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*Research Article*

# ENHANCEMENT OF BIOAVAILABILITY OF CARBAMAZEPINE BY SOLID DISPERSION TECHNIQUE

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**ABSTRACT**

The enhancement of oral bioavailability of poorly soluble drugs remains one of the most challenging aspects of drug development. Although salt formation solubilisation and size reduction have commonly been used to increase dissolution rate and there by oral absorption and bioavailability of such drugs. There are some practical limitations of these techniques. The solid dispersion approach has been widely and successfully applied to improve solubility, dissolution rate and consequently the bioavailability of poorly soluble drugs. Many hydrophilic excipients like fumeric acid, citric acid, mannitol, sorbitol, can be used to enhance the dissolution of drug. In the present study, an attempt was made to increase solubility and dissolution of drugs by solid dispersion technique using fumeric acid, citric acid by physical mixing and kneading methods.

**Keywords:** bioavailability, carbamazepine, physical mixing ,kneading method.

**The major objectives of the investigation areas follow**

1) To prepare solid dispersions of carbaazepin using various carriers by physical mixing and kneading method (KM)
2) To evaluate the drug release from solid dispersions by *in-vitro* dissolution rate studies.
3) IR studies to known the compatibility in between the drug ad polymer.

**MATERIALS**

1) The following materials were used in the present study:
2) Carbamazepine (gift sample from matrix laboratories ltd, Hyderabad)
3) Ethanol (qualigens chemicals ltd, Mumbai)
4) Fumeric acid
5) Citric acid
6) All other chemicals/solvents used were of AR grade.

**Preparation of carbamazepine solid dispersions**

The solid dispersions of carbamazepine were prepared in 1:1, 1:2 ratios by two methods as

1. **Physical mixing method**
   Carbamazepine and each of carriers of FA and CA were weighed accurately and mixed thoroughly in motor and pestle for 10 min. These mixtures were then passed through sieve number #120 and finally, stored in tight containers till further use.

2. **Kneading method**
   Carbamazepine and each of surface active carriers FA and CA were weighed accurately in various ratios (1:1, 1:2) and transferred to china dish sufficient quantity of ethanol was added and the thick slurry was needed for 1hr and then dried at $45^0$c until dryness. The dried mass was pulverized and sieved through sieve num #120.the resulting solid dispersions were stored for 24hrs in desiccators to congeal. The mass

obtained was crushed, pulverized. Finally dispersions were stored in air tight containers till further use.

**Experimental results**

The results were tabulated in table:1. table:2. table:3 table:4. table:5

**CONCLUSION**

The enhancement of dissolution rate and oral bioavailability of poorly soluble drugs remains one of the mostly challenging aspects of drug development. Among the various methods of enhancement of the dissolution rate and oral bioavailability, solid dispersion techniques were found to be more successful with a number of drugs. In the present investigation studies were carried out on enhancement of dissolution rate of carbamazepine by solid dispersion technology and for enhancing the dissolution rate of poorly soluble drugs.

From the results obtained the following conclusions were drawn:

- All the solid dispersions prepared were found to be fine free flowing powders.
- The drug content was uniform in a batch of solid dispersions in all the cases
- The dissolution of carbamazepine from all the solid dispersions higher than the dissolution of the corresponding pure drug. was rapid and several times
- Drug dissolution from all solid dispersions followed 1st order kinetics.
- All the dispersions parameters estimated i.e. $T_{10}$.$T_{50}$, DE30%, DE60, and $k_1$ values indicated rapid and higher dissolution of the drug from the solid dispersions than that of corresponding pure drug.
- Among the all solid dispersions tested fumeric acid solid dispersions prepared by kneading method in 1:2 ratios gave highest enhancement of dissolution rate and efficacy of carbamazepine.
- In each case the dispersions rate ($K_1$) and $DE_{30}$% and $DE_{60}$% were increased as the concentration of carriers in the solid dispersions was increased.
- Among these two carriers FA was found to be good carrier for solid dispersions for enhancing the dissolution rate of carbamazepine.
- From the solubility studies and IR studies found that there is no chemical reaction takes place between the drug and excipients.

