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ENHANCEMENT OF DISSOLUTION RATE OF OXCARBAZEPINE BY USING VARIOUS SOLID DISPERSION TECHNIQUES

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ABSTRACT

Oxcarbazepine is an anticonvulsant drug, mainly used as an add-on or first line treatment in adults and children. Due to sudden onset of attack, it is necessary to formulate antiepileptics into such a delivery system, which provide immediate relief. Hence, the present investigation was undertaken with a view to develop mouth-dissolving tablets of oxcarbazepine, which offers a new range of product having desired characteristics and intended benefits. The aim of this research wok is to formulate and evaluate Oxcarbazepine solid dispersions system by using the different techniques. This will increase the solubility of the drug or Oxcarbazepine and give the immediate release of the drug from the formulations. In this study, the mouth dissolving tablets were prepared using three different technologies like Physical mixing, solvent evaporation and Kneading techniques. The disintegrating agent used in the present study is Croscarmellose sodium. Solid dispersions of oxcarbazepine with Croscarmellose sodium in different weight ratios were prepared with a view to increase its water solubility. Oxcarbazepine solid dispersions with Croscarmellose sodium in 1:5 ratios of drug: carrier showed maximum drug release and hence, compressed along with other ratios into mouth dissolving tablet. Among the three different techniques used for preparation of solid dispersions Kneading method (KM) technique has shown the increase in dissolution rate that is the KM (III) was found to have a faster solubility and dissolution property which was prepared by using Croscarmellose sodium as a disintegrant in the ratio of 1:5. KM (III) which is prepared by using drug and disintegrant ratio of 1:5 ratios by using Kneading method (KM).

KEYWORDS: Oxcarbazepine; Mouth dissolving tablets; Solid dispersions; Croscarmellose sodium; Physical mixing; solvent evaporation and Kneading techniques; Dissolution rate.

1. INTRODUCTION

Improving oral bioavailability of drugs those given as solid dosage forms remains a challenge for the formulation scientists due to solubility problems. The dissolution rate could be the rate-limiting process in the absorption of a drug from a solid dosage form of relatively insoluble drugs. Therefore increase in dissolution of poorly soluble drugs by solid dispersion technique presents a challenge to the formulation scientists. Solid dispersion techniques have attracted considerable interest of improving the dissolution rate of highly improving wettability and forming amorphous particles. The term solid dispersion refers to a group of solid products consisting of at least two different components, generally a hydrophilic inert carrier or matrix and a hydrophobic drug.

Orally administered drugs completely absorb only when they show fair solubility in gastric medium and such drugs shows good bioavailability. Recently more than 40% NCE's (New Chemical Entities) developed in Pharmaceutical Industry are practically insoluble in water. These poorly water soluble drugs are allied with slow drug absorption leading to inadequate and variable bioavailability and gastrointestinal mucosal toxicity. Therefore, the improvement of drug solubility thereby its oral bio-availability remains one of most challenging aspects of drug development process especially for oral drug delivery system. There are numerous approaches available and reported in literature to enhance the solubility of poorly water soluble drug. The techniques are chosen on the basis of certain aspects such as properties of drug under consideration, nature of excipients to be selected and nature of intended dosage form.

The poor solubility and low dissolution rate of poorly water soluble drugs in the aqueous gastro-intestinal fluids often cause in sufficient bioavailability rather than the limited permeation through the epithelia and the formulation of poorly soluble drugs for oral delivery now presents one of the major challenges tom formulation scientists in the industries.[1] The term solubility is defined as maximum amount of solute that can be dissolved in a given amount of Solvent quantitatively it is defined as the concentration of the solute in saturated solution at a certain temperature in qualitative terms, solubility may be defined as spontaneous interaction of two or more substances to form a homogenous molecular dispersion.[2]

1.1 Mechanism of action

The exact mechanism by which Oxcarbazepine exerts its anticonvulsant effect is unknown. It is known that the pharmacological activity of Oxcarbazepine occurs primarily through its 10-monohydroxy metabolite (MHD). In-vitro studies indicate an MHD-induced blockade of voltage-sensitive sodium channels, resulting in stabilization of hyperexcited neuronal membranes, inhibition of repetitive neuronal discharges, and diminution of propagation of synaptic impulses. In addition, increased potassium conductance and modulation of high-voltage activated calcium channels may also contribute to the anticonvulsant effects.

1.2 Solid Dispersion

Solid Dispersions (SD's) traditionally have been used as an effective method to improve the dissolution properties and bioavailability of poorly water-soluble drugs. Since 1960.[3] many investigators have studied SD's of poorly water-soluble drugs with various pharmacologically inert carriers to increase the dissolution and oral absorption of poorly water-soluble drugs; however, only a few systems are useful commercially. Different types of drug–carrier interactions in solid-state dispersions have been suggested by Chios and Riegeman: simple eutectic mixtures, solid solutions, glass solutions and glass suspensions, amorphous precipitates in a crystalline carrier, and compound or complex formation. In SD's systems, a drug may exist as an amorphous form in polymeric carriers, and this may result in improved solubility and dissolution rates compared with crystalline material. The term solid dispersion refers to a group of solid products consisting of at least two different components, generally a hydrophilic matrix and a hydrophobic drug. The matrix can be either crystalline or amorphous. The drug can be dispersed molecularly, in amorphous particles (clusters) or in crystalline particles.[4]

