Innophos®

Chelamax®
Whitepaper

Proven Mineral Chelation

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Introduction

Dietary supplement makers use chelated minerals to provide increased bioavailability, which enhances efficacy and provides an edge in marketing against competitive products using the same minerals in a non-chelated form. But did you know that many ingredients sold as chelated minerals are in fact not fully chelated? And some are not chelated at all. At Innophos, we have developed an innovative three-step testing protocol to prove chelation. This unique testing methodology allows us to determine whether a mineral is fully chelated, with accuracy and precision that are unmatched in the industry.

Approximately nine out of ten Americans are deficient in at least one important mineral or vitamin.[1] Taking mineral supplements is a way to replenish deficits and restore those minerals to healthy levels. By using fully chelated minerals instead of mineral salts or oxides, a supplement manufacturer can deliver the maximum benefit of the nutrient to the consumer.

What is a chelated mineral?

The chelate structure helps enhance bioavailability, stability and digestibility.

Chelation occurs when a mineral ion is firmly bound to an organic molecule in two or more locations to form a ring structure. When this type of chemical bonding occurs, for example with amino acids or other organic molecules (ligands), a new molecule is formed, called a chelated mineral. The word chelate is derived from the Greek word *chele*, meaning claw of a crab. This is a good way to think about chelation: the ligand grabs onto the mineral like a claw, in two or more locations forming a ring, which acts as a protective shell around the mineral. This chelate structure helps enhance bioavailability, stability, and digestibility, and facilitates absorption in the intestine much more readily than the non-chelated mineral salt or oxide.

Ligands usually consist of common acids that are important for the body such as amino acids and citric acid, and the bonding generally involves the donation of two or more of the ligand's electron pairs to the mineral. The ligand choice can affect the physical properties of the molecule such as solubility. It is important to note that not every ligand can or will chelate to a mineral and not every mineral/ligand combination will form a chelated mineral. For example, glycine chelates to magnesium, but there is little evidence that it chelates to chromium in typical reaction conditions.

Fig. 1. Chelation occurs when a ligand bonds to a mineral in two or more locations.

Superior bioavailability of chelated minerals

Chelated minerals are used for supporting normal growth, building strong muscles and bones, improving immune system function, and overall health. The reason formulators choose chelated minerals as ingredients for dietary supplements is *superior* bioavailability.

Here's how chelation works to improve bioavailability: the protective organic shell of the chelated mineral enables it to withstand diverse challenges of the digestive system including varying pH levels and interactions with other dietary compounds. Chelated minerals maintain their solubility in the digestive tract, allowing the mineral to be readily absorbed. This is in sharp contrast to mineral oxides and salts (e.g. magnesium oxide) which are typically flushed through the intestine without being absorbed and are excreted as waste.

The increased bioavailability of chelates was demonstrated in a study where chelated calcium ascorbate was found to have an absolute bioavailability that was 2.6-times greater than that of calcium chloride.[2] The advantage of chelated minerals being more bioavailable than mineral oxides or salts has also been observed across mineral categories such as zinc and magnesium.[3] In a study using isotopically labeled zinc to compare the bioavailability of chelated zinc glycinate to zinc sulfate in rats, zinc glycinate was found to be superior, demonstrating 16% greater bioavailability.[4] In a clinical trial published in the *Journal of Nutrition*, zinc oxide was shown to have significantly lower bioavailability than chelated zinc citrate.[5] Similarly, chelated magnesium citrate has been found to be more readily absorbed than magnesium oxide.[6] Increased solubility along with the protection of chelated minerals from other potential dietary binders, such as phosphates or phytates, have been attributed as a possible mechanism of the increased bioavailability.[4, 7, 8, 9, 10]

Finally, chelated minerals have been shown to provide less gastrointestinal discomfort and better digestibility than their salt or oxide counterparts.[11,12] One study demonstrated that calcium ascorbate attenuated the high gastric acidity caused by ascorbic acid.[12]

