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# Efficacy Studies of Two Iron Supplements Irovit-1 and Irovit-2

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**Abstract.** Two preparations of iron supplements have been developed with vitamins, Irovit-1 and Irovit-2 containing 1 mg/mL and 2 mg/mL elemental iron respectively in complex form. Clinical trials of Irovit-1 and Irovit-2 have been conducted randomly on selected anemic males and females from urban population of Karachi, an improvement in hemoglobin levels were estimated for the treatments with Irovit-1 (10 mg Fe/day) and Irovit-2 (20 mg Fe/day). Both preparations have been found to be effective in increasing hemoglobin, Hematocrit and red blood cell count. The mean hemoglobin levels were observed increased 0.73 ± 0.25 g/dL and 1.10 ± 0.30 g/dL, after 5 weeks by oral intake of Irovit-1 and Irovit-2, respectively.

**Keywords:** iron saccharate, oral supplements, efficacy hemoglobin level

## Introduction

Iron deficiency anemia (IDA) is a major worldwide nutritional problem (Organization, 2011). Causes of anemia may be insufficient dietary iron intake; iron loses e.g. bleeding, parasite infestation and malabsorption of iron (Wiley Encyclopedia of Food Science and Technology, 1992). But all types of anemia have the same effect i.e. the lack of hemoglobin in red blood cells, which prevent proper oxygen transport through the body. Iron deficiency causes insufficient hemoglobin production, resulting in anemia symptoms (Campbell *et al*., 2018; Percy *et al*., 2017; Wong, 2017; Frewin *et al*., 1997). The average adult body contains 3g of iron. About 65% is found in the hemoglobin which carries oxygen from lungs to the various parts of the body (Krik-Oltmer Encyclopedia of Chemical Technology, 2005). A recent modification of WHO definition states that anemia in pregnancy when hemoglobin concentration falls below 11.0 g/dL (Organization, 2011).

The groups at greatest risk for developing IDA are menstruating females, pregnant or nursing females and young children (Minar *et al*., 2015; Wiley Encyclopedia of Food Science and Technology, 1992). Most athletes especially female have low-mid range hemoglobin values referred to as sports anemia thus affects their sports performance (Brownlie *et al*., 2002). Low concentration of Hb < 7 g/dL causes anemia with a few remarkable symptoms increasing lethargy, headaches, tinnitus and taste disturbances (Wiley Encyclopedia of Food Science and Technology, 1992). During pregnancy, womens have low mild range hemoglobin levels which is an extra demand for the fetus (Chandra *et al*., 2012). Food and nutrition board of the institute of medicine recommended routine use of 30 mg/day iron supplement during pregnancy. During pregnancy when the depletion of Hb level is fast, immediate administration of iron is essential to overcome this deficiency. This could only be accomplished by parenteral administration which is also the preferred route in patient which suffering from gastrointestinal disturbance caused by oral intake of iron, it is more pronounced during pregnancy. But the parenteral administration practices have their own drawbacks. Allergic side reactions, often fatal, also occur, such as hygienic safety problems described by (Feightner, 1994).

According to USP and BP the oral preparations usually used in iron deficiency anemia are mostly salts as shown in Table 1 (Birtish Pharmacopeia, 2008; United State Pharmacopeia /National Formulay, 2008). All these preparations are associated with high risk incidence of side effects including nausea, constipation and diarrhea. These side effects may be reduced by taking the drugs after meals or by the use of sustain released preparation of iron (complex form) (Frewin *et al*., 1997). Thus the following study described a preparation in the same context.

