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Original Research Article

Formulation and Characterization of Solid Dispersion of Oxcarbazepine

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Abstract: The purpose of the current study was to use the solid dispersion approach to improve the solubility of the medication oxcarbazepine, which is only moderately water soluble. The antiepileptic medication oxcarbazepine is used to treat seizures. Due to its high permeability and low water solubility, it falls under BCS class II. To prevent issues of this nature, it was imperative to increase the solubility of oxcarbazepine in accordance with British Pharmacopoeia (BP) solubility criteria since pure oxcarbazepine falls under the category of being only very slightly soluble. Solid dispersion technique has been used to try and increase the solubility of pure oxcarbazepine. Oxcarbazepine is also extensively metabolized by the liver. Attempt has been made to formulate solid dispersions containing oxcarbazepine to improve its solubility and dissolution rate to avoid first pass metabolism; to avoid difficulty.

Keywords: Oxcarbazepine, Solid dispersion, FT-IR & characterization.

INTRODUCTION

Solid dispersion (SD) simply means "drug dispersed in a solid matrix". It is one of the most successful and promising strategies that aim to enhance the solubility thereby increasing the oral B.A of poorly water soluble NCE. SD is simply defined as "molecular mixture of poorly water-soluble drugs in hydrophilic carriers, which present a drug release profile that is driven by polymer properties". Alternatively, "the dispersion of one or more active ingredients in an inert excipient or a matrix where by active ingredient could exist in finely crystalline, amorphous or solubilized state", also referred as SD [1]. Solid dispersion is an easier and more applicable approach as compared to chemical approach for improving the solubility of poorly water -soluble drugs [2].

Classification of Solid Dispersions

Solid dispersions can be classified as follows [3]:

1. Simple eutectic mixture,
2. Solid solution,
3. Glass solution or suspension,
4. Compound or complex formation,
5. Amorphous precipitation,
6. Combination of any of the above.

Solid solutions can be further divided based on whether the formulation is a continuous or a discontinuous solid solution. Additional they can be divided based on whether the formulation is a substitutional crystalline, interstitial crystalline or amorphous solid solution.

Advantage	Disadvantage
❖ Solid dispersion results in particles with reduced particle size and thus the surface area are improved and increased dissolution rate is attained. Hence bioavailability is increased [4]. The carrier used in the solid dispersion plays a major role in improving the wettability of the particles. Improved wettability results in increased solubility thus improving the bioavailability[5] ❖ In solid dispersion drugs are presented as supersaturated solutions which are considered to be metastable polymorphic form. Thus presenting the drug in amorphous form and increases the solubility of the particles [6].	❖ Major disadvantage is their instability. They show changes in crystallinity and a decrease in dissolution rate with ageing. Temperature and moisture have more deteriorating effect on solid dispersions than on physical mixtures. Difficulty in handling because of tackiness [7].

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Oxcarbazepine has been chosen as model active pharmaceutical ingredients in the present investigation for enhancement of solubility and dissolution rate. The major objectives of the present investigation are as follows;

- To find out the effect of hydrophilic polymers on enhancement solubility of pure drug.
- To formulate and evaluate solid dispersions by fusion method so as to improve the solubility and dissolution rate of oxcarbazepine.

MATERIAL AND METHOD

Table 1: List of materials used

Sr. No.	Category	Materials	Suppliers
1.	Drug	oxcarbazepine	Psycho remedies limited., ludhiana
2.	Carrier	Polyethene glycol 6000	Loba chemie Pvt. Ltd., Mumbai
3.	Complexing agent	cyclodextrin	Loba chemie Pvt. Ltd., Mumbai
4.	Disintegrants	Lepidium sativum	Kurukshetra

Compatibility Study of Drug with Carriers

Fourier Transform Infrared Spectroscopy

Extent of interactions between drug and matrix can be measured.

Preparation of Solid Dispersions of Oxcarbazepine by Fusion Method

Solid dispersions of oxcarbazepine in different ratio of drug and carriers were prepared using fusion method. Carrier's was fused and then drug was mixed with continuous starring. It was permitted to evaporate at room temperature for 48 hours. The process was used until the constant weight was attained. Prepared solid dispersion was crushed, pulverized and sifted through mesh number 50 and stored in desiccators [8].

Formulation of Oxcarbazepine Solid Dispersions

Solid dispersions batch were prepared in different drug to carrier ratios.

Table 2: Composition of solid dispersion of oxcarbazepine by fusion method

S. No.	Type of preparation	Drug carrier ratio	Method of preparation of solid dispersion	Drug (mg)	PEG 6000	Beta cyclodextrin	Lepidium sativum
1.	SD1	1:2:1:4	Fusion	500	1gm	500mg	2000mg
2.	SD2	1:2:4:1	Fusion	500	1gm	2gm	500mg
3.	SD3	1:4:1:2	Fusion	500	2gm	500mg	1000mg
4.	SD4	1:4:2;1	Fusion	500	2gm	1gm	500mg
5.	SD5	1:2:2:1	Fusion	500	1gm	1gm	500mg

Evaluation Parameters of Oxcarbazepine Solid Dispersions

Percentage (%) Practical Yield

It is useful to determine the efficiency of a preparation method. The practical yield is calculated by using following equation [9].

Practical yield (%) = (prepared solid dispersions) Weight /Theoretical weight Drug+ carrier] × 100

Estimation of Drug Content

Dissolve solid dispersions (equivalent to 100 mg of drug) in 100 ml of ethanol. The solution was filtered, diluted suitably and analysed at 373 nm by UV spectrophotometer. Percentage of drug content is calculated by following formula:

Percent drug content = (oxcarbazepine amount in weighed quantity of solid dispersions x 100)/ Theoretical amount of drug in solid dispersion.

