Insects as sources of iron and zinc in human nutrition

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Abstract

Dietary deficiencies in Fe and Zn are globally widespread, causing serious health problems such as anaemia, poor pregnancy outcomes, increased risk of morbidity and mortality, stunted growth and impaired physical and cognitive development. Edible insects, of which a diversity of over 2000 species is available, are dietary components for about 2 billion individuals and are a valuable source of animal protein. In the present paper, we review the available information on Fe and Zn in edible insects and their potential as a source of these micronutrients for the rapidly growing human population. The levels of Fe and Zn present in eleven edible insect species that are mass-reared and six species that are collected from nature are similar to or higher than in other animal-based food sources. High protein levels in edible insect species are associated with high Fe and Zn levels. Fe and Zn levels are significantly positively correlated. Biochemically, Fe and Zn in insects occur predominantly in non-haem forms, bound to the proteins ferritin, transferrin and other transport and storage proteins. Knowledge gaps exist for bioavailability in the human alimentary tract, the effect of anti-nutritional factors in other dietary components such as grains on Fe and Zn absorption and the effect of food preparation methods. We conclude that edible insects present unique opportunities for improving the micronutrient status of both resource-poor and Western populations.

Key words: Iron: Zinc: Insects: Anaemia: Bioavailability: Anti-nutritional factors: Food preparation methods

Introduction

Micronutrients, substances required in small amounts to sustain proper growth and development, enable the body to produce enzymes, hormones and other compounds essential for the maintenance of normal body functions. Micronutrient malnutrition affects over 2 billion individuals[1]. In terms of global public health significance, Fe, Zn, vitamin A and iodine are the most important micronutrients[2,3]. In the present review, we focus on Fe and Zn because: (a) both play a key role in preventing malnutrition and early stunting[3]; (b) deficiency of both is prevalent in areas of high cereal and low animal food consumption[4]; and (c) Fe and Zn from plant-based foods are generally poorly absorbed[4,5].

Because Fe and Zn play important roles in numerous biochemical pathways, deficiency of these micronutrients has negative effects on many physiological systems including the gastrointestinal tract, the central nervous system, and the immune, skeletal and reproductive systems. These health effects in the long run result in a high economic burden for individuals and countries[6]. The WHO estimates that compared with the year 2000, the number of individuals who died from Fe-deficiency anaemia (IDA) in the year 2015 increased from 61 000 to 78 000 and thus, as a result, the crude death rate due to IDA increased from 1·0 % to 1·1 %[7]. However, the *Lancet* series reported that there has been a significant reduction in the disability-adjusted life-years lost as a result of IDA (−3·3 (95 % CI − 4·8, −1·8) %)[8]. The WHO has called for integrated approaches to solving micronutrient deficiencies[2].

Globally, over 2 billion individuals are anaemic, many due to Fe deficiency[1]. In resource-poor areas, the Fe-deficiency situation is exacerbated by infectious diseases such as malaria, hookworm infestation, HIV/AIDS, schistosomiasis and tuberculosis[1]. The major health consequences of IDA include poor pregnancy outcome[9–11], increased risk of morbidity and impaired physical and cognitive development[11]. It has been proposed that treating IDA can not only restore personal health but also raise national productivity levels by 20 %[1].

The current WHO goal is to achieve a 50 % reduction in the prevalence of anaemia in women of reproductive age by 2025[10,12]. The solutions to Fe deficiency and anaemia can be both inexpensive and effective. Usually, multifactorial and multisector approaches that are tailored to local conditions and that take into account the specific aetiology of anaemia are favoured by policy makers in view of their sustainability. The WHO has recommended dietary diversification, food fortification and Fe supplementation. The simultaneous control of infections and prevention of other nutritional deficiencies such as vitamin B$_{12}$, folate, and vitamin A which are known to exacerbate Fe deficiency is also recommended.

Globally, 2·2 billion individuals are affected by Zn deficiency[13]. Recent estimates based on information from country food balance sheets indicate that, for 15–20 % of the global population, the absorbable Zn content of national food supplies may be inadequate to meet Zn requirements[14]. Zn deficiency in humans is a result of reduced dietary intake, inadequate absorption, increased loss or increased use, for example in the case of disease. Manifestation of Zn deficiency includes increased prevalence of diarrhoea, pneumonia and malaria as a result of impaired immune function[15]. Furthermore, it is associated with impaired cognitive functions such as learning and hedonic tone[13,16]. Stunting (percentage of children under 5 years of age with height-for-age below the expected range of a reference population) is 'the best known measure of the adverse outcomes associated with zinc deficiency in populations'[17].

