Ferrous gluconate

1. Clinical trials referenced for bioavailability and side effects

STUDIES SHOWING BIOAVAILABILITY LESS THAN SULFATE

(Brise and Hallberg 1962)
Includes two studies comparing different salts against sulfate, using the Hemoglobin incorporation RBV method.

Study A was for 10 days. Each person got sulfate one day and the test iron the next day. Each dose was 30mg elemental iron with 10mg ascorbic as a solution. Both iron types were labelled.

Study B had the same general design with labelled iron and fed on alternate days. This study went on for 24 days and the dose was 30mg elemental iron given 3 times a day between meals as tablets. No ascorbic acid. Subjects had a range of different iron status levels for both studies.

results

study A - 10 days, 30mg per day with iron in solution + ascorbic

Each patient had their iron amount adjusted relative to sulfate. Mean values were:
Ferrous sulfate - 100%
Ferrous fumarate - 101%
Ferrous gluconate - 80%
Ferrous succinate - 123%

Fig. 2. Absorbability of different iron compounds (solutions). Individual values in relation to ferrous sulphate.
study B - 24 days, iron as tablet, 3 x 30mg per day

Ferrous sulfate - 100%
Ferrous gluconate - 84%
Ferrous succinate - 93%

side effects.
More side effects occurred in study B with the larger dose sizes. Because of the nature of the study no comparison can be made of the side effects between types but the author states "When the same amount of iron is given, no differences in side-effects have been observed in the few published controlled studies."

My summary
This is quite a good test, as it lets each person become their own control so status doesn’t affect results. This study showed gluconate to a RBV of 80% when both were in solution, and a RBV of 84% when both were in tablet.

(Hurrell 2002)
No mention of how these figures were attained, except that it was adapted from his 1999 book http://trove.nla.gov.au/work/5703079?selectedversion=NBD20756571
Can’t source a version to find out more though.
Table 1. Characteristics of Conventional Iron Fortification Compounds

<table>
<thead>
<tr>
<th>Iron Compound</th>
<th>Approximate Fe (%)</th>
<th>Average Bioavailability</th>
<th>Potential for Adverse Organoleptic Changes</th>
<th>Approximate Relative Cost*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Freely water soluble</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ferrous sulfate 7H₂O</td>
<td>20</td>
<td>100</td>
<td>100</td>
<td>1.0</td>
</tr>
<tr>
<td>Dried ferrous sulfate</td>
<td>33</td>
<td>100</td>
<td>100</td>
<td>0.7</td>
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<tr>
<td>Ferrous gluconate</td>
<td>12</td>
<td>97</td>
<td>89</td>
<td>5.1</td>
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<tr>
<td>Ferrous lactate</td>
<td>19</td>
<td>—</td>
<td>106</td>
<td>4.1</td>
</tr>
<tr>
<td>Ferric ammonium citrate</td>
<td>18</td>
<td>107</td>
<td>—</td>
<td>2.1</td>
</tr>
<tr>
<td>Ferrous ammonium sulfate</td>
<td>14</td>
<td>99</td>
<td>—</td>
<td>2.3</td>
</tr>
<tr>
<td>Ferric chloride citrate</td>
<td>14</td>
<td>102</td>
<td>—</td>
<td>11.0</td>
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<tr>
<td>Poorly water soluble/soluble in dilute acid</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ferrous fumarate</td>
<td>33</td>
<td>95</td>
<td>100</td>
<td>1.3</td>
</tr>
<tr>
<td>Ferrous succinate</td>
<td>35</td>
<td>119</td>
<td>92</td>
<td>4.1</td>
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<tr>
<td>Ferric succinate</td>
<td>10</td>
<td>92</td>
<td>74</td>
<td>5.2</td>
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<td>Ferric glycerophosphate</td>
<td>15</td>
<td>93</td>
<td>low</td>
<td>10.5</td>
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<tr>
<td>Ferrous citrate</td>
<td>24</td>
<td>76</td>
<td>74</td>
<td>3.9</td>
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<tr>
<td>Ferrous tartrate</td>
<td>22</td>
<td>77</td>
<td>62</td>
<td>3.9</td>
</tr>
<tr>
<td>Water insoluble/poorly soluble in dilute acid</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ferric pyrophosphate</td>
<td>25</td>
<td>45–58</td>
<td>21–74</td>
<td>2.3</td>
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<tr>
<td>Ferric orthophosphate</td>
<td>28</td>
<td>6–46</td>
<td>25–32</td>
<td>4.1</td>
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<tr>
<td>Elemental Fe powders:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>electrolytic</td>
<td>97</td>
<td>16–70</td>
<td>75</td>
<td>—*</td>
</tr>
<tr>
<td>H-reduced</td>
<td>97</td>
<td>13–54</td>
<td>13–148</td>
<td>—*</td>
</tr>
<tr>
<td>Co-reduced</td>
<td>97</td>
<td>12–32</td>
<td>ND</td>
<td>—*</td>
</tr>
<tr>
<td>atomized</td>
<td>97</td>
<td>ND</td>
<td>ND</td>
<td>—*</td>
</tr>
<tr>
<td>carbonyl</td>
<td>99</td>
<td>35–66</td>
<td>5–20</td>
<td>—*</td>
</tr>
</tbody>
</table>

* Relative to ferrous sulfate 7H₂O = 1.0, for the same level of total iron.
* In general less expensive than ferrous sulfate. Cost of different powder types varies approximately sevenfold, with carbonyl iron being the most expensive.

