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Research Article

FORMULATION AND EVALUATION OF MOUTH DISSOLVING TABLETS OF OXCARBAZEPINE

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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. In this study, the mouth dissolving tablets were prepared using two different technologies, direct compression method and solid dispersion technology. Tablets produced by direct compression method contain crospovidone as a superdisintegrant and aspartame as a sweetener. Solid dispersions of oxcarbazepine with polyvinylpyrrolidone K-30 and polyethylene glycol 6000 in different weight ratios were prepared with a view to increase its water solubility. Oxcarbazepine solid dispersions with polyvinylpyrrolidone K-30 in 1:2 ratios of drug: carrier showed maximum drug release and hence, compressed along with other excipients into mouth dissolving tablet. The results compared for both the technologies showed that the oxcarbazepine tablets prepared using solid dispersion technology was found to have good technological properties and satisfying and reproducible drug dissolution profiles. Moreover the drug release was found to be comparable to the marketed dispersible tablet.

Keywords: Oxcarbazepine; Mouth dissolving tablets; PVP K30; PEG 6000; Solid dispersions; FT-IR; Dissolution rate.

INTRODUCTION

Many pharmaceutical dosages are administered in the form of pills, granules, powders, and liquids. Generally, a pill is designed for swallowing intact or chewing to deliver a precise dosage of medication to patients. The pills, which include tablets and capsules, are able to retain their shapes under moderate pressure. However, some patients, particularly pediatric and geriatric patients, have difficulty in swallowing or chewing solid dosage forms. Many pediatric and geriatric patients are unwilling to take these solid preparations due to a fear of choking. In order to assist these patients, several mouth-dissolving drug delivery systems have been developed. Mouth dissolving tablets can be prepared by various conventional methods like direct compression, wet granulation, moulding, spray drying, freeze drying and sublimation. MDTs disintegrate and/or dissolve rapidly in the saliva without the need for water, releasing the drug. Some drugs are absorbed from the mouth, pharynx and esophagus as the saliva passes down into the stomach. In such cases, bioavailability of drug is significantly greater than those observed from conventional tablet dosage form[1, 2].

Oxcarbazepine (10,11-dihydro-10-oxo-5H-dibenz[b,f]azepine-5-carboxamide) is a 10-keto analogue of carbamazepine with anticonvulsant activity [4]. Oxcarbazepine (as both monotherapy and adjunctive therapy) has shown efficacy in the treatment of partial onset seizures in children with epilepsy[3]. The drug having half-life of 2 h is completely absorbed and extensively metabolized to its

pharmacologically active 10-monohydroxy metabolite, which has a half-life of 9 h. Its pharmacological activity is primarily exerted through 10-monohydroxy metabolite[4]. Its insolubility in water and bland taste makes it an ideal candidate for fast disintegrating tablets with regards to palatability. Since epileptic patients have to strictly follow dosage regimen for preventing sub therapeutic concentration, MDT will avoid missing out of dose even during traveling or other situations where there is no access to water. The present investigation deals with the development of an effective and stable MDT of oxcarbazepine having adequate hardness, low disintegration time and pleasant taste.

MATERIALS AND METHODS

Oxcarbazepine was obtained as a gift sample from Psycho Remedies, Ludhiana. PVP K-30, PEG 6000 and other ingredients were obtained as a gift sample from Kwality Pharmaceuticals, Amritsar. Crospovidone CL (Kollidon) was purchased from BASF South East Asia Pvt. Ltd. All the other raw materials were of pharmacopoeial grade.

Pre-formulation study

Standardization of the drug was carried out using phosphate buffer pH 6.8 by UV spectrophotometer (UV-160A, SHIMADZU). Solubility analysis of drug in various solvents including water, phosphate buffer pH 6.8, and organic solvents like ethanol, methanol, chloroform and acetone was carried out.

Preparation of MDTs by direct compression method

Selection of excipients and optimization of their concentration:

Mouth dissolving tablets of oxcarbazepine were prepared firstly using different excipients (diluents and superdisintegrants) and then evaluated for various parameters like wetting time, friability, hardness, disintegration time and dissolution profile to select the best combination for preparation of oxcarbazepine mouth dissolving tablet. The combination with lowest disintegration time, optimum wetting time and hardness was selected for further study. Table 1 shows the composition of different trials, which were undertaken for formulating MDTs.

Table 1: Formula of different trials for the selection of excipients (data in mg).

Ingredients	A1	A2	A3	A4	B1	B2	B3	B4	C1	C2	C3	C4
Oxcarbazepine	100	100	100	100	100	100	100	100	100	100	100	100
Dicalcium Phosphate	164	179	164	179	-	-	-	-	-	-	-	-
Mannitol	-	-	-	-	164	179	164	179	-	-	-	-
Microcrystalline cellulose	-	-	-	-	-	-	-	-	164	179	164	179
Crospovidone	-	30	15	-	-	30	15	-	-	30	15	-
Croscarmellose sodium	-	-	30	15	-	-	30	15	-	-	30	15
Magnesium stearate	3	3	3	3	3	3	3	3	3	3	3	3
Aspartame	3	3	3	3	3	3	3	3	3	3	3	3

The excipients selected in the above trials were sieved through sieve no.40 and then mixed properly in mentioned proportions (Table 1) using pestle mortar or spatula. The formulae mixtures were then compressed and formulated into mouth dissolving tablets using single punch tablet machine[5]. The tablet weight was adjusted to300mg and then evaluated for various parameters.

