

BIOAVAILABILITY OF MINERALS AND TRACE ELEMENTS

Members of EC Flair Concerted Action No. 10: Measurement of micronutrient absorption and status*

COMPILED BY: SUSAN FAIRWEATHER-TAIT,¹
AND RICHARD F. HURRELL²

¹Institute of Food Research, Norwich Laboratory, Norwich Research Park, Colney, Norwich NR4 7UA, UK

²Swiss Federal Institute of Technology Zurich, Laboratory for Human Nutrition, P.O. Box 474, 8803 Rüslikon, Switzerland

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* Contributors: P. van Dael, Lausanne, Switzerland (selenium); W. van Dokkum, Zeist, The Netherlands (manganese); V. Ducros, Grenoble, France (chromium); S. Fairweather-Tait, Norwich, UK (introduction and magnesium); R. F. Hurrell, Rüslikon, Switzerland (introduction and iron); K. Cashman and T. A. Flynn, Cork, Eire (calcium), A. Alegria, R. Barbéa, R. Farré and M. J. Largada, Valencia, Spain (copper); F. Macleod and B. A. McGaw, Aberdeen, UK (iodine); B. Sandström, Frederiksberg, Denmark (zinc).

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INTRODUCTION

Essentiality of inorganic elements is not always easy to prove (Underwood & Mertz, 1987), but those considered to be essential for normal body functions include (i) the major elements, sodium (Na), potassium (K), calcium (Ca), magnesium (Mg), phosphorus (P), and chloride (Cl), (ii) the trace elements, cobalt (Co), chromium (Cr), copper (Cu), iron (Fe), iodine (I), manganese (Mn), molybdenum (Mo), selenium (Se) and zinc (Zn), and (iii) the 'newer' trace elements, arsenic (As), lead (Pb), lithium (Li), nickel (Ni), silicon (Si),

vanadium (V), and possibly fluorine (F) and tin (Sn). Well defined dietary deficiencies have been described in humans for Ca, Fe, I, Se and Zn, and, under special dietary circumstances such as total parenteral nutrition, for Mg, Cr, Cu and Mn. Deficiencies in Co may also occur but only in relation to deficiencies in vitamin B₁₂ of which Co is an integral part.

The bioavailability of a mineral or trace element is defined as the fraction of the ingested nutrient that is absorbed and subsequently utilized for normal physiological functions. For some of the elements this is the incorporation into various metalloproteins, such as Fe in haemoglobin. In addition, some elements, such as Ca and Mg, have a structural role in bones and teeth. Most elements are an integral part of a wide range of enzyme systems, for example Se in glutathione peroxidase. Earlier work suggesting that Cr (as glucose tolerance factor) potentiates the action of insulin has yet to be confirmed.

Physiological requirements for different inorganic nutrients vary widely, depending upon age, sex, stage of growth, pregnancy, and lactation. Dietary requirements are calculated from physiological requirements and efficiency of absorption from the diet, which ranges from less than 1% to almost 100%. The variation depends on dietary and host-related factors, including the amount of the element consumed.

Some inorganic nutrients, including Ca, Mg, Cu, I and Se, are relatively well absorbed, with reported fractional absorption values from mixed diets in man varying from 30% for Ca to almost 100% for I. Homeostatic mechanisms operate whereby absorption is up- or down-regulated when the supply of an element is limiting or excessive. When the amount of element absorbed is greater than immediate requirements, the excess is either stored in the body (e.g. iron in the liver), excreted in the urine (e.g. Ca) or excreted *via* gastrointestinal secretions or intestinal mucosal cells (e.g. Zn, Cu). Less well absorbed trace elements include Fe, Zn, Mn and Cr, with absorption varying widely according to the nutritional status (including body stores) of the individual and the composition of the diet. Typical mean values for absorption from individual foods for Zn are 10–50%, and for Fe < 1–30%. The fractional absorption of Mn and Cr may be less than 5%.

Dietary components greatly influence the absorption of most of the nutritionally important trace elements and minerals, with the exception perhaps of Se and I. The utilization of I by the thyroid, however, can be impeded by goitrogenic substances such as thiocyanate. Minor plant constituents, such as phytic acid and phenolics, can have a strongly inhibitory effect on absorption, peptide digestion products from dietary proteins can enhance or inhibit absorption depending on their nature, and there are several mineral–mineral interactions. Dietary components appear to have the greatest effect on the absorption of Fe and Zn, and consequently many human bioavailability studies have been made on these elements. Some elements, such as Mg, Cu, I and Se, are less well studied in man and clearly need further investigation.

In this review a brief summary will be given of the food sources, absorptive mechanism and subsequent metabolism of the nine minerals and trace elements identified as being nutritionally important. Physiological and dietary factors which influence their bioavailability in man are then discussed in more detail, and animal studies referred to only in the absence of data from human studies.

CALCIUM

FOOD SOURCES

Milk and milk products are the most important dietary sources of Ca followed by cereal products and fruits and vegetables (British Nutrition Foundation, 1989; National Research Council, 1989). Tinned fish, such as sardines, are rich sources of Ca but do not make a

significant contribution to intake for most people. Foods of plant origin are not particularly good sources of Ca, but the growing number of Ca fortified products is leading to a wider range of rich dietary sources of Ca.

ABSORPTION AND METABOLISM

Ca is absorbed in the intestine by two routes, transcellular and paracellular (Bronner, 1987). The transcellular route is saturable and subject to physiological and nutritional regulation *via* vitamin D while the paracellular route is non-saturable, essentially independent of nutritional and physiological regulation, and is concentration dependent. Most Ca absorption in humans occurs in the small intestine, but there is some evidence (Barger-Lux *et al.* 1989) for a small colonic component.

Plasma Ca concentration is maintained within narrow limits by the complex and integrated hormonal regulation of intestinal Ca absorption, urinary Ca excretion and bone turnover. A reduction in plasma Ca concentration evokes a parathyroid hormone mediated increase in plasma 1,25-dihydroxyvitamin D₃, which stimulates increased intestinal Ca absorption *via* the active transcellular route.

Efficiency of absorption is influenced by a variety of physiological factors (Allen, 1982). In general it falls with increasing age, menopause, vitamin D deficiency and disease states such as malabsorption syndromes, coeliac disease, Crohn's disease, chronic renal failure, diabetes, hypoparathyroidism and primary biliary cirrhosis. Increased efficiency of absorption is observed with vitamin D excess, Ca deficiency, phosphorus deficiency, pregnancy, lactation and certain disease states such as hyperparathyroidism, sarcoidosis and idiopathic hypercalciuria. Faecal excretion (incomplete absorption, desquamation and losses in digestive secretions) may account for up to 80% of the overall dietary Ca intake while urinary excretion is lower, between 10 and 35% of the intake (Davis *et al.* 1970).

DIETARY FACTORS AFFECTING CALCIUM ABSORPTION

Habitual calcium intake

The time period and physiological state of individuals are important determinants of the adaptive response. Ireland & Fordtran (1973) reported that the efficiency of Ca absorption was greater in human subjects adapted to a low Ca diet (300 mg/d) than a high Ca diet (2000 mg/d). Similarly, Fairweather-Tait *et al.* (1995*b*) found a higher efficiency of absorption in lactating Gambian mothers adapted to a low Ca diet (283 mg/d) than UK mothers on higher Ca intakes (1168 mg/d). Ca supplementation (300 mg/d) for 6 months resulted in a small reduction in fractional Ca absorption from a standard meal in Chinese children (Lee *et al.* 1995). Heaney (1991) concluded that absorption from a meal is influenced more by variations in Ca content than habitual Ca intake.

