Design, Preparation and *In-Vitro* Evaluation of Griseofulvin Mouth Dissolving Tablets

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Abstract:

Griseofulvin is a poorly water-soluble antifungal drug used in the treatment of dermatophytosis, whose conventional oral tablets show delayed onset of action and variable bioavailability. The present work aimed to develop mouth dissolving tablets (MDTs) of griseofulvin to improve patient compliance and enhance dissolution. Tablets were prepared by direct compression using sodium starch glycolate as superdisintegrant, microcrystalline cellulose as diluent, mannitol as filler, and suitable lubricants, in several formulations (F1–F8). Pre-compression blends were evaluated for bulk density, tapped density, Carr's index, Hausner's ratio, and angle of repose, while post-compression tablets were assessed for weight variation, thickness, hardness, friability, drug content, disintegration time, wetting time, and in-vitro dissolution in pH 6.8 phosphate buffer. FTIR studies confirmed absence of drug–excipient interaction. Among all batches, formulation F4 showed rapid disintegration, acceptable mechanical strength, and highest cumulative drug release (~99% within 60 min), with dissolution following Higuchi kinetics.

Stability studies of F4 at 40 °C/75% RH for 3 months showed no significant change in physical parameters or dissolution profile. These results indicate that mouth dissolving griseofulvin tablets prepared by direct compression (F4) are a promising alternative to conventional tablets, particularly for geriatric patients.

Keywords*: Griseofulvin superdisintegrants, FTIR studies, direct compression technique, in-vitro drug release studies.*

Introduction:

Griseofulvin is a fungistatic antibiotic derived from Penicillium griseofulvum, indicated for dermatophyte infections of skin, hair, and nails such as ringworm, tinea pedis, and onychomycosis. It binds to tubulin and disrupts mitotic spindle function while accumulating in keratin precursor cells, thereby protecting newly formed keratin from fungal invasion. Owing to its poor aqueous solubility and variable oral bioavailability (25–70%), conventional tablets may exhibit delayed onset and inconsistent therapeutic levels. Mouth dissolving tablets (MDTs) disintegrate within seconds in saliva without water, improving compliance in paediatric, geriatric, dysphagic, and travelling patients. MDTs can enhance pregastric absorption, reduce first-pass metabolism, and improve bioavailability for certain drugs. Use of superdisintegrants (e.g., sodium starch glycolate, crospovidone, croscarmellose sodium) and highly soluble excipients allows preparation of MDTs by simple direct compression, which is cost-effective and industrially scalable. The objective of the present study was to design, prepare, and evaluate griseofulvin MDTs by direct compression and to identify an optimized formulation exhibiting rapid disintegration and improved dissolution.

Materials And Methods:

Materials:

Griseofulvin was used as the model drug. Sodium starch glycolate served as superdisintegrant; microcrystalline cellulose (MCC) and mannitol were employed as diluent and filler; saccharin was used as sweetener; talc, magnesium stearate, and sodium stearyl fumarate functioned as lubricants/glidants. All other chemicals and reagents were of analytical grade.

Preformulation Studies

Organoleptic properties:

Colour and appearance of griseofulvin were recorded.

Melting point: Determined by capillary method to confirm identity and purity.

Solubility: Solubility was assessed in water, 0.1 N HCl (pH 1.2), and phosphate buffer pH 6.8.

FTIR compatibility: FTIR spectra of pure griseofulvin and physical mixtures with excipients (KBr pellet method) were recorded to detect possible interactions.

Formulation of Mouth Dissolving Tablets:

Griseofulvin MDTs were prepared by direct compression in eight formulations (F1–F8) using varying concentrations of sodium starch glycolate and other excipients. All ingredients were passed through #44 sieve and mixed thoroughly in geometrical dilution; lubricants (magnesium stearate, talc, sodium stearyl fumarate) were finally added and blended. The blends were compressed on a rotary tablet press using 8-mm flat-faced punches, targeting hardness of 3–3.5 kg/cm².

Evaluation of Powder Blends (Pre-compression):

Bulk density (g/ml):

Weight of powder divided by unsettled volume in a measuring cylinder.

Tapped density (g/ml):

Weight divided by tapped volume after standardized tapping.

Carr's index (%):

Carr's index = Tapped density – Bulk density / Tapped density X 100

Hausner's ratio:

Hausner's ratio = Tapped density / Bulk density

Angle of repose (θ):

Determined by fixed-funnel method using $\theta = \tan^{-1}(h/r)$

Micromeritic data indicated acceptable flow and compressibility suitable for direct compression; for griseofulvin blend, Carr's index (~4.6%) suggested good flow.

Evaluation of Tablets (Post-compression):

The prepared tablets (F1–F8) were evaluated as follows:

Weight variation:

20 tablets weighed individually; mean ± SD calculated.

