CODEN [USA]: IAJPBB ISSN: 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES

http://doi.org/10.5281/zenodo.1260873

Available online at: http://www.iajps.com Research Article

PREPARATION AND CHARACTERIZATION OF ESLICARBAZEPINE ACETATE SOLID DISPERSION

Sravani.P[1*], B. Mounika[1], P. Ganesh[1], Md.Zeeshanuddin[1], Y. Krishna reddy [1], A. Thangathirupathi [2], K.Rajeswar Dutt [3]

[1] Department of Pharmaceutics, Nalanda college of pharmacy, Nalgonda, Telangana.
[2] Department of Pharmacology, Nalanda college of Pharmacy, Nalgonda, Telangana.
[3] Department of Pharmaceutical analysis, Nalanda college of pharmacy, Nalgonda, Telangana.

Abstract

Solubility is one of the important parameters to achieve desired concentration of drug in systemic circulation for achieving required pharmacological response. Poorly water soluble drugs often require high doses in order to reach therapeutic plasma concentrations after oral administration. Low aqueous solubility is the major problem encountered with formulation development of new chemical entities. Solid dispersion method has been widely employed to improve the dissolution rate, solubility and oral absorption of poorly water soluble drugs. Solid dispersion technology is the science of dispersing one or more active ingredients in an inert matrix in the solid stage in order to achieve increased dissolution rate.The present work is on study of solubility parameters of eslicarbazepine acetate and evaluate its dissolution rate.

Key words: *Inert matrix, Plasma concentrations, Solubility, Solid dispersion, Eslicarbazepine acetate.*

Corresponding Author:

P.Sravani,
Department of Pharmaceutics,
Nalanda College of Pharmacy,
Nalgonda, Telangana.
Email:paramkushamsravani0218@gmail.com

QR code

Please cite this article in press P.Sravani et al., ***Preparation and Characterization of Eslicarbazepine Acetate Solid Dispersion,*** *Indo Am. J. P. Sci, 2018; 05(05).*

INTRODUCTION:

The oral bioavailability depends on several factors including aqueous solubility, drug permeability, dissolution rate, first-pass metabolism, presystemic metabolism, and susceptibility to efflux mechanisms. The most frequent causes of low oral bioavailability are attributed to poor solubility and low permeability.

Solubility is one of the important parameters to achieve desired concentration of drug in systemic circulation for achieving required pharmacological response. Poorly water soluble drugs often require high doses in order to reach therapeutic plasma concentrations after oral administration. Low aqueous solubility is the major problem encountered with formulation development of new chemical entities as well as generic development. Any drug to be absorbed must be present in the form of an aqueous solution at the site of absorption. Water is the solvent of choice for liquid pharmaceutical formulations. Most of the drugs are either weakly acidic or weakly basic having poor aqueous solubility.

Oral bioavailability of drugs is affected by variety of factors which influence their absorption from GIT. The solubility behavior of drug is important factor of its oral bioavailability.

Solubility of drug candidate has presented a challenge to the development of suitable formulation for oral administration.With the recent advances of screening of potential therapeutic agents the no of poorly soluble compounds for oral delivery now presents one of the most frequent and greatest challenges to formulation scientist in pharmaceutical industries.

Table 1 solubility

Descriptive term	Part of solvent required per part of solute
Very soluble	Less than 1
Freely soluble	From 1 to 10
Soluble	From 10 to 30
Sparingly soluble	From 30 to 100
Slightly soluble	From 100 to 1000
Very slightly soluble	From 1000 to 10,000
Practically insoluble	10,000 and over

MECHANISM OF SOLUBILIZATION: -

Polar solvents

1. Owing to their high dielectric constant, polar solvents reduces the force of attraction between oppositely charged ions in crystals

2. Polar solvents break covalent bonds of potentially strong electrolytes by acid base reactions

3. Polar solvents are capable of solvating molecules and ions through dipole interaction forces, particularly hydrogen-bond formation, which leads to the solubility of compound. However the nonpolar solvents won't obey the above mechanism of solubilization, so they are unable to dissolve the ionic and polar solutes.

