

Factors influencing the uptake of trace elements from the digestive tract

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Food tables or chemical analyses of duplicate food portions can at best give a value for total intake of trace elements for an individual or a population. However, for evaluation of the adequacy of trace element supply this information can be of limited value. Signs of zinc deficiency, for example, have been observed on diets providing 15–20 mg Zn/d (Halsted *et al.* 1972; Maleki, 1973) and 5–8 mg Zn/d (Krebs *et al.* 1984; Ross *et al.* 1986). In contrast to the major components of the diet, fat, carbohydrate and protein, only a fraction of most trace elements are absorbed from the digestive tract. Physiological factors and the chemical environment created by the food components and the intestinal secretions at the site of absorption influence the degree of trace element absorption from a diet. Our knowledge of these factors in relation to human trace-element absorption is still scarce, partly because of methodological difficulties in the study of mineral absorption in man.

Methodological considerations

The low degree of absorption, the intestine as the major route for excretion of most trace elements, and a slow intestinal transit in humans limits the use of conventional techniques, like chemical-balance studies, to identify individual factors influencing uptake of trace elements. It has, for example, been shown by Turnlund *et al.* (1982) that to get a complete collection of 1 day's Zn intake, the faecal samples needed can contain unabsorbed fractions of Zn derived from meals from 12 to 30 d before collection, as well as fractions of endogenous Zn excreted over the same period of time. Turnlund *et al.* (1986) have shown that the endogenous intestinal losses of Zn are of the same magnitude as the amount of Zn absorbed from the diet. The same is probably true for elements like copper and manganese. This can give values for apparent absorption of trace elements close to zero while the 'true' intestinal absorption can be as high as 30–40%.

With the use of isotopes, stable or radioactive, of the element of interest the degree of absorption can be determined with a much higher degree of accuracy than by using the balance technique. Stable-isotope techniques have been developed for Zn (Solomons *et al.* 1982; Turnlund *et al.* 1982), selenium (Janghorbani *et al.* 1981) and Cu (Turnlund *et al.* 1985). These techniques have the disadvantage that for most elements relatively high levels of the stable isotopes have to be added to the diet in order to achieve sufficient enrichment. This could influence the equilibrium between the native minerals of the diet and potential promoters or antagonists, and thus the degree of absorption. Radioisotopes with suitable γ -energy levels are available for iron, Zn, Se, chromium and Mn and, with access to a sensitive human whole-body counter, absorption from single composite meals can be determined by simple procedures. This allows systematic studies of factors that could influence absorption. The use of radioisotope techniques for food-mineral-absorption studies is best documented for Fe (Hallberg, 1980) and Zn (Arvidsson *et al.* 1978).

Physiological and endogenous factors

Knowledge of how physiological factors influence trace element uptake is limited. A significantly lower absorption of Zn from food in elderly men, 65–74 years, compared

with that of young men, 22–30 years, has been observed by Turnlund *et al.* (1986). Aamodt *et al.* (1983) also observed a declining absorption with age when a single dose of ^{65}Zn was given in the fasting state. This age effect could be due to a reduced digestive capacity or a response to a lower requirement for Zn, as indicated by smaller endogenous losses observed in the elderly men (Turnlund *et al.* 1986). The importance of an intact digestive capacity is well-documented for Fe. A lower food-Fe absorption has been reported after antrectomy and Billroth II partial gastrectomy (Magnusson, 1976), probably owing to an impaired gastric acid secretion. The relation between requirement and degree of absorption is also best known for Fe. Absorption from an aqueous reference dose of Fe is, in gastrectomized patients as well as in non-operated subjects, related to Fe stores determined by haemosiderin levels of bone-marrow smears (Magnusson, 1976). The large Fe requirement during late pregnancy is also to some extent met by a more efficient Fe absorption (Svanberg, 1975). To what extent the uptake of other trace elements is regulated by body need is not known. Findings for Zn (Turnlund *et al.* 1986) and Se (Levander & Morris, 1984) indicate that body homeostasis of these elements is regulated by excretion rather than by absorption. Despite the increased requirement for Zn during pregnancy no effect on Zn absorption compared with that in non-pregnant women has been observed (Swanson *et al.* 1983).

