Full Length Research Paper

Formulation and evaluation of gastro-retentive floating tablets of griseofulvin

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About 50% of an oral dose of griseofulvin passes through the gastro-intestinal tract unabsorbed and is excreted in faeces. Short residence time of the low soluble griseofulvin, in stomach and small intestine, limits its dissolution. Griseofulvin is highly soluble in acidic pH, and so a gastro-retentive floating matrix system was developed to control dissolution rate and thereby enhance solubility to develop an improved and convenient dosage form. Preformulation studies included selection of excipients and evaluation of compatibility with griseofulvin. Tablets were prepared by wet granulation technique with varying ratios of Methocel™, Accurel MP and Polyvinylpyrrolidone as determined by Design Expert software. Buoyancy capability and dissolution studies were carried out to assess the influence of the tablet components. Tablets that float immediately upon contact with dissolution medium and continue floating for over 12 h were achieved with at least 28% of Accurel MP. An increase in tablet hardness reduced the rate of griseofulvin release only up to 120 min. Methocel™ had the most significant influence on griseofulvin release, with an indirect proportion to the rate of griseofulvin release. Using Design Expert software, optimized formulation was achieved with 1% Polyvinylpyrrolidone, 30% Methocel™, 60% Accurel MP and hardness ranging between 8 and 9 N. Tablets produced floated immediately upon contact with the medium and remained floating for at least 12 h. Griseofulvin was released from the optimized tablets in a near zero order fashion, with a total of 80.8% griseofulvin released at the end of the 12-h dissolution test period.

Key words: Griseofulvin, gastro-retentive, floating tablets.

INTRODUCTION

Gastro-retentive dosage forms are systems that retain in the stomach for a sufficient time interval against all the physiological barriers and release active moiety in a controlled manner (Foda, 2011). Gastric retention
Griseofulvin has been observed to be highly soluble in acidic pH, making it a suitable candidate for gastro-retentive formulation in a bid to control dissolution rate and thereby enhance solubility and absorption (Persson et al., 2005). This study formulates floating tablets of griseofulvin using polypropylene foam powder (Accurel®), a low density polymeric carrier. Addition of Accurel® results in a matrix with a density less than 1 g/cm³, allowing tablets to float on gastric juice (Al-achi et al., 2013).

**MATERIALS AND METHODS**

Griseofulvin (Aspen Pharmacare, South Africa) was the active ingredient. Accurel MP (Membrana, Germany) was used as a low density polymer. Hydroxy Propyl Methyl Celulose (Methocel™ K100, Colorcon, England) was selected as the rate controlling polymer. Polyvinylpyrrolidone (PVP K-30, Fluka, United States) was used as a binder. Magnesium stearate (BDH Chemicals Ltd, England) was chosen as lubricant and ethanol (Sigma Aldrich, South Africa) was used as a granulating agent.

**Compatibility studies**

Compatibility studies were carried out to investigate the potential interactions between drug and excipients before formulation. A DSC-60 Shimadzu (Kyoto, Japan) instrument was used to record the DSC thermograms. Thermograms obtained in DSC were analysed based on the changes in appearance, disappearance or shift of endothermic or exothermic peaks of griseofulvin-excipient mixtures as compared to the pure griseofulvin and excipients (Heljo, 2007).

