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Comparative *in-vitro* Evaluation of Carbamazepine 200mg Tablets

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Abstract: ***Carbamazepine (CBZ) is widely used as an antiepileptic drug, primarily for the treatment of partial and tonic-clonic seizures. Bipolar disorder can be treated by this medicine it also can be used in treatment of neurological pain and trigeminal neuralgia. The drug is absorbed slowly and has irregular gastrointestinal absorption after oral administration due to its limited water solubility. The main purpose of the present study was to compare pharmaceutical quality of different Carbamazepine 200mg tablets dispensed in Tripoli pharmacies, The physicochemical equivalence of five different Carbamazepine 200mg tablets was investigated through the evaluation of the uniformity of weight, thickness, diameter, friability, hardness, disintegration time, drug content as well as dissolution rate. The results of all the five brands of Carbamazepine 200mg tablets passed the official tests as prescribed by the pharmacopoeia standards including uniformity of weight, thickness, hardness, friability, disintegration time, drug content as well as dissolution rate. Acceptable external features as well as uniformity in diameter and thickness revealed for all the tablets. The entire brands complied with the official specifications for uniformity of weight where no tablet showed a deviation more than ±5%. Brand B had the highest crushing strength while brand D had the highest disintegration time compared to the other brands. All the brands had values within the range specified for friability and assay in the USP. The dissolution profiles showed that none of the brands had dissolution less than 75% within 60 minutes. The entire brands evaluated in this study could be considered bioequivalence, therefore it can be interchanged in clinical practice, and the patient can be safety switch from one brand to another. This sort of study is good indicator for the evaluation of the idealness of commercial products.***

Keywords: Carbamazepine tablets, evaluation, bioequivalence.

1. Introduction

Carbamazepine is considered a first line drug in the treatment of epilepsy and specific analgesic for trigeminal neuralgia [1]. Carbamazepine is chemically (5H- dibenzo [b,f] azepine-5-carboxamide) with chemical structure in Figure (1). It is practically insoluble in water and has four different polymorphs and the dehydrate form [2]. In spite of the fact that carbamazepine is ineffectively solvent in water media, it has a high oral bioavailability in humans [3].The rate of absorption of carbamazepine can differ markedly with different pharmaceutical formulations [4.5]. Loss of seizure control and occurrence of side effects in many cases have been reported when one carbamazepine immediate release product is exchanged for another [6]. In another study on the pharmaceutical quality of carbamazepine immediate release tablets, it is reported that differences were observed in dissolution rate even within a single brand [7]. Carbamazepine is highly sensitive to moisture in tablets, resulting in a change in the dissolution rate *in vitro* and *in vivo* [8-11].

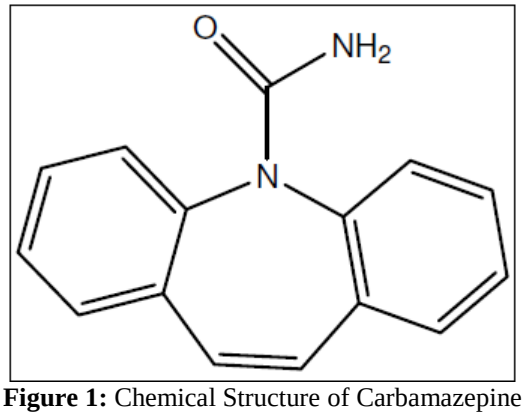

Figure 1: Chemical Structure of Carbamazepine

In Libya, there are many different brands of Carbamazepine tablets available from different multinational companies. Each brand has its own formulation which affects the release and delivery of drug and produce variable clinical responses. Evaluation of *in-vitro* release and the physicochemical properties of these brands are very important as it can be used to evaluate the bioavailability and pharmaceutical equivalence [12]. Various brands available in the market are considered pharmaceutically equivalent if they contain the same amount of active ingredients in the identical dosage form and meet the same compendia standards in strength, quality, purity and identity but may differ in shape, packaging, excipients, expiration time and labeling requirements. [13]

This study was conducted to evaluate and assess the pharmaceutical quality of different Carbamazepine 200mg tablets available in various pharmacy of Tripoli Libya. The assessment included the evaluation of weight uniformity, diameter, thickness, hardness, dissolution, disintegration, identification, and assay, to ascertain that all the brands under investigation are pharmaceutically equivalent.

2. Materials and Methods

Carbamazepine tablets having label strength of 200 mg of five different brands were purchased from local pharmacies in Tripoli Libya. The products were coded as A, B, C, D and E as illustrated in Table (1) and the study was performed within product expiration dates.

