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Formulation and evaluation of fast dissolving tablets of griseofulvin by solid dispersion

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Abstract
Superficial infections of the skin and nails are the most common fungal diseases in humans and affect ~25% (or ~1.7 billion) of the general population worldwide. Griseofulvin is antifungal antibiotic drug which is practically insoluble in water. (BCS class II) like other candidates in this class, it has solubility limited bioavailability. Solid dispersion is one of the widely and effective used techniques for solubility enhancement. The solid dispersions were prepared by physical mixing, kneading method, melting or fusion and solvent evaporation method using PEG 6000, PEG 4000, poloxamer 188, poloxamer 407 and crospovidone as polymer with ratio 1:1, 1:3, 1:5, 1:7 then formulating solid dispersion tablets of the best formulation of solid dispersion. Tablets formulations were prepared by direct compression technique using super disintegrants crospovidone, croscarmellose sodium and sodium starch glycolate in different concentrations. solid dispersion were evaluated for FTIR, DSC, in vitro dissolution profiles and developed tablets formulations were evaluated for various pharmaceutical characteristics viz. hardness, percentage friability, weight variation, drug content, disintegration time, wetting time, in vitro dissolution profiles. Among different formulations of solid dispersion, solid dispersion containing drug to polymer ratio 1: 1 (griseofulvin: crospovidone) gives best dissolution profile. The study reveals that the formulation F4 (6% of crospovidone) is found to be the optimized formulation with 98.23% drug release in 10 minutes and disintegration is found to be in (25sec.) in comparison with other super disintegrants. Results showed that crospovidone is a promising polymer for enhancing the solubility of griseofulvin.

Keywords: antifungal, solid dispersion, solubility, dissolution, griseofulvin

Introduction
Fungal infections, also called mycoses, are important causes of morbidity and mortality in humans. Fungal infections are divided into superficial infections (affecting skin, nail, scalp or mucous membranes) and systemic infections (affecting deeper tissues and organs). This large and diverse kingdom comprises more than 100,000 recognized species. Of this large group, only about 300 species have been identified as human pathogens; however, more than three fourths of these pathogens infect primarily the skin or subcutaneous tissues [1, 2].

Drug absorption from the GI tract can be limited by a variety of factors most significant contributor being poor aqueous solubility and poor membrane permeability of the drug molecule. When administered an active agent orally it must first dissolve in gastric and/or intestinal fluids before it can permeate the membranes of the GIT to reach systemic circulation. Hence, two areas of pharmaceutical research that focus on improving the oral bioavailability of active agents include; enhancing of solubility and dissolution rate of poorly water soluble drugs. Alteration of the solid state at the particle or molecular level involves a physical change in the drug and is an attractive option for improving drug solubility. Solid dispersions contribute by enhancing wettability and modulating the properties of the solvent. It is one of the widely and effective used techniques for dissolution enhancement. The basic procedures used to prepare solid dispersions are the physical mixing, kneading method, melting or fusion and solvent evaporation method [3]. Griseofulvin is one such drug belonging to class II according to biopharmaceutical classification system which shows poor water solubility but has good membrane permeability. Griseofulvin, a classical oral antibiotic first isolated as a metabolic product from a culture of penicillium griseofulvum. Griseofulvin works by interfering with fungal mitosis. The drug binds to tubulin, interfering with microtubule function, thus inhibiting mitosis. It binds to keratin in keratin precursor cells and makes them resistant to fungal infections. The drug reaches its site of action only when hair or skin is replaced by the keratin-griseofulvin complex [4].

Materials and Methods
Griseofulvin was gifted from Yarrow pharmaceuticals, Mumbai and all other chemicals used were of analytical grade.

Solubility enhancement of griseofulvin by solid dispersion technique
Preparation of physical mixture solid dispersions
For this method powders of griseofulvin and each of water soluble carriers viz PEG 6000, PEG 4000 poloxamer 188 and poloxamer 407 and crospovidone were weighed accurately and mixed in required proportion in mortar and pestle by simple blending for 30 min. and passed through 40 # sieve. The mixture was prepared in 1:1, 1:3, 1:5and 1:7 ratio of drug-carrier respectively [3, 5].

Preparation of kneading method solid dispersions
Weighed quantity of griseofulvin and PEG 6000, PEG 4000 poloxamer 188 and poloxamer 407 were placed in mortar and homogeneous paste of the drug and carriers were prepared by adding methanol in small quantity to maintain

suitable consistency of paste. The paste was dried in hot air oven at 40 ±2^{0}C and passed through 40 # sieve [6].

Preparation of melt method of solid dispersions

Griseofulvin and each of water soluble carriers such as PEG 6000, PEG 4000, poloxamer188, poloxamer 407 and crospovidone were weighed accurately and melted at 60^{0}C and cooled to room temperature to obtain a solid mass. The resulting solid dispersion was stored in desiccators until use [6, 7].

Preparation of solvent evaporation method of solid dispersions

Griseofulvin and each of water soluble carriers such as PEG 6000, PEG 4000 poloxamer 188, poloxamer 407 and crospovidone were added into methanol in mortar with constant stirring. Subsequently, methanol was evaporated in oven at 60^{0}C and resulting solid dispersion were stored for 24 hrs. In a desiccators to remove traces of organic solvent. The dried powder were triturated in a mortar and passed through 40 # sieve [7, 8].

Characterization of solid dispersions

Physical appearance

All batches of solid dispersion were evaluated for colour and appearance.

Saturation solubility studies

The saturation solubility study was carried out to determine increase in the solubility of pure griseofulvin as compared with the physical mixture (PM) and solid dispersions. The known excess amount of drug, PM and inclusion complexes were added to the 100 ml conical flasks containing 10 ml of water. Then the sealed flasks were maintained at 25°C for 48 hours. The saturated solution was sonicated for 20 min. and then centrifuged. Then, the supernatant were withdrawn through Whatman filter paper. The concentration of griseofulvin was determined by UV spectrophotometer at 291 nm [7, 8].

