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

Shaik Irfan Khan, Pilli Santhu, Papagatla Polireddy*
Nalanda College of Pharmacy, Cherlapalli, Telangana 508002

ABSTRACT :
The present study aimed to design, prepare, and evaluate mouth dissolving tablets (MDTs) of griseofulvin using the direct compression technique to enhance patient compliance and achieve rapid onset of action. Eight formulations (F1–F8) were developed employing different types and concentrations of superdisintegrants such as crospovidone and croscarmellose sodium. Pre-compression evaluation of powder blends revealed good flow and compressibility, as indicated by bulk density (0.549–0.574 g/cm³), tapped density (0.605–0.640 g/cm³), Carr's index (13.24–14.98%), Hausner ratio (1.17–1.29), and angle of repose (26°–30°). Post-compression parameters including weight variation, hardness, friability, drug content, disintegration time, and wetting time were assessed. The results showed uniform weight (398–401 mg), acceptable hardness (3.7–4.9 kg/cm²), low friability (<0.5%), and rapid disintegration (20–32 seconds) with wetting times of 79–101 seconds. Batches F5 and F6 exhibited the most favourable combination of mechanical strength, rapid disintegration, and uniform drug content. The study concludes that direct compression is a suitable and efficient method for preparing griseofulvin MDTs, and optimized formulations demonstrate potential for improved patient acceptability and enhanced therapeutic efficacy.
Keywords: Griseofulvin, crospovidone and croscarmellose sodium, FTIR Studies, In vitro drug release studies

I.INTRODUCTION

Oral drug delivery remains the most preferred route of administration due to its convenience, safety, and patient compliance. However, conventional oral solid dosage forms such as tablets and capsules often pose swallowing difficulties, particularly in pediatric, geriatric, and dysphagic patients.[1] To overcome these limitations, mouth dissolving tablets (MDTs) have emerged as an effective alternative dosage form that rapidly disintegrates or dissolves in the oral cavity without the need for water, resulting in faster onset of action and improved patient acceptability.[2]Mouth dissolving tablets offer a promising approach to improve the dissolution rate and bioavailability of poorly water-soluble drugs like griseofulvin. The incorporation of suitable superdisintegrants and optimized formulation techniques can facilitate rapid tablet disintegration in saliva, enhancing drug dissolution and absorption. Additionally, MDTs eliminate the need for water, making them particularly advantageous for patients with swallowing difficulties and for those requiring rapid therapeutic action.[3]Griseofulvin is a broad-spectrum antifungal agent widely used in the treatment of dermatophytosis. Despite its clinical effectiveness, griseofulvin exhibits poor aqueous solubility and low oral bioavailability, which can lead to delayed onset of action and variable therapeutic response.[4]The present research is focused on the design, preparation, and in vitro evaluation of griseofulvin mouth dissolving tablets.[5] The study aims to formulate MDTs using appropriate excipients and superdisintegrants to achieve rapid disintegration, acceptable mechanical strength, and enhanced drug release.[6] Various formulation parameters such as hardness, friability, drug content uniformity, disintegration time, wetting time, and in vitro dissolution behavior are evaluated to identify an optimized formulation with improved pharmaceutical performance.[7]

II. EXPERIMENTAL WORK

Materials and methods

Griseofulvin was procured from Hetero Labs, Hyderabad. Cross povidone and Sodium starch glycolate were obtained from Synpharma Research Labs, Hyderabad. Other chemicals and the reagents used were of analytical grade.

