The Effect of the Meat Factor in Animal-Source Foods on Micronutrient Absorption: A Scoping Review

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ABSTRACT

The EAT-*Lancet* Commission's planetary health guidelines suggest a reduction in the consumption of animal-source foods (ASFs) for better health and more sustainable food systems. ASFs are highly nutrient dense, therefore suited to address the widespread issue of micronutrient deficiencies, particularly in low-resource settings where diets are predominantly plant based. ASFs are also believed to contain the meat factor, a substance enhancing the absorption of micronutrients from plant-based foods. We conducted a scoping review with the objective of systematically mapping the available evidence on the meat factor. The MEDLINE/PubMed and Web of Science databases were searched for literature published up to September 2021. Articles eligible for inclusion were all studies assessing the effect of adding ASFs and/or ASF fractions on micronutrient absorption from a plant-based meal or the overall diet in animal models and human subjects. Screening and data extraction were performed, and results were charted into 12 categories. We identified 77 articles eligible for inclusion, 52 of which were conducted in human subjects, 24 in animal models, and 1 in both. The addition of muscle tissue and muscle tissue fractions to single plant-based meals steadily increased absorption of iron and zinc across studies. The efficacy of the meat factor in increasing iron and zinc absorption in the overall diet is less clear. No clear differences emerged between red meat, poultry, and fish in promoting the meat factor effect. No clear evidence indicates that milk and egg products contain the meat factor. Our review highlights the importance of muscle tissue for the potential of the meat factor to enhance absorption of micronutrients of concern. Although the literature supports including sustainable and economically accessible forms of these ASFs into the diet, we found limited studies in resource-poor countries and of diets with low meat intake. *Adv Nutr* 2022;13:2305–2315.

Introduction

In 2019, the EAT-*Lancet* Commission defined "planetary health guidelines," a holistic set of guidelines that lay out a framework for food systems to provide healthy and environmentally sustainable diets (1). These guidelines advocate for a shift in food production and consumption, with a reduction of animal-source foods (ASFs), defined herein as any food product of animal origin (including meat, fish, eggs, dairy products, and animal-derived ingredients), in the diet, in favor of plant-based foods, defined herein as any food not of animal origin. The reference diet identified by the Commission contains very limited levels of ASFs: reference egg and red meat intake is limited to 13 g/d and 14 g/d, respectively, whereas higher intakes are allowed for poultry (29 g/d), fish (28 g/d), and dairy (250 g/d). However, in the current historical context, factors embedded in, and impacting on, food systems are contributing to food insecurity, with consequences such as undernourishment, cognitive development impacts, and micronutrient deficiencies (MNDs) (2). The FAO estimates indicate that MNDs (or "hidden hunger") affect 2 billion people worldwide (3). Globally, as of 2021, 22% of children aged <5 y suffered

from stunting, 6.7% of children aged <5 y were wasted, and 29.9% of women of reproductive age suffered from anemia (4). Iodine, iron, and vitamin A deficiencies are currently the most widespread MNDs, followed by zinc and folate deficiency, which can all contribute to severe and life-threatening conditions, especially in children (5). In addition, evidence on disability-adjusted life-years due to MNDs provides the indication that the burden of hidden hunger disproportionately affects sub-Saharan Africa and South Asia (6), and the ongoing COVID-19 pandemic has only worsened this inequality (4).

In this context, ASFs can be a fundamental source of micronutrients, such as zinc, iron, riboflavin, calcium, vitamin B-12, and vitamin A (7), otherwise lacking or less bioavailable in cereals, roots, and tubers (8), which make up the highest percentage of total dietary calorie intake in most low- and middle-income countries (LMIC) (9). Indeed, evidence suggests that increasing the production or promotion of ASFs in LMIC can be an important strategy to increase intake and bioavailability of zinc (10), and, overall, that deficiencies in iron and zinc in these countries are attributable to the consumption of low-diversity plant-based diets and limited amounts of ASFs, or lack thereof (11). Furthermore, a randomized controlled trial conducted in Kenyan schoolchildren aged 6–14 y (median 7.4 y) demonstrated that supplementing young and stunted children with a beef-based snack led to improvements in linear growth, increases in levels of physical activity, and improved cognitive performance (12).