Absolute bioavailability of 2.6x

Table 1. Advantages of Fully Chelated Minerals

FEATURE	ADVANTAGE
Superior bioavailability	Greater absorption of the mineral
Greater stability	Less interaction with inhibitors and other nutrients
Lower chemical reactivity	Does not dissociate into charged particles which can react with and degrade vitamins and other ingredients in the supplement, rendering them useless
Enhanced solubility	More efficient transport of mineral molecules within the body
More digestible	Prevents dissociation of the mineral ion to reduce the risk of gastrointestinal side effects
Positive safety profile	Maximizes patient safety and consumer confidence

Three-step process verifies full chelation

A significant concern in supplement formulation is that many minerals sold as chelates are in fact not fully chelated and may not be chelated at all. To address this problem, Innophos has developed a novel three-step process for verification of full chelation in Chelamax® products. The three steps are: X-ray diffraction (XRD), thermogravimetric analysis (TGA), and Fourier transform infrared spectroscopy (FT-IR).

As a leading supplier of minerals to the nutrition market, Innophos developed this unique and integrated testing protocol to prove total chelation, which is linked to bioavailability of minerals in the human body.

This unique testing methodology is unmatched in the industry.

Table 2. Innophos Three-Step Testing Protocol

METHODS TO VERIFY CHELATION	RESULTS FROM ANALYSIS
Step 1: X-ray diffraction (XRD)	Confirms the structure of the compound
Step 2: Thermogravimetric analysis (TGA)	Confirms purity and hydration
Step 3: Fourier transform infrared (FT-IR) spectroscopy	Produces a fingerprint for lot-to-lot comparison

Step One:
X-ray Diffraction (XRD)

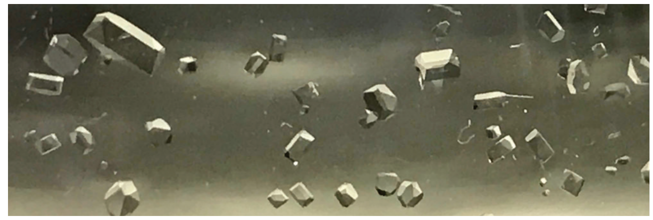
The first step of Innophos' three-step validation process is X-ray diffraction (XRD), which confirms the absolute structure of the entire molecule including the protective shell. First, we use single-crystal XRD, in which a crystal of a chelated mineral is centered within the X-ray beam creating a diffraction pattern, which is then analyzed to allow us to "see" the actual structure of the molecule. The analysis of the diffraction pattern reveals the arrangement of the atoms in the crystal, showing which specific ligands are present and how they arrange around the central mineral ion. This confirms if the ligand is arranged in a way to grab on to the mineral like a claw, chelating to the mineral, or if another type of bonding interaction is occurring. XRD confirms the molecular structure and therefore, formula of the molecule. For example, the structure of chelated magnesium glycinate contains two bound water molecules in addition to the two chelating glycinate ligands. The molecular formula of this compound is $Mg(C_2H_4NO_2)_2(H_2O)_2$ with a molecular weight of 208.5 g/mol and a magnesium content of 11.7%.

From this single crystal structure, we generate a powder XRD (PXRD) pattern that serves as a unique fingerprint for that crystal structure. The PXRD pattern of manufactured products is then compared to the known PXRD fingerprint of the proven chelate to confirm the molecular structure.

