Iron and Zinc Deficiencies in China: Existing Problems and Possible Solutions

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Dit onderzoek is uitgevoerd binnen de onderzoekschool VLAG
(Voeding, Levensmiddelentechnologie, Agrobiotechnologie en Gezondheid)

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Proefschrift
ter verkrijging van de graad van doctor
op gezag van de rector magnificus
van Wageningen Universiteit,
prof.dr. M.J. Kropff,
in het openbaar te verdedigen
op maandag 15 januari 2007
des namiddags te vier uur in de Aula

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Thesis Wageningen University – with summaries in English, Dutch and Chinese
ISBN: 90-8504-560-6

“The road to regional health and life-long productivity cannot be passed without removing the obstacle of vitamin and mineral deficiency.”

Joseph Hunt, Health and Nutrition Adviser, Asian Development Bank

# Abstract

Background: Micronutrient deficiencies affect the health and development of the population of China as well as its social and economic development. Iron and zinc deficiencies are quite prevalent, while insufficient intake and poor bioavailability are the major causes. Phytate is believed to be a potent inhibitor. Feasible, cost-effective and sustainable intervention programs to combat iron and zinc deficiencies need to be identified and developed.

Objectives: To examine the phytate content in foods, and in the diets, and its inhibitory effect on the bioavailability of iron and zinc.

To describe the magnitude of iron and zinc deficiencies and identify feasible, cost-effective and sustainable intervention strategies in China.

Methods: The phytate intake and zinc intake adequacy were assessed using data of 68,962 subjects from the 2002 China National Nutrition and Health Survey (a national representative survey). The dietary assessment data were collected using consecutive three days 24h recall by trained interviewers. The phytate content in the food samples was determined using the anion-exchange method. The phytate/minerals molar ratios of the foods and the diets were calculated. The following suggested critical values were used as the indicator for the inhibitory effect of phytate on the bioavailability of minerals: phytate/iron >1, phytate/zinc >15, phytate/calcium >0.24, phytate×calcium/zinc >200.

The costs and cost-effectiveness of supplementation, food diversification, and food fortification were estimated using the standard WHO ingredients-approach. For biofortification - a process of agronomic intervention or genetic selection of crop plants to increase the bioavailable concentrations of a component - the costs per capita were calculated according to the method in the literature. Cost-effectiveness of biofortification could not be determined. Biofortification of staples is believed to be a promising strategy for micronutrient deficiency.

Results: The phytate content of 60 foods ranged from 0 to 1878 mg/100 g. Of the samples, 53 foods had phytate/iron molar ratio >1, a total of 31 foods had phytate/zinc molar ratio >15. Phytate in commonly consumed foods in China impairs the bioavailability of iron and zinc.

The phytate intake was between 648 and 1433 mg/day. Urban residents consumed much less phytate than their rural counterparts (781 vs 1342 mg/day). The proportion of subjects with ratios above the critical values of phytate/iron and phytate/zinc were 95.4% and 23.1%. Phytate showed an inhibitory effect on the bioavailability of iron and zinc in the diets of people in China.

The overall prevalence of anaemia was 20.1%. Approximately, 30% of children (<2 years), adults (>60 years), pregnant and lactating women, and 20% of women of reproductive age were anemic. The proportions of zinc intake inadequacy were between 2.8% and 29.4%. Significantly higher proportions of zinc inadequacy were found in the category of phytate/zinc molar ratio >15 for both rural and urban residents. About 20% of rural children are "at risk" of inadequate zinc intakes.

The costs per capita for biofortification was the lowest intervention (International dollars (I$) = 0.01) for both iron and zinc deficiency. Food fortification was the most cost-effective for iron deficiency [I$ = 66/DALY (Disability Adjusted Life Years)], while dietary diversification for zinc deficiency (I$ = 103/DALY).

Conclusion: Iron and zinc deficiencies are of public health significance in China, which affects a large number of people. Phytate in the diets inhibits the bioavailability of iron and zinc, and plays an important role in the deficiencies of iron and zinc. Supplementation and fortification can be applied as short-term intervention, while dietary diversification and biofortification are the long-term strategies. Biofortification with improved varieties for micronutrient content and availability is a feasible, cost-effective and sustainable solution, especially for the rural Chinese population.

Contents

Chapter 1

Introduction

Micronutrients and Human Health

Micronutrients are essential minerals and vitamins that are needed in small amounts for various physiological functions of the human body. Because the body itself can not make the micronutrients or synthesize it in adequate quantities, humans need to obtain micronutrients from foods or other sources, like supplements. Deficiency may result from the shortage of one or more essential nutrients when the requirements are not met.

Iron

Human body requires iron for the synthesis of hemoglobin and myoglobin for transporting the oxygen, and for the formation of heme enzymes and other iron-containing enzymes which are particularly important for energy production, immune defense and thyroid function (1).

Most of the iron in the body is present in the erythrocytes. There is no active iron excretion from the body in urine or in the intestines. Iron is lost with cells of skin, intestines, urinary tract, and airways (2), and sweat iron losses are negligible (3). The body normally regulates iron absorption so as to replace the obligatory losses.

There are two types of dietary iron, heme iron from the hemoglobin and myoglobin of animal products, and non-heme iron presents in both plan and animal foods. Heme and nonheme iron are absorbed by separate pathways (4). Iron absorption in the body varies considerably depending on the food source. The absorption of heme iron is hardly influenced by the composition of the diet (5), and it depends mainly on the iron status of the individual. The absorption of heme iron varies between 15% and 35%.

The absorption mechanism of non-heme iron is different from that of heme iron. Non-heme iron enters a common non-heme iron pool in the gastric juice (6), the amount of iron absorbed depends to a large extent on the presence of enhancing and inhibitory substances in the meal and on the iron status of the individual (7-10). The absorption of non-heme iron ranges from 1 to 20%. The main enhancers of iron absorption are ascorbic acid (11) from fruits and vegetables and the partially digested peptides from muscle tissues (12). The main inhibitors are phytic acid from cereal grains (13) and legumes such as soy (14), and polyphenol compounds from beverages such as tea and coffee (15).

The proportion of the two forms of iron depends on the meal components. In populations with high meat consumption, heme iron contributes 40% or more to the total absorbed iron (8, 16, 17). In contrast, for most people living in developing countries, non-heme iron accounts for the majority of iron because of the low consumption of animal products. Heme iron only contributed 3.3% of the total dietary iron intake for people in

China (18), and urban residents consumed significantly more heme iron than their rural counterparts (1.3 vs 0.5 mg/d).

Zinc

Zinc is present in all body tissues and fluids. It is necessary for a wide range of biochemical, immunological and clinical functions (19). Zinc acts as a stabilizer of the structures of membranes and cellular components. Its biochemical function is as an essential component of a large number of zinc-dependent enzymes (20), particularly in the synthesis and degradation of carbohydrates, lipids, proteins and nucleic acids. Zinc plays a central role in the immune system (21, 22). The expression of the metallothionein gene, apoptosis and synaptic signaling is regulated by zinc. These biochemical functions of zinc give it a unique role for growth and development (23).

Zinc absorption is concentration-depended and it occurs throughout the small intestine. The absorption of zinc consists of a specific, saturable carrier-mediated component and a nonspecific, unsaturable diffusion-mediated component (24, 25). Zinc is likely to predominantly be transported via the saturable, specific transport mechanism. The body does not store zinc in the conventional sense. The major losses of zinc from the body are through the intestine, urine, skin and sweat.

Zinc absorption is influenced by several dietary factors (26). The amount of zinc in a meal affects zinc absorption (27), and fractional zinc absorption decreases with increasing amounts of zinc in the meal. The amount of protein in a meal is positively correlated to zinc absorption (28), while the effect of protein source on zinc absorption has not been explicitly studied (27, 29, 30). The major inhibitor of zinc absorption is phytate (31, 32), which is mainly from plant foods, especially cereals and legumes, binds zinc to form insoluble complexes in the intestinal lumen (26). It is reported that fiber in itself has no or little effect on zinc absorption (31, 33, 34). Studies indicated that calcium per se has no effect on zinc absorption (35-37). However, calcium with phytate and zinc form insoluble complexes when diets are high in both phytate and calcium, therefore, the zinc absorption will be impaired.

Meat and seafood are good sources of zinc. About 50% of zinc in the U.S. diet is provided by animal products (38-41). However, in many parts of the developing world, most zinc is provided by cereals and legume seeds. These plant foods are at the same moment high in phytate, which is a potent inhibitor of zinc absorption (13, 42). Information on food sources of zinc are lacking in developing countries including China.

In conclusion, both iron and zinc play important roles in human health. The dietary absorption of iron and zinc vary depending on the food source, and enhancing and inhibitory factors in the diets. Non-heme iron contributes the majority of total dietary iron for people in developing countries including China, making the absorption poor. Information on the food source of zinc is lacking and needs to be studied in China.

Micronutrients Deficiency

In 1990, the World Summit for Children endorsed the elimination of micronutrient malnutrition in developing countries by the year 2000, specifically deficiencies of vitamin A, iron and iodine. Zinc was added to the list at the Third Report of the World Nutrition Situation (43, 44).

In addition to protein-energy malnutrition, deficiencies of minerals and vitamins affect a high proportion of the world’s population, particularly in the developing world. Even in the developed countries micronutrient deficiencies affect a significant number of the population. Taken together, micronutrient deficiencies affect a far greater number of the world's population than protein-energy malnutrition.

Micronutrients deficiencies not only affect the health, mental and physical function (45-48), and survival of people (49), but also hamper the economic development of a region or a country. The World Bank has estimated that, at the levels of micronutrient malnutrition existing in South Asia, 5% of gross national product is lost each year due to just three nutrients deficiencies: iron, vitamin A and iodine. For each 50 million in population, an economic loss of $1 billion per year is accompanied.

Ross et al (50) estimated the effect of iron deficiency on the economic productivity in China using PROFILES, and found out that if adult anaemia has remained at the levels (women 35.6%, men 13.7%) in 2001, there would be RMB702 billion losses in productivity over the next ten years, while that of anaemia among children would be RMB2.4 trillion, which in total accounted for more than 3.6% Gross National Product (GNP) of China.

Iron Deficiency

Iron deficiency can decrease mental and psychomotor development in children (45, 51, 52), increase both morbidity and mortality of mother and child at childbirth, impair body temperature regulation (53), diminish work performance and decrease resistance to infection (54, 55).

It has been estimated that two to three billion of the world's population in developing countries are iron deficient. Women and children are particularly at risk of iron deficiency because of their elevated requirements for child-bearing and growth respectively. Iron deficiency anaemia affects about one billion people world-wide and is most prevalent in infants, children and women of child-bearing age in developing countries, where some 50% or more of these population groups may be anemic (56). An estimated 58% of the pregnant women in developing countries are anemic, and their infants are more likely to be born with low birth weight. WHO estimated that 31% of these children under 5 years old are also anemic.

The latest published data in China (57) indicated that the overall prevalence of anaemia is 20.1%. It is more prevalent among female residents than males (23.3 vs 15.8%), while it is more common in rural areas than in urban areas (20.8 vs 18.2%). It is revealed that 85-95% of anaemia in China is caused by iron deficiency (58-63).

The major causes of iron deficiency in developing countries include insufficient intake and poor bioavailability (64-66). Although the total intake of iron (24.4 mg/d) in the Chinese population is high, reaching about 177% of the Chinese Recommended Dietary Allowance (RDA) or 209% of the U.S. RDA (18), the iron deficiency is still prevalent, suggesting that the major cause of iron deficiency is low bioavailability in China (59, 67).

Zinc Deficiency

Zinc homeostasis in the body can be maintained over a wide range of zinc intakes by increasing or decreasing both zinc absorption and excretion, ultimately low zinc intake and/or bioavailability will result in zinc deficiency. When zinc is deficient, the body limits growth and/or reduces excretion in an effort to conserve zinc. Even in severe zinc deficiency situation, zinc concentrations in tissues may not be low because the body conserves zinc. There are no specific signs and symptoms associated with zinc deficiency; it may include retarded growth, depressed immune function, anorexia, dermatitis, skeletal abnormalities, diarrhea, alopecia and increased complication, and mortality during childhood (23, 68-71).

Zinc deficiency cases were first identified in the 1960s in the Middle East (72). Since then, marginal zinc deficiency and suboptimal zinc status have been recognized in many population groups in both less developed and industrialized countries (26). However, zinc deficiency has not received as much attention because of the shortage of the data of zinc contents and its anti-nutrients for local staple foods (73). There is no estimation of the global prevalence of zinc deficiency due to the paucity of generally accepted biomarkers of zinc status and of pathognomonic clinical features of zinc deficiency (69, 74). Although measurement of zinc consumption and/or plasma zinc concentration can be used to assess population zinc status, few countries have collected adequate data to permit estimation of the prevalence of zinc deficiency.

According to the estimation of the WHO (75), the percentage of the national populations at risk for low zinc intake ranges from 1 to 13% in the countries of Europe and North America to 68-95% in South and Southeast Asia, Africa, and the Eastern Mediterranean regions. Globally, nearly half of the world's population is at risk for inadequate zinc intake.

Although the cause of suboptimal zinc status in some cases may be inadequate dietary intake of zinc, inhibitors of zinc absorption are likely the most common causative factors (73, 76). The diets of people in developing countries are predominantly plant-based, especially for those living in rural areas. Available zinc for absorption is low as the consumption of animal products is low. Information on zinc intakes in developing countries is limited because of the paucity of data on the zinc content of the local foods. As the zinc content of foods is related to the mineral content of the soil (77, 78), it is not advisable to use the zinc data from other countries. Currently, few developing countries have information on zinc status at the national level.

Although the zinc contents of foods are available in the China Food Composition Table (79), the risk of zinc deficiency in populations has never been assessed because of the lack of data of phytate content of foods.

In conclusion, anaemia is prevalent in developing countries including China. The main cause of anaemia is the low bioavailability of iron because of the plant-food-based dietary pattern. The underlying mechanism needs to be studied in order to fight iron deficiency. Zinc deficiency has not been paid much attention because of the lack of sensitive and specific indexes. The magnitude of zinc adequacy of the population in China has not been assessed.

Phytate and Micronutrient Deficiency

The causes of micronutrients deficiencies include inadequate intakes, impaired absorption and/or utilization, excessive losses, increased physiological need (infancy, pregnancy, lactation) or a combination of these factors (73). It is reported that insufficient intake and poor bioavailability are major causes in developing countries, especially the latter (64, 65). Discounting the effect of individual's status, the bioavailability of the micronutrients is determined largely by its solubility in the intestine, which is affected by the presence of specific inhibitors of absorption.

Phytic acid is myo-inositol 1,2,3,4,5,6 hexakis phosphate (IP6), and it accumulates in cereal grains, nuts and legume seeds. Phytic acid is a strong chelator of divalent minerals such as iron, zinc, calcium, copper, and magnesium. Phytate exerts its inhibitory effect on the absorption of minerals by forming insoluble and indigestible complexes (42, 80-82). The effect of phytate on the bioavailability of minerals depends on not only the amount of phytate and minerals in the diets (34, 83), but also the ratio of phytate/minerals. Therefore, the phytate/minerals molar ratios are used to predict its inhibitory effect on the bioavailability of minerals in the food and diet (31, 84-89). The phytate/iron molar ratio >1 is regarded as indicative of poor iron bioavailability (90). The phytate/calcium molar ratio >0.24 will impair calcium bioavailability (85). Zinc absorption is greatly reduced and results in negative zinc balance when phytate/zinc molar ratio is >15 (31, 89, 91-93). Most plant-based diets have low calcium contents which does not inhibit zinc absorption. When diets are high in both phytate and calcium, phytate×calcium/zinc is better used to assess the zinc bioavailability than phytate/zinc molar ratio (84).

The inhibitory effect of phytate should be taken into account when assessing the micronutrient deficiency (75, 94). However, information on food contents and dietary intakes of phytate in developing countries is limited because of the paucity of data on the phytate content of the local foods. As there are wide variations of the phytate content of foods (95-98), the use of the database from other countries is not advisable because the mineral and phytate contents of plant-based foods tends to reflect local soil mineral levels, and food-preparation and processing techniques (92, 99). In order to assess the inhibitory effect of phytate on the bioavailability of minerals, the data of phytate contents in local foods should be available. The inhibitory effect of phytate on minerals has never been assessed in China because the above-mentioned reasons.

In conclusion, the inhibitory effect of phytate should be taken into account when assessing iron and zinc deficiencies. However, data on the phytate content of foods, and phytate intakes and its inhibitory effect on the bioavailability of iron and zinc are lacking in China.

Solutions for Micronutrient Deficiency

The World Bank indicated that interventions to end micronutrient deficiency were among the most cost-effective investments in the health sector (100). Failure to act in a country where micronutrient deficiency exists would result in a loss of 2-3% of the gross domestic product (64). Inevitably, investments are needed to implement the program(s), but the economic and social payoffs can reach as high as 84 times of the program costs (100). Ending micronutrient deficiency can provide the foundation for the elimination of poverty and for sustainable economic progress by preventing illness and death and by helping populations to become healthier, more intelligent, more educated and more productive.

Supplementation**, **food fortification and ***dietary diversification*** have been the three widely applied interventions for fighting micronutrient deficiency for the past decades. Each one has its advantages and disadvantages.

Supplementation is the addition of an element to the diet to make up for an insufficiency. Supplementation of vitamin A, iron and zinc has been proven in developing countries for rapid improvement of the mineral status in deficient individuals. Supplementation programs for the prevention of iron deficiency, particularly for pregnant women, are under way in 90 of 112 countries (101). The advantages of supplementation include easy to implement, and relatively rapid impact (102-105). However, the sustainability of these programs is questionable because of various economic, social and political difficulties that diminish their effectiveness at reaching all of the people at risk (106). To date, there is no large-scale national supplementation program in China, only a few research-oriented supplementation studies have been conducted (107-110).

Food fortification is the addition of an ingredient to food to increase the concentration of a particular element. It has been used for restoring nutrients removed during food processing, to replace nutrients in substitute, or to correct nutrient deficiency in populations (111). Fortification has been successfully used to improve the nutritional quality of the food supply in industrialized countries for many decades (112-114) but has only recently been applied in many developing countries (115, 116). Nowadays, about 50 countries are using food fortification as a strategy to fight micronutrient deficiency (117). For example, the introduction of iodine-fortified salt in China has decreased the incidence of goiter among primary students from 20% in 1992 to 8.3% in 2001 (116).

The advantages of food fortification include wide coverage, easy to implement, cheap, and increase the intake of multiple micronutrients simultaneously (118). The constraint is the reach of the most needed subset population who seldom consume processed cereals. More than 70% of populations live in rural areas in China, and many households have their staples processed at the local, small mill instead of getting processed cereals from the market.

In China, the most commonly consumed two staples, rice and wheat flour, are the suitable vehicles for food fortification. Soy sauce, consumed by more than 70% households in China, is also an ideal vehicle for fortification. In 2003, Global Alliance for Improved Nutrition (GAIN) funded fortification of wheat flour and soy sauce (NaFeEDTA) were launched in China (117). The result of a randomized, placebo-controlled intervention study showed that after 18-month of intervention, the intervention groups had significantly higher hemoglobin levels, lower anaemia prevalence, and higher plasma ferritin levels than the controls (116).

Dietary diversification is defined as the number of different foods or food groups consumed over a given reference period (119). A few studies conducted in Africa have demonstrated that the quality of diets could be improved significantly through dietary diversity (120-124). Dietary diversification can be used to alleviate several micronutrient deficiencies simultaneously without risk of antagonistic interactions (76).

Dietary diversification, the diet-based approach has the advantage that once the population changes its diet, it is likely to sustain this practice. The disadvantages are that very often it is difficult to change dietary practices, and that micronutrient-rich foods are often expensive, meaning that they may be beyond the reach of the poorest of the poor.

Lack of dietary diversity is a particular problem among the rural population in China because their diets are predominantly based on staples and often include less animal foods (125). Increasing the variety of foods across and within food groups is recommended in the dietary guidelines by the Chinese Nutrition Society (126). Nutrition education programs to disseminate the dietary guidelines have been conducted.

In recent years, more and more scientists believed that biofortification is a promising, cost-effective, and sustainable strategy in combating micronutrient deficiency, especially for developing countries. ***Biofortification*** is defined as the process of increasing the bioavailable concentrations of an element in edible portions of crop plants through agronomic intervention or genetic selection (127). Genetic variation in concentrations of iron, zinc, β-carotene, phytate, and enhancing factors exists among cultivars, which makes the selection of nutritionally appropriate breeding materials possible. The results of preliminary research on biofortification are encouraging. Zinc-dense wheat varieties have been developed and are already being grown on a commercial basis in Australia

(Adelaide, Victoria, Australia; 127). Golden rice, an advanced transgenic line containing 37 μg/g carotenoid, of which 31 μg/g is *β*-carotene, is now available (128, 129).

Compared with other strategies, biofortification provides a truly feasible means of reaching populations in remote and rural areas, delivering naturally-fortified foods to population groups with limited access to commercially-marketed fortified foods (130). It is easy to apply in most circumstances as there is no need to change the dietary behavior. Biofortification is cost-effective. The annually recurrent costs are low after the one-time investment to develop varieties, and germplasm can be shared internationally. Moreover, as the trace mineral requirements between human and plant nutrition are similar, biofortification could improve human nutrition as well as farm productivity.

Biofortification has the potential to have a major impact on the micronutrient intakes of people in China, whom derive 50% of their dietary energy, iron and zinc from two cereal staples, rice and wheat flour. By increasing the trace mineral content of staple foods through biofortification will have profound influence on the nutritional status of the entire population, the entire distribution curve could be shifted to the right. However, there are still a lot of questions which need to be answered, like the regulation and policy, the safety issues, the feasibility, the cost-effectiveness, the cost-benefit, and the acceptance by the consumers, before it is widely applied in China.

In conclusion, supplementation, food fortification and dietary diversification are the three widely applied strategies for fighting micronutrient deficiencies. Each has it advantages and disadvantages. Biofortification is a promising sustainable solution based on the latest preliminary research. However, information on its feasibility, cost-effectiveness, and safety is needed before it can be largely applied to combat micronutrient deficiency in China.

Rationale

The diets of Chinese people are still plant-food-based according to the report of the 2002 China National Nutrition and Health Survey (CNNHS) (125, 131). The daily consumption of cereal grains of urban and rural residents were 366g and 416g per reference man. Plant-foods including cereal grains, legumes, and tubers accounted for 52.6% and 66.3% of the energy intakes for urban and rural residents, while cereals and legumes provided 48.0% and 64.1% of protein for urban and rural resident, respectively.

Besides the important source of iron and zinc, plant-food-based diets are rich in bioactive compounds, which may prevent some types of non-communicable chronic diseases, such as cancer, diabetes mellitus, etc. (132, 133). On the other hand, plant-food-based diets also have high phytate content. Although phytate may have beneficial roles as an antioxidant and anticarcinogen (134), it can inhibit the bioavailability of critical nutrients such as zinc, iron, and calcium (33, 95).

There have been studies on the phytate contents of different foods and diets in other countries (96-98). However, these data are not suitable for use in assessing the phytate intake of people in China because of the fact that large discrepancies exist in food variety, food processing, cooking methods and food consumption between China and other countries. The phytate content and its inhibitory effect on the bioavailability of minerals in the foods and diets, and the adequacy of micronutrient intake have never been assessed in China because of the paucity of data in the China Food Composition Table (79). A sustainable intervention for micronutrient deficiency, which is cost-effective and feasible for the situation in China has not been identified and applied.

Hypothesis

The following hypotheses will be studied in this thesis:

- Phytate has an inhibitory effect on the absorption of iron and zinc in foods commonly consumed in China.
- The phytate intake of rural residents in China is significantly higher than that of their urban counterparts.
- The deficiency of iron and zinc is more common among rural than urban areas due to the inhibitory effect of phytate in the diets.
- Biofortification is a feasible and cost-effective solution for combating micronutrient deficiency in China.

