ALBION®
HUMAN NUTRITION

RESEARCH NOTES

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Implications of the "Other Half" of A Mineral Compound

As we know, the form of a mineral is often spoken of with the same interest as the mineral itself. Is it a chelate? A complex? Are Kreb-cycle complexes better than picolinates? Are citrates better than malates? Are taurinates more active than ∝keto-glutarates? Which amino acid is the best form of chelate? Glycinate? Aspartate? It would be easy for some to dismiss this type of debate and reduce the discussion to the basic benefit of the mineral involved: iron, magnesium, zinc, etc. After all, isn't it the mineral's biological benefit that we are after, when taking a mineral supplement?

Yes! But . . . This is a big "but." Although most nutritionists agree that it is the biological effect of the mineral that we are after, it is well known that the "other half" of the mineral compound can have a profound impact on the effectiveness of the mineral supplement. The "other half" of the mineral compound, the ligand, can impact bioavailability, tolerability, safety, tissue retention, chemical interactions and much more!

At Albion Laboratories, we are continuously called upon to answer questions that involve the "other half" of mineral compounds. Recently, a couple of issues have been raised that have caused us to deal with them in this newsletter. The issues, though brought to us in different contexts, are related in ways that have very important health implications.

The first issue involves the frequent use of the amino acid, glycine as the ligand ("other half") in many of Albion's patented chelates and complexes. The second issue involves questions about the use of picolinates as a ligand. Most often, this question comes up in regard to chromium or zinc picolinate. If the mineral end of the compound was all that mattered, the debate of glycine (amino acid) chelate versus picolinate chelate would probably be reduced to the relative bioavailability of the mineral as a glycine chelate versus a picolinate chelate. In which case, the glycine chelate would come out on top, because glycine is metabolized by the body after absorption and picolinic acid is not.

However, since Albion is more responsible in its considerations about the "other half" of the mineral compound, it is important to look at other issues about the choice of ligand, . . . issues that go beyond bioavailability, tissue retention and mineral effects.

Nutritionally Functional Mineral Chelates

In selecting an amino acid like glycine as the "other half" of its mineral chelate compounds, Albion has chosen to use a substance that is of nutritional value to the body. A mineral amino acid chelate properly formed is a nutritionally function mineral chelate. This means that every bit of the mineral compound has nutritional value to the body (100% nutrient density). Picolinic acid was not chosen by Albion as a ligand for many reasons. To begin with, picolinic acid is an excretory or waste product. It is not metabolized by, or useful to the body, however, the reasons that Albion chooses amino acids like glycine over picolinic acid do not stop with this one factor. There are more and very important factors that point to advantages for glycine and other amino acids - factors that go against the use of picolinates.

The Trouble with Picolinates

In the late 70's and early 80's, many were theorizing that the absorption of zinc was promoted by picolinic acid. In fact, much of this speculation was fueled by the finding that human milk, although lower in zinc content than bovine milk, had been shown to be a more bioavailable source for the mineral zinc. Many thought that a zinc-binding ligand unique to human milk could explain this higher bioavailability. Picolinic acid was one of the proposed ligands that was thought to increase the absorption of zinc from human milk. In line with this, Schwarz, Roth and Kirchgessner [Influence of Picolinic Acid and Citric Acid on Intestinal Absorption of Zinc in Vitro and in Vivo, Res Exp Med, 182(1):39-48 1983] conducted studies on zinc depleted and zinc supplied animals. They found that the zinc depleted animals showed a significantly higher rate of zinc uptake, as compared to the zinc supplied animals. However, they also found that the absorption of zinc, in vivo, did not vary in favor of the use of picolinate or citrate, when compared to zinc sulfate.

In a subsequent study, Roth and Kirchgessner [Effect of Different Concentrations of Various Zinc Complexes in Comparison With Sulfate on Zinc Supply Status in Rats, Z Ernahrungswiss, 22(1):33-44, 1983 Jan] demonstrated that zinc citrate was better absorbed that zinc picolinate. In fact, zinc picolinate was absorbed at a rate that was no better than zinc as sulfate. The authors went on to state that the higher absorption of zinc from human milk should not only be attributed to the presence of citrate, but is probably due to the protein composition of human milk.

Picolinates Can Do What?

