Ginger and Iron Deficiency Anaemia

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Ginger (*Zingiber officinale*) is rich in natural polyphenols and may potentially complement oral iron therapy in treating and preventing iron deficiency anaemia (IDA). Ginger possesses several health-promoting properties and has been traditionally used in East Asia to ease fatigue and weaknesses. Contemporarily, ginger is considered a functional food that can confer health benefits beyond its nutritional values for preventing, managing, or treating disease. As a rich source of natural polyphenols, ginger may potentially complement oral iron therapy in treating IDA and be a supportive dietary strategy for preventing IDA.

ginger iron deficiency anaemia iron

1. Nutritional Composition and Traditional Use of Ginger

Nutritional analysis has shown that ginger consists mainly of moisture, carbohydrate, protein, fibre, fat, and ash. It is rich in polyphenols and contains micronutrients including ascorbic acid, β-carotene, calcium, iron, and copper. However, it is worth noting that the nutritional composition of ginger can vary greatly depending on the varieties, origin, time of harvest, drying method, and storage condition. **Table 1** shows the approximate nutritional composition of dried ginger powder reported in the literature [1][2]. Ginger is, however, valued beyond its nutritional benefits. It is believed that the Indian and Chinese populations have used ginger as a tonic for over 5000 years [3]. In Shen Nong Ben Cao Jing, the oldest surviving Chinese materia medica circa 100BC, ginger was classified as a middle category of herb with little or no toxicity and was mainly used in combination prescription to treat deficiency to prevent illness or resist worsening disease [4]. Incidentally, ginger is also used in traditional Ayurvedic medicine to treat many diseases such as diabetes, flatulence, intestinal colic, indigestion, infertility, inflammation, insomnia, nausea, rheumatism, stomach ache, and urinary tract infections [5].

Table 1. Nutritional composition of dried ginger powder as reported by Ajayi et al. [1] and Sangwan et al. [2].

Nutrient	Amount	Unit
Carbohydrate	39.70–58.21	%
Protein	11.65–12.05	%
Crude fibre	8.30–21.90	%
Fat	9.89–17.11	%
Moisture	3.95–4.63	%

Nutrient	Amount	Unit
Ash	4.95–7.45	%
β-carotene	0.68–0.81	mg/100 g
Ascorbic acid	2.2–3.8	mg/100 g
Polyphenols	11.8–12.5	mg/100 g
Calcium	64.4–69.2	mg/100 g
Iron	1.5–1.8	mg/100 g
Copper	0.46–0.75	mg/100 g

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The following sections will explore available evidence from in vivo, ex vivo, in vitro, and human clinical studies to elucidate the potential benefits of ginger for IDA and its associated clinical manifestations of altered iron metabolism. A summary of the research findings is presented in **Table 2**.

Table 2. A summary of the research findings on ginger's beneficial properties in its applications for iron deficiency anaemia and associated clinical manifestations of altered iron metabolism.

Beneficial Property	Study Type	Research Findings	Reference
Iron absorption enhancement	Ex vivo	Ginger was the most potent spice for enhancing iron absorption by increasing uptake by 28.5 ± 2.09% in the jejunum of rats compared to control.	[6]
	In vitro	Adding ginger to food enhanced the bioaccessibility of dietary iron by 2- to 3-fold depending on the formulations.	[7]
	Human study	Ginger plus oral iron therapy improved haematological and iron parameters of anaemic patients better than oral iron therapy alone.	[8][9]
Antioxidant activity	In vivo	Adding ginger to the diet significantly increased the activities of antioxidant enzymes ($p<0.05$) at the intestinal and gastric mucosa of rats, demonstrating enhanced protective effects against oxidative stress.	[10]
	In vitro	The polyphenols and diarylheptanoid derivatives of ginger contributed to both radical scavenging and inhibitory effects of autoxidation.	[11]
	In vitro	Both red and white ginger variants possessed antioxidant capacities against free iron radicals in rat brains, but red ginger was superior at inhibiting Fe^{2}-induced lipid peroxidation and chelating Fe^{2}.	[12]
	In vitro	Water-based extract of ginger showed relatively low antioxidant activities compared to other spices due to reduced phenolic	[13]

