



## **In vitro Comparative Quality Evaluation of Formulated and Marketed Losartan Potassium 25 Mg Tablets**

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### **Authors' contributions**

*This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.*

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### **ABSTRACT**

**Background:** The outcome of the drug therapy depends largely on the quality of the drug product. The lower quality of the drug product can be the reason for therapeutic failure. The present study was designed to evaluate the quality standard of Losartan Potassium tablet brands available in Bangladesh market to get an idea of quality standard of drug product people consuming in this country.

**Materials and methods:** Three brands of losartan potassium were chosen randomly. Tablets of each brand were collected from individual retail outlets to gauge the qualitative evaluation and compare them by *in-vitro* drug release study. They were subjected to various quality control tests to measure the hardness, thickness, weight variation, friability, disintegration time, potency, stability, and dissolution profile. All these tests were performed according to the U.S. Pharmacopeia (USP) specification. Researchers further formulated a batch of tablet of Losartan Potassium and

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compared them with the existing brands. The formulation was prepared by optimizing the existing one available in the USP. Test results of the existing brands were taken into consideration during the optimization of the formulation.

**Results and discussion:** Two brands passed the weight variation test, while one brand exceeded the range ( $\pm 5\%$ ). The potency was determined instantly and 15 days after keeping the tablets in a stability chamber at 75% humidity and 60°C temperature. The potency of two brands degraded below the lower limit specified by the USP, while that of the remaining one was within the limits. Results of other tests were within the specified limits. Tablets prepared in the lab using an optimized formulation showed a better dissolution rate than the existing brands.

**Conclusion:** Some of the brands failed to meet the desired quality, so the quality control system of that companies should be upgraded and a proper monitoring system should be developed by the drug administration.

*Keywords: Losartan potassium; quality; evaluation; formulation; potency and marketed brands.*

## 1. INTRODUCTION

Hypertension is a familiar health problem, which is affecting around 1.39 billion people worldwide [1]. It occurs when blood creates an extended-term force on the artery wall and is associated with heart disease. In hypertension, systolic pressure is above 140 mmHg, and diastolic pressure above 90 mmHg [2]. If it develops, it requires life-long treatment. But one can lower/control blood pressure by losing weight, reducing salt intake, and regularly doing exercises [3]. However, these activities may not be enough for some individuals so they need medication for controlling the blood pressure.

Losartan is a non-peptide antihypertensive drug. It asserts its action by blocking the angiotensin-II receptors [4]. The orally active potassium salt of losartan is Losartan Potassium that passes through persistent first-pass metabolism by an enzyme named cytochrome P<sub>450</sub> [5] which converts it into a carboxylic acid metabolite. The resulting metabolite is found in human plasma and urine. Besides carboxylic acid metabolite, many other metabolites are also produced. It is a Biopharmaceutical Classification System (BCS) class III drug [6]. Chemically, it is (S)-1-[N-[(ethoxycarbonyl)-3-phenylpropyl]-L-alanyl]-L-proline and its empirical formula is C<sub>22</sub>H<sub>23</sub>ClKN<sub>6</sub>O [7]. It is a slightly yellowish solid substance with a molecular weight of 461 and a melting point of 183.5–184.5 °C. It is soluble in water (3.3 mg l<sup>-1</sup> at pH value of 7.8) and has a pKa value of 4.9. It is available on the pharmaceutical market in the form of tablets.

This study's primary objective was to evaluate the quality control parameters of Losartan Potassium tablets available on the market and also to propose its new formulation. When tablets

are manufactured, each tablet must comply with the standard quality. Still, they may or may not maintain the same quality after reaching the market, after a particular time.

## 2. MATERIALS AND METHODS

### 2.1 Chemicals and Reagents

All research-grade chemical reagents, such as reference standard Losartan Potassium tablets, distilled water, and other logistical supports were provided by Pharmaceutical Technology Lab, Department of Pharmacy, University of Asia Pacific (UAP), Dhaka-1205, Bangladesh.

### 2.2 Sample Collection

The marketed sample of three brands (twenty tablets of each brand) was collected from the retail shop situated in the Dhaka city. These three brands of tablets were marked as A, B, and C. Physical aspects, name of the manufacturer, batch number, manufacturing date, expiry date, manufacturing license number, Drug administration registration (DAR) number, and Maximum retail price (MRP) were appropriately checked at the time of collecting the tablets.