Dietary factors

Chemical form. The techniques used for analysing the trace element content of food, such as atomic absorption spectroscopy, usually require complete digestion of the samples. This gives no information about the chemical form(s) of the elements, which for some elements could affect the degree of absorption. The difference as regards absorption, between haem-Fe and other forms of Fe is a good example of this. Haem-Fe shows a high fractional uptake, more or less regardless of diet composition, while non-haem-Fe is strongly influenced by other components of the diet (Hallberg, 1982). A large supplement of Se (1 mg) in the form of selenate has been found to be absorbed better than Se as selenite (Thomson & Robinson, 1986). However, most trace elements are probably dissociated or in a soluble form at the low pH of the ventricle or during further digestion of the diet. The degree of absorption is then, to a large extent, influenced by the presence of other factors of the diet with a potential to act as promoters or antagonists of trace element absorption.

Fibre and phytic acid. Since the observations of Zn-responsive growth impairment on diets based on unleavened wholemeal bread (Ronaghy *et al.* 1974) the effect of unrefined cereals on trace element absorption has been a subject of great concern. The outer layers of grains and seeds contain not only the major part of most trace elements but also many substances that could influence trace element uptake, such as fibre, phytic acid and tannins. When purified fibre fractions have been used in mineral absorption studies no significant effect has been observed on absorption of Fe, Zn or Cu (Sandstead *et al.* 1978; Sandberg *et al.* 1983; Sandström *et al.* 1987b; Turnlund *et al.* 1984, 1985).

The strongest candidate for an antagonist of trace-element absorption from wholemeal bread is phytic acid (*myo*-inositol hexaphosphoric acid). Numerous studies have demonstrated an impairment of Zn absorption when phytate-rich diets have been given to animals (O'Dell & Savage, 1960; Davies & Olpin, 1979; Morris & Ellis, 1980; Forbes *et al.* 1984). Studies using stable or radioactive isotopes of Zn have confirmed that phytic acid can act as a strong antagonist for Zn absorption in humans. Addition of phytic acid to a low-fibre diet (Turnlund *et al.* 1984), to white bread to the levels found in wholemeal bread (Nävert *et al.* 1985) or to a cow's-milk-based infant formula to the level found in a soya-bean formula (Lönnerdal *et al.* 1984) reduced the absorption of Zn significantly

