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A Review on Comparative Assessment for Generic and Branded Medicine

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ABSTRACT

Background: Generic drugs are as effective as their branded counterparts in terms of safety and efficacy. Although their exists several myths about quality of generic medicines because of its less price as compared to branded counterparts. The more impoverished masses, the government has launched a countrywide *Jan Aushadhi* Campaign. Losartan Potassium is used for the present study which is an antihypertensive drug.

Objective: The present study aims to evaluate and compare the quality of generic medicine with their branded counterparts as per Indian Pharmacopeial standards and other validated methods of Losartan Potassium

Keywords: generics, branded medicine, Losartan potassium, *Jan Aushadhi*,

INTRODUCTION

Prescriptions with branded medicines by health professionals is thought to be one of the key causes of the high cost of medicine. The cost incurred by the manufacturer in drug research, production, storage, marketing, and distribution, etc., is directed to the patron.(1)

Branded medicine is the original product that has been developed by a pharmaceutical company. The company is given exclusive rights of manufacture and distribution of medicine for a certain period of time (patent). During this period, no one else can produce the same drug. Generic medicine is a replica of the original branded product, marketed after the patent period or expiry of other exclusive rights and hence supposed to be of low cost. Both branded and generics are manufactured by confirming to international standards. Generics can be sold by different brand name and may contain different fillers, binders and lubricants which give them a different color, shape, taste, smell, etc. Hence, generic can be marketed under non-proprietary name or as a branded generic. This enables the manufacturer to market the product in a way similar to the proprietary product.(1)

METHODOLOGY

MATERIALS AND METHODS:

Materials used: The materials used were either AR/LR grade or the best possible grade available as supplied by the manufacturer without further purification or investigation.

Table No. 1: Materials used for the formulation

Sr. No.	Materials	Source
1.	Losartan Potassium	Micro Labs, Bangalore.
2.	Hydrochloric acid	Vasa scientific co, Bangalore.
3.	Potassium ortho di phosphate	Vasa scientific co, Bangalore.
4.	Sodium hydroxide	Kemphasol , Mumbai
5.	Distilled water	Milton chemicals, Mumbai

Table No. 2: Equipments and instruments used

Sr. No.	Name of Instruments	Supplier / Manufacturer
1.	UV- Visible Spectrophotometer (Model UV-1800)	Shimadzu corporation, Japan.
2.	Dissolution Apparatus (TDT-08L)	Electolab Mumbai, India.
3.	Distillation apparatus	Bhanu scientific instruments Company, Bangalore.
4.	Monsanto tester	Krystal Industries, Ichalkaranji
5.	Vernier caliper	Esel International, Ambala
6.	Friabilator	Analab scientific instruments Pvt. Ltd, Vadodara
7.	Disintegration tester	Electronic India, Haryana

I. Preformulation studies:

a) Identification of drugs

- **Melting point determination:**

Melting point of Losartan Potassium was determined by open capillary method in Thiel's tube.(3)

II. Analytical method development:

a) Preparation of 1.2pH and 7.4pH:

- **Preparation of 0.1N Hydrochloric acid:**

Exactly measured 8.5ml of conc.0.1N hydrochloric acid was taken in 1000ml volumetric flask and final volume was made up to 1000ml with distilled water to get 0.1N hydrochloric acid.

- **Preparation of phosphate buffer (pH 7.4):**

Dissolve 2.38gm of disodium hydrogen phosphate, 0.1gm of potassium diortho phosphate and 8.0gm of sodium chloride in sufficient water to produce 1000ml. Adjust the pH, if necessary.(4)

b) Determination of λ_{max}

The λ_{max} of losartan potassium were determined in 0.1N hydrochloric acid and phosphate buffer pH 7.4 buffer solutions, which were scanned between 200-400 nm in the UV spectrophotometer.

c) Standard calibration of Losartan Potassium:

Accurately weighed 100mg Losartan Potassium was dissolved in 0.1N hydrochloric acid to get the first stock solution of 1000µg/ml. From the 1st stock solution 1ml aliquot withdrawn and further diluted to 100ml with 0.1N hydrochloric acid to get second stock of 10µg/ml. From the second stock, aliquot of 2ml, 4ml, 6ml, 8ml and 10ml were withdrawn and make volume up to 10ml with by 0.1N hydrochloric acid solution to get concentration of 2 µg/ml, 4 µg/ml, 6 µg/ml, 8 µg/ml and 10µg/ml respectively. The absorbance of the solutions was measured at 234nm by using UV-visible spectrophotometer.