Methodology

Drug excipient compatibility

Detect changes in characteristic functional-group bands (indicative of chemical interaction / new bond formation / salt formation).Sample prep: KBr pellet For pellets, mix ~1–2 mg sample in 100 mg KBr.Instrument settings: 4000–400 cm^{-1}, resolution 4 cm^{-1}, 32 scans.
Interpretation: compare spectrum of pure drug vs mixture and stored samples. Look for disappearance, shift (>10 cm^{-1}), or broadening of characteristic griseofulvin peaks (e.g., carbonyl, aromatic stretches) or new peaks. Small shifts ± a few cm^{-1} may be due to physical mixing — major shifts or new bands suggest interaction.[8]

Formulation table:
Table-1: Formulation table of MDTs

S.No	Ingredient	F1	F2	F3	F4	F5	F6	F7	F8
1	Griseofulvin	250	250	250	250	250	250	250	250
2	Cross povidone	25	50	75	100	-	-	-	-
3	Sodium starch glycolate	-	-	-	-	25	50	75	100
4	Lactose Monohydrate	112	87	62	37	112	87	62	37
5	Micro crystalline cellulose	5	5	5	5	5	5	5	5
6	Magnesium stearate	2	2	2	2	2	2	2	2
7	Talc	3	3	3	3	3	3	3	3
8	Aspartame	3	3	3	3	3	3	3	3
8	Total wt	400	400	400	400	400	400	400	400

Procedure
Direct compression technique

Accurately weigh all ingredients for the batch. Record lot and weight. Pass griseofulvin, Lactose, MCC and disintegrant separately through a suitable sieve (#40) to break lumps. Primary blending (API + diluent + part of disintegrant) Blend for 5–10 minutes to ensure uniform distribution. Add taste-masking agents, flavors Blend for additional 3–5 minutes.Glidant& lubricant addition: Add colloidal silicon dioxide (glidant) and blend for 1–2 minutes to uniformly distribute. Then add magnesium stearate (lubricant) and blend gently for not more than 1–2 minutes (overmixing with lubricant can reduce tablet hardness and slow disintegration). Compression: Set the tablet press to desired weight and thickness. Start with low compression force and make trial tablets.[9]

Evaluation of tablet[10,11,12]
Weight variation
Twenty tablets were randomly selected form each batch and individually weighed. The average weight and standard deviation of 20 tablets was calculated. The batch passes the test for weight variation test if not more then two of the individual tablet weight deviate from the average weight by more than the percentage.

Thickness
Twenty tablets were randomly selected form each batch and there thickness was measured by using vernier caliper. Thickness of three tablets from each batch was measured and mean was calculated.

Hardness
Hardness indicates the ability of a tablet to withstand mechanical shocks while handling. The hardness of the tablets was determined using Pfizer hardness tester. It is expressed in kg/cm2. Three tablets were randomly picked and hardness of the tablets were determined.

Friability
Friability test is performed to assess the effect of friction and shocks, which may often cause tablet to chip, cap or break. Roche friabilator was used for the purpose. This device subjects a number of tablets to the combined effect of abrasion and shock by utilizing a plastic chamber that revolves at 25 rpm dropping the tablets at distance of 6 inches with each revolution. Twenty tablets were weighed and placed in the Roche friabilator, which was then operated for 25 rpm for 4 min. After revolution Tablets were dedusted and reweighed. Compressed tablets should not loose more than 1% of their weight.
The percentage friability was measured using the formula,

$$\% F = \{1-(Wo/W)\} \times 100$$

Where,
% F = friability in percentage
Wo = Initial weight of tablet
W = weight of tablets after revolution

Content Uniformity
Powder equivalent of Griseofulvin was dissolved in phosphate buffer pH 6.8. Sufficient dilutions were made to obtain 10 mcg/ml solution. Absorbance of the resulting solution was measured using a T60 model UV/VIS spectrophotometer. From the absorbance values, amount of drug present in the given tablet was calculated. Procedure was repeated by using four more tablets from the same formulation and the average value of all five tablets was calculated.

Wetting time
A piece of tissue paper folded twice was placed in a small petridish containing ten milliliters of distilled water and water-soluble die. A tablet was placed on the paper and the time required for complete tablet wetting was measured. Complete wetting can be taken as the time at which colored water covered the entire tablet.

