Pesticide Use in Nepal: The Assessment of Residues and Risks

Govinda Bhandari

Pesticide Use in Nepal

The Assessment of Residues and Risks

Govinda Bhandari

Propositions

1. Data on the average use of pesticides in Nepal underestimates the current use of pesticides on vegetables.
(this thesis)

2. The use of organophosphate insecticides, particularly chlorpyrifos, poses risks to human health and the environment in Nepal.
(this thesis)

3. Soil health is important to ensure food safety and security.

4. Scientific data and information should be made easily available without charge for researchers from non-profit organisations.

5. With hard work you will get there but a good guide can help you to reach your destination faster.

6. Completing a PhD is a learning process, keep calm and carry on even when the process gets tough.

Propositions belonging to the thesis entitled:

Pesticide Use in Nepal: The Assessment of Residues and Risks

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February 2, 2021

Wageningen, The Netherlands

Pesticide Use in Nepal: The Assessment of Residues and Risks

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This research was conducted under the auspices of the Research School for Socio-Economic and Natural Sciences of the Environment (SENSE)

Pesticide Use in Nepal: The Assessment of Residues and Risks

Govinda Bhandari

Thesis
submitted in fulfilment of the requirements for the degree of doctor
at Wageningen University
by the authority of the Rector Magnificus
Prof. Dr A.P.J. Mol
in the presence of the
Thesis Committee appointed by the Academic Board
to be defended in public
on Tuesday 2 February 2021
at 01:30 p.m. in the Aula.

Govinda Bhandari
Pesticide Use in Nepal: The Assessment of Residues and Risks, 192 pages.

PhD thesis, Wageningen University, Wageningen, the Netherlands (2021)
With references, with summary in English

ISBN: 978-94-6395-640-6
DOI: https://doi.org/10.18174/536691

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1. General introduction

1.1 Pesticide use in conventional and integrated farming systems

A pesticide is a chemical or a complex mixture of different chemicals used in agriculture to keep plants healthy by protecting them from pests and infestations. In modern agriculture, the use of pesticides has become an integral part of minimizing the loss of crop yields and improving the storage of grains. Worldwide use of pesticides has been growing rapidly and expected to reach 3.5 million tonnes by the end of 2020 (Sharma et al., 2019). There are >1000 active ingredients in use globally (WHO, 2018). One of the reasons for increasing the global application of pesticides is due to the growing demand for food to feed the rising global population. The world population is expected to surpass >8 billion by 2030, and to surpass 9 billion by 2050 (UN, 2019). The risks related to pesticide use have become a worldwide concern exacerbated by poor agricultural practices (Sharma and Peshin, 2016). Risks are higher due to the toxicity of the pesticides being used. Pesticide exposure contributes to the deaths of 200 million people per year globally (Tariq et al., 2007). The challenge is how to feed the world in a sustainable way.

Although pesticides are considered easy and effective to use and offer immediate results (Aktar et al., 2009) for reducing crop losses, their misuse has become a serious issue in agricultural sustainability in Asia (Enserink et al., 2013). In this region, farmers often overuse pesticides on cash crops such as vegetables (Schreinemachers et al., 2020). In the absence of effective pesticide policies in developing countries, the use of toxic and persistent pesticides is increasing (Ecobichon, 2001; Phung et al., 2012). Integrated pest management (IPM) has emerged as a method to support sustainable agriculture and the wise use of chemical pesticides while increasing crop yields and household incomes (FAO, 2013). Global increases in crop yields can help nations meet the second of the United Nations 17 Sustainable Development Goals: "End hunger, achieve food security and improved nutrition and promote sustainable agriculture" by 2030 (UN, 2015). Sustainable agriculture reduces hunger, secures ecosystem functions and conserves biological diversity (Rockström et al., 2016).

Integrated farming system is based on cultural, chemical and biological methods for sustainable management of pests and diseases. This farming system emphasises growing healthy plants without hampering ecosystems and motivates biological pest control by empowering farmers. The benefits of this farming system are fewer pesticide applications and replacement of high-dose, more-toxic pesticides with low-dose, less-toxic and reduced-risk pesticides, including biopesticides. Integrated farming that comprises integrated pest management (IPM) methods is a viable option for sustainable agricultural production and meeting the future demand for food without any risk (Archer et al., 2019; Romeh, 2018; Rose et al., 2019). IPM methods are environmentally-friendly methods that are promoted by the EU as a framework for community action through its 2009/128/EC Directive related to pesticides (EU, 2009). IPM has shown to be affective for food safety and pest control (Abrol and Shankar, 2014; Mladenova and Shtereva, 2009). One of the goals of integrated farming system is to minimise pesticide use and reduce risk. Pesticide use in integrated farming system decreased by >50% compared to conventional farming system (Ahuja et al., 2015). In the same study, farmers using IPM methods increased net income and reduced risk, compared to conventional farmers. The IPM activities are limited in Nepal (Aryal et al., 2014), thus further investigation on the strength of IPM in Nepal would be an innovative task.

Conventional farming system has been shown to be based entirely on chemical pesticides disrupting a balance between organisms of the field ecosystems, pests and beneficial faunas and floras. Although productive, conventional farming has proven to be unsustainable, as it demands more investments, pesticides and technologies (Cristache et al., 2018). This farming system accelerates non-judicious application of pesticides resulting in the presence of pesticide residues in foodstuffs and soil, affecting human health and environment (Aktar et al., 2009). Despite the proven negative effects, conventional farming has become the top choice globally. Concentrations of pesticides in grapes from conventional farms exceeded their acceptable limits and posed higher risks than IPM farms (Turgut et al., 2011).

1.2 Pesticide use and human health

Although pesticides are beneficial, they can be fatal if not handled carefully. Farmers experience several health consequences after exposure (Esechie and Ibitayo, 2011; Gesesew et al., 2016; Karunamoorthi et al., 2012; Kim et al., 2017; Maumbe and Swinton, 2003; Ngowi et al., 2007; Zyoud et al., 2010). Of all stakeholders, exposure to pesticides typically occurs among farmers who work regularly in their fields (Damalas and Koutroubas, 2016) increasing their health risk. Developing countries are more vulnerable to the risks posed by pesticides due to the lack of training resources that would allow farmers and retailers to effectively deal with the hazards associated with handling pesticides (WHO, 2012). The other reasons for facing higher risks from pesticide exposure are linked to the use of banned pesticides, incorrect application methods, poor spraying equipment, inadequate storage facilities and the reuse of old pesticide containers for domestic purposes (Ecobichon, 2001; Ibitayo, 2006). Pesticide risk is also affected by the behaviour of a farmer during pesticide application (Lewis et al., 2016a). Most farmers and retailers in developing countries lack knowledge about the proper safety procedures as well as the technical skills needed when handling pesticides. Farmers are mainly exposed to pesticides during preparation and application, sprayer maintenance, re-entering the fields and spillage. Likewise, retailers are exposed while handling pesticides in their shops. Individuals are at risk not only during the handling of pesticides but also after its application through dietary and non-dietary exposure. The risk of pesticides depends upon many elements, including toxicity dose, frequency of application, duration of exposure and safety measures taken (Damalas et al., 2019). Previous studies stated knowledge, attitude and behaviour (KAB) of the farmers and retailers as the most influential factors for the safe use of pesticides (Akter et al., 2018; Gesesew et al., 2016; Jørs et al., 2014; Khan and Damalas, 2015b; Lekei et al., 2014b; Mohanty et al., 2013; Oesterlund et al., 2014). Moreover, fear of economic losses, absence of pesticide alternatives, use of faulty spraying equipment, misuse of pesticides, lack of proper maintenance of spraying equipment were the main barriers for farmers' safety behaviour (Khan, 2010; Raksanam et al., 2014b). Literature on safety behaviour of Nepalese farmers and pesticide retailers ("*agrovets*") are limited however, indicating a need for research on the KAB of pesticide handlers. Use of personal protective equipment (PPE) can reduce exposure to pesticides and associated risks, however there are a number of factors that prevented PPE use among farmers and retailers (Damalas and Hashemi, 2010; Walton et al., 2017; Yang et al., 2014). The risk of pesticide use is often underestimated in developing countries including Nepal. Convincing farmers and retailers to adopt adequate personal safety measures is a major challenge.

Safety precautions during pesticide application, storage and transport are minimal. A pesticide's label should appear clearly on packets and containers and must follow FAO and WHO guidelines (FAO, 1995). The USEPA and FAO pesticide safety suggestions include wearing impermeable hand gloves, long pants, long sleeve shirts, boots and a mask as major personal protective equipment. The correct use of PPE reduces pesticide exposure and associated risk (Garrigou et al., 2020). However, even the use of PPE at the time of pesticide application is found to be insufficient in many countries (Damalas et al., 2019; Kumari and Reddy, 2013; Levesque et al., 2012; Naidoo et al., 2010; Palis et al., 2006) including Nepal (Atreya et al., 2012; Khanal and Singh, 2016; Rijal et al., 2018).

1.3 Pesticide residues in the environment

After application, pesticides can be transported to unintended places via different routes and mechanisms such as uptake, drifting, volatilization, leaching, runoff, and adsorption all of which can cause risks to the environment and human health (Figure 1.1 A, B and C). Pesticides degrade slowly in the environment by different processes, including degradation by soil organism, chemical degradation (hydrolysis) and photo-degradation (photolysis). They form a long chain of residues in soil, ultimately reaching plants through pesticide uptake (Fantke et al., 2013; Ghanbari et al., 2017; Lehmann et al., 2017; Liu et al., 2016a;

Mtashobya, 2017; Valcke et al., 2017), and soil organisms (Aamir et al., 2018; Akoto et al., 2013; Gao et al., 2019; Ghanbari et al., 2017; Vasickova et al., 2019). The uptake of pesticides depends upon physiochemical properties of soil and pesticide as well as environmental factors such as precipitation, temperature and humidity (Biswas et al., 2018). The absorbed residues of pesticide are either metabolized by plant and animal system or accumulate in plants and animals, causing biomagnification in the environment (Gupta and Gupta, 2020). Pesticide drift, a source of pesticide exposure, has negative impacts on farm workers as well as people living near pesticide-treated farms (Coronado et al., 2011).

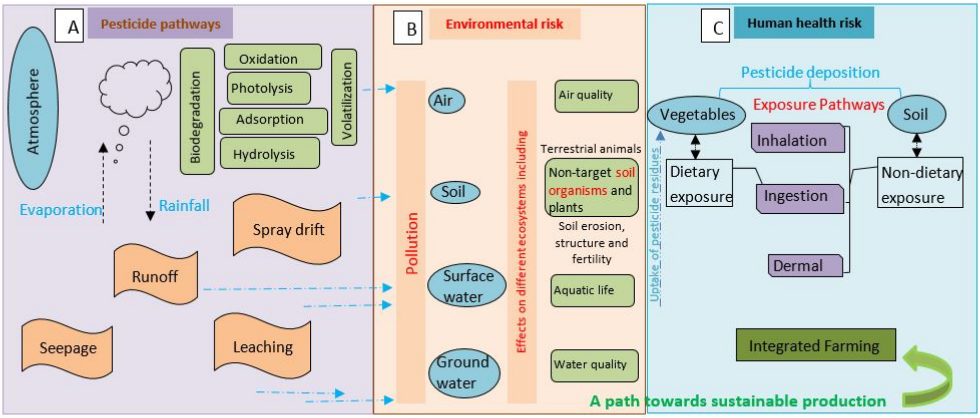


Figure 1.1 *Pesticide pathways and related risks to humans and the environment.*

1.4 Risk assessment related to pesticide used in agriculture

1.4.1 Human health risk

Pesticide risk for humans can be estimated using different methods such as hazard quotient (HQ) and hazard index (HI). The HQ measures risk of a single pesticide for humans, while HI measures cumulative risk of multiple pesticides with the same mode of action. Values from methods such as HQ or HI >1 indicate unacceptable risks to human health. Previous studies have also used these methods for human health risk assessment (Akoto et al., 2015; Chen et al., 2015; Gad Alla et al., 2015; Lozowicka, 2015; Seo et al., 2013). Pesticide risk assessment refers to an assessment process that is based on the characterization of effect and exposure (Hardy et al., 2012). The exposure assessment includes the environmental fate and behaviour of pesticides in different matrices such as soil, water and air (Figure 1.1 B). Likewise, the effect assessment refers to the characterisation of risk. This PhD study has adopted EFSA's 4 steps of risk assessment: i) identification of hazard, ii) characterisation of hazard, iii) assessment of exposure and iv) characterisation of risk.

Nowadays, food quality has become a serious issue due to the presence of significant pesticide residues in foodstuffs. Pesticides used in agriculture are more toxic and persistent and their residues deposited in foods and soils can pose risks for humans (Figure 1.1 C). For developing countries including Nepal, where hazardous pesticides are overused and misused (Atreya et al., 2011; Jallow et al., 2017a; Panuwet et al., 2012; Schreinemachers et al., 2012; Shammi et al., 2020; Tariq et al., 2007), it is a great challenge to make sure that pesticide concentrations in foods are safe to eat. Pesticides exposure due to food consumption has been reported globally (Aamir et al., 2018; Akomea-Frempong et al., 2017; Fang et al., 2015; Lehmann et al., 2017; Nougadere et al., 2020; Sieke et al., 2018; Valcke et al., 2017). Monitoring pesticide residues and their concentrations in food is crucial for the risk assessment. Databases compiled by FAO/WHO and the EU are the major which provide information on maximum residual limits (MRLs) of pesticides and their degradation products found globally in different foodstuffs. An MRL is the maximum concentration of a pesticide residue (expressed as mg/kg) in food that is legally accepted after the proper application of the pesticide. Concentrations of pesticides in food may exceed their MRLs, indicating poor agricultural practices (FAO, 2016). Furthermore, the EFSA and JMPR have their own human health-based toxic reference values for pesticides such as acute reference dose (ARfD) and acceptable daily intake (ADI) (both expressed in mg kg^{-1} body weight day^{-1}), which are used in risk assessment for humans.

A dietary risk in humans indicates exposure to pesticides via consumption of food. The acute and chronic dietary risk of pesticides is concerning i) when estimated short-term intake (ESTI) of a pesticide exceeds the acute reference dose (ARfD) of the pesticide and ii) when estimated daily intake (EDI) of a pesticide exceeds acceptable daily intake (ADI) of the pesticide. The short-term exposure to a pesticide is based on the presence of its residual concentration in a “large portion” consumption of a specific food in a day, while the long-term exposure is based on the presence of its residue on the average consumption of the food in question (EFSA et al., 2018). In the dietary risk assessment, there are many approaches for handling the food samples that have concentrations below the limit of detection (left-censored data). Of all the approaches, the use of substitution methods is frequently used (EFSA, 2010). The dietary risk of individual pesticides in humans can be evaluated by an index such as HQ, which is equal to ESTI/ARfD and EDI/ADI for the acute and chronic risks, respectively.

Non-dietary routes of human exposure to pesticides include inhalation, ingestion and skin contact (Damalas and Koutroubas, 2016). Looking at these exposure pathways and how they connect with pesticide concentrations found in soils may allow researchers to estimate cancer and non-cancer risks for humans. Human diseases related to genetics, reproduction, and endocrine disruption can be a result of chronic pesticide exposure (Gupta, 2004;

Sabarwal et al., 2018). Organochlorines have the possibility to induce lifetime carcinogenic health risks in humans (IARC, 2015). A recent study conducted in Nepal demonstrated a moderate cancer risk due to a non-dietary exposure to pesticides (Yadav et al., 2016). Based on the average daily non-dietary intake of organochlorines (CDI, mg/kg body weight), the lifetime cancer risk from the pesticide in humans can be estimated by using the guidance provided by USEPA and their associated threshold values. Cancer risks from pesticides can be calculated by multiplying CDI with the carcinogenicity slope factor (CSF) (USEPA, 1989). The cancer risk concerns scientists when the value from this calculation is $>1x10^{-4}$. Non-cancer risks from pesticides become concerns when the CDI value of a pesticide exceeds its human health-based toxic reference value. As mentioned in the dietary risk assessment above, the non-cancer risks are also evaluated based on indices such as HQ and HI.

1.4.2 Environmental risk

The environmental risk of pesticides consists of harmful effects on non-target soil organisms (FAO, 2017b; Stanley and Preetha, 2016; Uwizeyimana et al., 2017). Pesticide concentrations in soil exceeding their threshold levels impact ecosystem services, which is inevitable (Rodríguez-Eugenio et al., 2018). Furthermore, pesticide residues bioaccumulate in different trophic levels in ecosystems, gradually increasing ecotoxicity (Kapsi et al., 2019; Palma et al., 2004; Vasickova et al., 2019). The ecological risk assessment (EcoRA) of pesticides has been prioritized in many places, but not in developing countries like Nepal. Ecotoxicity differs with differences in soil physical, chemical and biological factors (Ellis et al., 2007; Lavtizar et al., 2016; Liu et al., 2013a; Vig et al., 2006; Zou et al., 2018), including other abiotic components (Thomatou et al., 2013). Thus, to monitor environmental risk of pesticides, a country should focus on their own legislative guidelines and thresholds (Wee and Aris, 2017). As there are limited ecotoxicological studies available in Nepal, the risk of pesticides used in agriculture for soil organisms is unknown. With this PhD thesis, we carried out EcoRA of chemical pesticides on earthworms, enchytraeids, springtails, mites and nitrogen as well as carbon mineralization organisms.

Pesticide risk for the environment can be estimated using different methods such as risk quotient (RQ) and toxicity exposure ratio (TER). The RQ and TER are used for the assessment of ecological risk of pesticides. The thesis adopted SANCO/10329/2002 recommended chronic toxicity exposure ratios (cTER) and indexes (RQ) for calculating toxicity of pesticides for earthworms and other soil organisms. RQ of pesticides can be categorised into 4 groups: no risk ($RQ<0.01$), lower risk ($0.01\leq RQ<0.1$), moderate risk ($0.1\leq RQ<1$) and higher risk ($RQ\geq1$) (Sánchez-Bayo et al., 2002). Furthermore, pesticide risk is unacceptable when its TER doesn't exceed trigger point values. For acute and chronic pesticide exposure, TER ≥10 and

≥5 assigned by the EU, respectively indicated acceptable trigger point values to soil organisms (EC, 2002; Jaabiri Kamoun et al., 2017). Studies done elsewhere have used these methods for the assessment of the environmental risk (Vasickova et al., 2019; Wee and Aris, 2017) of pesticide use, however in Nepal, there are nearly no similar kinds of risk assessment studies. The cTER is the ratio between the no observed effect concentration (NOEC) and the measured environmental concentration (MEC) or predicted environmental concentrations (PEC). For a precise risk assessment, pesticide concentrations in soils, such as MECs, based on two scenarios: i) general (considering the mean concentration of pesticide) and ii) worst-case (considering the maximum concentration of pesticide), were used. PECs are often estimated using mathematical models with default values based on the EUs' FOCUS-scenarios (EFSA et al., 2017). The index RQ of an individual pesticide is the ratio of the MEC or PEC to PNEC. The PNEC rests on the most susceptible organism and is obtained by dividing its concentration with the European Commission guidance assessment factor (AF) (EC, 2003). The AF ranged from 10 to 1000. The selection of the AF depended on the amount of accessible ecotoxicity data from literatures and databases.

1.5 Pesticide use in Nepal and associated risks

Nepal is an agricultural country with 3 ecological regions: Terai, Hilly and Mountainous. Over 65% of the population is engaged in agriculture. Agriculture's share of the GDP was large: 28% (AICC, 2018; MoF, 2017). Depending on the region, different cereals such as rice, wheat, maize, millet, legumes, oilseeds and vegetables are cultivated. Vegetables are planted as a cash crop across flat lands including river and road corridors. The average pesticide use is higher in the Terai region (flat land) than in other regions (PPD, 2015). Farmers in Nepal, especially in these specific areas, have gradually been shifting to commercial farming. Due to available human resources, employment opportunities, easy access to roads and markets, and the support of agricultural technology, production per unit area has been increased (Dahal et al., 2008; Raut et al., 2011). However, 35% of the agricultural production is lost due to pests, diseases and storage problems (PPD, 2013). The government of Nepal (GoN) has committed to intensifying agriculture with the aim of expanding agribusiness via higher inputs, including pesticides. As a consequence, pesticide consumption has been increasing by about 10-20% per year (Diwakar et al., 2008). In recent years, the import and application of pesticides in Nepal have grown notably, indicating farmers' dependency on chemical pesticides to grow crops. Overall, the average use of pesticides is approximately 396 g of active ingredient per ha (PPD, 2015), although pesticide use in vegetable farming is comparatively high. Jha and Regmi (2009) estimated that farmers used 2.63 kg of active ingredients per ha for Cole crops, for example. Therefore, commercial farmers who practiced conventional farming overused chemical pesticides mainly aiming at a maximum profit. Along with overuse, the other serious problems of pesticide use are: i) the lack of adequate knowledge of farmers and retailers on pesticide risks for humans and the environment, ii) the inadequate safety measures followed during pesticide handling, iii) the use of highly toxic pesticides that are banned in the EU, iv) the absence of effective monitoring systems for pesticide residues in food and the environment, and v) the inadequate pesticide rules and regulations. Up until the end of 2018, 170 different chemical compounds had been officially registered and used in Nepal. Most of the compounds used were insecticides (>35%) (PQPMC, 2019). From the total imported pesticides, >80% was used in vegetable production and storage (Adhikari, 2017; PPD, 2015), indicating a high risk for farmers cultivating vegetables. Soil quality on Nepalese farms has been decreasing as a result of the high chemical inputs (MoPE, 2000). Furthermore, pest resurgence has accelerated the application of higher doses of pesticides than recommended and farmers typically use a variety of pesticide cocktails (Chhetri et al., 2014). To avoid such misuse and associated risks to human and environmental health, the GoN has been upscaling good IPM-based agricultural practices (MoAD, 2016).

IPM focussed on reduced reliance on chemical pesticides. A previous study in Nepal has claimed that IPM-practicing farmers had reduced pesticide applications by 36% over non-practitioners (Kafle et al., 2014). IPM trained farmers have practised IPM techniques, for example, use of improved seeds, biopesticides, non-toxic chemical pesticides, proper irrigation and fertilizer (Bhandari, 2012). The farmers were motivated to adopt good agricultural practises such as appropriate use of pesticides, crop rotation and intercropping. Likewise, studies carried out elsewhere stated lower concentrations of residues on the IPM-farmed foodstuffs than on non-IPM (Baker et al., 2002; Mladenova and Shtereva, 2009; Singh et al., 2009). This clearly indicated that IPM farming could contribute to minimizing the effects of pesticides on health and the environment without decreasing crop yields (Bürger et al., 2008; Mariyono, 2008).

The pictorial representation of pesticides used in Nepal based on their target organism and toxic behaviour shown in Figure 1.2 and Figure 1.3, respectively.

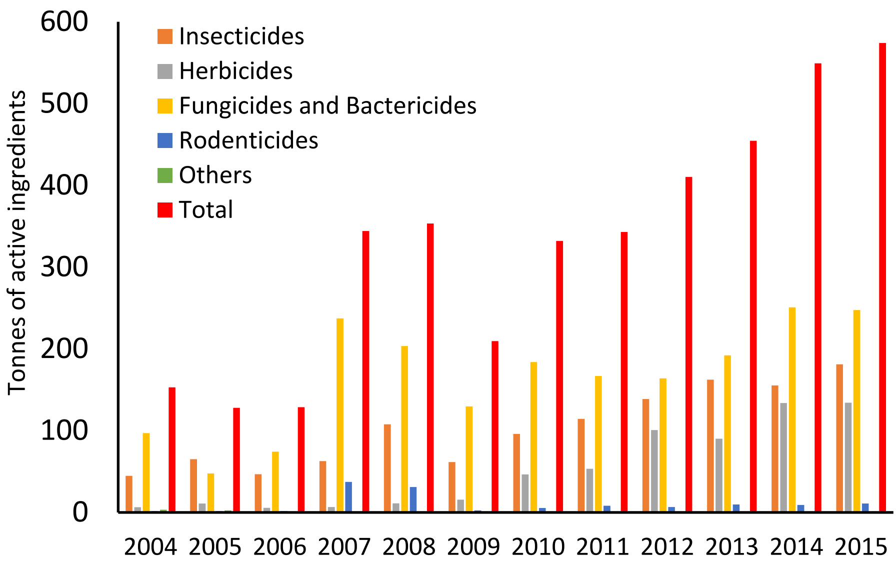


Figure 1.2 *Pesticide use in Nepal (2004-2017) (FAOSTAT, 2019).*

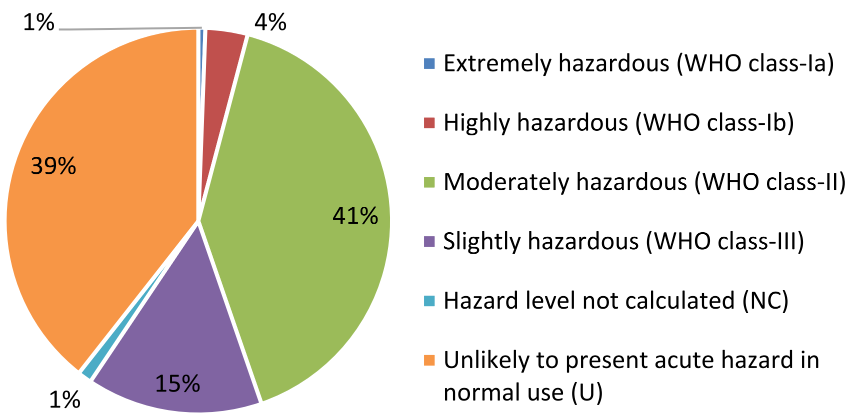


Figure 1.3 *Hazard categories of pesticides in Nepal based on WHO class (PQPMC, 2019).*

Vegetable farmers excessively applied pesticides and did not follow safety measures which resulted in higher risks of exposure (Aryal et al., 2014). While dietary exposure from pesticides can carry risks from both acute and chronic illnesses, non-dietary exposure from pesticides can carry both cancerous and non-cancerous risks. Due to acute exposure to pesticides, the most common health diseases reported were eye and skin irritation, headaches, respiratory discomfort, and asthma (Aryal et al., 2014; Atreya, 2008b; Vaidya et al., 2017). The health problems increased with the application of more hazardous pesticides (Lamichhane et al., 2019). Studies conducted elsewhere linked pesticide exposure with chronic diseases such as diabetes and Parkinson's disease (Evangelou et al., 2016; Schneider Medeiros et al., 2020). Nepal has already banned 16 compounds that are highly toxic, while 8 other compounds are in the process of being banned (PQPMC, 2019).

1.6 Overall aim of the thesis

This PhD study expands our understanding of chemical pesticide residues and their risks to human health and the environment in conventional and integrated farming systems. In this thesis, attention has been given to the estimation of pesticide residues in vegetables and soil, and to their risk assessments: dietary, non-dietary and ecological (Figure 1.1). Specifically, the research objectives are as follows:

1. Estimate pesticide use in vegetables and identify the factors affecting the safety behaviour of farmers and pesticide retailers on pesticide use and handling.
2. Evaluate the presence of pesticides and their degradation products in vegetables and agricultural soils from both IPM and conventional fields.
3. Assess the dietary risk to humans from pesticides in vegetable crops that were exposed to the highest doses of pesticides in the field.
4. Identify the human health risks from non-dietary intake of pesticides present in agricultural soils.
5. Investigate the ecological risk of pesticides detected in soils from both IPM and conventional fields.

The detail outline of the thesis is shown in Figure 1.4.

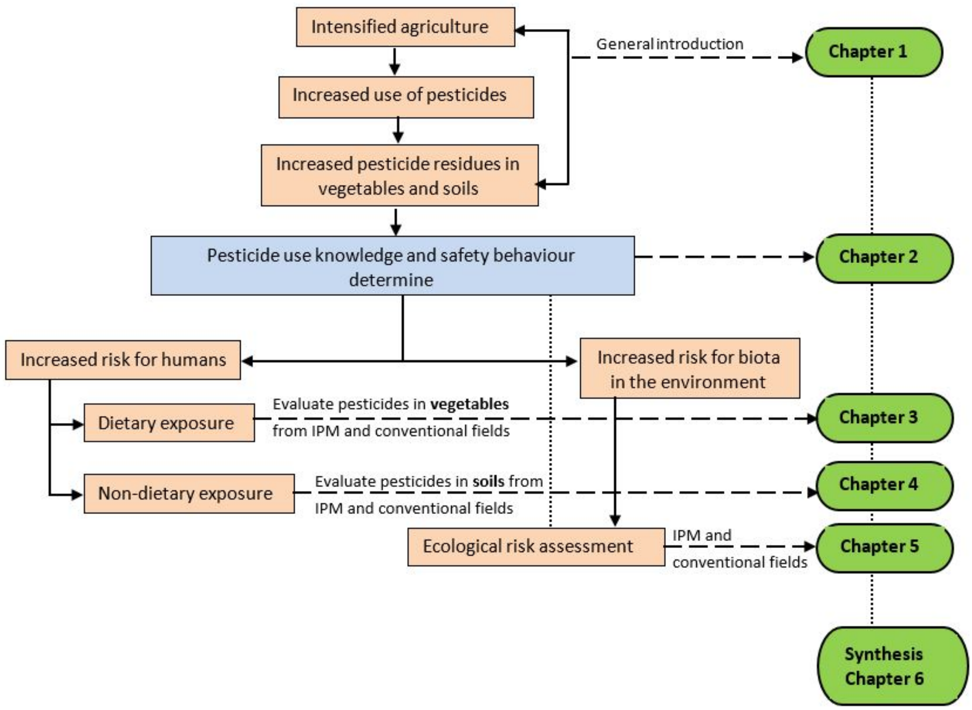


Figure 1.4 *Thesis outline.*

1.7 Outline of the thesis

This thesis includes 6 chapters. Chapter 1 comprises a general introduction to pesticide use, safety behaviour during pesticide application/handling, pesticide residues and the appropriate risk assessment methods to follow. The Chapter also discusses the significance of integrated farming, and increased use of pesticides in conventional farming and the associated risks.

Chapter 2 describes the perceptions of farmers and retailers for changing their pesticide behaviour based on a widely used model: Health Belief Model. Pesticide perceived threats, benefits and barriers to safety behaviour of farmers and retailers were analysed. Several ways of improving pesticide safety behaviour were recommended.

Chapter 3 identifies the pesticide residues in chilli, eggplant and tomato samples collected from two farming systems: i) conventional and ii) IPM. Dietary risk assessment of the pesticides was performed and the major contaminants were identified.

Chapter 4 identifies the pesticide residues in soil at three different depths: 0-5, 15-20 and 35-40 cm. The soils from conventional and IPM farms were studied separately. Non-dietary risk assessments of the pesticides including cancer and non-cancer risks were performed.

Chapter 5 assesses the ecological risks posed by pesticides in different depths of soil. Furthermore, it characterized the pesticide risk in different fields of farms: IPM and conventional, and the risk was correlated with farmers' knowledge and behaviour.

Chapter 6 summarizes the major outcomes of this study and discusses their strengths. Findings of this PhD thesis have significance for the i) safety and health of farmers and retailers; ii) food safety; iii) conservation of soil organisms, and iv) promotion of IPM techniques.

Chapters 2, 3, 4 have been published in peer-reviewed scientific journals. Methods, results, and the discussions of each chapter are presented separately and the publications can be assessed as shown at the beginning of each chapter.

1.8 Study area

The study area is located in Province 5, Rupandehi district in Nepal (Figure 1.5). The two administrative units, ward no. 6 and 7 of the Gaidahawa Rural Municipality (27° 35.429' N and 83° 19.215' E) were selected. The population is 47, 565, and the area is approximately 96.79 sq. km. Of the total land area (9679 ha), agriculture covers about 82%. The land is flat, fertile and the dominant soil textural classes are clays and silty clays, with some sandy clays, sandy clay loams and loamy sands. The sandier textured soils are found mainly along streams and rivers, near the banks where deposition occurs. At a few locations some silty soils may be found (mainly silt loams and silty clay loams) where regular flooding occurs and sediment carried by rivers or streams are deposited over a broad area. The average precipitation per annum is about 1391 mm. The maximum temperature in summer reaches 42.4°C and the minimum temperature in winter reaches 8.7°C. The duration of sunshine ranges from 4.76 hours (July) to 9.09 hours (April). The maximum evaporation is observed in the months of April and May and ranges from 4.02 mm to 11.69 mm while the minimum evaporation is observed in December, January and February and ranges from 0.09 mm to 4.18 mm. The major vegetables that are grown in agricultural fields are tomato, cauliflower, cabbage, radish, eggplant, bottle gourd, bean, bitter gourd, okra and chilli (GRM, 2018).

From the wards, a total of 12 villages were selected for questionnaire surveys (Figure 1.5). The villages were selected since most of the farmers were engaged in conventional farming and the agricultural activities were intensive. Few of the farmers in the areas of villages such as Kadamhawa, Loadpurahawa, Mujrahawa, Bisoria, Suryapura and Kanijahawa also practised integrated farming such as IPM farming. Pesticide retailers were randomly selected on the way to the villages. Soil samples from the villages and the standing vegetable crops such as tomatoes, chillies and eggplants were selected for pesticide analysis and risk assessment for adolescents and adults.

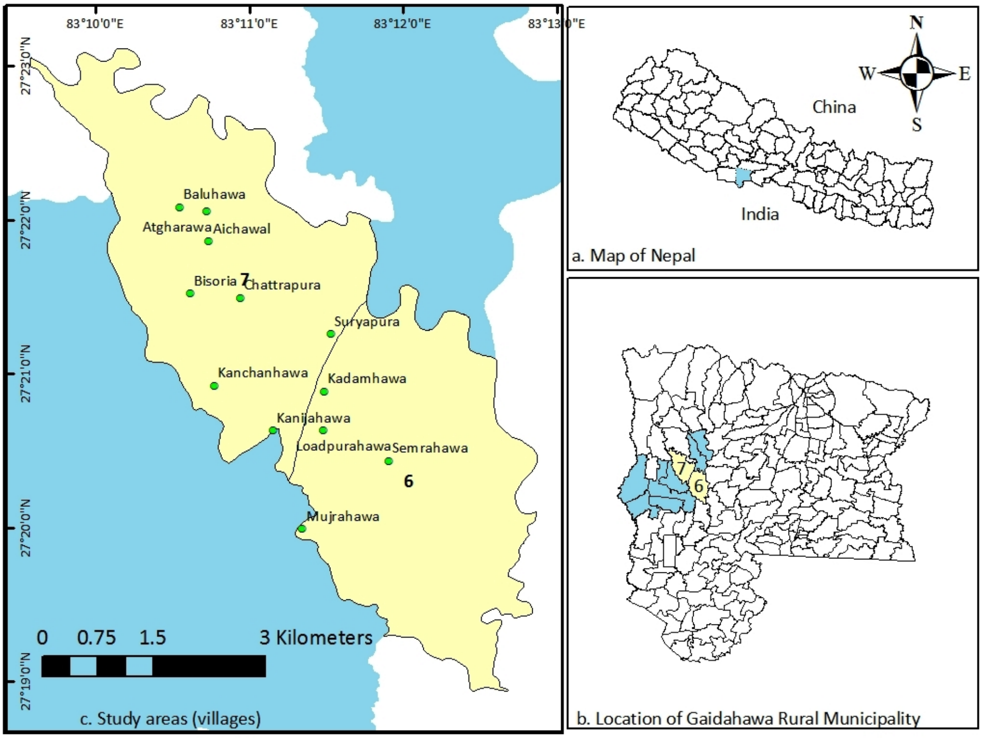


***Figure 1.5** Location of the study area.*

2. Factors affecting pesticide safety behaviour: The perceptions of Nepalese farmers and retailers

Indiscriminate use of pesticides in vegetable farming is an emerging problem resulting in increasing health and environmental risks in developing countries including Nepal. As there are limited studies focusing on farmers' and retailers' knowledge related to pesticide use and associated risks as well as safety behaviour, this study assesses their perceptions of pesticide use, associated impacts on human and environmental health and safety behaviours. This study is also intended to quantify pesticide use in vegetable farming. We used the Health Belief Model (HBM) to evaluate farmers' and retailers' safety behaviour associated with pesticides. We interviewed 183 farmers and 45 retailers. The study revealed that farmers applied pesticides at an average of 2.9 kg a.i./ha per crop per season; and insecticides, especially pyrethrins and pyrethroids as well as organophosphate, were the most frequently used. Retailers were more aware of the threats surrounding pesticide use and were thus more aware of the risks to their own health as well as to the health of animals, birds, fishes, and honey bees. Headache (73.8%) was the most commonly reported acute health symptom of pesticide use. Farmers often did not adopt the appropriate safety measures when handling pesticides sighting the constrained perceived barriers (direct path coefficient, DPC = -0.837) such as feeling uncomfortable and the unavailability of safety measures. Likewise, retailers lacked the incentive (direct path coefficient, DPC = 0.397) to adopt the necessary safety measures while handling pesticides. Training and awareness programs addressing safe handling practices and safety measures as well as education concerning the long-term risks of pesticide exposure on health and the environment, through radio, television and posters, may improve the safety behaviour of farmers and retailers.

Based on:

Bhandari, G., Atreya, K., Yang, X., Fan, L., Geissen, V., 2018. Factors affecting pesticide safety behaviour: The perceptions of Nepalese farmers and retailers. Science of The Total Environment 631/632, 1560-1571.

2.1 Introduction

The Health Belief Model (HBM) is a cognitive model that attempts to explain and predict health behaviours and has been used to understand the safety behaviour of farmers while handling pesticides (Khan, 2010; Raksanam et al., 2014b). The model (Figure 2.1) says that in order to adopt safety behaviour, individuals need to perceive themselves susceptible to the possible illnesses and perceive the illnesses as serious (i.e. perceived threat), believe that the healthy behaviours are beneficial (i.e. perceived benefit), and believe that the benefits of healthy behaviours exceed the costs (i.e. perceived barriers) (Buglar et al., 2010; Coppens, 2016). If individuals believe themselves to be susceptible to a risky condition, think that the condition would have severe consequences, understand that adoption of available resources would beneficially reduce the condition of susceptibility and severity, and admit that the benefits of taking action outweigh the barriers to action, they are likely to follow safety behaviours that they believe will reduce their risk (Champion and Skinner, 2008).

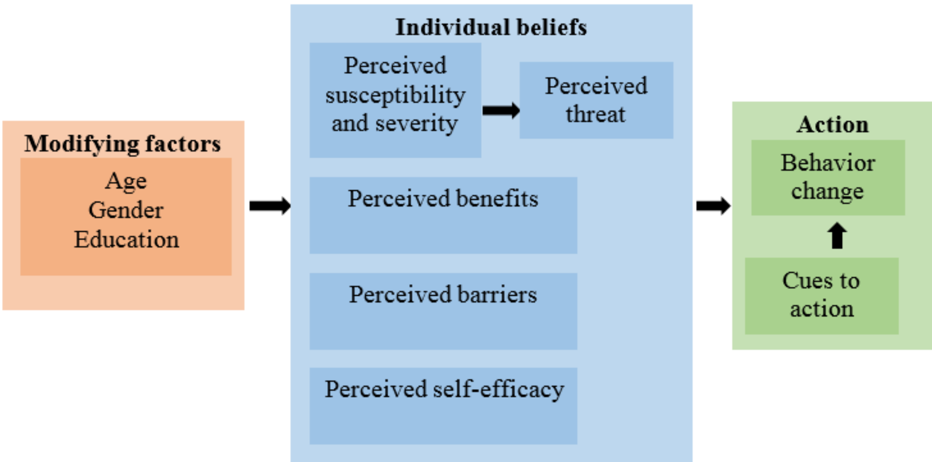


Figure 2.1 *The Health Belief Model (Champion and Skinner, 2008).*

Unsafe use of pesticides can be considered as a threat to human health and the environment and good safety behaviours can strongly reduce the threat (Damalas and Eleftherohorinos, 2011; Houbraken et al., 2016; Jin et al., 2017). Safety behaviour depends on the perceived susceptibility, the severity of the risks and benefits as well as the current inhibiting factors to adopting good safety behaviours (Abdollahzadeh et al., 2015; Rezaei et al., 2018; Sharifzadeh et al., 2017). Raksanam et al. (2012) found a strong relationship between farmers' perceived susceptibility to pesticide exposure, the perceived severity of the consequence of exposure and the perceived benefit of the farmers' safety behaviour. Farmers and retailers may perceive the threats from pesticide differently and thus their personal actions to reduce their risk vary accordingly. Some farmers perceive higher threats from pesticides and show more safety behaviours such as not drinking, smoking or eating during pesticide application as well as taking a bath and washing their cloths after spraying (Coppens, 2016). Similarly, farmers who had experienced health problems from applying pesticides may tend to adopt environmentally sound alternative pest management practices in order to reduce their pesticide risk (Lichtenberg and Zimmerman, 1999). The number of farmers who perceive higher threats from pesticide use corresponds to the increased use of safety measures such as gloves and shoes (Furlong et al., 2015; Hernandez-Valero et al., 2001). Considering this, our first hypothesis is that increased perceived threats from pesticide use is considered to have higher adherence to the safety behaviours.

Perceived barriers can affect the safety behaviours of farmers; the higher the perceived barrier, the lower the chances that farmers will report a higher adherence to safety behaviours (Khan et al., 2013; Raksanam et al., 2014a; Toan et al., 2013). Individual factors, such as the lack of time and comfort have been reported as barriers (Cabrera and Leckie, 2009; Levesque et al., 2012). Farmers may not use safety measures if they are an economical burden or a time restraint to performing the work (Snipes et al., 2009) or they are uncomfortable due to the heat stress and dampness experienced in the field (Walton et al., 2017). Factors such as the lack of training on safe pesticides use and the insufficient information provided on labels and package leaflets (normally in a foreign language) are considered the main barriers to the practice of good safety behaviour (Cabrera and Leckie, 2009; Damalas and Khan, 2017; Damalas and Koutroubas, 2017; Khan and Damalas, 2015a). Likewise, farmers who perceive the benefits of safety measures wear a combination of recommended safety gear such as long pants, long-sleeved shirts, aprons, hand gloves, protective masks, and hats during pesticide application (Salvatore et al., 2008; Walton et al., 2017). Thus, our second hypothesis is that increased perceived barriers decreases safety measure adherence, and increased perceived benefits of safety gear use increases the adherence to safety measures.

The Health Belief Model (HBM) comprises two additional components: cues to action and self-efficacy (Hanson and Benedict, 2002). Cues to action works as a 'trigger' and thus motivates individuals to change behaviours, while self-efficacy builds confidence in individuals to improve safety behaviours when handling pesticides (Bay and Heshmati, 2016). Farmers who are familiar with the short-term risk of poisoning during pesticide application adopt safety measures (Elmore and Arcury, 2001; Strong et al., 2008). Reoccurrence of symptoms such as headache and itching may act as internal stimuli to encourage the farmers to practice safe behaviours. External stimuli such as the provision of information via social media and trainings to facilitate the adoption of healthy behaviour (Kien, 2015) also act as triggers to encourage good pesticide practices. Safety hazards, safety culture, and production pressure can influence self-efficacy of individuals which in turn causes them to practice safe or unsafe behaviour (Brown et al., 2000; Rezaei et al., 2018). Providing proper safety equipment and work clothing would build a more positive work experience and increase job satisfaction thereby increasing the self-confidence of individuals (Wagner et al., 2013). Safety education positively determines farmers' self-efficacy and enhances their skills to perform work more safely (Pettinger, 2000). Accordingly, our final hypothesis is that increased cues to action and self-efficacy have a positive effect on safety behaviour.

The government of Nepal has launched a number of agricultural development plans and policies with the focus on prioritizing increased production and productivity of agricultural crops through intensive use of pesticides. Especially after instituting these new policies, the misuse of pesticides by farmers has become a common practice. Researchers discovered that farmers apply pesticides to vegetable crops at rates nearly four times higher than recommended (Jha and Regmi, 2009) and this indiscriminate use is increasing (Atreya et al., 2011; CBS, 2015; Sharma et al., 2012). Intensification of agriculture has led to the overuse of pesticides in vegetable farming resulting in human health problems and ecosystem degradation (Atreya et al., 2011; Sharma, 2015). The misuse of pesticides has also resulted in pesticide poisoning (Atreya, 2008a; Atreya et al., 2011), acetylcholinesterase depression (Atreya et al., 2012; Neupane et al., 2014) and increased health burden. Pesticides have adverse effects on animals and fishes (Klemick and Lichtenberg, 2008), birds (Iwaniuk et al., 2006), and honey bees (Prisco et al., 2013). The risks posed to humans and the environment from pesticide use are evident. The adverse effects are more acute in developing countries where farmers lack training and access to awareness programs on the safe use of pesticides (Damalas and Khan, 2017; Khanal and Singh, 2016).

In many rural areas of Nepal, farmers seek solutions from retailers to help manage pests and diseases in their crops (Aryal et al., 2014). Thus, pesticide retailers play a very important role in the pesticide supply chain. Unfortunately, pesticide retailers also practice unsafe behaviours such as selling unregistered, prohibited, or date expired pesticides; mixing, reweighing and repacking pesticides; trading on the open market; and using false labels on the pesticides (Sharma et al., 2012).

Farmers' and retailers' beliefs concerning pesticide use, their understanding of the adverse consequences of such use and their own personal safety behaviours have not yet been examined using the Health Belief Model in Nepal. Thus, we initiated this study in order to assess farmers' and retailers' knowledge, attitude and safety practices regarding pesticide use and their perceptions of the associated health risks to humans and the environment. This study also quantifies pesticide use in vegetable farming. Knowledge concerning the existing use of pesticide and farmers' and retailer' perceptions regarding risks may serve as a guide when formulating policies aimed at achieving sustainable vegetable farming. Identifying cognitive factors that affect safety behaviour may prove beneficial in the design of efforts, campaigns and activities that encourage better adherence to good safety behaviours. Identifying commonly used pesticides and educating people about the appropriate quantities of pesticides that should be used in vegetable farming could help encourage policy makers to take the necessary actions needed to prevent potential health risks of exposure.

2.2 Materials and methods

2.2.1 The study area

The study area is located in the Rupandehi district of Nepal, close to the India-Nepal border. The Gaidahawa Rural Municipality (27° 35.429’ N and 83° 19.215’ E) was selected (Figure 2.2) for this study. The population of the municipality is 47,565 individuals. The maximum temperature in summer reaches 42.4°C and the minimum temperature in winter reaches 8.7°C. The average annual rainfall is about 1391 mm. The main crop is rice followed by wheat, oilseeds and vegetables. Three crops are cultivated per year on irrigated land; while two crops are cultivated on non-irrigated land.

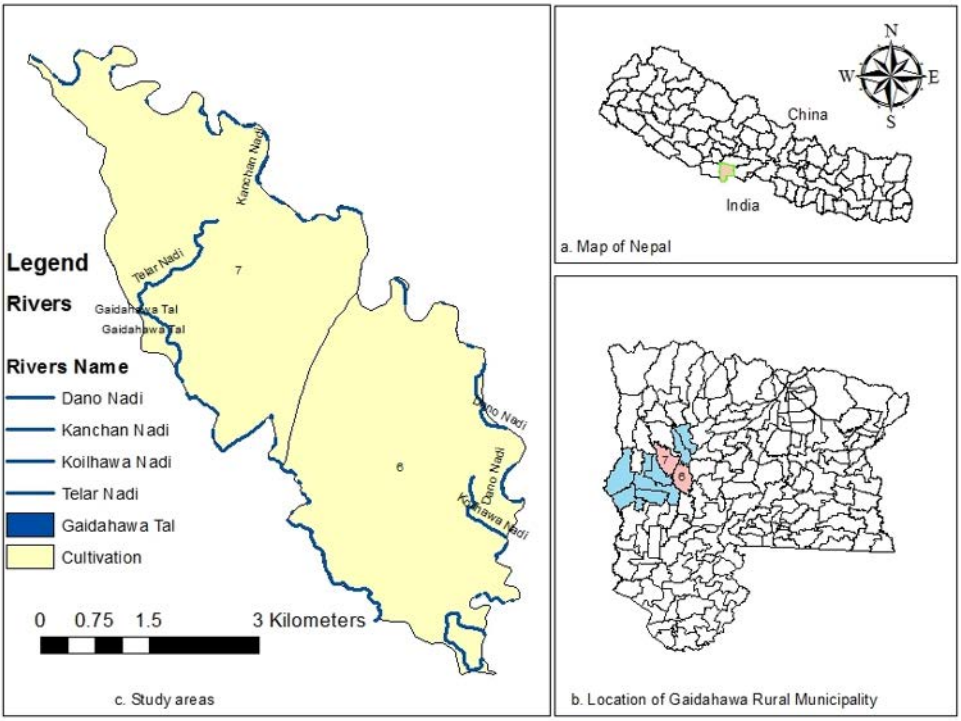


Figure 2.2 *Location of the study area.*

2.2.2 Sampling and data collection

The Gaidahawa Rural Municipality is comprised of nine wards – the smallest administrative unit. This study selected Ward 6 and 7 (Figure 2.2) where the majority of the farmers are engaged in commercial vegetable farming. Each ward is comprised of a number of villages. At the time of our study, the total number of households in both Wards was 1751 (CBS, 2012). We considered a random >10% of the households (183) which reflected a survey margin of error 6.8%. We used proportionate stratified random sampling of the Ward and village according to population density.

