



ADVANCED MINERAL CHELATION: ENHANCING BIOAVAILABILITY AND GASTROINTESTINAL TOLERANCE OF FERROUS BISGLYCINATE CHELATE THROUGH WBCIL'S FULLY REACTED MANUFACTURING STANDARDS

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ABSTRACT

Ferrous Bisglycinate (FBG) chelate is a technologically advanced iron supplement designed to overcome the limitations of traditional iron salts like ferrous sulfate. Unlike standard ionic iron, Ferrous Bisglycinate is a fully reacted bidentate chelate—specifically manufactured by West Bengal Chemical Industries Ltd., Kolkata, India (WBCIL)—where ferrous iron is chemically sequestered within two glycine rings. This unique molecular architecture ensures high stability in gastric acid and prevents the release of free reactive ions, thereby eliminating common gastrointestinal side effects such as nausea and constipation. Clinical data demonstrates that this chelated form utilizes both the standard DMT1 pathway and the high-capacity PepT1 dipeptide channel, resulting in bioavailability 2 to 4 times higher than traditional salts. Studies across diverse populations, including pregnant women and pediatric patients, consistently show that lower elemental iron doses of Ferrous Bisglycinate (e.g., 25mg) are as effective as higher doses of ferrous sulfate (e.g., 50 mg) in managing iron deficiency anemia. By leveraging the advanced manufacturing standards of WBCIL, this chelate addresses the chronic issue of patient non-compliance and emerges as a gold-standard delivery system for sensitive populations requiring efficient and tolerable iron repletion.

INTRODUCTION

Ferrous Bisglycinate (FBG) chelate represents a significant technological advancement in oral iron supplementation. It is a unique mineral complex designed to overcome the long-standing challenges associated with traditional iron salts, such as ferrous sulfate.^[1] At its chemical core, Ferrous Bisglycinate is a chelated compound. Chelation refers to a process where a mineral (in this case, iron) is chemically bonded to organic molecules—specifically amino acids.^[2] In this specific structure, one molecule of ferrous iron (Fe^{2+}) is bound to two molecules of glycine, the smallest and simplest amino acid.^[2]

The primary advantage of this chelated form lies in its molecular stability. Traditional iron salts dissociate (break apart) easily in the acidic environment of the stomach. This releases free iron ions which can irritate the gastrointestinal lining and interact with dietary inhibitors like phytates or tannins found in coffee and tea.^[3] Beyond GI distress, traditional iron salts cause liver problems by triggering hepatocyte oxidative stress. In contrast, FBG remains chemically neutral and stable throughout the digestive process. As iron is chemically shielded within two glycine rings, the body does not recognize it as a raw mineral. Instead, it is absorbed via the dipeptide pathway in the small intestine.^[4] This allows the iron to be taken up more efficiently without competing with other minerals like calcium for absorption sites. Also, Ferrous Bisglycinate protects hepatic antioxidant reserves by utilizing a regulated absorption pathway that prevents free iron surges in the portal circulation, thereby protecting hepatic antioxidant reserves and long-term liver function.^[4]

One of the most significant safety advantages of Ferrous Bisglycinate Chelate is its ability to mitigate the risk of iron overload and acute toxicity, a concern that is frequently associated with traditional iron salts like ferrous sulfate.^[2] Iron poisoning occurs when the body's natural regulatory systems are overwhelmed by an influx of free iron ions (Fe^{2+}), which can cause catastrophic oxidative damage to the liver, heart, and central nervous system.^[3] Ferrous Bisglycinate addresses this risk through two primary biological mechanisms: its unique dipeptide absorption pathway and its adherence to physiological regulation.^[3] Unlike traditional iron salts that might compel minerals into the bloodstream, FBG is absorbed by the body in a manner that remains sensitive to the person's actual iron stores.^[2,3] Research indicates that the uptake of iron from bisglycinate is inversely related to serum ferritin levels; if the body is already iron-deplete, it naturally downregulates the absorption of the chelate to prevent excessive accumulation.^[4] This absorption ensures that the iron is utilized primarily

to replenish deficiencies rather than being dumped into the system uncontrollably.^[4] Traditional iron salts dissociate rapidly in the stomach and intestines, releasing an overload of raw iron ions.^[4] If the dose is high, these ions can bypass the body's gated transport proteins (like DMT1) through passive diffusion, leading to systemic toxicity.^[5] Because the iron in FBG is chemically shielded or sequestered within glycine rings, it does not release these reactive free ions into the digestive tract. The molecule remains intact until it is processed by the mucosal cells.^[5]

