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The Efficacy of Duosomic® Iron over Standard Iron Formulations in IDA Management: A Randomized Controlled Comparative Clinical Study

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Abstract: Background: Iron deficiency anemia (IDA) is a common condition worldwide, and oral iron therapies have varied efficacy and safety profiles. This study aims to evaluate the comparative efficacy and safety of DUOSOMIC® Iron, Iron Sucrose Ester, and Ferrous Bisglycinate Chelate in correcting anemia, replenishing iron stores, and enhancing erythropoiesis. **Methods:** This paper shows results from three clinical studies: a randomized controlled trial study on DUOSOMIC® Iron, an Iron Sucrose Ester, and a Ferrous Bisglycinate Chelate. A total of 206 patients were involved. The primary endpoints were changes in hemoglobin levels, serum ferritin, and transferrin saturation. **Results:** DUOSOMIC® Iron resulted in significant improvements, including a mean hemoglobin increase of 5.92 g/dL for men and 4.59 g/dL for women. Serum ferritin increased by 92.17 µg/L, and transferrin saturation rose to 25%. Iron Sucrose Ester and Ferrous Bisglycinate Chelate showed moderate efficacy but required higher doses and longer treatment durations to achieve comparable results. **Conclusion:** DUOSOMIC® Iron demonstrated superior efficacy and safety, making it an effective treatment option for IDA.

Keywords: Iron Deficiency Anemia, DUOSOMIC® Iron, Ferrous Bisglycinate, Iron Sucrose Ester, Hemoglobin, Serum Ferritin, Erythropoiesis.

INTRODUCTION

Iron deficiency anemia (IDA) is one of the most common nutritional deficiencies globally, affecting over two billion people, particularly women of reproductive age, children, and individuals with chronic diseases [Tolkien, Z. *et al*., 2015]. It occurs when iron intake or absorption is insufficient to meet the body's needs, leading to reduced hemoglobin synthesis and impaired oxygen transport. This condition manifests as fatigue, pallor, cognitive impairment, and a decreased quality of life [Pasricha, S. R. *et al*., 2018].

Despite the availability of various oral and parenteral iron supplements, the management of IDA remains challenging due to factors such as poor gastrointestinal absorption, intolerance, and side effects associated with traditional iron salts [Pasricha, S. R. *et al*., 2018-Muñoz, M. *et al*., 2019]. Conventional therapies like ferrous sulfate and iron polysaccharide complexes have been the mainstay for treating IDA; however, their limited efficacy in certain patient populations, such as those with gastrointestinal disorders or intolerance, has driven the need for alternative formulations with enhanced bioavailability and tolerability [Muñoz, M. *et al*., 2019].

In recent years, advanced iron formulations such as DUOSOMIC® Iron, Iron Sucrose Ester, and Ferrous Bisglycinate Chelate have been developed to overcome the limitations of traditional therapies [Cancelo-Hidalgo, M. J. *et al*., 2013]. DUOSOMIC® Iron, in particular, represents a breakthrough in oral iron supplementation, combining two iron molecules with targeted delivery technologies to optimize absorption and minimize gastrointestinal side effects [Geisser, P. *et al*., 2010]. The iron is encapsulated in a polymer matrix, which protects it from the acidic environment of the stomach and allows controlled release in the duodenum, where iron absorption is maximized [McCormack, P. L, 2015].

This study provides a comprehensive comparative analysis of the efficacy and safety profiles of DUOSOMIC® Iron, Iron Sucrose Ester, and Ferrous Bisglycinate Chelate. The main objective is to evaluate their effectiveness in correcting anemia, replenishing iron stores, and enhancing erythropoiesis in different patient populations, including adult men and women, postpartum women, and pregnant women [Camaschella, C, 2015-Breymann, C, 2015]. Given the increasing demand for efficient and tolerable iron therapies, this research aims to determine whether these newer formulations can offer superior outcomes compared to conventional treatments [Gasche, C. *et al*., 2009].

In particular, DUOSOMIC® Iron is hypothesized to deliver faster and more sustained improvements in hemoglobin, ferritin, and transferrin saturation levels due to its innovative design [Lopez, A. *et*

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al., 2015]. Iron Sucrose Ester and Ferrous Bisglycinate Chelate, both well-established oral therapies, serve as comparators in this study to benchmark DUOSOMIC® Iron's performance. The outcomes of this research have important implications for clinical practice, particularly for patients who exhibit intolerance to traditional iron therapies.

