Symbiosis

www.symbiosisonline.org
www.symbiosisonlinepublishing.com

Review article Journal of Nutritional Health & Food Science Open Access

The Unresolved Wonder on Contaminant Iron Bioavailability: The Way Forward

*Demeke Teklu

Lead Researcher, Oromia agricultural research institute, Ethiopia

Received: February 15, 2017; Accepted: March 31, 2017; Published: April 20, 2017

***Corresponding author:** *Demeke Teklu, Lead Researcher, Oromia agricultural research institute, P.O. Box 41064, Addiss Ababa/Ethiopia, Tel: +251913038068; Fax: +251464412942; E-mail: demeketeklu@yahoo.com**

Abstract

Human can ingest extrinsic iron either involuntarily or deliberately. Contaminant iron from different sources like soil, processing equipment etc. in foods may lead to overestimation of the satisfaction of iron requirement while iron deficiencies remain a widespread health problem. The principal objective of this article is to review the existing *invitro* and *invivo* studies on contaminant iron bioaccessibility and bioavailability. The majority of the research findings, in both cases *invitro* and *invivo*, that are reviewed under this article suggest that soil contamination/geophagy does not enhance iron status and may even lower it in some cases. However, the mechanisms and degree to which geophagic substances adsorb or inhibit iron absorption remain unclear and with these circumstances it would be difficult to conclude that geophagy interferes with iron absorption. Few articles suggest that contaminant iron from soil and processing equipment could be a good source of dietary iron and iron bioavailability could be possibly enhanced with the combined effect of contamination and processing more specifically fermentation. However, more *invivo* contaminant iron bioavailability studies using golden method "rat hemoglobin repletion efficiency" should be conducted before drawing any conclusion on contaminant iron bioavailability since it depends on multiple effects that could not be covered under any of *invitro* iron bioavailability/bioaccessibility tests.

Keywords: *bioaccessibilty; bioavailabilty; contaminant iron; invitro; invivo;*

Introduction

The high prevalence of iron deficiencies which accounts more than two billion people has several adverse effects on the population especially in developing countries, particularly on women and children [13, 44]. As a result anemia leads to impaired psychomotor development in infant, impaired educational performance of schoolchildren, reduce working capacity in adults, and increase prenatal morbidity in pregnancy [16]. Iron deficiencies anemia is common in populations whose diet is mostly composed of plant-based foods which are attributed to the low mineral content of plant-based foods, as well as to their high chelating agent contents [25, 20].

Iron contamination in diet could perhaps result from: soil contamination during postharvest handling mainly cereals due to the traditional trashing of crops on the ground particularly in developing countries, processing equipments, and/or rarely from water. Controversial nutritional benefits of contaminant iron from different sources have been reported in the realization of iron requirement. *Invitro* and *invivo* human studies provide the majority of data available at present. Bioaccessibilty and bioavailability tests for contaminant iron have been investigated since early 1960th suggesting divisive ideas. These ideas may lead to two extinct conclusions in turn which leads to harmful outcomes: for instance 1) if it is concluded that contaminant iron is not bioavailable while it is, the supplement of iron will be suggested. Thus, this may lead to limited growth of children, exposure to infection, and oxidative stress due to excessive iron intake [21, 27, 34]. 2) if it is concluded that contaminant iron is bioavailable while it is not, this may lead to overestimation of the satisfaction of iron requirement while iron deficiencies remain the problem. Therefore, it is imperative to consider more tangible investigation to clear up the dilemma and this article, thus, was initiated to review the known unknowns about contaminant iron bioavailability and to suggest the possible way forward.

Soil contamination as a source of iron in cereal based food

Humans ingest soil both deliberately as geophagia or geophagy and accidentally (consequent implications to their mineral nutrition) [3]. Thus following the encounter with digestive fluids, chemical elements can be solubilised from soils and are potentially available for absorption, the so-called bioaccessible soil content.