Clinical research consistently highlights three main areas where Ferrous Bisglycinate outperforms older formulations. 1. Superior Bioavailability: Studies suggest it can be 2 to 4 times better absorbed than ferrous salts, meaning lower doses are required to achieve the same increase in serum ferritin levels.^[5] 2. Gastrointestinal Tolerance: Because it does not release free iron ions in the gut, users experience significantly fewer side effects, such as nausea, constipation, or abdominal cramping.^[5] 3. Reduced Food Interference: While most iron supplements must be taken on an empty stomach to be effective, Ferrous Bisglycinate maintains high absorption rates even when consumed with food because this chelated form has been shown to have minimal interference from dietary factors.^[5]

As iron deficiency remains one of the most prevalent nutritional disorders globally, Ferrous Bisglycinate chelate has emerged as a gold standard for sensitive populations.^[6] It is frequently the preferred choice for prenatal vitamins, athletes, and individuals with inflammatory bowel conditions who require effective iron repletion without the digestive distress typically associated with supplementation.^[7,8] West Bengal Chemical Industries Ltd., Kolkata, India (WBCIL) is a manufacturer of high-purity Ferrous Bisglycinate chelate. WBCIL has established itself as a specialist in mineral amino acid chelates and injectable iron APIs. Our manufacturing process is characterized by a commitment to WHO-GMP and ISO standards, ensuring that the chelation is chemically precise and free from contaminants. By leveraging advanced R&D and green chemistry principles, WBCIL produces a fully reacted chelate that maximizes stability and bioavailability. Our role is critical in the global supply chain, providing this novel formulation to nutraceutical industry to address iron deficiency with a focus on superior tolerance and safety.

Clinical studies on Ferrous Bisglycinate chelate

Table 1: Clinical Studies on Ferrous Bisglycinate Chelate.

Population	Comparator(s)	Key Findings & Outcomes
Pregnant Women (Danish cohort)	Ferrous Sulfate (50 mg)	Low Dose Efficiency: 25 mg of Ferrous Bisglycinate was as effective as 50 mg of ferrous sulfate in preventing iron deficiency anemia (IDA). ^[1]
Pregnant Women (2nd Trimester)	Ferrous Glycine Sulfate	Higher Hb Increase: Mean Hb rose by 2.48 g/dL (bisglycinate) vs. 1.32 g/dL (sulfate). Significantly lower incidence of side effects. ^[9]
Preterm Infants	Ferrous Sulfate	Reduced Dosage: 0.75 mg/kg/day of bisglycinate achieved similar ferritin levels as 3.0 mg/kg/day of sulfate—a 4x efficiency gain. ^[10]
Mixed Populations (17 RCTs)	Various Iron Salts	Meta-Result: Consistent evidence of higher Hb concentrations in pregnant women and a 64% lower risk of gastrointestinal side effects. ^[11]
Children with IDA	Iron Polymaltose Complex (IPC)	Superior Replenishment: Bisglycinate showed significantly higher increases in Serum Ferritin (29 ng/ml) compared to IPC (23 ng/ml) after 3 months. ^[12]
Orthopedic Surgery Patients	Previous Oral Iron (Failed)	Pre-Op Efficacy: Effectively managed preoperative anemia at low doses (14 mg/day) with zero reported side effects in patients previously intolerant to iron. ^[13]
Chronic Kidney Disease & Hemodialysis	Placebo / Conventional Salts	Alternative to IV: Improved serum iron and transferrin saturation in NDD-CKD patients, suggesting it as a viable oral alternative to IV iron. ^[14]

Clinical research on Ferrous Bisglycinate chelate has focused largely on its high bioavailability and gastrointestinal tolerability, particularly in comparison to traditional iron salts like ferrous sulfate, ferrous fumarate, and ferrous ascorbate. Recent systematic reviews and meta-analyses provide a clear picture of how this chelated form performs across different populations.