In light of the environmental and health concerns raised by the EAT-*Lancet* Commission on the consumption of certain ASFs (1), as well as the unaffordability of beef, chicken, and egg consumption in many LMIC (particularly in poor or rural communities), fish, and specifically small fish, are an affordable and vital option for consumption (13). Aquatic ASFs are an especially nutrient-dense class of ASFs because they are a rich source of vitamin D, iodine, and long-chain n–3 (ω-3) PUFAs (14).

Another way by which ASFs could improve the micronutrient status of individuals is through the presence of a "meat factor" (previously "meat-effect") (15), defined as an active substance, or substances, contained within animal muscle tissue, which has been shown to increase overall absorption of certain micronutrients, mainly iron and zinc, from plant-based meals (16,17). The meat factor is of particular importance for the global South, where the predominant sources of calories, protein, and micronutrients are whole grains, pulses, and tubers (9, 18), which tend to be rich in absorption-inhibitory compounds (11). Phytic acid, for example, which is mostly found in unrefined cereals, seeds, and pulses (19), can dose-dependently reduce zinc and nonheme iron absorption from a meal (20). In this case, bioavailability becomes crucial. First-published evidence of the meat factor dates back to 1968, when Layrisse et al. (21) demonstrated that the addition of fish muscle or veal muscle induced an increase in nonheme iron absorption from a maize-based meal. Although reviews have highlighted

the meat factor as an important reason for the inclusion of ASFs in the diet (17, 22), to our knowledge no effort to systematically map all the evidence available on the meat factor has been made.

Most of the evidence collected on the meat factor to date has focused on the role of meat, specifically red meat and its characteristic components (e.g., heme iron), on enhancing the absorption of iron and zinc from the meal (23, 24). However, as demonstrated by the initial studies presenting the meat factor also in ASF sources other than red meat (21), and in light of the guidelines defined by the EAT-*Lancet* Commission suggesting a reduction in the consumption of red meat (1), interest has grown on how other ASFs could be involved in enhancing micronutrient absorption through the meat factor. Furthermore, more clarity is needed on the involvement of eggs and dairy in the meat factor, because evidence has shown their consumption to have both enhancing and inhibiting effects on the absorption of these micronutrients (25). Moreover, publications emerging over the years have suggested variance in absorption of micronutrients other than iron and zinc, such as calcium, when consuming diets varying only in protein source between soy and meat (26). Thus, this warrants investigation into whether the meat factor might be involved.

In light of these considerations, we set out to conduct a scoping review to provide an overview of the published literature on the meat factor. The present scoping review was guided by the following research questions: "What is the meat factor and which ASFs contain it?" "What are the characteristics and methodologies used to investigate the meat factor?" and "What is the quality and quantity necessary to consume in order to maximize benefits from the meat factor?"

Furthermore, noting the important potential of aquatic ASFs to enhance micronutrient absorption, we set out to map the available literature on the meat factor in fish.

Methods
This scoping review was developed following the methodology outlined in Chapter 11 of the Joanna Briggs Institute Reviewer's Manual (27) and applying the Preferred Reporting Items for Systematic Reviews and Meta-Analyses for Scoping Reviews (PRISMA-ScR) (28). Following a preliminary search on the MEDLINE/PubMed database using the search terms "Meat-factor," "Animal-Source-Foods," and "Micronutrient-absorption," a preliminary analysis of the available literature was performed, based on which nonindexed and indexed (MeSH) terminologies were identified and a full search strategy was developed. The final comprehensive literature search was conducted on September 29, 2021. The databases were searched for all relevant literature published from an unlimited start date up to the date of the search (September 29). No start date was defined for the search to include any relevant publications that could have been published before the first recognized mention of the meat factor in 1968 (21). Articles were extracted from MEDLINE/PubMed and Web of Science databases. No search limitations were

placed regarding year of publication and publication status. The full search strategy implemented for each database is presented in **Supplemental Table 1**. Preliminary searches helped guide the development of eligibility criteria, which were then discussed and adjusted. Articles were deemed to be eligible for inclusion if they assessed the meat factor or, in general, the ability of ASFs to enhance absorption of micronutrients from plant-based foods, both in the context of single meals as well as complete diets.