**Preparation of floating tablets of griseofulvin**

A total of 25 runs, Table 1, were generated using Design Expert Software 9.0, specifically varying polymer ratios, binder concentration and compression force, as shown in Table 2. Magnesium stearate was kept at 1% for all the formulations. Tablets containing 100 mg of griseofulvin were prepared by wet granulation technique. Griseofulvin and all the other excipients were weighed accurately for a batch size of 200 tablets. To avoid segregation of materials, Accurel MP and other excipients were separately passed above powder blend, 60% ethanol (granulating agent) was added and mixed thoroughly with a bowl and stand mixer (Kenwood, United Kingdom) mixer for 10 min to form a homogeneous mixture. To the above powder blend, 60% ethanol (granulating agent) was added followed by mixing until the end point of granulation was observed. The wet granules were then passed through an 850 μm sieve, transferred onto a stainless steel plate covered with aluminium foil and placed in an oven. The granules were dried at 40°C (Labotec, South Africa) until the moisture content was less than 1.5%. The dried granules were transferred into a 1000 ml plastic beaker and mixed thoroughly with a wetting agent such as sodium lauryl sulphate or benzalkonium chloride. The resulting material is characterized as 'microsized' crystals of griseofulvin (Desai and Soon-Shiong, 2003). This has influenced griseofulvin to be commercially available as tablets containing 250 mg or 500 mg microsize or 125 mg or 165 mg ultramicrosize crystals of griseofulvin. It is also available as capsules containing 250 mg microsize griseofulvin and as an oral suspension containing 125 mg/5 ml microsize griseofulvin. However, micronization is costly and involves many steps. Griseofulvin has been observed to be highly soluble in acidic pH, making it a suitable candidate for gastro-retentive formulation in a bid to control dissolution rate and thereby enhance solubility and absorption (Persson et al., 2005). This study formulates floating tablets of griseofulvin using polypropylene foam powder (Accurel®), a low density polymeric carrier. Addition of Accurel® results in a matrix with a density less than 1 g/cm³, allowing tablets to float on gastric juice (Al-achi et al., 2013).

Pre-compression studies

Pre-compression studies were done to assess the flow properties of granules before compression. Bulk density, tapped density, angle of repose, loss on drying and compressibility of the granules were analysed before compression of the tablets, as per methods described by Wells and Aulton (2007).

Post-compression studies

Tablets were evaluated for the post-compression parameters which include physico-chemical parameters like weight variation, thickness, diameter, hardness, friability, in-vitro drug release (dissolution) and assay.

Buoyancy studies

Buoyancy test was performed as per the method of Taghizadeh et al. (2013). To determine the floating lag time, 6 tablets were put in
Table 1. Composition of Griseofulvin floating tablet formulations generated by Design Expert Software Version 9.0.

| Run | Methocel (mg) | Accurel mp (mg) | PVP k – 30 (%) | Hardness (N) |
|-----|---------------|-----------------|----------------|--------------|
| 1   | 65.500        | 100.000         | 2.080          | 10.000       |
| 2   | 25.000        | 91.375          | 1.000          | 9.000        |
| 3   | 72.625        | 25.000          | 2.17483        | 9.000        |
| 4   | 25.000        | 80.500          | 2.460          | 12.000       |
| 5   | 25.000        | 100.000         | 3.000          | 8.000        |
| 6   | 56.741        | 62.500          | 2.000          | 8.000        |
| 7   | 65.500        | 100.000         | 2.080          | 10.000       |
| 8   | 100.000       | 25.000          | 3.000          | 8.000        |
| 9   | 64.000        | 65.125          | 3.000          | 10.000       |
| 10  | 73.000        | 92.500          | 1.000          | 12.000       |
| 11  | 56.741        | 62.500          | 2.000          | 8.000        |
| 12  | 85.000        | 25.000          | 1.000          | 8.000        |
| 13  | 25.750        | 26.875          | 1.000          | 11.000       |
| 14  | 25.000        | 25.000          | 2.750          | 9.000        |
| 15  | 100.000       | 51.340          | 1.700          | 11.000       |
| 16  | 100.000       | 100.000         | 3.000          | 12.000       |
| 17  | 100.000       | 98.125          | 3.000          | 8.000        |
| 18  | 100.000       | 95.875          | 1.693          | 11.000       |
| 19  | 72.250        | 25.000          | 2.750          | 12.000       |
| 20  | 100.000       | 51.340          | 1.700          | 11.000       |
| 21  | 25.000        | 100.000         | 1.220          | 12.000       |
| 22  | 64.000        | 65.125          | 3.000          | 10.000       |
| 23  | 64.000        | 65.125          | 3.000          | 10.000       |
| 24  | 100.000       | 100.000         | 1.000          | 8.000        |
| 25  | 54.513        | 52.375          | 1.724          | 12.000       |

