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ORIGINAL ARTICLE

# Comparative Analysis of Five Brands of Lisinopril Tablets in Yemeni Market

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## Abstract:

**Background**: In poor countries such as Yemen, the cost of drugs is a factor affecting the patient's decision to buy it and generic medicines are introduced as cheaper alternatives to the high cost brands. Thus, this study aimed to identify the physicochemical similarity of five products of tablets comprising much Lisinopril (antihypertensive) taken from various pharmacies where retail medications are rendered to the Yemeni market.

**Methods:** In this study, the researcher has conducted an assessment to the quality and physicochemical uniformity of five various products of Lisinopril tablets. The uniformity of weight, friability, crushing strength, disintegration and dissolution tests and chemical test of the tablets were evaluated as major factors.

**Results:** Results showed that all five products of the Lisinopril 5 mg tablets were compatible to the standards of British Pharmacopoeia (BP) in terms of uniformity of weight (91.04 – 137.4%), the crushing strength/hardness test (3.93 – 7.92%) and the friability test (0.18 – 0.29%). All the products have showed good results about the disintegration time (15 sec – 7 min and 5 sec) and dissolution test (96.67 – 103.7%). The active content of products ranged from 102.8 – 108%.

**Conclusion:** The five brands of Lisinopril 5mg tablets, which were analyzed, have matched the BP quality standards and were physically and chemically consistent. Thus, cheap generic medicine can be used as alternative for innovator products.

**Key words:** Lisinopril, Brands drugs, Uniformity of weight, Disintegration, Friability, Hardness

## 1. Introduction

The increasing numbers of generic drug products are available in the market, making it possible to people involved in providing healthcare services to select a particular generic drug from several equivalent products (1). Internationally, statistics found that generic drugs are dramatically used, giving rise to a high cost of drug budgets. Since the use of generic drugs is a lower cost than the new products or brands, great savings in health care payment can be made. However, plenty of medical doctors have a doubt of quality of generic drugs (2, 3) and their reliability and to replace a particular drug (4). Empirical studies found that generic medications have lower therapeutic efficiency and value than branded products (5, 6) even though, they are bio-equivalents of their innovative peers and are produced under good manufacturing practices (7).

Statistics reported by countries in Central and Eastern Europe and some countries from the former Soviet Union showed that manufacturers of imported branded products promote that generic drugs are lower quality compared to the branded ones (8). To obtain approval from FDA for a generic drug, it must match the newly-produced drug in active ingredients, strength, dosage form, route of administration, the same usage indications, bioequivalent meet, batch requirements for identity, purity, quality and be manufactured in accordance with the strict standards of FDA's good manufacturing practice regulations required for innovative products (9).In Yemen as a poor country, the cost is the key factor in defining the patient access to health care. Many people postpone the use of medications required because of the high cost of branded products. Under these circumstances, locally manufactured medicines are offered as alternative due to their low cost. The objective of this study is to assess the quality of these five brands of Lisinopril tablets that are commercially available in the Yemeni market.

## 2. Materials and Methods

### *Samples*

Five commercial products (brands) of Lisinopril, labelled to contain 5 mg per tablets, from different manufacturers were purchased and coded as A, B, C, D and E and then separated (Table 1). Various analytical methods and tests which are important for the development and manufacture of pharmaceutical formulations (10) were performed for all the tablet brands of five formulations in the study.

**Table 1.** Country of origin, manufacture and expiry dates of five brands of list tablets

| Country | Brand | Code | Strength (mg) | Exp. Date |
|---|---|---|---|---|
| Sweden | Zestril® | A | 5mg | 12 \ 2014 |
| Yemen | Lotensin® | B | 5mg | 1\ 2014 |
| Yemen | Lisistril® | C | 5mg | 1 \ 2013 |
| Jordon | zenoril® | D | 5mg | 7 \ 2014 |
| India | cipril® | E | 5mg | 12 \ 2013 |

### *Weight Variation Test*

All the products were subjected to a number of weight variation tests. Thus, any variation in the weight of each single tablet is evidence that there is a similar variation in the content of the drugs. It is possible to achieve better tablet hardness and friability through a strict control for the tablet weights (11). The appropriate ratio for the deviation of the tablet weigh whose average weight of 250 mg or above should not exceed 5% (12). A weight test was performed individually for ten tablets which were selected from each of the product by using electronic balance (Kern, Germany, Model: D-72336). Their average weights were calculated. For all tablet products, the researcher used a mathematical equation for weight variation as follows (13):