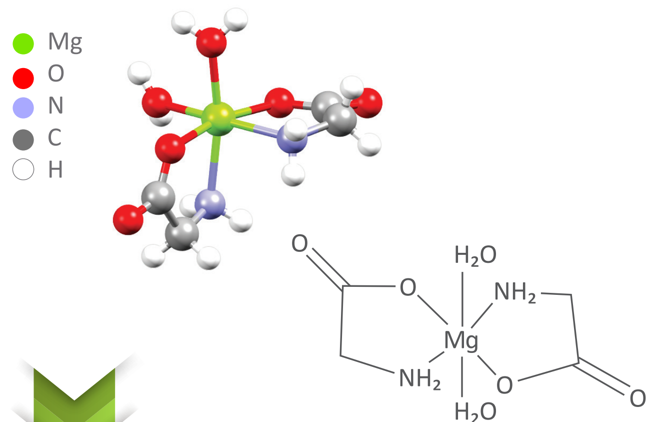
XRD allows us to "see" the actual structure of the molecule confirming chelation.

Fig. 2.

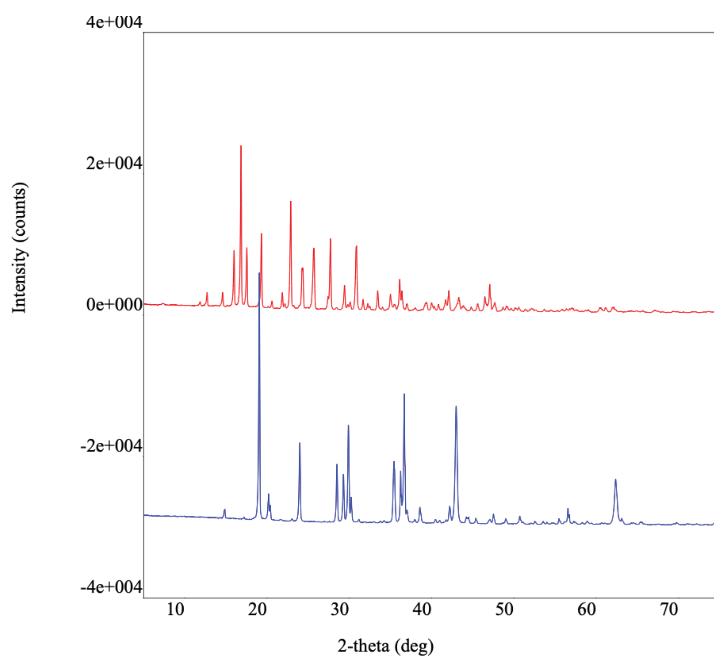
Single crystals grown in the lab which are used for XRD to determine the absolute structure of the molecule.



Structure of magnesium glycinate determined by XRD and the corresponding molecular diagram.



A PXRD fingerprint of the molecular structure is generated (red data) and can be easily compared to other samples. The blue data is from a sample that is not chelated and is clearly different than the chelated magnesium glycinate.

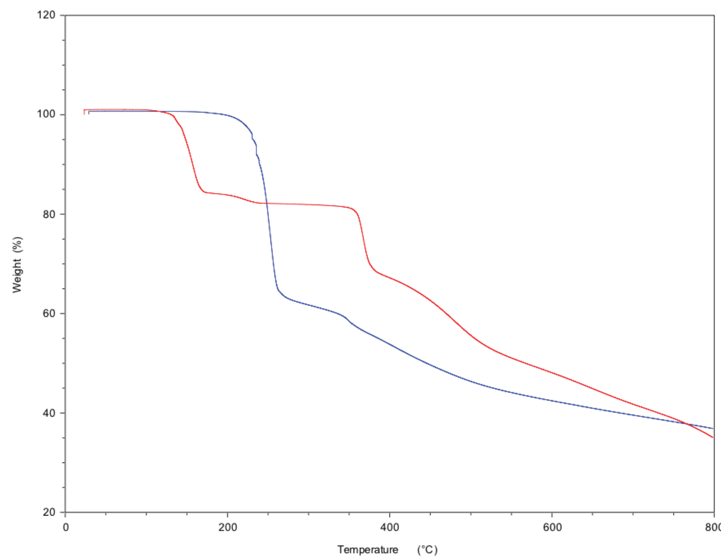


Step Two: Thermogravimetric Analysis (TGA)

TGA measures thermal decomposition of a sample by looking at mass loss as a function of increasing temperature. If there are unreacted (non-chelated) raw materials present in a sample, there will be a drop in mass at the temperature at which those raw materials decompose. The decomposition profile of unreacted or partially reacted products will be different from the profile of the pure, fully chelated product. TGA measurements showing *consistency in the decomposition profile of every sample* verify that all of the samples have the same composition.