So far, little attention has been paid to insects as sources of Fe and Zn in the human diet. In the following we review the available information on Fe and Zn contents and the biochemical forms occurring in edible insects. Next we discuss bioavailability of Fe and Zn in relation to anti-nutritional factors (ANF) in food sources and outline future directions for research in this area.

Iron and zinc concentrations in insects compared with livestock animals

Analyses of both Fe and Zn concentrations in the same edible insect species showed Fe contents ranging between 4 and 62 mg/100 g DM and Zn contents between 9 and 27 mg/100 g DM for eleven edible species that are mass-produced and six species that are collected from nature (Table 1). Fe content reported for the termite *Macrotermes subhyalinus* Rambur (Isoptera: Termitidae) is an outlier, causing the range for Fe contents to be wider than for Zn contents.

Comparing three commonly mass-reared insect species with common livestock species shows that the Fe and Zn concentrations in yellow mealworms, *Tenebrio molitor* L.

(Coleoptera: Tenebrionidae) are higher than for chicken and pork, but lower than for beef (Fig. 1). However, both African migratory locusts, *Locusta migratoria* L. (Orthoptera: Acrididae), and house crickets, *Acheta domesticus* L. (Orthoptera: Gryllidae), contain similar amounts of Zn and higher amounts of Fe, compared with chicken, pork and beef.

More detailed examination of the Fe, Zn and crude protein contents of insects reveals significant correlations between Fe and Zn contents (Spearman's $\rho = 0.592$; $P < 0.001$; n 48), and between Fe and Zn contents and body crude protein content (Spearman's $\rho = 0.443$; $P = 0.002$; n 48; and $\rho = 0.693$; $P < 0.001$; n 48 for Fe and Zn, respectively; Fig. 2). Factors that contribute to differences in Fe and Zn concentrations are species (Table 1), developmental stage and diet[18].

Species differences

Yellow mealworm larvae have a lower Fe content (3·3–10·0 mg/100 g DM) than African migratory locusts (7·8–21·7 mg/100 g DM)[19–26]. Large variation in Fe content (1·0–75·0 mg/100 g DM) has been reported for three species of termites belonging to the genus *Macrotermes* (Isoptera: Termitidae)[27–30]. Differences between species are not explained by taxonomic distance. For instance, adult yellow mealworms and morioworms (*Zophobas morio* Fabr.), both tenebrionid beetles, contain similar Fe concentrations (8·9 v. 9·2 mg/100 g DM), whereas their Zn concentrations differ (14·4 v. 8·3 mg/100 g DM)[31].

Developmental stages

Insects used as food are often consumed in a certain life stage, which is why few studies have reported on mineral concentrations in more than one life stage. Data on more than one life stage are available for the African migratory locust, adults of which have a higher Fe concentration compared with penultimate instars, whereas Zn content is similar for the two stages[21]. In house crickets Fe and Zn contents are similar for adults and nymphs[20].

Table 1. Protein, iron and zinc content for a selection of insect species consumed by humans (Mean values and standard deviations where available)

Species*	Scientific name	Crude protein (% DM)		Fe (mg/100 g DM)		Zn (mg/100 g DM)		References
		Mean	SD	Mean	SD	Mean	SD	
House cricket	*Acheta domesticus*	62·9	4·56	9·1	4·47	19·9	3·02	(19,20,23,25,26,82)
Jamaican field cricket	*Gryllus assimilis*	51·25		17·93		15·57		(26)
Two-spotted cricket	*Gryllus bimaculatus*	58·32		9·66		22·43		(24)
Tropical house cricket	*Gryllodes sigillatus*	70·00		4·23		13·9		(22)
Migratory locust	*Locusta migratoria*	59·0	3·11	13·7	4·35	14·8	1·09	(21)
Desert locust	*Schistocerca gregaria*	76		8·38		18·6		(22)
Lesser mealworm	*Alphitobius diaperinus*	67·85		21·80		26·80		(83)
Yellow mealworm	*Tenebrio molitor*	51·7	4·80	5·3	2·16	11·8	1·60	(19,20,22–26)
Superworm	*Zophobas morio*	42·9	3·22	3·8	1·00	7·7	0·77	(19,20,25)
Silkworm	*Bombyx mori*	51·8	2·23	15·9	7·23	16·8	5·55	(20,84,85)
Waxworm	*Galleria mellonella*	39·5	4·78	5·0	1·75	8·6	3·36	(19,20,23,25,86)
Termite	*Macrotermes subhyalinus*	38·8	0·57	61·9	8·61	9·5	1·43	(29,87)
Arboreal termite	*Nasutitermes* spp.	48·8		24·6		18·4		(88)
Palm worm	*Rhynchophorus palmarum*	28·0	9·26	5·1	1·25	12·9	1·39	(89)
Sago grub	*Rhynchophorus ferrugineus*	34·1	1·48	9·0	0·55	9·5	4·26	(90)
Longhorn grasshopper	*Ruspolia differens*	43·7	0·60	14·8	1·80	14·9	2·45	(30)
Cornfield grasshopper	*Sphenarium purpurascens*	65·2		18		42		(91)

