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Comparative *In-vitro* Evaluation of Different Captopril Tablet Brands Commercially Available in Sindh, Pakistan

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Authors' contributions

This work was carried out in collaboration among all authors. Author BS designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors MIA and AA managed the analyses of the study. Authors RI and TA managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

Pharmaceutical products of standard quality are very important in appropriate management of diseases. However, substandard drugs are failing to achieve the therapeutic outcomes. In this study, six brands of Captopril tables having two strengths (three brands of 50 mg, and three brands of 25 mg), were collected from local pharmacies of Sindh. Standards of United States of Pharmacopeia (USP) were used for comparison of Captopril brands. Wide ranges of physicochemical standard quality control tests of USP were performed and results were recorded. All six brands of captopril tablets met the standard of aesthetic test, and weight uniformity test,

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diameter test and thickness test and disintegration test in which dissolved within fifteen minutes. Four brands of captopril tablet meet the standard of hardness test, whereas two brands fails to meet the standard with average hardness in brand C25-2 (3.05 ± 0.32), and brand C25-3 (2.28 ± 0.40). Five brands of captopril tablet meet the standard of friability test whereas one brand C25-3 fail to meet the standard with average loss of 6.22%. All six brands of captopril tablet meet the standard of dissolution test and dissolved not < 80% in 20 minutes. In last all six brands of captopril tablet meet the standard of assay test and contain the captopril within 90-110%. It was concluded that all brands of Captopril tablets meet the standard of USP and are therapeutically equivalent, so Physicians can prescribe them cost-effectively and interchangeably.

Keywords: Pharmaceutical products; therapeutic; cardiovascular; morbidity.

1. INTRODUCTION

Pharmaceutical products of standard quality are very important in appropriate management of diseases, whereas substandard drugs are failing to achieve the therapeutic outcomes of therapy. It is very important that pharmaceutical products should be manufactured from quality material in aseptic environment by following standard protocols and procedures. At the same time, it is also very important that manufactured pharmaceutical products of standard quality should retain its standard during its transportation and shelf life till consumed by patient [1-3] Most of the pharmaceutical products are manufactured by following either standards of USP or British Pharmacopeia (BP). Similarly, USP or BP provides the standard quality control tests for testing any pharmaceutical product to assure that product is of standard, will maintain its standard until consumed by patient, and will deliver the appropriate active concentration of drug for producing desired effect on human body. The pharmaceutical products of standard are very necessary in controlling the epidemic as well nonepidemic diseases throughout the world [4-7]. Most of the substandard drugs are manufactured and distributed in developing countries. So, in current study two strength of Captopril tablets (50 mg and 25 mg) were selected for analyzing their quality by evaluation of physicochemical parameters of various brands of Captopril tablets commercially available in Sindh, Pakistan, and comparison of physicochemical equivalence, physicochemical parameters and appropriateness of their interchangeability. Captopril tablet is used for management of hypertension that is the main reason and significant cause in the progress of cardiovascular and chronic kidney diseases worldwide. Hypertension or in simple words increased blood pressure (BP) is among the chronic medical diseases that raises the blood pressure in arteries [8]. Hypertension is also included in one of the epidemic diseases affecting the majority of the population throughout the world. It is one of the major risk factor responsible for development of number of diseases especially premature cardiovascular diseases (CVD) [9]. In CVD, hypertension is one of the major risk factor of stroke and ischemic heart diseases (IHD) responsible for 54.0% and 47.0% of total stroke and IHD cases [10]. It is estimated that till 2025 hypertesnion will affect more than 1.5 billion poulation of the world. Pakistan is one of the increasing developing countries widely affected with hypertension. Prevalence of hypertension in Pakistan was 17.0% that raised to 35.0% in next three decades. In South Asian countries Pakistan is in top three countries responsible for high burden of hypertension. Increasing hypertension in developing countries such as Pakistan may be due to poor diet, physical inactivity, obesity, stress, and low income. The pathogenesis of hypertension is very complex and multifactorial, which cannot be clearly understood by simple one mechanism. In development of primary hypertension different system of human bodies are involved.

The objectives of this are to analyze the quality of captopril tablets by evaluation of physicochemical parameters of various brands of Captopril 25 mg 50 mg tablets commercially available in Sindh, Pakistan and to compare the physicochemical equivalence, physicochemical parameters and appropriateness of their interchangeability.

2. MATERIALS AND METHODS

In this study we have purchased the six brands of captopril tablets of different pharmaceutical industries. We performed the same tests as given in Fig. 1 on each brand for confirmation of their quality. Comparison of quality was also conducted between all selected brands of captopril tablets.