Beneficial Property	Study Type	Research Findings	Reference
		contents produced from hydro-distillation extraction.	
Anti-inflammatory action	Review	The bioactive compounds in ginger possessed broad anti-inflammatory properties that can block the activation of NF-κβ by suppressing pro-inflammatory cytokines of IL-1, TNF-α and IL-6, thus preventing hepcidin production.	[14]
	Human study	Ginger plus oral iron therapy significantly reduced the inflammatory marker TNF-α ($p<0.05$) in anaemic patients better than oral iron therapy alone.	[8][9]
Gut microbiota modulation	In vitro	Undigested ginger polyphenols significantly increased the abundances of *Bifidobacterium* ($p<0.05$) and *Enterococcus* ($p<0.01$) after faecal inoculated fermentation, accompanied by elevated levels of SCFA and decreased pH value.	[15]
	In vivo	Ginger supplementation could mitigate the detrimental impact of a high-fat diet in mice by promoting the abundance of *Bifidobacterium* genus and SCFA-producing bacteria (*Alloprevotella* and *Allobaculum*).	[16]
	In vivo	Ginger treatment significantly reduced antibiotic-associated diarrhoea symptoms ($p<0.05$) in rats with an associated increase in microbiota diversity and improved intestinal barrier integrity.	[17]
	Human study	Ginger juice consumption in healthy adults decreased the Prevotella-to-Bacteroides ratio and pro-inflammatory *Ruminococcus_1 and Ruminococcus_2* genus while increasing the Firmicutes-to-Bacteroidetes ratio, Proteobacteria and anti-inflammatory *Faecalibacterium*.	[18]
Erythropoiesis stimulation	In vivo	Ginger, with its bioactive compounds of 8-gingerol, 10-gingerol, 8-shogaol, and 10-shogaol, promoted the expression of Gata1 in erythroid cells of zebrafish embryos through the Bmp signalling pathway.	[19]
	In vivo	Ginger induced scl/runx1 expression through Bmp and Notch signalling pathways which up-regulated nitric oxide production for regeneration of haematopoietic stem/progenitor cells.	[20]
Iron overload prevention	In vivo	The bioactive lipids in ginger repressed some iron-related parameters, including reductions in 20% of ^{59}Fe absorption, 65% of pancreatic non-haem iron, and 40% to 50% of serum ferritin levels, compared to controls.	[21]
	In vivo	Ginger extract demonstrated strong protective effects against iron toxicity through its free radical scavenging activities in iron-overloaded rats.	[22]

Beneficial Property	Study Type	Research Findings	Reference
	Case series [6]	Ginger extract rich in 6-shogaol prevented iron overload in three patients with myelodysplastic syndrome. These patients had elevated serum ferritin (>300 g/µL) at baseline but achieved >40% reductions after three months through upregulation of hepcidin.	[23]
Ginger-synthesised iron nanoparticles	In vitro	Ginger was used to bio-reduce the metallic ions to nanoparticles (Fe^{3+} ions to FeNPs). Transmission electron microscopy showed that the FeNPs in ginger were in the range of 14.08–21.57 nm with almost spherical forms and demonstrated considerable radical scavenging properties and antimicrobial activities against Gram-positive and Gram-negative bacteria and fungi.	[24]
	In vitro	Ginger can be a suitable green material for synthesising iron nanoparticles with high antioxidant and antibacterial properties.	[25][26]

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Abbreviations: bone morphogenetic protein (Bmp); GATA-binding factor 1 (Gata1); interleukin (IL); short-chain fatty acids (SCFA); tumour necrosis factor alpha (TNF-α).

