World Journal of Pharmaceutical Sciences
ISSN (Print): 2321-3310; ISSN (Online): 2321-3086
Available online at: https://wjpsonline.com/
Research Article

FORMULATION AND IN VITRO EVALUATION OF CLOBAZAM ORAL THIN FILMS

Jyothi. G*, Nousheen Fathima, Vijaya Lakshmi, Sudhakar.M

*Department of pharmaceutics, Malla Reddy College of Pharmacy, Hyderabad, Telangana, India.

Received: 19-03-2025 / Revised Accepted: 23-03-2025 / Published: 02-04-2025

ABSTRACT:

Fast dissolving drug delivery system offers a solution for those patients having difficulty in swallowing tablets/capsules. The present research work is to develop oral thin films of Clobazam by using solvent casting method. Oral thin films were developed by using various super disintegrants like Ludiflash and crospovidone in different concentrations with Gelatin, Poly vinyl alcohol as a film forming agents. The prepared formulations of films were evaluated for film thickness measurement, folding endurance study, in-vitro disintegration time, in-vitro drug release pattern (in pH 6.8 phosphate buffer). Drug content, and drug-polymers interaction study (IR spectroscopy). Among all formulations, the formulation (F12) prepared by 180 mg of Ludiflash show good drug release (99.85±1.17%). The Optimized formulation F6 follows first order.

Keywords: Clobazam, Ludiflash, oral thin films, FT-IR.

INTRODUCTION

Because of its safety, convenience of use, and patient acceptance, the oral route is one of the most popular ways to administer medications. Oral solid dose forms are available for around 60% of traditional dosage forms.[1] The company switched to parenterals and liquid dosage forms due to the patients' dysphasia, limited bioavailability, and prolonged start of action. However, the inability to accurately dose liquid dosage forms (such as syrup, suspension, emulsion, etc.) and the discomfort associated with parenteral medication administration lead to patient noncompliance. Tablets and capsules are the most widely used oral dose forms; nevertheless, one significant disadvantage of these forms is their inability to be swallowed.[2] When it comes to ingesting oral dose forms, drinking water is crucial. while water is unavailable, many find it difficult to take pill dose forms, especially while traveling (motion sickness) or experiencing abrupt attacks of coughing during bronchitis, allergies, or the common cold. In these situations, tablets known as "fast dissolving tablets"—which dissolve or disintegrate quickly in the oral cavity—have garnered a lot of interest. Other names for fast-dissolving tablets include porous tablets, orodispersible tablets, mouth-dissolving tablets, and rapidmelts. Fast dissolving tablets dissolve or disintegrate within 60 seconds when placed in the mouth without drinking water or chewing. The active components reach the bloodstream after being absorbed by the mouth and gastrointestinal tract's mucous membranes.[3] However, a new technology was created as an oral dissolving strip because of some drawbacks, such as their physical solid form, psychological fear of swallowing, chewing, or choking, the friability of wafer-like porous and low pressure moulded tablets, and the high cost of packaging these dosage forms to keep them safe. Because they are more comfortable and flexible, oral dissolving strips are the most sophisticated type of oral solid dose form. [4] By dissolving in the oral cavity within a minute of coming into touch with saliva, it increases the effectiveness of APIs without requiring chewing or water for delivery. The oral mucosa's high blood flow and permeability, which are four to a thousand times larger than those of the skin, allow for rapid medication absorption and immediate bioavailability. Patients with illnesses including abrupt bouts of allergy reactions or coughing, as well as those who are bedridden, elderly, pediatric, or emetic, might benefit from using oral dissolving strips. Both systemic and local delivery are possible with them.

Address for Correspondence: Jyothi. G, Department of pharmaceutics, Malla Reddy College of Pharmacy, Hyderabad, Telangana, India, **Email:** gattujyothireddy@gmail.com.

How to Cite this Article: Jyothi. G, FORMULATION AND IN VITRO EVALUATION OF CLOBAZAM ORAL THIN FILMS. World J Pharm Sci 2025; 13(01): 180-188; https://doi.org/10.54037/WJPS.2022.100905

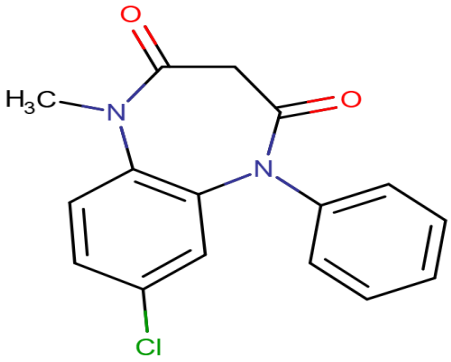

Figure.1 Structure of Clobazam

The creation of oral dissolving strips as a substitute for fast-dissolving tablets is gaining traction[5] because of their improved patient compliance, increased flexibility, and quicker rate of disintegration. Research on the utilization of oral dissolving strips as potentially effective delivery systems for a variety of active medicinal components has recently surfaced.[6-11]