Micromeritic Study (Physical Characterization of Oxcarbazepine Solid Dispersions)

- Bulk density,
- Tapped density,
- Angle of repose,
- Determination of Carr's index,
- Hausner's ratio.

Characterization of Solid Dispersions of Oxcarbazepine

The prepared solid dispersion was evaluated for practical percentage yield, micrometer properties, particle size analysis, saturation solubility analysis, XRD, SEM and determination of drug content [10].

RESULT AND DISCUSSION

The IR spectrum of Oxcarbazepine showed peaks at 3467 and 3340 cm−1 (corresponding to free anti-NH and hydrogen bonded syn-NH respectively), 1682 cm−1 (-C= O, ketone group vibration), 1651 cm−1 (-C=O, carboxamide group vibration), 1591 and 1562 cm−1 (range of –C=C vibration and-NH deformation) and 1407cm−1 (C−N stretch) These IR bands were matched with mentioned in literature and there for the drug is considered to be pure along with carriers PEG 6000 and beta cyclodextrin. Solid dispersion chromatograph of optimized batch (SD4)

shows slight shifting of the peak from the physical mixture of the drug. The result was tabulated in the table 3-6 and fig.1-5. Powder X-ray diffraction XRD was used to investigate the state of the drugs in the solid dispersions produced. Pure forms of the drugs and solid dispersions at 1:4 ratios were also investigated using XRD. The powder XRD patterns of OXC and their solid dispersions are shown in Figure 6-11. The diffraction spectra of the drug show numerous distinct lines of high intensity, indicating that they are in a highly crystalline state. The powder XRD patterns of the solid dispersions were completely different from those of pure drugs and showed no characteristic peaks. This demonstrates that the drugs were changed into an amorphous state in the solid dispersions. The loss of drug diffraction peaks in all drug–polymer solid dispersions indicated a change in their crystal form during the process. The percentage drug content of prepared solid dispersions was found to between 81.76% to 85.12 %. Saturated solubility studies excessive quantity of oxcarbazepine (10 mg) and solid dispersions equivalent to 10 mg was added to 10 mg of ethanol and phosphate buffer (pH 6. 8) and kept in a conical flask. These samples were maintained in a thermostatically controlled rotary mechanical shaker at 37°c for 48 h. Then the samples were kept for 24 h at room temperature to obtain equilibrium. Finally the samples were filtered and filtrates were diluted and scanned spectrophotometrically for drug content at 372 nm. Percentage practical yield of all the batches of solid dispersion was in the range of 81.76% to 85.12%. The photomicrographic of SEM studies shown in fig.12-19. The micrometric parameter of formulated preparation SD1-SD5 was tabulated in table 7.The % yield of various formulated SD was tabulated in table 8 & fig 20.

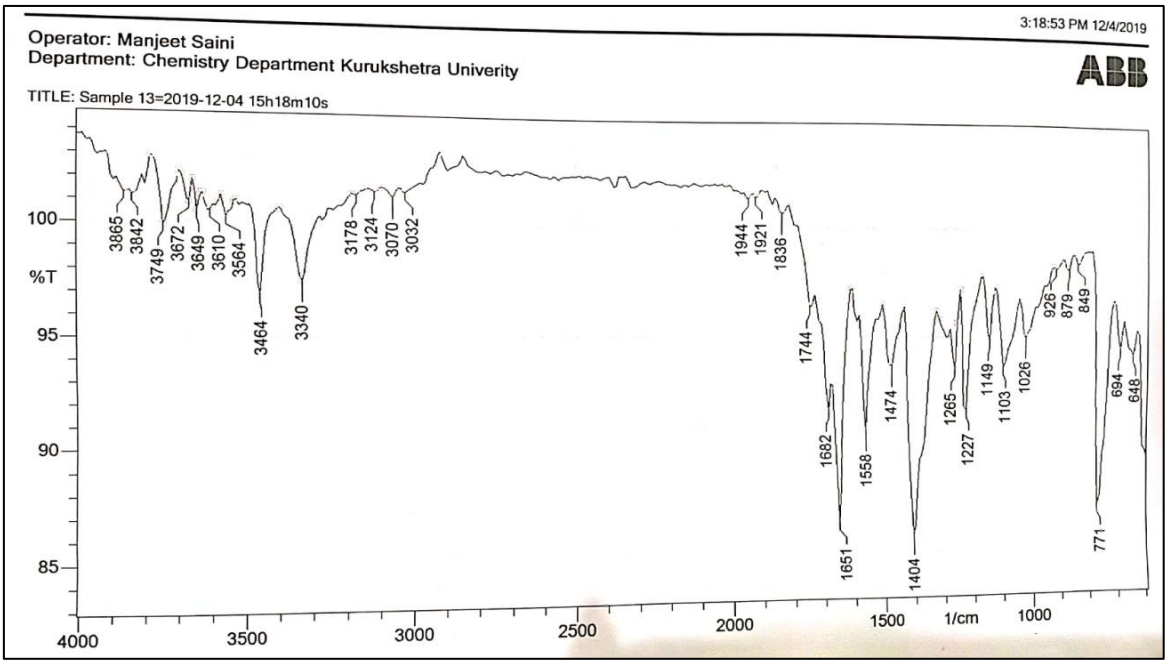

Figure 1: FTIR of oxcarbazepine

Table 3: Oxcarbazepine

Oxcarbazepine		
Sr. No.	**Peaks**	**Functional group**
1.	3467	NH and hydrogen bond
2.	3340	NH
3.	1685	C=O
4.	1407	C-N
5.	1558	(-C=C),NH deformation