In- Vitro Release study
The release rate of Griseofulvin from fast dispersible tablets was determined using dissolution testing apparatus II (paddle method). The dissolution test was performed using 900 ml of phosphate buffer pH 6.8 as a dissolution medium, at 37±0.5oC and 50 rpm. A sample (5 ml) of the solution was withdrawn from the dissolution apparatus at different time interval (minutes). The samples were filtered through a 0.45m membrane filter. Absorbance of these solutions was measured using a instrument T60 model UV/VIS spectrophotometer. Cumulative percentage of drug release was calculated using an equation obtained from a standard curve.

In vitro release studies
This in vitro release can be done by using USP dissolution apparatus I. The test is performed at 50 rpm. The media used were pH 1.2 buffer for initial 2 h, followed by 8 h in pH 6.8 phosphate buffer. The temperature was maintained at 37 ± 0.5°C. The samples were taken at predetermined time and the dissolution basket is replenished with the buffer. The taken samples were filtered through filtered through a 0.45 membrane filter. The absorbance was measured at 270 nm. For every trials, the experiments were done in triplicate. The release data of all the trials were analyzed to observe the release kinetics using zero order, first order and matrix, korsmeyer-peppas equations.

Release kinetics
The release kinetics can be understand basically by applying the obtained data to the release kinetics models.
Zero order
C = K0t
K0 - rate constant for Zero-order (concentration/time) t - Time (h).
First order
Log C = LogC0 – Kt / 2.303
Where C0 - Initial concentration of drug K = constant first order and t = Time (h)
Higuchi
Qt = Kt1/2
Where Qt - Amount of the drug release drug in time t K- Kinetic constant and t- is time in hrs Korsmeyer Pappas
Mt / M = Kt n
Where, Mt - amount of the released drug at time t, M- Overall drug amount released after 8 hrs K- Diffusion constant n- Diffusion exponent mechanism of release of drug.

Stability studies
The success of an effective formulation can be evaluated only through stability studies. The prepared disintegration tablets of Griseofulvin were placed on plastic tubes containing desiccant and stored at ambient conditions, such as at room temperature, 40±2oc and refrigerator 2-8oc for a period of 90 days.

III.RESULTS AND DISCUSSION

FT-IR Spectrum of Griseofulvin

All the formulations were uniform in drug content and the FTIR spectra of Griseofulvin and its fast disintegrating tablets are identical. The principle FTIR absorption peaks of Griseofulvin fast disintegrating tablets were observed and found to be identical with the spectra of Griseofulvin pure drug. Thus from the spectra it was understood that there was no interaction between Griseofulvin and the disintegrants used in the preparation of tablets.