The mechanisms for the enhancement of the dissolution rate of SD's have been proposed by several investigators. Molecular dispersion of drug in polymeric carriers may lead to particle size reduction and surface area enhancement, which result in improved dissolution rates. Furthermore, no energy is required to break up the crystal lattice of a drug during dissolution process and improvement in drug solubility and Wettbility due to surrounding hydrophilic carriers. Reduction or absence of aggregation and agglomeration may also contribute to increased dissolution. The methods used to prepare SD's include the melting method, the solvent method, and the solvent wetting method. Among the various approaches employed to improve the dissolution of poorly soluble drugs, Solid Dispersion has been proven successful.

Fast or immediate drug dissolution from Solid Dispersions has been observed due to increased wettbility, improved dispersibility of drug particles, and existence of the drug in amorphous form with improved solubility and absence of aggregation of drug particles.

1.3 Advantages of solid dispersion

Particles with reduced particle size, Particles with improved wettability, Particles with higher porosity, Drugs in amorphous state.[5]

Preparation methods of solid dispersions.[6]

(a) Solid dispersion techniques.

(b) Solvent evaporation method.

(c) Fusion method/melting method.

(d) Hot melt extrusion.

(e) Supercritical fluid technology (SCF).

(f) Dropping method.

(g) Electrostatic Spinning Method.

(h) Co-precipitation method.

2. MATERIALS AND METHODS

2.1 Materials

Oxcarbazepine (Novartis, Mumbai), Crosscarmellose sodium (Ozone international, Mumbai), Talc (Sd. Fine chemical Ltd. Mumbai), Magnesium stearate (Qualigen Chemical Ltd, Mumbai) Microcrystalline cellulose, P^H 101 (Signet Chemicals, (Wuhan), China), Methanol (Sd.fine chemicals Ltd.,Mumbai) and Sodium lauryl sulphate (Merck Specialities PVT.Ltd.,Mumbai).

2.2 Equipments

Dissolution Rate Test Apparatus IP/BP/USP single stage (LABINDIA DISSO 2000 Campbell Electronics), UV-Visible Spectrophotometer (Elico SL150), Electronic balance (Dhona 200 D), pH meter (Elico LI 120), Heavy rotary shaker (KEMI), Vortex mixer (KEMI), Heating mantle (KEMI), Hot air oven (Kandvil equipment), Disintegration test apparatus IP/BP/USP standards (Campbell Electronics), Roche Friabilator (Campbell Electronics), Tablet Hardness tester (Monsanto hardness tester), Tablet Compression machine (Cadmach-single punch tablet machine), Diameter test apparatus (Dial Vernier Calipers), Differential Scanning Calorimeter (DSC 823E, Aurobindo pharma Ltd, Unit-I: Mettler Toledo Star System),

Fourier Transform Infrared Spectrophotometer (Bruker, Germany) X-ray Diffractometer (Diffractometer system, XPERT-PRO).

2.3 Experimental methods

2.3.1 Estimation of Oxcarbazepine

A Simple Sensitive and accurate Spectrophotometric method was used for the measurement of Oxcarbazepine at a λ max 256nm.The absorbance of standard dilutions were measured at 256nm.

2.3.2 Procedure

An accurately weighed quantity of Solid Dispersions equivalent to 150 mg of OXC, was taken into a 100 mL volumetric flask and dissolved in methanol and filtered through a Whatman No.1 filter paper (0.45µ). The filtrates were diluted suitably with 0.1N Hydrochloric acid (Hcl) solution with 0.25% SLS of pH 1.2. The content of OXC was determined spectrophotometrically at 256 nm against suitable blank using UV-visible Spectrophotometer (Elico SL150).

2.3.3 Drug release studies

Dissolution studies on each formulation were performed in a calibrated eight station dissolution test apparatus equipped with paddles employing pH 1.2 phosphate buffers as medium. The paddles were operated to rotate at 75 rpm and the temperature was maintained at 37± 1^0c throughout the experiment. Samples were withdrawn at regular intervals up to 120 min and replaced with equal volume to maintain the constant volume of dissolution medium throughout the experiment.[7] Drug content of the samples was determined by UV Spectrophotometer at 256nm after suitable dilution of samples.[8] Necessary corrections were made for the loss of drug due to each sampling. The drug dissolved experiments were conducted in triplicate. The dissolution profiles were depicted in in **Tables: 4, 5, 6 to 7** and **Figure: 2 (a)-(c)** and **3 (a) to 5 (c)** respectively.

2.3.4 Determination of amount of drug content

The amount of drug substance present in the given dissolution samples were determined with the help of UV-Spectrophotometer at a wavelength of 256nm. The obtained absorbance values were substituted in the given equation to get the amount of drug substance at different time intervals of dissolution.

$$\text{Amount} = \frac{\text{Test o.d}}{\text{Standard o.d}} \times \text{dilution factor} \times 900 / 1000$$

2.3.5 Different formulation batches

Formulation 1 - PURE DRUG (100mg)

Formulation 2 – DRUG: POLYMER (1:1, 1:3, 1:5) Croscarmelose sodium.

