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Manufacturing of New Formulations of Ferrous Fumerate by Direct Compression Method

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ABSTRACT

In the present study new formulations of Ferrous Fumerate was manufactured by direct compression method using Talc, magnesium stearate. The present study is divided into two phases. In the first phase new formulation of Ferrous Fumerate was prepared by direct compression method . In the 2nd phase of present study new formulation is evaluated for their average weight variation, friability, hardness and other parameters like disintegration. The results showed that all parameters of new formulations are in accordance with the BP/USP limits ands. Weight variation, thickness, disintegration, are in accordance with BP/USP limits but hardness and friability was not in compliance with BP/USP limits.

Keywords: Ferrous Fumerate, Hardness, Thickness Friability, Disintegration

INTRODUCTION

Iron is an essential mineral nutrient that has a key physiological role and is required for numerous functions such as ATP production, DNA replication and oxygen transport. In normal healthy humans, the main source of iron loss is through sloughed gastrointestinal mucosal cells and shedding of skin. [1] Iron deficiency is one of the most common nutritional deficiencies throughout the world, and the most severe form manifests as anemia. Both iron deficiency and anemia have severe repercussions on, physical capacity for work, immune function and attention span [2-4].

Females are at high risk of iron deficiency due to regular menstrual blood loss and the increase of iron demand during pregnancy. Use of Non steroidal anti-inflammatory drugs and Peptic ulcer disease are common causes of blood (and therefore iron) loss. Anemia may be secondary to a diet lacking other micronutrients essential for iron metabolism such as vitamins C, A, B and folate, or to in flammatory

or infectious diseases. [5-9] The standard treatment involves supplementation with liquid or solid iron supplement preparations, usually of ferrous salt such as ferrous gluconate ferrous sulphate, or ferrous fumarate [10].

Ferrous fumarate is soluble in dilute acid but poorly soluble in water and is well absorbed as ferrous sulphate . It has an iron content of 32.87 %.(Hurrel et al., 1989; 1991; 2000).[11-13] In infants, iron absorption from ferrous fumarate is significantly higher than iron absorbed from ferric pyrophosphate

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(Davidsson et al., 2000; Meredith et al., 2003).[14,15]According to the British pharmacopoeia, ferrous fumarate tablets have been manufactured in combination with folic acid or alone, usually folic acid 0.1–0.5 mg and ferrous fumarate 150–200 mg.

Wet granulation methods used for tablet formulation are multistep and time consuming processes . However, in direct compression method tablets is compressed directly from mixtures of the drug and excipient without any preliminary treatment (British pharmacopoeia, 2004).[16] The direct-compression method provides high efficiency and has advantages over other manufacturing processes for tablets and (Zhang et al., 2003). [17] Direct compression is simple and more economical, it reduces the total time and manufacturing requirements, while wet granulation not only increases the processing time but also has certain limits imposed by thermolability and moisture sensitivity of the active pharmaceutical ingredient(s).Therefore, the pharmaceutical industry is now focusing more on the direct-compression process (Beyer et al., 2001; Yasmeen et al., 2005) [18-19]. The unnecessary exposure of any drug to moisture and heat can never be justified [20]. Tablets produced by the direct compression method give lower microbial levels than those prepared by the wet-granulation method (Ibrahim & Olurinola, 1991). A simple formula is composed of an active ingredient, binding agent, diluent, and a lubricant (Martino et al.,2004). [21]

METHODOLOGY

MATERIALS

Ferrous Fumerate, lactose, magnesium stearate, Talc and starch. All reagents used were analytical grade. Ferrous fumarate (B.P grade 93-101%) was used as the standard in quantitative analysis.

MANUFACTURING OF NEW FORMULATIONS: Check all raw materials on weighing order that are to be used in the manufacturing procedure for name, quantity, code number and appearance of material at the time of use in manufacture. Following steps are involved:

1. Transfer all ingredients into suitable polyethylene bag and mix for 15 minutes. If lumps are present, sieve it through mesh no.16.

2. Take out granules in suitable labeled container lined with polyethylene bag.

3. Adjust compression machine with die and punches.

TABLET SPECIFICATIONS

All parameters (wt. variation, thickness, hardness,friability disintegration,) of new formulations were carried out.

WEIGHT VARIATION TEST: Weight variation test of above mentioned tablets proved strictly that all the tablets were in accordance to the BP/USP requirements that not more than two tablets out of 20 tablets should cross ±7.5 % deviation. Similarly their statistical control chart(shewart chart)shows that new formulations of Ferrous Fumerate tablets were in range of the upper and lower limits.