Table 2. Factors and levels for factorial design.

| Factor                   | Lower | Level   |
|--------------------------|-------|---------|
| X₁ Methocel (mg)         | 0     | 100     |
| X₂ Accurel Mp (mg)       | 0     | 100     |
| X₃ PVP k- 30 (%)         | 1     | 3       |
| X₄ Tablet hardness (N)   | 8     | 12      |
| Dependent variable 1     | Lag time |         |
| Dependent variable 2     | Floating time |      |
| Dependent variable 3     | Drug release |        |

100 mL of 0.1 N HCL in a beaker, and the time required for each tablet to rise to the surface was measured. Then, the duration of each tablet that remained on the surface was determined as total floating time. Mean and standard deviation were calculated for the measurements obtained from 6 tablets.

Assay of tablets

Assay of the manufactured tablets was performed to assess the amount of griseofulvin contained, following BP method (BP, 2019). Twenty tablets per formulation run were weighed and powdered. To a quantity of powder containing 35 mg of griseofulvin, 60 ml of ethyl acetate was added. The solution was mixed and heated to 60°C with shaking for 20 min. The solution was allowed to cool and was diluted to 100 ml with ethyl acetate. Afterwards, the solution was centrifuged and two 5 ml aliquots of the clear supernatant liquid were transferred into separate 100 ml graduated flasks. To the first flask, 5 ml of 2 M methanolic methanesulfonic acid was added and the solution was allowed to stand at 20°C for 30 min. The solution
was diluted to 100 ml with methanol and labelled solution A. The contents of the second flask were diluted to 100 ml with methanol and labelled solution B. To a third flask, 5 ml of 2 M methanolic methanesulfonic acid was added and diluted to 100 ml with methanol. This solution was labelled solution C. The absorbance of each solution was measured at 266 nm. The content of griseofulvin was calculated from the difference between the absorbance obtained with solution A and the sum of the absorbances obtained with solutions B and C and from the difference obtained by repeating the operation using 35 mg of griseofulvin BPCRS (British Pharmacopoeia Catalogue Reference Standard, 2014) in place of the powdered tablets and from the declared content of griseofulvin in griseofulvin BPCRS. Acceptance criteria used: 95.0 - 105.0%.

In-vitro analysis of griseofulvin release from the floating tablets

A dissolution apparatus 2 (paddle apparatus) was used in 900 ml of dissolution medium containing 0.1 N hydrochloric acid and 4% sodium lauryl sulphate at 37 ± 0.5°C and a pH of 1.2. Rotation speed of paddle used was 100 rpm (USP, 2016). Samples (5 ml) were taken from the dissolution apparatus at set time intervals: 30, 60, 90, 120, 180, 240, 360, 480 and 720 min. The amount of griseofulvin dissolved was determined by employing a UV spectrophotometer at 296 nm. A standard calibration curve of griseofulvin in 0.1 N hydrochloric acid with 4% sodium lauryl sulphate was plotted and regression coefficient calculated to validate method.

RESULTS AND DISCUSSION

Compatibility studies

A comparison of the thermogram of griseofulvin to that of 1:1 (w/w) griseofulvin/Accurel MP mixture showed no significant change in enthalpy peak shape or onset, indicating the compatibility of griseofulvin with Accurel MP, as shown in Figure 1. No significant change was observed in the thermoanalytical profiles of griseofulvin and Methoce™, as shown in Figure 2. As well, no significant changes were observed in the endothermic peaks of griseofulvin and magnesium stearate (Figure 3). Magnesium stearate is the most common lubricant used in tableting. It is a white powder, which is insoluble in nature. Magnesium stearate reduces both wall friction and internal friction of powder and granules. This makes materials (powder/granules) glide better and be non-adherent, thereby enhancing flowability (Li and Wu, 2014).

The thermogram of griseofulvin/PVP k-30 mixture showed a slight broadening of the endothermic peak of griseofulvin, indicating a low degree of incompatibility between griseofulvin and PVP k-30 (Figure 4).