Both intervention and observational studies were eligible for inclusion, as were studies in human subjects and animal models. The decision was made to exclude in vitro and simulated absorption studies because these were considered less relevant to the scope of the present review as they are not reflective of normal dietary situations. Studies in English or Italian languages were included, whereas articles written in other languages were excluded due to limited translation resources. Given the exploratory nature of the present scoping review, allowance was made for articles not having "clean controls," that is, ASF-free groups. There are many reasons for this choice. Firstly, the decision to include animal-model studies entailed that most studies would include casein in the basal diet of the animals, therefore most studies would have otherwise been excluded. Secondly, the preliminary searches conducted indicated that eggs and dairy products most likely have a limited/null effect in enhancing micronutrient absorption from plant-based foods, therefore the addition of muscle tissue to the meal would be the real distinguishing factor. Lastly, the complexities of food traditions and the variability in methodologies applied to study the meat factor would strongly limit the number of included studies, if limited to articles including "clean" ASF-free control groups as a comparison. Therefore, it was also decided to include studies that tested ASFs in all groups, as long as noticeable differences, such as type of ASF, form of processing, and ASF quantity, were evident between groups. Finally, allowance was also made for studies assessing single ASF components added to the meal and to the diet, such as peptides, single amino acids, and fractions of other type, because they were considered relevant to the identification of the nature of the meat factor.

After the removal of duplicates, titles and abstracts were screened to remove nonrelevant articles and the remaining full-text articles were assessed for eligibility. Any doubts on eligibility of identified full-text publications were discussed and resolved among the authors, and the publications to include in the review were selected. The reference lists of randomly selected included publications were screened for any publications not identified through the systematic search. A data charting form to extract data was created before conducting the final search, tested and adjusted after an initial assessment of included studies. Data extracted were organized into 12 categories, by Author(s), Year of publication, Study country, Study objective, Study population (human/animal model, age, gender), Type of intervention, ASF tested (type and processing form), Micronutrient assessed (micronutrient, method for assessment, outcome measured),

Food composition data assessment, Group comparisons, Results, and Specification(s) on quality/quantity/frequency of consumption to benefit from the meat factor. The full data charting form is specified in **Supplemental Table 2**. The data were compiled in a spreadsheet and imported into Microsoft Excel (29) for coding and analysis of results. The results were then summarized in relation to the scoping review's research questions. On June 5, 2022, a new search was conducted to better account for the investigation of heme iron, hemoglobin, and myoglobin and their potential role as ASF fractions responsible for the meat factor. This was done through the use of the following search terms on our selected databases: ("hemoglobin" OR "myoglobin" OR "heme" OR "haem" OR "meat factor") AND ("nonheme") AND ("absorption"). As done with the primary search, all literature published up to the date of the search was screened.

Results
A total of 4533 citations were retrieved from the initial search, which resulted in 4057 articles after removing duplication. Screening of titles and abstract led to the identification of 124 potentially relevant citations, to be retrieved in full and assessed for eligibility. After assessing for eligibility, 75 citations were included in the scoping review. No further publications were identified from the reference lists of the randomly selected publications. The search conducted on June 5, 2022 resulted in the inclusion of 2 additional publications (30, 31). **Figure 1** represents the search flow of the scoping review. Citations were excluded for different reasons: citations were not relevant or unrecoverable; articles were reviews or conference reports not identified previously; some excluded articles assessed micronutrient absorption within supplements only, not in the context of a meal; citations were also excluded if they assessed micronutrient absorption from the ASF and not the plant-based food included in the meal; finally, articles were excluded if they assessed responses in absorption of micronutrients after protein quantity modifications, not specifying if modifications were resulting from addition or removal of ASFs.

Study characteristics
The general characteristics of the studies included in this scoping review are presented in **Table 1**.

Of the 77 citations included, 52 were intervention trials in human subjects, 1 was an intervention trial in both human subjects and in rats, and 24 were interventions exclusively in animal models, of which all but 1, conducted in piglets, were conducted in rats.

