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ORGANIC TRACE MINERALS

PART-A

- THE DIFFERENCE IN ORGANIC TRACE MINERAL SOURCES

PART-B

- SMALLER IS BETTER : NEW METHOD ANALYSES ORGANIC TRACE MINERAL POTENTIAL EFFICACY

"A"

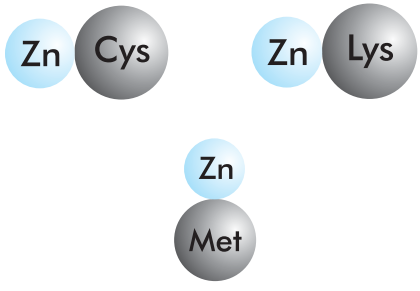
The Difference in Organic Trace Mineral Sources

The more nutritionists, veterinarians and livestock and poultry producers learn about factors that contribute to animal production, health and profitability, the more they turn their attention to trace mineral nutrition. But as they learn more about trace mineral nutrition, they discover that not all trace minerals are the same.

For example, different classes of minerals have different levels of bioavailability – the extent to which any nutrient is available for absorption and metabolism. Before a trace mineral can be absorbed, it must first become attached to an organic molecule, or "escort". This process allows it to pass through the intestine, into the bloodstream and on to tissues and organs for utilisation. If a trace mineral does not attach to an escort, it simply won't be absorbed, which is often the case with inorganic trace mineral supplementation.

There are currently five organic trace mineral product categories defined by the Association of American Feed Control Officials (AAFCO). Here are the definitions with some additional observations on how these categories differ.

Metal amino acid complex :



Metal amino acid complexes result from complexing a specific soluble metal salt (such as zinc, copper, manganese) with an amino acid.

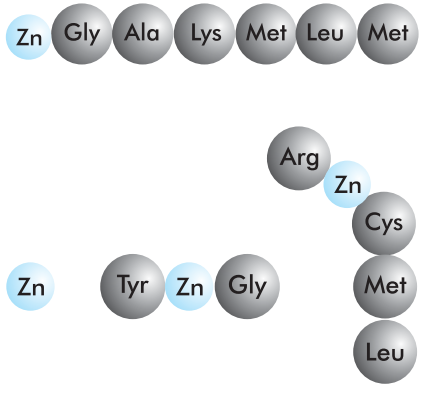
These metal-amino acid complexes are manufactured using a new patented "amino acid extraction process" that breaks down a pure source of protein into an intermediate product containing only free amino acids, without dipeptides, tripeptides or larger protein fragments. The free amino acids are then complexed in a one-to-one ratio – one amino acid molecule bonded to one metal ion.

Metal (specific amino acid) complex :

Metal specific amino acid complexes result from complexing a soluble metal salt with a *specific* amino acid.

Metal specific amino acid complex combine a single, known amino acid with a single metal ion to form a specific chemical entity such as zinc methionine. The end product is a new molecule containing one ion of the metal zinc and one molecule of the amino acid methionine.

Metal proteinate :

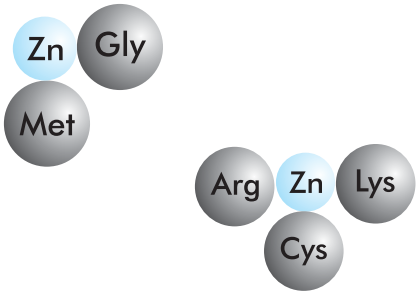


Metal proteinates result from

the chelation of a soluble salt with amino acids and/or partially hydrolysed protein.

The final product may contain single amino acids, dipeptides, tripeptides or other protein derivatives. Some research has shown that interaction with other dietary constituents may render proteinates unavailable for absorption and thus less bioavailable to the animal. Often, the resulting mixture is bound too weakly to withstand the environment of the digestive tract. Metal proteinates are not a defined chemical entity. These types of products tend to vary from one manufacturing run to the next.

