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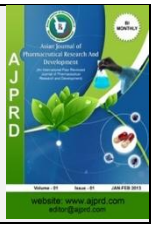

Open Access Research Article

Formulation and In-Vitro Evaluation of Oxcarbazepine Liquisolid Compacts

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A B S T R A C T

Objective: The solubility and dissolution properties of any drug are fundamental determinants of its oral bioavailability. The dissolution rate of weakly soluble, highly permeable (BCS-II) drugs, such as Oxcarbazepine, be capable of enhanced by use of the liquisolid (LS)technique

Methods: Oxcarbazepine liquid-solid compacts were formulated using PEG-600 as the non-volatile solvent, Avicel 102 as the carrier material, Aerosil 200 as the coating material Sodium starch glycolate as the disintegrant. Various batches of liquisolid compacts were set up by utilizing varied carrier-coating excipient ratio and different concentration of liquid medication. Flow parameters such as bulk density, tapped density, Carr's Index, Hausner's Ratio as well as an angle of repose were utilized to test the flowability of the powder mix. The liquid-solid system were made by direct compression strategy and were assessed for tests, for example weight variation, drug content, hardness, thickness, friability, wetting time, breaking down time also as well as the in vitro dissolution studies.

Results: The liquisolid system showed acceptable micromeritic properties. The tabletting properties of the liquisolid compacts were within the acceptable limits. delivery paces of liquisolid compacts were obviously higher compared with directly compressed tablets, due to expanding wetting properties and surface area of the drug. The liquisolid compacts showed enhanced bioavailability when compared with their conventional formulation

Conclusion: Liquid-solid tablet was measured as a hopeful system to enhance solubility and dissolution rate of poor-water soluble Oxcarbazepine.

Keywords: Oxcarbazepine, Solubility, Liquid-solid system, Dissolution rate

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INTRODUCTION

In recent years much attention has been focused on the drug bio-availability problem. The dissolution rate of a drug from its dosage form is now considered as an important parameter in the bio-availability[1].dissolution is the rate restricting step in the absorption of drugs from solid dosage forms, particularly when the medication is inadequately soluble. Different strategies, such as crystallization by solvent change, preparation of inclusion complexes with β-cyclodextrins, formation of water-soluble salts, micellar solubilisation, solid dispersion, lyophilisation, microencapsulation, liquisolid strategy and the incorporation of drug solutions or liquid drugs into soft gelatin capsules are a portion of the strategies that have been accounted for to improve the dissolution attributes of water-insoluble medications [2]. Liquisolid compaction is one of the promising procedures to upgrade the dissolution property of the medication and in this manner improve its

oral bioavailability. In this method, ineffectively soluble active pharmaceutical ingredient (API) is dissolved in a nonvolatile solvent and blended with the carrier and coating material. This leads to formation of a free-flowing dry powder, which has good compressibility.This dry powder is later compressed into tablet or filled into capsule[3]. Since the drug stays in solubilized state in nonvolatile solvents when directed, its dissolution rate is improved. The basic manufacturing process and low creation cost shows its adaptability at industrial scale. Recently, the dissolution upgrade of Tadalafil[4]. Using formulation strategy, a liquid medication can be changed over into a drylooking, non-adherent, free flowing, and readily compressible powder by mixing with selected powder excipients refers to as the carrier and coating materials [5]. In liquisolid compact, the drug is in a tablet or encapsulated dosage form and it is held in a solubilised liquid state, which therefore adds to expanded drug wetting properties,thereby enhancing drug dissolution. In liquisolid formulation the medicine is in either solubilised or molecularly dispersed state in the fluid vehicle, which is ingested into or onto the carrier and coating material individually. Hence, increased surface area of drug in powder form and enhanced dissolution of drug[6].

The strategy of liquisolid compacts has been effectively utilized to improve the in vitro release of poorly water-soluble drugs such as carbamazepine, famotidine, piroxicam, indomethacin, hydrocortisone, naproxen, furosemide, and prednisolone[7].

Oxcarbazepine (OXBZ) is chemically a dibenzazepine carboxamide derivative with an anticonvulsant property. OXBZ works by blockage of voltage gated Na channels and N and P type calcium channels[8]. The chemical structure of Oxcarbazepine was shown in fig.(1)

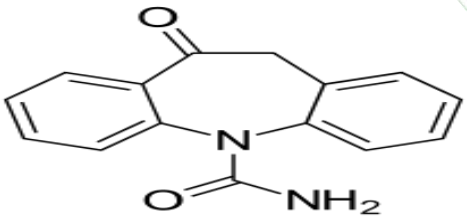

Fig 1: chemical structure of Oxcarbazepine

In the present study, a poorly soluble Oxcarbazepine were prepared as liquisolid compacts using water-miscible non-volatile solvents to enhance solubility and the dissolution rate with compare the *in vitro* drug discharge profile of formulated liquisolid tablets with the prepared direct compressed tablet.

