Panacea Journal of Pharmacy and Pharmaceutical Sciences
ISSN: 2349 7025

PJPPS
Panacea Research Library
http://internationaljournal.org.in/journal/index.php/pjpps

Original Research Article **Volume 15 Issue 3** **July-Sept 2026**

FORMULATION, DEVELOPMENT, EVALUATION OF CLOBAZAM AND SOLUBILITY, BIOAVAILABILITY ENHANCEMENT BY SOLID DISPERSION TECHNIQUES

***Pradeep Sahu, Dr. Amit Pandey, Mr. Sumit Dwivedi**

Department of Pharmaceutics, Shri Rama Krishna College of Pharmacy, Satna M.P.

* Corresponding Author's Email: bardadhi7@gmail.com

ABSTRACT

In this study, aim was to formulate Clobazam solid dispersions to modify the drug's solubility and enhance therapeutic effect. Clobazam suffers from poor aqueous solubility, which limits its bioavailability. Solid dispersions were prepared using as carriers in different drug-to-carrier ratios through solvent evaporation and physical mixing techniques. These dispersions were assessed for bulk density, particle size, tapped density, angle of repose, also drug release profile. The aim of this study was to enhance the dissolution rate of Clobazam using solid dispersion systems. Solid dispersion is a highly effective pharmaceutical strategy used to enhance the solubility and bioavailability of poorly water-soluble drugs. It works by dispersing a crystalline drug in an amorphous state within a hydrophilic polymer matrix, drastically increasing surface area and wettability. Solid dispersions are an effective method of increasing the solubility and bioavailability of poorly soluble drugs. In the present study to enhance solubility of Clobazam a poorly soluble drug by solid dispersion technique by employing solvent evaporation technique using PVP K 30 And PEG 8000 as carriers.. The prepared solid dispersions showed excellent improvement of drug solubility due to mean drug particle size reduction which lead to increase drug dissolution and bioavailability.

Key words:- Clobazam, PEG 8000, PVP K 30 and solid dispersion, bioavailability

INTRODUCTION:

Solubility refers to a substance's ability to dissolve in another substance, creating a homogeneous solution. This property depends on factors like the type of solvent used, temperature, and pressure. When the solubility limit is reached, further addition of solute does not increase its concentration in the solution. Solubility equilibrium occurs when dissolution and precipitation processes balance. Sometimes, solutions can become supersaturated, which is a meta stable state 1-2 . Solubility is not the same as the ability to dissolve, as it can also involve chemical reactions. Solubility is commonly expressed in units of concentration, and its methods of expression vary. Solubility plays a crucial role in drug development, especially for oral delivery. Solubility is the phenomenon of dissolution of solid in liquid phase to give a homogenous system and is one of the important parameter to achieve desired concentration of drug in systemic circulation for pharmacological response. Poorly water-soluble drugs after oral administration often require high doses in order to reach therapeutic plasma concentrations. The bioavailability of an orally administered drug depends on its solubility in aqueous media over different pH ranges. The insufficient dissolution rate of the drug is the limiting factor in the oral bioavailability of poorly water soluble compounds. Various techniques are used for the improvement of the aqueous solubility, dissolution rate, and bioavailability of poorly water soluble drugs include micronization, chemical modification, pH adjustment, solid dispersion, complexation, cosolvency, micellar solubilization, hydrotropy etc.

MATERIALS AND METHODS

Preformulation study

Physiochemical Properties of Clobazam

Physical evaluation It refers to the evaluation by sensory characters-taste, appearance, odor, feel of the drug, etc.

Sensory characters

S. No.	Sensory characters	Result
1.	Colour	White or off-white powder
2.	Odor	Odorless

Solubility of Clobazam

Solvent used	Clobazam
Distilled Water	Slightly Soluble
0.1 N Hydrochloric acid	Slightly Soluble
Ethanol	Soluble
Methanol	Freely soluble
Chloroform	Slightly Soluble

Melting point of the Clobazam

S. No.	Melting Point of Clobazam	Average Melting Point of Clobazam
1.	182 ºC-184 ºC	181 - 183°C
2.	181 ºC -183 ºC	
3.	181 ºC -183 ºC	

Procedure

Accurately weighed 10mg of powder was poured into the measuring cylinder carefully level the powder without compacting, if necessary and read the unsettled apparent volume, Vo, to the nearest graduated unit. Calculate the bulk density in gm per ml, gm/cc by the formula.

