ALBION®
HUMAN NUTRITION

RESEARCH NOTES

A COMPILATION OF VITAL RESEARCH UPDATES ON HUMAN NUTRITION

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A MATTER OF TASTE

According to a recent survey from the American Academy of Pediatrics, 86.7% of the doctors report that unpleasant taste is a major cause of non-compliance.

Taste is one of the most important parameters of compliance in the use of supplements and/or pharmaceutical products, especially when dealing with children. In nutritional supplement products, undesirable taste is one of several important formulation problems encountered. In this regard, iron is one of the nutritional ingredients that presents a challenge. Chewable tablets, lozenges, and any sort of beverage that contain iron will tend to have an unpleasant metallic aftertaste. So, any iron nutritional formulation of these types that offers a pleasing taste would be preferred over a competitor's, and would result in better compliance, as well as better sales. The desire to improve palatability in these products has prompted the development of various innovations designed to improve taste and acceptability.

The Taste-Free Iron Chelate

Several years back, Albion Advanced Nutrition developed a novel form of iron to be used in certain supplement formulations and foods. Albion Advanced Nutrition was already producing the finest iron compound in Ferrochel® (ferrous bisglycinate chelate); however, there was a need for a chelated iron that

lacked the metallic taste found in all iron compounds. It was determined that there are a few factors that are associated with the less pleasant taste of metals and metal amino acid chelates, such as iron and others. One of those factors involves the metal's coordination number. Iron exists in the primary valence state as the ferrous form (+2 oxidation state), which is easily oxidized to the ferric form (+3 oxidation state), a more stable state for iron. In addition to oxidation state, iron (and other metals) has a secondary valence that is referred to as their coordination number. The ferric form can have a coordination number of six (6). To decrease the metal taste of a mineral like iron, the coordination number of the metal must be satisfied by the electron donor groups of the organic ligand (from an amino acid, for instance) that forms an ionic or coordinate bond which is sufficiently stable within the pH environment involved. At least one ligand must be of the polydentate type of the alpha-amino acid configuration. Preferably two or more ligands will be of the polydentate type and are better as alpha-amino acid ligands. The overall charge must be balanced (a second taste factor). These are some of the considerations in the formation of the Taste-Free mineral amino acid chelates from Albion Advanced Nutrition, which form the basics to the US Patent #5,516,925 (Amino Acid Chelates Having Improved Palatability). To form a Taste-Free version of ferric iron, there must be sufficient ligands to provide ionic and coordinate covalent bonds equal to the coordination number of the central metal ion (with charge balance). To satisfy the coordination number for ferric iron, six such bonds would be formed, which would require three (3) bidentate ligands. From this concept, Albion Advanced Nutrition developed Ferric Trisglycinate Chelate.

The molecular structure, chemical formula, and molecular weight for Ferrochel® and the Iron Amino Acid Taste-Free Chelate are shown in Figure 1 below.

Bioavailability Is an Important Factor

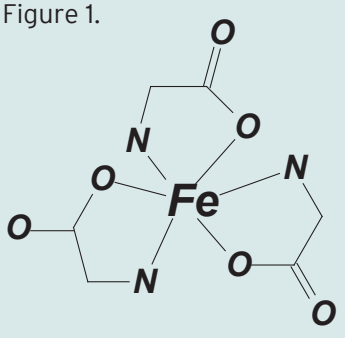
Ferrochel®, Albion Advanced Nutrition's exclusive ferrous bisglycinate chelate is known for its superior bioavailability. Clinical studies have demonstrated that Ferrochel®, a nutritionally functional mineral amino acid chelate, has much superior bioavailability, when compared to ferrous sulfate and other iron salt forms. In addition, Ferrochel® has many other clinical and organoleptic advantages over other forms of iron. Given the reputation of Albion's mineral amino acid chelates, Albion needed to develop a taste masked iron amino acid chelate that had good bioavailability. In line with this, a few independent clinical studies were done to evaluate the bioavailability of this Iron Amino Acid Chelate Taste-Free (Ferric Trisglycinate Chelate), starting quite some time ago.

Ferric glycinate iron bioavailability for rat, as determined by extrinsic radioisotopic labeling of infant formulas.

Langini S, et al.
Nutrition Reviews, October 1988,
Vol. 38, No. 4, 729-735.

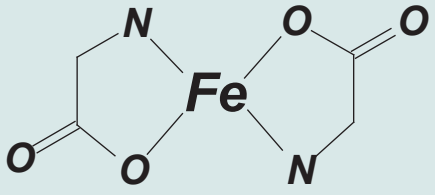
In this study, a casein based infant formula was fortified with each of the assayed iron sources: ferrous sulfate and ferric glycinate, and extrinsically labeled with $^{59}FeCl_3$. Ferrous sulfate had been the major iron source used for fortification; however it had shown prooxidant properties which impaired its nutritional and organoleptic qualities. In the study, male wistar rats were used. They were fed a protein basal diet devoid of iron for 24 hours prior to the test

Figure 1.