Drug content Estimation

Griseofulvin: Crospovidone complex equivalent to 125 mg of griseofulvin were weighed accurately and dissolved in 100 ml of methanol. Diluted suitably and drug content was analyzed at 291 nm by UV spectrophotometer. The concentration was calculated using the standard calibration curve of griseofulvin in methanol [5, 7].

FTIR spectral analysis

FTIR spectra of pure griseofulvin, crospovidone and with its solid dispersion were obtained by FTIR-8400S, CE (Shimadzu, Japan) spectrophotometer. The procedure consisted of dispersing samples with KBr and compressing into disc by applying a pressure for 5 min. in a hydraulic press. The pellet was placed in the light path and the scanning range used was 4000 to 400 cm^{-1} to obtain spectra [4, 5].

Spectroscopic Studies

Complex formation between griseofulvin and crospovidone was studied by UV spectrophotometric method. UV spectra of the solid dispersion and pure griseofulvin were taken by using UV spectrophotometer. The scans were recorded from 200 to 400 nm [4, 5].

Differential scanning calorimetry

Differential scanning calorimetry (DSC) thermograms of the drug, crospovidone and prepared solid dispersion complexes were recorded. These thermograms represent the rates of heat uptake from sample. About 2-5 mg samples were sealed in aluminum pans and scanned at a heating rate of 100^{o}C min^{-1} over a temperature range of 30 to 3000^{o}C under a nitrogen gas stream [4, 5].

Dissolution (*In vitro*) studies of solid dispersion

The dissolution rate of pure griseofulvin solid dispersion was studied in 900 ml of 0.1 N HCl using USP type-II (Paddle type) dissolution test apparatus with a paddle stirrer at 50 r.p.m. A temperature 37±0.5^{o}C was maintained throughout the study. Drug or solid dispersion equivalent to 125 mg of griseofulvin was used in each test. Samples of dissolution media (5ml) were withdrawn through a filter (0.45µ) at different intervals of time, suitably diluted and assayed at 241 nm. The samples of dissolution fluid withdrawn at each time were replaced with 5 ml of fresh fluid [3].

E) Evaluation of powder blends of griseofulvin solid dispersion

The powder blends were evaluated for the following flow parameters:

i) Angle of repose

Angle of repose is used to determine the flow properties of powders, granules. The method to find angle of repose is to pour the powder on a conical heap on a level, flat surface and measure the included angle with the horizontal

$$\text{Tan}^{-1}\,\theta = h/r$$

Where, h = height of the heap, r = Radius of the heap.

ii) Tapped density and bulk density

Tapped density was determined by placing graduated cylinder containing a known mass of granules and mechanical tapper apparatus, which was operated for a fixed number of taps until the powder bed volume has reached a minimum volume. Using weight of the drug in cylinder and this minimum volume, the tapped density may be computed [3, 8, 9].

$$\text{Tapped density} = \frac{\text{Weight of granules}}{\text{Tapped volume of granules}}$$

Bulk density of the granules was determined by pouring granules into a graduated cylinder via a large funnel and measuring the volume and weight.

$$\text{Bulk density} = \frac{\text{Weight of granules}}{\text{Bulk volume of granules}}$$

iii) Powder compressibility and Hausner's ratio

Powder compressibility is also known as Carr's index.

$$\text{Carr's compressibility index (\%)} = [(\text{Tapped density} - \text{bulk density}) \times 100]/\text{Tapped density}$$

Hausner's ratios were calculated from the bulk and tapped densities.

$$\text{Hausner's ratio} = \text{Tapped density}/\text{Bulk density}$$

E1) Development of directly compressible fast dissolving/fast disintegrating tablet by direct compression method

Directly compressed tablets were prepared using griseofulvin polymer complexes, variable concentration of other excipients. The powder blends equivalent to 125 mg of drug directly compressed using 10 mm flat faced round S.S punches. The tablets were evaluated for various tablet characteristics. Table No. 7.7 gives composition of these tablet formulations.

Table 1: Formulation of fast disintegrating/dissolving tablets of griseofulvin

Formulation No./ Excipients	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
Complex	250	250	250	250	250	250	250	250	250	250
Crospovidone	-	10	20	40	-	-	-	-	-	-
Croscarmellose sodium	-	-	-	-	10	20	40	-	-	-
Sodium starch glycolate	-	-	--	-	-	-	-	10	20	40
Microcrystallinecellulose	200	190	180	160	190	180	160	190	180	160
Lactose	20	20	20	20	20	20	20	20	20	20
Sodium saccharine	10	10	10	10	10	10	10	10	10	10
Magnesium stearate	10	10	10	10	10	10	10	10	10	10
Talc	10	10	10	10	10	10	10	10	10	10
Total weight (mg) of all FDDT's: 500 mg. And all excipients are in mg.										

Griseofulvin- Crospovidone complexes prepared by (KM).

Evaluation of directly compressible tablets

The tablets were evaluated for the following test parameters:

1. General appearance

All the tablet formulations were visually inspected for colour, odour, shape and visual defects.

2. Thickness and diameter

It was measured by using digital Vernier calipers. Ten tablets from prepared formulation randomly taken, thickness and diameter were measured [8, 9, 11].

3. Weight variation test

This test was performed as per I.P. (2010) ten tablets of each formulation were weighed individually using an electronic balance (0.1mg sensitivity). The average weight was calculated and individual tablet weight was compared with the average value and the deviation was recorded [8, 9].

4. Drug content uniformity

This was tested by taking 125 mg equivalent of griseofulvin was taken from the all formulation and then it was dissolved in 10 ml of methanol. From that 1 ml was pipetted out and it was make up to 10 ml using methanol and then its absorbance was calculated using UV-Visible Spectrophotometer at 291nm of wavelength [8, 9].

5. Hardness and friability

Hardness values three tablets of each formulation type were determined using Monsanto hardness tester. Friability testing was done using Roche friabilator. Ten tablets of each formulation were carefully de dusted and accurately weighed. Percentage weight loss was calculated [8].

