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Comparison and Evaluation of Marketed Tablet of Spironolactone

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ABSTRACT

The primary goal is to evaluate and compare the quality standards of branded and generic forms of the antihypertensive medication (Spironolactone). The drugs are evaluated and results showed that branded and generic meet the pharmacopoeial specifications. According to pharmacopeia, every tablet passed the test for weight fluctuation, hardness, friability, disintegration and dissolution. Thus, we can say that antihypertensive medications are equal.

Keywords: Spironolactone; Physicochemical test; In-vitro studies.

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INTRODUCTION

Spironolactone is a potassium-sparing diuretic under the brand name Aldactone, among others. Spironolactone was initially discovered in 1957 and was first introduced in 1959 by John A. Cella and Robert C. Tweit at G. D. Searle & Company.

Spironolactone is a particular pharmacologic antagonist of aldosterone that mainly works by competitively binding receptors at the distal convoluted renal tubule's aldosterone-dependent sodium potassium exchange site. Potassium is retained while spironolactone increases the excretion of water and sodium. By this mechanism, Aldactone functions as a diuretic and an antihypertensive mechanism.

Some of the marketed products of Spironolactone are Aldactone, Spilactone, Spironot. The drug used to treat hepatic scarring, renal illnesses and heart failure- related fluid buildup. It is also used to treat acne, hypokalemia, hypertension and excessive female hair growth. It's a steroidal 17-α-spironolactone with the chemical name for spironolactone is 17-hydroxy-7α-mercapto-3-oxo-17α-pregn-4-ene-21-carboxylic acid-γ-lactone acetate. Figure1 illustrate its structural formula.

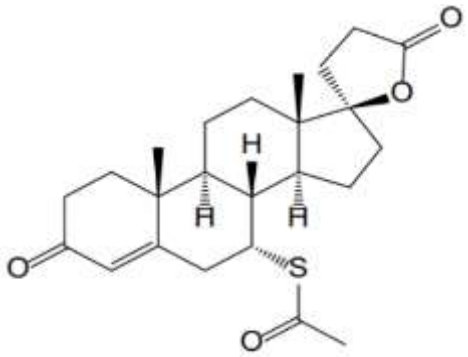

Figure 1: Chemical Structure of Spironolactone

Generic replacement is the prescribing different brand or non-brand drug which contains the same API at similar strength and dosage form. Branded drug products of top pharmaceutical companies are better as well as costly, that are hardly affordable to the poor people of under-developed and developing countries in comparison with the product manufactured by the low scale companies.

Table 1: Details about the Spironolactone tablet

Tablets	Price of strip (For 15 tablets)	Batch no	MFG Date	Expiry Date
Brand	13.60 Rs/-	02A23009	06/2023	05/2026
Generic	22.00 Rs/-	SSG2203	11/2022	10/2025

MATERIALS AND METHOD

Chemical and reagents

The spironolactone tablets were obtained from both government hospital pharmaceutical stores and a reputable pharmacy.

Preparation

The amount of spironolactone (mg/tablet) in each prepared tablet made using the wet granulation process.

PHARMACOKINETICS

Absorption

In healthy volunteers, the maximal plasma concentration (Cmax) of spironolactone is attained 0.5 to 1.5 hours post-dosage; the Cmax of the active metabolite canrenone is obtained 2.5 to 5 hours post-dosage. According to research, spironolactone takes 2-4 hours to start working.

Distribution

Over 90% of spironolactone and its metabolites are bound to plasma proteins.

Metabolism and excretion

Different metabolites are produced by the quick and widespread metabolism of spironolactone. When the sulfur in spironolactone is eliminated, a class of metabolites, including canrenone, is created. Another class of metabolites, such as 6-beta (β)-hydroxy-7-alpha (α)-thiomethyl spironolactone (HTMS) and 7-alpha (α) thiomethyl spironolactone (TMS), retain sulfur.

To become 7-α-thiospironolactone, Spironolactone must first undergo deacetylation. 7-α-thiospironolactone can be dethio acetylated to canrenone or s-methylated to TMS, the principal metabolite. It is possible to further metabolize TMS and HTMS.

- 7-α-thiospironolactone
- 7-α-thiomethyl spironolactone
- 6β,7α-thiomethyl spironolactone
- 3β-hydroxy-thiomethyl spironolactone
- 3α-hydroxy-thiomethyl spironolactone
- Canrenone

Urine is the primary excretion site for the metabolites, followed by bile. Spironolactone metabolites are eliminated as feces (14.2-14.6%) and urine (42-56%). The urine does not contain any unmetabolized spironolactone.

EVALUATION OF TABLETS

Weight variation:

Each formulation's twenty tablets were weighed using an electronic balance to get the average weight. The weights of each tablet were then compared to the average weight in order to examine weight variation. The percentage can be exceeded if two or more weights differ from the average weight.

% deviation= [(Average weight -Individual weight) ÷ Average weight] ×100.

Friability:

Twenty tablets were chosen at random and weighed for each formulation. The tablets were then put into the friability testing device, which was turned for four minutes at a speed of 25 rpm. Following that, the tablets were weighed, and the friability values are shown in Table 2.

