

QUALITY ANALYSIS OF DIFFERENT MARKETED BRANDS OF CARBAMAZEPINE AVAILABLE IN BANGLADESH

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Abstract

Carbamazepine is the medication commonly used in the treatment, and control of epilepsy, seizures, and neuropathic pain. As an anticonvulsant it is frequently used to treat seizures and neurological pain including diabetic neuropath, and a chronic pain condition that invades the trigeminal nerve known as trigeminal neuralgia. Bipolar disorder can also be treated by this medicine. The main objectives of this present study were to evaluate the quality of three commercial brands of Carbamazepine tablet formulation manufactured by different multinational and national companies in Bangladesh. To evaluate their quality using standard methods all the brands were tested for various parameters including weight variation, hardness, friability, disintegration time, and dissolution profile and finally the results were compared with the standards. It was observed that all of the brands meet the USP specification in weight variation test. All the brands passed the friability test according to USP (United State of Pharmacopeia) specification, and the products from multinational companies showed comparatively higher values. Tablets from every brand completely disintegrated within 15 minutes and thus complied with the USP specification. Besides, the release rate of different brands of carbamazepine was satisfactory within 45 minutes and ranged from 83.44% to 94.5%. Therefore, it can be concluded that almost all the brands of carbamazepine that are available in Bangladesh meet the USP specification for quality control analysis.

Keywords: *Carbamazepine, hardness, friability, disintegration time, dissolution time*

Introduction

A tablet is a pharmaceutical oral dosage form. It includes a mixture of active substances and excipients, generally in powder form, pressed or compacted from a powder into a solid dose. The packed tablet is the most well-known measurement structure being used today. Around 66% of all medicines are administered as strong dose structures, and half of these are packed tablets. A tablet can be detailed to convey a precise measurement to a particular site; it is generally taken orally, yet can be controlled sublingually, buccally, rectally and intra vaginally. The tablet is only one of the numerous structures that an oral medication can accept, for example, syrups, elixirs, suspensions, and emulsions (1). The excipients used for manufacturing include diluents (increase volume upto adequate volume), binders or grinding operators, glidants (stream helps), ointments (ensure proficient tableting), crumbles (advance tablet separation in the stomach related tract) sugars or flavors (improve taste) and shades (make the tablets outwardly alluring). A polymer covering is every now and again connected to make the tablet smoother and simpler to swallow, to control the discharge rate of the dynamic fixing, to make it increasingly impervious to the earth (expanding its timeframe of realistic usability), or on the other hand to improve the tablet's appearance (2, 3). Carbamazepine (CBZ) is considered as the essential medication for the treatment of fractional and tonic-clonic seizures. Seizure intensification has been once in a while saw in grown-ups, for the most part in the rationally hindered or in those with essential summed up epilepsy. Carbamazepine gave full oversight of fractional seizures more frequently than primidone or phenobarbital. It is prescribed medications of first decision for single-tranquilize treatment of grown-ups with fractional or summed up tonic-clonic seizures. It is additionally the medication of decision for trigeminal neuralgia and oftentimes utilized for treating bipolar sorrow likewise noted to have critical psychotropic impacts in epileptics. The originator patent terminated quite a while in the past (in 1986) and there are currently a few nonexclusive choices. Be that as it may, after the presentation of the conventional contender's worries have emerged about the wellbeing and

restorative proportionality of nonexclusive CBZ tablets. (4-9).

Carbamazepine may have restorative impacts in the treatment of certain uneasiness issue (alarm issue, posttraumatic stress issue), liquor and narcotic sleep inducing withdrawal states (10). CBZ has a narrow therapeutic index and the relationship between dose and plasma concentrations of CBZ may be unpredictable because of differences in genetics, age, gender, absorption, auto induction and disease state between individuals. Also, the presence of numerous clinically significant drug interactions supports the need of using therapeutic monitoring of CBZ as an essential tool in designing a safe and effective therapeutic regimen for patients with epilepsy (11, 12). It has been used since the 1960's for the treatment of trigeminal neuralgias and then approved as an anticonvulsant in the U.S. in 1974. In the last decade the use of carbamazepine has been expanded to include the treatment of certain disorders of mood and behavior (13).