The efficacy of two preparations Irovit-1 and Irovit-2 were assessed containing iron and multi-vitamins showed in (Table 2). Both preparations contain non-

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**Table 1.** Most common commercially available iron salts

| Preparations | Amount in mg/day | Fe content in mg/day |
|---|---|---|
| Ferrous fumarate | 200 mg | 65 mg |
| Ferrous gluconate | 300 mg | 35 mg |
| Ferrous succinate | 100 mg | 35 mg |
| Ferrous sulfate | 300 mg | 60 mg |

**Table 2.** Composition of Irovit-1 and Irovit-2

| Name of products | Ingredients | Amount per 10 mL syrup |
|---|---|---|
| Irovit-1 | Fe elemental (saccharated oxide of iron) | 10 mg |
| | Vitamins: | |
| | Thiamine HCl | 0.35 mg |
| | Riboflavin | 0.40 mg |
| | Nicotinamide | 4.50 mg |
| | Pyridoxine HCl | 0.35 mg |
| | Ascorbic acid | 20 mg |
| | Folid acid | 0.1 mg |
| Irovit-2 | Fe elemental (saccharated oxide of iron) | 20 mg |
| | Vitamins: | |
| | Thiamine HCl | 1.5 mg |
| | Riboflavin | 2.0 mg |
| | Nicotinamide | 20 mg |
| | Pyridoxine HCl | 2.0 mg |
| | Ascorbic acid | 40 mg |
| | Folid acid | 0.3 mg |

ionic colloidal form of saccharated oxide of iron, which ensures slow release of iron and maintain constant level of iron in the body (Martindale: extra pharmacopoeia, 1977). These preparations containing low levels, 1 mg/mL and 2 mg/mL of elemental iron are designed with a view to avoid well known gastrointestinal side effect of oral iron preparation containing high levels of elemental iron. Vitamins, especially vitamin C was added in the syrup to enhance absorption of iron (Hallberg *et al*., 1986).

## Material and Methods

**Preparation of Irovit-1 and Irovit-2.** Preparation of Irovit-1 and Irovit-2 comprised of two process (i) preparation of saccharated iron oxide and (ii) preparation of stabilized sugar base and addition of saccharated iron oxide and vitamins to this base.

***Preparation of saccharated iron oxide.*** Saccharated iron oxide was prepared by following the method developed earlier in our laboratory (Zaidi and Mahdihassan, 1962).

***Preparation of stabilized sugar base.*** The addition of saccharated iron oxide and vitamins to the base sugar (75 Kg), methyl-p-hydroxy benzoate (100 g), propyl p-hydroxy benzoate (50 g) and distilled water 15-20 L was placed in a 200 L stainless steel steam jacketed vessel, heated to 90ºC with vigorous stirring till the sugar dissolved completely. In another vessel carboxymethyl cellulose (180 g) was dissolved in hot water (50-60 ºC) and added to sugar solution, while hot. The mixture was left to cool at room temperature. Saccharated iron oxide containing 100 g of elemental iron was added to above mixture. Food colour (20 g) dissolved in water (20 mL) was added to the above mixture. pH of the mixture was adjusted to 7 by adding 28.5 g citric acid and finally orange flavor (125 mL) was added. Mixture of vitamins was also added to above solution and stirring continued till homogenous mixture obtained.

**Evaluation of efficacy and tolerability of Irovit-1 and Irovit-2.** 10 anemic patients (group-1) were selected for testing Irovit-1 and 15 anemic patients (group-2) were selected for testing Irovit-2 from urban area of Karachi. After taking their data, age, weight, height, blood pressure and initial blood sampling, they were provided with supplement 10 mL of Irovit-1 and Irovit-2 for 30-45 days. Subsequent blood sampling was done after 5 weeks. The parameters included in the study were, serum hemoglobin, hematocrit and RBC count.

Hemoglobin was estimated by cynamet hemoglobin method on Sysmax K1000 hematology auto-analyzer. Hematocrit and RBC count were also evaluated by the same machine.

