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COMPARATIVE STUDIES OF GENERIC AND BRANDED TABLETS OF DILTIAZEM HYDROCHLORIDE

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ABSTRACT
Diltiazem hydrochloride is a benzothiazepine derivative calcium-channel blocker with proven antianginal and antihypertensive capabilities. Generic drugs are identical or bioequivalent to a branded drug in dosage form, safety, strength, route of administration, quality and performance characteristic and intended use. Branded medicine is the original product that has been developed by a pharmaceutical company. The present study was to compare the generic and branded tablets of diltiazem hydrochloride by performing various tests like hardness, thickness, weight variation, drug content and dissolution rate. The selected generic tablets were coded as G1, G2 and branded tablets were coded as B1, B2. It was observed that the result obtained for branded medicines were comparatively better than the results obtained for that of generic medicines, but both the results were found to be within the permissible limits.

KEYWORDS: Generic drugs, Branded drugs, Benzothiazepine derivative, Diltiazem hydrochloride.

INTRODUCTION
A generic drug should be the same as a brand name drug in dosage, safety, strength, how it is taken, quality, performance, and intended use. The FDA (Food and Drug Administration), in order to issue approval for a generic drug product, has laid down quite a few strict, mandatory regulations on tests and procedures to guarantee that the generic drug can actually be substitute for the brand name drug. The FDA bases its approval for substitution, on the therapeutic equivalence, of generic drugs through specific scientific evaluations. By law, a generic drug product must contain identical amounts of the same active principle as the brand name product. Drug products considered therapeutically equivalent have exactly the same effect as the brand name product.[1]

For economic reasons, the use of generic substitution is increasingly being supported by health authorities. Potentially, this may be problematic for drugs with a narrow therapeutic window if quality control and/or bioequivalence is not optimal. Many developing countries do not have the resources or expertise to carry out appropriate quality control resulting in widespread distribution of substandard or even counterfeit drugs. Even in countries where procedures are well regulated, substandard drugs reach the market from time to time.[2] Generic drugs are equivalent to the brand formulation if they have the same active substance, the same pharmaceutical form and the same therapeutic indications and a similar bioequivalence respect to the reference medicinal product. The use of generic drugs is indicated from many countries in order to reduce medication price. However, some points, such as bioequivalence and the role of excipients, may be clarified regarding the clinical efficacy and safety during the switch from brand to generic formulations. In conclusion, the use of generic drugs could be related with an increased days of disease (time to relapse) or might lead to a therapeutic failure; on the other hand, a higher drug concentration might expose patients to an increased risk of dose-dependent side-effects.[3]

Generic medicines are produced by multiple manufacturers after the patent of the brand-name equivalent expires, most of them are significantly less expensive than their brand-name counterparts. To control pharmaceutical expenses, in the last two decades many payers and providers have encouraged the use of generic drugs, whose market share sharply increased and exceeded 40 % of the market volume in most developed countries in 2011.[4] Some prior studies have demonstrated improved adherence with generic drugs compared to brand-name drugs, likely due to price. Generics are approved by regulators based on evidence of pharmaceutical equivalence and bioequivalence with

the brand-name product, even though they may contain different inactive ingredients. Still, many patients and providers perceive generics to be less effective and less safe than their brand-name counterparts. Some patients explicitly express concerns about the effectiveness of generic drugs to treat their serious illnesses.[5]

The standard quality control tests such as weight variation, thickness, hardness, drug content and dissolution are carried out to compare generic and branded tablets of diltiazem hydrochloride.[6] In the current work, the branded and generic tablets were collected and subjected for the above-mentioned quality control tests.

MATERIALS AND METHODS

Materials

Different branded (DILZEM-30, ANGIZEM-30) and generic tablets (DILTIAZEM 30, DTM 30) of diltiazem hydrochloride were purchased from the nearby pharmacy store and used for the comparative study.

In the study, different product codes were used for representing different branded and generic tablets as follows; DTM 30 represented as G1, DILTIAZEM 30 as G2, DILZEM 30 as B1 and ANGIZEM 30 as B2.