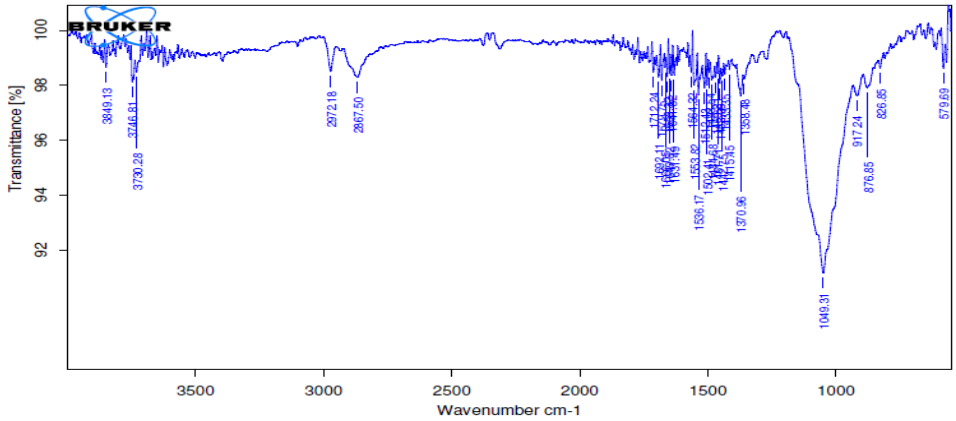

Fig-1: FTIR Studies of Drug

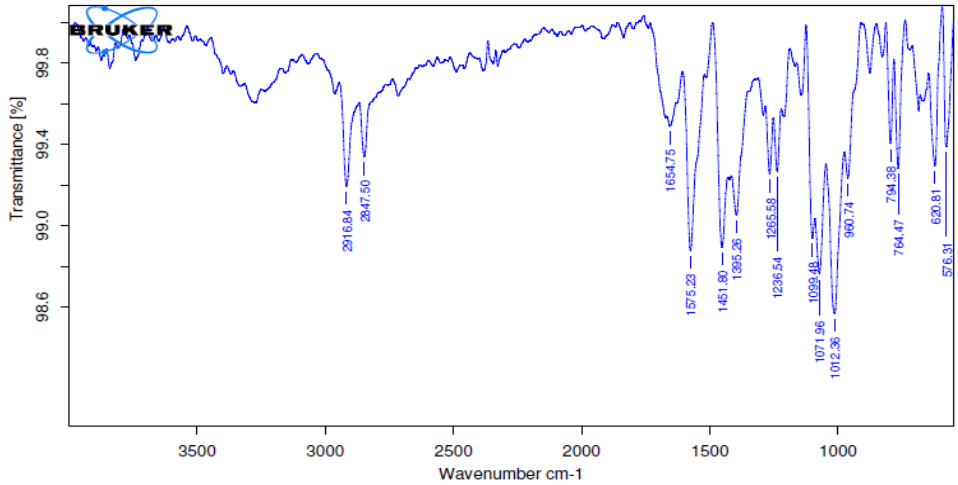

Fig-2: FTIR Studies of optimized formulation

Evaluation studies

Weight variation:

Tablet weights ranged from 398 mg to 401 mg, which is within ±5% of the target weight of 400 mg. This indicates uniform die filling during compression and consistent blending of the powder mixture. Compliance with pharmacopeial limits ensures dose uniformity, critical for therapeutic efficacy.

Thickness:

Thickness ranged from 2.1 mm to 3.7 mm, showing slight variability due to differences in compression force or formulation density. F4 (3.7 mm) is slightly thicker; F8 (2.1 mm) is thinner. Minor differences are acceptable as long as mechanical strength and disintegration are not compromised. Uniform thickness contributes to visual appeal and patient acceptability.

Hardness:

Hardness values ranged from 3.7 to 4.9 kg/cm². This range is adequate for MDTs, balancing mechanical strength and rapid disintegration. F7 (4.9 kg/cm²) is the hardest, which could slightly increase disintegration time; F4 (3.7 kg/cm²) is the softest but still acceptable.

Friability:
Friability values were between 0.32% and 0.43%, well below the USP limit of 1%. Low friability indicates that the tablets can withstand handling, packaging, and transport without significant breakage

Content Uniformity:
Drug content ranged from 76.98% to 83.69%. The slightly lower content in F3 (76.98%) may indicate minor content non-uniformity, possibly due to segregation during blending. Most batches (F2, F4, F5, F6, F7) have acceptable drug content near 80–84%, suitable for further development. Ensuring proper blending and avoiding segregation is essential to maintain assay within 95–105% of label claim in future scale-up.

Disintegration Time:
Disintegration times ranged from 20 sec to 32 sec, which is appropriate for MDTs (<60 sec). F6 showed the fastest disintegration (20 sec), likely due to higher superdisintegrant efficiency or optimal compression. F8 had the slowest disintegration (32 sec), possibly due to smaller thickness (2.1 mm) combined with slightly higher binder effect.

Wetting Time:
Wetting times ranged from 79 sec to 101 sec, reflecting tablet porosity and water absorption ability.

F3 had the highest wetting time (101 sec), which correlates with slightly slower penetration of water into the tablet matrix.

Lower wetting times in F1, F2, F5, F6 indicate faster saliva absorption, improving oral disintegration and patient convenience.