Thickness:

Measured with Vernier caliper for 3 tablets per batch.

Hardness:

Determined using Pfizer hardness tester (target 3.3–3.5 kg/cm²).

Friability:

20 tablets in Roche friabilator at 25 rpm for 4 min; % loss calculated (acceptable <1%).

Drug content:

Powder equivalent to one tablet dissolved in pH 6.8 buffer, suitably diluted, and assayed spectrophotometrically at 239 nm using a previously constructed calibration curve.

Wetting time: Determined using folded tissue paper in a Petri dish containing 6 ml Sorenson's buffer (pH 6.8); time for complete wetting recorded.

In-vitro disintegration time: Measured using IP disintegration apparatus in distilled water at 37 ± 2 °C; time for no palpable mass recorded.

***In-vitro* dissolution:**

USP II paddle apparatus, 900 ml phosphate buffer pH 6.8, 50 rpm, 37 ± 0.5 °C; 5-ml samples withdrawn at 5, 10, 15, 30, 45, 60 min and replaced with fresh medium.Samples were filtered, and absorbance was measured at 239 nm; cumulative % drug release was calculated using standard curves in pH 1.2 and 6.8 buffers.

Drug Release Kinetics:
Dissolution data for the optimized formulation were fitted to zero-order, first-order, Higuchi, and Korsmeyer–Peppas models. Linear regression coefficients (R^2) were used to identify the best-fit model.

Stability Studies:
Optimized formulation F4 was subjected to accelerated stability testing at 40 °C/75% RH for 3 months, packed in tubes with desiccant. At predetermined intervals, tablets were examined for appearance, hardness, friability, drug content, and dissolution profile.

Result And Discussion:

Pre-formulation studies:

API Characterization:

Table 1: Pre-formulation properties of Griseofulvin

S. No	API Characterization	Results
1	Physical Appearance	Griseofulvin is a white to pale cream- colored
2	Melting point	332 °C
3	Solubility	Slightly soluble in ethanol, chloroform, methanol, acetic acid, acetone, benzene& ethylacetate; practically insoluable in water & petroleum ether

Table 2: Pre-formulation properties of Mouth dissolving tablets

1	Bulk density	0.239 gm/ml
2	Tapped Density	0.228 gm/ml
3	Carr's index/Compressibility index	4.60
4	Hausner's Ratio	1.04
5	Angle of repose	32^0

Discussion: The value of the compressibility index is 4.60 % which is less than 15%. So, it indicates good flowability.

Micromeritic properties:

Table 3: List of Micromeritic properties of directly compressible powder of Griseofulvin

F. No	Bulk density	Tapped density	Compressibility index	Hausner ratio	Angle of repose
F1	0.254	0.246	3.14	1.03	30^0
F2	0.231	0.229	3.86	1.0	31^0
F3	0.245	0.239	2.44	1.02	31^0
F4	0.239	0.228	4.60	1.04	32^0
F5	0.248	0.238	4.03	1.04	31^0
F6	0.246	0.235	4.47	1.04	31^0
F7	0.250	0.241	4.41	1.03	30^0
F8	0.249	0.234	4.27	1.06	29^0

Discussion: All formulations show good compressible properties

Calibration of Standard Graph:

Standard graph of Griseofulvin in 0.1N HCl (1.2 pH buffer) & 6.8 Phosphate buffer:

The construction of the standard calibration curve of Griseofulvin was done by using 0.1N HCl (1.2 pH buffer and 6.8 Phosphate buffer) as the medium separately. Griseofulvin was found to have Iithe maximum absorbance at 239 nm. The standard graph of Griseofulvin in 0.1N HCl (1.2 pH buffer & 6.8 Phosphate buffer) was constructed by making the concentrations of 2µg/ml, 4µg/ml, 6 µg/ml, 8 µg/ml, and 10 µg/ml solutions. The absorbance of solutions was examined under UV- spectrophotometer at an absorption maximum of 239 nm. The standard graph of Griseofulvin was constructed by taking the absorbance on Y-axis and concentrations on X-axis.