6. Wetting time and water absorption ratio (R)

The wetting time of the tablets was evaluated by the use of a piece of double folded tissue paper placed in a petridish containing 6 ml of water in which eosin dye was dissolved. A preweighed tablet was placed on this paper and the time for complete wetting of tablet was noted as wetting time.

For measuring water absorption ratio the weight of the tablet before keeping in the petri- dish was noted (Wb). The wetted tablet from the petridish was taken and reweighed (Wa) water absorption ratio (R) was then determined according to following equation:

$$R = \frac{100\ (Wa - Wb)}{Wb}$$

Where, W_a and W_b are the weight after and before water absorption, respectively [8, 9].

7. *In vitro* disintegration study

It was carried out using digital tablet disintegration test apparatus. One tablet was placed in each of the six tubes of the basket assembly and disk was added to each tube. The assembly was the suspended in one litre beaker containing water maintained at 37 ± 2^0C. The time required for complete disintegration of the tablet was recorded.

8. *In vitro* dissolution study

The in-vitro drug release studies for all formulations were studied using USP type - II (Paddle) dissolution test apparatus. 900 ml of 0.1N HCl solution was used as dissolution medium. The speed of the paddle was set at 50 r.p.m. and the temperature of the medium was maintained at 37 ± 0.5°C and 5 ml sample was withdrawn at predetermined intervals up to 50 min. and replacements were done with fresh dissolution medium. The samples were suitably diluted and analysed for drug content by UV spectroscopy at 293 nm [8].

9. Stability study

The fast disintegrating /dissolving tablets were subjected to exaggerated conditions of temperature (40 ± 2^0C) and humidity (75 ± 5%RH) to test effect of various formulation additives on the stability of the drug and as well as that of the dosage form. These tablets were evaluated for contents of griseofulvin and dissolution profile over a period of 15 or 45 days [11].

Results and Discussion

Saturation solubility in water

Saturation solubility of griseofulvin in solid dispersions prepared by physical mixing (PM) and kneading method (KM)

Table 2: Saturation solubility of griseofulvin in solid dispersions prepared by physical mixing method

Sr. No.	Solid dispersion system (PM and KM)	Ratio	Saturation solubility (µg/ml) of physical mixture method	Saturation solubility (µg/ml) of kneading method
1.	Griseofulvin	Plain	155.3	155
2.	Griseofulvin: PEG 6000	1:1	200 **	205 **
3.	Griseofulvin: PEG 6000	1:3	195.78 **	195.78 **
4.	Griseofulvin: PEG 6000	1:5	178 **	178 **
5.	Griseofulvin: PEG 6000	1:7	184.56 **	184.56 **
6.	Griseofulvin: PEG 4000	1:1	195 **	195 **
7.	Griseofulvin: PEG 4000	1:3	194.2 **	194.2 **
8.	Griseofulvin: PEG 4000	1:5	190 **	190 **
9.	Griseofulvin: PEG 4000	1:7	195 **	188 **
10.	Griseofulvin: Crospovidone	1:1	205.32 **	210.32 **
11.	Griseofulvin: Crospovidone	1:3	200.5 **	198.5 **
12.	Griseofulvin: Crospovidone	1:7	195.98 **	190.29**
13.	Griseofulvin: Poloxamer407	1:1	198. **	198.26 **
14.	Griseofulvin: Poloxamer407	1:3	185.12 **	195.23 **
15.	Griseofulvin: Poloxamer407	1:5	182.25 **	185.56 **
16.	Griseofulvin: Poloxamer407	1:7	167.58 **	178.38 **
17.	Griseofulvin: Poloxamer188	1:1	198.23 **	199.58 **
18.	Griseofulvin: Poloxamer188	1:3	190.58 **	187.51 **
19.	Griseofulvin: Poloxamer188	1:5	194.45 **	179.54 **
20.	Griseofulvin: Poloxamer188	1:7	189.56 **	185.25 **

Saturation solubility of griseofulvin in solid dispersions prepared by melt method (MM) and solvent evaporation method (SEM)

Table 3: Saturation solubility of griseofulvin in solid dispersions prepared by MM and SEM

Sr. No.	Solid dispersion system (MM and SEM)	Ratio	Saturation Solubility (µg/ml) melt method	Saturation Solubility(µg/ml) solvent evaporation method
1.	Griseofulvin	Plain	155	155
2.	Griseofulvin: PEG 6000	1:1	205 **	204 **
3.	Griseofulvin: PEG 6000	1:3	189 **	197 **
4.	Griseofulvin: PEG 6000	1:5	195.2 **	194 **
5.	Griseofulvin: PEG 6000	1:7	198.3 **	191 **
6.	Griseofulvin: PEG 4000	1:1	200 **	201 **
7.	Griseofulvin: PEG 4000	1:3	194.7 **	165 **
6.	Griseofulvin: PEG 4000	1:5	200 **	189.4 **
7.	Griseofulvin: PEG 4000	1:7	190 **	190.3 **
8.	Griseofulvin: Crospovidone	1:1	205 **	198.9 **
9.	Griseofulvin: Crospovidone	1:3	190.63 **	199.89 **
10.	Griseofulvin: Crospovidone	1:5	189 **	185.56 **
11.	Griseofulvin: Crospovidone	1:7	185.02**	165 **
12.	Griseofulvin: Poloxamer407	1:1	198.23**	200.22 **
13.	Griseofulvin: Poloxamer407	1:3	185.23**	195.25 **
14.	Griseofulvin: Poloxamer407	1:5	182.30 **	192.89 **
15.	Griseofulvin: Poloxamer407	1:7	182.56 **	189.78 **
16.	Griseofulvin: Poloxamer188	1:1	198.35 **	190.45 **
17.	Griseofulvin: Poloxamer188	1:3	195.40 **	185.55 **
18.	Griseofulvin: Poloxamer188	1:5	189.05 **	182.29 **
19.	Griseofulvin: Poloxamer188	1:7	185.3 **	187.10 **

Note: Data analyzed by ANNOVA followed by Dunnett's test. Results considered significant at **P<0.01 vs griseofulvin (Control).