* The first eleven species are globally mass-reared; the last six species are collected from nature.
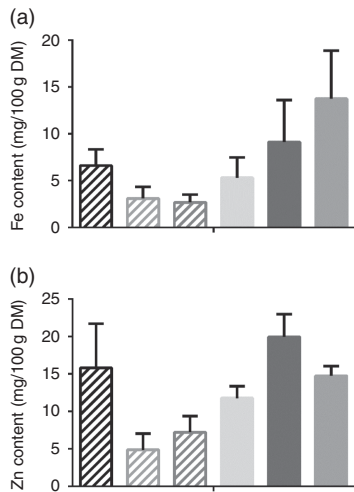
Fig. 1. Iron (a) and zinc (b) content on a DM basis in meat from conventional production animals (beef (▨); pork (▨); chicken (▨)) and in three insect species (yellow mealworm *Tenebrio molitor* L. (□), house cricket *Acheta domesticus* L. (■) and African migratory locust *Locusta migratoria* L. (■)). Data for conventional meat were adapted from the US Department of Agriculture (USDA) food database (USDA National Nutrient Database for Standard Reference, release 28; Agricultural Research Service, USDA, Nutrient Data Laboratory; http://www.ars.usda.gov/nea/bhnrc/ndl, selecting data on meat only (excluding pure fat and organs)) reporting both iron and zinc concentrations. Insect data were adapted from references[19,20,21,22,25]. Values are means, with standard deviations represented by vertical bars.

The same is true for yellow mealworms; data from several studies suggest similar concentrations of Fe (3·3–10·0 v. 3·7–8·9 mg/100 g DM) and Zn (9·5–13·7 v. 11·3–14·4 mg/100 g DM) for larvae and adults, respectively[19,20,22,24–26,31].

Dietary effects

In general, the chemical composition of insects is affected by the diet they consume[21,32,33]. Micronutrient contents are regulated in order to maintain body homeostasis and prevent toxic concentrations. For instance, the Jamaican field cricket (*Gryllus assimilis* Fabr.; Orthoptera: Gryllidae) decreases Zn assimilation and increases Zn excretion when provided with higher dietary Zn concentrations, such that a sixteen-fold increase in dietary Zn resulted in a twofold increase in Zn content in this cricket[34]. Hence, Zn levels seem to depend on dietary composition.