Research Questions

As described in the **Rationale**, the following research questions will be studied:

1. *What is the phytate content in foods commonly consumed in China and its inhibitory effect on the bioavailability of iron, zinc and calcium?*
2. *What is the phytate intake in the diets and its inhibitory effect on the bioavailability of zinc, iron and calcium of people in different geographical areas of China?*
3. *What is the magnitude of iron and zinc deficiency in China?*
4. *What is the feasible, cost-effective and sustainable intervention for iron and zinc deficiencies in China?*

In order to find the answers for the above-mentioned research questions, 60 food samples commonly consumed in China were collected and analyzed to provide the data of the contents of phytate, calcium, iron, and zinc and the molar ratios of phytate/calcium, zinc, and iron. The data of 2002 CNNHS was used to assess the phytate intake, and its inhibitory effect on iron, zinc, and calcium, and the food sources of iron and zinc in the diets of people in China. The standard WHO ingredients-approach method was used to calculate the costs of different intervention strategies.

Outline of the Thesis

A brief outline of the thesis is described below. The studies described in this thesis were conducted between 2002 and 2006.

Chapter 2 presents the contents of phytate, calcium, iron, and zinc and their molar ratios in 60 food samples commonly consumed in China, and assesses the inhibitory effect of phytate on the bioavailability of calcium, iron, and zinc in those foods.

Chapter 3 describes the phytate intake and the molar ratios of phytate to calcium, iron and zinc in the diets of people in China using the data of dietary intakes collected by consecutive 3 days 24h recall in 2002 CNNHS. The data of 68,962 residents from 132 study sites were analyzed. The effect of phytate on the bioavailability of iron, calcium and zinc in the diets of people in China was assessed.

Chapter 4 examines the inadequacy of zinc intake of subpopulations in China using the WHO suggested values, taken the inhibitory effect of phytate into account. The dietary intake data of 68,962 subjects in the 2002 CNNHS were analyzed.

Chapter 5 investigates the food sources of iron and zinc and the magnitude of iron and zinc deficiencies in China, and assesses the costs and cost-effectiveness of supplementation, fortification, dietary diversification and biofortification based on the situation in China, and provide information for policy makers for developing intervention strategies for combating micronutrient deficiencies in China.

Chapter 6 discusses the main findings of the studies described in this thesis, and draws conclusions with implications for policy, and future research.

Description of the Study

The 2002 CNNHS is a representative cross-sectional survey at national level that covered 31 provinces, autonomous regions and the municipalities directly affiliated to the Central Government (Hong Kong, Macao and Taiwan were not included). The multistage cluster sampling method was used for subject selection. Stage 1: all the 2,860 counties/districts/cities of China were divided into six areas (big cities, medium and small cities, rural 1, 2, 3 and 4) based on its type and the level of economic development (from high to low). Twenty-two counties/districts/cities from each area were randomly selected. A total of 132 counties/districts/cities were randomly selected at this Stage. Stage 2: three townships/sub-districts were randomly selected from each selected county/district/city. A total of 396 townships/sub-districts were randomly selected at this Stage. Stage 3: two villages/neighborhood committees were randomly selected from the selected townships/sub-districts. A total of 792 villages/neighborhood committees were randomly selected at this Stage. Stage 4: ninety households were randomly selected from each selected village/neighborhood, and finally, a total of 71,971 households were randomly selected to represent the national data. The sampling map is shown in Figure 1.

Figure 1 The Study Sites of 2002 CNNHS

The dietary survey was conducted among all members of 30 households that were randomly selected from the pre-selected 90 households. All family members above two years old of the selected households were invited for the dietary intake assessment.

The information on food intake was collected using a 24h dietary recall method for three consecutive days (two weekdays and one weekend day) by trained interviewers. The intakes of calcium, iron and zinc were calculated using the data of dietary recall and the 2000 China Food Composition Table (79). The contents of calcium, iron and zinc in foods were determined by atomic absorption spectrophotometry.

Fasting body weight and height (length) of subjects were measured following the standardized procedure (135) by trained investigators. Stunting is defined by measurements that fall below two standard deviations under the normal height for age (136).

Hemoglobin was determined using the cyanmethemoglobin method. The WHO definition of anaemia (64) was used. The hemoglobin values were adjusted according to the altitude of the study sites (64). Prevalence of anaemia was adjusted using the data of the 2000 China National Population Census (137) in order to eliminate the difference in proportion between the sampling and the whole population.

Table 1 presents the sample size of the 2002 China National Nutrition and Health Survey. A total of 221,044 individuals (urban 82,416; rural 138,628) completed the anthropometry measurements. The level of hemoglobin of 211,726 individuals (urban 79,672; rural 132,054) was determined.

Table 1. Sample Sizes of the 2002 China National Nutrition and Health Survey

	All	Big cities	Medium and small cities	Rural 1	Rural 2	Rural 3	Rural 4
Sampling population							
No. of survey site	132	22	22	22	22	22	22
No. of household	71971	12053	11981	12160	11919	11930	11928
No. of individual	243479	33356	35300	41640	44206	43343	45634
Anthropometric measurement	192500	29408	28270	32228	33766	34826	34002
No. of hemoglobin	184331	28456	27362	30760	32263	33610	31880
Dietary assessment							
No. of household	23470	3870	3817	4018	3964	3877	3924
No. of individual	68962	10570	10533	11639	11991	11824	12405
Additional samples							
Children < 2 yr	3025	851	898	480	266	342	188
Children 3-12 yr	20758	9993	10765	-	-	-	-
Pregnant women	4761	1071	1160	872	526	600	532
Anthropometric Measurement	28544	11915	12823	1352	792	942	720
No. of hemoglobin	27395	11351	12503	1253	771	857	660

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Chapter 2

Phytate, calcium, iron and zinc contents and their molar ratios in foods commonly consumed in China

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Journal of Agricultural and Food Chemistry 2005;53:10285-10290

Abstract

Objectives: To examine the phytate content in foods commonly consumed in China, and to assess the inhibility effect of phytate on the bioavailability of calcium, iron, and zinc in foods commonly consumed in China.

Methods: A total of 60 food samples commonly consumed in China were analyzed for phytate using the anion-exchange method and for calcium, iron and zinc using atomic absorption spectrophotometry. The foods analyzed included those based on cereal grains and soybean.

Results: Phytate contents expressed on a wet weight basis ranged from 0 for foods made from starches to 1878 mg/100 g for dried stick-shaped soybean milk film. The calcium contents were between 2.08 mg/100 g for ground corn and 760.67 mg/100 g for diced fried soybean curd. The lowest values of iron and zinc were 0.04 mg/100 g for Panjin pearl rice cooked with discarding extra water and 0.08 mg/100 g for potato and bean starches, while the highest values of iron and zinc were observed in dried stick-shaped soybean milk film. Although many foods were relatively rich in calcium, zinc, and iron, many also contained higher level of phytate. Of the 60 food samples, 34 foods had phytate/calcium molar ratio >0.24, 53 foods had phytate/iron molar ratio >1, 31 foods had phytate/zinc molar ratio >15, and only 7 foods had phytate×calcium/zinc >200.

Conclusion: Phytate in foods impair the bioavailability of calcium, iron, and zinc, which to some extend depends on food processing and cooking methods.

Keywords: phytate, calcium, zinc, iron, bioavailability, China

Introduction

The diets of people in China are based on plant foods, which provide at least 50% of dietary energy and nutrients (1). Plant-food-based diets are rich in bioactive compounds, which are believed to be beneficial for the prevention of non-communicable chronic diseases, such as cancer, diabetes mellitus, etc. However, on the other hand, plant-food-based diets are also rich in phytate. Phytate can decrease the bioavailability of critical nutrients such as zinc, iron, calcium (2, 3) and magnesium (4) because of its high binding affinities to minerals; on the other hand, phytate may act as an antioxidant and anticarcinogen (5).

Phytate exerts its inhibitory effect on the absorption of minerals by forming insoluble and indigestible complexes (6). The effect of phytate on the bioavailability of minerals depends on not only the amount of phytate and minerals in the diets, but also the ratio of phytate/minerals. The relative bioavailability of minerals can be predicted from the molar ratio of phytate/minerals in the food and diet (7-13).

There have been studies on the phytate contents of different foods and diets in other countries (14-16). However, these data may not suitable for use in assessing the phytate intake of people in China because of the fact that large discrepancies exist in food variety, food processing, cooking methods and food consumption between China and other countries. For this reason, the phytate contents and its inhibitory effect on the bioavailability of minerals has never been assessed in the foods and diets of people in China because of the lack of data in the China Food Composition Table (17). Therefore, the purpose of this study is, first, to examine the phytate content in foods commonly consumed in China and provide basic data for the China Food Composition Table; second, to assess the inhibitory effect of phytate on the bioavailability of calcium, iron, and zinc in foods commonly consumed; and last, to compare the phytate contents and its possible inhibitory effect on the bioavailability of minerals in China with other studies.

Materials and Methods

Samples Selection and Collection

The information on food consumption from the 2002 China National Nutrition and Health Survey (1) was used for food sample selection. A total of 60 kinds of food samples including 18 wheat flour and products, 14 soybean products, 9 rice products, 8 corn products, 6 other grains and 5 starch products were selected. A total of 5 different samples of each kind of food were purchased from 5 supermarkets in Beijing, China.

Panjin pearl rice was cooked with four methods in the lab of the National Institute for Nutrition and Food Safety, Chinese Center for Disease Control and Prevention. Tap water was added with a ratio 1.5:1 (weight/weight) before cooking. Rice was cooked for 10 min after boiling and discard extra water, then steamed for 20 min. Rice was cooked with electric pot for 40 min after boiling. Rice was steamed with pot for 40 min after boiling. Rice was cooked with a pressure pot for 10 min after boiling. The same amount of each of the 5 samples was ground (Phillip Model HR2839), mixed, and transferred into a screw-capped plastic bottle and was stored at –20°C until analysis.

Determination of Phytate, Calcium, Iron, Zinc, and Moisture

The Anion-exchange method (18) was used for determination of phytate content. Samples were accurately weighed (1.00-2.00 g) and transferred into 100 mL conical flasks. A total of 40-50 mL of Na_2SO_4 (100g/L)-HCl (1.2%) were added. Flasks were capped and shaken vigorously for 2 h on a rotator at ambient laboratory temperature. The supernatant solutions were then filtered through qualitative filter paper. In some instances, i.e., rice and oat cereals, a gel formed in the flask, and therefore, the sample was hard to filter. In those cases, the supernatant was centrifuged (Beckman TJ-6R, Lynchburg, VA) before filtration.

A total of 10 mL filtered extract was diluted to 30 mL with distilled water after mixing with 1 mL 30 g/L NaOH and then passed through an anion resin column (resin, AG1-X4, 100-200 mesh, Bio-Rad Laboratory, Inc., CA; column, 0.8×10 cm, Beijing Glass Instrumental Factory). The column was washed before use with 20 mL of 0.5 mol/L NaCl solution and deionized water till no Cl- can be detected.

The column was washed with 15 mL of distilled water and 20 mL of 0.05 mol/L NaCl solution after sample application. The eluate from the resin was eluted with 0.7 mol/L NaCl to 25 mL. The postcolumn reagent was made up as a 0.03% $FeCl_3$ solution containing 0.3% sulfosalicylic acid. A total of 4 mL of the reagent was added into 5 mL collected eluate and then centrifuged at 3000 rps for 10 min. The absorbance of the supernatant was measured at 500 nm using a spectrophotometer (LKB 4053, UK.).

A calibration curve for the colorimetric method was obtained by using phytate standards (P-8810 Sigma Co.). The phytate content of samples was calculated using the standard curve.

The contents of calcium, iron, and zinc in foods were measured by atomic absorption spectrophotometry (Perkin-Elmer 1100B, Norwalk, CT). Spectrophotometry measurements were calibrated using commercial standards (National Center for Standard

Substance, Beijing, China). The standard curves were controlled using chloride solutions of the metals. Relative standard deviations were less than 10%.

Quality Control

Duplicate sample solutions from each food sample were analyzed. The measurement was repeated until the relative standard deviation (RSD, %) was within 10%. Recovery experiments were done in every batch (6 samples) by adding 1mL of 10mg/mL standard phytate (P-8810 Sigma Co.) to the extracting samples. The average recovery rate of standard sample was 100.49% (n = 10, RSD = 1.30).

Statistical Analysis

The means and standard deviations of the phytate, calcium, iron, and zinc content of foods were calculated. The analysis results were expressed as M ± SD. A comparison of the difference in phytate contents between each two kinds of foods was applied using ANOVA factorial analysis with Turkey post-hoc comparison. Differences were considered significant at $P<0.05$. All statistical analysis was done with the SAS Statistical Package (SAS 8.2e for Windows, SAS Institute, Inc.).

Results and Discussion

Rice and Products

Rice is the staple food, especially for people from southern regions of China. On average, people consume 238 g rice and its products per day in China (1).

A total of 8 samples of rice and products were analyzed. The phytate, calcium, iron, and zinc content of the foods are presented in **Table 1**. Phytate contents ranged from 55 mg/100 g for Thailand rice to 183 mg/100 g for Heilongjiang rice, while calcium contents ranged from 2.52 mg/100 g for Panjin pearl rice to 4.74 mg/100 g for Tianjin Xiao Zhan rice. The range of iron contents was between 0.12 mg/100 g for Thailand rice and 0.19 mg/100 g for Heilongjiang rice, whereas that of zinc was between 1.09 mg/100 g for Tianjin Xiao Zhan rice and 1.76 mg/100 g for Thailand rice. Variations were found in phytate and minerals contents between different brands of commercial rice. The variability of the phytate content of rice was also found in other studies, which ranged from 6 to 60 mg/100 g (19-21).

The most common methods for cooking rice in China are boiling, steaming with or without discarding the excessive water. To study the effect of different cooking methods on phytate content, Panjin pearl rice was cooked with 4 different methods, i.e., steamed after boiling and discarding the excessive water and steamed, boiled, and cooked with pressure pot without discarding cooking water. Significant differences in phytate contents were found between uncooked and cooked rice for each cooking method ($P<0.001$). Rice steamed after boiling and discarding the excessive water had a greater degree of phytate reduction (78.6%) than cooked with pressure pot (48.7%), boiled (43.7%), and steamed (40.3%) without discarding cooking water. No significant differences in phytate content were found between steamed, boiled, and cooked with pressure pot. The result from the present study was similar to that of Almana (22), who reported that discarding excessive water in cooking rice may result in phytate degradation of 37-65%, while retaining the water only results in degradation of 12%. The influence on the minerals content was also found with different cooking methods. Both the iron and zinc content of rice with four methods decreased compared with the raw material, while calcium content increased which might be caused by to the high content of calcium in the cooking water (23).

Because phytate is heat stable, significant reduction during cooking or any conventional heat-processing method is not expected unless the cooking water is discarded, because some nutrients will be solved in the cooking water (24). Discarding cooking water will also result in a certain loss of nutrients at the same time. This method may not be effective in improving the bioavailability of minerals.

Studies in humans indicate that the absorption of zinc and iron form a meal corresponds directly to its phytate content (25, 26). The phytate/minerals molar ratios are used to predict its inhibitory effect on the bioavailability of minerals. The phytate/calcium molar ratio >0.24 will impair calcium bioavailability (8). The phytate/iron molar ratio >1 is regarded as indicative of poor iron bioavailability (27). Zinc absorption is greatly reduced and results in negative zinc balance when phytate/zinc molar ratio is 15 (10). When diets are high in both phytate and calcium, phytate×calcium/zinc is a more useful assessment of zinc bioavailability than phytate/zinc molar ratio (13).

Table 2 summarized the molar ratios of phytate/minerals of foods. The molar ratios of phytate/calcium of all rice were >0.24 except for rice steam-cooked with discarding cooking water, which was 0.11. All ratios of phytate/iron were >1, while that of phytate/zinc and phytate×calcium/zinc were below the critical values. These ratio indices indicated that the bioavailability of calcium and iron but not zinc would be impaired by phytate in rice and products.

Wheat and Products

Wheat and wheat products are another staple food, especially for people from northern regions of China. On average, people consume 140 g wheat and its products per day (1).

Phytate contents ranged from 3 mg/100 g for fresh wheat noodle to 420 mg/100 g for standard wheat flour, while calcium contents ranged from 11.1 mg/100 g for wheat flour (50% extraction rate) to 250.3 mg/100 g for wheat flake. The range of iron contents was between 0.41 mg/100 g for wheat flour (50% extraction rate) and 5.41 mg/100 g for fried wheat gluten, whereas that for zinc were between 0.47 mg/100 g for unleavened wheat pancake and 2.75 mg/100 g for fresh wheat gluten. Variations were found in both phytate and minerals contents between different foods made from wheat flour (**Table 1**). The phytate content in wheat gluten was comparable to that reported by Wallace and Satterlee (28).

The phytate content reported in other studies also shows a wide variation depending on flour extraction rate, flour types, and cooking method. The values reported for wheat flour were between 154 and 1750 mg/100 g (14, 15, 29-32). The phytate content in the present study is within the above range.

Because phytate is distributed in larger proportions in external covers in the pericarp and in the aleurone layer of wheat (33), therefore, simple dehulling or milling may be effective in removing significant amounts of phytate. However, it should be noticed that food processing and cooking will also result in the loss of minerals in some extents (34). In the present study, we have found that the phytate content of two refined flours decreased significantly as compared with the standard refined flour. At the same time, a certain amount of minerals loss was observed. A similar result can be seen in other reports (31, 35), an 80% extraction rate resulted in a reduction of 30-40% of phytate in comparison to the raw material.

People consume plenty of foods made from wheat flour. Steamed bread and pancake with and without fermentation process and noodles are most favorite foods for people in China. Studies indicated that the phytate contents varied considerably because of different preparation and cooking methods. During bread making, the content of phytate decreases as the action of phytases as well as the high temperature (36). Other factors affect phytate hydrolysis, including the type and extraction rate of flour and fermentation techniques (22, 37, 38).

In the present study, we found that the whole wheat bread had higher phytate value than white bread no matter whether it is baked or steamed, while the leavened pancake had only 50% of the phytate content as that of leavened pancake (7 vs 14 mg/100 g). This showed the effect of the processing and cooking on phytate hydrolysis. Similar results have been seen in other studies (7, 14, 38).

Of the 18 wheat and products, 16 had the phytate/iron molar ratio >1, 10 had a phytate/calcium ratio >0.24, and only 7 had a phytate/zinc molar ration above critical value. The molar ratios of phytate×calcium/zinc of foods were all below 200. The bioavailability of iron was more likely to be affected by phytate in this kind of foods.

Corn and Corn Products

Although less corn and products are consumed in comparison to rice and wheat, they are still frequently consumed foods, especially for people in some poor rural areas of China.

Phytate contents were between 18 mg/100 g for unleavened baked corn bread and 310 mg/100 g for corn flour, while calcium contents ranged from 2.08 mg/100 g for ground corn to 20.62 mg/100 g for leavened steamed corn bread. The phytate content of corn flour in the present study is much lower than 1078 mg/100 g reported by Garcia-Estepa et al (14, 29). The range of iron contents was between 0.34 mg/100 g for fresh corn and 2.58 mg/100 g for boiled fresh corn, whereas that of zinc was between 0.12 mg/100 g for fresh corn and 0.79 mg/100 g for corn flake.

Unlike for wheat and rice, 88% of phytate is present in the germ of corn (39); therefore, removing the germ portion is an effective way to remove a significant amount of phytate form corn. We have found that, on average, corn products had lower phytate values than those in corn and corn flour. This result indicated that phytate degrades to a certain degree during food processing and cooking.

The molar ratio of phytate/iron of all corn and products were >1, while that of phytate×calcium/zinc were <200. The molar ratios of phytate/calcium and zinc of corn and products were above the critical levels, except for unleavened baked corn bread and two corn bread (**Table 2**). This is indicated that phytate in most corn and products affect the bioavailability of minerals.

Other Grains

In general, the phytate content of other grains was higher than that of rice, wheat, and corn. Seed of Job's tears had the highest value of phytate, 1419 mg/100 g; zinc, 2.74 mg/100 g; and the lowest calcium content, 5.88 mg/100 g, while dried buckwheat noodle had the lowest phytate value, 223 mg/100 g. The highest values of calcium and iron were observed in black sesame powder. Sorghum had the lowest amounts of zinc and iron content as 0.41 and 0.94 mg/100 g, respectively (**Table 1**).

All of the molar ratios of phytate/minerals were above the critical values, excepts phytate/calcium for black sesame powder and phytate/zinc for buckwheat dried noodle (**Table 2**), which hence predicts a low bioavailability of calcium, iron, and zinc for these foods.

Soybean Products

Soy products are commonly consumed all over China. There are more than a hundred kind of soy products made by different methods. Soy and its products are good sources for both protein and minerals, and they are also the major source of phytate because of the high content.

Table 3 presents the phytate and minerals contents of soy foods. Soy foods products had the highest content of phytate as well as calcium, zinc, and iron as compared with other foods, although a wide variation was found. The ranges of phytate contents were between 130 mg/100 g for lactonic soybean curd and 1878 mg/100 g for dried soybean milk film. The range of calcium was between 12.55 mg/100 g for lactonic soybean curd and 760 mg/100 g for diced fried soybean curd. The iron contents ranged from 0.37 mg/100 g for lactonic soybean curd to 6.13 mg/100 g for dried soybean milk film, whereas that of zinc was from 0.37 mg/100 g for lactonic soybean curd to 3.50 mg/100 g dried soybean milk film. The phytate content of soy products was lower than reported by other studies (40-42).

The production of soy products undergoes soaking, grinding, and boiling. Phytate will be degraded throughout the procedures. Soaking may remove 6-28% phytate, and the longer the periods of soaking, the greater losses in the phytate content (18). Grinding enables endogenesis phytase to come into contact with more phytate and thus catalyzes the hydrolysis procedure. Boiling or pressure boiling may also cause certain loss of phytate. Then, different curdle reagents are added, and the curd may experience various squeeze methods and cooking methods, which may result in various degradation of phytate. However, the study indicated that food processing also lead to the decrease of minerals and vitamins content of foods (24, 38).

Table 4 lists the molar ratios of phytate/minerals of soy products. The ranges of phytate to calcium, iron, zinc, and phytate×calcium/zinc molar ratios were 0.06-0.63, 15.68-61.35, 34.72-68.06, and 10.89-1025.07, respectively. A total of 8 of 14 soy products had the phytate/calcium molar ratio above the critical level. All of the soy products had phytate to iron and zinc ratios above the critical values. A total of 7 of 14 soy products had phytate×calcium/zinc molar ratio were >200. When the four ratios are taken into account together, the phytate in soy products will inhibit the absorption of calcium, iron, and zinc.

Food Made from Starch

Table 5 presents the phytate and minerals contents of foods made from different starches. It shows that foods made of starch contained no detectable phytate. The calcium contents ranged from 5.58 mg/100 g for cornstarch to 63.09 mg/100 g for lotus starch, while the range of iron contents was from 0.38 mg/100 g for potato starch to 3.79 mg/100 g for sweet potato starch vermicelli. Potato and bean starch vermicelli had the lowest zinc value of 0.08 mg/100 g, while sweet potato starch vermicelli had the highest at 0.14 mg/100 g.

Because foods made of starch have undetectable phytate, the effect of phytate on the bioavailability of minerals in this kind of foods can be neglected.

Although a dietary pattern has changed in recent years in China, the diets of people are plant-based. Rice, wheat, and their products are staple foods for most people, while corn and corn products are staple foods for a few people living in rural areas. Grains are the main source of phytate. Both the phytate contents of grains and the molar ratios of phytate/minerals imply that phytate in the diet of people in China impair the bioavailability of iron and calcium.

In **conclusion**, variations of phytate contents are found in foods commonly consumed in China and can be observed in the same kind of food prepared by different processing and cooking methods. The indices of molar ratios of phytate/minerals predict that phytate shows the inhibitory effect on the bioavailability of minerals in those foods in certain extent; therefore, optimal food processing and cooking methods should be chosen in order to minimize this effect.