### 2.3 Study Design

The evaluation of weight variation, friability, hardness, disintegration time, and dissolution profile for quality analysis of Losartan Potassium brands of tablets available in Bangladesh was studied. For this study, various standard test methods related to estimating the quality of tablets were conducted.

### 2.4 Weight Variation

To estimate the weight variation, firstly, the weight of the first Losartan Potassium tablet was

measured using an electrical weight balance (Shimadzu, Japan). Then, the weight of the second tablet was measured and this process was repeated for the other 18 tablets. Following the same process, all of the 20 tablets of each brand were weighted, and the weight variation was determined [8].

By using the following equation, the percentage weight variation for each tablet was calculated:

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

## 2.5 Thickness and Diameter Test

Twenty tablets of each brand were taken and placed in a digital caliper (Anyi Instrument Co., Ltd.) horizontally and vertically to measure the tablet thickness and diameter, respectively. The diameter of tablets was measured in millimeters [9].

## 2.6 Hardness Test

To perform the hardness test, six tablets of each brand were placed one by one between the fixed and moving jaw of a hardness tester (Dr. Schleuniger Pharmaton), and the indicator's reading was adjusted to zero. The pressure was gradually applied to a tablet until it was broken. The pressure was expressed in Newton (N) [8]. Typically, the hardness of a coated tablet ranges from 4 to 8 kg (1 kg = 10 Newton).

The average hardness was calculated by using the following equation:

$$\text{Average Hardness} = \frac{\text{Total hardness of tablets}}{\text{No. of tablets}}$$

## 2.7 Friability Test

To perform the friability test, ten tablets of each brand were taken and their weight was measured. Those ten tablets were placed in a friabilator (Electrolab, India). The machine was running at 100 rpm for 4 minutes, where tablets were exposed to rolling and repeated shocks as they were falling six inches each turn within the apparatus. After stopping the machine, the tablets were taken out, wiped with tissue paper and weighted. Differences in the weight before and after running the friabilator were determined. The value was expressed in percentage. During this test, the loss of weight indicated the percent friability and it should not be more than one percentage [8].

By using the following equation, the percentage friability for each tablet was calculated-

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

## 2.8 Disintegration Test

To perform the disintegration test, four tablets of each brand were placed individually in each of the three tubes of the apparatus, and a disc was placed at the mouth of the tubes. This arrangement of the tubes was placed in a water medium. The basket rack assembly was positioned in 700 ml of water at  $37 \pm 2$  °C. The system was moving up and down from a distance of 5 to 6 cm at a frequency of 28 cyc/min. The time when no palpable mass remained in the apparatus was recorded using a stopwatch and considered as the disintegration time. The same procedure was performed for all three tablet brands [8]. Disintegration time for an uncoated or a film-coated tablet should not be more than 30 minutes. If one or two tablets fail to disintegrate, the process should be repeated with 12 tablets. So, 16 tablets out of 18 must completely disintegrate within the time. If two or more tablets are not disintegrated, the batch is rejected [10].

## 2.9 Potency Test and Stability Test

At first, the individual weight of four tablets of each brand was taken, and the average weight was calculated. Then, the tablets were crushed to form a fine powder in a mortar and pestle. The powdered tablets, equivalent to 10 mg of the active drug, were dissolved in 100 ml of distilled water in a 100 ml volumetric flask and kept in a sonicator for properly dissolving the powdered tablets. After that, the solution was filtered through filter paper. The same procedure was performed for all three tablet brands [11].

The potencies of the tablets were determined by using the following equation of measuring the drug content of the tablets-

$$\text{Drug present in a single tablet} = \frac{\text{conc} \left( \frac{\text{mg}}{\text{ml}} \right) \times \text{dilution factor} \times \text{total volume}(\text{ml}) \times \text{average weight}(\text{mg})}{\text{Sample taken}(\text{mg})}$$

After calculating the drug content of the tablets, the potencies of the tablets were calculated by using the following equation

$$\% \text{ Potency} = \frac{\text{drug present in a single tablet}}{\text{strength}} \times 100$$

Three tablets of each brand were taken and kept in a stability chamber at 75% humidity and 60°C temperature for 15 days. Their potency was calculated by performing the same procedure as above. Then, the potencies of the tablets before and after keeping them in a stability chamber were compared. According to the USP specification, the potency of a drug must be within 95-105%.