There were 13 pesticide retailers situated in the two Wards (DADO, 2015). However, a few farmers stated that they also buy pesticides from the retailers that are located on the way to a local market. Therefore, pesticide retailers situated on the way to the market were also considered. In the end, 45 pesticides retailers were interviewed.

We also conducted key informant interviews. Three officers from the Pesticide Registration and Management Division (PRMD) and four officers from District Agriculture Development Office (DADO) were interviewed. In addition, we also conducted focus group discussions. We made a questionnaire for the focus group discussions with the aim of acquiring information concerning: (i) pesticides use history, (ii) pesticides names, (iii) major crops grown and the pesticides used, (iv) pesticide poisoning, (v) acute health symptoms and possible diseases associated with exposure, (vi) pesticides and vegetable markets, (vii) safety practices and (viii) institutional support. Five focus group discussions, comprising 15-20 vegetable farmers, were conducted. Direct observations of the farmers' fields and retailers' stores were also made.

A semi-structured questionnaire containing modifying factors, individual beliefs and actions of the HBM (Figure 2.1) was designed based on previous questionnaires used in Atreya et al. (2012) and Bhandari (2014). A pilot study was conducted where 12 farmers and 2 retailers in a neighbouring village were interviewed to prepare the final survey questionnaire. Six students working on their Bachelor's degrees from the Institute of Agriculture and Animal Science (IAAS) at Tribhuvan University conducted the final household surveys. These students followed an all-day training program regarding the questionnaire where they learned how to effectively conduct the surveys. The survey questionnaire was mainly focused on (i) gender, age and education, (ii) pesticide use (iii) perceived susceptibility and severity, (iv) perceived benefits and barriers, and (v) self-efficacy and cues to action (Table 2.1). Prior informed consent from the respondent was obtained before conducting the face-to-face interview.

Table 2.1 *Descriptive statistics of variables used in data analysis.*

Factors	Variable description (binary, 0 = no, 1 = yes)		Farmer Mean (SD)	Retailer Mean (SD)
Perceived threat (PT)	Pesticides negatively affect	health	0.95 (0.22)	1 (0)
		Children's health	0.85 (0.36)	1 (0)
		livestock	0.92 (0.27)	1 (0)
		birds	0.66 (0.48)	1 (0)
		waterbodies	0.75 (0.43)	1 (0)
		fishes	0.80 (0.40)	1 (0)
		honeybees	0.78 (0.42)	1 (0)
	Pesticides' long-term health effects		0.44 (0.50)	0.67 (0.48)
	Exposure to pesticides while handling			0.84 (0.37)
	Pesticides entering human body		0.91 (0.29)	
Self-efficacy (SE)	Know the colour codes of pesticides		0.10 (0.31)	0.51 (0.51)
	Asking for information on the uses of pesticides during purchase		0.61 (0.49)	
	Received advice on pesticide use		0.74 (0.44)	
	Attended training on safe use and handling of pesticides		0.17 (0.38)	0.87 (0.34)
Perceived barrier (PBa)	Have participated in workshops and seminars related to pesticides			0.53 (0.50)
	Believed colour codes of pesticides not important			0.24 (0.43)
	Monitoring and support for pesticide retailers sufficient			0.27 (0.45)
	Attended training on protective equipment			0.13 (0.34)
	Training on safe handling of pesticides did not include experts from.....	Non-government organizations		0.96 (0.21)
		Government organizations		0.13 (0.34)
		Pesticide suppliers and companies		0.96 (0.21)
	Training on pesticide uses did not include experts from.....	Non-government organizations		0.98 (0.15)
		Government organizations		0.13 (0.34)
		Pesticide suppliers and companies		0.98 (0.15)
	Training on protective devices and clothing did not include experts from…..	Non-government organizations		0.98 (0.15)
		Government organizations		0.13 (0.34)
		Pesticide suppliers and companies		0.98 (0.15)
	While spraying do you perceive barrier on using	hat	0.52 (0.50)	
		long-sleeved shirt	0.23 (0.43)	
		long pants	0.23 (0.43)	
		gloves	0.88 (0.33)	
		mask	0.45 (0.50)	
Perceived benefit (PBe)	Suggest light trap for controlling insects and pests			0.16 (0.37)
	Suggest pheromone trap for controlling insects and pests			0.22 (0.42)
	Are farmers benefited by wearing…..while spray	hat		0.60 (0.50)
		glass		0.56 (0.50)
		long-sleeved shirt		0.93 (0.25)
		gloves		0.96 (0.21)
		mask		0.96 (0.21)
		long pants		0.96 (0.21)
	Go abroad (India) to buy pesticides			0.16 (0.37)
	Go far away from your business, such as Kathmandu, to buy pesticides			0.24 (0.43)
	Think bio pesticides and their use helps environment protection			0.78 (0.42)
	Do farmers need to …..after spraying	wash hands	0.99 (0.10)	
		take bath	0.85 (0.36)	
		wash cloths	0.76 (0.43)	
	During spraying, don't	drink	0.79 (0.41)	
		smoke	0.92 (0.28)	
		eat	0.95 (0.22)	
Cues to action (CtA)	Registered your business			0.87 (0.34)
	Renew registration certificates			0.56 (0.50)
	Received support from district agricultural office			0.40 (0.50)
	Participated in any social actions related to pesticides such as "No pesticide use week"			0.47 (0.50)
	Heard about unfortunate incidences related to pesticide poisoning		0.37 (0.48)	0.73 (0.45)
	Heard about unpleasant social stigma such as infertility			0.02 (0.15)
	Deaths in your family due to pesticides			0.07 (0.25)
	Do community farmers apply pesticides safely		0.93 (0.25)	

Table 2.1 *Descriptive statistics of variables used in data analysis (continued).*

Factors	Variable description (binary, 0 = no, 1 = yes)		Farmer Mean (SD)	Retailer Mean (SD)
Behavior change (BC)	Return pesticides that have expired or had labels removed to dealers			0.33 (0.48)
	Wash hands after handling pesticides			0.47 (0.50)
	While handling pesticides, do you wear	hat	0.43 (0.50)	0.04 (0.21)
		glass		0.11 (0.21)
		gloves	0.07 (0.26)	0.13 (0.34)
		mask	0.55 (0.50)	0.49 (0.51)
		long pants	0.74 (0.44)	
		long-sleeved shirt	0.75 (0.43)	

2.2.3 Quantification of pesticide use

The active ingredients (a.i.) in the different pesticides used in each of the 15 vegetable types grown in this area were estimated. The following formula was used.

P^e (kg a.i./0.03 hectare) = pesticide concentration (a.i.) per spray x total spray per frequency used for 0.03 hectare (ha) of land x total frequency of pesticide used in the particular vegetable growing season.

The average use of a pesticide for each type of vegetable was calculated by adding up the pesticide use in the major crops and dividing this number by the total number of crops. This study determined that 14 pesticides were used in the cultivation of the major 15 vegetable crops.

2.2.4 Data analysis

Survey questions consisted of a mixture of positive and negative items and were grouped according to the key factors of the HBM. Each question was given equal value: '1' for every "yes" answer and '0' for every "no" answer which is a common technique used in previous studies (Goldman et al., 2004; Strong et al., 2008). We did not check the reliability of the questionnaire due to the limited use of Cronbach's alpha (Sijtsma, 2009). The summative indices (SI) of each factor were calculated and represent the mean scores. Pearson Correlation Coefficients were calculated for all factors. The significant factors related to the safety behaviour of farmers and retailers were selected for path analysis as a supplement to separate direct and indirect effects and present the relative significance of factors (Wardell et al., 2012). Path analysis has been widely applied in past studies to investigate diverse topics, including organic food consumption (Lockie et al., 2004; Yazdanpanah et al., 2015), land transformation (Tong et al., 2016), water consumption (Fan et al., 2013) and pesticide use (Fan et al., 2015). Lockie et al. (2004), divided the effects of these factors into three groups of differing magnitudes: minor (<0.10), medium (0.10-0.19), and major (>0.20), which we adopted for this study. The study of factors causing minor effects on the safety behaviour of farmers and retailers was not a part of the current research.

2.3 Results and discussion

2.3.1 Gender, age and education

About 90% of the farmers interviewed were males. More than 25% of the interviewed farmers were ≤ 20 years old, 47% were 30 to 49 years old and the remaining 23% were above 50 years old. About 30% of the farmers were illiterate and the rest had different levels of education, such as primary (23%), lower secondary (20%), secondary (19%) and college (8.7%).

Likewise, about 80% of the retailers were males. Nearly 34% of the retailers were 40-49 years old. Forty five percent of the retailers were ≤20-39 years old and the rest were above 50 years old. Almost all retailers were literate. Most retailers (65%) had a college level education, while >31% had a secondary education (Table 2.2).

Table 2.2 *Characteristics of farmers and retailers.*

Respondent characteristic		Respondents			
		Farmer (N=183)	%	Retailer (N=45)	%
Gender	Male	164	89.6	36	80
	Female	19	10.4	9	20
Age	≤ 20	47	25.7	10	22.2
	30-39	42	23	10	22.2
	40-49	43	23.5	15	33.3
	50-59	33	18	8	17.8
	≥ 60	18	9.8	2	4.4
Education levels	Illiterate	54	29.5	0	0
	Primary (1-5 class)	42	23	1	2.2
	Lower secondary (6-8 class)	37	20.2	1	2.2
	Secondary (9-10 class)	34	18.6	14	31.1
	College (>10)	16	8.7	29	64.4

2.3.2 Types of vegetable grown

Vegetable farming was the primary source of income for farmers. Farmers grew a number of different vegetables in one year. Nearly 20% of the households cultivated tomato, followed by cauliflower (17.6%), cabbage (11.3%), radish (7%), brinjal (6.3%), and bottle gourd (5.2%) (Figure 2.3). Less than 5% of the households cultivated other vegetables such as bean, bitter gourd, okra, chilli, sponge gourd, potato, pea, broccoli, cucumber, pumpkin, chickpea, cowpea, carrot, onion, fennel, spinach, coriander, and fenugreek.

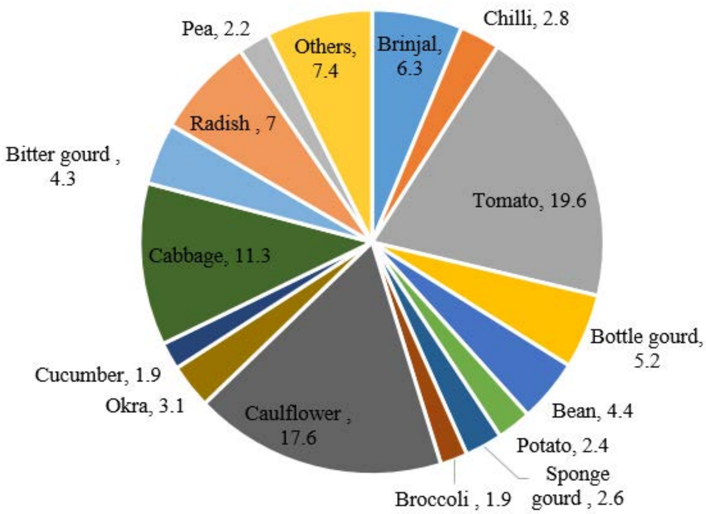


Figure 2.3 *Percentage of household cultivating major vegetable in the study area over the past 12 months.*

2.3.3 Use of pesticides in vegetable farming

The most commonly used pesticides in vegetable farming are listed in Table 2.3. WHO's class II insecticides were used more frequently than fungicides and herbicides which is consistent with studies done in Ethiopia (Mengistie et al., 2016), Vietnam (Dasgupta et al., 2007), Armenia (Tadevosyan et al., 2013) and Nepal (Neupane et al., 2014). A few banned organochlorine and organophosphate pesticides, such as endosulfan and phorate, were still in use. In a group discussion, farmers honestly mentioned that whenever they travel to the neighbouring country of India, they buy pesticides. The comparatively cheaper price of pesticides in India was their justification for buying the pesticides. Indian retailers are selling hazardous insecticides under the name of 'bio-pesticides' (FICCI, 2015) which might accelerate the introduction of extremely hazardous, unidentified, and banned pesticides into Nepal due to the open and porous border.

The application of pesticides differed for each type of vegetable. The average seasonal application ranged from 0.27 to 7.78 kg a.i./ha (mean 2.90, SD $\pm$2.33). This estimate is higher than a previous study (Jha and Regmi, 2009) that estimated about 2.37 kg a.i./ha for fungicides and 1.96 kg a.i./ha for insecticides. Similarly, our estimate of pesticide application rates differ strongly between regions in Nepal. For example, application rates were 1.85 kg a.i./ha in Kavre, 1.73 kg a.i./ha in Rautahat, 1.65 kg a.i./ha in Jhapa, 1.25 kg a.i./ha in Banke and 0.71 kg a.i. /ha in Chitwan (Chhetri et al., 2014).

The most commonly used pesticide, cypermethrin, was applied by 76% of the households (Table 2.3). On average, mancozeb had the highest application rate (7.78 kg a.i./ha), followed by dichlorvos, chlorpyrifos, profenfos, triazophos, dimethoate, carbendazim, metalaxyl, chlorantraniliprole, alphamethrin, imidacloprid, quinalphos, cypermethrin, and emamectin benzoate. A past study conducted in the hills of Nepal stated that mancozeb was a widely applied pesticide in vegetable farming (Atreya and Sitaula, 2011). We observed an extremely high use of dichlorvos (23.12 kg a.i./ha) on the brinjal. Farmers applied much higher doses than recommended for insecticides (Table 2.4a) and fungicides (Table 2.4b) in vegetable farming. Farmers typically made a mixture of 2 to 3 types of pesticides before application and used these mixtures on vegetables such as tomato, brinjal, cauliflower and cabbage, which is an observation consistent with previous studies (Damalas and Khan, 2017; Mengistie et al., 2015; Ngowi et al., 2007).

Table 2.3 *List of pesticides used in the study area.*

SN	Pesticides category	Pesticides group #	Common name	WHO class	% of HHs
1	Insecticides	Organophosphates	Profenofos	II	55.2
			Chlorpyrifos	II	44.3
			Dimethoate	II	41.5
			Dichlorvos	Ib	10.9
			Quinalphos	II	7.1
			Triazophos	Ib	5.5
			Phorate+	Ia	<1
		Organochlorines	Endosulfan+	II	<1
		Pyrethrins & Pyrethroids	Cypermethrin	II	76
			Alphamethrin	II	11.5
			Allethrin	II	<1
			Alphacypermethrin	II	<1
			Bifenthrin	II	<1
			Deltamethrin	II	<1
			Fenpropathrin	II	<1
			Fenvalerate	II	<1
			Lambda-cyhalothrin	II	<1
			Resmethrin	III	<1
		N-methyl carbamates	Carbofuran	Ib	<1
			Cartap hydrochloride	II	<1
		Other Insecticides and Acaricides	Imidacloprid	II	16.9
			Chlorantraniliprole	U	6
			Acetamiprid	II	<1
			Propargite	III	<1
		Biologicals and Insecticides of Biological Origin	Emamectin benzoate	II	23.5
2	Herbicides	Other Herbicides	Metsulfuron Methyl	U	<1
			Pendimethalin	II	<1
3	Other pesticides	Fungicides	Mancozeb	U	53.6
			Carbendazim	U	10.9
			Metalaxyl	II	6.6
			Cymoxanil	II	<1
			Thiram	II	<1
4	Unidentified Trade name	Sterlik, Mastrogen, Miret, Arjun, Megathane			

Note: Ia = Extremely hazardous; Ib = Highly hazardous; II = Moderately hazardous; III = slightly hazardous; U = Unlikely to present acute hazard in normal use; +banned pesticides; # Pesticides group is based on Roberts and Reigart (2013); HHs = Households.

Table 2.4a *Estimated (E) and recommended* (R) doses of pesticides for vegetable farming [kg active ingredient (a.i.)/ha] [mean (±Standard Deviation)].*

Pesticides/Crop	Brinjal	Chilli	Tomato	Bottle gourd	Bean	Sponge gourd	Broccoli	Cauliflower	Okra	Cucumber	Cabbage	Bitter gourd	Radish	Pea	Average use
Dichlorvos[E]	23.12 (21.51)			5.47 (6.77)				3.92 (1.48)	7.84 (8)		5.16 (1.87)	0.73 (0.90)			7.71 (7.90)
Dichlorvos[R]	na			0.500				na	na		na	0.500			
Chlorpyrifos[E]			11.59 (10.07)	5.74 (3.34)	4.18 (3.02)	2.52 (0.95)	3.98 (4.56)	2.51 (2.06)	1.48 (0.92)	1.69 (0.45)	4.75 (4.71)	4.89 (3.44)	6.8 (8.34)		4.56 (2.87)
Chlorpyrifos[R]			na	na	na	na	0.400	0.400	na	na	0.400	na	na		
Profenfos[E]	13.6 (16.19)	4.14 (3.35)	6.83 (4.36)	1.1 (0.96)	2.88 (1.72)	3.6 (1.27)	3.79 (4.72)	2.58 (3.61)			1.89 (1.88)	5.24 (7.16)	2.53 (2.95)	0.59 (0.35)	4.06 (3.46)
Triazophos[E]			2.33 (0.80)	5.4 (3.05)											3.87 (2.17)
Triazophos[R]			0.500	0.500											
Dimethoate[E]	8.72 (5.08)	1.79 (1.59)	3.38 (0)	2.97 (1.15)	2.52 (3.77)	0.59 (0.19)	1.24 (1.43)	1.87 (2.17)	1.68 (2.57)	5.87 (6.97)	4.12 (3.81)	0.62 (0.47)	0.83 (1.08)	0.39 (0.25)	2.61 (2.34)
Dimethoate[R]	0.600	na	0.300	na	na	na	0.200	0.200	0.600-0.700	na	0.200	na	na	na	
Quinalphos[E]					2.4 (1.7)			0.81 (0.98)					0.64 (0.58)		1.28 (0.97)
Quinalphos[R]					na			na					na		
Chlorantraniliprole[E]		2.10 (3.4)			0.92 (1.1)										1.51 (0.83)
Chlorantraniliprole[R]		0.111			0.185										
Alphamethrin[E]	3.54 (2.62)		2.56 (1.66)	0.66 (0.74)				1.03 (0.89)		0.75 (0.21)			0.17 (0.15)		1.45 (1.31)
Imidacloprid[E]	0.44 (0.29)		1.08 (0.80)		0.41 (0.52)			5.87 (12.84)			0.58 (0.59)		0.23 (0.18)		1.44 (2.19)
Imidacloprid[R]	na		na		na			na			na		na		
Cypermethrin[E]		1.10 (1.25)	1.34 (1.91)	0.28 (0.40)	0.50 (0.34)	0.4 (0.25)	0.4 (0.46)	0.27 (0.2)	0.15 (0.09)	0.17 (0.04)	0.33 (0.36)	0.62 (0.34)	0.18 (0.25)		0.48 (0.38)
Cypermethrin[R]		na	na	na	na	na	na	na	0.060-0.070	na	0.060-0.070	na	na		
Emamectin Benzoate[E]			0.77 (0.98)					0.15 (0.15)			0.13 (0.27)		0.04 (0.02)		0.27 (0.34)
Emamectin Benzoate[R]			na					na			na		na		

na = Not available; *Sources: (PRMD, 2013, 2016).

Table 2.4b *Estimated (E) and recommended* (R) fungicide use pattern in vegetable cultivation [kg active ingredient (a.i.)/ha] [mean (±Standard Deviation)].*

Pesticides/Crop	Brinjal	Tomato	Bottle gourd	Bean	Potato	Cauliflower	Cabbage	Radish	Pea	Average use
Mancozeb^{E}	12.85 (7.06)	16.51 (22.72)		10.63 (8.28)	5.48 (7.30)	4.25 (3.59)	2.14 (1.43)		2.59 (4.22)	7.78 (5.58)
Mancozeb^{R}	na	1.125-1.500		1.125-1.500	1.125-1.500	1.125-1.500	na		na	
Carbendazim^{E}		1.77 (0.99)	1.02 (1.1)	3 (2.12)		0.53 (0.35)		3.25 (3.99)		1.91 (1.19)
Carbendazim^{R}		0.050	na	0.250		0.100		na		
Metalaxyl^{E}		1.73 (1.19)								1.73 (1.19)
Metalaxyl^{R}		na								

na = Not available; *Source: (PRMD, 2016).

2.3.4 Pesticide related acute symptoms

Almost all farmers perceived acute health symptoms after pesticide application. The most frequently self-reported toxicity symptoms related to pesticides were headache (73.8%), skin irritation (62.3%), eye irritation (32.8%), weakness (22.4%), and muscle pain (19.1%) (Figure 2.4). These findings are consistent with past studies done in Nepal (Atreya, 2008b) and Vietnam (Dasgupta et al., 2007).

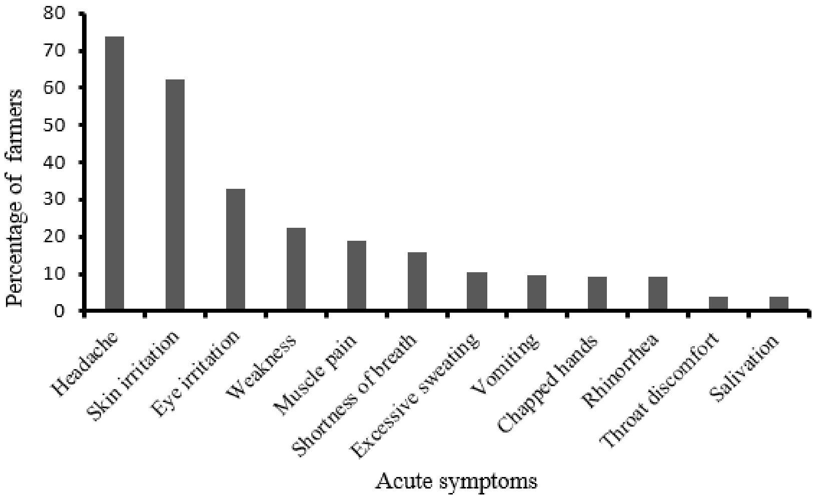


Figure 2.4 *Frequency of acute symptoms related to pesticide use.*

2.3.5 Pesticide safety behaviour of farmers

Farmers' safety behaviour was affected by several factors such as age, education, perceived threat, self-efficacy, perceived benefits, perceived barriers, and cues to action (Table 2.5).

This result should be interpreted with caution since there were very few female farmers in our study. The path analysis of farmers (Figure 2.5A) indicated that a perceived barrier (direct path coefficient, DPC = -0.837) had major negative effect on the safety behaviour, while self-efficacy (direct path coefficient, DPC = 0.104) and perceived benefits (direct path coefficient, DPC = 0.107) had medium positive effects. In our study, 53% farmers did not use hats, 24% did not use long-sleeved shirts and long pants, 88% did not use gloves and 45% did not use masks while spraying pesticides.

Table 2.5 *Correlations between farmers' and retailers' pesticide use safety behaviour and factors of the HBM.*

Construct	Farmers	Retailers
Age	-0.271**	0.017
Education	0.278**	-0.123
Gender	0.031	-0.164
Perceived threat	0.350**	0.482**
Self-efficacy	0.303**	0.186
Perceived benefits	0.182*	0.142
Perceived barrier	-0.886**	-0.077
Cues to action	0.172*	0.378*

* = significant at p <0.05 and ** = significant at p<0.01.

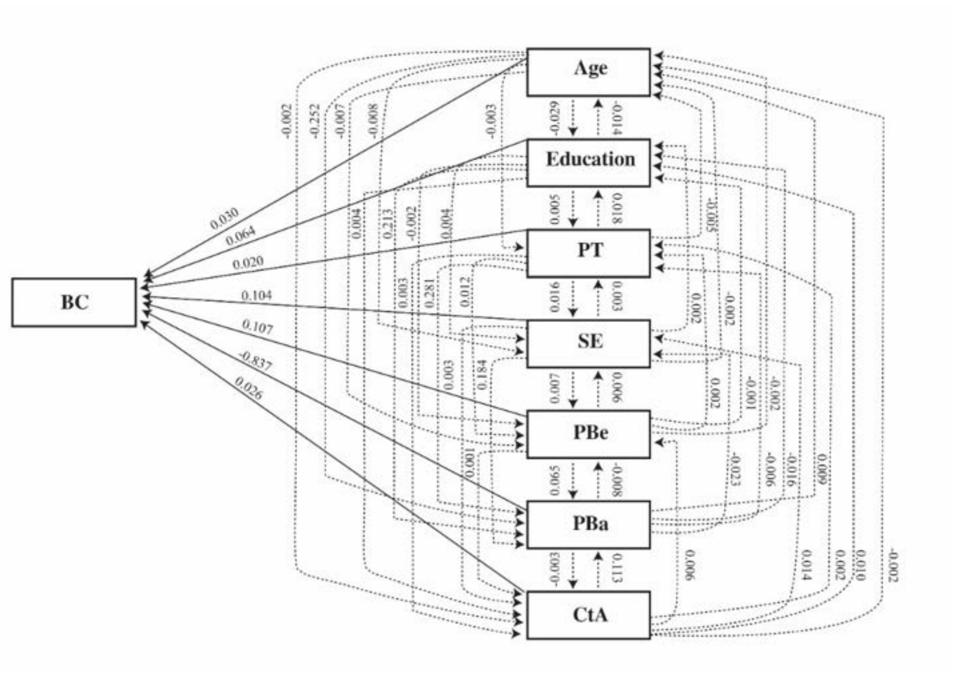


Figure 2.5A *Path analysis of factors affecting the safety behaviour of farmers while handling pesticides.*

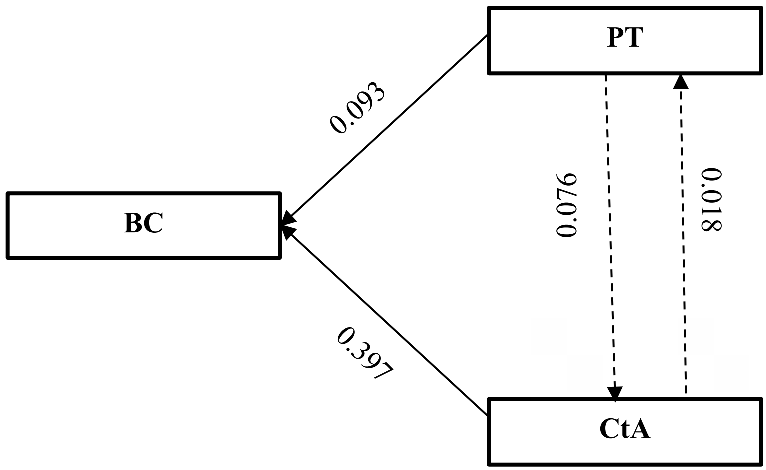


Figure 2.5B *Path analysis of factors affecting the safety behaviour of retailers while handling pesticides. Acronyms: PT, perceived threat; SE, self-efficacy; PBe, perceived benefit; PBa, perceived barrier; CtA, cues to action; BC, behaviour change. The solid arrows denote direct effects and the dotted arrows denote indirect effects. The numbers indicate the correlation coefficients between two variables joined by an arrow; the variable at the base of the arrow is the independent variable.*

This is because they perceived barriers such as unavailability, discomfort, inappropriateness, and unawareness (Figure 2.6), which is a finding consistent with a past study (Damalas et al., 2006). Farmers perceived higher barriers such as feeling discomfort wearing long pants and long-sleeved shirts while spraying, which might be due to heat stress. Age (indirect path coefficient, IPC = -0.252) had a major negative effect on perceived barriers whereas education (indirect path coefficient, IPC = 0.213) and perceived threats (indirect path coefficient, IPC = 0.281) had major positive effects. A farmers' education positively affected their safety behaviour, whereas perceived barriers negatively affected their behaviour. Young farmers perceived higher barriers regarding safety behaviour. About half of the farmers in our study were less than 40 years old. Most vegetable farmers had low levels of education and perceived lower severe threats, especially regarding the long-term health effects that accompanied low adherence to good safety behaviours while handling pesticides, which is a finding consistent with previous studies (Damalas and Hashemi, 2010; Jallow et al., 2017a).

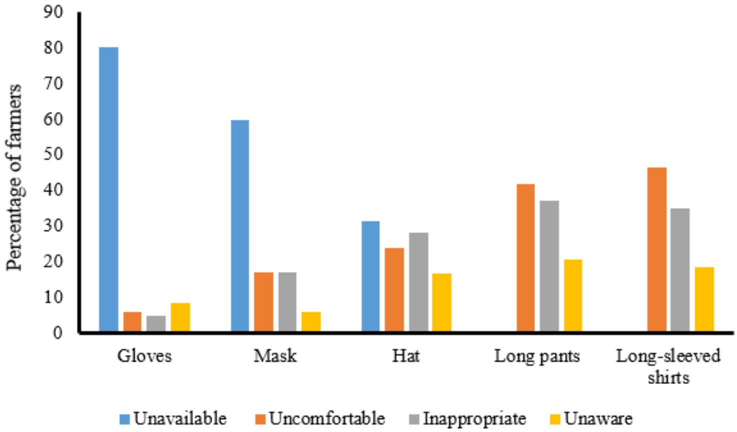


Figure 2.6 *Frequency of perceived barriers on personal protective behaviour.*

Self-efficacy (indirect path coefficient, IPC = 0.184) and cues to action (indirect path coefficient, IPC = 0.113) had medium positive effects on perceived barriers (Figure 2.5A). About 82% of the farmers had not received training concerning safe pesticide handling. "I am illiterate, not trained and unaware of pesticide safety items, I doubt on efficiency of the advertised protective measures and have no other option", a young farmer stated in a group discussion. Farmers often mixed pesticides with their bare hands due to their poor knowledge and higher illiteracy rate (Stadlinger et al., 2011). Education and training positively affected the safety behaviour of farmers (Damalas and Khan, 2017; Damalas and Koutroubas, 2017; Gaber and Abdel-Latif, 2012). Most farmers were unaware of the colour codes of pesticides and they had not yet heard about any unfortunate incidences related to pesticide poisoning. They believed that pesticide-related risks such as ill health (headache, skin and eye irritation) are short-term and things that regularly occurred during their daily agricultural life. One-quarter of farmers had not yet received any advice concerning safety precautions regarding pesticide use. "I have not meet the government extension service provider since many years, and when I need information on the use of pesticides, I go to nearby pesticide retailer", a commercial farmer in one group stated. However, about 40% of farmers did not receive information about pesticide use from retailers. Since most farmers lack training and education related to pesticide safety and are unaware of pesticide poisonings, they perceived larger barriers related to using protective items which led to their inadequate safety behaviours despite the overuse of pesticides. Vegetable farmers in the study area were at a higher risk of pesticide exposure.

2.3.6 Pesticide safety behaviour of retailers

Safety behaviour of retailers was associated with perceived threats and cues to action (Table 2.5). Path analysis of retailers indicated that cues to action (direct path coefficient, DPC = 0.397) had major positive effects on their safety behaviour (Figure 2.5B). Although 86% of retailers received training on the proper handling of pesticides, only half of them knew the colour codes of pesticides. Sixty percent of retailers did not get any support from district agricultural offices, while 53% did not participate in social actions, such as meetings, seminars and conferences against pesticide use. "Awareness on safety behaviour has not regularly been broadcasted in radio, television and newspaper, however, the new pesticides are frequently advertised in the area", a retailer stated in a group discussion. All retailers perceived higher threats to their health and the environment from pesticides. Surprisingly, some did not recognize the long term effects of pesticides and about 16% believed that they were not exposed to pesticides while handling them. A few retailers referred to pesticides as "medicines" rather than 'toxins'. When referring to pesticides as "medicines", only the functional aspect of these compounds was highlighted and retailers did not handle the pesticides safely, which is a finding similar to previous studies (Al Zadjali et al., 2014; Damalas et al., 2006; Jallow et al., 2017a). The registration of their businesses and the renewal of their certificates positively affected the safety behaviour of retailers, in line with Lekei et al. (2014b). Few retailers neither registered their business (13%) nor renewed their certificates (44%) even when they were involved in a pesticide-related business which might have affected their safety behaviour. Previous studies (Haj-Younes et al., 2015; Lekei et al., 2014b) reported that about 67% of the retailers sold expired pesticides to farmers.

This study provides useful information concerning farmers' and retailers' knowledge and behaviours related to pesticide use. The results should be interpreted with caution as there were certain limitations to this study. We conducted this study with a small sample size of farmers and retailers near to the India-Nepal border where large quantities of forbidden pesticides were available (Bhandari, 2014) and thus the results are not representative of other regions of Nepal. This study stands on the self-reports of individual perception and behaviour and that can be only partially validated since people often only want to report socially accepted behaviours on self-report studies (Damalas and Abdollahzadeh, 2016). However, this study was conducted in a friendly way and there was a good level of cooperation with farmers and retailers. Nonetheless, this study has accomplished several things: quantifies pesticide used in vegetable farming, farmers' and retailers' perceived risks from pesticide use, and their safety behaviours, all of which could help policy-makers towards sustainable management of pesticides and agricultural development in Nepal.

2.4 Conclusion

The largest amounts of pesticides were used on multiple harvest crops such as brinjal, chilli, and tomato. Farmers perceived lower pesticide threats to their health and the environment as well as lower benefits and higher barriers to their safety behaviours. The use of masks, gloves, and hats were very limited because of their availability and because farmers found them uncomfortable. In contrast to farmers, retailers perceived comparatively higher threats to their health and the environment from pesticides. However, their safety behaviour was not satisfactory due to inadequate triggers. Both farmers and retailers are exposed to higher risks from pesticide exposure. This study recommends the following interventions for improving pesticide use and safety behaviours for pesticide stakeholders: (i) increase educational programs, such as documentaries and talk shows as well as disseminating news through radio, television, and newspapers to raise awareness about good safety behaviours and the long-term consequences of pesticide use; (ii) provide training to retailers concerning safe pesticide handling practices and eco-farming alternatives; (iii) make protective safety devices more accessible and modify them to reflect local needs; and (iv) strengthen monitoring mechanisms to reduce the illegal import of banned pesticides, especially along the porous India-Nepal border.

Acknowledgements

We are grateful to the Netherlands Universities Foundation for International Cooperation (Nuffic) for funding this research (through NFP-PhD-5160957247). The authors thank local farmers and pesticide retailers for their cooperation and support during the survey. We would like to thank the students Garima Joshi, Samikshya Pandit, Sunil Ghimire, Kumar Pun Magar, Dipak Pandey, and Ravi Raj Mishra for their support during the field survey. We also thank Robin Palmer for English revision. The comments and suggestions received from the anonymous reviewers were also appreciated.

3. Pesticide residues in Nepalese vegetables and potential health risks

We conducted this study in order to assess the pesticide residues in vegetables and examine the related human health risk. Therefore, residues of 23 pesticides (organophosphates, organochlorines, acaricides, fungicides, and insecticides of biological origin) were analysed in the three main vegetable crops grown in Southern Nepal: 27 eggplant, 27 chilli and 32 tomato samples representing (i) conventional (N=67) and ii) integrated pest management (IPM) fields (N=19). Pesticide residues were found in 93% of the eggplant samples and in all of the chilli and tomato samples. Multiple residues were observed in 56% of the eggplant samples, 96% of chilli samples and all of the tomato samples. The range (µg/kg) of total detected pesticide residues in eggplants, chillies and tomatoes was 1.71-231, 4.97-507, 13.1-3465, respectively. The most frequently detected pesticides in these vegetables were carbendazim and chlorpyrifos. Chlorpyrifos residues exceeded the EU maximum residue limits (MRLs) in 11% of the eggplant and 19% of the chilli and tomato samples. In total, the residues of 4 pesticides such as triazophos, omethoate, chlorpyrifos and carbendazim exceeded the EU MRLs. Compared to chilli and eggplant crops, more carbendazim was sprayed onto tomato crops (p<0.05). Adolescent and adult dietary exposure were assessed using hazard quotient (HQ) and hazard index (HI) equations for the identified pesticides. HQs>1 were observed for chlorpyrifos and triazophos in tomatoes. The highest acute HQ (aHQ) was for triazophos (tomato) in adolescents (aHQ=3.21) and adults (aHQ=3.31), showing the highest risks of dietary exposure. The cumulative dietary exposure showed chronic HIs<1 for organophosphates in eggplants, chillies and tomatoes. The concentration of pesticide residues in the vegetable crops from the integrated pest management (IPM) fields was considerably lower, suggesting a greater ability of these systems to reduce the dietary risks from exposure to pesticides.

Based on:

Bhandari, G., Zomer, P., Atreya, K., Mol, H.G.J., Yang, X., Geissen, V., 2019. Pesticide residues in Nepalese vegetables and potential health risks. Environmental Research 172, 511-521.

3.1 Introduction

Pesticides are an important tool used in commercial agriculture to control insects, weeds and diseases and maintain crop yield by minimizing losses (Khanal and Singh, 2016; Schreinemachers et al., 2017; Wang et al., 2017b). However, pesticides have many harmful environmental impacts (Ibitayo, 2006; Yuantari et al., 2015) on non-target species, food webs and ecosystem functions (Atreya et al., 2011; Haj-Younes et al., 2015; Lekei et al., 2014a; Oesterlund et al., 2014). Many studies have documented that plants take up pesticides from soil (Fantke et al., 2013; Florence et al., 2015). The persistence and dissipation of pesticides in plants depend on plant characteristics (Lu et al., 2014). Of all the foodstuffs tested for pesticides in Nepal, vegetables were found to have the highest levels (Koirala et al., 2007). Many scholars have suggested integrated pest management (IPM) as an alternative approach to farming in order to minimize the use of chemical pesticides in the developing world (Hossain et al., 2017; Pretty and Bharucha, 2015). The government of Nepal has been promoting IPM since 2002. IPM is a technique used in agriculture that reduces a farmer's reliance on chemical pesticides and ensures the growth of healthy crops while conserving the environment and ensuring food safety and security at the same time. The integrated use of chemical pesticides, bio-pesticides (*Jholmol* in Nepali), and pheromone traps are a few successful and effective IPM practices used in Nepal (Joshi et al., 2017). However, the adoption of IPM at the field level has been very slow.

Pesticides residues in food pose a serious risk to consumers. In general, pesticides are sprayed directly onto crops. Infants, children, and adults can be exposed to these pesticides by consuming pesticide-contaminated food. Residues of chemical pesticides have been detected in many food commodities such as cereals (Akoto et al., 2013; Guler et al., 2010; Hou et al., 2013), seafood (Ernst et al., 2018; Kafilzadeh, 2015; Yahia and Elsharkawy, 2014), and tea (Amirahmadi et al., 2013; Chen et al., 2015; Seenivasan and Muraleedharan, 2011). Compared with other foodstuffs, even higher levels of pesticides were found in fruits and vegetables, the most important commodities foods in peoples' diets. In the worst case residual contents reach levels that render fruits and vegetables unsuitable for human consumption, as was the case in countries such as Burkina Faso (Lehmann et al., 2017), Kuwait (Jallow et al., 2017b), Tanzania (Kariathi et al., 2016), and Senegal (Diop et al., 2016). Therefore, food monitoring programs focused on testing pesticide levels have been put into place in different countries to improve food safety and agricultural practices as well as minimize economic losses. However, in Nepal, this program is in its infancy. To examine possible exposures, the government of Nepal uses the qualitative data derived from the Rapid Bioassay Pesticide Residue (RBPR) analysis program. This program is mainly focused on data collected around Kathmandu, the capital of Nepal. The country lacks scientific information concerning pesticide residues found on food in other parts of the country (Giri et al., 2012). Farmers in Southern Nepal grow different types of vegetables in one season and they often use higher doses of pesticides more frequently than recommended (Bhandari et al., 2018). This could result in chronic, sub chronic, and acute dietary exposure to pesticides (Essumang et al., 2008), especially for humans (Reiler et al., 2015; Sinha et al., 2012).

There are a number of methods used for assessing the cumulative risks of pesticides (Jensen et al., 2015; Wilkinson et al., 2000) and the indicators most often used are the hazard quotient (HQ) and hazard index (HI) (Bhanti and Taneja, 2007; Chen et al., 2011; Lehmann et al., 2017). The HQ is a tool that is used for the assessment of health risk (HR) due to human exposure to a single pesticide (Gad Alla et al., 2015). In order to assess the cumulative risk of different pesticides, the EFSA (2013b) has developed a methodology focused on cumulative assessment groups (CAGs) for assessing the cumulative risk index of pesticides that cause the same toxic effects in tissues, organs and physiological systems that can produce joint cumulative toxicity which is expressed as HI.

Since food intake is the major pathway by which most humans are exposed to pesticides, demand for food safety regulation has increased globally. To protect people from the toxic effects of exposure to pesticides, the EU, FAO/WHO and EPA have established limits on pesticide residues in foods. International Food Standards such as EU, EPA and CODEX (FAO/WHO) MRLs are applied in the benchmark assessment of exposure to pesticides (Chen et al., 2012). A maximum residue level is the highest concentration of a pesticide residue that is legally accepted in or on food when pesticides are applied correctly (refereed as Good Agricultural Practices). Safety reference values, such as maximum residue limits (MRLs), acute reference dose (ARfD), estimated daily intake (EDI) and acceptable daily intake (ADI) have been administered at national (Clever, 2017; Kurai, 2017; MPI, 2017) and international levels (EU, 2018; FAO/WHO, 2018) to prevent health risks and overexposure from pesticides. These kinds of safety regulations, particularly concerning chemical pesticides in food in Nepal, is still under development (CBS, 2013). Previous studies have found pesticide residues in vegetables but these studies did not assess the health risks associated with dietary intake of pesticides (Giri et al., 2012; Koirala et al., 2007; Lama, 2008). The dietary intake of pesticides (especially the amount consumed) differs in different age groups which may lead to different levels of exposure to pesticides. The concentration of dichlorvos in vegetables exceeded EU MRLs in Nepal (Rawal et al., 2012). In the same study, the EDI of dichlorvos exceeded the ADI in 18 types of vegetables. Higher levels of pesticide residues in vegetables may contribute to a greater health risk and hence, a detailed pesticide residue analysis and risk assessment is necessary. New knowledge about the current scenario concerning pesticides and their residues have been emerging in other parts of the world but not yet in Nepal. Research on this topic in Nepal is even more urgent considering the fact that several pesticides that have been banned for use on vegetable crops in the EU are still used in Nepal. The continuous application of these pesticides along with their persistent and toxic nature (for properties of the pesticides see Table S3.1) further support the necessity of this research. Furthermore, studies (Bhandari et al., 2018; Rijal et al., 2018) have already shown that pesticides are being applied at higher than recommended rates in vegetable farming.

Therefore, the objectives of this study were (i) to determine residues of chemical pesticides (organophosphates, OPs; organochlorines, OCs; acaricides, ACs; fungicides, FUs and insecticides of biological origin, INsB) used in vegetable farming in Nepal; and (ii) to assess the health risk of adolescents and adults due to the ingestion of pesticides in and on their vegetables.

3.2 Materials and Methods

3.2.1 Study area

The study area is located in the Rupandehi district of Nepal. The Gaidahawa Rural Municipality (27° 35.429' N and 83° 19.215' E) was selected for this study (Figure 3.1). The population of the Gaidahawa Rural Municipality is 47,565. The average annual precipitation is about 1391 mm. The maximum temperature in summer reaches 42 °C and the minimum temperature in winter reaches 9 °C.

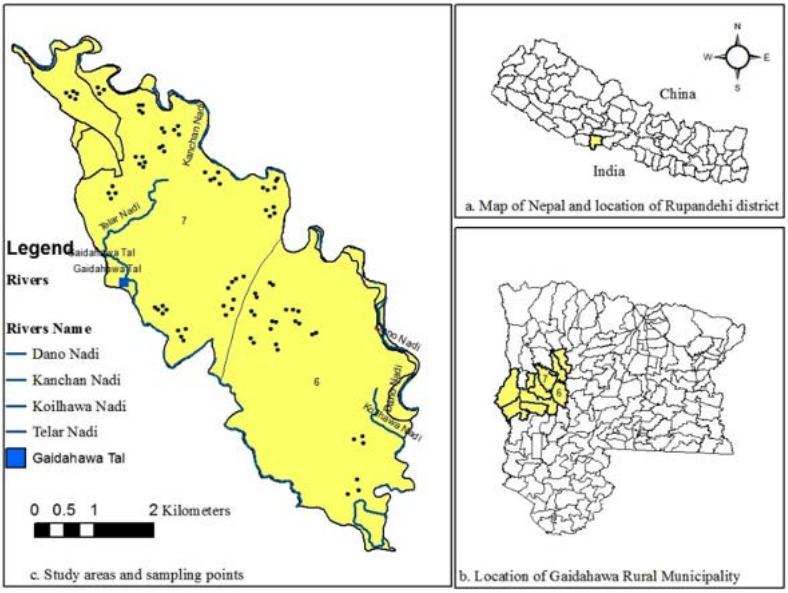


Figure 3.1 *Location map of the study area.*

3.2.2 Farming systems and pesticides applied

The major crop in Nepal is rice followed by wheat, maize, oilseeds and vegetables. While IPM is an ecosystem approach to crop production, contributing to reduce use of pesticides and health risks, few farmers in our study practiced IPM techniques, for example, use of hybrid seeds, ash, animal urine and dung. Few farmers practiced crop rotation or mixed cropping and the use of insect traps was minimal. Most farmers practiced conventional/intensive farming which was heavily dependent on pesticides application (Thapa, 2017). Farmers applied higher than the recommended amounts of pesticides to vegetable crops (Bhandari et al., 2018; Jha and Regmi, 2009). Of all the pesticides used within the study area, mancozeb had the highest application rate (7.78 kg a.i /ha), followed by dichlorvos, chlorpyrifos, profenfos, triazophos, dimethoate, carbendazim, metalaxyl, chlorantraniliprole, alphamethrin, imidacloprid, quinalphos, cypermethrin, and emamectin benzoate. Tomato, eggplant and chilli are the most common vegetable crops grown in the study area. Onto the aforesaid crops, growers applied higher doses of pesticides in different combinations (Bhandari et al., 2018). The planting and harvesting period for vegetables differed by crop. A detailed description of crop harvesting is provided in the Supplementary information (see Figure S3.1). Earlier studies (Arora, 2009; Baker et al., 2002; Ranga Rao et al., 2009) showed that food grown conventionally had higher concentrations of pesticide residues than food grown using IPM methods.

3.2.3 Sampling

Vegetable samples (27 eggplant, 27 chilli, and 32 tomato) from 54 local farmers' fields were collected during the winter of 2017. At the time of normal harvest, we collected vegetable samples from two types of farming systems: i) conventional farming (N=67) and ii) IPM fields (N=19). Altogether, 2-3 units of fresh vegetables were collected from each field (> 1kg each for tomato and eggplant and 0.5kg for chilli) in accordance with the procedures described in the FAO (1999). Samples were not rinsed/washed with water. A portion of each sample, without tops such as the sepal and peduncle, was prepared according to annex I of European Commission regulation 396/2005 EU (2010) using a knife and a chopping board and then thoroughly mixed. Next, 20 g of each sample was kept in a separate plastic bag at -20^{o}C until pesticide extraction and analysis could be carried out. Organically produced tomato samples (Greenland Organic Vegetable Grower Schalkwijk BV, Netherlands) were used as blanks.

3.2.4 Sample extraction and clean-up

A detail description of the analytical methods used in the pesticide analysis is provided in the Supplementary information (see extraction and clean-up methodology, p. S4).

3.2.5 Chemical analysis

All chemicals and reagents used were of analytical grade. Reference standards (in total 23) used for identification in this residue analysis were from Dr. Ehrenstorfer GmbH (Augsburg, Germany). Active substance standards used in this study had a purity of >95%. ^{13}C-Caffeine and PCB 198 (2,2',3,3',4,5,5',6-Octachlorobiphenyl) were used as internal standards.

