A COMPARISON AND EVALUATION OF LOOP DIURETIC FRUSEMIDE GENERIC Vs BRAND TABLETS

Abstract

Branded medications are the original products developed by pharmaceutical companies and generic drugs are copies of branded drugs whose patent has expired. The research work focused on comparisons and evaluations of generic V_S brand of frusemide tablets. The study includes some of the specifications that should tested in the finished products in tablets such as appearance, thickness, diameter, weight variation, hardness, friability, disintegration time, dissolution, hardness and thickness as per pharmacopoeial& non pharmacopoeial tests were performed. The generic and brand frusemide tablets quality control results showed within the range as per IP. The *in vitro*drug release of generic frusemide tablets was found to be 96.7 %in 45 min and branded tablets which showed drug release 98.3% in 45 min. Hence, it can be concluded that evaluation of loop diuretic frusemide tablets generic and brand frusemidetablets showed same deviations in the quality control results as per IP.

Key words: Frusemide, generic, brand, quality control test

Introduction

Pharmaceutical companies are developing a wide range of novel therapeutic compounds to treat illnesses through the creation of both branded and generic medications [1]. “The single comprehensive active pharmaceutical ingredient is formulated by various pharmaceutical companies by different brand names” [2]. “It is found that all thepharma industries are following the Pharmacopoeial standards which are maintained by pharmaceutical regulatory authoritiesduring the formulation of the drugs” [3].

“The generic drugs are the copy of branded drugs whose patent has expired and the branded drugs is the original product that has been developed by innovator of a pharmaceutical company” [4]. “Both products have same active ingredients, dosage form quality andperformance and generic drug are manufactured by different pharmaceutical companies under different brand names and sold under different cost either lesser or cost subsidized”[5]. “Still a significant proportion of lay people, doctors and pharmacists hold negative perceptions of generic medicines, perceiving generics as less effective, less safe, inferior in quality and more likely to cause side effects compared to their branded equivalents”[6].

But all the quality control tests for the pharmaceutical formulation are tested both in generic and brand drug as per Pharmacopoeial or in-house specification as per pharmaceutical company[7]. To keep in mind the above false suspect, the current studies aim thecomparison and evaluation of frusemide tablets generic and brand to throw away the blind belief of many people that branded medications have better therapeutic efficacy than the genericmedications [8].

"Frusemide promotes diuresis by blocking tubular reabsorption of sodium and chloride in the proximal and distal tubules, as well as in the thick ascending loop of Henle"[9]. "This diuretic effect is achieved through the competitive inhibition of sodium-potassium-chloride co-transporters expressed along these tubules in the nephron, preventing the transport of sodium ions from the lumenal side into the basolateral side for reabsorption"[10]. "This inhibition results in increased excretion of water along with sodium, chloride, magnesium, calcium, hydrogen, and potassium ions"[11].

Materials and methods

The current research focused to analyzecompared generic vs branded quality control tests forloop diuretictablets Frusemide(40mg), a potent loop diuretic drug used in the treatment of edema of pulmonary, cardiac, hepatic renal origin and in the management of chronic hypertension.There are many brands of frusemide tablets [Lasix(Sanofi India Ltd), Fru (Ind-Swift Limited),Frusenac(Geno Pharmaceuticals Ltd) Diaqua-2 , Lo-Aqua and etc.,] of different formulation manufactured and marketed, in our study one of the Frusemide tablets which has same strength of generic and brand product was selected.

Drug Profile

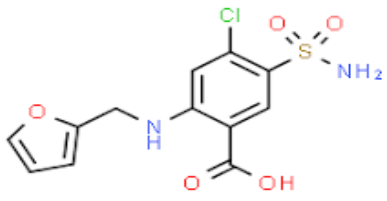

Fig 1: Structure of Frusemide

It is chemically 4-Chloro-2-[(furan-2-ylmethyl)amino]-5-sulfamoylbenzoic acid ($C_{12}H_{11}CIN_2O_5S$), molar mass 330.74g mol^{-1},category is a loop diuretic, it's bioavailability 43-69% through oral. Administration routes include subcutaneous, intramuscular, intravenous, and oral. The usual dose is 40-120 mg/day[12]. Adults with edema should take 20–80 mg once daily in one dose, or two doses of the same amount divided[13].

Chemicals and reagents

The frusemide tablet (both generic and brand) werepurchased from one of the reputed pharmacy in Chidambaram, Cuddalore district, manufactured by Zentiva private Ltd for brand and Unicure India Ltd for generic tabletswere selected in the research.Ingredients used was of analytical grade (AR grade) obtained from S.D Fine chemicals, Mumbai, India. Class A glasswares (Borosil Ltd., Mumbai, India) were used throughout the research work.