Biochemical forms of iron and zinc in insects

As for humans, dietary Fe and Zn are essential for proper physiological functioning of insects, fulfilling roles in DNA synthesis, oxidation, cuticle biosynthesis and acting as a cofactor in a variety of enzymes[35,36]. Transferrin and ferritin are two major proteins involved in Fe metabolism in insects, both having multiple functions. Transferrin is an Fe transporter, it might act as an antibiotic agent and it can be a vitellogenic protein[37]. Ferritin functions in Fe transport and storage and is present in the endoplasmatic reticulum, nuclear envelope and mitochondria of gut and fat body cells in particular, and extracellularly in the haemolymph[38,39]. Multiple studies investigating the transport mechanisms of Zn in insects have focused on
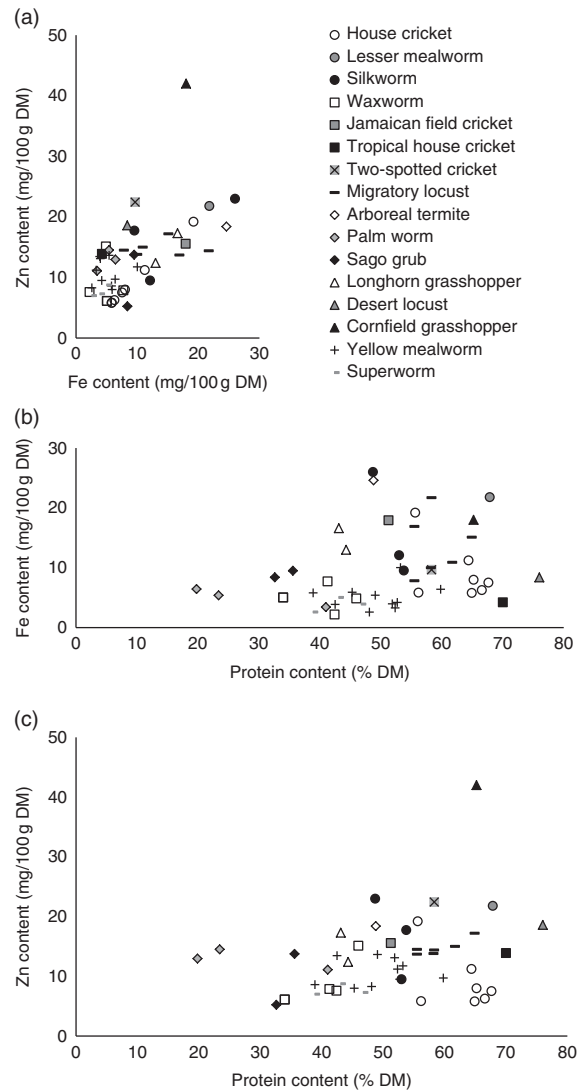

Fig. 2. Scatter plots of iron content, zinc content (both expressed as mg/100 g DM) and crude protein content (% DM) of sixteen of the seventeen insect species listed in Table 1. Data for *Macrotermes subhyalinus* were considered outliers and have been excluded. (a) Iron content (mg/100 g DM) plotted against zinc content (mg/100 g DM) (Spearman's ρ = 0·592; P < 0·001; n 48). (b) Iron content plotted against crude protein content (Spearman's ρ = 0·443; P = 0·002; n 48). (c) Zinc content plotted against crude protein content (ρ = 0·693; P < 0·001; n 48).

Zn transporters in the model species *Drosophila melanogaster*. Thus far, two families of Zn transporters have been identified, ten dZip and seven dZnT proteins[40]. These transporters are homologues to the human Zip (SLC39) and ZnT (SLC30) family members and are responsible for cellular influx and efflux, respectively. Zn transporters can be found ubiquitously or accumulated in specific organs/regions of the gastrointestinal tract, for example, the expression of dZip1 in the midgut and dZnT35C in the Malpighian tubules of *D. melanogaster*[40–42] that have roles in the absorption and excretion of Zn. Much less information is available on Zn storage in insects. Zn is present throughout the gastrointestinal tract of *D. melanogaster* with accumulation regions in the posterior midgut, the crop and the Malpighian tubules[43]. As most information on the physiological

functions of Fe and Zn in insects stems from research on *D. melanogaster*, it remains to be investigated whether the information is representative for the edible insect species which are the focus of the present review. Some differences in Fe metabolism between different insect orders have been demonstrated, showing different allocations of ferritin in midgut cells[39].

Bioavailability of iron and zinc in insect-derived food

Nutrient bioavailability refers to the proportion of a nutrient that is absorbed from the diet and used for normal body functions[44,45] and is governed by host-related and food-related factors such as the food matrix and the chemical form of the nutrient in question. Internal factors may include age, sex, nutrient status and life stage (for example, pregnancy). Nutrient bioavailability depends on different processes, including release of the nutrient from the physico-chemical food matrix; effects of digestive enzymes in the intestine; binding and uptake by the intestinal mucosa; transfer across the gut wall to the blood or lymphatic circulation; systemic distribution; systemic deposition; metabolic and functional use; and excretion via urine or faeces[45].

In vertebrates, Fe is usually found in muscles in the form of myoglobin and Hb. However, the primary form of haem-Fe in insects is found in cytochromes. It is presumed that the bioavailability of cytochrome haem-Fe is similar to that of myoglobin and Hb[35]. Fe in insects is predominantly present as the non-haem molecules ferritin and holoferritin. Because ferritin functions as a storage protein for Fe, each molecule is capable of containing thousands of Fe atoms, typically in the ferrous state, which increases their bioavailability. Insect ferritin has not yet been well characterised, although it is known to differ from the ferritin found in vertebrates[39]. Phyto-ferritin, present in legumes such as soya, appears to be better bioavailable than Fe in the form of reduced salts[46–51]. This is explained by protection of Fe from ANF, such as phytates, oxalates and tannins, by the protein complex. Although much of the diet-derived ferritin may not reach the intestinal absorption site intact, due to destruction during cooking and gastric digestion[52], the suggestion of a separate transporter for phyto-ferritin in human cells indicates that there is an absorption potential[53]. Even if only a small fraction of the original amount reaches the absorption site, it can have a tremendous impact due to the large number of Fe atoms present in ferritin proteins.