A standard stock solution of each pesticide was prepared in acetonitrile at a concentration of 2,000 µg/mL. A mixed standard solution was prepared at a concentration of 10 µg/mL from the individual stock solutions. The calibration curve for the LC measurements was prepared by diluting 10 µg/mL of the mixed standard solution to achieve final concentrations of 0.25, 0.5, 1, 2.5, 5, 10, 25, and 100 ng/mL in a mixture of acetonitrile and water (1:1, v/v). Stock and working solutions were stored at 4°C until use. Pesticides were analysed through Liquid Chromatography Triple Quadrupole Mass Spectrometry (LC-MS/MS) and Gas Chromatography Triple Quadrupole Mass Spectrometry (GC-MS/MS) using the same extraction and clean-up method, chemicals, mobile phases, column characteristics and instrumentation conditions (see the Supporting information for full details, p. S4-S6). All the validation procedures and analytical quality control criteria were in line with those described in the guidance document for pesticide residues analysis in food and feed (EU, 2017). Briefly, 23 pesticides (Table S3.1), from now on called analytes, were identified according to (i) the retention time and peak shape of the respective reference standards and (ii) the ion ratio, with ratios between the quantification and confirmation transitions within ±30% of the average ion ratio of the calibration standards. The concentration of the analytes was calculated based on bracketing calibration, with a matrix-matched calibration standard.

Quality assurance and quality control of the method was performed by spiking duplicate samples as well as examining recovery, linearity, ion ratios, retention time and the limit of detection (LOD, Table 3.1) in order to verify compliance with identification requirements as outlined in SANTE/11813/2017 (EU, 2017). A calibration curve was injected at the start of the sample sequences. For recovery assessment and method validation, organic tomato was used as blank samples and fortified with a standard mix solution at 1, 2.5, 5, 10, and 25 µg/kg. Next, 5 ng/g of a blank tomato matrix was frequently run to check any interference due to contamination from the apparatus, solvents or chemicals used.

Fortified blank tomato samples presented a recovery of all analytes between 70 and 120%. Similar recovery values (80-120%) were observed in vegetable samples fortified with the mixture of standards. The calibration curves presented satisfactory linearity of response versus concentration, with correlation coefficients above 0.99. The concentration in each of the two aliquots (replicates) was within ±35% of the mean concentration of both aliquots.

3.2.6 Risk assessment

The risk assessment process was carried out based on the EFSA's risk assessment steps: (i) hazard identification; (ii) hazard characterisation; (iii) exposure assessment; and (iv) risk characterisation.

3.2.6.1 Hazard identification

Hazard identification determines whether exposure to a pesticide can cause an increase in the incidence of specific adverse health effects. Exposure to pesticides may generate many different adverse effects in human populations such as carcinogenesis, neurotoxicity, cytogenetic damage, and endocrine disruption in addition to developmental, reproductive, and immunological disorders (Mansour, 2004; Nicolopoulou-Stamati et al., 2016; Nougadere et al., 2012). We adopted the Pesticide Properties Database (PPDB) and the Bio-Pesticides Database (BPDB) to assess the potential health issues due to consumption of vegetables contaminated with pesticides.

3.2.6.2 Hazard characterisation

Hazard characterisation seeks to identify the quantitative relationship between a dose level and the resulting incidence of disease. Intake of vegetables contaminated with pesticides can have acute and chronic risks which can be assessed adopting following equations.

Acute/short-term HQ assessment (aHQ)

The aHQ was calculated based on the estimated short-term intake (ESTI) and the acute reference dose (ARfD) as:

ESTI = (the highest level of residue x the highest large portion of food consumption per day)/body weight..(3.1)

aHQ = ESTI/ARfD..(3.2)

Information on ARfDs was obtained from the EU pesticides database (http://ec.europa.eu/food/plant/pesticides/eu-pesticides-database/public/?event=homepage&language=EN).

Chronic/long-term HQ assessment (cHQ)
The cHQ was calculated based on the estimated daily intake (EDI) and the acceptable daily intake (ADI) as:

EDI = (mean level of residue x average food consumption per day)/body weight...........(3.3)
cHQ = EDI/ADI..(3.4)

Information on ADIs was obtained from the EU pesticides database (http://ec.europa.eu/food/plant/pesticides/eu-pesticides-database/public/?event=homepage&language=EN).

3.2.6.3 Exposure assessment
We choose to estimate dietary risks of exposure to pesticides in adolescents and adults. Population groups adopted from the international standards of the WHO (2013) were 10-19 years for adolescents and >19 years for adults. As data of Nepalese large portion consumption of the vegetables was not available, for aHQ, the maximum consumption (g/day) value was assumed as: 500 (eggplant), 50 (chilli), and 300 (tomato) for adult. For cHQ, we used average vegetable consumption data derived from the national survey carried out by the Ministry of Health (MoH et al., 2017) and agricultural data from the Ministry of Agricultural Development (MoAD, 2017). Adults consumed on average 9.6 g/day of eggplant, 2.85 g/day of chilli, and 61.3 g/day of tomato. In adolescents, the vegetables consumption (g/day) was assumed to be half that of an adults' daily vegetable consumption. Individual body weight measurements adopted from the international standards of the WHO (2011) were 32 kg for adolescents and 62 kg for adults.

3.2.6.4 Risk characterisation
Risk characterisation presents an integrated picture of the adverse health effects in exposed populations. We characterised the potential health risk by using the Hazard Quotient (HQ) and, for chronic risk also the Hazard Index (HI). The HQ is used for assessing the potential risk due to a single pesticide, while the HI for mixture risk takes into account multiple pesticides (Posthuma et al., 2018). The HI is the sum of the HQs. An HQ or HI > 1 denotes potential risk to human health (Darko and Akoto, 2008) while an HQ or HI ≤ 1 indicates no risk (Chabukdhara and Nema, 2013; Sun and Chen, 2018). We calculated hazard indices based on this data due to its simplicity.

The HI is based on the cumulative effect of pesticides with similar mechanisms of action. Pesticides causing the same physiological effects in terms of site and nature were grouped to form CAGs. It is not likely that a sample will have the highest concentration of residues of all pesticides, henceforth, only the chronic HI was calculated by adding up the cHQs of pesticides of a group (only OPs) and was expressed as a hazard index (HI) as:

HI = $\sum_{i=1}^{n}$ cHQi..(3.5)

3.2.7 Statistical analysis

Data analysis was performed using SPSS base 23.0 software. The Shapiro-Wilk test of normality of the variables was checked prior to performing the tests (Thode, 2002). Mean concentrations of different pesticides grouped by vegetable type and farming systems were tested. The Kruskal-Wallis one-way ANOVA was used to compare distributions across groups at the 95% confidence interval.

3.3 Results

3.3.1 Pesticide residues in vegetables

Out of the 23 tested analytes, 14 (approximately 61% of the tested analytes) were detected. About 97% of the tested vegetable samples contained at least one analyte. The observed concentration of chlorpyrifos in eggplant, tomato and chilli samples ranged from 1.19 to 45.3 µg/kg (41% of the samples), 1.07 to 1772 µg/kg (94% of the samples) and 1.29 to 491 µg/kg (81% of the samples), respectively. Likewise, the concentration of carbendazim in eggplant, tomato and chilli samples ranged from 1.21 to 154 µg/kg (78% of the samples), 1.45 to 337 µg/kg (100% of the samples) and 1.11 to 95 µg/kg (81% of the samples), respectively. The analysis of the vegetables showed the presence of different metabolites with the following concentrations in tomato samples: omethoate (range 6.93-27.9 µg/kg, 6% of the samples) and N-(2,6-dimethylphenyl)-N-(methoxyacetyl) alanine (1.47 µg/kg, 3% of the samples). Likewise, the concentrations of 3,5,6-trichloro-2-pyridinol in eggplant samples and N-(2,6-dimethylphenyl)-N-(methoxyacetyl) in chilli samples ranged from 4.53 µg/kg to 30 µg/kg (22% of the samples) and 1.32 to 2.32 µg/kg (7% of the samples), respectively (Table 3.1). Of all the observed concentrations of pesticides, the mean concentration of carbendazim in tomato samples was significantly higher ($p<0.05$) than the concentration of this compound in chilli and eggplant samples.

The observed concentrations of pesticides that belong to different groups differed with respect to the type of vegetable and the order for detection of different groups of pesticides is shown in Figure 3.2. However, concentrations of pesticides that belonged to the group of fungicides were the same in all of the vegetables. Vegetables revealed a group diversity of the presence of different pesticides with a total of 8 combinations such as AC, AC+FU, AC+FU+OP, AC+OP, FU+OP, FU, OP, and INsB (for abbreviations, see Table 3.1). The most common combination in eggplant and tomato samples, FU+OP, corresponded to 37% and 68.8% of the samples, respectively. Furthermore, the most common combination in chilli, AC+FU+OP, corresponded to 44.4% of the samples.

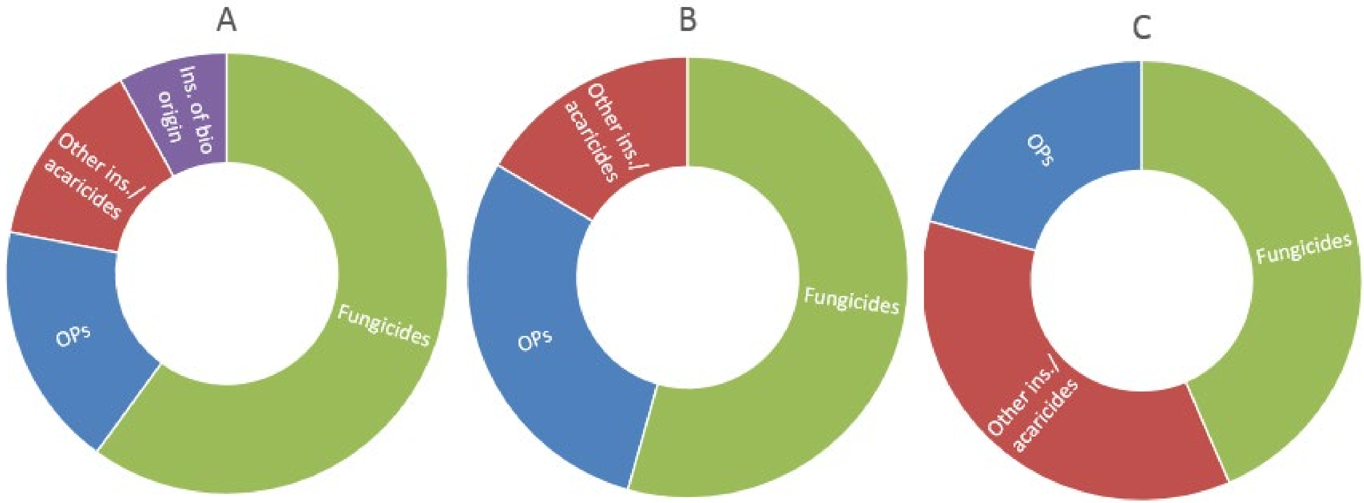


Figure 3.2 *The order of detection of different pesticides and their metabolites in the vegetables (A) eggplant, (B) tomato, and (C) chilli. Pesticides group is based on Roberts and Reigart (2013).*

Table 3.1 *Comparison of mean concentration of pesticides detected in vegetables and EU MRLs (µg/kg). The concentrations below the LODs (\) were not included when calculating the mean values.*

Pesticides group	Pesticides and metabolites	Eggplant (N=27)				Tomato (N=32)				Chilli (N=27)					
		Number and percentage (in brackets) of positive samples	Min-Max	Mean(±SD)	MRLs	Number and percentage (in brackets) of positive samples	Min-Max	Mean(±SD)	MRLs	Number and percentage (in brackets) of positive samples	Min-Max	Mean(±SD)	MRLs	LOD (µg/kg)	p-value
OPs	3,5,6-trichloro-2-pyridinol^{m}	6 (22)	4.53-30	13.4 (10.1)	NA	15 (47)	2.71-98.9	33 (32.1)	NA	5 (19)	2.96-13.5	6.47 (4.66)	NA	2.50	0.140
	Chlorpyrifos	11 (41)	1.19-45.3	11.1 (14.1)	10	30 (94)	1.07-1772	117 (341)	100	22 (81)	1.29-491	28.1 (104)	10	1	0.348
	Dichlorvos	\ (\)	NA	NA	10	\ (\)	NA	NA	10	3 (11)	1.35-2.76	2.18 (0.74)	10	1	NA
	Dimethoate	\ (\)	NA	NA	10	1 (3)	NA	NA	10	1 (4)	NA	NA	10	1	0.317
	Omethoate^{m}	\ (\)	NA	NA	10	2 (6)	6.93-27.9	17.4 (14.8)	10	\ (\)	NA	NA	10	1	NA
	Profenofos	1 (4)	NA	NA	10	22 (69)	1-1640	134 (353)	10000	8 (30)	1.16-228	40.6 (81.2)	3000	1	0.583
	Quinalphos	\ (\)	NA	NA	10	\ (\)	NA	NA	10	5 (19)	1.17-5.96	2.94 (1.79)	10	1	NA
	Triazophos	4 (15)	1.03-25.5	7.40 (12.1)	10	15 (47)	1.16-685	65 (182)	10	1 (4)	NA	NA	10	1	0.201
	Chlorantraniliprole	\ (\)	NA	NA	600	5 (16)	1.02-33.3	8.81 (13.9)	600	\ (\)	NA	NA	1000	1	NA
ACs	Imidacloprid	4 (15)	1.51-6.43	3.26 (2.23)	500	6 (19)	2.59-25.7	12.1 (9.02)	500	18 (67)	1.19-378	63.1 (108)	1000	1	0.281
	Carbendazim	21 (78)	1.21-154	19.7 (34)	500	32 (100)	1.45-337	50.3 (71.2)	300	22 (81)	1.11-95	20.1 (32.2)	100	1	0.002*
FUs	Metalaxyl	3 (11)	1.03-3.31	1.85 (1.27)	10	21 (66)	1.54-88.6	19.6 (29.3)	300	8 (30)	1.08-439	62.1 (153)	500	1	0.086
	N-(2,6-dimethylphenyl)-N-(methoxyacetyl)alanine^{m}	\ (\)	NA	NA	NA	1 (3)	NA	NA	NA	2 (7)	1.32-2.32	1.82 (0.71)	NA	1	1
INsB	Emamectin	1 (4)	NA	NA	20	\ (\)	NA	NA	20	\ (\)	NA	NA	20	1	NA

Code.

"m" = Metabolites; "\" = <LOD and "NA"= Not applicable; Organophosphates, OPs; acaricides, ACs; fungicides, FUs and insecticides of biological origin, INsB.

MRLs = Maximum residue level values set by EU for the corresponding pesticides and their metabolites in vegetables.

Organophosphates, OPs such as phorate and organochlorines, OCs such as p, p'-DDT; o, p'-DDT; p, p'-DDD; p, p'-DDE; α-Endosulfan; β-Endosulfan; α-HCH and γ-HCH were below the LOD in all samples and not included in the table.

* Significant at $p < 0.05$

Pesticides group is based on Roberts and Reigart (2013).

The concentration of pesticides and their metabolites with respect to the farming group, conventional farming and IPM, is shown in Table 3.2 and Figure S3.2. The total average concentration of pesticides in the vegetables from conventional farming was greater than the pesticides found on the vegetables farmed using IPM. The average concentration of few pesticide residues in vegetable samples from the two different farming systems differed significantly ($p<0.05$). In particular, the concentrations of imidacloprid, chlorpyrifos and 3,5,6-trichloro-2-pyridinol from conventional farming were significantly higher ($p<0.05$) than the residues detected in the vegetables from the IPM fields. However, concentrations of other pesticides did not vary based on farming techniques, which might be due to the small sample size.

Table 3.2 *Statistics of pesticides detected in vegetables from the two different farming groups (µg/kg). Only the positive samples were included in the calculation.*

Pesticides and metabolites	Farming group	N	Mean concentration	Std. Deviation	Std. Error Mean	p-value
3,5,6-trichloro-2-pyridinol[m]	IPM	3	3.05	0.31	0.18	0.014*
	Conventional	23	26	27.8	5.81	
Chlorpyrifos	IPM	13	3.62	2.63	0.73	0.012*
	Conventional	50	84.2	274	38.8	
Dichlorvos	IPM	1	NA	NA	NA	0.221
	Conventional	2	1.89	0.76	0.54	
Dimethoate	IPM	2	1.41	0.33	0.23	NA
	Conventional	0	NA	NA	NA	
Omethoate[m]	IPM	1	NA	NA	NA	0.317
	Conventional	1	NA	NA	NA	
Profenofos	IPM	4	25	42	21	0.906
	Conventional	27	118	321	61.9	
Quinalphos	IPM	2	2.54	0.13	0.1	1
	Conventional	3	3.21	2.47	1.43	
Triazophos	IPM	4	4.11	3.82	1.91	0.571
	Conventional	16	62.4	176	44	
Chlorantraniliprole	IPM	0	NA	NA	NA	NA
	Conventional	5	8.81	13.9	6.21	
Imidacloprid	IPM	8	8.59	18.1	6.41	0.005*
	Conventional	20	57.7	103	23	
Carbendazim	IPM	16	21.2	32.4	8.09	0.232
	Conventional	59	36	58.8	7.66	
Metalaxyl	IPM	7	21.4	30.7	11.6	0.305
	Conventional	25	30.5	88.2	17.6	
N-(2,6-dimethylphenyl)-N-	IPM	2	1.4	0.11	0.08	0.221
(methoxyacetyl)alanine[m]	Conventional	1	NA	NA	NA	
Emamectin	IPM	0	NA	NA	NA	NA
	Conventional	1	NA	NA	NA	
IPM[a]		19	39.5	54.2	12.4	0.008*
Conventional[a]		67	196	451	55.2	

Code.
[a] Total average concentration of pesticides; * Significant at $p < 0.05$; “NA” = Not applicable.

Overall, in only 2% of the vegetable samples no pesticide residues were detected. The number of residues of different pesticides and metabolites in tomato samples was higher than in chilli and eggplant samples (Figure 3.3). Vegetable samples from conventional farming were contaminated with up to 7 residues of pesticides.

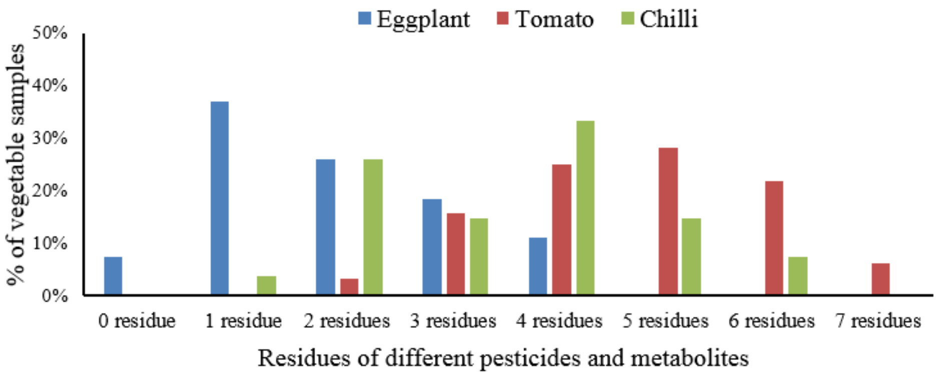


Figure 3.3 *The multiple residues of pesticides detected in vegetables from the two different farming groups.*

3.3.2 Hazard characterisation of the detected pesticides

Mostly, aHQ and cHQ for single pesticide were quite low, implying no risk. The HQs of dietary risks from vegetables contaminated with chemical pesticides for adolescents and adults is presented in Table 3.3a-3.3c. The consumption of tomato was found to imply a short-term risk (for both adolescent and adult individuals) due to triazophos and chlorpyrifos residues (Table 3.3b). Of all the pesticides and vegetables tested, consumption of tomatoes could carry the highest short-term risks for both adolescents and adults due to the high amounts of triazophos and chlorpyrifos found in these vegetables.

Table 3.3a *HQ and HI for detected pesticides in eggplant for the consumer group of adolescents and adults.*

Groups	Pesticides	ARfD	ADI	Adolescent					Adult					Source
				ESTI	aHQ	EDI	cHQ	cHI	ESTI	aHQ	EDI	cHQ	cHI	(ARfD, ADI)
		(mg kg-1 b.w. day-1)	(mg kg-1 b.w. day-1)	(mg kg-1 b.w. day-1)		(mg kg-1 b.w. day-1)			(mg kg-1 b.w. day-1)		(mg kg-1 b.w. day-1)			
OPs	Triazophos	1.00E-03	1.00E-03	1.99E-04	1.99E-01	1.64E-07 (LB) 2.92E-07 (UB)	1.64E-04 (LB) 2.92E-04 (UB)	8.44E-04 (LB) 1.07E-03 (UB)	2.06E-04	2.06E-01	1.70E-07 (LB) 3.02E-07 (UB)	1.70E-04 (LB) 3.02E-04 (UB)	8.71E-04 (LB) 1.10E-03 (UB)	JMPR
	Chlorpyrifos	5.00E-03	1.00E-03	3.54E-04	7.08E-02	6.78E-07 (LB) 7.67E-07 (UB)	6.78E-04 (LB) 7.67E-04 (UB)		3.65E-04	7.31E-02	7.00E-07 (LB) 7.92E-07 (UB)	7.00E-04 (LB) 7.92E-04 (UB)		EFSA
	Profenofos	1.00E+00	3.00E-02	5.77E-05	5.77E-05	4.10E-08 (LB) 1.85E-07 (UB)	1.37E-06 (LB) 6.18E-06 (UB)		5.95E-05	5.95E-05	4.23E-08 (LB) 1.91E-07 (UB)	1.41E-06 (LB) 6.38E-06 (UB)		JMPR
ACs	Imidacloprid	8.00E-02	6.00E-02	5.02E-05	6.28E-04	7.23E-08 (LB) 2.00E-07 (UB)	1.21E-06 (LB) 3.34E-06 (UB)	NC (LB) NC (UB)	5.19E-05	6.48E-04	7.47E-08 (LB) 2.07E-07 (UB)	1.24E-06 (LB) 3.44E-06 (UB)	NC (LB) NC (UB)	EFSA
FUs	Carbendazim	2.00E-02	2.00E-02	1.20E-03	6.02E-02	2.30E-06 (LB) 2.33E-06 (UB)	1.15E-04 (LB) 1.16E-04 (UB)	NC (LB) NC(UB)	1.24E-03	6.21E-02	2.37E-06 (LB) 2.40E-06 (UB)	1.18E-04 (LB) 1.20E-04 (UB)	NC (LB) NC (UB)	EFSA
	Metalaxyl	5.00E-01	8.00E-02	2.59E-05	5.17E-05	3.09E-08 (LB) 1.64E-07 (UB)	3.86E-07 (LB) 2.05E-06 (UB)		2.67E-05	5.34E-05	3.19E-08 (LB) 1.70E-07 (UB)	3.99E-07 (LB) 2.12E-06 (UB)		EU
INsB	Emamectin	1.00E-02	5.00E-04	1.95E-05	1.95E-03	1.39E-08 (LB) 1.58E-07 (UB)	2.78E-05 (LB) 3.17E-04 (UB)	NC (LB) NC (UB)	2.02E-05	2.02E-03	1.43E-08 (LB) 1.63E-07 (UB)	2.87E-05 (LB) 3.27E-04 (UB)	NC (LB) NC (UB)	EFSA

Table 3.3b *HQ and HI for detected pesticides in tomato for the consumer group of adolescents and adults.*

Groups	Pesticides	ARfD (mg kg^{-1} b.w. day^{-1})	ADI (mg kg^{-1} b.w. day^{-1})	Adolescent ESTI (mg kg^{-1} b.w. day^{-1})	Adolescent aHQ	Adolescent EDI (mg kg^{-1} b.w. day^{-1})	Adolescent cHQ	Adolescent cHI	Adult ESTI (mg kg^{-1} b.w. day^{-1})	Adult aHQ	Adult EDI (mg kg^{-1} b.w. day^{-1})	Adult cHQ	Adult cHI	Source (ARfD, ADI)
OPs	Omethoate	2.00E-03	3.00E-04	1.31E-04	6.54E-02	1.04E-06 (LB) 1.94E-06 (UB)	3.48E-03 (LB) 6.47E-03 (UB)	1.41E-01 (LB) 1.45E-01 (UB)	1.35E-04	6.75E-02	1.08E-06 (LB) 2.00E-06 (UB)	3.59E-03 (LB) 6.68E-03 (UB)	1.45E-01 (LB) 1.50E-01 (UB)	EFSA
	Dimethoate	1.00E-02	1.00E-03	7.69E-06	7.69E-04	4.91E-08 (LB) 9.77E-07 (UB)	4.91E-05 (LB) 9.77E-04 (UB)		7.94E-06	7.94E-04	5.07E-08 (LB) 1.01E-06 (UB)	5.07E-05 (LB) 1.01E-03 (UB)		EFSA
	Triazophos	1.00E-03	1.00E-03	3.21E-03	**3.21E+00**	2.92E-05 (LB) 2.97E-05 (UB)	2.92E-02 (LB) 2.97E-02 (UB)		3.31E-03	**3.31E+00**	3.01E-05 (LB) 3.07E-05 (UB)	3.01E-02 (LB) 3.07E-02 (UB)		JMPR
	Chlorpyrifos	5.00E-03	1.00E-03	8.31E-03	**1.66E+00**	1.05E-04 (LB) 1.05E-04 (UB)	1.05E-01 (LB) 1.05E-01 (UB)		8.57E-03	**1.71E+00**	1.09E-04 (LB) 1.09E-04 (UB)	1.09E-01 (LB) 1.09E-01 (UB)		EFSA
	Profenofos	1.00E+00	3.00E-02	7.69E-03	7.69E-03	8.82E-05 (LB) 8.85E-05 (UB)	2.94E-03 (LB) 2.95E-03 (UB)		7.94E-03	7.94E-03	9.10E-05 (LB) 9.13E-05 (UB)	3.03E-03 (LB) 3.04E-03 (UB)		JMPR
ACs	Imidacloprid	8.00E-02	6.00E-02	1.20E-04	1.51E-03	2.18E-06 (LB) 2.96E-06 (UB)	3.63E-05 (LB) 4.93E-05 (UB)	NC (LB) NC (UB)	1.24E-04	1.55E-03	2.25E-06 (LB) 3.05E-06 (UB)	3.75E-05 (LB) 5.09E-05 (UB)	NC (LB) NC (UB)	EFSA
	Chlorantraniliprole	NA	1.56E+00	1.56E-04	NC	1.32E-06 (LB) 2.13E-06 (UB)	8.45E-07 (LB) 1.36E-06 (UB)		1.61E-04	NA	1.36E-06 (LB) 2.20E-06 (UB)	8.72E-07 (LB) 1.41E-06 (UB)		EFSA
FUs	Carbendazim	2.00E-02	2.00E-02	1.58E-03	7.90E-02	4.82E-05 (LB) NA (UB)	2.41E-03 (LB) NA (UB)	NC (LB) NC (UB)	1.63E-03	8.15E-02	4.98E-05 (LB) NA (UB)	2.49E-03 (LB) NA (UB)	NC (LB) NC (UB)	EFSA
	Metalaxyl	5.00E-01	8.00E-02	4.15E-04	8.31E-04	1.23E-05 (LB) 1.26E-05 (UB)	1.54E-04 (LB) 1.58E-04 (UB)		4.29E-04	8.57E-04	1.27E-05 (LB) 1.30E-05 (UB)	1.59E-04 (LB) 1.63E-04 (UB)		EU

***Table 3.3c** HQ and HI for detected pesticides in chilli for the consumer group of adolescents and adults.*

				Adolescent					Adult					
Groups	Pesticides	ARfD	ADI	ESTI	aHQ	EDI	cHQ	cHI	ESTI	aHQ	EDI	cHQ	cHI	Source (ARfD, ADI)
		(mg kg-1 b.w. day-1)	(mg kg-1 b.w. day-1)	(mg kg-1 b.w. day-1)		(mg kg-1 b.w. day-1)			(mg kg-1 b.w. day-1)		(mg kg-1 b.w. day-1)			
OPs	Dimethoate	1.00E-02	1.00E-03	9.22E-07	9.22E-05	1.95E-09 (LB) 4.48E-08 (UB)	1.95E-06 (LB) 4.48E-05 (UB)	1.19E-03 (LB) 1.78E-03 (UB)	9.52E-07	9.52E-05	2.01E-09 (LB) 4.63E-08 (UB)	2.01E-06 (LB) 4.63E-05 (UB)	1.23E-03 (LB) 1.84E-03 (UB)	EFSA
	Triazophos	1.00E-03	1.00E-03	7.49E-06	7.49E-03	1.58E-08 (LB) 5.87E-08 (UB)	1.58E-05 (LB) 5.87E-05 (UB)		7.73E-06	7.73E-03	1.63E-08 (LB) 6.06E-08 (UB)	1.63E-05 (LB) 6.06E-05 (UB)		JMPR
	Chlorpyrifos	5.00E-03	1.00E-03	3.84E-04	7.67E-02	1.02E-06 (LB) 1.03E-06 (UB)	1.02E-03 (LB) 1.03E-03 (UB)		3.96E-04	7.92E-02	1.05E-06 (LB) 1.06E-06 (UB)	1.05E-03 (LB) 1.06E-03 (UB)		EFSA
	Profenofos	1.00E+00	3.00E-02	1.78E-04	1.78E-04	5.36E-07 (LB) 5.67E-07 (UB)	1.79E-05 (LB) 1.89E-05 (UB)		1.84E-04	1.84E-04	5.53E-07 (LB) 5.86E-07 (UB)	1.84E-05 (LB) 1.95E-05 (UB)		JMPR
	Dichlorvos	2.00E-03	8.00E-05	2.16E-06	1.08E-03	1.08E-08 (LB) 5.04E-08 (UB)	1.35E-04 (LB) 6.30E-04 (UB)		2.23E-06	1.11E-03	1.11E-08 (LB) 5.20E-08 (UB)	1.39E-04 (LB) 6.50E-04 (UB)		EFSA
ACs	Imidacloprid	8.00E-02	6.00E-02	2.95E-04	3.69E-03	1.87E-06 (LB) 1.89E-06 (UB)	3.12E-05 (LB) 3.15E-05 (UB)	NC (LB) NC (UB)	3.05E-04	3.81E-03	1.93E-06 (LB) 1.95E-06 (UB)	3.22E-05 (LB) 3.25E-05 (UB)	NC (LB) NC (UB)	EFSA
FUs	Carbendazim	2.00E-02	2.00E-02	7.42E-05	3.71E-03	7.30E-07 (LB) 7.39E-07 (UB)	3.65E-05 (LB) 3.69E-05 (UB)	NC (LB) NC (UB)	7.66E-05	3.83E-03	7.54E-07 (LB) 7.62E-07 (UB)	3.77E-05 (LB) 3.81E-05 (UB)	NC (LB) NC (UB)	EFSA
	Metalaxyl	5.00E-01	8.00E-02	3.43E-04	6.86E-04	8.19E-07 (LB) 8.51E-07 (UB)	1.02E-05 (LB) 1.06E-05 (UB)		3.54E-04	7.08E-04	8.46E-07 (LB) 8.78E-07 (UB)	1.06E-05 (LB) 1.10E-05 (UB)		EU

Code (Table 3.3).
NA: Not available; NC: Not characterized.
LB: Lower bound (results < LOD were replaced with 0).
UB: Upper bound (results < LOD were replaced with the value of LOD).
The aHQ and aHI values in bold represent potential dietary risk of the pesticides in adolescents and adults.
ARfD (mg kg^{-1} b.w. day^{-1}) and ADI (mg kg^{-1} b.w. day^{-1}) values were extracted from the EU pesticides database (http://ec.europa.eu/food/plant/pesticides/eu-pesticides-database/public/?event=homepage&language=EN).
The concentrations of organophosphates, OPs such as phorate and organochlorines, OCs such as p, p'-DDT; o, p'-DDT; p, p'-DDD; p, p'-DDE; α-Endosulfan; β-Endosulfan; α-HCH and γ-HCH were below the LOD in all vegetables (100% non-quantified) and not included in the calculation.
Data on ARfD and ADI of pesticides and metabolites such as quinalphos, 3,5,6-trichloro-2-pyridinol and N-(2,6-dimethylphenyl)-N-(methoxyacetyl)alanine was not available and not included in the calculation, therefore their potential health risks could not be ascertained. Chlorantraniliprole has only data on ADI, therefore the acute risk was not calculated. All tomato samples contained quantifiable carbendazim residues, therefore the UB was not available.
The body weight (b.w.) for adolescents and adults was 32 and 62 kg, respectively.
As data of Nepalese large portion consumption of the vegetables was not available, for acute risk estimation, the maximum consumption (g/day) value was assumed as: 500 (eggplant), 50 (chilli), and 300 (tomato) for adult. For chronic risk estimation, the average vegetables consumption (g/day) value is 9.6 (eggplant), 2.85 (chilli), and 61.3 (tomato) for adult. For adolescent, the maximum and average vegetables intake (g/day) is assumed as half of adults' consumption. The acute HI was not a priority of this research as the chance of having the highest residue in a sample for multiple pesticides is very low.
Pesticides group is based on Roberts and Reigart (2013).

3.3.3 Pesticides exposure

Our study detected mostly organophosphates in the investigated vegetable samples. A few of these samples exceeded the MRLs of these compounds set by Nepal and the EU. Chlorpyrifos exceeded the EU MRL in 19% of the tomato and chilli samples (Table 3.1). Likewise, chlorpyrifos exceeded the Nepalese foodstuff MRL (50 µg/kg) in 25% of the tomato samples and 4% of the chilli samples. Similarly, triazophos exceeded the EU MRLs in 4% of the eggplant samples and 6% of the tomato samples. The concentration of omethoate exceeded the EU MRL in 3% of the tomato samples. Carbendazim exceeded the EU MRL in 3% of the tomato samples, but it did not exceed the Nepalese foodstuff MRL (500 µg/kg). It is noteworthy to mention that all of the vegetable samples that were from the IPM fields had pesticide concentrations below EU MRLs. Measurements of omethoate, chlorpyrifos, triazophos and carbendazim exceeded the EU limits leading to unnecessary exposure to pesticides (Table 3.1).

3.3.4 Risk characterisation of the detected pesticides

Of all the pesticides groups and vegetables tested, the OPs that were detected in tomatoes posed the highest health risks. The chronic HIs for OPs in adults and adolescents were <1, indicating no risk of the vegetables consumption. HIs for other groups of pesticides could not be characterized, either due to their different modes of action or not applicable to characterize (Table 3.3a-3.3c). Pesticide-related health risks and diseases are presented in Table 3.4.

3.4 Discussion

The most frequently detected pesticides in the vegetables in this study were carbendazim and chlorpyrifos. Our vegetable samples tested negative for OCs and other pesticides banned in Nepal. However, previous studies (Bempah et al., 2016; Diop et al., 2016; Mtashobya, 2017) found OCs in vegetable samples (Table S3.2). One study carried out in Nepal (Koirala et al., 2007) detected OCs in vegetables that might have been due to past applications. For some pesticides, metabolites such as omethoate, N-(2,6-dimethylphenyl)-N-(methoxyacetyl)alanine, and 3,5,6-trichloro-2-pyridinol were detected in higher concentrations, probably due to their persistent nature (Xu et al., 2015). However, the occurrence of these pesticides in the vegetables varied (Table 3.1). Although farmers applied dimethoate to all vegetable crops (Bhandari et al., 2018), its metabolite (omethoate) was only detected in 6% of the tomato samples which might be due to the higher water solubility of this pesticide (Table S3.1). Farmers did not report the use of quinalphos in the sampled vegetables (Bhandari et al., 2018), but it was detected in 19% of the chilli samples. This might be due to the pesticide uptake from soil or spray drifting in from neighbouring farmers' fields or cross contamination by different vectors. Farmers apply dichlorvos the most often (Bhandari et al., 2018). However, its residue was detected in only 11% of the chilli samples, which might be due to higher water solubility and volatility of the compound. Along with its higher solubility in water, its shorter half-life time as well as its rapid disintegration in nature could also explain the values (Table S3.1). Further environmental factors such as rainfall, temperature, soil properties, and soil organisms also affect the occurrence of pesticides and their metabolites in different matrices (Bento et al., 2016). The detection frequency for fungicides was higher (Figure 3.2) which might have been due to its extreme use in vegetable farming in the study area (Bhandari et al., 2018). The multiple residues (resulting from the mixtures of different pesticides) occur due to plant uptake of pesticides (a mixture) of high persistence (Zhang et al., 2015), spray drift (Coronado et al., 2011) and poor agricultural practices. Farmers mix more than one kind of pesticide and sprayed it on tomato crops believing that the mixture would be more potent and more effectively kill the target pests (Bhandari et al., 2018). Therefore, we observed the highest number of residues in tomato. Tomato and green chillies are ready-to-eat foods and are consumed in salads, often without cooking. As a result, their detection suggest immediate action needs to be taken to minimize the risk of pesticide exposure. Previous studies showed that food grown conventionally had higher concentrations of pesticides than food grown on IPM fields (Mladenova and Shtereva, 2009; Singh et al., 2009). Our study also showed that most vegetables grown conventionally had higher levels of pesticide residues than food grown using IPM methods.

Nepalese farmers used pesticides on vegetables even when there was no disease or pests present (Pant et al., 2014). In our study, omethoate, chlorpyrifos, triazophos and carbendazim in the vegetables from conventional farming exceeded the EU MRLs, which further shows the poor agricultural practices of farmers leading to unnecessary exposure of consumers to pesticides. Farmers applied higher amounts of chlorpyrifos on tomato crops (Bhandari et al., 2018) and residue analysis of this crop revealed that 19% of the samples exceeded EU MRLs. This provides strong evidence of an indiscriminate use of pesticides in tomato crops. In our study, eggplant and tomato samples tested negative for dichlorvos (below LOD). However, Rawal et al. (2012) found the concentration of this compound in vegetables above EU limits. Of all the pesticides and vegetables examined in this current study, the consumption of tomatoes could pose highest potential human risks due to exposure to insecticides such as triazophos and chlorpyrifos. Acute pesticide poisonings from chlorpyrifos were also reported by hospitals in Nepal (Gyenwali et al., 2017; Lama, 2008). A study in Pakistan (Syed et al., 2014), however, estimated no risk of chlorpyrifos from consuming tomatoes. HQs not only depend on pesticide concentration but also on average body weight and quantity of food consumed (Javed and Usmani, 2016), all of which ultimately affect an individual's level of risk from pesticides.

OPs are routinely applied to vegetables to control insects and disease (Quijano et al., 2016). In our study, the OPs that were detected indicated the highest potential for health risks. Similar pesticide risk was observed in a previous study (Liu et al., 2016a). In our study, the pesticides such as triazophos and chlorpyrifos contributed significantly to higher cHI values for the OPs, which might be due to the overuse of these pesticides from the organophosphate group in the study area. The HI could be reduced by gradually minimizing the use of OPs. Moreover, we observed higher HQs for insecticides such as chlorpyrifos and triazophos, and fungicides such as carbendazim. These pesticides are responsible for many health problems such as endocrine disruption, reproductive disorders and neurological effects (Table 3.4). Previous studies in Nepal observed acetylcholinesterase depression in farmers applying chemical pesticides (Atreya et al., 2012; Neupane et al., 2014) and increased numbers of cancer patients in hospitals (Poudel et al., 2017). A recent study from Nepal (Yadav et al., 2016) concluded that there was a higher cancer risk associated with pesticides. Along with cardiovascular diseases, the occurrence of renal failure, Alzheimer's disease, Parkinson's disease, and strokes are also increasing in Nepal. Whether or not these diseases are linked to dietary exposure to pesticides warrants further investigation.

Table 3.4 *Pesticides detected in vegetables with their corresponding health issues^.*

Pesticides and metabolites	Carcinogen	Mutagen	Endocrine disrupter	Reproductive effects	Cholinesterase inhibitor	Neurotoxicant	Respiratory tract irritant	Skin irritant	Skin sensitiser	Eye irritant	Phototoxicant
3,5,6-trichloro-2-pyridinol^{m}	na	na	na	na	na	na	P	na	na	na	na
Carbendazim	P	Y	P	Y	X	X	X	X	na	X	na
Chlorantraniliprole	X	X	X	P	X	X	na	X	na	P	na
Chlorpyrifos	X	X	P	Y	Y	Y	X	X	P	X	X
Dichlorvos	P	Y	P	na	Y	Y	P	Y	P	Y	na
Dimethoate	P	X	X	P	Y	P	X	X	X	Y	na
Emamectin	X	X	na	P	X	P	na	X	P	Y	na
Imidacloprid	X	P	na	Y	X	P	X	P	na	P	na
Metalaxyl	X	X	X	X	X	X	X	X	P	X	na
N-(2,6-dimethylphenyl)-N-(methoxyacetyl)alanine^{m}	na	na	na	na	na	na	na	na	na	na	na
Omethoate^{m}	X	na	Y	X	Y	Y	na	Y	Y	X	na
Profenofos	X	na	na	X	Y	Y	na	Y	na	P	na
Quinalphos	X	na	na	P	Y	Y	Y	Y	na	Y	na
Triazophos	X	na	na	na	Y	Y	Y	Y	na	Y	na

Code.
Y = Yes, known to cause a problem; X = No, known not to cause a problem; P = Possibly, status not identified; na = Data not available.
^ Health issues were adopted from a PPDB database (https://sitem.herts.ac.uk/aeru/ppdb/en/index.htm) and BPDB (https://sitem.herts.ac.uk/aeru/bpdb/Reports/1326.htm).

OPs and their metabolites may translocate, accumulate or be deposited into vegetable tissues (Jeong et al., 2012). For compounds such as omethoate, N-(2,6-dimethylphenyl)-N-(methoxyacetyl)alanine, and 3,5,6-trichloro-2-pyridinol, neither CODEX, EU or EPA have set MRLs for the vegetables in this study and the WHO has no set values for ARfD or ADI which leads to difficulties in evaluating their risks on human health.

The 23 prioritized pesticides and metabolites assessed in the vegetables correspond to <20% of the active ingredients used, indicating that the total amount of pesticides in Nepalese vegetables might even be higher than presented in this study and the actual dietary risks even greater. This study was limited to small sample size consisting of only 3 types of vegetables. The levels of residues varies with seasons (Mtashobya, 2017), which might be inadequate to assess a total exposure to pesticides. Only certain pesticides sharing a common mode of action are subject to cumulative risk assessment. We used hazard indices to present the risks that pesticides in vegetables pose for human health and the dietary risk estimates were based on aHI and cHI for OPs only. Using HI as an approach for the risk assessment further limits the current risk assessment as complexity in the mixture of pesticides present in our foods and their different mode of actions has increased shortcomings on summation effects (Reffstrup et al., 2010). A balanced diet differs with respect to gender and age (DFTQC, 2012), and there is no clear information available on vegetable consumption and marketing, especially along the porous India-Nepal border. Activities such as cooking, washing, and peeling have been found to reduce pesticide residues in vegetables (Keikotlhaile et al., 2010; Kumari et al., 2003; Reiler et al., 2015; Shabeer et al., 2015). Overall, our results indicated that there is a potential for increased health risk for adults and adolescents following acute single and cumulative exposure to some pesticides used in vegetable farming in Nepal.

3.5 Conclusion

This study quantified pesticide residues in vegetables which could potentially threaten people's health in Nepal. Risks were mainly associated with the residues of OP pesticides in vegetables. The HQ and HI estimations revealed a serious potential risk for consumers. Due to multiple pesticide residues exceeding the MRLs for single residue concentrations, the consumers are exposed to pesticides. ARfD and ADI for multiple residues do not exist and therefore, this risk should urgently be studied. The consumption of some of the vegetables posed an unacceptable risk to human health.

The current study recommends the following interventions in order to reduce pesticide risk associated with the consumption of vegetables in Nepal: (i) extensive IPM training for farmers currently using pesticides, focusing on good agricultural practices such as pesticide spraying intervals and the importance of the waiting period; (ii) legal enforcement of pesticide residue limits to prevent, control and minimize health risks and (iii) decrease in the use of OPs, especially chlorpyrifos and triazophos.

Acknowledgements

We are grateful to the Netherlands Universities Foundation for International Cooperation (Nuffic) for funding this research (through NFP-PhD-5160957247). The authors thank local farmers for their cooperation and support during the sample collection. We would like to thank the students Dinesh Ghimire, Prashant Chaudhary, Santosh Gupta, and Ramesh Lodh for their support during the field work. We also thank Ron Hoogenboom, Ad Peijnenburg, Robin Palmer, Rita Boerrigter-Eenling, Joost Memelink, and Suryati Sunarto for their support. The comments received from the anonymous reviewers were also appreciated.

Supplementary Material

Table S3.1 *The properties of the pesticides tested and their metabolites^.*

Group	Pesticides and metabolites	MF/MW(g mol-1)	[a]CASRN	Water solubility (mg L-1)	[b]DT50	[c]Kd	[d]Koc	Vapour pressure (mPa)	[e]GUS index	[f]BCF
OPs	3,5,6-trichloro-2-pyridinol[m]	$C_5H_2Cl_3NO$/198.43	6515-38-4	81	75	na	149	137.32	4.88	3.20
	Chlorpyrifos	$C_9H_{11}Cl_3NO_3PS$/350.59	2921-88-2	1.05	28	127	5509	1.43	3.63	1374
	Dichlorvos	$C_4H_7Cl_2O_4P$/220.98	62-73-7	18000	na	na	50	2100	0.69	<100
	Dimethoate	$C_5H_{12}NO_3PS_2$/229.26	60-51-5	25900	7	na	na	0.247	1.01	8
	Omethoate[m]	$C_5H_{12}NO_4PS$/213.19	1113-02-6	500000	14	0.53	41.3	19	-2.38	75
	Phorate!	$C_7H_{17}O_2PS_3$/260.4	298-02-2	50	63	na	1660	112	1.25	483
	Profenofos	$C_{11}H_{15}BrClO_3PS$/373.63	41198-08-7	28	7	na	2016	2.53	0.59	1186
	Quinalphos	$C_{12}H_{15}N_2O_3PS$/298.3	13593-03-8	18	na	na	1465	0.346	1.1	na
	Triazophos	$C_{12}H_{16}N_3O_3PS$/313.31	24017-47-8	35	9	na	358	1.33	2.38	300
OCs	o, p'-DDT!	$C_{14}H_9Cl_5$/354.48	789-02-6	na	na	na	151000	na	-3.89	na
	p, p'-DDD!	$C_{14}H_{10}Cl_4$/320.04	72-54-8	0.09	na	na	131000	0.18	-2.46	na
	p, p'-DDE!	$C_{14}H_8Cl_4$/318.02	72-55-9	0.12	5000	50000	na	na	na	1800
	p, p'-DDT!	$C_{14}H_9Cl_5$/354.49	50-29-3	0.025	na	na	151000	na	-3.89	na
	α-Endosulfan!	$C_9H_6Cl_6O_3S$/406.93	959-98-8	0.32	86	na	11500	8.30	-0.1	2755
	α-HCH!	$C_6H_6Cl_6$/290.83	319-84-6	2	na	na	1888	5.99	1.62	na
	β-Endosulfan!	$C_9H_6Cl_6O_3S$/406.93	33213-65-9	0.45	na	na	na	na	na	na
	γ-HCH!	$C_6H_6Cl_6$/290.82	58-89-9	8.52	148	na	1270	4.40	3.95	1300
ACs	Chlorantraniliprole	$C_{18}H_{14}BrCl_2N_5O_2$/483.15	500008-45-7	0.88	204	3.18	362	6.3 X 10^{-09}	4.22	15
	Imidacloprid	$C_9H_{10}ClN_5O_2$/255.66	138261-41-3	610	174	na	na	4.0 X 10^{-07}	3.74	0.61
FUs	Carbendazim	$C_9H_9N_3O_2$/191.21	10605-21-7	8	22	na	na	0.09	2.53	25
	Metalaxyl	$C_{15}H_{21}NO_4$/279.33	58737-19-1	8400	39	na	162	0.75	2.79	7
	N-(2,6-dimethylphenyl)-N-(methoxyacetyl)alanine[m]	$C_{14}H_{19}NO_4$/265.3	87764-37-2	na	51	na	38	na	3.83	na
INsB	Emamectin	$C_{56}H_{81}NO_{15}$/1008.3	155569-91-8	24	1	na	377000	0.004	na	80

Code.

aCASRN, chemical abstracts service registry number; bDT50 (field), half-life time; cKd, soil sorption coefficient; dKoc, soil organic carbon-water partitioning coefficient; eGUS index, groundwater ubiquity score; fBCF, bio-concentration factor.