Table-2: Evaluation parameters of Griseofulvin mouth dissolving tablets

F. No.	Weight variation (mg)*	Thickness (mm)*	Hardness (kg/cm^2)*	Friability (%)	Drug content (%)	Disintegration time(sec)	Wetting time (sec)
F1	400	2.9	4.5	0.43	78.69	29	79
F2	399	3.1	4.3	0.38	80.12	30	81
F3	400	2.5	3.9	0.32	76.98	25	101
F4	398	3.7	3.7	0.41	82.16	27	98
F5	401	2.9	4.3	0.43	80.22	23	89
F6	400	2.8	4.2	0.35	83.69	20	93
F7	399	2.6	4.9	0.43	80.56	27	95
F8	400	2.1	4.5	0.40	79.89	32	99

Dissolution studies

All the 8 formulation of Griseofulvin mouth dissolving tablets were subjected to in vitro release studies these studies were carried out using dissolution apparatus. The dissolution medium consisted of 900 ml of Standard buffer pH 6.8 for period of time.

Table-3: Drug release studies of all formulations

Time	F1	F2	F3	F4	F5	F6	F7	F8
0	0	0	0	0	0	0	0	0
5	24.96	28.90	27.25	26.39	25.19	29.17	25.98	28.10
10	38.69	40.15	38.75	35.67	37.12	38.15	37.48	35.46
15	56.79	60.24	57.82	55.15	59.81	58.27	55.33	52.18
20	70.15	71.25	70.22	69.50	68.79	67.89	68.79	65.79
25	80.69	82.67	80.17	79.84	78.91	81.59	79.23	75.63
30	94.59	95.98	91.35	94.53	95.58	98.55	96.39	92.37