Preparation of solid dispersions and physical mixture

Solid dispersions of oxcarbazepine were prepared by solvent evaporation method using polyvinylpyrrolidone K30 (PVP K30) and polyethylene glycol 6000 (PEG 6000) as polymers in the different weight ratios of 1:1, 1:2 and 1:3 of drug: carrier polymers. Accurately weighed quantities of polymers (PVP K30 and PEG 6000) were added to the solutions of oxcarbazepine in acetone. The solutions were stirred at room temperature and the solvents were allowed to evaporate. Solid dispersions thus formed, were then dried in vacuum oven for 24 hours at room temperature, pulverized and sieved. After the preparation of solid dispersions, the powdered samples were stored in a closed container away from light and humidity until use[6]. Physical mixtures were prepared by mixing the appropriate amounts of oxcarbazepine and polymers (PVP K30 and PEG 6000) in mortar. The resulting mixtures were sieved, collected and stored in closed container away from light and humidity until use.

Phase solubility studies

Solubility studies were performed according to the method described by Higuchi and Connors[7]. An excess amount of oxcarbazepine was placed into 25ml glass flasks containing different concentrations of PVP K30 and PEG 6000 viz 2%,4%,6%,8%). Different concentrations include 2%, 4%, 6% and 8%. All flasks were closed with stopper and covered with cellophane membrane to avoid solvent loss. The content of the flasks were equilibrated by shaking for 72 hours in a thermostatically controlled water bath at 25°C[8]. After attainment of equilibrium the content of each flask was then filtered. The filtrate was then assayed spectrophotometrically for oxcarbazepine content at 306nm using UV spectrophotometer (UV-160A, SHIMADZU).

Dissolution studies of solid dispersions

Dissolution tests were performed in triplicate with USP Dissolution test apparatus II (LABINDIA DISSO 2000, Digital tablet dissolution test apparatus) in phosphate buffer (pH 6.8) at 37°C using paddle method at 50 rpm. Powdered samples of pure oxcarbazepine and solid dispersion preparations equivalent to 100 mg of oxcarbazepine were added to dissolution media. At appropriate time intervals of 10, 20, 30, 45 and 60 min., 10 ml of samples were withdrawn and filtered. The initial volume was maintained adding 10 ml of fresh dissolution medium. The removed samples were assayed for oxcarbazepine content by spectrophotometry at 306nm and the percent of drug dissolved was calculated[9].

Fourier transform infrared spectroscopy (FTIR)

The FTIR spectra were obtained using KBr on a Shimadzu 8400 FTIR spectrometer (8400 series, Shimadzu) [10]. The scanning range was 400-4000 cm^{-1} and the resolution was 1 cm^{-1}.

Differential scanning calorimetry

The DSC thermograms of samples (pure drug, PVP K30 and solid dispersions of oxcarbazepine and PVP K30) were recorded on a DSC (METTLER TOLEDO STAR^e System). The samples were heated in hermetically sealed aluminium pans over a

temperature range of 25°C to 350°C at a constant rate of 10°C/min under nitrogen purge (20 ml / min) [11].

Formulation and preparation of tablets of oxcarbazepine – PVP K-30 solid dispersions

Tablet formulation was developed from oxcarbazepine PVP K-30 solid dispersion that has shown maximum in vitro dissolution, using mannitol (13%), crospovidone (kollidon CL) as superdisintegrant (10%), magnesium stearate as glidant-lubricant (1%) and aspartame as sweetener (1%). For the preparation of tablets, powdered oxcarbazepine solid dispersions, containing amount equivalent to 100 mg oxcarbazepine, were mixed with other excipients and compressed on a single punch tablet machine. The average weight of the tablet was adjusted to 400mg.

Evaluation of tablets

Tablets were evaluated for various parameters such as hardness, friability, weight variation, wetting time[12, 13], water absorption ratio, disintegration time and *in vitro* drug release[14, 15]. Hardness was measured by monsanto hardness tester. Disintegration test was performed on six tablets using disintegration test apparatus II using distilled water as a disintegrating media at 25°C± 2°C. Friability was determined in Roche friabilator, by taking ten tablets. Drug release was carried out using USP Type II apparatus in phosphate buffer pH 6.8.The release was tested at rotational speed of 50 rpm. Samples were withdrawn at various intervals within a period of 60 min and analyzed using UV/Vis. spectrophotometer at wavelength of 306 nm. The drug release of the tablets was also compared with that of the marketed dispersible tablet of oxcarbazepine. Students t test was applied to the method with n=6**.**

RESULT AND DISCUSSION

The results of preformulation studies indicated that the drug was of acceptable standards with 99.8% purity. Drug was found to be insoluble in water, slightly soluble in buffers and in organic solvents viz. ethanol, methanol and chloroform and acetone.