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Table 1. Phytate, Calcium, Iron, and Zinc Content of Cereal-based Foods[a]

Food type	Moisture (g/100g)	Phytate (mg/100g)	Calcium (mg/100g)	Iron (mg/100g)	Zinc (mg/100g)
Rice and products (9)					
Thailand Rice	13.4	55 ± 2	3.77 ± 0.19	0.12 ± 0.04	1.76 ± 0.11
Tianjin Xiao Zhan	17.2	92 ± 3	4.74 ± 0.25	0.19 ± 0.02	1.09 ± 0.02
Heilongjiang Rice	13.3	183 ± 4	2.56 ± 0.06	0.19 ± 0.01	1.63 ± 0.02
Panjin Pearl Rice	14.1	131 ± 0	2.52 ± 0.19	0.16 ± 0.01	1.15 ± 0.06
Panjin Pearl rice, steamed after half boiling, discard extra water	61.4	14 ± 1	7.71 ± 0.69	0.04 ± 0.00	0.44 ± 0.01
Panjin Pearl rice, boiling	59.2	35 ± 1	9.06 ± 0.56	0.10 ± 0.02	0.56 ± 0.00
Panjin Pearl rice, steamed	58.6	38 ± 0	7.08 ± 0.47	0.10 ± 0.01	0.51 ± 0.00
Panjin Pearl rice, cooked with pressure pot	53.4	38 ± 0	9.07 ± 0.69	0.16 ± 0.00	0.56 ± 0.03
Rice noodle, dried	12.4	14 ± 3	14.01 ± 0.63	0.72 ± 0.03	0.46 ± 0.01
Wheat and products (18)					
Wheat flour, 85% extraction rate	12.0	420 ± 0	21.56 ± 1.36	1.35 ± 0.05	0.78 ± 0.02
Wheat flour, 75% extraction rate	12.3	117 ± 3	18.38 ± 0.79	1.27 ± 0.05	0.57 ± 0.01
Wheat flour, 50% extraction rate	12.7	37 ± 4	11.12 ± 1.06	0.41 ± 0.01	0.52 ± 0.04
Twisted wheat roll, steamed	37.3	77 ± 3	20.01 ± 1.20	0.68 ± 0.07	0.60 ± 0.01
Wheat bread, steamed	37.0	38 ± 0	15.87 ± 0.06	0.75 ± 0.04	0.53 ± 0.02
Whole wheat bread, steamed	42.6	173 ± 11	16.12 ± 0.06	1.00 ± 0.02	0.85 ± 0.02
Wheat bread, white, baked	31.3	20 ± 2	35.68 ± 0.15	0.68 ± 0.02	0.73 ± 0.01
Whole wheat bread, baked	32.0	176 ± 3	29.17 ± 1.55	0.88 ± 0.03	1.25 ± 0.12
Wheat pancake, unleavened	39.6	14 ± 0	14.17 ± 0.76	0.89 ± 0.12	0.47 ± 0.00
Wheat pancake, leavened	35.3	7 ± 1	23.74 ± 1.21	0.78 ± 0.04	0.58 ± 0.03
Wheat noodle, fresh	28.1	3 ± 0	22.12 ± 0.16	1.15 ± 0.08	0.57 ± 0.06

Wheat noodle, dried	11.7	158 ± 14	27.73 ± 0.80	1.87 ± 0.54	0.79 ± 0.02
Instant noodle	3.6	103 ± 3	15.83 ± 0.92	1.15 ± 0.26	0.55 ± 0.04
Spaghetti	10.7	248 ± 5	24.55 ± 1.31	0.87 ± 0.03	0.75 ± 0.03
Whole wheat biscuit	1.3	304 ± 21	39.32 ± 1.40	1.63 ± 0.15	0.71 ± 0.06
Wheat flake	2.4	138 ± 8	250.25 ± 7.29	3.22 ± 0.25	0.76 ± 0.02
Wheat gluten, fresh	63.1	134 ± 2	20.54 ± 0.33	3.02 ± 0.03	2.75 ± 0.04
Wheat gluten, fried	7.2	266 ± 4	27.19 ± 0.52	5.41 ± 0.39	1.98 ± 0.07
Corn and products (8)					
Fresh corn	57.9	300 ± 4	6.38 ± 0.02	0.34 ± 0.03	0.12 ± 0.00
Fresh corn, boiled	49.3	196 ± 7	2.71 ± 0.12	2.58 ± 0.25	0.13 ± 0.02
Ground Corn	13.4	100 ± 3	2.08 ± 0.03	0.43 ± 0.00	0.63 ± 0.08
Corn Flour	12.1	310 ± 6	5.01 ± 0.42	1.03 ± 0.02	0.63 ± 0.01
Corn flake	13.1	275 ± 0	2.58 ± 0.08	1.65 ± 0.01	0.79 ± 0.01
Baked corn bread, unleavened	41.8	18 ± 0	16.64 ± 0.26	0.61 ± 0.02	0.61 ± 0.00
Steamed corn bread, unleavened	41.1	61 ± 6	18.41 ± 0.62	0.83 ± 0.01	0.46 ± 0.03
Steamed corn bread, leavened	42.3	76 ± 2	20.62 ± 0.41	0.70 ± 0.00	0.54 ± 0.00
Other grains (6)					
Buckwheat noodle, dried	12.2	223 ± 5	54.29 ± 0.26	1.69 ± 0.05	1.69 ± 0.11
Oat flake	9.2	871 ± 44	45.83 ± 0.06	2.34 ± 0.39	1.26 ± 0.05
Millet	11.4	522 ± 18	10.70 ± 0.24	2.54 ± 0.09	1.80 ± 0.03
Sorghum	11.1	427 ± 9	6.48 ± 0.45	0.94 ± 0.09	0.41 ± 0.02
Black sesame powder	4.0	440 ± 22	327.74 ± 77.32	1.67 ± 0.35	0.84 ± 0.08
Seed of Job's tears	9.9	1419 ± 41	5.88 ± 0.10	1.85 ± 0.08	2.74 ± 0.13

[a] Data are expressed as mean ± SD on a wet weight basis.

Table 2. Molar Ratios of Phytate to Calcium, Iron, Zinc, and Phytate×Calcium/Zinc of Cereal-based Foods

Food type	Phytate /Calcium	Phytate /Iron	Phytate /Zinc	Phytate× Calcium/Zinc
Rice and products (9)				
Thailand Rice	0.88	39.40	3.07	0.29
Tianjin Xiao Zhan	1.18	40.46	8.29	0.98
Heilongjiang Rice	4.32	83.27	11.01	0.71
Panjin Pearl Rice	3.15	69.67	11.27	0.71
Panjin Pearl rice, steamed after half boiling, discard extra water	0.11	29.16	3.09	0.59
Panjin Pearl rice, boiling	0.24	29.89	6.20	1.40
Panjin Pearl rice, steamed	0.32	31.97	7.28	1.29
Panjin Pearl rice, cooked with pressure pot	0.25	20.02	6.64	1.51
Rice noodle, dried	0.06	1.64	2.96	1.04
Wheat and products (18)				
Wheat flour, 85% extraction rate	1.18	26.46	80.23	43.24
Wheat flour, 75% extraction rate	0.39	7.81	14.74	6.78
Wheat flour, 50% extraction rate	0.20	7.63	6.47	1.80
Twisted wheat roll, steamed	0.23	9.61	12.60	6.31
Wheat bread, steamed	0.14	4.24	7.05	2.80
Whole wheat bread, steamed	0.65	14.68	20.06	8.08
Wheat bread, white, baked	0.03	2.47	2.69	2.40
Whole wheat bread, baked	0.37	17.00	13.91	10.15
Wheat pancake, unleavened	0.06	1.37	3.02	1.07
Wheat pancake, leavened	0.02	0.79	1.24	0.74
Wheat noodle, fresh	0.01	0.24	0.58	0.32
Wheat noodle, dried	0.35	7.16	19.80	13.72
Instant noodle	0.40	7.64	18.37	7.27

Spaghetti	0.61	24.12	32.63	20.03
Whole wheat biscuit	0.47	15.87	42.29	41.56
Wheat flake	0.03	3.64	17.98	112.52
Wheat gluten, fresh	0.39	3.76	4.80	2.46
Wheat gluten, fried	0.59	4.17	13.25	9.01
Corn and products (8)				
Fresh corn	2.85	75.79	243.97	38.90
Fresh corn, boiled	4.39	6.45	149.68	10.13
Ground corn	2.91	19.68	15.61	0.81
Corn flour	3.75	25.48	48.18	6.03
Corn flake	6.44	14.15	34.18	2.21
Baked corn bread, unleavened	0.07	2.54	2.98	1.24
Steamed corn bread, unleavened	0.20	6.24	13.11	6.04
Steamed corn bread, leavened	0.22	9.23	13.85	7.14
Other grains (6)				
Buckwheat noodle, dried	0.25	11.21	13.04	17.70
Oat flake	1.15	31.59	68.14	78.04
Millet	2.96	17.46	28.53	7.63
Sorghum	3.99	38.60	103.21	16.72
Black sesame powder	0.20	22.33	51.83	169.05
Seed of Job's tears	14.62	65.07	51.03	7.51

Table 3. Phytate, Calcium, Zinc, and Iron Content of Soybean Foods[a]

Food type	Moisture (%)	Phytate (mg/100g)	Calcium (mg/100g)	Iron (mg/100g)	Zinc (mg/100g)
Lactonic soybean curd	91.6	130 ± 2	12.55 ± 0.20	0.37 ± 0.02	0.37 ± 0.02
Soybean curd, South	88.6	211 ± 2	217.45 ± 1.11	0.39 ± 0.01	0.58 ± 0.07
Soybean curd, North	79.5	446 ± 6	80.73 ± 0.71	1.43 ± 0.02	0.72 ± 0.06
Soybean curd slab	69.0	592 ± 6	137.33 ± 6.67	2.92 ± 1.42	1.30 ± 0.05
Soybean curd slab, soy sauce flavored	47.8	912 ± 20	377.96 ± 18.33	3.03 ± 0.03	2.25 ± 0.29
Soybean curd, chicken flavored	71.4	736 ± 1	523.39 ± 21.31	3.98 ± 0.00	1.07 ± 0.02
Fried soybean, shrimp flavored	2.2	1253 ± 5	216.03 ± 6.45	4.27 ± 0.03	2.32 ± 0.00
Smoked soybean curd	66.6	769 ± 16	245.65 ± 7.44	3.19 ± 0.18	1.96 ± 0.13
Fried soybean curd, diced	45.7	819 ± 11	760.67± 13.72	1.13 ± 0.02	1.50 ± 0.14
Flavored soybean curd slab	59.9	889 ± 16	118.47 ± 1.82	3.16 ± 0.48	1.82 ± 0.12
Thin sheets of bean curd	61.3	987 ± 12	97.03 ± 4.20	2.86 ± 0.02	1.65 ± 0.04
Soybean curd strip	61.1	987 ± 5	109.21 ± 5.95	1.77 ± 0.02	1.86 ± 0.21
Dried soybean milk film,					
Stick shaped	8.0	1878 ± 23	223.09 ± 0.18	6.13 ± 0.43	3.50 ± 0.06
Soybean powder	3.6	800 ± 2	306.18 ± 11.46	2.81 ± 0.13	1.53 ± 0.03

[a] Data are expressed as mean ± SD on a wet weight basis.

Table 4. Molar Ratios of Phytate to Calcium, Iron, Zinc, and Phytate×Calcium/Zinc of Soybean Foods

Food type	Phytate/ Calcium	Phytate/ Iron	Phytate/ Zinc	Phytate× Calcium/Zinc
Lactonic soybean curd	0.63	29.73	34.72	10.89
Soybean curd, South	0.06	46.06	35.61	193.59
Soybean curd, North	0.33	26.54	60.84	122.80
Soybean curd slab	0.26	17.21	44.74	153.59
Soybean curd slab, soy sauce flavored	0.15	25.53	39.83	376.38
Soybean curd, chicken flavored	0.09	15.68	68.06	890.49
Fried soybean, shrimp flavored	0.35	24.90	53.11	286.85
Smoked soybean curd	0.19	20.43	38.73	237.83
Fried soybean curd, diced	0.07	61.35	53.90	1025.07
Flavored soybean curd slab	0.45	23.88	48.02	142.22
Thin sheets of bean curd	0.62	29.31	58.76	142.54
Soybean curd strip	0.55	47.24	52.22	142.57
Dried soybean milk film, stick shaped	0.51	25.98	52.85	294.76
Soybean powder	0.16	24.20	51.46	393.93

Table 5. Phytate, Calcium, Iron, and Zinc Content of Foods Made of Starch[a]

Food type	Moisture (g/100g)	Phytate (mg/100g)	Calcium (mg/100g)	Iron (mg/100g)	Zinc (mg/100g)
Corn starch	12.2	0±0	5.58±0.55	0.57±0.05	0.11±0.01
Lotus starch	10.7	0±0	63.09±0.67	1.25±0.06	0.13±0.01
Potato starch	15.5	0±0	20.38±1.90	0.38±0.02	0.08±0.01
Bean starch vermicelli	14.4	0±0	24.69±0.83	0.84±0.11	0.08±0.01
Sweet potato starch vermicelli	13.5	0±0	36.04±1.01	3.79±0.12	0.14±0.01

[a] Data are expressed as mean ± SD on a wet weight basis

Chapter 3

Phytate intake and molar ratios of phytate to zinc, iron and calcium in the diets of people in China

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European Journal of Clinical Nutrition, 2006; 23 August, Epub.

Abstract

Objectives: To assess the phytate intake and molar ratios of phytate to calcium, iron and zinc in the diets of people in China.

Methods: 2002 China Nationwide Nutrition and Health Survey is a cross-sectional nationwide representative survey on nutrition and health. The information on dietary intakes was collected using consecutive 3 days 24h recall by trained interviewers. The data of 68,962 residents aged 2-101 years old from 132 counties were analyzed.

Results: The median daily dietary intake of phytate, calcium, iron, and zinc were 1186, 338.1, 21.2 and 10.6 mg, respectively. Urban residents consumed less phytate (781 vs 1342 mg/day), more calcium (374.5 vs 324.1 mg/day), and comparable amounts of iron (21.1 vs 21.2 mg/day) and zinc (10.6 vs 10.6 mg/day) than their rural counterparts. A wide variation in phytate intake among residents from 6 areas was found, ranging from 648 to 1433 mg/day. The median molar ratios of phytate to calcium, iron, zinc and phytate×calcium/zinc were 0.22, 4.88, 11.1 and 89.0, respectively, with a large variation between urban and rural areas. The phytate:zinc molar ratios ranged from 6.2 to 14.2, whereas the phytate×calcium/zinc molar ratios were from 63.7 to 107.2. The proportion of subjects with ratios above the critical values of phytate to iron, phytate to calcium, phytate to zinc and phytate×calcium/zinc were 95.4, 43.7, 23.1 and 8.7%, respectively. All the phytate/mineral ratios of rural residents were higher than that of their urban counterparts.

Conclusion: The dietary phytate intake of people in China was higher than those in Western developed countries and lower than those in developing countries. Phytate may impair the bioavailability of iron, calcium and zinc in the diets of people in China.

Key Words: phytate, dietary intake, phytate:zinc molar ratio, bioavailability, China

Introduction

Although the dietary intakes and nutritional status of people in China have been improved apparently along with the rapid economic development, micronutrient deficiencies are still the major nutritional problems among Chinese people. The diets of Chinese people are plant foods-based. The average daily intake of cereal grains was 402 g, which accounted for 57.9% of the total energy intake (1).

Plant foods-based diets are rich in bioactive compounds, which may prevent some types of non-communicable chronic diseases, such as cancer, diabetes mellitus, etc. (2, 3). Plant foods-based diets also have high phytate content. Although studies revealed that phytate may have beneficial roles as an antioxidant and anticarcinogen (4), owing to its ability to chelate and precipitate minerals, phytate can decrease the bioavailability of critical nutrients such as zinc, iron, calcium (5) and magnesium (6).

There have been many studies on the phytate contents of different foods; however, data on phytate intake are scarce. Studies on phytate intakes can be found in USA (7, 8), UK (9), Sweden (10), Italy (11), Nepal (12), Turkey (13), Taiwan (14), India (15), and Korea (16, 17). In China, with a wide variation in the diets (1), data on phytate intake is lacking (18).

Based on the 2002 China Nationwide Nutrition and Health Survey, we studied the following research questions: What are the levels of phytate intake in China? Are there differences between different geographical areas? What differences in phytate intake are observed compared to other countries? What is the possible effect of phytate on the bioavailability of zinc, iron and calcium?

Subjects and Methods

Sampling

The 2002 China Nationwide Nutrition and Health Survey is a nationally representative cross-sectional survey that covered 31 provinces, autonomous regions and the municipalities directly affiliated to the Central Government (Hong Kong, Macao and Taiwan were not included). Multistage cluster sampling method was used for subject selection. Stage 1: all the 2,860 counties/districts/cities of China were divided into six areas (big cities, medium and small cities, rural 1, 2, 3 and 4) based on its type and the level of economic development (from high to low). Twenty-two counties/districts/cities from each area were randomly selected. A total of 132 counties/districts/cities were randomly selected at this Stage. Stage 2: three townships/sub-districts were randomly selected from each selected counties/districts/cities. A total of 396 townships/sub-districts were randomly selected at this Stage. Stage 3: two villages/neighborhood committees were randomly selected from the selected townships/sub-districts. A total of 792 villages/neighborhood committees were randomly selected at this Stage. Stage 4: ninety households were randomly selected from each selected villages/neighborhoods, and finally, a total of 71,971 households were randomly selected to represent the national data.

Dietary Intake Assessment

The dietary survey was conducted among all members of 30 households that randomly selected from the pre-selected 90 households. All family members above 2 years old of the selected households were invited for the dietary intake assessment. A total of 23,470 households participated in the dietary survey (1).

The information on food intake was collected using a 24-h dietary recall method for 3 consecutive days (two weekdays and one weekend day) by trained interviewers. The intakes of calcium, iron and zinc were calculated using the data of dietary recall and 2000 China Food Composition Table (18). The contents of calcium, iron and zinc in foods were determined by atomic absorption spectrophotometry.

The phytate intake was calculated using the phytate content of foods we measured (19) owing to the lack of data in China Food Composition Table. The anion-exchange method (20) was used for determination of phytate content and the information on food consumption from the 2002 China Nationwide Nutrition and Health Survey was used for food sample selection. The average daily dietary intake of calcium, iron, zinc and phytate were calculated using the mean value of the 3 days intakes.

The molar ratios of phytate to zinc, calcium or iron are calculated as the millimoles of phytate intake per day divided by the millimoles of zinc, calcium or iron intake per day, respectively. The calcium×phytate/zinc molar ratio is expressed as milliomoles per day.

The proportion of subjects with ratios above the suggested critical values was calculated: phytate:calcium >0.24 (21), phytate:iron >1 (22), phytate:zinc >15 (23-25), phytate×calcium/zinc >200 (26, 27).

Statistical Analysis

Median and quartiles range were used to express the dietary intake of calcium, zinc, iron, phytate, the molar ratios of phytate to calcium, iron, zinc, and phytate×calcium/zinc as the values for the above-mentioned variables were not normally distributed.

The dietary phytate, calcium, iron and zinc intake of each individual was calculated. In order to eliminate the differences due to energy requirement in different age, sex, physical activity level and physiological condition, the reference man is used to adjust the dietary intakes of each individual. The reference man is defined as male adult aged 18 years and over, with light physical activity level, whose daily reference energy intake is 2400 kcal (28). The use of reference man allows the comparison with the results of 1982 (29) and 1992 Chinese National Nutrition Survey (30). The dietary phytate, calcium, iron and zinc intakes of each individual were calculated as phytate/calcium/iron/zinc intake (mg/day) times 2400 kcal divided by his/her RNI of energy (kcal) (28). The dietary intakes of phytate, calcium, iron and zinc were expressed as mg per day per reference man.

Considering the sampling method of equal-sample-size of the six areas and the proportion difference between the sampling and whole population, the data of 2002 China Nationwide Population Census (31) were used for the adjustment of areas in data analysis.

A general linear model factorial analysis was applied with Tukey's post hoc comparisons to compare the differences of daily phytate and mineral intakes and the ratios between different areas, age and sex were included as co-variables in the model to reduce the potential difference owing to age and sex proportion in six areas. The non-parameter one-way comparison with Wilcoxon's test was used to compare the difference between urban and rural areas. Multiple logistic regression analysis was performed to compare the percentage of people with ratios above the suggested critical level, while age and sex were also included in the models. All statistical analyses were done with the SAS Statistical Package (SAS 8.2e for Windows, SAS Institute Inc., Cary, NC, USA), and statistical significance was set at 0.05.

Results

Characteristics of the Subjects

Table 1 summarizes the characteristics of study population of 2002 China Nationwide Nutrition and Health Survey. A total of 68,962 subjects (33,551 male and 35,411 female) were included in this study. In all, 21,103 subjects were from urban areas, whereas 47,859 from rural areas.

Phytate Intakes of People in Six Areas

Table 2 shows the dietary intakes of phytate, calcium, iron and zinc of people in China. The median dietary intake of phytate, calcium, iron, and zinc were 1186, 338.1, 21.2 and 10.6 mg/day per reference man, respectively. Significant differences in phytate and calcium intakes were found between urban and rural areas. Rural residents consumed significantly higher phytate than their urban counterparts (1342 vs 781 mg/d). The calcium intake of rural residents was 324.1 mg/day per reference man, which was 50 mg less than that of their urban counterparts. The iron and zinc intakes of urban and rural residents were comparable (21.1 vs 21.2 mg/day; 10.6 vs 10.6 mg/day).

Variations were found in the intakes of phytate, calcium, iron and zinc between each two of 6 areas. The daily phytate intake ranged from 1433 mg for rural 3 to 648 mg for large cities. Calcium intakes were between 451.8 mg/day for large cities and 292.9 mg/day for rural 4. The range of iron intakes was from 22.7 mg/day for rural 3 to 20.7 mg/day for rural 4, while that of zinc was 11.2 mg/day for rural 1 and 9.9 mg/day for rural 3.

The Molar Ratios of Phytate:calcium, Phytate:zinc, Phytate:iron and Phytate×calcium/zinc

Table 3 presents the molar ratios of phytate to calcium, zinc, iron, phytate×calcium/zinc and the proportion of subjects with ratios above the suggested critical values. The median molar ratios of phytate to calcium, iron, zinc and phytate×calcium/zinc were 0.22, 4.88, 11.1 and 89.0, respectively. All the four ratios of rural residents were significantly greater than that of their urban counterparts. A wide variation was found in the four ratios among six areas. The phytate:calcium molar ratios were between 0.09 and 0.28. The phytate:calcium molar ratio of 43.7% subjects were above the proposed critical value. The phytate:iron molar ratios ranged from 2.55 to 5.72. The phytate:iron molar ratio of 95.4% subjects were greater than 1. The phytate:zinc molar ratios were between 6.2 to 14.2. 23.1% subjects had molar ratios above the proposed critical level. The phytate×calcium/zinc molar ratios varied from 63.7 to 107.2. The phytate×calcium/zinc molar ratios of 8.7% subjects were higher than 200.

Discussion

Phytic acid is Myo-Inositol 1,2,3,4,5,6 hexakis phosphate (IP6), and it accumulates in cereal grains, nuts and legume seeds. Phytic acid is a strong chelator of divalent minerals such as copper, calcium, magnesium, zinc and iron. As phosphate groups are progressively removed from the IP6, the mineral binding strength decreases and solubility increases (32). At phosphorylations ≥5, iron solubility was decreased (33), zinc (34) and calcium (35) absorption was inhibited. The phytate contents in food samples are determined using anion-exchange method (20) in the present study. Rice and wheat products are the staple foods in China. The phytate contents of staple foods ranged from 3 mg/100g for fresh noodle to 420 mg/100 for wheat flour (85% extraction rate) (19). The disadvantage of Anion-exchange method is the lack of specificity in distinguishing between IP6 and its hydrolysis products. IP3, IP4 and IP5 were included in this method. Another disadvantage is the difficulty of determining low IP6 levels. Therefore, the IP6 contents in foods in the present study were overestimated to some extent.