Methodology

Frusemide 40 mg uncoated tablet of both generic and brand was subjected for quality control test as per Indian pharmacopoeia 2018[14].

Evaluation tests for tablets

Tablets appearance

"20 tablets was selected and visually inspected for their external characters such as color, shape,surface texture, presence ofgrooves and surface defects"[15].

Weight variation (%)

"20 tablets from generic and brandwereweighed individually used electronic weighing balance(shimadzu).Their individual weights(X_1)were measured and recorded. Theaverage weight (X_A) of each sample was calculated and the deviation of each tablet weight fromthe average weight was determined"[14].

% weight variation = $(X_1-X_A)\times 100/ X_A$

Thickness(mm)

10tablets from the representative sample was taken and individual tablet thickness was measured by using digital verniercalipers(Labpro). Average valued of thickness and standard deviation values wascalculated[14].

Hardness(kg/cm^2)

Tablet hardness was measured by usedhardnesstester(Pfizer). From generic and brand, 10 tablets was observed and recorded for the hardness and average of ten values were noted along with standard deviation[14].

Friability(%)

Accurately weighed 6 tablets from generic and brand were placed separately in the Roche friabilator(Erweka, Germany)in the place of the drum. Rotated the drum for 100 rotations, at 25 rpm and removed the tablets,de-dusted and reweighed the tablets. The friability were calculated as the percentage loss of weight[14].% Friability= $(W_1 - W_2) \times 100 / W_1$

Where, W_1=Initial weight of tablets,W_2=Final weight of tablets.

Disintegration time(min)

"Disintegration time is considered to be one of the essential criteria in selecting the best formulation. The study was carried out used USP type II (Erweka, Germany) dissolution apparatus(paddle type)with water buffer as the disintegration medium.The medium was maintained at 37±0.5ºC at 28-32 cycles/min.The time point at which tablet completely disintegrates was noted as disintegration time"[14].

***In-vitro* dissolution studies**

The dissolution media used in this studied was pH 5.8 phosphate buffer of volume 900mL.

[Preparation of phosphate buffer: Solution I-Dissolve 13.61 g of potassium dihydrogen phosphate in sufficient water to produce 1000 ml. Solution II - Dissolve 35.81 g of disodium hydrogen phosphate in sufficient water to produce 1000 ml. Mix 96.4 ml of solution I with 3.6 ml of solution II].

"The apparatus(USP dissolution apparatus II)was set at the speed of 50rpm. The tablets was placed in each flask of the test apparatus. The samples were drawn for every 15 min time interval till 45 min. The volume of sample drawn was 5mL. 5mL of fresh buffer solution was replaced into the beaker to maintain the dissolution medium volume. Thus collected sample was taken and diluted to 5ml with the pH 5.8 phosphate buffer and the absorbance of these solutions was measured at 271 nm used UV Spectrophotometer"[14].

Assay of Frusemide tablet

Weighed and powdered 20 tablets and the equivalent quantity of the powder containing 0.1 g of Frusemide was weighed and mixed in 150 ml of 0.1 M sodium hydroxide(dissolving 0.4g in 100

ml water) for 10 min. Added sufficient 0.1 M sodium hydroxide to produce 250 ml and filtered using filter paper. Diluted 5 ml to 200 ml with 0.1 M sodium hydroxide and measured the absorbance of the resulting solution at the UV spectroscopy about 271 mm. Calculated the content of $C_{12}H_{11}CIN_2O_5S$ taking 580 as the specific absorbance at 271 nm[14].

Calibration curve

Scanning for λmax

The solutions of had a concentration of 10 µg / ml in phosphate buffer pH 5.8 was scanned in 200nm -400 nm in spectrum basic mode(Spheronics-pc based double beam spectrophotometer 2202).

Preparation of calibration curve

The stock solution of frusemide (100 µg / ml) were pipette out into a series of 10 ml volumetric flask and diluted with phosphate buffer pH 5.8 to got final concentration in the range of 2 – 10 µg / ml. The absorbancesof the resultant solutions was measured at 271nm for pH 5.8 phosphate buffer. Freshly prepared solutions was made for the calibration curves on 3 consecutive days[16].