Distilled water, 1% sodium lauryl sulfate, methanol, analytical balance, hardness tester (PTB), friability tester, full automated disintegration tester, semi-automated dissolution tester, UV-visible spectrophotometer

Table 1: Label information of five different brands of Carbamazepine 200mg tablets under investigation

Product code	Batch No.	Manufacture Date	Expire Date
A	T1413	01-2011	12-2013
B	040H	09-2010	09-2014
C	E10	-	05-2015
D	A5H100	08-2011	08-2016
E	7901	05-2010	05-2013

2.1 Visual Inspection

Samples of 20 tablets from each batch were selected randomly and inspected for their external characteristics such as color, surface texture and shape, presence of grooves; monograms and coat were described based on the visual observation.

2.2 Weight Uniformity

Twenty tablets of each product code were weighed using an electronic digital balance, each tablet was weighed individually then the average weight was calculated for each brand. Tablets were examined for their uniformity of weight and the percentage deviation allowed by USP generally ±10% for tablets weighing 130 mg or less, ±7,55 for tablets weighing more than 130 mg to 324 mg and ±5% for tablets weighing more than 324mg [14].

2.3 Hardness Test

Hardness, thickness, and diameter of samples of 20 tablets were determined using tablet combination tester.(Erweka TBH 320 WTD Multi-Check tester, Germany) In the hardness test, pressure was applied on the tablet and the force caused the tablet to break up was recorded.

2.4 Friability Test

Ten tablets from each brand were weighed and placed into the friability testing apparatus. Tablets were rotated at 25 rpm for 4 minutes. The tablet were removed, dusted and accurately weighed, and then the friability percentage was calculated for each batch, the friability value for the tablets must be less than 1% of the weight of tablets being tested.

2.5 Disintegration Test

Samples of six tablets were selected from each brand. Tablets were placed in six tubes of the basket-rack assembly of the disintegration time tester PTZ Auto 1EZ (Pharma test, Germany) and perforated cylindrical plastic discs were put on top surface of each tablet. The assembly was allowed to move up and down in a beaker containing 1 liter of distilled water at 37±0.5^{0}C. The time taken to break each tablet into small particles and pass out through the mesh at the bottom of the tube was recorded. Mean disintegration time was calculated for each one of the brands.

2.6 Content uniformity test

The amount of Carbamazepine in tablets from each brand was determined according to USP. A standard solution was prepared by dissolving pure carbamazepine in methanol and a sample solution was also prepared by dissolving 20 carbamazepine tablets from each batch in methanol. The absorbance of the prepared solutions was determined using spectrophotometer at 285nm. The Carbamazepine amount in each tablet was calculated using the equation for the calibration curve, not less than 92% and not more than 108% of the labeled amount of active drug.[15]

2.7 Dissolution Rate Determination

The dissolution medium used in this test was distilled water 900 ml with 1% sodium lauryl sulfate. Six samples of each batch were placed in the apparatus. All samples were submitted to 75 rpm on apparatus and 37 ± 0.5 ^{0}C aliquots were collected at definite time interval for one hour and analyzed using spectrophotometer at 285nm. The percentages of cumulative carbamazepine amounts released from the tablets were calculated, and then the data were plotted and evaluated. [15]

3. Results and Discussion

Five different Carbamazepine 200 mg tablets (Table 1) were assessed for their pharmaceutical quality according to the described requirements that are stated in the official compendia. The evaluation tests were performed on the samples while in their intended shelf life. The apparent physical characteristics of the samples based on visual inspection were conducted. All tablets were elegant attractive appearance with smooth surface texture; there were no defects in the tablets integrity.

3.1 Physicochemical Properties of Carbamazepine 200mgTablets:

Weight variation, hardness, disintegration time, dissolution percentage, assay percentage as well as thickness and diameter are shown in Table (2).

Table 2: Evaluated physicochemical parameters of the five brands of Carbamazepine 200mg tablets

Brands	Average weight g	Dissolution %	Hardness (kg/cm^2)	Disintegration time (min)	Assay (%)	Diameter (mm)	Thickness (mm)	Friability %
A	0.30 ±0.0316	91.26	14.81	0:01:04	96.43	12.095±0.355	4.5220	0.099
B	0.46±0.02	95.62	17.3	0:00:50	90.81	11.164±0	4.9390	0.131
C	0.28±0.014	78.33	8.13	0:00:23	101.41	9.553±0.01	4.410	0.035
D	0.25±0.02	97.68	13.15	0:02:54	98.7	9.538±0	3.0550	0.118
E	0.26±0.014	81.36	4.99	0:00:28	104.5	9.006±0	3.9140	0.039

All brands of Carbamazepine tablets were consistent in their weight and exhibited uniform geometrical dimension parameters (Table 2) the deviation of the tablets weight from the average weight were in the permitted limit with a

deviation less than ± 5%. Brand D and E exhibited quite similar average weight and all the investigated brands demonstrated similar diameters and thickness except brand B that showed to be the largest in average weight , diameter and thickness among the selected brands. The hardness test results (Table 2), showed that brand B exhibited greater capability to resist chipping, while Brand C and E demonstrated the lowest and weakest solidity in comparison to the other brands. The friability value should be less than 1% all the tablets tested was within the limit.