In addition, TGA can help in understanding the hydration state of the molecule. Water molecules can also be ligands and the difference between bound and free water molecules is often misunderstood. There is a stronger bonding interaction between a bound water molecule and the mineral ion which prevents the water from easily dissociating at typical drying temperatures. Therefore, the complete hydration state (free and bound) of a chelated mineral can be determined and verified via TGA. Material and water mass loss can be measured and compared against the theoretical mass loss of the compound structure. For example, for chelated magnesium glycinate, the product contains two water molecules that are bound to magnesium. This represents 17% of the mass of the molecule. The TGA profile will show a decomposition step of approximately 17% corresponding to the loss of both water molecules at around 150°C, confirming that these molecules are bound to the magnesium and will be present even after drying the product in typical conditions.

Fig. 3. TGA decomposition profiles of chelated magnesium glycinate (red data) and a sample that is not chelated (blue data). The mass loss step starting around 125°C in the red data is attributed to the decomposition of the two bound water molecules found in chelated magnesium glycinate. The non-chelated sample contains unreacted glycine which decomposes just above 200°C.



TGA measurements showing consistency in the decomposition profile of every sample verify that all of the samples have the same composition.

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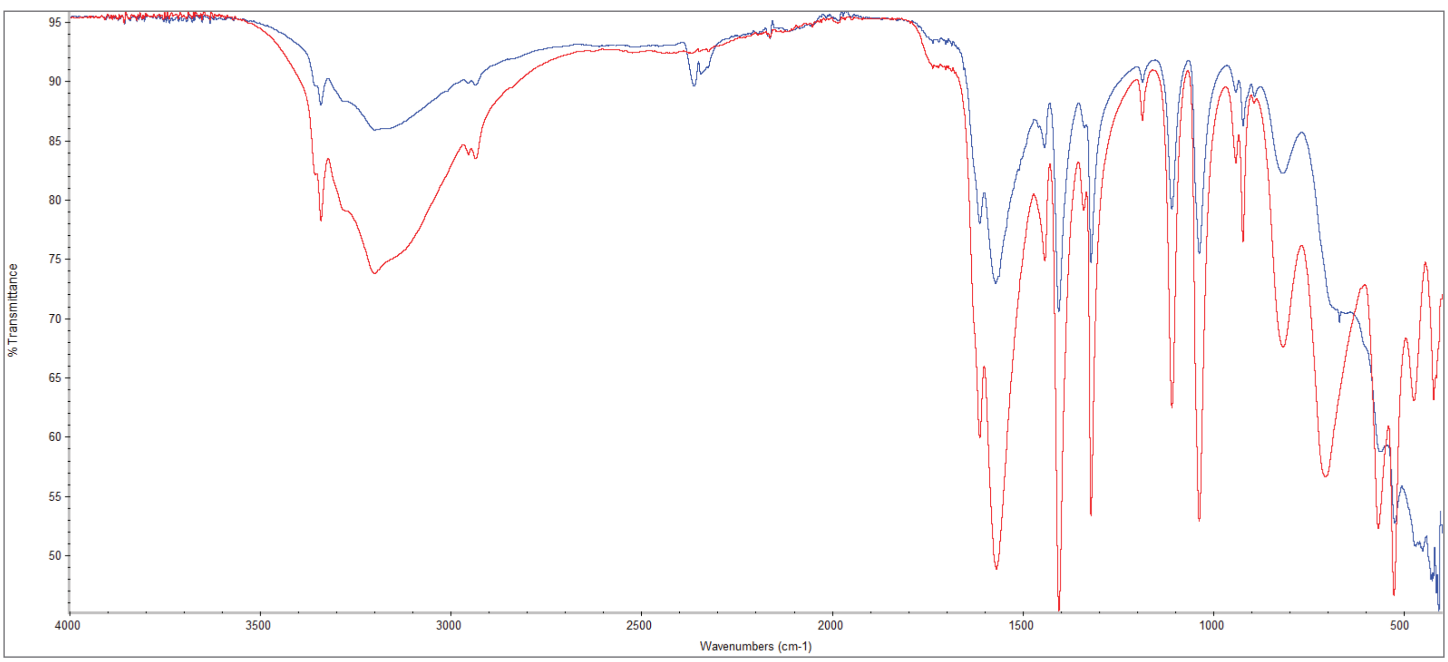
Step Three: Fourier Transform Infrared (FT-IR) Spectroscopy