^ = The properties of the pesticides were taken from PPDB (https://sitem.herts.ac.uk/aeru/ppdb/en/atoz.htm) and BPDB (https://sitem.herts.ac.uk/aeru/bpdb/atoz.htm) (Retrieved on: 30 March, 2018).

MF = Molecular formula; MW = Molecular weight; ! = Banned pesticides; na = Not available; m = Metabolites.

Organophosphates, OPs; organochlorines, OCs; acaricides, ACs; fungicides, FUs and insecticides of biological origin, INsB.

Table S3.2 *Comparison of pesticides level in vegetables in this study with previous studies across the world (µg/kg).*

Place, country	Pesticides	Levels of residues						References
		Eggplant	No. of samples	Chilli	No. of samples	Tomato	No. of samples	
Hyderabad, India (m)	Chlorpyrifos	24	10	na	na	179	10	(Sinha et al., 2012)
	Triazophos	0.86				3.01		
Andaman Islands, India (m)	Endosulfan	na	na	92	42	na	na	(Swarnam and Velmurugan, 2013)
Croatia (h)	Dimethoate	100	20	50	52	na	64	(Knežević et al., 2012)
	Endosulfan	na		na		40		
Bogota, Colombia (m)	Carbendazim	na	na	na	na	50	400	(Arias et al., 2014)
	Dimethoate					20		
	Imidacloprid					300		
	Metalaxyl					10		
Turkey (r)	Carbendazim	na	na	11–210	83	20–1200	177	(Bakirci et al., 2014)
	Chlorpyriphos			10-406		10–53		
	Endosulfan (α; β)			(230–430; 560–700)		na		
	Imidacloprid			10-1240		12–88		
	Metalaxyl			30-180		10–50		
Egypt (h)	Carbendazim	na	na	660	31	70	19	(Gad Alla et al., 2015)
	Chlorpyrifos			310		50		
	Metalaxyl			70		10		
	Profenofos			4300		410		
Ghana (r)	Endosulfan (α; β)	na	na	13–17; 6–10	60	15–19; 20–26	50	(Bempah et al., 2016)
	p,p'-DDD			9–13		25–31		
	p,p'-DDE			8–21		20–24		
	p,p'-DDT			20–26		23–29		
Niaga, Senegal (m)	∑DDTs	na	na	na	na	15	57	(Diop et al., 2016)
	Chlorpyrifos					135		
	Dimethoate					18		
Kuwait (r)	Imidacloprid	nd–90	14	nd–10	12	nd–510	16	(Jallow et al., 2017b)
	Metalaxyl	na		nd–10		nd–200		
	Profenofos	na		nd–30		20–390		
Burkina Faso (h)	Chlorpyrifos	na	na	na	na	667	17	(Lehmann et al., 2017)
	Imidacloprid					153		
	Profenofos					74		
	Triazophos					0.49		
Algeria (r)	Metalaxyl	na	na	na	na	4–412	10	(Mebdoua et al., 2017)
Uluguru, Tanzania (m)	α-HCH	na	na	na	na	2.20E-02	19	(Mtashobya, 2017)
	β-endosulfan					0.10		
	γ-HCH					1.70E-02		
Meru district, Tanzania (r)	Chlorpyrifos	na	na	na	na	833–603609	50	(Kariathi et al., 2016)
Pakistan (m, r)	Chlorpyrifos	250 (<90–570)	25	160(<90–270)	25	220(110–360)	25	(Latif et al., 2011)
	α-Endosulfan	640 (<150–1570)		660(<150–1330)		300(<150–580)		
	β-Endosulfan	290 (<230–730)		1260(<230–1610)		330(<230–870)		
Nepal (m)	Dichlorvos	6	3	4.20	3	11.4	3	(Rawal et al., 2012)
Rupandehi, Nepal	OPs, OCs, ACs, FUs, and INsB	Table 3.1						This study

na = Not available and nd = Not detected.

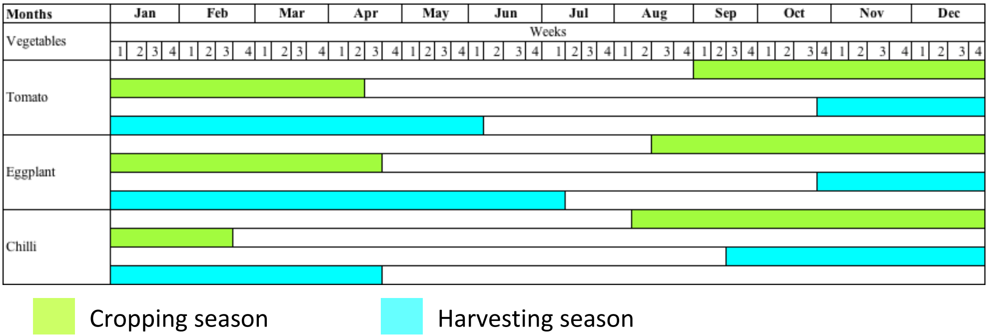


Figure S3.1 *Cropping calendar of vegetables.*

Extraction and clean-up methodology

20g of each vegetable sample was made into a slurry using a mortar and pestle. Matrix extracts were based on QuEChERS (Quick, Easy, Cheap, Effective, Rugged and Safe) method (Anastassiades and Lehotay, 2003), according to which, 5g of a homogenised sample was extracted with 10mL acetonitrile containing 1% acetic acid in a 50 mL tube. The tubes were shaken in a mechanical shaker (end-over-end) for 30 min. Next, a salt mixture consisting of 1g sodium acetate and 4g magnesium sulphate were added to each tube and immediately vortexed for 30 seconds to induce phase separation and partitioning. The tubes were then centrifuged at 3500 rpm for 10 minutes and resulted in the formation of a clear liquid-liquid partitioning layer. The extract at the top layer was transferred into a 12mL tube for storage. For LC analysis, 250µL crude extract and 250µL water were pipetted into a vial with an integrated filter. The filter cap was placed onto each vial and the vials were vortexed. The cap was pushed through the liquid in the vial and the liquid was analysed using LC-MS/MS. For GC analysis, the extract was cleaned using dispersive SPE by pipetting 25µL PCB 198 (internal standard), 250µL extract and 250µL ACN into an eppendorf tube containing 50 mg primary secondary amine (PSA) and 150 mg $MgSO_4$. The dispersive SPE with PSA removes many polar compounds such as lipids and chlorophyll in vegetable extracts that might help to get rid of peak interferences (Meimaridou et al., 2013). After vortexing for 30 seconds and centrifuging for 5 minutes, 150µL of the upper layer extract was pipetted into a GC-vial containing an insert and then analysed using GC-MS/MS (details of chemicals and reagents and tools and equipment are provided in Table S3.3 and Table S3.4 respectively).

***Table S3.3** Chemicals and reagents.*

S/N	Chemicals and reagents, purity (%)	Remarks
1	Pure water	Milli-Q© installation and with a minimum resistance of 18MΩ^{-cm} (Millipore Burlington, MA, USA)
2	Acetonitrile ULC-MS	UN 1648, Art. nr. 801022802 (Actu-All Chemicals b.v., Oss, The Netherlands)
3	Acetic acid (HAc), 96%	EMSURE 1.00062.1000 (Merck KGaA, Darmstadt, Germany)
4	Magnesium sulphate ($MgSO_4$), 98.9%	291184P, GPR RECTAPUR (VWR International bvba, Leuven, Belgium)
	Sodium acetate ($C_2H_3NaO_2$)	EMSURE 1.06268.1000 (Merck KGaA, Darmstadt, Germany)
5	DisQuE^{TM} extraction 2ml tube containing 150 $MgSO_4$ and 50mg PSA	186004572 (Waters, Ireland)
6	^{13}C-Caffeine, 99%	588598 (Sigma-Aldrich, Zwijndrecht, The Netherlands)
7	PCB 198	LGC Standards, Wesel, Germany
8	Formic acid, > 96%	251364 (Sigma-Aldrich, Zwijndrecht, The Netherlands)
9	Methanol, Ultra LC-MS	UN 1230, Art. nr. 813013802 (Actu-All Chemicals b.v., Oss, The Netherlands)
10	Ammonium formate, >99.99%	516961 (Sigma-Aldrich, Zwijndrecht, The Netherlands)
11	Reference standards	Sigma-Aldrich (Zwijndrecht, Netherlands) & LGC Standards (Wesel, Germany)

***Table S3.4** Tools and equipment.*

S/N	Equipment	Remarks
1	Centrifuge (50 mL PP tubes)	SN 42251949, Thermo Electron LED GmbH, Langenselbold, Germany
2	Centrifuge (eppendorf epps)	SN 41693362, Thermo Electron LED GmbH, Langenselbold, Germany
3	Head over head shaker	Reax 2, Heidolph Instruments, Schwabach, Germany
4	LC-MS/MS system	A Waters TQS MS linked to a Waters Acquity UPLC system (Waters, Millford, MA, USA)
5	UPLC column	Waters Acquity HSS T3-C18 column (2.1 X 100 mm, 1.7 µM particles); Waters part no. 186003539
6	GC-MS/MS system	Agilent 7890B GC coupled to a Agilent 7010B MS system (Agilent, Santa Clara, CA, USA)
7	GC column	Restek ClPesticides (30m x 0.25 mm, 25 µM film thickness) (Restek , Bellefonte, PA, USA)

Pesticide analytics

Pesticides were analysed using LC-MS/MS (parameters see Table S3.5) and GC-MS/MS (Table S3.6). GC-MS/MS was used for the more a-polar compounds that were difficult to analyse by LC-MS/MS. In the LC-MS/MS measurement positive ionisation was used, except for 3,5,6-trichloro-2-pyridinol which was analysed using negative mode.
LC flowrate was 0.4 ml/min, injection volume was 5 µL. Eluent A consisted of water, eluent B of MeOH:H_2O 95:5, both eluents contained 5 mM ammonium formate and 0.1 % formic acid. A gradient was used, starting at 100% A, after 1 min. %B was increased to 45% in 1.5 min., then in 6 minutes to 100%B, which was held for 2.5 minutes. In 0.5 minutes the gradient was returned to 100% A and the column was equilibrated for 2 min. before the next injection.

The GC injector was used in PTV solvent vent mode, injection volume was 5 µL. Temperature program of the GC oven: start 60°C, hold for 2 min, then with 20°C/min to 150°C, with 10 °C/min to 280°C and with 25°C/min to 320°C which was held for 5 min.

Table S3.5 *Compound dependent LC-MS/MS parameters.*

Compounds	Quantification transition	Qualifier transition	Dwell (sec)	Cone Volt	RT
3,5,6-trichloro-2-pyridinol	196>35/ 15	198>37/ 15	0.1	30	4.3
Chlorpyrifos	350>198/ 17	352>200/ 17	0.05	20	10.56
Dichlorvos	220.90 > 108.90/ 18	220.90 > 126.90/ 15	0.1	25	5.78
Dimethoate	230>125/ 20	230>199/ 10	0.025	22	4.36
Omethoate	214>155/ 17	214>183/ 10	0.025	22	3.05
Profenofos	373>96.7/ 33	373>302.9/ 18	0.05	30	9.86
Quinalphos	299>147/ 20	299>163/ 20	0.05	25	8.78
Triazophos	313.9>118.9/ 35	313.9>162/ 20	0.025	25	8.16
Chlorantraniliprole	482>283.9/ 10	484>285.9/ 10	0.025	20	7.38
Imidacloprid	256>175/ 20	256>209/ 20	0.025	30	3.99
Carbendazim	192>131.9/ 32	192>159.9/ 15	0.025	25	3.76
Metalaxyl	280>192/ 17	280>220/ 15	0.025	30	7.07
N-(2,6-dimethylphenyl)-N-(methoxyacetyl)alanine	266>160/ 22	266>220/ 10	0.025	40	6.43
Emamectin	886.50>126/ 40	886.5>158/ 37	0.05	40	10.24

Table S3.6 *Compound dependent GC-MS/MS parameters, top line was used for quantification for each compound.*

Compounds	Precursor Ion	Product Ion	RT	CE
o,p'-DDT	237	165	16.77	28
o,p'-DDT	235	165	16.77	28
p,p'- DDD (TDE)	165	17.07	28	28
p,p'- DDD (TDE)	165	17.07	28	28
p,p'-DDE	248	176	16.01	34
p,p'-DDE	246	176	16.01	34
p,p'-DDT	237	165	17.58	28
p,p'-DDT	235	165	17.58	28
Phorate	260	231	12.02	15
Phorate	260	75	12.02	2
α-Endosulfan	206	16.06	16	16
α-Endosulfan	160	16.06	8	8
α-HCH	183	12.07	6	6
α-HCH	145	12.07	16	16
β-Endosulfan	206	17.31	16	16
β-Endosulfan	160	17.31	8	8
γ HCH	183	12.71	6	6
γ HCH	145	12.71	16	16

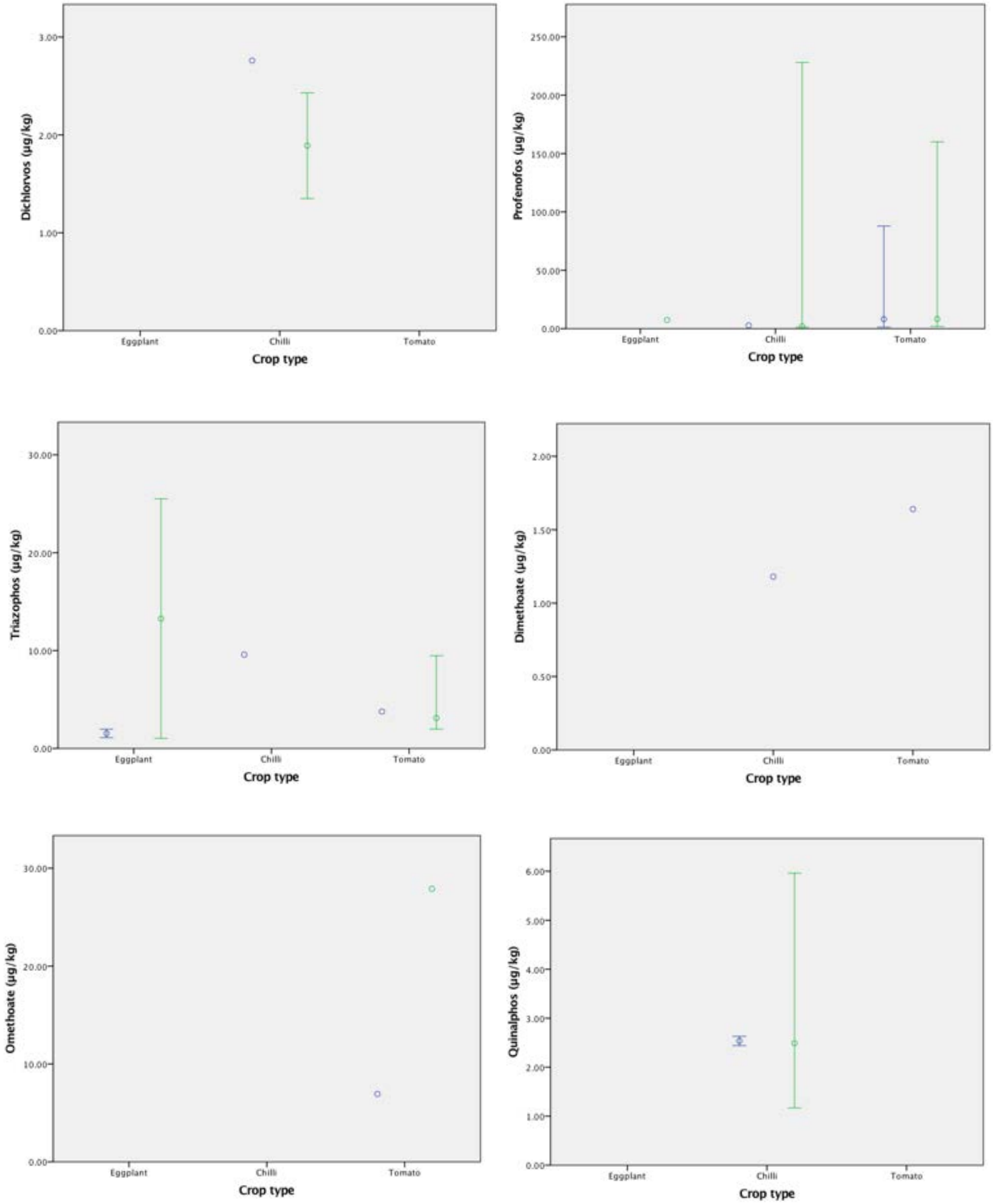
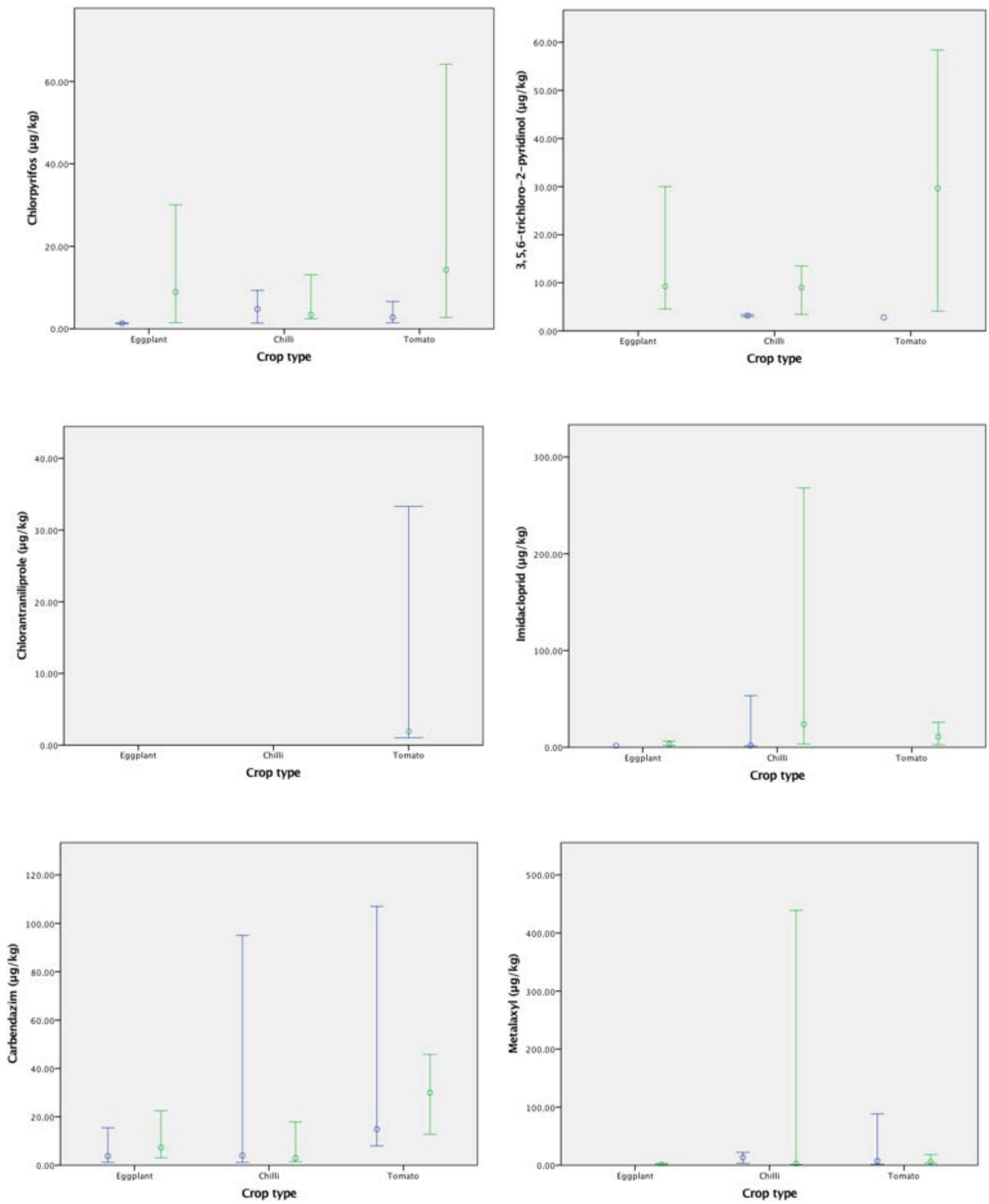


Figure S3.2 (continued on next page)



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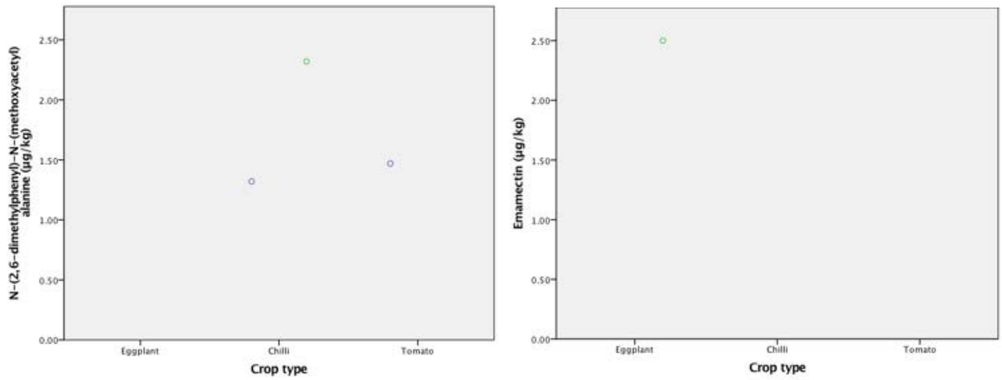


***Figure S3.2** The concentration (minimum, median and maximum) of pesticides and metabolites in vegetables with respect to different farming groups (error bars: 95% CI). Only measurements ≥LOD were considered in the graph.*

4. Concentration and distribution of pesticide residues in soil: Non-dietary human health risk assessment

Soil contamination by pesticide residues is a primary concern because of the high soil persistence of pesticides and their toxicity to humans. We investigated pesticide concentration and distribution at 3 soil depths in 147 soil samples from agricultural land and assessed potential health risks due to non-dietary human exposure to pesticides in Nepal. About sixty percent of the soil samples had pesticides (25% of the soil samples had single residue, 35% of the soil samples had mixtures of 2 or more residues) in 39 different pesticide combinations. Pesticide residues were found more frequently in topsoil. Overall, the concentration of pesticides ranged from 1.0 μg kg-1 to 251 μg kg-1, with a mean of 16 μg kg-1. The concentration of the primary group, organophosphates (OPs), ranged from 1.23 μg kg-1 to 239 μg kg-1, with a mean of 23 μg kg-1. Chlorpyrifos and 3,5,6-trichloro-2-pyridinol (TCP) were the predominant contaminants in soils. The ionic ratio of DDT and its degradation products suggested a continuing use of DDT in the area. Human health risk assessment of the observed pesticides in soil suggested negligible cancer risks and negligible non-cancer risks based on ingestion as the primary route of exposure. The predicted environmental concentrations (PECs) of pesticides were higher than the values found in the guidance for soil contamination used internationally. Low concentrations of residues in the soils from agricultural farms practicing integrated pest management (IPM) suggest that this farming system could reduce soil pollution in Nepal.

Based on:

Bhandari, G., Atreya, K., Scheepers, P.T.J., Geissen, V., 2020. Concentration and distribution of pesticide residues in soil: Non-dietary human health risk assessment. Chemosphere 253, https://doi.org/10.1016/j.chemosphere.2020.126594

4.1 Introduction

Chemical pesticides have been used in agriculture for decades in the effort to reduce crop loss and to meet the world's growing food demands. About one-third of agricultural commodities are produced using chemical pesticides (Zhang et al., 2011). If farmers worldwide all of a sudden stopped using pesticides, crop losses to pests of fruits, veggies and grains would increase by 78%, 54% and 32%, respectively (Cai, 2008). Global production of pesticides increased by 11% annually, from 0.2 million tons in the 1950s to >5 million tons by 2000 (Carvalho, 2017). In 2012, on average, around 3.8 million tons of chemical pesticides were applied to agricultural land (FAO, 2020). This amounts to a value of >40 billion US dollars (Pimentel, 2009). As a consequence of pesticide use, over two million people, mainly residing in developing nations, are at an elevated health risks (Hicks, 2019). The rate of pesticide use varies across the globe, even within the same region. For instance, the average rate of pesticide use is observed highest in Asia, where 6.5 to 60 kg ha^{-1} insecticides are used (Carvalho, 2017). However, in the regions of Nepal, pesticide use is relatively low at <400 g ha^{-1} (Sharma, 2015). One hundred and seventeen active ingredients of pesticides were registered and approved in Nepal, with annual imports of 410 tons of active ingredients consisting of 34% insecticides, 40% fungicides, 25% herbicides, 1.6% rodenticides, 0.03% biopesticides and 0.02% other botanical pesticides (PRMD, 2015).

Despite the benefits of using pesticides to improve food safety, intensive and widespread use of chemical pesticides can increase soil pollution, thereby increases environmental and health risks. Soil properties play a crucial role in the fate, behavior and dispersion of chemical pesticides (Lewis et al., 2016b) and has become the repository of pesticides used in agriculture. It adsorbs most pesticides and degradation products, which might negatively affect different food webs. Pesticides can ultimately reach to humans (Zhang et al., 2006), and are thereby subject to bio-amplification (Alamdar et al., 2014). Pesticides get washed away from soils by running water and thus find their way into water sources. Pesticides can also be emitted into the atmosphere through volatilization (Sweetman et al., 2005), which adversely affect air (Bidleman and Leone, 2004) and surface water quality (Mekonen et al., 2016). Runoff and flooding are two major pathways of movement of pesticides that may lead to unintentional diffusion and non-target contamination (Wong et al., 2017) that can ultimately negatively affect human health. The concentration of pesticides tend to increase with soil depth (Zhang et al., 2006) and thus, the concentrations found in the bottom soil layer may increase underground water pollution (Sankararamakrishnan et al., 2005). Different levels of pesticides were reported across the globe and have threatened humans and the environment (Houbraken et al., 2017; Sun et al., 2016). Along with analytical approaches, such as GC-MS and LC-MS, concentrations of pesticides are often estimated depending on their predicted environmental concentrations (PECs).

Farmers are exposed with pesticide-contaminated soils via different pathways such as dermal contact, direct ingestion, and inhalation (Li, 2018). The increasing probability of humans to develop cancer and non-cancer diseases as a result of such exposure was calculated by adopting USEPA standard models. Indices such as the hazard quotient (HQ) and the hazard index (HI) are used globally for health risk assessment and are mainly based on the concentration of pesticides (Hu et al., 2014; Pan et al., 2018; Sun et al., 2016). Likewise, risk of pesticides is often estimated based on their predicted environmental concentrations (PECs) (Silva et al., 2019; Vasickova et al., 2019), however, studies on PEC in the risk assessment of pesticide use are limited in literature. Further, monitoring pesticide residues in soils and examining their potential health risks is also scanty in Nepal. The application of hazardous insecticides and fungicides is increasing in the areas of Nepal where vegetables are cultivated for markets (Atreya et al., 2011; Bhandari et al., 2018). More than 80% of the pesticides applied in Nepal are used in vegetable farming (Adhikari, 2017). Vegetable farming is becoming increasingly more popular and is a good income option for farmers in Nepal. Adolescents and adults who work in the vegetable fields can be exposed to pesticides via different pathways such as non-dietary ingestion, dermal exposure and soil particle inhalation. In other parts of the globe, there is a growing evidences of human health risk due to pesticide use in agricultural (Ritz and Yu, 2000; Samsel and Seneff, 2013; Schreinemachers, 2003; Shelton et al., 2014). The dietary risks from pesticide ingestion is at the higher end, and thus considered unacceptable (Bhandari et al., 2019). In Nepal, studies have observed an emergence of higher cancer and non-cancer risks associated with pesticide use (PPDB, 2019; Yadav et al., 2016). Hazardous pesticides that are banned for use in the EU (pesticides use status in bold, Table S4.1, Supplementary information) are still used in Nepal. In addition, a recent study (Bhandari et al., 2018) showed that persistent and toxic pesticides are frequently applied to vegetable fields. This combined with the fact that farmers in Nepal are less likely to follow safe work practices and do not have access to personal protective equipment, resulting the pesticides exposure risks even larger. This study thus conducted to analyze pesticide residues in the soil of vegetable fields, and to estimate potential health risk for humans due to non-dietary exposure to pesticides in soil.

4.2 Materials and methods

Supplementary information presents information in support of the materials and methods.

4.2.1 Study area

Gaidahawa Rural Municipality (GRM) (27^o 35.429' N and 83^o 19.215' E) of Nepal was selected for the study (Figure 4.1). The area and population of the municipality is 96.79 sq. km and 47,565, respectively. About eighty-one percent (approx. 7900 ha) of the land is agricultural. The mean annual rainfall is about 1400 mm. The land is flat and the soil consists mainly of silt, clay and sand. The temperature may reach 42.4^{o}C and 8.7^{o}C in summer and winter, respectively (GRM, 2018).

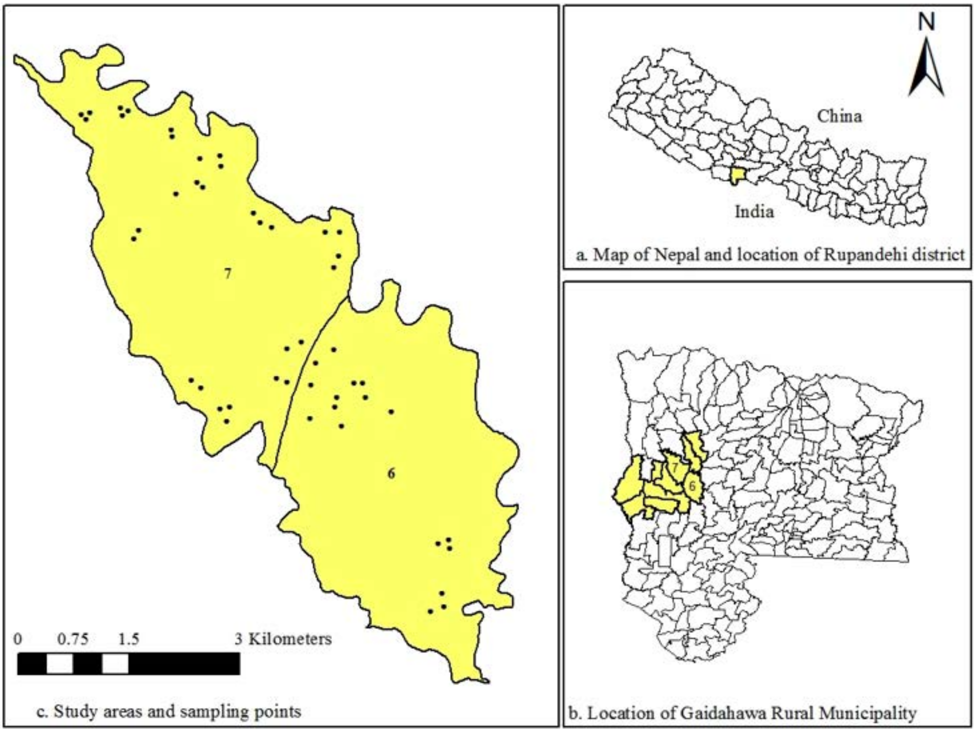


Figure 4.1 *Map of the study area.*

4.2.2 Farming practice and selection of pesticides

Bhandari et al. (2018) reported that farmers in the study area practice commercial vegetable farming. They grow many types of vegetables such as eggplant, chilli pepper, coriander, tomato, bean, onion, sponge gourd, pumpkin, broccoli, bitter gourd, fenugreek, cauliflower, spinach, okra, radish, cucumber, cabbage, fennel, bottle gourd, and pea. Application rate of pesticides differs by crops. A few farmers practice integrated pest management (IPM) techniques for controlling pests. IPM techniques included were the use of insect traps, animal dung and urine, ash, alcohol, and tobacco. The existing farming system is heavily dependent on the application of chemical pesticides at significantly higher than recommended doses, however IPM fields were less likely to receive high amount of chemical pesticides. The frequency of applications is also higher than recommended, indicating poor agricultural practices. Farmers use thirty litre lever-operated Knapsack sprayers. Of all the pesticides used, the general trend in application rate (kg ha^{-1}) of top five pesticides was: mancozeb > dichlorvos > chlorpyrifos > profenofos > triazophos (Bhandari et al., 2018). Farmers even apply these pesticides as cocktails.

The present study accounted commonly used following pesticide groups: 7 organophosphates (OP), 1 anthranilic diamide (AD), 1 neonicotinoid (NND), 1 benzimidazole (BD), 1 phenylamide (PA), 1 micro-organism derived (MOD) and 2 unclassified degradation products (UDP). In addition to these compounds, one organophosphate and 8 organochlorines (OC), which are banned in the EU and Nepal due to their high soil persistence and toxicity (Table S4.1, Supplementary information) were also considered. Due to analytical limits, namely poor recoveries (< 70%) as well as logistic and financial limitations, some compounds were excluded.

4.2.3 The soil samples

At the time of soil sampling, farmers had not sprayed their fields with pesticides for 7 days. Soil samples were collected following the principals laid out in the EU guidelines (Theocharopoulos et al., 2001). The municipality consists of 9 wards, which is the smallest administrative unit of government. Each ward consists of a number of villages. The soil samples were collected from randomly selected villages in the 6th and 7th wards where most farmers were involved in vegetable farming following either IPM or intensive farming practices. The pesticide groups in the areas represented the use and pollution of pesticides in Nepal. Furthermore, the soil sampling areas were the same from where vegetable samples were selected for a study (Bhandari et al., 2019). The soil samples were taken from a total of 49 farmers' standing vegetable fields at 3 depths (0-5 cm, 15-20 cm and 35-40 cm).

There were 27 samples from eggplant fields, 36 samples from chilli fields and 84 samples from tomato fields, altogether 147 soil samples were collected during the vegetable growing season in 2017. An auger was used to collect soil samples. Ten samples from each sampling field were collected and mixed thoroughly after foreign materials such as stones, leaves, pebbles, gravel and roots were removed. A composite and representative sample was then collected by quartering and compartmentalization. Furthermore, a twenty gram of sample from each sampling field was kept in a separate plastic bag with a zipper and labelled with a unique sample identity. Sterile gloves were used to prevent contamination during the whole process. Final samples were kept in the refrigerator at -20 ^{o}C until complete analysis. Collected soil samples were grouped and labelled one of two ways: i) fields where intensive/ conventional farming was practiced (n = 114) and ii) fields where IPM was practiced (n = 33).

4.2.4 Chemical determination and quality control

Soil samples, labelled as clean by Wageningen Food Safety Research and which did not contain any of the 23 tested pesticides examined (list of pesticides including LODs, see Table 4.1) were considered as blanks. The analytical determination, chemicals and reagents, instrumentation, and quality assurance of the method are described in Bhandari et al. (2019). The chemical analysis and the quality control were performed as per the European Commission guidelines (SANTE/11813/2017) (EC, 2017). In the case where different LODs of the pesticide were observed, the highest LOD of the pesticide was used as the reporting limit and was considered as the final LOD of the pesticide. The calibration curves showed linearity within the range of 70-120%, with a regression coefficient (R^2) > 0.99. Relative standard deviations were <10%, indicating reliability and accuracy of the method.

4.2.5 Human health risk assessment

The selected pesticides have been found to induce either cancer or non-cancer diseases (PPDB, 2019) (Table S4.2, Supplementary information). DDT was categorized as a probable carcinogenic for humans by the International Agency for Research on Cancer (IARC). In 2015, the IARC found positive associations between exposure to DDT and diseases such as non-Hodgkin lymphoma, testicular cancer, and liver cancer (IARC, 2015). In order to assess health risks posed to humans, we adopted USEPA models that have been proven successful and adopted worldwide (Liu et al., 2013b). The threshold values of the models and the concentrations of pesticides found in our soils were used to assess human health risks (for the threshold values used in the risk assessment, see Table S4.3, S4.4 and S4.5 in Supplementary information, page 5).

To facilitate the process, the risk assessment process for humans is divided into 3 steps: i) hazard identification (HaI), ii) exposure assessment (ExA), and iii) risk characterization (RiC). HaI involves the identification of pesticides in the study area that can have health risks to humans. The persistence and toxicity of pesticides that have risks were identified based on PPDB (2019). ExA was done for pesticides that posed potential health risks. Cancer and non-cancer risks from pesticides exposure were estimated following USEPA models and hazard quotient (HQ) and hazard index (HI) indices, respectively. The relationship between pesticides concentration and the resulting incidence of impacts was based on mathematical models to determine risks to humans via different exposure pathways such as ingestion, inhalation and dermal contact. RiC incorporates information derived from HaI and ExA. It involves the estimation of health risk due to single and multiple pesticides. Total cancer risk (TCR), HQ and HI were used to characterize risks to human health.

4.2.5.1 Assessment of cancer risk (CR) for OCs

Exposure to DDTs is potentially linked with CR (Band et al., 2011; Wong et al., 2015). Considering the incidental ingestion, inhalation and dermal contact with contaminated soil, (USEPA, 2018), the chronic (average) daily non-dietary intake (CDI, mg kg^{-1} day^{-1}) of compounds (pp'-DDT, pp'-DDE and pp'-DDD) in adolescents and adults can be estimated using the following equations.

$$CDI_{ing}=\frac{C_{soil}\times EF\times ED\times IR_{ing}}{AT\times BW}\times CF \quad (4.1)$$

$$CDI_{der}=\frac{C_{soil}\times SA\times SAF\times ABS\times EF\times ED}{AT\times BW}\times CF \quad (4.2)$$

$$CDI_{inh}=\frac{C_{soil}\times EF\times ED\times IR_{inh}}{PEF\times AT\times BW} \quad (4.3)$$

where CDI_{ing}, CDI_{der} and CDI_{inh} are the average daily doses via ingestion, dermal contact and inhalation (mg kg^{-1} day^{-1}), respectively.

C_{soil} (mg kg^{-1}) = concentration of pesticides in soil

The details of other parameters/exposure factors such as IR_{ing}, EF, ED, BW, CF, AT, SA, SAF, ABS, IR_{inh}, and PEF are listed in Table S4.3. The incremental lifetime CR denotes the increasing possibility of humans to get cancer during their lifespan via exposure to a carcinogenic compound. In our study, the CR in adolescents and adults over their lifetime exposure to DDT and its degradation products was calculated following USEPA (2001) and Yadav et al. (2016).

$$\mathrm{CR} = \mathrm{CDI} \times \mathrm{SF} \quad (4.4)$$

where, SF = carcinogenicity slope factor (details in Table S4.4)
CDI = estimated average chronic daily non-dietary intake (Table S4.6)
If multiple carcinogenic compounds are present, the total CR (TCR) from all of the compounds and possible routes is calculated following Yadav et al. (2016).

$$\mathrm{TCR} = \sum_{k=1}^{n} \mathrm{CRi} \quad (4.5)$$

where, i = different exposure pathways
In general, TCR values between $1x10^{-6}$ and $1x10^{-4}$ are considered to be acceptable, while those exceeding $1x10^{-4}$ are considered to constitute a lifetime carcinogenic risk to humans. A risk factor $<1x10^{-6}$ is regarded as negligible or no risk (USEPA, 1989).

4.2.5.2 Assessment of non-cancer risk (NCR)
The NCR was calculated following USEPA (2019), which was also adopted in a past study (Pan et al., 2018). The NCR for the pesticides of interest for a specific exposure route can be expressed as Hazard Quotient (HQ). HQ of a pesticide is the ratio of CDI, and RfD (reference dose) of the pesticide.

$$\mathrm{HQ} = \frac{\mathrm{CDI}}{\mathrm{RfD}} \quad (4.6)$$

The total NCR of pesticides belonging to OPs via two primary routes such as soil ingestion and dermal contact can be denoted as HI, which was estimated by following Equation 4.7.

$$\mathrm{HI} = \sum_{k=1}^{n} \mathrm{HQi} \quad (4.7)$$

where, HQ_i = hazard quotient of exposure pathway i
RfD (mg kg^{-1} day^{-1}) = daily maximum permissible concentration of OPs, including the reference doses for exposures such as ingestion (RfD_{ing}) and dermal contact (RfD_{der}). The RfD_{ing} = RfD and RfD_{der} = RfD x ABS_{GI}. ABS_{GI} is the gastrointestinal absorption factor (dimensionless). Pesticides belonging to OPs have their common mode of action (Table S4.1), therefore HI was estimated for only the OPs.

The details of parameters such as RfD and ABS_{GI} used in NCR assessment are listed in Table S4.5. HQ or HI greater than one shows potential NCR, while HQ or HI ≤ 1 means negligible or no risk. Our study could not estimate the potential NCR via inhalation because reference concentration (RfC) values for the pesticides of interest were not available in the PPDB (2019).

4.2.6 Predicted environmental concentration (PEC)

PEC is an indicator of the expected pesticide concentrations in soil, taking into account the default values (EFSA et al., 2017). The PEC was estimated with the default values (otherwise stated) using the Equations 4.8 to 4.12. For multiple applications of chemical pesticides, the maximum time-weighted average (TWA) concentrations for exposure days of 1, 2, 4, 7, 14, 28, 50, and 100 were estimated using a moving time-frame (MTF) Excel spreadsheet. For a given exposure period, the spreadsheet calculates the TWA concentrations for period starting times ranging from day of first application to day of last application (MTF), and scans for the highest value (EC, 2004).

$$PEC_{s,ini} = \frac{A(1-f_{itn})}{100\ DEPTH_{soil} bd_{soil}} \quad (4.8)$$

$$PEC_{s,act} = PEC_{s,ini} e^{-k_{soil}t} \quad (4.9)$$

$$PEC_{s,twa} = PEC_{s,ini} \frac{(1-e^{-k_{soil}t})}{k_{soil}t} \quad (4.10)$$

$$PCEC_{s,ini,n} = \frac{PEC_{s,ini,1}(1-e^{-nk_{soil}i})}{(1-e^{-k_{soil}i})} \quad (4.11)$$

$$PEC_{s,act,n} = PEC_{s,int,n} e^{-k_{soil}t} \quad (4.12)$$

where, A = application rate (g/ha); f_{int} = fraction intercepted by crop cover; $DEPTH_{soil}$ = depth of soil (cm); bd_{soil} = bulk density of soil (g cm^{-3});
$PEC_{s,ini,1}$ = initial PECs after one application; n = number of applications; i = application interval (d); k_{soil} = degradation rate in soil (d^{-1}) = ln(2)/half-life

PECs of pesticides are estimated for the different farms at three different time points (after pesticide application) for each pesticide prediction: the initial PECs (immediately), the short-term PECs (1-4 days) and the long-term PECs (7-100 days). Since the farmers in our study hadn't applied pesticides for a week prior to our first sample measurement, predicted concentrations ($PEC_{s,act,7\ days\ after\ pesticide\ application}$) of pesticides would be suitable for making possible comparisons with their measured environmental concentrations (MECs). Likewise, since farmers followed poor agricultural practices, we used the initial PECs of pesticides in order to compare measurements with the international guidelines of soil quality standard. All the tested pesticides had a 90% degradation time under a year, thus the background concentrations and the PECs that accumulated were not considered in this study. Human health risk (HR) was evaluated by comparing the PECs of the pesticides in soils with international guidelines of soil quality such as pesticide soil regulatory guidance values (PSRGVs), the maximum concentrations of pesticides present in soil without hampering the environmental balance (Li and Jennings, 2017) and Chinese Soil Quality Standard (GB 15618-2018) (MoEP, 2018). Past studies (Qu et al., 2015; Wang, 2007) also followed similar methods for the evaluation of the health risk.

4.2.7 Statistical analysis

The data analysis was performed using Canoco 5 and SPSS 23. To avoid underestimating soil concentrations of pesticides, only pesticide residue concentrations ≥ LODs were considered in data analysis. Concentrations below the LOD were not included in the analysis (Sun et al., 2016). The normality of the data was tested by the Kolmogorov–Smirnov test. In the cases of normal distribution, a one-way ANOVA was used to compare the number of pesticide residues and the total pesticide concentrations in soil between conventional and IPM farming practices, vegetable farms (eggplant, chilli and tomato), and three depths of soil. In case of significant effects at the 95% confidence level ($p < 0.05$), the Bonferroni post hoc test was conducted. Principal component analysis (PCA) and Pearson correlation coefficients were used to study relationships between the pesticide concentrations and the pesticide properties.

4.3 Results

4.3.1 Number of pesticides in soil

Pesticide residues analysis in soils revealed the presence of a variety of pesticide combinations. Thirty-nine pesticide combinations were detected in soils. One single pesticide residue was detected in 25% of the soil samples, while multiple residues were present in 35% of the soil samples (Figure 4.2A). The number of residues varied significantly with soil depths, vegetable fields, and farming practices (Figure 4.2B). Pesticide residues were found less frequently in the depth 35-40 cm and more frequently in the top soil (0-5 cm) (p=0.001). A large number of pesticide residues (up to 7 residues) was detected in 2% of the tested top soils.

The number of pesticide residues detected in soils from eggplant fields was significantly lower than tomato fields (p=0.025; Figure 4.2B). Seventy-three percent of soil samples from tomato fields and half of the soil samples from chilli fields contained detectable pesticide residues.

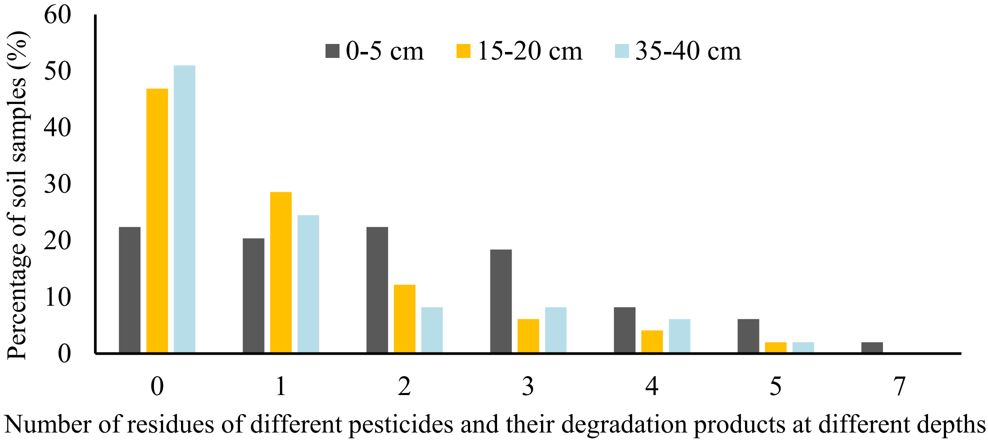


Figure 4.2A *Number of residues of different pesticides and their degradation products at different soil depths and the frequency (in percentage of soil samples).*

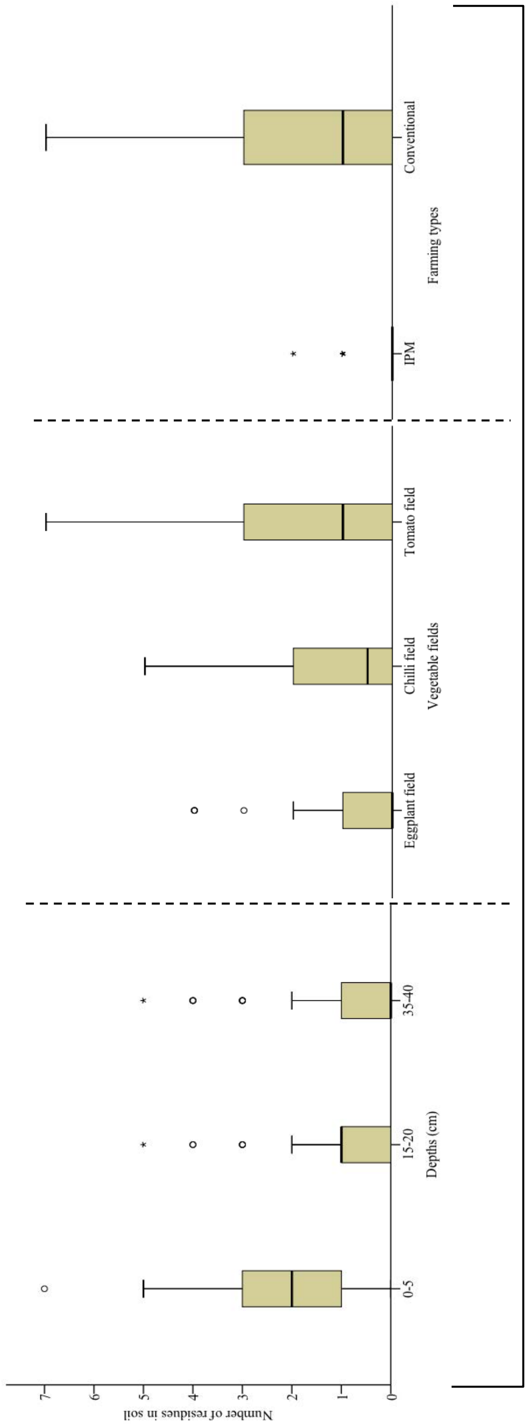


Figure 4.2B *Box plots for comparison of mean number of residues at different soil depths detected in different vegetable fields of two farming types and the p-values.*

Soils from IPM fields had a significantly smaller number of observed pesticide residues >LOD than the soils from conventional fields ($p < 0.01$; Figure 4.2B and LODs in Table 4.1). Only fifteen percent of the soil samples from the IPM fields contained detectable pesticide residues. On the other hand, about seventy-three percent of soil samples from the conventional fields contained detectable residues of pesticides.