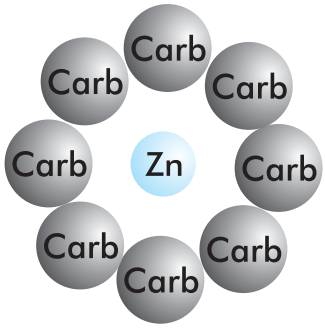
Metal amino acid chelate :



Chelates are formed from the reaction of a metal ion from a soluble metal salt with amino acids having a mole ratio of one mole of metal to one, two or three (preferably two) moles of amino acids to form coordinate – covalent bonds. In simpler terms, chelation refers to a specific mineral that becomes surrounded by and bonded to two or more nonspecific amino acids.

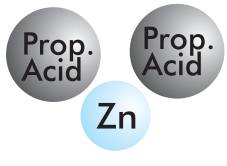
There are various products on the market claiming to be metal chelates. A "true" chelate is formed only when a coordinate covalent bond exists between the metal and the amino acid. However, the process is deficient because of its inability to specify which amino acids – and how many – are being chelated.

Metal polysaccharide complex :



Metal polysaccharide complexes result from complexing a soluble salt with a polysaccharide solution declared as an ingredient of the specific metal complex. There are limited published research results of metal polysaccharide complex use. Also, the product is more of an organic mineral matrix without any chemical bonding between the mineral and the polysaccharide.

Metal propionate :



Although not new to the feed industry, metal propionate research is limited. First recognised in 1891, metal propionates are the result of combining soluble metals with soluble organic acids. Resulting products are highly soluble and generally disassociate in solution.

"B"

Smaller is Better : New Method Analyses Organic Trace Mineral Potential Efficacy

Key Findings :

- Increasing trace mineral status by increasing uptake and absorption leads to improve animal performance.
- Molecular size is a major factor in determining bioavailablity of organic trace minerals.
- Testing now exists for determining structural differences between commercial sources of organic trace minerals.

Introduction :

Organic trace mineral (OTM) inclusion in animal diets continues to expand around the world. Commercially available products represent a wide spectrum of chemical entities that have different physical and chemical properties and, consequently, produce different nutritional responses. Often the terminology used in describing these products does not take into account the differences between the various chemical entities. As a result, nutritionists, veterinarians, feed manufacturers and producers may be unaware of these distinct differences and may consider all OTM products to be similar and, therefore, to have similar effects on animal performance.

This discussion will attempt to clarify the differences between the various OTMs and underscore the

qualities that increase bioavailablity and improve animal performance.

Improving Metabolic Parameters

The primary role of OTMs is to increase the bioavaliablity of supplemental trace minerals from the diet. The beneficial effects of OTMs are attributed to the association of the metal with an organic molecule, the ligand. The increased bioavailability of the trace mineral in a properly designed and carefully manufactured OTM is believed to be the result of :

Increased solubility :

The OTM is readily soluble in the intestinal contents. This enables the product to be homogeneously distributed in intestinal contents and to be able to reach the surface of the intestinal tract for absorption. However, solubility alone is not sufficient criteria to prove increased bioavailability.

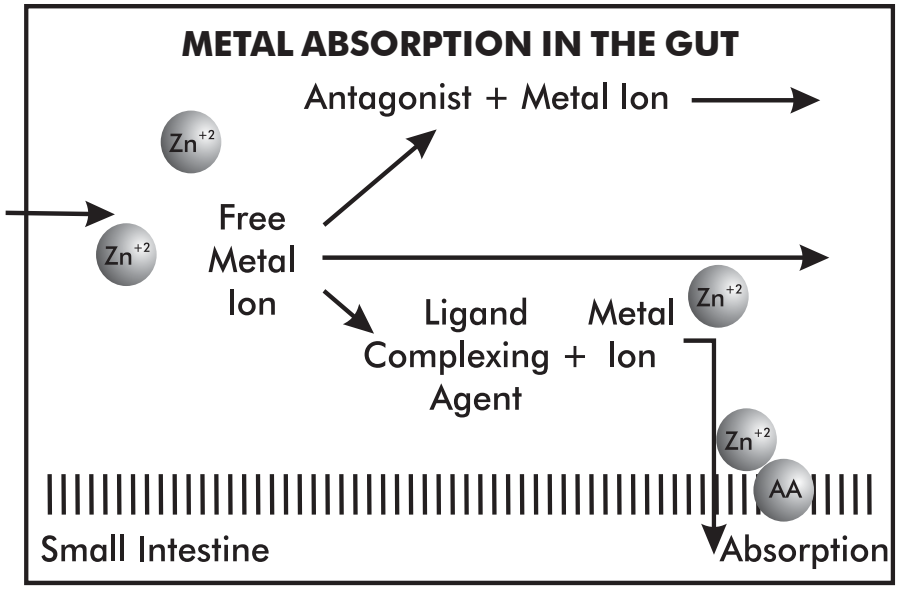
Greater stability in the gut :