ND = not determined.
Source: adapted from Hurrell, reference 2.

**Gluconate - 89%**

Fumarate - 100%

Succinate - 92%

carbonyl - 5-20%

*(Zariwala 2013)*

Used the two-stage in vitro dissolution-absorption protocol ie. basically the best in vitro method. It looked at both dissolution and absorption

results

This showed the dissolution part, interesting to see how FerrogradC which was the ferrous sulphate plus AA took too long for dissolution

In the paper there is no table of data just the graph below, so these values are taken from the graph. These values are RBV adjusted against 'ultrapure' sulfate, which were used as a reference standard.
Ferrous sulfate tablet- 41%, Ferrous fumarate tablet- 32%, Ferrous gluconate tablet- 31%, Ferrous sulfate slow release plus ascorbic - 29% (Ferrograd C), Ferrous gluconate syrup plus folic - 34%, Ferrous gluconate syrup plus ascorbic - 32% (Floradix)

My summary
In vitro test that uses the whole supplement with all its excipients (binding and other parts of the supplement) rather just in its pure form. This often can’t be done when using the in vivo labeling method. To adjust their results so they work for me, i’ve made sulfate 100%, which gives:
Ferrous fumarate tablet- 78%, Ferrous gluconate tablet- 76%, Ferrous sulfate slow release plus ascorbic - 71% (Ferrograd C), Ferrous gluconate syrup plus folic - 83%, Ferrous gluconate syrup plus ascorbic - 78% (Floradix)

Adding ascorbic and a liquid form usually increase available, so I’m surprised that they were only minimally better here. I wonder if Floradix contains some inhibitors, quite possibly looking at the ingredients list.

STUDIES SHOWING BIOAVAILABILITY SAME AS SULFATE

(Casparis et al. 1996) - could only access abstract
Study of 40 women with IDA. Divided into 4 groups and for 30 days given either ferrous gluconate liquid - 75mg/day  
ferrous gluconate tablet - 80mg/day  
ferrous sulphate tablet - 105mg/day  
ferric protein succinylate liquid - 80mg/day

All the usual test were done (red blood cells, hemoglobin, hematocrit and serum iron) at the end of the treatment and no significant difference between results. Can’t see what all the ferritin results were.
side effects
Glucconate liquid had no reported side effects and no dropouts. The rest had 1 or 2 dropouts, not too sure about number of side effects.

my summary
glucconate was as effective as sulfate at a lower dose. less side effects but a small sample.

SIDE EFFECT STUDIES

(Hallberg, Ryttinger, and Sölvell 1966)
A series of three tests that compare different iron supplements against a placebo. One of the few that compares with a placebo, and at a dosage that is standard. 1496 subjects of blood donors. Given 222mg/day so a high dose, broken into three doses /day.

% of subjects that reported negative side effects
sulphate 27.9
fumarate 26.4
gluconate 31.5
placebo 13.9
(no statistical difference between the three irons )
Interesting to see how high the placebo is.

(Cancelo-Hidalgo et al. 2013)
For this review 111 studies were included, with data on 10,695 patients. Basically an analysis of a whole lot of studies.

Overall AE’s (adverse events)
Ferrous sulfate with mucoproteose (Slow Release) - 4.1%
iron protein succinyllate - 7.3% (1.96 relative to FS SR) (not statistically significant difference)
ferrous glycine sulfate - 18.5%
ferrous gluconate - 29.9% (11.06 relative)
ferrous sulfate without mucuproteose 32.3% (11.21 relative)
ferrous fumarate - 43.4% (19.87 relative)

so a little less side effects compared to normal release sulfate but not significant

Things to note
Can’t know details like if patients were anemic, what food it was taken with, double blind or not or dosage, but a big dataset.

(Fochi, Ciampini, and Ceccarelli 1985)
This study for ferritin doesn’t say much about side effects, but references these results from (Kerr and Davidson 1958).
Hard to interpret as different doses and only one study for gluconate, however it looks about the same as sulfate for the same dose

![Image](image.jpg)

**OTHER STUDIES**

(Babayan 2008)

50 anemic women were given either floradix or femineral - two types of liquid forms of ferrous gluconate. Both groups given 10ml per day, but they contained different amounts of iron. 10ml for femineral and 15ml for floradix. Usual tests done after 28 days.

**Results**

Both groups had significant improvement of serum iron levels. Only the femineral group showed significant improvements in Hb. Not sure why ferritin levels weren’t measured.

**my summary**

Femineral had more Hb increase despite the lower iron content. So maybe floradix had more inhibitors/less enhancers or alternatively the other ingredients in femineral helped increase the Hb. Both did increase serum iron by about 27μg/dL. Not sure what to take out of this one except that things get complicated when lots of ingredients are added with the iron. No doubt that there are herbs that increase iron, but also plenty that inhibit so it’s a lot of guess work if you go down that route.

**2. Info and sources regarding inhibitors and enhancers**

Haven’t seen any specific information on this, only that they are affected.


An iron salt of gluconic acid. It is composed of iron, bound to two molecules of gluconic acid, which is the acid form of glucose.
3. References used in this section