CBZ (5H-dibenzo [b, f] azepine-5-carboxamide) is insoluble in water, dissolvable in liquor, acetonitrile and $\text{CH}_3)_2\text{CO}$. CBZ is accessible in market with the brand names Carbamazepine, Carbatrol, Carbamazepine, Carbelan, Carbazin, Tegretol, Zeptol and Epitol. In spite of the fact that CBZ is ineffectively solvent in watery media, it has a high oral bioavailability in humans (14). In the amphibian condition, pharmaceuticals have been generally found. Among them, carbamazepine is recognized at the most noteworthy recurrence. The antiepileptic sedate is by all accounts exceptionally industrious in the earth, hence it qualifying as a reasonable marker for anthropogenic impacts in the sea-going condition (15, 16). According to the predicted no environmental concentration (PNEC) just carbamazepine has been identified in all sewage treatment plants with the best focuses (17). Carbamazepine showed a checked abatement in the seriousness of social dyscontrol and examples of pharmacological reaction may give pieces of information to organic components basic dysphoria and conduct dyscontrol (18). Carbamazepine may have prophylactic just as intense viability in patients with the two periods of hyper burdensome disease, including a few patients who don't react to lithium. Restorative impacts were accomplished with 600-1600 mg/day at blood dimensions of 8-12

microgram/ml with generally few symptoms. It is proposed that carbamazepine is a valuable medication for the prophylaxis of hyper burdensome sickness and double-blind, placebo-controlled parallel trial for acute mania (19-22).

Digestion happens basically in the liver through the cytochrome P-450 oxidase framework, creating carbamazepine-10, 11-epoxide (CBZ-EP) which is as dynamic and may achieve a dimension up to a large portion of that of CBZ. This is on the whole changed over to carbamazepine-trans-10, 11-dihydrodiol (CBZ-Di OH) by epoxide hydrolase before discharge in the pee. Degradation was observed in CBZ samples under stress conditions like acid hydrolysis, photolysis and thermal exposure. Mild degradation was observed for alkaline hydrolysis and exposure to oxidation by hydrogen peroxide (23, 24). The introduction of clozapine metabolism by carbamazepine might be partly mediated by CYP3A4 (25). Carbamazepine (CBZ) therapy is associated with cutaneous adverse reactions in up to 10% of patients. Predisposition to these hypersensitivity reactions has been linked to the human leukocyte antigen (HLA) genotype (26).

Methods

Collection of sample:

For the analytical studies, the sample products of Carbamazepine were collected from local market. The samples were properly checked for their batch number and expiry date. Here we used sample Carbazin, Tegretol and Zeptol respectively from local pharmaceutical companies.

Weight variation test:

The weight variety is routinely estimated to help guaranteed that a tablet contains appropriate measure of drug. Weight variation is measured by using an electronic balance (OHAUS). The % of weight variation is calculated by the following formula.

% of weight variation = $\frac{\text{Individual weight} - \text{Average weight}}{\text{Average weight}} \times 100$

Hardness test:

Hardness trial of material is demonstrative of its quality. Then again, one can say it additionally shows opposition capacity to harm its flawlessness. For tablet, it mirrors the inside holding quality of granules/powder which can ready to hold composite structure under connected outer power. Hardness

is also so called crushing strength. The hardness of the tablet was found by utilizing Monsanto type tablet hardness analyzer.

Criteria: Tablet hardness should lie between 5 to 10 kg / cm² (27).

Friability test:

Friability is the misfortune in weight of tablet in the holder because of expulsion of fine molecule from their surface. The friability of the tablet was resolved utilizing Friability analyzer (Shimadzu). It is communicated in rate (%). Limit is not more than 1% (28).

The % friability was then calculated by the following formula:

F = $\frac{\text{Initial weight} - \text{Final weight}}{\text{Initial weight}} \times 100$

Disintegration time test of tablet:

About 900ml water was taken in 1000ml beaker and the beaker was placed into the disintegration tester (Magumps). One Carbamazepine tablet was placed in each tube of basket rack and plastic disk is placed over each tablet and the basket rack is accurately positioned into the beaker. The temperature was maintained as 37±5. A motor driven device helps to move the basket up down through a distance of 5-6cm at a rate of 28-32 cycles per minutes. As Carbamazepine is an uncoated tablet and the tablet is manufactured according to USP so disintegration test was observed in water medium. The time at which all the Carbamazepine tablets went through the strainer was the crumbling time and the normal breaking down time were determined. In this way disintegration time was determined for three different brands of Carbamazepine tablets and the observed result for each sample was recorded.