Uniformity of content of griseofulvin Uniformity of content of griseofulvin in solid dispersions prepared by PM and KM

Table 4: Uniformity of content of griseofulvin in solid dispersions prepared by PM and KM

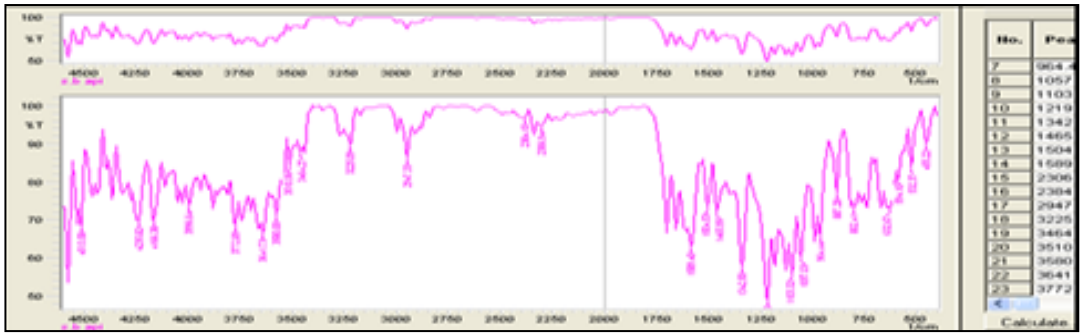
Sr. No.	Solid dispersion system (PM and KM)	Ratio	% Drug content ±SD of physical mixture	%Drug content ± SD of kneading method
1.	Griseofulvin: PEG 6000	1:1	97.59±0.12	98.5±1.44
2.	Griseofulvin: PEG 6000	1:3	98.25±0.23	97.47±0.71
3.	Griseofulvin: PEG 6000	1:5	97.75±0.28	97.85±0.75
4.	Griseofulvin: PEG 6000	1:7	98.84±0.56	97.21±0.56
5.	Griseofulvin: PEG 4000	1:1	97.25±1.23	98.38±1.45
6.	Griseofulvin: PEG 4000	1:3	98.20±0.58	98.52±0.52
7.	Griseofulvin: PEG 4000	1:5	98.56±0.89	97.36±0.32
8.	Griseofulvin: PEG 4000	1:7	97.32±0.98	97.85±0.58
9.	Griseofulvin: Crospovidone	1:1	98.96±0.25	98.36±0.14
10.	Griseofulvin: Crospovidone	1:3	98.63±0.86	98.96±0.97
11.	Griseofulvin: Crospovidone	1:5	98.15±0.94	98.25±1.32
12.	Griseofulvin: Crospovidone	1:7	97.28±0.56	97.36±0.78
13.	Griseofulvin: Poloxamer 407	1:1	97.23±0.78	98.69±0.36
14.	Griseofulvin: Poloxamer 407	1:3	96.56±0.70	98.78±0.21
15.	Griseofulvin: Poloxamer 407	1:5	97.17±0.36	98.36±0.28
16.	Griseofulvin: Poloxamer 407	1:7	97.10±0.25	97.21±0.98
17.	Griseofulvin: Poloxamer 188	1:1	97.89±0.45	98.56±1.23
18.	Griseofulvin: Poloxamer 188	1:3	97.95±0.58	98.23±0.58
19.	Griseofulvin: Poloxamer 188	1:5	97.51±0.40	98.40±0.48
20.	Griseofulvin: Poloxamer 188	1:7	97.10±0.26	97.23±0.25

Uniformity of content by melt method and solvent evaporation method

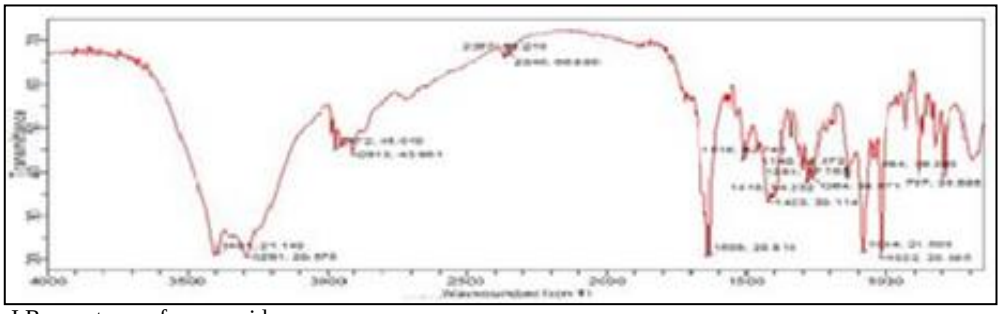
Table 5: Uniformity of content of griseofulvin in solid dispersions prepared by (MM) and SEM