THICKNESS TEST: Thickness of new formulations including average , standard deviation, upper and lower limits are in accordance with BP/USP.

HARDNESS: Hardness test of new formulations of Ferrous Fumerate tablets was found to be in conjunction with the stated guidelines as given in BP/USP. Similarly the official range of hardness stated in BP/USP is not less than 4.00 Kg of pressure is required to break any tablets.

FRIABILITY TEST: The phenomenon where by tablet surfaces are damaged and/or show evidence of lamination or breakage when subjected to mechanical shock or attrition.(British Pharmacopoeia 2000).Friability of tablets was not less than 1%. Therefore it is not compliance with the BP/USP standards.

DISINTEGRATION TEST: Disintegration test was

conducted on new formulation of Ferrous Fumerate tablets. The official range in BP/USP for uncoated tablets is not more than 15> mins. Results of all showed that our tablets were in accordance to BP/USP.

RESULTS AND DISCUSSION

WEIGHT VARIATION TEST: Wt. variation test of new formulation tablets proved statistically that all the tablets were in accordance to the BP/USP requirements (Table 1).

THICKNESS TEST: Thickness of all tablets of new formulation are in accordance with BP/USP (Table-2-3)

HARDNESS TEST: Hardness test of new formulation was found to not be in conjunction with the stated guidelines as given in BP/USP (Table-4-5).

FRIABILTY TEST: Friability of new formulation tablets was not less than 1%. Therefore it is not compliance with the BP/USP standards. It's data is given in (Table-6).

DISINTEGRATION TEST: was conducted on new formulation and we know the official range given in BP/USP is not >15 minutes. And our results were in accordance to BP/USP (Table-7)

Table 1: Statistical Weight Variations

no. of tablets	Average (Gm)	Standard deviation	Upper limit (X+3S)	Lower limit (X-3S)
20	0.50355	0.008964228	0.53044	0.4766

Table 2: Thickness of 10 tablet

Tablets	1	2	3	4	5	6	7	8	9	10
Thickness	4.0	4.3	4.3	4.3	4.4	4.4	4.3	4.4	4.4	4.4

Table 3: Statistical Thicknes

no. of tablets	Average Thickness (mm)	Standard deviation	Upper limit (X+3S)	Lower limit (X-3S)
10	4.32	0.1166	4.669	3.9702

Table 4: Hardness of 10 tablets from the optimised formulation

No of tablets.	Result (Kg)	BP/USP Specification	Deviation from BP/USP Specification
10	1.564	Not less than 4.00 KG	Not Within specified limit

Table 5: Statistical Hardness

no. of tablets	Average (Kg)	Standard deviation	Upper limit (X+3S)	Lower limit (X-3S)
10	1.564	0.512357	3.101	0.0269

Table 6: Friability Test

No of tablets	Result (%)	BP/USP Specification	Deviation from BP/USP Specification
10	3.273	Not more than1%	Not in specified limit

Table 7: Disintegration Test

No of tablets	Disintegration time (min:sec)	BP/USP Specification	Deviation from BP/USP Specification
10	10 min 48 sec	Not more than 15min	Within specified limit

DISCUSSION

In the present study new formulation of Ferrous Fumerate was manufactured . For manufacturing of

new formulations Direct compression method method was used. Direct Compression has the advantage over other metods in that it is a simple and less time consuming process. In addition the method is also economical. All parameters of(wt. variation, thickness, hardness,disintegration) of new formulation were carried out and results showed that they are in accordance with the BP/USP limits. In the pharmaceutical industry, hardness of the tablets is an important parameter. Tblets must have sufficient ability to survive the handling forces during packaging and shipping. However, if the hardness exceeds a certain limit, it increases the disintegration time, which ultimately affects the bioavailability (Lachman et al., 1976) . In our trials, hardness varied from 0.40 kg to 236 kg. The average hardness for the optimised formulation was found to be 1.564 Kg.Friability is another important parameter that is related to hardness. According to the U.S.P the allowed limit of friability is not more than 1% of weight Loss. In our trials Disintegration time was found to be 10 minutes and 48 seconds which is within specified BP\USP limit.

CONCLUSION

All parameters (wt. variation, thickness, hardness, friability, disintegration,) of new formulations were carried out and results showed that wt. variation, thickness, disintegration, are in accordance with BP/USP limits but hardness and friability wan not in compliance with BP/USP limits. So we conclude that we prepare this preparation with folic acid to improve our formulation and or by using other method. But advantage of this method is that this method is quite simple, less time consuming and economical therefore we use this method.

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