Bioaccessibility (*in vitro* solubility or dialysability of a nutrient)[54] of micronutrients present in various species of edible insects has not been widely studied but is expected to follow trends of meat, fish and poultry. However, the non-haem-Fe present in most edible insects may be poorly soluble under intestinal conditions and may also be affected by other components of the diet[44]. Furthermore, the impact of known enhancers and inhibitors of nutrient bioavailability on (micro)nutrients present in edible insects is not known. Examples of nutrient enhancers include the 'meat factor' present in meat, fish and poultry thought to be a result of muscle protein, which enhances absorption of Fe from all foods[44]. Protein (more specifically: amino acids such as histidine and methionine) is known to enhance non-haem-Fe and Zn absorption[44,55]; therefore, insects with a high protein content might promote the uptake of these minerals.

Recently, the *in vitro* solubility and availability of Fe and Zn from various insect species (grasshopper, cricket, mealworms and buffalo worms) have been compared with those from sirloin beef using a Caco-2 cell model. It was found that Fe and Zn solubility was significantly higher from the insect samples than from beef, but bioaccessibility of Fe (measured as the ferritin concentration in Caco-2 cells) was more diverse, with the highest response for buffalo worms (*Alphitobius diaperinus* Panzer; Coleoptera: Tenebrionidae), followed by beef, yellow mealworms, cornfield grasshoppers (*Sphenarium purpurascens* Charp.; Orthoptera: Pyrgomorphidae), and two-spotted crickets (*Gryllus bimaculatus* Geer; Orthoptera: Gryllidae)[56]. In the same study by Latunde-Dada *et al.*[56], it was shown that the addition of insects to wheat flour (1:1) was superior to beef in increasing Fe and Zn solubility in the composite mixtures.

Based on the above, it is likely that the addition of insects to current starch-based diets, exemplary for individuals living in many low- and middle-income countries (LMIC), will provide additional Fe and Zn, that could potentially fill the requirement gap, and maybe increase the bioavailability of native and fortification Fe in the starchy foods. As an example, a complementary feeding cereal enriched with locally derived dried caterpillars showed a small increment in Hb concentrations in infants and children in the DRC Congo[57]. A better understanding of the bioavailability of Fe and Zn from insects may help to improve the design of such a strategy. In addition, good bioavailability of Fe and Zn will also mean that insects are a valuable food item for consumers in other parts of the world, including Europe and North America.

Anti-nutritional factors

ANF are compounds that interfere with the absorption of one or more nutrients from human food, animal feed or water[58]. Diets laden with ANF such as phytic acid can cause micronutrient malnutrition by reducing the bioavailability of micronutrients such as Fe and Zn. In many LMIC, micronutrient malnutrition is further exacerbated by the consumption of monotonous staple food-based diets which contain enough energy to ease hunger pangs but not enough micronutrients. In addition, the staple foods are usually high in ANF.

An important ANF reducing Fe and Zn absorption is phytic acid, which is the storage form of P in grains, nuts and legumes. When chelated to a mineral in the seed, phytic acid is known as phytate. Phytic acid is highly abundant in some plant foods (wholegrain cereals, pulses, seeds, nuts) and it binds minerals such as Fe, Zn and Ca, thereby decreasing their bioavailability[59]. This is because it forms soluble or insoluble complexes that cannot be absorbed[60]. Similarly, other inhibitors of nutrient absorption may bind the nutrient, render the nutrient insoluble, or compete for the same uptake system. The latter has been observed in the interaction between Ca and non-haem-Fe, especially when Ca and/or Fe supplements are used outside the meal setting[61].