2.3.6 Methods used in the present work

In the present study three methods were used to enhance the solubility of poorly soluble drug Oxcarbazepine *i.e.,* Physical mixture method, Solvent evaporation method and Kneading method.

A. Physical mixture method (PM)

In Physical mixture method the drug Oxcarbazepine and surface active carriers Croscarmelose sodium (CCS), in proposed ratios *i.e.* 1:1, 1:3 and 1:5 were weighed accurately and triturated by using mortar and pestle. This is continued for nearly 15min. The resultant product was then filled in glass bottles, sealed and stored in a desiccator until further use.[9]

B. Solvent Evaporation method (SE)

In this method solid dispersion of drug was prepared by using Croscarmelose sodium (CCS) as a disntegrant in the three different mass ratios (1:1, 1:3and 1:5) by using solvent evaporation method.

C. **Kneading method (KM)**

In Kneading method the drug (Oxcarbazepine) and surface active carriers Croscarmelose sodium (CCS) in the ratio of i.e. 1:1, 1:3 and 1:5 were weighed accurately and triturated in a mortar and pestle by adding drop by drop of methanol for size reduction of the particles. This method was continued for nearly 45 min and made into dough like mass.

Table: 1. Preparation methods of Solid Dispersions

METHODS	MASS RATIO	SOLVENT	TRITURATION/ KNEADED TIME	TEMP.TIME	SIEVE NO:
Physical method (PM)	1:1, 1:3, 1:5	……	15 (min)	……..	#80
Solvent	1:1, 1:3, 1:5	Methanol	……..	HAO at 50°C	#80

Evaporation method (SE)				For 24 hrs	
Kneading method (KM)	1:1, 1:3, 1:5	Methanol	45 (min)	HAO at 50°C For 24 hrs	#80

Table: 2 Composition of OXC Solid Dispersion with CCS

Solid Dispersion composition	Method	Drug-Carrier ratio	Formulation Code
Oxcarbazepine : Croscarmellose sodium (CCS)	Physical mixture (PM)	1:1	PM I (1:1)
		1:3	PM II (1:3)
		1:5	PM III (1:5)
	Solvent Evaporation method (SE)	1:1	SE I (1:1)
		1:3	SE II (1:3)
		1:5	SE III (1:5)
	Kneading method (KM)	1:1	KM I (1:1)
		1:3	KM II (1:3)
		1:5	KM III (1:5)

1. RESULTS AND DISCUSSION

Trial-1

This trail was done by using pure drug; it has shown poor dissolution property because of less solubility of drug in the dissolution medium.

Calibration Curve of Oxcarbazepine

Concentration and Absorbance obtained from Calibration curve of Oxcarbazepine in 0.1N Hydrochloric acid (Hcl) solutons with 0.25% SLS (pH 1.2).

The present analytical method obeyed Beer's law in the concentration range 2-10µg/mL and is suitable for the estimation of Oxcarbazepine. The value of R^2 (correlation coefficient) for the linear regression equation was found to be 0.997. The results are reported in **Table: 3** and **Figure: 1.**

Table: 3 Calibration curve data for the estimation of Oxcarbazepine

SI No.	Concentration (µg/mL)	Absorbance (at 256 nm)
1	2	0.075
2	4	0.157
3	6	0.221
4	8	0.284
5	10	0.352

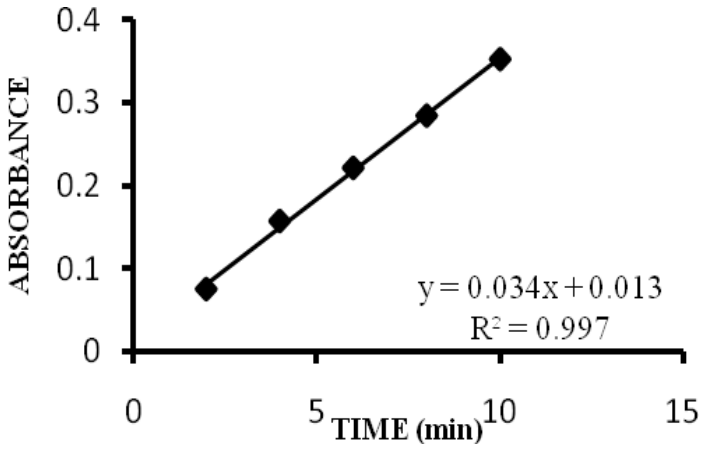

Figure: 1 Standard plot of Oxcarbazepine

Table: 4 Dissolution profile data of Pure OXC (PD)

TIME (min)	% Oxcarbazepine released			Mean%OXC releasd ±SD
	TRAIL-1	TRAIL-2	TRAIL-3	
0	0	0	0	0
5	17.31	18.05	18.21	17.85±0.48
10	18.22	19.85	19.33	19.13±0.83
20	20.88	21.47	21.01	21.12±0.31
30	24.19	23.66	23.32	23.72±0.43
40	26.41	25.82	25.22	25.81±0.59
60	31.25	29.75	30.52	30.50±0.75
90	38.81	37.69	37.51	38.00±0.70
120	43.56	45.12	44.22	44.30±0.78

Improvisation

As pure drug has shown poor dissolution property, in order to enhance the dissolution rate we used different methods for preparing solid dispersions.

