Neonicotinoids and Pollinators, Both in Service of Food Supply

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This article is based on a talk given by Tjeerd Blacquière at the 2014 BBKA Spring Convention and was much appreciated by the audience.

Since the onset of human agriculture thousands of years ago, selection for reduced human toxicity and improved human digestibility of seeds and tubers has led to crops that are more vulnerable to diseases and pest organisms than their ancestral wild relatives (Fresco, 2012). For many pests, farmers' cuisine is preferred over natures' cuisine. Wild plants avoid being eaten (by insects, herbivores and us) while crop plants are made for being eaten (eaten by us, but also easily by herbivores, insects and fungi). Therefore, pests need to be controlled if people wish to harvest a high share of the yield of their crops. In her book Fresco explains that people in former times had not so much grip upon their harvest of food, and food was therefore surrounded by many rituals and incantations. Only in recent centuries has food production become more reliable, and hunger has almost disappeared in recent decades.

Among the pests attacking human food crops, insects take a big share. Insecticides have therefore long been used to control insect pests in crops. Several classes have passed by because of evolved resistance of pests against specific insecticides and sometimes because of problematic side-effects e.g. DDT, although this is still used in several parts of the world. Several newer insecticides have systemic properties which make their application through addition to seeds in seed coatings possible, a method that strongly reduces the amount of active ingredient to be used. An important share in this class is taken by the neonicotinoids. Neonicotinoids have the additional advantage that they show much higher affinity to insect nicotinic acetylcholine receptors than to mammalian and bird receptors, which reduces risks for farmers and birds (Casida & Durkin, 2013). Neonicotinoids have been used since the 1990s on a growing range of crops.

Toxicity of neonicotinoids

Neonicotinoids are highly toxic to target pest insects as well as non-target insects, (partly) beneficial ones, among which are bees and other pollinators. Since honey bees are one of the default organisms on which insecticides for crop protection need to be tested, ample toxicity data are available in the registration files presented to registration boards and to a large extent also in the public peer-reviewed scientific literature (Blacquière *et al*., 2012). Because of their high toxicity, neonicotinoids, and a few other systemic insecticides, have often been considered a threat to bees, and suspected to be implicated in the losses of colonies of honey bees occurring in some parts of the world.

Exposure

In the real world, toxicity only leads to hazard when exposure to the toxin occurs. For that reason much of the risk-assessment (RA) criteria are about the expected exposure and possible avoidance or mitigation of too high exposures. Because they are systemic, neonicotinoids may end up in nectar and pollen of crops and hence may be consumed and harvested by pollinators. Exposures will, based on the RA, typically be in the non-lethal or so called sub-lethal ranges (Blacquière *et al*., 2012). These ranges extend from just below the lethal dose for 50% of the individuals, the LD50, to several orders of magnitude lower. Exposures in the field are in general at least one but generally a few orders of magnitude lower than the laboratory estimated LD50s. Surprisingly the majority of testing is done with dosages close to the LD50s (Walters, 2013). This may be one important cause for discrepancies experienced between laboratory studies and field studies.

The most important exposure routes for bees to neonicotinoids are the residues in pollen and nectar of treated crops collected by foragers and brought to the colony. Concentrations of the major neonicotinoids in pollen and nectar are in the low nanograms per gram range (Blacquière *et al*., 2012), exposing bees that collect ~25–50 mg of food per trip to ~60–120 picograms/bee (although most of this is not consumed but only loaded and carried, see Fournier *et al*., 2014). Oral LD50s are ~4 nanograms/bee. Exposures through dust at sowing can be much higher, but can be mitigated (better coating with no dust and better drilling equipment), as well as those by guttation droplets from crop plants, which will probably not be harvested by bees.

Sub-lethal effects at low exposures

Sub-lethal effects are all those effects that do not cause death of an individual, or a colony in case of honey bee colony loss, but which to any extent affect its performance (Cresswell, 2011). Learning and memory can be tested with the proboscis extension response, or through learning and memorising the route through a complex maze. More or less at field-scale the homing response of bees can be evaluated as an endpoint incorporating several contributing, and possibly affected, components such as orientation ability, memorising of the surroundings as well as muscular flight capacity. If homing is negatively affected this will immediately draw back on the performance of colonies through reduced food gain and reduced longevity of individuals leading to reduced colony strength (Henry *et al*., 2013). Homing is one of the tests suggested by the European Food Safety Agency (EFSA) to be included in risk-assessment, however at field-realistic dosages or exposures effects may be hard to determine.