Sr. No.	Solid dispersion system (MM and SEM)	Ratio	%Drug content ± SD of melt method	%Drug content ± SD of solvent evaporation method
1.	Griseofulvin: PEG 6000	1:1	98.36±1.35	98.28±0.15
2.	Griseofulvin: PEG 6000	1:3	98.29±1.25	98.25±0.56
3.	Griseofulvin: PEG 6000	1:5	97.23±0.25	98.16±0.49
4.	Griseofulvin: PEG 6000	1:7	97.46±0.56	97.30±0.26
5.	Griseofulvin: PEG 4000	1:1	98.33±0.28	98.23±1.25
6.	Griseofulvin: PEG 4000	1:3	97.12±0.45	97.65±0.45
7.	Griseofulvin: PEG 4000	1:5	97.35±0.59	97.18±0.86
8.	Griseofulvin: PEG 4000	1:7	97.10±.057	97.10±0.25
9.	Griseofulvin: Crospovidone	1:1	98.58±0.40	98.58±0.54
10.	Griseofulvin: Crospovidone	1:3	97.56±0.15	98.60±0.45
11.	Griseofulvin: Crospovidone	1:5	98.63±1.23	98.25±0.15
12.	Griseofulvin: Crospovidone	1:7	97.20±0.25	97.58±0.18
13.	Griseofulvin: Poloxamer 407	1:1	97.89±0.58	98.10±0.48
14.	Griseofulvin: Poloxamer 407	1:3	98.23±0.89	98.23±0.26
15.	Griseofulvin: Poloxamer 407	1:5	97.25±0.78	97.58±0.85
16.	Griseofulvin: Poloxamer 407	1:7	97.85±0.45	97.45±0.72
17.	Griseofulvin: Poloxamer 188	1:1	99.10±0.40	98.10±0.57
18.	Griseofulvin: Poloxamer 188	1:3	98.25±0.48	98.01±0.61
19.	Griseofulvin: Poloxamer188	1:5	98.05±0.50	98.23±0.82
20.	Griseofulvin: Poloxamer 188	1:7	97.56±0.25	97.25±0.10

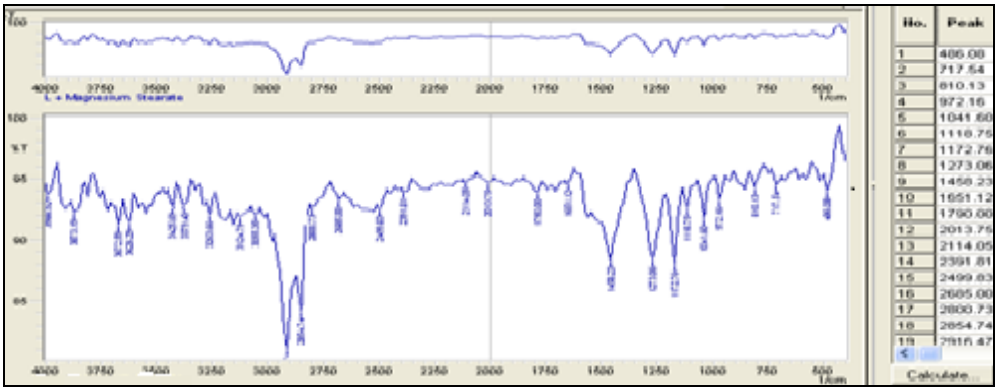
Infra-Red spectral characteristics



I.R. spectrum of pure sample of griseofulvin



I.R. spectrum of crospovidone



I.R. spectrum of griseofulvin+crospovidone solid dispersion

Fig 1: Infra-Red spectral characteristics

Differential scanning calorimetric characteristics

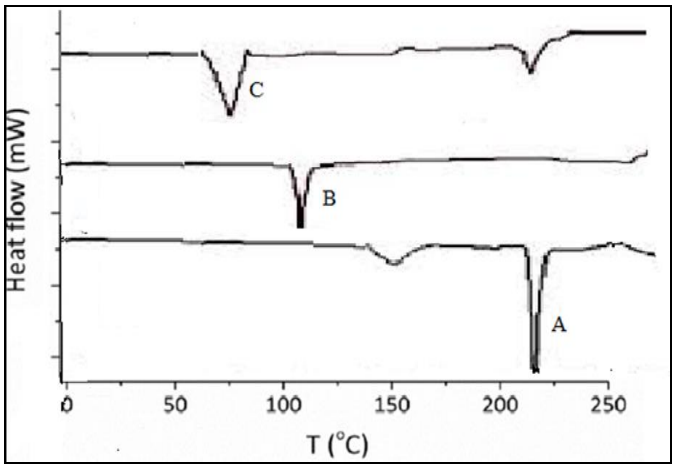


Fig 2: Differential scanning calorimetrythermogram of A) Griseofulvin B) Crospovidone C) Solid dispersion complex

DSC analysis provides additional evidence that solid dispersion was formed. DSC thermogram of griseofulvin shows sharp endothermic peak at 220^0C, which indicates that griseofulvin is in pure crystalline state. DSC thermogram of complex shows a small peak at 220^0C, which indicates that griseofulvin is complexes with crospovidone.

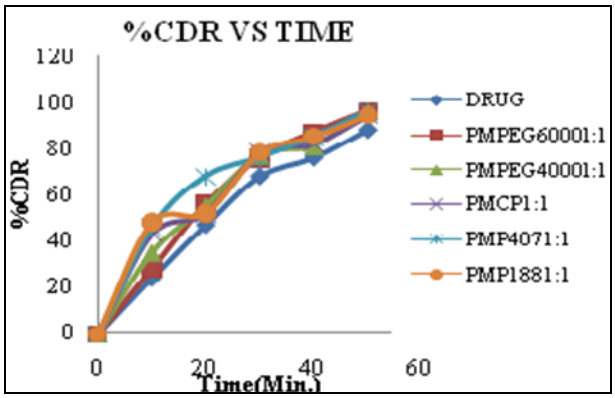
Dissolution of griseofulvin (*In vitro*) release from solid dispersions

Griseofulvin solid dispersions presented better dissolution performance as compared to the pure drug in a given time course.

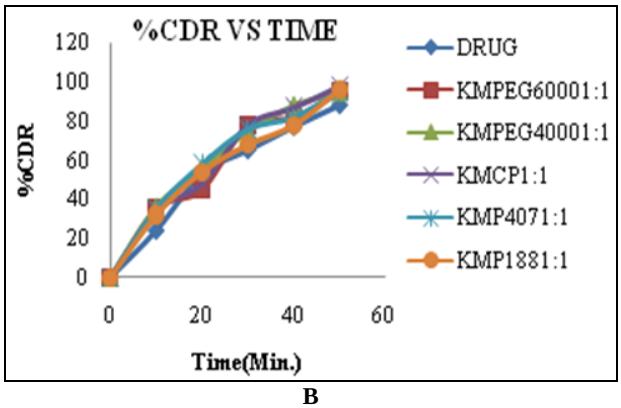
The trend was plotted for all the four methods of all the carriers of ratio 1:1 which gives best dissolution release.