Same procedure was followed to obtain standard calibration curve of Losartan Potassium in phosphate buffer (pH 7.4), only difference is that we had used phosphate buffer (pH 7.4) instead of 0.1N hydrochloric acid as a dilution medium. (5)

II. Evaluation of marketed drug:

a) Quality control test

- **General appearance**

The formulated tablets were assessed for its general appearance and observations were made for Shape, Colour, Diameter, Thickness and Odour.

- **Weight Variation**

Individually weighed 20 tablets and calculated the average weight not more than two of the individual weights deviate from the average weight by more than the percentage deviation shown in Table 3 and more deviated by more than twice that percentage.

$$\text{Percentage Deviation} = \frac{[\text{Weight of tablet (mg)} - \text{Average weight of tablet (mg)}]}{\text{Average weight of tablet (mg)}}$$

Table No.03: Limits for weight variation

Average weight of the tablet (mg)		Maximum percentage deviation
IP	USP	
130 or less	80 or less	±10
130 or 324	80 or 250	±7.5
324 or more	250 or more	±5

Note: The values presented are arthematic mean ± SD's of three determination

- **Thickness**

Thickness mainly depends up on die filling, physical properties of material to be compressed under compression force. The thickness of the tablets was measured by using Digital Vernier Callipers. Desired thickness: 2.0 - 4.0 mm

- **Hardness**

Hardness of the tablet is defined as the force required in breaking a tablet in a diametric compression test. Pfizer tester and Monsanto tester are the equipments used to test hardness. In this test, a tablet was placed between two anvils, force was applied to the anvils and the crushing strength that just causes the tablet to break is recorded. Hence hardness is sometimes referred to as Crushing Strength. Tablets require certain amount of strength or hardness to withstand mechanical shocks of handling in manufacture, packaging and shipping

. Desired hardness: 4-12 Kg/cm2

- **Friability**

Friability is defined as the loss in weight of tablet in the container due to removal of fine particle from their surface. It is expressed in percentage (%). A pre weighed tablet sample (20 tablets) was placed in the friabilator chamber and rotated for 10 revolutions. In each revolution the tablets are carried up and are allowed to freely fall from a height of 6 inches. After 100 revolutions the tablets are removed from the chamber, dusted and reweighed. When capping is observed during friability test, tablets should not be considered acceptable, regardless of percentage weight loss.

% Friability was then calculated using the following formula-

Friability = [(Initial wt – Final wt)/ Initial wt] X 100

Limit: Friability should be less than 1%

- **Disintegration Test**

The process of breakdown of a tablet into smaller particles is called as disintegration. The in vitro disintegration time of a tablet was determined using disintegration test apparatus as per IP specifications. Place one tablet in each of the 6 tubes of the basket. Add a disc to each tube and run the apparatus by using Water, 0.1N HCl, Phosphate buffer pH- 7.4 as the immersion liquid and maintained a temperature at 37°± 2°C. The time in seconds/minutes taken for complete disintegration of the tablet with no palpable mass remaining in the apparatus was measured and recorded.(2)

a) Drug content:

Triturate the marketed generic and branded tablet separately in mortar and transfer in 100 ml volumetric flask. Add littlie 0.1N hydrochloric acid to the flask. Shake well and then make the volume up to 100ml mark with 0.1N hydrochloric acid. 1ml of this solution is diluted to 100ml in another volumetric flask. Absorbance of both solutions is seen in UV-visible spectrophotometer at 234nm.