***Table 4.1** Comparing mean concentrations of pesticides detected in soils from different farming systems during the growing season (μg kg^{-1}). The concentrations <LODs (na) were excluded when calculating the average values. Dichlorvos, dimethoate, omethoate, phorate, α-β-endosulfan and α-γ-HCH had concentrations < LOD (i.e. <1 μg kg^{-1}) and do not appear in the table. Abbreviations of pesticides are shown in parenthesis. NA = not applicable.*

Chemical group	Pesticides and degradation products	Type of farming						LODs	p-value
		IPM (N=33)			Conventional (N=114)				
		NPS (%)	Min-Max	Mean (SD)	NPS (%)	Min-Max	Mean (SD)		
UNC	3,5,6-trichloro-2-pyridinol^m (TCP)	NA	NA	NA	36(32)	2.63-57.4	10.4(9.98)	2.5	NA
OPs	Chlorpyrifos (CHLPY)	NA	NA	NA	11(10)	10.5-177	40.8(49.35)	10	NA
	Profenofos	NA	NA	NA	4 (4)	1.09-3.37	1.75(1.09)	1	NA
	Quinalphos	NA	NA	NA	3(3)	1.06-2.47	1.59(0.77)	1	NA
	Triazophos (TRIZO)	NA	NA	NA	6(5)	1.05-8.12	3.28(2.73)	1	NA
OCs	o, p'-DDT!	NA	NA	NA	3(3)	1.60-4.28	2.85(1.35)	1	NA
	p, p'-DDD!	NA	NA	NA	3(3)	1.95-11.1	7.11(4.69)	1	NA
	p, p'-DDE!	NA	NA	NA	18(16)	1-13.9	3.31(3.16)	1	NA
	p, p'-DDT!	NA	NA	NA	10(9)	1.05-78.4	12.1(24.5)	1	NA
AD	Chlorantraniliprole (CHLNITR)	NA	NA	NA	35(31)	1.08-14.2	3.17(2.62)	1	NA
NND	Imidacloprid (IMDA)	2(6)	1.02-1.17	1.10 (0.11)	26 (23)	1.16-31.6	5.52(6.52)	1	0.354
BD	Carbendazim	NA	NA	NA	18(16)	1.03-6.45	2.12(1.54)	1	NA
PA	Metalaxyl (MA)	3(9)	1.22-3.80	2.19 (1.41)	12(11)	1.12-8.97	3.25(2.4)	1	0.482
UNC	N-(2,6-dimethylphenyl)-N-(methoxyacetyl)alanine^m (MMB)	1(3)	NA	NA	2(2)	1.11-1.56	1.34(0.32)	1	0.207
MOD	Emamectin	NA	NA	NA	1(1)	NA	NA	1	NA

Notation.

Chemical group: UNC = Unclassified; OPs = organophosphates; OCs = organochlorines; AD = Anthranilic diamide; NND = Neonicotinoid; BD = Benzimidazole; PA = Phenylamide and MOD = Micro-organism derived.

NPS = Number of positive samples; m = degradation product; ! = banned pesticides.

The concentrations of residues of dichlorvos, dimethoate, omethoate, phorate, α-β-endosulfan and α-γ-HCH were < LOD and do not appear in Figure 4.3A.

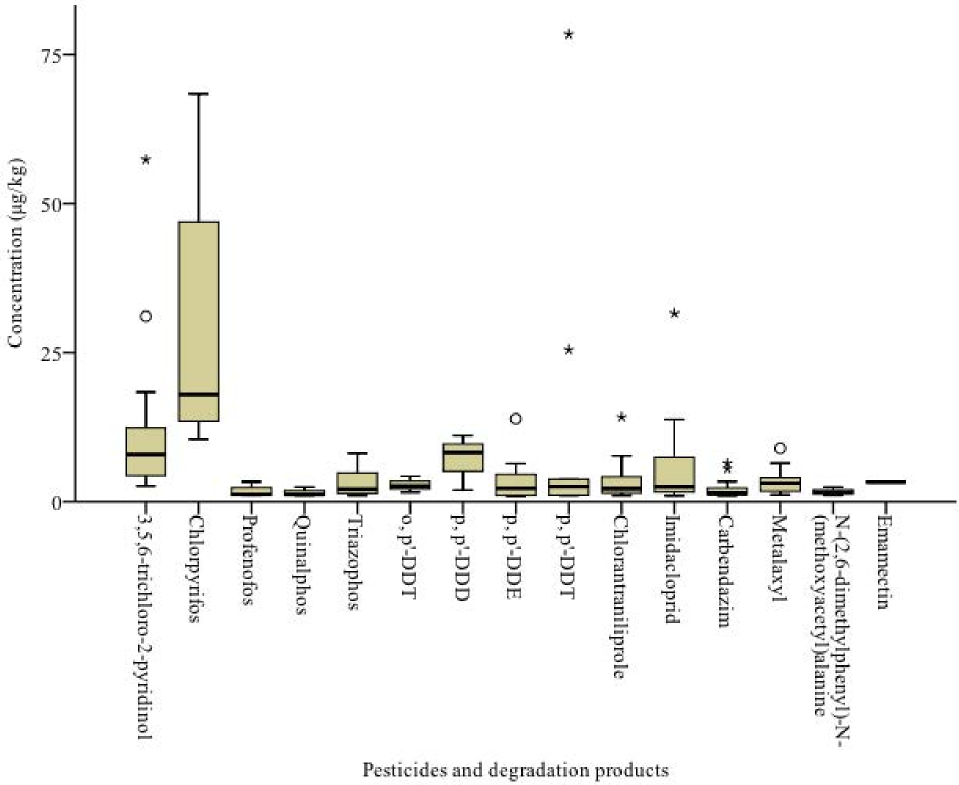


Figure 4.3A *Distribution of pesticide concentrations and pesticide degradation products in soils.*

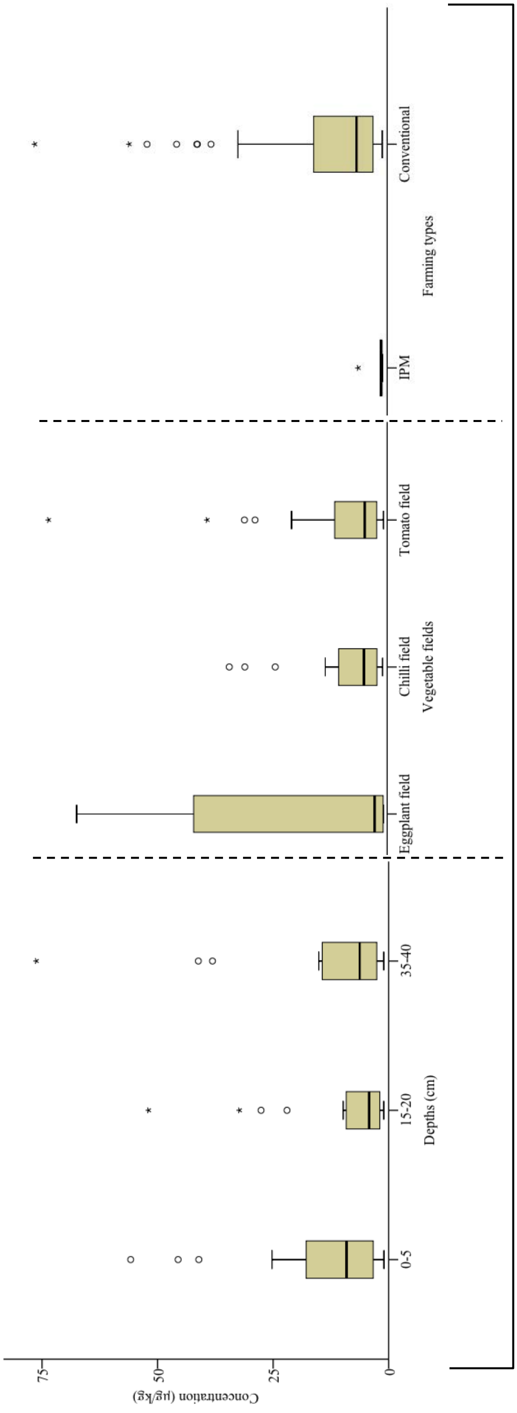


Figure 4.3B *Box plots for comparison of mean concentration of pesticide residues at different soil depths detected in different vegetable fields of two farming types and the p-values.*

4.3.2 Types of pesticide residues and their combinations

Fifteen different pesticide residues (approximately 65% of the tested pesticides) were observed in the soils (Table 4.1). Residues of dichlorvos, dimethoate, omethoate, phorate, α-γ-HCH and α-β-endosulfan were below LOD (< 1 μg kg^{-1}). The six most common pesticide mixtures (for abbreviations of pesticides, see Table 4.1) detected in soils were:

(i) CHLNITR + IMDA
(ii) CHLNITR + CHLPY + TCP + TRIZO
(iii) MA + TCP
(iv) CHLNITR + p,p'-DDE + p,p'-DDT
(v) IMDA + p,p'-DDE and
(vi) o,p'-p,p'-DDTs + p,p'-DDE + p,p'-DDD

Chlorantraniliprole and imidacloprid residues were the most prominent with 11% and 5% of the total soil samples with detectable residue levels, respectively, and found frequently at the soil depth 15-20 cm. The most common pesticide, CHLNITR, was found in 17% of the soil samples from tomato fields. In IPM fields, most soil samples (85%) were residues free however, residues of MA, IMDA, and MA + MMB were detected.

Of all the detected pesticides in our samples, about 60% of the pesticides were non-persistent or moderately persistent compounds. Persistent and very persistent compounds represented about 13% and 27% of the detected pesticides, respectively. Four of the compounds such as o,p'-p,p'-DDTs; p,p'-DDE and p,p'-DDD, detected in soils were degradation products of active substances that are currently banned in Nepal. Overall, eight percent of the soils contained quantifiable residues of DDT and its degradation products.

4.3.3 Hazard identification

Our study found 4 organophosphates (chlorpyrifos, profenofos, quinalphos and triazophos), 4 organochlorines (o,p'-DDT, p,p'-DDT, p,p'-DDD and p,p'-DDE), 1 anthranilic diamide (chlorantraniliprole), 1 neonicotinoid (imidacloprid), 1 benzimidazole (carbendazim), 1 phenylamide (metalaxyl), 1 micro-organism derived (emamectin) and 2 unclassified degradation products [TCP and N-(2,6-dimethylphenyl)-N-(methoxyacetyl)alanine] in soil samples (Table 4.1). The mean concentration of pesticides in soil samples was 16.05 μg kg^{-1} with a range of 1.02-251.28 μg kg^{-1}. Total pesticide concentrations in soils differed according to the farming practices, vegetables cultivated, and soil depths as seen in Table 4.1 and Figure 4.3B. A significant correlation existed between total pesticide concentration and farming practices, vegetables cultivated, and soil depth ($p < 0.05$). The identified hazards are the most commonly detected pesticides in soils such as carbendazim, imidacloprid, chlorantraniliprole, p,p'-DDT, p,p'-DDE, metalaxyl, chlorpyrifos, and TCP (Table 4.1). Except chlorantraniliprole, concentrations of the other pesticides in soils showed relationship with each other, indicating positive or negative correlation (Table 4.2).

Table 4.2 *Correlations between the most common pesticides and degradation products detected in soils (positively correlated in bold font).*

Pesticides and degradation products	N	CARBE	IMDA	CHLNITR	p,p'-DDT	p,p'-DDE	MA	CHLPY	TCP
CARBE	18	1							
IMDA	28	-0.53	1						
CHLNITR	35	-0.05	0.42	1					
p,p'-DDT	10	na	-1.00**	0.20	1				
p,p'-DDE	18	**1.00****	0.07	0.04	0.32	1			
MA	15	-0.28	-0.97	0.91	na	na	1		
CHLPY	11	**0.99***	-1.00**	-0.95	na	na	na	1	
TCP	36	**0.95****	0.08	0.67	na	0.41	**0.72***	**0.89****	1

Notation.
CARBE = Carbendazim, IMDA = Imidacloprid, CHLNITR = Chlorantraniliprole, MA = Metalaxyl, CHLPY = Chlorpyrifos and TCP = 3,5,6-trichloro-2-pyridinol.
"*" and "**" represented significant correlation at the levels 0.05 and 0.01 (both 2-tailed), respectively.
"N" = Number of positive soil samples, "na" = Cannot be calculated because at least one of the variables is constant.

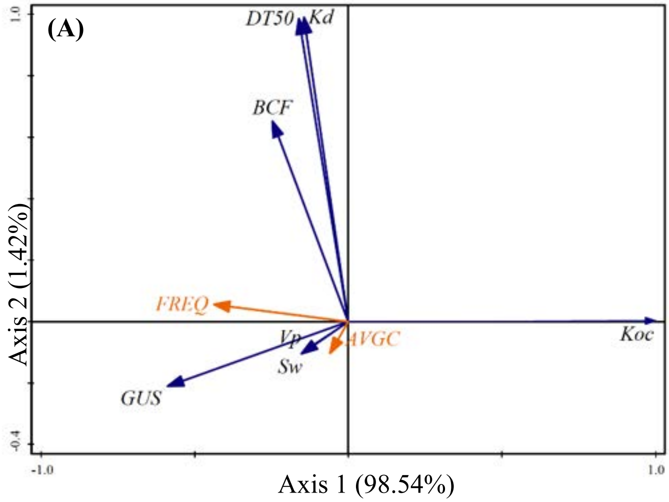
The average concentration of the pesticides was weakly correlated with their properties such as H_2O solubility, DT50, adsorption and mobility, vapour pressure, GUS index, and BCF; while the frequency of detection of the pesticides had a significant positive correlation with GUS index (Table 4.3). Principal Component Analysis (PCA) was performed to make the results of the table more informative and easily interpretable (Figure 4.4). Except p,p'-DDE, all the DDTs made a similar contributions to the OCs and suggested a similar source of origin.

Table 4.3 *Correlations between the parameters, frequency and concentration of pesticides detected in soils (positively correlated in bold font).*

Parameters of pesticides	N	WS	DT_{50}	K_d	K_{oc}	VP	GUS	BCF	FREQ	AVGC
WS (mg L^{-1})	13	1								
DT_{50}	11	-0.13	1							
K_d	3	-0.99	**1.00***	1						
K_{oc}	12	-0.19	-0.31	**1.00****	1					
VP (mPa)	11	-0.10	0.05	**1.00****	-0.18	1				
GUS index	13	0.14	0.59	-1.00**	-0.92**	0.41	1			
BCF	10	-0.26	**0.65***	0.69	-0.24	-0.21	-0.46	1		
FREQ	15	0.04	0.09	-0.24	-0.39	0.54	**0.59***	-0.35	1	
AVGC	15	-0.13	-0.11	-0.50	-0.11	0.09	0.12	0.39	0.06	1

Notation.
WS (mg L^{-1}) = Water solubility, DT_{50} = Half-life, K_d = Soil distribution Coefficients, K_{oc} = Soil adsorption Coefficient, VP (mPa) = Vapour pressure, GUS = Groundwater Ubiquity Score, BCF = Bio-concentration factor, FREQ = Frequency, and AVGC = Average concentration.
"N" = Number of pesticides corresponding to the parameters.
"*" and "**" represented significant correlation at the levels 0.05 and 0.01 (both 2-tailed), respectively.

TCP and chlorantraniliprole contributed the most to the total frequency of detection, while chlorpyrifos and p,p'-DDT had the highest pesticide concentration in soils with a maximum concentration of 177 and 78.4 µg kg^{-1}, respectively. These two compounds also pose the highest health risks. The compounds that had lower concentrations such as carbendazim and p,p'-DDE were comparable to those of metalaxyl and chlorantraniliprole, respectively. For all the DDTs, the concentration of p,p'-DDT (40 µg kg^{-1}) and p,p'-DDD (11.1 µg kg^{-1}) was higher in the depth 35-40 cm. Likewise, the concentration of p,p'-DDE (5.70 µg kg^{-1}) and o,p'-DDT (4.28 µg kg^{-1}) was higher in the depth 15-20 cm.



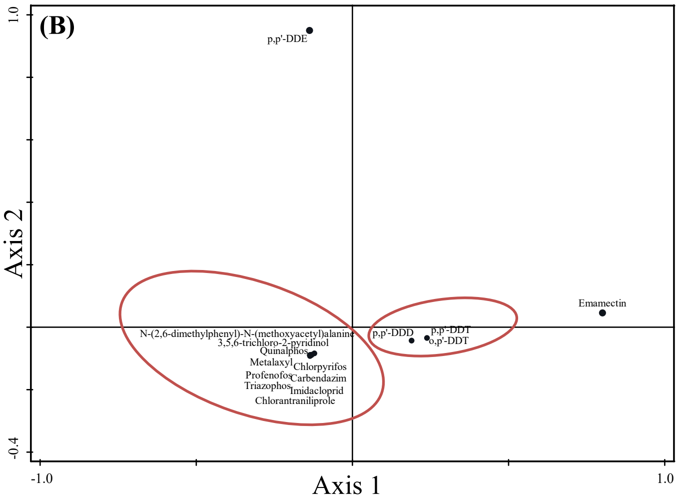


Figure 4.4 *Loading plots of PCA. Loading plot of PCA (A) showed loadings of the frequency of detection (FREQ) and average concentration of detected pesticides (AVGC) in soil with the pesticide properties such as DT50-soil half-life time (days); K_d-soil distribution coefficient (mL g^{-1}); Koc-organic carbon-water partition coefficient (mL g^{-1}); Sw-H_2O solubility at 20°C (mg L^{-1}); Vp-vapor pressure at 25°C (mPa); GUS-leaching potential index; BCF-bio-concentration factor (l kg^{-1}). Loading plot of PCA (B) showed the distribution of sources of different pesticides observed in soil (N = 15).*

Predicted concentrations ($PEC_{s,act,7\ days\ after\ pesticide\ application}$) of pesticides in soils from tomato, eggplant and chilli farms are presented in the Supplementary information, Table S4.7. $PEC_{s,act,7}$ of most of the pesticides were much higher than their measured environmental concentrations (MECs). Carbendazim, dichlorvos, imidacloprid and profenofos showed higher initial PECs of pesticides than their global pesticide soil regulatory guidance maximum values, indicating that farmers might be at greater risks from the pesticides (Table S4.7 and Table S4.8).

4.3.4 Exposure assessment for farm workers

The non-dietary chronic daily intake from exposure to p,p'-DDE, p,p'-DDT and p,p'-DDD in soils via non-dietary ingestion, dermal contact, and inhalation are presented in Table S4.9. Similarly, the total average cancer risks (CR) resulting from exposure to OCs are presented in Table 4.4. The CR posed by p,p'-DDE, p,p'-DDT, and p,p'-DDD in soils for adults were 1.30E-09, 4.75E-09, and 1.97E-09, respectively, which were slightly lower than those for adolescents (1.38E-09, 5.03E-09, and 2.09E-09, respectively). Likewise, the carcinogenic effects of p,p'-DDT in adults and adolescents was comparable and was higher than that of p,p'-DDE and p,p'-DDD in adolescents and adults, respectively.

Table 4.4 *The cancer risks (CR) of adolescents (adol) and adults (adul) resulting from the pesticides exposure in soils.*

Pesticides	CR- (adol-ing)	CR- (adol-der)	CR- (adol-inh)	CR- (adul-ing)	CR- (adul-der)	CR- (adul-inh)	TCR(adol)	TCR(adul)
p,p'-DDD	1.02E-09	1.06E-09	1.33E-13	1.13E-09	8.38E-10	1.46E-13	2.09E-09	1.97E-09
p,p'-DDE	6.75E-10	7.03E-10	8.79E-14	7.47E-10	5.54E-10	9.61E-14	1.38E-09	1.30E-09
p,p'-DDT	2.46E-09	2.56E-09	3.21E-13	2.73E-09	2.02E-09	3.51E-13	5.03E-09	4.75E-09

4.3.5 Risk characterization for farm workers

The estimated CR of three OCs such as p,p'-DDE, p,p'-DDT and p,p'-DDD in adolescents and adults via different pathways were found below $1x10^{-6}$ (Table 4.4) and showed no CR due to the exposure to the pesticides in soils. Even after considering the TCR as cumulative, the CR for adolescents and adults were below the USEPA bench mark ($1x10^{-6}$).

The average HI for OPs was < 1 and posed negligible NCR. The HI (mean±SD) estimated for adolescents via dermal contact exposure routes and soil ingestion was 8.02E-05±1.04E-04 and 1.10E-04±1.43E-04, respectively. Likewise, the HI (mean±SD) estimated for adults via dermal contact exposure routes and soil ingestion was 2.95E-05±3.83E-05 and 5.69E-

05±7.38E-05, respectively. The total HIs for adolescents and adults were 1.90E-04 and 8.64E-05, respectively, showing a negligible NCR.

The non-cancer risks of the OPs to farmers via dermal contact pathways and soil ingestion are presented in Figure S4.1 and Figure S4.2. The HQ and HI (of the total OPs) were found <1 for both adolescents and adults, indicating negligible NCR.

4.4 Discussion

4.4.1 Pollution assessment

In general, top soils (0-5 cm) contained higher concentrations and numbers of pesticide residues. However, DDT and its degradation products were less frequently found in the top soils. According to the Chinese standard (GB 15618-2018), risk screening value for the total DDT is 100 µg kg^{-1}. Likewise, Ma et al. (2016) classified soil into (i) negligible contamination, with DDT concentration <50 µg kg^{-1}; (ii) lower contamination, with DDT concentration 50-500 µg kg^{-1}; (iii) medium contamination, with DDT concentration 500-1000 µg kg^{-1}, and (iv) higher contamination, with DDT concentration >1000 µg kg^{-1}. Although DDT has been banned in Nepal since 2001, we found DDT concentration <50 µg kg^{-1} in 99% of the total soil samples.

Farmers applied most of the pesticides with higher application rates, greater numbers of applications and shorter application intervals (Bhandari et al., 2018). This might have contributed to higher predicted environmental concentrations (PECs) of pesticides (see Table S4.7 in Supplementary information). The PECs after 7 days of pesticide application ($PEC_{s,act,7}$) for most pesticides, except for dichlorvos and emamectin, were much higher than their measured concentrations (Table 4.1 and Table S4.7, Supplementary information). In the same study, they applied dimethoate and dichlorvos at higher than their recommended levels. However, soils were free from pesticide residues such as dimethoate and its degradation product (omethoate), dichlorvos, phorate, α-β-endosulfan and α-γ-HCH (<LOD). Dimethoate, omethoate and dichlorvos have higher water solubility (Table S4.1) and phorate, α-β-endosulfan and α-γ-HCH have been banned for many years which may explain why their residues were absent in the soils. Soils from conventional systems had significantly higher numbers of pesticide residues than the soils from IPM farming. In the IPM farms, about 85% of the soil samples were clean, and the remaining samples had pesticide concentrations close to their corresponding LODs (Table 4.1). In an another study, we observed higher residues of pesticides in vegetables from conventional farms than that of IPM farms (Bhandari et al., 2019).

The fate of pesticides in soils is determined by their various factors: mobility, persistence, and volatility. Furthermore, other pesticide properties such as phosphorus and nitrogen levels, organic carbon content, and soil pH affect distribution and occurrence (Gong et al., 2004; Pan et al., 2018). Few of the pesticides detected in soils have lower soil organic carbon-water partitioning coefficients (Koc) and thus, moderate leaching potential which suggests a risk of ground water pollution. The sorption of chemical pesticides was the highest for the soils with greatest OC content (Zbytniewski and Buszewski, 2002).

Conventional fields contain less OC than IPM fields and this might enhance the mobility of pesticides and could thus increase groundwater pollution (Sánchez-González et al., 2013). About ninety percent of total inhabitants in the study area drink water from tube wells adjacent to their vegetable fields (GRM, 2018) which could increase their HR. Pesticides may contaminated groundwater and make it unsuitable for drinking, which is the case for Nigeria (Sosan et al., 2008) and the Philippines (Castaneda and Bhuiyan, 1996). The mean concentrations of the pesticides in our soil samples are at lower end in comparison to other countries (Table 4.5).

Table 4.5 *Comparison of pesticide levels in soils from conventional farming in this study with past studies across the globe. To find the relevant literature, Web of Science database was considered by using the search phrase pesticide and soil and *concentration*. Hyphens indicate that no information was available. Pesticides concentration in µg kg^{-1}. The mean concentration of the most pesticides in this study is lower than the other studies abroad.*

Pesticides	Abroad		Nepalese agricultural soil
	Place, country/land use/mean concentration	Reference	Mean concentration (this study)
3,5,6-trichloro−2-pyridinol	-	-	10.4
Chlorpyrifos	Okara, Pakistan/cotton, wheat/1393	(Rafique et al., 2016)	40.8
	China/persimmons and jujubes/17.15	(Liu et al., 2016a)	
	China/nuts/42.2	(Han et al., 2017)	
	Dormaa West, Ghana/cocoa/30	(Fosu-Mensah et al., 2016)	
Profenofos	Okara, Pakistan/cotton, wheat/89.79	(Rafique et al., 2016)	1.75
	Dormaa West, Ghana/cocoa/30	(Fosu-Mensah et al., 2016)	
Quinalphos	-	-	1.59
Triazophos	Okara, Pakistan/cotton, wheat/99.74	(Rafique et al., 2016)	3.28
o,p′-DDT	Nagaon, India/paddy fields, tea gardens and others/150	(Mishra et al., 2012)	2.85
	Hong Kong/different types of land use/0.05	(Zhang et al., 2006)	
	Shanghai, China/agriculture/1.66	(Jiang et al., 2009)	
	Beijing, China/school yards/42.38	(Wang et al., 2008)	
	Moldavia, Romania/forest/0.7	(Tarcau et al., 2013)	

Table 4.5 *Comparison of pesticide levels in soils..................... (continued).*

Pesticides	Abroad Place, country/land use/mean concentration	Reference	Nepalese agricultural soil Mean concentration (this study)
p,p′-DDD	Limuru, Kenya/rural and semi urban areas/1.71	(Sun et al., 2016)	7.11
	Nagaon, India/paddy fields, tea gardens and others/73	(Mishra et al., 2012)	
	Hong Kong/farmland/0.05	(Zhang et al., 2006)	
	Shanghai, China/agriculture/4.56	(Jiang et al., 2009)	
	Beijing, China/school yards/6.47	(Wang et al., 2008)	
	Moldavia, Romania/forest/1.2	(Tarcau et al., 2013)	
p,p′-DDE	Limuru, Kenya/rural and semi urban areas/0.97	(Sun et al., 2016)	3.31
	Nagaon, India/paddy fields, tea gardens and others/276	(Mishra et al., 2012)	
	Hong Kong/farmland/1.73	(Zhang et al., 2006)	
	Shanghai, China/agriculture/16.14	(Jiang et al., 2009)	
	Beijing, China/school yards/27.29	(Wang et al., 2008)	
	Moldavia, Romania/forest/10	(Tarcau et al., 2013)	
p,p′-DDT	Limuru, Kenya/rural and semi urban areas/11.76	(Sun et al., 2016)	12.1
	Nagaon, India/paddy fields, tea gardens and others/351	(Mishra et al., 2012)	
	Hong Kong/farmland/0.02	(Zhang et al., 2006)	
	Shanghai, China/agriculture/3.26	(Jiang et al., 2009)	
	Beijing, China/school yards/17.54	(Wang et al., 2008)	
	Moldavia, Romania/forest/8.1	(Tarcau et al., 2013)	
Chlorantraniliprole	-	-	3.17
Imidacloprid	Okara, Pakistan/cotton, wheat/548.7	(Rafique et al., 2016)	5.52
Carbendazim	Basrah, Iraq/agricultural soil/1259	(Raheem et al., 2017)	2.12
Metalaxyl	Spain/agricultural areas/ 3.82	(Sánchez-González et al., 2013)	3.25
N-(2,6-dimethylphenyl)-N-(methoxyacetyl)alanine	-	-	1.34
Emamectin	-	-	-

Depending on the date of pesticides application, the $PEC_{s,act,7}$ were correct for only dichlorvos and emamectin. However, the PECs of other pesticides in different fields (see Table S4.7 in Supplementary information) were much higher than their MECs (measured environmental concentrations or the mean concentration) (Table 4.1) and pesticide soil regulatory guidance values (Table S4.8, Supplementary information). The farmers' pesticide use behaviours such as the application rates were self-reported and observed higher than recommended (Bhandari et al., 2018). The differences between MECs and PECs are several orders of magnitude that might be due to the estimation of PECs from the realistic worst-case scenario. Since PSRGVs might be risk-based, the values could more accurately reflect the potential environmental and health risks which are worth consideration. In addition, immediate predicted environmental concentrations ($PEC_{s,act,0}$) of contaminated soils and their effects on human health should not be neglected.

Our predicted environmental concentration in soil (PEC_S) for dimethoate on tomato after multiple applications was much higher than their respective values in the draft assessment report (DAR) of the European Commission (EC, 2004). The possible reason for higher PEC_S for dimethoate might be due to the fact that the pesticide was applied at level higher than its recommended dose (Bhandari et al., 2018). Likewise, the PEC_S for other pesticides from eggplant and chilli farms could not be compared due to unavailability of their DARs.

4.4.2 Source identification of DDT

DDT is a mixture of its degradation products: 15% o,p'-DDT and 85% p,p'-DDT (Zheng et al., 2009), and the half-life has been estimated >15 years in the environment. Parent DDT disintegrates to DDE and DDD, more stable compounds than their parent. The ratio o,p'-DDT/p,p'-DDT is used to differentiate dicofol from DDT. The ratio between 0.2 and 0.3 corresponds to the occurrence of technical DDT, while the ratio between 1.9 and 9.3 or higher corresponds to the presence of dicofol (Qiu et al., 2005). In our study, the ratio ranged between 0.03 and 0.17, except in one sample, signifying the application of technical DDT. One sample showed the ratio comparatively higher which corresponds with dicofol use in the area. The ratio (p,p'-DDE+p,p'-DDD)/p,p'-DDT assesses the time and degree of disintegration of p,p'-DDT in soil (Qiu et al., 2004). Ratios greater than one indicate aged mixtures, while ratios < 1 indicate fresh applications of the parent DDT in soil. In our study, the ratios ranged from 0.21 to 2.20. The ratio was less than one in two samples, specifying the ongoing use of DDT and the ratio was > 1 in another sample, indicating its historical use (Dhimal et al., 2014). The current use of DDT might be due to conventional farming and/or expansion of diseases such as malaria fever and dengue (Awasthi et al., 2017; Shah et al., 2012). Similar findings have been reported from other regions of Nepal (Yadav et al., 2017; Yadav et al., 2016). Potential source analysis indicated that DDT and related compounds mainly originated from a recently applied DDT, possibly due to: (i) the illegal entry due to the porous India-Nepal border; (ii) inadequate execution of the ban and/or (iii) application of DDT for dengue control.

DDT disintegrates to DDD from anaerobic degradations while it changes to DDE from aerobic degradations. The ratio DDD/DDE indicates whether DDT is degraded aerobically or anaerobically. In our study, the ratio DDD/DDE ranged from 0.30 to 2. The ratio was less than one in a higher number of samples, indicating higher percentages of DDE than DDD and thus, DDT was aerobically degraded. Our results were different from those in soils from China (Ma et al., 2016), where the ratio was > 1 in a higher number of samples, indicating higher percentages of DDD than DDE and thus, DDT was anaerobically degraded. The disintegration of DDT-DDE-DDD can occur directly or indirectly (Wenzel et al., 2002). The ratios of DDE:DDT, DDD:DDE, and DDD:DDT decide dechlorination paths in soils. DDT to DDE was the major disintegration route, as the ratios were: DDE:DDT (1.73) > DDD:DDE (0.96) > DDD:DDT (0.33). These results coincide with Zhang et al. (2006), but differed with Ma et al. (2016). This differences can be explained by dissimilarities in the precipitation, temperature, humidity, soil moisture, soil texture, microbes, CEC, and OM, which affect the conversion of DDT into DDE-DDD (Aislabie et al., 2010; Chattopadhyay and Chattopadhyay, 2015).

PCA estimates the source and disintegration behaviour of pesticides (Yang et al., 2012). In our study, pesticides belonging to the groups such as organophosphates, anthranilic diamide, neonicotinoid, benzimidazole, phenylamide and unclassified degradation products were aligned together indicating similar source and degradation behaviour, while OCs were separated, suggesting different source and fate of the pesticides.

4.4.3 Carcinogenic and non-carcinogenic risk

TCR and CR via dermal and ingestion pathways of exposure to DDTs for adolescents and adults were below $1x10^{-6}$, indicating negligible cancer risk (Table 4.4). Adolescent and adult exposure to single non-carcinogenic pesticides (HQ) and multiple pesticides (HI) was < 1, suggesting no appreciable non-cancer health risk. Likewise, HIs of pesticides via ingestion and dermal exposure for adolescents and adults were also negligible (< 1) (Figure S4.1 and Figure S4.2). However, other pathways of exposure such as inhalation could still exist in Nepal and cannot be excluded for a non-cancer risk assessment. The risk via inhalation was not considered in this study because essential parameters were unavailable. Furthermore, metabolism and excretion of pesticides in humans were excluded from this study. All soil samples came from farmers' fields close to their houses thus, children may have had direct contact with these soils on a daily basis.

Overall, the cancer and non-cancer risks of pesticides for adolescents were relatively higher than those for adults. Previous studies (Landrigan and Goldman, 2011; Pan et al., 2018) also indicated relatively higher risks for children than adults. The possible reason for higher risks for adolescents might be due to their higher exposure to given doses of OCs and OPs. The soil ingestion was the main pathway of OP exposure and added to 58% and 66% of the total risks in adolescents and adults, respectively [Figure S4.1 (b) and Figure S4.2 (b), Supplementary information]. Even though the soil samples of GRM were contaminated with pesticides, a negligible health risk from the exposure to the pesticide contaminated soil was observed in this study.

This study considered the worst case scenario (only positive samples and their total average concentrations): replacing the non-detects with 0 (Yadav et al., 2016) would even further decrease the CR, HQ and HI values. However, children are more likely to unintentionally ingest significant amounts of contaminated soil because of their childish behavior such as putting contaminated hand or fingers in their mouths (Rasmussen et al., 2001). Henceforth, this study warrants further research to investigate the implications of exposure for children through all of the possible pathways.

4.4.4 Limitations and future recommendations

Pesticide residues could move from neighbouring fields via water and wind and be deposited in surrounding environments (Silva et al., 2018) and accumulate in higher concentrations on the topsoil (1-2 cm) than deeper soil (Yang et al., 2015). Future research should consider soil samples and the distribution of residues in the topmost surface layer. We used conservative risk assessment methods that are generally used for risk assessment of contaminated sites and their applications in farmland needs further research. The PECs of pesticides in soils were based on information related to the pesticide application history in our earlier study (Bhandari et al., 2018) and thus, the results may not be representative of other areas and the latest pesticides use statistics. The twenty-three prioritized pesticides and degradation products assessed in Nepalese soil correspond to <20% of the active ingredients imported for use, indicating that the total pesticides in soils might even be higher than detected in our study and the pesticide mixtures may even be more complicated. Reference concentrations (RfC) of the pesticides and degradation products for the estimation of inhalation exposure were not available thus, risks due to the exposure to pesticides could not be estimated. Worldwide PSRGVs (Table S4.8) were not calculated comprehensively in humans (Li and Jennings, 2017) and comparison of the PECs with the global values for pesticides in soil may be inadequate for the assessment of HR. Further, whether or not the PECs are reasonable to evaluate the risk of pesticides in the area compared with the PSRGVs could not be answered. Despite such limitations, we have used widely accepted models and indices for the risk assessment.

4.5 Conclusion

Pesticides applied to vegetables farming in Nepal pollutes soils. Adoption of IPM techniques could reduce pesticide pollution in soils, as this study showed a notably smaller number of pesticide residues and their minimum concentration in the soil samples collected from IPM fields, compared to conventional farming. OCs concentration were sufficiently low in most soil samples (<LOD). However, DDTs were detected with p,p'-DDE being the predominant compound. There is no appreciable health risk from pesticides residues in soils, based on direct dermal contact and/or ingestion in adults or adolescents. The focus should be placed on DDT pollution and the recommendations from the United Nations treaty, the Stockholm Convention should be implemented. A few pesticides detected in soils have a potential of leaching thus, there is a risk of ground water pollution.

Predicted environmental concentrations (PEC_s) for most of the frequently applied pesticides used on vegetables in Nepal did not appear in the European Commission (EC) draft assessment reports thus, the estimated PECs is of minimal use. The PECs 7 ($PEC_{s,act,7\ days\ after\ pesticide\ application}$) for almost all of the pesticides were much higher than their measured environmental concentrations (MECs). The initial PECs of carbendazim, dichlorvos, imidacloprid and profenofos were much higher than their guidance values in soil. The PECs scenario based on the poor agricultural practices is insufficient to claim an increasing health risk of farm workers which warrants future research on PECs and health risk from pesticides in soils from other locations.

Acknowledgements

We are thankful to the Nuffic for supporting this work through project No. PhD-5160957247. We would like to thank the farmers for their help in fields. We thank the students who supported researchers carrying out the sample collection: Dinesh Ghimire, Ramesh Lodh, Prashant Chaudhary, and Santosh Gupta. We would also like to thank Robin Palmer, Ad Peijnenburg, Ron Hoogenboom and Paul Zomer for their support of this study, reviewing the manuscript and helping with the laboratory work, respectively.

Supplementary Material

Table S4.1 *The properties of the pesticides tested and their degradation products^.*

Group	Pesticides and degradation products/type	Mode of action	Use status (EC/NE)	Major pests controlled	MF/MW(g mol^{-1})	[a]CASRN	WS	[b]DT50	[c]Log P	[d]Koc	VP	[e]GUS index	[f]HLC	gKd	hBCF
UNC	3,5,6-trichloro-2-pyridinol[m]/ins	NA	NA	na	$C_5H_2Cl_3NO$/198.43	6515-38-4	81	75	3.21	149	137.32	4.88	1.10	na	3.20
OP	Chlorpyrifos/ins	NSY with contact, inhalation and stomach action; AChE inhibitor	AP/AP	Scale; Wooly aphid; Leaf roller; Caterpillars; Worms; flies; Ants; Cockroaches; Beetles; Termites	$C_9H_{11}Cl_3NO_3PS$/350.59	2921-88-2	1.05	28	4.7	5509	1.43	3.63	0.478	127	1374
	Dichlorvos/ins	Respiratory; contact and stomach action, ChE inhibitor	**NP/AP**—	Beetles; Weevils; Borer; Flies; Mosquitoes; Cockroaches; Aphids; Thrips	$C_4H_7Cl_2O_4P$/220.98	62-73-7	18000	na	1.9	50	2100	0.69	$2.58x10^{-2}$	na	<100
	Dimethoate/ins	SYS with contact and stomach action, AChE inhibitor	AP/AP	Aphids; Thrips; Flies; Grasshoppers; Jassids; Spidermites; Leaf and plant hoppers	$C_5H_{12}NO_3PS_2$/229.26	60-51-5	25900	7	0.75	na	0.247	1.01	$1.42x10^{-6}$	na	8
	Omethoate[m]/ins	SYS with contact and stomach action, ChE inhibitor	NP/NP	Aphids; Mites; Caterpillars; Beetles; Mealybugs; Scale	$C_5H_{12}NO_4PS$/213.19	1113-02-6	500000	14	-0.9	41.3	19	-2.38	$4.62x10^{-9}$	0.53	75
	Phorate!/ins	SYS with contact and stomach action, AChE inhibitor	NP/NP	Leaf miners; Beetles; Flies; Nematodes; Mites; Rootworms	$C_7H_{17}O_2PS_3$/260.4	298-02-2	50	63	3.86	1660	112	1.25	$5.90x10^{-1}$	na	483
	Profenofos/ins	NSY with contact and stomach action, AChE inhibitor	**NP/AP**	Aphids; Bugs; Worms; Leaf webber; Whitefly; Spidermites; Caterpillars; Cotton leaf-perforator	$C_{11}H_{15}BrClO_3PS$/373.63	41198-08-7	28	7	1.7	2016	2.53	0.59	$1.65x10^{-3}$	na	1186
	Quinalphos/ins	NSY with contact and stomach action, AChE inhibitor	**NP/AP**	Caterpillars; Aphids; Mealybugs; Mites; Bollworms; Leaf hoppers; Borers	$C_{12}H_{15}N_2O_3PS$/298.3	13593-03-8	18	na	4.44	1465	0.346	1.1	$4.70x10^{-3}$	na	na
	Triazophos/ins	NSY, broad spectrum with contact and stomach action, ChE inhibitor	**NP/AP**—	Aphids; Thrips; Midges; Beetles; Sawflies; Apple suckers; Spidermites; Scale insects, Fruit flies	$C_{12}H_{16}N_3O_3PS$/313.31	24017-47-8	35	9	3.55	358	1.33	2.38	$4.90x10^{-3}$	na	300

Table S4.1 *The properties of the pesticides.........(continued)*

Group	Pesticides and degradation products/type	Mode of action	Use status (EC/NE)	Major pests controlled	MF/MW(g mol^{-1})	[a]CASRN	WS	[b]DT50	[c]Log P	[d]Koc	VP	[e]GUS index	[f]HLC	gKd	hBCF
OC	o, p'-DDT!/ins	Central nervous system (CNS) stimulant	NP/NP	Mosquitoes; Houseflies; Body lice; Beetles; Gypsy moths	$C_{14}H_9Cl_5$/354.48	789-02-6	na	na	na	151000	na	-3.89	na	na	na
	p, p'-DDD!/ins	NSY stomach and contact action	NP/NP	Mosquitoes; Lice	$C_{14}H_{10}C_{14}$/320.04	72-54-8	0.09	na	6.02	131000	0.18	-2.46	$4.0x10^{-6}$	na	na
	p, p'-DDE!/ins	CNS stimulant; A weak androgen receptor antagonist	NA/NP	\	$C_{14}H_8Cl_4$/318.02	72-55-9	0.12	5000	6.51	na	na	na	na	50000	1800
	p, p'-DDT!/ins	CNS stimulant; GABA-gated chloride channel antagonist	NP/NP	Mosquitoes; Houseflies; Body lice; Beetles; Gypsy moths	$C_{14}H_9Cl_5$/354.49	50-29-3	0.025	na	6.91	151000	na	-3.89	na	na	na
	α-Endosulfan!/ins	NSY with contact and stomach action	NP/NP	Mites; Ticks; Tstetse fly; Beetle; Aphids; Leaf hoppers	$C_9H_6Cl_6O_3S$/406.93	959-98-8	0.32	86	4.74	11500	8.30	-0.1	1.48	na	2755
	α-HCH!/ins	NA	NP/NP	Soil-dwelling and plant eating insects	$C_6H_6Cl_6$/290.83	319-84-6	2	na	3.82	1888	5.99	1.62	na	na	na
	β-Endosulfan!/ins	NSY with contact and stomach action	NP/NP	Mites; Ticks; Tstetse fly; Beetle; Aphids; Leaf hoppers	$C_9H_6Cl_6O_3S$/406.93	33213-65-9	0.45	na	3.83	na	na	na	na	na	na
	γ-HCH!/ins	CNS stimulant with contact and stomach action	NP/NP	Soil-dwelling and plant eating insects	$C_6H_6Cl_6$/290.82	58-89-9	8.52	148	3.50	1270	4.40	3.95	$1.48x10^{-6}$	na	1300
AD	Chlorantraniliprole/ins	Ryanodine receptor	AP/AP	Cabbage loopers; Corn borers; Armyworms; Cutworms	$C_{18}H_{14}BrCl_2N_5O_2$/483.15	500008-45-7	0.88	204	2.86	362	$6.3 X 10^{-9}$	4.22	$3.2x10^{-9}$	3.18	15
NND	Imidacloprid/ins	SYS with contact and stomach action	AP/AP	Plant hopper; Aphids; Termites; Beetle; Fleas; White grups, Craneflies; Ants; Crickets	$C_9H_{10}ClN_5O_2$/255.66	138261-41-3	610	174	0.57	na	$4.0 X 10^{-7}$	3.74	$1.7x10^{-10}$	na	0.61
BD	Carbendazim/fun	SYS with curative and protectant activity	**NP/AP**	Husk spot; Grey mould; Crown rot	$C_9H_9N_3O_2$/191.21	10605-21-7	8	22	1.48	na	0.09	2.53	$3.6x10^{-3}$	na	25

Table S4.1 *The properties of the pesticides..........(continued)*

Group	Pesticides and degradation products/type	Mode of action	Use status (EC/NE)	Major pests controlled	MF/MW(g mol^{-1})	aCASRN	WS	bDT50	cLog	dKoc	VP	eGUS index	fHLC	gKd	hBCF
PA	Metalaxyl/fun	SYS with curative and protective action	AP/AP	Downy mildew; Foliar and tuber blight; Damping-off	$C_{15}H_{21}NO_4$ /279.33	58737-19-1	8400	39	1.75	162	0.75	2.79	1.6×10^{-5}	na	7
UNC	N-(2,6-dimethylphenyl)-N-(methoxyacetyl)alanine[m]/fun	NA	NA	na	$C_{14}H_{19}NO_4$ /265.3	87764-37-2	na	51	na	38	na	3.83	4.54	na	na
MOD	Emamectin/ins	NSY, acts by causing insect paralysis; Chloride channel activator	AP/AP	Lepidoptera species; Mites; Thrips; Leafminers; Emerald ash borer; Caterpillars	$C_{56}H_{81}NO_{15}$/1008.3	155569-91-8	24	1	5	377000	0.004	na	1.7×10^{-4}	na	80

Notation.
aCASRN, chemical abstracts service registry number; WS (mg L^{-1}), water solubility [L–Low (WS <50), M–Moderate (WS: 50–500), H–High (WS >500)]
bDT50 (field days), half-life time [NP–Non-Persistent (DT50 <30), MP–Moderately Persistent (DT50: 30–100), P–Persistent (DT50: 100– 365), VP–Very Persistent (DT50 >365)]
cLog P, Octanol-water Partition Coefficient [LB-Low bioaccumulation (Log P<2.7), MB-Moderate bioaccumulation (Log P: 2.7-3), HB-High bioaccumulation (Log P: >3)]
dKoc (mL/g), soil organic carbon-water partitioning coefficient [VM-Very mobile (Koc <15), M-Mobile (Koc: 15-75), MM-Moderately mobile (Koc: 75-500), SM-Slightly mobile (Koc: 500-4000), NM-Non mobile (Koc: >4000)]
VP (mPa), vapour pressure [L–Low volatility (VP <5.0), M–Moderately volatile (VP: 5.0–10.0), H–Highly volatile (VP >10.0)]
eGUS index, groundwater ubiquity score [L–Low leachability (GUS <1.8), T–Transition state (GUS: 2.8–1.8), H–High leachability (GUS >2.8)]
fHLC (Pa m^3 mol^{-1}), Henry's Law Constant [HV-Highly volatile (HLC >100), MV-Moderately volatile (HLC: 0.1-100), NV-Non volatile (HLC: <0.1)]
gKd, soil sorption coefficient
hBCF, bio-concentration factor [LW-Lower potential (BCF<100), THC-Threshold for concern (BCF: 5000-100), HP-Higher potential (BCF>5000)]
Status is based on EC regulation 1107/2009 and Pesticide Registration and Management Division, Government of Nepal
^ = Pesticide properties were retrieved from the PPDB and the BPDB databases which were maintained by the University of Hertfordshire, UK (Retrieved on: 23 November, 2019)
AP = Approved; NP = Not approved; "–" = still in use but in the process to ban; MF = Molecular formula; MW = Molecular weight; ! = Banned pesticides; na = Not available; m = Degradation products; NA = Not applicable
Group: Unclassified, UNC; Organophosphates, OP; organochlorines, OC; Anthranilic diamide, AD; Neonicotinoid, NND; Benzimidazole, BD; Phenylamide, PA; Micro-organism derived, MOD. The group is based on PPDB (2019)
NSY/SYS= Non-systemic/systemic; AChE/ChE = Acetylcholinesterase/Cholinesterase

Table S4.2 *Detected residues in soils with their corresponding human health consequences#.*

Pesticides and degradation products	Cancer	Genotoxicity	Endocrine disruption	Reproductive disorders	Cholinesterase inhibition	Nervous system disorders	Respiratory problems	Skin irritation	Skin sensitization	Eye problems	Phototoxicity
3,5,6-trichloro-2-pyridinol	DU	A3; B3; C3; D0; E0	DU	PSNI	DU	DU	DU	DU	DU	DU	DU
Carbendazim	PSNI	A2; B3; C3; D0; E1	PSNI	C	NC	NC	NC	NC	DU	NC	DU
Chlorantraniliprole	NC	A3; B0; C3; D0; E3	NC	PSNI	NC	NC	DU	NC	DU	PSNI	DU
Chlorpyrifos	NC	A3; B3; C3; D0; E3	PSNI	C	C	C	NC	NC	PSNI	NC	NC
Emamectin	NC	A3; B0; C0; D0; E3	DU	PSNI	NC	PSNI	DU	NC	PSNI	C	DU
Imidacloprid	NC	A3; B3; C3; D3; E2	DU	C	NC	PSNI	NC	PSNI	DU	PSNI	DU
Metalaxyl	NC	A3; B0; C0; D0; E3	NC	NC	NC	NC	NC	NC	PSNI	NC	DU
N-(2,6-dimethylphenyl)-N-(methoxyacetyl)alanine	DU	A0; B0; C0; D0; E0	DU	DU	DU	DU	DU	DU	DU	DU	DU
o,p'-DDT	C	A0; B0; C0; D0; E0	C	C	NC	C	DU	C	DU	DU	DU
p,p'-DDD	C	A0; B0; C0; D0; E1	C	C	DU	DU	C	C	DU	NC	DU
p,p'-DDE	C	A0; B0; C0; D0; E2	C	C	DU	C	DU	C	DU	NC	DU
p,p'-DDT	C	A0; B0; C0; D0; E1	PSNI	C	DU	C	DU	C	DU	PSNI	DU
Profenofos	NC	A3; B0; C0; D0; E0	DU	NC	C	C	DU	C	DU	PSNI	DU
Quinalphos	NC	A0; B0; C0; D0; E0	DU	PSNI	C	C	C	C	DU	C	DU
Triazophos	NC	A3; B0; C0; D0; E0	DU	DU	C	C	C	C	DU	C	DU

Notation.
C = Known to cause health consequences; NC = Known not to cause health consequences; PSNI = Possibly, status has not been identified; DU = Data unavailable
# Human health consequences were retrieved from the PPDB and the BPDB databases which were maintained by the University of Hertfordshire, UK (Retrieved on: 23 November, 2019)
Genotoxicity: A, Chromosome aberration; B, DNA damage/repair; C, Gene mutation; D, Genome mutation; E, Unspecified genotoxicity type (Data sources: EFSA database and others)
0: Data not available; 1: Positive; 2: Mixed/ambiguous results; 3: Negative

Table S4.3 *Constant parameters and their values for the cancer and non-cancer risk estimation (USEPA, 2002; Wang, 2007).*

Exposure factors	Unit	Adolescent (ado)	Adult (adu)
Average life span (AT)	days	LTx365	LTx365
Body weight (BW)	kg	32	62
Dermal absorption factor (ABS)	unit less	0.13	0.13
Dermal adherence factor (SAF)	mg cm^{-2}	0.2	0.07
Exposure duration (ED)	years	14	30
Exposure frequency (EF)	days yr^{-1}	350	350
Ingestion rate (IR_{ing})	mg day^{-1}	100	100
Inhalation rate (IR_{inh})	m^3 day^{-1}	17.7	17.5
Lifetime (LT)	years	70	70
Particle emission factor (PEF)	m^3 kg^{-1}	1.36×10^9	1.36×10^9
Surface area (SA)	cm^2 day^{-1}	2800	5700
Conversion factor (CF)	kg mg^{-1}	10^{-6}	10^{-6}

Notation.
BW is based on WHO (2011); for non-cancer risk estimation, AT = ED x 365

Table S4.4 *The carcinogenicity slope factor (SF) [(mg kg^{-1} day^{-1})$^{-1}$] of pesticides through different exposure routes (Qu et al., 2015).*

Pesticides	$CSF_{ingestion}$	CSF_{dermal}	$CSF_{inhalation}$
p,p'-DDD	2.40E-01	3.43E-01	2.40E-01
p,p'-DDE	3.40E-01	4.86E-01	3.40E-01
p,p'-DDT	3.40E-01	4.86E-01	3.40E-01

Table S4.5 *Pesticides with their corresponding reference dose (RfD) and gastrointestinal absorption factor (ABS_{GI}) values for cancer and non-cancer risk estimation (USEPA, 2018).*

Pesticides	RfD (mg kg^{-1} day^{-1})	ABS_{GI} (unit less)
3,5,6-trichloro-2-pyridinol[m]	na	na
Carbendazim	0.02	1 [dv]
Chlorantraniliprole	1.56	1 [dv]
Chlorpyrifos	0.001	1
Emamectin	0.0005	1 [dv]
Imidacloprid	0.06	1 [dv]
Metalaxyl	0.08	1
N-(2,6-dimethylphenyl)-N-(methoxyacetyl)alanine[m]	na	na
Profenofos	na	na
Quinalphos	0.0005	1
Triazophos	0.001	1[dv]

RfC values (mg/m^3) of the pesticides were not available (na) in Integrated Risk Information System (IRIS) developed by US EPA, hence assessment of non-cancer risk via inhalation is excluded from this study. Furthermore, ABS_{GI} values of some pesticides did not appear in the system therefore, a default value (dv) of 1 was used for the pesticides (except profenofos and other degradation products, m) in the calculations. Profenofos and other degradation products are excluded in the calculations as their RfD values did not appear.