## 2.10 Dissolution Test

At first, three tablets of each brand were taken. Then, 900 ml of distilled water was poured into three dissolution vessels. Type II apparatus (paddle) was taken. The temperature was set to 37±2 °C, and rpm was 50. When the temperature reached up to 37 °C, the machine was started. After that, one tablet of each brand was introduced in each vessel, and a stopwatch was turned on. At predetermined time intervals (0, 5, 15, 30, 45, and 60 minutes), 10 ml of the sample was withdrawn from each vessel and immediately replaced with the same volume of fresh distilled water.

The solution was filtered so that we get the active drug other than additives. From the filtrate, 2 ml of the solution was taken and diluted with distilled water up to 10 ml. The solution was then run through an ultraviolet (UV) spectrophotometer, and the absorbance was taken at  $\lambda_{max}$  of 203 nm [12]. According to the USP specification, the percentage of drug release should be not less than 75% at 30 minutes.

## 2.11 Proposed Formulation and Preparation of a Tablet

A batch of Losartan Potassium tablet was prepared by using direct compression technique. The composition of granules is summarized in Table 1. The calculated amount of the active drug was mixed with the excipients thoroughly. The mixture was tightly compressed by using a KBr press (laboratory scale hydraulic press, UK), with a compression force of 3 tons, to prepare a tablet, and then a dissolution test was performed.

The amount of a binder and a disintegrant was adjusted to obtain the desired percentage drug release.

## 3. RESULTS

A weight variation test was performed to assure uniformity of weight of tablets of each brand and investigate tablet-to-tablet variation in terms of

weight, which should be within the limits of percentage deviation, according to the USP specification. Weight variation test results of Losartan Potassium 25 mg tablets are given in Table 2. Tablet of brand B showed 5.45% weight variation which was beyond the acceptable limit. Tablets of each brand were randomly selected to conduct the thickness test. Test results are given in Table 2. Results showed that none of the brands showed a deviation greater than ±5%, based on the calculation. The average hardness of three brands of Losartan Potassium tablets is shown in Table 2. Friability test helps determine the tablet's strength to withstand the physical and mechanical hazards during transportation. A disintegration test is provided to determine whether the tablets disintegrate within the prescribed time when placed in a liquid medium under the experimental conditions. Test results are given in Table 2. The results of dissolution studies of Losartan Potassium tablets are shown in Fig. 1.

## 4. DISCUSSION

In the present study, the pharmaceutical evaluation of various Losartan Potassium brands of tablets applied different approaches to investigate the quality control parameters. Drug manufacturers must ensure that their final products are consistent, safe, and effective. During this study, weight variation, which is the key to controlling the crushing strength and friability of tablets, was assessed. Test results revealed that nearly all of the Losartan Potassium brands of tablets passed the weight variation uniformity test specified in the USP (not exceeding ±5% variation). There was no significant difference in thickness of tablets of different brands. If a tablet is less thick, it can be broken down more easily. On the other hand, a thicker tablet is difficult to swallow. So, the uniform thickness of tablets of each brand is needed to ensure quality. Friability test is designed to evaluate the tablet's ability to withstand abrasion during packaging, handling, and shipping, and it is also closely related to the tablet's hardness. Conventional compressed tablets that lose less than 0.5 to 1% of their weight are considered acceptable. In the friability test, tablets of each brand showed impressive friability values.

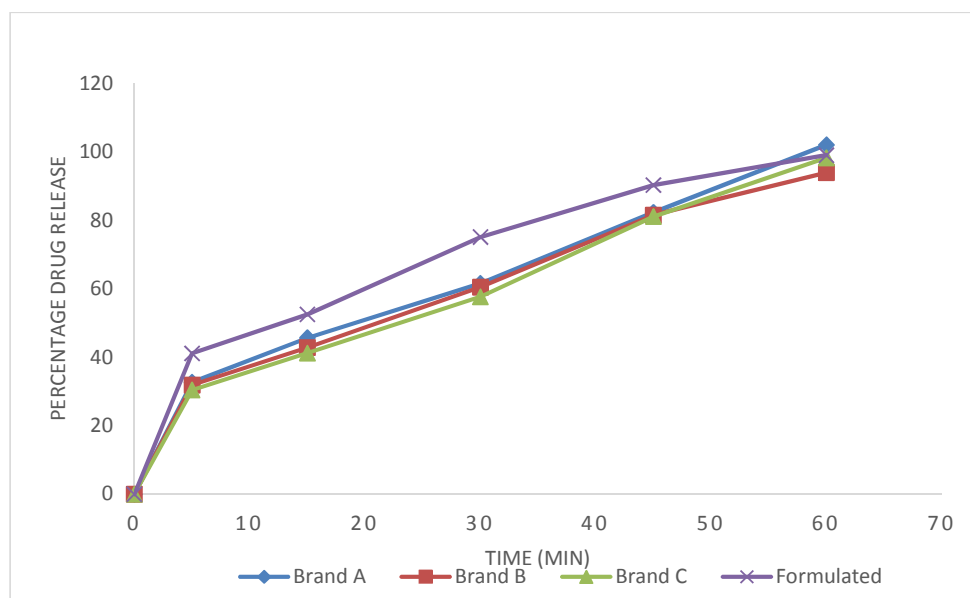
Dissolution is the rate-limiting step of drug absorption from a solid dosage form. As drugs need to be dissolved in the gastrointestinal tract before absorption, *in-vitro* dissolution data can be