Ferric Trisglycinate

Molecular Formula: $FeC_6H_{12}O_6N_3$
Molecular Weight: 278 amu



Ferrous Bisglycinate

Molecular Formula: $FeC_4H_8O_4N_2$
Molecular Weight: 204 amu

period. Hematological parameters were assessed. The animals were allotted to two groups with equal average hemoglobin values, FEP/Hb ratio and body weight. The animals were then fed the experimental formula meals via gastric tube. Then body counts of radioiron were taken of the animals at 2 hours (this was to be the level at 100% absorption for the iron compounds), and then daily for two weeks. For both iron sources, the whole blood radioiron content on day 14 were approximately 85% of the retained tracer. The apparent iron absorption as percent of dose was determined. For the ferrous sulfate group, there was an absorption rate of 15.8%, while the ferric glycinate group had an absorption rate of 30.9%, demonstrating a superior bioavailability for the ferric glycinate.

Iron absorption from ferrous bisglycinate and ferric trisglycinate in whole maize is regulated by iron status.

Bovell-Benjamin AC, et al.
Am J Clin Nutr 2000;71:1563-1569.

The objective of this study was to compare iron absorption from ferrous sulfate, ferrous bisglycinate, and ferric trisglycinate in whole-maize meal; to determine whether iron from ferrous bisglycinate and ferrous sulfate exchanges in the intestinal pool; and to assess iron absorption from ferrous bisglycinate and ferric trisglycinate over a range of iron statuses. There were four parts (1a, 1b, 2a, and 2b) to this research trial, and the ferric trisglycinate was involved in study 2b. Parts 1a and 1b found that the average iron absorption from ferrous bisglycinate was 4.7 times greater than the iron absorption from ferrous sulfate. In study 2a, the subjects consumed ferrous sulfate (with ascorbic acid) and bisglycinate separately in water on two different days; in study 2b, the same subjects consumed ferric trisglycinate in water and in maize on two different days. The ferric trisglycinate was poorly absorbed when administered in the maize porridge (2.3%), however, it was absorbed at 39% when given in water, which was slightly superior to the absorption of Ferrochel® in water. Overall the researchers concluded that iron from ferrous bisglycinate (Ferrochel®) is better absorbed than that from ferrous sulfate in maize or the presence of the absorption inhibitors in whole maize, and that Ferrochel® is an effective and safe source of iron and is particularly useful in diets rich in phytates. The ferric trisglycinate was found to be ineffective as an iron source when given in a diet high in phytates. More research is needed to determine why this is the case. However, it should not be overlooked that iron from ferric trisglycinate was fairly well absorbed when given in water.

The use of sugar fortified with iron trisglycinate in the prevention of iron deficiency anemia in preschool children.

Regiane A. Cardoso de Paula and Mauro Fisberg.
Archiovos Latinoamericanos de Nutricion S V51; N1, 2001, pp54-59.

In this study, the effectiveness of the use of ferric trisglycinate chelate as a sugar fortificant in the prevention or control of iron deficiency anemia was evaluated. The study ran for six months and involved 93 children (ages 10-48 months) attending a day care center in Sao Paulo, Brazil. All of the children consumed 20 grams of fortified sugar per day for five days a week at breakfast. The children were assigned to one of two groups. Group one consumed a sugar fortified to deliver 2% of the RDA and group two received sugar fortified to deliver 20% of the RDA at the quantity consumed. After six months, both groups showed significant increases in the weight/height ratio. Both groups had highly significant increases in hemoglobin levels (0.4 g/dL). When one considered the anemic children only, the average increase in hemoglobin was 1.4 g/dL. In the anemic children, there was also a very significant increase in serum ferritin. The increase in serum ferritin was highest in the children receiving the higher level of iron per day. The fortified sugar was well tolerated and accepted. The researchers concluded that ferric trisglycinate is a bioavailable source of iron and its use to fortify sugar (even at low doses) is a safe and effective means in preventing iron deficiency anemia in populations at risk.

Overview and Summary

Iron Amino Acid Chelate Taste-Free (ferric trisglycinate chelate) is a fine, red-brown powder. It is practically insoluble in water, and has a fairly neutral pH. Despite its lack of water solubility, it was shown to be fairly well absorbed when given in a water carrier (Bovell-Benjamin AC, et al, AJCN 2000;71:1563-1569). A study on its sensory quality and storage

stability in whole maize (Bovell-Benjamin AC, et al, J Food Science 1999;64(2):371-376) has shown that ferric trisglycinate chelate scores high for its lack of negative effects on this food form. The other iron forms caused a bad taste and rancidity. The researchers felt that the lack of reactivity (electrochemical neutrality, charge balance) and low solubility give ferric trisglycinate this advantage when used to fortify certain foods.

Iron Amino Acid Chelate Taste-Free has been shown to have a relative absorption that is about midway between ferrous sulfate (at the low end) and Ferrochel® (at the high end). It has been shown to be an effective way to treat and prevent iron deficiency anemia due to its bioavailability and safety. Ferric trisglycinate chelate from Albion Advanced Nutrition is a great choice for iron in supplement and food products that need to have a palatable form of iron. It is truly Taste-Free!

Ferrochel® is a registered trademark of Albion Laboratories, Inc.

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