Highest weight variation = (Highest weight − Average weight/Average weight) × 100

Lowest weight variation = (Lowest weight − Average weight/Average weight) × 100

*Hardness test*

Hardness refers to the strength of a tablet to resist machine-driven shocks during handling process of manufacturing, packaging and shipping (14). The adequate value of hardness or crushing strength of tablet is 4kg or above (15). During the study, the researcher adopted a Tablet Breaking Force Tester to determine the hardness of all tablets, Germany (PHARMA TEST: PTB). For all categories, five tablets of each product were selected and their hardness was also indentified.

*Friability test*

Friability test is designed to assess the ability of a tablet resistance to abrasion in packing, handling and transporting. In this study, the researcher adopted PHARMA TEST: PTB. Friabilator (Germany) to determine friability. The percentage (%) was the ratio of friability. Ten tablets for each brand were initially weighed and transferred into friabilator which was operated at 25 rpm for 4 minutes (up to 100 revolutions). The tablets were weighted weighting again. The following formula shows the ratio of their friability after being weighted (13):

% Friability = (Weight before test − Weight after test/Weight before test) × 100

In most cases, the substantial level of weight loss of conventional compressed tablet is not more than 0.5 to 1% (14).

*Disintegration time test*

Disintegration refers to the tablet fraction process into smaller pieces. It is deemed to be the primary move to dissolution. The maximum disintegration time for USP uncoated tablet must be as short as 5 minutes but most of the tablets have a maximum disintegration time of 30 minutes (14). The method used as defined in the USP/NF was (PHARMA TEST: PTZ S) (1980). For individual tablet of all the products, the average of disintegration instrument used amounted at 100 ml of 0.1N HCl whereas the temperature was maintained at 37±1°C all over the testing process. The researcher, thus, selected six tablets of each product and placed them in each of the cylindrical tubes of the basket. In addition, the disc was also used. During the time test process, the researcher of this study recorded the time consumed to break each tablet into small pieces and pass out through the net. Calculation of the total disintegration time was performed for each tablet of the products (16).

*The dissolution rate test*

In most cases, test of dissolution is performed to define drug release pattern during a short period of time (17). In this experiment, the researcher used Dissolution Tester – Germany (PHARMA TEST: D-63512) to test dissolution rate of each tablet of all the products. In order to define the dissolution rate for each of the tablet products, an amount of 900 ml of phosphate buffer, pH 2 was used as a dissolution medium. The speed of the experiment was 50 rpm at temperature of 37±1ºC for individual test. Besides, amount of 5 ml as samples was taken at a regular time period of 10 minutes as pre-estimated. The same formula continued up to 30 minutes by replacing equal amount of fresh dissolution medium (phosphate buffer, pH 2). As a result, the accepted samples were subjected to suitable dilution and analysis by using HPLC at 215 nm for Lisinopril. Absorption was measured and the rate of drug release was calculated (17, 13). All measurements were performed in triplicate.

*Content of uniformity test*

Content of uniformity of the active ingredient in tablets was carried out by HPLC (Shimadzu CLharASS-VP V6.12 SP3, Kyoto, Japan). The mobile phase consisted of (Mono basic phosphate buffer: Acetonitrile) (80:20) pH=2.0. The experiment showed that 2.0 ml/min was the aggregate rate, and 20 µl for the injection volume and 215 nm for the detection wavelengths (Lisinopril). ODS hypersil C18 Column (25cmx4.6mm packed with 10 µm silica) was used throughout the experiments. Tests for chemical compliance and content of dynamic ingredient uniformity were performed in accordance with the standard method specified in BP 2002.

*Data Analysis*

In this study, the researcher used the mean ± standard deviation to analyze data for weight uniformity test, friability, crushing strength and the disintegration and dissolution times of the tablets.

## 3. Results

All the samples used for the study were within their shelf life at the time of investigation. The results of the physicochemical properties of the various brands of Lisinopril are presented in Table 2 and 3.

The uniformity of weight determination for all brands of Lisinopril tablets ranges from 91.04% to 137.4. The tablet crushing strength of A, B, C, D and E brands of Lisinopril ranged from 3.93 to 7.92. All Lisinopril brands showed friability values ranging from 0.18% to 0.29% (Table 2).