Table 4: Standard graph of Griseofulvin in 0.1N HCl (1.2 pH buffer)

S. No.	Concentration(µg/Ml)	Absorbance
1	0	0
2	2	0.117
3	4	0.253
4	6	0.415
5	8	0.533
6	10	0.672

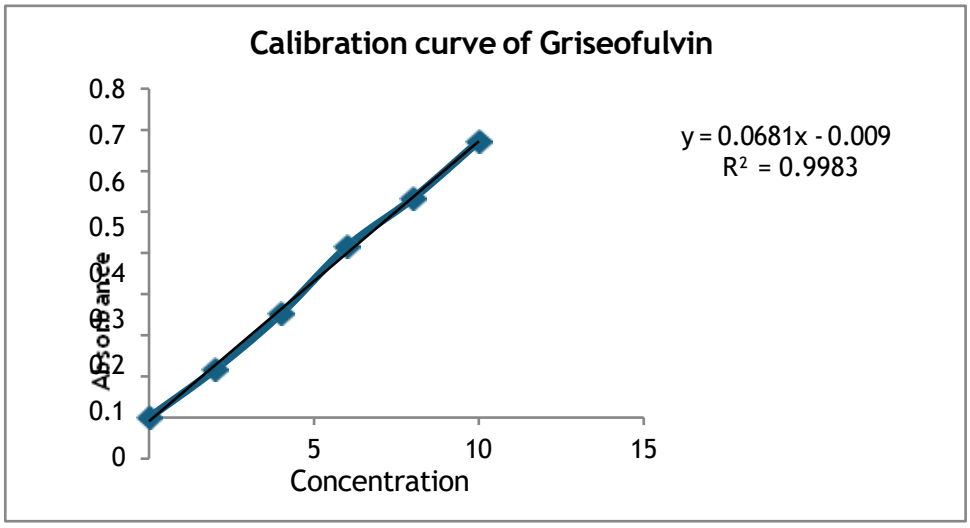

Figure 1: Calibration curve of Griseofulvin in 0.1N HCl (1.2 pH buffer)

Table 5: Standard graph of Griseofulvin (6.8 pH phosphate buffer)

S. no.	CONCENTRATION(µg/ml)	ABSORBANCE
1	0	0
2	10	0.213
3	20	0.387
4	30	0.567
5	0	0.763
6	50	0.942

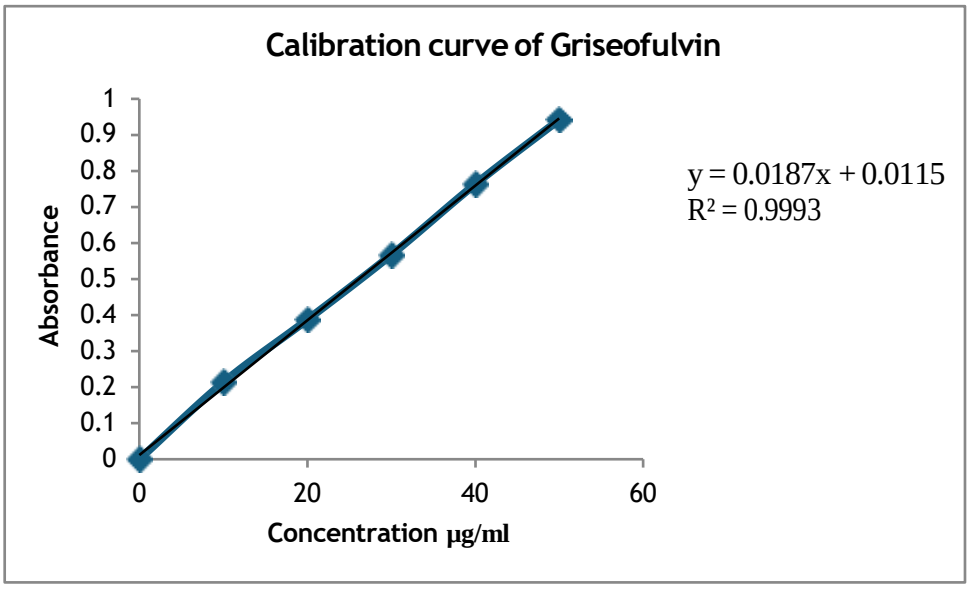

Figure 2: Calibration curve of Griseofulvin in (6.8 pH phosphate buffer)

Fourier Transformation Infra-red (FTIR) analysis:

Infra-red spectroscopy analysis was performed by Fourier Transformation Infrared Spectrophotometer Shimadzu. The instrument was calibrated by using polystyrene film.

