An Evaluation of Liquid Vitamin-Mineral Supplement Technology

GERHARD N. SCHRAUZER, D.Sc. FACN, CNS

ABSTRACT

Liquid multivitamin-mineral preparations are gaining popularity among those who believe that liquid (or colloidal) nutrients are better absorbed from a liquid than when ingested in tablets or pills. Critics have argued that this claim is not supported by any studies-but is this really true? This article provides answers to this and other frequently asked questions about these products.

INTRODUCTION

ALTHOUGH VITAMINS AND MINERALS are customarily taken in solid (tabletted, cap suled, or chewable) forms, liquid preparations have recently become available and have rapidly found wide customer acceptance, based in part on the marketing argument that supplements in solution are better absorbed than those taken in solid form. Liquid supplements are as such are not new; the first were developed decades ago but were prescribed mainly for elderly persons, infants, and patients with digestive problems. They were not in general use and did not become widely known. The recent upsurge of the popularity of liquid supplements started 10 years ago with the promotion of products designated as "plant-derived minerals" or "colloidal minerals." Unlike the conventional supplements, which as a rule use chemically defined compounds of single elements in solid form, the plant-derived minerals are offered in solution. They are promoted as being superior to conventional mineral supplements in that they contain not just the usual elements, such as iron or zinc, but instead virtually all elements, essential and nonessential, that are present in mineral-rich humic shale deposits. They contain iron and a number of essential trace elements at nutritionally significant amounts, but many of the other elements listed on the labels are present at very low levels.

The popular acclaim of these preparations is difficult to rationalize on the basis of their mineral content alone; if anecdotal reports are believed, they appear to have additional healing or tonicizing effects and act somewhat like elixirs, the possible reasons for which will be discussed later. These liquid mineral extracts are also not new products; they were claimed to have been used as remedies by Native Americans for centuries in regions of Utah where such humic shale deposits occur, and this is how they became known to white settlers in the region, one of whom started to market them some 75 years ago. Their continuing popularity among users is attributed primarily to the high bioavailability of the elements present in these extracts. However, it has been charged that this claim is unsupported by evidence; in addition, the chemical nature, composition, and safety of the extracts have been called into question (Schauss, 1997a, 1997b). Indeed, the various products that were being marketed initially differed considerably in quality and composition. After these criticisms, manufacturers standardized their products with respect to composition and purity, but the general uncertainty as to the nature and health value of these natural mineral extracts still persists. In a broader sense, this uncertainty extends to liquid vitamin-mineral supplements as a whole, and questions are still raised as to whether vitamins or minerals are indeed better absorbed from solutions than from tablets or whether any other advantages are offered by liquid preparations compared with conventional solid supplements.

The present account was prepared to address these questions without directly or indirectly promoting any specific line of products. At first, the bioavailability and absorption of liquid and solid vitamins and minerals is discussed on general principles. Then, studies are reviewed in which liquid supplements were tested for against solid forms. Finally, the nature of the plant-derived mineral extracts is disclosed and questions regarding their apparent efficacy, mechanism of action, and safety are addressed.

NUTRIENT BIOAVAILABILITY AND ABSORPTION

Bioavailability is defined as the proportion of a nutrient in food that can be absorbed and made available for use and storage; absorption is the physiological process that permits passage of a dietary nutrient from the intestinal lumen to the body fluids and tissues (Bender, 1989). Because bioavailability is a prerequisite of absorption, solid supplements must be soluble in the stomach fluid. Most supplements are formulated to meet this requirement, but their increasing complexity makes solubility difficult to achieve.

The United States Pharmacopeial Convention, Inc. (USP) has established manufacturing standards for vitamins and minerals with regard to quality, purity, potency, and the dissolution and disintegration properties of supplements. However, only a few manufacturers state on the label that their products meet the USP requirements. It therefore has been suggested (Blonz, 1996) that consumers test questionable pills themselves, by placing them in half a glass of vinegar, to simulate the acidic environment of the stomach. According to USP, calcium supplements should dissolve in 30 minutes, magnesium supplements in 45 minutes; for vitamin E tablets, a 45-minute disintegration is acceptable, and for multivitamin and mineral combinations, a 60-minute dissolution. However, for people with low stomach acid production, the in vitro dissolution tests may be of little value.

In the liquid supplements, the vitamins and minerals are already dissolved and therefore are immediately bioavailable. Furthermore, the liquid supplements usually are acidic; specifically, they are formulated to contain citric acid, ascorbic acid, and other substances that increase the bioavailability of minerals, such as carbohydrates (glucose, lactose), polyols (sorbitol), amino acids (arginine, lysine), vegetable gums, peptides, and emulsifying agents. Solid vitamin-mineral preparations instead contain inert excipients and are usually buffered so as not to cause gastric discomfort on ingestion, although this may reduce mineral bioavailability.

