ALBION®
HUMAN NUTRITION

RESEARCH NOTES

A COMPILATION OF VITAL RESEARCH UPDATES ON HUMAN NUTRITION

August, 2000 Volume 9, No. 2

IS IT A REAL CHELATE ?

Unfortunately, the health food industry has permitted the use of some terms for mineral forms that has caused a great deal of confusion. In spite of the official adaption of mineral definitions by NNFA, the industry has allowed certain marketers to use the definitions to sell minerals that don't meet the defined criteria. For example, many claim to be making mineral amino acid chelates, but are they? What does it take to make a real totally reacted metal amino acid chelate? Albion Laboratories has been manufacturing this type of mineral under patented processes for many years. This method for the manufacturing processes of the various mineral amino acid chelates, as well as other Albion manufactured nutritionally functional mineral chelates can be reviewed in any of the many patents that Albion holds.

Here are a few things that make Albion's mineral chelates stand out:

1. Albion possesses over 70 patents in the field of mineral technology.
2. Only Albion's mineral amino acid chelates have been given CAS Registry Numbers.
3. Only Albion mineral amino acid chelates are Kosher-Parvé.
4. Albion metal amino acid chelates have been chemically validated, and consequently, are the only known chelates that meet the NNFA definition.
5. Virtually all published research on metal amino acid chelates has been done using Albion metal amino acid chelates.

No other mineral amino acid chelate manufacturer can make these claims. Why is virtually all published clinical research on mineral amino acid chelates done on Albion produced material? In fact, one might want to ask the question, "why" to all of the above listed statements. Patents, CAS Registry Numbers, Kosher-Parvé status, chemical validation, and clinical research all increase the amount of scrutiny that the mineral amino acid chelate in question must undergo. Only a company that knows that the integrity of its product will stand up to such scrutiny would expose itself to such review. Only a company that manufacturers a totally reacted, nutritionally functional mineral amino acid chelate can claim all of the above listed accolades.

Can you define a mineral amino acid chelate? A nutritionally functional mineral amino acid chelate? If you are putting them into your products, or buying them in a supplement, it is important that you know what they really are. If it is not an Albion patented mineral amino acid chelate, chances are it's not the real thing.

THE NNFA DEFINITION OF MINERAL AMINO ACID CHELATES

Metal Amino Acid Chelate is the product resulting from the reaction of a metal ion from soluble metal salt with amino acids with a mole ratio of one mole of metal to one to three (preferably two) moles of amino acids to form coordinate covalent bonds. The average molecular weight of the hydrolyzed amino acids must be about 150 AMU (Atomic Mass Units) and the resulting chelate must not exceed 800 AMU. The Minimum elemental metal content must be declared. It will be declared as a METAL amino acid chelate: e.g. Copper amino acid chelate.

Adopted by the NNFA Board of Directors July, 1996.
NNFA Today, Pg. 15, Aug. 96.

CHELATION

To gain a common understanding of what a chelate is, it is necessary to first establish a definition. The word "chelate" is derived from the

Greek word che´le for the pincer-like claws seen in the lobster or crab. The term "chelate" was first proposed by Morgan and Drew in 1920 to describe a class of metal complexes in which the metal atom is held in the complex through more than one point of attachment in this pincer grip, and form a ring structure.[1]

Minimum Chelation Requirements

The minimum requirements, or conditions, for the creation of a chelate are set down below. If any of theses conditions are not met, chelation will not occur regarding less of what a manufacturer claims. The formation of a metal chelate does not guarantee the mineral's absorption and metabolism. These are additional requirements that are elaborated on in the later section on 'Nutritionally Functional Chelates'.

1. The chelating ligand must contain two atoms that can bond to the same metal ion.[2] The ligand atoms must be donor atoms that are capable of donating one or both electrons to the metal-ligand bond formation (coordinate covalent bonds). Examples of donor atoms are nitrogen, oxygen, sulfur and phosphorus. In addition, donor atoms may function as an acidic or basic functional group, such a –COOH (carboxyl), =O (carbonyl), or –NH2 (amino).

2. The ligand must form a heterocyclic ring with the metal as the closing member of the ring.[3] If the ligand must contain two donor atoms that bind to the same metal atom then it must form a ring structure upon chelation. A metal complex can be different than a metal chelate. In a complex, the metal can be attached to only one atom in the ligand, forming a straight chained molecule. Examples of both a metal chelate and metal complex as defined by NNFA are shown in Figure 1. It should also be noted that metals in Group IA of the Periodic Table of the Elements (Li, K, Na, etc.) cannot be chelated due to the low electro negativity and high tendency to release electrons. Currently, these metals can only be complexed. A buyer should be wary of any manufacturer that claims otherwise.