Since early 1960th different scholars suggest that the higher iron content of cereals like maize, wheat, teff is due to the soil contamination as a result of uncontrolled traditional threshing on the ground [5, 12]. Though these works had not been confidential since there was no control/reference, they were giving an important insight to the area for many scholars. According to Saturni *et al* and Umeta et al, teff is an excellent source of iron for most of the population in Ethiopia [33, 39]. However, some authors argue that teff's highest content of iron is due to soil contamination as a result of threshing the crop on the ground [1, 6, 10]. A significant proportion of the iron in the teff diets of Ethiopia is extrinsic to food, usually referred to as contaminant iron and the complete removal of extrinsic iron from teff is not possible [9, 39].

Iron contamination due to food processing

Plant material and extract

Other sources of extrinsic iron may be originated from equipment during food processing like milling, or from iron leaching from iron/steel pots into food during cooking and storage.

Iron content is significantly increased in *invitro* study from 2 to 7 mg/100g in the flour after milling [30]. In another recent study, increase in iron content ranging from 43 to 138% have been measured between maize grains and flours, which increased with milling intensity [15]. A study comparing the iron contents of rice flour and polished rice from the same Thai market show a difference in iron content of 28.6 mg/100 g, which was attributed to contamination of whish 60 % iron was metal particles originating from the miller as it was manifested by strong magnet [17].

According to Park and Brittin, the iron content of most foods cooked in stainless steel utensils can be higher than that of the same foods cooked in glassware [29]. Similarly, another study conducted in Ethiopia shows double-fold increases of iron in foods cooked in iron pots than in the same foods cooked in aluminum or clay pots [4]. What matters is not whether the source of iron is extrinsic or not, rather the point is what is the impact of this contaminant iron on iron status of an individual, which is left controversial yet.

Invitro contaminant iron bioavailability tests

A study conducted in Benin published in 2010 assesses the impact of different processing method and contaminant iron boiaccessibility on different maize based meal. Evaluation of iron bioaccessibility was performed by *invitro* enzymatic digestion followed by dialysis. Finally the researchers conclude that iron bioaccessibility in mawè and owo products showed that only a small part of the contaminant iron originating from the mill was available for absorption. However it appears that fermentation can greatly increase the amount of bioaccessible iron. Thus, combined effect of contamination and fermentation resulted in enhanced levels of iron potentially accessible for absorption and further *invivo* study were suggested by the authors [14]. However, another study which follows the same iron bioaccessibilty test from Burkina Faso, published in 2013 disagrees with the previous authors. The researcher's intention was to measure iron contamination levels in millet and sorghum after decortications and milling and to assess the bioaccessibility of contaminant iron. The bioaccessibility of contaminant iron was measured using *invitro* digestion followed by measurement of dialyzable, soluble and insoluble iron. At the end of the research phytate/iron molar ratios were lower in iron contaminated flours, suggesting an improvement in iron bioavailability. However, measurement of bioaccessibility in iron contaminated to (traditional food) showed that contaminant iron was mainly insoluble and thus not available for absorption and has poor nutritional interest [22].

Invitro digestion/Caco-2 cell model in which ferritin formation was used as an index of iron bioavailability were used in a study conducted in Zanzibar, Tanzania, and Uganda and published in 2013. The researcher were aimed at assessing the *invitro* iron bioavailability and the capacity of geophagic earths and clay minerals to inhibit dietary iron absorption using methods that better approximate human physiology. Authors, then, concluded that although geophagic earths have high iron concentrations compared to iron-rich foods, this iron is not bioavailable, and that some geophagic earths inhibit dietary iron absorption [35]. However, some authors, in contrast to the above authors, suggests that the fraction of iron mineral that is soluble in the gastrointestinal environment and available for absorption, after conducting more sophisticated studies of the iron content of geophagic earth using the *invitro* methods [19, 24, 36]. Hallberg and Bjrn-Rasmussen, also found that amount of iron absorbed increased from 0.14 to 0.18 mg or about 30% due to the contamination as it is calculated from the iron exchangeability of contaminated food [17]. These results show that contaminant iron can be a good dietary source of iron.