Effect of method of preparation employed and type of polymer on dissolution profile of griseofulvin from different solid dispersions

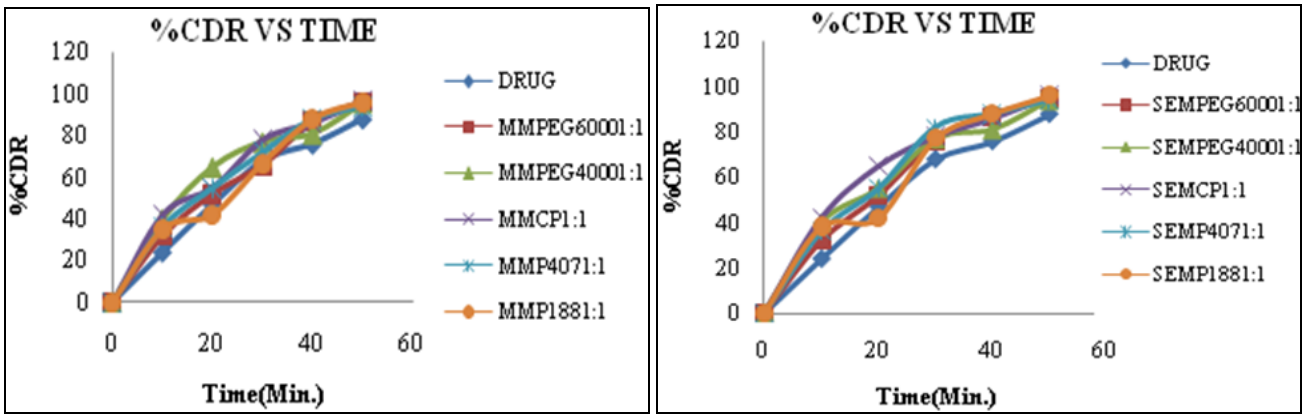
Solid dispersion of griseofulvin prepared by KM produced maximum drug release than those prepared by other methods.



A



B



C **D**

Fig 3: Effect of method and polymers on %drug release (*In vitro*) of griseofulvin from solid dispersion **A:** (PM 1:1), **B:** (KM 1:1), **C:** (MM 1:1), **D:** (SEM 1:1) Characteristics of powder blends used for preparation of tablets

Table 6: Flow properties of solid dispersion of griseofulvinand formulation additives for FDDT's

Blend	Angle of repose (Ø) (Mean ± S.D.)	Compressibility Index %) (Mean ± S.D.)	Hausner's ratio (Mean ± S.D.)	Tapped density (Mean ± S.D.)
F1	25.27±0.2	24.58±0.41	1.33±0.04	0.714±0.23
F2	24.98±0.5	11.10±.048	1.16±0.12	0.625±0.14
F3	23.60±0.15	11.42±0.08	1.12±0.24	0.645±1.23
F4	22.44±0.40	11.73±0.56	1.13±0.45	0.666±0.58
F5	22.14±0.47	17.12±0.48	1.20±0.26	0.689±0.04
F6	21.80±1.2	14.70±0.45	1.17±0.45	0.689±0.02
F7	19.84±0.25	15.38±0.25	1.18±0.68	0.606±0.36
F8	20.10±0.20	16.21±0.01	1.19±0.01	0.645±0.45
F9	20.55±0.02	17.24±0.45	1.21±0.12	0.833±0.12
F10	22.73±0.58	15.62±0.25	1.23±0.23	0.770±0.45

Evaluation of fast disintegrating tablet

1. General appearance

All tablets were white in colour and round shaped tablet.

2. Thickness and diameter

Thickness and diameter values for of all tablets were in the range of 4.21mm to 3.28 mm and 10.05mm to 10.20 mm respectively as shown in Table No.1.7

3. Weight variation

Weight variation of all tablets was found within the specifications of I.P. Average weight of one tablet of all the formulations was in the range of 496mg to 498mg as shown in Table No. 1.7.

4. Hardness and friability

Hardness of tablets of all formulations was in the range of 8.0Kg/cm^2 to8.6 Kg/cm^2 (Table No.1.7).

Friability of all the formulations was in the range of 0.1904 % to 0.5076% (Table No.1.7).

5. Content uniformity (%)

Drug content of all formulations were found in the range of 96.72 % to 98.03% (Table No.1.7).

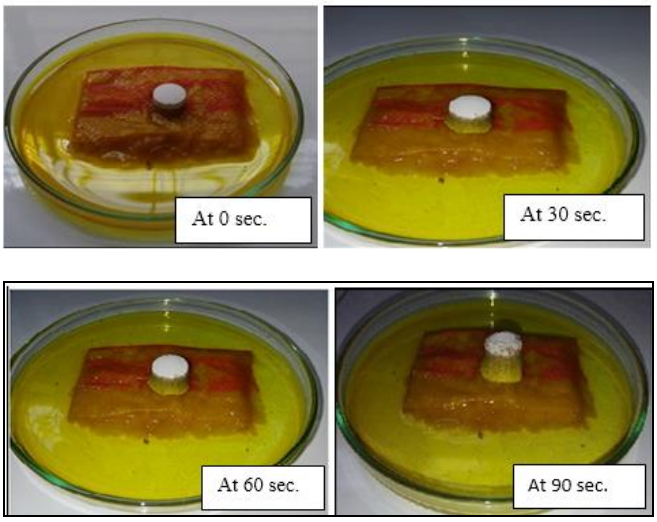
Table 7: Characteristics of griseofulvin: crospovidone (1:1) solid dispersion FDDT's by direct compression method

