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Research Article

FORMULATION DEVELOPMENT AND EVALUATION OF FAST DISSOLVING TABLET OF CARBAMAZEPINE

MALI P.A., BHARATE S.D., BARI M.M., LOHARE G., JANJALE M

Shree Sureshdada Jain Institute of Pharmaceutical Education & Research, Jamner, Maharashtra, India.

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ABSTRACT

To obviate the problem of dysphasia & to improve patient compliance, FDT have gained considerable attention over the conventional dosage form such as tablet & capsule. Carbamazepine is dibenzapine derivative with structure resembling that of tricyclic antidepresent,is used in epilepsy. The major problem of this drug is very low solubility in biological fluid & poor bioavailability after oral administration. The present work focus on the effect of superdisintegrents (such as crosspovidone, sodium starch glycolate & pregelatinized starch.) on wetting time,disintegrating time,drug content, in vitro drug release, stability parameter studied. No chemical interaction between drug & excipient was confirmed by DSC & FTIR studies. Among all formulation F was considered best. The result concluded that FDT of poorly soluble drug carbamazepine, showing enhanced dissolution, will lead to improved bioavailability, improved effectiveness& hence better patience compliance.

Keywords: Fast dissolving tablets, Carbamazepine, Crosspovidone, Sodium starch glycolate & Pregelatinized starch.

INTRODUCTION

In recent decade a variety of pharmaceutical research has been conducted to developed new dosage forms, considering quality of life, ease of medication, or novel drug delivery. Among the dosage form developed to facilitate ease of medication, the fast dissolving tablets is one of most widely employed as commercial products[1] Conventional dosage form such as tablet & capsule posses one important drawback of dysphasia (i.e. difficulty in swallowing)or chewing in some patients particularly in pediatric & geriatric patients. the problem of swallowing is common phenomenon in geriatric patients due to fear of chocking, hand tremors, & in young patients due to underdeveloped muscular & nervoussystem & in schizophrenic patients which leads to poor patient compliance [2] FDT has much attention because of it avoid the problem of dysphasia & improve patient compliance. FDT is solid dosage form that disintsgrate s & dissolves in mouth without water. Most fast dissolving tablets must include substance to mask the active ingredient. FDT begin to disintegrate immediately after coming into contact with saliva, with complete disintegration normally occurring in 30-50 seconds after administration.[3]

Carbamazepine, a dibenzapine derivative with structure resembling the tricyclic antidepressants, is used in the treatment of epilepsy, one of the major problem with this drug is its very low solubility in biological fluids & its biological half life between 18 to 65 hrs that result into poor bioavailability after oral administration[4]. It shows erratic dissolution profile in gastric & intestinal fluid ue to its poor water solubility. The peak plasma concentration cmax & time taken to reach cmax (tmax) depend upon extent & rate of dissolution can be increased by increasing the surface area of available drug by various methods (micronisation, complexation) [5]. The dissolution of drug can also influenced by disintegration time of the tablets. Fast disintegration time of tablets delivers a fine suspension of of drug particles resuling in higher surface area & faster dissolution [6]

MATERIALS AND METHOD

Materials

Carbamazepine drug was procured as gift sample from Cadila Health Care, Ahemedabad, Gujrat.Crosspovidone, sodium starch glycolate, pregelatinised starch were obtained as gift samples from Dr. Reddys Laboratories, Hyderabad. Magnesium stearate, talc & poly vinyl pyrolidone purchased from S.D. Fine chemicals Ltd., Mumbai. All other materials were of pharmaceutical grade.

Method

Carbamazepine tablets were prepared by direct compression method. The composition of each tablet is shown in **table (no.1)**. the drug, dilulents, superdisintegrant, & sweetner were passed through sieve # 40. All the ingredients were properly mixed together. Talc & magnesium stearate were passed through mesh # 80,mixed, blended with initial mixture in a polybag. The powder blend was compressed into tablets on a ten station rotary punch tableting machine using 8 mm punch[7]

Table 1: Composition of carbamazepine fast dissolving tablets

Ingredient(mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9
Carbamazepine	100	100	100	100	100	100	100	100	100
Crosspovidone				2.5	5.0	7.5	-	-	-
Sodium starch glycolate	2.5	5.0	7.5				-	-	-
Pregelatinized starch	-	-	-	-	-	-	2.5	5.0	7.5
Microcrystalline cellulose	40	40	40	40	40	40	40	40	40
Mannitol	42.5	40	37.5	42.5	40	37.5	42.5	40	37.5
Aspartame	10	10	10	10	10	10	10	10	10
Talc	3	3	3	3	3	3	3	3	3
Magnesium stearate	2	2	2	2	2	2	2	2	2

Evaluation of carbamazepine tablets

The prepared tablets were evaluated for the following parameters.

Thickness

Thickness of tablets was measured by using digital venire calipers.[8]

Uniformity of weights

20 tablets were weighed collectively & individually. from the collective weight, average weight was calculated. Each tablet weight was then compared with average weight to ascertain weather it was within permissible limits or not.[9]

Hardness

Hardness of the tablet was determined using the Monsanto hardness tester[10].