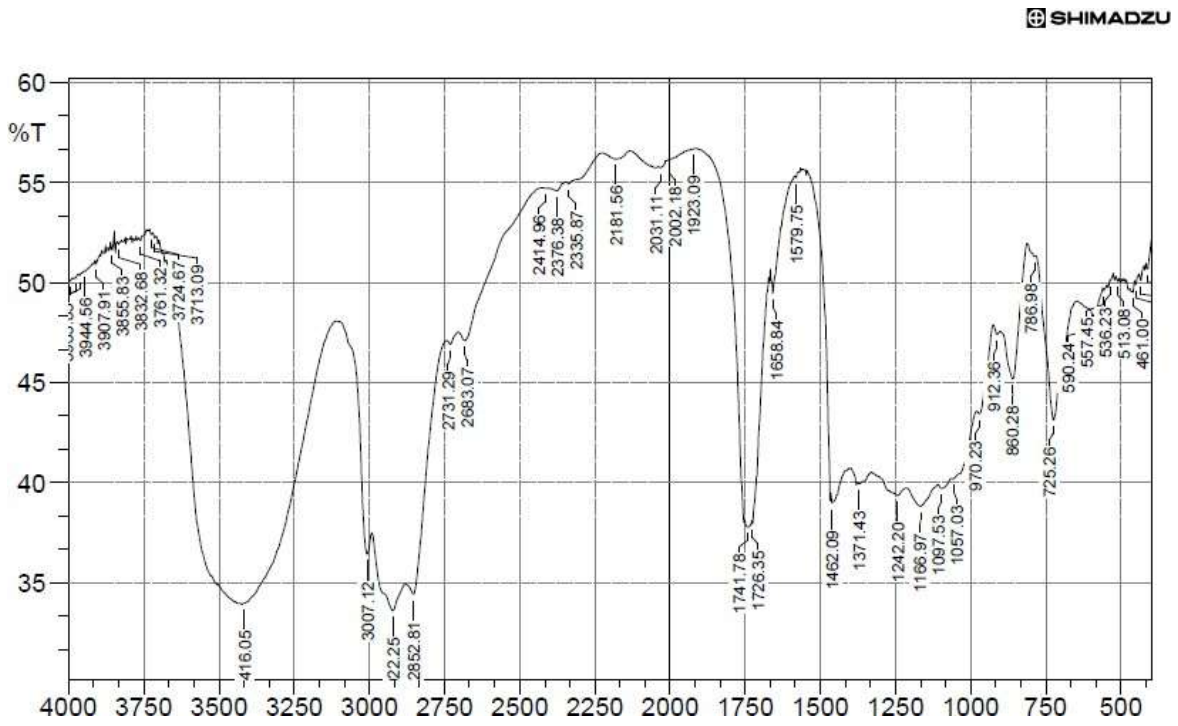

Figure 3: FTIR Studies of Griseofulvin

Table 6: Characteristic Peaks for Griseofulvin

S. No.	Characteristic Peaks	Frequency range (cm-1)	Frequency (cm-1)
1	OH stretching	4000-3000	3907.91
2	OH Bending	1500-1000	1371.43
3	C-H stretching	3000-2500	2852.81
4	C=O stretching	2000-1500	1726.36