A wide variation in phytate intakes was calculated in the diets of people in China. The average phytate intakes of people in China are higher than those in developed countries, and lower than those in Africa and Asia. It is reported that the average American consumes about 750 mg phytate per day (7). The estimates of daily phytate intakes in the United Kingdom range from 600 to 800 mg (36). Average phytate intake in Finland has been estimated to be 370 mg/day (37). The average national phytate intakes in Italy were 219 mg/day (11). Swedish people appear to consume very low levels of phytate (180 mg/day) (10). Nigerians consume as much as 2000-2200 mg/day (38) phytate, which is about three times more than the North Americans. Middle Eastern inhabitants also have very high amounts of phytate in their diets (36). A few studies in Asia indicate that phytate intake is higher compared to Western countries. Indian people consume as much as 1560-2500 mg phytate per day (15). Kwun and Kwon reported that the phytate intake of South Koreans was 1676.6 mg/day (16). The daily average phytate intake of people in China was higher than that in western countries (7, 10-11, 36-37), and less than that of Korean (16), Indian (15) and Nigerians people (38). A large variation was found in phytate intakes between people from different areas of China. It ranged from 781 mg/day for urban residents to 1433 mg/day for rural residents.

The variation in dietary pattern may be responsible for the discrepancy in intakes of phytate and minerals between urban and rural areas. The report of the 2002 China Nationwide Nutrition and Health Survey (1) indicated that the daily consumptions of cereal grains of urban and rural residents were 366 g and 416 g per reference man. Plant foods including cereal grains, legumes and tubers accounted for 52.6% and 66.3% to the energy intakes for urban and rural residents, whereas cereals and legumes provided 48.0 and 64.1% of protein for urban and rural residents, respectively. Although variation was found between urban and rural areas, the diets of people in China are still plant food-based. Plant foods are also the major resource of minerals, which provided most of the dietary intakes of calcium (54.6 vs 71.7%), iron (76.9 vs 86.1%) and zinc (61.2 vs 76.9%) for urban and rural residents in China. Differences in age proportion between urban and rural areas may not explain the phytate and minerals differences, as the differences were still significant after including the age and sex in the models as co-variables.

The influence of phytate on the bioavailability of minerals depends not only on the phytate contents in the diet, but also on the interaction between phytate and minerals. The phytate to minerals molar ratios are used to predict the inhibitory effect of phytate on the bioavailability of minerals. Phytate:calcium molar ratio >0.24 will impair calcium absorption (27). Phytate:iron molar ratio >1 will significantly decrease the iron absorption (22). Turnlund et al. (24) indicated that zinc absorption is greatly reduced and results in negative zinc balance when phytate:zinc molar ratio is 15.

Iron, zinc and calcium are essential minerals that are often lacking in human diets, either due to insufficient intake or poor absorption. There are two types of food iron-haem iron from animal foods, and non-haem iron from both animal and plant foods. The absorption of haem iron is little influenced by dietary pattern. The absorption of non-haem iron is influenced by both enhancing and inhibitory factors in the diets. Ascorbic acid from fruits and vegetables and meat/fish/poultry are the main enhancing substances for iron absorption (39, 40). Phytic acid from cereal grains and legumes (41, 42), and polyphenol compounds from tea and coffee (43) are the major inhibitory substances. It is reported that 85-95% anaemia in China is caused by iron deficiency (44-47). As the iron intakes were high (1), low iron bioavailability is considered a major factor in the aetiology of iron deficiency anaemia (48). When phytate:iron molar ratio >1 is used as the critical value (22), the bioavailability of iron in most subjects (95.4%) was inhibited. Phytate may play an important role in the anaemia problem in China.

Milk and milk products are the most important sources of calcium for people living in developed countries, whereas plant foods are the main source of calcium for people in China. Oxalate is a potent dietary inhibitory of calcium absorption (49) with phytic acid possessing a much smaller inhibitory effect (50). It is considered that the major factor resulting in an inadequate supply of calcium in the diets of people in China is low calcium intake from a low consumption of milk products, rather than low bioavailability. In the present study, we found that one-fifth of the urban residents and one-half of the rural residents have phytate:calcium molar ratio above the critical level, which implies the calcium bioavailability of this portion of population, was affected by phytate.

Meat and sea foods are good sources of zinc. However, meat and sea foods only provided 17.5% of zinc, while cereals and legumes contributed 56.8% zinc for people in China (unpublished data). These plant foods are high in phytic acid, which is a potent inhibitor of zinc absorption (51). The median phytate:zinc ratio was 11.1, which is similar to that in the diets of Taiwanese (14) and Korean (17), but lower than those of American lacto-ovo vegetarians (52), Middle Easterners (36), and Indian (15); and higher than those of a typical American hospital diet (53) and omnivorous diets. Our data suggest that phytate has little influence on zinc bioavailability of most residents in large cities of China. As 19-45% of rural residents had phytate:zinc molar ratios above the critical level, suggesting that phytate might increase the risk of impaired zinc bioavailability for rural residents in China.

It is suggested that the effect of other factors such as calcium on zinc bioavailability should be taken into consideration in diets that are both high in phytate and calcium but low in zinc (26). Considering the low calcium intake, phytate×calcium/zinc molar ratio might not be suitable for predicting the interaction effect of phytate and calcium on the absorption on zinc for people in China.

In **conclusion**, people in China consume more phytate in their diets than those in developed countries, and less than those in developing countries. A wide variation was found in phytate intake of people in different areas of China. The inhibitory effect of phytate on iron bioavailability for both urban and rural residents, and zinc bioavailability for rural population should be addressed.

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Table 1. Characteristics of Study Population

Sex	Age (years)	Total		Urban				Rural					
				All		Large Cities	M & S Cities	All		Rural 1	Rural 2	Rural 3	Rural 4
Total	All	68962		21103		10570	10533	47859		11639	11991	11824	12405
	2~	7185	(10.4)	1373	(6.5)	477	8896	5812	(12.1)	1325	1409	1306	1772
	10~	9309	(13.5)	2221	(10.5)	980	1241	7088	(14.8)	1544	1823	1863	1858
	20~	7537	(10.9)	2192	(10.4)	1066	1126	5345	(11.2)	1067	1379	1263	1636
	30~	12966	(18.8)	3655	(17.3)	1418	2237	9311	(19.5)	2166	2344	2354	2447
	40~	11760	(17.1)	3904	(18.5)	2053	1851	7856	(16.4)	2096	2039	2008	1713
	50~	10209	(14.8)	3474	(16.5)	1993	1481	6735	(14.1)	1809	1681	1703	1542
	60~101	9996	(14.5)	4284	(20.3)	2583	1701	5712	(11.9)	1632	1316	1327	1437
Male	All	33551		10027		4984	5043	23524		5762	5813	5752	6197
	2~	3857	(11.5)	718	(7.2)	256	462	3139	(13.3)	721	733	712	973
	10~	4954	(14.8)	1166	(11.6)	515	651	3788	(16.1)	836	965	981	1006
	20~	3359	(10.0)	978	(9.8)	479	499	2381	(10.1)	491	590	554	746
	30~	5934	(17.7)	1678	(16.7)	650	1028	4256	(18.1)	982	1070	1048	1156
	40~	5490	(16.4)	1791	(17.9)	933	858	3699	(15.7)	985	954	936	824
	50~	4930	(14.7)	1558	(15.5)	899	659	3372	(14.3)	927	845	834	766
	60~96	5027	(15.0)	2138	(21.3)	1252	886	2889	(12.3)	820	656	687	726
Female	All	35411		11076		5586	5490	24335		5877	6178	6072	6208
	2~	3328	(9.4)	655	(5.9)	221	434	2673	(11.0)	604	676	594	799
	10~	4355	(12.3)	1055	(9.5)	465	590	3300	(13.6)	708	858	882	852
	20~	4178	(11.8)	1214	(11.0)	587	627	2964	(12.2)	576	789	709	890
	30~	7032	(19.9)	1977	(17.8)	768	1209	5055	(20.8)	1184	1274	1306	1291
	40~	6270	(17.7)	2113	(19.1)	1120	993	4157	(17.1)	1111	1085	1072	889
	50~	5279	(14.9)	1916	(17.3)	1094	822	3363	(13.8)	882	836	869	776
	60~101	4969	(14.0)	2146	(19.4)	1331	815	2823	(11.6)	812	660	640	711

The values in parentheses are the percentage of the cases in the age group of the total cases within the same gender category.

Table 2. Dietary Intakes of Phytate, Calcium, Iron and Zinc of People in China (mg/day/reference man[1])

	Phytate (mg) Median (P_{25}-P_{75})	Calcium (mg) Median (P_{25}-P_{75})	Iron (mg) Median (P_{25}-P_{75})	Zinc (mg) Median (P_{25}-P_{75})
All	1186 (823–1603)	338.1 (240.9–471.8)	21.2 (16.8–27.1)	10.6 (8.5–13.3)
Urban	781 (443–1205)	374.5 (254.0–549.4)	21.1 (16.3–27.6)	10.6 (8.2–13.8)
Large cities[2]	648 (343–1034) [a]	451.8 (309.5–642.4) [a]	21.5 (16.7–28.0) [a]	10.7 (8.3–13.7) [a]
M & S cities[2]	833 (483–1272) [b]	343.9 (232.1–512.6) [b]	21.0 (16.2–27.5) [b]	10.6 (8.1–13.9) [a]
Rural[3]	1342 (970–1757)*	324.1 (235.8–441.8) *	21.2 (17.0–26.9) *	10.6 (8.6–13.1) *
Rural 1[2]	1271 (952–1651) [c]	380.2 (273.5–526.7) [c]	21.2 (16.8–26.9) [b]	11.2 (9.1–13.8) [b]
Rural 2[2]	1361 (981–1772) [d]	315.8 (230.7–426.1) [d]	21.0 (17.0–26.6) [c]	10.6 (8.6–12.9) [c]
Rural 3[2]	1433 (971–1975) [e]	303.9 (231.7–401.0) [e]	22.7 (18.4–27.9) [a]	9.9 (8.1–12.3) [d]
Rural 4[2]	1309 (956–1693) [f]	292.9 (206.9–412.0) [e]	20.7 (16.2–26.9) [c]	10.4 (8.1–13.4) [a]

[1]The reference man is used to adjust the dietary intakes of each individual, the equation is expressed as dietary intakes (mg/day) × 2400/individual RNI of energy.

[2]A general linear model is performed with Tukey's post hoc analysis to compare the effects of area. Values not sharing the same letters (a–f) denote significant difference between areas, $P < 0.05$.

[3]Compared to urban area, Wilcoxon's signed rank sum test, $^{*}P < 0.05$

Table 3. Molar Ratios of Dietary Phytate to Calcium, Iron, Zinc and Phytate×calcium:zinc of People in China

	Phytate : Calcium			Phytate : Iron			Phytate : Zinc			Phytate×Calcium:Zinc		
	Median	(P25-P75)	> 0.24 (%)[1]	Median	(P25-P75)	>1 (%)[1]	Median	(P25-P75)	>15 (%)[1]	Median (mmol/day)	(P25-P75) (mmol/day)	>200 (%)[1]
All	0.22	(0.14–0.31)	43.7	4.88	(3.28–6.51)	95.4	11.1	(8.1–14.2)	23.1	89.0	(57.8–131.7)	8.7
Urban	0.13	(0.06–0.21)	20.5	3.11	(1.76–4.77)	87.7	7.3	(4.4–10.6)	8.0	64.1	(36.6–104.8)	5.4
Large cities[2]	0.09 [a]	(0.05–0.15)	7.5 [a]	2.55 [a]	(1.36–4.05)	83.3	6.2 [a]	(3.4–9.2)	3.1 [a]	63.7 [a]	(33.8–109.5)	6.4 [a]
M & S cities[2]	0.14 [b]	(0.07–0.24)	25.7 [b]	3.33 [b]	(1.92–5.06)	89.4	7.7 [b]	(4.8–11.2)	10.0 [b]	64.3 [b]	(37.7–103.0)	5.0 [b]
Rural[3]	0.25 *	(0.17–0.35)	52.6*	5.56*	(3.86–7.18)	98.4	12.5*	(9.5–15.6)	28.9*	98.7*	(66.1–142.0)	10.0*
Rural 1[2]	0.20 [c]	(0.13–0.29)	37.7 [c]	5.20 [c]	(3.76–6.66)	97.0	11.3 [c]	(8.7–14.1)	18.9 [c]	103.6 [c]	(70.1–151.1)	11.9 [c]
Rural 2[2]	0.26 [d]	(0.18–0.35)	55.6 [d]	5.72 [d]	(3.91–7.36)	99.2	12.8 [d]	(9.7–15.6)	29.8 [d]	98.2 [d]	(65.3–142.0)	10.1 [c d]
Rural 3[2]	0.28 [e]	(0.18–0.41)	60.4 [e]	5.53 [e]	(3.93–7.10)	98.0	14.2 [e]	(10.4–18.1)	44.6 [e]	107.2 [d]	(71.7–148.9)	9.4 [d]
Rural 4[2]	0.26 [f]	(0.18–0.40)	56.7 [e]	5.54 [f]	(3.70–7.31)	97.8	12.2 [f]	(9.1–15.5)	27.9 [d]	87.9 [e]	(59.4–125.6)	7.4 [e]

[1]Logistic regression analysis, Values not sharing the same letters (a–f) denote significant difference between areas, $P < 0.05$

[2]A general linear model is performed with Tukey's post hoc analysis to compare the effects of area. Values not sharing the same letters (a–f) denote significant difference between areas, $P < 0.05$.

[3]Compared to urban area, Wilcoxon's signed rank sum test, * $P < 0.05$

Chapter 4

Assessment of zinc intake inadequacy and food source of people in China

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Public Health Nutrition (in press)

Abstract

Objectives: To assess the zinc intake inadequacy and food sources of people in China.

Methods: Diets of 68,962 subjects aged 2-101 years (urban 21,103, rural 47,859) in the 2002 China National Nutrition and Health Survey were analyzed. Dietary intake was assessed using 24h recall for three consecutive days. Zinc intake inadequacy was calculated based on the WHO suggested values.

Results: The median daily zinc intakes ranged from 4.9 mg/day (urban girls, 2-3 years) to 11.9 mg/day (rural male, 19+ years). The zinc density of urban residents (2-3, -19+ years) was 5.0-5.2 mg/day/1000 kcal, which significantly higher than that of their rural counterparts (4.7-4.8 mg/day/1000 kcal). Differences in food sources of zinc from cereal grains (27.4-45.1 vs 51.6-63.2%) and animal foods (28.4-54.8 vs 16.8-30.6%) were found between urban and rural residents. Zinc from vegetables and fruits (8.2-13.8 vs 9.7-12.4%), and legumes (1.3-3.3 vs 2.5-3.4%) were comparable between urban and rural residents. The proportions of zinc intake inadequacy were between 2.8% (urban female, 19+ years) and 29.4% (rural lactating women). Rural residents had higher proportions of zinc intake inadequacy than their urban counterparts. Significantly higher proportions of zinc inadequacy were found in the category of phytate:zinc molar ratio >15 for both rural and urban residents.

Conclusion: About 20% of rural children are "at risk" of inadequate zinc intakes with phytate as a potential important inhibitor. Moreover, lactating women are also considered a vulnerable group.

Key words: zinc, phytate, dietary intake, China National Nutrition and Health Survey

Introduction

Zinc is an essential mineral that performs important biochemical functions for maintaining human health (1-6). Zinc deficiency may be widespread in developing countries, but the true magnitude of mild and moderate zinc deficiency is unknown, in part because of the lack of a reliable and specific index of zinc status (7, 8). Recommended Dietary Allowance (9) and the estimated average requirement (10, 11) are suggested to be used in estimating the prevalence of nutrient inadequacy in a group.

Zinc deficiency may arise from low dietary intakes, low bioavailability and/or interaction with other nutrients and losses through disease process (12-14). Inhibitors of zinc absorption are believed to be the more likely causative factor (15). Phytate, present in whole grains, cereals and legumes, is a strong inhibitor for zinc absorption. Phytate in plant-based diets is high, which is the major inhibitory factor for zinc absorption. A phytate:zinc molar ratio is used to predict the inhibitory effect of phytate on the bioavailability of zinc (8, 16, 17). WHO suggests that the assessment of dietary zinc status should take inhibitory factors into account, and phytate data must be available (8). However, the inhibitory effect of phytate on the bioavailability of zinc has not been examined in China due to the lack of the information on phytate content in the China Food Composition Table (18). In 2005, the phytate content of 60 food samples commonly consumed in China was analyzed (19) using an anion-exchange method, which made it possible to assess the dietary zinc intake of people in China taking the inhibitory effect of phytate into account. The purpose of the present study was: (1) to assess the prevalence of zinc intake inadequacy in relation to the effect of phytate in the diets; (2) to examine if zinc intake inadequacy differs by age, sex and region in China; (3) to describe the food sources of zinc.

Subjects and Methods

Sampling

The 2002 China National Nutrition and Health Survey (CNNHS) is a nationally representative cross-sectional survey that covered 31 provinces, autonomous regions and the municipalities directly affiliated with the Central Government (Hong Kong, Macao and Taiwan were not included). Multi-stage cluster sampling method was used for subject selection. Stage 1: all the 2860 counties/districts/cities of China were divided into six areas (big cities, medium and small cities, rural 1, 2, 3 and 4) based on its type and the level of economic development (from high to low). Twenty-two counties/districts/cities from each area were randomly selected. A total of 132 counties/districts/cities were randomly selected at this Stage. Stage 2: three townships/sub-districts were randomly selected from each selected counties/districts/cities. A total of 396 townships/sub-districts were randomly selected at this Stage. Stage 3: two villages/neighborhood committees were randomly selected from the selected townships/sub-districts. A total of 792 villages/neighborhood committees were randomly selected at this Stage. Stage 4: ninety households were randomly selected from each selected village and neighborhood, and finally, a total of 71,971 households were randomly selected to represent the national data.

Dietary Intake Assessment

The dietary survey was conducted among all members of 30 households that randomly selected from the pre-selected 90 households. All family members above two years old from the selected households were invited for the dietary intake assessment. A total of 23,470 from 71,971 households participated in the dietary intake assessment (20).

The protocol of the survey was approved by the Ethical Committee of National Institute for Nutrition and Food Safety, Chinese Center for Disease Control and Prevention. A signed consent form was obtained from each subject or his/her parent or guardian.

Information on food intake was collected using the 24h dietary recall method for three consecutive days (two weekdays and one weekend day) by trained interviewers. The parent or guardian was interviewed for children aged 2 to 16 years.

Zinc intake was calculated using the data of+ dietary recall in conjunction with the China Food Composition Table. The composition of infant formula is available in the Table and was included in the calculation. Zinc content of foods in the China Food Composition Table was determined by atomic absorption spectrophotometry (18). Duplicate food samples were analyzed. Standard reference materials (SRM) were obtained from the China National Center of Standard Material for quality control. The relative standard deviation (RSD, %) was within 10%.

Sixty food samples including rice, wheat flour, corn and soybean products commonly consumed in China were selected based on the frequency of foods consumed of 2002 CNNHS (19). The phytate content of food samples was determined using an Anion-exchange method (21). The phytate intake was calculated using the phytate content in conjunction with the dietary recall data. The average daily dietary intake of zinc and phytate were calculated using the mean value of the three days' intakes.

The contributions of individual foods to zinc were calculated by summing the amount of zinc consumed from each food by all subjects in each age group and dividing by the total intake from all foods for all subjects in the respective age group.

Phytate:zinc molar ratio was calculated as the millimoles of phytate intake per day divided by the millimoles of zinc intake per day. The proportion of subjects with different phytate:zinc molar ratios (<5, 5-15, >15) were calculated. The percentage of people with zinc intake below the WHO normative requirement (8) at a different phytate:zinc molar ratio was calculated. The average individual normative requirement for zinc from diet are developed according to zinc availability, the three (high, moderate and low) bioavailability levels corresponding to 50%, 30% and 15% absorption (8). The normative requirements of first trimester for pregnant women, and the first three months for lactating women were used to assess the inadequacy zinc intake for these groups.

Statistical Analysis

Values of dietary zinc intake were expressed as median and inter-quartile range. Zinc intake was expressed as mg/day, and zinc density as mg/day/1000 kcal. Normal probability plots and Kolmogorov-Smirnov tests were used to determine whether variables followed a normal distribution. To analyze the associations of sex, age, region and their interactions with dietary zinc intake, a general linear model factorial analysis was applied with Tukey's post-hoc comparisons. The results are presented by sex, age, and region for the significant interactions found between sex and age, and between age and region. Differences in zinc intake of subjects by sex and region were compared using Wilcoxon's signed rank sum test. The proportion of subjects with different phytate:zinc molar ratios was calculated while the proportion of zinc intakes less than the WHO suggested normative requirement (8) was calculated by region and phytate:zinc molar ratio. Differences in the above-mentioned proportions between urban and rural areas were compared using Chi-square test. All statistical analyses were applied with the SAS Statistical Package (8.2e for windows, SAS Institute Inc. Cary, NC). Statistical significance was set at 0.05.

Results

The Characteristics of the Study Population

A total of 68,962 subjects were included in the present analysis. A total of 21,103 subjects (male 10,027, female 11,076) were from urban areas, while 47,859 (male 23,524, female 24,335) from rural areas. There were 310 pregnant women and 470 lactating women. The means of BMI and dietary energy intake of different age group and region are presented in **Table 1**.

The Dietary Zinc Intake of People in China

The median zinc intakes by age, sex and region are presented in **Table 2**. There were significant effect of age [F (6, 68956) = 372.8; P<0.001], sex [F (1, 68961) = 113.8; P<0.001], and first level interactions between region and age [F (6, 68956) = 22.5; P<0.001], and between age and sex [F (6, 68956) = 15.5; P<0.001], for dietary zinc intakes. The median of zinc intakes ranged from 4.9 mg/day (urban girls, 2-3 years) to 11.9 mg/day (rural male, 19+ years). The zinc intake of urban boys aged 2-3 years was higher than that of their rural counterparts (6.2 vs 5.1 mg/day). In contrast, the zinc intake of rural adults (19+ years) was significantly higher than that of their urban counterparts (male 11.9 vs 10.5 mg/day; female 10.2 vs 8.9 mg/day). The younger the age group, the less the zinc intake. Rural lactating women consumed higher zinc than their urban counterparts (11.0 vs 9.8 mg/day) whereas urban pregnant women consumed comparable amounts of zinc as their rural counterparts (10.7 vs 10.9 mg/day).

There were significant effect of age [F (6, 68956) = 4.9; P<0.001], region [F (1, 68961) = 278.8; P<0.001], and first level interactions between region and age [F (6, 68956) = 4.2; P<0.001], and between age and sex [F (6, 68956) = 3.3; P<0.001], as well as second level interactions between sex, region and age [F (4, 68958) = 3.9], for dietary zinc density. The median zinc density of all age groups was between 4.7 and 5.7 mg/day/1000 kcal (**Table 2**). The zinc density of urban residents (2-3, -19+ years) was 5.0-5.2 mg/day/1000 kcal, which significantly higher than that of their rural counterparts (4.7-4.8 mg/day/1000 kcal). No significant difference was found between different age group. Variation in median zinc intake was found between male and female within the same region and same age group. The zinc density of urban boys (2-3 years) was higher than that of their female counterparts; In contrast, the rural boys (2-3 years) and rural adults consumed less zinc density than their female counterparts. Urban pregnant women had higher zinc density intakes than their rural counterparts (5.7 vs 4.7 mg/day/1000 kcal). No difference in zinc density was found between urban and rural lactating women.

The Food Source of Zinc

The dietary zinc from cereal grains including rice, wheat flour and its products was 27.4-63.2%, while 16.8-54.8% zinc was from animal foods. Vegetables and fruits provided 8.2-13.8% of dietary zinc, while legumes contributed only 1.3-3.4% of dietary zinc. Large discrepancies were found in the food sources of zinc from staple and animal foods between urban and rural residents within the same age group. Staple foods provided 27.4-45.1% zinc for urban residents, 51.6-63.2% for rural residents. Dietary zinc of urban residents 28.4-54.8% was from animal foods, and was much higher than that of their respective rural counterparts (16.8-30.6%). Vegetables, fruits and legumes provided comparable zinc for both urban and rural residents. Detailed information on the food source of dietary zinc intake stratified by age, sex and region was shown in **Table 3**.

The Proportion of Subjects with Different Phytate:zinc Molar Ratios

Variations in the proportions were found between different age and/or sex subgroups with the same phytate/zinc molar ratio (**Table 4**). Of 28.6-46.8% urban residents and 3.9-8.0% rural residents had phytate/zinc molar ratios <5, while 48.7-65.7% of residents had phytate/zinc molar ratios between 5 and 15, and 4.5-18.2% of urban residents and 27.8-36.4% of rural residents had phytate/zinc molar ratios >15. The proportion of rural residents with phytate/zinc molar ratios >15 was significantly higher than that of their urban counterparts. Significant effect of age on the proportion of subjects with different phytate:zinc molar ratios was found in all subgroups. Significant sex difference was only found in rural children aged 9-13 years (**Table 4**).