A study from England suggest geophagical soils consumed by ethnic Bengali communities were found a significant source of bioaccessible iron [2]. The consumption may be of benefit to the geophagist although with the quantities of soil that can be deliberately consumed. On the other hand, the absorption of elements into the human body following soil consumption can also be reduced attributable to; for example, the adsorptive properties of ingested earth materials that can lower bioaccessible concentrations. The sorption potential of some geophagical soils in lowering the bioaccessibility of copper, iron and zinc, although other materials were identified to be a source of calcium, magnesium and manganese that humans could potentially utilize [19].

Beside their limited number researches that are conducted on the bioavailability of contaminant iron in the diet, the *invitro* methods might be less appropriate to analyze bioavailability of contaminant iron in the diet. The actual absorption and utilization of iron for normal metabolic processes in human involves digestion (soluble/dialysable mineral), uptake (intestinal enterocytes), transport into the circulation and retention, utilization, storage. However, the *invitro* methods attempt to assimilate only one or two former processes and could not effectively predict bioavailability: This is because:

a.Dialysis or solubility technique - which is a two step digestion at simulated physiological conditions: gastric phase (pepsin, HCl, pH 2) and intestinal phase (pancreatic enzymes, bile acids, $NaHCO_3$, pH 7) measure the soluble or dialysable minerals. This technique can be useful to identify enhancers , inhibitors, (phytate and degradation products, polyphenols, ascorbic acid) but does not predict same magnitude of response as in humans; since A) small polyphenolic compounds and organic acid complexes is dialysable but not bioavailable, B) large molecules like ferritin can be absorbed but is not dialyzable.

b.Caco-2 cell model – which involve two-step *invitro* digestion simulating gastric phase, intestinal phase, uptake/absorption measured as ferritin formation in Caco-2 cells after 22 hours and partial transport into circulation. The model is quit better as compared to the dialysis/solubility technique but not far enough compatible with the magnitude of response in humans as the model assume ferritin formation proportional to iron uptake and does not include hepcidin controlled transport, uptake is only considered for cell but not blood. Duizer et al., also indicate that caco-2 cells are colon cells – transport rates of hydrophilic compounds paracellular lower, less leaky, less discrimination on the basis of molecular size of compounds transported parallellary compared to duodenum cells [11]. Therefore, the model can be an excellent predictor of direction of response but not magnitude of response in human.

c.Absorption prediction algorithm–which involves the prediction of iron bioavailability in the meal based on the calculation of heme and non-heme iron composition and their bioavailability, balanced factors that enhance or inhibit the iron absorption. According to Reddy, the model is inaccurate for quantitative measurement since all factors effect are assumed to be independent and additive rather than interactive [31]. Knowledge about the exact amount of contaminant iron and its bioavailability in soil contaminated foods may be a prerequisite for proper interpretation of algorithm to predict absorption unless the prediction only apply to intrinsic iron [9].

d.Phytic acid/Mineral molar ratio – which involve the calculation of molar ratio of phytic acid to iron. The model is not the sufficient indicator of iron bioavailability since it only based on the inhibition effect of phytic acid while there are other factors like tannin, calcium, fiber etc which can possibly inhibit iron absorption. According to Baye et al., [9] knowing the exact amount of contaminant iron and its bioavailability in soil contaminated cereal foods may be a prerequisite for use of phytic acid/iron molar ratio to correctly predict bioavailability in food containing contaminant iron.

Invivo contaminant iron bioavailability studies

Invivo studies which have used human as a study subjects have investigated the effect of geophagy on iron absorption using Turkish, Texan, and South African geophagic earth. Minnich et al., have been studied the effect of geophagy on iron absorption on 31 healthy and iron deficient human subjects [28]. Even though the researchers investigated that Turkish geophagic earth effectively blocks iron absorption, they suggest that the effect of clay and soil on iron absorption may not be the sole factor in time of anemia production. Nutritional and parasitic factors are usually involved as well. Another study from the same country which was conducted on 12 patients who are between 8 and 21 years of age, with iron deficiency anemia and geophagia. Then, decreased iron absorption was detected respectively in the patients against the elevated absorption curves in control subjects [8]. However, a study from USA, Texas which was conducted on 27 healthy human subjects and 5 patients deficient in iron concludes that pica does not impair iron absorption [38]. Although these studies have a number of limitations, including outdated methods, very small sample sizes, unblocked confounding factors, and inadequate statistical analyses, they represent the only available *invivo* data [35, 41].