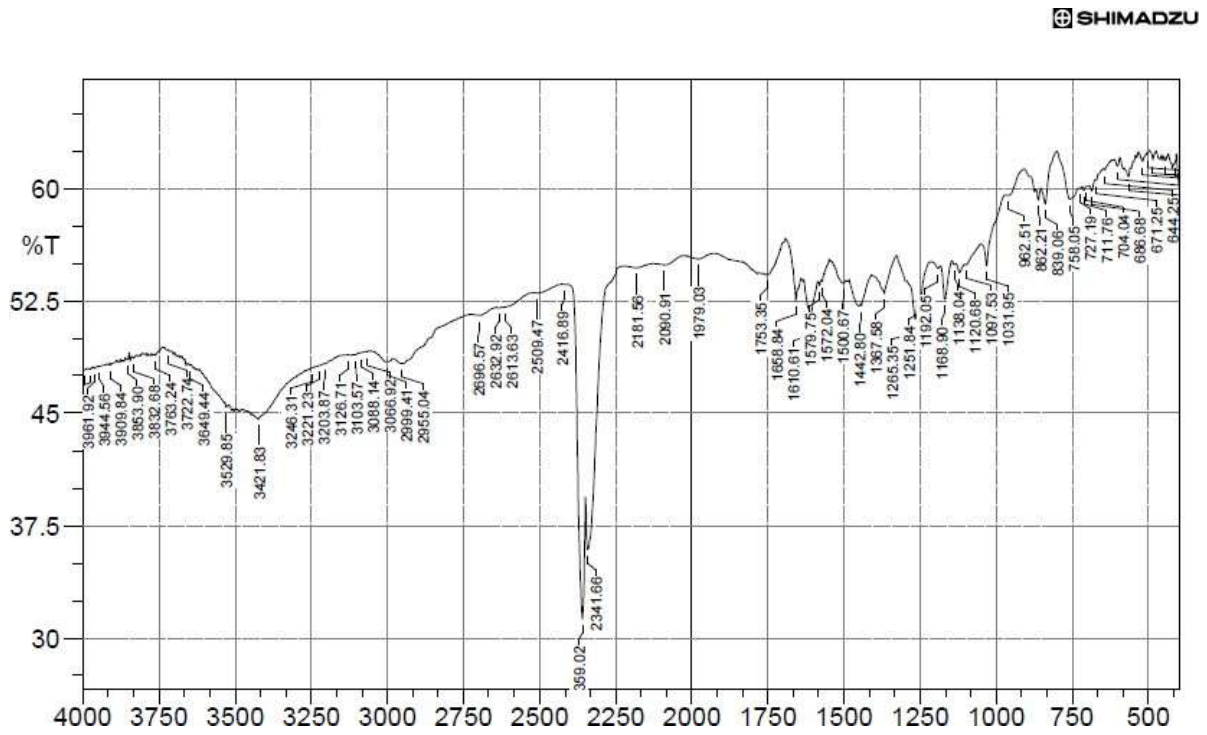

Figure 4: FTIR Studies of Physical mixture of drug and excipients

Table 7: Characteristic Peaks for drug and excipients

S. No.	Characteristic Peaks	Frequency range (cm-1)	Frequency (cm-1)
1	OH stretching	4000-3500	3909.15
2	OH Bending	3000-2500	2955.68
3	C=O stretching	2000-1500	1753.23

Discussion: The IR spectrum of the Griseofulvin and Drug Excipients mixture was shown in figure number 3 & 4 respectively. In the present study, it has been observed that there is no chemical interaction between Griseofulvin and the polymers used. From the figure, it was observed that there were no changes in these main peaks in the IR spectra of a mixture of drugs and polymers, which show there were no physical interactions because of some bond formation between drugs and polymers. This further confirms the integrity of pure drug and compatibility of them with excipients.

Evaluation of the Prepared Tablets for Physical Parameters:

Table 8: Evaluation Parameters for Optimized formulation

Parameter	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**
Weight variation	99	98	98	100	100	100	99	100
Thickness (mm)	3.8	3.5	3.4	3.8	3.1	3.4	3.7	3.5
Hardness (kg/cm^2)	3.41	3.42	3.5	3.9	3.3	3.5	3.3	3.4
Friability (%)	0.46	0.44	0.48	0.43	0.42	0.40	0.42	0.43
Disintegration time (seconds)	12.30	10.20	8.21	7.03	25.1	29.07	33	36
Drug content	88	93	91	97	88	92	90	96
Wetting time(sec)	18	20	23	24	20	22	32	26
Water absorption ratio	99	98	96	92	85	101	99	102

Uniformity of weight:

All the prepared mouth dissolving tablets of Griseofulvin was evaluated for weight variation. The weight of all the tablets was found to be uniform with low values of standard deviation and within the prescribed IP limits of ± 5%.

Hardness and friability:

The hardness of the tablet formulations was found to be in the range of 3.3 to 3.5 kg/cm^2 The friability values were found to be in the range of 0.40 to 0.48 %.

Uniformity of drug content:

The low values of standard deviation indicate uniform drug content within the tablets The percent drug content of all the tablets was found to be in the range of 88 to 97 percent (which was within the acceptable limits of ±5%.).

Discussion: All Formulations tested for Physical parameters like Hardness, thickness, Weight Variation, Friability, and found to be with in the Pharmacopoeial limits. The results of the tests were tabulated. The drug content of the formulation was determined and was found to be within the permissible limit. This study indicated that all the prepared formulations were good.

In-vitro Dissolution studies: The dissolution conditions used for studying drug releases:

Apparatus: USP apparatus II (Paddle)

Agitation speed (rpm): 50 rpm

Medium: 0.1N HCl (1.2 pH) and 6.8pH Phosphate buffer

Volume: 900 ml

Temperature: 37.0 ± 0.5 ^{0}C

Time: 5,10,15,30,45,60 min

Table 9: In-vitro dissolution Profiles for tablets

Time (min)	F1	F2	F3	F4	F5	F6	F7	F8
0	0	0	0	0	0	0	0	0
5	18.64	17.54	18.85	19.26	16.76	20.55	18.59	21.48
10	40.93	35.72	27.91	39.72	24.70	39.74	34.68	48.78
15	63.70	48.82	52.25	56.41	46.85	52.45	48.92	60.42
30	89.62	79.72	73.94	73.15	69.23	68.20	78.90	73.19
45	92.21	85.92	88.92	89.98	77.23	87.90	97.92	85.65
60	95.52	92.83	95.13	99.21	90.65	98.16	97.34	96.90

