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Original Research Article

FORMULATION DEVELOPMENT AND EVALUATION OF FILM-COATED IMMEDIATE RELEASE TABLETS OF FERROUS ASCORBATE AND FOLIC ACID BY WET GRANULATION TECHNIQUE

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Abstract: Iron deficiency anaemia remains a major global health concern, particularly among women and pediatric populations. Ferrous ascorbate and folic acid are commonly prescribed together due to their synergistic role in erythropoiesis; however, challenges such as metallic taste, poor aqueous solubility, stability issues, and gastrointestinal intolerance affect patient compliance. The present study was undertaken to develop and evaluate film-coated immediate release tablets of ferrous ascorbate and folic acid using the wet granulation technique to improve oral delivery, taste masking, and stability. Pre-formulation studies were carried out to characterize the drugs and assess powder flow properties. Tablets were prepared in multiple formulation trials, optimized, and subsequently film-coated. The prepared tablets were evaluated for physical appearance, weight variation, hardness, friability, disintegration time, content uniformity, in-vitro dissolution, and stability studies as per pharmacopeial guidelines. The optimized formulation (WGM3) demonstrated satisfactory mechanical strength, rapid drug release, uniform content, and stability under accelerated conditions. The study concludes that wet granulation followed by film coating is a suitable and effective approach for developing stable and patient-acceptable immediate release tablets of ferrous ascorbate and folic acid.

Keywords: Ferrous ascorbate, Folic acid, Wet granulation, Film-coated tablets, Immediate release

INTRODUCTION

Iron deficiency anaemia is one of the most common nutritional disorders worldwide and represents a major public health problem, particularly among women of reproductive age, pregnant women, children, and adolescents1. It is characterized by reduced haemoglobin levels due to inadequate iron availability, leading to fatigue, impaired cognitive function, reduced work capacity, and compromised immunity. Nutritional deficiencies, poor absorption, increased physiological demand, and chronic blood loss are the primary causes of iron deficiency anaemia, especially in developing countries. Hence, effective and patient-compliant oral iron therapy is essential for its prevention and management2,3.

Ferrous ascorbate is a preferred iron salt due to its high elemental iron content and superior bioavailability. The presence of ascorbic acid enhances iron absorption by maintaining iron in the ferrous form and improving its solubility in the gastrointestinal tract. Folic acid plays a complementary role in erythropoiesis by supporting DNA synthesis and red blood cell maturation. Combined administration of ferrous ascorbate and folic acid is therefore widely recommended to correct nutritional anaemia and promote effective haemoglobin synthesis2,4.

However, conventional oral iron formulations often suffer from formulation and patient-related limitations such as metallic taste, poor palatability, instability, and gastrointestinal irritation, which negatively affect patient compliance. Additionally, folic acid is sensitive to light and moisture, requiring careful formulation to ensure stability. Immediate release tablets remain the most convenient and cost-effective dosage form, but challenges related to flowability, content uniformity, and compressibility must be addressed5.

Wet granulation is a widely used tablet manufacturing technique that improves powder flow, uniform distribution of low-dose drugs, and mechanical strength of tablets. Film coating further enhances product quality by masking unpleasant taste, improving appearance, and protecting moisture- and oxygen-sensitive drugs. Therefore, the present study focuses on the development and evaluation of film-coated immediate release tablets of ferrous ascorbate and folic acid using the wet granulation technique to achieve optimal stability, rapid drug release, and improved patient compliance5,6.

Objectives

1. To carry out pre-formulation studies of ferrous ascorbate and folic acid.
2. To develop immediate release tablets using the wet granulation technique.
3. To evaluate the formulated tablets for physicochemical and in-vitro performance.
4. To study the stability of the optimized film-coated formulation.

MATERIAL AND METHODS

Ferrous ascorbate and folic acid were used as active pharmaceutical ingredients. Lactose monohydrate and maize starch were employed as diluents. Croscarmellose sodium served as a superdisintegrant. Polyvinyl pyrrolidone K-30 was used as a binder. Sodium metabisulfite acted as an antioxidant, sodium lauryl sulfate as a wetting agent, colloidal silicon dioxide and talc as glidants, magnesium stearate as a lubricant, and isopropyl alcohol as a granulating solvent. Film coating materials included Instamoist Shield (seal coat) and Opadry (color coat).

Methods

- **Preparation of Tablets:** Immediate release tablets of ferrous ascorbate and folic acid were prepared by the wet granulation technique. Precisely weighed quantities of ferrous ascorbate, folic acid, lactose monohydrate, maize starch, croscarmellose sodium, sodium metabisulfite, and colloidal silicon dioxide were blended uniformly to obtain a homogenous powder mixture. Granulation was carried out by slowly adding a binding solution of polyvinyl pyrrolidone K-30 prepared in isopropyl alcohol with continuous mixing until a cohesive wet mass was formed[7,8].