Table 4: PEG6000

PEG 6000		
1.	1705	C=O
2.	1651	C=C
3.	2885	C–H
4.	3502	N–H

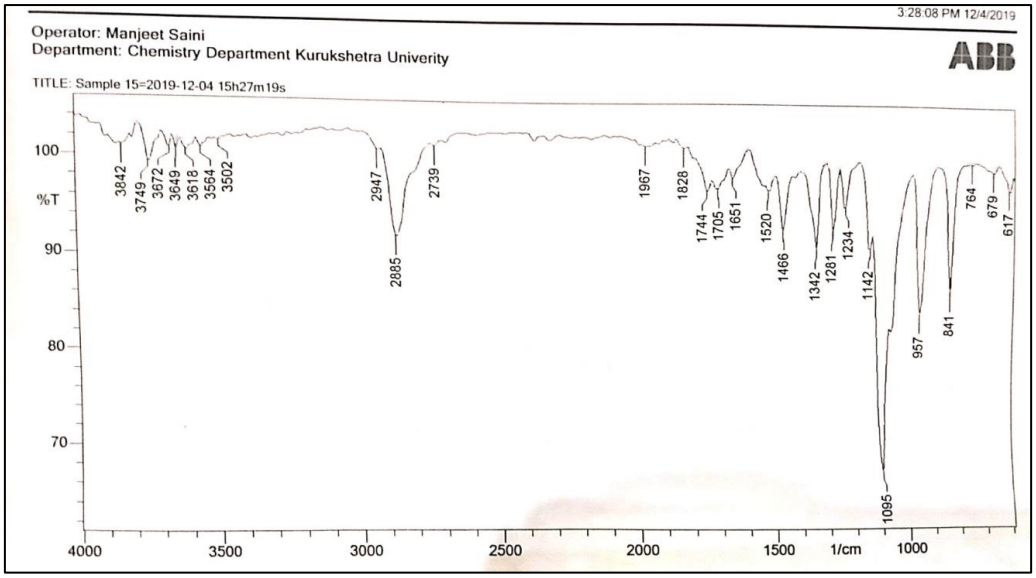

Figure 2: FTIR of PEG6000

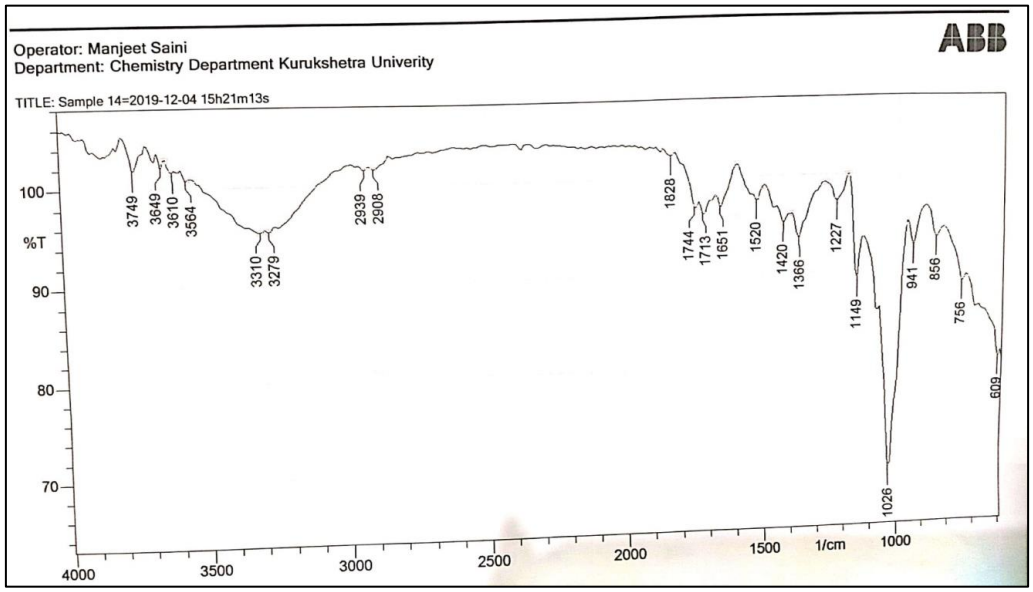

Figure 3: FTIR of beta cyclodextrin

Table 5: Beta-cyclodextrin

Beta cyclodextrin		
1.	2947	C-H
2.	1651	COOH
3.	1520	C=C
4.	1342	C=O

Table 6: Physical mixture

Physical mixture		
1.	3340	NH
2.	3467	NH AND HYDOGEN BOND
3.	1651	C=O
4.	1404	C-N
5.	1543	(-C=C)
6.	1705	C=O
7.	2885	C-H
8.	1520	C=C