In vivo iron bioavailability assessment methods

Human and animal trial are used to evaluate the iron bioavailability and considered as a golden standards. Determining the iron bioavailability in human is complicated by the fact that once a food is consumed, it mixes with in the gastrointestinal tract with the other foods that are consumed at about the same time or may be because the iron is present in a mixture of sources available in the diet. Moreover, human iron bioavailability study is cumbersome, complicated, costly and time consuming to perform [7, 23]. Despite human trial, animal hemoglobin repletion bioassay is good for efficacy study because their environment condition can be controlled properly and the most common method in use [43]. However, animal bioavailability studies have limitations because of different iron requirements, metabolism, digestive capacity, sensitivity to iron absorption inhibitors and promoters as compared to human [7]. Despite this fact rat hemoglobin repletion efficiency has been used for determining the relative biological values of iron by numerous scholars for the last three decades [7, 26, 32, 31, 40, 42]. Moreover, the study which compared *in vitro,* animal and clinical determination of iron bioavailability suggest that rat hemoglobin depletion-repletion model serves as the most reliable predictor of iron bioavailability in human (Forbes *et al.,* 1989).

Conclusion

The majority of the studies (in both cases *invitro* and *invivo*) that are reviewed under this article suggest that soil contamination/geophagy does not enhance iron status and may even lower it in some cases. However, the mechanisms and degree to which geophagic substances adsorb or inhibit iron absorption remain unclear. Thus, with these circumstances it would be difficult to conclude that geophagy interferes with iron absorption. Few articles suggest that contaminant iron could be a good source of dietary iron and iron bioavailability which could possibly be enhanced by the combined effect of contamination and processing more specifically fermentation. However, results from *invitro* studies must always be confirmed by *invivo* and more *invivo* contaminant iron bioavailability test using golden method “Rat Hemoglobin Repletion Efficiency” before drawing any conclusion on contaminant iron bioavailability; since it depends on multiple effects that could not be entirely addressed under any of the *invitro* iron bioavailability/bioaccessibility tests.

References

1. Abebe Y, Bogale A, Hambidge k, Stoecker B, Bailey K, Gibson R. Phytate, Zink, iron and calcium content of selected raw and prepared foods consumed in rural Sidamo, Southern Ethiopia, abd implication for bioavailability. Journal of food composition and analysis. 2007;20(3):161-168.
2. Abrahams W, Follansbee H, Hunt A, Smith B, Wragg J. Iron nutrition and possible lead toxicity: an appraisal of geophagy undertaken by pregnant women of UK Asian communities. Appl Geochem.

2006;21(1):98–108.

3. Abrahams W. Involuntary soil ingestion and geophagia: A source and sink of mineral nutrients and potentially harmful elements to consumers of earth materials. Appl Geochem. 2012;27(5):954–968.

4. Adish A, Esrey S, Gyorkos T, Jean-Baptiste J, Rojhani A. Effect of consumption of food cooked in iron pots on iron status and growth of young children: a randomized trial. J.-Lancet. 1999;353(9154):712-716.

5. Almgard G. High content of iron in teff, Eragrostis abyssinica Link., and some other crop species from Ethiopia-a result of contamination. Lantbrukshogskolans Annaler. 1963;29:215-220.

6. Ambaw A. Determination of iron fractions of laboratory and field threshed teff flour, fermented past and enjera: implication to iron bioavailability (Master's Thesis). Addis Ababa University, Center for food science and nutrition. 2013.

7. Aragon J, Ortiz D, Pachon H. Comparison between *invitro* and *invivo* methods to screen iron bioavailability. Journal of Food. 2012;10(2):103-111.

8. Arcasoy A, Çavdar A, Babacan E. Decreased Iron and Zinc Absorption in Turkish Children with Iron Deficiency and Geophagia. Acta Haematol. 1978;60(2):76–84.