Calcium load

Ca absorption is dose dependent (Heaney, 1991). Fractional Ca absorption from Ca gluconate solution, administered to human subjects through an intestinal perfusion system, decreased with increasing Ca load but absolute Ca absorption increased (Ireland & Fordtran, 1973).

Milk and milk products

Ca in milk and milk products has a relatively high bioavailability. Mean Ca absorption from cows' milk in healthy human adults ranges from 20 to 45% (Heaney *et al.* 1988; Fairweather-Tait *et al.* 1989*a*; Griessen *et al.* 1989; Heaney & Weaver, 1990).

Plant foods

Ca absorption from a meal containing Ca oxalate is less than from a meal containing Ca carbonate (Heaney *et al.* 1990). Thus vegetables which are rich in oxalate may have low Ca bioavailability, e.g. 5.1% from spinach compared to 27.6% for milk, at an equivalent Ca load (Heaney *et al.* 1988), whereas Ca absorption is higher from low oxalate vegetables, kale (41%), and watercress (27%) (Fairweather-Tait *et al.* 1989*a*; Heaney & Weaver, 1990).

Phytate reduces Ca absorption (McCance & Widdowson, 1942; Reinhold *et al.* 1973; Morris & Ellis, 1985). Ca absorption from high phytate soyabeans (31%) is lower than that from low phytate soyabeans (41%) (Heaney *et al.* 1991), but wheat products, with the exception of high phytate wheat bran, do not have a negative effect on Ca absorption from the diet (Weaver *et al.* 1991).

Fat

In the healthy adult, the amount of fat in the diet does not affect Ca absorption (Allen, 1982), but with fat malabsorption Ca absorption is reduced (Agnew & Holdsworth, 1971), probably owing to the formation of insoluble soaps in the intestinal lumen.

Calcium supplements

Differences in chemical solubility between Ca supplement preparations do not affect Ca absorption apart from highly insoluble salts (Sheikh *et al.* 1987; Heaney *et al.* 1990). However, there is some evidence of enhanced absorbability of Ca citrate malate (CCM) (Smith *et al.* 1987; Miller *et al.* 1988). Salts that require acid for solubilization may be poor sources of Ca for individuals with impaired gastric acid secretion unless ingested with a meal (Bo-Linn *et al.* 1984; Recker, 1985). Co-ingestion of a light meal increases Ca absorption, which may be due to slower gastric emptying, and thus a slower presentation of Ca to intestinal absorption sites (Heaney *et al.* 1989).

DIETARY FACTORS AFFECTING URINARY EXCRETION

Urinary Ca excretion is influenced by a number of dietary factors, of which protein and sodium are the most important. Zemel (1988) has estimated that doubling protein intake will increase urinary Ca excretion by 50% when dietary Ca and phosphorus are held constant. The effect of protein is more marked when purified proteins (casein, lactalbumin, gelatin or egg white) are administered in controlled experiments than when high protein foods are consumed since the concomitant intake of phosphate partly offsets the calciuric action of dietary protein (Spencer *et al.* 1988).

Increasing dietary sodium intake as sodium chloride has been shown to increase urinary excretion of Ca in humans (Castenmiller *et al.* 1985; Shortt *et al.* 1988). Healthy individuals who have adequate Ca and vitamin D intakes and who absorb dietary Ca efficiently adapt to high salt intakes by increasing Ca absorption to compensate for the increased urinary Ca loss (Fujita *et al.* 1984). However, the increase in Ca absorption may not be sufficient to balance the increase in urinary Ca excretion (Breslau *et al.* 1982).

CONCLUSION

Ca absorption may be influenced by a number of dietary factors. Further studies in humans using radio- or stable isotopes are needed to quantify their influence on Ca bioavailability and to evaluate the extent to which physiological adaptation can compensate for differences in Ca bioavailability in foods.

CHROMIUM

FOOD SOURCES AND EFFECTS OF PROCESSING

Richest dietary sources of Cr are spices such as black pepper, brewer's yeast, mushrooms, prunes, raisins, nuts, asparagus, beer and wine. Refining of cereals and sugar removes most of the native Cr, but stainless steel vessels in contact with acidic foods may contribute additional Cr. Beverages, including milk, may provide up to one-third of the daily intake of Cr. However, the insulin potentiating activity of foods (see below) may not correlate with total Cr content (Khan *et al.* 1990).

ABSORPTION, TRANSPORT AND METABOLISM

Intestinal absorption of inorganic trivalent Cr is less than 3%, irrespective of dose, but hexavalent Cr from industrial compounds, which is considered highly toxic, is better absorbed. There is no evidence that natural complexes of Cr (e.g. as found in brewer's yeast) are better absorbed than simple Cr salts. Cr is absorbed in the small intestine, primarily in the jejunum in humans (Doisy *et al.* 1976). The mechanism is not well understood, but a non-saturable passive diffusion process seems likely (Anderson & Kozlovsky, 1985). Absorption is reported to be higher in women than in men, and higher urinary Cr values are reported for the elderly, suggesting that Cr retention changes with age (Offenbacher, 1992). Elevated urinary Cr levels are also present during various forms of stress, such as strenuous exercise, physical trauma and infection.

Glucose loading tests have been performed in human subjects to examine the link between Cr deficiency and carbohydrate metabolism. The disappearance of plasma Cr after an oral glucose tolerance test cannot be explained by increased urinary loss but might be due to transient changes between Cr and insulin-sensitive tissues (Morris *et al.* 1992).

DEFICIENCY

Glucose intolerance is one of the principal signs of Cr deficiency. Cr acts by increasing the activity of insulin and consequently less insulin is required to control glycaemia. These aspects are reviewed by Mertz (1993).

DIETARY FACTORS AFFECTING ABSORPTION AND UTILIZATION

Amino acids

At neutral or basic pH, hydrated Cr polymerizes and forms an inert precipitate. Ligands, such as amino acids and keto acids, compete with the hydroxide ions in biological solutions, prevent precipitation, and form rapidly diffusing Cr complexes of low molecular weight. In rats, Cr absorption is facilitated by certain amino acids, such as histidine which chelates Cr in the small intestine (Dowling *et al.* 1990).

Vitamins

An acute dose of ascorbic acid enhanced ⁵¹Cr absorption in rats and ascorbate-depleted guineapigs (Seaborn & Stoecker, 1992). A combination of nicotinic acid and Cr is required to optimize human glucose metabolism (Urberg & Zemel, 1987).

Carbohydrates

There is little or no evidence that carbohydrates can affect Cr bioavailability but diets high in simple sugars increase urinary Cr excretion in humans (Kozlovsky *et al* 1986).

Metals

In animals, interactions with Cr have been noted for Zn, Fe, V and Ca. An oral dose of zinc decreased the absorption of ^{51}Cr in Zn deficient rats, and it is possible that Cr and Zn are being absorbed by a common mechanism. Similarly the administration of Fe inhibits the absorption of Cr, indicating that Cr and Fe also share a common gastrointestinal transport mechanism. Antacid (CaCO_3) reduces Cr uptake and retention in rats (Seaborn & Stoecker, 1990).

Chelating substances

Chelating substances such as oxalate have been reported to increase Cr absorption whereas citrate and EDTA are apparently without effect. Conversely, phytates have been shown to decrease Cr transport through the rat intestine (Chen *et al.* 1973).

CONCLUSIONS

Animal studies suggest that some amino acids and nicotinic acid increase Cr absorption whereas Zn and Fe reduce it. There are few studies on Cr bioavailability in man but the use of stable isotopes offers a possibility of investigating this further.

