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(Research Article)

Potency and Dissolution Property of Several Brands of Commercial Iron Capsules Marketed in Bangladesh

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ABSTRACT

The aim of this study was to assess the quality of some iron capsules locally marketed in Bangladesh, in terms of potency (drug content) and dissolution. Two different categories of combined ferrous iron-folic acid containing oral capsules were collected randomly from different medicine shops of Dhaka city. One category contained iron as ferrous sulfate salt and the other category contained iron as carbonyl iron. Collected nine different brands of dried ferrous sulfate (DFS) containing capsules were coded as DFS-01 to DFS-09, while carbonyl iron (CI) containing capsules (10 different brands) were coded as CI-01 to CI-10. DFS and CI capsules were analyzed by using UV-VIS spectrophotometer and atomic absorption spectrophotometer (AAS) respectively. Potency of all the DFS capsules complied with British Pharmacopoeial (BP) specification, whereas only three of the ten brands of CI capsules (CI-01, CI-02 and CI-10) showed satisfactory amount of carbonyl iron per capsule amounting to 49.9mg (99.8%), 50.2mg (100.4%) and 50.06mg (100.1%) respectively. Dissolution data of half of the carbonyl iron capsules (viz CI-03, CI-05, CI-07, CI-08 and CI-10) did not meet pharmacopoeial specification i.e., their Q value (percent released of the labeled amount of the drug) was below the acceptance limit (<75%) of USP. To conclude, only the ferrous sulfate capsules were of good quality in terms of potency but most of the capsules of carbonyl iron form showed unsatisfactory assay and dissolution property.

Key Words: Potency, Dissolution, Ferrous iron, Carbonyl iron, Pharmacopoeial specification.

INTRODUCTION

Iron deficiency anemia (IDA) is the most common nutritional deficiency worldwide. It can cause reduced work capacity in adults[1] and impact motor and mental development in children and adolescents[2]. There is some evidence that iron deficiency without anemia affects cognition in adolescent girls[3] and causes fatigue in adult women[4]. IDA may affect visual and auditory functioning[3] and is weakly associated with poor cognitive development in children[4].

Oral iron therapy is usually the first-line therapy for patients with IDA[5]. The choice of iron salt to be used for replacement therapy is based on bioavailability, side effects and cost effectiveness of various iron salts. Since all iron has to be reduced to ferrous form for absorption, ferrous salts are preferred for treatment of IDA[6-8] and specifically ferrous sulfate. Ferrous sulfate in liquid form is not stable; hence other ferrous salts are used in these formulations[9].

Carbonyl iron has been used in food fortification industry. The main advantage with this form of iron is its small particle size which contributes to increased bioavailability. In an Indian study, a modified release form of carbonyl iron has been found to have 147 % bioavailability compared to ferrous fumarate[10]. Hb rise with carbonyl iron and ferrous sulfate is reported to be similar from another study[11].

Iron deficiency is the most pervasive nutritional problem in the world, especially among infants and young children in the developing countries[12]. Prevalence of IDA among children under 5 years of age in South Asia is estimated to be 75%, 55% and 56% in India, Bangladesh and Pakistan, respectively[13,14]. The World Health Organization (WHO) estimates that 39% of children younger

than 5 years, 48% of children between 5 and 14 years, 42% of all women, and 52% of pregnant women in developing countries are anemic[15].

There are three (3) main strategies for correcting iron deficiency in populations, which can be used alone or in combination: (1) education combined with dietary modification or diversification to improve iron intake and bioavailability; (2) iron supplementation; and (3) iron fortification of foods. Although dietary modification and diversification has been traditionally thought of as the most sustainable approach, change of dietary practices and preferences is difficult and foods that provide highly bioavailable iron (such as meat) are expensive[16]. Iron supplementation in the form of tablets or capsules is the most common strategy currently used to address iron deficiency in developing countries.