Maternal Health and Pregnancy Outcomes

In maternal health, the primary goal of iron therapy is to maintain optimal hemoglobin levels while ensuring consistent compliance. A landmark randomized trial demonstrated that a low dose of 25 mg of elemental iron from Ferrous Bisglycinate was as effective as 50 mg of iron from ferrous sulfate in preventing iron deficiency and anemia during pregnancy.^[1] Furthermore, a 2023 meta-analysis published in *Nutrition Reviews* found that pregnant

women taking Ferrous Bisglycinate for 4–20 weeks achieved a significantly higher increase in hemoglobin concentrations compared to those taking other iron salts (Standardized Mean Difference of 0.54 g/dL).^[9] Some studies have even noted slightly higher newborn birth weights in the bisglycinate group, suggesting more effective systemic iron support for the developing fetus.^[10]

Gastrointestinal (GI) Tolerance and better Compliance

The compliance barrier is the most frequent cause of iron therapy failure, as traditional salts often cause nausea, constipation, and epigastric pain. Ferrous Bisglycinate significantly addresses this issue; a 2023 meta-analysis showed a 64% reduction in reported GI adverse events compared to traditional iron salts (Incidence Rate Ratio of 0.36).^[11] This superior tolerance exists because the iron is chemically shielded by glycine, preventing it from interacting with and irritating the gut mucosa. The impact on compliance is substantial: in one study of pregnant women, 73% of those in the chelate group maintained perfect adherence to their regimen, compared to only 35% in the ferrous sulfate group.^[12]

Besides, the risk of compliance barrier extends beyond the GI symptoms and gut. The liver is the primary site of iron storage and detoxification. Poorly absorbed iron salts can lead to labile or free iron entering the portal circulation. This can trigger oxidative stress within hepatocytes, potentially leading to long-term liver dysfunction. Ferrous Bisglycinate significantly addresses these systemic risks. Because the chelate is absorbed more efficiently and follows a regulated pathway, it minimises the formation of non-transferrin bound iron (NTBI). By preventing these free iron surges in the portal circulation, Ferrous Bisglycinate mitigates the risk of oxidative damage to hepatocytes and deplete hepatic antioxidant reserves.^[13]

Efficacy in Children and Infants

For pediatric populations, the ease of administration and the rapid, lasting restoration of iron stores are critical factors. Research in Mexican School children found that while both ferrous sulfate and bisglycinate increased ferritin, the bisglycinate group maintained significantly higher ferritin levels six months post-supplementation, indicating a more robust restoration of long-term iron stores.^[13] Additionally, studies in children with Iron Deficiency Anemia have shown that Ferrous Bisglycinate outperforms Iron Polymaltose Complex (IPC) in raising both hemoglobin levels and mean corpuscular volume (MCV) over a three-month period.^[14] This is further supported by evidence in preterm infants, where a significantly lower dose of

bisglycinate (0.75 mg/kg/day) achieved similar ferritin levels to a much higher dose of sulfate (3.0 mg/kg/day).^[15]

Ferrous Bisglycinate versus Ferrous Sulfate in terms of bioavailability and side effects

Table 2: Summary Table: Ferrous Bisglycinate vs. Ferrous Sulfate.

Feature	Ferrous Sulfate	Ferrous Bisglycinate Chelate
Elemental Iron Dose	Usually higher (60–100mg)	Often lower (15–30mg)
Bioavailability	10% - 15% (lower)	30% - 40% (higher)
GI Side Effects	High (nausea, constipation)	Low to None
Food Interference	Inhibited by tea/coffee/phytates	Minimal interference
Absorption Pathway	DMT1 (ion channel)	Dipeptide/PepT1 (amino acid path)