FT-IR spectroscopy measures the absorption of infrared light by a molecule due to vibrational frequencies of the bonds within the molecule. When a mineral ion forms a bond with a ligand, the vibrational frequencies of the functional groups involved in the bond formation are altered. There are many types of bonding and therefore many vibrational frequencies that can occur in a molecule. Simply comparing the FT-IR spectra of bonded ligands with free ligands does not provide absolute proof of chelation. This only provides evidence that an interaction has occurred, such as bridging, terminal binding, or even hydrogen-bonding, but it does not confirm the ligand is chelating or provide information regarding the actual structure of the molecule. Additional characterization is needed to prove chelation and the absolute molecular structure.

Our standard FT-IR spectra, supported by extensive XRD and TGA test data, are proprietary to Innophos. The test data enables us to know with certainty that the standard FT-IR spectrum we designate for a product is actually representative of the chelated structure. By comparison, many chelated mineral suppliers use only FT-IR, unsupported by additional data. Claims of full chelation based on this inadequate testing protocol are spurious at best. Therefore, manufacturers that characterize their products using FT-IR only, do not know whether their particular IR spectrum is that of the chelated molecule or another type of interaction or structure.

Claims of full chelation based on FT-IR alone are inadequate.

Fig. 4. FT-IR spectra of the proven chelated magnesium glycinate (red data) and that of a sample that is not fully chelated (blue data)



Complete Transparency

Innophos is the only company using a data-based three-step verification process to prove our products are fully chelated. Extensive XRD, TGA, and FT-IR data, available to our customers, demonstrates 100% chelation of Chelamax® products. We are committed to full transparency and freely share data with our customers that demonstrate which products are fully chelated and how we know that they are.

Some mineral products are labeled as fortified or buffered and are advertised as being more potent – which can be misleading to both manufacturers and consumers. For a manufacturer, the higher potency may seem to provide a reduced cost in use for a formulation. For the consumer, the higher potency may incorrectly suggest a higher level of dietary benefit. However, in many cases the potency is achieved by fortifying a chelated product with a non-chelated product of higher potency. In other cases, the two products are merely physically mixed with no chemical reaction taking place at all. The result in both cases is a less bioavailable mineral for the consumer. With Chelamax® products you know exactly what you are getting.

For example, fully chelated Chelamax® magnesium glycinate has a potency (magnesium content) of 11.7%, because chemically, this is the maximum amount of magnesium that can be fully chelated by two glycine ligands due to the chemical structure of the molecule. By comparison, magnesium oxide has a potency of 60%. Though the potency of the magnesium oxide is higher, it is not as readily absorbed as chelated magnesium glycinate and is less bioavailable in the body.

