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Whitepaper

Chelamax®

Chelamax Zinc Bisglycinate: A Superior Alternative to Traditional Zinc

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Executive Summary

Chelamax® zinc bisglycinate has several advantages over zinc oxide:

- Greater solubility, stability and bioaccessibility
- 3x the dissolution rate
- Physical properties suited for today's preferred supplement forms

The link between nutrition and good health has never been more important. During the pandemic, demand for nutritional supplements has skyrocketed as consumers seek to fortify their diets and to improve their immune systems. But not all mineral forms are alike.

At Innophos, we focus on manufacturing the highest performance minerals as well as understanding the differences between mineral forms. We developed the only 3-step verification process available on the market to characterize the molecular structure of minerals. Using our methodology, we have verified the fully chelated nature of the products in our portfolio. The advantage of chelation is consistent solubility throughout the digestive tract, which is critical for bioaccessibility and mineral absorption[1,2].

Chelation in Mineral Absorption

Chelation is known to enhance the absorption of zinc. Animal studies have shown that chelated zinc has greater efficacy than inorganic zinc in mineral supplements[3-6]. Furthermore, chelated zinc has increased absorption in human clinical studies as well[7,8].

Given the growth and interest in zinc supplementation due to its role in improving immune health[9,10], we compared the solubility and dissolution of Chelamax® zinc bisglycinate vs. zinc oxide. In the studies below, we show the advantages of Chelamax® fully chelated zinc bisglycinate over zinc oxide. Chelamax® zinc bisglycinate, based on its physical and chemical properties, is a superior alternative to other zinc sources such as zinc oxide and therefore, ideal for the delivery forms preferred today.

Figure A. Shows the structure of a fully chelated mineral. Each ligand bonds to the metal in two positions creating a ring. The two ligands create a stable compound with zinc which does not break down in gastric conditions.

Bioavailability in the GI Tract

The bioaccessibility of mineral oxides and salts vary significantly as it is driven by the solubility of the mineral in the gastrointestinal tract. The overall diet will have an effect on this uptake as well. For instance, phytates, an antinutrient which is found in grains, legumes and other foods, drastically reduce the effectiveness of inorganic minerals. However, chelated minerals have up to 129% more absorption than inorganic salts in the same conditions[11]. Chelation provides stability to the mineral for improved mineral absorption. The daily requirement for zinc is 8-11 mg for an adult[12], but if that zinc source is not bioavailable, the supplement will not be efficacious.

BIOACCESSIBLE	VS	BIOAVAILABLE
the QUANTITY of a compound that is AVAILABLE FOR ABSORPTION *(in supplements it is solubility in the GI tract)*		**the FRACTION of the compound that is ACTUALLY ABSORBED** *(influenced by food eaten, bioaccessibility, individual metabolism, concentration in the body i.e. deficiency)*

Link Between Solubility and Bioaccessibility

Soluble minerals are needed in today's preferred delivery forms like gummies and soft gels. Understanding the solubility of these minerals in biological conditions is critical to gaining an understanding of absorption. Solubility is routinely tested in the laboratory using distilled water, but that has limited value when considering biological absorbance. For comparison, both samples were tested for solubility in water, as well as gastric and intestinal pH conditions. As shown in Table 1, Chelamax® zinc bisglycinate is much more soluble under conditions that mimic the intestine where zinc is mainly absorbed.

Primary uptake for zinc in the body is at the small intestine. Supplements are exposed to both acidic pH conditions in the stomach and neutral pH conditions when reaching the small intestine. The solubility of inorganic zinc sources is reduced as the pH moves from acidic to neutral, while Chelamax® zinc bisglycinate is soluble throughout the GI tract. The chelated compound remains intact, stable and bioaccessible[1, 10], while the oxide is precipitated and no longer available for absorption.

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BIOLOGICAL CONDITIONS

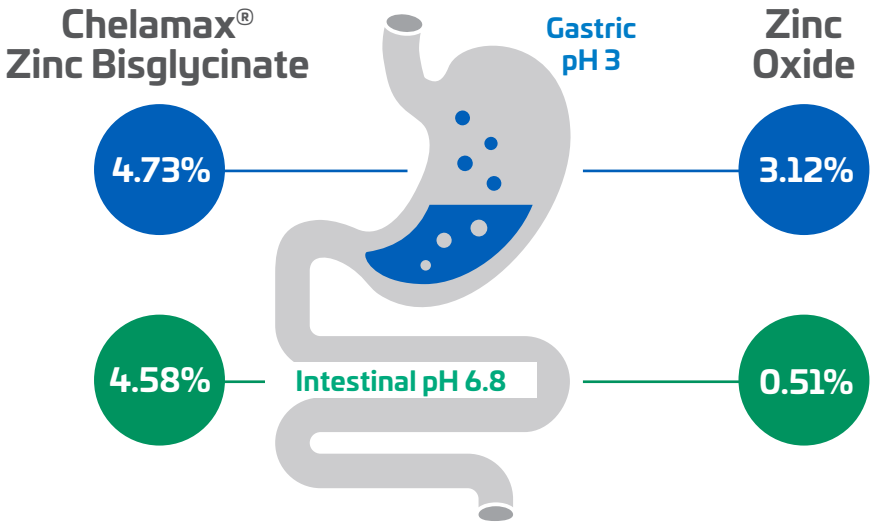
Table 1. Solubility differences of Chelamax® zinc bisglycinate and zinc oxide[13].