Limit: Less than 1.0%

Friability= [(Initial weight (W1) - Final weight (W2)) ÷ Initial weight (W1)] ×100

Hardness:

Ten tablets were tested for each formulation's hardness using the Pfizer hardness tester; the average results are displayed in the table 2.

Thickness:

A vernier caliper was used to measure the thickness of the tablet. For every batch, ten tablets were utilized. Table 2 displays the outcomes.

Test for disintegration:

Using a tablet disintegration tester, six tablets from each generic and brand were used for the test in distilled water at 37°C, following the guidelines provided by the United State pharmacopeia 2014. The duration needed for the tablet to fully dissolve is known as the disintegration time (DT), and it was recorded.

Table 2 Evaluation of Spironolactone

Sr. No	Tablets	Weight variation	Friability Test	Hardness Test	Thickness Test	Disintegration Test	Dissolution Test	Assay
	Standard as per IP	<7.5 for 300mg	<1%	3-10Kg/cm^2	±5%	30 mins	Not less than 70%	97-102%
1	Brand	±4.7%	0.57%	5.1	± 0.2%	70 sec	86.5%	100%
2	Generic	±2.3%	0.99%	4.4	± 1.2%	20 sec	89.4%	98.7%

Dissolution Test:

Apparatus No: 1

Medium: 1000ml of 0.1M hydrochloric acid containing 0.1 percent w/v of sodium dodecyl sulphate. Speed and time: 75 rpm and 60 minutes. Take off an appropriate amount of the medium and pass it through membrane filter disc whose average pore diameter is not more than is 0.1µm. Measure the absorbance of the filtrate, suitable diluted, if necessary, at the maximum at about 242nm. Calculate the content of spironolactone in the medium taking 445 as the specific absorbance 242nm.Not less than 70.0 percent of the stated amount of Spironolactone.

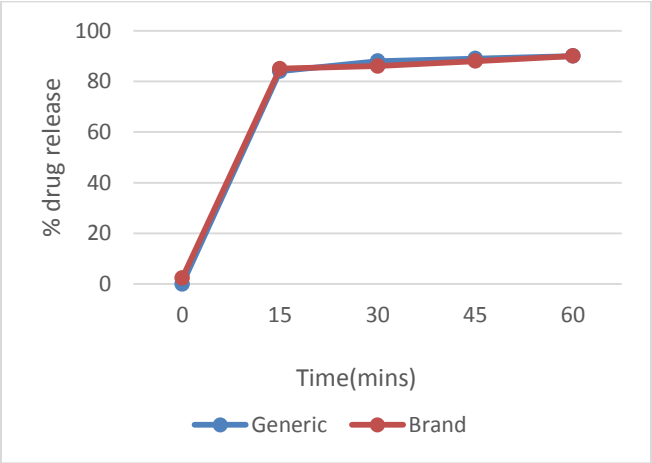

Figure 2: Dissolution profile of generic and non-generic drug of spironolactone

Assay:

Preparation of standard stock solution

Accurately weighed Spironolactone (10.0mg) was transferred to 100ml volumetric flask, dissolved in about 50ml of methanol and volume was made up to 100ml with methanol to obtain stock solution of 100µg/ml.

Preparation of working Solution

From the standard stock solution 0.5ml, 1.0ml, 1.5ml, 2.0ml, 2.5ml, 3.0ml and 3.5ml were pipette out into 10ml volumetric flask and volume was made up to the mark with methanol to produce the concentration ranging from 5-35µg/ml respectively. The process of choosing the analytical wavelength involved scanning 10µg/ml in the 400-200nm wavelength range using methanol as a blank. The wavelength that corresponded to the maximum absorbance was determined to be 238nm. Figure 3 displays the corresponding UV spectrum.

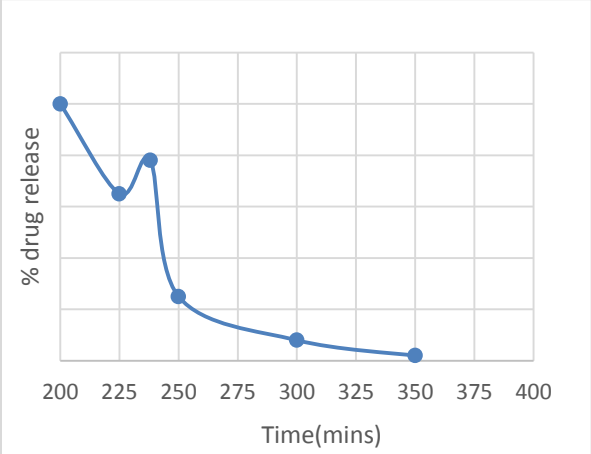

Figure 3: UV Spectrum of Spironolactone

RESULTS AND DISCUSSION

Within limits that are established, the outcomes of our study on antihypertensive spironolactone tablets, both generic and brand names, fulfilled the IP requirements of quality control testing. In vitro study is used to do it. As long as the tablet fluctuation, friability, hardness, thickness, disintegration time, dissolution and assay are all within the pharmacopoeial standards, it is said to be in compliance. The tablets were all determined to be in compliance with pharmaceutical criteria, it can be assumed.

CONCLUSION

The work concludes that branded (non-generic) and generic medications had comparable outcomes. To lower prescription costs and make therapy more affordable, generic versions of the drug should be given out broadly. So, the expense of the medication can be covered by the generic public as well.

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