A number of iron preparations are currently marketed in Bangladesh - ferrous, ferric, as well as various iron complexes, which are being used to treat iron deficiency. The potency (drug content) and dissolution property of a solid dosage form are the two most important parameters need to study for assessing the safety and efficacy of any drug products. There are several reports on unsatisfactory dissolution and assay data of marketed drug products both in the developed as well as developing countries[17-19]. The present research work was therefore aimed to study potency (drug content) and dissolution property of iron capsules available in local market as these two parameters (drug content and dissolution property) indicate the drug's efficacy level in treating iron deficiency anemia.

MATERIALS AND METHODS

Collection and Coding of Locally Marketed Iron Preparations

Nine different brands of dried ferrous sulfate (DFS) capsules and ten carbonyl iron (CI) containing locally manufactured and marketed capsules were collected randomly from different medicine shops of Dhaka city, Bangladesh.

To preserve brand identity, DFS Capsule brands were coded randomly as DFS-01 to DFS-09, while carbonyl iron containing capsules were similarly coded as CI-01 to CI-10.

Reagents

Ferrous sulphate heptahydrate working standard (WS) was kindly donated by popular pharmaceuticals Ltd, Bangladesh. 2, 2-bipyridine was purchased from Loba Chemie, India. Ammonium acetate was bought from Merck, India. All other reagents used were of analytical reagent grade. Distilled water was used to prepare solution with the reagents.

Iron Content Determination

Ferrous iron as ferrous sulphate from ferrous sulphate salt containing iron capsules was determined by molecular absorption spectroscopy using a UV-Vis Spectrophotometer (Simadzu UV-VIS spectrophotometer 1601, Japan) according to BP (2007) method. Ferrous sulphate heptahydrate WS was used as a standard in this determination. Absorbance of each DFS sample was recorded at 523 nm against a blank (water). The amount of ferrous sulphate per capsule (in mg) was calculated from the respective absorbance data and taking into consideration of potency of standard (99%), conversion factor for ferrous sulphate heptahydrate to dried ferrous sulphate, dilution factor, weight of standard and sample.

Iron as carbonyl iron from carbonyl iron containing capsules was determined using Atomic Absorption Spectrophotometer (AA-6300,Japan). As carnonyl iron containing products were INN products and hence analytical method was adopted from a pharmaceuticals company of Bangladesh. One ppm ferrous iron was taken as standard in this method. Not less than 20 times of theoretical fill weight of each brand of capsule pellets was weighed and finely powdered. An accurately weighed and finely powdered sample, equivalent to 100mg carbonyl iron was transferred into a 250mL volumetric flask. 30ml of water and 10ml of 37% HCl were added to it and then heated and shaken for homogeneous mixing. Five mL of this solution was taken into a 100mL volumetric flask, diluted up to the mark with water and mixed well. Absorbance of both the standard and sample solution was taken at 284.3nm using atomic absorption spectrophotometer (AA-6300, Japan). The amount of elemental iron per capsule (in mg) was calculated from respective absorbance data and taking into consideration of the sample and standard weight and dilution factor of sample solution.

Dissolution Study

USP dissolution test apparatus II (paddle) was used for analysis of percent carbonyl iron release from the capsules[20]. Temperature of the vessel and whole tank was maintained at 37°C throughout the test and 1 litre 0.1N HCl was used as dissolution medium in each vessel. Paddle rpm was maintained at 100. The dissolution processes was run for 2 hours. One capsule's fill weight was given per vessel. After 2 hours, 5mL of solution from each vessel was taken and diluted to 50 mL with water. The sample was then analyzed using atomic absorption spectroscopy for the percentage of carbonyl iron released. Absorbance of both the

standard and sample solutions was taken at 284.3nm in the atomic absorption spectrophotometer (AA-6300, Japan). Six (6) capsules for each brand was taken for each dissolution test and percent drug release of each capsule was calculated using absorbance value of both the sample and standard and taking into consideration of their weight taken, potency of standard and dilution factor of sample solution.