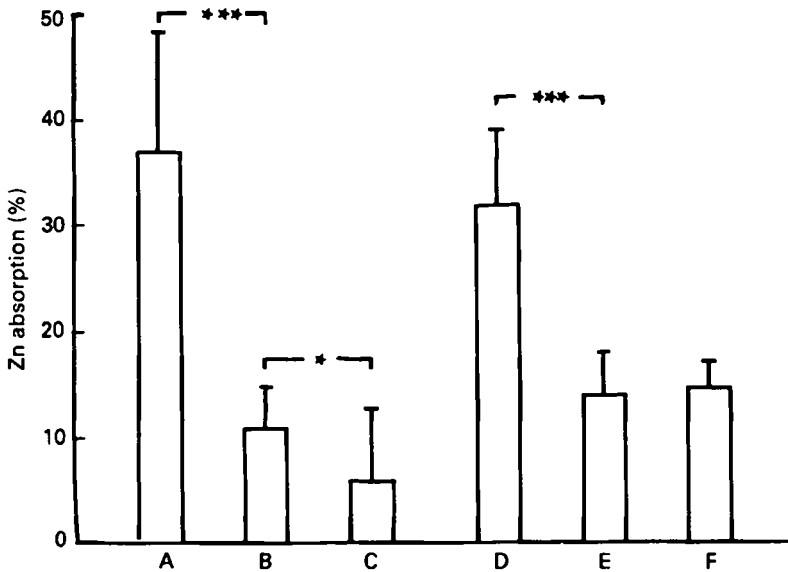


Fig. 1. The effect on zinc absorption of the addition of sodium phytate to white bread and a cow's-milk-based infant formula compared with the absorption found with wholemeal bread and soya-bean-protein infant formula. A, White bread; B, wholemeal bread; C, white bread + sodium phytate; D, cow's-milk formula; E, soya-bean-protein formula; F, cow's-milk formula + sodium phytate. Values are means, and standard deviations represented by vertical bars. Differences were statistically significant: * $P < 0.05$, *** $P < 0.001$.

(Fig. 1), while reduction of the phytic acid content of bran by leavening in bread significantly improved Zn absorption (Nävert *et al.* 1985). Recent studies of Fe absorption have shown that phytates are the main cause of an inhibitory effect of bran on Fe absorption (Hallberg *et al.* 1987). In contrast, phytic acid does not seem to influence Cu absorption (Turnlund *et al.* 1985) despite the observation *in vitro* that Cu has a higher tendency than Zn to complex with phytic acid (Vohra *et al.* 1965).

It is, however, possible that components of whole-grain cereals other than phytic acid could affect trace-element absorption. Studies of meals based on sorghum indicate that tannins are potential antagonists for Fe absorption (Gillooly *et al.* 1984). The presence of tannins is also the probable explanation for the strong negative effect of tea on non-haem-Fe absorption (Rossander *et al.* 1979).

Proteins. The protein source and amount have been found to influence the uptake of several trace elements. Formation of small peptides or free amino acids during digestion could render the trace elements more easily absorbed while, on the other hand, an incomplete protein digestion could bind or occlude trace elements and reduce absorption. Meat and fish proteins strongly stimulate Fe absorption (Björn-Rasmussen & Hallberg, 1979). Indications of a positive effect of protein on Se absorption have also been observed (Greger & Marcus, 1981). The chemical properties of the proteins are also a probable explanation for the less-efficient absorption of Zn from cow's milk and cow's milk- or soya-bean-protein-based infant formulas compared with that from human milk (Sandström *et al.* 1983a,b).

A nutritionally important effect of dietary protein is to counteract the inhibitory effect of phytic acid on Zn absorption. A reasonable intake of animal protein together with wholemeal bread improves Zn absorption to a similar degree as when the amount of phytic acid is reduced by long-time fermentation (Fig. 2).