Active transport

The vitamins and minerals in foods are normally present at low concentrations. Accordingly, active transport systems have evolved to ensure their absorption. Active transport across the intestinal mucosa may require specific carrier proteins and cofactors and is energy dependent (usually adenosine triphosphatase dependent) (Serfaty-Lacrosniere et aL, 1995). Carrier proteins are often highly substrate specific, although in the case of metals the same carrier can bind several different metals with similar ionic radii and charges. Active transport is an important mechanism of homeostatic control and may be subject to adaptation that is, it may increase in response to deficiency or decrease if a nutrient is supplied in excess. However, active transport mechanisms are subject to genetic damage and may change with age or in response to disease. It therefore is difficult to predict, on a case-to-case basis, to what extent a bioavailable nutrient is absorbed. As a general rule, the more of an actively transported nutrient that is supplied, the less that is absorbed. This situation favors liquid supplements because, if taken as directed, they provide the nutrients in lower concentrations than solid supplements do.

Facilitated absorption

The absorption of certain vitamins and minerals is facilitated by endogenous carrier proteins or by exogenous factors acting as complexing agents. The endogenous carrier proteins are located on the two faces of the cell membrane and exist in two conformational states. Metal binding occurs first at one and then at the other site on the membrane (SerfatyLacrosniere et al., 1995; Stein, 1986). Facilitated absorption occurs mainly by diffusion and is not an energy-dependent process; the driving force is the concentration difference of the ion between the two sides of the membrane. In general, facilitated absorption is more rapid than simple diffusion, but it is limited by the carrier capacity and the amount of binding factor available. If a specific endogenous carrier or binding factor is not produced under pathological conditions, intestinal absorption of the nutrient may be negligible. In order not to overwhelm the available

absorption capacity, vitamins and minerals should be supplemented at low concentrations over a period of time rather than suddenly. These conditions are more easily met with liquid than with solid supplements: The former are ingested in comparatively high dilution, whereas the latter on ingestion may release the vitamins and minerals at concentrations much higher than those normally encountered in foods and in excess of the available absorption capacity. Time-release supplements were developed to obviate this problem.

Absorption by passive diffusion

Simple or passive diffusion represents the simplest possible mechanism of absorption (Serfaty-Lacrosniere et al., 1995). It is an energy-independent process and occurs best from isotonic solutions. The degree of absorption depends on the concentration of the nutrient on both sides of the membrane and its relative solubility in the lipid bilayer. Liquid supplements readied for ingestion are, or should be, nearisotonic solutions, so as to favor nutrient absorption by passive diffusion. A solid supplement, in contrast, may dissolve in the stomach to yield an initially hypertonic solution. When this solution is passed into the small intestine, it is first diluted with body fluid, via osmosis through the intestinal membrane, until isotonicity is reached. Because of the attendant increase of intestinal content, peristalsis may be activated, resulting in gastric discomfort, diarrhea, and diminution of absorption. In elderly subjects or patients with intestinal disorders, the normally spontaneous process of rendering an hypertonic solution isotonic may be generally disturbed. For such subjects, special isotonic liquid feeding mixtures have been developed.

Inhibitors of absorption

The ingestion of solid supplements with foods is sometimes recommended to increase bioavailability. However, foods may actually diminish the bioavailability or absorption of nutrients. For example, long-chain fatty acids from ingestion of lipids form insoluble calcium and magnesium salts, which are poorly absorbed. In the liquid vitamin-mineral preparations, the comparatively low solubility of the citrates of calcium and magnesium compounds results in the formation of suspensions. Bioavailability is not reduced, because these compounds readily dissolve when added to orange juice. Phytic acid (inositol hexakisdihydrogen phosphate), a compound present in unprocessed whole grains and unleavened bread, forms insoluble complexes with iron, zinc, copper, calcium, and manganese and greatly reduces their bioavailability (Davies and Nightingale, 1975; Hallberg, et al, 1987; Navert et al., 1985). Copper forms an insoluble sulfide when ingested with egg yolk (Schultze, et al., 1936). Dietary fiber, oxalic acid in vegetables, and tannins in coffee and tea also inhibit the absorption of iron and other minerals (Morck, 1983). Tannins form poorly absorbable, complexes with metals as well with vitamin Bl (thiamine) (Friedrich, 1987). Raw fermented fish contain an enzyme (thiaminase) that inactivates thiamine; thiamine absorption is also inhibited by alcohol. Naturally occurring antagonists of vitamin B2 (riboflavin), vitamin B6 (pyridoxal), and biotin are known. The uptake of vitamin K is inhibited by vitamin E (Friedrich,1987).