The studies that were identified and included were published between 1968 and 2017, more than half (68%) of which were published before the year 2000. No other studies conducted after 2017 were identified by our search. The majority of the interventions were conducted in 1 country, of which the United States was the most prominent, with 29 studies. Additionally, 2 studies were conducted in >1 country, one in Sweden and Thailand, and the other across Brazil, Chile, Mexico, Argentina, Peru, and Venezuela. Of
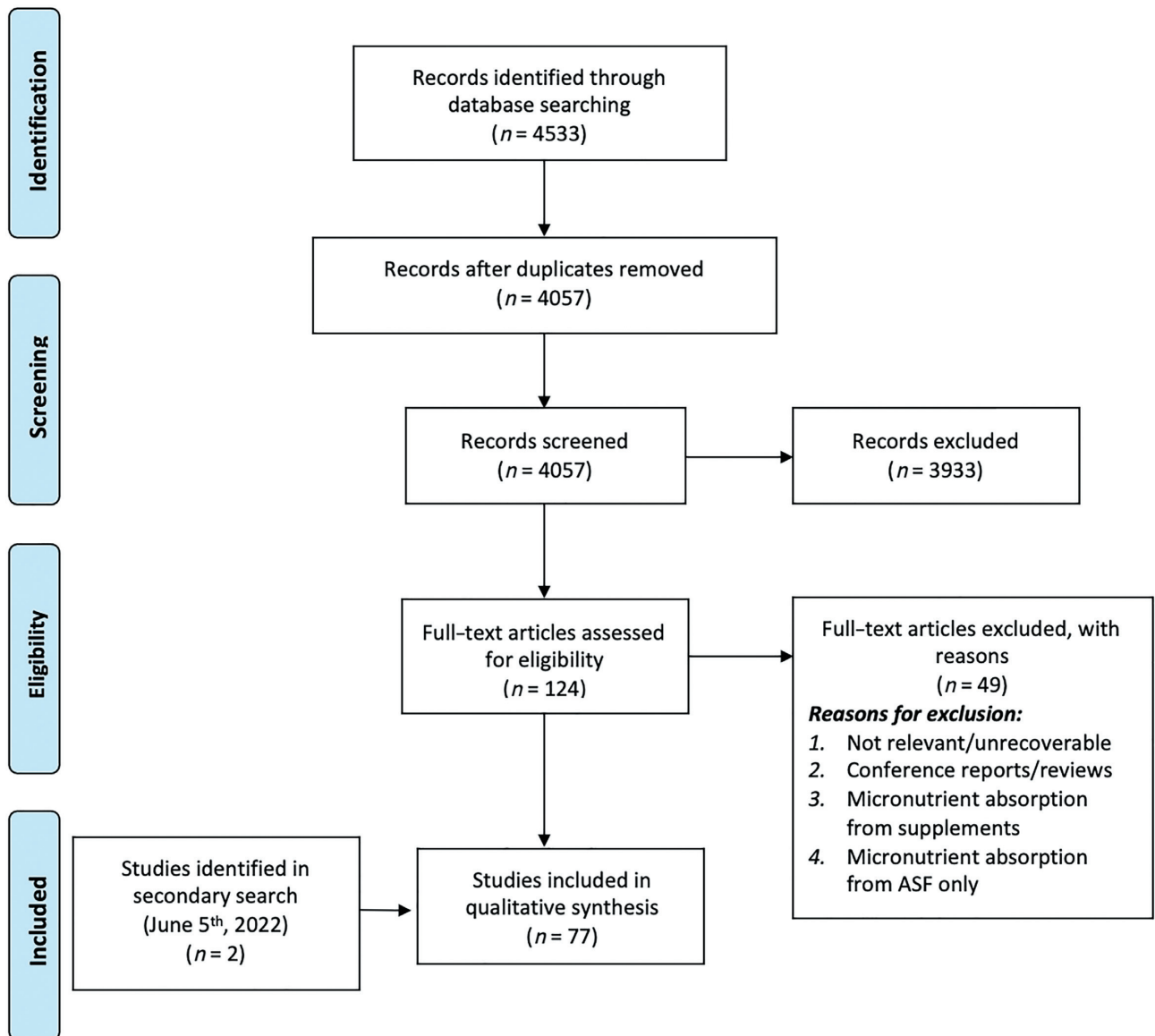
FIGURE 1 Schematic describing the search flow of the scoping review. The search flow was adapted from the Preferred Reporting Items for Systematic Reviews and Meta-Analyses 2009 statement. ASF, animal-source food.

these 77 interventions, 17 were conducted in countries in the global South.

Regarding the sex and age of the human study participants, 40 studies were conducted in adults aged >18 y, of which 21 involved both men and women, 15 involved women only, 3 involved men only, and 1 study didn't specify the sex of the participants. Four studies on men and women involved adults aged >18 y as well as adolescents older than 14 y.

Four studies were conducted in children: 1 was conducted in male and female infants aged 6 mo; 1 in male and female infants aged between 43 and 49 wk; 1 was conducted in boys and girls 4–8 y old; and 1 was conducted in girls 7–9 y old. Finally, 4 studies were conducted in male and female subjects of unspecified ages, and 1 study was conducted in subjects for whom age and sex were not specified.