The table illustrates a clear clinical transition from traditional high-dose iron salts to high-efficiency chelated iron, highlighting that Ferrous Bisglycinate chelate offers a more targeted physiological response.^[16] The data demonstrates that because of its superior bioavailability—often double or triple that of ferrous sulfate—clinical outcomes like hemoglobin and ferritin recovery can be achieved using significantly lower elemental iron doses (e.g., 25 mg vs. 50 mg).^[14] This low-dose, high-impact profile is largely due to the dipeptide absorption pathway, which prevents the iron from being blocked by dietary inhibitors and, more importantly, keeps it from irritating the gastric lining.^[15] Consequently, the table reflects a massive reduction in gastrointestinal side effects, solving the chronic issue of non-compliance that typically plagues traditional iron therapy.

The specialized absorption mechanism of Ferrous Bisglycinate chelate is centered on its ability to utilize multiple entries into the bloodstream, distinguishing it from the singular pathway used by traditional iron salts.^[16] In the human gut, standard iron (such as ferrous sulfate) must rely almost exclusively on the Divalent Metal Transporter 1 (DMT1).^[17] This pathway is easily saturated and can be blocked by inhibitors in our diet, such as the phytates in grains or the polyphenols in coffee.^[18]

However, because Ferrous Bisglycinate is a chelated molecule, the iron is protected within two glycine amino acid rings, allowing it to be recognized as a protein fragment rather than a raw mineral.^[19] This enables the compound to utilize the Peptide Transporter 1 (PepT1) pathway—the same high-capacity channel the body uses to absorb dipeptides from protein.^[20] By utilising this amino acid transport system, the iron bypasses luminal competition and dietary blockers that typically limit iron uptake.^[20] Furthermore, since the iron remains bound until it reaches the mucosal cells, it does not release free reactive ions in the stomach,

effectively eliminating the oxidative stress and inflammation that cause the nausea and constipation associated with conventional supplements.^[21,22]

Ferrous Bisglycinate versus Ferrous Fumarate and Ferrous Ascorbate

Table 3: Comparison of Chemical and Absorption Properties among Ferrous Bisglycinate Chelate, Ferrous Fumarte, and Ferrous Ascorbate

Feature	Ferrous Bisglycinate Chelate	Ferrous Fumarate	Ferrous Ascorbate
Molecular Charge	Neutral (Electrically stable)	Ionic (Dissociates)	Ionic (Dissociates) ^[23]
Absorption Path	Dual (DMT1 and PepT1)	Single (DMT1)	Single (DMT1) ^[23]
Effect of Food	Minimal interference	Significant interference	Absorption is enhanced by Vitamin C but blocked by phytates. ^[23]
Bioavailability	Very High (3-4x vs Sulfate)	Moderate	High (due to Ascorbate) ^[23]

Table 4: Comparison of Clinical Tolerability and Performance.

Parameter	Ferrous Bisglycinate	Ferrous Fumarate	Ferrous Ascorbate
GI Side Effects	Lowest (highly tolerated)	Moderate to High	Moderate ^[24]
Metallic Taste	Negligible	Strong / Common	Mild to Moderate ^[24]
Typical Dose (mg)	15 mg – 30 mg	60 mg – 100 mg	50 mg – 100 mg ^[25]
Clinical Focus	Pregnancy, IBD, sensitive stomachs	General anemia (cheap)	Pregnancy and pediatrics ^[25]
Stability in Gut	High (does not break down early)	Low (dissociates in gastric acid)	Low (breaks down to release free iron) ^[25]

While fumarate is a common organic salt, it still dissociates in the stomach, releasing free iron ions that can cause oxidative stress and constipation.^[23] Ferrous Bisglycinate remains intact until it reaches the absorption sites in the small intestine, making it significantly more favourable to stomach. Ferrous ascorbate is designed to keep iron in its more absorbable ferrous state using Vitamin C.^[24] However, it still relies on the DMT1 pathway. Ferrous Bisglycinate outperforms ascorbate because it uses the additional PepT1 pathway, allowing it to be absorbed even when the DMT1 path is saturated or inhibited by dietary factors like calcium or tea.^[25]