## Results and Discussion

The efficacy of saccharated iron oxide as oral preparation has never been evaluated before. Two trials were conducted to assess the effectiveness of Irovit-1 and Irovit-2. For these studies patients with low hemoglobin level were selected and divided in two groups. After supplementation an improvement in hemoglobin level was observed in both groups more significantly in patients belonging to group-2 treated with Irovit-2. Patients treated with Irovit-1 showed Hb increased from 0.3 g/dL to 1.0 g/dL, whereas patient treated with

Irovit-2 showed Hb increased from 0.8 g/dL to 1.7 g/dL with a mean value of 0.7 ± 0.25 g/dL in group-1 and 1.10 ± 0.3 g/dL in group-2 (Table 4). The concentration of hemoglobin increase was more rapid in group-2 receiving 20 mg elemental iron daily. Our findings were also supported by longitudinal studies in which 30-200 mg iron were given daily to bring about significant increase of 1.0 to 1.7 g/dL in hemoglobin content (Feightner, 1994). In another study low dose (20 mg/day) of iron has been given to pregnant women. This strategy was found to be effective in preventing IDA and ID in the treated subject (Makrides *et al*., 2003). Food and Nutrition Board of the Institute of Medicine recommended daily oral intake of iron supplement containing 30 mg/day during pregnancy.

Other blood parameters in these patients like hematocrit, red blood cell (RBC) counts and platelets were also studied which are shown in (Table 3). The significant increase in hematocrit (%) was observed from 27.97 ± 3.76 to 31.54 ± 3.5. The mean difference in increase was 3.56 ± 2.20 within 5 weeks of supplementation. RBC count increases from 4.05 x $10^6$/uL ± 0.69 to 4.36 x $10^6$/uL ± 0.53. The mean significant increase in RBC was noted 0.30 x $10^6$/uL ± 0.89 after 5 weeks of supplementation. The platelets increases from 267.73 x $10^3$/uL ± 104.98 to 274.8 x $10^3$/uL ± 97.02. The mean significant increase in platelets was 7.07 x $10^3$/uL after 5 weeks of supplementation.

**Table 3.** Status of RBC & HGB, PLT & Hematocrit in patients before and after taking Irovit-2

| Parameters | Units | Mean ± SD at 0 week | Mean ± SD at 5 weeks | Mean difference ± SD |
|---|---|---|---|---|
| Hemoglobin | g/dL | 8.16 ± 1.34 | 9.26 ± 1.24 | 1.10 ± 0.30 |
| Hematocrit | % | 27.97 ± 3.76 | 31.54 ± 3.50 | 3.57 ± 2.20 |
| RBC count | x$10^6$/µL | 4.05 ± 0.69 | 4.36 ± 0.53 | 0.31 ± 0.89 |
| Platelets | x$10^3$/µL | 267.73 ± 104.98 | 274.8 ± 97.02 | 7.07 ± 3.23 |

**Table 4.** Comparison of the mean hemoglobin value at 0 and after 5 weeks in Group-1 (Irovit-1) and Group-2 (Irovit-2)

| | Units | Mean ± SD at 0 week | Mean ± SD at 5 weeks | Mean increase ± SD |
|---|---|---|---|---|
| Group-1 | g/dL | 9.53 ± 1.57 | 10.26 ± 1.50 | 0.73 ± 0.25 |
| Group-2 | g/dL | 8.16 ± 1.34 | 9.26 ± 1.24 | 1.10 ± 0.30 |

## Conclusion

Both the preparation indigenously produced Irovit-1 and Irovit-2 have low iron concentrations and are readily absorbed. The normal side effects associated with other oral iron preparations were missing. Our investigation has shown that low iron doses (20 mg/day) is sufficient to manage iron deficiency anemia effectively. Moreover, very low doses of iron (10 mg/day) are also beneficial for anemia treatment, but not as effective as 20 mg/day, resulting in a substantial increase in the level of hemoglobin.

The significance increase in hematocrit % 3.56 ± 2.20 and RBC counts x $10^6$/uL 0.30 ± 0.89 shows significant rise from base line suggested the better absorption and cure of anemia by using the Irovit-2 (20 mg Fe/10 mL) within 5 weeks.

**Conflict of Interest.** The authors declare no conflict of interest.

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