RESULTS AND DISCUSSIONS

Iron Content Determination

Nine different brands of dried ferrous sulphate (DFS) capsules and ten different brands of carbonyl iron (CI) capsules were bought at retail price from the medicine shops of Dhaka city, Bangladesh. They were coded as stated in the material part to preserve their brand identity. Chemical nature of iron of the two categories of capsules were divers - DFS contained ionic iron while CI contained elemental iron. Composition of representative brands of the said two different categories of iron capsules is presented in the Table-1. It is clear from the Table 1 that, DFS capsules were of two component system but CI capsules were of three component system. Folic acid content in both the categories of iron preparations was same.

Results of potency analysis of ten (10) different brands of DFS capsules is shown in the Figure 1. It is clear from the Figure 1 that all the tested brands of DFS complied with the BP specification (95 to 105%). To be precise, DFS-01 and DFS-05 exhibited optimum percent of ferrous iron amounting to 100.57% and 100.27%, respectively while DFS-02, DFS-04 and DFS-09 marginally met BP specification (not less then 95%). Although all the DFS brands were not of the same self life, but iron content as ferrous salt (in percentage) retained in all the tested brands and thus indicated that all the samples were of good quality in term of potency.

Ten (10) commercially available capsules containing carbonyl iron (CI) were assayed using atomic absorption spectroscopy. The estimated content of carbonyl iron from the AAS data are shown in the Figure 2. It was claimed by the manufacturer that each capsule contained 51mg carbonyl iron (elemental iron 50 mg) where as the observed analytical data (Figure 2) exhibited significant difference from that for most of the brands. In particular, only three of the brands (CI-01, CI-02 and CI-10) showed satisfactory amount of iron per capsule and the amounts were 49.9mg (99.8%), 50.2mg (100.4%) and 50.06mg(100.1%) respectively which fell within the acceptable limit (not less than 98% iron) claimed by the manufacturers. In contrast, CI-03 to CI-09 did not meet the specification (Figure 2).

It is not clear why most of the CI brand capsules did not meet the specification while such problem was not observed for DFS brands (Figure 1). Even if some elemental iron was changed to ionic form in CI brands during self life, it should not cause to lower iron content in the determination of AAS. Therefore, initial addition of elemental iron in the CI capsules might have low. Manufacturers of those brands had not much reputation in the country too. Relevant authority should take strict measures to the companies who are not following good quality control practice in the country.

Dissolution study

Nowadays, the study of dissolution *in vitro* is considered as a fundamental requirement in the pharmaceutical industry in order to assure the quality of solid pharmaceutical dosage forms for oral use[21-23]. In the present study, carbonyl iron containing capsules of ten (10) different brands were allowed to dissolute separately in a simulated environment of stomach (pH 1.2) for two hours. The experiment was carried out following USP with a dissolution tester (USP apparatus II). Obtained results are presented in the Figure 3. This figure shows the relative percent release of carbonyl iron from the tested CI brands within the stipulated time (2 hour) of the experiment. According to USP 2010[20], dietary supplements should contain not less than 75% of the labelled content (Q value) of elemental iron and it should be dissolved in 1 hour in 0.1 N HCl. It is clear that only two brands (CI-04 and CI-06) released more than 80% of carbonyl iron (Figure 3) and met the USP specification nicely. Percent release of carbonyl iron for each of the brands CI-01, CI-02 and CI-09 were slightly higher than the USP specification limit (75%) while the rest brands (CI-03, CI-05, CI-07, CI-08 and CI-10) did not qualify the USP specification and they were thus of spurious category. It was a mater of surprise that 50% of the tested brands did not release the active ingredient properly, which means if any of those branded capsules is taken for the remedy of iron deficiency that will not impart any beneficial effect to the patient rather it will come out through the feces like undigested stone material.

CONCLUSION

Inappropriate amount of iron content and inadequate percent of release of it from the substandard brands might be due to defect in the manufacturing process. Manufacturer as well as drug regulatory authority should take proper measures to maintain quality of any product including iron preparations so that after using those

products, one can get rid of unexpected sufferings from any disease or of nutritional deficiency.