Adverse interactions in supplements

Solutions of the B vitamins are more stable in acidic rather than in neutral or alkaline solutions, which is one of the reasons why citric and ascorbic acids are added to the liquid vitamin-mineral preparations. However, the resulting mixtures are extremely oxygen sensitive. To prevent loss of vitamins during manufacture and storage, liquid supplements must be protected from air as much as possible; opened bottles should be kept refrigerated. Destructive oxidation reactions may also take place in powdered mixtures of minerals and vitamins and even in the finished tablets, thereby reducing the shelf-life of the products. Accordingly, special precautions are taken during manufacture of the supplements, oxygen is excluded where necessary, and reactive ingredients either are not combined or are prevented from interacting through microencapsulation or the use of excipients. In some cases tablets with a layered structure are produced; the vitamins typically form the central core, which is surrounded by mineral salts and a

protective layer of calcium carbonate. Other manufacturers obviate this problem by offering packages of five or more tablets or capsules containing water-soluble vitamins, fat-soluble vitamins, and minerals separately.

BIOAVAILABILITY AND ABSORPTION OF VITAMINS

Many (but not all) of the water-soluble and fat-soluble vitamins are absorbed by passive diffusion when they are present at sufficiently high concentrations (Serfaty-Lacrosniere et al.,1995) (Table 1). At low, physiological levels the absorption of vitamins is often active, facilitated, and cofactor dependent, which provides an argument against megadosing. As is well known, oral vitamin B12 is absorbed regardless of oral dose only to the extent that it is bound to intrinsic factor; impaired excretion of this factor by gastric mucosal cells results in B12 deficiency. The absorption of vitamin C (ascorbic acid) in humans is active and saturable. At dosages up to 180 mg/ day, 80-90% of the vitamin is absorbed; at 2,000 mg/ day, absorption drops to 44%, and at 5,000 mg/ day, to 20.9% (Horning et al., 1980). The human organism can maximally absorb 1,160 mg of ascorbic acid per day. Vitamin C is better absorbed in a natural citrus extract containing bioflavonoids, proteins, and carbohydrates (Vinson and Bose, 1988). In therapeutic applications, multiple smaller oral doses are in general preferable to single large doses. This was confirmed for vitamin C in a study wherein three divided doses per day caused a more significant increase of serum ascorbate levels than the same amount given in one daily dose (Vinson et al., 1998).

Selenium is included in Table 1 because it occurs in foods, mainly in the form of selenomethionine (Le., an organic rather than an inorganic form). Baker's or Brewer's yeast naturally converts selenium into selenomethionine and is widely used in supplements, although yeast-free selenomethionine-containing supplements are also available. Selenomethionine is absorbed like methionine, by active transport; its selenium is not immediately bioavailable but becomes so after enzymatic degradation. In some products, selenomethionine is replaced by sodium selenite or other inorganic selenium salts. Inorganic selenium salts are also added to yeast, which is then offered as "organic" even though it does not contain selenomethionine. Selenomethionine is compatible with vitamin C, but selenite is reduced by it to the bio-unavailable elemental selenium (Schrauzer and McGinness, 1979). The use of selenite in solid or liquid nutritional supplements should therefore be discouraged; also, the need for accurate labeling of supplemental selenium products is apparent.

TABLE 1. INTESTINAL ABSORPTION OF VITAMINS AND OF, Fooo-FoRM ORGANIC SELENIUM (SELENOMETHIONINE)

Vitamin	Site of absorption	Mechanism of absorption
A	Proximal and distal small intestine Duodenum, jejunum	Facilitated (carrier-dependent) diffusion at low concentrations, simple diffusion at higher concentrations. Absorption increases with fats; salts of bile acids increase resorption
D	Duodenum, jejunum Proximal small intestine Terminal ileum Jejunum	Simple diffusion; fats and emulsification facilitate absorption Active transport; unsaturated fatty acids, vitamin E, inhibit absorption
D, E, and carotenes K1	Duodenum	Simple diffusion Synergistic absorption with sodium; conversion to absorbable metabolites