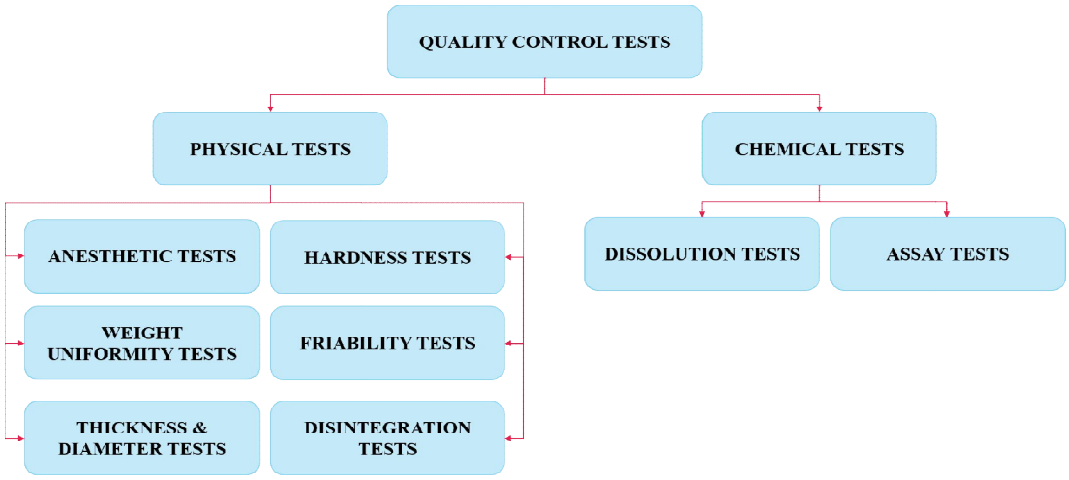

Fig. 1. Quality control tests for captopril tablets

In weight variation test required number of tablets of each brand were selected at random and weighed individually by using Shimadzu analytical weighing balance by following the standard procedure given in USP. For hardness test crushing strength of required number of tablets of each brand was determined by using Monsanto tablet hardness tester that was hard enough to bear the stress not less than 4.00 kg to break a tablet in to two halves. The force required to break tablets in to two halves was noted and observed for complying with U.S.P limits. The thickness and diameter of required number of tablets of each tablet brand will was determined by using Vernier Caliper Neiko 01407A which evaluates the degree of compaction during the punching of tablets and average value of tablets thickness and diameter was observed for complying with USP limits. Friability is a phenomenon in which mechanical shocks applied on tablets to check the crushing strength, capping and lamination of tablets. In this test required numbers of tablets of each brand were cause to cascade in Friabilator of origin Pharma test- Germany rotated at 25 rpm for 4 minutes. The weight loss was determined as a percentage of the initial weight and results were observed for complying with U.S.P limits that is 0.5 to 1%. In disintegration and dissolution tests required numbers of tablets of each brand were analyzed in disintegration apparatus Pharma test / Germany and dissolution USP Apparatus 1 (Basket), DT 800H, Erweka, Germany respectively to determine the tablet disintegration time and dissolution amount as per limits given in U.S.P. The assay of drug content in tablets involves the grinding of large sample followed by analysis of an aliquot. Analysis was performed by the method prescribed in the monograph by using HPLC Shimadzu 1100 Series, Germany and test results were compare according to limits given in U.S.P.

In this research six different brands of captopril tablets used for hypertension management were collected from different local medical stores of Sindh. Selected brands of captopril tablets were evaluated for pharmaceutical quality control tests. For standard procedures and standards of captopril tablets USP was used as a reference. For research captopril tablet of two strength were selected i.e., 25 mg, and 50 mg. For research three brands of captopril 50 mg and three brands of 25 mg were selected and given different codes for ease.

Table 1. Code names of selected brands

S: No	Code	Strength (mg)
01	C50-1	50
02	C50-2	50
03	C50-3	50
04	C25-1	25
05	C25-2	25
06	C25-3	25

3. RESULTS AND DISCUSSION

In Aesthetic test, twenty tablets of each brand of captopril were selected and evaluated with human eye. All tablets pass the test and met the standard criteria of USP except product C25-03 in which powder was observed in blisters. Results of anesthetic test are summarized in Table 2.