In view of these findings on picolinate and zinc absorption, and considering the fact that picolinic acid (an excellent mineral chelator) is excreted into the urine unchanged, further studies on

Glycine Has Other Functions

Glycine is one of the more often used ligands in Albion's mineral amino acid chelates. As mentioned in this newsletter, there have been some positive findings associated with glycine intake. The fact that this component of an Albion chelate is of biological use makes an Albion chelate nutritionally functional. Amino acids whose catabolism yields pyruvate or one of the intermediates of the citric acid cycle are termed gluconeogenic or glycogenic (see figures 1 and 2 below). These intermediates are substrates for gluconeogenisis, and therefore, can give rise to the net formation of glycogen in liver and muscle.

Creatine, which is inherently involved in the production of muscular energy is synthesized from glycine and the guanidino group of arginine, plus the methyl group from S-adenosylmethionine, as depicted in figure 3 below.

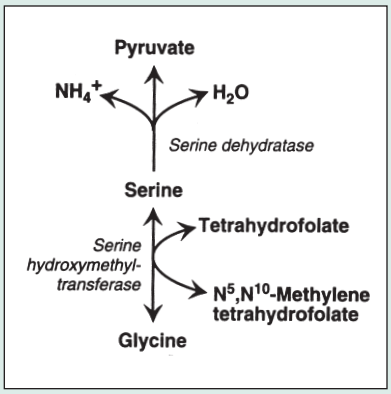

Figure 1

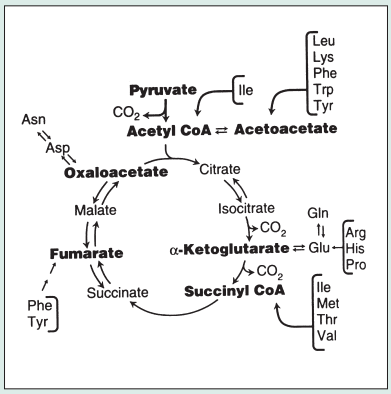

Figure 2

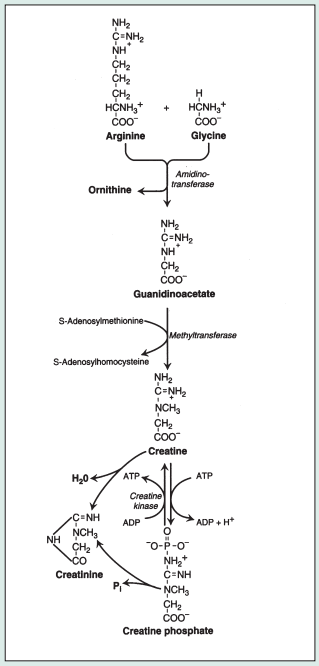

Figure 3

the effects of picolinic acid on zinc and other minerals metabolic fates were warranted.

In another animal study, Seal and Heaton, [Effect of Dietary Picolinic Acid on the Metabolism of Exogenous and Endogenous Zinc in the Rat, J Nutr, 115(8):986-93 1985 Aug], examined the effect of picolinic acid on the metabolic balance of zinc in three differently designed experiments. In all three experiments, the use of picolinic acid led to an increase in urinary and fecal output of zinc. In addition, the residual zinc levels in the tissues of the animals were reduced in the picolinate fed animals, even in the animals that were fed diets containing 0.8 mmol Zn/Kg. These observations indicated that picolinic acid increased the turnover of endogenous zinc and it enhances the excretion of ingested (supplemental) zinc. This gives cause to question the use of picolinate as a chelating ligand for supplemental zinc.

Seal performed further research on the effects of picolinates on mineral metabolism [Influence of Dietary Picolinic Acid on Mineral Metabolism in the Rat, Ann Nutr Metab, 32(4):186-91, 1988]. In this research, differing amounts of zinc and picolinate were fed to the research animals and balance studies were preformed. The animals fed 25 ppm zinc were in negative zinc and copper balance during the experiment. Zinc excretion was elevated with increasing zinc in the diet. The urinary zinc, copper and magnesium increased with increasing picolinate supply. Tissue zinc was not improved by the dietary zinc picolinate. The research concluded that picolinic acid forms soluble complexes with minerals that are absorbed, but are then re-excreted in urine and may not be available for metabolism or incorporation into tissues.

Another Thing About Picolinates

[Reading SA, Chromium Picolinate, J Fla Med Assoc: vol 83 iss 1, 1996, P29-31].