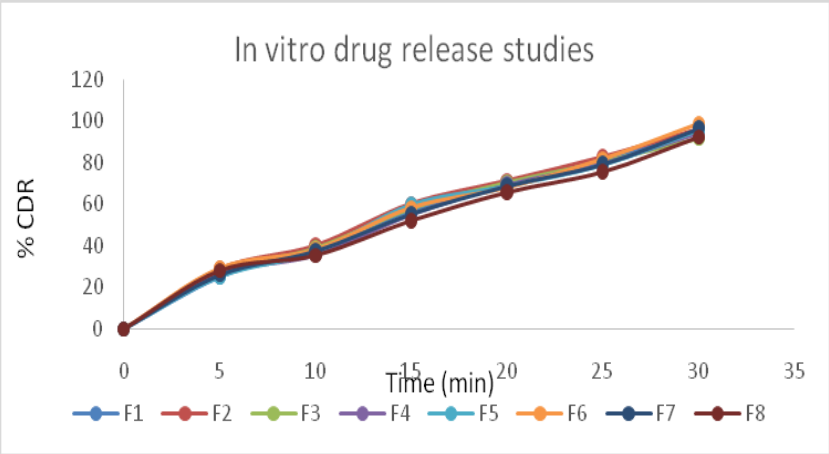

Table-3: Dissolution Profile of F1 to F8 formulations

Drug release kinetics studies

Zero order kinetics

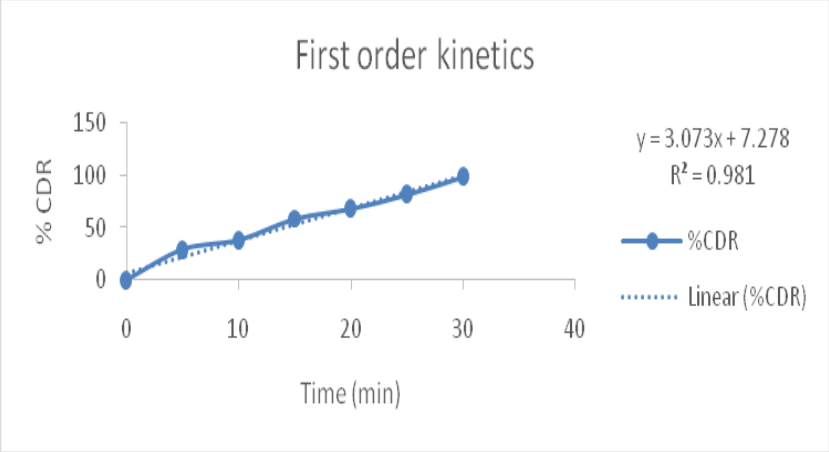

Fig-4: Zero order kinetics of optimized formulation

First order kinetics

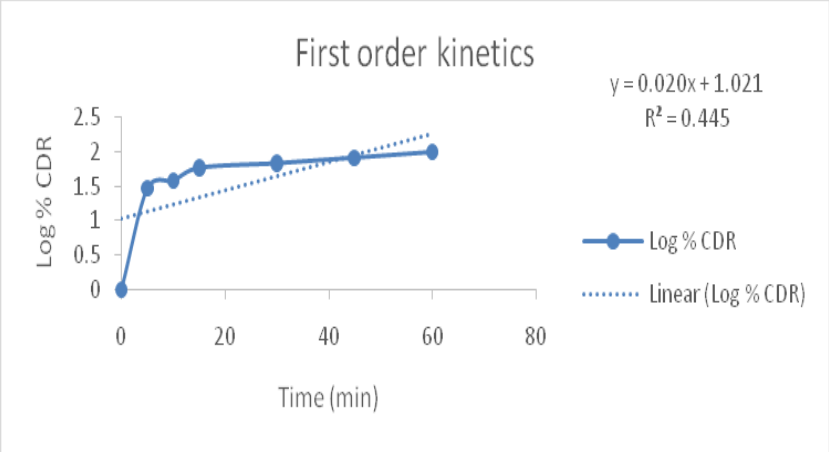

Fig-5: First order kinetics of optimized formulation

Higuchi model

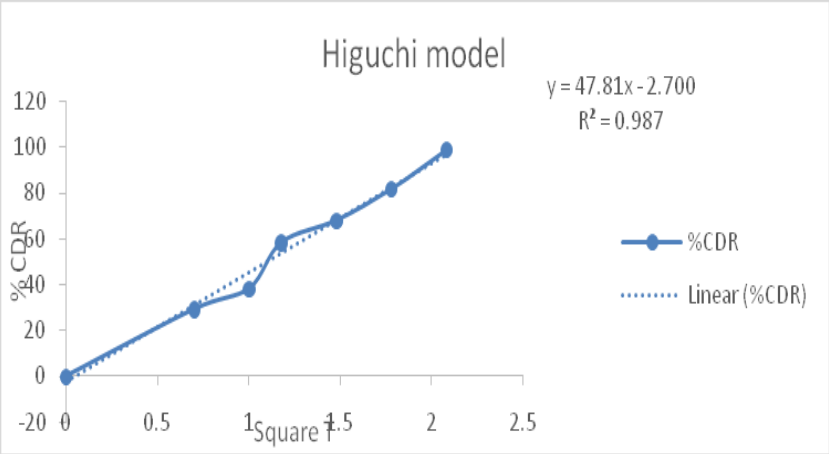

Fig-6: Higuchi model of optimized formulation

korsmeyer peppas

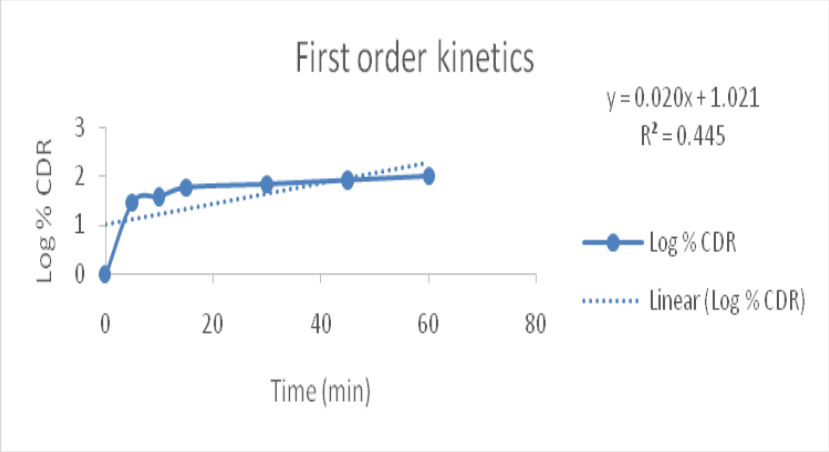

Fig-7: Korsmeyer peppas of optimized formulation

Stability Study

There was no significant change in physical and chemical properties of the tablets of formulation F-6 after 3 months. Parameters quantified at various time intervals were shown.