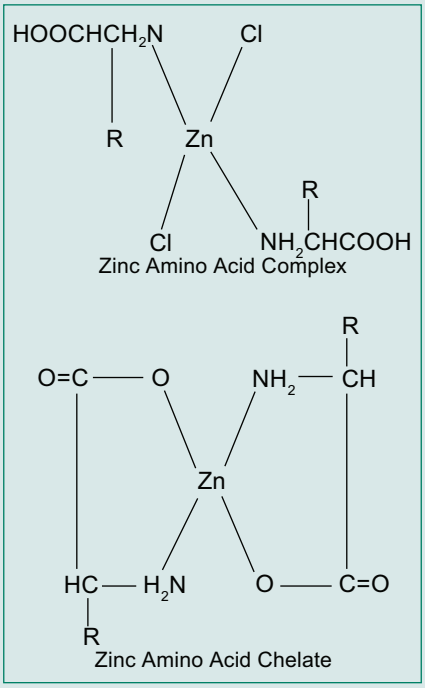

Figure 1.
Structural differences between a metal amino acid complex and a metal amino acid chelate.

3. It must be sterically possible to chelate the metal.[4] Steric hindrance is the interference or inhibition of an otherwise feasible reaction because the size of one or the other reactant moiety prevents approach to the required distance for reactivity. The steric hindrance is a function of not only the ligand, but also the radius of the metal atom. As far as the ligand is concerned it is sterically and energetically unlikely that a large polypeptide or a ligand with bulky side chains such as partially hydrolyzed protein would be able to chelate metal. Their two potential donor atoms would be too far apart to bend far enough for both to reach the reactivity zone of the metal. The radius of the metal atom must also be a consideration. One may visualize this as holding a marble between the index finger and the thumb and counting the number of additional people who can grasp the same marble in a similar fashion. It

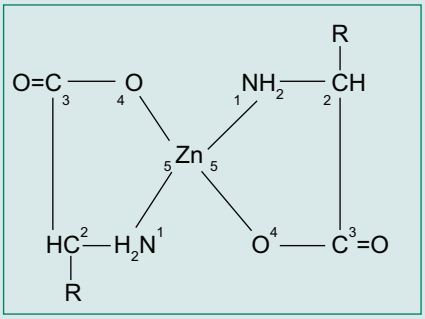

Figure 2.
Example of two five membered rings joined at the Zn atom.

The smaller the metal ion, the fewer the number of ligands that can potentially position themselves in such a way as to chelate the cation.

becomes obvious that only a limited number of people can hold the marble at the same time. If the marble is larger, more people can grasp it. If it is smaller, less people can hold it. The same is true of chelating ligands and single metal atoms. The smaller the metal ion, the fewer the number of ligands that can potentially position themselves in such a way as to chelate the cation. The larger the ligand, the more that can be involved in chelate formation. Furthermore, if the angles between the elements forming the heterocyclic ring are too acute due to too few numbers (four or less) the chelate will be unstable and break apart easily. Too many members (seven or more) will also result in an unstable chelate. The most stable chelate rings are those that are five and six membered rings as shown in Figure 2.[5]

4. The molar ration of the ligand to the metal must be at least 1:1. If the quantity of ligands is inadequate for the quantity of metal to be chelated, then a complete chelation reaction is impossible. The chemical reaction for chelate formation must be balanced by molar equivalents of substrates rather than by simple weight percentages. Many companies do not understand this essential requirement and try to balance the equation by weight percentages, which results in insufficient ligands for total chelation. One must know the molecular weights of the ligand and metal in order to calculate correct molar equivalents. If it were sterically possible to form chelates with proteins or partially hydrolyzed proteins, balancing the molar equivalents for complete reaction would be very difficult.

Requirements for a Nutritionally Functional Chelate

The previously mentioned criteria are the minimum requirements for chelation to occur, but chelation does not guarantee mineral absorption and there are some other qualifications that are necessary for a nutritionally functional chelate, that is, a chelate that can be absorbed and metabolized safely without further modifications by the body. Chelation is not a "magic" word. A mineral must be chelated in a specific manner for maximum absorption and metabolism to occur. A nutritionally functional chelate is one that meets all of the chelation requirements which have been previously discussed, plus the following:

1. The chelate must have a molecular weight of less than 1000 daltons.[6,7,8] The Association of American Feed Control Officials (AAFCO) has set an upper limit for a metal amino acid chelate of 800 daltons.[9] It is known that only these low molecular weight amino acid chelates cross the intestinal wall intact,[10] and it has been documented that the intestine absorbs the metal in these low molecular weight chelates not as a metal-ligand complex, but as an intact small polypeptide chelate (usually a di- or tri-peptide like molecule).[11] This avoids the energetically costly and inefficient process of ionization in the gut, avoidance of interfering chemical reactions that reduce the absorption of minerals from the gut, and the re-chelation required for transport of a metal ion or a larger chelate or complex.[12] Therefore, although unlikely, if a metal were to be chelated to a large polypeptide, such as soy protein, that protein must give up the metal during the digestion process of the soy protein in the stomach and intestines. If the metal is released during the digestion process, it is subject to the many gastro-intestinal reactions experienced by a common metal salt even though at one time it was theoretically chelated. Had that same metal been chelated to an amino acid, there would have been no further digestion in the gut, and the chelate would have been absorbed into the mucosa as the same molecule that was ingested. Thus it is of little, if any, nutritional value to chelate a metal protein or partially hydrolyzed protein with a molecular weight greater than 1000 daltons (even if it were chemically possible) because they are not absorbed as such and require further digestion in the gut.

2. The chelate must be electrically neutral. The reason for this is that there are positive and negative charges on the membrane of each intestinal cell. If a chelate is not electrically neutral, it will either be repelled or bound to the membrane and later sloughed off. In either case, no absorption occurs. In order to achieve this electrically neutral state, the following two requirements must be fulfilled:

A. The chelate must not be complexed with an easily ionizable anion, such as a halogen or a sulfate group. If this condition is not met, the chelate may chemically interact

in the gut to form an insoluble metal hydroxide or phosphate. An example of a chelate complexed to a halogen (Cl) is shown in Figure 3.

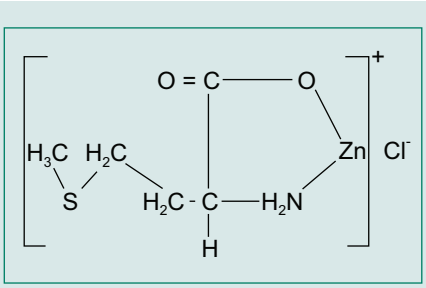

Figure 3.
A Zn methionine chelate complexed with a chlorine anion.

B. The ligand must satisfy both the oxidative state and a coordination number of the metal atom. This type of bonding is referred to as coordinate covalent bonding. This requirement will also have an effect on the ligand: metal molar ratio. For example, if a mole of a divalent metal cation such as Mg++ were to be chelated, then it is necessary to use two moles of amino acids or one mole of some other ligand with two donor atoms or groups that are acidic in nature, or a mole of a multiple donor atom ligand, such as EDTA. I should be remembered in these cases that only the amino acid chelate is absorbed as a nutritionally viable molecule.

3. The chelate must have a high enough stability constant to avoid competitive chemical interactions in the gut prior to absorption.[13] These chemical interactions include the formation of hydroxides, phosphates and oxides, all of which could break the chelate ring if the stability constant is too low. Furthermore, the ligand must not allow the release in the stomach or intestines of the metal it had originally chelated which would allow it to interact with other metal ions. The stability constant of the chelate must be higher than competitive ligands in the gut and the mucosal cell membrane in order to preserve the chelate structure intact for absorption. If the chelate is capable of disassociating at the mucosal membrane due to a low stability constant, it will disassociate in the gut prior to reaching the intestinal cells. On the other hand, the stability constant cannot be so great that the mucosal cells or other cells within the body cannot strip the metal from the ligand after absorption and utilize both the mineral and amino acids structurally or metabolically.

4. ***The ligand must be easily metabolized.***[14] Chelates made from ligands that are not metabolized, such as EDTA and picolinic acid, are not considered nutrtionally functional. Chelates manufactured from these types of ligands may be counterproductive through their ability to remove of minerals from the body.[15] Amino acids are the ideal ligand for the nutritional presentation of essential minerals. Certain other nutrients can form chelates, but few meet all of the requirements of a *nutritionally functional chelate*.

SUMMARY AND CONCLUSION

The requirements and conditions that a molecule must meet in order to be considered a nutritionally functional mineral amino acid chelate are very explicit. They involve specific bonding, ring formation, ligand/mineral molar ratios, molecular weights, electric neutrality, stability constants and ease in metabolism. The end point of all the parameters set for a nutritionally functional mineral amino acid chelate is a mineral form that has the following benefits:

GREAT ABSORPTION POTENTIAL
GREAT TOLERABILITY
LOW TOXICITY
MORE FREEDOM FROM DIETARY INTERFERENCE
LESS EFFECT ON ORGANOLEPTIC PROPERTIES, WHEN ADDED TO FOOD
GREATER FORMULATION STABILITY

Albion Laboratories, Inc. manufactures the only nutritionally functional mineral amino acid chelate that is backed by published clinical research – Research that supports the benefits listed above.

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