Nonpolar solvents can dissolve the nonpolar solute with similar internal pressure through induced dipole interactions. In short solubilization takes place by consideration of, 1. Polarity 2. Dielectric constant, 3. Association, 4. Salvation, 5. Internal pressure, 6. Acid-base reaction.

Factors affecting solubility

1.Temperature Generally as the T increases the solubility increases.For effect of T on solubility we have to take consider two criteria. Basically, solubility increases with temperature. The situation is though different for gases. With increase of the temperature they became less soluble in each other and in water, but more soluble in organic solvents.

Endothermic reactions During dissolution process the energy (heat) is absorbed. Thus rise in T will lead to an increase solubility of a solid in the solution with a positive heat of solution.

Exothermic reactions During dissolution process the energy (heat) is evolved. Thus rise in T will lead to a decrease solubility of a solid in the solution with a negative heat of solution.

Non-polar compounds The forces holding the particles together are small, and any interaction between solute and solvent is small. Not detectable heat effect on non polar substance.

Polar compounds Either decrease or increase in solubility. In polar substances, it takes energy to separate the molecule from surrounding molecules & if energy is supplied in the form of heat, producing a cooling effect. Also there is the possibility of interaction between the solute and solvent with formation of a dipole-dipole type bond, and this interaction will tend to give off heat. Depending on which of the two interactions is greatest you can get an increase or decrease in temperature,pH.

Table.2 BCS classification

BCS class	Solubility	Permeability	Absorption pattern	Examples
I	High	High	Well absorbed	*Metoprolol, Diltiazem, Propranolol*
II	Low	High	Well absorbed	*Phenytoin, Nifedipine, Danazol*
III	High	Low	Variable	*Cimetidine, Acyclovir, Captopril*
IV	Low	Low	Poorly absorbed	*Hydrochlorothiazide, Taxol, Furosemide*

3. Particle size As the particle size decreases solubility increases due to increase in the surface area. But after very small particle size decrease in P.S will decreases solubility due to formation of agglomerates.

4. Crystal structure Amorphous form of drugs is more soluble than Crystalline form.

Solubility: solvates >anhydrous > hydrates

5.Molecular structure Change in the molecular structure highly affects solubility of compound eg. Introduction of the hydrophilic group in hydrophobic substance may improve solubility.Introduction of hydrophilic group Benzene into phenol with increased solubility.Conversion into salt Generally all salt forms are soluble. Esterification Chloramphenicol into palmitate form for taste masking.

6. Pressure Solid and liquid solutes For majority of solid and liquid solutes, pressure does not affect solubility. Gas Solute for gases the Henry's law states that solubility of gas is directly proportional to the pressure of this gas. This is mathematically presented as: p = kc, where k is a temperature dependent constant for a gas.

BCS classification is a framework for classifying a drug substance based on its solubility and intestinal permeability.BCS takes in to account three major factors i.e, solubility, intestinal permeability and dissolution rate. Biopharmaceutics classification system (BCS) is a scientific classification of a drug substance based on its aqueous solubility and intestinal permeability that correlates *in vitro* dissolution and *in vivo* bioavailability of drug products. When combined with *in vitro* dissolution characteristics of the drug product, BCS takes into account two major factors: solubility and intestinal permeability, which govern the rate and extent of oral drug absorption from solid dosage forms and ultimately, its bioavailability. Due to this reason, BCS is the fundamental tool in the drug development especially in the development of oral drug products. Biopharmaceutics Classification System (BCS) with characteristics of drugs.

To improve the solubility of drug candidates there are different solubilisation techniques which increases drug dissolution and oral bioavailability

Solid dispersion

Solid dispersion method has been widely employed to improve the dissolution rate, solubility and oral absorption of poorly water soluble drugs. Solid dispersion technology is the science of dispersing one or more active ingredients in an inert matrix in the solid stage in order to achieve increased dissolution rate. A solid dispersion technique has been used by various researchers who have reported encouraging results with different drugs The first drug whose rate and extent of absorption was significantly enhanced using the solid dispersion technique was sulfathiazole by Sekiguchi and Obi . Technique for the preparation of solid dispersions, Lyophilization has also been thought of as a molecular mixing technique where the drug and carrier were co-dissolved in cyclohexanol, frozen and then sublimed under vacuum to obtain a lyophilized molecular dispersion.