The Industrial Standard: Ensuring a Fully Reacted Chelate

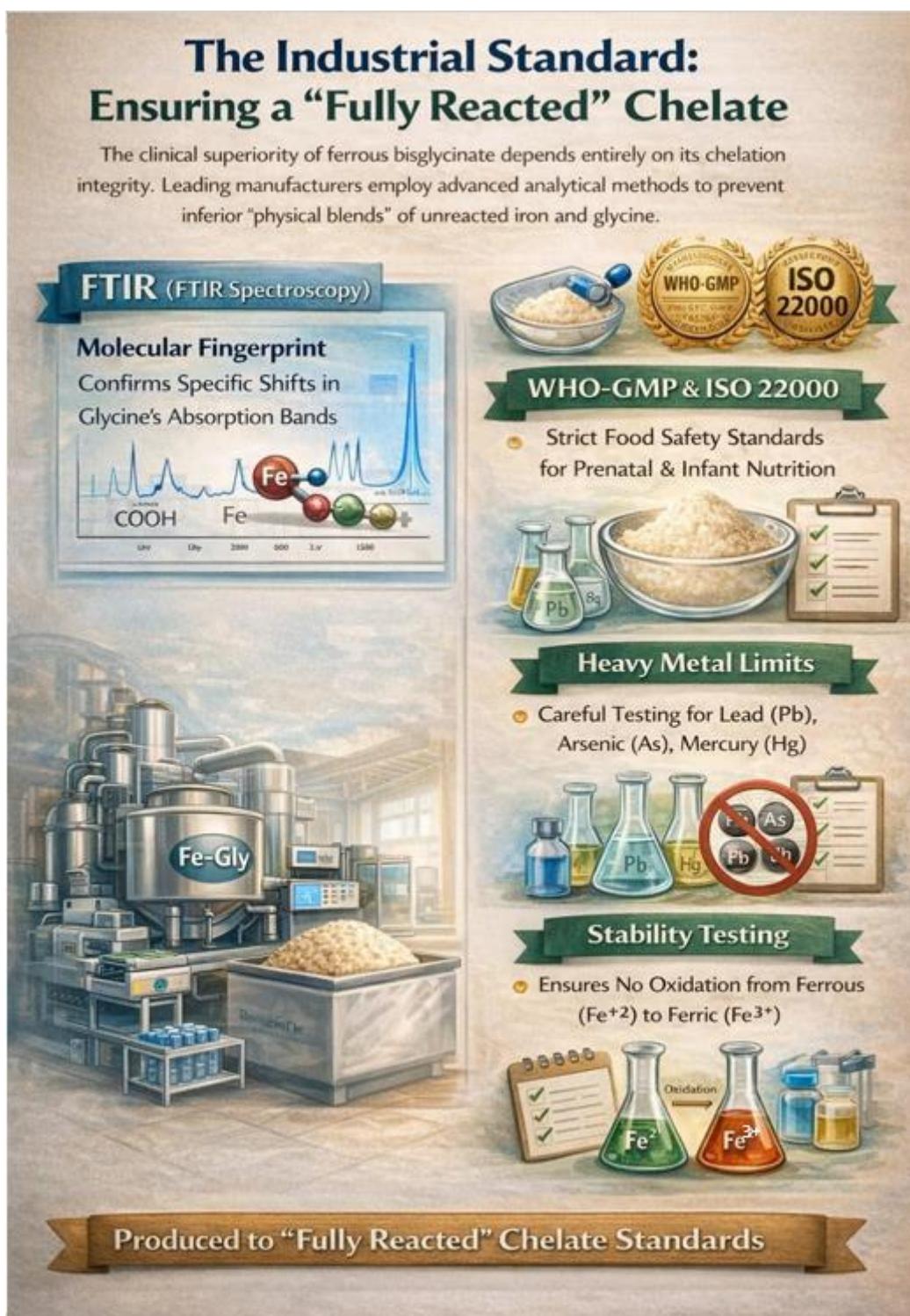


Figure 1: The Industrial Standard Maintained to Ensure a Fully Reacted Chelate.