The OTM is stable in the digestive tract. It protects the metal from antagonists present in the diet and from changes in the pH as it moves through the digestive tract. The ligand in the OTM should resist degradation by digestive enzymes and gut microflora.

Enhanced absorption across the intestinal membrane :

The OTM is absorbed more readily than the inorganic form of the metal. This may be the result of the ligand serving as a carrier for the metal across the intestinal brush border.

Figure 1:



Improved metabolic utilisation :

The OTM improves metabolic utilisation of the trace mineral by reducing interaction, protecting it from sequestration in cells and binding with dietary and physiological constituents. OTMs also improve metabolic utilisation by maximising trace mineral status and increasing uptake into critical tissues while decreasing elimination in feces, urine and bile.

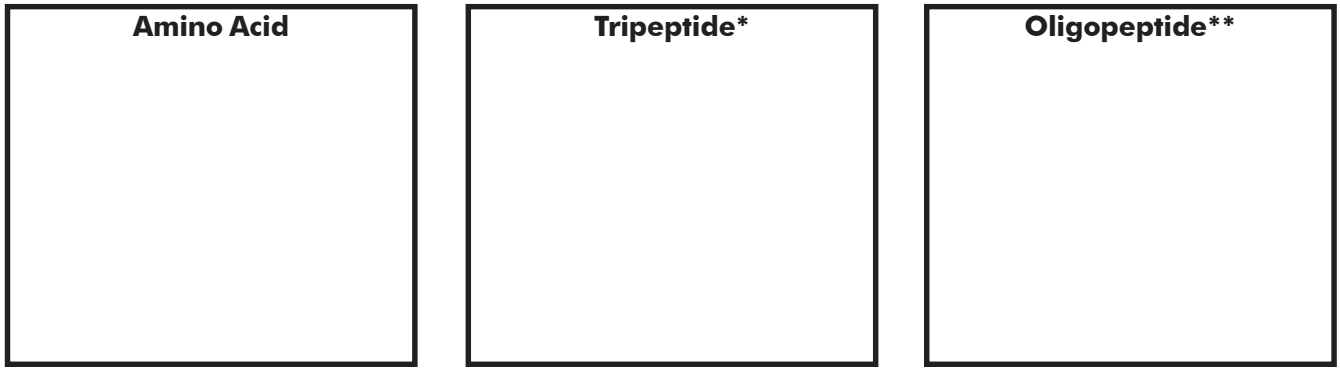
The exact mechanisms by which OTMs improve the bioavailablity of trace minerals are not known. However, the effects of some OTMs on enhanced bioavailablity and improved animal performance are well documented. It is important to recognise that all OTMs are not the same and that the nature of the ligand will have a significant impact on the efficacy of OTMs.

Several different types of OTMs are commercially available. The most widely used forms are products in which the ligand is either an amino acid or a peptide. Synthetic amino acids or amino acids produced by the complete hydrolysis of protein are used as ligands in one type of OTM product. The OTM in which the ligand is a peptide is often a mixture, depending on the type and degree of hydrolysis of the protein. The molecular size of OTMs will depend on the nature of the ligand and the molecular ratio of ligands to the metal. The variations in the molecular size of OTMs affect the bioavailability and, ultimately, the ability to improve animal performance.