The Prevalence of Zinc Intake Inadequacy

Table 5 presents the prevalence of zinc intake inadequacy by age, sex and region. The proportions of zinc intake inadequacy were between 2.8% (urban female, 19+ years) and 29.4% (rural lactating women). The distributions were much higher when a phytate/zinc molar ratio >15 was calculated: 10.3% for rural female, 19+ years, and 100% for urban lactating women. The proportions of zinc intake inadequacy of urban residents were 2.8-16.4%, which were significantly lower than that of their rural counterparts (3.6-29.4%). Prevalence of zinc intake inadequacy was significantly higher among male adults (19+ years) than their female counterparts. The zinc intake of 5.5% pregnant and 29.4% lactating women was inadequate.

Discussion

Information on zinc intake in developing countries is limited because of the paucity of data on the zinc content of local staple foods (22). China has developed a China Food Composition Table since the 1960s and kept it updated using reliable and valid determination methods (18). The composition of fortified foods is also available in the

China Food Composition Table. The strength of the present study is the use of 3-day, 24h dietary recall data of a national representative sample population in conjunction with the China Food Composition Table. One limitation of this study is that the zinc from dietary supplements was not taken into account. As the dietary supplement use in China (23) is low (urban, 10.3%; rural, 2.9%) compared with that (39.5%) in U.S. (9), we assumed that the zinc intake was underestimated to a small extent. This limitation suggests that the use of dietary supplements and their contribution to total nutrient intake in the population in China, especially for urban persons, should be monitored in future surveys.

The present study found that the zinc intake of people in China was lower than that of the U.S. population (9,24, 25), but comparable with that of the population in the U.K. (26, 27), Germany (28) and New Zealand (29). People in China consumed more zinc than their counterparts in Chile (30), India (31) and Korea (32). However, the adequacy of zinc intake depends not only on the amount, but also its bioavailability. The inhibitory factors that may interact with zinc should be examined when assessing the dietary intake of zinc (8, 33). People consuming a diet that provides marginal zinc intake may not absorb adequate amount of zinc if they are also consuming foods high in phytate. The average phytate intake of people in China (1186 mg/day) (34) was higher than that in western countries (35, 36), and less than that of Korean (37) and Indian people (38). The proportion of people with inadequate zinc intake was considerably high in the phytate:zinc molar ratio >15 category, indicating that zinc in the diets of those populations would be affected by their high phytate intake. The vulnerable groups of zinc deficiency in China are children, adolescents and lactating women, especially those in rural areas. As zinc plays an important role for children's growth (39) and pregnancy (40, 41), zinc deficiency will impact on human health severely (42), including growth retardation, abnormal immune function, impaired cognitive function, increased maternal morbidity, prolonged gestation and increased risk to the fetus.

Information on the inadequacy of dietary zinc intakes should be interpreted together with data derived from other assessment methods. The national prevalence of stunting among children under 5 years can be used as an indirect indicator of a population's risk of zinc deficiency (43, 44). The national prevalence of stunting in China is 3.3-8.6% for urban children <5 years and 17.3-20.9% for their rural counterparts (45). It can be concluded that the level of risk of zinc deficiency is low for the urban population and moderate for the rural population in China. Further population assessment of zinc status by serum zinc concentrations in a representative sample of the population should be made in order to identify segments of the population at high risk. Appropriate intervention strategies including supplementation, food fortification, dietary diversification and biofortification should be developed to target different populations.

In conclusion, urban people in China are at low risk of zinc deficiency, whereas the rural population is at a moderate level of risk of zinc deficiency. Lactating women and rural children in China are vulnerable populations. Effective strategies correcting these problems should be developed and implemented in targeted risk groups.

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Table 1. Characteristics of the Study Population

Group	Urban					Rural				
	N	BMI (kg/m^2)		Energy (kcal/day)		N	BMI (kg/m^2)		Energy (kcal/day)	
		M	SD	M	SD		M	SD	M	SD
Male										
2-3 yr	154	16.2	1.8	1386.8	1006.7	623	16.2	1.7	1212.8	613.4
4-8 yr	455	15.9	2.3	1528.3	694.6	2049	15.2	1.5	1589.7	585.9
9-13 yr	641	17.4	2.9	1858.0	711.9	2641	16.5	2.4	2007.1	652.4
14-18 yr	554	19.7	3.1	2196.0	808.5	1461	18.8	2.5	2414.2	700.2
19+ yr	8223	24.0	3.5	2129.9	790.0	16750	22.4	3.2	2600.2	750.1
Female										
2-3 yr	108	15.7	1.4	1439.0	2510.9	466	15.6	1.5	1160.7	537.7
4-8 yr	436	15.3	2.0	1392.8	557.0	1758	14.8	1.4	1512.6	618.4
9-13 yr	598	17.0	2.9	1700.1	645.2	2351	16.4	2.4	1830.0	571.6
14-18 yr	484	20.3	3.0	1816.0	656.3	1259	19.8	2.5	2076.9	694.1
19+ yr	9340	23.9	3.8	1808.0	749.2	17831	22.9	3.5	2238.6	678.1
Pregnant	55	22.5	3.2	1938.7	603.3	255	24.2	3.5	2380.7	714.4
Lactating	55	22.3	2.0	1979.1	635.6	415	23.2	4.4	2421.6	742.7

Table 2. Quartile of Zinc Intakes and Zinc Density by Age, Sex and Region (P_{25}, P_{50}, P_{75})

Group	Zinc (mg/day)						Zinc (mg/day/1000 kcal)					
	Urban			Rural			Urban			Rural		
	P_{25}	P_{50}	P_{75}	P_{25}	P_{50}	P_{75}	P_{25}	P_{50}	P_{75}	P_{25}	P_{50}	P_{75}
Male												
2-3 yr	4.7	6.2^{c}	7.9	3.9	$5.1^{*,e}$	6.9	4.5	5.3	6.4	4.1	4.7^{*}	5.4
4-8 yr	5.2	7.1^{c}	9.3	5.5	7.1^{d}	9.0	4.3	5.0	6.0	4.2	4.7^{*}	5.3
9-13 yr	6.9	9.1^{b}	12.1	7.3	9.0^{c}	11.2	4.4	5.0	6.3	4.3	4.7^{*}	5.2
14-18 yr	8.4	10.7^{a}	13.8	8.9	11.0^{b}	13.6	4.3	5.1	6.0	4.3	4.7^{*}	5.2
19+ yr	8.1	10.5^{a}	13.6	9.7	$11.9^{*,a}$	14.4	4.4	5.1	6.1	4.3	4.7^{*}	5.2
Female												
2-3 yr	3.7	$4.9^{\S,cd}$	7.2	3.7	5.1^{a}	7.0	4.2	$5.1^{\S}$	6.1	4.2	$4.8^{\S}$	5.5
4-8 yr	5.1	6.7^{c}	8.9	5.2	$6.8^{\S,b}$	8.6	4.4	5.1	6.1	4.2	4.7	5.3
9-13 yr	6.3	$8.2^{\S,ad}$	10.9	6.7	$8.3^{\S,c}$	10.3	4.4	5.1	6.0	4.3	4.8^{*}	5.3
14-18 yr	7.0	$8.9^{\S,ab}$	11.8	7.6	$9.3^{\S,d}$	11.8	4.4	5.1	6.3	4.3	4.8^{*}	5.2
19+ yr	6.9	$8.9^{\S,b}$	11.6	8.3	$10.2^{*,\S,e}$	12.5	4.4	5.2	6.2	4.3	$4.8^{*,\S}$	5.3
Pregnant	8.1	10.7^{ab}	14.1	8.9	10.9^{ef}	13.6	4.5	5.7	6.6	4.2	4.7^{*}	5.3
Lactating	7.1	9.8^{abcd}	11.9	9.0	$11.0^{*,fg}$	13.3	4.2	4.9	5.9	4.3	4.8	5.3

A general linear model performed with Tukey's post-hoc analysis to compare the effects of age (by sex and by region). Values not sharing the same letters (a–e) denote significant difference between age groups of same sex, $P < 0.05$;

*Significant difference between urban and rural residents within same age and sex group, Wilcoxon's signed rank sum test, $^{*}P<0.05$

§Sex difference within same age and region, Wilcoxon's signed rank sum test, $^{\S}P<0.05$

Table 3. Food Sources of Dietary Zinc by Age, Sex and Region (%)

Group	Urban						Rural					
	Cereal Grains	Animal Foods	Vegetables & Fruits	Legumes	Nuts, Cake, Sauce, Oil	Other	Cereal Grains	Animal Foods	Vegetables & Fruits	Legumes	Nuts, Cake, Sauce, Oil	Other
Male												
2-3 yr	28.9	51.8	8.4	2.4	2.4	6.0	51.6	30.6	9.7	3.2	1.6	3.2
4-8 yr	40.0	38.8	10.0	1.3	3.8	6.3	60.0	20.0	12.0	2.7	2.7	2.7
9-13 yr	41.6	34.7	10.9	3.0	4.0	5.9	61.2	18.4	11.2	3.1	3.1	3.1
14-18 yr	42.2	35.3	10.3	2.6	4.3	5.2	63.2	17.9	11.1	2.6	2.6	2.6
19+ yr	42.2	34.5	11.2	2.6	4.3	5.2	61.9	18.3	11.1	3.2	3.2	2.4
Female												
2-3 yr	27.4	54.8	8.2	1.4	2.7	5.5	53.4	27.6	10.3	3.4	1.7	3.4
4-8 yr	41.3	34.7	10.7	2.7	4.0	6.7	58.9	20.5	12.3	2.7	2.7	2.7
9-13 yr	41.8	34.1	12.1	3.3	3.3	5.5	61.8	16.9	12.4	3.4	3.4	2.2
14-18 yr	37.6	38.6	10.9	2.0	4.0	6.9	62.4	16.8	11.9	3.0	3.0	3.0
19+ yr	40.0	34.0	13.0	3.0	4.0	6.0	62.0	17.6	12.0	2.8	2.8	2.8
Pregnant	43.1	28.4	13.8	2.6	4.3	7.8	58.6	18.1	12.1	3.4	3.4	4.3
Lactating	45.1	30.4	11.8	2.9	4.9	4.9	60.2	20.3	11.9	2.5	2.5	2.5

Table 4. Proportion of Subjects with Different Phytate:zinc Molar Ratio (%)

Group	Urban			Rural		
	Phytate:Zinc Molar Ratio			Phytate:Zinc Molar Ratio*		
	< 5	5-15	> 15	< 5	5-15	> 15
Male						
2-3 yr	46.8	48.7	4.5	8.0	64.2	27.8*
4-8 yr	28.6	62.9	8.6	5.0	65.2	29.9*
9-13 yr	32.6	58.8	8.6	5.6	61.8	32.5*
14-18 yr	32.1	59.7	8.1	4.8	61.7	33.5*
19+ yr	32.4	60.6	7.0	5.2	61.7	33.1*
Age effect	χ^2=21.6, *P*<0.01			χ^2=25.3, *P*<0.01		
Female						
2-3 yr	35.2	59.3	5.6	7.7	64.4	27.9*
4-8 yr	30.3	59.6	10.1	5.7	65.7	28.6*
9-13 yr	33.1	57.5	9.4	3.9	63.1	33.0*,§
14-18 yr	34.1	59.9	6.0	5.8	59.5	34.7*
19+ y	32.7	60.2	7.1	4.9	61.1	34.0*
Pregnant	30.9	50.9	18.2	6.3	61.6	32.2*
Lactating	29.1	63.6	7.3	5.1	58.6	36.4*
Age effect	χ^2=22.0, *P*<0.05			χ^2=45.4, *P*<0.01		

*Significant difference between urban and rural residents, χ^2–test, *P<0.05

§Sex difference within same age and region, χ^2–test, §P<0.05

Table 5. Proportion of Zinc Intakes Less Than WHO Normative Requirement (%)

Group	Urban				Rural			
	Phytate:Zinc Molar Ratio			Total	Phytate:Zinc Molar Ratio			Total
	<5	5-15	>15		<5	5-15	>15	
Male								
2-3 yr	0.0	8.8	33.3	6.3	4.5	9.1	69.5	25.8*
4-8 yr	0.9	9.0	69.7	11.9	0.0	1.1*	46.1*	14.7
9-13 yr	0.0	7.3	55.3	8.9	0.0	0.9*	49.3	16.8*
14-18 yr	2.8	6.3	67.6	10.2	1.9	1.6*	47.4*	17.2*
19+ yr	0.2	2.8	43.6	4.8	0.4	0.3*	19.4*	6.6*
Female								
2-3 yr	2.9	5.9	80.0	8.8	3.2	6.7	62.5	21.7*
4-8 yr	1.0	3.4§	55.0	8.6	0.0	2.6§	46.5	15.1*
9-13 yr	0.0	6.0	51.0	8.3	0.0	1.9*,§	42.5§	15.6*
14-18 yr	0.7	5.1	50.0	5.9§	1.6	2.5*	49.7	18.8*
19+ yr	0.1	1.3§	27.8§	2.8§	0.1	0.2*,§	10.3*,§	3.6*,§
Pregnant	0.0	0.0	40.0	7.3	0.0	0.0	17.1	5.5
Lactating	0.0	14.3	100.0	16.4	0.0	2.9*	76.2	29.4*

*Significant difference between urban and rural residents, χ^2–test, *P<0.05

§Sex difference within same age and region, χ^2–test, §P<0.05

Chapter 5

Iron and zinc deficiencies in China: what is a feasible and cost-effective strategy?

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Submitted for publication

Abstract

Objectives: In order to prioritize the interventions for micronutrient deficiencies in China, the affected populations of iron and zinc deficiencies were assessed based on the data of the 2002 China National Nutrition and Health Survey.

Methods: The costs and cost-effectiveness of supplementation, food diversification, and food fortification were estimated using the standard WHO ingredients-approach.

Results: The results indicated that 30% of children (<2 years), adults (>60 years), pregnant and lactating women, and 20% of women of reproductive age were anemic, which affected 245 million populations. Approximately, 100 million population were affected by zinc deficiency (zinc intake inadequacy and stunting), the majority living in rural areas. For iron and zinc deficiency intervention, biofortification showed the lowest costs per capita, international dollars (I$) =0.01, while dietary diversification through health education represented the highest costs with I$=1148. The cost-effectiveness of supplementation, food fortification and dietary diversification for iron deficiency alone was I$179, I$66, and I$103/DALY, respectively, Data for biofortification are not known. For zinc deficiency, the corresponding figures were I$399, I$153, and I$103/DALY, respectively.

Conclusion: Iron and zinc deficiencies are of public health significance in China. Of the two long-term intervention strategies i.e., dietary diversification and biofortification with improved varieties, the latter is especially feasible and cost-effective for rural population. Supplementation and fortification can be used as the short-term strategies for specific groups.

Key words: micronutrient deficiency, iron, zinc, cost-effectiveness, China

Introduction

The latest WHO estimates revealed that undernutrition is an underlying cause of 53% of all deaths in children <5 years of age (1). It has been estimated that more than 2 billion of the world population, nearly all in developing countries, are iron deficient (2, 3). Billions of individuals are also at risk for zinc deficiency (4).

Micronutrient deficiency not only affects the health and development of humans (5-9), but also hinders the social and economic development of a country. It is estimated that the losses in economic productivity due to iron deficiency in China would be more than 3.6% Gross National Product (GNP) (10).

The causes of micronutrients deficiencies include inadequate intakes, impaired absorption and/or utilization, excessive losses, increased physiological need or the combination of these factors (11). Insufficient intake and poor bioavailability are major causes in developing countries (12-14). Micronutrient content and bioavailability can be improved apparently by either increasing the quantity of a micronutrient or increasing enhancing factors/decreasing inhibiting factors in the foods using different techniques or sources. Strategies for increasing effective nutrients supply fall into two categories, supplementation and food-based approaches. Supplementation is the addition of an element to the diet to dissolve insufficiency. Food-based approaches consist of food diversification (increase the number of different foods or food groups consumed over a given reference period (15) and fortifications. Food fortification is the addition of an ingredient to food to increase the concentration of a particular element, while biofortification is the process of increasing the bioavailable concentrations of an element in edible portions of crop plants through agronomic intervention or genetic selection (16). Supplementation, food fortification and dietary diversification have been the three widely applied interventions for micronutrient deficiency for the past decades. Each intervention has its advantages and disadvantages (17).

Information on the magnitude of micronutrient deficiencies, the cost and cost-effectiveness of intervention strategies is needed for prioritizing the significance, and for developing public policy. However, at the moment, there is a lack of this kind of information in China. The 2002 China National Nutrition and Health Survey (CNNHS) conducted in 2002 makes it possible to assess the current situation of micronutrient deficiencies in China and provide information for policy makers. Therefore, the purpose of the present study was (1) to estimate the population affected by iron and zinc deficiencies; (2) to identify the vulnerable population for intervention; (3) to estimate the cost and cost-effectiveness of four interventions; (4) to provide information for policy makers for developing intervention strategies.

Methods

Estimation of Affected Populations with Micronutrient Deficiencies

The 2002 CNNHS was a nationally representative survey, which recruited 243, 479 individuals from 71, 971 households of 132 sites in 31 provinces, autonomous regions and the municipalities (18). More detailed information on the study design (19) and quality control (20) has been described elsewhere.

Hemoglobin was determined using the cyanmethemoglobin method (National Committee for Clinical Laboratory Standards, 1994). The WHO definition was used for defining anaemia (21). The hemoglobin values were adjusted according to the altitude of the study sites. Prevalence of anaemia was adjusted using the data of 2000 China National Population Census (22) in order to eliminate the difference in proportion between the sample and the whole population.

Fasting body weight and height (length) of subjects were measured following the standard procedure (23) by trained investigators. The duplicate measurements in subgroups showed a high reproducibility (correlation coefficients of duplicate measurements was 0.99 for height and 0.98 for weight). Stunting is defined by the WHO z-score of height-for-age criteria (24).

The information on food intake was collected using 24h dietary recall method for three consecutive days (two weekdays and one weekend day) by trained interviewers (19). Zinc intake was calculated using the data of dietary recall in conjunction with the China Food Composition Table (25). The WHO normative requirement (26) was used to assess the inadequacy of zinc intake. The percentage of people with zinc intake below the WHO normative requirement at different phytate/zinc molar ratios was calculated (27 Ma et al, unpublished).

The prevalence of anaemia, stunting and zinc intake inadequacy in combination with the data of 2000 China National Population Census (22) was used for the estimation of the absolute number of affected subjects.

Food Source of Iron, and Zinc

The contribution of individual food to iron/zinc was calculated by summing the amount of iron/zinc consumed from each food by all subjects in each age group and dividing it by the total intake from all foods for all subjects (28).

Estimated Costs and Cost-effectiveness of Different Interventions

The costs per capita and cost-effectiveness of supplementation and fortification for iron and zinc were obtained from the results of the total population-level costs for the Western Pacific Region B for the year 2000 by WHO (29, 30). The standard WHO ingredients-approach with separate specification of units of utilization and costs is adopted (29). Costs are expressed in international dollars (I$) to facilitate more meaningful comparisons across regions. An international dollar has the same purchasing power as the US$ has in the USA. Costs in local currency units are converted to international dollars by use of purchasing power parity (PPP) exchange rate rather than official exchange rates (30). The costs of an intervention program are costs per year (I$, millions) per one million population, i.e. cost per capita. The cost-effectiveness is measured by cost per disability-adjusted life-year (DALY) saved.

The costs per capita and cost-effectiveness of health education through mass media for the entire population (31) were used for dietary diversification through health education because more specific information is not available.

The costs of biofortification were calculated based on the literature (32). The areas of rice and wheat harvested were 28×10^6, and 22×10^6 hectare in China (33). For a single staple crop, the estimated central fixed costs of developing iron-/zinc-dense varieties over 10 years will be I$$12.5\times10^6$ (32). The central fixed costs include costs of nutritional studies to establish efficacy and to demonstrate impact after adoption. The costs for developing iron-dense/zinc-dense rice and wheat varieties will be I$$25\times10^6$ for a 10 years period.

The estimated costs for adaptive breeding per province for growing conditions in China for the same 10 years periods will be I$$2.5\times10^6$. There are 17 provinces for growing rice and 9 provinces for growing wheat. The estimated costs of two crops in those areas will be I$$65\times10^6$ ($17\times2.5\times10^6 + 9\times2.5\times10^6$).

The extension costs are estimated to be I$1 per adopted hectare. If adoption occurs on 50% of the rice and wheat areas in China, there will be 25×10^6 hectare ($50\%\times28\times10^6$ + $50\%\times22\times10^6$). The fixed undiscounted extension cost will be I$$25\times10^6$. The total investment of iron-/zinc-dense rice and wheat will be I$115×$10^6$ in 10 years, which is I$11.5×$10^6$/year. The estimated costs per capita will be I$0.01 (**Table 4**).

Results

Affected Populations by Iron and Zinc Deficiencies in China

Table 1 presents the prevalence of anaemia and the estimated affected populations by anaemia and iron deficient anaemia in China. The overall prevalence of anaemia was 20.1% and 31.1% of children <2 years were anemic. Nearly 30% of adults >60 years, pregnant and lactating women, and 20% women of reproductive age were anemic. The estimated affected populations by anaemia were 245 million, and 208 million of those were due to iron deficiency. Three-fourths of these affected populations were found in rural areas.

The zinc intake inadequacy, stunting and the estimated affected population in China is shown in **Table 2**. More rural residents had inadequate zinc intake than their urban counterparts (8.2 vs 4.6%). Zinc intake inadequacy among rural children was 2-3 folds in comparison with their urban counterparts. In addition, 14.3% of rural children <5 years were stunting. The estimated population affected by zinc intake inadequacy and stunting were 86 million and 10 million, respectively, and the majority of them were living in rural areas.

Food Sources of Iron and Zinc of People in China

The food sources of iron and zinc are presented in **Table 3**. The highest proportions of iron (47.7%) and zinc (53.9%) were found in staple foods including rice, wheat and their products. Staple foods provided even more iron (52.1 vs 37.0%) and zinc (58.9 vs 41.4%) for rural residents as compared with their urban counterparts. Animal products provided as expected more iron (19.6 vs 10.5%) and zinc (34.5 vs 18.6%) for urban residents than their rural counterparts because of their higher meat intake. Staple foods were also the major sources of phytate for both rural (82.1%) and urban (77.6%) residents. Vegetables contributed about 17% of iron, 11% of zinc, and only 7% of phytate.

The Costs per Capita and Cost-effectiveness of Different Interventions

Table 4 presents the costs per capita and the cost-effectiveness of four interventions for iron and zinc deficiencies. For intervention for iron deficiency, the costs/capita per year of dietary diversification, supplementation, food fortification, and biofortification were estimated to be I$1148, 11.4, 0.06 and 0.01, respectively. The cost-effectiveness for supplementation, food fortification and dietary diversification were I$179, I$66, and I$103/DALY, respectively, and that for biofortification could not be determined.

For zinc deficiency intervention, the costs/capita per year of dietary diversification, supplementation, food fortification, and biofortification were I$1148, 0.05, 0.01 and 0.01, respectively. The cost-effectiveness for supplementation, food fortification and dietary diversification were I$399, I$153, and I$103/DALY, respectively.

Discussion

The present study indicated that iron and zinc deficiencies affected over 300 million people in China, most of them were women and children living in rural areas. It turned out that staple foods provided about 50% of iron and zinc intake, but, at the same time, they contained most of the phytate, which inhibits the bioavailability of iron and zinc. The costs per capita and the cost-effectiveness varied for different intervention strategies considerably. This information is crucial for developing the public health policy in China.

The strength of the present study is that the latest national representative data was used for the estimation of the magnitude of iron and zinc deficiency and for the identification of vulnerable groups. The second strength is the quality of the dietary assessment method, including an updated food composition table. Moreover, the standard WHO ingredients-approach was used for the estimation of costs and cost-effectiveness of the different interventions. One limitation is that the cost-effectiveness of biofortification could not be estimated because of not enough biofortified foods available at present, and the lack of the effectiveness study of biofortified foods on the micronutrient status of human subjects.