Types of solid dispersion

(A) Eutectic Mixtures When a mixture of A and B with composition E is cooled, A and B crystallize out simultaneously, whereas when other compositions are cooled, one of the components starts to crystallize out before the other. Solid eutectic mixtures are usually prepared by rapid cooling of a co-melt of the two compounds in order to obtain a physical mixture of very fine crystals of the two components. When a mixture with composition E, consisting of a slightly soluble drug and an inert, highly water soluble carrier, is dissolved in an aqueous medium, the carrier will dissolve rapidly, releasing very fine crystals of the drug. The large surface area of the resulting suspension should result in an enhanced dissolution rate and thereby improved bioavailability.

(B) Solid Solutions According to their miscibility two types of solid solution are Continuous Solid Solutions In a continuous solid solution, the

components are miscible in all proportions. Theoretically, this means that the bonding strength.
Theoretically, this means that the bonding strength between the two components is stronger than the bonding strength between the molecules of each of the individual components.

Discontinuous Solid Solutions In the case of discontinuous solid solutions, the solubility of each of the components in the other component is limited. A typical phase diagram, show the regions of true solid solutions. In these regions, one of the solid components is completely dissolved in the other solid component. Below a certain temperature, the mutual solubilities of the two components start to decrease.

Substitutional crystalline solid dispersion is a type of solid solutions which have a crystalline structure, in which the solute molecules substitute for solvent molecules in the crystal lattice. Substitution is only possible when the size of the solute molecules differs by less than 15% or so from that of the solvent molecules.

Interstitial Crystalline Solid Solutions In interstitial solid solutions, the dissolved molecules occupy the interstitial spaces between the solvent molecules in the crystal lattice. As in the case of substitutional crystalline solid solutions, the relative molecular size is a crucial criterion for classifying the solid solution type. In the case of interstitial crystalline solid solutions, the solute molecules should have a molecular diameter that is no greater than 0.59 of the solvent molecule's molecular diameter. Furthermore, the volume of the solute molecules should be less than 20% of the solvent.

(C)Amorphous Solid Solutions In an amorphous solid solution, the solute molecules are dispersed molecularly but irregularly within the amorphous solvent. Using griseofulvin in citric acid Other carriers urea and sugars such as sucrose, dextrose and galactose, organic polymers such as polyvinylpyrrolidone (PVP), polyethylene glycol and various cellulose derivatives have been utilized for this purpose.

(D) Glass Solutions and Glass Suspensions A glass solution is a homogenous, glassy system in which a solute dissolves in a glassy solvent. The term glass can be used to describe either a pure chemical or a mixture of chemicals in a glassy or vitreous state. The glassy or vitreous state is usually obtained by an abrupt quenching of the melt. It is characterized by transparency & brittleness below the glass transition temperature.

Selection of A Carrier

A carrier should meet the following criteria to be suitable for increasing the dissolution rate of a drug.
1. Freely water-soluble with intrinsic rapid dissolution properties.
2. Non-toxic and pharmacologically inert.
3. Heat stable with a low melting point for the melt method.
4. Soluble in a variety of solvents and pass through a vitreous state upon solvent evaporation for the solvent method.
5. Able to preferably increase the aqueous.
5. Able to preferably increase the aqueous solubility of the drug and
6. Chemically compatible with the drug and not form a strongly bonded complex with the drug .
First generation carriers
Example: Crystalline carriers: Urea, Sugars, Organic acids .
Second generation carriers
Example: Fully synthetic polymers include povidone (PVP), polyethyleneglycols (PEG) and polymethacrylates. Natural product based polymers are mainly composed by cellulose derivatives, such as hydroxypropylmethylcellulose (HPMC), ethylcellulose or hydroxypropylcellulose or starch derivates, like cyclodextrins
Third generation Carriers
Example: Surface active self emulsifying carriers:Poloxamer 408,Tween80, and Gelucire 44/14

Advantage of solid dispersion

The reasons for solid dispersion or advantages of solid dispersions are as follows:
• Particles with reduced particle size
• Particles with improved wettability
• Particles with higher porosity
• Drugs in amorphous state