***Trial -2* In-vitro dissolution studies of OXC and its Solid Dispersions**

In-vitro dissolution studies data of Pure drug and its dispersions prepared by Physical mixture, Solvent evaporation method and Kneading method are shown in **Tables: 4, 5, 6 to 7** and **Figure: 2 (a)-(c)** and **3 (a) to 5 (c)** respectively.

In-vitro **dissolution studies of OXC and its Solid Dispersions**

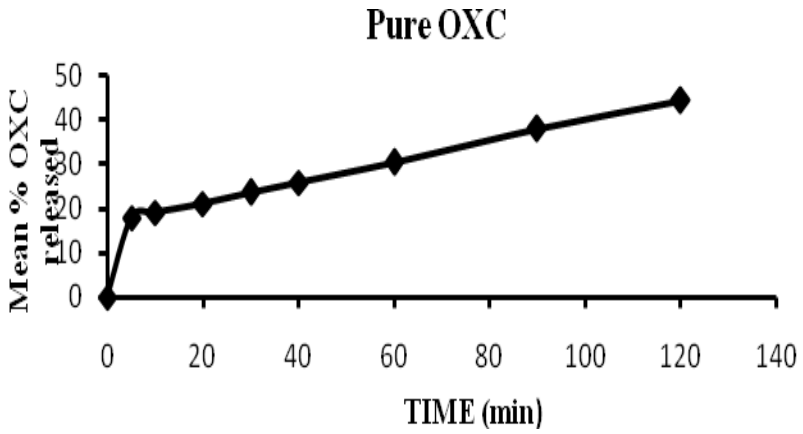

Figure: 2 (a) Dissolution profile plot for pure drug of Oxcarbazepine

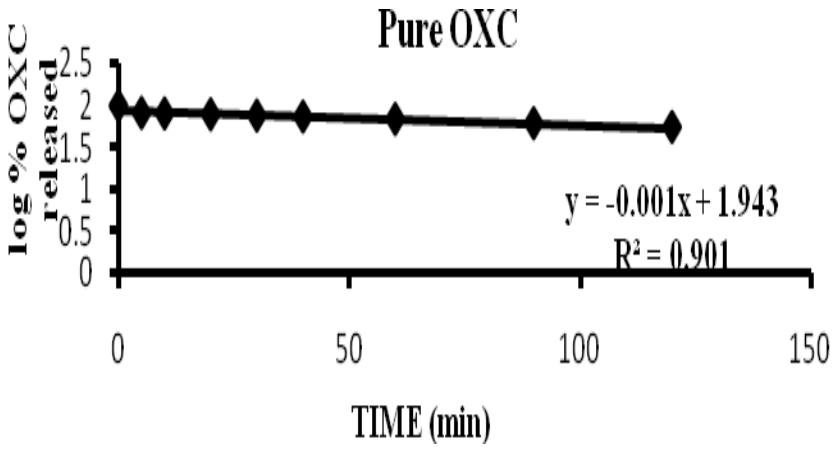

Figure: 2 (b) First order kinetic plot for Pure Oxcarbazepine

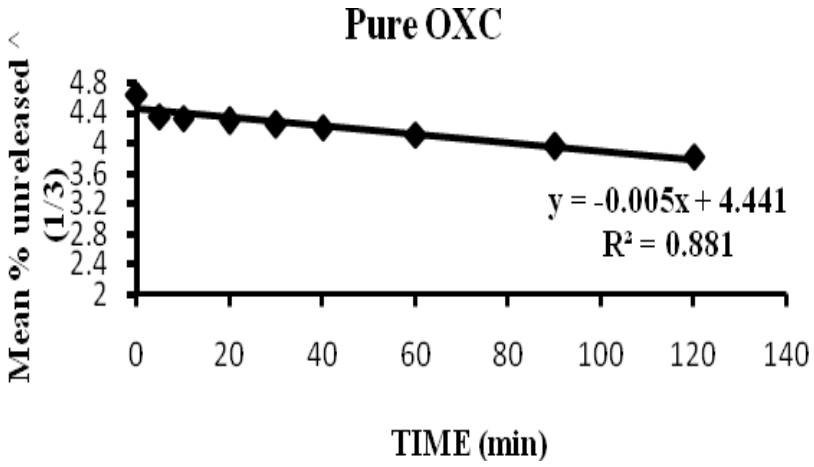

Figure: 2 (c) Hixson-Crowell's dissolution plot of Pure Oxcarbazepine

Table: 5 Dissolution profiles of Oxcarbazepine Solid Dispersion prepared by Physical mixture method using CCS