9. Baye K, Mouquet-Rivier C, Icard-Verniere C, Picq C, Guyot J. Changes in mineral absorption inhibitor consequent to fermentation of Ethiopian enjera: implications for predicted iron bioavailability and bioaccessibility. International journal of food sience and technology. 2014;49(1):174-180. OI: 10.1111/ijfs.12295.

10. Bokhari F, Derbyshire E, Brennan C, Stojceska V. A study to establish whether food-based approaches can improve serum iron levels in child-bearing aged women. J Hum Nutr Diet. 2012;25(1):95-100. doi: 10.1111/j.1365-277X.2011.01185.x.

11. Duizer E, Penninks A, Stenhuis W, Groten J. Comparison of permeability characteristics of the human colonic Caco-2 and rat small intestinal IEC-18 cell lines. Journal of Controlled Release. 1997;49(1):39–49.

12. Ethiopia Nutrition Survey (ENS)(1959). A report by the Interdepartmental Committee on Nutrition for National Defense. CJFD 45 (26). Washington, D. C.

13. Gibson S. Zinc: The missing link in combating micronutrient malnutrition in developing countries. Proceedings of the Nutrition Society. 2006;65(1):51–60.

14. Greffeuille V, Mouquet-Rivier C, Icard-Verniere C, Ouattara L, Avallone S, Hounhouigan J, et al. Traditional recipe of millet-, sorghum-, and maize-based dishes and related sause frequently consumed by young children in Burkina Faso and Benin. INSTAPA, Europian Union's Seventh Fremwork Program, ISBN. 2010;978-90-8585-903-3.

15. Greffeuille V, Kayodé A, Icard-Vernière C, Gnimadi M, Rochett I, Mouquet-Rivier C. Changes in iron, zinc and chelating agents during traditional African processing of maize: effect of iron contamination on bioaccessibility. Food Chem. 2011;126(4):1800–1807. doi: 10.1016/j.foodchem.2010.12.087

16. Hall A, Bobrow E, Brooker S, Jukes M, Nokes K, Lambo J, et al. Anaemia in school children in eight countries in Africa and Asia. Public health nutrition. 2003;4(3):749-756.

17. Hallberg L, Björn-Rasmussen E. Measurement of iron absorption from meals contaminated with iron. Am J Clin Nutr. 1981;34(12):2808–2815.

18. Harvey W, Dexter B, Darnton-Hill L. The impact of consuming iron from non-food sources on iron status in developing countries. Public Health Nutrition. 2000;3(4):375-383.

19. Hooda P, Henry K, Seyoum T, Armstrong L, Fowler M. The potential impact of soil ingestion on human mineral nutrition. Sci Total Environ. 2004;333(1-3):75–87.

20. Hurrell R, Egli I. Iron bioavailability and dietary reference values. American Journal of Clinical Nutrition. 2010;91(5):1461S–1467. doi: 10.3945/ajcn.2010.28674F.

21. Iannotti L, Tielsch J, Black MM, Black RE. Iron supplementation in early childhood: Health benefits and risks. The American Journal of Clinical Nutrition. 2006;84(6):1261- 1276.

22. Icard-Verniere C, Hama F, Guyot J, Picq C, Diawara B, Mouquet-Rivier C. Iron contamination during in-field milling of millet and sorghum. J Agric Food Chem. 2013;61(43):10377-10383. DOI: 10.1021/jf402612k.

23. Ismail M. The use of Caco-2 cell as an *invitro* method to study bioavailability of iron. Mal J Nutr. 1999;5(1):31-45.

24. Kikouama J, Cornec F, Bouttier S, Launay A, Bald´e L, Yagoubi N. Evaluation of trace elements released by edible clays in physicochemically simulated physiological media. Int J Food Sci Nutr. 2009;60(2):130–142. DOI: 10.1080/09637480701614956.

25. Lonnerdal B. Dietary factors influencing zinc absorption. Journal of Nutrition. 2000;130(5S Suppl):1378S–1383.

26. Lucia D, Toste V, Silveria M, Bordalo A, Roddrigues C, Ana P, et al. Iron bioavailability in Wistar rat fed with fortified rice with Ultra Rice R technology with or without addition of yacon flour (Smallanthus Sonchiflolius). Archivos LatinoAmericanos De Nutricion. 2013;63(1):64-73.