MATERIALS & METHODS USED: Clobazam API was procured from Kekule Pharma Limited, and Gelatin, Propylene Glycol, Citric acid, Ludiflash and Aspartame were procured from S.D Fine Chemicals, Crospovidone were procured from Signet Chemical Corp., Mumbai and Trusil mixed flavor R.S.V were procured from International flavours of fragnance India Ltd.

Preparation Method:

Formulation of Oral Thin Films of Clobazam:

The oral thin films of Clobazam was prepared by solvent casting technique. The Oral Thin Films were prepared using polymers like Gelatin, PVA. Propylene glycol is used as a plasticizer and super disintegrants like Ludiflash and Crospovidone. The calculated amount of polymers i.e film forming agents and disintegrants were dispersed in the three-fourth volume of a beaker with continuous stirring using magnetic stirrer and the final volume was adjusted with distilled water. The calculated amount of Clobazam was incorporated in the polymeric solutions after levitation with required volume of Propylene Glycol, citric acid, Aspartame and Vanilla Flavor. The solution was cast onto Glass Plate then kept in hot air oven at 400c. The films were punched into size of 4cm2 containing 10mg of Clobazam . By carrying out the trial and error method different concentrations for a film forming polymers were used like Gelatin, PVA. It has been found that 200mg of gelatin, 200 mg of PVA shows better films. Which these concentrations of films were prepared by dissolving different quantities of film forming polymers in required amount of water.

Table.1 Formulation details of Clobazam Oral thin films

Formulation Code / Ingredients(mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
Clobazam	90	90	90	90	90	**90**	90	90	90	90	90	90
Gelatin	200	200	200	200	200	**200**	-	-	-	-	-	-
PVA	-	-	-	-	-	-	200	200	200	200	200	200
Ludiflash	30	60	90	120	150	**180**	-	-	-	-	-	-
Crospovidone	-	-	-	-	-	-	30	60	90	120	150	180
Aspartame	10	10	10	10	10	**10**	10	10	10	10	10	10
Citric acid	5	5	5	5	5	**5**	5	5	5	5	5	5
Vanilla Flavor(mg)	10	10	10	10	10	**10**	10	10	10	10	10	10
Propylene Glycol(ml)	30	30	30	30	30	**30**	30	30	30	30	30	30
Distilled water	Q.S	Q.S	Q.S	Q.S	Q.S	**Q.S**	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S

Calculation of dose for Ezogabine:

The dose of Clobazam is 90 mg. Therefore, amount of Clobazam required in 4 cm2 film is 10 mg.

- Length of glass plate =6 cm.
- Width of glass plate =6 cm.
- Area of the plate =36 cm2.
- No. of 4 cm2 films present whole plate =36/4 =9 films.
- Therefore, Each films contains 10 mg of drug
- 9 films contain 90 mg drug (9*10).
- So, the Labelled claim of drug = 10 mg

a) Physical appearance and surface texture of film:

This parameter was checked simply with visual inspection of films and evaluation of texture by feel or touch.

b) Weight uniformity of films

Three films of the size 4cm square were weighed individually using digital balance and the average weights were calculated.

c) The thickness of films

The thickness of the films was measured using screw gauge with a least count of 0.01mm at different spots of the films. The thickness was measured at three different spots of the films and average was taken.

d) Folding endurance of films

The flexibility of films can be measured quantitatively in terms of folding endurance. Folding endurance of the films was determined by repeatedly folding a small strip of the films (approximately 4 cm^2) at the same place till it broke. The number of times films could be folded at the same place, without breaking gives the value of folding endurance.

e) Surface pH of films

Surface pH was determined by the films were allowed in contact with 1ml of distilled water. The surface pH was noted by bringing a combined glass electrode or pH paper near the surface of films and allowing equilibrate for 1 min.

f) In vitro disintegration time of films

Disintegration test was performed in the USP disintegration time testing apparatus. 6.8 pH Buffer solution used as a medium. The films were placed in the tubes of the container and disintegration time was recorded.