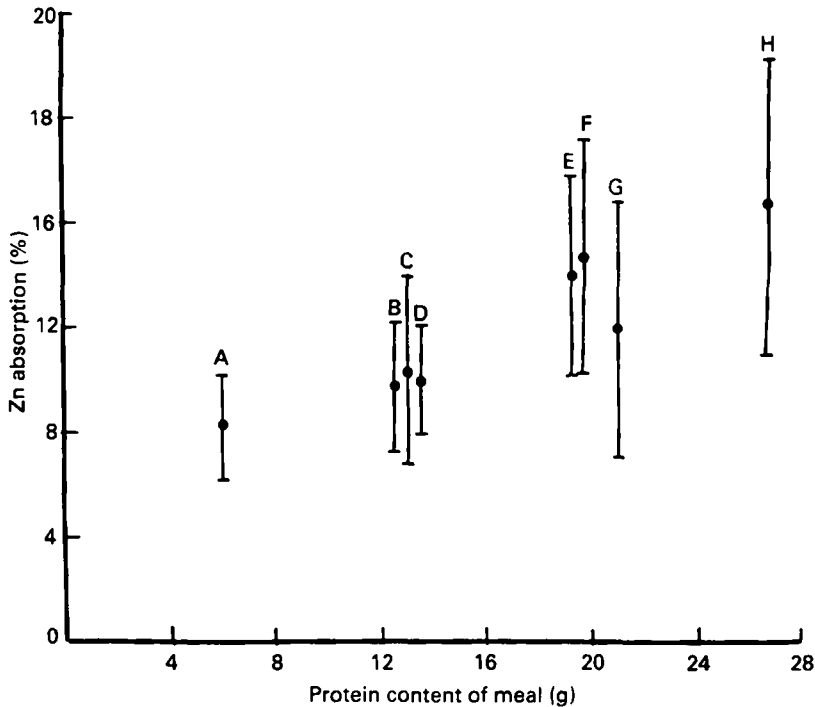


Fig. 2. The effect on zinc absorption of the addition of increasing amounts of animal-protein sources to wholemeal bread. The content of Zn was made similar in the meals by the addition of zinc chloride. A, Wholemeal bread; B, + milk; C, + beef; D, + egg; E, + milk and cheese; F, + egg and milk; G, + egg; H, + milk, cheese and casein. Values are means, and standard deviations represented by vertical bars. A significant correlation ($P < 0.05$) between protein content of the meal and Zn absorption was observed.

Ascorbic acid. Ascorbic acid is known to be a potent promotor of non-haem-Fe absorption (Hallberg *et al.* 1986). The effect is dose-dependent over a large range of intakes and similar with ascorbic acid-rich foods as with ascorbic acid supplements. Its effect is believed to be due to its reducing potential and it is unlikely that ascorbic acid affects ions not prone to change valency. This lack of effect has been confirmed for Zn (Solomons *et al.* 1979; Sandström & Cederblad, 1987).

A negative effect of ascorbic acid on absorption of Se has been suggested from observations of a reduction of selenite to elemental Se in parenteral solutions in the presence of ascorbic acid (Shils & Levander, 1982). However, ascorbic acid does not seem to affect selenate absorption as determined by changes in plasma Se levels (Mutanen & Mykkänen, 1985). Neither was selenite absorption influenced by simultaneous intake of orange juice, while mixing of selenite and ascorbic acid 2 h before intake seemed to reduce Se absorption to almost zero (Robinson *et al.* 1985).

Mineral-mineral interactions. Similarities in chemical properties might lead to biological antagonism. The chemical basis for these interactions was outlined by Hill & Matrone (1970) and many of their hypotheses have later been confirmed in animal studies. Such similarities exist, for example, between Cu^+ and Zn^{2+} and between Fe^{3+} and Mn^{2+} . Pharmacological levels of Zn have been shown to interfere with Cu absorption and as Cu is necessary for Fe metabolism low Cu absorption may lead to anaemia (Patterson *et al.* 1985). A similar effect of high levels of Cu on Zn absorption have not been observed in man and at the levels found in human diets Cu has no effect on Zn absorption (Valberg *et al.* 1984). Interactions between Fe and Mn have been

confirmed in animal studies and in man (Thomson *et al.* 1971). High levels of tin, as can be found in foods kept in unlacquered cans, have been found to impair Zn absorption (Johnson *et al.* 1982; Valberg *et al.* 1984).

Competition at specific uptake sites or transport mechanisms has also been suggested for Fe and Zn (Solomons, 1986). In an aqueous system, high Fe levels impaired Zn absorption (Valberg *et al.* 1984; Sandström *et al.* 1985). However, inorganic Fe had no effect on Zn absorption from a composite meal (Fig. 3). It should be noted that, even at a Fe:Zn molar ratio of 25:1 in an aqueous solution, fractional Zn absorption is significantly higher than at the ratio of approximately 1:1 found in a normal composite meal. The mechanisms and pathways used for absorption from 'pure' aqueous solutions of trace elements may differ from those used when the trace elements are presented to the mucosa as a digested composite meal. Interactions observed in studies using trace-element solutions may not necessarily, therefore, be occurring at a normal dietary intake of trace elements. Haschke *et al.* (1986) observed no effect of Fe content on Zn absorption from formula diets in balance studies in infants. The results suggested instead that the absorption of Cu was influenced by the Fe concentration.