Table S4.6 *The average CDI values (mg kg^{-1} day^{-}1) of pesticides for adolescents (ado) and adults (adu).*

Pesticides	CDI-ing(ado)	CDI-der(ado)	CDI-inh(ado)	CDI-ing(adu)	CDI-der(adu)	CDI-inh(adu)
p,p'-DDD	4.26E-09	3.10E-09	5.55E-13	4.71E-09	2.44E-09	6.06E-13
p,p'-DDE	1.99E-09	1.45E-09	2.59E-13	2.20E-09	1.14E-09	2.83E-13
p,p'-DDT	7.25E-09	5.28E-09	9.43E-13	8.02E-09	4.16E-09	1.03E-12

Table S4.7 *Predicted environment concentrations [(PECs) μg/kg] of pesticides (in soil) that farmers applied in different fields.*

Fields	Pesticides	[ar]Application rate (g/ha)	[np]No. of applications	[ai]Application interval (days)	PECs, act (days after pesticide applications)									Reference
					0	1	2	4	7	14	28	50	100	
Tomato	**Carbendazim**	1770	17	15	3130	3030	2940	2760	2510	2010	1300	650	0	This study
	Chlorpyrifos	11590	19	15	24900	24300	23700	22500	20900	17600	12400	7200	0	
	Dichlorvos	23120	19	15	15400	4900	1500	200	0	0	0	0	0	
	Dimethoate	3380	25	10	1430	1300	1180	970	720	360	90	10	0	
	Emamectin	770	21	15	510	260	130	30	0	0	0	0	0	
	Imidacloprid	1080	15	15	7350	7320	7290	7230	7150	6950	6570	6020	0	
	Metalaxyl	1730	20	15	4900	4820	4730	4570	4330	3820	2980	2020	0	
	Profenofos	6830	15	15	5890	5330	4830	3960	2940	1470	370	40	0	
	Triazophos	2330	11	30	1720	1600	1480	1270	1010	590	200	40	0	
	Chlorantraniliprole	2100	17	15	6530	6510	6490	6440	6380	6230	5940	5510	0	
Eggplant	Dimethoate	8720	24	15	7510	6810	6160	5060	3760	1880	470	50	0	
	Imidacloprid	440	14	30	2120	2110	2100	2080	2060	2000	1890	1730	0	
	Profenofos	13600	10	30	9560	8660	7840	6430	4780	2390	600	70	0	
Chilli	Dimethoate	1790	8	30	1260	1140	1030	850	630	310	80	10	0	
	Profenofos	4140	13	15	3570	3230	2930	2400	1780	890	220	30	0	

Notation.

Except for dimethoate (tomato) and chlorantraniliprole (chilli), 80%, the fraction intercepted by the vegetable cover for other pesticides is 50%; Depth of soil = 5 cm and bulk density = 1.5 g cm^{-3} (EFSA, 2002); ar, np and ai were based on our previous study (Bhandari et al., 2018). In the respective fields, few pesticides in bold showed higher PECs (days after pesticides application, 0) than their global pesticide soil regulatory guidance maximum values, indicating greater risks for farm workers.

Table S4.8 *List of studied pesticides and their global pesticide soil regulatory guidance values [(PSRGVs) (µg kg^{-1})] selected randomly from a past study (Li and Jennings, 2017). For pesticides with multiple PSRGVs, the maximum values were considered for possible comparison.*

S.N.	Pesticides	Countries	PSRGVs								
1	Carbendazim	Belarus, Georgia, Ukraine	100								
2	Chlorpyrifos	Australia|Florida (US), Bahamas|Alberta| BC (Canada)| Lithuania|Malaysia|New Zealand|Spain|Ukraine	160000-340000	250000	49000-95000	180	100000	180000	61000	200000	200
3	Dichlorvos	Belarus, Armenia, Georgia|Florida (US), Bahamas|Malaysia, New Zealand|BC (Canada)|China|Moldova, Tatarstan, Russia	30	300	1700	17	1000	100			
4	Dimethoate	China|Armenia, Belarus|Florida (US), Bahamas|Alberta|Malaysia, New Zealand|Vietnam	2000	100	13000	5.5-5.8	12000	50			
5	Imidacloprid	Georgia	40								
6	Metalaxyl	Armenia, Georgia, Ukraine|BC (Canada)|Malaysia, New Zealand	50	3700	3700000						
7	o,p′-DDT	Bulgaria|BC (Canada)|China, Moldova, Tatarstan, Russia	100	15	100						
8	p,p′-DDD	Andorra| Bulgaria|Georgia (US)|BC (Canada)|China|Ecuador|Montenegro|New Zealand|Russia	700	100	660	15	500	100	10	700	100
9	p,p′-DDE	Andorra| Bulgaria|Georgia (US)|BC (Canada)|China|Ecuador|Montenegro|New Zealand|Russia	600	100	660	15	500	100	10	700	100
10	p,p′-DDT	Andorra| Bulgaria|Georgia (US)|BC (Canada)|China|Ecuador|Montenegro|New Zealand|Russia	200	100	660	15	500	100	10	700	100
11	Phorate	New Zealand|Florida (US), Bahamas|Alberta|Malaysia|BC (Canada)	12210	16000	75-140	12000	12				
12	Profenofos	Georgia|Ukraine	100	1							
13	Quinalphos	BC (Canada)| Arizona, New Zealand, Malaysia	31	31000							
14	Triazophos	Georgia (US)	25000								
15	α-Endosulfan	Bahamas, Florida (US)|Ecuador|Panama|Victoria	450000	100	500	1000					
16	α-HCH	Serbia, Italy, Hungary, Ecuador, Czech Republic, Andorra|Bulgaria|BC (Canada)|China, Croatia|Estonia, Singapore|GermanyLatvia|Lithuania|EU	10	1	0.9	100	200	10000	2000	400	50000
17	β-Endosulfan	Bahamas, Florida (US)|Ecuador|Panama|Victoria	450000	100	500	1000					
18	γ-HCH	Serbia, Italy, Hungary, Ecuador, Czech Republic, Andorra|Bulgaria|BC (Canada)|China, Croatia|Estonia|Germany|Latvia|Lithuania|EU	10	1	0.01	100	200	10000	2000	400	50000

Notation.

PSRGVs of omethoate, 3,5,6-trichloro-2-pyridinol, chlorantraniliprole, N-(2,6-dimethylphenyl)-N-(methoxyacetyl)alanine and emamectin were not noticed and did not apear in the list.

Table S4.9 *The non-dietary chronic daily intake for adolescents (ado) and adults (adu) derived from exposure to the pesticides in soils. Only the positive samples were included in the calculation. CDI values in mg kg^{-1} day^{-1}.*

Pesticides	CDI-(ado-ing)	CDI-(ado-der)	CDI-(ado-inh)	CDI-(adu-ing)	CDI-(adu-der)	CDI-(adu-inh)	CR-(ado-ing)	CR-(ado-der)	CR-(ado-inh)	CR-(adu-ing)	CR-(adu-der)	CR-(adu-inh)
p,p'-DDE	5.99E-10	4.36E-10	7.80E-14	6.63E-10	3.44E-10	8.53E-14	2.04E-10	2.12E-10	2.65E-14	2.25E-10	1.67E-10	2.90E-14
	6.83E-10	4.97E-10	8.89E-14	7.56E-10	3.92E-10	9.72E-14	2.32E-10	2.42E-10	3.02E-14	2.57E-10	1.90E-10	3.31E-14
	3.85E-09	2.80E-09	5.01E-13	4.26E-09	2.21E-09	5.48E-13	1.31E-09	1.36E-09	1.70E-13	1.45E-09	1.07E-09	1.86E-13
	8.33E-09	6.06E-09	1.08E-12	9.21E-09	4.78E-09	1.19E-12	2.83E-09	2.95E-09	3.69E-13	3.13E-09	2.32E-09	4.03E-13
	3.33E-09	2.42E-09	4.33E-13	3.68E-09	1.91E-09	4.73E-13	1.13E-09	1.18E-09	1.47E-13	1.25E-09	9.27E-10	1.61E-13
	6.59E-10	4.80E-10	8.58E-14	7.29E-10	3.78E-10	9.38E-14	2.24E-10	2.33E-10	2.92E-14	2.48E-10	1.84E-10	3.19E-14
	8.87E-10	6.46E-10	1.15E-13	9.81E-10	5.09E-10	1.26E-13	3.02E-10	3.14E-10	3.92E-14	3.34E-10	2.47E-10	4.29E-14
	6.53E-10	4.76E-10	8.50E-14	7.22E-10	3.75E-10	9.30E-14	2.22E-10	2.31E-10	2.89E-14	2.46E-10	1.82E-10	3.16E-14
	6.29E-10	4.58E-10	8.19E-14	6.96E-10	3.61E-10	8.96E-14	2.14E-10	2.23E-10	2.78E-14	2.37E-10	1.75E-10	3.04E-14
	1.40E-09	1.02E-09	1.82E-13	1.54E-09	8.01E-10	1.99E-13	4.75E-10	4.94E-10	6.18E-14	5.25E-10	3.89E-10	6.76E-14
	1.32E-09	9.60E-10	1.72E-13	1.46E-09	7.56E-10	1.88E-13	4.48E-10	4.66E-10	5.83E-14	4.96E-10	3.68E-10	6.38E-14
	2.76E-09	2.01E-09	3.60E-13	3.06E-09	1.58E-09	3.93E-13	9.39E-10	9.78E-10	1.22E-13	1.04E-09	7.70E-10	1.34E-13
	2.85E-09	2.07E-09	3.70E-13	3.15E-09	1.63E-09	4.05E-13	9.68E-10	1.01E-09	1.26E-13	1.07E-09	7.94E-10	1.38E-13
	2.57E-09	1.87E-09	3.34E-13	2.84E-09	1.47E-09	3.65E-13	8.72E-10	9.08E-10	1.14E-13	9.65E-10	7.15E-10	1.24E-13
	1.01E-09	7.33E-10	1.31E-13	1.11E-09	5.78E-10	1.43E-13	3.42E-10	3.56E-10	4.46E-14	3.79E-10	2.81E-10	4.87E-14
	1.82E-09	1.33E-09	2.37E-13	2.02E-09	1.05E-09	2.59E-13	6.19E-10	6.45E-10	8.06E-14	6.85E-10	5.08E-10	8.82E-14
	1.82E-09	1.33E-09	2.37E-13	2.02E-09	1.05E-09	2.59E-13	6.19E-10	6.45E-10	8.06E-14	6.85E-10	5.08E-10	8.82E-14
	5.99E-10	4.36E-10	7.80E-14	6.63E-10	3.44E-10	8.53E-14	2.04E-10	2.12E-10	2.65E-14	2.25E-10	1.67E-10	2.90E-14
p,p'-DDT	2.28E-09	1.66E-09	2.97E-13	2.53E-09	1.31E-09	3.25E-13	7.76E-10	8.08E-10	1.01E-13	8.59E-10	6.37E-10	1.10E-13
	1.53E-08	1.11E-08	1.99E-12	1.69E-08	8.77E-09	2.17E-12	5.20E-09	5.41E-09	6.76E-13	5.75E-09	4.26E-09	7.39E-13
	4.70E-08	3.42E-08	6.12E-12	5.20E-08	2.70E-08	6.69E-12	1.60E-08	1.66E-08	2.08E-12	1.77E-08	1.31E-08	2.27E-12
	6.29E-10	4.58E-10	8.19E-14	6.96E-10	3.61E-10	8.96E-14	2.14E-10	2.23E-10	2.78E-14	2.37E-10	1.75E-10	3.04E-14
	1.89E-09	1.37E-09	2.46E-13	2.09E-09	1.08E-09	2.69E-13	6.42E-10	6.68E-10	8.35E-14	7.10E-10	5.26E-10	9.13E-14
	2.02E-09	1.47E-09	2.63E-13	2.23E-09	1.16E-09	2.87E-13	6.87E-10	7.15E-10	8.94E-14	7.59E-10	5.63E-10	9.77E-14
	8.99E-10	6.54E-10	1.17E-13	9.94E-10	5.16E-10	1.28E-13	3.06E-10	3.18E-10	3.98E-14	3.38E-10	2.51E-10	4.35E-14
	1.16E-09	8.42E-10	1.51E-13	1.28E-09	6.64E-10	1.65E-13	3.93E-10	4.09E-10	5.12E-14	4.35E-10	3.22E-10	5.60E-14
	6.59E-10	4.80E-10	8.58E-14	7.29E-10	3.78E-10	9.38E-14	2.24E-10	2.33E-10	2.92E-14	2.48E-10	1.84E-10	3.19E-14
	6.77E-10	4.93E-10	8.81E-14	7.49E-10	3.89E-10	9.64E-14	2.30E-10	2.40E-10	3.00E-14	2.55E-10	1.89E-10	3.28E-14
p,p'-DDD	1.17E-09	8.51E-10	1.52E-13	1.29E-09	6.70E-10	1.66E-13	2.80E-10	2.92E-10	3.65E-14	3.10E-10	2.30E-10	3.99E-14
	4.96E-09	3.61E-09	6.46E-13	5.49E-09	2.85E-09	7.06E-13	1.19E-09	1.24E-09	1.55E-13	1.32E-09	9.76E-10	1.69E-13
	6.65E-09	4.84E-09	8.66E-13	7.36E-09	3.82E-09	9.47E-13	1.60E-09	1.66E-09	2.08E-13	1.77E-09	1.31E-09	2.27E-13

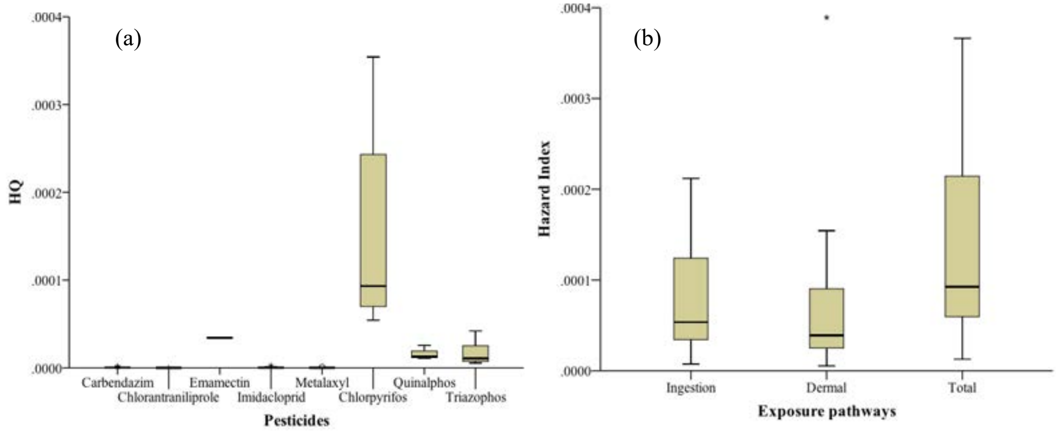


Figure S4.1 *Box plots showing non-cancer risks of pesticides for adolescents (a) and comparison of exposure pathways (b). Only the positive samples were included in the calculation of HQ and HI.*

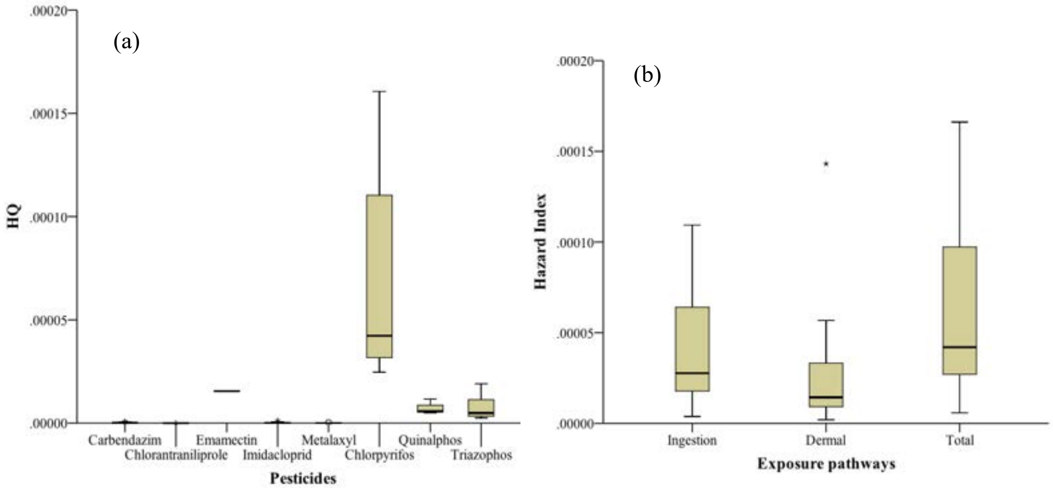


Figure S4.2 *Box plots showing non-cancer risks of pesticides for adults (a) and comparison of exposure pathways (b). Only the positive samples were included in the calculation of HQ and HI.*

5. Ecological risk assessment of pesticide residues in soils from vegetable production areas: A case study in S-Nepal

Pesticides pose a serious risk to ecosystems. In this study, we used European Food Safety Authority methods, such as risk quotient (RQ) and toxicity exposure ratios (TER), to assess the potential ecological risks of 15 pesticide residues detected in agricultural soils in the Gaidahawa Rural Municipality of Nepal. The mean and maximum concentrations of the detected pesticide residues in the soil were used for risk characterization related to soil organisms. RQ_{mean}, TER_{mean} and $RQ_{maximum}$, $TER_{maximum}$ were used to determine general and the worst-case scenarios, respectively. Of all the detected pesticides in soils, the no observed effect concentration (NOEC) for 27% of the pesticides was not available in literature for the tested soil organisms and their TER and RQ could not be calculated. RQ threshold value of ≥1 indicates high risk for organisms. Similarly, TER threshold value of ≥5, which is acceptable trigger point value for chronic exposure, indicates an acceptable risk. The results showed that the worst-case scenario ($RQ_{maximum}$) indicated a high risk for soil organisms from chlorpyrifos [$RQ_{maximum}$ >9 at depths (cm) of 0-5, 15-20 and 35-40 soil layer]; imidacloprid (1.78 in the 35-40 cm soil layer) and profenofos (3.37 in the 0-5 cm and 1.09 in the 35-40 cm soil layer). Likewise, for all the soil depths, the calculated TER for both the general and worst-case scenarios for chlorpyrifos ranged from 0.37 to 3.22, indicating chronic toxicity to F. candida. Furthermore, the risk of organophosphate pesticides for soil organisms in the sampling sites was mainly due to chlorpyrifos, except for two study sites where the risk was from profenofos. Ecological risk assessment (EcoRA) of the pesticide use in the study area indicated that the EFSA soil organisms were at risk at some of the localities where farmers practiced conventional farming. Farmer awareness and training related to pesticide effects on ecological entities and the safe disposal behaviour for pesticide containers including leftover pesticides are urgently needed.

Based on:

Bhandari, G., Atreya, K., Vašíčková, J., Yang, X., Geissen, V., 2020. Ecological risk assessment of pesticide residues in soils from vegetable production areas: A case study in S-Nepal. Submitted to the Environmental Pollution.

5.1 Introduction

Over 4 million tons of pesticides are used annually worldwide (FAO, 2017a). Unfortunately, this number is only expected to increase due to the burgeoning world population demanding more food from shrinking agricultural lands that suffer from declining soil quality. As if that wasn't enough, climate change and the emergence of new pests and diseases are throwing all kinds of new challenges into the mix (Brain and Anderson, 2019; Delcour et al., 2015; Xu et al., 2008). Modern farming methods rely on chemical pesticides to control insects and diseases, thereby improving food quantity. However, both the abundant use and in some cases, misuse of pesticides have contributed to soil pollution (Tsaboula et al., 2016). Research has discovered that pesticides can bioaccumulate and become biomagnified in soil, leading to even greater possible risks for the environment (Haj-Younes et al., 2015; Yuantari et al., 2015). There should be systematic monitoring of pesticide levels in soil that should include an evaluation of pesticide toxicity as well as an ecological risk assessment (EcoRA).

Many ecotoxicological studies have stated that pesticides can induce DNA injury, disturb hormone activity, decrease growth and survival rates, affect reproduction, alter individual food consumption, and diminish the density of earthworm communities (Jager et al., 2007; Uwizeyimana et al., 2017; Wang et al., 2019). Pesticides in soils induced behavioural changes in some organisms thus affecting the environmental system and impairing predator-prey interactions (Dinh Van et al., 2014). A number of toxicological studies (Table S5.1) have confirmed that pesticides are harmful to soil fauna. According to the Regulation SANCO/10329/2002, the European Food Safety Authority (EFSA) recommended risk assessment methods such as risk quotient (RQ) and toxicity exposure ratios (TER) for soil organisms (EFSA et al., 2017). With these laws in place, ecotoxicological testing and systematic monitoring of pesticides in soil are being carried out in Europe and are slowly emerging from other parts of the world. Unfortunately, this testing is not yet a common occurrence in Nepal.

Pesticide application in Nepal has been increasing with the annual import going from 404 tons in 2012 to 635 tons in 2018 (CBS, 2019). The government of Nepal estimated the average application of pesticides to be about 396 g of active ingredients per ha in 2014 (PPD, 2014). About 80% of the imported pesticides were applied to vegetable fields (Adhikari, 2017). There were 169 types of active ingredients in pesticides registered and approved for use in agriculture in 2019 (GC and Neupane, 2019). Earlier studies have shown misuse and overuse of pesticides in agriculture (Aryal et al., 2014; Sharma et al., 2012), mainly in vegetable farming (Atreya et al., 2011; Chhetri et al., 2014). Unsustainable agricultural practices in Nepal expose soils to a mixture of pesticides that could decrease the country's rich biodiversity, which currently includes 17,097 known fauna species (MoFE, 2018). Soil biota such as bacteria, fungi, nematodes, earthworms, enchytraeids, microarthropods (springtails and mites), and insect larvae along with several other organisms help to maintain soil quality: structure and properties, pivotal functions and major ecosystem services. Soil health is of crucial importance as it determines the quality and quantity of food production, biodiversity, and resilience to climate change. Increased use of pesticides carries a greater risk to soil health that may destroy ecological cycles, including the breakdown of organic material, sequestration of carbon, cycling of nutrients, pest suppressiveness of soil and soil fertility (Keesstra et al., 2016; Lavelle et al., 2006).

For the sustainable management and responsible application of pesticides, ecological risk assessment (EcoRA) is necessary. The EFSA's risk assessment procedure mainly involves an assessment of exposure and a characterization of risk (Figure S5.1). The risks posed by pesticides depend on the exposure concentrations and intrinsic (eco) toxicity, expressed as Toxicity-Exposure- Ratio (TER). The TER is interpreted using trigger standards as defined in the EU number 546/2011 (EC, 2002). TERs are identified for single assessments and single organisms. The TER explains the toxicity of a pesticide and provides an impression of the exposure estimates for each species separately. A trigger value equal to 5 represents "safety factors" for earthworms and other soil organisms. TER values <5 and ≥5 indicate high risk (unacceptable) and low risk (acceptable), respectively. The ratio of a measured soil concentration (MSC) or a predicted soil concentration (PSC) to a predicted no-effect concentration (PNEC) is used to calculate RQ (EC, 2002; Palma et al., 2014; Vasickova et al., 2019) which represents no risk (RQ<0.01), lower risk (0.01≤RQ<0.1), moderate risk (0.1≤RQ<1) and higher risk (RQ≥1). Earlier studies conducted elsewhere used both the TER and the RQ to define an EcoRA for pesticides (Thomatou et al., 2013; Vasickova et al., 2019; Wee and Aris, 2017). However, there are scant scientific studies examining the ecological risks of pesticides on soil organisms in Nepal.

This study aims 1) to investigate the potential risk posed by pesticide residues following the EFSA's guidelines for soil organisms [including earthworms *(Eisenia fetida),* enchytraeids *(Enchytraeus crypticus),* springtails *(Folsomia candida),* and mites *(Hypoaspis aculifer)* as well as nitrogen and carbon mineralization microorganisms, which are the recommended invertebrate subjects for ecotoxicological studies (EFSA et al., 2017; Jänsch et al., 2006)]; and 2) to compute the correlation between pesticide risk and a farmer's knowledge about pesticide use and behavior in the environment. This study provides the first evidence of the ecological risk of exposure to the most commonly applied pesticides in Nepal. The findings can be useful in developing effective pesticide risk mitigation strategies and national pesticide policy.

5.2 Materials and Methods

5.2.1 Pesticide residues in the study area

In a previous study (Bhandari et al., 2020) we studied pesticide residues in soils (3 depths) from 11 integrated and 38 conventional vegetable farms of the Gaidahawa Rural Municipality in the Rupandehi district, Nepal. Of the 23 pesticides analysed in our previous study, residues of 15 different pesticides were detected frequently and heavily in soils from conventional farms (Bhandari et al., 2020). Details of these pesticide residues are included here in Table S5.2. In this study we focus on the assessment of ecological risk of these residues. Detailed descriptions of the study area including the soil sampling points and the residues detected are stated in our previous paper (Bhandari et al., 2020). To the best of our knowledge, a residual limit for pesticides in soil has not yet been developed in Nepal. Therefore, we compared the measured concentration of pesticide residues with the guidance values established for different countries (Li and Jennings, 2017). The guidance values are the maximum concentration of individual pesticide residues present in soils posing no ecological risk.

5.2.2 Risk Assessment

Pesticide EcoRA included an assessment of exposure and ecotoxicity (effects) (Figure S5.1). We used two common methods: a) the TER for 4 selected species of the EFSA soil organisms (EC, 2002), and b) the risk quotient (RQ) for each pesticide residue (Renaud et al., 2018). When the no observed effect concentration (NOEC) value for a pesticide was available via systematic review, the RQ and TER were estimated to assess chronic EcoRA. When the value was not known, the risk could not be assessed. Additionally, we compared pesticide concentrations in soils with pesticide soil regulatory guidance values (PSRGVs) to see if findings using the TER and the RQ methods corresponded with the guidance values. The concentrations of banned pesticides such as DDT and its principal metabolites in soils were compared with the existing threshold values for soils. A farmer’s field was denoted as a “site”. The risk of organophosphate in pesticide mixtures was estimated by adding up all the individual pesticide risks with a common mode of action (Damodaran, 2019) based on the concentration addition (CA) technique (Bundschuh et al., 2014). The risk of pesticide mixtures for other chemical groups could not be computed because ecotoxicity data was not available.

5.2.2.1 Assessment of exposure

The concentration of pesticide residues detected in the 3 depths (0-5, 15-20 and 35-40 cm) (Bhandari et al., 2020) was used for the risk assessment. The geometric mean and maximum pesticide levels detected at the studied sites were used as the mean measured soil concentration (MSC_{mn}) and the maximum measured soil concentration (MSC_{mx}). In the first case, the value gives a general scenario (GS) (TER_{mn} or RQ_{mn}) and, in the second case, the value gives the worst-case scenario (WS) (TER_{mx} or RQ_{mx}) (Palma et al., 2014).

5.2.2.2 Assessment of toxicity

The toxicity assessment was based on the available ecotoxicological data from i) the pesticide properties database (PPDB) https://sitem.herts.ac.uk/aeru/ppdb/; ii) the draft assessment reports (DARs) from the EFSA; and iii) a basic literature search using the Web of Science Core Collection and Scopus databases. The search terms included:

(i) Pesticide AND soil AND *toxic*
(ii) Pesticide AND soil AND organism

A systematic review of literature was conducted based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (Moher et al., 2009) for the assessment of toxicity including the effect of pesticides on soil organisms (Supplementary material, Figure S5.2 and Table S5.1).

In order to assess the ecological risks of pesticides, there are several ecotoxicological aspects that can be examined such as the no observed effect concentration (NOEC) and/or the lethal concentration at which 50% of the examined organisms exhibit mortality (LC_{50}), as well as a median effective concentration (EC_{50}) for organisms such as the earthworm *(E. fetida),* the enchytraeid *(E. crypticus),* the springtail *(F. candida),* the mite *(H. aculifer)* and the nitrogen and carbon mineralization microorganisms. These are organisms that need to be included in any study assessing pesticides for approval by the EFSA for the European Union. Data from past studies that were in agreement with the Organisation for Economic Co-operation and Development (OECD) standardized procedures for the organisms was considered for the current study. Since the toxicological dose descriptors listed above differed with their corresponding ecotoxicological output, they could not be compared. Although pesticides detected in soil have their LC_{50} as well as EC_{50}, the present study was based on the available NOEC endpoints. If multiple NOEC values were available for a single organism, the geometric mean was considered and used. Of the 15 pesticides (Table S5.2), the NOEC for DDD, DDE, quinalphos and triazophos were not available for the tested species thus, the TER and RQ for these compounds could not be calculated.

Using the NOEC value, we derived the predicted no-effect concentration for the most sensitive species ($PNEC_{mss}$). To overcome issues such as insufficient toxicity data, errors and inaccuracy related to the conservative approach, the $PNEC_{mss}$ value was estimated as the lowest long-term NOEC divided by the assessment factor (AF). The most susceptible organism for each pesticide was selected to obtain the $PNEC_{mss}$ with an AF to account for potential chronic risks. The selection of the AF was based on the guidance document of the EU (EC, 2002) and could range from 10 to 1000: (i) an AF of 1000 was used in a case where at least one LC_{50} at one ecological level was available; (ii) an AF of 100 was used in a case where data from a long term assay was available; and (iii) an AF of 50 and 10 were used in the cases where two and three or more NOECs were available, respectively. In the present study, based on available long-term NOECs, we used an AF of 100, 50 and 10 (Table 5.1).

Table 5.1 *Ecotoxicology (NOEC and NSDE in µg/kg) of pesticides for E. fetida (earthworm), E. crypticus (enchytraeid), F. candida (springtail), H. aculeifer (mite), and N and C mineralization organisms extracted from different sources (see details in footnote). Degradation products of chlorpyrifos and metalaxyl such as 3,5,6-TCP and N-alanine indicated 3,5,6-trichloro-2-pyridinol and N-(2,6-dimethylphenyl)-N-(methoxyacetyl)alanine, respectively. The N-alanine was referenced as CGA 62826 in the EFSA document and hence its NOEC was used in the calculation. PNEC = Predicted no-effect concentration; NOEC = No observed effect concentration; AF = Assessment factor.*

Group	Compound	*E. fetida,* NOEC	*E. crypticus,* NOEC	*F. candida,* NOEC	*H. aculeifer,* NOEC	NSDE for N|C mineralization microorganisms	Critical concentration	PNEC AF	$PNEC_{mss}$
AD	Chlorantraniliprole	1000000d	na	390d	100000d	700ad|700ad	390	10	39
BD	Carbendazim	1000a,d	100b◊	na	na	4800d^|4800d^	100	10	10
MOD	Emamectin	2000d	na	na	na	400d^|na	2000	50	40
NND	Imidacloprid	178a	1000g	1250d	≥2670d	na	178	10	17.8
OC	DDT	280000ah	na	176000ah	na	na	176000	50	3520
OP	Chlorpyrifos	12700a	5000e	65c	na	na|4800ad	65	10	6.5
	Profenofos	na	na	<50f	na	250△|na	50	50	1
PA	Metalaxyl	40000ad	na	125000d#	na	1350d^|1350d^	40000	10	4000
UNC	3,5,6-TCP	4600a,d	na	na	na	4150d^|4150d^	4600	50	92
	N-alanine	500000d	na	na	na	na	500000	100	5000

Note.
Data stated as "≥"number or "<"number, the given number was used in a calculation.
a Lewis et al. (2006).
b Novais et al. (2010); ◊ = Data for *Enchytraeus crypticus* was not found in literatures, hence NOEC of carbendazim is used for *Enchytraeus albidus*.
c (Herbert et al., 2004); d Data collected from the EFSA documents that are available online; e (Carniel, 2019).
f (Liu et al., 2012); △= nitrification rate; g (de Lima et al., 2017).
h (RIVM, 2015).
$PNEC_{mss}$ = the lowest long-term NOEC of the most susceptible species/AF.
na = Information on toxicity was not available in the refereed databases.
NSDE = No significant adverse effect. ^ = <25% effect considered as NSDE.
In the case of metalaxyl, NSDE data for ridomil gold was used. # = Toxicity data of metalaxyl to *Folsomia candida* was not available, hence the data of ridomil was used in the calculation.
Pesticides group: AD = Anthranilic diamide; UNC = Unclassified; OP = Organophosphate; NND = Neonicotinoid; OC = Organochlorine; BD = Benzimidazole; PA = Phenylamide; MOD = Micro-organism derived.

5.2.2.3 Risk characterization of a single pesticide

The most commonly used methods for assessing ecological risk are the Toxicity-Exposure-Ratio (TER) (EC, 2002) and the Risk Quotient (RQ) (Renaud et al., 2018). TERs based on NOECs for single test organisms, which included *E. fetida, E. crypticus, F. candida, H. aculifer* as well as nitrogen and carbon mineralization microorganisms were considered.

Based on EC (2009), the TER approach relates toxicity and exposure. As mentioned earlier, in the cases denoted as "≥ value" or "< value", the given value was used. The TER for each pesticide was estimated by using the TER for the test organisms ($TER_{species}$) and the following Equation 5.1.

$$TER_{species} = \frac{NOEC_{species}}{MSC_{maximum\ or\ mean}} \quad (5.1)$$

where, NOEC = No observed effect concentration and MSC = Measured pesticide concentration in soil.

The EC (2002) defined cut-off (trigger point) values of 5 and 10 for chronic and acute toxicity for soil organisms, respectively. Pesticide risk was considered negligible if the TER exceeded the cut-off values. TER values of ≥10 or ≥5, which are acceptable trigger point values for acute and chronic exposure, respectively, indicated an acceptable risk for the organisms (Jaabiri Kamoun et al., 2017).

The risk quotient of a pesticide i (RQ_i) provided an index for the risk of a single pesticide and was calculated as described in Equation 5.2.

$$RQ_i = \frac{MSC_{soil}}{PNEC_{mss}} \quad (5.2)$$

where, MSC = Measured pesticide concentration in soil and $PNEC_{mss}$ = Predicted no-effect concentration for the most sensitive species.

The classification of the risk quotient was based on the previous existing studies (Sánchez-Bayo et al., 2002; Vryzas et al., 2011): no risk ($RQ<0.01$), lower risk ($0.01 \le RQ < 0.1$), moderate risk ($0.1 \le RQ < 1$) and higher risk ($RQ \ge 1$).

5.2.2.4 Risk characterization of pesticide mixtures-concentration using addition model

The widely accepted concentration addition (CA) approach was used to calculate the toxicity of pesticide cocktails (Vasickova et al., 2019; Wee and Aris, 2017). Multi-pesticide exposures can lead to additive actions. The mixture RQ (RQ_{mix}) of organophosphates (OP) was estimated by adding up the individual RQ_i of each pesticide that belongs to the OP group. Furthermore, the total risk of multiple pesticide residues of a site ($\sum RQ_{site}$) was estimated using the concentration addition (CA) based on the mixture risk assessment method (Bundschuh et al., 2014). CA, the most suitable model to use in ecotoxicological studies (Chen et al., 2014), is based on the assumption that all pesticides in a cocktail have the same mode of action and can be stated as in Equation 5.3.

$$\sum(RQ_{site} \text{ or } RQ_{mix}) = \sum_{k=1}^{n} RQ_i = \sum_{k=1}^{n} (MSC_i/PNEC_i) \quad (5.3)$$

where, RQ_{site} = Risk quotient of a site; RQ_{mix} = Risk quotient of pesticide mixtures; RQ_i = Risk quotient of a pesticide i; MSC_i = Measured soil concentration of a pesticide i; $PNEC_i$ = Predicted no-effect concentration of a pesticide i; n = number of pesticides.

The classification of RQ_{mix} was based on Sánchez-Bayo et al. (2002) and Vasickova et al. (2019) as mentioned for the RQ above.

To correlate the classified RQ at sites where the pesticide knowledge and behaviour of farmers was known, we developed a summative score based on farmer's replies to the survey questions (Table 5.2).

Table 5.2 *Variables (n=6) for farmers pesticide use KNB score. Results of the questionnaire survey among the farmers was based on our previous study (Bhandari et al., 2018). Commercial vegetable farmers from different villages were selected for the survey conducted in 2017. Of the 183 farmers, this study included the scores of 49 farmers that were selected randomly.*

Variables	Description	KNB values (1 or 0)
ANIMALS	Do pesticides negatively affect animals?	0=no, 1=yes
BIRDS	Do pesticides negatively affect birds around you?	0=no, 1=yes
FISHES	Do pesticides negatively affect fishes?	0=no, 1=yes
HONEYBEES	Do pesticides negatively affect honeybees?	0=no, 1=yes
PESCONT	Do you throw pesticides container at field after use?	0=yes, 1=no
UNUSEDPES	Do you throw unused/leftover pesticides at field?	0=yes, 1=no

The contribution of each RQ_i to RQ_{site} or RQ_{mix} was derived following Equation 5.4.

$$\%\ \text{contribution} = \left(\frac{RQ_i}{\sum(\mathrm{RQ_{site}}\ \text{or}\ \mathrm{RQ_{mix}})}\right) \quad (5.4)$$

where, RQ_i = Risk quotient of a pesticide i; RQ_{site} = Risk quotient of a site; RQ_{mix} = Risk quotient of pesticide mixtures.

5.2.3 Statistical analysis

Data analysis on the concentration of pesticides ≥LODs was performed. Data entries where pesticide concentrations were <LODs were left empty and excluded from the study (Sun et al., 2016). We used the Spearman's rho correlation coefficient to calculate the linear correlation of the risk quotient (RQ_{site}) calculated for the soil depths (0-5, 15-20 and 35-40 cm) and the knowledge and behaviour (KNB) of farmers. A p-value less than 0.05 was considered significant. The correlation was also used to demonstrate if there was a positive relationship between the risks of pesticides at different sites and the farmers' pesticide KNB scores. The score was based on the sum of values from each variable listed in Table 5.2.

5.3 Results

5.3.1 Risk assessment

5.3.1.1 Ecological risk based on the TER approach

Data from ecotoxicological tests conducted following the ISO/OECD procedures were considered for this research. Most ecotoxicological information about pesticides included data for only a single organism. Toxicological information for several detected pesticides was unavailable and thus assessment of their potential ecological risk was not possible. Data on the NOEC for *E. fetida* was available for 60% of the 15 detected pesticides (Table 5.1). In Nepal, ecotoxicological studies have not been carried for many of the pesticides that have been approved for agricultural use. However, ecotoxicological studies from other countries have been used (Table S5.1).

The toxicity exposure ratio (TER) for a general scenario (GS) and a worst-case scenario (WS) are presented in Table 5.3a-5.3c. For both scenarios, chronic risk for *E. fetida, E. crypticus, and H. aculifer* was negligible for all assessed pesticides at all the depths of soil, except chlorpyrifos. Both TER_{mx} and TER_{mn} calculated for different depths were above the cut-off value of 5 for chronic toxicity. Pesticides such as carbendazim, chlorantraniliprole, DDT, emamectin, metalaxyl and N-alanine notably showed high TERs at different depths. Of all pesticides, chlorantraniliprole showed the highest TER (TER=494430) at 35-40 cm for *E. fetida* under the GS.

Table 5.3a *Maximum and mean toxicity exposure ratios (TER_{mx} and TER_{mn}) for soil organisms at 0-5 cm. TER values <5 (in bold) and >5 indicated risk and no risk, respectively. WS = worst scenario and GS = general scenario. MSC_{mx} and MSC_{mn} indicated the maximum and mean concentration of pesticides in soils (in µg/kg), respectively. DDT represented the sum of p, p'-DDT and o, p'-DDT concentrations. "NA" = not applicable. Degradation products such as 3,5,6-TCP and N-alanine indicated 3,5,6-trichloro-2-pyridinol and N-(2,6-dimethylphenyl)-N-(methoxyacetyl)alanine, respectively.*

Pesticides	MSC_{mx}	MSC_{mn}	E. fetida Chronic		E. crypticus Chronic		F. candida chronic		H. aculeifer chronic	
			TER_{mx} (WS)	TER_{mn} (GS)	TER_{mx} (WS)	TER_{mn} (GS)	TER_{mx} (WS)	TER_{mn} (GS)	TER_{mx} (WS)	TER_{mn} (GS)
3,5,6-TCP	57.4	8.69	80.1	529	NA	NA	NA	NA	NA	NA
Carbendazim	6.45	1.62	155	617	15.5	61.7	NA	NA	NA	NA
Chlorantraniliprole	14.2	3.23	70423	309723	NA	NA	27.5	121	7042	30972
Chlorpyrifos	177	32.5	71.8	391	28.3	154	**0.37**	**2.00**	NA	NA
DDT	5.41	3.53	51756	79330	NA	NA	32532	49865	NA	NA
Emamectin	3.30	3.30	606	606	NA	NA	NA	NA	NA	NA
Imidacloprid	13.8	3.94	12.9	45.2	72.5	254	90.6	317	193	678
Metalaxyl	6.49	2.44	6163	16382	NA	NA	19260	51194	NA	NA
N-alanine	2.49	2.49	200803	200803	NA	NA	NA	NA	NA	NA
Profenofos	3.37	1.74	NA	NA	NA	NA	14.8	29	NA	NA

Table 5.3b *The TER at 15-20 cm. The pesticide concentration in µg/kg. N-alanine and profenofos residues were not detected at the depth, hence did not appear here.*

Pesticides	MSC_{mx}	MSC_{mn}	E. fetida Chronic		E. crypticus Chronic		F. candida Chronic		H. aculeifer Chronic	
			TER_{mx} (WS)	TER_{mn} (GS)	TER_{mx} (WS)	TER_{mn} (GS)	TER_{mx} (WS)	TER_{mn} (GS)	TER_{mx} (WS)	TER_{mn} (GS)
3,5,6-TCP	15.9	7.26	289	633	NA	NA	NA	NA	NA	NA
Carbendazim	5.55	2.01	180	498	18.0	49.8	NA	NA	NA	NA
Chlorantraniliprole	4.22	2.06	236967	485546	NA	NA	92.4	189	23697	48555
Chlorpyrifos	68.4	20.2	186	629	73.1	248	**0.95**	**3.22**	NA	NA
DDT	29.8	7.98	9402	35088	NA	NA	5910	22055	NA	NA
Imidacloprid	7.57	2.06	23.5	86.6	132	486	165	608	353	1299
Metalaxyl	4.23	2.67	9456	14961	NA	NA	29551	46752	NA	NA

Table 5.3c *The TER at 35-40 cm. The pesticide concentration in µg/kg.*

Pesticides	MSC_{mx}	MSC_{mn}	E. fetida Chronic		E. crypticus Chronic		F. candida Chronic		H. aculeifer Chronic	
			TER_{mx} (WS)	TER_{mn} (GS)	TER_{mx} (WS)	TER_{mn} (GS)	TER_{mx} (WS)	TER_{mn} (GS)	TER_{mx} (WS)	TER_{mn} (GS)
3,5,6-TCP	31.1	7.26	148	634	NA	NA	NA	NA	NA	NA
Carbendazim	3.41	2.23	293	448	29.3	44.8	NA	NA	NA	NA
Chlorantraniliprole	6.52	2.02	153374	494430	NA	NA	59.8	193	15337	49443.02
Chlorpyrifos	60.6	26.4	210	481	82.5	189	**1.07**	**2.46**	NA	NA
DDT	81.1	13.5	3454	20734	NA	NA	2171	13033	NA	NA
Imidacloprid	31.6	3.35	5.63	53.2	31.7	299	39.6	373	84.5	797.68
Metalaxyl	8.97	2.41	4459	16582	NA	NA	13935	51818	NA	NA
N-alanine	1.56	1.32	320513	379967	NA	NA	NA	NA	NA	NA
Profenofos	1.09	1.09	NA	NA	NA	NA	45.9	45.9	NA	NA

The calculated TER of chlorpyrifos for GS and WS at all depths of soil was lower than the corresponding trigger value which indicated potential risk (TER <5) to non-target soil organisms. It has been observed that MSC_{mx} and MSC_{mn} of chlorpyrifos posed a risk to *F. candida* based on TER_{mx} and TER_{mn}, respectively. Furthermore, chlorpyrifos showed the lowest TER (TER=0.37) at 0-5 cm for *F. candida* under the WS.