Code of formulation	Diameter (mm) (Mean ± S.D.)	Thickness (mm) (Mean ± S.D.)	Wt. variation (mg) (Mean ± S.D.)	Content Uniformity (%) (Mean ± S.D.)
F1	10.20±0.010	4.21±0.005	499.00±0.50	97.00±0.55
F2	10.05±0.005	4.26±0.017	497.84±1.75	97.84±1.75
F3	10.14±0.010	4.22±0.010	499.03±0.50	96.03±0.50
F4	10.03±0.011	4.25±0.035	498.35±1.23	98.30±1.20
F5	10.06±0.015	4.24±0.015	496.72±1.23	97.72±1.23
F6	10.17±0.005	4.21±0.010	498.03±0.98	96.03±0.98
F7	10.08±0.010	4.23±0.010	497.33±1.25	96.83±1.28
F8	10.12±0.010	4.26±0.010	498.72±1.21	98.42±1.24
F9	10.15±0.010	4.28±0.010	498.78±1.25	97.68±1.28
F10	10.05±0.010	4.28±0.010	498.78±1.25	98.28±1.21

6. Wetting time and water absorption ratio (R)

Table 8: Wetting time and water absorption ratio (R)

Code of formulation	Wetting time (Sec.) (Mean ± S.D.)	Water absorption ratio (R) (Mean ± S.D.)
F1	84±8.0	30±0.2
F2	78±8.7	52±0.23
F3	76±8.2	56±0.56
F4	69±7.5	68±0.89
F5	85±1.2	98±1.45
F6	65±3.2	45±1.45
F7	95±2.3	64±0.12
F8	78±5.4	52±1.12
F9	68±0.2	38±0.85
F10	84±1.0	48±0.42



Photograph 1: Wetting time of the tablet formulation (F4)

7. Disintegration time of tablets

All tablet formulations reported disintegration time between 25.38 sec.to 35.64 sec. The control formulation (F1) indicated disintegration time was 68.40 sec. (Table No.1.9).

From these findings it can be claimed that the addition of the superdisintegrants has certainly improved the disintegration time of tablets. Disintegration time of tablets was observed in order of crospovidone>croscarmellose> sodium starch glycolate.

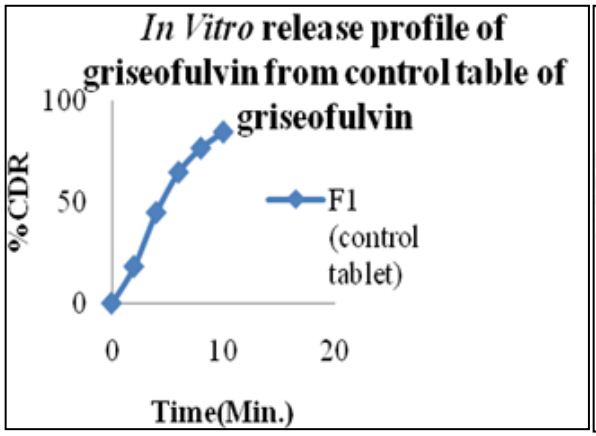
Table 9: Hardness, friability and disintegration time of fast dissolving tablets of griseofulvin

Code of formulation	Hardness (Kg/cm^2) (Mean ± S.D.)	Friability (% W/W loss) (Mean ± S.D.)	D.T. (*In vitro*) (Sec.) (Mean ± S.D.)
F1	8.30±0.10	0.5276±0.08	68.40±0.57
F2	8.60±0.15	0.3420±0.06	33.33±0.50
F3	8.34±0.05	0.4015±0.06	30.71±1.52
F4	8.30±0.10	0.4102±0.09	29.51±2.05
F5	8.20±0.15	0.3004±0.18	33.94±2.58
F6	8.30±0.10	0.5904±0.12	30.64±0.51
F7	8.43±0.05	0.3034±0.10	25.38±1.11
F8	8.30±0.10	0.3015±0.25	34.71±2.40
F9	8.20±0.15	0.4109±0.08	33.75±2.34
F10	8.54±0.04	0.2254±0.15	30.74±2.32

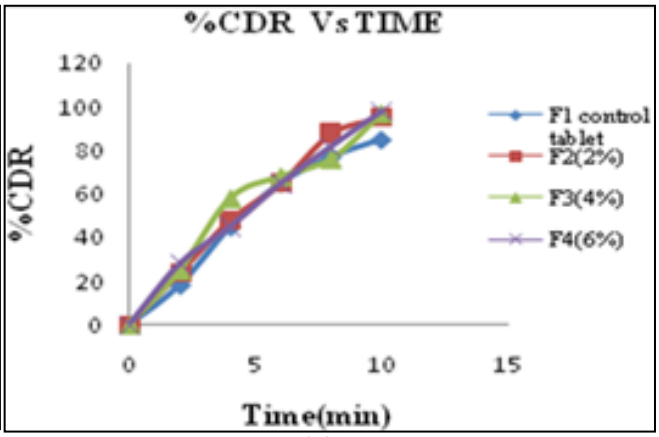
8. Dissolution characteristics of FDDT's in 0.1 N HCL

Dissolution profile of control formulation (F1) i.e. formulation without addition of any superdisintegrant (F1). Formulations F2, F3, and F4 which contain increasing concentrations of crospovidone (2%,4%,6%).Formulations F5, F6, and F7 which contain increasing concentrations of crosscarmellose sodium (2%, 4%,6%).

Formulations F2, F4, and F5 which contain increasing concentrations of sodium starch glycolate (2%, 4%, 6%).