Same procedure is followed to determine drug content in phosphate buffer (pH 7.4) but only difference is that here we have used pH 7.4 except 0.1N hydrochloric acid solution.

b) Dissolution studies:

The release rate of marketed generic and branded tablet was determined by employing USP type 2 apparatus by rotating basket method. The dissolution test was performed using 900 ml 0.1 N hydrochloric acid for 2 hours then followed by 7.4 pH phosphate buffer for next 5-6 hrs. in 37 ± 0.5°C at 50 rpm. 50mg of marketed generic and branded tablet were placed in a basket. A sample (5 ml) of the solution was withdrawn from the dissolution apparatus at predetermined time interval and the same volume was replaced with 5 ml of fresh dissolution medium. The samples absorbance of these solutions was measured at 234 nm.

Table No.04: Dissolution parameters

Dissolution medium	Dissolution medium volume	Apparatus	Speed of rotation	Temperature	Volume of sample withdrawn	Sampling time interval (min)	Measurement of Absorbance
0.1N HCL	900ml	USP XXIII (Basket type)	50rpm	37±0.5°C	5ml	5,10,15,30, 60,90,120	234nm
Phosphate Buffer 7.4pH	900ml	USP XXIII (Basket type)	50rpm	37±0.5°C	5ml	15,30,60, 90,120, 150,180, 210,240	234nm

Note: The values presented are arthematic mean ± SD's of three determination

c) **Drug release kinetics and data analysis:**

To analyze the mechanism for the release and release rate kinetics of the dosage form, the data obtained was fitted into, zero order, first order, Higuchi matrix and Krosmeyer and Peppas model. In this by comparing the r – values obtained, the best fit model was selected.(6)

1) Zero order kinetics:

Drug dissolution from pharmaceutical dosage forms that do not disaggregate and release the drug slowly, predicting that the area does not change and no equilibrium conditions are obtained can be represented by the following equation,

$$\mathbf{Q_t = Q_0 + K_0 t}$$

Where,

Q_t = amount of drug dissolved in time 't'

Q_0 = initial amount of the drug in the solution.

K_0 = zero order release constant.

This relationship can be used to describe the drug dissolution of several types of modified release pharmaceutical dosage form.

2) First order kinetics:

To study the first order release rate kinetics the release rate data was fitted to the following equation,

$$\log Qt = \log Q_0 + \frac{K_1 t}{2.303}$$

Where,

Qt = amount of drug release in time't'

Q_0 = initial amount of the drug in the solution.

K_1 = first order release constant.

This relationship can be used to describe the drug dissolution in pharmaceutical dosage forms such as those containing water soluble drugs in porous matrices.

3) Higuchi model:

Higuchi developed several theoretical models to study the release of water soluble and low soluble drugs incorporated in semisolids and/or solid matrices. Mathematical expressions were obtained for drug particles dispersed in a uniform matrix behaving as the diffusion media, and the equation is,

$$Q_t = K_H t^{\frac{1}{2}}$$

Where,

Q_t = amount of drug release in time't'

K_H = Higuchi dissolution constant

This relationship can be used to describe the drug dissolution from several types of modified release pharmaceutical dosage forms.

4) Krosmeyer and Peppas release model:

To study this model the release rate data are fitted to following equation,

Where, $\frac{M_t}{M_\infty}$ = the fraction of drug release.

K = release constant

t = release time

n = diffusional exponent for the drug release i.e. dependent on the shape of the matrix dosage form.(7)

CONCLUSION

The present study was aimed to compare the Branded and Generic tablets based on the *in-vitro* drug release rate. For this study we have selected a Losartan Potassium drug, branded (LOSAKIND-50) and generic (*Jan Aushadhi* Store) tablet which is anti-hypertensive drug. From the evaluation parameters it was observed that all the quality control test including the drug content and *in-vitro* drug release profile showed similar results for generic drug and Branded drug. The mechanism of drug release was followed to be zero order kinetics for Branded and Generic drugs.

Both Branded and Generic tablets of Losartan Potassium had identical quality and they fulfilled all the criteria prescribed by the Indian pharmacopoeia. The government and healthcare professionals must take up generic promotional schemes (*Jan Aushadhi)*, Creating public awareness by advertisements in print as well as electronic media, general awareness programs on quality of generics to build confidence among prescribers, pharmacists, and consumers. This confirms that the generic medications are of equivalent and comparable quality of the branded medicines available in the market.

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