Polyvinylpyrrolidone, also known as povidone is a binder used in both wet and dry granulation. Polyvinylpyrrolidone facilitates agglomeration of powder material to form granules of desired hardness and size (Cantor et al., 2008).

Pre-compression studies

Table 3 shows results of pre-compression studies. All formulations had values of Carr's Index and Hausner ratios of less than 20.0 and 1.25, respectively. Run 2 had
Figure 2. Thermograms of griseofulvin, Methocel™ and 1:1 (w/w) griseofulvin / Methocel™ mixture.

Figure 3. Thermograms of griseofulvin, magnesium stearate and 1:1 (w/w) Griseofulvin / magnesium stearate.
Figure 4. Thermograms of griseofulvin, PVP-k30 and 1:1 (w/w) griseofulvin/PVP-k30 mixture.

Table 3. Pre-compression parameters of Griseofulvin tablets formulation runs.

| Batch | BD (g/ml) | TD (g/ml) | CI (%) | H    | C     | AR (ɵ) ± S.D | FP | LOD (%) |
|-------|-----------|-----------|--------|------|-------|-------------|----|---------|
| Run 1 | 0.18      | 0.27      | 17.73  | 1.18 | Fair  | 37.4 ± 1.3  | Fair | 0.43    |
| Run 2 | 0.20      | 0.21      | 7.59   | 1.08 | Excellent | 32.2 ± 1.4 | Good | 0.21    |
| Run 3 | 0.22      | 0.26      | 18.00  | 1.18 | Fair  | 34.5 ± 1.5  | Good | 0.32    |
| Run 4 | 0.18      | 0.21      | 14.89  | 1.18 | Fair  | 32.2 ± 0.9  | Good | 1.65    |
| Run 5 | 0.17      | 0.19      | 10.76  | 1.12 | Good  | 30.5 ± 0.7  | Good | 2.71    |
| Run 6 | 0.19      | 0.22      | 13.69  | 1.16 | Good  | 32.8 ± 1.4  | Good | 0.54    |
| Run 7 | 0.18      | 0.22      | 19.56  | 1.24 | Fair  | 33.6 ± 1.3  | Good | 3.43    |
| Run 8 | 0.23      | 0.27      | 16.67  | 1.20 | Fair  | 33.3 ± 0.8  | Good | 2.21    |
| Run 9 | 0.18      | 0.21      | 12.35  | 1.14 | Good  | 33.9 ± 2.1  | Good | 0.25    |
| Run 10| 0.18      | 0.21      | 12.50  | 1.14 | Good  | 32.4 ± 0.6  | Good | 1.58    |
| Run 11| 0.19      | 0.22      | 13.57  | 1.16 | Good  | 34.4 ± 0.7  | Good | 2.73    |
| Run 12| 0.26      | 0.30      | 12.69  | 1.15 | Good  | 34.9 ± 1.4  | Good | 4.65    |
| Run 13| 0.21      | 0.25      | 13.72  | 1.16 | Good  | 34.4 ± 0.7  | Good | 2.54    |
| Run 14| 0.22      | 0.27      | 19.35  | 1.24 | Fair  | 33.8 ± 1.9  | Good | 3.44    |
| Run 15| 0.19      | 0.22      | 14.2   | 1.17 | Good  | 35.1 ± 0.7  | Good | 0.87    |
| Run 16| 0.19      | 0.21      | 11.98  | 1.14 | Good  | 34.9 ± 1.2  | Good | 1.74    |
| Run 17| 0.18      | 0.21      | 13.78  | 1.16 | Good  | 35.7 ± 1.7  | Good | 1.32    |
| Run 18| 0.18      | 0.20      | 12.80  | 1.14 | Good  | 32.4 ± 1.6  | Good | 0.13    |
| Run 19| 0.20      | 0.23      | 14.46  | 1.17 | Good  | 35.6 ± 1.4  | Good | 3.72    |
| Run 20| 0.19      | 0.22      | 12.09  | 1.14 | Good  | 33.2 ± 2.0  | Good | 1.93    |
| Run 21| 0.16      | 0.19      | 14.16  | 1.16 | Good  | 32.4 ± 1.3  | Good | 1.21    |
| Run 22| 0.19      | 0.23      | 14.52  | 1.17 | Good  | 32.8 ± 1.5  | Good | 0.34    |
| Run 23| 0.19      | 0.21      | 12.78  | 1.15 | Good  | 33.1 ± 1.3  | Good | 2.38    |
| Run 24| 0.19      | 0.21      | 13.00  | 1.15 | Good  | 33.4 ± 1.4  | Good | 0.67    |
| Run 25| 0.19      | 0.22      | 13.59  | 1.16 | Good  | 35.2 ± 1.2  | Good | 2.43    |