Ginger can also be used as a food additive to enhance the bioavailability of non-haem iron. A study by Jaiswal et al. [7] compared the effects of iron bioaccessibility by adding various spices (ajwain, cumin, cinnamon, fennel, black pepper, and ginger) at 1 or 2% weight to wheat flour and different Indian bread formulations. The bioaccessibility of iron was measured through an in vitro dialysis method. Adding spices at 2% significantly enhanced iron bioaccessibility ($p < 0.0001$). Ginger, in particular, was shown to increase iron bioaccessibility in all food formulations by 2- to 3-folds. The authors attributed effects to the ascorbic acid and amino acids within ginger that favour iron absorption [7]. However, with its low vitamin C content (**Table 1**), iron bioaccessibility is likely to be assisted by other bioactive compounds in ginger.

The effects of ginger in enhancing iron availability have been confirmed in a human intervention study. Kulkarni et al. [8][9] conducted a human clinical study to demonstrate the potential use of ginger supplements in the treatment of IDA along with oral iron therapy. The study recruited 62 patients with anaemia following the WHO Hb cut-off levels, consisting of 12 males and 50 females, from a hospital in India. Their conditions were likely due to nutritional deficiency since those with chronic conditions, pregnancy, and blood donors were excluded. Participants were divided into two groups. The intervention group (n = 30) took 1.5 g of ginger powder with oral iron therapy, whereas the control group (n = 32) received only oral iron therapy as routine care. Fasting blood samples were collected at baseline and after 30 days. Pre- and post-treatment comparisons of haematological and iron parameters found significant increases ($p<0.05$) in all parameters in both groups. However, the intervention group achieved a more remarkable improvement in percentage difference than the control group in Hb (+8.23% vs. +2.3%), iron status (+19.63% vs. +5.54%), total iron-binding capacity (−7.23% vs. −4.47%), and SF (+45.11% vs. +34.11%). However, the authors did not report whether there were significant differences in the mean differences between groups. Notwithstanding, based on the published sample size, means, and standard deviations, the p-values could be easily estimated. The mean difference between groups for serum iron levels was significantly different post-treatment ($p<0.007$). Hence, the study demonstrated that ginger could assist in iron absorption and improve the efficacy of oral iron therapy for IDA.

The study by Kulkarni et al. [8][9] had several drawbacks. The first is its short duration of trial with only 30 days. Although patients with uncomplicated anaemia are expected to show improvement after 4 weeks of oral iron treatment, replenishment of iron store will take longer to achieve [27][28]. Secondly, the study did not track the adverse events experienced by the participants. Thus, there was no data on ginger's effects on any side effects of oral iron therapy. Thirdly, there could be selection bias in the study design as it is unclear how the group assignment was carried out. Hence, the results from this research need further validation with more well-designed clinical trials.

2.2. Antioxidant Activity

Another study by Prakash and Srinivasan [10] showed that ginger can significantly enhance the activities of antioxidant enzymes ($p<0.05$), including superoxide dismutase (SOD), catalase (CAT), glutathione reductase (GR), and glutathione-S-transferase (GST), in both gastric and intestinal mucosa in vivo. For eight weeks, eight male Wistar rats were fed ad libitum with a basal diet enriched with 0.05% ginger powder. Compared to the control group provided with the basal diet only, the ginger group showed 48%, 11%, 67%, and 50% stimulation in the activities of CAT, SOD, GST, and GR, respectively, in the intestinal mucosa. In rats subjected to ethanol-induced oxidative stress, ginger treatment demonstrated higher SOD, GST, and GR activities in the gastric mucosa by 35%, 39%, and 30%, respectively, compared to controls. Moreover, the ginger-fed group also had 56% higher mucin content of gastric mucosa than the ethanol-treated controls. In short, this research illustrated the gastrointestinal protective effects of dietary ginger against oxidative stress.