**Table 1: Construction of calibration curve in phosphate buffer (pH6.8)**

| S.No | Concentration (µg/ml) | Absorbance |
|---|---|---|
| 1 | 5 | 0.196±0.5 |
| 2 | 10 | 0.257±0.3 |
| 3 | 15 | 0.375±0.2 |
| 4 | 20 | 0.468±0.4 |
| 5 | 25 | 0.547±0.1 |

**Table 2: Cumulative % drug release profile**

| Time | Pure drug | Ca 1:1KM | FA 1:1 KM | CA 1:2KM | FA 1:2KM |
|---|---|---|---|---|---|
| 5 | 1.73±1.22 | 2.59±1.22 | 10.8±0.23 | 23.32±1.06 | 22.43±0.70 |
| 10 | 2.30±0.23 | 3.45±2.24 | 11.66±0.62 | 26.78±1.02 | 25.34±0.47 |
| 15 | 3.17±0.47 | 5.66±1.93 | 13.39±1.22 | 30.88±0.81 | 37.08±0.47 |
| 30 | 4.61±0.47 | 8.06±1.69 | 16.56±0.47 | 34.99±1.29 | 48.81±1.03 |
| 45 | 7.2±2.24 | 10.22±1.47 | 25.78±0.81 | 46.38±1.08 | 51.41±1.71 |
| 60 | 6.76±1.31 | 12.82±0.47 | 34.27±2.09 | 54.14±1.22 | 59.47±0.05 |
| 90 | 9.22±1.24 | 22.46±1.69 | 41.33±1.07 | 58.32±0.62 | 67.53±0.47 |
| 120 | 38.59±1.17 | 42.91±0.40 | 43.92±0.23 | 65.52±0.47 | 70.27±.0.62 |

**Table 3: Solubility and drug content**

**data for solid dispersions**

| Batch | ratio | Drug content | Solubility(mg/ml) |
|---|---|---|---|
| CA | | | |
| | 1:1PM | 96.32±0.65 | 0.12 |
| | 1:1KM | 97.98±0.77 | 0.16 |
| | 1:2PM | 98.61±0.90 | 0.19 |
| | 1:2KM | 95.35±0.23 | 0.23 |
| FA | | | |
| | 1:1PM | 97.56±0.79 | 0.22 |
| | 1:1KM | 98.74±0.73 | 0.25 |
| | 1:2PM | 94.76±0.37 | 0.26 |
| | 1:2KM | 99.36±0.26 | 0.28 |

**Table 4: Cumulative % drug release profile**

| Time | Pure Drug | CA 1:2KM | FA 1:2 |
|---|---|---|---|
| 5 | 1.73±1.22 | 38.73±0.31 | 55.58±0.75 |
| 10 | 2.30±0.23 | 42.19±0.25 | 69.84±0.91 |
| 15 | 3.17±0.47 | 53.56±0.71 | 82.24±0.93 |
| 30 | 4.61±0.47 | 65.81±0.62 | 85.25±1.03 |
| 45 | 7.2±2.24 | 71.58±1.51 | 92.25±0.56 |
| 60 | 6.76±1.31 | 74.48±0.47 | 109.87±1.42 |
| 90 | 9.22±1.24 | 77.22±1.64 | |
| 120 | 38.59±1.17 | 81.93±1.38 | |

Mean ± SD.n=3

**Table 5: Dissolution kinetics of carbamazepine solid dispersion**

| Batch | ratio | $DE_{30}$% MIN | $T_{10}$ MIN | $T_{50}$ MIN | FIRST ORDER RATES($MIN^{-1}$) | |
|---|---|---|---|---|---|---|
| | | | | | $K_1$ | $R^2$ |
| CARBAMAZEPINE | | 0.00178 | 2.9 | 7 | 0.002303 | 0.686 |
| CA | | | | | | |
| | 1:1PM | 0.00181 | 3.5 | 12.1 | 0.002303 | 0.875 |
| | 1:1KM | 0.00141 | 13.3 | 36 | 0.0046 | 0.906 |
| | 1:2PM | 0.0187 | 25.21 | 43 | 0.0069 | 0.971 |
| | 1:2KM | 0.0280 | 42.1 | 51 | 0.0092 | 0.888 |
| FA | | | | | | |
| | 1:1PM | 0.00857 | 11.66 | 16.2 | 0.004606 | 0.960 |
| | 1:1KM | 0.00119 | 22.4 | 38.14 | 0.0046 | 0.946 |
| | 1:2PM | 0.00225 | 25.34 | 46.52 | 0.0046 | 0.974 |
| | 1:2KM | 0.00483 | 52.4 | 58.64 | 0.02763 | 0.794 |

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