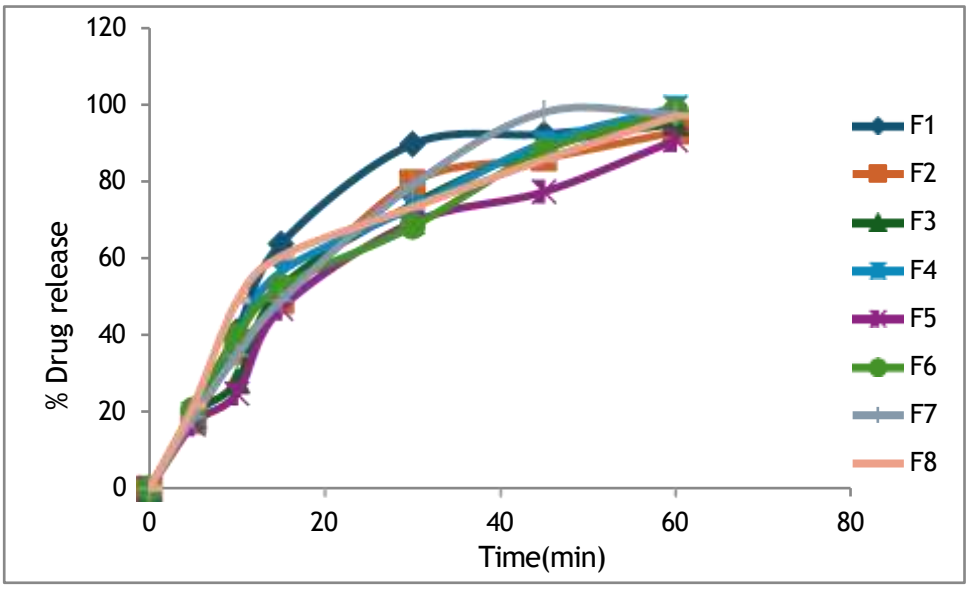

Figure 5: In-vitro dissolution Profiles for tablets

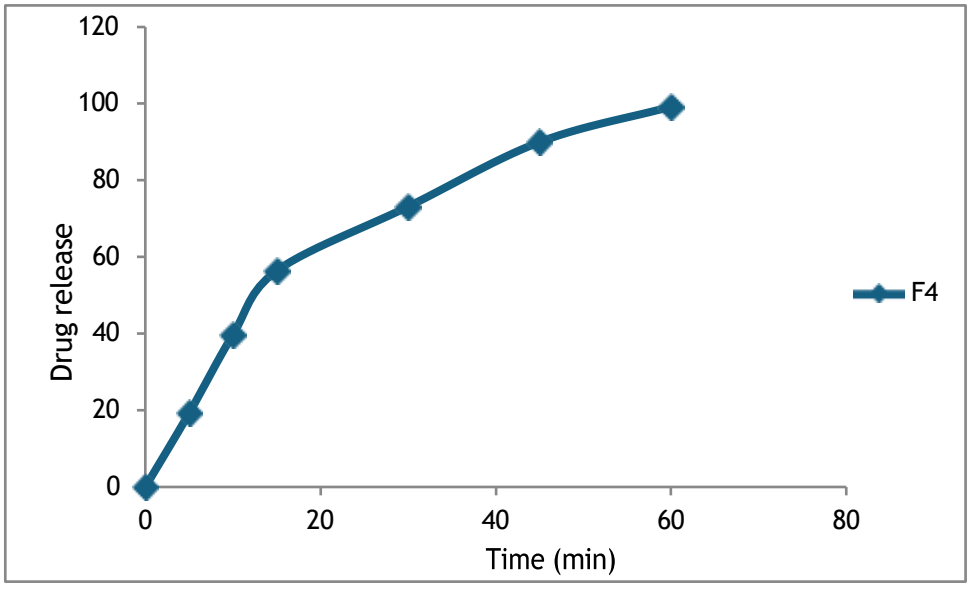

Figure 6: Drug release studies of optimized formulation

Conclusion: Among all formulations, F4 shows better drug release when compared with all other formulations. So, formulation F4 was selected as the optimized formula.

Discussion:

In vitro dissolution studies were performed on the above promising formulation, namely, formulation 4.

Drug release kinetics

Table 10: Kinetic studies for optimized formulation

Time	% CDR	Log % CDR	Log T	Square T	ARA	Log % ARA
0	0	0	0	0	0	0
5	19.26	1.2846563	0.69897	2.236068	80.74	1.9070887
10	39.72	1.5990092	1	3.162278	60.28	1.7801732
15	56.41	1.7513561	1.176091	3.872983	43.59	1.6393869
30	73.15	1.8642143	1.477121	5.477226	26.85	1.4289443
45	89.98	1.954146	1.653213	6.708204	10.02	1.0008677
60	99.21	1.9965554	1.778151	7.745967	0.79	-0.102373

Zero-order kinetics:

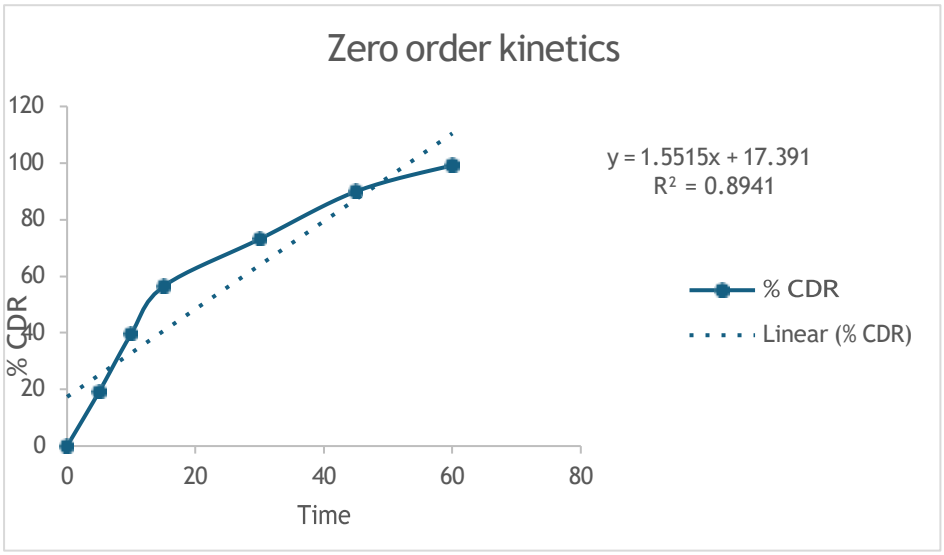

Figure 7: Zero Order Plot For best preparation

First-order kinetics:

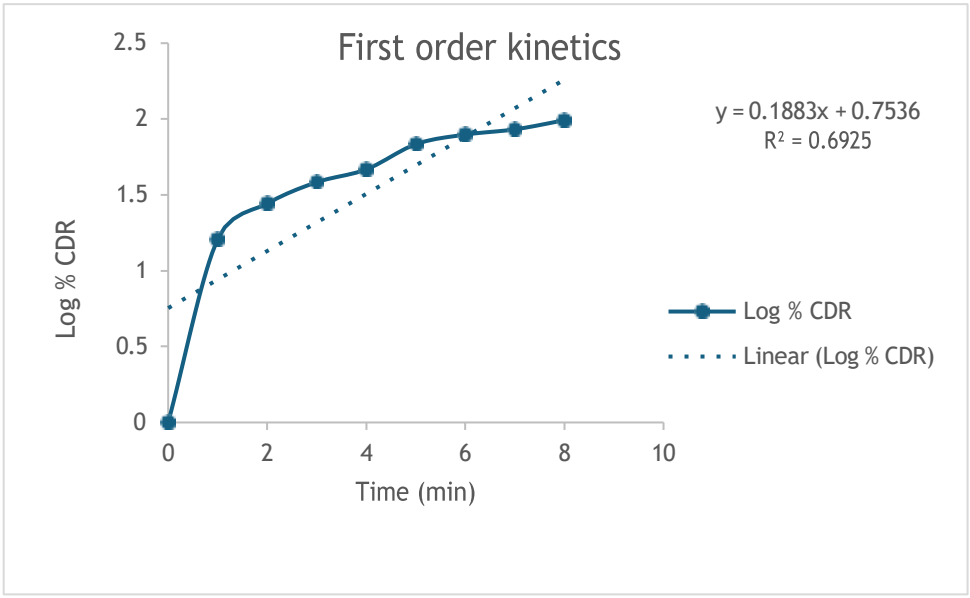

Figure 8: First Order Plot for best preparation

Higuchi Model:

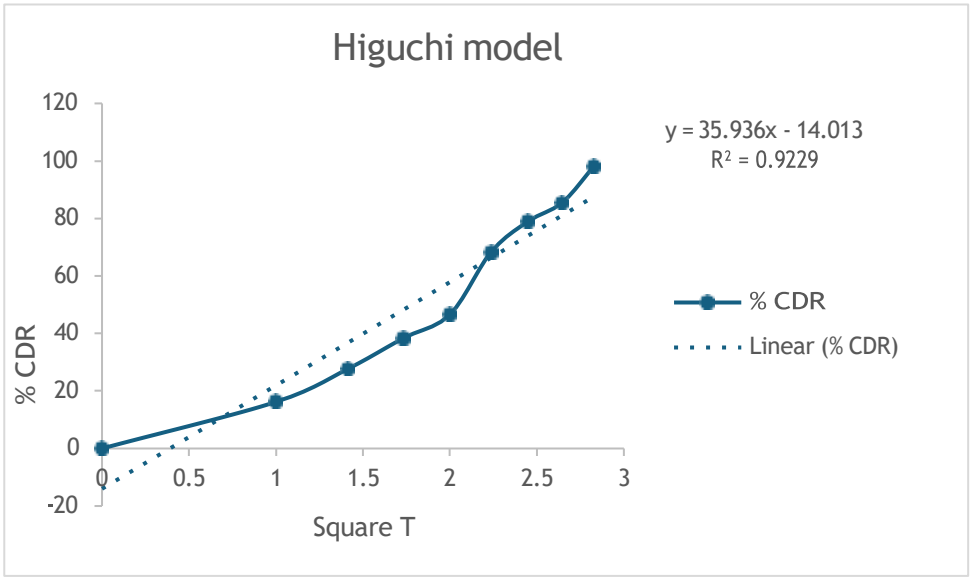

Figure 9: Higuchi Plot for best preparation

Korsmeyer Peppas equations:

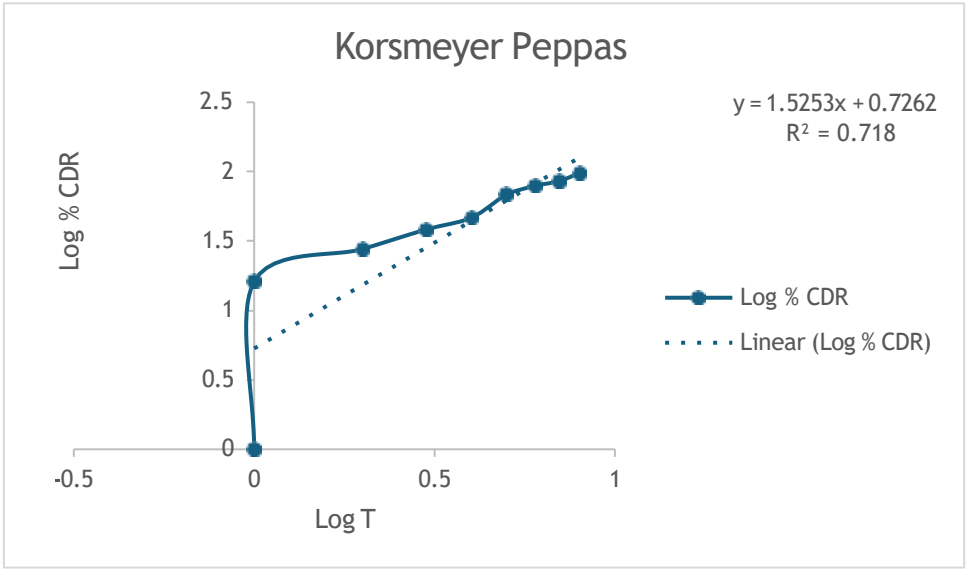

Figure 10: Korsmayer Peppas Plot For best preparation

Table 11: Drug release kinetics

S.no	Kinetic model	R^2 value
1	Zero-order kinetics	0.894
2	First-order kinetics	0.692
3	Higuchi model	0.922
4	Krosmayer Peppas	0.718

Model-Dependent Approaches:

Release Kinetics:

To know the drug release kinetics from these formulations, the dissolution data were subjected to different kinetic models such as Zero-order and Higuchi's square root kinetics model. The line of equations and regression coefficient of kinetic study for all the formulations are shown in the table. The regression coefficient was considered as the main parameter to interpret release kinetics. From the above results obtained the drug release mechanism was found to be dissolution control.

Stability Studies:

Table 12: Stability Studies of Optimized Formulation F4

S. No	ime in days	Physical changes	Mean % drug content ± SD		
			Mouth-dissolving tablet		
			25^0C/60%	30^0C/75%	40^0C/75%
1.	01	No Change	99.21	99.21	99.21
3.	30	No Change	99.12	99.17	99.05
5.	60	No Change	98.76	98.86	98.73
7.	90	No Change	98.64	9856	98.62

Discussion:

There was no significant change in physical and chemical properties of the tablets of formulation F4 after 3 Months, parameters like % drug release and assay values at various

conditions (at 40^0C/ 75% RH) as per ICH guidelines quantified at various time intervals were shown in Table and dissolution profile.

Conclusion:

Mouth dissolving tablets of griseofulvin were successfully formulated by direct compression using sodium starch glycolate as a super disintegrant, achieving rapid disintegration and improved dissolution compared with conventional tablets. Pre-compression and post-compression evaluations confirmed suitable flow properties, mechanical strength, content uniformity, and fast disintegration times for all formulations. Among the batches, formulation F4 showed the most favorable performance, releasing about 99% of griseofulvin within 60 min and following Higuchi diffusion-controlled kinetics, while remaining stable under accelerated storage. These findings support F4 griseofulvin MDT as a promising patient-friendly dosage form, particularly for populations with swallowing difficulties.

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