Friability test

Tablets equivalent to 6.5gm were placed in Roche friabilitor, which was given 100 revolutions & the tablets were reweighed. [9&8]

Drug content

Twenty tablets of each formulation were weighed & powered. The quantity of powder equivalent to 10 mg of carbamazepine was weighed solution was filtered, diluted suitably with 1% sodium lauryl sulphate in phosphate buffer pH 7.4 & drug content was analysed at 320nm by UV-Visible spectrophotometer.[11]

Wetting time & water absorption ratio

A piece of tissue paper folded double was placed in petridish contenting 5ml of water. The tablet was placed on the paper & the time for complete wetting of tablet was measured in seconds. Water absorption ratio(R) was determined by using the following equation[12]

$$R = 10X (Wa-Wb) / Wb$$

Wa= weight of tablet before water absorption

Wb= weight of tablet after water absorption

Disintegration test

DT was measured using disintegration test apparatus. One tablet was placed in each tube of basket. The basket with bottom surface made of stainless steel screen(#10) was immersed in water bath at 370C.the time required for complete disintegration of tablet in each tube was determined [13]

Test for dispersion

Two tablets were placed in 100ml water & stirred gently until it was completely dispersed & smooth dispersion was obtained. The dispersion liquid was passed through sieve no. 22. No residue should remain over the sieve[13]

In vitro dissolution studies

Dissolution rate of carbamazepine tablets was studied using USP dissolution test apparatus (Electro lab) type 2(paddle). 900ml of the dissolution medium (1% SLS solution) was taken in covered vessel & temperature was maintained at 37 oc. the speed of the paddle was set at 75 rpm. Sampling was done at every min. interval. For each sample 5ml of the dissolution medium was withdrawn & the same amount of dissolution medium at 37oc was replenished to the dissolution medium. The sample was withdrawn & diluted with 1% SLS solution & analyzed in UV spectrophotometer at 287 nm. [14]

Characterization of Carbamazepine Tablets

FTIR Studies

IR spectra for drug, & powdered tablets were recorded in a Fourier transform infrared spectrophotometer with KBr pellets[10]

DSC Studies

DSC scans of about 10 mg, using an automatic thermal analyzer system were performed with accurately weighed carbamazepine & formulation(Mettler Toledo, USA). Sealed & perforated aluminum pans were used in the experiments for all samples. Temperature calibrations were performed using indium as standard. An empty pan sealed in the same way as the sample was used as a reference. The entire samples were run at a scanning rate of 10oc / min. from 100-300 ^{o}C. [10]

RESULT & DISCUSSION

The values of precompression parameters evaluated were within limits & indicated good free flowing property. The data obtained from post compression parameters such as hardness, friability, uniformity of weight, drug content, wetting time, shown in table no. 3

Table 2: Solubility study data of carbamazepine in various solvents & buffer

S. No.	Name of solvent	Concentration (mg/ml)
1	Phosphate buffer pH6.8	2.1
2	Phosphate buffer pH7.2	0.87
3	Phosphate buffer Ph7.4	0.78
4	1% sodium lauryl sulphate	6.3
5	2%sodium lauryl sulphate	5.1

Table 3: Result of post compression parameters

Formulations	Hardness (Kg/cm2)	Friability (%)	Drug content ((mg%)	Weight variation	Wetting time
F1	3.1±0.11	0.54±0.6	99.5±0.5	200±1.8	33.11±0.12
F2	3.3±0.11	0.59±0.7	99.8±0.1	201±1.5	58.21±0.54
F3	3.3±0.13	0.52±0.9	99.22±0.3	199±1.5	66.40±0.32
F4	3.2±0.14	0.61±0.4	99.4±0.5	200±1.4	22.34±0.65
F5	3.1±0.12	0.65±0.5	99.6±0.7	202±1.4	19.87±0.98
F6	3.2±0.14	0.56±0.3	99.3±0.2	200±1.5	17.87±0.76
F7	3.3±0.13	0.67±0.1	99.1±0.4	198±1.2	23.5±0.98
F8	3.1±0.11	0.69±0.6	99.4±0.6	199±1.3	18.±0.87
F9	3.2±0.12	0.64±0.2	99.54±0.3	197±1.6	15.67±0.54

All the tablets prepared were found to contain the medicament within 100±2% labeled claim. The drug content of all the prepared tablets was found to be in the range of 99.1-99.8%. the values obtained were found to be within limit. Hardness of tablets was found to be in range of 3.1-3.3Kg/cm2. Friability of tablets was less than 1%.