Dissolution rate test of tablet:

Disintegration is the property or propensity of a medication to experience arrangement, which influences the rate of medication absorption. In the pharmaceutical business, sedate disintegration testing is routinely used to give basic in vitro medication discharge data for both quality control purposes, i.e., to survey bunch to-clump consistency of strong oral measurements structures, for

example, tablets, and medication advancement, i.e., to foresee in vivo medication discharge profiles. To determine dissolution of tablet dissolution test apparatus USP (VEEGD) and UV visible spectrophotometer (Beckman) are used. Standard stock solution of Carbamazepine was prepared by dissolving 10 mg of API in 100 ml of distilled water to produce a concentration of 0.1 mg/ml or 100mcg/ml. Each Carbamazepine tablet of each brand was placed into each beaker which contains 900 ml of 0.1N HCL solution into 1000ml beaker of dissolution apparatus. The disintegration medium was warmed up to $37 \pm 0.50^{\circ}\text{C}$ by an auto radiator and 100 RPM was balanced and the machine was begun. In every 15-min interval 5 ml of the solution was drawn out from the machine and it was then again recovered with the rest solution. The solution was then run through UV spectrophotometer (Beckman) and absorbance was collected at 287 nm. The experiment was repeated thrice and the mean value of the three was taken to calculate the dissolution time.

$$\% \text{ of release drug} = \frac{\text{Abs. of sample} \times \text{Conc. Of standard}}{\text{Abs. of standard} \times \text{Conc. Of sample}} \times \text{Potency} \times 100$$

Statistical analysis: The data was expressed as mean \pm S.E.M. (standard mistake of the mean). understudy's t-test was utilized for the assessment of information and $p < 0.05$ acknowledged as huge.

Results

Weight variation:

The weight variations of three brands of Carbamazepine were determined and the observed results are shown in the following table.

Hardness Test:

The hardness of three brands of Carbamazepine tablet was determined and the observed results are shown in the following table.

Friability Test:

Ten tablets from each brand of carbamazepine were selected to conduct the friability test. According to the pharmacopoeia (USP 30, NF 25), the friability value for the tablets must be less than 1%.

Disintegration time:

This is the measurement time of a tablet to disintegrate tablets into particles in contact with gastrointestinal fluid. The disintegration time of all brands of Carbamazepine tablet has met the specification of disintegration time is 15 minutes for uncoated tablet specified in USP.

Dissolution Test:

The dissolution rate of three brands of Carbamazepine tablets was determined. According to the official United States pharmacopoeia (USP 30, NF 25), all the brands must release more than 70% of active pharmaceutical ingredient within 45 min.

Discussion

Weight variation:

The USP specification of weight variation: $\pm 7.5\%$ for 130 to 324mg normal load of tablet & $\pm 5\%$ for more than 324mg of average weight of tablet. The highest average weight variation was found for Zeptol brand, 301.7mg and the lowest average weight value for Carbazin brand was recorded 280.2mg. The average weight value for Tegretol was recorded 275.2mg. It was observed that all of the brands meet the USP specification.

Hardness Test:

From the above results it was appeared that all brands of Carbamazepine tablets comply with the pharmacopoeia specification of hardness.

Friability Test:

From the (Table 3), it was found that all the brands of Carbamazepine had meet the friability specification as mentioned in the Pharmacopoeia.

Disintegration time:

It was seen from the result (Table 4) that none of the marketed Carbamazepine sample exceeded the specification and therefore it can be said that the entire marketed sample complied with the pharmacopoeia specification for tablet disintegration time. All the brands had shown rapid disintegration time and this rapid disintegration time was found for the type and amount of disintegrate used in that formulation.

Dissolution Test:

The dissolution behavior of all brands have shown in the Figure 1-3. The drug release % was plotted against the times. It was observed that all of the brands had released at least 70% of content within 30 minutes and 80% of content within 45 minutes.

Conclusion

Carbamazepine tablets have been analyzed to find their current quality status. For this purpose, the marketed sample of three brands of Carbamazepine tablets was analyzed by using established methods and apparatus. The result of weight variation, hardness, disintegration time, dissolution tests of all marketed products comply with pharmacopeia limit. Weight variation is within the limit for all brands, hardness is within the limit for all brands, disintegration time is also within the pharmacopoeia limit for all brands. Dissolution rate of each brands are also within the pharmacopoeia limit that no brands release not more than 10% drug in treatment with 0.1N HCL for 1 hour. All of the brands have proved that they have the potency which meets the pharmacopoeia limit / specification. The present study, although performed on a limited scale yet on the basis of professional judgment the data reported in this study can help the Drug Control Authority to get an idea about the quality status of the marketed Carbamazepine preparations in Bangladesh.

Acknowledgments

The authors are thankful to Head, Department of Pharmacy, Daffodil International University for all sorts of supports throughout the study.