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Table-1: Composition of Iron Containing Capsules

Sample Code	Composition
DFS-01 to DFS-10	Each capsule contains ferrous sulphate 150mg and folic acid 0.5 mg
CI-01 to CI-09	Each capsule contains carbonyl iron 51mg (elemental iron 50mg), folic acid 0.5 mg and zinc sulphate monohydrate 61.8mg (elemental zinc 22.5mg)

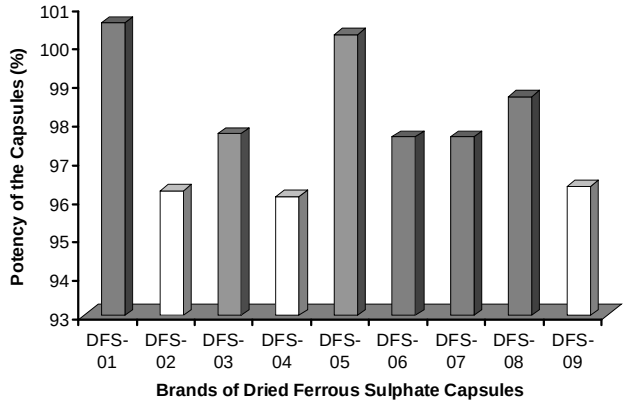

Figure-1: Potency of Ferrous Iron in the Marketed Ferrous Sulphate Capsules.

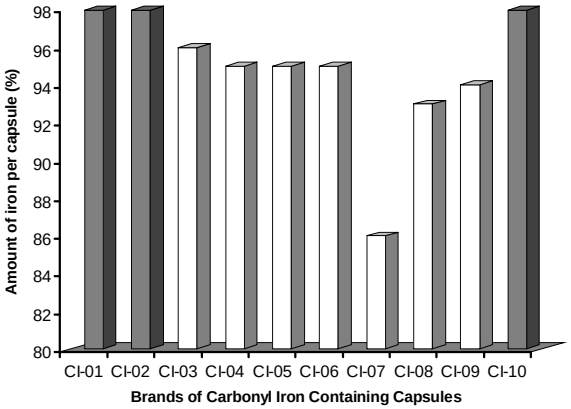

Figure-2: Potency of Commercial Carbonyl Iron Capsules.

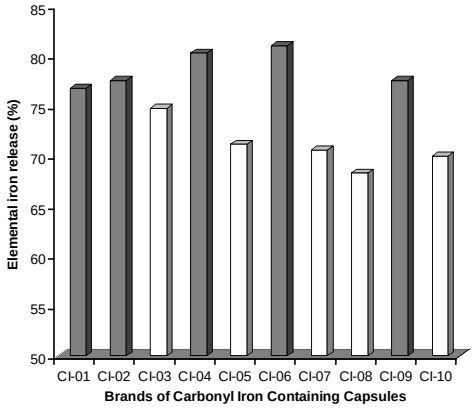

Figure-3: Dissolution of Carbonyl Iron Capsules in 0.1N HCl (pH 1.2)