COPPER**FOOD SOURCES**

The Cu content of food reflects its geographical origin and the processing conditions it undergoes prior to consumption. Foods high in copper include liver, kidney, shellfish, wholegrain cereals and nuts. Soft or acidic water passing through copper pipes can also contribute copper to the diet.

ABSORPTION, TRANSPORT AND METABOLISM

Cu absorption in humans ranges from 25 to 70%, the major site being the small intestine. Intestinal absorption (active and passive) is regulated by nutritional status, the chemical form of the element, and interactions with dietary components (Johnson *et al.* 1988). There appears to be no effect of age or sex on net Cu absorption (Johnson *et al.* 1992).

Newly absorbed Cu is transported in the plasma loosely bound to albumin and incorporated into caeruloplasmin in the liver (Davis & Mertz, 1987). Approximately 0.5–1.5 mg absorbed Cu is re-excreted in the bile and hence lost in faeces. Very small amounts are excreted in the urine, sweat and skin. Genetic defects in Cu metabolism result in Cu deficiency (Menkes' syndrome) or toxicity (Wilson's disease).

DEFICIENCY

Cu deficiency has been observed in premature infants, infants exclusively fed on cows' milk, infants with Menkes' syndrome, malabsorption conditions, and patients given inadequate Cu in parenteral nutrition fluids (Mills, 1992).

DIETARY FACTORS AFFECTING ABSORPTION

Bioavailability has been reviewed by Sandstead (1982) and Turnlund (1988).

Level of intake

Turnlund *et al.* (1989) demonstrated that Cu absorption is strongly dependent on dietary intake, and that most young men can achieve Cu balance from a diet of 0.8 mg Cu/d, by adaptive changes in Cu absorption and endogenous faecal losses. Neither urinary Cu nor salivary Cu are affected by dietary Cu levels (Turnlund *et al.* 1990), and as skin and menstrual losses contribute little to overall Cu losses, they have only a minor effect on Cu balance (Turnlund *et al.* 1991).

Dietary protein

Significantly more Cu is retained from a high protein than a low protein diet (Greger & Snedeker, 1980). Cu balance is more positive with animal than plant protein diets, because endogenous Cu losses are lower (Turnlund *et al.* 1991).

Dietary fibre

Although Cu can form complexes *in vitro* with phytate, hemicellulose and lignin fractions of dietary fibre (Cheryan, 1980), there is no evidence that fibre or phytate affects Cu absorption in man, but α -cellulose and/or phytate may affect Cu utilization or endogenous losses (Turnlund *et al.* 1985).

Ascorbic acid

Results from animal experiments suggest that high dietary levels of ascorbic acid can have a negative affect on Cu bioavailability, but in humans the situation is less clear. Finley & Cerklewski (1983) reported that supplementation with 1500 mg ascorbic acid/d for 2 months produced a significant drop in serum caeruloplasmin activity. Jacob *et al.* (1987) found that 600 mg ascorbic acid/d did not depress intestinal Cu absorption but it reduced caeruloplasmin oxidase activity.

Influence of fructose on copper balance

A comparison made by Reiser *et al.* (1985) of the effects of isoenergetic levels of fructose and cornstarch on Cu metabolism in men showed that superoxide dismutase was lower and Cu retention higher in the group fed fructose, although serum Cu and caeruloplasmin were similar. In a similar study, Holbrook *et al.* (1989) observed that the group consuming a low Cu fructose diet had significantly more positive balances and a greater apparent absorption for Cu, Zn, Fe, Mn, Ca and Mg than the group on the low Cu corn starch diet, suggesting that fructose increases the absorption of these minerals.

Interactions with other elements

Fe–Cu: The fact that serum Cu has been found to be low in some cases of iron deficiency anaemia suggests that iron status has an effect on Cu metabolism. Interaction between Fe and Cu seems to be due to impaired utilization of one in the absence of the other (Turnlund, 1988).

Zn–Cu: A reduction in Cu absorption has been reported in the presence of excessive Zn. The level necessary to impair bioavailability is unknown but results from balance studies

indicate that it must exceed normal dietary intakes; therapeutic levels (150 mg/d) of Zn supplements over extended periods of time (Turnlund, 1988) produce symptoms of Cu deficiency, but the effect of a Zn–Cu ratio of 15:1 is less than that of Cu restriction (August *et al.* 1989). The interaction may be reciprocal because low plasma Zn is often accompanied by high plasma Cu.

Mo–Cu: Dietary Mo slightly above the recommended intake increased urinary Cu significantly in one balance study in human beings (Doesthale & Gopalan, 1974). High dietary Mo may mobilize Cu stores and could have the potential to induce Cu deficiency in men.

Cd–Cu: Cd affects Cu status adversely, but human diets are not likely to contain enough Cd to be toxic (Sandstead, 1982).

Drugs

Penicillamine is used to reduce the toxic levels of endogenous Cu in Wilson's disease (Mason, 1979). Cu deficiency may occur when large quantities of antacids are taken (Turnlund, 1988).

CONCLUSIONS

Cu absorption in humans ranges from 25 to 70%. The efficiency of intestinal absorption depends on dietary Cu level and nutritional status. Dietary components that can influence Cu bioavailability include amino acids and proteins, carbohydrates (fructose), dietary fibre and phytate, ascorbic acid and other mineral elements (Fe, Zn, Mo) that can interact with Cu. Amino acids, protein and fructose increase Cu absorption, while ascorbic acid and phytate decrease it. Drugs, such as antacids, can also negatively affect Cu absorption.

IODINE

FOOD SOURCES

The concentration of I in plants and animals is greatly influenced by the soil. In the Western world, milk and its products are good sources of I (Lamand & Tressol, 1992), especially where cattle feed iodination occurs (e.g. Finland, Norway and the UK). Seafood also contains large amounts of I from seawater. Bread, which contains iodate products as dough strengtheners, and processed foods containing iodized salt are also good sources of inorganic iodide. In countries where I prophylaxis exists, iodized salt has been the main source, and in this form absorption approaches 100% (Delange & Bürgi, 1989).

Excess I intake can result in hyperthyroidism (Pennington, 1988) when the thyroid gland is overstimulated.

ABSORPTION AND METABOLISM

In food, I is present mainly as inorganic iodide, which is almost completely absorbed by the gastrointestinal tract. Other forms of I are converted to inorganic iodide prior to absorption (Pennington, 1988). I is transported in the plasma, loosely attached to the plasma proteins. In the thyroid gland, the iodide ions are oxidized to iodine and react with the tyrosine components of thyroglobulin to produce the organic components mono- and di-iodotyrosine which form the thyroid hormones thyroxine (T4) and triiodothyronine (T3).

Excess I (inorganic form) is excreted in the urine (85–90%), with smaller amounts in the faeces and in sweat (Lamberg, 1993). Both organic and inorganic I are secreted into the gastric juice and saliva; inorganic I is completely reabsorbed but the organic I is excreted in the faeces (Alexander *et al.* 1967; Pennington, 1988).

DEFICIENCY

Dietary I deficiency in man results in goitre, hypothyroidism, cretinism and other iodine deficiency disorders (IDD) (Dunn, 1993; Lamberg, 1993). I deficiency stimulates an increase in the production of thyroid stimulating hormone which causes the thyroid to increase the uptake of I and results in thyroid gland enlargement.