Bulk density = Bulk Mass/ Bulk Volume

Bulk density of Clobazam

S. No.	Bulk mass	Bulk volume	Bulk density	Avg. bulk density
1.	1 gm	1.52 ml	0.657 g/ml	0.660±0.0094
2.	1 gm	1.49 ml	0.671 g/ml	
3.	1 gm	1.53 ml	0.653 g/ml	

Procedure

Accurately weighed 10mg of powder was poured into the measuring cylinder carefully level the powder and read the tapped volume (after 50-60 times tapping), V_t to the nearest graduated unit. Calculate the tapped density in gm per ml, gm/ cm^3 by the formula:- Tapped density = Bulk Mass/ Tapped Volume

Tapped density of Clobazam

S. No.	Bulk mass	Tapped volume	Tapped density	Avg. tapped Density
1.	1 gm	1.12 ml	0.892 g/ ml	0.885±0.008
2.	1 gm	1.13 ml	0.885 g/ ml	
3.	1 gm	1.14 ml	0.877g/ ml	

Compressibility index (Carr's index)

Compressibility index (C.I.) is an important measure that can be obtained from the bulk and tapped densities. Carr's index a material having values of less than 20% to 30% is defined as the free flowing material (Wells, 1998). It can be calculated as per given formula:

$$C.I. = \frac{100\ (V0-Vf)}{V0} \qquad ORC.I. = \frac{\text{Tapped density- Bulk density}}{\text{Tapped density}} \times 100$$

Compressibility index of Clobazam

S. No.	Bulk density	Tapped density	C.I.
1.	0.660±0.0094	0.885±0.008	25.42

Hausner ratio:

It indicates the flow properties of the powder and is measured by the ratio of tapped density to bulk density.

Hausner ratio = Tapped density / Bulk Density

Hausner ratio of Clobazam

S. No.	Bulk density	Tapped density	Hausner ratio
1.	0.660±0.0094	0.885±0.008	1.340

Moisture content determination

S. No.	Drug	KF Factor	Amount of KF Reagent Consumed	Moisture content
1	Clobazam	0.545	0.2ml	0.109

Determination of λ_{max} of Clobazam:-

The λ_{max} of Clobazam was determined by running the spectrum of drug solution in double beam ultraviolet spectrophotometer.

Procedure:-

Accurately weighed 10 mg of drug was dissolved in 10 ml of ethanol solutions in 10ml of volumetric flask. The resulted solution 1000µg/ml and from this solution 1 ml pipette out and transfer into 10 ml volumetric flask and volume make up with ethanol solution prepare suitable dilution to make it to a concentration range of 5-25 **µg**/ml. The spectrum of this solution was run in 200-400 nm range in U.V. spectrophotometer (Labindia-3000+). The spectrum peak point graph of absorbance of Clobazam versus wave length was shown in figure 6.2:

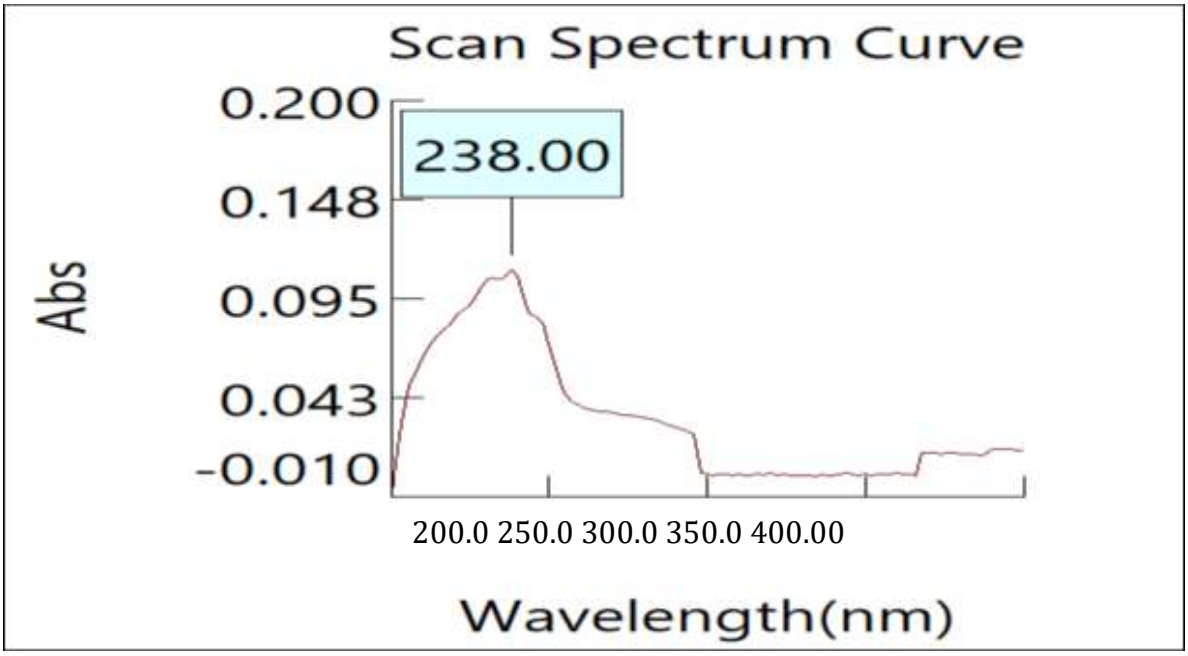

Figure:- Wavelength maxima of Clobazam in Ethanol

Calibration curve of Clobazam Observation table:-

Calibration curve of Clobazam

S. No.	Concentration (µg/ml)	Absorbance (Mean ± SD)
1	5	0.125 ± 0.005
2	10	0.248 ± 0.003
3	15	0.369 ± 0.004
4	20	0.478 ± 0.006
5	25	0.598 ± 0.004

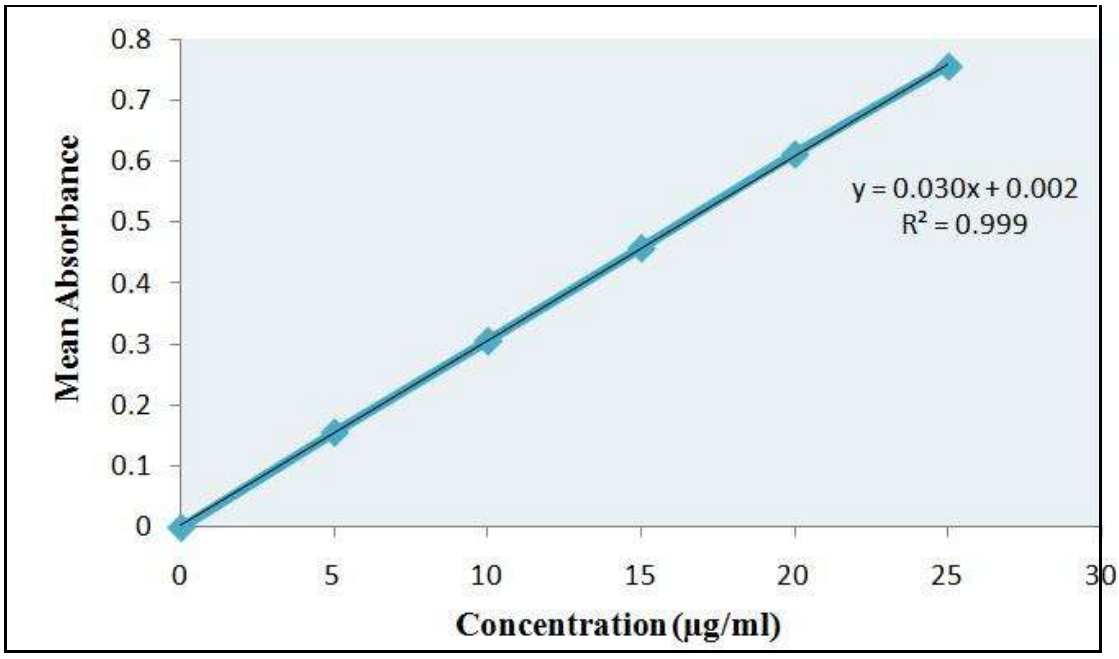

Figure :- Calibration curve of Clobazam in methanol

The linear regression analysis was done on Absorbance data points. The results are as follow for standard curve