K2 Thiamin	Proximal jejunum	Active transport at physiological concentrations, at higher levels by simple diffusion; thiamine at 10 times daily dose produces only minor increase of serum level because of rapid excretion
Riboflavin	Proximal jejunum	Absorption is probably regulated hormonally, with sodium acting synergistically (?) after conversion into coenzyme form (flavine mononucleotide) in intestinal mucosa. Synergistic absorption with sodium (?), and simple diffusion Rapid intestinal absorption at all concentrations
Nicotinic acid Nicotinamide B6	Not known	Simple diffusion, facilitated by conversion into metabolites (rat, hamster); pyridoxamine, pyridoxal and pyridoxine pass intestinal mucosal cells by passive diffusion; at low levels, a partial phosphorylation and dephosphorylation, transport by passive diffusion
Folic acid	Jejunum	Free folic acid is absorbed by simple diffusion at high concentrations; tenfold daily dose is rapidly absorbed
Biotin	Proximal small intestine	Synergistic absorption with sodium; active absorption or by diffusion (hamster)
Pantothenic acid B12 (cobalamin)	Ileum	Probably primarily by simple diffusion Cobalamin complex with intrinsic factor (IF) is bound to specific receptors in ileum; the IF-cobalamin complex or free cobalamin is then transported into the mucosal cell
C (ascorbic acid)	Ileum	At physiological levels, active, carrier, and sodium dependent absorption that is saturable; in some animals, absorption by diffusion
Se (selenomethionine)	Small intestine	Active transport, similar to methionine

W. Friedrich, 1987, modified.

BIOAVAILABILITY AND ABSORPTION OF SELECTED MINERALS

Table 2 summarizes available data on the site and mechanism of absorption of essential minerals and trace elements (Berthon, 1995). As may be seen, the absorption of metals is often subject to endocrine control. A separate discussion of several selected mineral elements and of the so-called colloidal minerals follows.

TABLE 2. INTESTINAL ABSORPTION OF ESSENTIAL MINERALS

Mineral	Site of absorption	Mechanism of absorption
Na,K	Small intestine	Passive and associated with water absorption; regulation of sodium/ potassium balance in higher animals and humans occurs in the kidney
Ca	Small intestine	Uptake is regulated by parathyroid hormone, vitamin D, calcitonin, phosphate; citrate, orotate, ascorbate increase Ca bioavailability; phytic and oxalic acid decrease bioavailability
Mg	Small intestine	Mechanism of absorption in animals and humans is probably related to that of Ca, but in general less Mg is absorbed
Fe	Duodenum and small intestine	Passive absorption facilitated by stomach hydrochloric acid, citric acid, ascorbic acid, lactic acid, succinic acid, etc., inhibited by polyphenols, phytic acid, coffee, tea, dietary calcium
Cu	Small intestine, duodenum	Active transport with a diffusion component, facilitated under acidic conditions, by citric and ascorbic acid; diminished by carbohydrates, notably fructose, excess ascorbic acid, also by zinc
Zn	Jejunum, duodenum, colon	Active and carrier-mediated, inducible in rodents and humans (metallothionein); absorption is increased by glucose, low-molecular weight compounds, inhibited by phytic acid, calcium, vitamin D
Mn	Duodenum	Absorption increased by low intestinal pH, but not specifically by ascorbic acid; absorption inhibited by calcium
Cr	Jejunum, ileum, duodenum	Facilitated diffusion, absorption very low; absorption is increased by oxalate, amino acids, transferrin, albumin, starch, ascorbic acid; absorption decreased by antacids, zinc, iron, vanadium must dissolve in 30 minutes to at least 75% in 0.10 mollL HCl at 37°C

(Blanchard, 1989).

Calcium

The most commonly prescribed calcium supplements contain calcium carbonate. Although calcium carbonate is soluble in acids and therefore should dissolve in the stomach, the solubilities of calcium carbonate-based supplements vary considerably (Blanchard, 1989). Because the failure to dissolve is in some cases caused by the compactness of the tablets, a disintegration test in simulated gastric fluid under standardized conditions was introduced to assess calcium bioavailability (United States Pharmacopoeia, 1985). However, because this test measured only disintegration and not dissolution, it overestimated bioavailability. Therefore, since 1987, the official USP requirement for labeling of calcium supplements has included a dissolution test, by which the tablets.