Methods

Determination of absorption maxima

The λ_{max} of diltiazem hydrochloride was determined by using UV spectrophotometer. The solution containing 10µg/ml concentration of Diltiazem HCI was prepared in phosphate buffer pH 6.8 and scanned over the range of 200-400nm against buffer pH 6.8 as blank using double beam UV spectrophotometer.[7]

Weight variation

20 tablets of each branded and generic were collected randomly and weight of individual tablet was determined. The average weight of the 20 tablets was calculated. Percentage deviation in weight of each tablet from the average weight was determined. Weight variation of tablets was determined by using following formulas.[8]

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

$$\text{Positive \% Deviation} = \frac{\text{Maximum weight} - \text{Average weight}}{\text{Average weight}} \times 100$$

$$\text{Negative \% Deviation} = \frac{\text{Minimum weight} - \text{Average weight}}{\text{Average weight}} \times 100$$

Thickness

The thickness of tablets was measured in mm by using screw gauge. The 5 tablets were selected randomly; the thickness of individual tablet and the average thickness of the tablets was noted. Total reading was calculated by using following formula.[9]

Total reading = P.S.R + [(C.H.R ± Z) × L.C

Where,
P.S.R = Pitch Scale Reading
C.H.R = Coinciding Headscale Reading
Z = Zero correction
L.C = Least Count

Hardness

Hardness of tablet was measured using Monsanto hardness tester. It is the pressure required to fracture diametrically placed tablets by applying the force. The hardness of the generic and branded tablets (5 tablets each) was determined which was expressed in kg/cm^2.[10,11]

Drug content

Drug content of generic and branded diltiazem tablets was determined. For this purpose, six tablets were weighed and crushed with pestle in a small glass mortar. The fine powder was weighed to get 180 mg (equivalent to 30 mg of diltiazem hydrochloride), and transferred to 250 ml conical flask containing 100 ml of pH 6.8 phosphate buffer and stirred for 45 min in ultra sonicator. Solution was filtered and the filtrates obtained were analysed UV spectrophotometrically by using following formula.[12]

$$\% \text{ Drug content} = \frac{\text{Concentration}}{1000} \times DF \times 100$$

In vitro Dissolution

The dissolution studies for branded and generic diltiazem tablets were carried out in USP type II (paddle type) apparatus. The release studies were performed at 75 rpm in 900 ml of phosphate buffer pH 6.8. 5ml aliquots were withdrawn at predefined intervals (15, 30, 45, 60, 75min) and the volume of the dissolution medium was maintained by adding the same volume (5ml) of fresh dissolution medium. The absorbance of the withdrawn samples was measured spectrophotometrically.[13]

RESULTS AND DISCUSSIONS

Determination of λ_{max}

The λ_{max} of diltiazem hydrochloride was determined by using phosphate buffer pH 6.8 which was scanned between 200-400nm in the UV spectrophotometer. The absorption maxima (λ_{max}) of 238 was selected for the present study. The following graph represents the (λ_{max}) of diltiazem hydrochloride.

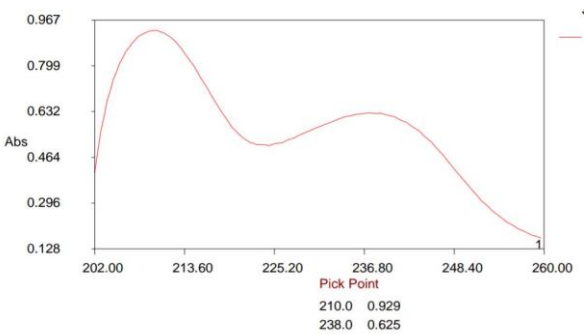

Figure No. 1: Determination of λ_{max}.

Weight Variation

According to I.P. specification, tablet weighed 80 mg to 250 mg can have the maximum of ±7.5% deviation. From the obtained results, it was observed that, no single tablet of generic and branded product crosses the percentage deviation.

Table No. 1: Interpretation of weight variation results.

Product code	Average Weight (mg)	Maximum Weight (mg)	Minimum Weight (mg)	Positive% deviation (%)	Negative % deviation (%)	Permitted value	Comments
G1	181	190	180	4.972	-0.552		
G2	173	180	170	4.046	-1.734	±7.5%	Passes the
B1	185	190	180	2.702	-2.702		limit
B2	188	190	180	1.063	-4.255		

Tablet thickness

It was found that the variation of tablets thickness was within the accepted limit of ±5%, where it was ranged from 0.046% to 0.187%.

A difference between the tablets was seen in the thickness values which is most likely due to the different choices in production which depends upon desire of each pharmaceutical company.

Hardness

The following table represents hardness of the two different diltiazem hydrochloride tablets from each of generic and branded formulation.

Table No. 2: Hardness of diltiazem hydrochloride tablets.