5.3.1.2 Ecological risk based on RQ approach

The risk quotient (RQ) values under GS and WS for the studied pesticides are shown in Table 5.4. Chlorpyrifos in all the depths showed RQs >1 for both MSCs geometric mean and MSCs maximum. Profenofos showed RQs >1 for both MSCs at 0-5 cm and 35-40 cm depths. In addition to chlorpyrifos and profenofos, our results suggested a potential risk of imidacloprid to soil organisms at 35-40 cm under the WS. Due to the higher RQ values at all depths and scenarios, the risk posed by chlorpyrifos was worrisome. The top 3 pesticides ranked in decreasing order of their toxicity to the in-soil organisms were: chlorpyrifos > profenofos > imidacloprid, indicating the highest toxicity for organophosphates (OPs).

Table 5.4 *The Risk Quotient (RQ) for the most sensible organisms at different depths of soil. RQ values for an individual pesticide at the depth calculated as a ratio of the measured soil concentrations [($MSC_{mx\ or\ mn}$) µg/kg] divided by the $PNEC_{mss}$ µg/kg (reported in Table 5.3a-5.3c and Table 5.1). WS = worst scenario and GS = general scenario. The calculated values of RQ were categorised into 4 risk levels: no risk (RQ<0.01), lower risk (0.01≤RQ<0.1), moderate risk (0.1≤RQ<1) and higher risk (RQ≥1). RQ values in bold indicated higher risk. DDT represented the sum of p, p'-DDT and o, p'-DDT concentrations. "NA" = not applicable. Degradation products such as 3,5,6-TCP and N-alanine indicated 3,5,6-trichloro-2-pyridinol and N-(2,6-dimethylphenyl)-N-(methoxyacetyl)alanine, respectively.*

Pesticides	Risk Quotient (RQ)					
	0-5 cm		15-20 cm		35-40 cm	
	RQ_{mx} (WS)	RQ_{mn} (GS)	RQ_{mx} (WS)	RQ_{mn} (GS)	RQ_{mx} (WS)	RQ_{mn} (GS)
3,5,6-TCP	0.62	0.09	0.17	0.08	0.34	0.08
Carbendazim	0.65	0.16	0.56	0.20	0.34	0.22
Chlorantraniliprole	0.36	0.08	0.11	0.05	0.17	0.05
Chlorpyrifos	**27.23**	**4.99**	**10.52**	**3.10**	**9.32**	**4.06**
DDT	<0.01	<0.01	0.01	<0.01	0.02	<0.01
Emamectin	0.08	0.08	NA	NA	NA	NA
Imidacloprid	0.78	0.22	0.43	0.12	**1.78**	0.19
Metalaxyl	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01
N-alanine	<0.01	<0.01	NA	NA	<0.01	<0.01
Profenofos	**3.37**	**1.74**	NA	NA	**1.09**	**1.09**

Furthermore, 84% of the sites represented no risk (∑RQ_{site} <0.01) and 16% showed a higher risk (∑RQ_{site} ≥1). The highest risk based on RQ_{site} was 30.60 for a conventional farmer's site with the identification code F53 and was indicated for the depth of 15-20 cm (Table S5.3). All IPM sites such as F4, F5, F7, F32, F36, F56, F62, F102, F109, F143 and F158 showed no risk (RQ<0.01). The contribution for the RQ was 98% and 2% for chlorpyrifos and profenofos, respectively. Table S5.3 presents pesticide contributions measured at 8 sites with a higher risk (∑RQsite≥1) to the overall risk. Although multiple pesticide residues were observed at a single site, this doesn't infer that pesticides contributed equally to the overall risk posed by the pesticide cocktail. Table S5.3 shows that chlorpyrifos contributed higher than profenofos to the overall risk at one site (∑RQ_{site}). The RQ of OPs at depths (cm) 0-5, 15-20 and 35-40 ranged from 0-11, 0-31 and 0-9, respectively (Table 5.5).

Table 5.5 *Correlation matrix between risk quotient (RQsite) of organophosphates (OPs) and knowledge and behaviour (KNB) score at different depths (cm) of soil (n=49). Descriptive statistics of the variables in parenthesis. Values in bold represented either positively or negatively correlated.*

Variables (Min-Max; Mean±SD)	RQ _0-5	RQ _15-20	RQ _35-40	KNB
RQ _0-5 (0-11; 0.34±1.57)	1	**0.57***	0.27	**-0.44***
RQ _15-20 (0-31; 0.96±4.45)		1	**0.62***	**-0.60***
RQ _35-40 (0-9; 0.25±1.36)			1	**-0.38***
KNB (1-6; 3.63±1.81)				1

* Correlation is significant at the 0.01 level (2-tailed). OPs included in the analysis were profenofos and chlorpyrifos.

Overall, both the RQ and TER methods seemed conservative as the $PNEC_{mss}$ applied an assessment factor of 10-1000 due to the scarcity of NOEC values and thus considered as the worst-case scenarios. For example, in this study, we considered the RQ_{mn} with geometric mean of positives only, and the RQ_{mx} with maximum measured soil concentration. Among the 15 compounds that were detected (Table S5.2), a higher risk (RQ_{mx}>1) was observed for imidacloprid, profenofos and chlorpyrifos, while a higher risk for sites ($\sum RQ_{site}$>1) was posed by chlorpyrifos and profenofos only (Table S5.3).

5.3.2 Perspectives on pesticide risk and farmers' knowledge and behaviour (KNB)

Data on farmers' knowledge and behaviour originated from our previous study (Bhandari et al., 2018). The knowledge score (mean±SD) of farmers about the effect of pesticides on animals, birds, fishes and honeybees was 0.84±0.37, 0.51±0.51, 0.59±0.50 and 0.51±0.51, respectively. Likewise, the behaviour score (mean±SD) of farmers concerning pesticide waste management and correct application was 0.45±0.50 and 0.73±0.45, respectively. The knowledge score ranged from 1 to 4 and the behaviour score ranged from 1 to 2. About 45% of the farmers managed their pesticide packets/containers by burning the waste at a designated area, while 73% of the farmers kept the leftover pesticides and reused them. During a visit to a farmer's field, packets and containers of pesticides were observed simply discarded on the ground, which was unsafe and indicated poor hygiene in fields (Figure 5.1). The total KNB score (mean±SD) for farmers was 3.63±1.81, ranging from 1 to 6. The score indicated a level of awareness of farmers related to pesticide effects and waste management.

Figure 5.1 *Unsafe disposal of pesticide packets and containers at fields.*

The correlation between the KNB score and the risk quotient (RQ) of pesticides at different farm sites is shown in Table 5.5. The pesticide risk at sites at all depths was negatively correlated (p<0.01) with the KNB score. A significant positive correlation was observed among RQs of organophosphate at depths (cm) 0-5 and 15-20 as well as 15-20 and 35-40.

5.4 Discussion

5.4.1 Pesticide residues in the soils

Although mathematical equations have been used for estimating predicted pesticide environmental concentrations (PEC), the use of real measured concentrations in the agricultural fields (MSC) instead of modelled (PEC) for the pesticide EcoRA provides significant benefits since it gives an accurate measurement of pesticides and includes the inherent heterogeneity of ecosystems (ECOFRAM, 1999). The use of modelled PEC data in the pesticide evaluation process has also been criticized due to its limitation on reflecting the dissipation of pesticides in the environment (Vasickova et al., 2019). Due to higher application rates of pesticides, PEC of most pesticides were much higher than their MSC, indicating that the risk of pesticides could be overestimated due to the use of PEC in the risk assessment processes (Bhandari et al., 2020).

Of all pesticides, chlorpyrifos showed the highest concentration at all the depths. DDT, an organochlorine insecticide has been banned for use in Nepal since 2001 (PQPMC, 2019), however its residues were detected at all the depths as they degrade very slowly in the environment (Boul, 2010). Similar studies (Tan et al., 2020; Xu et al., 2020) done elsewhere showed the highest concentration of carbendazim. Residues of HCH and DDT were detected at higher concentrations in bottom soils from Hong Kong (Zhang et al., 2006). At the 35-40 cm depth, residues of N-alanine were more frequently detected. Risk was due to higher concentrations of DDT and endosulfan, the frequently occurring residues in soil (Yadav et al., 2016). Most frequently detected pesticides in Chinese agricultural topsoil were imidacloprid and emamectin benzoate (Tan et al., 2020). The presence of several pesticides in soil increased the ecotoxicity and caused several effects (Table S5.1), including the death of non-target soil organisms (Cang et al., 2017; Tiwari et al., 2019).

5.4.2 Ecological risk based on TER, RQ including threshold and guidance values

Ecotoxicological data is a prime requisite when performing studies on EcoRA (Frampton, 2000). The ecotoxicity was especially high due to chlorpyrifos residues in soils (Table 5.3a-5.3c). Thomatou et al. (2013) demonstrated a non-acceptable ecological risk due to chlorpyrifos methyl in Greece. In the same study, pesticides with the highest ecotoxicity were organophosphates (OPs). The major contributors to ecotoxicity in many different studies were triazoles (Vasickova et al., 2019), OPs (Wee and Aris, 2017), triazines and OPs

(Palma et al., 2014), and triazoles, carbamates and neonicotinoids (Xu et al., 2020). In our study, OPs most notably contributed to the ecological risk, while the other groups didn't.

The ecological risk based on TER under general scenario (GS) and worst-case scenario (WS) is shown in Table 5.3a-5.3c. Of all pesticides and soil organisms, chlorpyrifos exhibited higher toxicity under both scenarios for *F. candida* due to its higher toxicity persistence in a tropical climate (Watts, 2012). The higher toxicity might be due to higher concentrations of chlorpyrifos and its lower NOEC. Chlorpyrifos was indicated as one of the most acutely as well as chronically toxic pesticides for soil organisms (USEPA, 2009). For imidacloprid, the TER_{mx} value of *E. fetida* at 35-40 cm under the WS was observed closer to its trigger point value which might be due to its exposure to the pesticide. In a multi-level ecotoxicological study, Wang et al. (2019) also demonstrated a toxicity of imidacloprid for *E. fetida*. Of all pesticides and organisms examined in a previous study (de Lima et al., 2017), imidacloprid was found to be the most toxic compound to *F. candida*, which is known to be very susceptible to pesticides and is one of the most susceptible among soil invertebrates (Fountain and Hopkin, 2005). Although chlorantraniliprole was applied in higher doses than recommended on vegetables such as chillies (Bhandari et al., 2018), it showed greater TER values (Table 5.3a-5.3c), indicating negligible risk at all depths of soil. However, the risk assessment of the pesticide applied to a fruiting vegetable by EFSA presented a chronic risk to *F. candida* (TER=3) (EFSA, 2013a). In the same study, the ecotoxicity of chlorantraniliprole was observed for *F. candida* in fruits such as grapes (TER=1.9) and pomes (TER=1.4).

Our study presented a contradictory trend for chlorpyrifos and profenofos. Both the pesticides demonstrated higher risks (RQs > 1) for both scenarios: general and worst-case. In a previous study on risk assessment, chlorpyrifos presented a similar trend (Wee and Aris, 2017). The major contribution to the higher risk for 6 sites was only for chlorpyrifos and ranged from 98 to 100%. A similar study (Chen et al., 2020b) indicated that chlorpyrifos and butachlor were the main pollutants. In the arable soils of the Czech Republic, Vasickova et al. (2019) identified that 11% of sites had no risk and 35% of sites had higher risk. One study reported a higher risk in 29% of the sites, mainly due to the use of chemical pesticides that have been banned in Europe (Iturburu et al., 2019). In our study, chlorpyrifos significantly contributed to the overall risk of a site ($\sum RQ_{site}$), a finding similar to a previous study (Wee and Aris, 2017). Chlorpyrifos, profenofos and imidacloprid have an ability to persist in soil (Lewis et al., 2006) and were used in higher doses than the recommended (Bhandari et al., 2018); all of which might have caused moderate to higher ecological risks (RQ). Li et al. (2018) also estimated lower to moderate ecological risks due to simazine. As described by Montuori et al. (2016), the RQ values may be less relevant in other regions because of the variation in seasons, agricultural practices, contamination levels, and distribution of pollutants. For all the pesticides that showed higher risk (RQ>1), a future site-specific risk assessment is required to better understand the risks of specific pesticides (Pivato et al., 2017). It is noteworthy to mention that all of the sites that were from the integrated farming had no risk (∑RQsite <0.01); however, 21% of the sites from conventional farming had high risk (∑RQsite ≥1).

The threshold value of DDT in soil (μg/kg) for the safety of soil organisms is 10 (Jongbloed et al., 1996). The Dutch ecological limit for DDT as well as DDD and DDE in soil is 10 μg/kg (RIVM, 2015), the maximum permissible concentration in soil based on direct ecotoxicology. The DDT (o, p'-DDT+p, p'-DDT) mean concentration in 35-40 cm from our study area was above 10 μg/kg (Table 5.3c), indicating the higher ecotoxicity associated with DDT. Furthermore, the mean concentration of p, p'-DDD at the same depth was slightly greater than the Dutch standard for DDD in soil (Table S5.2), which might affect soil organisms. However, the mean concentration of p, p'-DDE in soils did not exceed the standard. The high TER and low RQ values for DDT in Table 5.3a-5.3c and Table 5.4, respectively, further supported the finding. Our previous study (Bhandari et al., 2020) indicated that fungicides such as carbendazim and metalaxyl and insecticides such as chlorpyrifos and imidacloprid had concentration in soils below the guidance values (PSRGVs). However, the current EcoRA showed moderate to high risks to soil organisms from the aforementioned pesticides and did not converge with the guidance values, except for metalaxyl which showed negligible risks. Different methods and databases used in the EcoRA may preclude the effective comparison among the estimated risks (Wang et al., 2009), henceforth our results are less consistent. In the PSRGVs, Ukraine considered 1 μg/kg as a benchmark for the concentration of profenofos in soil. The profenofos concentrations in 3% of our soil samples were above this benchmark, indicating that ecological risk associated with profenofos pollution should be considered. Furthermore, the PSRGVs for 3,5,6-TCP, N-alanine and chlorantraniliprole were not found, hence their estimated risk (TER and RQ) could not be compared.

5.4.3 Risk quotient and its relationship with farmers' knowledge and behaviour (KNW)

A significant correlation ($p<0.01$) existed between pesticide risk (RQ) at a farm site and the farmer's KNW related to the effects and management of pesticides. Farmers who were aware of the ecological effects of pesticides and the appropriate waste management measures that should be taken had a negligible pesticide risk at their sites. Although demonstrating no relationship between pesticide risk and knowledge (Lekei et al., 2014a), many other studies have highlighted the significance of a farmer's knowledge regarding pesticide effects and management (Mohanty et al., 2013; Wang et al., 2017a; Wang et al., 2017b; Yang et al., 2014). Farmers were at high risk due to the lack of knowledge and training related to pesticides (Akter et al., 2018; Atreya et al., 2012). A few farmers randomly disposed of pesticide containers in fields after carrying out pesticide applications (Figure 5.1). A similar disposal method for pesticide packaging was common among farmers in Tanzania (Lekei et al., 2014a) and Ghana (Okoffo et al., 2016). Furthermore, unacceptable levels of exposure to organophosphates caused high ecological risk (RQ>1) in Malaysia (Wee and Aris, 2017). In Costa Rica, an RQ>1 was observed and believed to be due to exposure to pyrethroids (Fournier et al., 2018) and in China, the same can be said for organochlorines (Chen et al., 2020a). Organophosphate pesticides are commonly used in Nepal (Aryal et al., 2014). This study demonstrated that there was a high risk of organophosphate exposure at farm sites and the risk was linked to poor knowledge and behaviour related to chlorpyrifos and profenofos exposure and waste management.

5.4.4 Uncertainty and variability related to risk assessment

In this section, uncertainty and variability regarding the EcoRA performed are recognized and discussed. For every EcoRA, uncertainty and variability is inevitable and the risk cannot be estimated with absolute certainty (USEPA, 2004). Of course, the EcoRA rests on and is limited by the availability of data and handling (i.e. strength and excellence) (Wee and Aris, 2017). Pesticides were not detected in most of the soil samples (due to the limits of detection) (Table S5.2). In our study, data on pesticide concentrations <LOD were excluded which could have led to an overestimation of the mean concentration of pesticides and their associated risks. However, the TER_{mx} and RQ_{mx} of pesticides (values in bold of Table 5.3a-5.3c and Table 5.4) allows us to say that, considering the worst-case scenario, the ecological risk of several pesticides is notably high. Variability in endpoint data and risk assessment models accelerate the uncertainty (Chen, 2005). Uncertainty related to ecotoxicity data and models can be anticipated since we used the NOEC data from studies with known ISO/OECD procedures and the models for risk assessment were based on EFSA methods.

For reducing uncertainties due to variations in soil quality, Dutch EC_{50} values were corrected for location-specific differences in samples, considering the organic content and clay material in soils (Rutgers et al., 2008). Therefore, the use of NOEC values in this study without any correction for differences in backgrounds such as with Nepalese soil properties, pesticide application practices and meteorological parameters has brought a higher level of uncertainty. Furthermore, the use of international pesticide soil regulatory guidance values for comparisons with measured pesticide concentration (MSC) in our soil samples without corrections could also increase uncertainty. The aforementioned properties, practises and parameters may vary within the country. Generalization of results from the site-specific research conducted in previous studies may not represent the current scenario of risks, thus conclusion should be drawn with caution when comparing findings to other areas of Nepal. Nevertheless, information from this study provides a baseline of pesticide EcoRA for policy makers of Nepal.

Ecotoxicological information about chemical pesticides and their degradation products are not always available and should be incorporated in future risk assessments. For instance, the EcoRA of N-alanine should be considered more in testing protocols because of its persistence in soils. Furthermore, the ecotoxicity of the degradation product of chlorpyrifos was higher than chlorpyrifos itself (Baskaran et al., 2003). Higher tier risk assessment methods directed at improving risk assessments should also be considered to better understand pesticide risk rising from the current (first tier) risk assessment. For comprehensive EcoRA, future studies should also consider acute toxicity which can be derived from using toxicity data such as EC_{50} and an assessment factor of 1000 (Wang et al., 2020). Our study dealt with a few pesticides and limited ecotoxicological information (Table 5.1). It isn't likely that it provided a complete assessment of pesticide risks in the environment. The present risk assessment depends upon deterministic methods and conservative approaches. Various elements including the test organisms, the regional meteorology and hydrology, and the local soil qualities can directly influence pesticide ecotoxicity (Huguier et al., 2015; Jegede et al., 2017). Consequently, studies need to be conducted with recent soil samples and the findings of these studies need to be integrated into Nepalese pesticide risk assessments after developed models are validated.

5.5 Conclusions

1. Based on TER and RQ methods under two scenarios: general and worst-case, our results identified chlorpyrifos as the main soil pollutant and revealed the highest ecological risks at all depths, particularly for *Folsomia candida*.
2. Pesticide residues in soils revealed the presence of multiple residues (pesticide cocktails) in 35% of the soil samples, including a diversity of pesticide combinations (Bhandari et al., 2020). We considered the additive effect for the pesticides with a similar mode of action, however their interaction in a cocktail may have been the result of either antagonistic or synergistic effects rather than the additive, signifying that the resulting risks due to such effects are unknown.
3. Generally, the TER values are only assigned for single compounds, thus only applicable when estimating a potential ecological risk associated with a single compound, hence other methods should be explored.

4. To reduce the ecological risk of pesticides, programs such as awareness and capacity building training related to pesticide effects and waste management should be provided to farmers.
5. Ecotoxicological research is limited in Nepal. Our findings may be used to argue for a comprehensive EcoRA in future research as well as setting national benchmarks for pesticide concentrations in soil.
6. All the IPM sites revealed no ecological risk.

Acknowledgements

We are grateful to the Nuffic for providing the funds to conduct this study (through Project No. 5160957247). We would like to thank Jakub Hofman and Paul van den Brink for providing comments and suggestions during the manuscript preparation. We thank Robin Palmer for reviewing the English language.

Supplementary Material

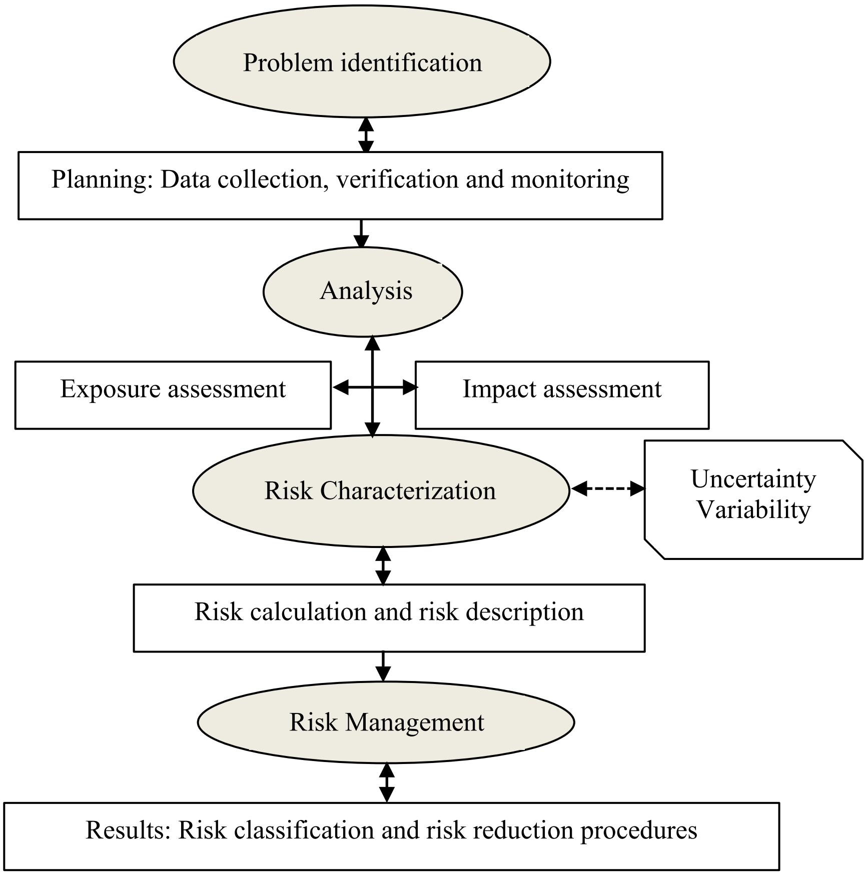


Figure S5.1 *The framework of ecological risk assessment [modified Ying (2018)].*

Assessment of hazard and pesticides effect

Literature published from 2000 to 2019 was considered for the assessment. Pesticides and their degradation products in Table S5.2 and organisms such as E. fetida, E. crypticus, F. candida, H. aculifer and N as well as C mineralization microorganisms were considered for the search 1 and 2 separately (Figure S5.2). For 1 and 2, article inclusion criteria were that the titles should contain *toxic* and *effect*, respectively.

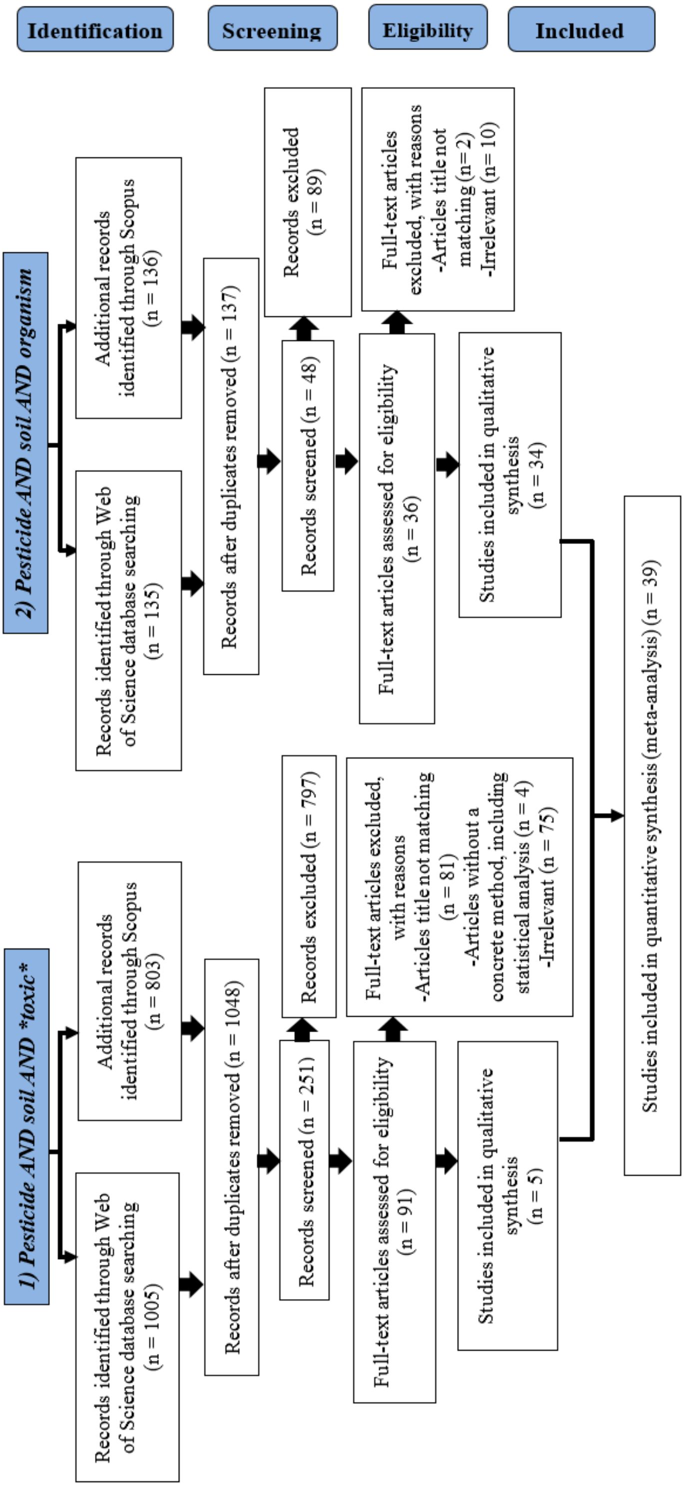


***Figure S5.2** The PRISMA flowchart based on (Moher et al., 2009).*

***Table S5.1** Overview of studies on the pesticides effect in soil invertebrates. The order of pesticides has been sorted alphabetically.*

Pesticides	Test organisms/species	Effects	References
3,5,6-trichloro-2-pyridinol	Earthworms	Low risk	(EFSA, 2005)
Carbendazim	Earthworms/Eisenia fetida	Impact on the weight and reproduction	(Yasmin and D'Souza, 2007)
	Earthworms	DNA damage	(Huan et al., 2016)
	Enchytraeid	Impaired the antioxidant system	(Novais et al., 2014)
	Earthworms	Population of earthworms decreased at higher concentrations	(Burrows and Edwards, 2002)
	Earthworms/Eisenia fetida	Harmful effects on embryo development and genetic factor	(Huan et al., 2016; Rico et al., 2016)
Chlorantraniliprole	Earthworms/Eisenia fetida	Inhibition of growth, reproduction and destruction of biomacromolecules	(Liu et al., 2018)
	Springtails/Folsomia candida	Affect locomotor abilities	(Lavtizar et al., 2016)
Chlorpyrifos	Earthworms/Eisenia fetida	Alterations of SOD activity	(Wang et al., 2012)
	Earthworms/Eisenia fetida	Morphological abnormalities and inhibition of AChE	(Venkateswara Rao et al., 2003)
	Springtails/Folsomia candida	AChE inhibition and oxidative damage	(Jager et al., 2007)
	Mites/Hypoaspis aculeifer	Affect survival and reproduction	(Jaabiri Kamoun et al., 2017)
	Earthworms/Eudrilus eugeniae	Changes in activities of AChE, enzymes related to oxidative stress, contents of LPO, GSH and GST including changes in morphology	(Tiwari et al., 2019)
	Earthworms/Pheretima peguana	Decreases neutral-red retention time (NRRT) for the coelomocyte and inhibits AChE	(Muangphra et al., 2016)
	Earthworms/Eisenia fetida	DNA damage in earthworms	(Casabé et al., 2007)
	Earthworms/Eisenia fetida	Growth retardation	(Zhou et al., 2011)
	Earthworms/A. caliginosa	Inhibited and depressed CbE activity and AChE activity, respectively	(Sanchez-Hernandez et al., 2014)
	Earthworms/L. terrestris	Chlorpyrifos inhibited the activity of cholinesterases and AChE	(Sanchez-Hernandez et al., 2018)
	Earthworms/Eisenia fetida	Effect on development and fecundity in earthworm	(Shi-ping et al., 2007)
	Earthworms/P. excavatus	Effect on growth, development and reproduction	(De Silva et al., 2010)
DDT	Earthworms/Eisenia fetida	Increased GST and CAT activities; inhibition of survival and growth	(Shi et al., 2016)
Emamectin	Earthworms	Low risk	(EFSA, 2012)
Imidacloprid	Earthworms/Eisenia fetida	Inhibition of reproduction	(Wang et al., 2019)
	Earthworms/Eisenia fetida	Avoidance behavior as well as changes in Hsp70 levels	(Dittbrenner et al., 2012)
	Earthworms/Eisenia fetida	Damage of DNA	(Wang et al., 2016)
	Springtails/Folsomia candida	Changes in GST activity, GST mRNA as well as glutathione (GSH) level	(Sillapawattana and Schaffer, 2017)
	Springtails/Folsomia candida	Lethal toxicity (effect on survival and reproduction)	(van Gestel et al., 2017)
	Springtails/Folsomia candida	Reduction in reproduction	(Alves et al., 2014)
	Earthworms/Eisenia fetida	Disruption of a balance between antioxidant enzymatic activities and reactive oxygen species (ROS) contents	(Zhang et al., 2014)
	Earthworms/Eisenia fetida	Effect on reproduction, growth, AChE and DNA	(Wang et al., 2015b)
	Earthworms/Eisenia fetida	Inhibited cellulase activities; damaged cells of epidermal layer and midgut	(Wang et al., 2015a)
Metalaxyl	Earthworms/Eisenia fetida	Accumulation of the pesticide in earthworms (enantioselective)	(Xu et al., 2011)
Profenofos	Earthworms/Eisenia fetida	Neurotoxicity as well as changes in morphology and histology	(Chakra Reddy and Venkateswara Rao, 2008)
	Earthworms/ F. candida	Effect on survival, reproduction and hsp70 gene expression	(Liu et al., 2012)
Triazophos	Earthworms/Eisenia fetida	Inhibition of growth and reproduction	(Khandelwal, 2017)
	Earthworms	Oxidative stress, cell damage and tissue injury	(Yang et al., 2019)

Note.
CbE = Carboxylesterase; AChE = Acetylcholinesterase; SOD = Superoxide dismutase; CAT = Catalase; GST = Glutathione -S-transferase; LPO = Levels of lipid peroxidation; and reduced glutathione (RG).
No information related to effects was available in the literature for pesticides and their degradation products such as quinalphos, N-(2,6-dimethylphenyl)-N-(methoxyacetyl)alanine, DDE and DDD, henceforth did not appear in the table.

Table S5.2 *Descriptive statistics of pesticides and their degraded product concentrations (µg/kg) at different depths of soil. "NA" = not applicable. The concentration was based on our previous study (Bhandari et al., 2020). LOD (µg kg^{-1}) = Limit of detection.*

Group	Pesticides (n=15); LOD	Soil depths (cm) 0-5							15-20							35-40						
		No	%	Min	Max	Median	Mean	SD	No	%	Min	Max	Median	Mean	SD	No	%	Min	Max	Median	Mean	SD
AD	Chlorantraniliprole; 1	16	33%	1.09	14.20	2.86	3.23	3.30	10	20%	1.08	4.22	1.80	2.06	1.21	9	18%	1.08	6.52	1.57	2.02	2.03
BD	Carbendazim; 1	11	22%	1.03	6.45	1.42	1.62	1.56	4	8%	1.10	5.55	1.67	2.01	2.07	3	6%	1.42	3.41	2.30	2.23	1.00
MOD	Emamectin; 1	1	2%	3.30	3.30	3.30	3.30	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
NND	Imidacloprid; 1	15	31%	1.02	13.80	2.67	3.94	4.47	6	12%	1.17	7.57	1.71	2.06	2.45	7	14%	1.16	31.60	2.47	3.35	11.04
OC	o, p'-DDT; 1	1	2%	1.60	1.60	1.60	1.60	NA	1	2%	4.28	4.28	4.28	4.28	NA	1	2%	2.66	2.66	2.66	2.66	NA
	p, p'-DDD; 1	1	2%	1.95	1.95	1.95	1.95	NA	1	2%	8.28	8.28	8.28	8.28	NA	1	2%	11.10	11.10	11.10	11.10	NA
	p, p'-DDE; 1	10	20%	1.00	6.42	1.94	2.07	1.76	4	8%	1.09	13.90	3.90	3.85	5.67	4	8%	1.00	5.55	2.67	2.23	2.31
	p, p'-DDT; 1	4	8%	1.05	3.81	2.13	1.93	1.41	4	8%	1.13	25.50	2.65	3.70	11.72	2	4%	1.50	78.40	39.95	10.84	54.38
OP	Chlorpyrifos; 10	5	10%	13.10	177.00	25.90	32.45	69.49	4	8%	10.50	68.40	15.25	20.18	27.48	2	4%	11.50	60.60	36.05	26.40	34.72
	Profenofos; 1	3	6%	1.10	3.37	1.42	1.74	1.23	NA	NA	NA	NA	NA	NA	NA	1	2%	1.09	1.09	1.09	1.09	NA
	Quinalphos; 1	2	4%	1.23	2.47	1.85	1.74	0.88	1	2%	1.06	1.06	1.06	1.06	NA	NA	NA	NA	NA	NA	NA	NA
	Triazophos; 1	3	6%	1.05	8.12	1.43	2.30	3.98	2	4%	1.86	2.35	2.11	2.09	0.35	1	2%	4.84	4.84	4.84	4.84	NA
PA	Metalaxyl; 1	8	16%	1.12	6.49	2.78	2.44	1.87	2	4%	1.69	4.23	2.96	2.67	1.80	5	10%	1.20	8.97	1.94	2.41	3.24
UNC	3,5,6-TCP; 2.5	16	33%	2.63	57.40	8.89	8.69	13.06	9	18%	3.03	15.90	5.94	7.26	4.75	11	22%	3.02	31.10	7.13	7.26	8.04
	N-alanine; 1	1	2%	2.49	2.49	2.49	2.49	NA	NA	NA	NA	NA	NA	NA	NA	2	4%	1.11	1.56	1.34	1.32	0.32

Note.
N-alanine = N-(2,6-dimethylphenyl)-N-(methoxyacetyl)alanine; Pesticides group: AD = Anthranilic diamide; UNC = Unclassified; OP = Organophosphate; NND = Neonicotinoid; OC = Organochlorine; BD = Benzimidazole; PA = Phenylamide; and MOD = Micro-organism derived.

***Table S5.3** Sum of the risk quotient (RQ) and contribution (%) of the organophosphate (mixture of 2 pesticides) at the different depths. The sum of RQ ($\sum RQ_{site}$) of a given site was computed by summing up all the RQs for each of the pesticide residues ≥LOD. The contribution (%) was not available for pesticides concentrations <LOD. The calculated values of $\sum RQ_{site}$ were categorised into 4 risk levels as: no risk (∑RQsite <0.01), lower risk (0.01≤∑RQsite <0.1), moderate risk (0.1≤∑RQsite <1), and higher risk (∑RQsite ≥1). Because of privacy, the location of the sites could not be shown on a map. CHL = Chlorpyrifos and PRP = Profenofos.*

Sites (n=49)	Soil depths (cm) 0-5				15-20				35-40			
	Sum of the RQ based on the CA effect	Risk	% contributed CHL	% contributed PRP	Sum of the RQ based on the CA effect	Risk	% contributed CHL	% contributed PRP	Sum of the RQ based on the CA effect	Risk	% contributed CHL	% contributed PRP
F4	0.00	No			0.00	No			0.00	No		
F5	0.00	No			0.00	No			0.00	No		
F7	0.00	No			0.00	No			0.00	No		
F8	0.00	No			0.00	No			0.00	No		
F19	0.00	No			0.00	No			0.00	No		
F21	0.00	No			0.00	No			0.00	No		
F22	0.00	No			0.00	No			0.00	No		
F30	0.00	No			0.00	No			0.00	No		
F32	0.00	No			0.00	No			0.00	No		
F34	0.00	No			0.00	No			0.00	No		
F35	0.00	No			2.77	Higher	100%		1.77	Higher	100%	
F36	0.00	No			0.00	No			0.00	No		
F40	0.00	No			0.00	No			0.00	No		
F52	0.00	No			0.00	No			0.00	No		
F53	1.62	Higher	100%		30.60	Higher	98%	2%	0.00	No		
F55	0.00	No			1.42	Higher		100%	0.00	No		
F56	0.00	No			0.00	No			0.00	No		
F58	0.00	No			0.00	No			0.00	No		
F59	0.00	No			0.00	No			0.00	No		
F60	0.00	No			0.00	No			0.00	No		
F61	0.00	No			0.00	No			0.00	No		
F62	0.00	No			0.00	No			0.00	No		
F76	0.00	No			0.00	No			0.00	No		
F77	0.00	No			0.00	No			0.00	No		
F83	0.00	No			0.00	No			0.00	No		
F102	0.00	No			0.00	No			0.00	No		
F103	0.00	No			0.00	No			0.00	No		
F109	0.00	No			0.00	No			0.00	No		
F129	0.00	No			0.00	No			0.00	No		
F133	0.00	No			0.00	No			0.00	No		
F136	0.00	No			0.00	No			0.00	No		
F140	0.00	No			0.00	No			0.00	No		
F143	0.00	No			0.00	No			0.00	No		
F144	0.00	No			0.00	No			0.00	No		
F146	0.00	No			0.00	No			0.00	No		
F148	0.00	No			0.00	No			0.00	No		
F149	0.00	No			2.02	Higher	100%		0.00	No		
F155	2.55	Higher	100%		3.98	Higher	100%		0.00	No		
F156	0.00	No			0.00	No			0.00	No		
F157	0.00	No			0.00	No			0.00	No		
F158	0.00	No			0.00	No			0.00	No		
F163	0.00	No			0.00	No			0.00	No		

Table S5.3 *Sum of the risk quotient (RQ) and contribution (%) of the organophosphate (mixture of 2 pesticides) at the different depths................(continued).*

	0-5				15-20				35-40			
			% contributed				% contributed				% contributed	
Sites	Sum of the RQ based on the CA effect	Risk	CHL	PRP	Sum of the RQ based on the CA effect	Risk	CHL	PRP	Sum of the RQ based on the CA effect	Risk	CHL	PRP
F167	0.00	No			1.10	Higher		100%	1.09	Higher		100%
F169	0.00	No			0.00	No			0.00	No		
F170	0.00	No			0.00	No			0.00	No		
F173	0.00	No			0.00	No			0.00	No		
F179	0.00	No			0.00	No			0.00	No		
F180	2.14	Higher	100%		0.00	No			0.00	No		
F183	10.52	Higher	100%		5.12	Higher	100%		9.32	Higher	100%	

Legend No risk (grey) Higher risk (red)

6. Synthesis

This thesis mainly focussed on understanding (i) pesticide use and the related safety behaviour among farmers and retailers, (ii) dietary and (iii) non-dietary risks due to pesticide residues in vegetables and soil, respectively, and (iv) the ecological risks posed by pesticides. Here, I present the thesis findings according to the key objectives stated in the general introduction section and schematically shown in Figure 6.1.

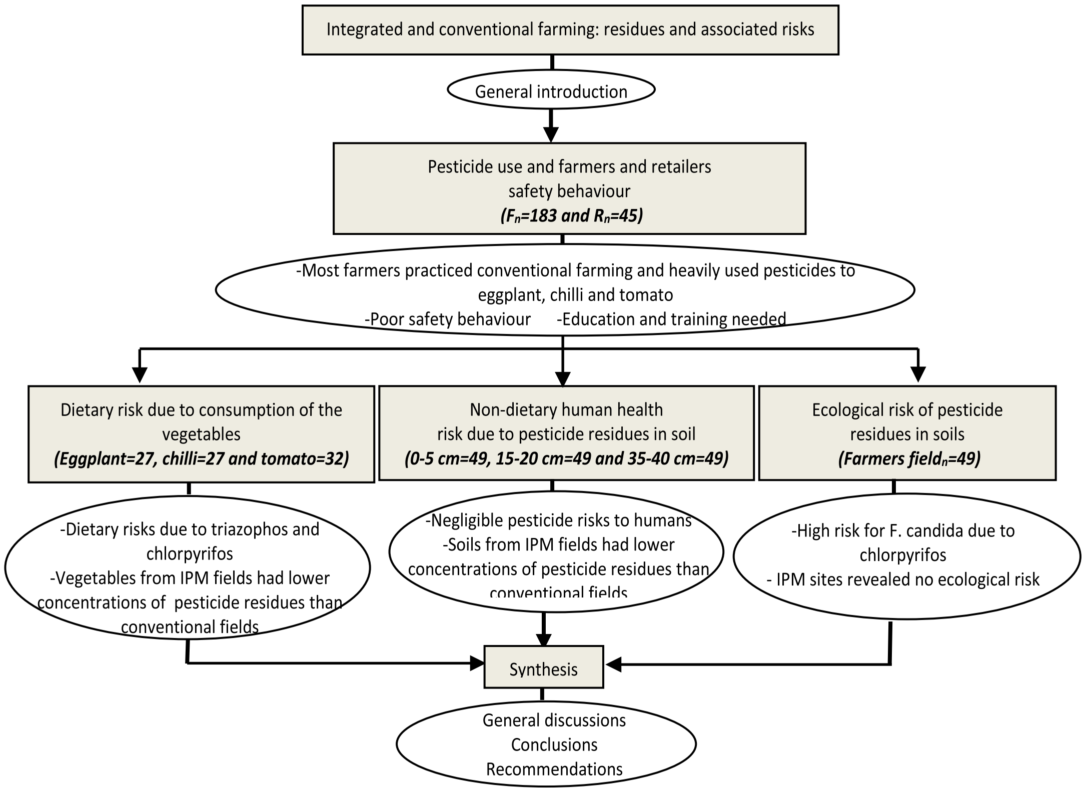


Figure 6.1 *The outline of this thesis with the learning objectives as noted in the rectangular boxes. Based on the application of pesticides (Chapter 2), the eggplant, chilli and tomato samples were analysed and dietary risk assessment was carried out (Chapter 3). The cultivated soils were analysed for non-dietary health risks (Chapter 4). The ecological risk of pesticides in soil was examined (Chapter 5). Data between parenthesis are italicized, representing sampling units. IPM = integrated pest management; KAB = knowledge and behaviour.*

6.1 General discussion

6.1.1 Pesticide use on vegetable crops and safety behaviour of farmers and pesticide retailers

Farmers used mainly insecticides and fungicides on vegetable crops. On average, 3 active ingredients were used per vegetable. Farmers mostly applied pyrethroids, organophosphates and carbamates on different vegetable crops such as eggplant, chilli, tomato, bottle gourd, bean, sponge gourd, broccoli, cauliflower, okra, cucumber, cabbage, and bitter gourd. The most frequently used insecticides were cypermethrin (76% of the farmers) and profenofos (>55% of the farmers). Similarly, 54% of the farmers applied the fungicide, mancozeb. However, insecticides such as carbofuran and cartap hydrochloride from the groups such as carbamate and thiocarbamate, respectively were applied the least often. Our results showed that farmers' application of pesticides on eggplants, tomatoes and chillies was much higher than their recommended doses (Chapter 2). Our results also observed that banned insecticides such as endosulfan and phorate were also applied. The use of banned pesticides in agriculture was also reported in Ethiopia (Haylamicheal and Dalvie, 2009) and India (Devi et al., 2011; Joseph et al., 2020). The average pesticide use for vegetables was 2.9 kg a.i./ha, however it depended on the types of vegetables and pesticides (Chapter 2). Organophosphate was excessively used for vegetables (for example, dichlorvos for eggplants was 23.12 kg a.i./ha). Farmers used several fungicides in vegetable farming, however the application of mancozeb was found to be the highest (7.78 kg a.i./ha). Our results showed higher rates of pesticide use in vegetables compared to previous studies in other regions (Chhetri et al., 2014; Jha and Regmi, 2009).

Pesticides can be very useful when used wisely. Integrated farming based on IPM methods uses pesticides judiciously. In our study, very few farmers adopted such methods, for example, use of ash, pheromone trap, compost manure, animal dung and urine for vegetable farming. Farmers and pesticide retailers often lack sufficient knowledge on the safe use of pesticides and eco-friendly methods for pests control (Akter et al., 2018; Atreya, 2007; Gesesew et al., 2016; Mohanty et al., 2013; Oesterlund et al., 2014; Rijal et al., 2018; Vaidya et al., 2017). Our results showed that most farmers overused pesticides in vegetable and practiced conventional farming. They regularly sprayed chemical pesticides even when there were no sign of plant diseases. Farmers mixed more than one pesticide and sprayed cocktails, which is more harmful than spraying a single pesticide (PAN, 2020). Farmers were uneducated and untrained and did not follow the minimum safety precautions while working, thus exposing themselves to pesticides. The EU regulation 2016/425 states the significance of personal protective equipment (PPE) to protect from various forms of exposure (EU, 2016). Safety behaviours such as wearing proper PPE can reduce pesticide exposure (Yarpuz-Bozdogan, 2018) and associated risks (Houbraken et al., 2016). The use of safety measures helped to avoid about 44% of pesticide-related illness in Vietnam (Dasgupta et al., 2007). The level of education and knowledge of farmers and retailers on pesticide use determined their safety behaviour (Ali et al., 2020; Sapbamrer and Thammachai, 2020). Furthermore, climate (Watson et al., 2019) and economic conditions (Damalas et al., 2006; Garrigou et al., 2020) influenced the safety behaviour of farmers. Our study also found that farmers suffered from headaches and irritation, two of the most frequently reported short-term illnesses due to pesticide handling. Previous studies also reported chronic health problems, particularly related to reproduction, hormone disruption and mutation (Gupta, 2004; Kim et al., 2017; Sabarwal et al., 2018).

Age, education, individual beliefs, and cues to action determined the safety behaviour of farmers (Chapter 2) (Figure 6.2). Farmers perceived higher barriers for the safety measures thus used hats, long-sleeved shirts, long pants, gloves, and masks less frequently during pesticide handling. The perceived barriers mentioned above refer to the suggested clothing as being uncomfortable or unavailable, or farmers were simply unaware of the benefits of wearing such clothing during pesticide application. For example, wearing long pants and long-sleeved shirts while spraying pesticides caused farmers discomfort due to overheating. The perceived barriers were also found to inhibit the safety behaviour of farmers in Iran during pesticide handling (Sharifzadeh et al., 2019).