DIETARY FACTORS INFLUENCING BIOAVAILABILITY

Goitrogens

The most studied factors relating to I bioavailability are the goitrogens, but these only have a significant impact on IDD when the usual dietary intake of I is low. Goitrogens can reduce the levels of I uptake by the thyroid, or impair its metabolism (Pennington, 1988; McDowell, 1992*a*). Thioglucosides are the most common goitrogens, as found in brassica vegetables, e.g. cabbage, cauliflower, broccoli and turnip. On hydrolysis thioglucosides yield thiocyanates and isothiocyanates (Pennington, 1988) which inhibit the selective concentration of I by the thyroid (McDowell, 1992*a*). Thiocyanates are also formed by hydrolysis in foods such as nuts, cassava, maize and sweet potatoes (Pennington, 1988).

Different foods

Few data have been produced on the absorption of I from specific foodstuffs since the balance studies of von Fellenberg (1926). From faecal and urinary monitoring, I absorption, estimated from balance studies, was 93% for cod liver oil, 65% for cress and 89% for KI (von Fellenberg, 1926); there was a strong correlation between I intake and urinary excretion. High I absorption (approximately 100%) was found from eggs and a seaweed, but a much lower absorption (10%) from a second seaweed, possibly owing to the physical structure of the seaweed preventing the release of I on digestion (Katamine *et al.* 1987). Another exception to the high bioavailability of I is erythrosine, a red food colourant, which has high I content (58% w/w) but low absorption (2–5%), most erythrosine being excreted directly in the faeces (Pennington, 1988). Absorption is increased when erythrosine is used in foods which are processed at very high temperatures (Katamine *et al.* 1987).

Minerals and trace elements

High dietary As, F or Ca, very low or high Co levels, high K and low Mn levels adversely affect I bioavailability (McDowell, 1992*a*).

Selenium deficiency

Recent studies in northern Zaïre (Vanderpas *et al.* 1990, 1992) and northwestern China (Ma *et al.* 1993) have shown that Se deficiency is an important factor in these IDD-endemic areas. The biochemical basis for these observations is suggested to be the fact that Se is a

co-factor in two enzyme systems involved in the synthesis and metabolism of thyroid hormones, namely: Se-containing glutathione peroxidase (Se-GPX) and type I iodothyronine 5'-deiodinase (ID-1). It is thought that the lack of Se-GPX causes a decrease in the functional activity of the thyroid gland owing to a build up of cytotoxic levels of H_2O_2 , whereas a lack of ID-1 decreases the conversion of serum T4 into the more biologically active T3 (Arthur *et al.* 1993; Vanderpas *et al.* 1993).

CONCLUSION

The amount of bioavailable I in a diet depends mainly on level of I and not so much on chemical form/dietary constituents; however, some factors such as goitrogens and Se deficiency play a secondary role. Few measurements have been made on the bioavailability of I from food. It is assumed to be high but there are some exceptions.

IRON

FOOD SOURCES

Fe is widely distributed in meat (30–70% is haem iron), vegetables and cereals, but the concentration in milk and fruits and vegetable is low (Thompson, 1988). Fe in the water supply is also low; the maximum permitted level in drinking water in the US is 0.3 mg/l (Thompson, 1988). The Fe content *per se* of individual foods has little meaning since Fe bioavailability varies considerably.

ABSORPTION, TRANSPORT AND METABOLISM

Fe is absorbed into the mucosal cells of the small intestine, primarily in the duodenum, by an active, saturable process (Charlton & Bothwell, 1983). Efficiency of absorption is increased with iron deficiency and reduced when erythropoiesis is depressed. Some absorbed Fe is stored temporarily as ferritin in the mucosal cell either to be mobilized later or to be excreted when the cell is exfoliated. The haem iron molecule is taken up intact into the mucosal cell, where the Fe is released and enters the non-haem Fe pool. The adult male loses about 1 mg Fe/d *via* epithelial cells, gut secretions, urine and skin; in menstruating women, additional losses when averaged over 28 d can be a further 1.4 mg/d (Herberg *et al.* 1987).

Fe is transported in the plasma bound to transferrin which delivers it to the cells or to the bone marrow. In the adult male, 95% of the Fe required for haemoglobin synthesis is derived from degraded red blood cells (Dallman *et al.* 1980). The body has no active mechanism for excreting Fe and any in excess of needs is stored as ferritin or haemosiderin, principally in the liver and spleen.

DEFICIENCY

Iron deficiency occurs when stores are depleted, and anaemia when the haemoglobin level in blood falls below the normal level for the individual (British Nutrition Foundation, 1995). Anaemia is most common in infants, preschool children, adolescents and women of child bearing age, particularly in developing countries. Anaemia can have an adverse effect on psychomotor and mental development in children, mortality and morbidity of mother and infant during pregnancy, work performance and resistance to infection (Herberg *et al.* 1987).

DIETARY FACTORS INFLUENCING BIOAVAILABILITY

Non-haem iron

Non-haem Fe bioavailability is strongly influenced by dietary components mainly as a result of luminal interactions (reviewed by Hallberg, 1981; British Nutrition Foundation, 1995). Since Fe is not excreted, Fe bioavailability and Fe absorption are synonymous, and vary from less than 1% in the most inhibitory meals to more than 90% for the most bioavailable forms of Fe, e.g. ferrous sulphate together with ascorbic acid given to Fe deficient individuals in the fasting state (Bezwoda *et al.* 1979).

Haem iron

Haem Fe is always relatively well absorbed (15–35%) and is little influenced by physiological or dietary factors (Monsen *et al.* 1978). It has been used to fortify foods (MacPhail *et al.* 1985) but is severely limited by its intense colour and low Fe concentration. Haemoglobin is better absorbed than haem Fe administered without the globin and is further enhanced by the presence of meat, possibly because protein digestion products prevent polymerization of haem in the lumen (MacPhail *et al.* 1985). Recently, the addition of Ca (165 mg) to a hamburger meal was shown to reduce the haem Fe absorption (Hallberg *et al.* 1992).

Phytic acid

Phytic acid (myoinositol hexaphosphate) is found in cereal grains and legume seeds and is a major determinant of the low Fe bioavailability in these foods. It is thought to form an insoluble complex with Fe, other minerals and peptide degradation products in the intestinal lumen, from which the Fe cannot be absorbed (Hurrell *et al.* 1992). The degradation of phytic acid in wheat bran almost completely removes the inhibitory effect of wheat bran on Fe absorption (Hallberg *et al.* 1987) and adding phytic acid to wheat rolls inhibits iron absorption dose dependently (Hallberg *et al.* 1989). Phytic acid is a major inhibitory factor in isolated soya protein. Fe absorption increased significantly when phytic acid free soya protein isolates were fed to adults in a liquid formula meal (Hurrell *et al.* 1992) or to infants in infant formula (Davidsson *et al.* 1994a). Some traditional food processes such as fermentation, germination or soaking can activate native phytases in cereal grains which then degrade phytic acid and improve Fe absorption. The results from human studies with pure fibre fractions, such as cellulose and pectin, indicate that fibre *per se* does not influence Fe absorption (Rossander *et al.* 1992). The inhibitory effect of bran can be attributed almost entirely to its high phytate level (Hallberg *et al.* 1987).