MATERIALS AND METHODS

Materials

Oxcarbazepine was acquired as a gift sample from Organosis Ltd, Noida. (U.P.),India; Avicel PH 102 (SD fine chemical Ltd. Haryana) ; Aerosil 200 (SD fine chemical Ltd. Haryana); PEG-600 as well as Sodium Starch Glycolate were purchased from(SD fine chemical Ltd. Haryana) ,India. Every other material and reagents utilized were of logical reagent grade.

METHODS

Solubility studies:

The solubility of oxcarbazepine will assessed in different non-volatile solvents such as distilled water, Tween 80, polyethylene glycol-600, and propylene glycol. Saturated solutions were prepared by adding excess amount of oxcarbazepine was mixed with four non-volatile solvents separately in 50ml vials.The mixures were shaken on the rotatory shaker for 48 hr at 25^0C under constant vibration . At that point solutions were were separated through 0.45µ layer channel and diluted appropriately with 1% sodium lauryl sulfate (SLS) and examined UV spectrophotometrically at 256 nm for their medication content. The concentration of a dissolved drug is determined using the standard equation[9].

Angle of slide

In assessing the liquid retention potential of carrier and coating material angle of a slide is utilising as the parameter. The weighed amount of carrier and coating material was set toward one side of a shiny metal plate. At that point, this end was gradually raised until the plate with the even surface framed a point at which the sample was about to slide. The experiment was done in triplicate and the average of the angle of the slide was calculated[10].

Binding capacity of adsorbents for the solvents: Binding limit is characterized as the limit of powder excipients to hold fluid without change in their flow properties. It was determined by the following simple method. A constant weight of 5g of different powder excipients were put into a mortar and PEG-600 was added in increments of 0.01mL. The blend was ground up after every expansion to help dissemination of the fluid all through the powder particles. Addition of liquid was continued until lumps appeared in the powder mixture[11].

Assessment of load factor:

In a liquisolid system, the amount of fluid held by the carrier and coating materials relies upon the excipient proportion (R) while keeping up adequate flow and compression properties.

Theexcipient ratio R (R=Q/q) of a powder is defined as the ratio between the weights of carrier (Q) and coating materials (q) present in the formulation[12]. Arrangement of a liquisolid framework with an adequate flow rate and compressibility is conceivable when a most extreme measure of held liquid of the carrier material is not exceeded. This feature amount of liquid is termed as liquid load factor (L*f*). The liquid load factor (L*f*) is substitute as the mass ratio of the liquid medication (W) and carrier powder (Q) in the system (i.e., L*f*=W/Q) [13]. To calculate the loading factor, propylene glycol (liquid medication without drug) was add on to 10g carrier material and blended for 1min.The above method was repeated until a powder with sufficient flow rate was obtained.

Preparation of liquisolid system

The measure of excipients used to prepare liquisolid compact relies on their ϕ-values as well as liquid load factors. In recent studies, Avicel 102 was used as carrier whereas Aerosil 200 was used as coating material.

The liquid load factor (Lf) is calculated by using following formula

$Lf = \phi + ø\ (1/R)$ (1)

$Lf = W/Q$ (2)

$R = Q/q$ (3)

Where, ϕ and ø are the estimations of the carrier and the covering powders in a specific order while R is excipient proportion. The Oxcarbazepine was suspended in PEG 600 in the concentration (% Cd) of 50, 70 and 90 %. The total 9 batches were formulated as given in Table no.1.