The overall disintegration time for Lisinopril tablet brands was between 15 seconds to 7 minutes and 50 seconds. It was observed that all the samples had the dissolution time ranging from 96.67% to 103.7%. The active content of products was between 102.8% – 110.8 % (Table 3).

**Table 2.** Results of unofficial quality control tests conducted on the Lisinopril tablets

| Code | Weight uniformity test, mg Mean (± SD) | Crushing Strength Kgf Mean (± SD) | Friability Mean (± SD) |
|---|---|---|---|
| A | 106.3 (0.9) | 4.61(0.195) | 0.188 (0.111) |
| B | 99.12 (1.8) | 7.92 (0.608) | 0.202(0.022) |
| C | 101.2 (2.5) | 3.93 (0.452) | 0.494(0. 0111) |
| D | 91.04 (2.2) | 5.61(1.558) | 0.231(0.192) |
| E | 137.4 (2.7) | 4.12(0.564) | 0.291(0.142) |
| **LIMITS** | | >4 kg/cm$^2$ | <1% |

**Table 3.** Results of official quality control tests conducted on the Lisinopril Tablets

| Code | Disintegration Time (min) Mean (± SD) | Dissolution after 30 min Mean (± SD) | Active Content Uniformity test Mean (± SD) |
|---|---|---|---|
| **A** | 0.67 (0.102) | 101.03 (1.04) | 110.8 (1.414) |
| **B** | 0.25 (0.012) | 103.7 (0.496) | 110.4 (2.969) |
| **C** | 5.36 (0.313) | 96.67 (4.21) | 106.65 (6.611) |
| **D** | 7.50 (0.504) | 103.43 (1.193) | 106.87(2.142) |
| **E** | 4.44 (0.455) | 99.68 (3.751) | 102.8 (1.555) |
| **LIMITS** | < 15 | >70% | 95-105% |

## 4. Discussion

In this study, five branded products of Lisinopril tablets were selected from different pharmacies in Sana'a, Yemen. To assess and measure their quality control, five branded products were subjected to a number of tests. The result of the uniformity of weight for all the products showed compliance with the official specifications, since no brand deviated by up to 5% from their means. A variation beyond the pharmacopoeia limits indicates unacceptable brands (18). All the products gave less than 0.5%w/w loss in weight with the friability test determination, which is less than the official specification of 1%w/w, showing that all the

brands could resist abrasion without loss of tablet integrity (18). Suitable tablet hardness and reasonable friability are required for the satisfaction of consumers (19). The mean crushing strength which measures the level of hardness of the tablets is within the limits. In spite of the crushing strength is not an official method of tablet quality evaluation, it is still valuable in evaluating the integrity of tablet dosage forms (18). According to the specification of BP criteria, it has been shown that all the products have passed the disintegration test (18). The BP shows that not less than 70%w/w labeled content should dissolve at 45 minutes. The study results has shown that the five brands reached more than 96% at 30 minutes which mean that the five brands may show good bioavailability profile in vivo. Dissolution rate has been reported to have a direct bearing on the bioavailability profile of tablet dosage forms as it can be used to predict the drug release pattern in vivo (20).

According to the United State Pharmacopeia (USP), a Lisinopril tablet should contains not less than 90% and not more than 110% of Lisinopril. The results of the active content of products of the five brands in this study were within the limits which are in parallel with other studies which demonstrated brand-brand equivalence with the innovator product (21, 22). On the other hand, An empirical study on 85 generic brands from 21 countries found that 91% of the evaluated generic Piroxicam products failed to meet the routine in vitro USP quality assurance criteria for potency and/or dissolution (23). For such variation in dissolution, it may give rise to altered bioavailability and efficacy, and hence therapeutic failure. Furthermore, this study is incompatible with most recent studies that were conducted in Nigeria to compare between different products of Lisinopril tablets using HPLC and UV Spectrophotometer (24).

## 5. Conclusion

This study concluded that Lisnopril from all brands demonstrated compliance with the official specifications in terms of uniformity of weight, hardness, disintegration, friability and chemical content. Thus, cheap generic medicine can be used as alternative for innovator products.


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### Conflict of interest

The author declares that there is no conflict of interest.

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