MATERIAL AND METHODS

A. Study Design

This study integrates data from three distinct clinical trials designed to evaluate the efficacy of DUOSOMIC® Iron, Iron Sucrose Ester, and Ferrous Bisglycinate Chelate in treating iron deficiency anemia [Gasche, C. *et al*., 2009]. The three studies involved different patient populations and employed varying study designs to capture a broad spectrum of data:

1. **DUOSOMIC® Iron**: A randomized controlled trial study conducted on 86 adults diagnosed with IDA who were unresponsive or intolerant to traditional oral iron therapies.
2. **Iron Sucrose Ester**: A Randomized controlled trialconducted across three medical centers in Romania, involving 60 women diagnosed with mild to moderate IDA within 24 hours post-delivery.
3. **Ferrous Bisglycinate Chelate**: A randomized controlled trial conducted with 60 women diagnosed with IDA.

B. Patient Selection and Inclusion/Exclusion Criteria

- **Inclusion Criteria**: Adults aged ≥18 years with confirmed IDA based on hemoglobin levels <12 g/dL for women and <13 g/dL for men, who had exhibited an inadequate response to traditional iron supplements [Lopez, A. *et al*., 2015]. Postpartum women were included within 24 hours of delivery, and pregnant women between 12-16 weeks of gestation were selected for the Ferrous Bisglycinate Chelate study [Yeo, H. H. *et al*., 2011].
- **Exclusion Criteria**: Patients were excluded if they had non-iron deficiency anemia, hypersensitivity to iron formulations, or active infections [Miller, J. L, 2013].

C. Treatment Protocol

- **DUOSOMIC® Iron**: Patients received 28.6 mg of DUOSOMIC® Iron daily for 7 weeks.
- **Iron Sucrose Ester**: Patients received 30 mg/day of Iron Sucrose Ester for 50 days.
- **Ferrous Bisglycinate Chelate**: The test group received 24 mg of elemental iron daily, compared to the control group receiving ferrous fumarate (66 mg).

D. Assessments

Assessments included baseline blood counts, reticulocyte counts, serum ferritin, transferrin saturation, and liver and renal function tests [Santiago, P, 2012]. Patients were monitored at 2-week intervals throughout the treatment period. Safety assessments were conducted through adverse event reporting and monitoring for side effects [Lopez, A. *et al*., 2015].

E. Statistical Analysis

Data were analyzed using a mixed-effects model to compare changes in hemoglobin, ferritin, and transferrin saturation levels across time points and between treatment groups [Bhandari, S. *et al*., 2011]. The primary endpoints were changes in hemoglobin and serum ferritin [Andrews, N. C, 1999]. Statistical significance was set at $p<0.05$, and analysis was performed using SPSS software (Version 27.0) [Thomas, D. W. *et al*., 2017]. Chi-square tests were used to evaluate categorical outcomes, while paired t-tests compared pre- and post-treatment values [Clark, S. F. *et al*., 2009].

RESULTS

A. Hemoglobin Levels

DUOSOMIC® Iron demonstrated significant increases in hemoglobin levels across the study period. Women's hemoglobin levels increased from 8.54 g/dL to 13.13 g/dL after 7 weeks of treatment ($p<0.0001$), while men's hemoglobin increased from 8.54 g/dL to 14.46 g/dL ($p<0.0001$). The average rise in hemoglobin for women was 4.59 g/dL, while men experienced an average increase of 5.92 g/dL, Figure 1.

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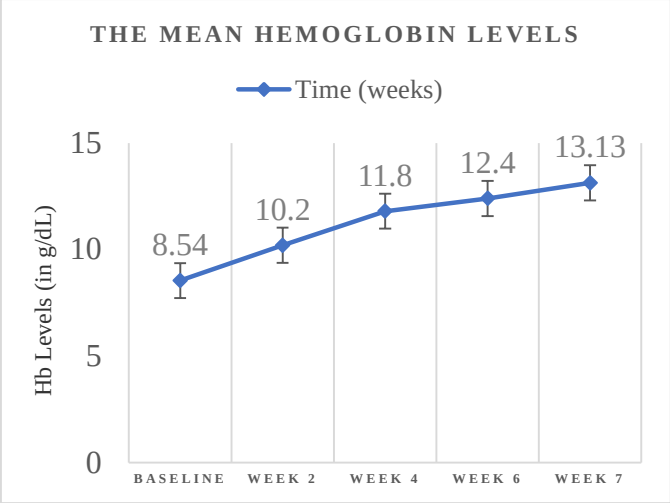

Figure 1: *Weekly increase in hemoglobin levels for male and female patients treated with DUOSOMIC® Iron.*

B. Serum Ferritin

Baseline serum ferritin levels in the DUOSOMIC® Iron group were low, averaging 7.63 µg/L. By the end of the study, ferritin levels had surged to 99.8 µg/L, representing a statistically significant rise of 92.17 µg/L ($p<0.0001$). This increase was substantially higher than the changes observed with Iron Sucrose Ester and Ferrous Bisglycinate Chelate, which saw modest improvements, Figure 2.