Slope = 0.030

The intercept = 0.002

The correlation coefficient (r^2) = 0.999

Preparation of solid dispersion complexes

S. No.	**Solid Dispersion**		
	Drug: PEG 8000	**Drug: PVP K30**	**Drug: SLS**
1.	1:1	1:1	1:1
2.	1:2	1:2	1:2
3.	1:4	1:4	1:4
4.	1:8	1:8	1:8

Results of solubility study

Solubility of different solid dispersion complexes

F. code	**Complex**	**Solubility (mg/ml)**		
		Physical method	**Kneading method**	**Solvent evaporation method**
	Pure drug		0.188 mg/ml	
CSDF1	**Drug: PEG 8000 (1:1)**	0.190	0.225	0.332
CSDF2	**Drug: PEG 8000 (1:2)**	0.196	0.325	0.365

CSDF3	**Drug: PEG 8000 (1:4)**	0.223	0.365	0.421
CSDF4	**Drug: PEG 8000 1:8)**	0.245	0.378	0.565
CSDF5	**Drug: PVP K 30 (1:1)**	0.223	0.332	0.356
CSDF6	**Drug: PVP K 30 (1:2)**	0.256	0.356	0.458
CSDF7	**Drug: PVP K 30 (1:4)**	0.325	0.385	0.556
CSDF8	**Drug: PVP K 30 (1:8)**	**0.456**	**0.398**	**0.658**
CSDF9	**Drug: SLS (1:1)**	0.321	0.325	0.221
CSDF10	**Drug: SLS (1:2)**	0.456	0.395	0.265
CSDF11	**Drug: SLS (1:4)**	0.569	0.421	0.369
CSDF12	**Drug: SLS (1:8)**	0.625	0.485	0.421

Results of drug content

Formulation	**Label Claim (mg)**	**Amount Found (mg)**	**Label Claim (%) Mean ± SD**	**RSD**
CSDF8	10	9.92	99.20 ± 0.03	0.125

Drug: PVP K 30 (1:8)

***Average of three determination**

Release kinetics of Clobazam solid dispersion

Table :- IN-VITRO drug release data for optimized formulation CSDF8

Time (min)	Square Root of Time(h)$^{1/2}$	Log Time	Cumulative*% Drug Release	Log Cumulative % Drug Release	Cumulative % Drug Remaining	Log Cumulative % Drug Remaining
15	3.873	1.176	11.23	1.050	88.77	1.948
30	5.477	1.477	22.23	1.347	77.77	1.891
60	7.746	1.778	36.65	1.564	63.35	1.802
120	10.954	2.079	43.32	1.637	56.68	1.753
240	15.492	2.380	49.98	1.699	50.02	1.699