Because stomach acid production diminishes with age, elderly persons may be unable to utilize calcium as the carbonate. An effective carrier for facilitated absorption of calcium is citric acid, which may explain why calcium carbonate dissolved in orange juice shows generally superior bioavailability (Whiting and Pluhator, 1992) and, under these conditions, does not interfere with iron absorption (Mehansho et a1., 1989). Other calcium compounds that are well soluble and provide bioavailable calcium include the orotate and the ascorbate. Calcium absorption and the incorporation of calcium into bone are biochemically complex, hormonally controlled processes in which several additional trace elements and phosphate play contributory roles (Bucci, 1991). To this effect, more sophisticated liquid and solid calcium supplements have been formulated that contain calcium and magnesium as the citrates and orotates, microcrystalline hydroxyapatite, and vitamin D, with boron and other trace elements believed to be working synergistically to improve calcium absorption and incorporation into bone.

Magnesium

Some studies indicate that soluble magnesium compounds such as magnesium citrate are more bioavailable than magnesium oxide (Lindberg et a1., 1990). Magnesium absorption may be enhanced by the addition of a glucose polymer solution (Bei, et a1., 1986). Some studies, however, indicate that the intestinal absorption of magnesium is the same so long as it is free and in the ionized form (Lindberg et a1., 1990). Only about 21 % of the magnesium is normally absorbed through the intestine; excesses after storage compartments are filled are excreted, about 70% via the intestine and 30% renally. The mechanism of intestinal absorption of magnesium resembles that of calcium; physiological concentration and excretion are hormonally controlled. Excess magnesium stimulates calcium excretion, and excess calcium impairs absorption of magnesium. Mineral waters containing magnesium and calcium as the bicarbonates provide good sources of both elements. In some liquid vitamin-mineral supplements, ocean-derived minerals, Dead Sea minerals, or minerals from the Great Salt Lake are added to increase the magnesium content and to add additional naturally occurring trace elements. The magnesium is present in the form of the chloride, which is well absorbed from dilute solutions but acts as a cathartic if ingested in larger amounts.

Iron

Subclinical iron deficiency is widespread in the general population. In adults, migraine headaches, lack of appetite, aversion to eating meat, breathlessness on exertion, heart palpitations, brittle nails, constipation, cold sensitivity, sore tongue, and weak or fragile bones can be caused by iron deficiency. In children, growth retardation, pale complexion, unhealthy appearance, fatigue, depression, dizziness, inability to concentrate or to think clearly, and irritability are caused by iron deficiency.

For the treatment of simple iron deficiency anemias, pills containing a high dose of iron, usually as the sulfate, are prescribed. Iron sulfate taken in excess is toxic; in the home, it poses a serious health hazard, and accidental ingestion of an overdose, especially by infants, can be fatal. For some years, therefore, powdered elemental iron (Ferrum reductum) was used to treat iron deficiency anemias. Elemental iron is less toxic than ferrous sulfate, but because of its poor bioavailability 500 mg (approximately 7.5 grains) must be taken three or four times daily after meals (The Dispensatory, 1995a). Even ferrous sulfate must be taken daily for months because so little of the iron is absorbed. It may cause stomach upset and constipation, and patient compliance is often poor; children, especially, tend to refuse to take iron sulfate pills for any extended period. To obviate the compliance problem in an experiment with preschool children aged 2-6 years, iron fortified bread was given for 6 months; however, this regimen failed to produce positive results. A significant increase of hemoglobin levels in the children resulted only when a small amount of iron (20 ppm Fe as ferrous sulfate) was added to the drinking water. At the conclusion of the test, after 8 months of supplementation, hemoglobin levels increased from 10.6::!: 1.1 to 13.0::!: 1.1 g/dl, serum ferritin from 13.7 ::!: 8.9 to 25.6 ::!: 10.5 p,g/L (N = 31), and "no problems related to the (iron) salt addition or to the children drinking the iron-enriched water" occurred (Dutra de Oliveira et a1., 1994). Iron is discussed further in the section on colloidal minerals. Liquid vitamin-mineral supplements contain vitamin C and vitamin A, which increase iron bioavailability and absorption, respectively.

Zinc, copper, manganese, chromium

The bioavailability and absorption of zinc, copper, manganese, and chromium are lowered by dietary components (e.g., phytic acid, tannin, fiber, phosphate). Absorption is increased by certain amino acids, decreased by others. The bioavailabilities of ionic forms of these metals are mutually interdependent. Supplemental iron, for example, impairs the absorption of zinc (Solomons and Jacob, 1981), copper (Haschke et a1., 1985), and manganese (Thomson et a1., 1971), whereas calcium may reduce chromium absorption (Seaborn and Stoecker, 1990). Ingestion of multiple

minerals may provide assurance against imbalances induced by single elements. In solid supplements, the presence of calcium and magnesium may impair absorption of these metals. Vitamin C may decrease gastrointestinal absorption of copper. More research is required on both solid and liquid supplements to establish the optimal concentration of these elements for supplementation.