Interventions to end micronutrient malnutrition are known to be the most cost-effective investments in the health sector (34, 35). Actions to solve this problem comprehensively and sustainable would cost less than 0.3% of the Gross Domestic Product (GDP). In contrast, failure to take actions would result in a loss of 2-3% of the GDP (36). The economic and social payoffs from intervention programs can reach as high as 84 times the program costs.

Supplementation, food fortification and dietary diversification have been the three widely applied interventions for micronutrient deficiencies for the past decades. Supplementation of vitamin A, iron and zinc has been proven to be effective in developing countries for rapid improvement of the mineral status in deficient individuals

(17, 37-40). However, its sustainability is questionable because of various economic, social and political difficulties that diminish their effectiveness at reaching all of the people at risk (41). Considering the high prevalence of iron and zinc deficiencies among important subpopulations in China and recommendations (42, 43), supplementation program(s) targeting the population “at risk” can be considered as a short-term intervention.

Fortification has been successfully applied to improve the nutritional quality of the food supply in industrialized countries for many decades (44-47), but has only recently been adopted in developing countries (48, 49). It has the advantage of wide coverage, easy to implement, and cost-effective (50). The constraint is to reach the most needed subset of the population who seldom consume processed cereals. In China, more than 60% of populations live in rural areas and almost all households have their staples processed at the local, small mill instead of getting processed cereals from the market. It is a challenge to reach those people and the subpopulations living in remote and mountainous areas. No national program is needed in China at present because a program of wheat flour and soy sauce fortification has been implemented since 2003 (51).

Lack of dietary diversity is a particular problem among the rural population in China because their diets are predominantly based on staples and often including low amounts of animal foods (52). The permanent solution is to persuade people to change their diets. Once the program is successful, it will sustain and not require regular re-supply of supplementation/fortification. However, very often it is difficult to change dietary practices, micronutrient-rich foods are often expensive, and the poor cannot afford those (53). Although the costs are high, from a sustainability perspective, it would be useful to develop a national health education program and combine it with existing programs such as the Poverty Reduction and Health Education for Peasants so that the resources will be used in the best way.

In recent years, more and more scientists, in the field of both agriculture and nutrition, believed that biofortification is a promising, cost-effective, and sustainable intervention for alleviating micronutrient deficiency, especially for developing countries. Genetic variation in concentrations of minerals and phytate exists among cultivars, which makes the selection of nutritionally appropriate breeding materials possible (16). Zinc-dense wheat varieties have been developed and are already being grown on a commercial basis in Australia (Adelaide, Victoria, Australia; 16).

Biofortification has the potential to have a major impact on the micronutrient intake of people in China, who derive about 50% of their iron and zinc from two staples: rice, wheat and their products. By increasing the mineral content and decreasing the phytate content simultaneously of staple foods through biofortification, it will directly have a profound influence on the nutritional status of the entire population. Biofortification of vegetables can also be considered as an option, especially with adequate energy in the food, because vegetables are rich in ascorbic acid enhancing iron absorption and play an important role in the daily diets. Biofortification provides a feasible means of reaching populations in remote and rural areas, delivering naturally-fortified foods to people with limited access to supplementation/commercially-marketed fortified foods (54), in this way, there is no need to change the dietary practice. Biofortification is cost-effective (55, 56), although detailed cost-effectiveness estimates are not available. The annually recurrent costs are low after the one-time investment to develop varieties, and germplasm with increased minerals and decreased phytate content can be shared internationally. Moreover, as the trace mineral requirements between human and plant nutrition are similar, biofortification could improve human nutrition as well as plant yield in a way that is environmentally beneficial (37, 39). However, there are still a lot of questions left to be answered, like the regulation and policy, the safety, the bioavailability, the cost-effectiveness, and the acceptance of the consumer before it can be widely applied. A link between the agriculture and nutrition sector needs to be established to solve the problem of micronutrient deficiency. The agricultural sector must adopt a specific goal of improving human nutrition and health, while the nutrition and health sectors must adopt agricultural interventions as a primary tool to fight malnutrition (57).

It is acknowledged that no single intervention by itself can solve the micronutrient deficiency problem. The success of biofortification does not mean there is no need for other strategies in the future. Supplementation, fortification and dietary diversification will continue to be used for not only ending nutritional deficiencies but also preventing diet-related diseases (58).

In **conclusion**, iron and zinc deficiencies affect a large number of populations in China, especially women and children in rural areas. Supplementation and fortification can be used as short-term intervention for micronutrient deficiencies, while dietary diversification and biofortification will be the long-term interventions. Biofortification is a feasible, cost-effective and sustainable solution for the rural population in China.

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Table 1. Prevalence of Anaemia and Estimated Affected Populations in China

	Prevalence (%)	Estimated affected populations (million)	
		Anaemia	Iron deficiency anaemia*
Anaemia (0-101 yrs)			
All	20.1	245.4	208.6
Urban	18.2	61.8	52.5
Rural	20.8	183.6	156.1
Children (< 2 yrs)			
All	31.1	12.7	10.8
Urban	29.3	2.9	2.5
Rural	31.6	9.8	8.3
Adults (> 60 yrs)			
All	29.1	37.2	31.6
Urban	22.5	7.8	6.6
Rural	31.5	29.4	24.5
Women (15-50 yrs)			
All	19.9	68.3	58.1
Urban	18.8	19.4	16.5
Rural	20.4	48.9	41.6
Pregnant women			
All	28.9	3.1	2.6
Urban	25.3	1.2	1.0
Rural	30.4	1.9	1.6
Lactating women			
All	29.5	6.2	5.3
Urban	27.3	2.4	2.0
Rural	30.4	3.8	3.3

* Anaemia due to iron deficiency is estimate at 85%

Table 2. Prevalence of Zinc Intake Inadequacy and Stunting, and Estimated Affected Populations in China

	Prevalence (%)	Estimated affected populations (million)
Zinc intake inadequacy (2-101 yrs)		
All	7.1	86.0
Urban	4.6	15.3
Rural	8.2	70.7
Children, 2-3 yr		
Urban	7.4	0.5
Rural	24.0	5.0
Children, 4-6 yr		
Urban	12.0	1.3
Rural	16.0	6.1
Children, 7-10 yr		
Urban	8.4	1.4
Rural	14.0	8.6
Children, 11-18 yr		
Urban	8.4	3.9
Rural	17.6	23.6
Stunting (children < 5 yrs)		
All	14.3	9.8
Urban	4.9	0.8
Rural	17.3	9.0

Table 3. Food Source of Iron, Zinc and Phytate of People in China (%)

Food type	All	Urban	Rural
Iron			
Rice and products	22.1	16.8	24.3
Wheat and products	25.6	20.2	27.8
Vegetables	16.9	16.1	17.2
Animal foods	13.1	19.6	10.5
Others	22.3	27.3	20.2
Zinc			
Rice and products	33.8	25.5	37.2
Wheat and products	20.1	15.9	21.7
Animal foods	23.3	34.5	18.6
Vegetables	10.9	9.8	11.3
Others	10.9	14.3	11.2
Phytate			
Rice and products	52.3	50.9	52.7
Wheat and products	28.9	26.7	29.4
Vegetables	7.4	7.6	7.3
Others	11.4	14.7	10.6

Table 4. The Cost per Capita and Cost-effectiveness of Interventions

	I$ cost per capita	Average I$ cost per DALY averted
Iron deficiency		
Supplementation	11.4	179
Food fortification	0.06	66
Dietary	1148	103
Diversification		
Biofortification	0.01	n.a.
Zinc deficiency		
Supplementation	0.05	399
Zinc Fortification	0.01	153
Dietary	1148	103
Diversification		
Biofortification	0.01	n.a.

n.a. not applicable

Chapter 6

General Discussion

The studies in this thesis focused on the phytate content of foods, the phytate intake, the inhibitory effect of phytate on the bioavailability of iron and zinc, the magnitude of iron and zinc deficiencies, and the cost-effective and sustainable intervention for iron and zinc deficiencies in China. The results from these studies are summarized in this chapter. The main findings as well as the internal validity and external validity are discussed. The conclusion, public health implications and recommendation for future research are also described.

Main Findings

The main findings of this thesis are summarized in **Table 1** of **Chapter 6** and described briefly below.

Phytate Content in Commonly Consumed Foods in China

The content of phytate, iron, zinc and calcium of 60 food samples commonly consumed in China and the phytate/mineral molar ratios, described in **Chapter 2,** showed a wide range of phytate content (0-1878 mg/100 g) in different foods. Many foods were relatively rich in zinc, iron, and calcium and contained higher levels of phytate as well. Of the 60 food samples, 53 foods had phytate/iron molar ratio >1, a total of 31 foods had phytate/zinc molar ratio >15, a total of 34 foods had phytate/calcium molar ratio >0.24, and only 7 foods had phytate×calcium/zinc >200. Phytate in commonly consumed foods in China impair the bioavailability of iron and zinc.

Phytate Intake and its Inhibitory Effect on the Bioavailability of Iron and Zinc

The phytate intake and molar ratios of phytate to iron, zinc and calcium in the diets of people in China, described in **Chapter 3**, indicated a wide variation in phytate intake (648-1433 mg/day) among residents from different areas in China. Urban residents consumed much less phytate than their rural counterparts (781 vs 1342 mg/day). The proportion of subjects with ratios above the critical values of phytate/iron, phytate/calcium, phytate/zinc and phytate×calcium/zinc were 95.4%, 43.7%, 23.1% and 8.7%, respectively. All the phytate/mineral ratios of rural residents were higher than that of their urban counterparts. Phytate showed an inhibitory effect on the bioavailability of iron and zinc in the diets of people in China.

The Zinc Intake Inadequacy of People in China

The assessment of the zinc intake inadequacy of people in China, described in **Chapter 4,** indicated that the proportions of zinc intake inadequacy were between 2.8%

and 29.4%. Rural residents had higher proportions of zinc intake inadequacy than their urban counterparts. Significantly higher proportion of zinc inadequacy were found in the category of phytate/zinc molar ratio >15 for both rural and urban residents. About 20% of rural children are "at risk" of inadequate zinc intake with phytate as a potent inhibitor. Lactating women are also considered a vulnerable group for zinc intake inadequacy.

The magnitude of iron and zinc deficiencies in China, and the cost-effectiveness of interventions, were estimated in **Chapter 5**, showing that the prevalence of anaemia was 20.1%. Approximately, 30% of children <2 years, adults >60 years, and pregnant and lactating women, and 20% of women of reproductive age were anemic. Anaemia was more prevalent in rural areas than in urban areas. For iron and zinc deficiency intervention, the lowest cost per capita was biofortification with international dollars (I$) =0.01. The cost-effectiveness of supplementation, food fortification and dietary diversification for iron deficiency alone was I$179, I$66, and I$103/DALY, respectively, and for biofortification not known. For zinc deficiency, the corresponding figures were I$399, I$153, and I$103/DALY, respectively.

In conclusion, anaemia is epidemic in both rural and urban areas of China, and affects a large number of the population. Zinc deficiency is more prevalent among children in rural areas. Phytate plays an important role in iron and zinc deficiencies in China. Supplementation and fortification can be used as the short-term strategies for those "at high risk" of iron and/or zinc deficiencies, while dietary diversification and biofortification are the long-term intervention strategies. Biofortification with improved varieties is feasible and cost-effective for the rural population.

Table 1. Summary of Main Findings

Research question	Main findings
What is the phytate content in foods commonly consumed in China and its inhibitory effect on the bioavailability of zinc, iron, and calcium? (**Chapter 2**)	Phytate content in foods Rice and rice products: 55-183 mg/100 g Wheat and wheat products: 3-420 mg/100 g Corn and corn products: 18-310 mg/100 g Soybean products: 130-1878 mg/100 g Other grains: 223-1419 mg/100 g **Wide variations in phytate content of different foods** Phytate/mineral molar ratios (of 60 food samples) Phytate/iron > 1: 53 foods Phytate/zinc < 15: 31 foods Phytate/calcium > 0.24: 34 foods Phytate×calcium/zinc > 200: 7 foods **Phytate has inhibitory effect on iron and zinc in foods**
What is the phytate intake of people in different geographical areas of China? (**Chapter 3**) What is the inhibitory effect of phytate on the bioavailability of zinc, iron and calcium in the diets of people in different areas of China? (**Chapter 3**)	Phytate intake (median, per day per reference man) Large cities: 648 mg Medium and small cities: 833 mg Rural 1: 1271 mg; Rural 2: 1361 mg Rural 3: 1433 mg; Rural 4: 1309 mg **Rural areas consumed more phytate than urban areas** Phytate/mineral molar ratio in the diets Phytate/iron > 1 urban: 87.7%; rural: 98.4% Phytate/zinc > 15 urban: 8.0%; rural: 28.9% Phytate/calcium > 0.24 urban: 20.5%; 52.6% Phytate×calcium/zinc >200 urban:5.4%; rural: 10.0% **The inhibitory effect of phytate on iron and zinc in rural areas was greater than in urban areas**
What is the magnitude of iron and zinc deficiency in China? (**Chapter 4-5**)	Anaemia All: 20.1%; urban: 18.2%; rural: 20.8% Children <2 years: 31.1%; urban 29.3%; rural: 31.6% Pregnant women: 28.9%; urban:25.3%; rural: 30.4% Lactating women: 29.5%; urban: 27.3%; rural: 30.4% Women of reproductive age: 19.9%; urban: 18.8%; rural: 20.4% Zinc intake inadequacy children 2-3 years: male: urban: 6.3%; rural: 25.8% female: urban: 8.8%; rural: 21.7% children 4-8 years: male: urban: 11.9%; rural: 14.7% female: urban: 8.6%; rural: 15.1%

<table>
<tr><td></td><td>children 9-13 years: male: urban: 8.9%; rural: 16.8%
female: urban: 8.3%; rural: 15.6%
children 14-18 years: male: urban: 10.2%; rural: 17.2%
female: urban: 5.9%; rural: 18.8%
children 19+ years: male: urban: 4.8%; rural: 6.6%
female: urban: 2.8%; rural: 3.6%

Stunting
Children< 5 years: all 14.3%; urban: 4.9%; rural: 17.3%</td></tr>
<tr><td>What is the feasible, cost-effective and sustainable intervention for iron and zinc deficiencies in China?
(Chapter 5)</td><td>Children and women are vulnerable subpopulations for iron and zinc deficiencies, zinc intake inadequacy was more prevalent among rural children

The estimated affected populations (million)
Anaemia: all: 245.4; urban: 61.8; rural: 183.6
Iron deficiency: all: 208.6; urban: 52.5; rural: 156.1
Zinc intake inadequacy:
All: 86.0; urban: 15.3; rural: 70.7
Stunting: children < 5 yrs: 9.8; urban: 0.8; rural 9.0
Large number of population affected by iron and zinc deficiencies

Cost and cost-effectiveness of interventions
Iron deficiency I$/capita I$/DALY
Supplementation 11.4 179
Food fortification 0.06 66
Dietary diversification 1148 103
Biofortification 0.01 n.a.

Zinc deficiency I$/capita I$/DALY
Supplementation 0.05 399
Food fortification 0.01 153
Dietary diversification 1148 103
Biofortification 0.01 n.a.
Fortification is cost-effective intervention for iron and zinc deficiencies</td></tr>
</table>

n.a. not applicable

Internal Validity

Study Population

The data used in **Chapter 3-5** were from the 2002 China National Nutrition and Health Survey (CNNHS), which is a national representative survey. In order to be national representative, the multiple stage (four stages) stratified random sampling with equal-sample-size method was used. The study sites covered six types of social and economic areas. For each stage of the four stage sampling, random selection was used. In order to ensure the sufficient number of pregnant and lactating women, and children <12 years, addition samples were randomly selected.

The demographic indexes (gender ratio, family size, and proportion of minority) of the sampling of the 2002 CNNHS were compared with that of the 2000 China National Population Census (1), and no significant differences were found. The test of goodness of fit was used to compare the age distributions of the two surveys, and no significant differences were found (2).

We concluded that the sampling of the study population was representative for six types of areas of China and at national level as well.

Food Intake Assessment

A valid and reliable dietary assessment method is crucial in evaluating the dietary intake in a population-based study. It is inevitable that variation exists in dietary assessment. Variation may come from two sources, one is within subject (intrasubject) variation, and another is between subjects (intersubject). Intrasubject variation is the day-to-day difference in nutrient intake within individual, while intersubject variation is the difference between intakes of individuals over time. These sources of variation contribute to errors in the estimations of usual nutrient intakes. Gibson (3) indicated that, unlike with measurement errors, no attempt should be made to minimize inter- and intrasubject variations because they characterize the true usual intake. The two sources of variability in dietary assessment should be separated and estimated statistically by using analysis of variance. In order to achieve this, the food intake of each individual should be measured for more than one day.

In the present study, the households participated in the dietary assessment were randomly selected. All family members in the selected households participated in the dietary assessment. The information on food intakes of the subjects were collected by using the 24h recall method for three consecutive days (two weekdays and one weekend day). The amounts of cooking oil and condiments consumed during the three survey days were obtained from a food weighing method. In a sub-sample of 23 198 subjects, the information on dietary intake was collected by using food weighing, in addition to 3-day 24h recall at the same time period. The interviewers were trained for both interviewing and weighing foods. The same interviewer performed the dietary recall and food weighing during the three survey days. The analysis showed that the correlation coefficients of food intakes between food weighing and 24h recall method were 0.58-0.88 (4).

The intakes of energy and nutrients were calculated using the data of dietary intakes and the 2000 China Food Composition Table (5). The China Food Composition Table has been developed since 1960s and has been kept updated using reliable and valid determination methods of energy and nutrients analysis. The means of energy and nutrient intakes of three days were calculated to reduce the effect of day-to-day variation.

In conclusion, the dietary assessment in the present study is reliable and valid.

Phytate Determination

Phytic acid (IP6) is hydrolyzed to lower inositol phosphates, inositol pentaphosphate (IP5), inositol tetraphosphate (IP4), inositol triphosphate (IP3), and the inositol diphosphate (IP2) and monophosphate (IP1) during storage, fermentation, germination, food processing and digestion in the human gut (6). Only IP6 and IP5 have a negative effect on a bioavailability of minerals (7).

Many methods of phytate determination have been developed (6, 8-17). Among these techniques, anion exchange column chromatography and HPLC were shown to be best suited for separation of inositol phosphates.

The anion-exchange method used in our study is an adopted AOAC method (12). The disadvantage of Anion-exchange method is the lack of specificity in distinguishing between IP6 and its hydrolysis products. IP3, IP4 and IP5 were included in this method. ***Therefore, the IP6 content in foods in the present study were overestimated to some extent.***

Anthropometric Measurements

Accurate measurement of anthropometric indexes is extremely important for the assessment of the physical growth and development. The scale and measuring tape for weight and height produced by the same factory were provided to each study site. The equipments were recalibrated daily. The measurements were taken twice by trained investigators following the standard procedure (18) and the average of the two measurements was computed (19).

The quality control results indicated that the duplicate measurements in subgroups showed a high reproducibility (correlation coefficients of duplicate measurements was 0.99 for height and 0.98 for weight) (20). ***We conclude that the quality of anthropometric measurements in the present study is adequate.***

Hemoglobin Measurement

The 10 μl capillary made in USA was supplied to each study site. The hemoglobin was determined using the cyanmethemoglobin method (National Committee for Clinical Laboratory Standards, 1994). Duplicate measurements were taken for every sample. Reference sample for quality control was determined for each batch of the sample analysis. ***The results of the determination of blind reference samples showed that all labs for hemoglobin determination were qualified.***

Data Analysis

Specific software for data entry was developed for the 2002 CNNHS by SPSS Inc. by using Surveycraft software (20).

Workshops were held to train the participants from each study province who were responsible for data entry. Data cleaning was taken following a procedure developed by statistical experts. The missing values or doubtful values were sent back to the province and checked with the data of the original questionnaires.

A technical expert group was organized for the data analysis. The analysis procedures were double checked by the expert.

The WHO definition of anaemia was used to calculate the prevalence of anaemia. The hemoglobin values were adjusted according to the altitude of the study sites (21). Prevalence of anaemia was adjusted using the data of 2000 China National Population Census (1) in order to eliminate the difference in proportion between the sampling and the whole population.

Confounding

The confounders in the study were considered at the design of the study, the data collection and analysis. We minimized the effect of confounders by using random sample selection. In order to eliminate the differences due to energy requirement in different age, sex categories, physical activity level and physiological condition, the reference man is used to adjust the dietary intakes of each individual (22). Considering the sampling method of equal-sample-size of the six areas and the proportion difference between the sampling and whole population, the data of the 2002 China National Population Census (1) were used for the adjustment of areas in data analysis.

External Validity

Generalizibility

The major strength of this study is the analyses were based on a large-scale national representative data. The international criteria/methods were applied for the definition of anaemia (21), stunting (18), zinc adequacy assessment (23), and the determination of phytate (12). The use of the WHO method for the cost-effectiveness of interventions made it possible to make the cross country or region comparison (24).

From this study, the magnitude of iron and zinc deficiencies are identified, the information on the cost-effectiveness of interventions is provided, which may help policy makers in China and other countries in Western Pacific Regions to develop interventions for micronutrient deficiency in their own situation.

Phytate Content of Foods

Variation was found in phytate content of different rice varieties. The published data of phytate content of rice ranged from 6 (25) to 220 mg/100 g (26-28). We found in our study that phytate content of rice was between 55 and 183 mg/100 g (29).

Variation in phytate content was found among foods made from wheat flour in our study, which ranged from 3 to 420 mg/100 g. The phytate content of wheat products reported in other studies also shows a wide variation depending on flour extraction rate, flour types, and cooking method. The reported values for wheat flour and products were between 154 and 1750 mg/100 g (30-36).

In the present study, we found that the whole wheat bread had a higher phytate value than white bread no matter whether it is baked or steamed, while the leavened pancake had only 50% of the phytate content as that of leavened pancake (7 vs 14 mg/100 g). This showed the effect of the processing and cooking on phytate hydrolysis. Studies indicated that phytate contents can be reduced by 20-90% using fermentation, germination, soaking, and baking, etc. (30, 37-39).

The reported phytate content of corn flour was 1078 mg/100 g (30, 32), which is much higher than what we found (18 and 310 mg/100 g).

Soy products had the highest content of phytate as compared with other foods. The ranges of phytate contents were between 130 and 1878 mg/100 g, which were within the scope (1460-2900 mg/100 g) reported by others (40-42).

Phytate Intake

Variation in phytate intake was found in studies in both developed and developing countries. The phytate intake in developed countries varied between 200 and 800 mg/day. Swedish (43) and Italian (44) people consumed low levels of phytate (180; 219 mg/day). The average phytate intake in Finland was estimated to be 370 mg/day (45), while the daily phytate intake in the United Kingdom (46) and United States (47) was between 600-800 mg.

People in developing countries consumed much more phytate than those in developed countries. Kwun and Kwon reported that the phytate intake of South Koreans was 1676.6 mg/day (48), while Indian people consumed as much as 1560-2500 mg phytate per day (49). Middle Eastern inhabitants also have very high amounts of phytate in their diets (47). Nigerians consumed as much as 2000-2200 mg/day (50).

The average phytate intake (1186 mg/day) of people in China is higher than those in developed countries, and lower than those in Africa and Asia. A wide variation in phytate intake was found between urban residents and rural residents of China (781 vs 1342 mg/day). The phytate intake of urban residents in China was similar to that in some western countries (43-47), while rural residents consumed comparable phytate with Korean (48), Indian (49) and Nigerian people (50).

Iron and Zinc Deficiency

It has been estimated that more than two billion of the world population, nearly all in developing countries, are iron deficient (51). Women and children are particularly at risk of iron deficiency.

In Asia, high prevalence of anaemia among pregnant women was reported, 87% in India (52), 73% in Nepal (53), 65% in Sri Lanka (54), and 40-50% in Bangladesh (55, 56). The prevalence of anaemia among pregnant women (25.3-30.4%) in our study was about half of those mentioned-above, however, it was higher than the 18% in developed countries (51). Iron deficiency has often been claimed to be the predominant cause of anaemia. 55% of anaemia among pregnant women in Bangladesh was due to iron deficiency, while 6-30% of pregnant women in European countries had iron deficiency anaemia (57, 58).