REPARATION AND CHARACTERIZATION

Zero order release kinetics of formulation CSDF8

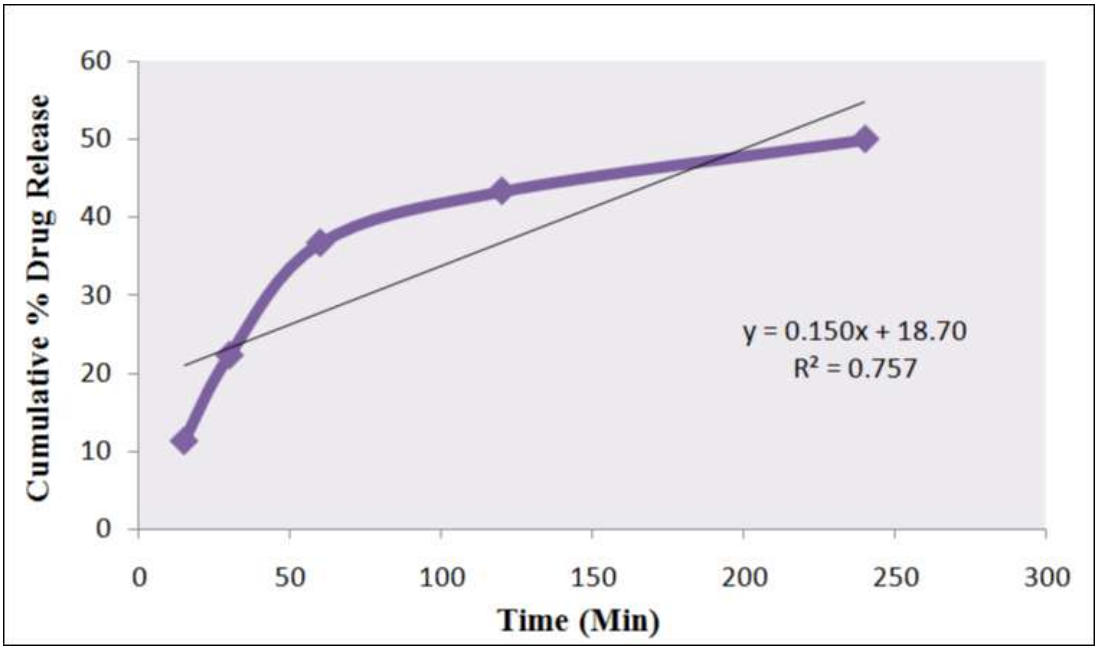

Figure:- Graph of zero order release Kinetics of formulation CSDF8

First order release Kinetics of formulation CSDF8

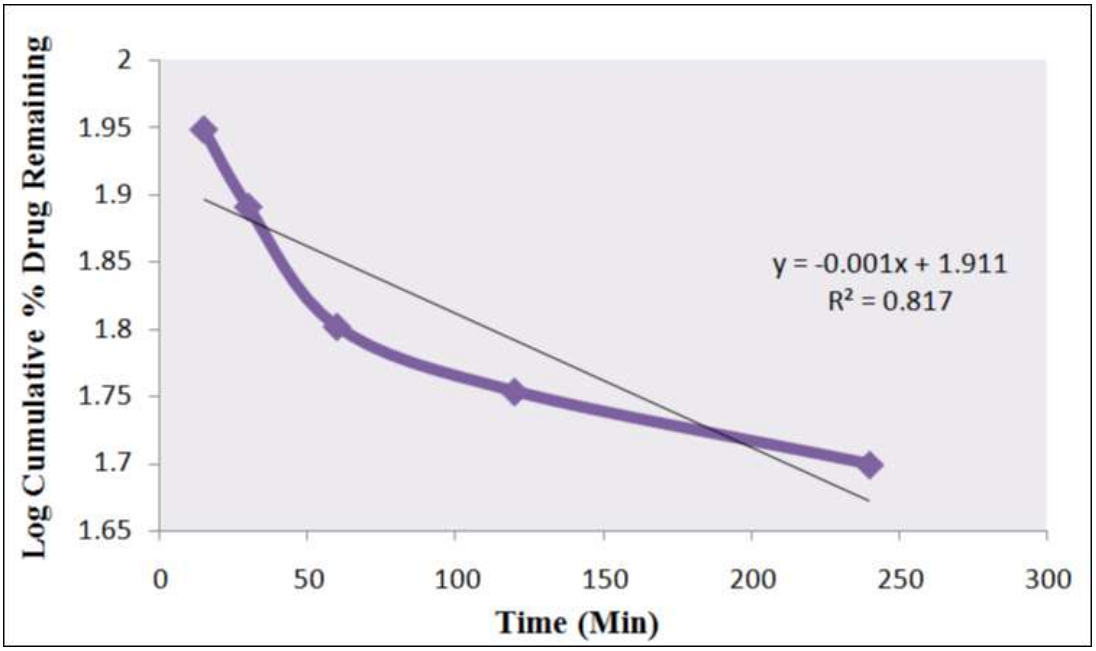

Figure:- Graph of first order release kinetics of formulation CSDF8

Table:- Regression analysis data

Batch	**Zero Order** r^2	**First Order** r^2
CSDF8	0.757	0.817

When the regression coefficient values of were compared, it was observed that **'r'** values of First order was maximum i.e. 0.817 hence indicating drug release from formulations was found to follow first order kinetics.

Differential scanning calorimetry (DSC)

Thermal analysis was carried out with a DSC instrument. Sample was weighed into a non-hermetically sealed aluminum pan. The samples were heated from 25 to 400 °C at a

heating rate of 5°C/min for drug and solid dispersion. The instrument was calibrated by using indium.