The clinical superiority of Ferrous Bisglycinate is entirely dependent on the integrity of the chelation process. In the manufacturing sector, particularly at specialized facilities like WBCIL, the focus is on producing a fully reacted compound.^[26] A common pitfall in the

supplement industry is the use of physical blends, where ferrous sulfate and glycine are simply mixed together. These do not offer the same biochemical benefits.^[27] To prevent this, manufacturers use sophisticated analytical techniques. Fourier-Transform Infrared (FT-IR) is used to fingerprint the molecule.^[28] A true chelate will show specific shifts in the absorption bands of the carboxylate group of glycine, proving that a coordinate covalent bond has formed with the iron atom.^[29] Since this formulation is often used in prenatal care and infant nutrition, the regulatory threshold is exceptionally high. Leading manufacturers must adhere to WHO-GMP & ISO ensuring consistent batch-to-batch quality and food safety, heavy Metal Limits: Strict monitoring of Lead (Pb), Arsenic (As), and Mercury (Hg) levels, often keeping them significantly below USP (United States Pharmacopeia) limits, and stability Testing ensuring the iron does not oxidize from Ferrous (Fe^{2+}) to Ferric (Fe^{3+}) over the shelf life of the product, as the ferric form is much harder for the body to absorb.^[30]

The analytical validation of Ferrous Bisglycinate manufactured by WBCIL focuses on proving its identity as a fully reacted, bidentate chelate rather than a simple mechanical mixture. Using FT-IR spectroscopy, WBCIL verifies that the elemental ferrous iron (Fe^{2+}) is chemically locked between two glycine molecules to create stable, heterocyclic rings. This rigorous characterization confirms that the compound is held together by coordinate covalent bonds, resulting in an electrically neutral and highly stable structure. By ensuring the total absence of unreacted free components—such as raw iron salts or unbound glycine—WBCIL produces a gold-standard delivery system. This molecular architecture allows the iron to bypass common absorption obstacles, remain stable against stomach acid, and eliminate the gastric distress and oxidative damage typically caused by unchelated iron.

METHODOLOGY

The spectroscopic measurements were conducted using an Agilent Technologies (USA) FT-IR spectrometer. Samples were analyzed using Attenuated Total Reflectance (ATR), where a small amount of material is placed in direct contact with the ATR crystal to ensure high-quality, repeatable data. By scanning the mid-infrared region from 400–4000 cm^{-1} , WBCIL captures the full coordination environment, providing definitive evidence that the iron and glycine have successfully merged into a single, bioactive chelate.

In the context of mineral nutrition, a fully reacted chelate refers to the total chemical transformation of raw materials into a single, stable complex with no residual ingredients left behind. Achieving complete chelation means that every available glycine molecule has

successfully bonded to a ferrous ion. If free or unattached glycine remained, it would indicate an unfinished chemical reaction, which compromises the bioavailability and structural integrity of the supplement. To certify that WBCIL's Ferrous Bisglycinate is a genuine chelate, we monitor the specific shifting and disappearance of functional group peaks during spectral analysis. The formation of the heterocyclic ring gives the compound covalent-like properties, making it behave differently in the body than standard ionic mineral salts.

By ensuring that no inorganic iron remains in its raw salt form, WBCIL eliminates the primary cause of intestinal irritation. This is vital because it is the free reactive iron ions that trigger the nausea, constipation, and stomach pain often reported with lower-quality products. WBCIL utilizes FT-IR spectroscopy to provide physical proof of this high-purity state, using the molecular fingerprint of the chelate to confirm two key indicators: a total disappearance or significant shift of peaks linked to free glycine, particularly the NH_3^+ (Amine) and a distinct symmetric COO^- shift to identify the change from a simple ionic interaction to a stable, bidentate chelate defined by coordinate covalent bonding.

RESULTS AND DISCUSSION

Table 5: Key FT-IR spectral shifts observed in glycine and our Ferrous Bisglycinate (FBG).