Table 1: Formulation of liquisolid compact of Oxcarbazepine

Formulations	OXZ (mg)	PEG-600 (mg)	Avicel 102 (mg)	Aerosil 200 (mg)	SSG (mg)	Total weight (mg)
F1	150	200	404.3	35.7	10	800
F2	150	200	412	26	12	800
F3	150	200	415	20.4	15	800
F4	150	200	377	53.5	20	800
F5	150	200	401	39	10	800
F6	150	200	407	31	12	800
F7	150	200	355	80.3	15	800
F8	150	200	371	58.5	20	800
F9	150	200	394.1	45.9	10	800

The weighed amount of Oxcarbazepine was dispersed in the determined measure of non-volatile solvent (PEG-600) named as liquid vehicle. The mixing procedure was conducted in three stages as described by Spireas et al.[22]. Firstly, the weighed quantity of carrier material (Avicel 102) was blended with liquid medication in order to evenly distribute the liquid medication into the powder. At that point, the determined amount of coating material (AEROSIL® 200) was added to the system under persistent grinding up under in a mortar. At last, to the above binary mixture super disintegrating agent i.e., sodium starch glycolate was added and blended for a time of 10 to 20 min producing the final liquisolid powder which was compressed using rotary tablet press machine with 12 mm round and flat punch with a compression force that provides acceptable tablet hardness[23]. The concluding formulation of solid liquid compacts is shown in table no. 1.

Preparation of Oxcarbazepine tablets

The liquisolid powder blend containing Oxcarbazepine was compressed straightforwardly by utilizing single punch tablet machine to get tablets of 10, 12 and 14mm diameter with wanted thickness and hardness.

EVALUATION OF LIQUISOLID TABLETS

Physical parameters of tablets

Tablets were assessed via doing tests for weight variation, uniformity of tablet thickness and diameter, friability and hardness. All the tests were carried out in triplicate as per the compendial specifications[14,15].

Content uniformity

The drug content consistency was resolved as per IP 1996. The 20 tablets were weighed and powdered. The quantity of powder equivalent to 100 mg of drug was weighed and transferred to 100 ml volumetric flask containing 60 ml of ethanol (95%). The flask was shaken to dissolve the drug and volume was adjusted with ethanol. 10 ml of this solution was filtered and diluted to 100 ml with ethanol and absorbance of resulting solution was measured spectrophotometrically at maximum wavelength of 256 nm[16].

Disintegration test

For the vast majority of the tablets, the first significant advance towards arrangement is breakdown of tablet into more modest particles or granules, a process known as disintegration. The disintegration test was completed as portrayed under strategy for uncoated tablets in IP 1996. The assembly was suspended in the liquid medium (water) in the appropriate vessel, ideally in 1000 ml beaker. The volume of the fluid such that the wire mesh at its maximum point is at least 25 mm lower the surface of liquid and its lower point is at least 25 mm above the base of the container. A thermostatic arrangement was made for heating the liquid and maintaining the temperature at 37 ± 2°C. Assembly was suspended in beaker containing 1000 ml of distilled water and the apparatus was operated for specified time. Also disintegration time of tablet was recorded. Finally the assembly was removed from liquid[16].

Dissolution studies

The dissolution test was used to compare the release of Oxcarbazepine from liquisolid tablets and marketed tablet.

The USP Apparatus 2 was used with 900 ml of 1% sodium lauryl sulphate solution (1% SLS) at 37 ± 0.5^{0}C, and rotated at 50 rpm. 1 (ml) sample was withdrawn after specified time intervals and sink condition was maintained. The samples were filtered, diluted properly and analysed spectrophotometrically at 256 nm wavelength[17].Dissolution profiles of formulations were compared on the basis of dissolution efficiency (DE) and mean dissolution time (MDT) with marketed formulation.

RESULTS AND DISCUSSION

Solubility studies

The solubility of oxcarbazepine was assessed in different non-volatile solvents such as distilled water, Tween 80, polyethylene glycol-600, and propylene glycol.were indicated in table no. 2 .Highest solubility was found in PEG 600 (5.231µg/ml) and lowest in Distilled water (0.100 µg/ml). This is due to dispersion of higher fraction of drug in PEG 600 which helps to improve dissolution of drug.

Table 2: Solubility studies of oxcarbazepine in non-volatile solvents

Sr no.	Solvent	Solubility(µg/ml)
1	Distilled water	0.100
2	PEG 600	5.231
3	TWEEN-80	4.893
4	Propylene glycol	3.925

Evaluation of liquisolid tablet

Physical parameters of tablets

All the physical parameters of liquisolid tablets are shown in Table no. 3 and pre-compression results are shown in Table no.4 .Hardness of liquisolid compacts were ranged from 4.7 ± 0.70 to 4.5 ±0.04 mm and friability of all the liquisolid compacts was found to be in the range of 0.5 to 0.6% . It was seen that liquisolid compact formulated by utilizing Avicel 102 as carrier indicated more noteworthy compactibility as compared to other carriers. This may be due to hydrogen bonding between adjacent cellulose molecules in Avicel 102 which causes deformation of the particles plastically leading to formation of strong compact[19].