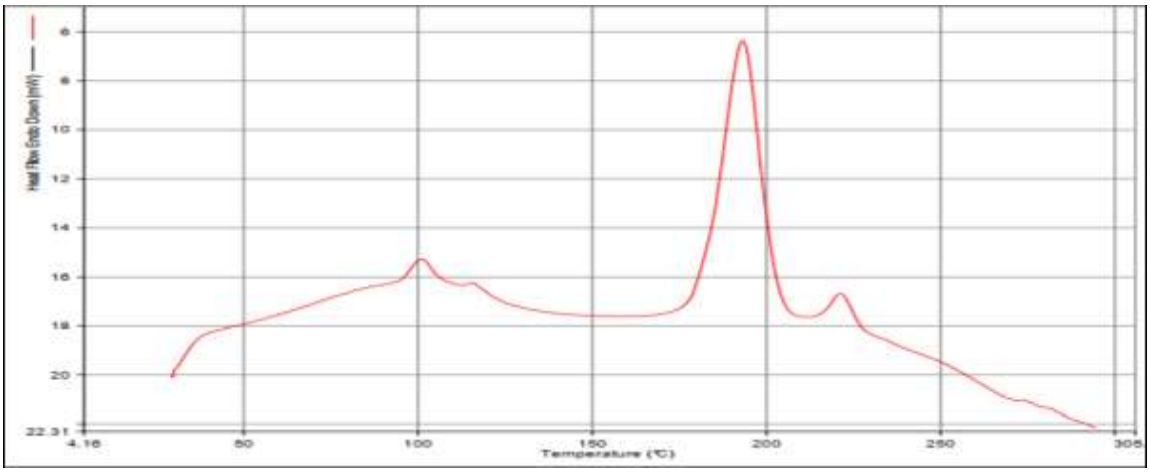

Figure :- DSC analysis of pure Clobazam

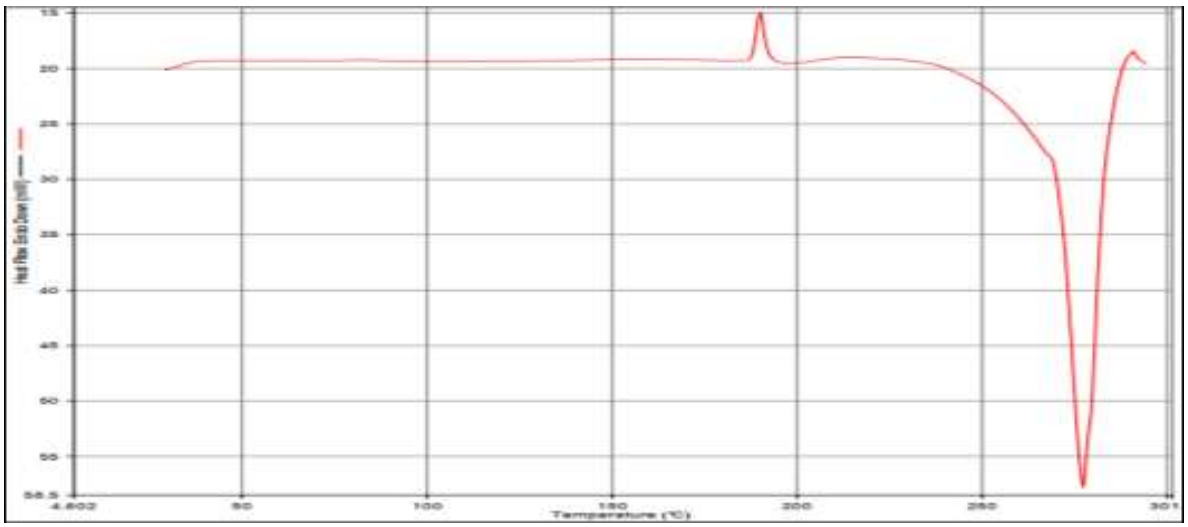

Figure :- DSC analysis of optimized batch SDF8

As the solid dispersion exhibited no endothermic peak corresponding to the melting point of drug that the drug is dispersed amorphously in solid matrix.