For the preparation of mouth dissolving tablets of oxcarbazepine, various excipients were screened for the best formulation and their concentrations were optimized there after. Batches A1-A4, B1-B4, C1-C4 were prepared to select the diluents and the superdisintegrants and their concentration to be used for the preparation of tablets. Table 2 shows that the tablets containing mannitol as a diluent i.e. batches B1-B4 exhibit quick disintegration time and wetting time along with optimum hardness and lower friability in comparison to the batches containing dicalcium phosphate i.e. batches A1-A4 and microcrystalline cellulose as diluent i.e. batches C1-C4. The probable reason of better results with batches containing mannitol as a diluent might be due to its water soluble nature and presence of large granular particles as suggested by Debord et al[16]. Mannitol is shown to disintegrate instantaneously when comes in contact with saliva as compared to microcrystalline cellulose which is water insoluble and has high compression and binding properties and dicalcium phosphate which is an inorganic diluent[17]. Hence, further investigations were carried out using mannitol as diluent. Among the batches containing mannitol (B1 – B4), batches B1 and B2 i.e. having crospovidone exhibited lowest disintegration and wetting time as compared to batches B3 and B4 (containing croscarmellose sodium). It might be due to low water uptake and more gelling tendency of croscarmellose sodium than crospovidone[18], which is shown to have low

swelling efficiency, high water uptake capacity and spongy nature, which yield porous tablets that disintegrate in matter or fractions of second. Batches B1 and B2 were prepared to optimize the amount of crospovidone and mannitol.

Table 2: Evaluation parameters of prepared tablets

Batch No	Disintegration time (sec)	Wetting time (sec)	Hardness (kg/cm^2)	Friability (% w/w)
A1	59.6 ± 3.51	55.6 ± 1.52	3.4 ± 0.34	0.76 ± 0.02
A2	63.0 ± 1.0	60.6 ± 1.52	3.7 ± 0.11	0.72 ± 0.02
A3	75.0 ± 3.0	72.0 ± 2.0	2.0 ± 0.2	>1%
A4	75.3 ± 3.21	72.6 ± 2.51	2.1 ± 0.49	>1%
B1	30.6 ± 2.08	27.0 ± 3.60	3.6 ± 0.30	0.92 ± 0.02
B2	39.6 ± 1.52	33.3 ± 1.52	3.0 ± 0.20	0.82 ± 0.02
B3	43.6 ± 2.62	40.6 ± 4.50	3.6 ± 0.11	0.86 ± 0.03
B4	53.6 ± 4.72	50.2 ± 1.52	2.4 ± 0.2	>1%
C1	55.6 ± 2.08	54.3 ± 2.51	2.0 ± 0.30	>1%
C2	55.0 ± 3.60	52.0 ± 3.0	3.2 ± 0.11	0.95 ± 0.03
C3	62.0 ± 2.0	61.6 ± 3.51	2.4 ± 0.40	>1%
C4	63.6 ± 2.51	62.0 ± 4.0	2.2 ± 0.30	>1%

Batch B1 exhibited lesser disintegration and wetting time as compared with batch B2. The optimum concentration of the crospovidone and mannitol for preparation of mouth dissolving tablets would be 10% and 54.6% respectively. Thus, better tablet results were obtained at low concentrations of diluent and high concentrations of superdisintegrant. The mouth dissolving tablets of oxcarbazepine were ultimately prepared by using mannitol as a diluent, crospovidone as a superdisintegrants, magnesium stearate as lubricant and aspartame as a sweetener using single punch tableting machine. The prepared tablets were subjected to various quality control tests and the data observed from the various tests on prepared mouth dissolving tablets by direct compression methods are given in Table 3.

Table 3: Results of evaluation parameters for MDTs prepared by direct compression

Evaluation Parameters	Observations
Appearance	Light Yellowish round flat tablets
Thickness	4.0 ± 1.0mm
Uniformity of weight	Complies
Disintegration time	30 ± 5 sec
Wetting time	50 ± 10 sec
Water absorption ratio	75 ± 10%
Friability	0.8 ± 0.1%
Hardness	3.0 ± 1.0 kg/cm^2
Dissolution test USP	< 60% in 60 min
Taste	Acceptable

From the dissolution behavior as shown in the Fig 1, it was concluded that the dissolution rate of the drug from the tablets was low as expected when compared with the dissolution profile of pure drug. The percentage drug release from the MDTs at first 10 min was found to be comparable with the pure oxcarbazepine i.e. 19.5% but as the sampling time increases, the % drug release goes on decreasing. It might be due to stronger binding or larger compression force, which restricted the drug release from the tablet. In spite of lesser disintegration time, lesser wetting time and high water absorption ratio, the dissolution rate was so low. The tablets showed 52.5% release in 60 min. The reason behind this effect must be due to lesser solubility of oxcarbazepine in the media. Thus, the tablets prepared by direct compression technology showed lesser efficiency as far as drug release is concerned.