Glycine		FBG	
Wavenumber	Significance	Wavenumber	Significance
~2600-3000	NH_3^+ broad bands	2800-3500	Broad band for NH_2 stretching indicating amine bond between Iron and Glycine
3112	NH_3^+ stretching	1574.8	Evidence of ring formation
1124	NH_3^+ rocking	1340	Symmetric COO^- shift indicating bonding to carboxyl group
635	COO^- bending		
~606	COO^- wagging		
504	COO^- rocking		

The provided IR spectroscopy data offers definitive proof of the successful chelation of iron with glycine to form a fully reacted Ferrous Bisglycinate. By comparing the wavenumbers of pure glycine with those of the resulting complex, we can identify specific shifts that confirm the transition from a physical mixture to a stable coordinate covalent compound.

Confirmation of Amine Bonding and Ring Formation

The most critical change occurs in the nitrogen-containing groups. In pure glycine, the broad bands at $\sim 2600-3000 \text{ cm}^{-1}$ and the specific stretching at 3112 cm^{-1} represent the protonated

amine group (NH_3^+) (Figure 2). In the Ferrous Bisglycinate complex, these shift to a broad band between 2800–3500 cm^{-1} , signalling the presence of NH_2 stretching. This shift confirms that the nitrogen atom from the glycine molecule has formed a direct amine bond with the iron center. Furthermore, the appearance of a peak at 1574.8 cm^{-1} provides molecular fingerprint evidence of the actual glycine-iron ring formation, proving the mineral is sequestered within the amino acid structure.

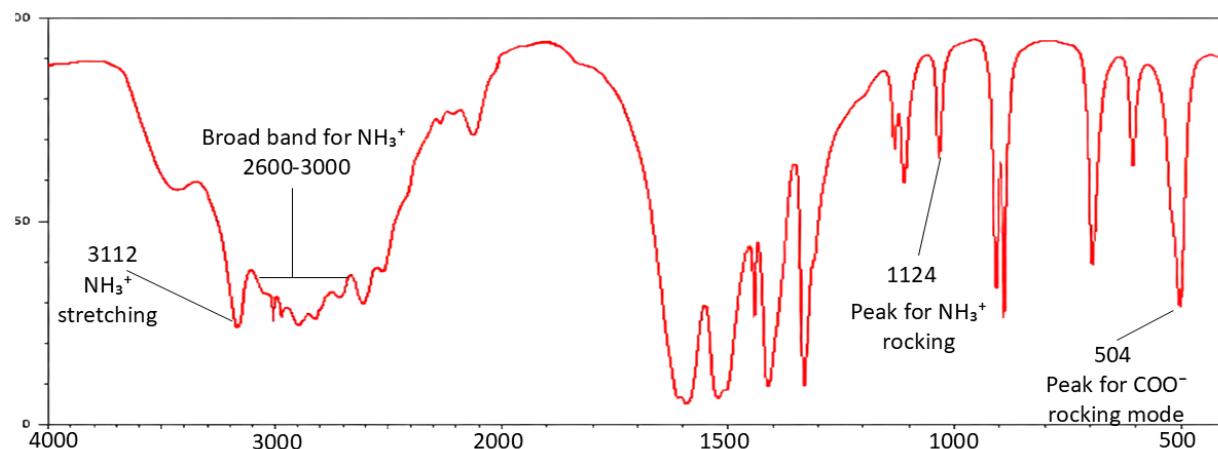


Figure 2: FT-IR spectra of Glycine.

Evidence of Carboxyl Group Coordination

The infrared results also track the behavior of the carboxyl group (COO^-). While pure glycine exhibits various bending, wagging, and rocking motions (at 635, 606, and 504 cm^{-1}), the Ferrous Bisglycinate complex shows a distinct symmetric COO^- shift at 1340 cm^{-1} (Figure 3). This shift is significant as it indicates that the oxygen atom of the carboxyl group has bonded to the iron atom. This dual bonding—through both the nitrogen (amine) and oxygen (carboxyl) sites—is what defines a true chelate ring, ensuring the iron remains chemically neutral and protected throughout the digestive process.

These FTIR results are essential for quality control to distinguish a true chelate from a simple physical blend of ferrous sulfate and glycine. Without these specific shifts in absorption bands, the supplement would dissociate prematurely in the stomach, leading to the same gastrointestinal side effects and low bioavailability seen in traditional iron salts. By confirming a fully reacted state through IR spectroscopy, manufacturers ensure the product will utilize the dipeptide absorption pathway, maximizing efficacy and tolerance.