27. Majudar, Paul P, Talib V, Ranga S. The effect of iron therapy on the growth of iron-replete and iron deplete children. Journal of Tropical Pediatrics. 2003;49(2):84-88.

28. Minnich V, Okuolu A, Tarkon Y, Arcasoy A, Cin S, Yrucoglu O, et al. Pica in Turkey II. Effect of Clay upon Iron Absorption. American Journal of Clinical Nutrition. 1968;21(1):78-86.

29. Park J, Brittin H. Increased iron content of food due to stainless steel cookware. J Am Diet Assoc. 1997;97(6):659–661.

30. Prabhavathi T, Narasinga B. Contaminant iron in foods and its bioavailability predicted by *invitro* method. Indian J Med Res. 1981;74:37–41.

31. Reddy M. Algorithm to assess non-heme iron bioavailability. Int J Vitam Nutr Res. 2005;75(6):405-412. DOI: 10.1024/0300-9831.75.6.405

32. Rohner F, Ernst F, Arnold M, Hilbe M, Biebinger R, Ehrensperger F, et al. Synthesis, characterization and bioavailability in rats of ferric phosphate nanoparticles. J Nutr. 2007;137(3):614-619.

33. Saturni L, Giannia F, Bacchetti T. The gluten-free Diet: Safety and National Quality. Nutrients. 2010;2(1):16-34. DOI:10.3390/nu2010016.

34. Sazawal S, Black R, Ramsan M, Chwaya HM, Stoltzfus RJ, Dutta A, et al. Effect of routine prophylactic supplementation with iron and folic acid on admission to hospital and mortality in preschool children in high malaria transmission setting: Community based, randomized, placebo-controlled trial. The lancet. 2006;367(9505):133-143.

35. Seim G, Ahn C, Bodi M, Luwedde F, Miller D, Hillier S, et al. Bioavailability of iron in geophagic earth and clay minerals and their effect on dietary iron absorption using in virto digestion/Caco-2 cell model. Food Funct. 2013;4(8):1263-1270. DOI: 10.1039/c3fo30380b.

36. Smith B, Rawlins B, Cordiero M, Hutchins M, J. V. Tiberindwa, L. Sserunjogi, et al. The bioaccessibility of essential and potentially toxic trace elements in tropical soils from geophagic earths. J Geol Soc. 2000;157:885–891. doi: 10.1144/jgs.157.4.885
37. Swain H, Newman M, Hunt R. Bioavailability of elemental iron powders to rat is less than Bakery-grade ferrous sulfate and predicted by iron solubility and particle surface area. J Nutr. 2001;133(11):3546-3552.
38. Talkington K, Gant N, E Scott D, Pritchard A. Effect of ingestion of starch and some clays on iron absorption. Am J Obstet Gynecol. 1970;108(1970):262–267.
39. Umeta M, West C, Fufa H. Content of Zinc, Iron, Calcium and their absorption inhibitors in foods commonly consumed in Ethiopia. Journal of food composition and analysis. 2005;18(8):803-817.
40. Urga K, Narasimha V, Sasikala V, Vishwanatha S. Bioavailability of iron and zinc from in rats. Bull Chem Soc Ethiop. 1998;12(2):95-103.
41. Young S. Pica in Pregnancy: New Ideas About an Old Condition. Annual Review of Nutrition. 2010;30:403-422. DOI: 10.1146/annurev.nutr.012809.104713.
42. Weber T, Freitas C, Amanco O, Mmorais M. Effect of dietary fiber mixture on growth and intestinal iron absorption in rats recovering from iron-deficiency anemia. British journal of nutrition. 2010;104(10):1471-1476. doi: 10.1017/S0007114510002497.
43. Wienk J, Marx J, Beynen C. The concept of iron bioavailability and its assessment. Eur J Nutr. 1999;38(2):51-75.
44. Zimmermann M, Hurrell F. Nutritional iron deficiency. Lancet. 2007;370(9586):511-520.