Plant-derived liquid or colloidal minerals

Some of the liquid vitamin-mineral supplements contain aqueous extracts of minerals found in deposits in humic shales. The extracts contain predominantly the sulfates of iron, and aluminum; in addition, zinc, silicon, nickel, manganese, magnesium, lithium, calcium, boron, chromium, copper, and silicon and traces of 60 or more other elements are present, or claimed to be present, depending on the sensitivity of the analytical method employed. In some extracts, traces of organic compounds such as humic or fulvic acids are detectable. The safety of these extracts became a concern after it was suggested that some could contain possibly radioactive or toxic elements such as strontium and aluminum (Schauss, 1997a, 1997b). These concerns have since proved to be unfounded with respect to radioactivity and the presence of unusually high levels of strontium. In our own tests, using a scintillation technique approved by the U.S. Environmental Protection Agency, none of 10 extracts tested showed radioactivity above background, and a previously quoted high value for strontium was actually that of sulfur.

The levels of aluminum in some of the earlier, more concentrated versions of extracts could exceed 4,000 ppm, but these have been lowered in most products to one third of that value or less. At current levels, 1 ounce of extract provides 10-20 mg of aluminum, which is within the nutritional range. Aluminum is widely distributed in foods, from which a certain amount is absorbed, and the absorption appears to occur in proportion with iron. Although iron is retained, excess aluminum is excreted, causing the adult human body invariably to contain only about 0.5 g of aluminum, compared with 4-5 g of iron. Several studies attest that aluminum may have beneficial or essential physiological functions in animals; past postulated links between oral aluminum intake and Alzheimer's disease have been discredited (Watt, 1997).

Thus, recent comparisons of the levels of mineral elements in the subcortical region and the frontal cortex of the brains of AD patients give no evidence that Al is an etiological factor in AD. Instead, these studies revealed significant accumulations of calcium and zinc in the frontal cortex of AD brains, suggesting that mineral transport systems in the brain cells of AD patients are defective (Kienzl et a1., 1996).

Because the humic shale extracts contain sulfates of iron and aluminum, they are weakly acidic and contain equilibrium amounts of free sulfuric acid and traces of colloidal metal hydroxides. It was the presence of the latter that led to their marketing name, "colloidal minerals," although most of the elements are actually present in ionic forms. An extract may typically contain 300 ppm of iron, predominantly as ferrous sulfate. One ounce of extract in 8 ounces of orange juice provides almost 10 mg of iron at a dilution that makes it both well tolerable and highly bioavailable. This fact provides a basis for the disputed promotional claim that the plant-derived minerals are 10-12 times more bioavailable than in their elemental form. The fact that elemental iron has a low bioavailability is well known; the literature lists it as ranging from 0.5% to 2%. In contrast, the bioavailability of iron in the form of ferrous sulfate is given as 12-16% (Auterhoff, 1968).

The presence of iron in the extracts could be responsible for some of their claimed beneficial effects: Iron supplementation in cases of subclinical iron deficiency often results in striking improvements of the general condition. However, the extracts also provide nutritionally significant amounts of several other essential elements. The extracts bear a close chemical resemblance to the iron sulfate-containing mineral springs or "vitriol waters" found in Europe.

These have been described as possessing astringent, tonicizing, and antiseptic properties. They were widely recommended at the turn of the 20th century for treatment of iron deficiency anemias and especially of chlorosis, the then common form of anemia occurring in young girls, because it was already known that dissolved iron is more bioavailable than that in conventional iron preparations (Tilenius, 1925). Vitriol waters were prescribed as tonics after acute diseases or blood loss; to treat exhaustion and fatigue; and for diseases of the spleen, liver, and kidneys, various chronic diseases, nervous disorders, "sciatica," disorders of the thyroid gland, diseases of the mucous membranes, and so on (Tilenius, 1925). These claims may appear excessive or difficult to rationalize, but they were based on empirical observations made over the years by the local balneologists.