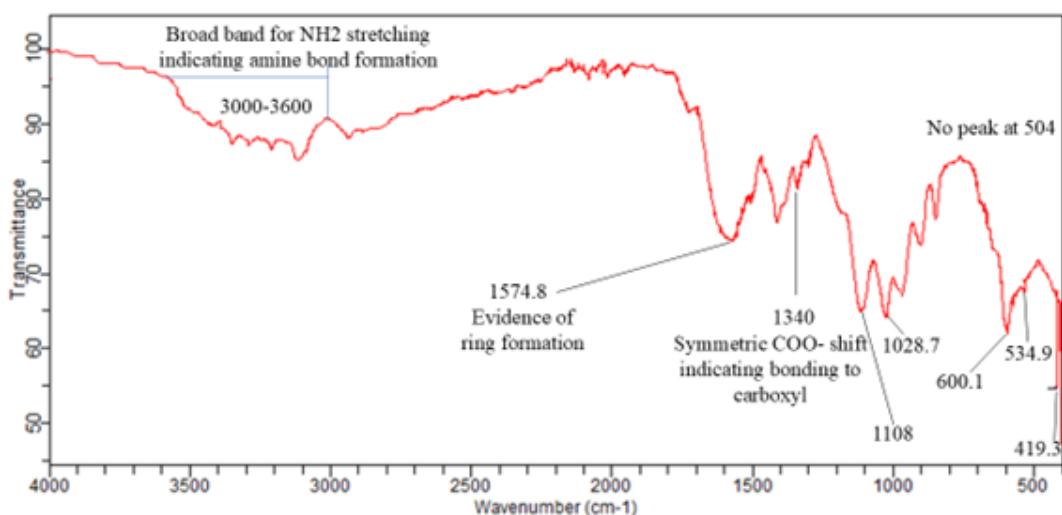


Fig. 3: FT-IR spectra for Ferrous Bisglycinate (FBG).

Thus, the overall results of FT-IR analysis of Ferrous Bisglycinate chelate confirm successful chelation through distinct shifts in the absorption bands of the glycine ligand. The most characteristic evidence is the disappearance of the vibration peak at 2125 cm^{-1} , which represents the torsional vibration of the NH_3^+ group in free glycine zwitterions, indicating that the amine group has coordinated with the ferrous ion. Additionally, the FTIR spectra typically show a shift in the carboxylate (COO^-) stretching vibrations: the asymmetric stretching band (around 1576 cm^{-1}) and the symmetric stretching band (around 1411 cm^{-1}) move toward different wavenumbers, signifying the formation of a stable five-membered heterocyclic ring between the iron and the glycine molecules. These results demonstrate that the iron is chemically shielded within the glycine rings, which accounts for the compound's high stability and its ability to remain intact through the acidic environment of the stomach.

CONCLUSION AND FUTURE ASPECTS

Ferrous Bisglycinate chelate manufactured by WBCIL represents a superior alternative to traditional iron salts due to its unique chemical structure and absorption mechanism. By sequestering iron within two glycine rings, this fully reacted chelate prevents the release of reactive free ions in the stomach, thereby eliminating common gastrointestinal side effects and ensuring high compliance. The use of dual absorption pathways—utilizing both DMT1 and the high-capacity PepT1 peptide channel—allows for 2 to 4 times higher bioavailability compared to ferrous sulfate, even in the presence of dietary inhibitors. Through the rigorous use of analytical validation like FT-IR, WBCIL guarantees a high-purity, bidentate structure that maximizes both efficacy and tolerance in sensitive populations.

Future applications are likely to grow within prenatal and pediatric care, where the low-dose, high-impact profile is essential for safety and long-term iron restoration. Emerging evidence suggests that high-efficiency oral chelates could serve as a viable alternative to IV iron for persons with non-dialysis-dependent chronic kidney disease, potentially reducing healthcare costs and invasive procedures.

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