	CHELAMAX® ZINC BISGLYCINATE (%)	ZINC OXIDE (%)
In Water	7.6	Insoluble
In 0.1N HCl (Gastric)	4.7	3.1
In pH 6.8 Buffer (Intestinal)	4.6	0.5

DIGESTIVE SYSTEM

Solubility in Gastric and Intestinal Conditions

Figure B. Chelamax® zinc bisglycinate is significantly more stable throughout the intestinal tract where zinc is absorbed.



Dissolution Rates of Zinc Tablets

Tablets are widely used as a dosage form in mineral supplementation. The kinetics of solubility are influenced by the tablet hardness, other ingredients, and the dissolving media. For the study, tablets were produced on a Piccola 8 station rotary press equipped with SMI Director software. The formulation for each tablet is shown in the graphic below. To match tablets sold commercially, the zinc target concentration was set to 200% daily value (DV) in a 660 mg tablet. The final zinc concentration was tested to between 186-188% DV based on the average 10-tablet mass seen in the figure on page 5.

Utilizing an Agilent 708-DS paddle stirring dissolution apparatus, 660 mg tablets containing zinc oxide and Chelamax® zinc bisglycinate were analyzed in phosphate buffer (pH 6.8) according to the USP 724 dissolution monograph[14]. Tablets were introduced to the buffer and 1 ml samples of the supernatant media were collected every three minutes for 30 minutes using an Agilent 850 DS sampling station. The supernatant samples were further diluted to 15 mL in 3% nitric acid and analyzed for zinc content (in triplicate across three wavelengths) using an Agilent 5800 ICP-OES system.

A-Tab® MD, a multi-functional co-processed excipient specially formulated to enhance compressibility and simplify formulations in pharmaceutical and nutraceutical tablets, was used in both tablets.

ZINC TABLETS MADE WITH A-TAB® MD

Table 2. Zinc tablets made with A-Tab® MD results in enhanced compressibility and simplified formulation.

INGREDIENTS	%	%
Zinc Source	11.5	4.2
A-Tab® MD	83.6	90.9
Magnesium Stearate	0.9	0.9
Croscarmellose Sodium	3.9	3.9
TOTAL	**100**	**100**

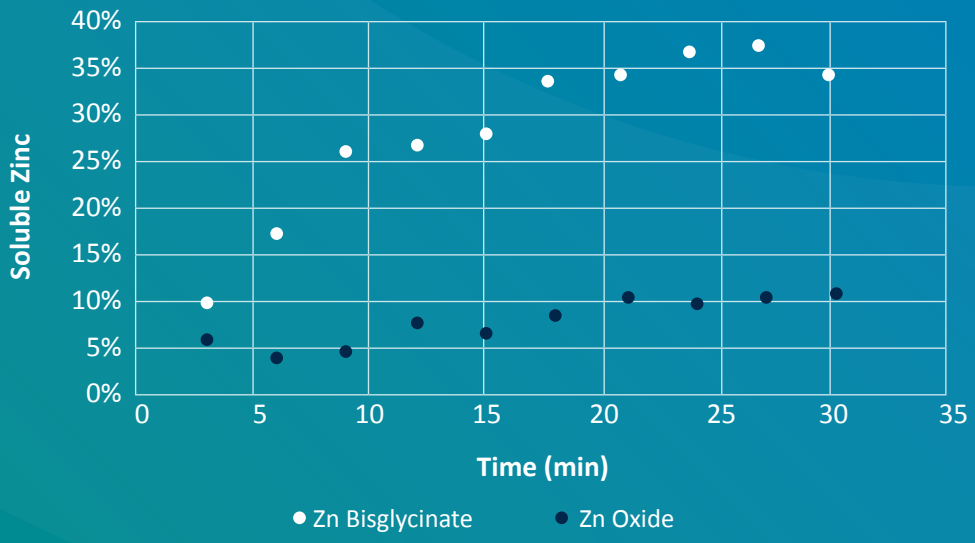
The tablets were evaluated by standard USP protocols[14]. Eighteen tablets were tested using a Vankel VK100 for disintegration and the results were averaged. For all other tests (USP 1216, 1217), ten tablets were tested in each case and the results were averaged. The tablets had acceptable hardness, friability and disintegration for the dissolution study.

Table 3. Tablet results from both formulas, zinc 186-188% DV[15].