REFERENCES

1. Haas JD, Brownlie T, Iron deficiency and reduced work capacity: a critical review of the research to determine a causal relationship, J. Nutr,131, 2001,676S-88S.
2. Halterman JS, Kaczorowski JM, Aligne CA, Auinger P, Szilagyi PG, Iron deficiency and cognitive achievement among school-aged children and adolescents in the United States, Pediatrics,107, 2001,1381-6.
3. Algarin C, Peirano P, Garrido M, Pizarro F, Lozoff B, Iron deficiency anemia in infancy: long-lasting effects on auditory and visual system functioning, *Pediatr Res*,53, 2003, 217-23.
4. Verdon F, Burnand B, Stubi CL, Bonard C, Graff M, Michaud A, *et al*, Iron supplementation for unexplained fatigue in non-anaemic women: double blind randomised placebo controlled trial, *BMJ*,326, 2003, 1124.
5. Crosby WH, The rationale for treating iron deficiency anemia, Arch Intern Med, 144, 1984, 471-2.
6. Glader B, Anemias of inadequate production. In: Kliegman RM, Jenson HB, Behrman RE, Stanton BF, editors. Nelson Textbook of Pediatrics,18th ed. Elsevier, New Delhi, 2008. p. 2014-2016.
7. Andrews NC. Disorders of iron metabolism and sideroblastic anemia. In: Nathan DG, Ginsburg D, Orkin SH, Look AT, edotors. Nathan and Oski's Hematology of Infancy and Childhood, WB Saunders, Philadelphia, 2003, p. 455-497.
8. Adamson JW. Iron Deficiency and other Hypoproliferative Anemias. In: Kasper DL, Braunwald E, Fauci AS, Hauser SL, Longo DL, Jameson JL, editors. Harrison's Principles of Internal Medicine. New York : McGraw Hill; 2007. p. 586- 592.
9. Nagpal J, Choudhury P, Iron formulations in pediatric practice. Indian Pediatr,41, 2004, 807-815.
10. Desai BB, Desai A, Gawde A, Baliga V, Comparative assessment of bioavailability and safety of a modified r-release (MR) carbonyl iron tablet and conventional iron preparation in adult Indian patients with nutritional iron deficiency anemia, J Indian Med Assoc, 103, 2005, 338-342.
11. Devasthali SD, Gordeuk VR, Brittenham GM, Bravo JR, Hughes MA, Keating LJ, Bioavailability of carbonyl iron: a randomized, double-blind study, Eur J Haematol, 46, 1991, 272-278.
12. UNICEF. Delivering essential micronutrients: Iron. Available at: http://www.unicef.org/nutrition/index_iron.html. Accessed on August 1, 2011.
13. MI/UNICEF. Vitamin and mineral deficiency. A global progress report. 2004.
14. Proceedings from the national workshop on methodologies for assessment of vitamin A deficiency, iron deficiency anemia and iodine deficiency disorders, New Delhi, September 13-15, 2004. All India Institute of Medical Sciences, India, 2004.
15. WHO/UNICEF/UNU. Iron Deficiency Anemia: Assessment, Prevention and Control. Geneva, Switzerland: World Health Organization, 2001.
16. Zimmermann MB, Hurrell RF, Nutritional iron deficiency. Lancet, 370, 2007, 511-520.

17. A. El-Sayed, N.A. Boraie, F. A. Ismail, L.K. El-Khordagui, S. A. Khalil, Assessment of the pharmaceutical quality omeprazole capsule brands marketed in Egypt, Eastern Mediterranean Health Journal, 13(6), 2007, 1427-1437.
18. Tajnin Ahmed, Afia Ferdous, Subrata Kumar Biswas, Farhana Sharif, Assessment of dissolution profile of aceclofenac tablets available in Bangladesh. Stamford Journal of Pharmaceutical Sciences, 3(1), 2010, 1-3.
19. Dimple Pabla, Fatemeh Akhlaghi, Hossein Zia, A comparative pH-dissolution profile study of selected commercial levothyroxine products using inductively coupled plasma mass spectrometry, European Journal of Pharmaceutics and Biopharmaceutics, 72, 2009, 105–110.
20. Disintegration and Dissolution of Dietary Supplements, Revision Bulletin, March 2010. The United States Pharmacopeial Convention 2010.
21. Adams E, De Maesschalck R, De Spiegeller B, Heyden Y V, Smeyers-Verbeke J, Massart D L, Evaluation of dissolution profiles using principal component analysis. Int. J. Pharm, 212, 2001, 41-53.
22. Dressman J B, Amidon G L, Reppas C., Shah V P, Dissolution testing as a prognostic tool for oral drug absorption: immediate release dosage forms, Pharm. Res, 15, 1998, 11-22.
23. Skoug J W, Halstead G W, Theirs D L, Freeman J E, Fagam D T, Rohs B R, Strategy for the development and validation of dissolution tests for solid oral dosage forms, Pharm. Technol, 20, 1996, 58-72.

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