The gingerol-related polyphenols and diarylheptanoids derived from the rhizomes of ginger possess remarkable free radical scavenging activities [11]. However, the antioxidant potency may vary across ginger varieties. In an in vitro experiment, Oboh et al. [12] studied the antioxidant effects of two types of gingers (red and white) against free iron radicals in rat brains. Although both variants possessed antioxidant capacities against Fe^2, the study found red ginger (*Z. officinale* var. Rubra) superior to white ginger (*Z. officinale* Roscoe) at inhibiting Fe^2-induced lipid peroxidation and chelating Fe^2, likely due to its higher ascorbic acid, phenol, and flavonoid contents.

Hinneburg et al. [13] demonstrated in another study that the contents of total phenols in various spices had significant positive correlations with their antioxidant properties in terms of iron reduction ($r^2 = 0.8871$, $p<0.001$) and inhibition of lipid peroxidation ($r^2 = 0.7327$, $p<0.01$). Specifically, the hydro-distilled ginger extract showed relatively low Fe^3 to Fe^2 reducing activity and Fe^2 chelating capacity compared to basil, parsley, juniper, cumin, and fennel extracts. The reduced antioxidant activities were attributed to the low total phenols/extractable compounds ratio of only 7.8% for ginger versus 59.7% for basil. The water-based extraction method used in Hinneburg et al. [13] could not preserve the antioxidant activity of essential oils from ginger. Hence, the variety, extraction and processing methods can greatly affect the antioxidant properties of ginger.

2.3. Anti-Inflammatory Action

The anti-inflammatory action of ginger and its potential application in AI were aptly reviewed by Kumar et al. [14]. Inflammation stimulates hepcidin production in response to pro-inflammatory cytokines such as IL-1, tumour necrotic factor (TNF)-α and, in particular, IL-6. As an acute phase protein, hepcidin's role is to inhibit iron absorption and thus minimise the free iron supply to invading pathogens. Hence, sustained elevation of hepcidin will cause hypoferremia leading to anaemia. Additionally, an increase in IL-6 activates the nuclear factor kappa B (NF-κβ) pathway, resulting in the synthesis of CRP from the hepatocytes. The rising CRP levels indicate systemic inflammation and can blunt the erythropoiesis stimulation response in AI, especially in chronic kidney disease [14]. The bioactive compounds in ginger, such as 6-gingerol, 6-shogaol and 6-paradol, are known to possess broad anti-inflammatory properties that can block the activation of NF-κβ by suppressing pro-inflammatory cytokines [14][29].

The human intervention study on ginger and iron absorption reported by Kulkarni et al. [8][9] mentioned earlier also measured malondialdehyde (MDA) as the serum biomarker for oxidative stress and TNF-α as the inflammatory marker of the 62 participants receiving either ginger and iron treatment or oral iron therapy only. Both groups had an insignificant difference in mean MDA and TNF-α levels at baseline. After 30 days, both oxidative stress (MDA: −18.62%, $p<0.001$) and inflammatory markers (TNF-α: −20.11%, $p<0.05$) were significantly reduced in the oral iron plus ginger group. Conversely, in the control group taking only oral iron therapy, there was a significant decrease in post-trial MDA levels (−9.67%, $p<0.05$) and a non-significant increase in TNF-α (+3.86%, $p>0.05$) [9]. The estimated mean difference between groups was not significant in changes in MDA but was significant in TNF-α ($p<0.05$). It can be inferred from these results that, compared to oral iron therapy alone, combining ginger with oral iron therapy can better alleviate oxidative stress and reduce inflammation in patients with IDA while correcting their anaemic condition.

2.4. Gut Microbiota Modulation

Both iron deficiency and excess iron can lead to dysbiosis, characterised by an imbalance in the gut microbial community, and are associated with diseases [30]. Recent research has found ginger to exact prebiotic effects that improve gut microbiota composition. In a study that stimulated digestion and fermentation in vitro, 85% of the polyphenols in a dry ginger powder were still detectable in the digestive fluids after simulated digestion [15]. These polyphenol constituents include 6-, 8-, 10-gingerols and 6-shogaol. The undigested ginger extract significantly modulated faecal microbiota structure following mixed-culture fermentation with faecal inoculation compared with the control group. After 12 h of fermentation, the abundances of the beneficial bacterial groups of *Bifidobacterium* ($p<0.05$) and *Enterococcus* ($p<0.01$) were significantly higher in the ginger group than in the control group. The study also found elevated levels of short-chain fatty acids (SCFA) accompanied by decreased pH value after fermentation with ginger extract compared to control. The results demonstrated that ginger and its polyphenol compounds could improve human health through gut microbiota modulation [15].