g) Drug content uniformity study of films

The films were tested for drug content uniformity by a UV-Spectrophotometric method. Films of 2 cm diameter were cut from three different places from the casted films. Each film was placed in 100 ml volumetric flask and dissolved in 6.8 pH Buffer solution and 0.2 ml is taken and diluted with Buffer up to 10 ml. The absorbance of the solution was measured at 232 nm using UV/visible spectrophotometer (Single beam spectrophotometer (YIS-294)). The percentage drug content was determined using the standard graph and the same procedure was repeated for three films.

h) In-vitro Dissolution Study

In vitro dissolution of Clobazam Oral thin films was studied in modified USP type 5 apparatus dissolution test apparatus 900ml 6.8 pH Buffer solution was used as dissolution medium. The stirrer was adjusted to rotate at 50rpm.The temperature of dissolution medium was maintained at 37±0.5ºC throughout the experiment. One film was used in each test. Samples of dissolution medium (5ml) were withdrawn by means of a syringe fitted with pre-filter at known intervals of time and analyzed for drug release by measuring the absorbance at 232 nm. The volume withdrawn at each time interval was replaced with the fresh quantity of dissolution medium. Cumulative percent Clobazam released was calculated and plotted against time.

i) Drug Release Kinetics

To analyze the mechanism of the drug release rate kinetics of the dosage form, the data obtained were plotted as:

1) Cumulative percentage drug released Vs time (In-Vitro drug release plots)
2) Log cumulative percentage drug remaining Vs Time (First order plots)

RESULTS AND DISCUSSIONS

In the present study, an attempt has been made to formulate and evaluate oral thin films of Clobazam by the solvent casting method using Crospovidone and Ludiflash as super disintegrants.

Solubility

The solubility of Clobazam was carried out at 250C using 0.1 N HCL, 6.8 pH phosphate buffer, 7.4 pH Phosphate buffer and purified water.

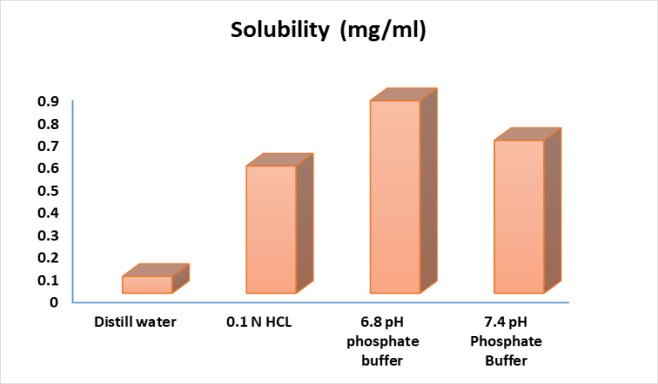

Figure.2 Solubility graph

Discussion:
From the conducted solubility studies in various solutions, we can say that 6.8 pH phosphate Buffer solutions have more solubility when compared to other buffer solutions.

Flow properties of the pure drug:

Table.2 Flow properties of the pure drug

Angle of repose	**27.02±1.21**
Bulk density	**0.348±0.004**
Tapped density	**0.457±0.008**
Carr's index	**14.26±1.27**
Hausner's ratio	**1.16±0.04**

Discussion: From the above flow properties of the pure drug, it was concluded that the all the parameters are within the limits indicating the free flow of drug.

UV spectrum of Clobazam:

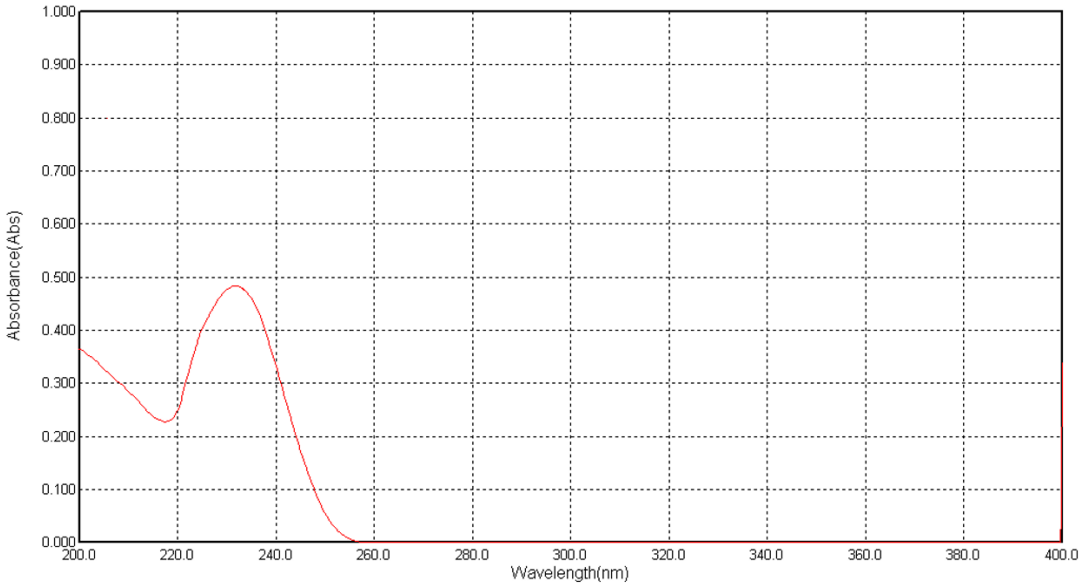

Figure.3 Absorption maxima of Clobazam in 6.8 pH phosphate buffer

Discussion:
A solution of Clobazam containing the conc. 8 µg/ ml was prepared in 6.8 pH Buffer buffer and UV spectrum was taken using Single Beam Spectrophotometer(YIS-294). The solution was scanned in the range of 200 – 400 nm. The maximum absorbance was found to be at 232 nm.

Standard Calibration Curve of Clobazam In 6.8 pH Phosphate Buffer:
Standard calibration curve of Clobazam was drawn by plotting absorbance vs concentration. The λmax of Clobazam in 6.8 pH phosphate buffer was determined to be 232 nm as shown in Fig. The absorbance values are tabulated in Table. Standard calibration curve of Clobazam in the Beer's range between 0-30 µg/ml is shown in Fig.

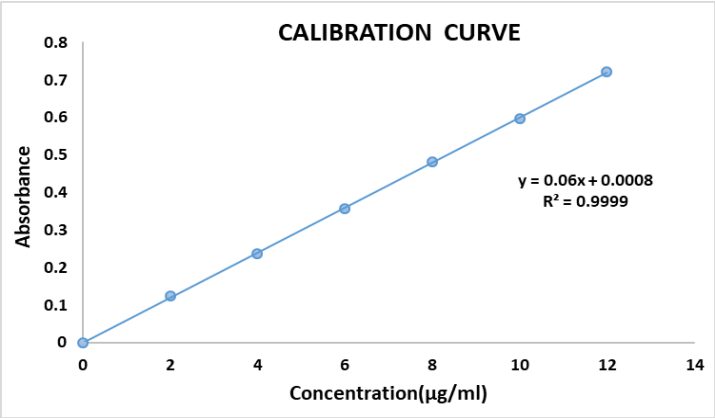

Figure.4 Standard calibration curve for Clobazam in 6.8 pH phosphate buffer at λmax 232 nm.

Discussion:

The linearity was found to be in the range of 2-12 g/ml in 6.8 pH phosphate buffer. The regression value was closer to 1 indicating the method obeyed Beer-lambert's law.

Compatibility Study:

Pure Drug:

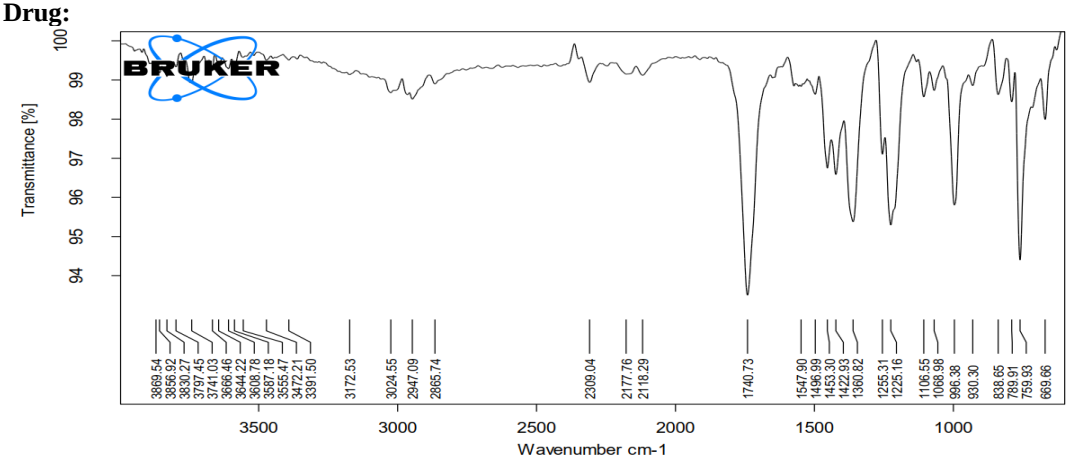

Figure.5 I.R. Spectra of pure drug

Optimized formulation:

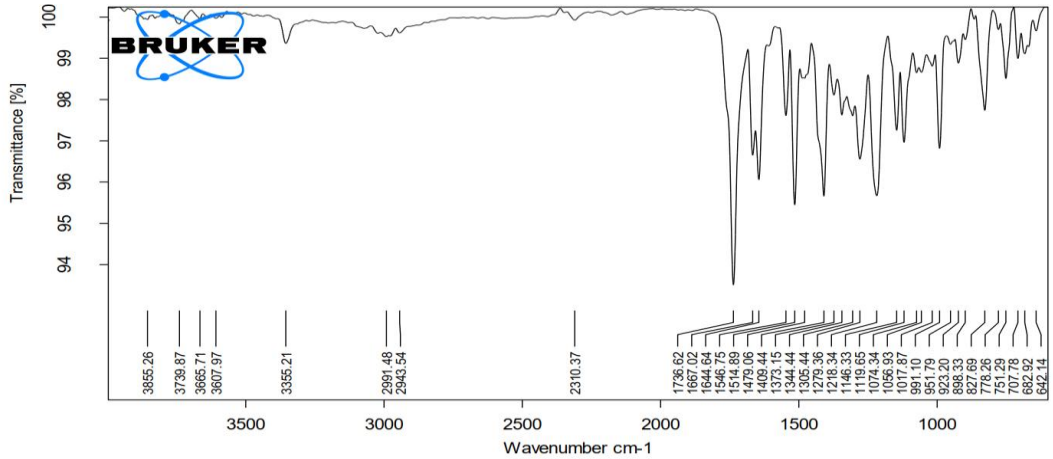

Figure.6 I.R. Spectra of optimized formulation

Discussion: From the drug excipient compatibility studies we observed that there are no interactions between the pure drug (Clobazam) and optimized formulation (Clobazam + excipients) which indicates there are no physical changes.

Evaluation of Oral Thin Films Formulations:

Physical appearance and surface texture of films:

Table.3 Evaluation Parameters

Formulation Code	Physical appearance	Surface of Film
F1	Semi transparent	Smooth surface
F2	Semi transparent	Smooth surface
F3	Semi transparent	Smooth surface
F4	Semi transparent	Smooth surface
F5	Semi transparent	Smooth surface
F6	Semi transparent	Smooth surface
F7	Semi transparent	Smooth surface
F8	Semi transparent	Smooth surface
F9	Semi transparent	Smooth surface
F10	Semi transparent	Smooth surface
F11	Semi transparent	Smooth surface
F12	Semi transparent	Smooth surface

Discussion: These parameters were checked simply with visual inspection of films and by feel or touch. The observation suggests that the films are having the smooth surface and they are semitransparent enough to see

Evaluation parameters of oral thin films

Table.4: Evaluation of Oral Thin Films of Clobazam

Formulation Code	Avg. Weight (mg	Avg. Thickness (mm)	Avg. Folding Endurance
F1	41.25±1.12	0.23±0.02	147±1
F2	45.71±1.34	0.29±0.01	149±2
F3	49.32±1.42	0.22±0.02	156±4
F4	52.60±1.56	0.24±0.03	151±1
F5	56.43±1.19	0.22±0.01	158±3
F6	59.27±1.24	0.25±0.02	169±1
F7	42.43±1.27	0.27±0.01	154±2
F8	46.20±1.46	0.29±0.02	167±2
F9	48.33±1.21	0.23±0.02	148±3
F10	51.07±1.37	0.24±0.01	151±4
F11	55.46±1.49	0.26±0.02	153±2
F12	58.27±1.20	0.28±0.02	157±1

Discussion:

The average weight the films was found in between 41.25±1.12- 450.85±0.16. The average thickness of the films was found in between the range of 0.22±0.01-0.29±0.02mm. The average folding endurance of the films was been found in between the ranges of 147±1-169±1.

Table.5: Evaluation of Oral thin films of Clobazam

Formulation Code	Avg. Drug Content Uniformity (%)	Avg. In Vitro Disintegration(sec)	Avg. Surface pH
F1	93.37±1.42	28±1.2	6.7±0.08
F2	95.45±1.36	25±1.4	6.5±0.05
F3	96.61±1.48	23±1.5	6.8±0.04
F4	97.89±1.65	20±1.4	6.5±0.09
F5	98.34±1.29	17±1.2	6.6±0.07
F6	99.45±1.47	14±1.2	6.8±0.06
F7	93.26±1.65	32±1.2	6.5±0.05
F8	94.20±1.48	29±1.1	6.7±0.03
F9	94.88±1.25	25±1.5	6.7±0.04
F10	96.37±1.29	23±1.3	6.8±0.05
F11	97.42±1.42	20±1.2	6.6±0.08
F12	98.29±1.26	17±1.5	6.7±0.07

Discussion:

The average content uniformity of the formulations from F1 to F12 was found in between 90.45±0.42% - 98.98±0.26. The Disintegration time of the films from F1 to F12 was in between the range of 19±1.22-10±1.08. The average surface pH of the films was in the range of pH 6.5±0.05-6.8±0.06.