Table: 3 Physical Parameters of Oxcarbazepine tablets

Formulations	Weight variation ± SD (mg)	Hardness ± SD Kg/cm^2	Friability±SD (%)
F1	1.8±0.71	4.7±0.70	0.5±0.05
F2	2.0±0.10	3.4±0.98	0.5±0.04
F3	1.2±0.32	4.0±0.81	0.5±0.05
F4	1.5±0.45	3.2±0.32	0.6±0.03
F5	2.0±0.96	3.8±0.11	0.5±0.02
F6	1.1±0.65	3.5±0.45	0.5±0.01
F7	1.0±0.67	3.3±0.22	0.6±0.01
F8	1.1±0.54	3.0±0.06	0.4±0.06
F9	1.3±0.34	4.5±0.04	0.6±0.01

Table: 4 Pre – compression results

Formulations	Angle of repose	Bulk density (g/ml)	Tapped density (g/ml)	Carr"s index %	Hausner's ratio
F1	23.34	0.4756	0.5579	14.8	1.23
F2	27.85	0.4664	0.6219	25.0	1.25
F3	27.01	0.4918	0.6383	22.9	1.44
F4	21.34	0.4812	0.6162	12.53	1.22
F5	23.50	0.4556	0.6387	16.34	1.30
F6	24.39	0.4623	0.5854	23.07	1.27
F7	27.32	0.4715	0.6088	14.42	1.12
F8	30.45	0.4428	0.6234	18.51	1.24
F9	27.46	0.4763	0.6236	23.07	1.23

Disintegration time

Disintegration time of liquisolid tablets is shown in Table no.5 and agrees according to IP particulars for every formulated batches.

Table 5: Evaluation of Oxcarbazepine liquisolid formulations

Formulation code	Disintegration time (min)	% Drug Content
F1	37.62±1.54	96.5±0.56
F2	26.20±1.22	95.9±0.34
F3	25.68±1.34	97.76±0.55
F4	30.19±1.39	98.54±1.04
F5	23.24±1.56	98.18± 0.50
F6	21.50±1.35	97.97±0.00
F7	28.24±1.45	94.89±0.32
F8	22.34±1.30	97.75±0.01
F9	19.20±1.22	98.98±0.33

Content uniformity

A key quality trait for all drug preparations is the requirement for a constant dose of drug between individual tablets. Uniform drug content was observed for all the formulations which is as per the IP specification[20].

Dissolution Studies Figure no.2 illustrates the *in vitro* drug release profile of the liquisolid formulations. It was discovered that the drug release rate from the formulations was influenced by disintegration time, grouping of medication in PEG 600 and the properties of the carrier and coating material. The formulations which exhibited minimum disintegration time and low drug concentration in PEG 600 showed rapid drug release. A decrease in concentration of drug in PEG 600 increases the dispersion of drug at molecular level which may further enhance the dissolution rate of the drug. To comprehend impact of carriers on drug dissolution various batches with same excipient proportion and concentration of drug in non volatile solvent were compared.

The enhanced dissolution rates of liquisolid compacts compared to marketed tablet may be attributed to the fact that, the drug is already in PEG 600 while at the same time, it is carried by the powder particles. Thus, its release is accelerated due to its increased wettability and surface availability to the dissolution medium. The wettability of the compacts by the dissolution media is one of the proposed mechanisms for explaining the upgraded dissolution rate from the liquisolid compacts[21].PEG encourages wetting of drug particles by diminishing interfacial tension between dissolution medium and tablet surface. the liquisolid tablet F9 had the highest percentage 49 % of Oxcarbazepine dissolved in 10 min, while 32% of the drug was released from direct compressed tablets. All liquisolid tablets show completely 80% of drug release at 30 min,except F1. However, marketed direct compressible tablet show less drug release at this time.