Interactions

Sub-lethal impairments of behaviour might result in reduced social immunity responses such as grooming or hygienic behaviour, on top of possible direct negative effects on the individual (cellular) immune response (Wilson-Rich *et al*., 2009). Much concern has arisen about possible additive and synergistic interactions between exposure to neonicotinoids and to pathogens. Several studies have tested combined exposure to neonicotinoids and pathogens in a laboratory setting, and demonstrated effects on the mortality of bees and development of the pathogen, both additive and synergetic. Sometimes expression of specific genes was evaluated

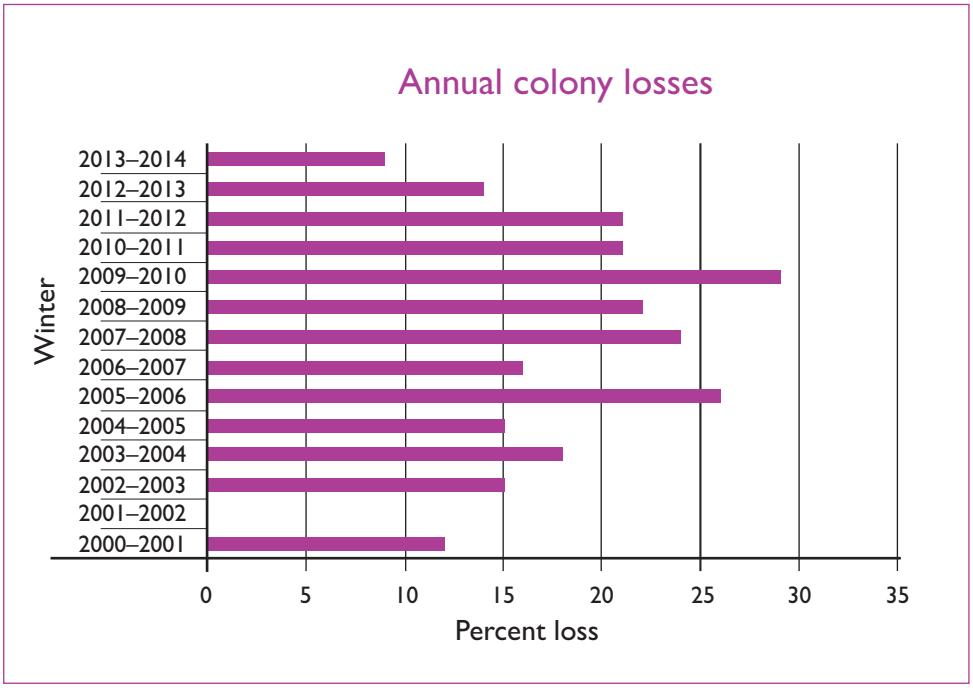

Figure 1. Colony losses in the Netherlands since 2001. *Data are based on surveys by Bees@wur from Wageningen University and Research, by beekeepers associations NCB/ZLTO and by Beemonitoring.org. Most data are from voluntary responses to enquiries with many questions. The data from 2013 and 2014 are based on an active telephone poll by bees@wur and the NBV begin in April among a random sample of the members of the beekeeping associations. In this case only three questions were asked: beekeepers address, number of colonies wintered, and number of colonies surviving to date.*

High losses in 2005–06 are unexplained, although it was a severe winter. The 29% loss in 2009–10 was increased by the use of winterfeed with high HMF content. This accounted for a loss of 6%, leaving 23% for 'normal' losses.

as the endpoint. However, in most cases no effects have been found with similar treatments in the field at colony level. Studying synergisms asks for sophisticated approaches. In these cases it is not enough merely to test exposure to the neonicotinoid, chronically, and at a field-realistic rate and method of application; the suspected synergistically-acting pathogen needs also be tested at a realistic 'infection dosage' and in a 'natural' manner of exposure.

Cresswell (2012) concluded using Hill's Epidemiological Criteria that neonicotinoids were an improbable cause for honey bee colony declines, although the conclusion might be provisional, since there is a lack of certain data. To partly fill that gap, in our 2012 review (Blacquière *et al*., 2012) we recommended to the chemical industry that it publishes as much as possible of these field studies, although it will not be easy to publish big studies showing 'no effect', which actually translates as: 'safe'. Although it is easier to publish papers which do show positive results which might translate to: 'risk', I would strongly call for inclusion of at least one field-realistic exposure/dosage in every study conducted.

In perspective: other factors contributing to honey bee declines

Many factors have been mentioned in the literature, e.g. Kluser *et al*, 2011. In Germany in a large multi-year monitoring it was found that when the varroa mite infestation of colonies was very low through good beekeeping practice, losses were reduced to ~4% (Genersch *et al*., 2010). In two quick surveys in the Netherlands in spring 2013 and 2014, it was found that 70% of the beekeepers did not lose any colonies. The mean loss of 14% (2013) and 9% (2014) was therefore just caused by one third of the apiaries, which were just distributed among the no-loss apiaries. See Figure 1 for an overview of colony losses in the Netherlands since 2001.

Beekeepers should concentrate on good beekeeping practice firstly, which includes proper varroa control. And we should, scientists as well as beekeepers and citizens, take care to do proper experiments, at relevant exposure rates, and to keep up sober reasoning. Agriculture needs both the use of crop protection products as well as pollinators. We all are dependent on both, by clever applications we will benefit from both.

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