(A)



(B)

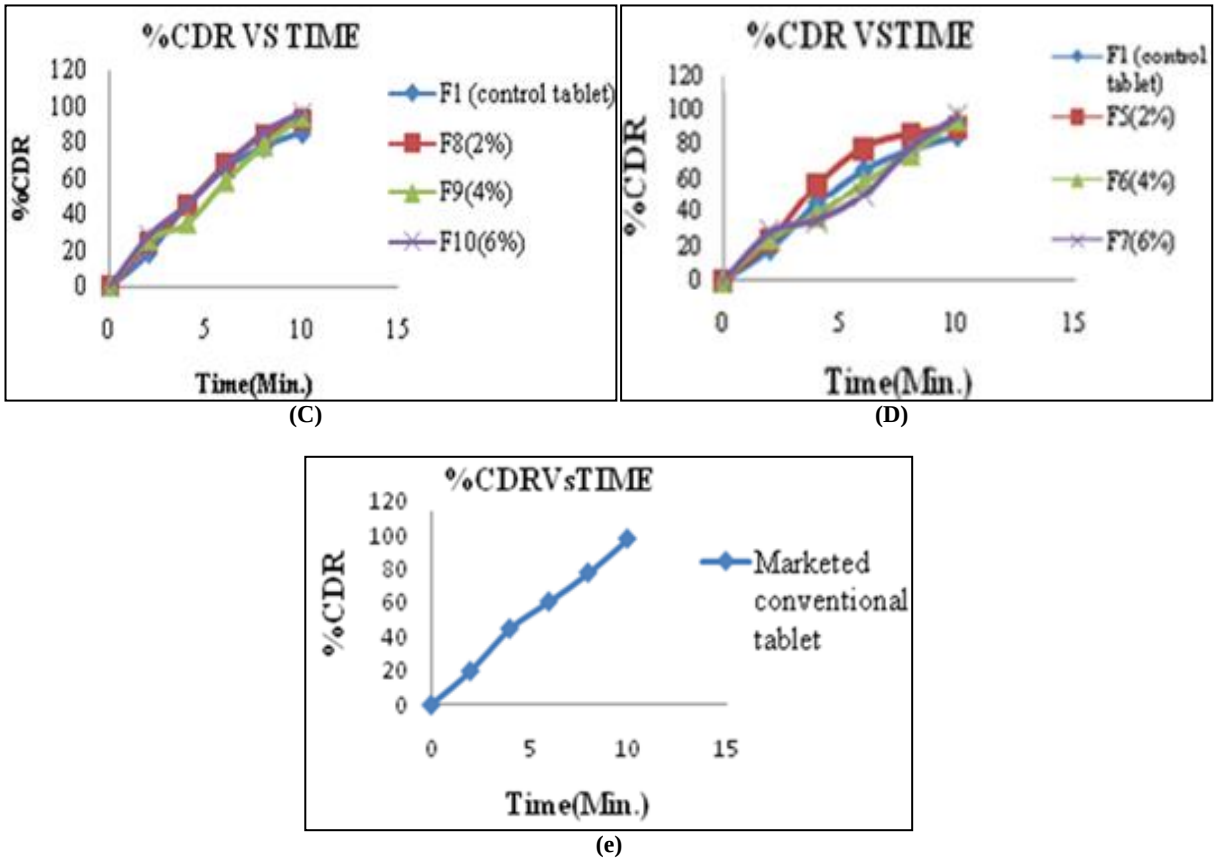


Fig 4. A. Dissolution profile (*In vitro*) of control formulation (F1) **B.** Effect of concentration of crospovidone on dissolution profile of griseofulvin from FDDT's **C.** Effect of concentration of crosscarmellose sodium on release of griseofulvin from FDDT's **D.** Effect of concentration of sodium starch glycolate on release of griseofulvin from FDDT's **E.** Effect of marketed conventional tablets of griseofulvin dissolution profile

Comparative assessment of dissolution characteristics of experimental FDDT's and marketed conventional tablet formulation

Table No.1.10 gives Difference factor (f1) and similarity factor (f2) of all FDDT's and marketed conventional tablet formulation:

Table 10: Difference factor (f1) and similarity factor (f2) of all FDDT's and marketed conventional tablet formulation

Sr. No.	Code of formulation	f1 (dissimilarity factor)	f2 (similarity factor)	Inference (f1 1-15 and f2 50-100)
1.	F1	7	60	Passable
2.	F2	8	63	Good fit
3.	F3	9	57	Passable
4.	F4	5	67	Acceptable
5.	F5	16	49	Passable
6.	F6	7	67	Acceptable
7.	F7	10	56	Passable
8.	F8	8	64	Good fit
9.	F9	8	62	Good fit
10.	F10	7	63	Good fit

Stability study of fast dissolving/disintegrating tablet of griseofulvin

Table 11: Stability studies of optimized formulation (F4)

Sr. No.	Parameters	Observations (Mean ± S.D.)	
		0 day	45 day
1.	Physical appearance	White coloured, smooth free from cracks	White coloured, smooth free from cracks
2.	Hardness (kg/cm^2)	8.60±0.15	8.55±0.10
3.	*In vitro* disintegration time(Sec.)	30.51±2.05	30.71±1.45
4.	Content uniformity	98.42±1.24	98.41±1.07
5.	Weight variation	499.03±0.50	498.93±0.40
6.	% drug release within 10 min.	96.23±1.20	96.12±0.28

Conclusion

Solid dispersion preliminary solubility analysis was carried out for the selection of carriers and solid dispersion was prepared with PEG 4000, PEG 6000, poloxamer 407, poloxamer 188 and crospovidone. These solid dispersions were analysed for the solubility and *Invitro* dissolution profile The solid dispersion of griseofulvin prepared by kneading method showed better dissolution compared to pure drug. The characterization of powdered blend of all the batches was done for determination of pre-compression parameters. The values of pre- compression parameters like bulk density, tapped density, Hausner ratio, Compressibility index and angle of repose of all the batches were evaluated which were within prescribed limits and indicated a good flow property. The result for characterization of blend indicates good flow properties. Further it was formulated to fast dissolving tablets with optimised solid dispersion using different concentration of superdisintegrants. After compression of powder blend, the tablets were evaluated for various post compression parameters i.e. friability, wetting time, hardness and disintegration time, weight variation and percentage drug content. The effect of concentration and type of superdisintegrants on in vitro drug release used in formulation of fast dissolving tablet was also investigated. The study reveals that the formulation prepared by 6% Crospovidone (F4) is the best formulation in comparison with other superdisintegrants.

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