		Hardness	(Kg/cm^2)	
Trial No.	**DTM-30* (G1)**	**DILTIAZEM 30* (G2)**	**DILZEM 30* (B1)**	**ANGIZEM 30* (B2)**
1	5.2±0.17	5.4±.23	6.2±.017	6.8±0.15
2	5.5±0.21	5.6±0.30	6.0±0.19	6.6±0.16
3	5.2±0.14	5.2±0.19	6.0±0.22	6.6±0.35
4	5.4±0.19	5.0±0.24	6.2±0.15	6.8±0.42
5	5.4±0.25	5.2±0.16	6.0±0.22	7.0±0.22
Average	5.34±0.35	5.28±0.32	6.02±0.14	6.76±0.62
IP Specification		5-8Kg/cm^2		
Comments		Accepted		

*Values expressed as mean of 3 readings ± standard deviation (n=3)

The obtained hardness values indicate good mechanical strength with an ability to withstand physical and mechanical stress conditions while handling. According to IP specification, tablet hardness of diltiazem hydrochloride should range between 5-8 Kg/cm^2. Depending on this specification, it can be observed that hardness values were greater for branded tablets when compared to generic tablets but both were within the limits.

Drug content

The following table represent percentage drug content of the two different diltiazem hydrochloride tablets from each of generic and branded formulation.

Table No. 3: Drug content of generic and branded tablets.

Product name	% Drug content * (%)	Comments
DTM 30	73.45±0,95%	
DILTIAZEM 30	70.91±0.52%	Accepted
DILZEM 30	75.84±0.12%	
ANGIZEM 30	78.45±0.87%	

*Values expressed as mean of 3 readings ± standard deviation (n=3)

***In vitro* dissolution**

The generic and branded tablets used in the current study, found to have good %CDR that is in the range of 94.75% to 98.45% within the allowed time i.e 75min which indicates good bioavailability of the drugs.

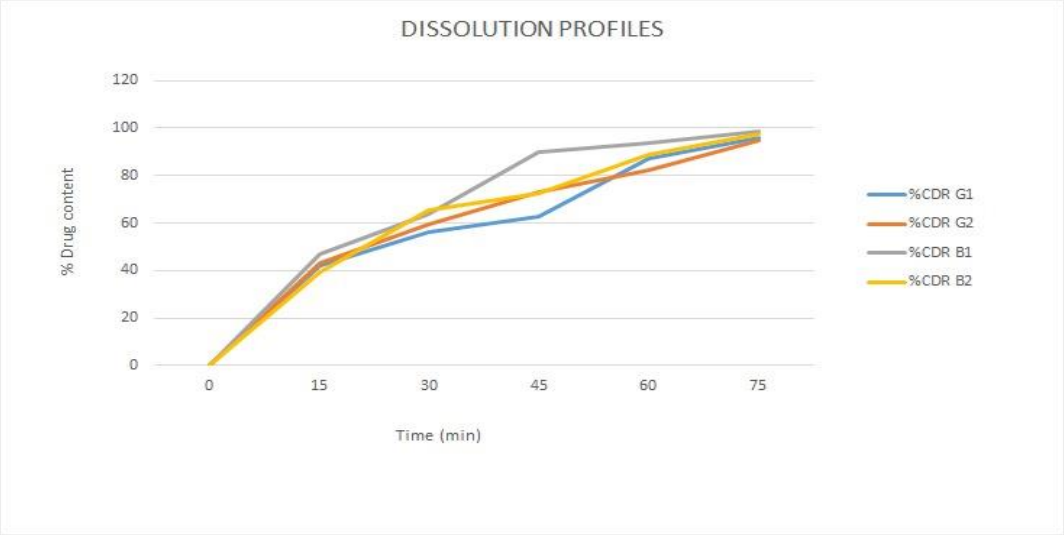

Figure No. 2: Dissolution profiles of generic and branded tablets.

CONCLUSION

For this study we have selected two different tablets of diltiazem hydrochloride from each generic and branded formulation which are antianginal and antihypertensive. The selected generic tablets were coded as G1, G2 and branded tablets were coded as B1, B2.

The tests performed were hardness, thickness, weight variation, drug content and dissolution rate. All the generic and branded tablets met the requirements and are within the limits of Pharmacopeial specification. It was observed that the weight variation, hardness, thickness, drug content and dissolution test showed better results for branded drugs compared to generic drugs, but both the values were found to be within the limits.

Hence, when compared to branded medications, generic pharmaceuticals are an appropriate alternative that is safe and effective. These medications are an affordable option for medication because they are bioequivalent, secure, and far less expensive than their branded counterparts.

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