Children are another vulnerable group. The prevalence of anaemia among children in developing countries ranged from 9.5 to 62.6% (59-65), while in industrialized countries that ranged from 2 to 8% (66-70). The anaemia prevalence of children <2 years was 31.1%, rural children showed higher prevalence than their urban counterparts.

Indicators of zinc deficiency in populations include: stunting among preschool children, inadequate zinc intake at national level based on the national food supplies or dietary assessment data (71). Data on the prevalence of stunting are collected routinely in many countries and are compiled in the WHO Global Data Base on Child Growth and Malnutrition (72). The stunting prevalence of the present study was comparable to that for China (14.3 vs 15.6%) from the WHO database. Discrepancies in the intakes of zinc (10.1 vs 12.4 mg/d), zinc density (4.3 vs 4.8 mg/1000 kcal), and phytate intake (1186 vs 2056 mg/d) were found between our study and the WHO database, which may be caused by the resources of information on dietary intake and phytate. ***As dietary intake from the national representative data in 2002, and the phytate content of foods were measured in China (73, 74), therefore, our results are more reliable.***

Cost-effectiveness of Interventions

The information on the cost-effectiveness of interventions was obtained from the results of WHO CHOICE (24). The advantage is that CHOICE is the standard method developed by WHO for the assessment of costs, and cost-effectiveness of different interventions. These methods mean that the results of intervention analysis can be compared more meaningfully across interventions and across locations. CHOICE provides results in such a way that analysts from countries within a region can adapt them to their own setting if they wish.

One limitation is that the cost-effectiveness of biofortification was not provided because there are not enough biofortified foods available at present, and the lack of the effectiveness study of biofortified foods on the micronutrient status of human subjects.

Suggestions for Future Research

Phytate and Micronutrient Deficiency

There have been studies on the phytate content of food and the effect of food processing and cooking method on the phytate hydrolyzation. However, this kind of information is lacking in China. As the phytate and mineral content of foods are influenced by the soil and other conditions, and the cooking methods in China differ a lot from other countries, the phytate content of different food varieties need to be determined by using HPLC method. In addition, the effect of different cooking methods on the hydrolyzation of phytate needs to be investigated as well.

The Causes of Anaemia in China

Iron deficiency has often been claimed to be the predominant cause of anaemia (75, 76). However, it is not well known how common iron deficiency is and to what extent it is associated with anaemia. It is reported that the ranges of anaemia due to iron deficiency were between 30% (56, 64) and 87% (59, 72). This kind of information is lacking at the national level in China. Therefore, a cross-sectional study with a national representative sample of women of childbearing age, children and adolescents should be designed to clarify the major cause of anaemia in China. Information on the indicators of iron status (serum ferritin, transferrin saturation), and parasitic infection, etc should be included. ***The results from the study will be used to further improve the intervention programs in China.***

Efficacy, Feasibility, Acceptability, and Cost-effectiveness of Biofortification.

Information on the efficacy, cost-effectiveness, feasibility and acceptability of biofortification is lacking. The information is crucial for facilitating policy makers to select the most feasible, cost-effective and sustainable intervention with limited resources. Firstly, research is needed to find out the acceptance of consumers, including the appearance, taste and texture, etc.. Secondly, intervention trial(s) should investigate the efficacy of biofortified food(s) on the micronutrient status of populations at-risk. Finally, the cost-effectiveness of biofortification needs to be estimated based on the intervention trials.

Conclusion

The findings from this thesis revealed that deficiency of iron and zinc is of significance for public health in China. Children, women and older people in both urban and rural areas are the vulnerable groups for iron deficiency, while children in rural areas are at high risk of zinc deficiency. Low intake and poor bioavailability of iron and zinc in plant-based-diets are the main causes of the deficiencies and phytate plays a major role in the deficiency of iron and zinc in China.

Of the two short-term strategies, supplementation is the preferred choice for the above mentioned vulnerable groups, while food fortification can be applied to reach the population at large with high cost-effectiveness.

Of the two long-term strategies, dietary diversification through health education is a more permanent approach, while biofortification is especially feasible and cost-effective for the rural population.

Implications for Public Health

Micronutrient deficiency affects human health and development. Even mild levels of micronutrient deficiency may damage cognitive development, lower disease resistance and increase the risk for the offspring. The costs of these deficiencies in terms of lives lost and poor quality of life are tremendous. Moreover, micronutrient deficiency will hinder the social and economic development. Investments to prevent micronutrient deficiency will be returned in two ways, i.e. the improvement of people's health as well as economic development through the prevention of illness and the improvement of productivity.

In our present studies, we observed that millions in the population of China suffer from micronutrient deficiencies, especially children, pregnant and lactating women and women of reproductive age. ***Therefore, both short-term and long-term intervention strategies should be developed in order to improve the health of people in China as well as the social economic development. Supplementation and food fortification can be applied as the short-term intervention for people "at risk", while dietary diversification through health education and biofortification can be used as the long-term strategy.***

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Summary

Deficiencies of micronutrients affect a high proportion of the world's population, particularly in the developing countries. The physical and mental development of humans as well as their economic development is impaired.

It is believed that insufficient intake and poor bioavailability of minerals are the major causes of micronutrient deficiencies, and that phytate is a potent inhibitor. However, information on the phytate content in foods, and in the diets and the inhibitory effect of phytate on the bioavailability of iron and zinc is lacking in China. Therefore, in order to identify feasible, cost-effective and sustainable intervention strategies, the following research questions are addressed in this thesis:

1. *What is the **phytate content in foods** commonly consumed in China and its inhibitory effect on the bioavailability of iron, zinc and calcium?*
2. *What is the **phytate intake in the diets** and its inhibitory effect on the bioavailability of zinc, iron and calcium of people in different geographical areas of China?*
3. *What is the **magnitude** of iron and zinc deficiency in China?*
4. *What is the feasible, cost-effective and sustainable **intervention** for iron and zinc deficiencies in China?*

In order to answer these research questions, the content of phytate, zinc, iron, and calcium of 60 foods commonly consumed in China was determined, and the phytate/mineral molar ratios were calculated (**Chapter 2**). A wide range of phytate content (0-1878 mg/100 g) in different foods was found. Many foods were relatively rich in iron, zinc, and calcium, and contained higher levels of phytate as well. Of the 60 food samples, 53 foods had phytate/iron molar ratio >1, a total of 31 foods had phytate/zinc molar ratio >15, a total of 34 foods had phytate/calcium molar ratio >0.24, and only 7 foods had phytate×calcium/zinc >200. Phytate in foods commonly consumed in China impairs the bioavailability of iron and zinc.

Based on the data of phytate content in foods in **Chapter 2**, the dietary assessment data of 68,962 subjects from the 2002 China National Nutrition and Health Survey were used for calculating the phytate intake and phytate to mineral molar ratios in the diets of people in China (**Chapter 3**). We found a wide variation in phytate intake (648-1433 mg/day) among residents from different areas in China. Urban residents consumed much less phytate than their rural counterparts (781 vs 1342 mg/day). The proportion of subjects with ratios above the critical values of phytate/iron, phytate/zinc, phytate/calcium, and phytate×calcium/zinc were 95.4, 23.1, 43.7, and 8.7%, respectively. All the phytate/mineral molar ratios of rural residents were higher than that of their urban counterparts. Phytate showed an inhibitory effect on the bioavailability of iron and zinc in the diets.

The diets of 68,962 subjects from the 2002 China National Nutrition and Health Survey were analyzed (**Chapter 4**) to assess the zinc intakes inadequacy taking the inhibitory effect of phytate into account. Zinc intake inadequacy was calculated based on the WHO suggested values. The median daily zinc intakes ranged from 4.9 to 11.9 mg. The zinc density of urban residents was significantly higher than that of their rural counterparts (5.0-5.2 vs 4.7-4.8 mg/day/1000 kcal). The proportions of zinc intake inadequacy were between 2.8% and 29.4%. Rural residents had higher proportions of zinc intake inadequacy than their urban counterparts. Significantly higher proportions of zinc inadequacy were found in the category of phytate/zinc molar ratio >15 for both rural and urban residents. In conclusion, about 20% of rural children are “at risk” of inadequate zinc intakes with phytate as a potential important inhibitor.

In order to prioritize the interventions for micronutrient deficiencies in China, the magnitude of iron and zinc deficiencies were estimated based on the data of the 2002 China National Nutrition and Health Survey. The costs and cost-effectiveness of supplementation, food diversification, and food fortification were estimated using the standard WHO ingredients-approach (**Chapter 5**). We found children and women, especially those in rural areas, are vulnerable populations. Approximately, 245 million were affected by anaemia, while 100 million individuals by zinc deficiency (zinc intake inadequacy and stunting). For iron and zinc deficiency intervention, the lowest costs per capita was biofortification with I$0.01. The cost-effectiveness of supplementation, food fortification and dietary diversification for iron deficiency were I$179, I$66, and I$103/DALY, respectively. For zinc deficiency, the cost-effectiveness of supplementation, food fortification and dietary diversification were I$399, I$153, and I$103/DALY, respectively. We concluded that iron and zinc deficiencies are of public health significance in China. Biofortification is a feasible, cost-effective and sustainable solution for the rural population. This means that breeding of wheat and rice varieties with sufficient amounts of micronutrients which are highly bioavailable is needed.

The main findings from the present study are summarized and discussed in the general discussion (**Chapter 6**). Subsequently, the internal validity including the sampling method, food intake assessment, phytate determination, anthropometric measurements, and data analysis was discussed. The findings from our study including the phytate content of foods, phytate intake of populations, iron and zinc deficiencies, and the cost-effectiveness of interventions were compared with other studies. Moreover, suggestions for future research are made. Finally, implications for public health are proposed, including the necessity of developing feasible, cost-effective and sustainable intervention strategies for micronutrient deficiencies.

In **conclusion**, iron and zinc deficiencies are epidemic in China, and affect a large number of people. Phytate plays an important role in deficiencies of iron and zinc. Supplementation and fortification can be used as short-term intervention for micronutrient deficiencies, while dietary diversification and biofortification will be the long-term interventions. Biofortification is a feasible, cost-effective and sustainable solution, especially for the rural population in China.

Samenvatting

Tekorten aan micronutriënten komen voor in grote delen van de wereld, vooral in ontwikkelingslanden. Daardoor verslechtert de lichamelijke en geestelijke ontwikkeling van mensen, maar ook de economische ontwikkeling van landen.

Doorgaans wordt aangenomen dat onvoldoende inneming en slechte biobeschikbaarheid van mineralen een belangrijke oorzaak is van deze micronutriënt deficiënties, mogelijk doordat fytaat de opname afremt. Gegevens over fytaatgehaltes in voedingsmiddelen en de voeding en de remmende werking van fytaat op de biobeschikbaarheid van ijzer en zink zijn niet beschikbaar in China. Daarom is gezocht naar haalbare, kosten-effectieve en duurzame interventie strategieën om de volgende onderzoeksvragen te kunnen behandelen in dit proefschrift.

1. *Wat is het* ***fytaatgehalte in veelgebruikte voedingsmiddelen*** *in China en wat zijn de remmende effecten op de biobeschikbaarheid van ijzer, zink en calcium?*
2. *Wat is de* ***inneming van fytaat uit de voeding*** *en wat zijn de remmende effecten van fytaat op de biobeschikbaarheid van ijzer, zink en calcium van de bevolking in verschillende geografische regio's in China?*
3. *Wat is de* ***omvang*** *van ijzer en zink deficiënties in China?*
4. *Wat is een haalbare, kosteneffectieve en duurzame* ***interventie*** *om ijzer- en zinktekorten in China tegen te gaan?*

Om deze onderzoeksvragen te beantwoorden zijn in 60 veelgebruikte voedingsmiddelen de gehaltes van fytaat, zink, ijzer en calcium bepaald. Hieruit zijn vervolgens fytaat/mineraal molaire verhoudingen berekend (**hoofdstuk 2**). Het fytaatgehalte in de diverse voedingsmiddelen had een brede range (0-1878 mg/100 g). Veel voedingsmiddelen hadden relatief hoge ijzer-, zink- en calciumgehaltes en bevatten tevens hoge fytaatgehaltes. In 53 van de 60 voedingsmiddelen werd een fytaat/ijzer molaire verhouding >1 gevonden, 31 voedingsmiddelen hadden een fytaat/zink verhouding >15, in 34 producten een fytaat/calcium verhouding >0.24 en in slechts zeven producten werd een verhouding fytaat×calcium/zink >200 gevonden. Fytaat in veelgebruikte voedingsmiddelen in China vermindert de biobeschikbaarheid van ijzer en zink.

De gegevens over fytaatgehaltes in producten uit **hoofdstuk 2** zijn gecombineerd met de voedingsgegevens van 68.962 mensen van de *China National Nutrition and Health Survey* uit 2002. De fytaatinneming en de fytaat/mineraal molaire verhoudingen van voeding van de Chinese bevolking werden hieruit berekend (**hoofdstuk 3**). De fytaatinneming vertoonde een grote variatie (648-1433 mg/dag) over de verschilde regio's. Stedelingen consumeerden veel minder fytaat dan bewoners op het platteland (781 vs 1342 mg/dag). De fractie van deelnemers met een ratio boven de kritische waarden voor fytaat/ijzer, fytaat/zink, fytaat/calcium en fytaat×calcium/zink waren respectievelijk, 95.4%, 23.1%, 43.7%, en 8.7%. Voor alle fytaat/mineraal molaire verhoudingen gold dat ze hoger waren bij plattelandsbewoners dan stedelingen. Fytaat had een remmend effect op de biobeschikbaarheid van ijzer en zink in de voeding.

De voedingen van de 68.962 deelnemers aan de *China National Nutrition and Health Survey* uit 2002 werden geanalyseeerd (**hoofdstuk 4**) om de inneming van zink te bepalen, waarbij rekening is gehouden met het remmende effect van fytaat. Om een gebrekkige inneming van zink vast te stellen is gebruik gemaakt van data van de WHO. De dagelijkse zink inneming (mediaan) varieerde van 4.9 tot 11.9 mg. De zinkdichtheid bij stedelingen was significant hoger dan die van de plattelandsbewoners (5.0-5.2 vs 4.7-4.8 mg/dag/1000 kcal). De fracties van gebrekkige zinkinneming lagen tussen de 2.8% en 29.4%. Plattelandsbewoners hadden een groter percentage gebrekkige zinkinneming vergeleken met stedelingen. Significant hogere fracties hiervan werden gevonden in de fytaat/zink molaire verhouding >15 voor zowel stedeling als plattelandsbewoners. Samengevat heeft ongeveer 20% van de plattelandskinderen een risico op gebrekkige zinkinneming waarbij fytaat mogelijk een belangrijke remmer is.

De gegevens over ijzer en zink deficiëntie op basis van de *China National Nutrition and Health Survey* (2002) werden ook gebruikt om te bepalen welke interventies voor micronutriënten deficiënties in China kans van slagen zouden hebben. De kosten en kosteneffectiviteit van suppletie, voedsel diversiteit en voedsel verrijking werden geschat door de standaard WHO ingrediënten-aanpak te gebruiken (**hoofdstuk 5**). Vooral kinderen en vrouwen in plattelandsgebieden waren kwetsbare groepen. Ongeveer 245 miljoen mensen waren getroffen door anemie, terwijl 100 miljoen individuen zinktekort hadden (gebrekkige zinkinneming en 'stunting'). Met betrekking tot ijzer- en zinkinterventies had biofortificatie de laagste kosten per hoofd van de bevolking (International dollars (I$) = 0.01). De kosteneffectiviteit van suppletie, voedselverrijking en voedsel diversiteit voor ijzertekort was respectievelijk I$179, I$66 en I$103/DALY. Voor zinkdeficiëntie was de kosteneffectiviteit van suppletie, voedselverrijking en voedsel diversiteit I$399, I$153 en I$103/DALY. Hieruit werd geconcludeerd dat ijzer- en zinkdeficiënties een grote invloed hebben op de volksgezondheid in China.

Biofortificatie is een haalbare, kosteneffectieve en duurzame oplossing voor toepassing op het platteland. Dit houdt in dat het telen van granen en rijst soorten met voldoende hoeveelheden micronutriënten met hoge biobeschikbaarheid nodig is.

De belangrijkste bevindingen van deze studies zijn samengevat en aan een nadere beschouwing onderworpen in de discussie (**hoofdstuk 6**). Daarin wordt de interne validiteit, inclusief de steekproeftrekking, verzameling van voedingsdata, fytaatbepaling, anthropometrische metingen en data analyse besproken. Daarna worden de bevindingen over fytaatgehaltes in voedingsmiddelen, fytaatinneming in de diverse groepen, ijzer- en zinkdeficiënties en de kosteneffectiviteit van de interventie vergeleken met andere studies. Ook worden aanbevelingen voor nader onderzoek gedaan. Tot slot worden voorstellen voor de implicaties voor de volksgezondheid gedaan, waarbij ook de noodzaak voor het ontwikkelen van haalbare, kosteneffectieve en duurzame interventie strategieën voor micronutriënt deficiënties worden besproken.

Samengevat kan worden gesteld dat ijzer- en zinktekort epidemische vormen aanneemt in China waardoor grote delen van de bevolking worden getroffen. Fytaat speelt een belangrijke rol bij ijzer- en zinkdeficiënties. Suppletie en verrijking kunnen op korte termijn worden ingezet, terwijl voedseldiversiteit en biofortificatie een lange termijn benadering zijn voor het probleem. Biofortificatie is een haalbare, kosten effectieve en duurzame oplossing, vooral voor de rurale gebieden in China.

总结

微量营养素缺乏影响世界上特别是发展中国家人群的健康，它不仅影响人类体格和智力的发展，而且还对社会经济的发展带来负面影响。

膳食摄入不足和膳食中生物利用率低是导致微量营养素缺乏的两个主要原因，植酸是其中的主要抑制因子。但是，在中国，有关食物中植酸的含量、膳食植酸的摄入量以及植酸对铁和锌生物利用率抑制作用方面的研究还基本没有开展，缺乏全国有代表性的数据。为制定切实可行的、成本-效益高的和可持续性的干预措施，本论文针对以下问题开展研究：

1. *中国居民经常消费的食物中植酸的含量及其对铁、锌和钙的抑制作用？*
2. *中国居民膳食植酸的摄入量及其对铁、锌和钙生物利用率的抑制作用？*
3. *中国居民中铁和锌缺乏的现况？*
4. *针对铁和锌缺乏的切实可行的、成本-效益高、可持续的干预措施？*

为了回答这些问题，论文的**第二章中**分析了中国居民经常消费的 60 种食物中植酸的含量并计算了这些食物中植酸和矿物质的摩尔分子比。结果发现，不同食物中植酸含量的差别很大，从 0 到 1878 mg/100g。许多食物中铁、锌和钙的含量较高，但同时植酸的含量也高。所测定的 60 种食物中，有 53 种植酸/铁的分子摩尔比>1，31 种的植酸/锌的分子摩尔比>15，34 种食物的植酸/钙分子摩尔比>0.24，只有 7 种食物的植酸×钙/锌的比值>200。说明一半以上的食物中的植酸抑制铁、锌和钙的生物利用率。

论文的**第三章**中利用 2002 年中国居民营养和健康状况调查中 68,962 人的膳食数据计算中国居民膳食植酸的摄入量及植酸和矿物质的分子摩尔比。结果发现，不同地区居民植酸的摄入量差别很大，为 648-1433 mg/day。城市居民植酸的摄入量（781 mg/day）显著少于农村居民（1342 mg/day）。膳食中植酸/铁、植酸/锌、植酸/钙分子摩尔比和植酸×钙/锌的比值大于推荐值的比例分别为 95.4%，23.1%，43.7%和 8.7%。农村居民膳食中上述比值大于推荐值的比例都高于城市居民。中国居民膳食中植酸对铁和锌的生物利用有抑制作用。

论文的**第四章**利用 2002 年中国居民营养和健康状况调查中 68,962 人的膳食数据并考虑植酸的抑制作用，用世界卫生组织推荐的方法来评价中国人群锌摄入状况。结果发现，中国居民膳食摄入锌的中位数为 4.9 mg/day 到 11.9 mg/day，城市居民锌的能量密度（5.0-5.2 mg/day/1000 kcal）显著高于农村居民（4.7-4.8 mg/day/1000 kcal）。农村居民中锌摄入不足的比例远高于城市居民。不论是在城市、还是在农村居民中膳食植酸/锌分子摩尔比>15 中锌摄入不足的比例都显著高。农村儿童中有 20%的处于锌摄入不足的危险，植酸是主要的抑制因素。

论文的**第五章**中，为制定中国的微量营养素缺乏的干预措施，根据 2002 年中国居民营养与健康状况调查的数据对全国铁和锌缺乏的情况进行估计，并利用世界卫生组织推荐的方法计算补充剂、食物强化和食物多样三种干预措施的人均花费及成本-效益。结果发现，儿童和妇女，特别是农村的是易感人群。全国有约 2450 万的人贫血，1000 万人锌营养不足（包括锌摄入不足和身材矮小）。针对铁和锌缺乏的干预措施中，生物强化的人均花费最低，为 0.01I$/人。铁缺乏的干预措施中，补充剂、食物强化和食物多样化三种干预措施的成本-效益比分别为 I$179, I$66 和 I$103/DALY；锌缺乏的干预措施中，补充剂、食物强化和食物多样化三种干预措施的成本-效益比分别为 I$399, I$153 和 I$103/DALY。从以上结果可以得出，铁和锌缺乏在中国是一个重要的公共卫生问题，生物强化是一个切实可行、成本-效益比高和可持续的针对农村人群的措施。因此，需要利用生物强化培育微量营养素和生物利用率均高的小麦和稻米品种。

论文的第六章对本论文的主要发现进行了总结和讨论。然后，对内部有效性包括抽样方法、膳食调查方法、植酸含量测定方法、体格测量和数据分析进行了讨论。把本文的主要发现，包括食物中植酸含量、人群植酸摄入量、铁和锌缺乏及干预措施的成本-效益比和其他研究者的结果进行比较。在此基础上提出今后研究的方向，并提出了本研究结果的公共卫生意义，即亟需制定针对微量营养素缺乏的切实可行、成本-效益比高和可持续性的干预措施。

综上所述，铁和锌缺乏在中国处于流行状态，影响大量的人群。植酸是铁和锌缺乏的主要抑制因素。补充剂和食物强化可以作为微量营养素干预的短期措施，膳

食多样化和生物强化是根本和长效的措施，特别是对于农村人群的微量营养素缺乏，生物强化是一个切实可行、成本-效益比高和可持续性的措施。

Acknowledgements

I was 39 years old when I started my PhD program in the Division of Human Nutrition at Wageningen University, The Netherlands in 2002. At that time, I was not quite sure how and when I could complete this program. Four years passed, I am very glad that I have finished my thesis and ready for the public defence. I understand that I could not be successful in fulfilling this goal without the help of many people. I would like to take this opportunity to acknowledge all those who have helped, supported me and contributed to this thesis.

I would like to thank Professor **Xiaoguang Yang** for providing the opportunity for me when he was the director of the Institute of Nutrition and Food Hygiene, Chinese Academy of Preventive Medicine. **Professor Yang** is the principal investigator of the 2002 China National Nutrition and Health Survey. Without the completion of the survey, it would not have been possible for me to finish my thesis. My sincere thanks go to all the team members of the 31 provinces and all participants from the 132 study sites for their contribution to this survey.

Professor Fengying Zhai and I met **Professor Evert Schouten** at the workshop on Nutritional and Lifestyle Epidemiology at Wageningen, in June 2001. **Professor Schouten** introduced **Professor Frans J Kok** to us. We discussed the possibility of starting my sandwich PhD program at that time. Special thanks go to **Professor Schouten** for that. I would like also to thank **Professor Schouten** for the close collaboration in organising the workshop on Nutritional and Lifestyle Epidemiology for Chinese students in Beijing and Nanjing, China. My gratitude goes to **Professor Zhai** for her support, encouragement and contribution to my thesis.