TABLET CHARACTERISTICS	CHELAMAX® ZINC BISGLYCINATE	ZINC OXIDE
Compression Force (KN)	20	20
Disintegration (min)	4:29	6:30
Friability (%)	0.21	0.23
Hardness (kp)	18.6	19.6
Avg. Mass (mg, 10 pieces)	615.7	614.7

Solubility of Chelamax® Zinc Bisglycinate

Figure C. Zinc solubility over time as a percent of the total zinc in the tablet made at 20 KN force[16].



The chelated zinc has a 3-fold increase in solubility

The results in Figure C clearly show the improved solubility of Chelamax® zinc bisglycinate over zinc oxide. Over the course of 30 minutes in pH 6.8 buffer solution, the chelated zinc has a 3-fold increase in solubility. The zinc oxide tablet quickly reaches a maximum solubility of about 10% of the total zinc present, while Chelamax® zinc bisglycinate continues to improve in solubility over the entire 30 minute experiment. Tablet disintegration time for the 20 KN tablets are between 4 and 6 minutes respectively (Table 3). The advantage of chelation is consistent solubility throughout the digestive tract, which is critical for bioaccessibility and mineral absorption[1, 2].

Physical Properties and Applications

Table 4. The table highlights the physical properties of Chelamax® zinc bisglycinate.

PARAMETER	AVERAGE RESULT	APPLICATION
Bulk Density (g/ml)	0.68	Powder Drink Mixes
Tapped Density (g/ml)	1.02	Capsules, Tablets
Through 60 Mesh %	93	Tablets
Through 80 Mesh %	84	Softgels
Solubility (mg/ml)	76	Powdered Drink, Softgels, Gummies
pH	7.77	Liquid Application, Neutral Taste

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Conclusion

Chelamax® zinc bisglycinate is a superior alternative to traditional zinc sources, and suitable for a wide variety of applications. The solubility and dissolution properties show a clear advantage in bioaccessibility over traditional inorganic zinc sources like zinc oxide. Our 3-step validation process sets a new standard in testing and proof of chelation. This work has demonstrated our Chelamax® line has greater bioaccessibility and provides the foundation of our upcoming Chelamax® bioavailability program. We look forward to sharing more soon.

Contact Innophos today to learn how Chelamax® fully chelated minerals can help you get the most from your mineral supplements.

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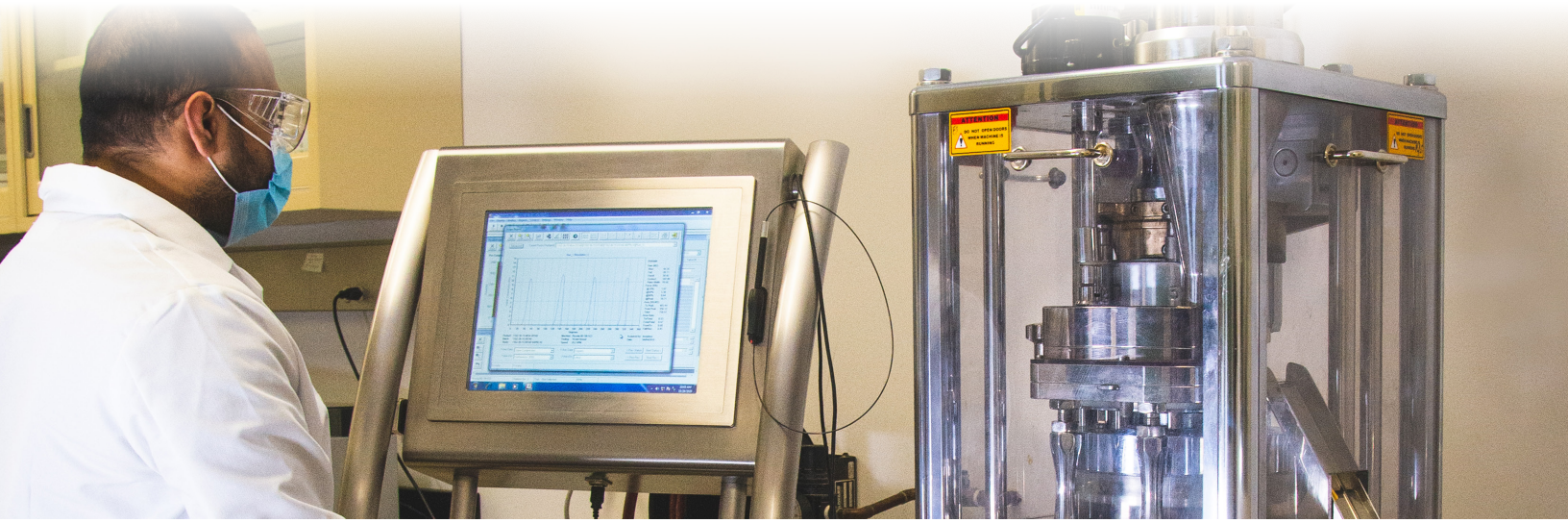

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