Study methodology

The methodological characteristics of included publications are presented in **Table 2**.

The majority (92%) focused on assessing the effect of the meat factor on 1 micronutrient alone, whereas the remaining publications assessed changes in absorption of ≥2 micronutrients. Iron was the micronutrient most investigated across publications (78%), followed by zinc (23%), calcium (8%), phosphorus (4%), magnesium (4%), and, finally, manganese (1%). Regarding the methodology used to assess the absorption of investigated micronutrients, extrinsic labeling of the meal with radioisotopes was the most used across studies (53%). This was followed by extrinsic labeling with stable isotopes (12%), the assessment of apparent absorption (10%), intrinsic labeling with radioisotopes (8%), and hemoglobin

TABLE 1 Description of the main characteristics of publications assessing the effect on micronutrient absorption of adding animal-source foods to a plant-based meal

Study characteristics	Intervention details	Studies, n (% of total of 77)
Subjects	Studies in humans	52 (68)
	Studies in animal model	24 (31)
	Studies in humans and animal models	1 (1)
Publication date	1968–2000	52 (68)
	2000–2017	25 (32)
Study country	USA	29 (38)
	Sweden	11 (14)
	Spain	7 (9)
	Denmark	6 (8)
	Venezuela	6 (8)
	United Kingdom	3 (4)
	China	2 (3)
	Switzerland	2 (3)
	Philippines	2 (3)
	Benin	1 (1)
	India	1 (1)
	Japan	1 (1)
	Myanmar	1 (1)
	South Korea	1 (1)
	Thailand	1 (1)
	Tunisia	1 (1)
Multicountry studies	Sweden and Thailand	1 (1)
	Brazil, Chile, Mexico, Argentina, Peru, and Venezuela	1 (1)
Age and sex of human participants	>18 y old	40 (52)
	Male and female	21 (27)
	Female	15 (19)
	Male	3 (4)
	Not specified	1 (1)
	>14 y old	4 (5)
	Male and female	
	7–9 y old	1 (1)
	Female	
	4–8 y old	1 (1)
	Male and female	
	6–12 mo	2 (3)
	Male and female	
	Not specified	4 (5)
	Male and female	
	Not specified	1 (1)
	Not specified	

regeneration efficiency (for the assessment of iron only, 6%). Other assessments used less frequently were relative biological value for studies assessing iron, dual extrinsic and intrinsic labeling with radioisotopes, gastric intubation of FeSO$_4$, and atomic absorption spectrometry.

The ASF content of the meal varied widely across studies, with slightly more than half of the publications (53%) testing the effect of adding only 1 source of ASF, and the remaining testing >1 source. The most studied ASF ($n = 51$) class was red meat, considered as either beef, veal, pork, or lamb; this was followed by dairy products and eggs ($n = 31$), fish and seafood ($n = 28$), ASF fractions ($n = 19$), poultry ($n = 17$), and meat of unspecified origin ($n = 5$). ASF fractions considered were either derived from protein fractions (egg white protein, casein, casein phosphopeptides,

cysteine, beef extracts, amino acids, glutathione and histidine, methionine and lactalbumin, pork proteins, anchovy-derived protein fractions) or other tissue fractions [L-α-glycerophosphocholine, sardine oil, anchovy-derived lipid fractions, L-α-phosphatidylcholine, chondroitin sulfate (CS), hyaluronic acid (HA), beef tallow, heme concentrate].

The full list of outcomes as extracted in the data charting form is presented in **Supplemental Table 3**.

Animal model results

Of the 25 animal studies included, 17 publications showed that the addition of ASFs to the meal had an enhancing effect on micronutrient absorption. Of these, 13 were studies on iron, 4 were zinc studies, and 1 study was on phosphorus and calcium. Of the remaining publications, 5 showed no

TABLE 2 Description of the main methodological characteristics of publications assessing the effect on micronutrient absorption of adding ASFs to a plant-based meal[1]