Food processing. An important future research area is the effect of food processing and preparation on trace-element absorption. Differences in Zn availability from soya-bean proteins depending on the method of processing have been observed in rats (Ketelsen *et al.* 1984). Extrusion cooking of a bran product reduced the apparent absorption of Zn in ileostomy subjects (Kivistö *et al.* 1986). A lower Zn absorption from toasted cornflakes compared with cooked corn grits was observed by Lykken *et al.* (1986) and attributed to heating- and toasting-reaction-products binding Zn. In contrast, studies in rats indicate that the absorption of Zn from maize can be improved by extrusion cooking (Fairweather-Tait & Symss, 1985).

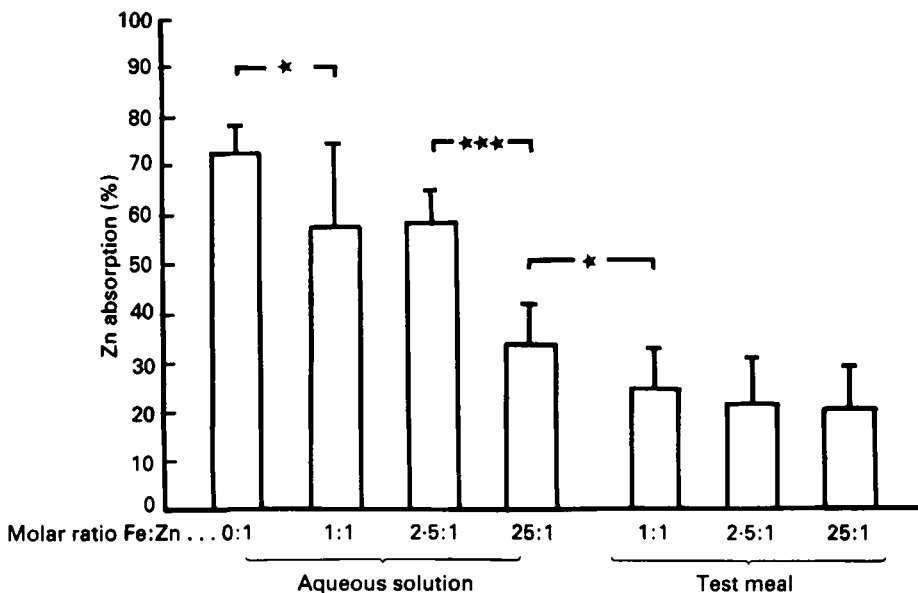


Fig. 3. The effects on zinc absorption of increasing iron content of an aqueous solution, or a test meal containing 40 μmol Zn. Values are means, and standard deviations represented by vertical bars. Differences were statistically significant: * $P < 0.05$, *** $P < 0.001$.

Implications for dietary evaluation

Present knowledge hardly allows a prediction of the degree of absorption of trace elements from a certain diet. A rough estimate can be made for Fe based on the intake of haem-Fe and non-haem-Fe and the amount of meat and ascorbic acid in the diet (Monsen *et al.* 1978). For Zn, the molar ratio of phytic acid:Zn has been suggested as an index of Zn absorption (Oberleas & Harland, 1981). However, as is obvious from Fig. 2, where all meals had the same ratio, as well as from Zn absorption studies from soya-bean-protein meals (Sandström *et al.* 1987a), this ratio can at best be used to compare meals with otherwise similar nutrient compositions.

It is also important to notice that the effects of dietary components on trace-element absorption are related to each individual meal. A high intake of ascorbic acid for breakfast has no effect on Fe absorption from the dinner. Neither can the absorption of a trace element be evaluated for a single food, in case this food does not constitute the total or major component of a meal. For assessment of the adequacy of trace-element supply, it would therefore be valuable if information relating to food selection and meal types were reported, together with nutrient intake values, in dietary surveys.

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