Demerits of solid dispersion

The commercial utilization is very limited. Problems of solid dispersion involves
• Formulation of solid dispersion into dosage forms is not easy
• The physical and chemical stability of drugs and vehicles is not easy to maintain
• Drug permeability
• Drug solubility in carrier
• Dose accuracy
• Drug : carrier ratio

Mechanism involved in enhanced drug solubilization by solid dispersion technique

The basic principle includes complete removal of drug crystallinity and molecular dispersion of the poorly soluble compound in a hydrophilic polymeric carrier. When the solid dispersion is exposed to aqueous media, the carrier dissolves and the drug

releases as fine colloidal particles. This increases surface area of dissolution rate and hence bioavailability of poorly water soluble drugs. Drug in soluble hydrophilic carrier improves the dissolution rate by reducing particle size and increasing the particle porosity. Remaining drug is in amorphous state and Improving wettability and hence possibility bioavailability for poorly water soluble drug. The potential advantage of this technique is enormous.

DRUG PROFILE

Drug Name Eslicarbazepine acetate

Structure

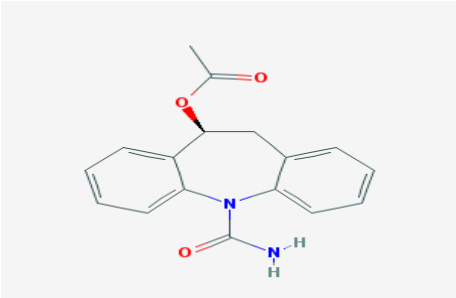

Figure 1 Structure of eslicarbazepine acetate

Chemical name :(9S)-2-carbamoyl-2-azatricyclo[9.4.0.0^{3,8}]pentadeca-1(15),3,5,7,11,13-hexaen-9-yl acetate

Molecular weight : 296.326

Indication Eslicarbazepine acetate is indicated as adjunctive therapy in the treatment of partial-onset seizures that are not adequately controlled with conventional therapy in epileptic patients.

Pharmacodynamics Eslicarbazepine acetate is associated with a dose- and concentration-dependant increase in heart rate and prolongation of PR interval.

Mechanism of action Eslicarbazepine acetate is converted to the active metabolite eslicarbazepine which carries out its anticonvulsant activity. The exact mechanism of action is unknown, but it is thought to involve the inhibition of voltage-gated sodium channels. In in vitro electrophysiological studies, eslicarbazepine was shown to inhibit repeated neuronal firing by stabilizing the inactivated state of voltage-gated sodium channels and preventing their return to the activated state. In vitro studies also showed eslicarbazepine inhibiting T-type calcium channels, which likely also has a role in anticonvulsant activity.

Absorption Eslicarbazepine active metabolite has a high bioavailability and reaches peak serum concentration 1-4 hours after a given dose. Eslicarbazepine acetate absorption is not affected by food.

Volume of distribution The apparent volume of distribution of eslicarbazepine is 61.3 L for a body weight of 70 kg based on population PK analysis.

Protein binding Eslicarbazepine is bound to plasma proteins at a relatively low rate of <40%, independent of concentration. In vitro studies have shown that plasma protein binding is not relevantly affected by the presence of other medications such as warfarin, diazepam, digoxin, phenytoin or tolbutamide. Similarly, the binding of these medications was not significantly affected by the presence of eslicarbazepine.

Metabolism Eslicarbazepine acetate is rapidly and extensively metabolized to its major active metabolite, eslicarbazepine, via hydrolytic first-pass metabolism. Eslicarbazepine corresponds to about 92% of systemic exposure. Minor active metabolites (R)-licarbazepine and oxcarbazepine consist of <5% of systemic exposure. Active metabolites are then metabolized to inactive glucuronides that correspond to about 3% of systemic exposure.

Eslicarbazepine had a moderate inhibitory effect on CYP2C19 and a mild activation of UGT1A1-mediated glucuronidation when studied in human hepatic microsomes. It has been shown to induce CYP3A4 enzymes in vivo.

Route of elimination Eslicarbazepine acetate and its metabolites are eliminated primarily via renal excretion. Eslicarbazepine active metabolite is excreted two-thirds in the unchanged form and one-third as a glucuronide conjugate. This accounts for around 90% of total metabolites excreted, with the remaining 10% being minor metabolites. Renal tubular reabsorption is expected to occur with eslicarbazepine.