Results and Discussion

Table 1:Labelcontents

Item	Cost of tablets - For 10 tablets Rs.	Batch No.	Manufacture Date	Expiry Date	Manufacturer
Generic	10	FST1012	11/2022	10/2024	Unicure India Ltd
Brand	5	3P1454A	04/2023	03/2026	Zentiva private Limited

Table 2: Results of appearance features of the different brands of frusemide 40 mg tablets

Parameter	Generic	Brand
Shape & Color	Round & white	Round & white
Surface texture &Convexity	Smooth & flatwith bevelededges	Smooth & flatwith bevelededges
Presence ofcracks& chips	None	None

Table 3:Results of evaluation test for Tablets

Evaluation Test for Tablets								
Drug	**Average weight (mg)**	**% weight variation**	**Hardness test**	**Thickness test**	**Friability**	**disintegration test**	**Dissolution rate**	**Assay**
	Standard as per IP	<7.5%	3-10 kg/cm^2	± 5 %	<1%	30mins	Not less than 70%	90-110%
Generic	131.7	3.120	6.2	1.014	0.94	1 min39sec	96.7	101.2
Brand	165.3	2.955	6.4	0.406	0.77	1 min25sec	98.3	105.1

Table 4:Result of Calibration curves data of frusemide using pH 5.8 phosphate buffer

S.no	Concentration (µg /ml)	Absorbance
1	2	0.107
2	4	0.226
3	6	0.343
4	8	0.436
5	10	0.578