My PhD life started in the middle of November 2002 in Wageningen. I worked on the study proposal under the supervision of **Professor Clive West**. I have gained a lot from his advice and keen thinking. I finished the research plan in two months which has set up a good beginning for my whole thesis. **Professor West**'s death is a most regrettable loss in the field of nutrition. It is a pity that he can not see this thesis. Deeply cherish the memory of **Professor Clive West**.

My heartfelt thanks go to my current supervisor, **Professor Frans J Kok**. He has played many roles in the process of my PhD program since I met him in 2001. **Professor Kok** is not only my supervisor, but also a model, a collaborator and a friend. I have learnt

plenty from him on the methodology of research, skills of leadership and communication, and many others. Under his supervision, three of four manuscripts of my thesis have been published or accepted now. It is really a great pleasure to work with him. Thank you indeed, **Frans**, for all your support and encouragement. Thanks also go to **Anneroos** for hosting me every time I visit Wageningen and sharing the different experience and culture with me.

Special thanks go to **Professor Evert Jacobsen**, my supervisor. **Professor Jacobsen** works in the field of agriculture. He and **Professor West** tried to build a bridge between agriculture and human nutrition. The study of my thesis is a pilot for doing so. **Professor Jacobsen** has kept his eyes upon the progress of my thesis both in The Netherlands and in China. When I finalized my thesis in August 2006, he spent his vacation to give his advice and comments, from which I have benefited a lot.

I would like to thank **Dr. Guusje Bonnema**, the coordinator of the INREF program. Your advice and support are crucial for the completion of my PhD program. Thank you very much. I would also like to express my gratitude to those working in the same program, **Dr. Jianjun Zhao** and **Ms. Jian Wu,** for sharing their information and comments with me.

As there is a lack of information on the phytate content of foods in the China Food Composition Table, we had to determine the phytate content of foods ourselves in China. Many thanks go to **Ms. Ying Jin** from our Institute for her great contribution to this hard work, including collection of food samples and the laboratory analyses. And also my gratitude for **Professor Jianhua Piao, Ms. Ning Qu** and **Ms. Ruihua Zhou** from the National Institute for Nutrition and Food Safety, China CDC, **Professor Beizhong Han** and **Ms. Jianfen Liang** from the University of Agriculture, China for their support and assistance.

Many people have been involved in the data collection, cleaning and analyses of the 2002 China National Nutrition and Health Survey. It is impossible to list all their names here. Sincere thanks go to **Ms. Yanping Li**, my former student and current colleague, for her great contribution to this thesis. Thanks also go to **Ms. Songming Du** for her contribution in the data analyses.

Specially, I would like to thank my two paranymphs, **Ms. Huaidong Du** and **Ms. Andrea Werkman**, for assisting me in finalising my thesis and arranging many practical things related to the public defence. I met **Ms. Huaidong Du** at Wageningen when she

was doing her master program. Although she is busy doing her PhD program in the Dutch National Institute for Public Health and the Environment (RIVM) at this moment, she is really helpful in many aspects, including arranging accommodation for me when I visited Wageningen, editing and handing in the reading version of my thesis, and others.. Thank you so much for your great help, your patience and your time. **Ms. Andrea Werkman** and I travelled together to attend the 12th Seminar on the European Nutrition Leadership Program in Luxembourg in March 2006. I learnt a lot from our conversation. Many thanks go to **Andrea** for translating the summary into Dutch.

Sincere thanks go to those who helped me with my PhD program, **Ms. Gea Brussen, Ms. Marie Jansen**, **Ms. Lous Duym, Ms. Lidwien van der Heyden, Ms. Riekie Janssen,** and **Mr. Eric van Munster**.

Thanks go to **Mr. Tong Zhao** for designing the wonderful cover for my thesis.

I would like to express my gratitude to my **Mom** for giving me life, supporting my university study, and many things more. I talk with my Mom over the phone almost every weekend. Although she does not quite understand what her son is doing for the PhD, she knows I am doing the right thing.

Special thanks go to my wife, **Yongfang Wang**, and my son, **Jack Ma** for supporting me any time when I met difficulties. My wife took care of our son and our family while I studied abroad. Without her assistance and contribution, it was impossible for me to go to Wageningen to accomplish the program. Thank you so much, my wife and my son, I love you!

Curriculum Vitae

Guansheng Ma was born on April 8th 1963, in Guan County, Shandong Province, China. He was enrolled by Shandong Medical University in 1981. He studied medicine in the university between 1981 and 1986. He did his master program in public health in Shanghai Medical University during 1986-1989. He sought advanced study on health education and health promotion at the School of Public Health, University of North Carolina at Chapel Hill, U.S.A in 1992-1993. He finished his fellowship training on behavior and health in the Department of Social Medicine, Harvard Medical School, U.S.A. between 1997 and 1998.

He started his research work in the Institute of Nutrition and Food Hygiene, Chinese Academy of Preventive Medicine in 1989. As a research associate in the Department of Community Nutrition in 1989-1994, he was responsible for training, and nutrition education in the UNICEF supported project entitled *Surveillance and Improvement of Children's Nutrition*. He was nominated as the chief and responsible for establishing a new department, the Department of Student Nutrition, in the institute in 1994. He was promoted as professor in 2001. He has been responsible for more than 10 research projects supported by UNICEF, IAEA, WHO, Nutricia Nutrition Foundation, and Danone Nutrition Foundation as principal investigator. He was also the major co-investigator of the 2002 China National Nutrition and Health Survey. He has attended many academic conferences and meetings at the national and international level. He has been also participating in several expert meetings organized by WHO, IAEA, FAO and WFP.

He worked for United Nations Office for Humanitarian Co-ordination in Iraq for three months for evaluating the Oil-for-food program in 1998. He worked as the governor assistant for one year in A-ba Zang and Qiang Autonomous Prefecture, Sichuan, China during 2003-2004. He was responsible for anti-poverty project in this remote and mountainous area.

He is promoted as the Deputy Director of Institute of Nutrition and Food Safety, Chinese Center for Disease Control and Prevention in 2002 after the integration of the two former institutes. He is responsible for the management of research projects, training, and international collaboration in the institute.

He is the Secretary-general of Chinese Association for Student Nutrition Promotion; Committee Member of Codex Committee, Ministry of Health, China; Editorial Board of Chinese Journal of School Health, Food and Nutrition in China, Journal of Hygiene Research, Chinese Journal of Pediatrics.

He has published 23 papers in the international peer-reviewed journals, and 77 papers in Chinese journals. He is also the editor of the Report of the 2002 China National Nutrition and Health Survey: Behavior and Lifestyle.

Research Publications

Publication in peer-reviewed English Journals

1. **Ma G.** (1998). Nutrition knowledge, attitude, food practice and its changes in China. Australian Journal of Nutrition and Dietetics. 55(1):S9-S11.
2. Yao M, Roberts SB, **Ma G**, Pan H, McCrory MA. (2002). Field methods for body composition assessment are valid in healthy Chinese adults. Journal of Nutrition. 132(2):310-317.
3. Yao M, McCrory MA, **Ma G**, Li Y, Dolnikowski GG, Roberts SB. (2002). Energy requirements of urban Chinese adults with manual or sedentary occupations, determined using the doubly labeled water method. European Journal of Clinical Nutrition. 56(7):575-584.
4. **Ma G.** (2002). Environmental factors leading to pediatric obesity in the developing world. Nestle Nutrition Workshop Series Pediatric Program Volume 49. Lippincott Williams & Wilkins, Philadelphia. 49:195-207.
5. Shetty P, Iyengar V, Sawaya A, Diaz E, **Ma G**, et al. (2002). Application of stable isotopic techniques in the prevention of degenerative diseases like obesity and NIDDM in developing societies. Food and Nutrition Bulletin. 23(3Suppl):174-179.
6. **Ma G**, Li Y, Hu X, Ma W. (2002). Effect of television viewing on pediatric obesity. Biomedical and Environmental Sciences. 15:291-297.
7. Yao M, McCrory MA, **Ma G**, Tucker KL, Gao S, Fuss P, Roberts SB. (2003). Relative influence of diet and physical activity on body composition in urban Chinese adults. American Journal of Clinical Nutrition. 77(6):1409-1416.
8. Li Y, **Ma G**, Zhang Q, Du W, Pan H. (2003). Validity of body fat percentage using skinfold measurement in 12-14-Year-old Chinese boys and girls. International Journal of Body Composition Research. 1(2):53-58.
9. Yao M, Lichtenstein AH, Robert SB, **Ma G**, Gao S, Selhub J, Tucker KL, McCrory MA. (2003). Relative influence of diet and physical activity on cardiovascular risk factors in urban Chinese adults. International Journal of Obesity. 27(8):920-932.

10. Li Y, Zhang Q, Du W, Pan H, **Ma G.** (2003). Comparison between air-displacement plethymography and dual energy X-ray absorptiometry in 176 Chinese adolescents. International Journal of Body Composition Research. 1(4):131-136.
11. Gao X, Yao M, McCrory MA, **Ma G**, Li Y, Roberts SB, Tucker KL. (2003). Dietary pattern is associated with homocysteine and B vitamin status in an urban Chinese population. Journal of Nutrition. 133(11):3636-3642.
12. **Ma G**, Li Y, Gao S, Pan H. (2003). Risk factors for obesity in Chinese adults. Report on the third Research Coordinating Meeting of Coordinated Research Project on Application of nuclear techniques in the prevention of degenerative diseases (obesity and non-insulin dependent diabetes) in ageing NAHRES-76. 53-68.
13. **Ma G**, Yao M, Liu Y, Lin A, Zou H, Urlando A, Wong WWL, Nommsen-Rivers L, Dewey KG. (2004). Validation of a new pediatric air-displacement plethysmograph for assessing body composition in infants. American Journal of Clinical Nutrition. 79(4): 653-660.
14. Du X, Zhu K, Trube A, Zhang Q, **Ma G**, Hu X, Fraser DR, Greenfield H. (2004). School-milk intervention trial enhances growth and bone mineral accretion in Chinese girls aged 10-12 Years in Beijing. British Journal of Nutrition. 92(1):159-168.
15. Zhu K, Du X, Greenfield H, Zhang Q, **Ma G**, Hu X, Fraser DR. (2004). Bone mass in Chinese premenarcheal girls: the roles of body composition, calcium intake and physical activity. British Journal of Nutrition. 92(6):985-993.
16. Cui Z, Li Y, Di Y, Ba L, Hu X, **Ma G.** (2004). The relative influence of diet and physical activity on obesity in China. Journal of Community Nutrition. 6(3):125-130.
17. Cui Z, Li Y, Liu A, Zhang Q, Du W, **Ma G.** (2004). Relative risk of metabolic syndrome in middle aged adults with different weight living in urban Beijing, China. Journal of Community Nutrition. 6(3):131-136.
18. **Ma G**, JinY, Piao J, Kok FJ, Bonnema G, Jacobsen E. (2005). Phytate, calcium, iron, and zinc contents and their molar ratios in foods commonly consumed in China. Journal of Agricultural and Food Chemistry. 53:10285-10290.

19. Li Y, Yang X, Zhai F, Piao J, Zhao W, Zhang J, **Ma G.** (2005). Disease risks of childhood obesity in China. Biomedical and Environmental Sciences. 18:401-410.

20. **Ma G**, Li Y, Hu X, Cui Z, Yang X, Chen C. (2006). Report on childhood obesity in China (2) verification of BMI classification reference for overweight and obesity in Chinese children and adolescents. Biomedical and Environmental Science. 19:1-7.

21. Zhu K, Zhang Q, Foo LH, Trube A, **Ma G**, Hu X, Du X, Cowell CT, Fraser DR, Greenfield H. (2006). Growth, bone mass, and vitamin D status of Chinese adolescent girls 3 y after withdrawal of milk supplementation. American Journal of Clinical Nutrition. 83:714-721.

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23. Li Y, Zhai F, Yang X, Schouten EG, Hu X, He Y, Luan D, **Ma G**. Determinants of childhood overweight and obesity in China. British Journal of Nutrition. (in press)

Publication in Chinese Journals

1. **Ma G**, Shi K, Cheng W, et al. (1991). The determination of selenium levels and the concentration of nitrosamine in patients with gastric cancer, dysphasia, chronic atrophic gastritis and superficial gastritis. Tumor. 11(2):92-96.

2. **Ma G,** Shi K, Cheng W, et al. (1992). Blockage of MNNG mutagenesis by selenium. Tumor. 12(6):272-273.

3. **Ma G**, Zhai F, Li Y, et al. (1994). Parents' nutrition knowledge, attitude, and behavior regarding infant feeding in the poor areas of China. Acta Nutrimenta Sinica. 16(4):396-399.

4. **Ma G**, Zhai F, Li Y, et al. (1994). Training on nutrition field workers and its evaluation. Journal of Hygiene Research. 23(6):368-369.

5. **Ma G**, Zhai F, Ao M, et al. (1994). Use of focus group discussion in developing nutrition education materials for infants' parents in the poor areas of China. Chinese Journal Health Education. 10(2):42-43.

6. He Y, Li W, Change Y, Zhai F, **Ma G,** Lin H. (1995). Dietary pattern and its influencing factors of pre-school children in relatively poor rural areas of China. Journal of Hygiene Research. 24(1):44-47.
7. Sun J, **Ma G,** Hu X, et al. (1995). A survey on nutrition knowledge and dietary behavior for students' parents. Chinese Journal School Health. 16(5):348-349.
8. Hu X, **Ma G,** Sun J, et al. (1995). A K-A-P survey on nutritional knowledge among Beijing middle school students. Chinese Journal of Health Education. 11(8):11-14.
9. **Ma G,** Sun J, Hu X, et al. (1995). A survey on nutrition knowledge and dietary behavior for pupils in four primary school in Beijing. Acta Nutrimenta Sinica. 17(4):446-448.
10. Ge K, **Ma G,** Zhai F, et al. (1996). Dietary nutrients intakes of Chinese students. Acta Nutrimenta Sinica. 18(2): 129-133.
11. Li W, Chang Y, Zhai F, He Y, **Ma G**. (1996). The nutritional status of pre-school children in 101 relatively poor counties in China. Journal of Hygiene Research. 25:S74-S82.
12. Li Y, Zhai F, **Ma G,** et al. (1996). Evaluation of a nutrition education activity for rural children's parents in China. Journal of Hygiene Research. 25(5):316-319.
13. Li Y, Zhai F, Li W, **Ma G**. (1996). Nutrition education methods for rural children's parents in China. Journal of Hygiene Research. 27(4):275-276.
14. Zhai F, Li Y, He Y, **Ma G**. (1998). The effective measures in promoting the nutritional status of preschool children in rural China. Chinese Food and Nutrition. 6:19-22.
15. **Ma G**, Hu X, Gao S. (1999). The effect of energy intake at breakfast on school performance. Journal of Hygiene Research. 28(5):286-288.
16. Du L, Li Y, Ren Y, Ma W, **Ma G**. (2000). The snack pattern of children in Guangzhou. Chinese Journal of School Doctor. 14(5):325-326.
17. **Ma G**, Liu X, Li X, et al. (2000). A cross-sectional study of K-A-P on health of technical school students. Chinese Journal of School Doctor. 14(2):93-95.
18. **Ma G**, Liu X, Li X, et al. (2000). Effectiveness of health education among technical students. Chinese Journal of Health Education. 16(3):134-137.
19. Wu J, **Ma G**, Hu X, et al. (2000). The fast food consumption of Chinese children. Chinese Journal of School Health. 21(4):244-246.

20. Ma W, **Ma G**, Hu X, Wu J. (2000). Analysis of breakfast practice and relative factors of children and adolescents in four cities. Guang Dong Anti-epidemic. 26(4):3-7.
21. **Ma G**, Hu X, Ma W, Wu J. (2001). Dietary behavior of children and adolescents living in urban China. Food and Nutrition in China. 1:16-18.
22. Ma W, **Ma G**, Hu X, et al. (2001). The beverage consumption practice of Chinese children in four urban areas. Chinese Journal of School Health. 22(2):102-104.
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24. Gao S, **Ma G**, Zhai F, Ge K. (2001). Breakfast variety of Chinese students. Chinese Journal of School Health. 22(3):196-199.
25. **Ma G**, Hu X, Ma W, et al. (2001). The snacking pattern of children and adolescents from four cities of China. Acta Nutrimenta Sinica. 23(2):177-180.
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33. Hu X, Zhang H, Gao S, Liu A, Pan H, **Ma G**. (2002). The perceptions, attitudes and needs of school administrators towards school health education. Chinese Journal of School Health. 23(1):9-10.
34. Hu X, **Ma G**, Ma W, et al. (2002). The food preference of children and adolescents in urban China. Chinese Journal of School Doctor. 16(2):107-109.
35. Li Y, **Ma G**, Hu X, Ma W. (2002). Logistic analysis of relative factors affecting television-viewing time of children and adolescents living in urban China. China Public Health. 18(suppl.):9-11.
36. **Ma G**, Hu X, Li Y, Ma W. (2002). Environmental and behavior factors leading to childhood obesity in four cities of China. Chinese Journal of Prevention and Control Non-communicable Disease. 10(3):114-116.
37. **Ma G**, Li Y, Hu X, et al. (2002). The television viewing time of children and adolescents living in urban China. Chinese Journal of Health Education. 18(7):411-413.
38. **Ma G**, Hu X, Ma W, et al. (2002). The food purchase practice and its influencing factors of families living in urban China. Chinese Journal of School Doctor. 16(3):193-195.
39. **Ma G**, Zhai F, Gao S, Ge K. (2002). Impact of breakfast frequency on energy and nutrients among Chinese primary and secondary school students. Chinese Journal of School Health. 23(4):289-291.
40. Zhang H, Hu X, **Ma G**, et al. (2002). The perceptions, attitudes and needs towards health education of teachers in China. Chinese Journal of School Health. 23(4):295-296.
41. Hu X, **Ma G**, Zheng X, et al. (2002). The perceptions, attitudes and needs towards health education of food service stuffs in China. Chinese Journal of School Health. 23(4):297-298.
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57. Li Y, **Ma G**, Pan H, Cui Z, et al. (2003). The comparison of prevalence of overweight and obesity of adolescents using different references. Chinese Journal of Prevention and Control of Non-communicable Diseases. 11(6):281-282.
58. Liu A, **Ma G**, Pan H, Zhang Q, Hu X. (2003). The reliability and validity study of 1-Year physical activity questionnaire for elementary students. Chinese Journal of School Doctor. 17(1):4-7.
59. Zhang Q, Du W, Hu X, Liu A, Pan H, **Ma G**. (2004). The relation between body mass index and percentage body fat among Chinese adolescent living in urban Beijing. Chinese Journal of Epidemiology. 25(2):113-116.
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65. Lai J, Yin S, **Ma G**, Piao J, Xu J, Meng J, Yang X. (2005). Distribution of feeding index and association between feeding index and growth of infants and young child aged 6-24 months. Journal of Hygiene Research. 34(5):617-619.
66. Liu A, Li Y, Song J, Pan H, Han X, **Ma G**. (2005). Study on the validation of the computer science application's activity monitor in assessing the physical activity among adults using doubly labeled water method. Chinese Journal of Epidemiology. 26(3):197-200.

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69. **Ma G**, Zhu D, Hu X, Luan D, Kong L, & Yang X. (2005). The Drinking practice of people in China. Acta Nutrimenta Sinica. 27(5):362-365.

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77. Li Y, Song J, Pan H, Yao M, Hu X, **Ma G**. (2006). Validity of food frequency questionnaire to investigate the dietary energy and nutrients intake. Acta Nutrimenta Sinica. 28(2):143-147.

78. Li Y, He Y, Zhai F, Yang X, Hu X, Zhao W, **Ma G**. (2006). Comparison of assessment of food intakes by using 3 dietary survey methods. Chinese Journal of Preventive Medical. 40(4):273-280.

Educational Programme

1. Participated in Nutritional and lifestyle epidemiology workshop. 8-17 June 2001. Wageningen University, the Netherlands.
2. Oral presentation: Vegetables, fruits and health. 2001 China International Conference on fruits and vegetables. 11-14 October 2001. Xiamen, China.
3. Oral presentation: Dietary assessment. 2002 China National Nutrition and Health Survey training workshop. 5-15 January 2002. Chengdu, Sichuan, China.
4. Oral presentation: Vitamin and mineral supplements. Seminar on Standards for Infant Formula. 24 January 2002. Beijing, China.
5. Oral Presentation: Water-soluble Vitamins. Nutrition training workshop. 27 January 2002. Beijing, China.
6. Presented at 2002 Annual Meeting of National Food and Nutrition Consultation Committee. 1st February 2002. Beijing, China.
7. Presented at The 26th Clinical Congress of the American Society for Parenteral and Enteral Nutrition. 23-27 February 2002. San Diego, California, USA.
8. Presented at The Symposium and Workshop on Forging Effective Strategies for Prevention and Management of Overweight and Obesity in Asia. International Life Science Institute. 22-24 April 2002. Singapore.
9. Presented at Xiang Shan Scientific Meeting: nutrition, health and social development. 28-29 April 2002. Beijing China.
10. Organized and lecture in China-Netherlands Nutritional and lifestyle epidemiology workshop. 21-25 May 2002. Beijing, China.
11. Oral Presentation: The nutritional situation of school children in China. The Experts Meeting on School Feeding Research Copenhagen. Invited by United Nations University, World Food Program. 30-31 May 2002. Copenhagen, Denmark.
12. Oral presentation: Effect of milk supplementation on the physical development of Chinese school girls. International seminar on milk and bone health of adolescents. 15-16 September 2002. The 5th meeting on maternal and child nutrition, China Nutrition Society. Dalian, China.

13. Presented at the Symposium on Plant metabolism and bioavailability of iron, zinc and vitamin A in commonly consumed foods in developing countries. 5-6 December 2002. Copenhagen, Denmark.
14. Presentation: Dietary Patterns and the Relative Role of Cereals and Vegetables in Meeting the Nutrition Requirement of People in China. Wageningen University. 10 February 2003. Wageningen, the Netherlands.
15. China Central TV interview on diet and health. 9 September 2003. Beijing, China.
16. Present at Forum on food safety, nutrition and development. National Food and Nutrition Consultation Committee. 22 September 2003. Beijing, China.
17. Oral presentation: The nutritional status of Chinese school children. At The Children's Hospital at Westmead of University of Sydney. 31 October 2003.
18. Oral presentation: Milk and the nutrition of Chinese school children. At Dairy Australia. Victoria Australia. 5 November, 2003.
19. Oral presentation: The nutritional status of Chinese school children. At School of Health Science of Deakin University. 5 November, 2003. Victoria Australia.
20. Oral presentation: Dietary patterns and the relative role of cereals and vegetables in meeting the nutrition requirement of people in China. On Plan Genomics: from crop production to healthy food. At Chinese Academy of Agricultural Science. Beijing, China. 10-15 November, 2003.
21. Oral presentation: The relation of fast food consumption and obesity prevalence among children and adolescents living in 4 cities of China. Beijing, China. Conference on Obesity of Children and Adolescents. 13-14 November, 2003.
22. Oral presentation: The relative contributions of energy expenditure on body composition and weight gain to the evolution of the risk of the obesity. The First research coordination meeting of the International Atomic Energy Agency. 29 March-2 April 2004. Vienna, Austria.
23. Temporary adviser for Joint WHO/FAO workshop on Fruit and Vegetables for Health. 1-3 September, 2004. WHO Center for Health Development. Kobe, Japan.
24. Oral presentation：Eating practice and its influencing factors. The 9th National Nutrition Conference of China Nutrition Society. 12-14 October, 2004. Beijing, China.
25. Presented at the 2nd Asian Congress of Pediatric Nutrition. 1-4 December 2004. Jakarta, Indonesia.

26. WHO expert meeting on childhood obesity. 20-24 June, 2005. WHO Center for Health Development. Kobe, Japan.
27. Oral presentation: Childhood obesity in China. The XVIIth IEA World Congress of Epidemiology 21-25 August 2005. Bangkok, Thailand.
28. Oral presentation: Physical activity and NCDs in China. Behavior, lifestyle and health workshop. 10 January 2006. Beijing, China.
29. The 18th International Congress of Nutrition. 19-23 September, 2005. Durban, South Africa.
30. The 12th European Nutrition Leadership Training Seminar. 8-16 March 2006. Luxembourg.
31. China- Netherlands Nutritional and lifestyle epidemiology workshop. 20-25 April 2006. Beijing, China.