TIME (min)	Mean % OXCARBAZEPINE released (x ± SD, n=3)			
	PD	PM I (1:1)	PM II(1:3)	PM III (1:5)
0	0	0	0	0
5	17.85±0.48	19.21±0.51	20.18±0.98	21.05±1.03
10	19.13±0.83	19.98±0.22	21.04±0.64	22.26±1.25
20	21.12±0.31	21.45±0.81	23.14±1.03	26.35±1.24
30	23.72±0.43	24.17±0.27	30.38±1.17	35.64±1.05
40	25.81±0.59	26.22±0.35	33.57±1.32	41.72±0.24
60	30.50±0.75	30.81±1.40	40.88±0.52	45.52±0.64
90	38.00±0.70	38.82±1.32	45.26±0.24	51.08±0.36
120	44.30±0.78	45.91±1.02	51.44±0.37	59.68±0.51

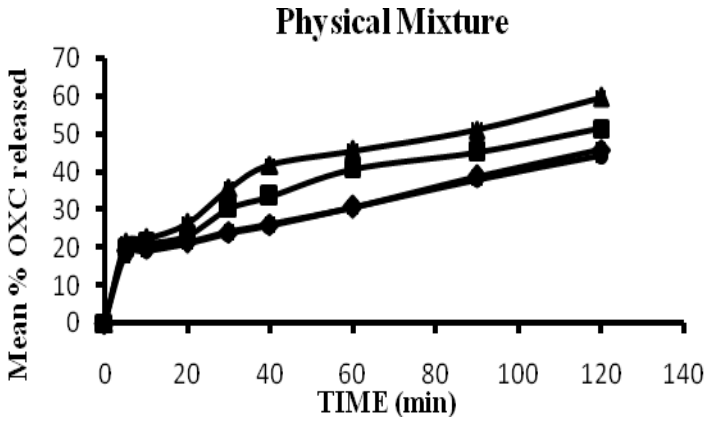

Figure: 3 (a) Comparative *in-vitro* dissolution profiles of Oxcarbazepine Solid Dispersions by Physical mixture method using CCS [PM-I (1:1), PM-II (1:3), PM-III (1:5)] and Pure Drug (PD) (Mean ± SD., n = 3).

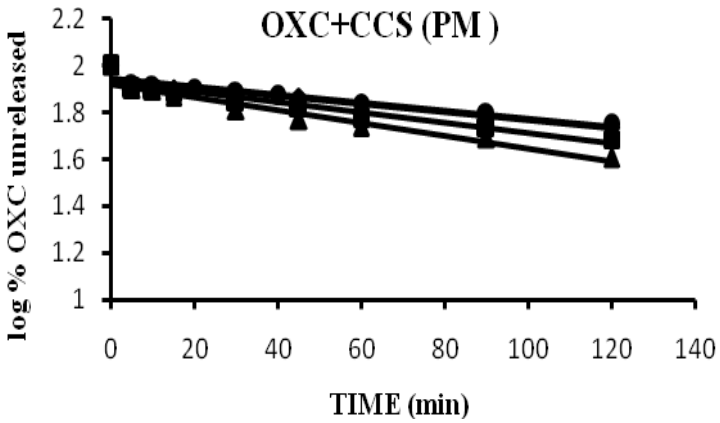

Figure: 3 (b) First order plot of Oxcarbazepine dispersion by Physical mixture method using CCS [PM-I (1:1), PM-II (1:3), PM-III (1:5)] and Pure Drug (PD).

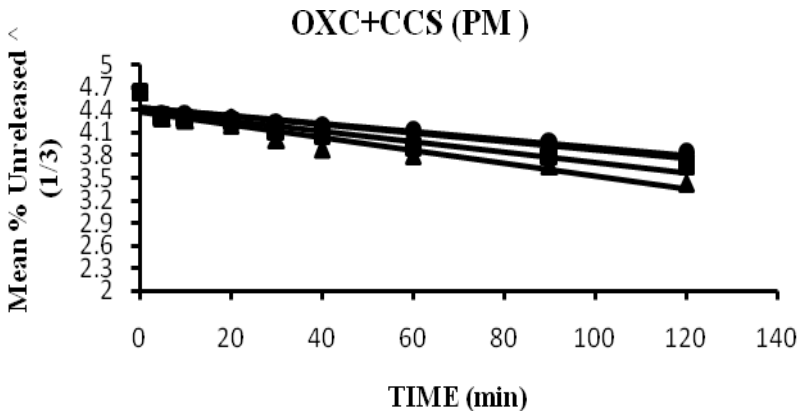

Figure: 3 (c) Hixson-Crowell's dissolution plots of Oxcarbazepine Solid Dispersions by Physical mixture method using CCS [PM-I (1:1), PM-II (1:3), PM-III (1:5)] and Pure Drug (PD).