The weight of all three brands of captopril 50 mg tablets is greater than 130 mg therefore standard limit for each captopril 50 mg tablets is ± 7.5%, whereas all three brands of captopril 25 mg tablets is less than 130 mg therefore standard limit for each captopril 25 mg tablets is ± 10% and their results are summarized in Table 2. Result shows that all six brands of captopril tablets passed the weigh uniformity test. In diameter and thickness tests, ten tablets of each band of captopril were evaluated and results are summarized in Table 3. Allowed limit for average diameter and thickness of all captopril tablets is ±5%, and their results shows that all six brands of captopril tablets passed the diameter test and thickness tests. The significance of these three physical tests such as weight variation, diameter and thickness tests ensure that the tablets in each brand are within the appropriate size range. Another physical test like hardness and friability test are used to measure the ability of the tablets to resist chipping, abrasion or breakage under conditions of storage, transportation and handling before storage. The allowed limit for average hardness of uncoated captopril tablet is 4-8 Kg/cm^2, and their results are summarized in Table 3. which shows that all three 50 mg brand and one 25 mg brand having code C25-1 pass the test, whereas two 25 mg brand having codes C25-2, and C25-3 completely fail the test and no tablet was within the limit. All tablet of both brands breaks by applying force lower than 4 Kg/cm^2. Whereas allowed limit for friability of uncoated captopril tablet is less than 1%, and results summarized in table 02 shows that all three 50 mg brand and two 25 mg brand pass the test, whereas one 25 mg brand having codes C25-3 failed in this test. This failure in hardness and friability among the few brands of captopril my resulted from the use of inappropriate or little amount of binding excipient during formulation, inadequate moisture content during compression or insufficient compression pressure during tableting. The last physical test performed on each captopril brand was disintegration test in which six tablets were selected from each brand, and then test was performed on disintegration test apparatus. The allowed limit for disintegration of captopril tablet is 15 minutes, and their results are summarized in Table 3 that shows all six brands of captopril tablets passed the disintegration test. The chemical analysis start with dissolution test of captopril in which six tablets were selected from each brand then test was performed on dissolution test apparatus, and samples for result of dissolution test of captopril were collected at twenty minutes for checking the absorbance of each sample on UV-Visible spectrophotometer at 205nm. Table 3 shows the dissolution and statistical analysis of all captopril brands that all tablets met the standard and dissolved more than 80% within 20 minutes. In last, assay of captopril tablets was performed on HPLC for determination of the amount of captopril present in each formulation. Table 3 shows the assay results of all captopril brands are within limit i.e., 90-110% and relative standard deviation (RSD) met the standard i.e., RSD should not be more than 2%.

Table 2. Aesthetic characteristic of captopril tablets

Observation	C50-1	C50-2	C50-3	C25-1	C25-2	C25-3
Color	White	Pale green	White	White	White	White
Color Shade	Light	Light	Light	Dark	Light	Light
Uniformity of color	Uniform	Uniform	Uniform	Uniform	Uniform	Uniform
Tablet finish	Smooth & Uncoated	Smooth & Uncoated	Smooth & Uncoated	Smooth & Uncoated	Smooth & Uncoated	Smooth & Uncoated
Shape	Oval, convex	Oval, biconvex	Round, convex	Square, convex	Round, convex	Round, convex
Cracking / Mottling	No	No	No	No	No	No
Blister Packing	Comply with standard	Comply with standard	Comply with standard	Comply with standard	Comply with standard	Powder material seen in blisters
Primary carton	Comply with standard	Comply with standard	Comply with standard	Comply with standard	Comply with standard	Comply with standard

Table 3. Physico-chemical test results of the six selected brands of captopril tablets

Brand	Wt. variation (gm)	Hardness (kg/cm^2)	Friability (%)	Disintegration (min)	Dissolution rate % at 20 min	Drug content (%)
C50-1	0.203±0.009	4.90±1.32	0.26	7.37±0.18	93.58 ± 4.59	94.8 ±0.084
C50-2	0.196±0.004	6.25±0.69	0.0	5.43±0.35	101.47 ± 6.06	90.1±0.183
C50-3	0.180±0.006	5.50±0.87	0.58	1.89± 0.49	100.77 ± 4.50	98.1±0.003
C25-1	0.099±0.003	6.47±0.48	0.54	2.47± 0.52	95.52 ± 7.06	99.7±0.102
C25-2	0.124±0.001	3.05±0.32	0.43	1.43±0.10	120.87 ± 9.52	94.5±0.146
C25-3	0.127±0.006	2.28±0.40	6.22	0.88±0.35	92.17 ± 4.68	95.0±0.547

4. CONCLUSION

All selected brands of Captopril tablets met the standard of USP. All selected brands of Captopril tablets pass the aesthetic, weight uniformity, diameter and thickness test. Four selected brands of Captopril tablets pass the hardness test except C25-2, and C25-3 brand that breaks at lower than 4 Kg. Five selected brands of Captopril tablets pass the friability test except C25-3 brand that shows the loss of 6.22% drug concentration. All brands of Captopril tablets also met the standard of USP for dissolution and disintegration test. Most importantly, all brands of Captopril tablets met the standard of assay test. All selected captopril tablet available in market of Sindh are therapeutical equivalent and of standard of USP, and can be prescribed interchangeably. All selected captopril tabletsare of standard, so Physician can prescribe the cost-effective drug for management of hypertension.

DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

CONSENT

It is not applicable.

ETHICAL APPROVAL

P.M.C.H Nawabshah Ethics Committee approved the study.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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