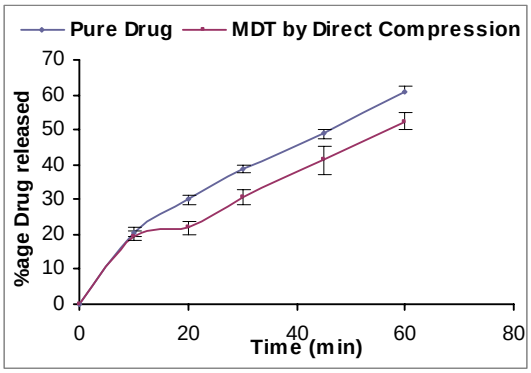


Fig. 1: Comparative in vitro release of pure Oxcarbazepine and its MDT prepared by direct compression method.

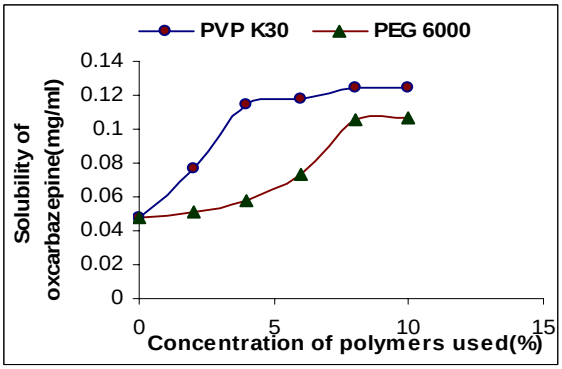


Fig. 2: Phase solubility diagram of oxcarbazepine with PVP K30.

The results of phase solubility studies revealed that PVP K30 has more pronounced effect on increasing the solubility of oxcarbazepine as compared to PEG 6000. As The concentrations of polymers were increased from 2% to 10%, the solubility of oxcarbazepine gets increased (fig 2) The linear A_L type phase solubility diagrams were indicative of a definite interaction in solution between drug and polymer and of soluble complex formation[7]. However more pronounced and linear results were obtained from PVP K-30. This may be attributed to the improved wetting of oxcarbazepine in the presence of PVP K-30 probably due to formation of intermolecular hydrogen bonding between the carbonyl group of PVP K-30 and the hydrogen atom in the NH_2 group[7].

Figures 3 and 4 illustrate the dissolution profiles of solid dispersions with PVP K 30 and PEG 6000 respectively in different weight ratios. Dissolution profile of PVP K30 solid dispersions showed pronounced increase in the release rate of oxcarbazepine. From 1:1 solid dispersions, the release rate was 69.8% in 60 min. As the ratio was increased from 1:1 to 1:2, further increase in the release rate was observed, the release was 98.2% in 60 min. On further increasing the polymer concentration to drug: polymer ratio of 1:3, there was a slight decrease in the release rate of the drug. Similar findings were reported with solid dispersions of

ibuprofen-PVP in different ratios, where a linear relationship was found between the polymer concentration and the dissolution rate constant[19].