Table: 6 Dissolution profiles of Oxcarbazepine Solid Dispersion prepared by Solvent Evaporation method using CCS

TIME (min)	Mean % OXCARBAZEPINE released (x ± SD, n=3)			
	PD	SE I (1:1)	SE II (1:3)	SE III (1:5)
0	0	0	0	0
5	17.85±0.48	22.43±0.67	25.29±0.71	29.42±0.43
10	19.13±0.83	26.18±0.24	32.63±0.64	38.56±0.52
20	21.12±0.31	33.82±0.53	48.26±0.44	63.18±0.66
30	23.72±0.43	41.42±0.82	55.18±0.35	75.82±0.53
40	25.81±0.59	48.64±0.36	69.07±0.28	81.22±0.42
60	30.50±0.75	60.24±0.54	76.36±0.75	87.25±0.26
90	38.00±0.70	69.27±0.22	85.73±0.43	91.34±0.91
120	44.30±0.78	74.62±0.19	92.15±0.24	99.73±0.44

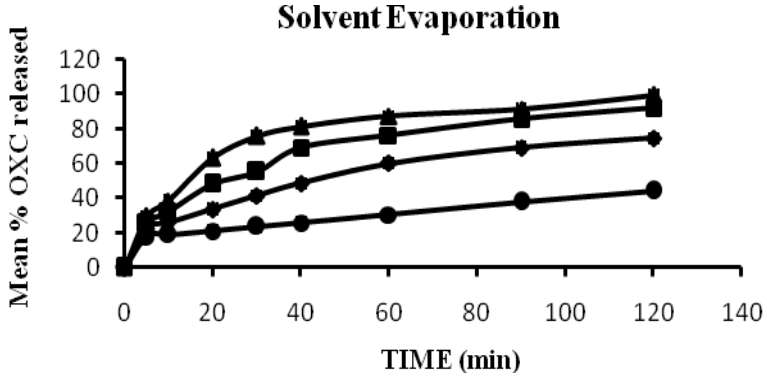

Figure: 4 (a) Comparative *in-vitro* dissolution profiles of Oxcarbazepine Solid Dispersions by Solvent Evaporation method using CCS [SE-I (1:1), SE-II (1:3), SE-III (1:5)] and Pure Drug (PD) (Mean ± SD., n=3).

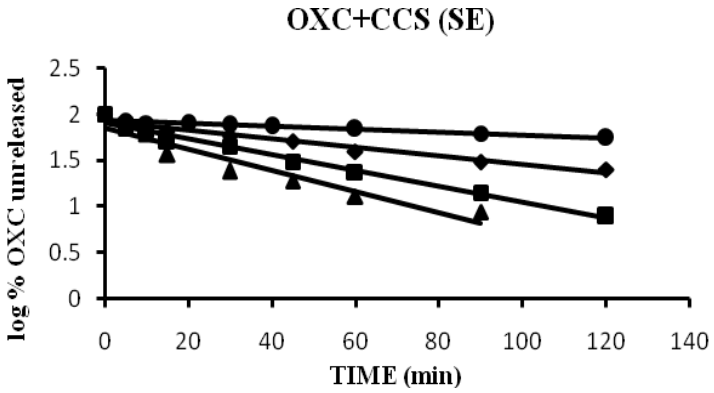

Figure: 4 (b) First order plot of Oxcarbazepine dispersion by Solvent Evaporation method using CCS [SE-I (1:1), SE-II (1:3), SE-III (1:5)] and Pure Drug (PD).

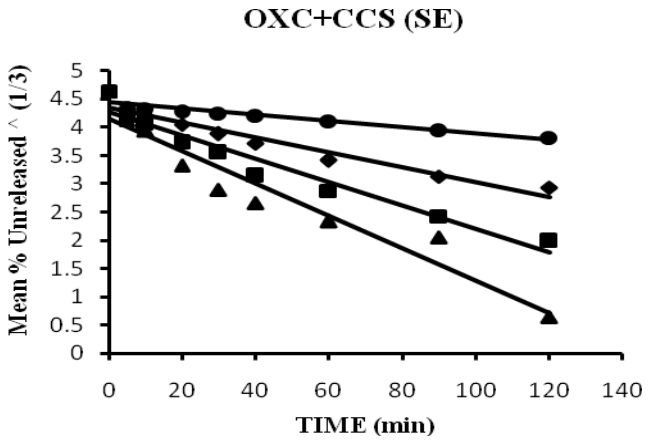

Figure: 4 (c) Hixson-Crowell's dissolution plots of Oxcarbazepine Solid Dispersions by Solvent Evaporation method using CCS [SE-I (1:1), SE-II (1:3), SE-III (1:5)] and Pure Drug (PD).

Table: 7 Dissolution profiles of Oxcarbazepine Solid Dispersion prepared by Kneading method using CCS

TIME (min)	Mean % OXCARBAZEPINE released (x ± SD, n=3)			
	PD	KM III (1:1)	KM III(1:3)	KM III (1:5)
0	0	0	0	0
5	17.85±0.48	30.75±0.42	33.36±0.46	35.81±0.67
10	19.13±0.83	40.62±0.39	42.17±0.84	44.42±0.69
20	21.12±0.31	54.43±0.24	56.46±0.36	60.19±0.55
30	23.72±0.43	64.24±0.18	65.34±0.27	76.29±0.37
40	25.81±0.59	72.63±0.44	78.21±0.23	85.47±0.62
60	30.50±0.75	82.16±0.37	84.52±0.42	91.22±0.54
90	38.00±0.70	90.45±0.72	93.18±0.53	99.98±0.32
120	44.30±0.78	96.53±0.46	99.08±0.37	0.00