Polyphenols

The phenolic compounds present in plant foods include tannic acids, phenolic acids, flavonoids and polymerization products. They are particularly high in beverages such as tea, coffee, herb teas, cocoa and red wine. Hydrolysable tannins of black tea have been shown to be a most potent inhibitor of iron absorption. Disler *et al.* (1975) found a four-fold reduction in Fe absorption from a meal with tea. Chlorogenic acid, the phenolic compound in coffee, is also inhibitory (Brune *et al.* 1989) and coffee also reduces Fe absorption (Morck *et al.* 1983). The monomeric flavonoids of herb teas (Brown *et al.* 1990) and the polymeric flavonoids of red wine (Cook *et al.* 1995) also inhibit Fe absorption but are less potent than black tea. A glass of red wine reduced Fe absorption from a small bread meal by 75% (Cook *et al.* 1995) but had no inhibitory effect when consumed with a meal of string beans, potatoes and hamburger (Hallberg & Rossander, 1982), presumably because other components in the meal offset the inhibitory effect of red wine. Phenolics in

vegetables can also strongly inhibit Fe absorption (Tuntawiroon *et al.* 1991) and there is a strong inverse relationship between their polyphenol content and Fe absorption in man (Gillooly *et al.* 1983).

Calcium

Ca can inhibit Fe absorption but its effect depends on quantity and on the size and composition of the meals, being more pronounced in small, simple meals such as bread rolls or a hamburger but absent in larger more complex meals. In a small bread meal, inhibition of Fe absorption was dose-related up to 300 mg Ca added as Ca chloride, and was similarly inhibited with 165 mg Ca added as the inorganic Ca compound or as 150 ml milk (Hallberg *et al.* 1991), or when 200 ml milk or a milkshake was consumed with a simple hamburger meal (Hallberg *et al.* 1992). With more complex meals 150–250 ml milk did not elicit a significant reduction (Hallberg & Rossander, 1982; Galan *et al.* 1991), presumably because of the combined effect of all the modifiers of iron absorption present in the meal.

Protein

Peptides can both inhibit or enhance Fe absorption, depending on their nature. Fe absorption from liquid meals containing soya protein, whey protein, casein and egg white were lower than from bovine serum albumin or muscle tissue (Hurrell *et al.* 1989*b*). The inhibitory effect of soya protein isolate was only partly removed by degrading the phytic acid (Hurrell *et al.* 1992) which may be due to inhibitory peptides binding Fe (Lynch *et al.* 1994). Other legume proteins are similarly inhibitory (Macfarlane *et al.* 1988). The inhibitory effect of commercial whey protein concentrate is due to its high Ca content and not to whey *per se* (Hurrell *et al.* 1990), whereas the effect of casein is probably due to casein phosphopeptides, formed on digestion, chelating Fe in an insoluble complex. Complete hydrolysis of casein (Hurrell *et al.* 1989*b*) or enzymic removal of the phosphorus groups from serine phosphate side chains largely removes its inhibitory effect (Hurrell *et al.* 1990).

Lactoferrin has often been suggested as the facilitator of Fe absorption in breast milk, but there is no evidence to support this hypothesis (Davidsson *et al.* 1994*b*). However, many studies have confirmed the enhancing effect of muscle tissue on Fe absorption (Layrisse *et al.* 1968), which may be related to the high level of cysteine (Martínez-Torres & Layrisse, 1970) since at equivalent quantities of cysteine, free cysteine, glutathione or beef similarly increased Fe absorption from a maize meal (Layrisse *et al.* 1984). The facilitating effect of an enzymically digested beef extract on Fe absorption was removed by oxidizing the cysteine residues before feeding (Taylor *et al.* 1986). Their potential to chelate Fe and to reduce ferric Fe to the more soluble ferrous Fe could explain the enhancing effect of cysteine-containing peptides on Fe absorption.

Ascorbic acid

Ascorbic acid is the best known and most potent enhancer of Fe absorption both in its natural form in fruit and vegetables (Ballot *et al.* 1987) and when added as the free compound (Cook & Monsen, 1977). The enhancing effect is dose-related over the range 25–1000 mg (Cook & Monsen, 1977). At high enough concentrations, ascorbic acid can overcome the inhibitory effect of phytic acid in cereals (Hallberg *et al.* 1989) and in soya formula (Davidsson *et al.* 1994*a*), and it can partly overcome the effect of polyphenols from tea (Disler *et al.* 1975). Ascorbic acid increases the bioavailability of all Fe fortification compounds (Hurrell, 1992) but is sensitive to losses during storage and cooking. Its facilitating effect is thought to be due to its ability to convert ferric to ferrous Fe at low pH and to its chelating properties.

Fortification iron

As reviewed recently by Hurrell (1992), Fe compounds used in food fortification vary considerably in bioavailability owing to their different solubility in the gastrointestinal tract. Freely water-soluble compounds such as ferrous sulphate dissolve instantaneously and have the highest relative bioavailability, but insoluble compounds such as elemental Fe, ferric pyrophosphate and ferric orthophosphate never dissolve completely in gastric juice and have low and varying absorption. Since freely water-soluble compounds often cause unacceptable colour and flavour changes in many foods, insoluble compounds which are organoleptically inert are often used in food fortification, particularly in cereal products. Ferrous fumarate and ferrous succinate are poorly soluble in water and cause fewer organoleptic problems, but are readily soluble in dilute acid and are similarly absorbed to ferrous sulphate (Hurrell *et al.* 1989*a*).

The International Nutrition Anemia Consultative Group (INACG) has recently recommended the use of NaFeEDTA as an iron fortificant in developing countries (INACG, 1993). The EDTA moiety in this compound protects Fe from reacting with phytic acid and Fe absorption from cereal and legume products is 2–3-fold greater than with ferrous sulphate.

Contamination iron

Food can be 'contaminated' with Fe either from soil (Hallberg *et al.* 1983) or by the cooking equipment used industrially or at home (Brittin & Nossaman, 1986). Contamination Fe from soil is of limited bioavailability (Hallberg *et al.* 1983), but Fe from cooking equipment may be readily absorbed, such as beer brewed in Fe containers (Derman *et al.* 1980) or food cooked in Fe pots (Martinez & Vannucchi, 1986; Fairweather-Tait *et al.* 1995*a*).

CONCLUSIONS

Food Fe is present as haem Fe and non-haem Fe. Haem Fe absorption is relatively unaffected by diet composition, but it is increased by muscle protein and decreased by Ca. On the other hand, non-haem Fe absorption is very sensitive to dietary components, being facilitated in the presence of ascorbic acid or muscle protein and inhibited by phenolic compounds, phytic acid, Ca and certain proteins. With the possible exception of Ca, the effects take place in the intestinal lumen where the facilitators and inhibitors compete to bind Fe in soluble or insoluble forms.

MAGNESIUM**FOOD SOURCES**

Mg is widely distributed in plant and animal foods, especially nuts, legumes, green vegetables (present as the inorganic ion of chlorophyll), cereals, and chocolate. Hard drinking water may also be an important source of dietary Mg.

ABSORPTION, TRANSPORT AND METABOLISM

Mg is absorbed primarily in the small intestine, both by a facilitated process and by passive diffusion. Absorption increases but fractional absorption falls with increasing dose (Fine *et al.* 1991). There is a wide range in efficiency of absorption, ranging from 10% on high Mg

diets to 75% on Mg restricted diets. Endogenous faecal excretion from Mg secreted into the gastrointestinal tract secretions is about 25–50 mg/d. Absorbed Mg is retained either for tissue growth or replacement, with the skeleton acting as a store, and the remainder is excreted in the urine. When intake decreases, the kidney is very efficient at conserving Mg in order to maintain homeostasis.