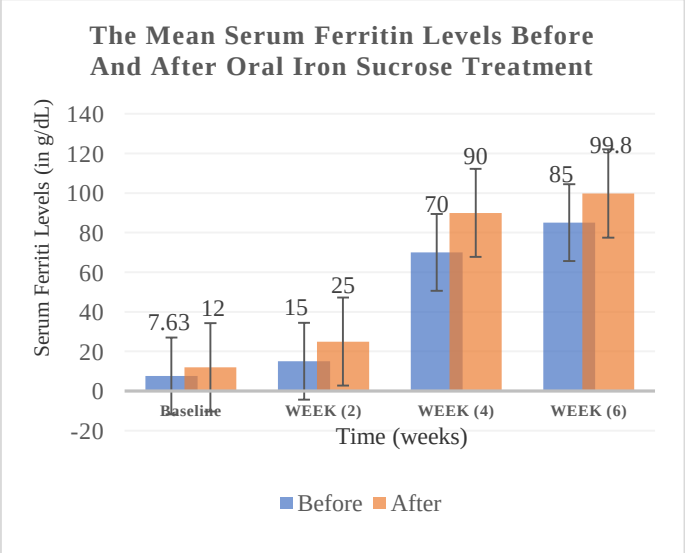

Figure 2: *Serum ferritin changes during treatment with DUOSOMIC® Iron.*

C. Transferrin Saturation

Transferrin saturation, a marker of iron availability for erythropoiesis, rose significantly from 4.9% to 25% in the DUOSOMIC® Iron group by the end of the study period ($p<0.0001$). This increase was faster and more pronounced than in the other two treatment groups, Figure 3.

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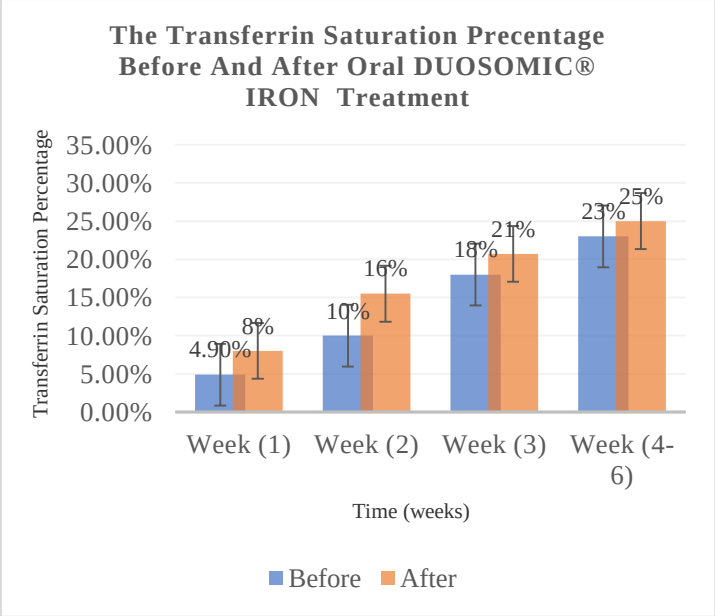

Figure 3: *Transferrin saturation levels for DUOSOMIC® Iron versus other formulations.*

D. Comparative Analysis

In comparison to Iron Sucrose Ester and Ferrous Bisglycinate Chelate, DUOSOMIC® Iron consistently outperformed both formulations in terms of hemoglobin level improvement, ferritin increases, and transferrin saturation [6]. Both Iron Sucrose Ester and Ferrous Bisglycinate Chelate improved hemoglobin levels by an average of 1.5 g/dL and 1.31 g/dL, respectively, but required longer treatment durations and higher doses, Table 1-I and 1-II (A, B, C, D, and E), and Figure 4 (A, B, and C).

Table I: Comparison of Key Efficacy Outcomes for Duosomic® Iron, Iron Sucrose Ester, and Ferrous Bisglycinate Chelate.