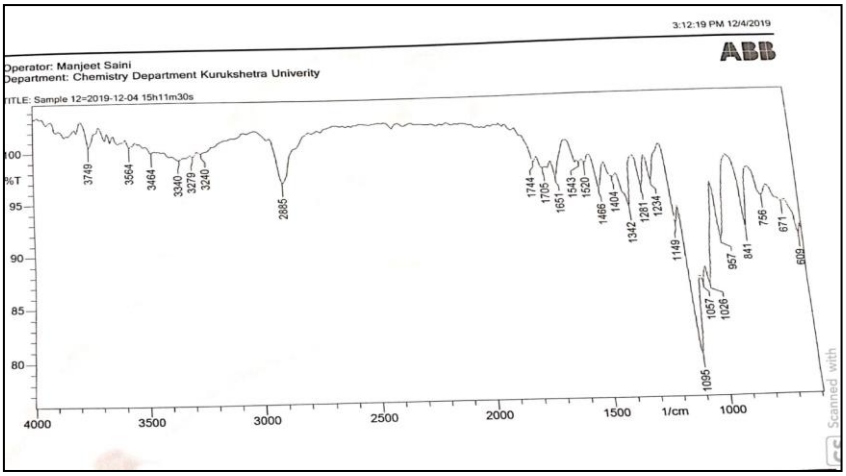

Figure 4: FTIR of Physical mixture

Solid dispersion chromatograph of optimized batch (SD4)

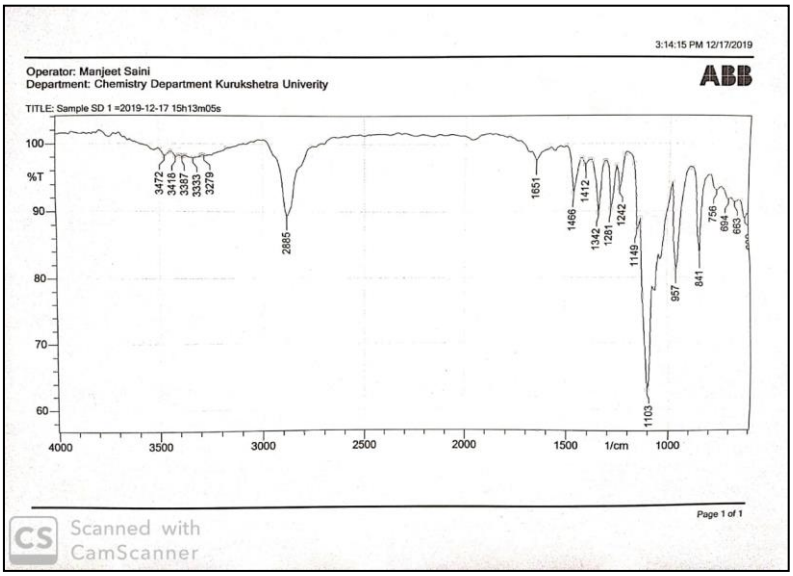

Figure 5: FTIR of (E) Solid dispersion

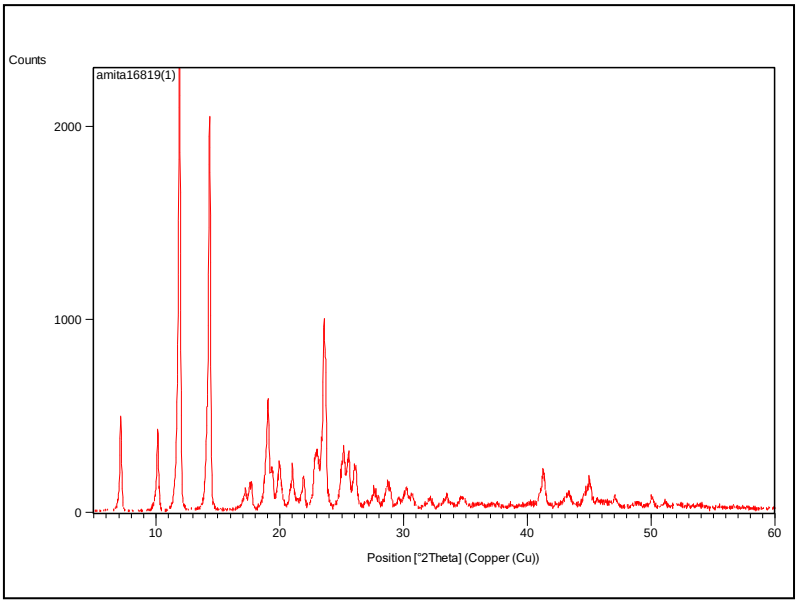

Figure 6: X-Ray difractogram (oxcarbazepine)

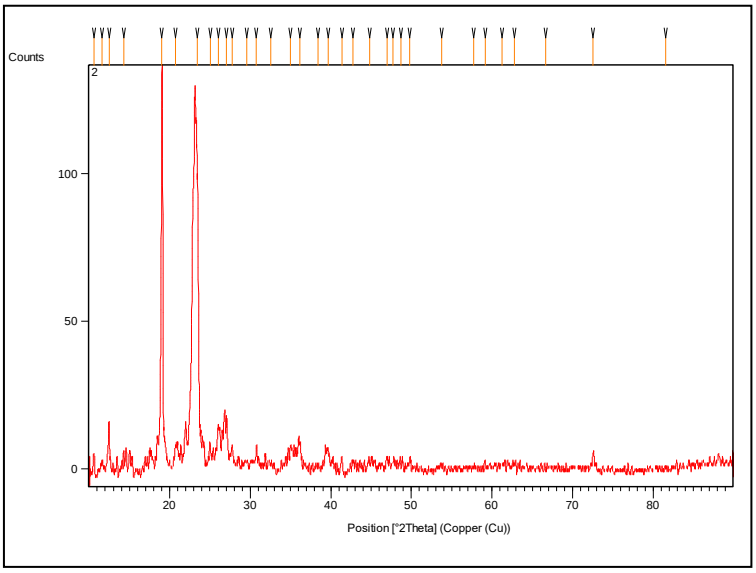

Figure 7: X-ray diffractogram (physical mixture)