DEFICIENCY

Clinical Mg deficiency in humans is rare. First described by Hirschfelder & Haury (1934), it has been reported in alcoholics, and in patients on Mg-free intravenous solutions (Shils, 1988). Hypomagnesaemia, generally accompanied by hypocalcaemia, is also induced by starvation, malabsorption syndromes, acute pancreatitis, alcoholism, and prolonged diarrhoea or vomiting (Foy, 1980), and is treated with intravenous Mg. Lack of Mg has also been implicated in certain chronic diseases (e.g. coronary heart disease, hypertension, and premenstrual syndrome).

FACTORS AFFECTING BIOAVAILABILITY

Very little is known about the absorption of Mg from different foods, and research on Mg bioavailability has been impeded by the lack of a satisfactory isotope. The short half-life of the radioisotope ^{28}Mg (21.3 h) has restricted its use in absorption studies where faecal collections need to be carried out for longer periods than those optimal for ^{28}Mg detection by methods other than whole body counting. However, enriched sources of the stable isotope ^{26}Mg can be used in conjunction with ^{28}Mg to measure true absorption from plasma or urine collected shortly after dosing (Schwartz, 1984), applying a double-label stable isotope technique. Apparent Mg absorption can be measured from the determination of faecal and urinary ^{26}Mg excretion following oral administration of ^{26}Mg -labelled foods. However, in practice, the high natural abundance of ^{26}Mg (11.01%) blunts the sensitivity with which the isotope can be measured in body fluids and excreta, and it can only be accurately measured for 2–4 d after administration, depending upon the size of the dose (Schwartz *et al.* 1984).

Animal studies indicate that Mg is better absorbed from milk than from cereals, legumes and meat (Hazell, 1985). The proportion of soluble Mg differs between milks; in human milk 92% of the total Mg is in the soluble fraction, in whey-predominant infant formula it is 83% and in casein-predominant formulas it ranges from 70 to 91% (Lönnerdal *et al.* 1993). The remainder of the Mg is found with the casein and fat fractions.

Most Mg in cereals is present in the aleurone layer, probably in the form of phytin (Ca_3Mg phytate) or as potassium-magnesium-phytate, and the rest is found as phosphates and sulphates. In plant cell walls Mg may be bound by lignin but not by pectin. The Mg in green vegetables is primarily found within chlorophyll, and the tetrapyrrole ring of chlorophyll may offer Mg some protection from dietary inhibitors. However, hydrogen can replace Mg during food processing, leading to the formation of pheophytin and hence a significant loss of green colour. Schwartz *et al.* (1984) intrinsically labelled leafy vegetables (collards, turnip greens, lettuce and spinach) with ^{26}Mg and measured net absorption (by faecal and urinary balance) from muffins in which the bran was replaced with the vegetables in adult male volunteers. In addition, an i.v. dose of ^{28}Mg was given in order to calculate true absorption of ^{26}Mg from measured plasma isotope ratios. True absorption ranged from 52% for bran to 62% for lettuce, with intermediary values for the other vegetables. Net absorption was, as expected, significantly lower, ranging from 42% for bran to 54% for collards and turnip greens. The lower absorption of Mg in bran is probably due to its

higher phytate content, since phytic acid has been found to bind Mg and reduce its bioavailability (Roberts & Yudkin, 1960; Seelig, 1980).

Several dietary constituents have been suggested to have an influence on Mg bioavailability. Enhancers include protein and amino acids (Schwartz, 1988), and inhibitors include phosphate, phytate and dietary fibre (Reinhold *et al.* 1976; Kelsay *et al.* 1979). However, much of the human research on dietary Mg bioavailability was performed a number of years ago using balance techniques. The experimental design generally involved the addition or substitution of fibre or phytate in diets, which introduced other changes in dietary factors apart from those of primary interest. Thus the individual effect of enhancers and inhibitors of Mg absorption is not clear.

The bioavailability of Mg salts has been studied fairly extensively in recent years, usually by comparing Mg elimination in 24-h urine during placebo and treatment periods. Mg oxide has a lower bioavailability than citrate (Lindberg *et al.* 1990) or Mg-L-aspartate-HCl (Muhlbauer *et al.* 1991). There are no significant differences between Mg lactate, citrate and hydroxide (Bohmer *et al.* 1990) but Mg orotate has a higher bioavailability than Mg hydroxycarbonate (Schlebusch *et al.* 1992). Mg from almonds, a high-Mg food, is as bioavailable as soluble Mg acetate, but enteric-coated Mg chloride is much lower (Fine *et al.* 1991).

CONCLUSION

Mg absorption and bioavailability is one of the least well understood aspects of Mg metabolism. The Mg content of Western diets that include a substantial amount of refined foods is relatively low and increased intakes of alcoholic beverages may, in some instances, lead to a reduction in Mg utilization and hence a depletion in body levels. The substitution of whole grain for refined cereal products can significantly increase dietary Mg intake, but high intakes of dietary fibre and phytate may reduce its bioavailability.

MANGANESE

FOOD SOURCES

Relatively high concentrations of Mn have been reported in cereals (20–30 mg/kg), brown bread (100–150 mg/kg), nuts (10–20 mg/kg), ginger (280 mg/kg) and tea (350–900 mg/kg dry tea) (Wenlock *et al.* 1979). Concentrations of Mn in crops are dependent on soil factors such as pH whereby increasing soil pH decreases plant uptake of Mn (Xilinas, 1983). Animal tissues contain very low amounts of Mn.

ABSORPTION, METABOLISM AND FUNCTION

Mn absorption, probably as Mn^{2+} , is relatively inefficient, generally less than 5%. Homeostatic regulation of Mn is brought about primarily through excretion (mainly *via* bile) rather than through regulation of absorption (Korc, 1988; Keen & Zidenberg-Cherr, 1990). Most absorbed Mn is transported *via* α -2-macroglobulin (as Mn^{2+}) and transferrin (as Mn^{3+}). The Mn-containing enzyme arginase is responsible for urea formation, pyruvate carboxylase catalyses the first step of carbohydrate synthesis from pyruvate, and Mn-superoxide dismutase catalyses the transformation of the superoxide radical to hydrogen peroxide. Other roles of manganese in carbohydrate and lipid metabolism have been described (Leach & Lilburn, 1978; Korc 1988; Keen & Zidenberg-Cherr, 1990), and it appears to play an important role in brain function in which biogenic amines are probably involved (Leach & Lilburn, 1978).

DEFICIENCY

Signs of Mn deficiency have been demonstrated in several animal species, including impaired growth, skeletal abnormalities, depressed reproductive function and defects in lipid and carbohydrate metabolism (McDowell, 1992*b*). The frequently cited single case of Mn deficiency in man is a male subject who was fed a purified diet deficient in vitamin K which was accidentally also deficient in manganese, causing weight loss, dermatitis, growth retardation of hair and nails, reddening of black hair, and a decline in levels of blood lipids (Doisy, 1972). Mn deficiency may be more frequent in infants owing to the low concentration of Mn in human breast milk and varying levels in infant formulas (Korc, 1988).

DIETARY FACTORS AFFECTING BIOAVAILABILITY

Mn absorption and bioavailability have not been studied extensively in humans. In animals, high amounts of Ca, P, fibre and phytate increase the requirement of Mn, probably *via* the formation of insoluble Mn complexes, resulting in reduction of the soluble fraction available for absorption (Keen & Zidenberg-Cherr, 1990). Most of the Mn in tea infusions is in a soluble form and therefore likely to be well absorbed (Hazell, 1985). Mn from soya protein was found to be better absorbed than from casein protein (Lee & Johnson, 1989). Fe–Mn interactions have been demonstrated whereby Fe deficiency increases Mn absorption, and high amounts of dietary Fe inhibit Mn absorption (Davis *et al.* 1992), possibly by competition for similar binding and absorption sites of (non-heme) Fe and Mn.