Half life The apparent plasma half-life of eslicarbazepine is 10-20 hours in healthy subjects and 13-20 hours in epilepsy patients. Steady-state plasma concentrations are attained after 4 to 5 days of once daily dosing.

Clearance Renal clearance of eslicarbazepine was found to be approximately 20 mL/min in healthy subjects with normal renal function.

Toxicity There are no adequate and well-controlled studies of the use of eslicarbazepine acetate in pregnant women. In studies conducted in pregnant mice, rats, and rabbits, eslicarbazepine acetate did show developmental toxicities, including teratogenicity, embryolethality, and fetal growth retardation, at clinically relevant doses. Drug-induced liver injury ranging from mild to moderate elevations in transaminases (>3 times the upper limit of normal) to rare cases with concomitant elevations of total bilirubin (>2 times the upper limit of normal) have been reported with the use of eslicarbazepine. Overdose with eslicarbazepine acetate appears similar to its known adverse reactions and includes symptoms of hyponatremia, dizziness, nausea, vomiting, somnolence, euphoria, oral paraesthesias, ataxia, and diplopia. There is no specific antidote for eslicarbazepine acetate overdose and it should be treated primarily with supportive measures. If required, the drug may be removed by gastric lavage, partially by hemodialysis or inactivated with activated charcoal.

MATERIALS AND METHODS:

Eslicarbazepine acetate, Sodium starch glycollate, Cross caramellose,Ethanol.

Formulation of solid dispersions

The Kneading method (KM) was used for the preparation of solid dispersion (SD). drug: Carrier ratios (1:1, 1:2, 1:3,) were used.Drug and carrier of different ratios were triturated using a small volume of methanol-water (1:1) solution to give obtain a thick paste, which was kneaded for 30minutes and then dried at 40°C in an oven. The dried mass was then pulverized, passed through 30 mesh no. 30, stored in a vacuum desiccator (48 h) and passed through 60 mesh no. 60 before packaging in an airtight container.

Evaluation

Percent Practical Yield (PY) Percentage practical yield were calculated to know about percent yield or efficiency of any method, thus its help in selection of appropriate method of production. Solid dispersions were collected and weighed to determine practical yield (PY) from the following equation .

PY (%) = Practical Mass (SD) / Theoretical Mass (Drug + Carrier) × 100

Determination of drug content The drug content was calculated by dissolving solid dispersion equivalent to 2 mg of drug was transferred to 100 ml volumetric flask and dissolved in minimum amount of methanol; and the volume was made up to 100 ml with phosphate buffer (pH 7.4) and then solution was filter through 0.45-µm membrane filter paper and assayed for drug content using UV double beam spectrophotometer at its specific wavelength.

Solubility Determination Excess amount of solid dispersion were added to 25 ml phosphate buffer (pH 7.4) taken in a stoppered conical flasks, and mixture were shaken for 24 hrs in a rotary flask shaker. After shaking to achieve attain equilibrium, 2 ml aliquots were withdrawn at 1 hr intervals and filtered through whatman filter paper no 40. The filtrate was analyzed spectrophotometrically. Shaking was continued until three consecutive reading were the same

***In vitro* drug release** Accurately weighed preparations equivalent to 2 mg of preparation were added to 900 ml of dissolution media (7.4 phosphate buffer) contained in USP dissolution apparatus II and stirred at a speed of 50 rpm at 37±0.5˚C. Five milliliter aliquots were withdrawn at 10, 20, 30, 40, 50 60 minute and replaced by 5 ml of fresh dissolution media (37˚C). The collected samples were analyzed after suitable dilution using UV-visible spectrophotometer against the blank. The dissolution of pure was done similarly.