Figure 1: Prepared Granules and Lubricated granules by wet granulation technique

- The wet mass was passed through a suitable sieve to obtain granules, which were then dried to achieve optimum moisture content. Dried granules were re-sieved to obtain uniform particle size. Extragranular excipients such as croscarmellose sodium, sodium lauryl sulfate, talc, colloidal silicon dioxide, and magnesium stearate were blended with the granules to improve disintegration, flow, and lubrication. The final blend was compressed into tablets using a rotary tablet compression machine fitted with capsule-shaped punches[8].
- The compressed tablets were subjected to seal coating using a non-aqueous coating system to protect the tablet core and minimize moisture interaction. Subsequently, color coating was performed using an aqueous film-coating system to improve appearance, taste masking, and patient acceptability[9].

- **Evaluation of Granules:** The prepared granules were examined for bulk density and tapped density using graduated cylinder methods. Flow characteristics were assessed by calculating Carr's index and Hausner's ratio. Particle size distribution was determined by sieve analysis to ensure uniform granule size and satisfactory flow during compression[10,11].
- **Evaluation of Tablets:** The prepared tablets were visually inspected for color, shape, surface texture, and overall appearance. Tablet thickness was measured using a vernier caliper, while weight variation was determined by weighing individual tablets and comparing them with the average tablet weight. Mechanical strength was evaluated by hardness testing, and resistance to abrasion was assessed using a friability apparatus[12,13].

Disintegration time was determined using a standard disintegration test apparatus in 0.1 N hydrochloric acid maintained at 37 ± 0.5 °C to confirm immediate release characteristics. Drug content uniformity and percent assay were performed by dissolving tablets in a suitable solvent followed by spectrophotometric analysis to ensure accurate and uniform dosing of both ferrous ascorbate and folic acid[11,14].

Drug release behavior was studied using USP Type II (paddle) dissolution apparatus operated at 50 rpm in 0.1 N hydrochloric acid. Samples were withdrawn at predetermined time intervals and analyzed spectrophotometrically to calculate cumulative percentage drug release[15-17].

The optimized formulation was subjected to accelerated stability testing at 40 °C ± 2 °C and 75% ± 5% relative humidity. Tablets were periodically evaluated for physical appearance, assay, and dissolution performance to assess formulation stability[18,19].

RESULTS AND DISCUSSION

- **Pre-Formulation and Pre-Compression Studies:** Ferrous ascorbate and folic acid exhibited acceptable physical characteristics suitable for tablet formulation. Pre-compression studies of granules indicated good flow and compressibility, especially for the optimized formulation (WGM3), ensuring uniform die filling and reproducible tablet weight.

Table 1: Pre-Compression Parameters of Optimized Formulation (WGM3)

Sr. No.	Parameter	Observation
1	Bulk density (g/cm³)	0.4708
2	Tapped density (g/cm³)	0.6000
3	Carr's index (%)	21.46
4	Hausner's ratio	1.27

- **Post-Compression Evaluation**

All formulations complied with pharmacopeial limits. The optimized batch (WGM3) showed superior hardness, acceptable friability, uniform drug content, and rapid disintegration.

Figure 2: Compressed tablet by WGT and seal coated by NAC

*WTG – Wet Granulation Technique, *NAC -Non-Aqueous Coating

Table 2: Physical Evaluation of Optimized Tablets (WGM3)

Sr. No.	Parameter	Result
1	Average weight (mg)	1350
2	Thickness (mm)	6.60–6.68
3	Hardness (kg/cm²)	10.5–11.5
4	Friability (%)	0.62
5	Disintegration time (min)	8–9

- **Content Uniformity and Assay**

Both ferrous ascorbate and folic acid content were within acceptable limits, indicating uniform distribution of drugs.

Table 3: Content Uniformity and Assay of WGM3

Sr. No.	Drug	Result
1	Ferrous ascorbate	103.1%
2	Folic acid	196.6%

- **In-Vitro Dissolution Study**

The optimized formulation showed rapid and complete drug release, confirming immediate release behavior.

Table 4: In-Vitro Drug Release of WGM3

Sr. No.	Time (min)	% Drug Released
1	15	72.4
2	30	88.6
3	45	101.5

- **Stability Study**

No significant changes were observed in physical appearance, drug content, or dissolution profile during accelerated stability testing.

Table 5: Stability Study Summary (WGM3)

Sr. No.	Parameter	Observation
1	Appearance	No change
2	Assay	Within limits
3	Dissolution	Complies
4	Microbial limits	Passed

CONCLUSION

Film-coated immediate release tablets of ferrous ascorbate and folic acid were successfully developed using the wet granulation technique. The optimized formulation (WGM3) demonstrated satisfactory mechanical strength, rapid disintegration, complete drug release, and stability under accelerated conditions. Film coating effectively masked metallic taste and enhanced product stability. The developed formulation is suitable for the management of iron deficiency anemia with improved patient compliance.

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Conflict of Interest

The authors declare no conflict of interest.

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