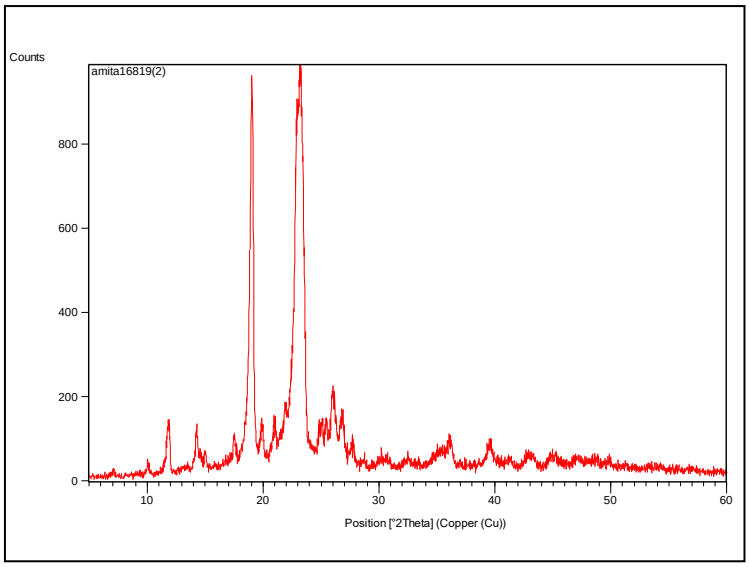

Figure 8: X-ray diffractogram (SD1)

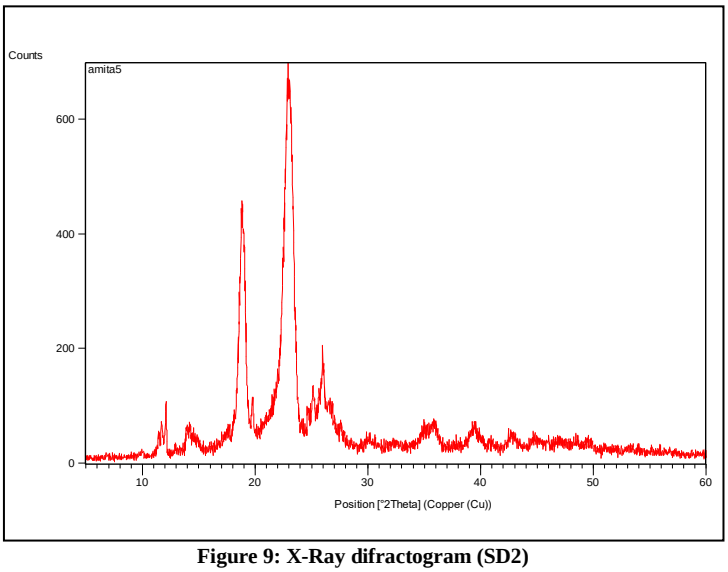

Figure 9: X-Ray difractogram (SD2)

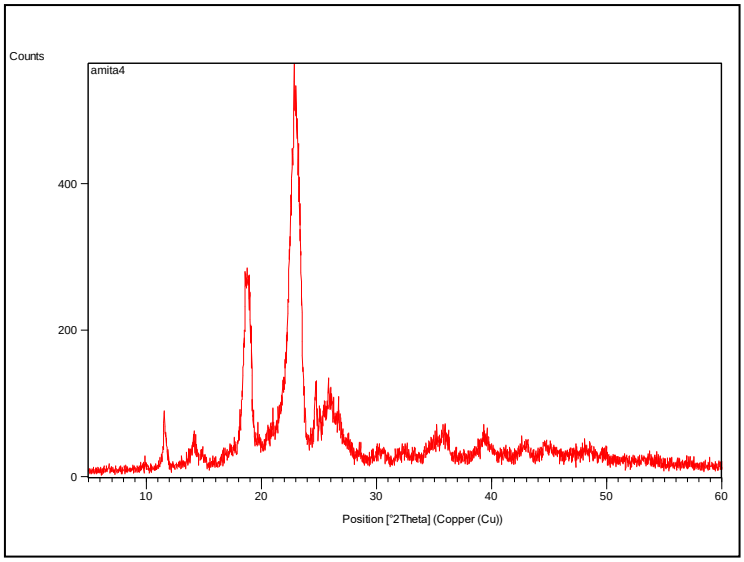

Figure 10: X-Ray difractogram (SD3)

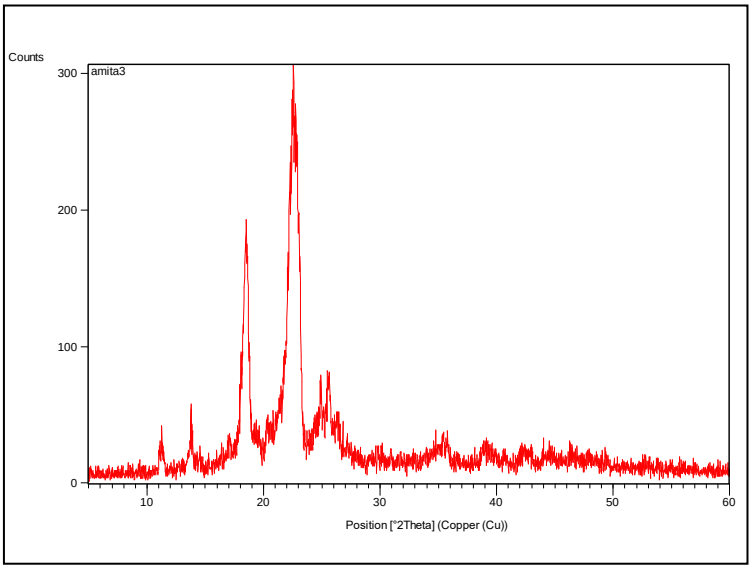

Figure 11: X-Ray difractogram (SD4)