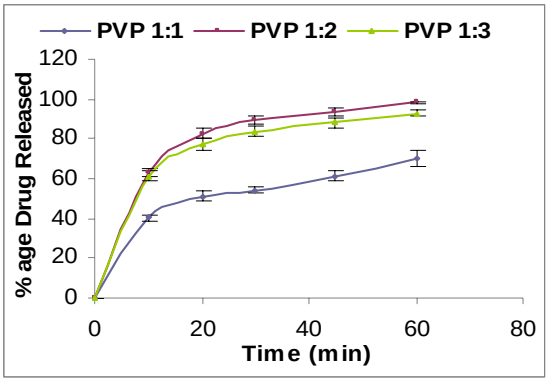


Fig. 3 : Dissolution profiles of oxcarbazepine from PVP K30 solid dispersions

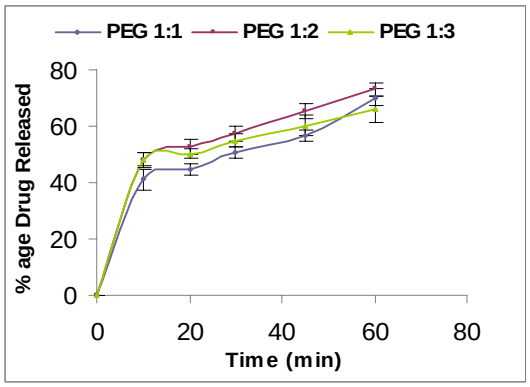


Fig. 4 : Dissolution profiles of oxcarbazepine from PEG 6000 solid dispersions

Several mechanisms have been proposed to account for the increase in dissolution kinetics of drugs from solid dispersions. These mechanisms include the carrier controlled dissolution[20, 21, 22], the continuous drug layer formation and that involving the release of intact particles with dissolution occurring over a large surface area[23]. The later mechanism has been suggested to be important at low drug levels. It is also clear that a modification of the surface properties and hence a reduction of the contact angle value improves the wettability of the powder and it leads to an increase of dissolution rate. From the data obtained for the PEG 6000 solid dispersions, it was observed that the dissolution rate was increased in comparison to the pure drug, but the release was less in comparison with dispersions obtained from PVP K30. From 1:1 PEG solid dispersions, the release was found to be 70.2% in 1 hour, which was found to be comparable to the release data obtained from 1:1 PVP solid dispersions. However when the concentration of polymer was increased from 1:1 to 1:2, there was slight increase in the release rate i.e. 73.1% release in 1 hour. On further increasing the concentration of the polymer to drug: polymer ratio of 1:3, the release rate was found to decrease.

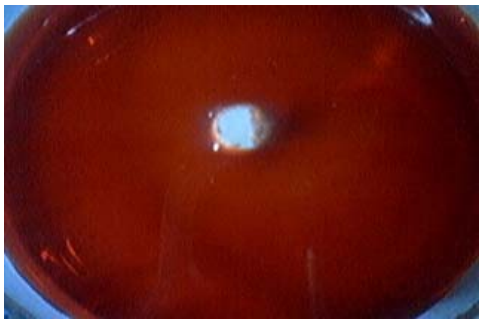
The reason for the lesser release rates with the PEG dispersions in comparison to the PVP solid dispersions may be due to the presence of crystallinity in PEG dispersions and improper wetting of drug with PEG which results in lower release rates in comparison with PVP dispersions.

In order to gain information on the physicochemical characteristics of the prepared solid dispersions, FT-IR analysis was conducted. The purpose of this study was to evaluate possible interaction between oxcarbazepine and carrier used in solid state. The spectrum of oxcarbazepine is characterized by the presence of strong absorption band at 3334 cm^{-1}, which is indicative of amines (-NH- group). The carbonyl-stretching mode appears as a very strong doublet at 1693 cm^{-1} (C=O stretching) and 1645 cm^{-1}. Other characteristic bands were found at 1556 cm^{-1}, 1568 cm^{-1}, which was indicative of presence of aromatic rings.

The spectrum of PVP K30 showed important bands at 2948 cm^{-1} (C-H stretch) and 1647 cm^{-1} (C=O). A very broad band was also visible at 3446 cm^{-1}, which was attributed to the presence of water confirming the broad endotherm detected in the DSC experiment. The spectra of PEG 6000 are characterized by the C-H stretching vibrations at 2883 cm^{-1} and C-O (ether) stretching at 1105 cm^{-1}**.** From the spectra of physical mixture of drug with PVP K30, it was observed that the strong absorption band of oxcarbazepine was shifted from 3334 cm^{-1} to 3340 cm^{-1}, which indicates the presence of H- bonding between the drug and the polymer. On the other hand, in case of physical mixture of drug with PEG 6000, the absorption spectrum of drug has been shifted from 3334 cm^{-1} to 3338 cm^{-1}. That indicates lesser interaction between the drug and the polymer when mixed together. In the spectra obtained for the solid dispersions of drug with PVP K30, the characteristic bands of drug gets shifted from 3334 cm^{-1} to 3338 cm^{-1} and the absorption bands of polymer shifts from 1647 cm^{-1} to 1654 cm^{-1}. This data depicts the presence of H- bonding between the –NH group of drug and C=O group of the polymer which shifts the absorption spectra. The spectra of solid dispersion of drug with PEG 6000 showed the shift in the absorption band of drug from 3334 cm^{-1} to 3340 cm^{-1}, which indicates the presence of some type of interaction. Also, the absorption spectrum of polymer was found to have a shift from 2883 cm^{-1} to 2885 cm^{-1} and 1105 cm^{-1} to 1107 cm^{-1}[1]From the above data obtained, the interaction is expected between oxcarbazepine and polymers (PVP K30 and PEG 6000) in the solid state, it should reasonably involve the –NH- (amine) group of oxcarbazepine and the carbonyl group in polymers. As the intensity is found to increase in all the cases, the H- bonding must be due to intermolecular association between the drug and the polymer.