All brands passed the disintegration time test according to the official limit. Tablets were broken up and disaggregated in to their original granules and particles within 15 minutes. Brand C and E demonstrated very rapid disintegration time compared to the other brands (Table 2). While brand D showed a more prolonged disintegration time (2:54min). The calibration curve of carbamazepine was shown in figure (2). It was found that all brands were in compliance with the standard limit for dissolution test (Figure 3). The drug release values were more than 75% in 60 minutes. All the assessed brands exhibited similar patterns of drug dissolution excluding brand C and E which had the highest drug release in 15min. The results obtained from the evaluation of active ingredients content were within the limits (92-108%), results were showed in (Table 3) so content uniformity test of all brands fit the criteria.

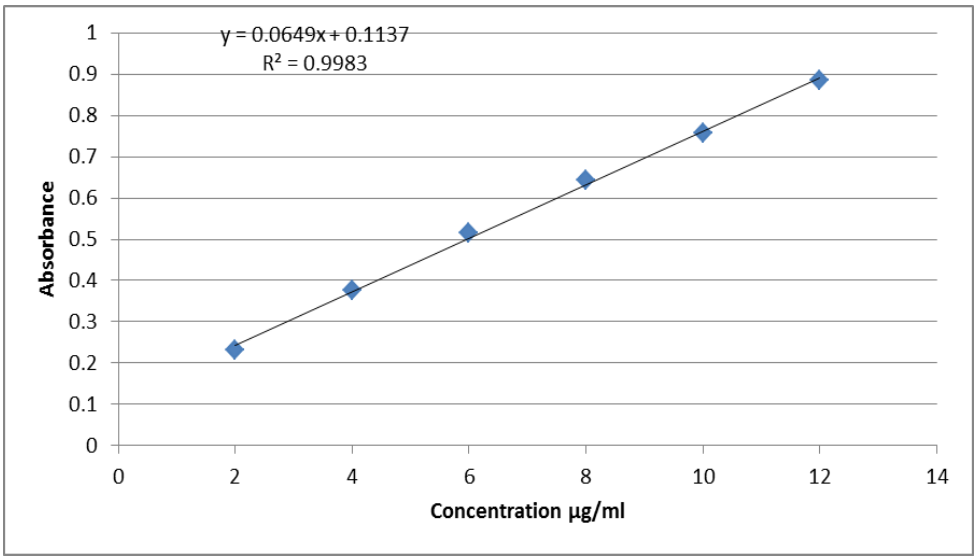

Figure 2: Calibration curve

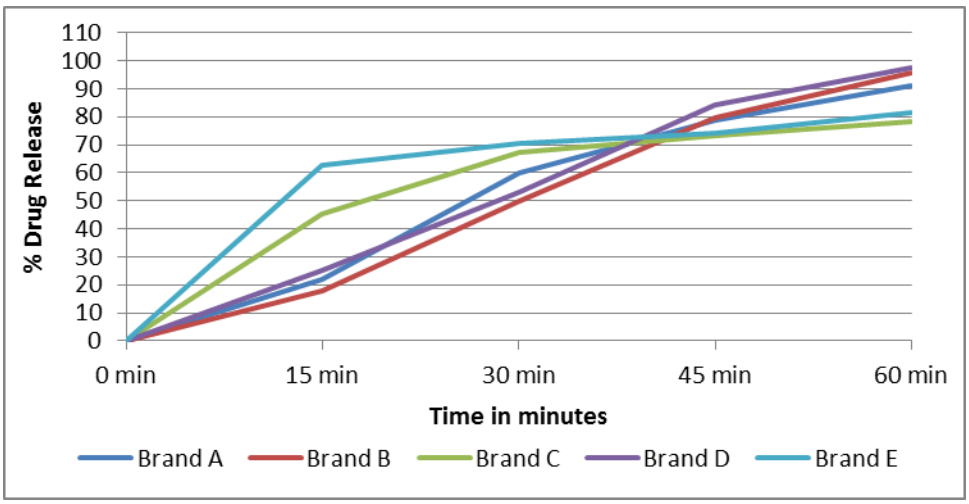

Figure 3: Dissolution curve of different brands of Carbamazepine tablet

4. Conclusion

From the result of this study, all brands of Carbamazepine 200mg tablets available in local market of Tripoli Libya complied with USP standards, even though the manufacture is different, there are no problems found just relates different between brands, and these variation do not indicate any defects, but it may be the industrialization or the steps of manufacturing in plant or different in additives in each brand and environmental conditions used during manufacturing. All brands can be interchangeable while there was no significant variation in the quality of the tested drugs, it can be inferred that the brands tested of Carbamazepine 200mg tablets are pharmaceutically equivalent. This study highlights the need for focusing on the post marketing evaluation of pharmaceutical products circulating in the markets originated from different manufacturers especially in developing countries.

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