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Table 1. Weight Variation of Carbamazepine (Carbazin, Tegretoland Zeptol 200mg)

Sl. No.	Brand Name	Average Weight(mg)	Average weight variation %	SD	RSD%
1	Carbazin	280.2	0.97	3.22	1.15
2	Tegretol	275.2	1.03	3.48	1.26
3	Zeptol	301.7	0.56	2.11	0.69

Table 2. Hardness of Carbamazepine (Carbazin, Tegretoland Zeptol 200mg)

Sl. No.	Sample	Mean weight(mg)	SD	RSD%
1	Carbazin	8.55	2.18	25.58
2	Tegretol	6.58	0.53	8.07
3	Zeptol	8.36	0.78	9.38

Table 3. Result of friability test

Sample	Initial weight of 10 Tablets in mg	Final weight of 10 Tablets in mg	Friability (%)
Carbazin	1368	1368	0(%)
Tegretol	1359	1349	0.73(%)
Zeptol	1507	1495	0.79(%)

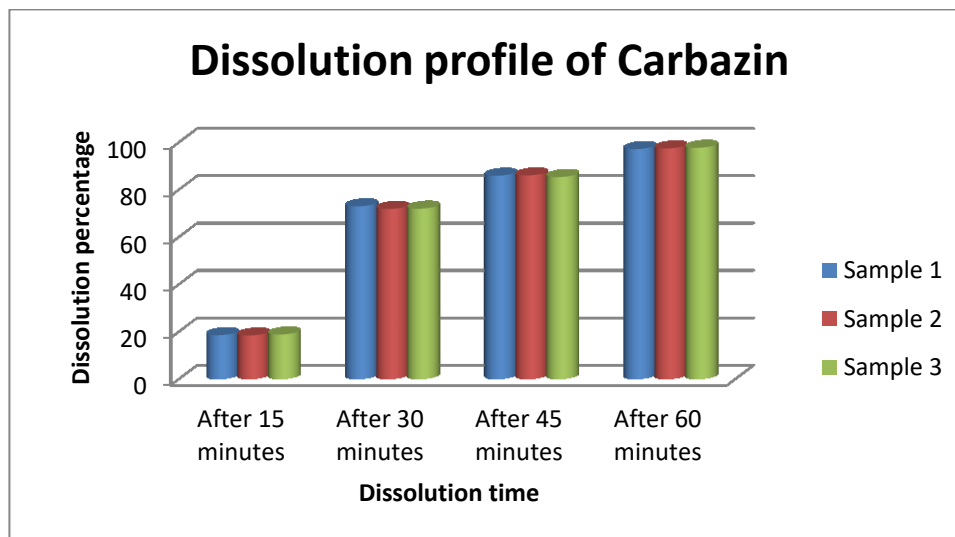
Table 4. Disintegration Time of Carbamazepine (Carbazin, Tegretoland Zeptol 200mg)**Figure 1.** Absorbance data of Carbazin

Figure 2. Absorbance data of Tegretol

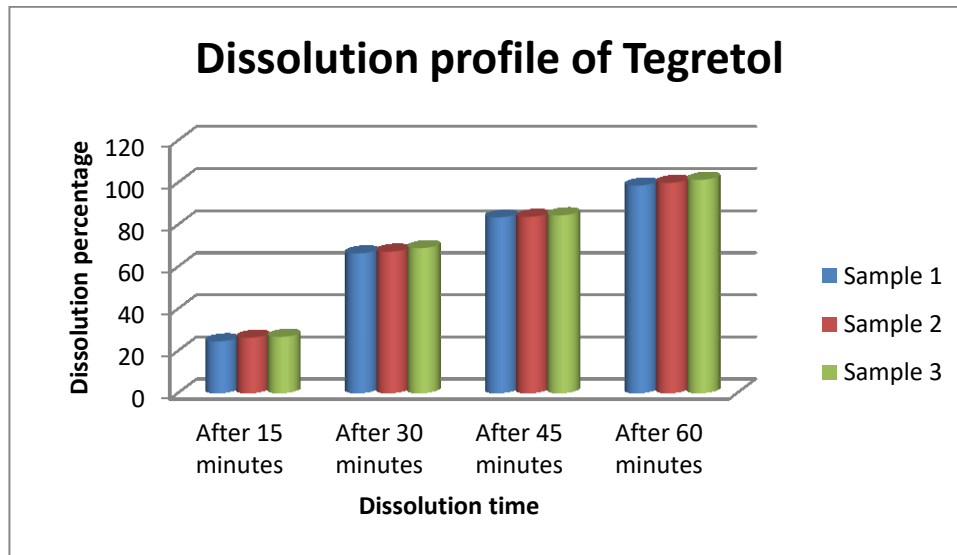


Figure 3. Absorbance data of Zeptol