The tablets were subjected for evaluation of in vitro disintegration time. The in vitro disintegration time varies from1.5 to 3.5 minute. it shown in table no.4. **figure 1** depicts the disintegration behavior of tablets. It was observed that when crosspovidone is used as disintegrant, the tablet disintegrates rapidly in short time due to easy swelling ability of crosspovidone compared to other tablet composed of sodium starch glycolate & pregelatinized starch. Disintegration time of tablet containing sodium starch glycolate increase as conc. of sodium starch glycolate. While the disintegration time of tablet containing crosspovidone & pregelatinized starch decrease as the conc. of crosspovidone & pre gelatinized starch increase[16]

Table 4: Result of disintegration time (minute)

Series	Sodium starch glycolate (series1) (min.)	Crosspovidone (series2)	Pregelatinized starch (series3)
Category1	2.5	2.4	2.4
Category2	2.9	2.3	2.1
Category3	3.0	1.9	1.7
Category4	3.4	1.6	1.4

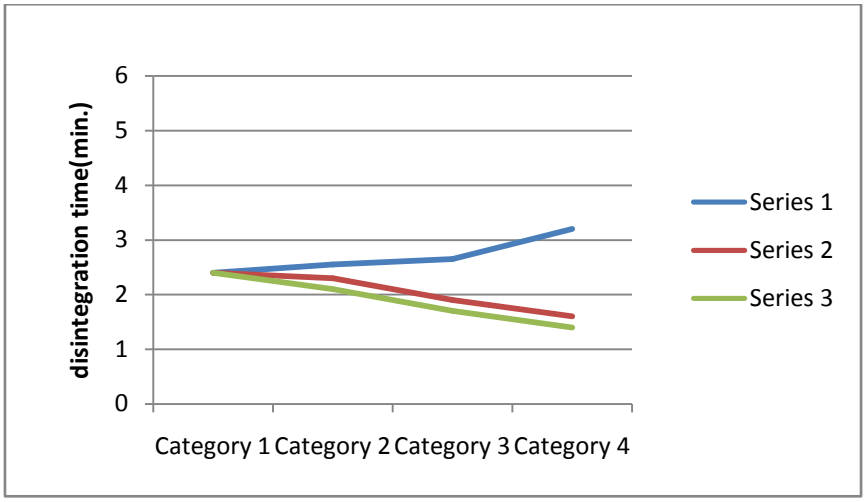

Fig. 1: Effect of superdisintegrants on the disintegration time of carbamazepine tablet.

Dissolution process depend on wetting time followed by disintegration of tablet. Wetting time was rapid in crosspovidone followed by sodium starch glycolate & pregelatinized starch.The influence of super disintegrant on the dissolution from tablet as shown in table no. 5. the t50% & t90% (time for 50%or 90% release) values decreased with increase in conc. of crosspovidone & pregelatinized starch. While it is oppose condition in case of sodium starch glycolate.the tablet prepared with sodium starch glycolate, disintegrate due to rapid uptake of water, followed by rapid swelling[17] into primary particle but more slowly[18] due to the formation of viscous gel layer by sodium starch glycolate.[16] Crosspovidone exhibits high capillary activity & pronounced hydration with a little tendency to gel formation & disintegrate tablet rapidly.[17] & disintegrantes the tablet rapidly but into larger masses of aggregated masses[19] The F6 formulation showed 90% drug release in 3.9 minute.

Table 5: Dissolution parameter of carbamazepine tablet

Formulation	t50%	t90%
F1	0.90±0.3	5.90±0.8
F2	0.99±0.5	6.99±0.7
F3	1.87±0.6	7.23±0.2
F4	0.83±0.7	5.21±0.1
F5	0.76±0.4	4.72±0.2
F6	0.69±0.6	3.93±0.3
F7	0.79±0.1	4.02±0.4
F8	0.71±0.3	3.95±0.6
F9	0.65±0.2	3.94±0.5

Stability study: the stability study for carbamazepine tablet was carried out at 40 0c& 75 % RH for 4 weeks by storing the sample in stability chamber. No appreciable change in disintegration time, hardness, drug content was observed after 4 weeks as shown in table no.6

Table 6: Stability study data observed after 4 weeks.

Formulation	Disintegration time	Hardness (Kg/cm2)	Drug content (mg%)
F1	2.9	3.1±0.11	99.5±0.5
F2	3.0	3.3±0.11	99.8±0.1
F3	3.4	3.3±0.13	99.22±0.3
F4	2.3	3.2±0.14	99.4±0.5
F5	1.9	3.1±0.12	99.6±0.7
F6	1.6	3.2±0.14	99.3±0.2
F7	2.1	3.3±0.13	99.1±0.4
F8	1.7	3.1±0.11	99.4±0.6
F9	1.4	3.2±0.12	99.54±0.3

CONCLUSION

The major problem of carbamazepine it is erratically absorbed from GIT, its limited aqueous solubility which may hinder dissolution may decrease bioavailability. The above result showed that functionality differences bet. Superdisintegrant, the carbamazepine tablet could be prepared by using any of suprdisintegrant used. Overall result indicates formulation f6 which contain 7.5 % crosspovidone was better one. & satisfy all criteria of fast dissolving tablet. Carbamazepine show enhanced dissolution, improved bioavailability, effectiveness, & hence better patience compliance.

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