Ginger's effects on gut microbiota modulation were also confirmed in a mice model in an in vivo study [16]. Five-week-old C57BL/6J male mice were fed a high-fat diet with or without ginger supplementation for 16 weeks. With ginger treatment, mice on a high-fat diet showed lower body weight and amelioration of liver steatosis, low-grade inflammation, and insulin resistance compared to controls. Analysis of the gut microbiome showed an increase

in *Bifidobacterium* genus and SCFA-producing bacteria (*Alloprevotella* and *Allobaculum*) and increases in faecal SCFA concentrations. As a high-fat diet promotes oxidative stress and chronic low-grade inflammation associated with metabolic dysfunction, this research demonstrated that ginger supplementation could mitigate the detrimental impact of a high-fat diet on gut microbiota composition to promote health.

Another in vivo study also found ginger to have therapeutic effects in relieving diarrhoea after antibiotic use through gut microbiota recovery [17]. The study used 5-week-old Sprague-Dawley rats treated with antibiotics by gavage for seven days before administering ginger extract for another seven days. The study found ginger treatment significantly reduced diarrhoea symptoms ($p<0.05$) compared to the control group that did not receive ginger treatment. Furthermore, the ginger treatment also considerably increased microbiota diversity in the gut, showing accelerated recovery. Specifically, the abundance of Proteobacteria phyla was increased by antibiotics treatment but restored significantly after ginger administration ($p<0.0001$). In contrast, antibiotic treatment depressed the abundance of Bacteroidetes phyla and saw significant improvement with ginger treatment ($p<0.001$). The study found *Escherichia Shigella* decreased at the genus levels, whereas Bacteroides increased the most in relative abundance. Histopathological observation of the colon also revealed evidence of intestinal barrier integrity improvement with ginger treatment associated with restoring tight junction protein Zonula occludens-1.

Changes in gut microbiota compositions in humans were also observed after consumption of ginger in a recent RCT [18]. The study recruited 138 healthy adults. All participants were advised to consume their usual diet but avoid ginger-rich products, probiotics, and prebiotics for one week before starting the study. During the intervention period, the participants were randomly assigned to take either fresh ginger juice (ginger group, n = 68) or sterile 0.9% sodium chloride (control group, n = 66) daily for seven days. Blood serum and faecal samples were collected at baseline and after seven days. A total of 4 participants in the control group and 7 in the ginger group were lost to follow-up, with only 123 participants completing the study. The study found increased counts of intestinal bacterial species when comparing the taxonomic composition between the ginger and control groups. The ginger juice intervention decreased the relative abundance of the Prevotella-to-Bacteroides ratio and the pro-inflammatory *Ruminococcus_1* and *Ruminococcus_2* genus and increased the Firmicutes-to-Bacteroidetes ratio, *Proteobacteria* and anti-inflammatory *Faecalibacterium*. Hence, the study concluded that consuming ginger juice for a short period had substantial effects on the composition and function of gut microbiota in healthy people.

There is currently no known pre-clinical and clinical study on the effect of ginger on the gut microbiota in the case of anaemia or iron deficiency. Nevertheless, prebiotics, such as inulin, are known to affect gut microbiota to improve iron absorption in IDA [31]. Thus, it is logical to assume a similar positive impact of ginger on IDA through inferences. This is an area of further research.