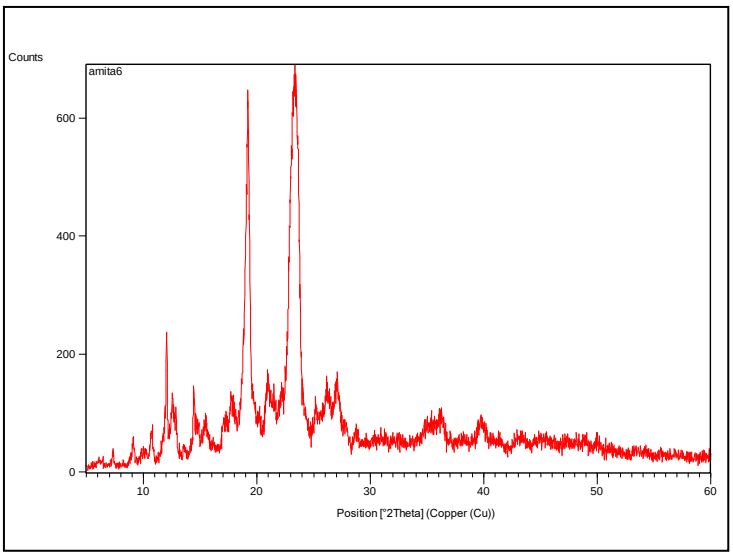

Figure 12: X-Ray difractogram (SD5)