Medline Abstract: Chromium Picolinate is a dietary supplement gaining in popularity among Americans, especially those seeking a weight-reduction program. Although the mechanism(s) responsible for the purported actions of chromium picolinate have not been thoroughly investigated, studies suggest that the biochemical, physiological and behavioral actions of chromium picolinate may be a consequence of the effects of picolinic acid on the CNS [central nervous system]. Analogues of picolinic acid have been shown to induce profound alterations in the metabolism of serotonin, dopamine and norepinephrine in the brain. Thus, caution should be used with chromium picolinate supplements, especially in individuals prone to behavioral disorders.

Interesting Findings About the Positive Effects of Glycine

As mentioned earlier, glycine is the predominant amino acid ligand used by Albion in its chelates and complexes. Due to this, concerned individuals have asked about the effects of an increased dietary intake of glycine in association with the taking of Albion minerals. Glycine is a very safe substance, even at a high chronic dose. Glycine helps slow the degeneration of muscle tissue as one of three components needed to synthesize creatine. It is necessary for CNS function and is needed for the maintenance of a healthy prostate. The body uses glycine to form nonessential amino acids for the immune system and it is involved in the energy system.

In addition, glycine has been thoroughly researched and found to have a number of other additional side benefits.

1. "Glycine accelerates recovery from alcohol-induced liver injury", [Yin, et al, J Pharmacol Exp Ther, 286(2):1014-9 1998 Aug].

Glycine prevents hepatic damage caused by hypoxia-reoxygenation, diminishes mortality due to endotoxin and minimizes alcoholic injury by decreasing blood ethanol. This study's results indicate that a glycine containing diet expedites the process of recovery from ethanol-induced liver injury and may lead to its clinical application in alcoholic hepatitis.

2. "Dietary glycine prevents increases in hepatocyte proliferation caused by peroxisome proliferator" [WY-14, 643", Rose, et al; Chem Res Toxicol, 10(10):1198-204 1997 Oct].

Peroxisome proliferators are a group of nongenotoxic carcinogens which include a number of hypolipidemic drugs, solvents and industrial

plasticizers. Liver Kupffer cells are stimulated to produce things like tumor necrosis factor alpha (TNF alpha) by these peroxisome proliferators. This study showed that a glycine-enriched diet prevented the stimulation of the Kupffer cells from forming TNF alpha and raised the possibility that dietary glycine could be effective in fighting cancer caused by these types of carcinogens.

3. Glycine was shown to have significant anti ulcer and cytoprotective properties against chemically induced gastric ulcers [Tariq and Al-Moutaery, Res Commun Mol Pathol Pharmacol, 97(2):185-98 1997 Aug].

4. Dietary glycine was found to be a safe and effective treatment to reduce the nephrotoxicity of cyclosporines. [Thurman RG, et al, Transplantation, 63 (11):1661-7 1997 Jun 15].

5. Glycine diet (5%) was shown to totally prevent mortality and reduce liver and lung injury in animals exposed to endotoxin shock. [Ikejim, et al, Am J Physiol, 271 (1PT1):G97-103 1996 July].

6. Glycine minimizes alcohol-induced liver injury by preventing ethanol from reaching liver by activating first-pass metabolism in the stomach. [Iimuro y, et al, Gastroenterology, vol 110, iss 5, 1996, P1536-42].

Summary

There are more reports that could be listed about glycine protecting against other chemically induced damage from things like chlorpromazine, cisplatin and other hepato or nephro toxic agents, but the point is well made. Glycine is a good thing.

From our standpoint, glycine is an excellent choice for an amino acid chelate ligand for more than one reason. It is the smallest amino acid and thus, forms mineral chelates of the smallest possible molecular weight (greatest absorption potential). The stability constant that glycine possesses is excellent, as well. It allows for the chelate to remain intact throughout the pH range of the gastrointestinal tract, but it is not too strong - allowing for the efficient release of the minerals to the biological tissues in need of them. Unlike picolinic acid, glycine (and other amino acids) is also a useful nutrient to the body.

The Bottom Line: Minerals that are chelated via the Albion process with amino acids, like glycine, are safer and more effective than minerals bound to picolinic acid.

Albion Human Nutrition

100 Maple Park Blvd., Suite 110
St. Clair Shores, Michigan 48081 USA
[P] 586•774•9055 | [TF] 800•222•0733
[F] 586•774•8838
[e] info@AlbionMinerals.com