Why is Molecular Size Important ?

Molecular size of an organic trace mineral is critical to the performance of the OTM product. A properly designed, well manufactured OTM with the optimum molecular size will meet the design criteria of increased solubility, greater stability, enhanced absorption and improved metabolic

Figure 2 : Comparison of single amino acid and peptides



* Tripeptide consists of three amino acids
** Oligopeptide refers to a peptide consisting of 8-50 amino acids and may have a molecular weight of 1,200-8,000 daltons

utilisation. OTMs with optimum molecular size are more bioavailable than inorganic forms and produce a consistent improvement in animal performance in field studies.

Figure 1 illustrates graphically a proposed model of metal absorption in the gut. The effects of molecular size on the efficiency of metal absorption described by this model and other factors that contribute to increased bioavailablity are briefly discussed in the following paragraphs.

Solubility :

Most nutrients are solubilised for efficient intestinal absorption. Readily soluble OTM become homogenously distributed in the intestinal contents and are able to reach the absorbing surfaces of the intestinal tract. Forms of trace metals, including OTMs that have low solubility in the intestinal contents are not absorbed in appreciable amounts. This is well demonstrated by the low bioavailability of inorganic trace minerals such as Zinc oxide. Copper oxide (CuO) is particularly insoluble and so net absorption from CuO is thought to be less than 1%.

Molecular size significantly affects solubility of OTMs. OTMs that have single amino acid ligands are usually readily soluble in intestinal contents. The solubility of the OTM decreases as the size of the ligand increases from a single amino acid to a dipeptide, tripeptide, etc. As the size of the ligand exceeds a tetra or pentapeptide, the ligand is nearly insoluble in the intestinal contents.

Stability within the gut :

The role of OTM is to protect the metal from antagonists present in the diet and from changes in the pH as it moves through the digestive tract. For example, it is thought that only 1-5% of dietary Copper is absorbed in the ruminant (NRC Dairy – 2000) due to antagonistic factors in the diet (i.e., 95-99% will be excreted). The ability of the OTM to protect the metal depends on the stability of the complex formed between the metal and ligand. This stability is quantitatively expressed by the stability constant of the complex and depends on the nature of the ligand and is unique to each of the trace metal. In general, complexes between metals and amino acids are more stable than those formed between the same metal and dipeptides. As a rule of thumb, the stability constant of a dipeptide-metal complex is about one-half that of the same metal and a single amino acid. Large peptides and proteins form weaker complexes with metals.

Absorption across the intestinal brush border membrane :

The increased bioavailablity of OTM may be a result of the ligand serving as a carrier for the metal across the intestinal brush border. Previous studies have shown that single amino acids, dipeptides and tripeptides are absorbed intact and can be found in the portal blood of animals (Koeln and Webb, 1982). The size of a high proportion of these peptides were estimated to be less than 300 daltons (Schlaghek and Webb, 1984). Large peptides and protein molecules must be digested into single amino acids, di-and/or tripeptides before absorption takes place. Trace minerals must be bound to either a single amino acid, or di-or tripeptides, in order for the transport theory to be valid.

Other studies evaluating the effect of amino acids and some "derivatives" on Copper absorption showed that, in general, the Copper complexes

of mononumeric (one) amino acids are better absorbed than dimeric (two) or trimeric (three) or polymeric (four or more) amino acids (Kirchgessner and Grassmann, 1967, 1969).

Improved Metabolic utilisation :

An OTM containing a small ligand such as a single amino acid, dipeptide or tripeptide is likely to be absorbed intact. After absorption, the ligands of the absorbed OTM will protect the trace mineral from sequestration in cells and binding with plasma proteins as well as improve metabolic utilisation by increasing uptake into tissues and decreasing elimination in feces and bile. Larger peptide ligands are not likely to survive digestive enzymes and OTMs containing these ligands are not likely to be absorbed intact. These OTM do not provide the desired improvement in metabolic utilisation.

