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Research Article

Design and Characterization of a Novel Sugar Free Formulation of Ferrous Gluconate in Oral Vial with Plunger and Tear Off Cap (VPTC)

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ABSTRACT

Aim of present study was to provide a sugar free formulation that contains ferrous gluconate in a suitable pharmaceutical dosage form which consists of a plunger containing ferrous gluconate closed with a tear-off cap and an umber vial contains solution which is prepared specially to dissolve ferrous gluconate. Final form is closed and securely fastened with a plastic cap. This dosage form combines advantages of liquid dosages with those of solid dosages. Product in its final form was evaluated for many parameters like appearance, pH of solution part and assay. Results of all tests were found within the limits. It could be concluded that oral vial with plunger and tear off cap may be used as an alternative dosage form for ferrous gluconate.

Keywords: Ferrous gluconate, VPTC, Stability, Oral vial.

INTRODUCTION

Ferrous gluconate is used as a source of iron for iron –deficiency anemia (Martindale, 2009)[1]. (C. A. Johnson and J. A. Thomas, 1954)[2] have referred to that It is generally held that ferrous iron is much more readily adsorbed than ferric and it is desirable therefore that any oxidation which may occur should be restricted to a minimum. Aqueous solutions of ferrous gluconate are stabilized by the addition of glucose (The Merck Index, 2001)[3]. So most pharmaceutical markets offer ferrous gluconate in the dosage forms tablets, capsules or oral solutions with sugar. Tablets remain popular as a dosage because of the advantages afforded both to the manufacturer (e.g. Simplicity and economy of preparation, stability, and convenience in packaging, shipping, and dispensing) and the patient (e.g. accuracy of dosage, compactness, portability, blandness of taste and ease of administration). Liquid dosage forms are useful for a number of reasons. They can be formulated for different routes of administration: orally, introduction into body cavities or external application the dose can easily be adjusted by dilution, making the oral liquid form ready to be administered to children or people unable to swallow tablets or capsules. Much has been written about the biopharmaceutical properties of solid dosage forms. Many researchers begin their absorption studies of drugs administered in solution to assess the bioavailability relative to tablets and capsules. Absorption occurs when drugs are in a dissolved state, thus it is frequently observed that the bioavailability of oral dosage forms decreases in the following order: aqueous solution > aqueous suspension> tablets or capsule(Remington, 2005)[4]. Our research presented the product in the dosage form oral vial with plunger and tear off cap (VPTC); this dosage form is used in Italy; it combines advantages of liquid dosages with those of solid dosages. (Ruba Kello, 2014)[5] has Shown the advantages of this dosage form. It is ideally suited to formulations that are not possible to present in the dosage form "oral solution" due to many reasons like stability. it is suitable for children and patients who have trouble swallowing; it has also fast absorption, good stability and accurate dosing. Use the dosage form as shown in figure 1, remove plastic cap, then

press the plunger into the vial shaking well then drink the whole solution. Our research presented the product as sugar free, it doesn't contain sugar at all. The FDA defines the label " Sugar Free " as a claim that may be used on a food that contains Less than 0.5 g sugars per RACC(Reference amounts customarily consumed) and per labeled serving.

MATERIALS AND METHODS

Tear-off caps, molded DED umber glass vial 10 ml, plastic caps were purchased from P.P.I (Italy), ferrous gluconate (BP) was purchased from Careth (India), sodium benzoate was purchased Chem-Base laboratories (China), sorbitol solution 70% was purchased from Roquette (France), Glycerin was purchased from Acidchem (Malasia), Sucralose was purchased from Zim (India), citric acid monohydrate was purchased from Weif and Ensign (China), sodium Citrate dehydrate was purchased from Changzhou (China), vanillin flavor was purchased from Jiaxing (China), peppermint oil flavor was purchased from Nectar (India), Strawberry flavor and soluble caramel color were purchased from Sensiet (Italy).

Ingredients included in the plungers

Ferrous gluconate was filled manually into plungers and closed with tear off caps, each cap was contained 335.72 mg of ferrous gluconate equivalent to 37.50 mg iron (II) . 5% an overage of ferrous gluconate was used to compensate for expected degradation during products shelf life. So the target fill weight is 352.51 mg. The ingredients included in the plungers are listed in table1.