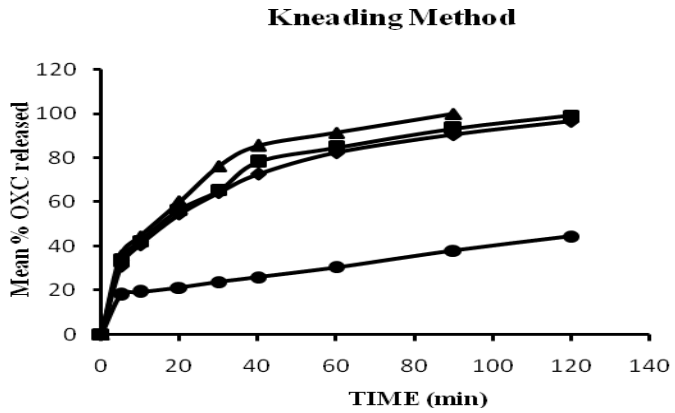

Figure: 5 (a) Comparative *in-vitro* dissolution profiles of Oxcarbazepine Solid Dispersions by Kneading method using CCS [KM-I (1:1), KM-II (1:3), KM-III (1:5)] and Pure Drug (PD) (Mean ± SD., n=3).

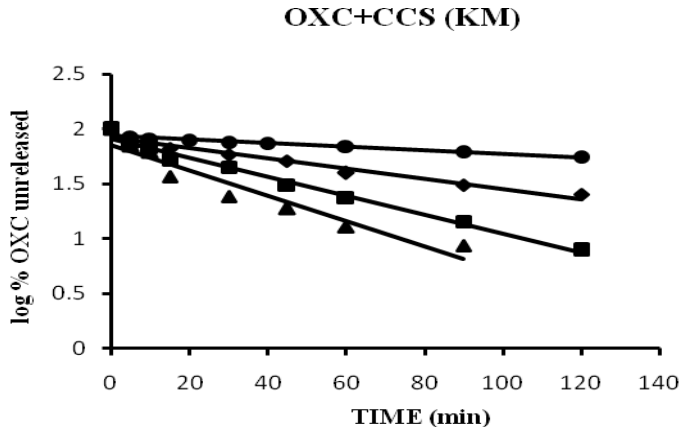

Figure: 5 (b) First order plot of Oxcarbazepine dispersion by kneading method using CCS [KM-I (1:1), KM-II (1:3), KM-III (1:5)] and Pure Drug (PD).

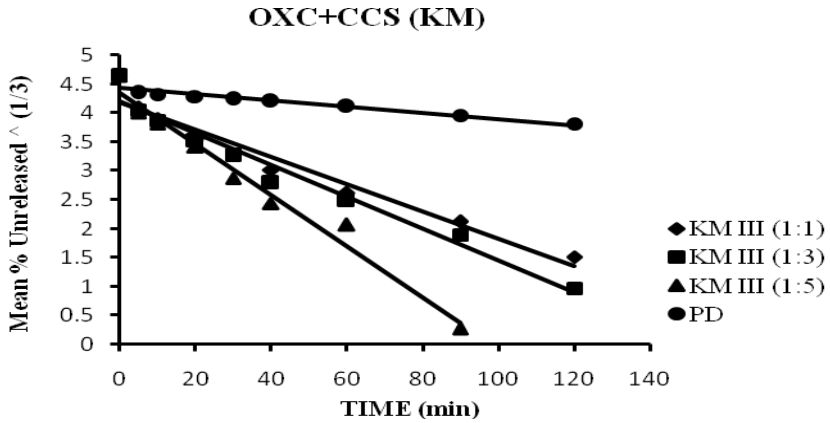

Figure: 5 (c) Hixson-Crowell's dissolution plots of Oxcarbazepine Solid Dispersions by Kneading method using CCS [KM-I (1:1), KM-II (1:3), KM-III (1:5)] and Pure Drug (PD).

Here dissolution study of pure drug data showed that 25.81±0.59 percent of drug was released within 40 min.

Croscarmellose sodium (CCS)

1:1 ratio

In Physical mixture dissolution study of OXC with CCS data showed that 26.22±0.35 % of drug was released within 40 minutes. In solvent evaporation method was found to be 48.64±0.36 % drug released within 40 min. In Kneading method the drug release in 1:1 ratio was found to be 72.63±0.44 % within 40 min. For initial periods of time for 10 and 20 minutes, the drug release in 1:1 ratios of physical mixture was found to be 19.98±0.22 % and 21.45±0.81 % respectively. In other methods (SE and KM) the drug release found to be 26.18±0.24 %, 33.82±0.53 % and 40.62±0.39 %, 54.43±0.24 % within 10 and 20 minutes.

Kneading method (KM) containing 1:1 molar ratios of drug and CCS showed faster dissolution rate, about 90.45±0.72 % drug release was observed within 90 min. In other methods Physical mixture and Solvent evaporation (PM and SE) showed dissolution rate, about 38.82±1.32% and 69.27±0.22% drug release were observed within 90 min, respectively. The dissolution data given in **Tables: 3, 4, 5 to 6** and **Figure: 3 (a)-(c)** and **4 (a) to 6 (c)** respectively.