2.5. Erythropoiesis Stimulation

Erythropoiesis, the process of producing RBCs, is impeded in IDA due to insufficient dietary iron intake, impairment in iron absorption as affected by inflammation, or an imbalance between surging iron requirements and iron available resulting from rapid growth or heavy blood loss [32]. In fact, the use of ginger for haematopoiesis has an

ethnomedicinal origin. Dry ginger is used in traditional Chinese medicine as a warm herb to promote blood flow, remove blood stasis, and alleviate weakness and fatigue. As such, ginger is used in many blood tonic herbal formulas for treating blood circulation, anaemia, and haemorheological conditions [33][34]. Ginger is also a tonic food recommended for postpartum women during the one month confinement period immediately after delivery for recovery from blood loss. Specifically, in Southern China, traditional postpartum dietary practices include the 'ginger vinegar soup' made from sweet vinegar, ginger, egg, and pig's trotters [35]. This is an example of iron-rich food leveraging ginger as a functional ingredient to improve iron bioavailability and promote erythropoiesis. Thus, the ability of ginger to stimulate erythropoiesis can be an added benefit to the effectiveness of oral iron therapy for IDA treatment.

In a study that utilised zebrafish embryos to investigate the effect of ginger extract on haematopoiesis in vivo, Ferri-Lagneau et al. [19] found ginger, with its bioactive compounds of 8-gingerol, 10-gingerol, 8-shogaol, and 10-shogaol, promoted the expression of GATA-binding factor 1 (Gata1) in erythroid cells. Gata1 is an early marker and key regulator of erythropoiesis. Moreover, increases in the expression of haematopoietic progenitor markers cmyb and scl were also observed. The study also identified 10-gingerol as the most potent stimulator in promoting the primitive wave of erythropoiesis in early developing zebrafish embryos. The study further confirmed that the haematopoiesis effect of ginger was mediated through the bone morphogenetic protein (Bmp) signalling pathway.

In a subsequent study, the same group of researchers further demonstrated that ginger/10-gingerol can rescue the expression of haematopoietic stem/progenitor cells (HSPC) in zebrafish embryos with genetic defects [20]. Ginger was found to induce scl/runx1 expression through Bmp and Notch signalling pathways that led to arteriogenesis and HSPC formation. Bmp and Notch are known to regulate nitric oxide (NO) production, which plays an active role in the modulation of haematopoietic cell growth and differentiation. The study also showed that ginger produced a robust up-regulation of NO in the rescued mutant zebrafish embryos. Therefore, the combined effect of ginger on Bmp, Notch and NO production can be beneficial for the regulation of erythropoiesis for regeneration/recovery.

2.6. Iron Overload Prevention

Ginger's ability in modulating iron absorption in the case of overload was an unexpected finding in a study that used ginger nanoparticle-derived lipid vectors (GDLV) to deliver DMT-1 short-interference RNAs (siRNA) that suppressed DMT-1 mRNA expression to reduce iron absorption in an iron-loading mice model [21]. The study found that GDLV containing negative control appeared to repress some iron-related parameters similar to the DMT-1 siRNA treatment. The observed effects were reductions of 20% in ^{59}Fe absorption, approximately 65% of pancreatic non-haem iron, and 40 to 50% lower SF compared to controls. Hence, the authors suggested that the bioactive lipids in ginger could influence iron absorption and homeostasis.

In another animal model, Gholampour et al. [22] showcased the protective properties of ginger against the deleterious effects of iron overloading. To induce iron overload, male Wistar rats were given ferrous sulphate at 30 mg/kg/day, dissolved in 1 mL distilled water, intraperitoneally for 14 days. These rats showed significantly higher serum hepatic markers and bilirubin levels, elevated MDA levels, lower serum albumin levels, total protein,