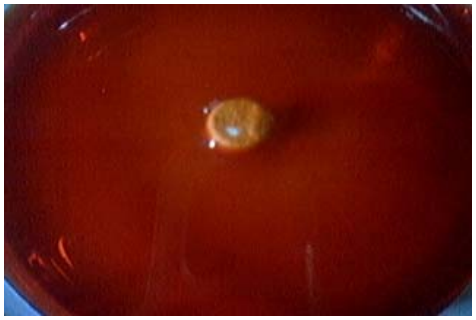
The thermograms of oxcarbazepine, PVP K30 and solid dispersions of oxcarbazepine-PVP K30 over the temperature range from 20-350°C were observed. In the pure drug a sharp endotherm at ~230°C was observed which could be the melting point. Two less significant endotherms at ~269°C and 281°C were also observed which could be some heat base transitions and needs investigation. In the thermogram of PVP K30, an endotherm was observed at ~231°C and no other significant peaks were observed. However, during the scanning of PVP K30, a broad endotherm was observed at ~80°C. This hump in the initial phase could be attributed to the presence of moisture. The thermogram of solid dispersions showed a shift in the endothermic peaks of both drug as well as polymer. The endotherm was observed at ~207°C. However, the peak was found to be extended upto ~223°C. This data suggests the complete amorphization of drug in the polymer. Moreover some degree of interaction was reported which was dictated by the shift in the endotherms to a lower value**.** The PVP K-30 solid dispersion showing maximum dissolution rate (1:2 ratio) was converted into tablet formulation with improved dissolution. The mean hardness was found to be 3 kg/cm^2. The results of disintegration test revealed that the prepared tablets disintegrated rapidly i.e. within 30 s. The tablets were found to have 85% water absorption ratio and showed wetting time in the range of 30 sec. For predicting the wetting and disintegration time, a prepared mouth dissolving tablet was put in the petri plate and wetting and disintegration rate was noted at the intervals

of 5, 10, 15, 20, 25 and 30 seconds. The images (Fig 7) show the various stages in the wetting of the prepared mouth dissolving tablets at different time intervals. It was observed that the tablet wetted and disintegrated completely in 30 seconds, which is an essential requirement for mouth dissolving tablets.



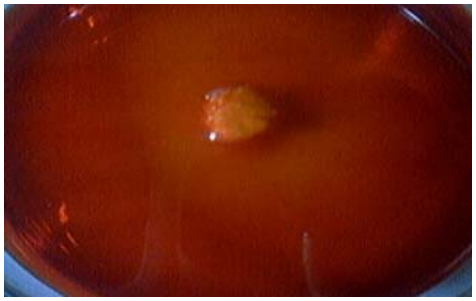
INITIAL

After 5 sec

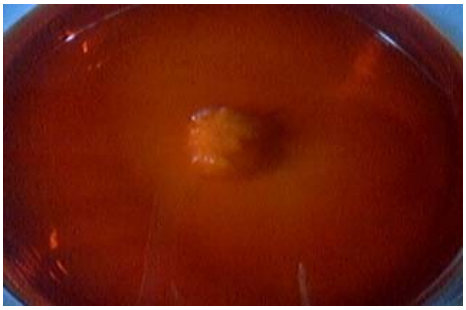


After 10 seconds

After 15 seconds



After 20 seconds



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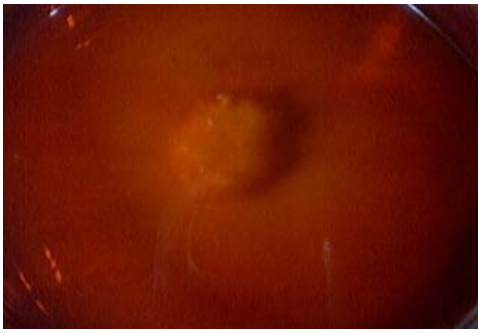
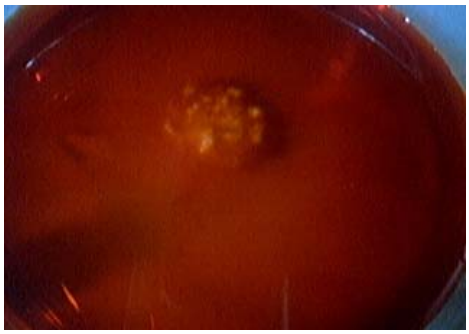


After *27* seconds



After 30 seconds

Fig. 7: Images showing wetting time of MDTs.

The drug release studies were performed on the prepared MDTs using phosphate buffer pH 6.8. From the graph shown in Figure 8, it is evident that the solid dispersion technique has improved the dissolution rate of oxcarbazepine to a great extent. The mouth dissolving tablet prepared from solid dispersions showed a release of 63% in first 10 min, and more than 95% release in 60 min. From the study, it was reported that the release from tablets were found to be less as compared to the solid dispersions themselves. It might be attributed to the compression force required during tableting which results in a small decrease in the drug release profile of mouth dissolving tablets. The in vitro release profile of prepared mouth dissolving tablets was compared with the marketed oxcarbazepine tablets. Fig 9 shows the dissolution profile of marketed dispersible oxcarbazepine tablet. The drug release profile of prepared MDTs was found to be comparable with the marketed dispersible tablets of oxcarbazepine. The release was found to be uniform over the range of 60 min.

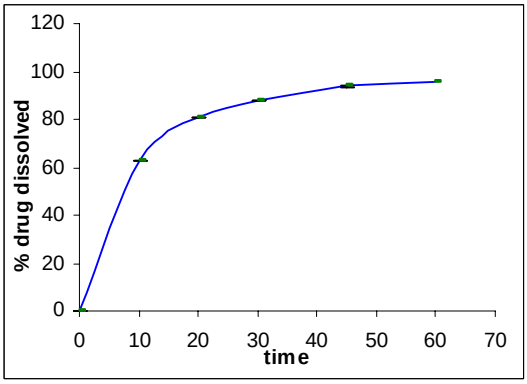


Fig. 8: Dissolution profile of oxcarbazepine MDTs prepared from solid dispersions.