Result by pictorial representations of evaluation test for Tablets

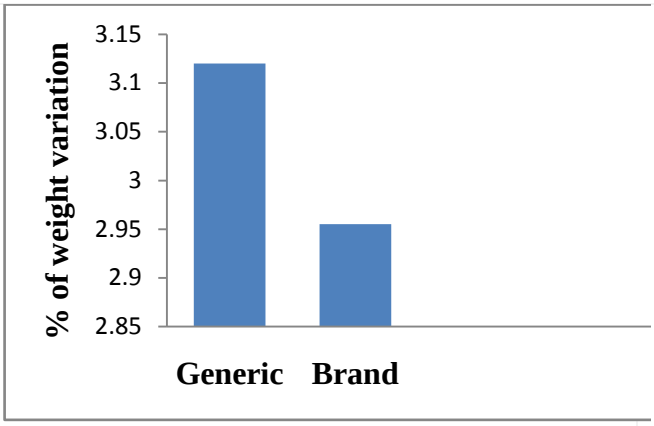

Fig 2 : % of weight variation of frusemide tablets

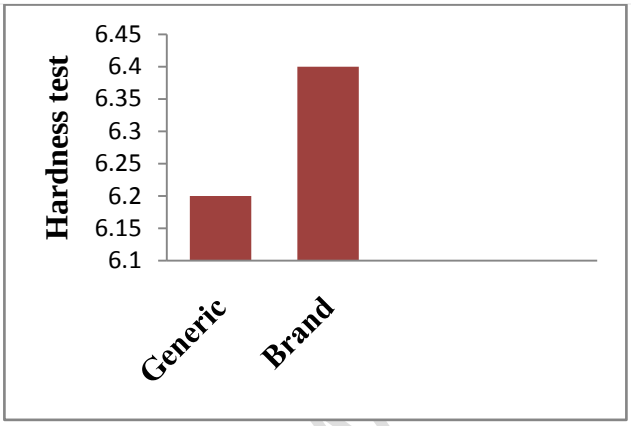

Fig 3 : Hardness of frusemide tablets

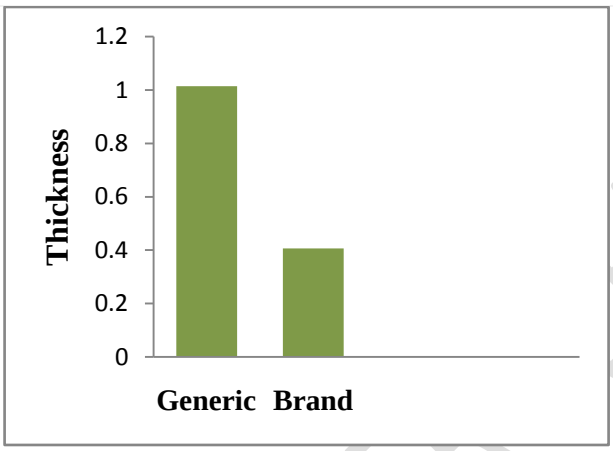

Fig 4 : Thickness of frusemide tablets

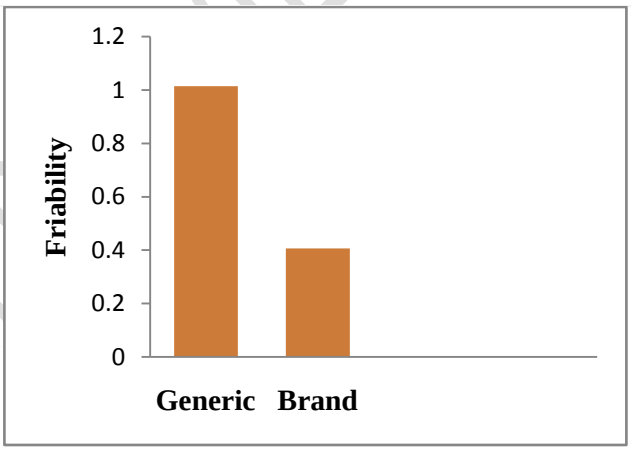

Fig 5 : Friability of frusemide tablets

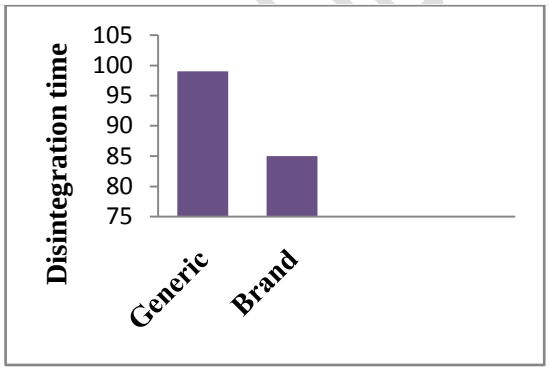

Fig 6 : Disintegration time of frusemide tablets

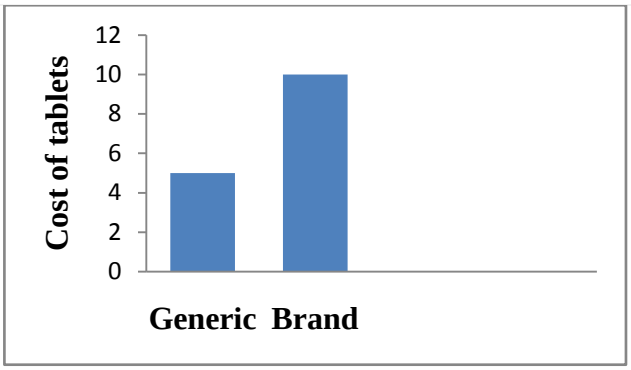

Fig 7 : Cost of frusemide tablets

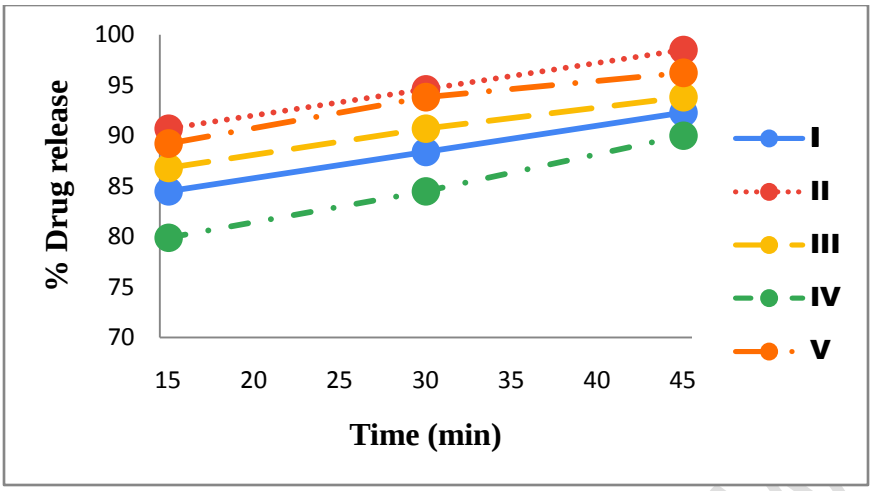

Fig 8 : Dissolution profile for generic drug

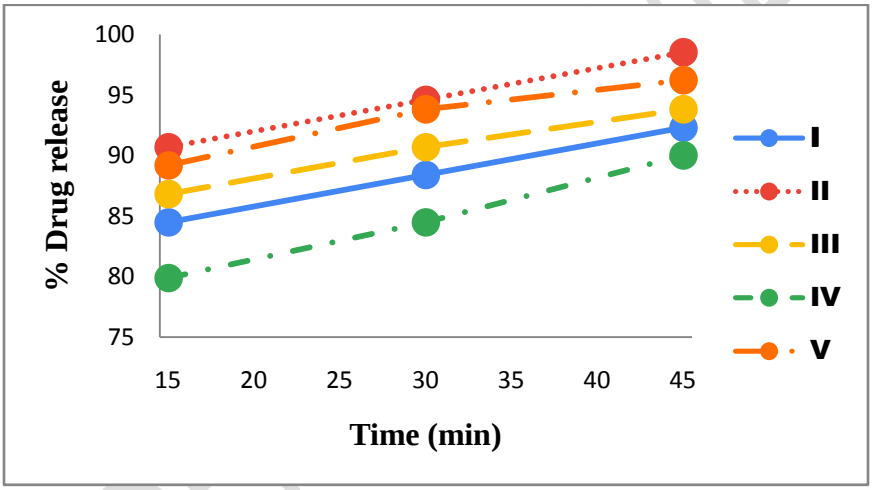

Fig 9:Dissolution profile of branded drug

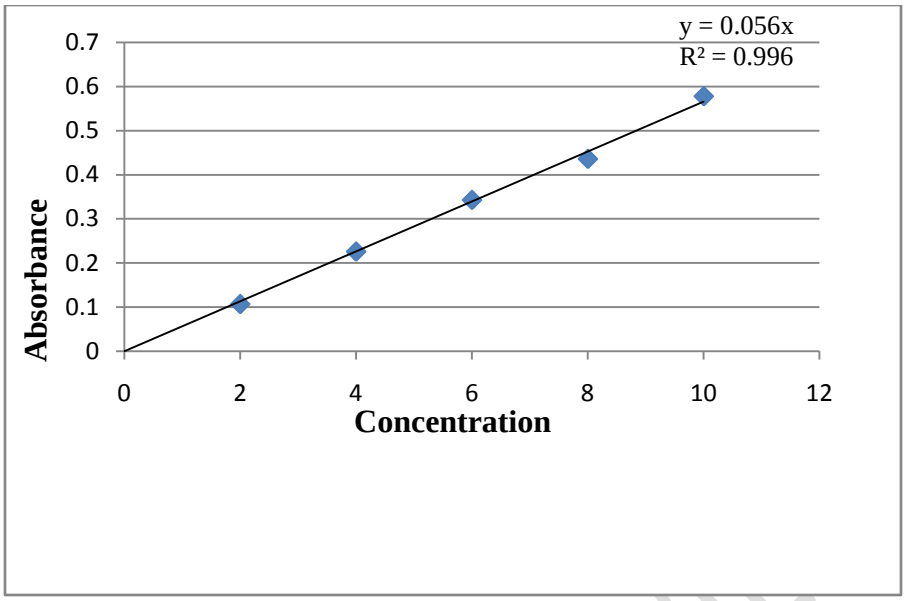

Fig 10: Calibration curve of frusemide drug

The results of our research work conducted on generic and brands of loop diuretics frusemide tablets, met the IP requirements of quality control tests within specified limits. Shape (brand-round, generic-round) & Color (brand -white, generic-white, Surface texture (brand -smooth, generic-smooth) & Convexity (brand –flat with beveled edges, generic- flat with beveled edges) presence of cracks & chips (brand -none, generic-none). The various physical parameters of tablets like weight variation (brand -2.955%, generic-3.120%), hardness (brand -6.4kg/cm^2, generic-6.2kg/cm^2), thickness (brand -0.406%, generic - 1.014%), friability (brand –0.94%, generic-0.77%), dissolution(brand -98.3%, generic-96.7%), assay (brand -105.1%, generic-101.2%) and disintegration time (brand –1 min 25 sec, generic -1min 39 sec) are accessed were within the pharmacopoeial specifications. Drug release of generic tablet was found to be 96.7 % in 45 min which is lesser than the branded tablets which showed drug release 98.3% in 45 min. Hence, it could been concluded that tablets were all found have been as per pharmaceutical specifications.

Conclusion

Finally, study suggests that generic and branded (non-generic drugs) shown equal results. Hence generic form of the drug could been widely prescribed to reduce the medication cost and make the treatment economical. Cost of the generic tablet was Rs 5 per 10 tablets,whereas cost of the brand tablet was found to be Rs 10 per 10 tablets. The generic tablet was cheaper than branded tablets. So that general people can also meet the medication cost.Generics did not had to invest

major amounts of time and research because FDA testing and approval of the brand drug's ingredients is already complete generics can get to market quicker and been sold for much cheaper than brand drugs.Generic medicine contains the same active ingredient that had undergone all clinical trials and quality testing during its patent when it was manufactured by a brand as the non-generic medicine. Therefore, these were considered havebeen safe further thepharmacovigilance centers monitor the safety and side effects of medications.

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