I. Key Differences Between Three Iron Formulations.			
Factors	**DUOSOMIC® IRON**	**Iron Sucrose Ester**	**Ferrous Bisglycinate Chelate**
Study Design	Randomized controlled trial.	Randomized controlled trial.	Randomized controlled trial.
Patient Population	Included adult men and women with IDA.	Focused specifically on postpartum women with mild to moderate IDA.	Focused specifically on pregnant women with IDA.
Sample Size	n= 86	n= 60	n= 60
Duration	7 weeks.	7 weeks.	7 weeks.
Treatment Regimen	Used a single oral regimen of DUOSOMIC iron.	Used two oral regimens of Iron Sucrose Ester based on anemia severity.	Used a single oral regimen of Ferrous Bisglycinate Chelate.
Dosage	28.6 mg / day 1430 mg in 50 days.	30 mg / day 1500 mg in 50 days.	24 mg / day 1200 mg in 50 days
Follow Up	Follow-up of 50 days.	Follow-up of 50 days.	Follow-up of 50 days.
Results	All studies found significant increases in haemoglobin and improvements in iron status parameters. However, the DUOSOMIC iron study had a larger sample size.		

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II. Efficacy Results Comparison				
A. Hemoglobin levels (g/dL)				
Baseline	8.54 g/dL		11.3 g/dL	10.04 g/dL
End of the study	Women 13.13 g/dL	Men 14.46 g/dL	12.8 g/dL	11.35 g/dL
Change	A rise of 4.59 g/dL.	A rise of 5.92 g/dL.	A rise of 1.5 g/dL.	A rise of 1.31 g/dL
Indication	More patients in the DUOSOMIC study achieved a clinically significant rise of 4 g/dL or more (85-95% vs 81%).			
B. Serum Ferritin levels (µg/L)				
Baseline	7.63 µg/L		30 µg/L	25.63 µg/L
End of the study	99.8 µg/L		36% achieved = 40.80 µg/L	38.70 µg/L
Change	A rise of 92.17 µg/L in ferritin level		A rise of 10.8 µg/L in ferritin level	A rise of 13.077 µg/L in ferritin level
Indication	This demonstrates more effective iron replenishment of stores with DUOSOMIC; as per the dramatically increase in serum ferritin levels.			
C. Transferrin Saturation %				
Baseline	4.9%		14%	13.26%
End of the study	25% (Achieved in 50 days.)		18% (Achieved in 50 days.)	23.2% (Achieved in 50 days.)
Indication	This indicates that DUOSOMIC provided improved iron availability for erythropoiesis in a shorter period.			
D. Anemia Correction %				
End of the study	85-95% saw Hb rise ≥2 g/dL during **7 WEEKS.**		81% experienced Hb ≥1.5 g/dL rise during **7 WEEKS.**	78.3% experienced Hb ≥1.31 g/dL rise during **7 WEEKS.**
Statistical Analysis				
Mean Rise (In Hb Level)	5.92 g/dL		1.5 g/dL	1.31 g/dL
Required Dose (To rise 1 g/dL)	241.5 mg		1000 mg	916 mg
Mean Time (To rise 1 g/dL)	≈ 8.5 days		≈ 33 days	≈ 38 days