*BD = Bulk Density, TD = Tapped Density, CI = Compressibility Index, H = Hausner ratio, AR = Angle of Repose, LOD = Loss On Drying, C = Compressibility, FP = Flow properties; S.D: Standard deviation.
excellent compressibility, 18 runs had good compressibility and 6 runs had fair compressibility. Carr’s Index and Hausner ratios which reflect the impact of tapping on particle packing and are influenced by particle size, shape and cohesivity predicted that all the formulations were compressible. Twenty four of the runs had granules with good flowability. The only exception, Run 1, had granules with fair flowability. However, all formulations had an angle of repose less than 40°, an angle acute enough to predict weak intermolecular forces of attraction between granules. It was thus satisfactory to proceed to compression without any further recommendations to aid flowability of the granules. All formulation runs had water content (loss on drying) of less than 5.0%.

Post-compression studies

The results of quality control tests done on formulated tablets are presented in Table 4. Consistency of tablet weight within each run was assessed by the weight variation test. From a sample of twenty tablets from each run, not more than two tablets were outside a weight range of 7.5% from their mean. This confirmed consistency of weight uniformity and all formulation runs passed weight variation test.

Table 4. Post-compression parameters of griseofulvin floating tablets formulation runs.

| Batch | WV (g) ± S.D | H (N) ± S.D | D (mm) ± S.D | T (mm) ± S.D | F (%) |
|-------|-------------|-------------|-------------|-------------|-------|
| Run 1 | 0.2909 ± 0.009 | 10.1 ± 1.2 | 12.00 ± 0.1 | 3.40 ± 0.1 | 0.14  |
| Run 2 | 0.2282 ± 0.006 | 8.8 ± 0.6  | 12.00 ± 0.1 | 2.70 ± 0.1 | 0.06  |
| Run 3 | 0.2357 ± 0.018 | 10.8 ± 1.6 | 12.01 ± 0.1 | 2.22 ± 0.1 | 0.08  |
| Run 4 | 0.2274 ± 0.012 | 8.6 ± 1.0  | 12.03 ± 0.1 | 2.52 ± 0.1 | 0.10  |
| Run 5 | 0.2392 ± 0.010 | 11.3 ± 1.1 | 12.02 ± 0.1 | 2.46 ± 0.1 | 0.05  |
| Run 6 | 0.2474 ± 0.007 | 9.0 ± 1.0  | 12.00 ± 0.1 | 2.68 ± 0.1 | 0.21  |
| Run 7 | 0.2834 ± 0.014 | 11.4 ± 1.8 | 12.00 ± 0.1 | 3.08 ± 0.1 | 0.12  |
| Run 8 | 0.2652 ± 0.009 | 8.6 ± 0.7  | 12.00 ± 0.1 | 2.58 ± 0.1 | 0.06  |
| Run 9 | 0.2491 ± 0.009 | 11.7 ± 0.9 | 12.01 ± 0.1 | 2.52 ± 0.1 | 0.08  |
| Run 10| 0.2981 ± 0.009 | 12.1 ± 1.3 | 12.00 ± 0.1 | 3.20 ± 0.1 | 0.14  |
| Run 11| 0.2278 ± 0.017 | 9.1 ± 0.5  | 12.00 ± 0.1 | 2.00 ± 0.1 | 0.06  |
| Run 12| 0.1963 ± 0.014 | 7.2 ± 1.5  | 12.00 ± 0.1 | 1.90 ± 0.1 | 0.04  |
| Run 13| 0.1292 ± 0.005 | 6.6 ± 1.4  | 12.00 ± 0.1 | 1.18 ± 0.1 | 0.12  |
| Run 14| 0.1546 ± 0.008 | 9.7 ± 0.4  | 12.00 ± 0.1 | 1.24 ± 0.1 | 0.06  |
| Run 15| 0.2512 ± 0.010 | 11.0 ± 1.3 | 12.04 ± 0.1 | 2.50 ± 0.1 | 0.02  |
| Run 16| 0.2922 ± 0.013 | 10.4 ± 0.6 | 12.00 ± 0.2 | 3.26 ± 0.1 | 0.07  |
| Run 17| 0.3062 ± 0.013 | 10.0 ± 0.8 | 12.00 ± 0.1 | 3.38 ± 0.1 | 0.08  |
| Run 18| 0.3069 ± 0.014 | 8.4 ± 0.9  | 12.02 ± 0.1 | 3.46 ± 0.1 | 0.04  |
| Run 19| 0.1871 ± 0.009 | 8.2 ± 0.3  | 12.00 ± 0.1 | 1.64 ± 0.1 | 0.14  |
| Run 20| 0.2497 ± 0.016 | 11.4 ± 1.6 | 12.00 ± 0.1 | 2.30 ± 0.1 | 0.01  |
| Run 21| 0.2258 ± 0.009 | 11.3 ± 1.0 | 12.00 ± 0.1 | 2.30 ± 0.1 | 0.04  |
| Run 22| 0.2442 ± 0.010 | 10.5 ± 1.0 | 12.03 ± 0.2 | 2.54 ± 0.1 | 0.08  |
| Run 23| 0.2447 ± 0.006 | 11.0 ± 0.5 | 12.00 ± 0.1 | 2.51 ± 0.1 | 0.11  |
| Run 24| 0.3267 ± 0.014 | 10.0 ± 1.0 | 12.00 ± 0.1 | 3.84 ± 0.1 | 0.05  |
| Run 25| 0.2113 ± 0.007 | 11.6 ± 0.7 | 12.01 ± 0.1 | 2.06 ± 0.1 | 0.08  |