triglyceride, cholesterol, and glucose, decreased creatinine clearance and higher fractional excretion of sodium compared to controls ($p<0.001$). The histopathological examination further confirmed their liver and kidney damage. A separate group of iron overloaded rats was fed with a hydroalcoholic ginger extract at 400 mg/kg/day dissolved in 1 mL distilled water and given by gavage for 11 days from the fourth day of ferrous sulphate injection. The feeding of ginger markedly reversed the adverse impacts of iron overload, as evidenced in the significantly higher levels of hepatic serum markers, renal functional markers and lipid peroxidation markers in this group compared to the iron only group ($p<0.01$). Moreover, depleted serum total protein, albumin, glucose, triglycerides, and cholesterol were restored with bilirubin concentration decreased in the blood. Hence, ginger extract demonstrated strong protective effects against iron toxicity potentially through its free radical scavenging activities. The preservation of the liver and kidney was also corroborated through histological examinations.

The potential of ginger, especially its 6-shogaol derivative, in preventing iron overload is further demonstrated in a case series reported by Golombick et al. [23]. 6 early-stage, transfusion-independent patients with myelodysplastic syndrome (MDS) were given a daily supplement of 20 mg of a ginger extract standardised for 20% 6-shogaol. Blood and urine samples were collected monthly. At three months, the study found that 6-shogaol was able to reduce the SF levels (>40% reductions) of three of the patients who had elevated SF (>300 g/µL) at baseline. Two of the patients who had SF reduction repeated the study for another 3 months after a washout period. Again, a greater than 40% reduction in SF was observed in the repeat tests for both patients. The two patients were tested for their serum hepcidin levels at the repeat tests. Both patients demonstrated elevation of serum hepcidin that accompanied the SF reduction. Furthermore, one patient who had high liver function enzymes due to alcohol consumption also saw normalisation of liver function with a greater than 40% reduction in these enzymes at the end of the study. The restoration of liver function was achieved without changing alcohol consumption habits. The research concluded that ginger extract rich in 6-shogaol prevented iron overload in MDS patients through upregulation of hepcidin, potentially with liver function restoration.

2.7. Ginger-Synthesised Iron Nanoparticles

Nanotechnology, the understanding and control of matter generally in the 1–100 nm dimension, is gaining much medical research as it holds the potential for breakthroughs in preventing, diagnosing, and treating various diseases due to the unique physicochemical properties of nanomaterials [36][37]. Unsurprisingly, iron nanoparticle (FeNP) preparations have also been developed to overcome the inherent limitations of conventional ferrous and ferric iron formulations in the treatment of IDA. Pre-clinical studies showed that iron nanoparticles have high bioavailability, are non-toxic, and induce lesser side effects than conventional iron preparations for IDA, even though the delivery and safety issues in humans for therapeutic use required further research [38]. The high bioavailability of iron nanoparticles is also ideal for food fortifications as the nanoparticles do not cause unacceptable taste or colour in food vehicles. Hence, it is suggested that nanosized iron salts can have potential applications in food fortification to reduce IDA worldwide [39].

Ginger has been used in the green approach for metallic nanoparticles, including iron. The green synthesis approach is preferred to avoid the production of unwanted or harmful chemical by-products and achieve a cost-

effective and sustainable supply of nanoparticles [40]. El-Refai et al. [24] used ginger and garlic extracts to synthesise silver, copper, iron, and zinc nanoparticles, and their antioxidant and antimicrobial activities were evaluated. The high flavonoid and phenolic contents in garlic and ginger water extracts revealed in the phytochemical analysis strongly support the potential of garlic and ginger to bio-reduce the metallic ions to their respective nanoparticles (e.g., Fe^{3+} ions to FeNPs). Transmission electron microscopy showed that the FeNPs in ginger were in the range of 14.08–21.57 nm with almost spherical forms. In comparison, the particle size of FeNPs in garlic ranged from 60.30 to 82.63 nm with tetragonal structures. All nanoparticles extracted in this research, including FeNPs from ginger, demonstrated considerable radical scavenging properties and antimicrobial activities against Gram-positive and Gram-negative bacteria and fungi [24]. Other researchers have similarly shown ginger to be a suitable green material for synthesising FeNPs with high antioxidant and antibacterial properties [25][26].

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