Improved animal performance :

Based on the factors discussed above, OTMs containing a single amino acid, a dipeptide or a tripeptide ligands are expected to produce consistent, predictable improvements in animal performance. Indeed, numerous published studies have demonstrated that high quality OTMs consisting of a bond between a single amino acid and a metal ion have produced consistent improvements in animal performance. Further evidence of the effectiveness of these OTMs is demonstrated by *in vivo* bioavailablity research which supports increased uptake of metal bonded to a single amino acid versus inorganic trace minerals and larger peptide/ proteinated OTM (Baker, 1992; Wedekind *et al*., 1992; Ward *et al*., 1996).

A summary of 8 dairy trials feeding Zinc bonded to a single amino acid demonstrated highly significant responses for increased milk production and reduction of somatic cell count (Kellogg *et al*., 1990).

A summary of 22 feedlot cattle trials using the same Zinc product demonstrated significantly positive responses in average daily gain, feed conversion and improved carcass quality.

A summary of 8 swine nursery studies evaluating the effects of supplementing copper bonded to amino acid demonstrated consistent and significant improvements in daily gain and increased feed intake (Coffey *et al*., 1994).

A summary of 14 broiler studies feeding Zinc and Manganese bonded to a single amino acid demonstrated significant improvements in body weight, average daily gain, feed conversion, reduced mortality and increased breast meat yield.

Although some research has demonstrated a neutral effect, the majority of research work with a single amino acid bonded to a metal ion is overwhelmingly positive.

Products produced by bonding a single metal ion to a peptide have also shown varied results, some positive but many neutral. Copper bioavailability of an OTM produced by bonding Copper to a peptide was higher than inorganic copper forms for ruminants (Kincaid *et al*., 1986; DeBonis and Nockels, 1992), but many other researchers obtained contradictory results (Wittenberg *et al*., 1990 ; Ward *et al*., 1993, 1996; Kegley and Spears, 1994; Engle and Spears, 2000) demonstrating no difference between inorganic copper and this OTM copper peptide form.

Zinc response of an OTM product produced by bonding zinc to a peptide showed a positive result in reducing somatic cell count (Anon, 1993a) but others reported no effect on somatic cell count (Spain *et al*., 1994; Whitaker *et al*., 1997).

Analysis of Organic Trace Minerals

Molecular size clearly plays a role in the effectiveness of an OTM. Understanding the molecular size of OTM products provides a useful assessment as to a product's potential efficacy. Until recently, there has been no method of analysis to objectively measure the molecular size of protein based OTM products. All protein-based OTM manufacturers claim their products are specifically designed to include single amino acids, dipeptides or tripeptides. These claims have been left unchallenged because the feed industry was unable to investigate, analyse and/or substantiate these claims.

A recently developed patent pending method of analysis enables practical and reliable analysis of protein based OTM products.

The OTM method of analysis investigates important criteria for determining the potential effectiveness of a product. The protein based OTM is solubilised and then passed

through a series of different size Millepore™ molecular filters. The Millepore filter is used to determine the molecular size and quantify the amount of each protein fraction in the product. Millepore filters are available in sizes of 500,000 daltons, 100,000 daltons, 30,000 daltons, 10,000 daltons, 3,000 daltons, 1,000 daltons and 500 daltons. OTMs passing through the 500 dalton sieve filter reflect a molecular size believed best for maximum absorption.

Metal content is also measured for each protein fraction to demonstrate the potential for uniform bonding throughout the product. This procedure allows everyone involved in the industry to place an objective measurement on the important issue of OTM molecular size. They may then apply reasonable expectations based on these findings regarding solubility, absorption, stability and predictability of performance.

Summary

All prospective and current OTM customers share the issue of risk assessment when purchasing an OTM for inclusion in their animal production systems. There is a real risk of investing in expensive OTM supplementation and not getting the expected animal performance result or return on investment.

Evaluation of bioavailability data, depth and significance of animal efficacy data, combined with OTM molecular size and variation analysis, is crucial to support improved "risk assessment" and ROI decision making.

When purchasing protein based organic trace minerals, remember :
SMALLER IS BETTER .

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