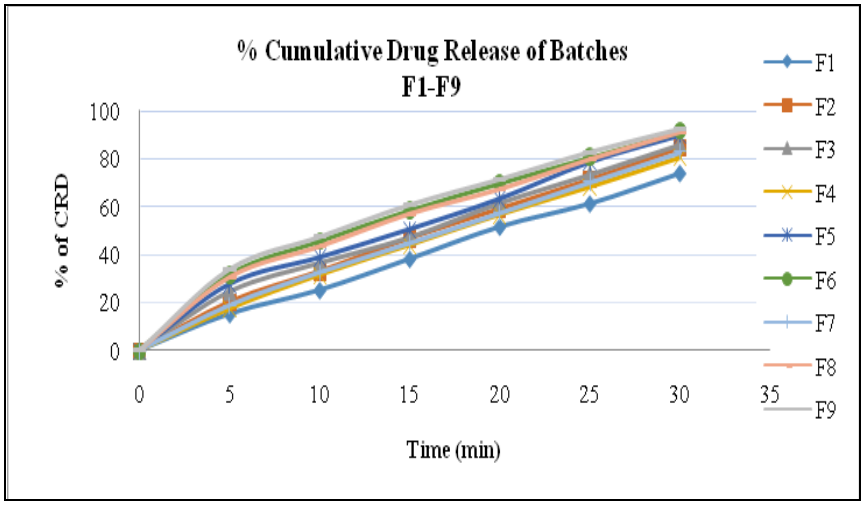

Figure: 2 Cumulative drug release study of batches F1-F9

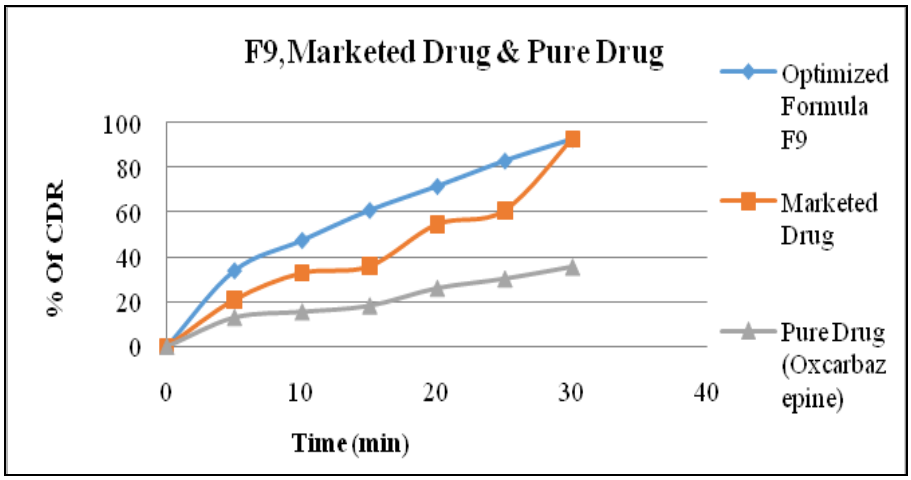

Figure 3: Optimized Formula Compared with the Pure Drug and Marketed Drug

DISCUSSION

Oxcarbazepine is very slightly soluble in water; so the study plan was done, to improve the solubility of oxcarbazepine by liquisolid technique, and then was to formulate liquisolid compacts.

The *in vitro* release studies revealed that the liquisolid compacts formulations showed a faster drug release when compared to the physical mixture and pure drug.

CONCLUSION

The solid liquid compacts were effectively formulated utilizing the suitable amount of non-volatile solvent, carrier and coating material as well as the disintegrant which were calculated based on the loading factor and factor and the fluid maintenance capability of carrier and coating material. The consequences of the different assessment tests show that the solid liquid compacts delivered were inside satisfactory cutoff points. Oxcarbazepine exhibits high permeability through biological membranes, but its absorption after oral administration is limited by its low dissolution rate due to its very low aqueous solubility. Hence, the use of the liquisolid technique was chosen to enhance the dissolution properties of Oxcarbazepine. The Oxcarbazepine liquisolid compacts were prepared using Avicel PH102 and Aerosil 200 as the carrier and coating material,respectively. The flow properties of Oxcarbazepine liquisolid compacts showed an acceptable flowability. The hardness, friability, weight variation and disintegration tests were within adequate limits. The *in vitro* dissolution study affirmed upgraded drug discharge from liquisolid compacts compared with directly compressed counterparts and this was autonomous of the sort and volume of the dissolution medium. The liquisolid compacts indicated an enhancement in bioavailability compared with their directly compressed counterparts. The dissolution rate results show that the main objective of this research has been met because there is a marked improvement in the dissolution profile of the F9 when compared to that of the conventional tablet. Hence, it is concluded that liquid-solid compact technique is a novel approach that can be employed to increase the solubility and dissolution rate of oxcarbazepine.

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CONFICTS OF INTEREST

The authors declare no conflict of interest in this research article.