**Table 1. Composition of formulated losartan potassium tablet**

Ingredients	Quantity (mg)	Range (%)	Justification
Losartan potassium	25		Active ingredient
Mannitol	62.82 (43.32%)	10-90	Diluent
Maize starch	14.5 (10%)	5-20	Disintegrant
Avicel pH 101	29 (20%)	20-90	Binder
Purified talc	4.35 (3%)	1-10	Lubricant
Aerosil 200	0.58 (0.4%)	0.1-0.5	Glidant
Sodium starch glycolate	5.8 (4%)	2-8	Disintegrant
Magnesium stearate	2.95 (2%)	0.25-5.0	Lubricant

**Table 2. Quality control parameter (*In-vitro*) evaluation of different brands of Losartan potassium 25 mg tablets**

Brand of Losartan Potassium Tablets	A	B	C
% Weight Variation	3.72	<b>5.45</b>	2.73
% Deviation of Thickness	0.49	1.77	0.85
% Deviation of Diameter	0.24	0.35	0.28
Average Hardness(N)	58.17	82.83	64
% Friability	0.155	0.466	0.293
% Potency (Normal)	105.4	101.85	106.7
% Potency (Stability)	81.4	88.2	103.4
Disintegration Time (sec)	1262.25	802.25	649.5
% Drug Release (30 min)	69.514	54.491	76.087
% Drug Release (60 min)	97.079	95.353	101.361
% Drug Release of the Formulated Tablets(30min)	<b>90.28</b>		

**Fig. 1. Dissolution profile of three marketed tablets and one formulated losartan potassium tablets**

correlated with the drugs' bioavailability. A higher rate and complete drug dissolution will ensure greater bioavailability [13]. According to the USP specification, the Losartan Potassium tablet's

drug release rate should not be less than 75% at 30 minutes. Unfortunately, it was found that only one brand out of three brands met up this criterion in this study. Losartan Potassium is

readily soluble in water [14]. The hardness of the tablets was also within the specified limit, so the poor dissolution rate of these formulations might be the due composition of the formulations. The release of the drug mainly depends on the amount of binder and disintegrants used in the formulation. Excess binder hinders drug release while disintegrants aids in drug release from the tablet [15]. So, a new batch of Losartan Potassium tablets was manufactured in the laboratory optimizing the existing formulation. The prepared formulation showed a satisfactory release rate compared to the existing ones.

According to the USP specification, the *in-vitro* physical and chemical evaluation of selected commercial brands of Losartan Potassium 25 mg tablets in Bangladesh passed the quality tests. As the quality control parameters are related to the drug's pharmacological action, a high-quality tablet should meet all the standard quality parameters for proper therapeutic response. However, despite the variation, most drug products are within the official limits. This reflects that formulations of Losartan Potassium are producing the desired effects as an antihypertensive drug.

## 5. CONCLUSION

This study assessed the quality as well as physicochemical properties of three brands of Losartan Potassium using *in-vitro* methods. However, despite the variation, most drug products are within the official limit. It reflects that these formulations are producing the desired effects as an antihypertensive drug. Some of the brands failed to meet the desired quality, so the quality control system of that companies should be upgraded and a proper monitoring system should be developed by the drug administration. So, the prescribing patterns should be changed depending upon the socio-economic status of patients.

## 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.

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## CONSENT

Not applicable.

## ETHICAL APPROVAL

Not applicable.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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