RESULTS AND DISCUSSIONS:

Table.3: % Yield, Solubility, %drug content

Formulation	%Yield	Solubility (µg/ml)	%Drug Content
F1	80.1	0.897	75.1
F2	72.35	1.092	65.5
F3	64.23	1.679	92.3
F4	82.5	1.725	95.1
F5	45.6	0.985	66.25
F6	85.1	0.658	54.2
F7	76.23	1.152	79.3
F8	81.6	1.120	86.5

Table.4: Invitro dissolution studies

Time(Mins)	F1	F2	F3	F4	F5	F6	F7	F8
0	-	5.2	12.63	15.83	8.2	10.56	15.36	14.9
5	10.6	15.5	22.39	28.69	10.89	21.3	25.96	29.7
10	21.9	19.99	30.65	35.24	26.9	30.56	34.87	33.54
15	26.9	24.36	35.35	48.9	30.5	41.2	46.21	47.6
30	31.2	30.25	38.12	58.9	32.6	45.6	58.6	58.2
45	35.8	40.69	42.15	67.4	40.8	50.2	66.1	66.32
60	40.2	52.39	48.62	82.4	41.9	60.23	70.2	76.8
80	45.36	55.32	65.63	85.1	46.8	72.9	82.99	80.3

Percentage Yield Solid dispersion prepared by solvent kneading method using different carriers in different ratios like shows varied percentage yields.It shows more percent yield occurred in the orderF4>F6>F8>F1>F2>F3>F5

Solubility Studies Solid dispersions are prepared to improve the solubility of the drug by carriers like sodium starch glycollate and cross caremellose. The results shown improved solubility in case of F4 which was having 1:4 ratio of drug carrier eslicarbazepine acetate and SSG followed by more improvement of solubility seen in f3> f7>f8>f2>f1>f5>f6

Determination of Drug content The drug content was more for F4 formulation with 1:4 drug carrier ratio of SSG carrier that was about 95.1% followed by F3with 92.3%, F8 with 86.5%.

***In vitro* Disssolution studies** The cumulative % drug release of different formulation after one hour shown maximum drug release out of which max drug release shown was 82.4% within 60 min where shown more improvement in drug dissolution and showing the constant drug release through out the time later on by other formulations likeF7& F8.

CONCLUSION:

Solubility is one of the important parameters to achieve desired concentration of drug in systemic circulation for achieving required pharmacological response. Low aqueous solubility is the major problem encountered with formulation development of new chemical entities. Solid dispersion method has been widely employed to improve the dissolution rate, solubility and oral absorption of poorly water soluble drugs.The present work is on study of solubility parameters of eslicarbazepine acetate and evaluate its dissolution rate.By preparaing solid dispersion by solvent kneading method using two different carriers like SSG &CCM were showing improved dissolution rates. In solvent kneading method the reducing the size of the particle which shows more surface area and using carriers of optimum ratio making it more soluble and high permeable.In this solid dispersion prepared by Drug and Carrier SSG ratio as 1:4 showing more about 85.1% drug relase in short period of time.

REFERENCES:

1 Ketan T. Savjani, Anuradha K. Gajjar, and Jignasa K. Savjani Drug Solubility: Importance and Enhancement TechniqueISRN Phharmaceutics,2012

2. Naveen Dutt Dixit, Suneel Kumar Niranjan A Review: Solid Dispersion World Journal Of Pharmacy And Pharmaceutical Sciences Volume 3, Issue 9, 238-257,2014

3. Ingle U.S,Gaikwad, review on solid dispersion a dissolution technique, International journal of research in ayurveda and pharmacy,2(3),2011, 751-757.

4. Sakina Sultana and A H M Saifuddin, Review article: Solid dispersion currently practiced in pharmaceutical field, International Journal of Advancements in Research & Technology, Volume 5, Issue 3, March-2016

5. Sameer Singh1, Raviraj Singh Baghel, A review on solid dispersion, International journal of pharmacy & life sciences, 2(9): Sep., 2011.

6. Dhirendra K, Lewis S, Udupa N And Atin K, Solid Dispersions: A Review, Pak. J. Pharm. Sci., Vol.22, No.2, April 2009, Pp.234-24

7. Jinal N. Patel, Dharmendra M. Rathod, Techniques to improve the solubility of poorly soluble drugs, International Journal Of Pharmacy & Life Sciences, Int. J. Of Pharm. & Life Sci. (Ijpls), Vol. 3, Issue 2: Feb.: 2012, 1459-1469.