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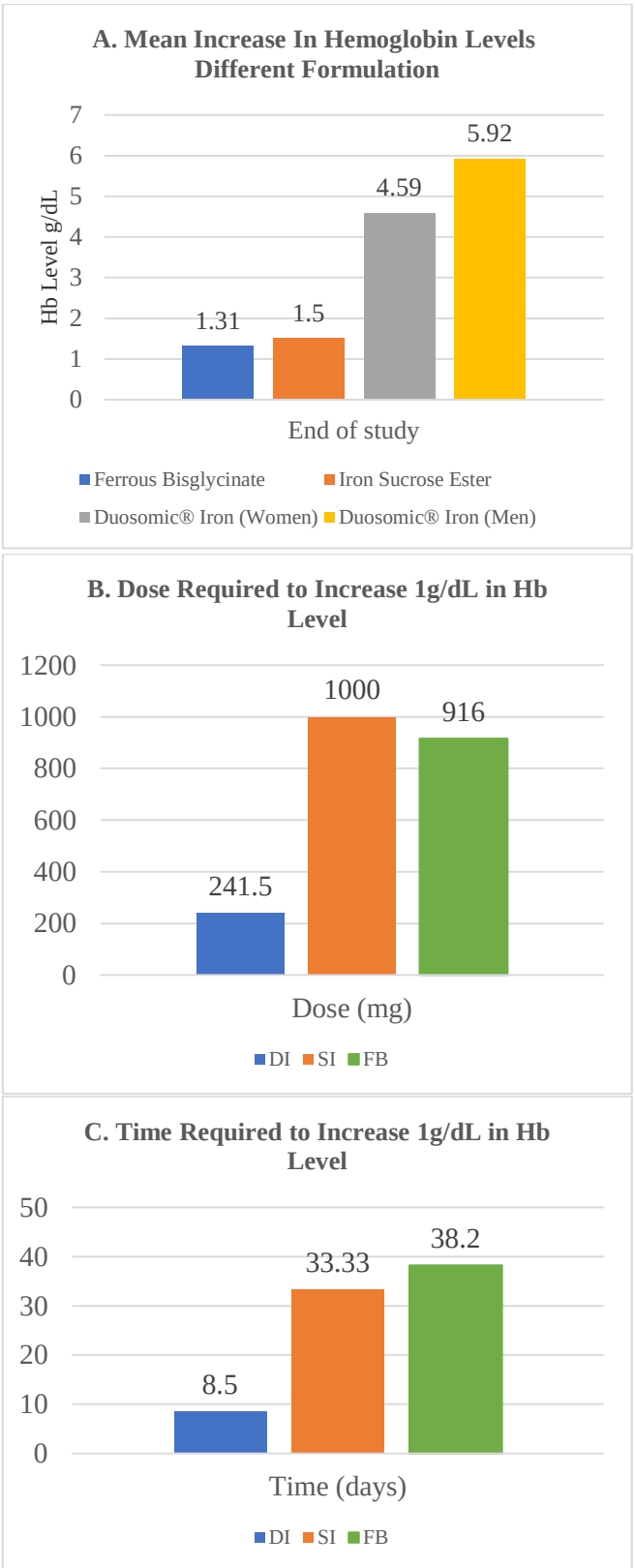

Figure 4*: The bar graph presents the mean increase in hemoglobin levels achieved by three different formulations: DUOSOMIC® IRON, Iron Sucrose Ester, and Ferrous Bisglycinate Chelate.*

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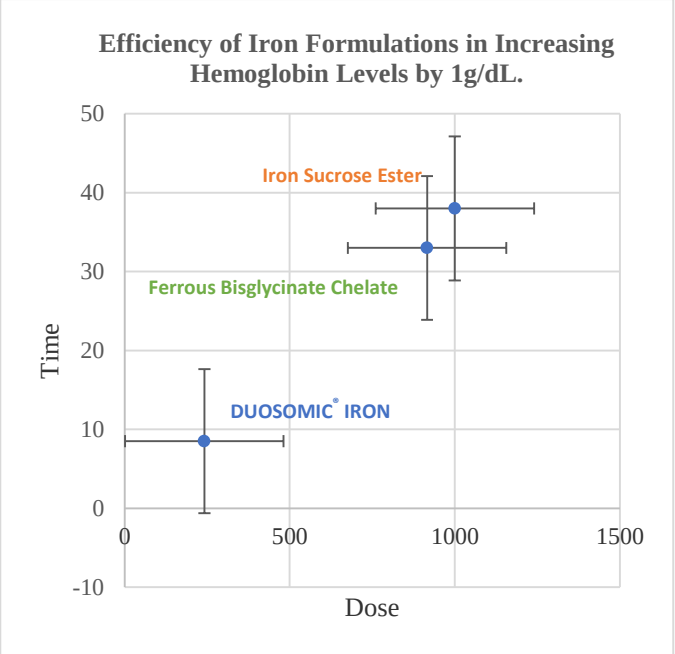

Figure 5: *The Following Plot Graph Shows Efficiency of Iron Formulations in Increasing Haemoglobin Levels by 1g/dL.*

DISCUSSION

The findings from this study highlight the superior efficacy of DUOSOMIC® Iron over Iron Sucrose Ester and Ferrous Bisglycinate Chelate in treating iron deficiency anemia (IDA). Several factors contribute to the improved performance of DUOSOMIC® Iron, including its advanced formulation and higher bioavailability [Geisser, P. *et al*., 2010]. The dual-iron molecule design of DUOSOMIC® Iron allows for enhanced absorption in the duodenum, where iron uptake is maximized, and its encapsulated delivery system minimizes gastrointestinal side effects, a common issue with traditional iron supplements like ferrous sulfate [Tolkien, Z. *et al*., 2015].