Phytic acid content varies greatly among plants due to the type/species of seed, environmental condition, climate and soil quality[59]. In grains, phytic acid is primarily found in the bran while in legumes it is found in the cotyledon layer[59]. With the exception

of phytic acid, the extent to which other ANF such as polyphenols and tannins affect the bioavailability of Fe and Zn in humans is not clearly established. Management and control of dietary inhibitors and enhancers is critical. For example, the bioavailability of non-haem-Fe, such as that found in plant foods, eggs and milk, is inhibited by phytates but may be enhanced by vitamin C. Practical ways to reduce dietary inhibitors and increase Fe absorption also include fermentation, germination, malting and adopting food fortification practices, i.e. dietary modification strategies to either include in a meal foods that can promote the absorption of a micronutrient or to exclude foods that inhibit its absorption. Whether Zn and the biochemical form of Fe present in edible insects are affected by ANF is a critical consideration worth further research because cereal-based staple foods are consumed in the same meal as the insects.

Nutrient bioavailability also responds to systemic factors such as deficiency of a nutrient or changes in the physiological state, for example during pregnancy[61]. This may result in the up-regulation or down-regulation of the absorption of a nutrient. Similarly, infections and inflammation may reduce the absorptive capacity of the gut[62]. It is important to know the bioavailability of nutrients such as Fe, Zn, folate, Ca, Mg and vitamin A in order to translate their physiological requirements into actual dietary requirements[61].

Effect of food preparation methods on the mineral content of edible insects

The nutrient quality of different foods can be altered by different methods of food processing such as frying and boiling[63]. Cooking loss of minerals may be caused by the outflow of minerals from the food materials[64]. These losses can be prevented by various methods such as: (a) eating the boiled food with the soup made using the water/stock of the boiled food; (b) boiling in salted water (up to about 1% NaCl); (c) avoidance of too long boiling; and (d) using cooking methods that cause a lesser amount of mineral losses, for example, stewing, frying or parching[64]. Most insects are either sautéed, baked, ground into a paste before addition to foods, stewed, boiled or fried. Numerous websites offer recipes for cooking insects[65]. As is the norm for any food product, consumer education aimed at the retention of nutrients from edible insects before, during and after cooking must be systematically introduced alongside the insect products. So far, the effect of various food preparation methods on the micronutrient/mineral content of various insect sources has not been fully investigated.

Conclusions and implications

The relative contribution of diets rich in edible insects towards solving micronutrient malnutrition needs to be quantified. Preliminary findings suggest that Fe biofortification of staple food crops can be efficacious for improving Fe status[66–69]. Furthermore, although the inclusion of animal foods in the diet can be a good strategy to combat micronutrient malnutrition, this is often not affordable for the individuals suffering from micronutrient malnutrition and thus often is an unsuitable option. The *Lancet* series on interventions for improvement of maternal and child nutrition identified the need for innovative community-based strategies for scaling up the coverage of nutrition interventions that have the potential to reach especially the poor populations[3].

The information on Fe and Zn contents in edible insects is at present still limited and best documented for the species discussed in the present paper which feature in human diets around the world[70] and which are also good sources of protein, fat and dietary fibre[18]. Consumption of edible insects is widely practised in parts of Africa, Asia and Latin America. Current estimates are that insects form part of the diet of about 2 billion individuals, in particular in tropical areas of the world[71]. Therefore, insects are receiving increasing attention for their potential to alleviate the projected protein shortage by 2050[71,72].

Although the consumption of edible insects has been shown to contribute to protein intake[73–77], the contribution of edible insects to the micronutrient pool has not been explored. We postulate that the addition of edible insects to the human diet, either whole, in-part, or processed, will greatly contribute towards the achievement of the 'zero hunger' sustainable development goal target, especially because the large majority of the hungry individuals (98% of 795 million individuals) who also suffer from hidden hunger live in LMIC[78] where edible insects are widely accepted.

The global human population is growing rapidly and is expected to reach 9–10 billion individuals by 2050. At present, 70% of the global agricultural land is used to produce livestock that provide meat and dairy products as favoured protein sources[71]. Increasing the production of livestock is seriously constrained by the availability of agricultural land and will aggravate climate change[79]. Insect production requires much less agricultural land per unit protein produced and contributes much less to climate change than livestock[80].

Regarding bioavailability of Fe and Zn from insect-derived food, only data from an *in vitro* experiment are available. Although the results are promising, *in vivo* studies on human subjects are required to quantify the absorption efficiency of Fe and Zn from insect-containing foods. Insects are receiving increased attention primarily due to their high protein content which is favourable for enhancing the uptake of Fe and Zn. Factors that may interfere with Fe and Zn absorption from insects such as processing, preservation, preparation and combinations with other foods need to be addressed in controlled studies to allow full utilisation of the potential of insects as Fe and Zn sources in human diets[81].

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