8. PrakashKhadka ,JieunRo Pharmaceutical particle technologies: An approach to improve drug solubility, dissolution and bioavailability Asian Journal of Pharmaceutical Sciences, Volume 9, Issue 6, December 2014, Pages 304-316

9. PekanwarS.S,Kankude A.D, Formulation and evaluation of solid dispersion of lopanavir, International jresearch journal of pharmacy,6(9),2015,663-669.
10..Arno A. Enose,Priya K. Dasan, Formulation and Characterization of Solid Dispersion Prepared by Hot Melt Mixing: A Fast Screening Approach for Polymer Selection, Journal of PharmaceuticsVolume 2014
11.Ankit Gupta, Mahesh Kumar Kataria , Formulation And Evaluation Of Solid Dispersion Of Glipizide For Solubility And Dissolution Rate Enhancement International Journsl Of Pharmaceutics And Drug Analysis, Vol: 2; Issue: 2, 2014
12.Mohammad Barzegar-Jalali, Mohammad Reza Siahi-Shadbad, Development and Characterization of Solid Dispersion for Dissolution Improvement of Furosemide by Cogrinding Method Advanced Pharmaceutical Bulletin, 2014, 4(4), 391-399.
13.Yangzhaotiegangxin, Solid Dispersion In The Development Of A Nimodipine Delayed-Release Tablet Formulation Asian Journal Of Pharmaceutical Sciences Volume 9, Issue 1, February 2014, Pages 35-40
14.Prasanth VV, Abhilash M Formulation and Evaluation of Solid Dispersion of Melitracen, International Journal Of Pharmaceutical And Chemical Sciences, Vol. 2 (3) Jul-Sep 2013.
15.B.V.Ramana, C.S.Parameshwari, Dissolution Rate Enhancement of Aceclofenac By Solid Dispersion Technique, Scholars Academic Journal of Pharmacy (SAJP), , 2013; 2(2):113-118
16.Mogal S. A, Gurjar P. Solid dispersion technique for improving solubility of some poorly soluble drugs, Der Pharmacia Lettre, 2012, 4 (5):1574-1586.
17.K. Arunprasad1, N. Narayanan, Preparation And Evaluation Of Solid Dispersion Of Terbinafine Hydrochloride, International Journal Of Pharmaceutical Sciences Review And Research, Volume 3, Issue 1, July – August 2010; Article 027.
18.N Prasanthi, N Rama Rao, Studies On Dissolution Enhancement Of Poorly Water Soluble Drug Using Water Soluble Carriers, Asian Journal Of Pharmaceutical And Clinical R esearch, Vol.3 Issue 2, April-June 2010.
19.Ganesh Chaulang, Piyush Patel, Formulation and Evaluation of Solid Dispersions of Furosemide in Sodium Starch Glycolate, Tropical Journal of Pharmaceutical Research, February 2009; 8 (1): 43-51.
20.K. Arunprasad1, N. Narayanan, Preparation And Evaluation Of Solid Dispersion Of Terbinafine Hydrochloride, International Journal Of Pharmaceutical Sciences Review And Research, Volume 3, Issue 1, July – August 2010; Article 027.
21.N Prasanthi, N Rama Rao, Studies On Dissolution Enhancement Of Poorly Water Soluble Drug Using Water Soluble Carriers, Asian Journal Of Pharmaceutical And Clinical R esearch, Vol.3 Issue 2, April-June 2010.
22.Ganesh Chaulang, Piyush Patel, Formulation and Evaluation of Solid Dispersions of Furosemide in Sodium Starch Glycolate, Tropical Journal of Pharmaceutical Research, February 2009; 8 (1): 43-51.
23.Shobit kumar,Sathish kumar guptha,Dissolution rate enhancement by solid dispersion techniques,Asian journal of pharmacy and life sciences, vol. 1 (4), oct-dec, 2011
24.B.Kusum, CH. Krishna Chatanya, M. Naga Madhu, Dissolution enhancement of efavirenz by solid dispersion and PEGylation techniques, Int J Pharm Investig. 2011 Jan-Mar; 1(1): 29–34.
25.A.Sharma and C.P. Jain, Preparation and characterization of solid dispersions of carvedilol with PVP K30, Res Pharm Sci. 2010 Jan-Jun; 5(1): 49–56.