Methodological characteristics	Intervention details	Studies, n (% of total of 77)
Number of micronutrients tested	One micronutrient	71 (92)
	Two or more micronutrients	6 (8)
Micronutrients assessed	Iron	60 (78)
	Human	42 (55)
	Animal	17 (22)
	Both	1 (1)
	Zinc	18 (23)
	Human	11 (14)
	Animal	7 (9)
	Calcium	6 (8)
	Human	3 (4)
	Animal	3 (4)
	Phosphorus	3 (4)
	Human	1 (1)
	Animal	2 (3)
	Magnesium	3 (4)
	Human	1 (1)
	Animal	2 (3)
	Manganese	1 (1)
	Human	
Assessment methodology	Extrinsic labeling with radioisotopes	40 (53)
	Extrinsic labeling with stable isotopes	9 (12)
	Apparent absorption	8 (10)
	Intrinsic labeling with radioisotopes	6 (8)
	HRE (iron only)	5 (6)
	RBV	3 (4)
	Intrinsic and extrinsic labeling with radioisotopes	2 (3)
	Gastric intubation of $FeSO_4$	2 (3)
	Atomic absorption spectrometry	2 (3)
ASF content of meal	One source of ASF	41 (53)
	Two or more sources of ASF	36 (47)
Type of ASF in meal	Red meat	51 (66)
	Dairy products and eggs	31 (41)
	Fish and seafood	28 (37)
	ASF fractions	19 (25)
	Poultry	17 (23)
	Unspecified meat	5 (7)

[1] ASF, animal-source food; HRE, hemoglobin regeneration efficiency; RBV, relative biological value.

significant impact of ASFs on micronutrient absorption [3 studies adding ground beef (32–34), 1 casein (35), and 1 egg white (36)] and 2 studies showed a negative impact on absorption of micronutrients, in 1 case when casein was compared with soy protein (37), and in the other case when fish was substituted for casein (38).

Human study results

Of 33 publications assessing the impact of adding muscle tissue to a single meal, 31 found a positive impact on absorption of iron and zinc from the meal. The lowest recorded quantities of muscle tissue necessary for the enhancing effect were 40 g fish [raw weight before cooking (39)] and 17 g cooked bacon (40). No clear indication emerged that the addition of milk products or eggs has an enhancing effect on micronutrient absorption from a meal. Two studies on zinc absorption indicated that the addition of protein from milk and eggs can enhance absorption (16, 41), as did 1 study on the enhancing effect on iron absorption when a spray-dried milk formula was compared with a soy-based formula (42); however, most studies demonstrated either a null effect or a reduction in absorption of both zinc and iron.

Of 3 studies assessing zinc absorption from overall diets varying in meat quantity (0–289 g/d), only 1 found an increase in zinc absorption when subjects consumed 184 g meat/d, compared with subjects consuming a vegetarian diet (43). Similarly, the only study assessing calcium absorption from an overall diet showed no significant differences between soy-based and meat-based diets (26).

In contrast, 5 studies (22, 44–47) showed a higher enhancement of iron absorption when diets contained greater quantities of meat ($\leq$294 g/d) compared with little to no meat (0–54 g/d), whereas 1 study showed no effect (48).

ASF fractions

Results trying to identify the meat factor vary widely based on the ASF fraction examined. The most examined ASF fractions derived from the protein fraction of muscle tissues. When protein fractions and the full spectrum of amino acids from pork, beef, poultry, and fish were tested, they led to an increased iron absorption, in both animal models and human subjects [15, 21, 25, 49, 50]. Moreover, studies assessed the effect of single amino acids representative of these food groups to further investigate the nature of the meat factor. The most commonly investigated amino acid was cysteine, with 3 studies indicating an enhancement of iron absorption [51–53], and 1 study indicating an enhancement of zinc absorption when added to rats' meals in addition to methionine or if double the quantity was supplemented [54]. One publication also found that glutathione, but not histidine, enhanced iron absorption in humans [52]. One publication conducted in infants aged 6 mo [31] investigated the potential role of heme in the meat factor by adding 2.5 mg heme concentrate to a commercial weaning food given to 6-mo-old infants. This, however, did not result in an improvement in nonheme iron absorption from the meal.

The lipid fraction from anchovies was tested in rats and increased iron absorption noticeably [55], as did sardine oil [56, 57]. When lipid fractions from raw sardines were compared with lipid fractions from fried sardines, only the raw sardines induced an increase in zinc, phosphorus, and calcium absorption [58, 59].

Other ASF fractions tested were casein, glycosaminoglycans (HA and CS), and choline. Whereas casein had a null effect on zinc, magnesium, and calcium in 1 rat study [35], the addition of 1 and 2 g casein phosphopeptide increased zinc absorption from a rice-based gruel in adult human subjects [60].

Choline was tested in 2 studies, which showed enhanced iron absorption in rats consuming anchovy-derived L-α-phosphatidylcholine [55] and in humans consuming L-α-glycerophosphocholine in quantities present in a medium portion of beef (46 mg) [61].