Mn absorption is higher from human milk than from cows' milk (Lönnerdal *et al.* 1983; Davidsson *et al.* 1989). The difference may be due to high bioavailability of lactoferrin bound Mn, the low bioavailability of casein bound Mn, or the higher Ca content of cows' milk (Lönnerdal *et al.* 1983; Davidsson *et al.* 1991). Mn absorption in adults is higher from lettuce and spinach than from wheat and sunflower seeds, possibly because of the influence of fibre and phytate (Johnson *et al.* 1991). However, Davidsson *et al.* (1991) observed no effect of phytate, phosphate or ascorbic acid on Mn absorption in adults from infant formulas. Addition of Fe and Mg to wheat bread did not affect Mn absorption in adults (Davidsson *et al.* 1991).

CONCLUSIONS

Mn deficiency in man is rare; homeostatic regulation is primarily brought about through excretion of manganese *via* bile, rather than through changes in the efficiency of Mn absorption. High amounts of Ca, P, fibre and phytate appear to inhibit Mn absorption, and Mn–Fe interactions have been demonstrated. Mn absorption from human milk is higher than from cows' milk.

SELENIUM

FOOD SOURCES

Se is present in food from both animal and vegetable origin. The Se concentration in food varies between different food items and reflects soil Se content (Combs, 1988); thus animal tissues show smaller variations in their Se than vegetable products owing to homeostatic regulation (Behne, 1989).

Cereals, seafood and meat products are the richest sources of Se and are the main contributors to the daily Se intake, whereas vegetables, fruits and beverages are generally

low in Se (Combs, 1988). Low dietary Se intake levels have been reported for people living in low Se areas (Combs, 1988) and for population groups with special or restricted feeding regimes (Roekens *et al.* 1986).

Only limited information is available on the Se species in food. Selenomethionine (Se-Met) has been identified as a major Se compound in wheat (Olson *et al.* 1970), soyabeans (Yasumoto *et al.* 1988) and high Se-yeast (Korhola *et al.* 1986), while selenocysteine (Se-Cys) has been identified in several mammalian proteins (Sunde, 1990). Inorganic Se forms have been identified in drinking water (Robberecht & Van Grieken, 1982).

ABSORPTION, TRANSPORT AND METABOLISM

The efficiency of absorption of Se is fairly high (50–95%) and depends on the dietary form (Robinson & Thomson, 1983). SeMet is absorbed by an active mechanism similar to that of its S-analogue methionine (Wolffram *et al.* 1989). Compared with inorganic forms, it is absorbed very rapidly throughout the small intestine (Vendeland *et al.* 1992*a*). The absorption is further enhanced at low methionine (Met) intake levels (McConnell & Cho, 1965). Se-Cys absorption has not yet been fully clarified, but some evidence exists that it shares a common active transport mechanism with basic amino acids (Wolffram *et al.* 1989). Selenite is absorbed from the small intestine by diffusion, stimulated, in the presence of certain thiols and selenate by a carrier mediated system shared with sulphate. Both inorganic forms are most readily absorbed in the ileum (Ardüser *et al.* 1986; Vendeland *et al.* 1992*a*).

Se metabolism has not yet been elucidated but the liver appears to play a central role in metabolism and homeostasis, and plasma is the transport medium for absorbed and metabolized Se components (Kato *et al.* 1992; Patterson *et al.* 1993). Retained Se can be incorporated into tissue proteins as Se-Met or into specific Se proteins as Se-Cys. Glutathione peroxidase (GSH-Px), type I-iodothyronine deiodinase and selenoprotein P have been identified as specified Se proteins containing Se-Cys as their Se moiety (Sunde, 1990). Several other, not yet fully characterized, Se proteins have been isolated during the last decade (Sunde, 1990; Zachara, 1992). Skeletal muscle is reported to be the major Se body pool accounting for approximately half of total body Se (Oster *et al.* 1988).

Excretion of absorbed Se as methylated Se compounds, e.g. trimethylselenonium, occurs mainly through urine (Robinson & Thomson, 1983). The composition of the urine has been reported to depend on the level of dietary Se (Zeisel *et al.* 1987).

DEFICIENCY

Keshan disease, a fatal cardiomyopathy, occurs in certain low Se areas in China and affects mostly young children and pregnant women (Nève *et al.* 1985). Low Se states have also been reported for population subgroups with very specific dietary habits, such as infants, in particular preterm and very-low-birthweight infants (Lockitch *et al.* 1989), and patients on total parenteral nutrition (Rannem *et al.* 1993).

DIETARY FACTORS AFFECTING BIOAVAILABILITY

Absorption studies, responsiveness of indices of Se status and the prevention of nutritional deficiency diseases have been used to assess Se bioavailability (Levander, 1983). Absorption studies measure the retention of dietary Se, but neglect its utilization, whereas status assessment relates to a functional parameter, but does not give information on the absorption or retention of administered Se.

Intake

Retention of Se is inversely related to intake; low Se intake results in lower urinary excretion and in increased body retention of Se (Martin *et al.* 1989*a*).

Chemical form

Se bioavailability depends to a great extent on the Se compound. Se-Met is readily absorbed, and results in higher blood Se concentration than inorganic Se, whereas GSH-Px activity seems to be unaffected by the chemical form of dietary Se (Xia *et al.* 1992).

Fish and mushrooms, although containing high concentrations of Se, have relatively low bioavailability (Mutanen, 1986; Meltzer *et al.* 1993), whereas meat, wheat and high Se yeast are reported to contain highly bioavailable Se (Levander *et al.* 1983; Van der Torre *et al.* 1991). This is almost certainly the result of differences in chemical form of Se in the foods. High Se yeast and wheat both contain Se-Met which, as a discrete component, is readily available, whereas fish and mushrooms must contain a chemical form of lower availability.

Dietary factors

The main dietary factors which influence Se bioavailability are Met, thiols, heavy metals and vitamin C. Dietary Met influences the absorption of Se-Met owing to the identical absorption mechanism for both amino acids (McConnell & Cho, 1965; Waschulewski & Sunde, 1988). With a Met deficient diet, Se-Met will be used to replace Met in protein synthesis, which will result in increased tissue Se levels and a decreased incorporation into specific Se enzymes such as GSH-Px. Conversely, increased dietary Met can compete with the intestinal absorption of Se-Met and lead to a lower Se nutritional status.

Certain thiols in the gastrointestinal tract enhance selenite absorption (Scharrer *et al.* 1992), probably owing to formation of selenocomplexes with thiol compounds which are more rapidly absorbed by the intestinal epithelium through various Na⁺-dependent and independent mechanisms (Scharrer *et al.* 1992; Vendeland *et al.* 1992*b*).

The influence of vitamin C on Se bioavailability depends on the ingested form of Se. The bioavailability of natural food Se is enhanced, whereas that of selenate is unaffected in the presence of vitamin C (Mutanen & Mykkänen, 1985). A high vitamin C consumption (1g/d) resulted in higher fractional and apparent absorption as well as enhanced retention of selenite, which might be due to the protection by vitamin C of critical sulphhydryl groups involved in gastrointestinal selenite uptake (Martin *et al.* 1989*b*). The well documented interaction of Se with heavy metals is reported to decrease the utilization of Se in certain foods through the formation of bonds between the heavy metals and Se (Whanger, 1981).