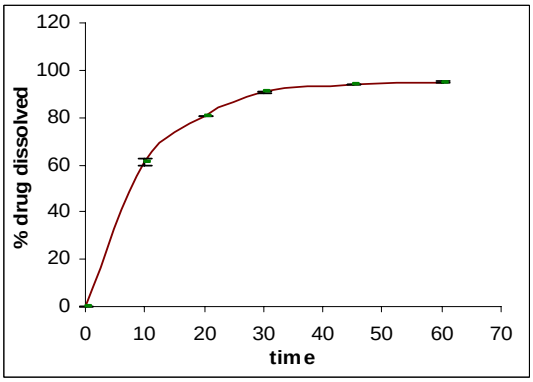


Fig. 9: Dissolution profile of marketed dispersible oxcarbazepine tablet.

Fig 9 shows the drug release profiles of the tablets prepared from direct compression and solid dispersion technologies. The release from mouth dissolving tablets prepared by direct compression was only 55% in 1 hr, compared to release from mouth dissolving tablets of solid dispersions that was more than 95% in 1 hr.

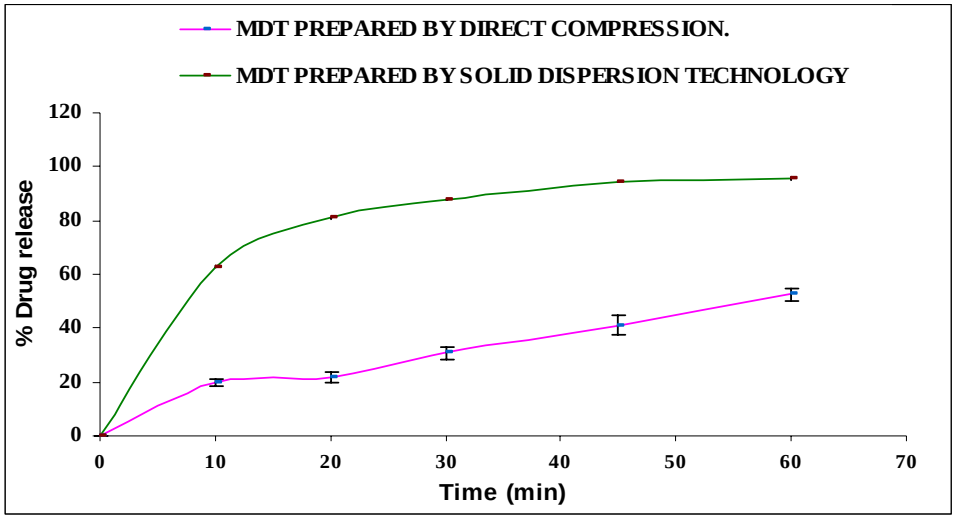


Fig. 9: Comparison of the release profiles of the MDTs of oxcarbazepine prepared by different technologies

The use of oxcarbazepine- PVP solid dispersions allowed preparation of tablets with good technological properties and satisfying and reproducible drug dissolution profiles. Thus, solid dispersion technology is found to be best suited for the formulation of mouth dissolving tablets of poorly water-soluble drugs. From the above study, it is concluded that the mouth dissolving tablets prepared by solid dispersion technology shows the better dissolution rates in comparison to the pure drug and mouth dissolving tablets prepared by direct compression technology.

CONCLUSION

The present investigation successfully formulated mouth-dissolving tablets of oxcarbazepine with improved drug release profile. Two different technologies, direct compression and solid dispersion technology were employed for the formulation of mouth dissolving tablets. Among different excipients used, crospovidone (Kollidon CL) as a superdisintegrant, mannitol as a diluent, magnesium stearate as a lubricant and aspartame as a sweetener were used. The tablets prepared by direct compression method passed all the pharmacopoeial tests. The only problem encountered with the tablets prepared by this method involves the lesser drug release rate, which has been attributed to the lower solubility and thus wettability of the drug into the media.

Solid dispersions of oxcarbazepine were prepared using PVP K30 and PEG 6000 as the carrier polymers in three different drugs to carrier ratios of 1:1, 1:2 and 1:3 using solvent evaporation method. Phase solubility studies showed the increase in solubility of drug on increasing the polymer concentration. FT-IR and DSC studies revealed the presence of some degree of interaction between PVP K30 and oxcarbazepine. Solid dispersions of PVP K30 in drug- carrier ratio of 1: 2 markedly improved the dissolution rate of oxcarbazepine. The mouth dissolving tablets of solid dispersions prepared using 1:2 dispersions of oxcarbazepine-PVP K30 (equivalent to 100mg of oxcarbazepine), mannitol (13%), crospovidone (10%), magnesium stearate (1%) and aspartame (1%) showed better dissolution profiles in comparison with tablets produced with direct compression method, giving 95% drug release in 60 min. Moreover, the drug dissolution rate from the developed tablets were comparable with those obtained from marketed dispersible oxcarbazepine tablets, thus confirming the effectiveness of using solid dispersed drug in tablet formulation.