Anchovy-derived CS did increase iron absorption in rats [55]; however, CS and a sodium salt of HA did not increase iron absorption in humans [62].

Discussion

This scoping review set out to provide an overview of all the published literature and identify current gaps in the knowledge on the meat factor. To our knowledge, this is the first attempt at systematically summarizing the knowledge available on the present topic.

Overall results indicate there is strong evidence for ASFs, in particular muscle tissue, having an enhancing effect on iron and zinc absorption from a plant-based meal. Although the present review has not identified a single food component responsible for this increased uptake, it has been suggested that peptides, phospholipids, and mucopolysaccharides released during digestion of muscle tissue contribute in facilitating iron uptake by mediating the formation

of readily absorbable ferric oxohydrate nanoparticles [55]. Publications identified suggest the enhancement in nonheme iron absorption is not at all influenced by the presence of heme in the muscle tissue. Indeed, adding heme concentrate or hemoglobin directly to the meal did not significantly enhance nonheme iron absorption [24, 31]. On the contrary, heme-free beef and heme-free chicken protein maintained the enhancing effect on nonheme iron absorption [30, 50]. In our review we could not identify a mechanism through which the meat factor could enhance zinc absorption. However, the evidence synthesized herein indicates that zinc absorption is enhanced in meals containing the same amount of protein and zinc, even in low-phytate-containing meals, when muscle tissue is added, suggesting that the difference in absorption is likely attributable to the protein source [63].

The amount of added muscle tissue necessary to obtain the "meat factor" effect from a single meal appears to be relatively low (from a Western diet perspective), with amounts as low as 40 g fish [based on raw edible parts [39]] and 17 g cooked bacon [40] being identified. This could be advantageous for communities with low incomes and lack of access to ASFs; however, some of the identified publications suggest that higher quantities of muscle tissue consumption could be even more beneficial [22].

In contrast, evidence for the effect of ASFs on phosphorus, calcium, magnesium, and manganese absorption from plant-based meals is weak, because too few studies have investigated these micronutrients, and results are inconclusive. Assessments of the potential of the meat factor to enhance the absorption of micronutrients other than those mentioned in the present review are lacking. The presence and consequent absorption of trace elements such as iodine and selenium in plant-based foods, whose deficiency rates are extremely widespread [64, 65], are mostly dependent on regional soil content [66], and are therefore unlikely to be affected by the meat factor. However, gaps in the literature might warrant further investigation into the role of the meat factor for relevant micronutrients for which evidence is limited or lacking completely.

Whether dairy and egg products can enhance micronutrient absorption from meals is also uncertain. Studies included in the present review show mixed results, and published data indicate that casein varies in its ability to bind calcium, iron, and zinc, thus impacting absorption [67], and that egg yolk proteins can inhibit iron, calcium, and magnesium absorption [68].

Knowledge gaps

The present scoping review has identified several knowledge gaps that must be addressed in future research. Firstly, the majority of studies conducted on the meat factor date back to before the year 2000. This is significant because the majority of studies in this period were conducted using the extrinsic labeling with radioisotopes method, which for ethical concerns cannot be used in vulnerable populations, such as children and pregnant or lactating women. Because the stable isotope technique, which can be safely applied in

these populations, was introduced into nutrition science only starting from the 1990s ([69]), evidence is currently lacking on the impact of the meat factor in children and pregnant and lactating women, who are the populations who could arguably benefit the most from interventions to address MNDs ([4]).

Secondly, the review highlights the lack of studies assessing the meat factor in overall diets, which is an important element to consider when assessing the magnitude of effect of nutritional interventions. This is further complicated by the fact that the evidence has a strong bias toward Western countries in terms of geographical representation, where ASF consumption is higher ([70]). This can, in turn, lead to limited evidence on the effect of adding small amounts of ASFs to more predominantly plant-based diets that could contain varied amounts of uptake inhibitors, such as phytate, or promoters. Indeed, whereas some of the highlighted evidence suggests 40 g ASF is sufficient to benefit from the meat factor ([39]), the higher baseline consumption of Western countries could, in fact, mask benefits from even lower portions.