*WV = Weight Variation, H = Hardness, D = Diameter, T = Thickness, F = Friability & S.D: standard deviation.
Buoyancy studies

All formulation runs that produced tablets that floated had densities less than 0.00091 g/cm\(^3\). Using Design Expert 9.0, a linear model was the best fit model for both lag time and floating time with sequential p-values of 0.0003 and 0.0021, and lack of fit values of 0.8541 and 0.9118, respectively (Figures 5 and 6).

It was determined that only Accurel MP had a significant influence on lag time and floating time, with a "Probability > F" value of less than 0.0001. An increase in Accurel MP decreased lag time, as shown in Figure 7. Accurel MP, polypropylene foam powder, is a low density polymer used in floating drug delivery systems. When included in a matrix, Accurel MP adsorbs the drug, excipients and entraps air. The entrapped air reduces the density of the formulation and allows the unit to float when exposed in an aqueous environment (Al-Achi et al., 2013). Accurel Mp was directly proportional to floating time. Approximately 28% w/w of Accurel MP was sufficient to achieve immediate flotation of tablets and floatation of at least 24 h.

Assay of griseofulvin tablets

The quantity of griseofulvin in the compressed tablets was calculated and results obtained are shown in Table 5. The British Pharmacopoeia (BP) specifies that griseofulvin tablets should contain not less than 95.0% and not more than 105.0% of the labelled amount. As shown in Table 5, all formulation runs had percentage griseofulvin content within the acceptable range and hence the formulated tablets complied with the USP specification. The formulated tablets contained the claimed amount of griseofulvin, 100 mg.

In-vitro drug release studies

Highest percentage drug release was achieved by formulation runs that had the least amount of Methocel™
Figure 6. Statistical analysis of model of fit for floating time using design expert.