In-Vitro Dissolution Study: The in-vitro drug release study of oral thin films from each batch (F1 to F12) was carried out in 6.8 pH phosphate buffer solution for 30 mins and the values are shown in Table. The plot of % Cumulative drug release V/s time (mins) were plotted and depicted as shown in Fig & Table

Table.6 In vitro dissolution studies

Time(min)	F1	F2	F3	F4	F5	F6
0	0	0	0	0	0	**0**
5	32.12 ±1.48	44.17 ±1.47	49.48 ±1.35	55.37 ±1.20	64.48 ±1.37	**71.45 ±1.65**
10	44.45 ±1.54	59.65 ±1.45	57.20 ±1.15	68.48 ±1.16	78.46 ±1.25	**79.43 ±1.24**
15	57.18 ±1.46	63.38 ±1.47	68.47 ±1.25	76.37 ±1.25	86.45 ±1.32	**87.45 ±1.16**
20	71.57 ±1.45	77.45 ±1.28	76.13 ±1.65	85.45 ±1.37	93.18 ±1.45	**96.38 ±1.37**
25	79.65 ±1.37	88.34 ±1.45	89.24 ±1.13	93.45 ±1.12	95.35 ±1.25	**99.85 ±1.17**
30	86.47 ±1.12	93.67 ±1.12	98.45 ±1.14	99.14 ±1.37	99.74 ±1.16	
35	97.32 ±1.48	98.85 ±1.75				

Table.7 In vitro dissolution studies

Time(min)	F7	F8	F9	F10	F11	F12
0	0	0	0	0	0	0
5	34.47 ±1.25	42.44 ±1.52	45.47 ±1.48	49.37 ±1.54	53.76 ±1.18	63.42 ±1.21
10	46.47 ±1.37	58.32 ±1.63	59.52 ±1.54	62.18 ±1.37	65.45 ±1.20	79.47 ±1.23
15	59.54 ±1.78	65.32 ±1.84	68.41 ±1.69	70.45 ±1.28	72.26 ±1.15	85.45 ±1.20
20	75.39 ±1.58	73.35 ±1.28	77.26 ±1.78	79.37 ±1.18	85.37 ±1.45	97.46 ±1.37
25	88.32 ±1.87	89.76 ±1.15	90.42 ±1.27	87.45 ±1.19	89.45 ±1.28	99.14 ±1.20
30	93.28 ±1.68	94.48 ±1.36	96.34 ±1.24	98.79 ±1.25	99.53 ±1.17	
35	98.42 ±1.46	98.76 ±1.75	99.12 ±1.38			

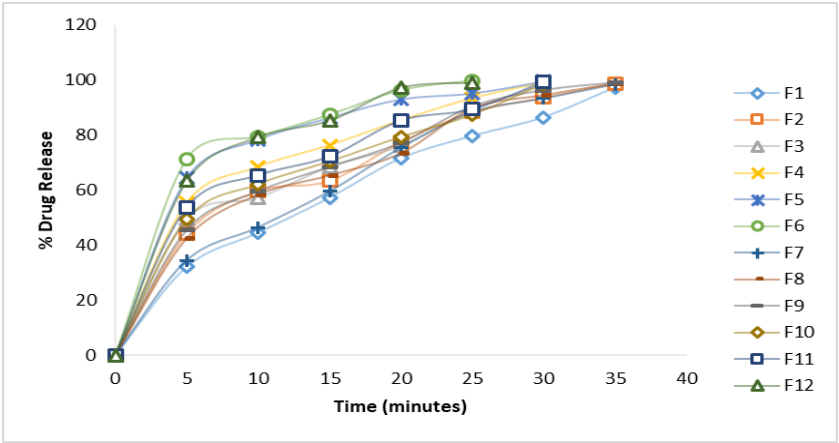

Figure.7 In-vitro drug release of formulations (F1-F12)

Discussion:

From the Invitro dissolution studies it was identified that the Formulations containing Ludiflash in the concentration of 30mg, 60mg, 90mg, 120mg,150mg and 180mg and Gelatin in concentration of 200mg i.e.,(F1-F6) shows 97.32±1.48%, 98.85±1.75% at the end of 35mins, 98.45±1.14%, 99.14±1.37% and 99.74±1.16% at the end of 30mins.While Formulation F6 Shows 99.85±1.17% release at the end of 25 mins. Formulations containing Crospovidone in the concentration of 30mg, 60mg, 90mg, 120mg,150mg and 180mg and PVA in concentration of 200mg i.e,(F7-F12) shows 98.42±1.46%, 98.76±1.75%, 99.12±1.38% at the end of 35mins, 98.79±1.25% and 99.53±1.17% at the end of 30mins.While Formulation F12 Shows 99.14±1.20% release at the end of 25 mins. This shows that effectiveness of super disintegrants is in the order of Ludiflash>Crospovidone. The concentration of super disintegrant's in the formulations also increased the dissolution rates. In all the formulations 200mg concentration of Gelatin and 180 mg of Ludiflash, there was linearly increase in dissolution rate. At higher concentration, all the formulations showed increase in dissolution rate.

Drug Release Kinetics of Clobazam

Zero Order Release Kinetics

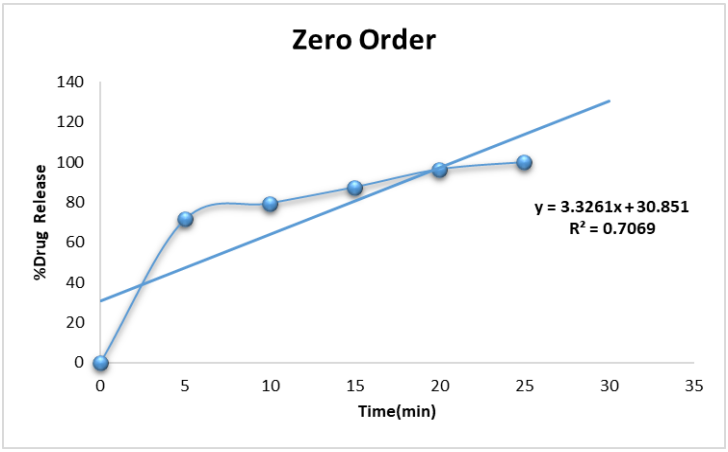

Figure.8 Zero order release profile of Clobazam Best formulation (F6)

First Order Release Kinetics Data

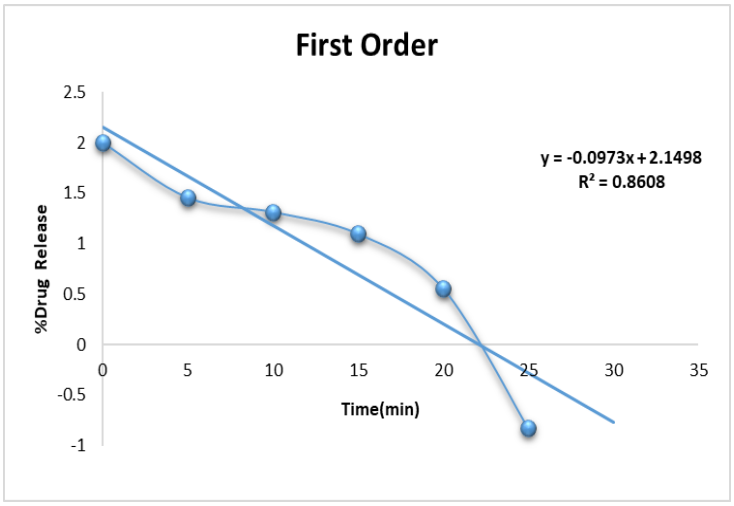

Figure.9 First order release profile of Clobazam Best formulation (F6)

Discussion: The in vitro dissolution data for best formulation F6 were fitted in different kinetic models i.e, zero order, first order. Optimized formulation F6 follows first order.