Thirdly, this review highlights that most of the included evidence focused on assessing the meat factor from red meat. The first studies to demonstrate the meat factor also included fish in their investigation ([21]); however, later studies shifted the focus mostly to red meat, likely driven by the consumption patterns of the countries in which the studies were conducted. Although it is clear that red meat is common among many households, especially in countries that most represent the available evidence ([70]), emerging environmental and health concerns ([1]) suggest that future research should place more focus on other ASFs, such as poultry, fish, and other aquatic foods. Fish and pelagic small fish are nutrient-dense ASFs suited to address micronutrient deficiencies in an economically accessible ([71]) way and with substantial possibilities for an environmentally sustainable scale-up of aquaculture activity ([72]). Aquatic ASFs can also have the co-benefit of helping reduce, or in part attenuate, the consumption of red and processed meat ([14]). Furthermore, the evidence highlighted in this review indicates that consuming fish with a plant-based meal has similar benefits to red meat in terms of the meat factor, therefore highlighting that fish and small fish can be a sustainable alternative for ASF inclusion into the diet.

Finally, given the importance of processed (sun-dried, smoked, etc.) fish in diets in low-resource areas and the role of food processing for the reduction of food loss ([73]), especially in countries with less access to cold-chain storage and transport ([74]), it is fundamental that future research investigates the impact of common forms of ASF processing, and specifically fish processing, on the magnitude of effect of the meat factor.

Strengths and limitations

This scoping review strived to be as transparent as possible throughout the entire process, by following the framework outlined by Chapter 11 of the Joanna Briggs Institute Reviewer's Manual ([27]) for conducting scoping reviews and the PRISMA-ScR guidelines ([28]).

The search strategy was developed to systematically identify all available literature on the topic, and despite efforts to be as comprehensive as possible, this review was not designed to be exhaustive, although the screening of randomly selected reference lists resulted in no new findings and the secondary search to expand inclusion to heme's involvement resulted in only 2 new inclusions, thus increasing confidence that most publications have been identified.

This scoping review also presents several limitations. Firstly, the heterogeneity of interventions complicated the definition of control conditions. As mentioned in the Methods section, leeway was given in selecting publications that included comparisons between groups and meals even when ASFs were present in both comparison conditions. This was followed by critical assessments of the results of each study when these conditions existed; however, this could have nonetheless impacted on the results. Secondly, some of the publications included contained several known inhibitors or enhancers of micronutrient absorption within the same meal as ASFs, and this could strongly impact overall magnitude of effect.

Finally, there are numerous complexities in measuring micronutrient absorption. Nonheme iron absorption, for example, is determined by iron status, presence of concomitant nutritional deficiencies, and presence of inflammation ([17]). On the other hand, zinc absorption is not determined by zinc status, but rather by zinc, protein, and phytate intake, as well as food processing and various physiological factors ([75]). Further, zinc lacks a validated gold standard biomarker for defining zinc status of individuals and populations ([76]).

Therefore, it is clear that all the above limitations play an important role in influencing the evidence available on the meat factor, and future research should focus on addressing these issues as much as possible.

Conclusions

In conclusion, this scoping review highlighted the role of ASFs in enhancing iron and zinc absorption from plant-based meals. These observations confirm previous findings that ASFs are an essential element to consider within the context of transforming food systems to tackle some of the most common micronutrient deficiencies in LMIC ([77]).

The EAT-*Lancet* Commission has highlighted important environmental and health concerns regarding the current food consumption patterns and food system outputs, and the resulting reference diet emphasizes a mainly plant-based diet, with little-to-no quantities of ASFs ([1]). However, the micronutrient density of ASFs, their benefits for cognitive performance and linear growth, the high variability in their consumption across the globe, and the evidence on the meat factor highlighted here, suggest that although consumption patterns should mostly shift away from the overconsumption of red meat toward more sustainable forms of ASFs, such as fish and small fish, overall, the consumption of modest amounts of ASFs can be extremely beneficial. This

shift would result in a 2-fold benefit: on one side, LMIC would see an increase in absorption of micronutrients of critical importance; on the other side, high-income countries would benefit from a reduction of red and processed meat consumption while maintaining consumption of nutrient-dense foods, with consequent reductions in rates of noncommunicable diseases ([14]). However, it is important that this shift is adapted to context, with cultural aspects of diets and concern for all forms of sustainability (economic, social, and environmental) at the center ([78]–[80]).

Future research should build upon the evidence summarized in this review, possibly in low-resource settings, to investigate the role of economically accessible, environmentally sustainable, and healthy ASFs, in fresh and processed forms, to further investigate the meat factor and its potential for interventions in the communities that are most vulnerable.

Acknowledgments

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