There is some evidence that dietary protein and phosphorus levels affect Se retention (Greger & Marcus, 1981). Faecal losses were highest and urinary excretion lowest in adult men with low protein diets, regardless of the phosphate content. The lowest apparent Se retention was observed on a low protein, high phosphorus diet.

The soluble fibre, guar gum, was reported to increase faecal Se excretion in human subjects and to decrease Se balance, due to decreased Se absorption from the gastrointestinal tract (Choe & Kies, 1989).

CONCLUSIONS

Se can be present in different organic and/or inorganic forms in human diets. The absorption, retention and metabolism of dietary Se are largely dependent on its chemical forms, which are responsible for differences in the overall utilization or bioavailability of different Se food sources. In addition to the dietary forms, the bioavailability of Se is

influenced by the presence of certain dietary constituents (e.g. Met concentration, thiols, heavy metals, vitamin C) which may enhance or decrease the utilization of dietary Se.

ZINC

FOOD SOURCES

The Zn content of foods varies from up to 2000 mg/kg fresh weight in oysters to below 5 mg/kg in refined foods or foods with a high fat content. In legumes and animal products Zn is associated with protein components. In meat products the Zn content to some extent follows the colour of the meat, so that the highest content, approximately 50 mg/kg, is found in lean red meat, at least twice that in chicken. In cereals, most of the Zn is found in the outer fibre-rich part of the kernel, thus the degree of refinement determines the total Zn content. Wholegrain products provide 30–50 mg/kg while a low extraction rate wheat flour contains 8–10 mg/kg. The major dietary determinants for the total Zn intake are the amount of animal protein, the extraction rate of the cereals and the fat content of the diet.

ABSORPTION, TRANSPORT AND METABOLISM

Zn in foods is absorbed *via* a carrier mediated transport process (Lee *et al.* 1989), which under normal physiological conditions appears not to be saturated (Sandström, 1992). Zn is transported in plasma by albumin and α -2-macroglobulin, and is present in all organs, tissues and fluids of the body. It is primarily an intracellular ion and only approximately 0.1% of body Zn is found in plasma. Bone and skeletal muscle account for more than 80% of body Zn. Body Zn content is regulated by homeostatic mechanisms over a wide range of intakes by changes in fractional absorption (normally 20–40%) and urinary (0.5 mg/d) and intestinal (1–3 mg/d) excretion.

DEFICIENCY

The clinical manifestations of severe Zn deficiency in man are growth retardation, a delay in sexual and skeletal maturation, dermatitis, alopecia, loss of appetite and behavioural changes (Hambidge, 1986). Mild Zn deficiency is more difficult to diagnose. Reduced growth rate in children and impaired immune function are regarded as early signs of Zn deficiency.

DIETARY FACTORS AFFECTING BIOAVAILABILITY

The bioavailability of dietary Zn depends on dietary enhancers and inhibitors and host-related factors. Soluble, low molecular weight organic substances such as amino acids and organic acids act as Zn binding ligands and facilitate absorption. Other organic compounds forming stable complexes with Zn at intestinal pH reduce its absorption, and ions with physicochemical properties similar to Zn compete for binding sites. The effects of several of these factors on Zn absorption have been identified in single meal studies.

Intake

A dose relationship has been shown both in single meal studies with radioisotopes (Sandström, 1992) and in studies of single meals or total diets using stable isotopes (Istfan *et al.* 1983; Wada *et al.* 1985; August *et al.* 1989; Taylor *et al.* 1991; Sian *et al.* 1993). At low Zn intakes, in the absence of phytate, more than 50% of dietary Zn can be absorbed. This increased absorption at low intakes is, however, not obvious for high phytate diets where absorption seldom exceeds 20%.

Phytate

In plant food based diets, the content of phytate present in whole grain cereals and legumes is probably the single most important factor for Zn absorption as it is a potent inhibitor of Zn absorption. With high phytate meals (e.g. wheat bran), absorption is only 5–10% (Rossander *et al.* 1992). The effect of phytate seems to be significant in single meals at molar ratios of phytate:Zn above 10. Fermentation of wholemeal bread reduces the phytate content and improves Zn absorption (Nävert *et al.* 1985). During fermentation and other food processes the hexaphosphate form of inositol is gradually degraded. The penta form seems to have a similar Zn absorption depressing effect as the hexa form whereas lower inositol phosphates have less or no effect (Sandström & Sandberg, 1992). Animal protein improves Zn absorption from phytate-rich meals (Sandström *et al.* 1980) which could explain why substitution of wholemeal bread for white bread did not reduce Zn absorption from a meat based sandwich (Fairweather-Tait *et al.* 1992). Isolated dietary fibre preparations with no phytate do not affect Zn absorption (Rossander *et al.* 1992).

Metals

In aqueous solutions Fe impairs Zn absorption (Valberg *et al.* 1984; Sandström *et al.* 1985), but this interaction does not take place when Fe is added to an animal protein meal, indicating different uptake mechanisms for solutions and solid foods. Tin in large doses inhibits Zn absorption (Valberg *et al.* 1984), but the ratio between Cu and Zn does not affect Zn absorption (August *et al.* 1989). Animal studies have suggested an interaction between Ca and Zn in phytate-rich diets, but this has not been confirmed in human studies. When a Ca-rich food such as milk was added to a phytate-containing meal and when the Ca content of a soya formula was increased, Zn absorption was improved or unchanged (Lönnerdal *et al.* 1984; Sandström *et al.* 1987). However, it remains to be shown whether or not intake of Ca supplements in a phytate-containing diet reduces Zn availability.

Human milk

Absorption of Zn from human milk is high (40% in adults), lower (~30%) from cows' milk based formula and cows' milk, and even less (14%) from an infant soya formula (Sandström *et al.* 1983). The high bioavailability of Zn in human milk has been attributed to low molecular weight ligands such as citrate or to specific proteins. However, when individual dietary components were added to cows' milk protein based infant formula the depressing effect of phytate was confirmed, but neither the protein nor the carbohydrate source had any measurable influence on Zn absorption (Lönnerdal *et al.* 1984).

Processing

Food processing can affect mineral binding and availability, such as the reduction in phytate with leavening of bread. A lower absorption of Zn from toasted cornflakes compared with corn grits has been reported (Lykken *et al.* 1986) but extrusion cooking of wheat bran did not affect Zn absorption (Fairweather-Tait *et al.* 1989*b*). Other studies have shown that the extrusion cooking process affects the intestinal degradation of phytate which affects absorption, while there is no effect of the extrusion cooking *per se* (Rossander *et al.* 1992).

Total diet studies

Relatively few studies of Zn uptake from total diets have been performed and in the majority of these studies formula diets, often with added Zn salts, have been used. The inhibiting effect of phytate on Zn has been confirmed; the addition of phytate to a formula

diet (molar ratio phytate:Zn 15) halved Zn absorption (Turnlund *et al.* 1984). There was no difference in Zn absorption between an animal protein diet with a phytate:Zn molar ratio of 5.7 and a diet made from mainly plant products with a ratio of 11.6 (Swanson *et al.* 1983).

CONCLUSIONS

The bioavailability of Zn can vary from 5 to 50%. Diets can be roughly classified as having a low, medium or high bioavailability, according to the content of Zn, phytate and animal protein. The highest absorption, 30–50%, is found in refined low Zn diets with low phytate content or in animal protein based formula diets. From a mixed animal and plant product diet, 20–30% Zn absorption can be expected. The lowest absorption, 10–15%, is seen from diets dominant in developing countries, based on cereals and legumes with a high phytate content and with negligible amounts of animal protein.

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