Table-11: Stability studies of all formulations

Formulation Code	Parameters	Initial	1st Month	2nd Month	3rd Month	Limits as per Specifications
F-6	**25^{0}C/60%RH % Release**	98.55	97.58	95.55	94.10	**Not less than 85 %**
F-6	**30^{0}C/75% RH % Release**	98.55	96.37	95.63	94.25	**Not less than 85 %**
F-6	**40^{0}C/75% RH % Release**	98.55	96.20	95.22	94.26	**Not less than 85 %**

CONCLUSION

The study confirms that griseofulvin MDTs can be successfully prepared by direct compression, producing tablets that are mechanically strong, fast-disintegrating, and patient-friendly. Pre- and post-compression

evaluations demonstrate that proper selection and concentration of superdisintegrants, along with careful blending and compression parameters, are critical to achieving uniformity, rapid disintegration, and acceptable drug release.Among the eight formulations, F5 and F6 are identified as the most suitable batches for further in-vitro dissolution studies and potential scale-up, as they exhibit the best balance between mechanical properties and rapid disintegration, fulfilling the objectives of developing a mouth dissolving griseofulvin tablet.

REFERENCES

1. Sheshala, Formulation and in vivo evaluation of ondansetron orally disintegrating tablets using different superdisintegrants, 2011 Nov;34(11):1945-56.
2. Seager H. Drug-delivery products and the Zydis fast-dissolving dosage form. J Pharm Pharmacol. 1998;50(4):375–382.
3. Fu Y, Yang S, Jeong SH, Kimura S, Park K. Orally fast disintegrating tablets: developments, technologies, taste-masking and clinical studies. Crit Rev Ther Drug Carrier Syst. 2004;21(6):433–475.
4. Bandari S, Mittapalli RK, Gannu R, Rao YM. Orodispersible tablets: An overview. Asian J Pharm. 2008;2(1):2–11.
5. Kuchekar BS, Badhan AC, Mahajan HS. Mouth dissolving tablets: A novel drug delivery system. Pharm Times. 2003;35(7):3–10.
6. Lachman L, Lieberman HA, Kanig JL. The Theory and Practice of Industrial Pharmacy. 3rd ed. Philadelphia: Lea &Febiger; 1986.
7. Sharma D, Soni M, Kumar S, Gupta GD. Fast dissolving tablets: A new era in novel drug delivery system. Int J Pharm Sci Rev Res. 2010;4(2):49–57.
8. Rajnikant M. Suthar, Formulation and Evaluation of Fast Dissolving Tablets of Ondansetron by Solid Dispersion in Superdisintegrants, Indian Journal of Pharmaceutical Education and Research | Vol 47 | Issue 3 | Jul–Sep, 2013
9. Praveen Khirwadkar et al., Formulation and evaluation of mouth dissolving tablets of atenolol, International Journal Of Pharmacy&Technology, IJPT, March-2011, Vol. 3, Issue No.1 , 1876-1888.
10. AmareshPrustyFormulation and in-vitro evaluation of amlodipine besylate-hp-b-cd inclusion complex incorporated mouth dissolving tablets Bulletin of Pharmaceutical Research 2014;4(3):124-8.
11. Sunidhimahant, formulation and evaluation of mouth dissolving tablets of ondansetron hydrochloride using plantago ovata (isapghula) mucilage as natural super disintegrating agent j herbmedpharmacol. 2015; 4(3): 102-109.
12. Basawaraj S Patil Formulation and evaluation of mouth dissolving tablets of nimesulide by new coprocessed technique Research Journal of Pharmaceutical, Biological and Chemical Sciences 2010 RJPBCS 1(4).