REFERENCES

1. Kulkarni A.S, Alookar N.H, Mane M.S & Gaja J.B. Liquid solid systems. *IJPSN*, 2010; 3(1):795-802.
2. Saharan V, Kukkar V, Kataria M. Dissolution enhancement of drugs.part i : technologies and effect of carriers. *International Journal of Health Research*, 2009; 2(2): 207-223.
3. Mahapatra Anjan K, Sastry G.M, Swain Ranjit P, Murthy PN & Palei Narahari N. Liquisolid technique: a novel approach in pharmaceutical formulation development. J*ournal. Of Chemical and. Pharmaceutical Research,2014;* 6(14): 529-543.
4. Lu M, Xing H, Yang T.Dissolution enhancement of tadalafil by liquisolid technique. *Pharmaceutical Development and Technology.2017;* 22(1): 77–89.
5. Yadav V.B, Yadav A.V. Improvement of Solubility and Dissolution of Indomethacin by Liquisolid and Compaction Granulation Technique .*Journal of Pharmaceutical Sciences and Research*, 2009;1(2): 44-51.
6. Karmarkar A.B. Effect of Ceolus KG-802 on the dissolution rate of fenofibrate liquisolid tablets: Preformulation and formulation development studies.*Drug discoveries & therapeutics*, 2010; 4(6):493-498.
7. Nagabandi V, Tadikonda R, Jayaveera K. Formulation development and evaluation of liquisolid systems to improve the dissolution rate of ketoprofen. *IJBR*.2011;2:530-41.
8. Schachter S.C. Oxcarbazepine:current status and clinical applications, *Experimental opinions of Investigative Drugs*,1999;8(7):1-10.
9. Sisinthy S.P, Sarah C.Y.L, Nalamolu K.R. Optimization of coconut oil based self-micro emulsifying drug delivery systems of olmesartan

medoxomil by simplex centroid design. *International Journal of Applied Pharmaceutics*, 2016;8(4):47-52.
10. Prajapati S.T, Bulchandani H.H, Patel D.M, Dumaniya S.K, Patel C.N. Formulation and evaluation of liquisolid compacts for olmesartan medoxomil. *Journal of Drug Delivery* 2013;1-9.
11. Javadzadeh J, Siahi-Shadbad M.R, Barzegar-Jalali M.Enhancement of rate of Piroxicam using Liquisolid compacts. *Farmaco* 2005; 60: 361-365.
12. Shah C.V, Gonjari I.D, Karmarkar A.B.Evaluation of in-vitro dissolution profile comparison methods of sustained release tramadol hydrochloride liquisolid compacts. *Digest Journal of Nanomaterials and Biostructures*, 2012; 4(4):651-661.
13. El-Say Khalid M, Samy Ahmed M, Fetouth Mohamed I, *International journal of Pharmaceutical Sciences.* 2010; 3(1):135-142.
14. The United States Pharmacopoeia National Formulary. USP28 NF23 ed. Canada: The United States Pharmacopoeial Convention; 2005.p.342-343.
15. British Pharmacopoeia. IV.ed. London: The Stationary Office; 2004.p. A256-A274
16. Indian Pharmacopoeia. Vol I & II. Delhi: The Controller of publications; 1996.p. 137-8
17. Tayel S.A, Soliman II, Louis D. Improvement of dissolution properties of Carbamazepine through application of the liquisolid tablet technique. *European Journal of Pharmaceutics and Biopharmaceutics*. 2008; 69(1):342–7.
18. Lobo M.S, Costa P. Modeling and comparison of dissolution profiles. *European Journal of Pharmaceutical Sciences*.2001; 13(2) :123–33.
19. Shangraw R. Compressed Tablets by Direct Compression Granulation Pharmaceutical Dosage Forms: Tablets. 2nd Ed, USA: Marcel Dekker; 1989.p.195-246.
20. Indian Pharmacopoeia. Vol I & II. Delhi: The Controller of publications; 1996.p. 137-138.
21. Fahmy R.H, Kassem M.A. Enhancement of famotidine dissolution rate through liquisolid tablets formulation: *In vitro* and *in vivo* evaluation. *European Journal of Pharmaceutics and Biopharmaceutics*. 2008; 69(3):993-1003.
22. Sanka k, Poienti S, Mohammad A.B & Divan P.V.*Powder Technology*.2014; 256(4):336-344.
23. Naveen C, Narra N, Rao T.R. Preparation and characterization of liquidsolid compacts for improved dissolution of telmisartan. *Journal of Drug Delivery* 2014;1-10