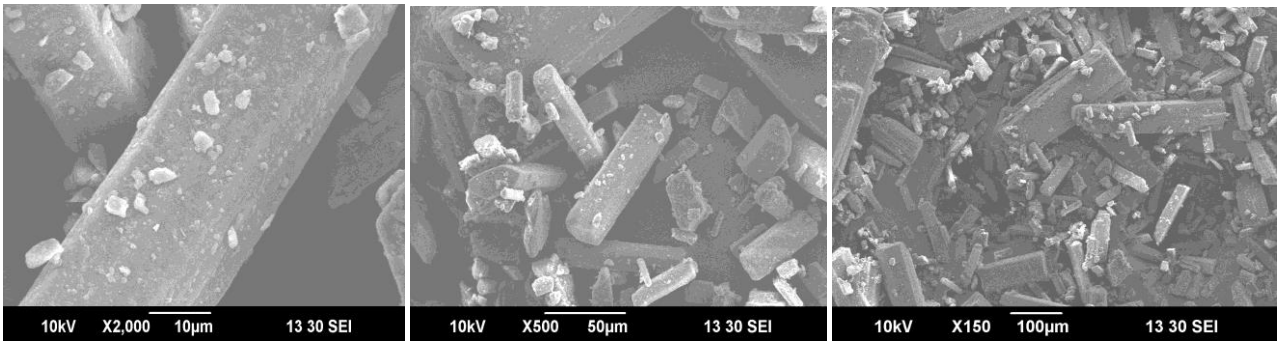

Figure 12: Photomicrograph of drug oxcarbazepine at different magnifications

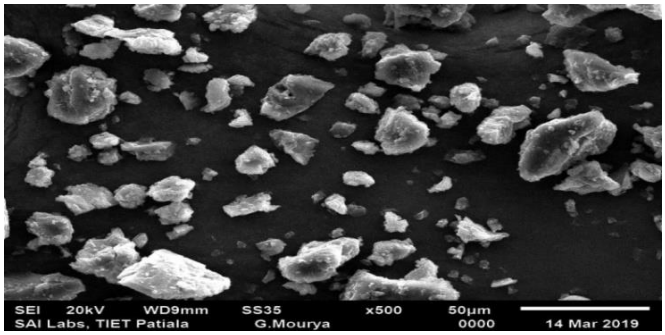

Figure 13: Photomicrograph of PEG 6000

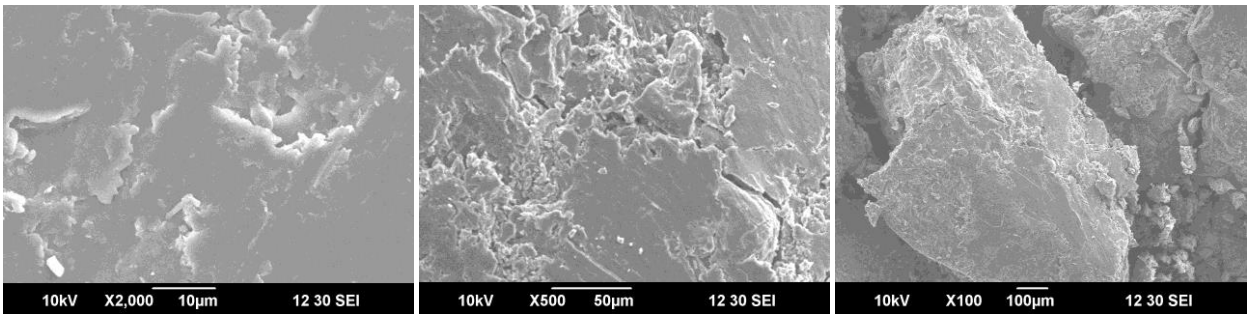

Figure 14: Photomicrograph of Solid dispersion (SD1) at different magnifications

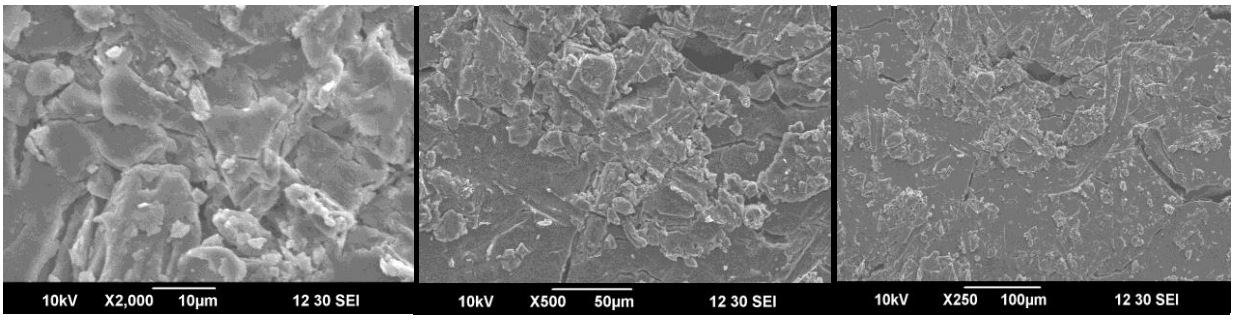

Figure 15: Photomicrograph of solid dispersion (SD2) at different magnifications

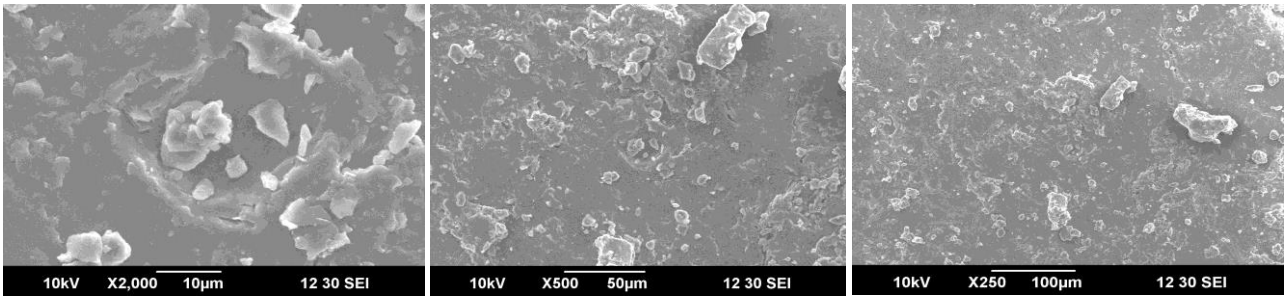

Figure 16: Photomicrograph (SD2)

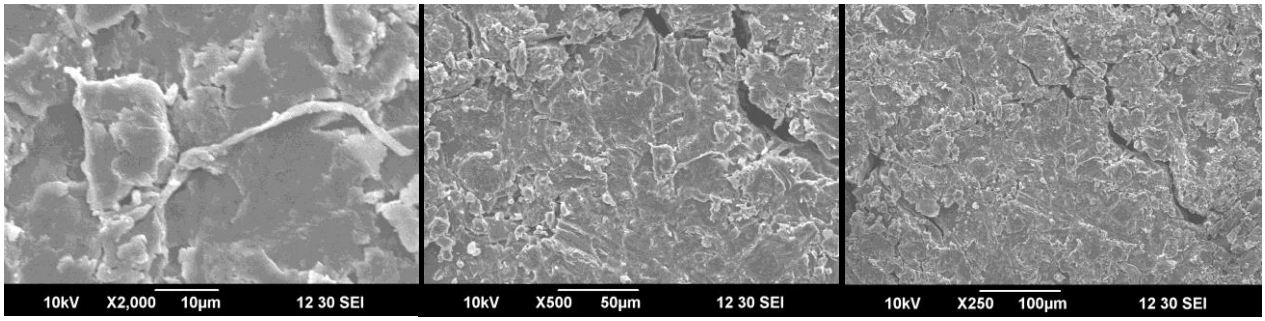

Figure 17: Photomicrograph (SD3)

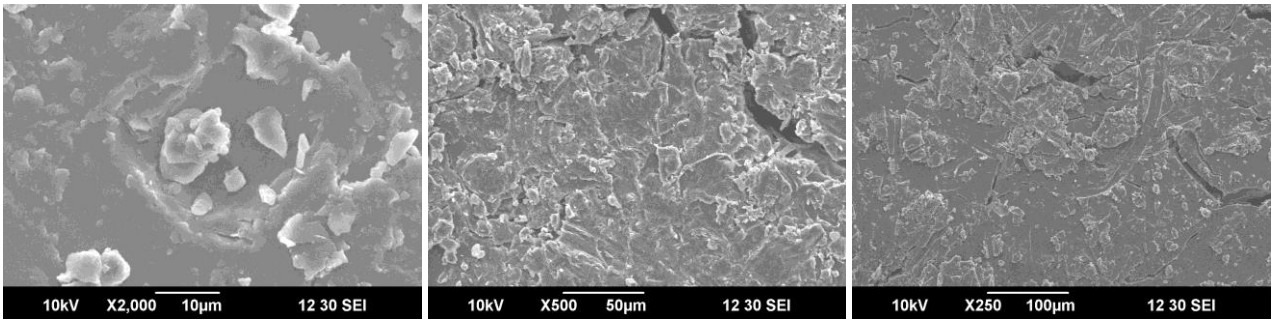

Figure 18: Photomicrograph (SD4)