SUMMARY AND CONCLUSION

The solubility of pure drug was significantly increased in the presence of different hydrophilic carriers lite. PEG 8000, PVP K 30 and SLS solid dispersion were used on the prepare at weight ratios of 1:1, 1:2, 1:4 and 1:8, using three different preparation

methods, physical trituration, kneading and solvent evaporation in various weight ratios to enhance the solubility of pure drug and dissolution.The increased dissolution rate was observed with increase in hydrophilic carrier concentration. From the selected hydrophilic carrier, PVP K 30 in the ratio of (1:8) has shown significant impact on the aqueous solubility and dissolution rate of Clobazam when compared to the reaming two hydrophilic carriers. It means solid dispersion of clobazam with increased solubility of dissolution increased the bioavailability of the drug.

BIBLIOGRAPHY

1. Ahuja N, Katare OP, Singh B. Studies on dissolution enhancement and mathematical modeling of drug release of a poorly water-soluble drug using water-soluble carriers. Int J Pharm. 2006;44-54.
2. Charbit G, Badens E, Boutin O. Supercritical fluid technology for drug product development. Drugs and Pharmaceutical Sciences. Vol. 138. New York: Marcel Dekker Inc.; 2004.
3. Chiou WL, Riegelman S. Preparation and dissolution characteristics of several fast-release solid dispersions of griseofulvin. J Pharm Sci. 1969;58:1505.
4. Chokshi R, Zia H. Hot melt extrusion technique: A review. Int J Pharm Res. 2004;3:3-16.
5. Constantinides PP. Lipid microemulsions for improving drug dissolution and oral absorption: Physical and biopharmaceutical aspects. Pharm Res. 1995;12:1561-72.

6. Jung J, Perrut M. Particle design using supercritical fluids: Literature and patent survey. J Supercrit Fluids. 2001;20:179-219.

7. Kakumanu VK, Bansal AK. Supercritical fluid technology in pharmaceutical research. Business Briefing: Labtech. 2004;70-72.

8. Kaushal AM, Gupta P, Bansal AK. Amorphous drug delivery systems: Molecular aspects, design, and performance. Crit Rev Ther Drug Carrier Syst. 2004;21(3):133-93.

9. Leuner C, Dressman J. Improving drug solubility for oral delivery using solid dispersions. Eur J Pharm Biopharm. 2000;50(1):47-60.

10. Mayersohn M, Gibaldi M. New method of solid-state dispersion for increasing dissolution rates. J Pharm Sci. 1966;55:1323-34.

11. Maghsoodi M, Nokhodchi A. Agglomeration of celecoxib by quasi emulsion solvent diffusion method: Effect of stabilizer. Adv Pharm Bull. 2016;6(4):607-16.

12. Shamsuddin, Fazil M, Ansari SH, Ali J. Development and evaluation of solid dispersion of spironolactone using fusion method. Int J Pharm Investig. 2016;6(1):63-68.

13. Varalakshmi TSNS, Siva Ramesh C, Jyothi I, Jyothi Y, Bharathi G, Chinni Babu P. Formulation and evaluation of solid dispersions of valsartan for dissolution rate enhancement. J Pharm Res. 2015;9(2):139-44.

14. Jafari E. Preparation, characterization and dissolution of solid dispersion of diclofenac sodium using Eudragit E-100. J Appl Pharm Sci. 2013;3(8):167-70.

15. Vemula VR, Lagishetty V, Lingala S. Solubility enhancement techniques. Int J Pharm Sci Rev Res. 2010;5(1):41-51.

16. Tapas AR, Kawtikwar PS, Sakarkar DM. Enhanced dissolution rate of felodipine using spherical agglomeration with Inutec SP1 by quasi emulsion solvent diffusion method. Res Pharm Sci. 2009;4(2):77-84.

17. Chaulang G, Patel P, Hardikar S, Kelkar M, Bhosale A, Bhise S. Formulation and evaluation of solid dispersions of furosemide in sodium starch glycolate. Trop J Pharm Res. 2009;8(1):43-51.

18. Patil AD. Does orally dissolving formulation of clobazam provide clinical advantage over its standard formulation? Indian J Pharmacol. 2016;48:339-40.