Formulation of the solution part

To about 2.8 liter of distilled water its temperature about 45 C°, the following materials were added with continuous mixing. Sorbitol 70 %, glycerin, Sucralose, sodium benzoate, vanillin powder, peppermint oil, strawberry flavor, sodium citrate, citric acid monohydrate and soluble caramel color. Then the volume was completed to 3 liter with distilled water and solution was adjusted the pH 3.5–4.0. Solution was filled manually into 10 ml molded DED umber glass vials. The vials were closed with tear off caps and Final forms were closed and securely fastened with a plastic caps. The ingredients of the solution part are listed in table 2.

Batch size

3 liter of the solution part, each unit contains 352.51mg of ferrous gluconate in the plunger and 10 ml of the solution part in the vial.

pH evaluation

For the evaluation of pH, pH meter (Crison,Switzerland) calibrated with buffers, potassium tetraoxalate 0.05m, pH 1.68 and potassium biphthalate 0.05 m, pH 4.01. For each measurement, a 10 ml sample was collected and placed in an amber glass flask. The pH was measured by dipping the electrode directly into the solution, at room temperature.

Assay of Ferrous Gluconate

Dissolve 0.5 g of sodium hydrogen carbonate in a mixture of 30 ml of dilute sulphuric acid and 70 ml of distilled water. Weight the content of 20 tears off caps. Calculate the Average weight. When the effervescence stops, dissolve an equivalent to 1.00 g of Ferrous Gluconate with gentle shaking. Using 0.1 ml of ferroin as indicator, titrate with 0.1 M ammonium and cerium nitrate until the red color disappears. Each 1 ml of 0.1 M ammonium and cerium nitrate is equivalent to 5.585 mg of iron (II).

RESULTS AND DISCUSSIONS

Evaluation of the parameters of the Ingredients included in the plungers

The Ingredients included in the plungers, as shown in table 1, include ferrous gluconate as active ingredient, it was included in this part to get the maximum stability and to present the product as sugar free solution because aqueous solutions of ferrous gluconate are stabilized by the addition of glucose (The Merck Index, 2001)[3]. so the separation between ferrous gluconate in a plunger and the solution in a vial then dissolve it by pressing the plunger into the vial through tear off cap just before taking the medicine is the best choice to get stable and sugar free solution product. The Ingredients included in the plungers were evaluated for appearance and assay. Physical parameters of the Ingredients included in the plungers are shown in table 3. Appearance test results for the Ingredients included in the plungers were within the specification i.e. greenish–yellow granules. Assay was conducted and results was found within the limits. Results of assay were found as following: Trial 1: 7.0 ml of 0.1 M ammonium and cerium nitrate equivalent to 39.095 mg of iron (II) = 104.253 %. Trial 2: 6.9 ml of 0.1 M ammonium and cerium nitrate equivalent to 38.537 mg of iron (II) = 102.764 %. Trial 3: 6.9 ml of 0.1 M ammonium and cerium nitrate equivalent to 38.537 mg of iron (II) = 102.764 %.

Average = 103.259 %, SD = 0.858 and RSD = 0.831 %. Results are shown in table 4.

Evaluation of the parameters of the solution in the vial

The ingredients of the solution in the vial as shown in table 2 include Sorbitol 70% as sweetening agent and vehicle in the formulation, Glycerin as viscosity increasing agent and cosolvent, sucralose as sweetening agent, Sodium benzoate as antimicrobial preservative, citric acid monohydrate and sodium citrate as buffering agent, Soluble caramel color as coloring agent, Vanillin powder, peppermint oil and Strawberry flavor as flavoring agent (Handbook of Pharmaceutical Excipients, 2009)[6]. Ferrous gluconate is freely but slowly soluble in water (British Pharmacopoeia, 2011)[7] and to overcome the problem of slow solubility of it in water, we chose also to use glycerin as cosolvent. Because ferrous gluconate is soluble in glycerin (Sax NI, 1975)[8]. Oxidation of ferrous gluconate solutions is retarded and stability improved by buffering to pH of 3.5 to 4.5 with citrate buffer (Osol, A. and J.E. Hoover, et al, 1975)[9]. we consider this value although the contact time between ferrous gluconate in the plunger and solution in the vial is very short but choose the value to be 3.5 - 4.0 to get tasty taste and to present the product in an optimal specifications. An umber vial was used to protect ferrous gluconate in the tear off cap and plunger completely from light because ferrous gluconate is affected by light (Osol, A. and J.E. Hoover, et al, 1975)[9]. The solution in the vial was evaluated for its appearance and it was within the specification i.e. caramel colored solution. Results are shown in table 4.