CONCLUSION:

In the present study Oral drug delivery system of Clobazam were successfully developed in the form of oral thin films which offers a suitable and practical approach in serving the desired objective of faster disintegration and dissolution characteristics with increase bioavailability. Oral thin films of Clobazam were prepared by using Crospovidone and Lufiflash as super disintegrants. Under the pre-formulation studies, API characterization and drug-excipient compatibility studies were carried out. The API characterization showed compliance with the drug characteristics. The disintegrants and other excipients were selected based on the satisfying results

produced during drug- excipient compatibility studies to develop the final formulation. The final suitable formulation (F6) was achieved fruitfully by the solvent casting method using Gelatin as film forming agent and Ludiflash as disintegrant which exhibited a rapid disintegration time (14±1.2 sec) and in vitro drug release (99.85±1.17%) ate the end of 25minutes. Considering the results of batches containing Ludiflash and crospovidone as disintegrant it can be concluded that the formulation F6 was meeting the higher in-vitro correlation limits and in less instance of time when subjected to the comparison with other formulation with Ludiflash as the disintegrating agent. It was also observed that solvent casting method was the best suitable method used for immediate drug release. Finally, The in vitro dissolution data for best formulation F6 were fitted in different kinetic models i.e, zero order, first order. Optimized formulation F6 follows first order.

BIBLIOGRAPHY:

1. Arya A, Chandra A, Sharma V, Pathak K. Fast dissolving oral films: an innovative drug delivery system and dosage form. International Journal of ChemTech Research. 2010;2(1):576–583. [Google Scholar]
2. Sharma K, Pfizer WR, Ghosh TK. Quick-dispersing oral drug delivery systems. Drug Delivery to the Oral Cavity Molecule to Market. 2005;145:262–287. [Google Scholar]
3. Cilurzo F, Cupone IE, Minghetti P, Selmin F, Montanari L. Fast dissolving films made of maltodextrins. European Journal of Pharmaceutics and Biopharmaceutics. 2008;70(3):895–900. doi: 10.1016/j.ejpb.2008.06.032. [DOI] [PubMed] [Google Scholar]
4. Yellanki SK, Jagtap S, Masareddy R. Dissofilm: a novel approach for delivery of phenobarbital; design and characterization. Journal of Young Pharmacists. 2011;3(3):181–188. doi: 10.4103/0975-1483.83756. [DOI] [PMC free article] [PubMed] [Google Scholar]
5. Hanawa T. Development of a new and kindly oral dosage form for elderly. Journal of Pharmaceutical Science and Technology. 1997;13(4):251–258. [Google Scholar]
6. Goel H, Rai P, Rana V, Tiwary AK. Orally disintegrating systems: innovations in formulation and technology. Recent Patents on Drug Delivery and Formulation. 2008;2(3):258–274. doi: 10.2174/187221108786241660. [DOI] [PubMed] [Google Scholar]
7. Mishra R, Amin A. Formulation development of taste-masked rapidly dissolving films of cetirizine hydrochloride. Pharmaceutical Technology. 2009;33(2):48–56. [Google Scholar]
8. Shimoda H, Taniguchi K, Nishimura M, et al. Preparation of a fast dissolving oral thin film containing dexamethasone: a possible application to antiemesis during cancer chemotherapy. European Journal of Pharmaceutics and Biopharmaceutics. 2009;73(3):361–365. doi: 10.1016/j.ejpb.2009.08.010. [DOI] [PubMed] [Google Scholar]
9. Borsadia SB, O'Halloran D, Osborne JL. Quick-dissolving films—a novel approaches to drug delivery. Drug Development and Delivery. 2003;3(3):63–66. [Google Scholar]
10. Peh KK, Wong CF. Polymeric films as vehicle for buccal delivery: swelling, mechanical, and bioadhesive properties. Journal of Pharmacy and Pharmceutical Sciences. 1999;2(2):53–61. [PubMed] [Google Scholar]
11. Corniello CM. Quick dissolve strips: from concept to commercialization. Drug Delivery Technology. 2006;6:68–71. [Google Scholar]
12. Ali S, Quadir A. High molecular weight povidone polymer-based films for fast-dissolving drug delivery Application. Drug Delivery Technology. 2007;7:36–43. [Google Scholar]
13. Kulkarni KS, Deokule HA, Mane MS, Ghadge DM. Exploration of different polymers for use in the formulation of oral fast dissolving strips. Journal of Current Pharmacy Research. 2010;2:33–35. [Google Scholar]
14. Malke S, Shidhaye S, Desai J, Kadam V. Oral films-patient compliant dosage form for pediatrics. Internet Journal of Pediatrics and Neonatology. 2010;11(2) [Google Scholar]
15. Martineau B. A look at fast-dissolving drug delivery systems. Drug Delivery Technology. 2009;9(4):36–38. [Google Scholar]
16. Keene DL, Whiting S, Humphreys P. Clobazam as an add-on drug in the treatment of refractory epilepsy of childhood. Canadian Journal of Neurological Sciences. 1990;17(3):317–319. doi: 10.1017/s0317167100030651. [DOI] [PubMed] [Google Scholar]