Figure 7. Influence of Accurel MP on lag time and total floating time.

of 25 mg, whilst formulation runs that had the highest amount of Methocel™, 100 mg showed the least drug release rate and the least total drug release, as shown in Figure 8.
Table 5. Assay of griseofulvin tablets.

| Batch  | Quantity ± SD (mg) | Percentage assay | Batch  | Quantity ± SD (mg) | Percentage assay |
|--------|--------------------|------------------|--------|--------------------|------------------|
| Run 1  | 98.7 ± 2.4         | 98.7             | Run 14 | 104.6 ± 0.4        | 104.6            |
| Run 2  | 95.7 ± 1.6         | 95.7             | Run 15 | 101.6 ± 2.7        | 101.6            |
| Run 3  | 102.9 ± 2.6        | 102.9            | Run 16 | 96.4 ± 2.1         | 96.4             |
| Run 4  | 99.4 ± 2.1         | 99.4             | Run 17 | 97.8 ± 2.4         | 97.8             |
| Run 5  | 95.7 ± 0.9         | 95.7             | Run 18 | 95.3 ± 1.5         | 95.3             |
| Run 6  | 96.6 ± 2.1         | 96.6             | Run 19 | 96.3 ± 2.1         | 96.3             |
| Run 7  | 97.9 ± 1.5         | 97.9             | Run 20 | 98.1 ± 2.4         | 98.1             |
| Run 8  | 97.0 ± 1.8         | 97.0             | Run 21 | 95.3 ± 1.3         | 95.3             |
| Run 9  | 96.2 ± 1.1         | 96.2             | Run 22 | 95.5 ± 1.2         | 95.5             |
| Run 10 | 104.6 ± 0.4        | 104.6            | Run 23 | 97.6 ± 1.3         | 97.6             |
| Run 11 | 101.6 ± 1.9        | 101.6            | Run 24 | 96.2 ± 1.8         | 96.2             |
| Run 12 | 96.4 ± 2.2         | 96.4             | Run 25 | 97.8 ± 2.1         | 97.8             |
| Run 13 | 97.8 ± 3.1         | 97.8             |        |                    |                  |

Figure 8. *In-vitro* drug release profile of the formulation runs with (a) 25% Methocel™, (b) 50 to 75% Methocel™ and (c) 100% Methocel™.
Initial drug release followed a quadratic model, with a sequential p-value of 0.0290 and a lack of fit p-value of 0.0208. Methocel™ had the most pronounced effect on initial drug release whilst Accurel MP had less effect on drug release and an increase in tablet hardness slightly decreased release of griseofulvin (Figure 9). Methocel™, also known as hydroxypropyl methylcellulose (HPMC), is a water-soluble, non-ionic cellulose ether. It retains chemical stability over a pH range of 3.0-11.0 and resists enzymatic degradation (Dow, 2000). HPMC has a cellulose backbone with ether linked methoxyl and hydroxypropyl side group substituents attached through ether linkages to the cellulose chain hydroxyl groups. A combination of 30 mg Methocel™ and 60 mg Accurel MP provided the most optimum formulation (Figure 10).

The formulation produced tablets that floated immediately with floating time above 12 h with 80.8% release of griseofulvin (Figures 11 and 12). Evaluation of drug release kinetics revealed a zero order model to best fit griseofulvin release data from the tablets, with a
correlation coefficient of 0.9983 (Figure 13).

**Conclusion**

Design Expert generated 25 formulation runs which were compressed to assess the influence of Methocel™, Accurel MP, tablet hardness and polyvinylpyrrolidone on buoyancy and drug release. Accurel MP concentration was directly proportional to lag time and total floating time of tablets. Methocel™ concentration was indirectly proportional to release rate of griseofulvin from tablets. The optimized formulation, of ratio Methocel™:Accurel MP:hardness 30:60:8-9, respectively was chosen and floating tablets were compressed. Compressed tablets float immediately upon contact with dissolution medium.
and float for more than 12 h. Griseofulvin was released in a zero order fashion over 12 h, with 80.8% released within that period. Tablets were of acceptable quality according to USP standards.

CONFLICT OF INTERESTS

The authors have not declared any conflict of interests.

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