CONCLUSION

The results of our investigation demonstrated that oral vial with plunger and tear off cap can be used as an alternative dosage form for ferrous gluconate and allowed to present ferrous gluconate as sugar free solution. Therefore, the separation between ferrous gluconate and the solution then dissolve it just before taking the medicine is the best choice to get stable and sugar free solution product.

RECOMMENDATION

- The general and suitable specifications of granules which are filled into the plungers by filling machine will be determine in the next article.
- The formulation should be subjected to stability studies as per ICH guidelines at temperatures and humidity of 40 C°/ 75% RH ± 5% RH for six months (accelerated conditions) and at 25°C ± 2°C/60% RH ± 5% RH (long-term condition).

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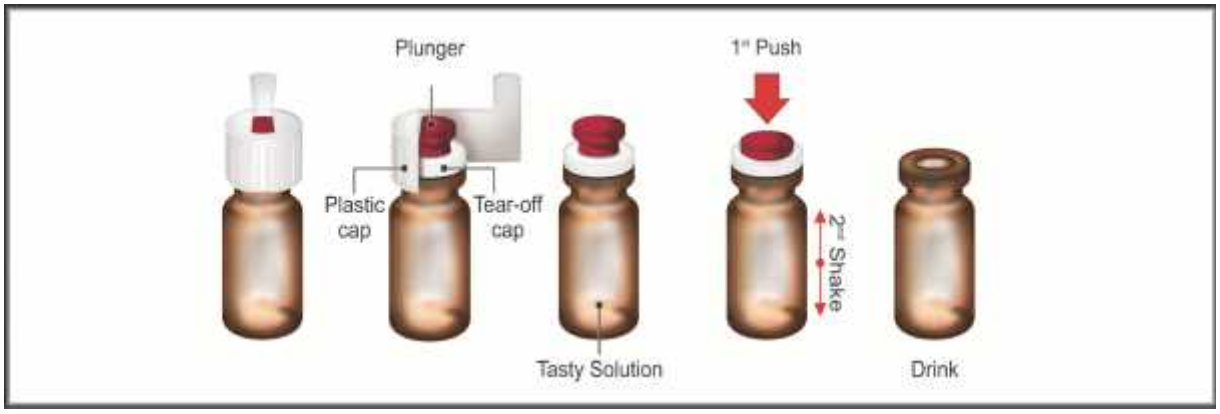

Fig 1
how to use the dosage form (VPTC)

Table 1
Ingredients included in the plungers

Ingredients	Theoretical amounts mg/unit	Actual amounts mg/unit
Ferrous gluconate	335.72 mg equivalent to 37.50 mg of iron (II)	335.72+ (overage 5%*) = 352.51

*5 % an overage of ferrous gluconate was used to compensate for expected degradation during products shelf life.

Table 2
ingredients of the solution part

Ingredients	**Quantity g / unit**
Sorbitol 70%	2.40000
Sucralose	0.00500
Sodium Benzoate	0.02500
Citric Acid monohydrate	0.03500 Or to get the required pH
Sodium Citrate	0.00223
Vanillin powder	0.00150
Peppermint oil	0.00030
Strawberry liquid	0.05000
Glycerin	1.60000
Soluble caramel color	0.00320
Purified water	Up to 10.00000 ml

Table 3
Physical parameters of the formulation

Physical parameters	**Limits**	**Reference**
Appearance of the Ingredients included in the plungers	greenish–yellow granules	In house specification
Appearance of the solution part	caramel colored solution	In house specification
pH of solution part	3.5-4.0	In house specification
Assay	93.0-107.0 %	In house specification

Table 4
Results of initial values of the formulation

Test	Initial values
Appearance of the Ingredients included in the plungers	greenish–yellow granules
Appearance of the solution part	caramel colored solution
pH of solution part	3.8
Assay	103.259 %

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