Today, similar claims are made by users of the "colloidal minerals" products. If one is willing to accept them as true, these apparent healing effects cannot be attributed solely to the iron present. To rationalize them, it must be considered that the preparations contain sulfates of iron and other metals, which causes them to be acidic as a result of the presence of equilibrium amounts of sulfuric acid. Dilute sulfuric acid, Acidum sulfuricum dilutum, was used for hundreds of years internally as a tonic and medicine for a wide variety of conditions-to promote convalescence from protracted fevers, to reduce fatigue, to stimulate the appetite, to improve digestion, and to treat gastric hypoacidity, menopausal hot flashes, thyroid diseases, and so on. The administration of dilute sulfuric acid was recommended still relatively recently as a "constitutional agent" (Aschner, 1995). In U.S. pharmacies it was available in flavored alcohol solution known as Elixir of vitriol or Acidum sulfuricum aromaticum (The Dispensatory, 1995b), and in Europe as Elixir acidum halleri or Aqua rabelii (Schulz, 1903). The plant mineral extracts or colloidal mineral preparations therefore may owe their apparent efficacy also to the presence of sulfuric acid. They could be regarded as natural versions of "elixirs of vitriol." Sulfuric acid, or sulfate, is the terminal product of the metabolism of sulfur amino acids. Sulfate is required for biosynthesis of the all-important chondroitin sulfates and for detoxification of physiological metabolites, natural products, and pharmaceuticals, including adrenaline, thyroid hormones, phenols, and a wide variety of drugs. Sulfate may also detoxify heavy metals such as lead and barium.

SUMMARY AND OUTLOOK

Because the industry is now offering both solid and liquid vitamin-mineral preparations, health professionals have a wider choice in searching for the right supplements for their patients. Solid vitamin and mineral preparations have the obvious advantage that single or multiple nutrients can be prescribed and dispensed at accurate dosages. They are also easier to ship and store, but, as we have seen, they may cause problems with respect to bioavailability and compliance. Liquid supplements contain the nutrients in a more highly bioavailable form, are gentler to the stomach, and sometimes are more suitable than solid supplements, especially for children and elderly patients, as was shown specifically for iron. The liquid mixtures containing numerous vitamins and minerals are probably better suited for routine general supplementation than for treatment of a defined deficiency. Those containing humic-shale or plant-derived minerals are tonics as well as supplements and therefore belong in a special category. In general, the preparation of any supplement poses a challenge, and some of the newer liquid products need to be further refined and improved. However, the liquid technology is here to stay and offers opportunities for numerous new products. It is hoped that further development of the liquid supplement technology will ultimately lead to a more balanced and economical use of vitamins and minerals.

REFERENCES

Aschner, B. (1995). *Technik der Konstitutionstherapie*, ed 7.
(KF. Haug, Heidelberg) pp 52, 56, 120.
Auterhoff, H. (1968). *Textbook of Pharmaceutical Chemistry*,
ed 5. (Wiss. Verlagsges., Stuttgart) pp 85-86.

Bender, AE. (1989). Nutrient availability: Chemical and biological aspects. In *Bioavailability* "88." D. Southgate, I. Johnson, G.A Fenwick, eds. (Royal Society of Chemistry, Cambridge, UK) p. 3.

Bei, L., Wood, RJ., and Rosenberg, I.H. (1986). Glucose polymer increases jejunal calcium, magnesium and zinc absorption in humans. *Am J Clin Nutr* 44, 244-247.

Berthon, G. (1995). *Handbook of Metal-Ligand Interactions in Biological Fluids* Vol. 1. (Marcel Dekker, New York) Chapter 2.

Blanchard, J. (1989). Calcium and osteoporosis: Some caveats and pleas (editorial). *Calcify. Tissue Int*. 44, 67-68.

8Ionz, E. (1996). Food Section, *The San Diego Union-Tri*
bune, Thursday, Dec. 5.

Bucci, L.R (1991). Osteoporosis treatment: Much more
than calcium. *Today's Chirop* 20, 38.

Davies, N.T., and Nightingale, R (1975). The effects of phytate on intestinal absorption and secretion of zinc and whole body retention of zinc, copper, iron and manganese in rats. Br *J Nutr* 34, 243-258.

Dutra de Oliveira, J.E., Ferreira, J.B., Vasconsellos, V.P., and Marchini J.S. (1994). Drinking water as an iron carrier to control anemia in preschool children in a daycare center. *JAm Coll Nutr* 13,198-202.

Friedrich, W. (1987). *Handbuch d. Vitamine*. (Urban and
Schwarzenberg, Baltimore).

Hallberg, L., Rossander, L., and Skanberg, AB. (1987).
Phytates and the inhibitory effect of bran on iron ab
sorption in man. *Am J Clin Nutr* 45, 988-996.

Haschke, F., et al. (1985). Effect of iron fortification of in
fant formula on trace mineral absorption. *J Pediatr Gas*
troenterol Nutr 5, 768-773.

Homing, D., Vuilleumier, J.P., and Hartmann, D. (1980).
Int J Vitam Nutr Res 50, 818.