In our study, almost all farmers perceived the benefits of washing their hands after spraying, however a few of them did not take baths (15%) or wash their clothes (24%) after spraying. Furthermore, there were farmers who preferred to drink, smoke and eat during pesticide application which increases the risk of exposure. Educated farmers perceived higher pesticide threats and were aware of the long-term effects of pesticides on humans, animals, birds, fishes, and honeybees. Self-efficacy and cues to action had positive effects on farmers' safety behaviour. Educated and trained farmers in China (Fan et al., 2015) and Bangladesh (Akter et al., 2018) had good protective behaviours. Most farmers in our study were neither educated nor trained, thus 90% of them did not know the colour codes used for pesticides. Of all the factors, perceived barrier was the most reliable predictor of a farmer's safety behaviour (Sharifzadeh et al., 2019). Government authorities should concentrate efforts on minimizing the barriers to safety behaviour for farmers.

Perceived threats and cues to action also determined the safety behaviour of pesticide retailers (Chapter 2). Although 100% of the retailers perceived higher threats to their health and environmental entities from pesticides, some retailers (33%) did not believe the long-term detrimental health effects of pesticide exposure. A few farmers even stated that pesticides were "medicine" instead of "poison". Furthermore, some retailers (16%) did not think that they were exposed to the pesticides while handling them. Retailers who registered their businesses and renewed their licences regularly had good safety practices while handling pesticides, a finding consistent with a past study conducted among Tanzanian retailers (Lekei et al., 2014b). Retailer participation in the meetings, seminars, and workshops on pesticide use triggered their safety behaviour, however only 47% of them were given any opportunity to follow any of these events. Any training related to the safe handling of pesticides motivated retailers to improve their safety actions.

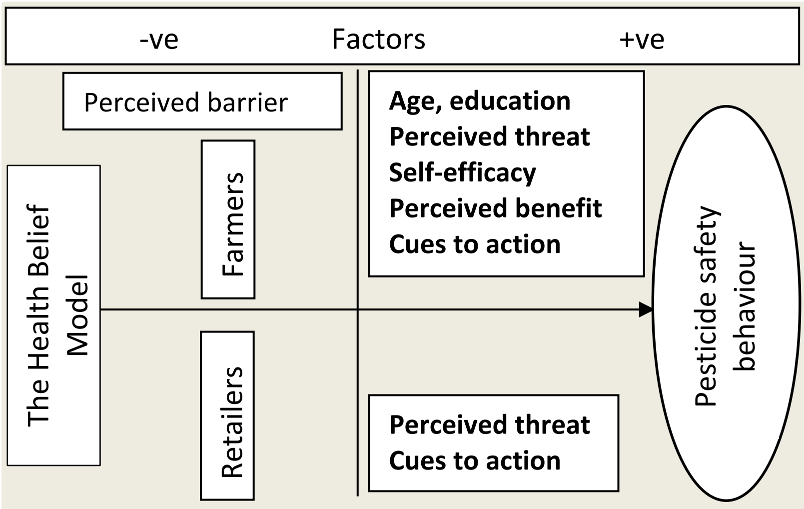


Figure 6.2 *Results based on the Health Belief Model for understanding the safety behaviour of farmers and retailers. The factors that affected the pesticide safety behaviour of farmers and retailers positively (+ve) are in bold.*

6.1.2 Dietary risk for humans

The survey (Chapter 2) found overuse of pesticides on eggplants, chillies and tomatoes. Pesticide residues can be taken up by plants or stay on the soil surface after application. Dietary consumption of these residues may contribute to human exposure. We tested the vegetable samples for 23 pesticides (along with their degradation products). Of the pesticides, only 14 were detected in the vegetables, and we examined dietary risks of these pesticide residues in adults and adolescents (Chapter 3). In our study, 100% of the tomato and chilli and 93% of the eggplant samples contained pesticide residues. About 7% of the eggplant samples were free from pesticide residues. Carbendazim (fungicide) in tomato was significantly higher than chilli and eggplant. Chlorpyrifos (insecticide) residues exceeded the EU maximum residue limits (MRLs) in 11% of the eggplant and 19% of the chilli and tomato samples. Although 170 active ingredients are registered and used in Nepal, the government only sets pesticide limits on 36 active ingredients in foodstuff. Of the pesticide residues detected in our study (Chapter 3), Nepalese MRLs for food grains, legumes and pulses were available for only 3 pesticides, namely dichlorvos (1000 µg/kg), chlorpyrifos (50 µg/kg) and carbendazim (500 µg/kg) (Lama, 2008).

In comparison to eggplant and chilli samples, a higher number of residues were present in tomato samples. Up to 7 residues of different pesticides were present in 6% of the tomato samples from conventional farming. Furthermore, multiple pesticide residues were detected in eggplants (56% of the samples), chillies (96% of the samples), and tomatoes (100% of the samples). Studies done elsewhere also observed contaminated fruits and vegetables with multiple pesticide residues (Jallow et al., 2017b; Liu et al., 2016a; Liu et al., 2016b).

Carbendazim (fungicide) and chlorpyrifos (insecticide) were detected most frequently in vegetables, a finding consistent with a past study (Quijano et al., 2016). A recent study conducted in Saudi Arabia contained mainly insecticides and fungicides in 100% of the chilli, 96% of the tomato and 85% of the eggplant samples studied (Ramadan et al., 2020). Both, fungicides and insecticides were major groups detected in Turkey (Golge et al., 2018). Of all foods tested by Koirala et al. (2007), a higher number of vegetable samples were contaminated with higher concentrations of organochlorines (i.e. BHC and DDT) and organophosphates (i.e. malathion and methyl-parathion). Although Nepal has banned endosulfan and methyl-parathion insecticides for their use in agriculture, Dhakal (2016) detected residues of those insecticides in fruits, indicating current application of banned pesticides in the country. Our study also detected pesticides that are not approved for use in the EU: dichlorvos, profenofos, quinalphos, triazophos and carbendazim.

Integrated Pest Management (IPM) motivates farmers to decrease the use of chemical pesticides (Gautam et al., 2017). Therefore, the concentration of insecticides and their degradation products such as imidacloprid, chlorpyrifos and 3,5,6-trichloro-2-pyridinol (TCP) in vegetables from IPM fields were significantly lower ($p < 0.05$) than the insecticides and their degradation products found on the vegetables from conventional fields. Furthermore, the total average concentration of the detected pesticides on vegetable samples from IPM fields (39.5µg/kg) was significantly lower ($p < 0.05$) than the pesticide concentrations found on the vegetables from conventional fields (196 µg/kg). Foodstuffs from IPM fields were either free from pesticides (Polat and Tiryaki, 2019) or had lower concentrations of insecticides and fungicides (i.e. below MRL) than non-IPM fields (Baker et al., 2002; Mladenova and Shtereva, 2009; Singh et al., 2009).

Triazophos exceeded the European Union Maximum Residue Limit (EU MRLs) in 4% of eggplant and 6% of tomato samples. Likewise, chlorpyrifos exceeded the EU MRLs in eggplants (11% of the samples), chillies (18.5% of the samples) and tomatoes (19% of the samples). Both omethoate and carbendazim in 3% of the tomato samples exceeded the EU MRLs; all indicating poor agricultural practices. Overall, 44% of the tomato samples exceeded the EU MRLs. All the vegetable samples exceeding the EU MRLs were from conventional farming. A detailed list of pesticide concentration ranges in vegetables with their EU MRLs can be found in Chapter 2. Of all detected pesticides, imidacloprid significantly exceeded its MRLs in fruits and vegetables in a study performed in Kuwait (Jallow et al., 2017b). The MRLs were set for just single pesticides at a time, ignoring the “cocktail effect”. In our study, vegetables showed a group diversity of pesticide combinations, which makes it challenging to protect humans the risks of pesticide exposure. Farmers used pesticides in much higher rates than recommended on vegetables such as tomatoes, chillies and eggplants (Chapter 2), therefore we estimated dietary risk of pesticides due to the consumption of these vegetables. The dietary risk assessment of the pesticides indicated that consumption of tomatoes could cause potential health risks due to mainly organophosphates such as chlorpyrifos and triazophos. The risk might be due to the higher persistency and application rates of these compounds. Chlorpyrifos used on fruits and vegetables caused health risks elsewhere (Kariathi et al., 2016; Lehmann et al., 2017; Mojsak et al., 2018; Reiler et al., 2015). Organophosphate residues contributed health risks due to the consumption of tomatoes in Bolivia (Reiler et al., 2015). Its dietary risk for humans was demonstrated elsewhere (Abdelbagi et al., 2020; Kariathi et al., 2016; Lehmann et al., 2017; Mojsak et al., 2018; Salamzadeh et al., 2018). However, the risk was of less concern in the EU regions (Jensen et al., 2015; Quijano et al., 2016). In the studies, pesticide concentrations in foodstuffs didn’t pose health risks for the Danish and Spanish consumers, indicating their lower estimated short-term intake (ESTI) and estimated daily intake (EDI) than the acute reference dose (ARfD) and the acceptable daily intake (ADI), respectively. In our study, adults were at higher risks from dietary exposures than adolescents which might be due to consumption of more food by adults than adolescents. The exposure to a pesticide is dependent on its dose in food (ICAR, 2019), thus the more you eat, the greater your potential risk. Generally, the MRL, ADI and ARfD values are only assigned for single active ingredients, thus only applicable when estimating a potential risk associated with a single residue of a pesticide. However, when estimating the risk posed by multiple pesticide residues, there is still doubt whether the risk estimation methods currently used, which were based on single MRL, ADI and ARfD values, can be considered accurate. Multiple pesticide residues in foods could lead to synergistic or antagonistic effects once they are absorbed in the human body (Prutner et al., 2013).

6.1.3 Non-dietary human health risk

As mentioned in Chapter 1, pesticides that are persistent in soil remain at different depths and concentrations due to their physical and chemical properties, as well as environmental characteristics (WHO, 2008). Overall, 15 pesticide residues, including their degradation products, were detected in three different soil depths (cm): 0-5, 15-20 and 35-40 (Chapter 4). The residues were more frequently observed in upper layers of soil. From the 147 soil samples, about 60% contained pesticide residues with a mean of 16 µg kg^{-1}, ranging from

1.0 µg/kg to 251 µg/kg. Overall, 35% of the soil samples had multiple pesticide residues, with 2% of the upper layer soils from conventional farming containing up to 7 residues per sample. Among organophosphates (OPs), chlorpyrifos was the most frequently occurring insecticide followed by triazophos, profenofos and quinalphos with their concentrations of (µg kg^-1) 40.8, 3.28, 1.75 and 1.59, respectively. Soil samples contained organochlorine (OC) residues mainly o, p'-DDT (2% of the samples); p, p'-DDE (12% of the samples); p, p'-DDD (2% of the samples) and p, p'-DDT (7% of the samples). Of all the DDTs, residues of p, p'-DDE were most frequently found in soils, while p, p'-DDT residues had higher concentrations with an average of 12.1 µg kg^{-1}. The isomeric ratio of DDTs suggested ongoing use of DDT, a finding consistent with a past study (Yadav et al., 2016). DDT has been banned in Nepal since 2001, but due to the persistent nature of it, the residues are still present in soils. From the different chemical pesticide groups, OC pesticides are very persistent, toxic and have the tendency to bioaccumulate and biomagnify (Briz et al., 2011; Contreras López, 2003; Gao et al., 2013). The other pesticides and their degradation products such as chlorantraniliprole, imidacloprid carbendazim, metalaxyl, emamectin, N-(2,6-dimethylphenyl)-N-(methoxyacetyl)alanine and TCP had their average concentration (µg kg^-1) in soil as 3.17, 5.21, 2.12, 3.04, 3.30, 1.72 and 10.3, respectively. Furthermore, higher precipitation can wash out soil pesticide residues and ultimately contaminate other sources (Pokhrel et al., 2018). For example, in our study, a few of the soil samples from IPM fields had pesticide residues.

Human health risk assessment consists of acute and chronic risk due to organophosphate (OP) and organochlorine (OC) residues in soil, respectively. The soil residues may reach humans via different exposure pathways such as inhalation, ingestion and dermal contact. Our findings suggest negligible non-cancer risk of OP residues in soils to humans through ingestion and dermal exposure (HQ and HI <1) which was consistent with a study in China (Pan et al., 2018). Toxicological reference values for profenofos and degradation products such as 3,5,6-trichloro-2-pyridinol [TCP] and N-(2,6-dimethylphenyl)-N-(methoxyacetyl)alanine [N-alanine] were not available in the databases we referred to, thus their risk assessment was not possible. However, concentrations of profenofos including other detected pesticides were compared with their globally established guidance/threshold values in soils (Chapter 4). Similarly, our findings suggested negligible cancer risk (considering all the aforementioned pathways), particularly due to OC residues as the estimated value of total incremental lifetime cancer risk was $<1\times10^{-6}$. Chapter 4 includes all the details of the USEPA procedures and parameters used in the health risk assessment. DDT and its degradation products were extensively detected in Chinese soils (Gong et al., 2004; Hu et al., 2014; Ma et al., 2016), thus a potential cancer risk was observed (Qu et al., 2015). Previous studies have established relationships between pesticides and their human health consequences (Ennaceur et al., 2008; Shinomiya and Shinomiya, 2003), including cancer (Ennour-Idrissi et al., 2019; Louis, 2019) and non-cancer risks such as hormone disruptions and reproductive problems (Frye et al., 2012; Younglai et al., 2004). Although health risk due to pesticides in soil was of less concern, adolescents were exposed relatively more than adults which might be due to adolescent body weights being relatively less than that of adults. Of all the exposure pathways, potential exposure to OP was mainly through ingestion.

For estimating non-dietary health risk due to pesticide mixtures, we considered the additive effect for the pesticides with a common mode of action. However, residual interactions in a mixture may have been the result of either antagonistic or synergistic effects rather than the additive effects (Alexander et al., 2008), which means that the resulting risks due to such effects are unknown.

6.1.4 Ecological risk of pesticide residues detected in soil

Earthworms play an important role in soil fertility maintenance by influencing organic content, soil structure and microscopic organisms (Fragoso et al., 1997; Hole et al., 2005). However, chemical pesticides induce negative effects on ecosystems and ecosystem services (Carriquiriborde et al., 2014; Utsumi et al., 2011). In Chapter 5, we assessed ecological risks of 9 pesticides from different groups, including their degradation products such as 1 organochlorine insecticide (DDT), 2 organophosphate insecticides (profenofos and chlorpyrifos), 1 phenylamide fungicide (metalaxyl), 1 neonicotinoid insecticide (imidacloprid), 1 anthranilic diamide insecticide (chlorantraniliprole), 1 benzimidazole fungicide (carbendazim), and 2 unclassified group metabolites (TCP and N-alanine) at 3 layers (cm) of soil: 0-5, 15-20 and 35-40. The other pesticides such as DDD, DDE, quinalphos and triazophos were detected in soils but excluded from the risk assessment as their ecotoxicity data was not available in literature. The risk assessment was based on the EFSA standard procedures and test organisms such as the earthworm *(Eisenia fetida),* the enchytraeid *(Enchytraeus crypticus),* the springtail *(Folsomia candida),* the mite *(Hypoaspis aculifer)* and N as well as C mineralization microorganisms. Therefore, the toxicity exposure ratio (TER) for the aforementioned pesticides was estimated for assessing ecotoxicity at 3 depths of soil, while the risk quotient (RQ) was estimated for assessing individual and mixture toxicity of pesticides. The ecological risk of pesticides was assessed by comparing their TER with trigger values and international standards that have been adopted elsewhere (Devi et al., 2015; Vasickova et al., 2019; Wee and Aris, 2017). Furthermore, we compared the measured concentrations of pesticides with their corresponding pesticide soil regulatory guidance values.

TER values of chlorpyrifos, an organophosphate insecticide, notably contributed chronic toxicity to *F. candida* for all 3 depths (cm) (0-5, 15-20 and 35-40). However, the TER values of other pesticides for the depths indicated no significant risk of the pesticides for *E. fetida, E. crypticus, and H. aculifer.* Moreover, insecticides such as profenofos and chlorpyrifos contributed risk for 16% of the sites. Organophosphate and neonicotinoid insecticides contributed risk to soil organisms elsewhere (Chagnon et al., 2015; Giesy et al., 2014). Based on RQ, our study showed a potential ecological risk for the soil organisms due to 3 insecticides, profenofos at depths (cm): 0-5 and 35-40; imidacloprid at a depth of 35-40; and chlorpyrifos at all the depths. Additionally, compared with the Ukrainian standards for profenofos in 3% of the soil samples, the ecological risk associated with the pesticide cannot be ignored. High ecological risk due to insecticides was observed for the river ecosystems in Malaysia (Wee and Aris, 2017). However, fungicides and herbicides in the Czech Republic and China, respectively posed ecological risks (Li et al., 2018; Vasickova et al., 2019). It was found that ecotoxicity, particularly the TER associated with DDT and metalaxyl, was negligible. The findings converge with the results based on their RQ, where the pesticides did not show a significant risk. A few compounds such as p,p'-DDD, p,p'-DDE, quinalphos and triazophos were discarded from the risk assessment due to the unavailability of their ecotoxicity data, hence neither their RQs nor TERs were known. Pesticide cocktails in soil resulting from diverse groups can affect soil organisms. Our study was primarily based on the additive effects of pesticides, particularly organophosphate insecticides, therefore, ecological risk of pesticides due to other effects such as synergistic and antagonistic is still unknown. Several pesticide packets and containers were observed at different sites during the survey, indicating unsafe behaviour of farmers. Such behaviour was common among Ethiopian farmers, with the discarded containers polluting soil and water due to the residual chemicals left in them (Mequanint et al., 2019).

The summative index of farmers' knowledge and behaviour was correlated with the mixture toxicity of organophosphates, RQ ($\sum RQ_{mix}$), indicating that the ecological risks of the pesticides at sites is negatively associated with the pesticide knowledge and safety behaviours of farmers. Moreover, the risk can be reduced by increasing farmers' knowledge of pesticide effects on health and the environment. Enhancing awareness and providing pesticide use and safety training among farmers can minimize the environmental risks of pesticides.

6.2 General conclusions and major findings

This thesis focussed on the factors affecting safety behaviour of farmers and retailers, dietary and non-dietary risk of pesticide exposure and assessment of ecological risk of pesticide use. The EFSA risk assessment procedures were applied because of the lack of such procedures for Nepal. The use of chemical pesticides is increasing in Nepal and unfortunately, farmers have been overusing pesticides, especially in vegetable farming, ultimately leading to health and environmental degradation. This study focussed on risk assessment of a pesticide (HQ or RQ) as well as pesticide mixtures resulting from a combined exposure (HI) based on information on individual pesticides with a similar mode of action-additive effects. As there is a lack of sufficient information on synergism and antagonism of complex mixtures of pesticides in vegetables and soils, our study could not examine the combined effects further and thus the effects are still unknown. However, this study provides a baseline risk for the current use of pesticides in Nepal. The knowledge gained from this research is crucial for enhancing the safety behaviour of farmers and retailers and is also important for minimising dietary and non-dietary exposure to pesticides from vegetables and soil, respectively.

The major findings are:

1. Very few farmers in our study practiced IPM techniques. Farmers practicing conventional farming used almost all groups of pesticides in vegetable cultivation. Of the pesticides used, 78% were insecticides, 16% were fungicides and 6% were herbicides. We estimated higher application rates for insecticides and fungicides than the recommended doses. We found over 30 active ingredients being used in vegetable farming. However, farmers were unaware of the negative effects of pesticides and pesticide toxicity labels, thus they often used banned pesticides. The average application of fungicides such as mancozeb and insecticides such as dichlorvos were the highest. The highest application rates were observed in eggplant, chilli, and tomato. Interestingly, retailers had a good knowledge of pesticides and their health and environmental consequences, however, they lacked sufficient safety measures at their shops. Therefore, both stakeholders have a higher risk of pesticide exposure. Education and training support for the farmers and retailers, and implementation of legal framework, are important for the safety of human health and the environment.

2. Vegetables from IPM fields contained notably lower concentrations of pesticides than from conventional fields, indicating that the IPM foods were comparatively safer. Up to 7 different pesticide residues were detected in individual sample from conventional farming forming pesticide cocktails. The percentage of vegetable samples containing pesticide cocktails in conventional and IPM fields was 88 and 47, respectively. In eggplants, tomatoes and chillies from the conventional fields, the concentration of insecticides (i.e. triazophos, omethoate and chlorpyrifos) and a fungicide (i.e. carbendazim) exceeded the EU MRLs, indicating poor agricultural

practices. The estimated dietary intake of pesticide residues (ESTI, mg kg^{-1} body weight day^{-1}) through consumption of vegetables, particularly tomatoes from conventional fields, was higher than their human health based toxicological reference values (ARfD, mg kg^{-1} body weight day^{-1}), posing acute health risk for consumers. The dietary risk was mainly due to organophosphate insecticides such as chlorpyrifos and triazophos.

3. Pesticide residues were more frequently detected in the upper soil layer. Ingestion was the main pathway of pesticide exposure. However, non-dietary consumption of their residues did not pose a significant human health risk, including cancer and non-cancer. The pesticides in soils from non-IPM fields had notably higher concentrations of residues than IPM fields. The predicted concentration (PEC) of most pesticides in soil based on the EFSA procedures were much higher than their measured soil concentrations, thus their predicted values do not coincide with real field measurements.

4. Insecticides, mainly profenofos, imidacloprid and chlorpyrifos, posed ecological risks for soil organisms particularly in conventional farms/sites. *F. candida* was the most sensitive to pesticides. There was also an association between the increase in the ecological risk due to the inadequate knowledge of farmers and their lack of safety measures with regards to pesticide use. The cocktail effect of pesticides was unknown.

6.3 Implications and recommendations

6.3.1 Implications for management of pesticide use and safety practices

This study identified factors affecting pesticide use safety behaviour of farmers and retailers. Government agencies should provide education on and awareness of good agricultural practices, especially the safe use of chemical pesticides for farmers, and offer training for the retailers on pesticide alternatives. The training packages would enhance retailers' knowledge and capacity and encourage them to follow precautionary measures while handling pesticides. This information will help policymakers to make effective pesticide policies on pesticide use and safety behaviour in Nepal. Illegal import of banned pesticides through open Nepal-India boarders warrants severe punishment. When pesticide application doses exceeded their recommended rates, harmful effects to humans and the environment are inevitable (Meena et al., 2020). Good agricultural practices such as proper pesticide application, including safe pre-harvest intervals, and following recommended doses and application frequencies could increase agricultural production without hampering human health and the environment.

6.3.2 Implications for developing food safety and promoting integrated farming

To meet an increasing demand for food, famers have been using many chemical pesticides to protect their crops from pests and plant diseases. Globally, pesticide application has minimized crop loss and increased agricultural production. However, pesticide persistence and farmers' poor agricultural practices have raised several issues, including residues of pesticides in foods. While food safety has been considered a serious issue in developed nations, developing countries such as Nepal are still using toxic and persistent chemical pesticides on vegetable crops that are banned in the EU. Toxicological and risk assessment studies have been conducted worldwide and authorities have established pesticide MRLs in food commodities to ensure food safety. However, the government of Nepal has not yet established pesticide MRL legal framework for the most common foodstuffs, including vegetables, that would prevent consumer exposure to pesticides. Pesticide toxicity and risk assessment should also be conducted to achieve agricultural sustainability and food safety (Damalas and Koutroubas, 2016). However, risk assessment tools as well as comprehensive safety levels of pesticides in Nepalese foods have not yet developed.

The current use of OP insecticides, especially chlorpyrifos and triazophos, has a negative effect on human health via consumption of vegetables, particularly tomatoes. The vegetables from non-IPM fields contained higher concentrations and numbers of pesticides than IPM fields, therefore, this study recommends extensive IPM programs focussing especially on rural vegetable growers. Farmers should also be encouraged to adopt good agricultural practices to ensure food safety. Furthermore, regular monitoring of pesticide residues in different commodities may help to reduce dietary exposures in humans. This thesis (Chapter 3) examined the risk of insecticides due to tomato consumption. The current use of chlorpyrifos and triazophos in vegetables should be managed by enforcing strict regulations and an effective control mechanism.

6.3.3 Implications for occupational safety, including non-dietary exposure to pesticides

While working in fields treated with pesticides, farmers can be exposed to the residues present in soil. This also holds true for the people coming into contact with pesticides at their workplace. Due to pesticides drift, populations in the immediate areas surrounding agricultural lands are also exposed via different exposure pathways such as inhalation, ingestion and dermal contact. As mentioned in Chapter 1, in developing countries including Nepal, farmers do not use proper safety measures while handling pesticides and can be exposed even when mixing and applying pesticides. Most Nepalese farmers ignored sanitation behaviours such as washing hands, wearing clothes and taking baths after spraying and they did not follow safe pesticide use practices (Chapter 2). Despite the poor safety practices of farmers during spraying and working in the fields, exposure to pesticides via the non-dietary pathways was negligible. Of all pathways, ingestion contributed higher risks, although the risks were not serious. As soils from conventional fields had higher concentrations of residues than IPM fields, current exposure due to ingestion of contaminated soil particles may further increase health risks in the future. Therefore, it is important to regularly monitor the pesticide residues in soil, especially soils from the conventional fields, to gauge the potential non-dietary exposure to pesticides.

6.3.4 Implications for the protection of soil communities in Nepal

The aim of sustainable agricultural development is to feed increasing populations without hampering health and the environment. Indiscriminate use of pesticides in intensive agriculture is a major threat to non-target species, including soil organisms (Mojsak et al., 2018; Schulz, 2004). Pesticides adversely affect soil health, including microbes and their diversity, composition and biological processes (Meena et al., 2020). In Chapter 5, we assessed the ecological risk of pesticides detected in soils. Of all the pesticides studied, organophosphates such as profenofos and chlorpyrifos as well as neonicotinoids such as imidacloprid showed higher ecological risks. Therefore, pesticides belonging to these groups should be accounted for in future ecological risk assessments. Pesticide risk at sites increased with a decrease in farmers' knowledge of the effects of pesticides and their personal safety behaviour. Farmer awareness of the ecological effects of pesticides and the effective safety management of their packets and containers may help to reduce the current ecological risk. Furthermore, higher tiered future risk assessment studies for different ecosystems, focusing especially on organophosphates and neonicotinoids, are needed to safeguard biota and maintain ecosystem services.

6.4 Research challenges and future research directions

We conducted surveys with farmers and retailers focused on their knowledge, attitude and behaviour. This thesis adds value to the understanding of the safety behaviour and pesticide use of farmers and retailers. This was an attempt to identify factors affecting pesticide safety behaviour, assessing human health and environmental risk. We encountered a few challenges during the research period. Data on Maximum Residue Limits (MRLs), Acute Reference Dose (ARfD), Acceptable Daily Intake (ADI), and No Observed Effect Concentration (NOEC) for some pesticides detected in this study, including their degradation products, were not available. Furthermore, ADI and ARfD were based on No-Observed-Adverse-Effect level (NOAEL) that involved a default uncertainty factor (Alexander et al., 2008).

Future studies could be directed towards:

1. Upscaling a survey by including pesticide importers, formulators, and professional sprayers.
2. For a comprehensive dietary risk analysis, the number of samples and active ingredients should be increased, including imported foodstuffs. A 24-hour dietary recall method can be adopted during a survey for a more precise intake and risk estimation. A gender- based dietary risk study could be another option.
3. Continuous monitoring of pesticide residues in topsoil and including more pesticides that are used in vegetable farming during different seasons. Researchers should prioritize assessing the health and environmental risks posed by persistent and toxic OP insecticides that are currently applied.
4. Higher tiered risk assessment studies focusing on ecological risk to organisms in different ecosystems should conducted. Acute risk based on LD $(LC)_{50}$ might be conducted. The cocktail effect of pesticides should be assessed deploying a holistic risk assessment approach.

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English summary

Globally, crop loss has decreased with the increased application of chemical pesticides. Nonetheless, food safety has become an emerging challenge. Farmers prefer to use chemical pesticides because they are quick and effective at controlling plant diseases, insects and pests. Although the use of pesticides has minimized crop loss and helped maintain yields, pesticide misuse and overuse has ultimately put humans and the environment at great risk. Pesticides persist in the environment and have been shown to traverse the placenta and cause abnormalities in the fetus.

Every year, Nepal imports tons of pesticides mainly from two countries: India and China. These pesticides are mostly used for agriculture, particularly in the Terai region where vegetables are cultivated. The high use and misuse of chemical pesticides may lead to land pollution which can affect human health and ultimately cause ecosystem degradation. In Nepal, there is very little legal framework and few policies concerning pesticide use. Due to insufficient monitoring and supervision, even the policies that are in place are ineffective. For instance, Nepal has banned persistent and toxic pesticides such as phorate and endosulfan for many years, however they are still used in rural areas. Most of the rural farmers in Nepal lack education and are unaware of the toxic effects of the pesticides they use in their fields. Most pesticide retailers (*agrovets*) also lack sufficient training and knowledge. This makes them incapable of properly diagnosing plant diseases and recommending the appropriate chemical pesticides to farmers. Farmers and retailers are exposed to harmful chemicals when handling pesticides which puts them at risk. The fate and behaviour of pesticides differ with differences in biotic and abiotic factors such as soil, weather, climate, flora, farming practice and pesticide properties, all of which influence ecotoxicity.

Chapter 2 of this thesis aimed to examine pesticide use in a rural area of Nepal. We looked at pesticide use on vegetable crops and identified factors affecting the safety behaviour of farmers and pesticide retailers. We analysed interview data from 183 farmers and 45 retailers from the Gaidahawa Rural Municipality, Nepal. The Chapter made use of the Health Belief Model (HBM) to present the study results. Correlations between HBM constructs and the safety behaviour of farmers revealed that factors such as education, perceived threat and benefit, self-efficacy, and cues to action positively affected their pesticide use safety behaviour. Farmers perceived that pesticides posed low threats to humans and ecosystems. Due to the perceived lower threats from pesticides, farmers perceived that the use of personal protective equipment (PPE) had low benefits and high barriers such as unavailability and discomfort while using. Likewise, for retailers, perceived threat and cues

to action affected their safety behaviour. Although few retailers were aware of the effects of pesticides on their health and the environment, most retailers complained that there was not enough training on pesticide safety behaviour. While age and perceived barrier negatively affected farmers' safety behaviour, there was no such relationship seen in retailers. Farmers applied the highest amount of organophosphate insecticides and carbamate fungicides on eggplants, chillies and tomatoes. The short-term risks associated with pesticide exposure in farmers were headaches (>70%), skin irritation (>60%) and eye irritation (>30%). Most farmers perceived pesticides as a "medicine" and not a poison since pesticides cured plant diseases. This Chapter recommends that more educational activities be made available to farmers and retailers. These educational activities could include organizing pesticide-related documentaries and talk shows, broadcasting news via the radio, television, newspapers and mobile applications in order to increase the levels of knowledge and awareness among farmers and retailers. The government or scientists should provide them with training on how to safely handle pesticides and implement the best integrated pest management methods. The illegal import of chemical pesticides (including banned pesticides) in and around the border areas in Nepal is running rampant.

The study in Chapter 3 presents data from two different farming types: integrated pest management (IPM) and conventional farming. In this study, based on interview with farmers we looked at 23 pesticide residues, including their metabolites, in three vegetable crops: chillies (n=27), tomatoes (n=32) and eggplants (n=27). We used our results to assess the possible health risks from dietary exposure to pesticides. The study detected 14 different pesticide residues, including insecticides and fungicides, in the vegetables. The number of pesticides in cocktails from IPM and conventional farming systems ranged from 0-6 and 1-7, respectively. About 88% of the vegetables from conventional farming contained pesticide cocktails, while from IPM it was 47%. The study assessed adults' and adolescents' dietary risk of 6 organophosphate (OP) insecticides (dichlorvos, omethoate, dimethoate, triazophos, chlorpyrifos, profenofos), 1 neonicotinoid insecticide (imidacloprid), 1 anthranilic diamide insecticide (chlorantraniliprole), 1 benzimidazole fungicide (carbendazim), 1 phenylamide fungicide (metalaxyl), and 1 micro-organism derived insecticide (emamectin). OP insecticides such as quinalphos and other metabolites such as 3,5,6-trichloro−2-pyridinol (TCP) and N-(2,6-dimethylphenyl)-N-(methoxyacetyl)alanine lack human health-based toxicological reference values such as Acute Reference Dose (ARfD) and Acceptable Daily Intake (ADI), thus the health risks were unknown. The study adopted EFSA's risk assessment methods: hazard quotient (HQ) and hazard index (HI). ARfD and ADI information was obtained from the EFSA, JMPR and EU databases.

We detected residues of pesticides in over 90% of the sampled eggplant crops and 100% of the sampled tomato and chilli. The concentration of triazophos, omethoate, chlorpyrifos and carbendazim residues exceeded the EU MRLs (triazophos, 10 µg/kg; omethoate, 10

µg/kg; chlorpyrifos, 10-100 µg/kg; carbendazim, 100-500 µg/kg) in some samples. One individual tomato sample from conventional farming system contained up to 7 different residues, forming pesticide cocktails. The average concentration of imidacloprid, chlorpyrifos and its metabolite TCP in the vegetables sampled from conventional farming were found to have higher concentrations ($p < 0.05$) than the vegetables sampled from IPM farming. This shows that the adoption of IPM farming may significantly reduce pesticide residues in vegetables. Of all the vegetables and pesticides, carbendazim in tomatoes was high ($p < 0.05$).
The dietary risk assessment showed that the consumption of tomatoes could impose an acute risk from triazophos and chlorpyrifos for adults and adolescents. This Chapter recommends strengthening legal frameworks and offering alternative programs that support food safety. It recommends to either ban or strongly restrict the use of triazophos and chlorpyrifos in tomatoes. We also suggest the adoption of IPM farming to assure the safety of vegetables meant for human consumption.

The study in Chapter 4 aimed to assess non-dietary risk due to pesticide residues in soils by examining three major exposure pathways in humans: dermal contact, direct ingestion, and inhalation. We measured the concentration and distribution of pesticides at three depths (0-5 cm, 15-20 cm and 35-40 cm) of soil samples (n=147) from 2 farming types: integrated pest management (IPM) and conventional. We predicted the concentration of pesticides and their degradation products and compared these values with their internationally adopted soil regulatory guidance values. Hazard quotient and hazard index were used to characterize non-cancer risk in adults and adolescents. We used the USEPA models to assess cancer risk based on the average daily dose of pesticide exposure via the different exposure routes. We found pesticide residues more frequently in upper layers of soil (0-5 cm). We detected up to 7 residues in an individual soil sample from conventional farming. Soils from eggplant fields had a higher number of pesticide residues ($p < 0.05$) than tomato fields. Likewise, soils from conventional farming had a significantly higher number of pesticide residues ($p < 0.05$) than the soils from IPM farming. TCP and chlorantraniliprole residues were detected the most frequently. Of all tested pesticides and their degradation products (n=23), we detected 15 in soils, where chlorpyrifos and p,p'-DDT residues were found to be in the highest concentrations. Overall, the human health cancer and non-cancer risks posed by the pesticides in soils was negligible. Predicted concentrations of pesticides (PEC) were higher than their guidance values for most pesticides. This Chapter recommends promotion of IPM methods for reducing pesticide pollution in soils. We also urge future research focused on the risk that water pollution poses to humans.

Chapter 5 assesses ecological risk of pesticides (n=9) at 3 depths of soil. We performed a correlation analysis between the risk at a farmer's site and the farmer's knowledge and behaviour related to pesticide effects and waste management. We adopted globally used methods for risk assessment such as toxicity exposure ratio (TER) and risk quotient (RQ). We estimated risk for EFSA's soil organisms such as earthworms *(Eisenia fetida),* enchytraeids *(Enchytraeus crypticus),* springtails *(Folsomia candida),* mites *(Hypoaspis aculifer)* and nitrogen and carbon mineralization microorganisms. We made a comparison between the measured pesticide concentrations in soils and the pesticide permissible concentration (or the soil regulatory guidance value for pesticides whose RQ and TER could not be calculated). Profenofos, imidacloprid and chlorpyrifos showed a higher risk (RQ>1) at 2 depths (0-5 cm and 35-40 cm), 1 depth (35-40 cm) and 3 depths (0-5 cm, 15-20 cm and 35-40 cm), respectively. Estimated TER for most pesticides and their metabolites did not show chronic risks of pesticide exposure for soil organisms, except for *F. candida*. The TER of chlorpyrifos was <5 at all depths of soil which posed a chronic risk for *F. candida*. About 16% of the sites posed ecological risks, determining chlorpyrifos to be a main soil pollutant. The risk at sites increased significantly when farmers had poor pesticide knowledge and waste management practices. Ecotoxicity data related to soil organisms was not sufficient for all the pesticides, thus the risk assessment was not possible for all of the pesticides detected in soils. For pesticides to which the risk assessment was not possible, we compared their concentration with the existing threshold or guidance values in soil. A higher tiered method of risk assessment including residue cocktails could create a better picture of pesticide risks for ecological entities that future research might focus on.

Acknowledgements

The time has come to acknowledge and express my very great appreciation to all who helped me in my PhD journey. I would like to thank various people and institutions in The Netherlands and Nepal whose help made me to complete my PhD thesis.

First of all, my deepest thanks to Chair, Soil Physics and Land Management Group (SLM)- Prof. Dr. Coen Ritsema. I cannot forget the day you wrote an email that I got awarded Netherlands Universities Foundation for International Cooperation (Nuffic) fellowship for my PhD. Thank you so much for your trust and support during my PhD period. I would like to thank the Nuffic for funding me to pursue my PhD.

I would like to express my sincere and deepest gratitude to my promotor Prof. Dr. Violette Geissen for your support during the long journey of my PhD. Prof. Violette, thank you so much for accepting me as a Sandwich PhD under your supervision. I remember the first days in Wageningen University and Research (WUR) when we met at Atlas building and you helped me to connect with the staffs and students of our research group, SLM. Since then, I never felt alone and have nice memories. Your skilful, energetic and positive attitude really amazed me. I got generous freedom to be creative that helped me to think critically and act logically. You helped me a lot throughout my PhD providing reminders, suggestions, ideas and feedbacks that made me able to publish articles. At the time when I was in Nepal, I had many skype calls and discussions with you when I struggled while writing articles. I am also thankful to you for putting me in contact with Dr. Liangxin Fan and Prof. Paul T.J. Scheepers from School of Surveying and Land Information Engineering, Henan Polytechnic University, China and Radboudumc, Radboud Institute for Health Sciences, Netherlands, respectively. In a nutshell, I enjoyed very much working with you and thank you so much for everything!

I also want to express my gratitude to my co-promotors Dr. Kishor Atreya and Dr. Xiaomei Yang, for your patient guidance, enthusiastic encouragement and useful critiques during my PhD. Dr. Kishor, thank you so much for your support. Your help during my field survey and guidance on data entry was invaluable and countless. Your dedication towards research and publication inspired me and motivated to work harder. You used to ring me at the time when internet was not possible, which helped me to keep my progress on schedule. Thank you for all your timely and constructive comments, edits, corrections, suggestions and discussions in all the published articles. Thank you for your warm welcome to your office and home for guidance and discussions. Dr. Xiaomei, your teaching and encouragement were crucial for me, I learned a lot with you since I started my PhD. You helped me in preparing my PhD proposal focusing on pesticide residues and risk assessment before submitting it to the Graduate school, WIMEK. You were always available for help when I was in need during my PhD period.

Moreover, I would like to thank Prof. Paul T.J. Scheepers, Dr. Liangxin Fan, Dr Hans Mol and Dr. Jana Vašíčková (RECETOX) for your corrections and suggestions as well as co-authorship with my publications. Your critical comments to the manuscripts helped me learn more and successfully publish articles.

I am also grateful to Paul Zomer, Rita Boerrigter-Eenling, Joost Memelink, Nicolas Beriot and Suryati Sunarto for all their help and sharing of knowledge during my lab work in Wageningen Food Safety Research, part of WUR. I learned a lot about pesticide analytics as well as GC-MS/MS and LC-MS/MS with you. Your guidance and support helped me a lot and the lab work ended well.

Moreover, I would like to thank all the colleagues who greatly helped me a lot during questionnaire survey as well as vegetables sample collection at the field. Thank you Garima Joshi, Samikshya Pandit, Sunil Ghimire, Kumar Pun Magar, Dipak Pandey and Ravi Raj Mishra for your help in the survey. Thank you Dinesh Ghimire, Prashant Chaudhary, Santosh Gupta and Ramesh Lodh for your help in the sample collection. I would like to thank all the residents of the study area who helped me by responding during the survey. Thank you for the Gaidahawa Rural Municipality officials who cooperated during the survey and provided the information of the municipality. Special thanks to Santosh Bhusal, agricultural extension officer of the municipality for your advice in selecting the villages and sampling locations during the fieldwork. Thank you Prof. Dr. Roshan M. Bajracharya, Prof. Dr. Keshab R. Adhakari, Dr. Bhaba Prasad Tripathi, Dr. Jagannath Joshi, Dr. Sanjeev Bhuchar, Samden Lama Sherpa, Sarkardeep Shrestha, Dil Bahadur Bhattarai, Bihani Thapa, Shova Shrestha for hosting Dr. Johannes Botschek and his team as well as helping me to organize a field visit for them in a course entitled “Human Induced Land Degradation”. Thank you Standy Christianto for providing me the field photos. I would also like to thank Shikhar Prasad Lamichhane for your help and skills with graphics that I needed for some of my articles. I would like to thank Poshan Niraula for teaching me basics of the ArcGIS. Thank you Sunil Shrestha for your help in booking air tickets and accommodation during my travel in and out.

A special thanks goes to all staff members from SLM research group for their help, friendship and cooperation. I would like to thank Dr. Jos van Dam for all your help in refining the PhD research proposal. I had my first experience of canoeing in Netherlands and you helped me to do it. Thank you Marnella van der Tol and Rianne Maasen for all your help and support, including documentation, accommodation as well as solving technical issues when needed.

I am thankful to Marnella as you received me very well in Atlas building for the first time and helped me to move my luggage to my room with your nice car. Thank you Robin Palmer and Jaclyn Bandy for your help in English revision of the articles. I want to thank Geert Belgers and Kees van der Klift who handled administrative and financial matters throughout my PhD study. I want to convey special thanks to my WUR colleagues: Shyam Shrestha, Ashok Subedi, Carlos Faundez Urbina, Ammar Ali, Vera Felix da Graca Silva, Raoul Kpegli, Karrar Mahdi, Yueling Qi, Ricardo Teixeira da Silva, Mousumi Akter, Nicolas Beriot, Murilo Vianna, Kaveh Hosseini and Godeberthe Nkeshimana for your friendship during the last 4.5 years. Thank you Dr. Isaurinda Baptista and Dr. Suman Bajracharya for inviting me to your PhD party that inspired a lot to make me confident enough since the early days of my PhD journey. Thanks to my previous Nepalese colleagues in WUR: BP Dhakal, TN Joshi, Sudip Subedi, RP Mainali, Binita Thapa, Aakash Koirala, Deny Kumar Shrestha, Kriti Shrestha, Pragya Shrestha and Dr. Arun Kumar Pratihast for your wonderful friendship. I can remember the typical Nepalese food that we had together in the past that made a homely environment for me during my stay in The Netherlands. Thanks to my corridor international friends in Bornsesteeg: Kashmira Bandal and Ade Ryane for celebrating with international foods in weekends.

I am grateful to my colleagues at the Progressive Sustainable Developers Nepal (PSD-Nepal) for arranging everything before and during my PhD period. I would like to thank Dr. Sangeeta Poudel, Dr. Peter Matthews, Dr. Banalata Sen, Dr. Prakash Bhave, Ambika Pandey, Suman Dangol, Sioux Cumming, Roshan Nepal, Pradip Shrestha, Bhanu Panthi and Jeevan Thapa for helping in moving the PSD-Nepal projects smoothly during my absence.

Last but not least, I am very grateful to my family members, including my father, mother, sisters and brothers-in-law. My loving wife Ambika Bhandari and my beautiful daughter Aaravi Bhandari deserve very special thanks for their continuous moral support, pray and blessings. Ambika, you were always there to support me and encourage me when I felt bad due to rejections of articles and frustrations. During the last year of my PhD, I could stay in Nepal with you and your endless love and support which I will never forget.

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About the author

Govinda Bhandari (1984), son of Thaneshwar Bhandari and Kamala Devi Bhandari, was born in the village of Bastu in Gulmi district, Nepal. His father is a retired government secretary of a village in the district, while his mother is a house wife.

Govinda completed his 10+2 level from Terai, Rupandehi district. Later, he went to the capital city, Kathmandu to do his BSc in Environmental Science. After the completion of BSc from Tribhuvan University, he got an opportunity to do MSc in Ecology and Environment from Sikkim Manipal University, India. After completing his MSc, he worked as a Lecturer at Hilbert International College, Kamaladi, Kathmandu for 2 years. Later, started an Non-Government Office (NGO) named Progressive Sustainable Developers Nepal (PSD-Nepal), which aimed primarily for working in the areas of health and environment in Nepal. In the NGO, he is the President and actively engaged in research training and capacity building for Nepalese junior researchers as well as helping them with their thesis and reports. His interests grew in scientific writing and publishing. Within a short period after the NGO, he started a scientific journal, the *International Journal of Environment* (eISSN: 2091-2854), an official journal of PSD-Nepal. He is the Editor-in-Chief of the journal since 2013.

In the year 2016, he was awarded a Nuffic fellowship through a project NFP-PhD-5160957247, funded by the Dutch government to do his Sandwich PhD in the Wageningen University and Research, The Netherlands. He then started his PhD work in the Soil Physics and Land Management Group (SLM) supervised by Prof. Dr. Violette Geissen and co supervised by Dr. Xiaomei Yang and Dr. Kishor Atreya. During his PhD, he tried to explore the pesticide residues in Nepalese vegetable and soils as well as assessed their risk to human health and the environment, which is quite a new contribution for science and a baseline for pesticide perspectives in Nepal.

During his PhD research, Govinda participated in workshops, trainings and conferences organized in Nepal and The Netherlands. He organized capacity building trainings on scientific writing and publishing for Nepalese researchers. In his free time, Govinda likes playing badminton and listening Nepalese folk songs. After his PhD, Govinda is looking forward to working in projects related to ecotoxicology in Nepal or elsewhere in the globe.

Latest publications

Bhandari G, Atreya K, Yang X, Fan L, Geissen V. Factors affecting pesticide safety behaviour: The perceptions of Nepalese farmers and retailers. Science of The Total Environment 2018; 631-632: 1560-1571.

Bhandari G, Zomer P, Atreya K, Mol HGJ, Yang X, Geissen V. Pesticide residues in Nepalese vegetables and potential health risks. Environ Res 2019; 172: 511-521.

Bhandari G, Atreya K, Scheepers PTJ, Geissen V. Concentration and distribution of pesticide residues in soil: Non-dietary human health risk assessment. Chemosphere 2020; 253: 126594.

Manuscript (under review)

Ecological risk assessment of pesticide residues in soils from vegetable production areas: A case study in S-Nepal. Environmental Pollution.

Acknowledgements of financial support

This PhD research was financially supported by the Netherlands Universities Foundation for International Cooperation (Nuffic)-through the PhD grant number NFP-PhD-5160957247.

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SENSE PhD Courses

- Environmental research in context (2016)
- Basic Statistics (2016)
- Research in context activity: 'Organising seminar and the Nepal excursion 'Human induced land degradation' (2017)

Other PhD and Advanced MSc Courses

- Information Literacy PhD including EndNote Introduction, Wageningen Graduate Schools (2016)
- Reviewing a Scientific Paper, Wageningen Graduate Schools (2016)
- Training course on GIS and GPS for faculty members, researchers, MSc and PhD students, Nepal GIS Society (2017)
- Journal Publishing Practices and Standards, INASP and Tribhuvan University (2017)
- Peer Review course for researchers and journal editors, INASP (2019)
- Publication Ethics course for researchers and journal editors, INASP (2020)
- Copyright and Licensing course for researchers and journal editors, INASP (2020)

Management and Didactic Skills Training

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- Teaching in the MSc course 'Scientific writing and publishing' (2019)
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Oral Presentations

- *Land Degradation in Nepal: A Case of Pesticide Pollution.* Human induced Land Degradation, 2-10 September 2017, Kathmandu, Nepal

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