Thus, it has been concluded that solid dispersion technology can be used as a better alternative to the direct compression technology for the formulation of mouth dissolving tablets especially for drugs having poor water solubility.

References

1. Seager H. Drug-delivery Products and the Zydis Fast-dissolving Dosage Form. J Pharm Pharmacol 1998; 50:375-382.
2. Bradoo R, Shahani S, Poojary S, Deewan B, Sudarshan S. Fast Dissolving Drug Delivery Systems. JAMA India 2001; 4(10): 27-31.
3. Bang L, Goa K. Oxcarbazepine: a review of its use in children with epilepsy. Paediatr Drugs 2003; 5(8): 557-73.
4. Wellington K, Goa KL. Oxcarbazepine: an update of its efficacy in the management of epilepsy. CNS Drugs 2001; 15(2): 137-63.
5. Toshifusa S, Hideshi S, Kenji H, Kunio I. Studies of rapidly disintegrating tablets in oral cavity using co ground mixtures of

mannitol with crospovidone. Chem Pharm Bull 2002; 50(2): 193-198.
6. Franco M, Trapani G, Latrofa A et al. Dissolution properties and anticonvulsant activity of phenytoin-PEG 6000 and PVP K30 solid dispersion. Int J Pharm 2001; 225:63-73.
7. Higuchi T, Connors KA. Phase solubility techniques. Adv Anal Chem Instrum 1965; 4:117-212.
8. Sethia S, Squillante E. Solid dispersion of carbamazepine in PVP K30 by conventional solvent evaporation and supercritical methods. Int J Pharm 2004; 272: 1-10.
9. Ahmad M Abdul-Fattah, Bhargva HN. Preparation and in vitro evaluation of solid dispersion of halofantrine. Int J Pharm 2002; 235:17-33.
10. Van den Mooter G, Augustijns P, Blaton N, Kinget R. Physicochemical characterization of solid dispersions of temazepam with polyethylene glycol 6000 and PVP K30. Int J Pharm 1998; 164:67-80.
11. Ryh-Nan P, Jing-Huey C, Rhei-Long C. Enhancement of dissolution and bioavailability of piroxicam in solid dispersion system. Drug Dev Ind Pharm 2000; 26(9): 989-994.
12. Dobetti L. Fast melting tablets: Development and technology. Pharm Tech Drug Delivery 2001; 44-50.
13. Bi Y, Sunada H, Yonezawa Y, Danjo K, Iida K. Preparation and evaluation of compressed tablets rapidly disintegrating in the oral cavity. Chem Pharm Bull (Tokyo) 1996; 44: 2121-2127.
14. Andries F. Marais, Mingna Song, Melgardt M. de Villiers. Effect of compression force, humidity and disintegrant concentration on the disintegration and dissolution of directly compressed furosemide tablets using croscarmellose sodium as disintegrant. Tropl J Pharm Res 2003; 2:125-135.
15. Shenoy V, Agrawal S, Pandey S. Optimizing fast dissolving Dosage form of Diclofenac Sodium by rapidly disintegrating agents. Indian J Pharm Sci 2003; 65(2): 197-201.
16. Debord B, Lefebvre C, Guyot Hermann AM, Bouche R, Guyot JC. Study of different crystalline forms of mannitol comparative behavior under compression. Drug Dev Ind Pharm 1987; 13:1533-1546.
17. Pharmapedia.http://www.pharmpedia.com /Tablet:Formulation_of_tablets/Diluents.
18. Patel DM, Patel NM, Shah RR, Jogani PD, Balapatel AI. Studies in formulation of orodispersible tablets of rofecoxib. Ind J Pharm Sci 2004; 66(5): 621-625.
19. Najib NM, Suleiman M, Malakh A. Characteristics of the in vitro release of ibuprofen from polyvinylpyrrolidone solid dispersions. Int J Pharm 1986; 32:229-236.
20. Corrigan OI, Murphy CA, Timoney RF. Dissolution properties of polyethylene glycols and polyethylene glycol-drug systems. Int J Pharm 1979; 4:67-74.
21. Dubois JL, Ford JL. Similarities in the release rates of different drugs from polyethylene glycol 6000 dispersions. J Pharm Pharmacol 1985; 37:494-495.
22. Craig DQM, Newton JM. The dissolution of nortriptyline hydrochloride from polyethylene glycol solid dispersions. Int J Pharm 1992; 78:175-182.
23. Saers Sjökvist E, Craig DQM. An investigation into the mechanisms of dissolution of alkyl p-aminobenzoates from polyethylene glycol solid dispersions. Int J Pharm 1992; 83:211-219.