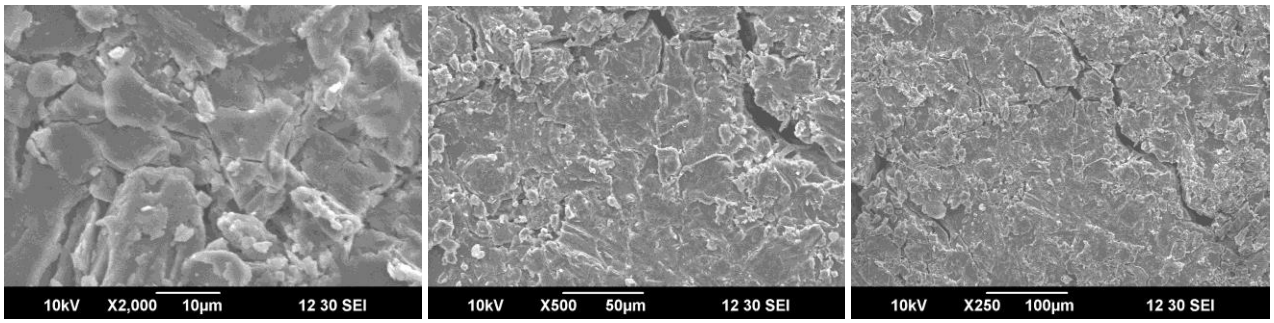

Figure 19: Photomicrograph (SD5)

Table 7: Micromeritic parameters

Sr. No.	Batch code	Bulk density (g/cm^3)	Tapped density (g/cm^3)	Hauser's ratio	Compressibility (%)	Angle of repose (^{O})
1.	SD1	0.5033	0.7473	1.2042	22.32	31.26
2.	SD2	0.5142	0.7685	1.2397	23.95	30.74
3.	SD3	0.5345	0.7919	1.3263	25.72	29.11
4.	SD4	0.5193	0.7500	1.2401	21.36	28.42
5.	SD5	0.5219	0.7793	1.1690	21.45	26.56

Table 8: Percentage practical yield of solid dispersions formulation

Sr. No.	Batch code	Percentage practical yield
1.	SD1	81.76
2.	SD2	82.14
3.	SD3	85.12
4.	SD4	82.12
5.	SD5	83.14

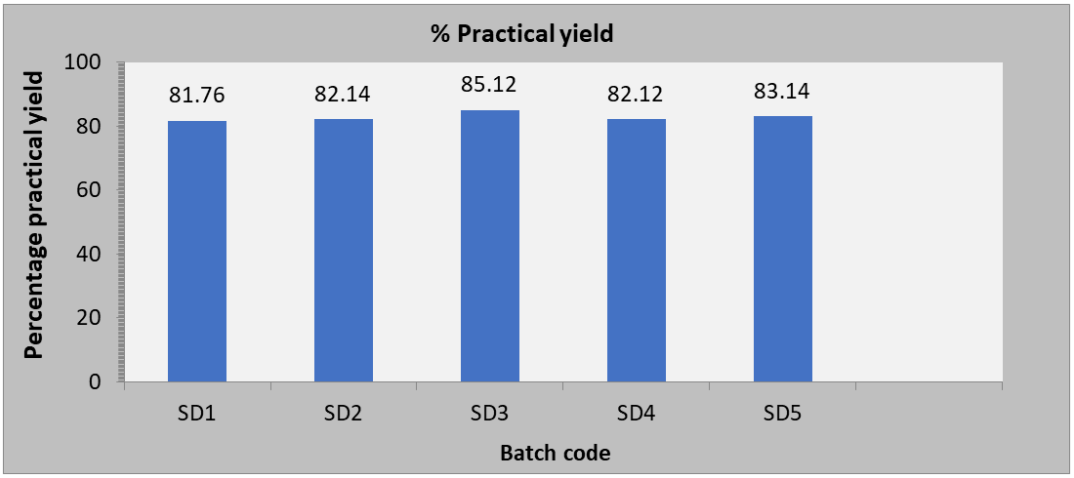

Figure 20: Percentage practical yield of solid dispersions formulation

CONCLUSION

Poor water solubility of oxcarbazepine restrains the absorption and bioavailability of the drug. Present work was aimed to resolve the problems associated with the poor bioavailability of oxcarbazepine by preparing its solid dispersions using PEG 6000, lapidium sativum and beta cyclodextrine as suitable carriers. Oxcarbazepine is an anticonvulsant it works by decreasing nerve impulses that cause seizures and pain first made in 1966. However, therapeutic utilization is limited owing to their low solubility, lack of standardization and poor apparent quality. Solid dispersions technology has attracted considerable interest as a means of enhancing the solubility and dissolution rate oxcarbazepine. In the present work, solid dispersions technique was used to enhance the solubility profile of oxcarbazepine using PEG 6000, beta cyclodextrin, lapidium sativum as carriers. All formulations were found to be fine and free flowing. Prepared solid dispersions depicted enhanced dissolution rate as compared to pure drug. Oxcarbazepine solid dispersions were developed using fusion method and investigated for various parameters like FTIR, SEM, XRD & drug content.

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