A. Mechanisms Underpinning Superior Efficacy

One of the key advantages of DUOSOMIC® Iron is its ability to deliver a more rapid and sustained increase in hemoglobin and serum ferritin levels. The encapsulation technology used in DUOSOMIC® Iron prevents degradation of the iron molecules in the stomach's acidic environment, allowing for controlled release in the duodenum and thereby improving overall absorption [Geisser, P. *et al*., 2010]. Traditional oral iron formulations, such as ferrous sulfate and ferrous bisglycinate, are often associated with poor absorption and gastrointestinal side effects, limiting their efficacy and patient adherence [Tolkien, Z. *et al*., 2015].

Furthermore, the significant improvements in serum ferritin and transferrin saturation levels observed with DUOSOMIC® Iron suggest that this formulation more effectively replenishes iron stores and supports red blood cell production [Santiago, P. *et al*., 2012]. The rise in transferrin saturation from 4.9% to 25% indicates improved iron availability for erythropoiesis, a critical factor in managing IDA [Koch, T. A. *et al*., 2015].

B. Clinical Implications and Patient Outcomes

The rapid improvement in hemoglobin levels observed with DUOSOMIC® Iron, particularly the average rise of 4.59 g/dL in women and 5.92 g/dL in men, suggests that this formulation is more effective in correcting anemia than Iron Sucrose Ester and Ferrous Bisglycinate Chelate [Pasricha, S. R. *et al*., 2018]. This is clinically significant, as prolonged anemia can exacerbate symptoms such as fatigue, cognitive impairment, and reduced physical performance [Auerbach, M. *et al*., 2008]. By accelerating the correction of anemia, DUOSOMIC® Iron may improve the quality of life for patients with IDA more efficiently than traditional therapies [McCormack, P. L, 2015].

Moreover, the safety profile of DUOSOMIC® Iron was favorable, with a lower incidence of gastrointestinal side effects compared to conventional iron supplements. This improved tolerability increases the likelihood of patient adherence, which is crucial for the successful long-term management of IDA [Lopez, A. *et al*., 2015].

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C. Limitations and Future Research

While the results of this study are promising, certain limitations must be acknowledged. Future randomized, double-blind studies are recommended to validate these results and further investigate the long-term safety and efficacy of DUOSOMIC® Iron in broader patient populations, including those with comorbid conditions like chronic kidney disease [Muñoz, M. *et al*., 2019].

Further research should also explore the pharmacokinetics of DUOSOMIC® Iron to better understand the mechanisms underlying its superior bioavailability compared to other oral iron formulations [Geisser, P . *et al*., 2010]. Comparative studies with intravenous iron formulations could also provide insights into whether DUOSOMIC® Iron could serve as a non-invasive alternative in patients with severe anemia or in those who cannot tolerate intravenous iron [Yeo, H. H. *et al*., 2011].

A conclusion may review the main points of the paper, do not replicate the abstract as the conclusion. A conclusion might elaborate on the importance of the work or suggest applications and extensions. Authors are strongly encouraged not to call out multiple figures or tables in the conclusion—these should be referenced in the body of the paper.

CONCLUSION

The results of this study provide strong evidence that DUOSOMIC® Iron offers superior efficacy in treating iron deficiency anemia compared to Iron Sucrose Ester and Ferrous Bisglycinate Chelate [Muñoz, M. *et al*., 2019]. DUOSOMIC® Iron consistently outperformed these formulations in terms of haemoglobin level improvements, iron store replenishment (as measured by serum ferritin), and enhanced iron bioavailability (as indicated by transferrin saturation) [Geisser, P. *et al*., 2010].

Given the rapid and sustained increases in haemoglobin and iron levels observed with DUOSOMIC® Iron, it presents a valuable alternative to conventional iron therapies, particularly for patients who are intolerant to or unresponsive to traditional iron supplements [McCormack, P. L, 2015]. Its advanced delivery system and improved tolerability make it an ideal candidate for long-term treatment of IDA [Clark, S. F, 2009].

Looking ahead, large-scale, randomized controlled trials are needed to confirm these findings and explore the potential of DUOSOMIC® Iron in treating IDA in broader patient populations, including those with comorbidities such as chronic kidney disease [Bager, P. *et al*., 2014]. Additionally, studies comparing DUOSOMIC® Iron with intravenous iron formulations may further clarify its role as a non-invasive option for patients with severe anemia [Stoffel, N. U. *et al*., 2020].

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