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Comparison of Innophos with Other Mineral Suppliers

Many products, even those in which the word chelate is part of the ingredient name (e.g., chromium glycinate chelate), may not be fully chelated – and therefore are likely to have inferior bioavailability. Innophos' Chelamax® chelated minerals provide the full nutritional benefit of fully chelated minerals with none of the product or testing deficiencies that these competitive minerals have. Here are some of the typical flaws found in a few popular brands of so-called "chelated minerals":

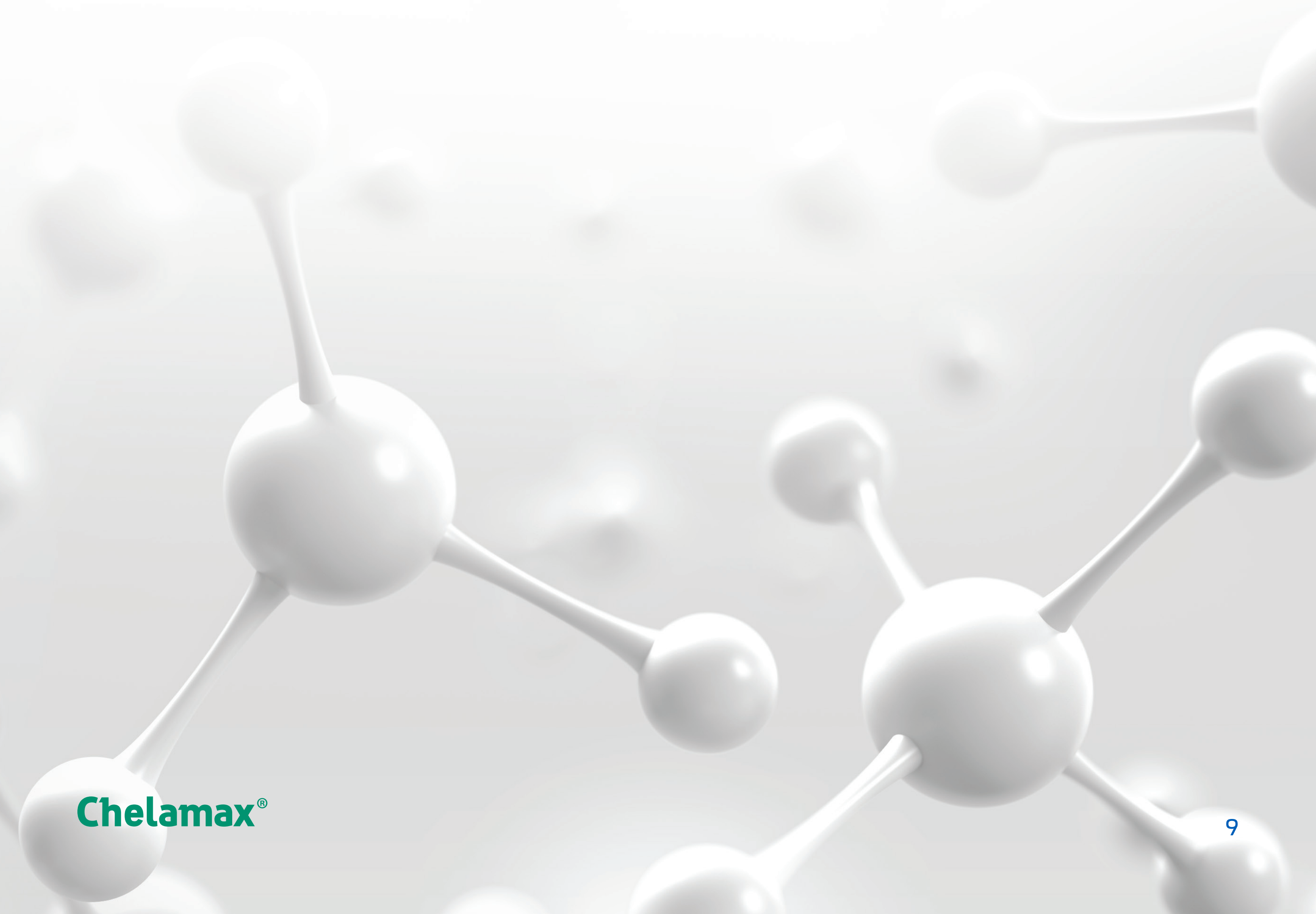
Did you know that many ingredients sold as chelated minerals are in fact not fully chelated?