Kienzl, E., Jellinger, K., Wruss, W., Sorbager, S., and Puchinger, L. (1996). Distribution of individual elements in Alzheimer disease brain tissue. *In Metal Ions in Biology and Medicine* Vol. 4. P. Collery, J. Corbella, J.L. Domingo, et aI., eds. Gohn Libbey Eurotext, Montrouge, France) pp. 617-619.

Kobrin, S.M., Goldstein, S.J., Shangraw, RF., and Raja, RM. (1989). Variable efficacy of calcium carbonate tablets. *Am J Kidney Dis* 14,461-465.

Lindberg, J.5., Zobitz, M.M., Poindexter, J.R, and Pak, c.Y. (1990). Magnesium bioavailability from magnesium citrate and magnesium oxide. *J Am Coli Nutr* 9, 48-55.

Mehansho, H., Kanerva, RL., Hudepohl, G.R, and Smith, K.T. (1989). Calcium bioavailability and iron-calcium interaction in orange juice. *J Am Coli Nutr* 8, 61-68.

Morck, T.A (1983). Inhibition of food iron absorption by
coffee. *Am J Clin Nutr* 37, 416-420.

Navert, B., Sandstrom, B., and Cederblad, A (1985). Reduction of the phytate content of bran by leavening in bread and its effect on zinc absorption in man. *Br J Nutr* 53, 47-53.

Schauss, AG. (1997a). Colloidal mienrals: Clinical implications of clay suspension products sold as dietary supplements. *Am J Nat Med* 4, 3-10.

Schauss, AG. (1997b). An analysis of colloidal mineral
claims. Health Counselor 9, 60-62.

Schrauzer, G.N., and McGinness, J.E. (1979). Observations
on human selenium supplementation. *Trace Substances*
in Environmental Health 13, 64-67.

Schulz, H. (1903). *Vorlesungen iiber die Wirkungen und An wendung der unorganischen Arzneistoffe*, ed. (K.F. Haug, Berlin) pp. 246-247.

Schultze, M.a., et al. (1936). Further studies on the bioavailability of copper from various sources as a supplement to iron in hemoglobin formation. *J Bioi Chem* 115, 453-457.

Seaborn, C. and Stoecker, B. (1990). Effects of antacid or ascorbic acid on tissue accumulation and urinary excretion of chromium. *Nutr Res* 10, 1401-1407.

Serfaty-Lacrosniere, c., Rosenberg, I.H., and Wood, RJ. (1995). The process of mineral absorption. In *Handbook of Metal-Ligand Interactions in Biological Fluids*, Vol. 1. (Marcel Dekker, New York) pp 322-330.

Solomons, N.W., and Jacob, RA (1981). Studies on the bioavailability of zinc in humans. *Am J Clin Nutr* 34, 475-482.

Stein, W.D. (1986). *Transport and Diffusion Across Cell Mem branes*. (Academic Press, New York).

The Dispensatory of the United States of America, ed 25. (1955a). G.B. Lippincott, Philadelphia) p 721-722.

The Dispensatory of the United States of America, ed 25. (1995b). G.B. Lippincott, Philadelphia) pp. 1373-1374.

Thomson, AB.R, et al. (1971). Interrelation of intestinal transport system for manganese and iron. *J Lab Clin Med* 73, 6422.

Tilenius, O. (1925). Iron Springs etc. [German). In *Biider Almanach* 1925. (Berlin). pp 203-205.

United States Pharmacopoeia. (1985). SXXl/NF XVI Sup plement 5. (U.S. Pharmacopoeial Convention, Rockville, MD).

United States Pharmacopoeia. (1987). SXXl/NF XVI Sup plement 5. (U.S. Pharmacopoeia Convention, Rockville, MD).

Vinson, J.A, and Bose, P. (1988). Comparative bioavail ability to humans of ascorbic acid alone or in a citrus extract. *Am J Clin Nutr* 48,601-604.

Vinson, J.A, Roberts, K., Stonebrook, K., Jahner, D.K.W., and Berman, J.G. (1998). Comparative nutrient absorption after daily supplementation with multivitamin/multimineral tablets in young adults. *J Am Coli Nutr* 17, 531.

Watt F. (1997). Berkeley Newsletter. June/July 1997.

Whiting S.J. and Pluhator, M.M. (1992). Comparison of in vitro and in vivo tests for determination of availability of calcium from calcium carbonate tablets. *J Am Coli Nutr* 11, 553-560.

Address reprint requests to:
Gerhard N. Schrauzer
Biological Trace Element Research Institute
11526 Sorrento Valley Road, Suite A
San Diego, CA 92121