1:3 ratio

In Physical mixture dissolution study of OXC with CCS data showed that 33.57±1.32 % of drug was released within 40 minutes. In solvent evaporation method was found to be 69.07±0.28 % drug released within 40 min. In Kneading method the drug release in 1:3 ratios was found to be 78.21±0.23% within 40 min. For initial periods of time for 10 and 20 minutes, the drug release in 1:1 ratios of physical mixture was found to be 21.04±0.64 % and 23.14±0.63 % respectively. In other methods (SE and KM) the drug release found to be 32.63±0.64 %, 48.26±0.44 % and 42.17±0.84%, 56.46±0.36 % within 10 and 20 minutes.

Kneading method (KM) containing 1:3 molar ratios of drug and CCS showed highest dissolution rate, about 93.18±0.53 % drug release was observed within 90 min. In other methods Physical mixture and Solvent evaporation (PM and SE) showed dissolution rate, about 45.26±0.24% and 85.73±0.43% drug release were observed within 90 min, respectively. The dissolution data given in **Tables: 3, 4, 5 to 6** and **Figure: 3 (a)-(c)** and **4 (a) to 6 (c)** respectively.

1:5 ratio

In Physical mixture dissolution study of OXC with CCS data showed that 41.72±0.24 % of drug was released within 40 minutes. In solvent evaporation and kneading methods were found to be 81.54±0.42 % and 85.47±0.62 % drug released within 40 min. For initial periods of time for 10 and 20 minutes, the drug release in 1:1 ratios of physical mixture was found to be 22.26±1.25 % and 26.35±1.24 % respectively. In other methods (SE III and KM III) the drug release found to be 38.56±0.52 %, 63.18±0.66 % and 44.42±0.69 %, 60.19±0.55 % within 10 and 20 minutes.

Kneading method (KM III) containing 1:5 molar ratios of drug and CCS showed the highest dissolution rate, about 99.98±0.32% drug release was observed within 90 min. In other methods Physical mixture and Solvent evaporation (PM III and SE III) showed dissolution rate, about 51.08±0.36% and 91.34±0.91% drug release were observed within 90 min, respectively. The dissolution data given in **Tables: 3, 4, 5 to 6** and **Figure: 3 (a)-(c)** and **4 (a) to 6 (c)** respectively.

CONCLUSION

This study was undertaken with an aim to formulate an Oxcarbazepine drug in the form solid dispersion to overcome the poor solubility drawback of the drug. The drug Oxcarbazepine is having poor solubility in the water, under class 2 of BCS of classification of drug its solubility was tried to increase by formulating in the form of solid dispersion with polymer by using various techniques. Solid dispersions were prepared by using the Crosscarmelose sodium as a disintegrant in 1:1, 1:3 and 1:5 ratio of different techniques.

Among the three different techniques used for preparation of solid dispersions Kneading method (KM) technique has shown the increase in dissolution rate that is the KM (III) was found to have a faster solubility and dissolution property which was prepared by using Croscarmellose sodium as a disintegrant in the ratio of 1:5. Hence finally it was concluded that KM (III) as an optimized formula with an increased rate of dissolution rate and solubility. KM (III) which is prepared by using drug and disintegrant ratio of 1:5 ratio by using Kneading method (KM).

REFERENCES

1. Amidon GL, Lennernas H, Shah VP, Crison JR. Theoretical basis for a biopharmaceutical drug classification: the correlation of in vitro drug product dissolution and in vivo bioavailability, Pharm Res., 1995; 12(3): 413-420.
2. Breitenbach J. Melt extrusion from process to drug delivery system. Pharm Res., 2002; 12: 1269-1292.
3. Sekiguchi K, Obi N; Studies on absorption of eutectic mixtures. I.A. comparison of the behaviour of eutectic mixtures of sulphathiazole and that of ordinary sulphathiazole in man, Chem. Pharm. Bull., 1961; 9: 866-872.
4. Buck ton G, Darcy P. The use of gravimetric studies to asserts the degree of crystalanity of predominantly crystalline powder. Int J Pharm., 1995; 123: 265-271.
5. Ghaderi R, Artursson P, Carifors J. Preparation of biodegradable micro particles using solution enhanced dispersion by supercritical fluids (SEDS). Pharm Res., 1999; 16: 676-681.
6. Karavas E, Ktistis G, Xenakis A, Georgarakis E. Effect of hydrogen bonding interactions on the release mechanism of felodipine from nanodispersions with polyvinylpyrrolidone, Eur J Pharm Biopharm., 2006; 63: 103-114.
7. Luenberger H. Spray freezed drying the process of choice for low water soluble drugs, J nano partical research., 2004: 111-119.
8. Patil et al. Improvement in dissolution efficiency of poorly soluble naproxen. The Eastern pharmacist., 2001; 521: 107-110.
9. Franco M, Trapani G, Latrofa A et al. Dissolution properties and anticonvulsant activity of Phenytoin-PEG 6000 and PVPK30 Solid Dispersion. Int J Pharm., 2001; 225: 63-73.