Company A bases their full chelation claim on FT-IR data alone, which is not conclusive proof of chelation. In addition, some products they claim to be fully chelated cannot be based on the chemistry of the particular mineral and ligand combination.

Company B offers a line of chelated minerals, but they do not mention their analytical methods in their promotional materials.

Company C markets a line of products including 20 amino acid chelates. Their catalog does not mention "full chelation," nor does it say how or even whether chemical structure has been verified.

Company D competes primarily on price and offers only one apparently chelated product.



Chelamax® Product Families

Table 4. Chelamax® Chelated Minerals—Core Products

PRODUCT	MINERAL POTENCY	MOLECULAR FORMULA	MOLECULAR WEIGHT (G/MOL)	CAS #
Calcium ascorbate	9.4%	$Ca(C_6H_7O_6)_2(H_2O)_2$	426.3	5743-28-2
Calcium glycinate	17.9%	$Ca(C_2H_4NO_2)_2(H_2O)_2$	224.2	35947-07-0 (anhydrous)
Chromium picolinate	12.4%	$Cr(C_6H_4NO_2)_3$	418.3	14639-25-9
Magnesium citrate	12.3%	$Mg_3(C_6H_5O_7)_2(H_2O)_8$	595.2	153531-96-5 (nonahydrate)
Magnesium glycinate	11.7%	$Mg(C_2H_4NO_2)_2(H_2O)_2$	208.5	14783-68-7 (anhydrous)
Zinc citrate	32.1%	$Zn_3(C_6H_5O_7)_2(H_2O)_2$	610.4	5990-32-9
Zinc glycinate	28.2%	$Zn(C_2H_4NO_2)_2{\cdot}H_2O$	231.5	14281-83-5

At Innophos, we continue to strive to provide the best science and highest quality products in the industry. We are excited to launch three additional Chelamax® products:

Table 5. Chelamax® Chelated Minerals—New Products

PRODUCT	MINERAL POTENCY	MOLECULAR FORMULA	MOLECULAR WEIGHT (G/MOL)	CAS #
Calcium citrate	21.1%	$Ca_3(C_6H_5O_7)_2(H_2O)_2{\cdot}2H_2O$	570.49	5785-44-4
Bismaltolato oxo vanadium (BMOV)	16.1%	$VO(C_6H_5O_3)_2$	317.14	38213-69-3
Zinc picolinate	21.1%	$Zn(C_6H_4NO_2)_2$	309.59	17949-65-4

These products have been subjected to our rigorous three-step testing protocol and have been verified to be fully chelated. Chelamax® calcium citrate and zinc picolinate add depth to our existing line of chelated calcium and zinc products, to serve an even wider range of applications across the industry. It is difficult to find a truly chelated vanadium source since the chemistry of vanadium can be so challenging. Our Chelamax® BMOV is carefully reacted in a controlled process to ensure a complete reaction and verified to be chelated. These are exciting new additions to the Chelamax® product line, which will continue to grow as we validate more products through our three-step process.

Conclusion

At Innophos, we verify full chelation of our mineral products with a degree of transparency, rigor, and scientific data unmatched in the industry. These verification procedures and data points help prove the quality of what you are buying and the value you are getting. Innophos has raised the bar in terms of transparency and validation in the chelated minerals industry. Our customers can be confident that our Chelamax® products are superior to other brands of chelated minerals, which simply lack the same level of testing, verification, and supporting data.

Contact Innophos today about using Chelamax® minerals in one of your product formulations.

Innophos is the only company using a data-based three-step verification process to prove our products are fully chelated.

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