

# Comparative Evaluation of Branded and Generic Medicines - Ranitidine & Metformin HCl

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**Abstract**—Ranitidine is H2 receptor antagonist used to treat Duodenal ulcers, Metformin HCl is Biguanide Antihyperglycemic agent used for treating non-Insulin dependent Diabetes Mellitus (NIDDM) and as anti-diabetic used for the treatment of Type-2 Diabetes Mellitus. The present study was to compare and evaluate the Quality and Price of Ranitidine and Metformin HCl Branded and Generic medicines. The selected Branded and Generic tablets are coded as C1, C2, C3, C4. Each tablets were evaluated for evaluation parameters such as Weight variation, Hardness, Friability, Disintegration, Assay, in-vitro Dissolution. From the results based on the Evaluation tests of Tablets and in-vitro dissolution rate studies, the Branded Medicines showed better Drug release and followed First order kinetics of Drug Release.

**Keywords**— Branded Drug, Generic Drug, Drug Codes, Ranitidine, Metformin HCl, H2 Receptor Antagonist, Anti-Diabetic.

## I. INTRODUCTION

A drug that has a trade name and is protected by a patent (can be produced and sold only by the company holding the patent). It is also known as “Innovator Drugs”. A drug product that is comparable to a brand or reference listed drug product in dosage form, strength, route of administration, quality and performance characteristics, and intended use. Generic drug are made by a company other than the company that developed the original medicine. They are chemically identical to the original drug and have the same active ingredients.<sup>1,2</sup>

Brand name and generic medications don't always have the same exact ingredients. To ensure that the company can make profit, after money spent research and creating the drug, the company will patent the drug, preventing other companies from selling the generic drug. The FDA states that the only way they would allow generics on the market is if both types of the drugs are bioequivalent. The FDA's standard is that the drugs have the same exact active ingredient, but the inactive ingredients can be different but at a certain potency.<sup>3</sup> To ensure that the company can make profit, after money spent research and creating the drug, the company will patent the drug, preventing other companies from selling the generic drug. But when looking at the brand name and generic medication the look of the medications even look different, which confuses many people into thinking they picked up the wrong drug, when it actually is just the generic instead of the brand name.<sup>3</sup>

Brand-name medicines are originator products or medicines that have been discovered by a company and are patented to maximise any economic gain that may result from being the sole company producing a new drug treatment for a particular illness or disease condition. In Generic-name medicines are bioequivalent to branded medicines. On expiration of the originator product's patent term protection, other manufacturing companies may file submissions to

regulatory authorities for approval to market generic versions of the originator medicines<sup>4</sup>

## II. METHODOLOGY<sup>5-15</sup>

TABLE 1. Details of drugs.

S.No	Type of Drug	Name of the Drug	Code
1	Branded	Ranitidine	C1
	Generic		C2
2	Branded	Metformin HCl	C3
	Generic		C4

TABLE 2. Details of drug prices.

S.No	Type of Drug	Name of the Drug	Code	Price (Rs For 10 Tab)	
				M.R.P	Retailer Price
1	Branded	Ranitidine	C1	7.29	5.82
	Generic		C2	7.10	5.79
2	Branded	Metformin HCl	C3	15.00	12.25
	Generic		C4	10.00	5.00

### Standard Calibration Curve of Ranitidine

#### (a) Stock Sample Preparation:

Accurately weighed 100mg of drug (Ranitidine) was first dissolved 100ml of 0.1N HCl in 100ml of volumetric flask and to make a concentration of 1000µg/mL (primary stock solution). 5ml of primary stock solution was pipetted out into 50 ml of volumetric flask and volume was adjusted 0.1HCl to make a concentration of 100µg/mL (secondary stock solution).

#### (b) Sample Preparation

From the secondary stock solution various concentrations such as 0-10 µg/mL were prepared for calibration curve. Standard curve was plotted by taking absorbance in UV double beam spectrophotometer at 322nm.

### Standard Calibration Curve of Metformin HCl

(a) Stock Sample Preparation: Accurately weighed 100mg of drug was first dissolved 100ml of Phosphate buffer pH 6.8 in 100ml of volumetric flask to make a concentration of 1000µg/mL (primary stock solution). 5ml of primary stock

solution was pipette out into 50 ml of volumetric flask and volume was adjusted Phosphate buffer pH 6.8 to make a concentration of 100µg/mL (secondary stock solution.

**(b) Sample Preparation**

From the secondary stock solution various concentrations such as 0-10 µg/mL were prepared for calibration curve. Standard curve was plotted by taking absorbance in UV double beam spectrophotometer at 232nm.

**Evaluation Tests for Tablets**

**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.

$$\text{Percentage deviation} = \frac{[\text{Weight of tablet (mg)} - \text{Average weight of tablet (mg)}]}{\text{Average weight of tablet (mg)}} \times 100$$

TABLE 3. Limits for weight variation.

Average weight of tablets(mg)		Maximum Percentage Deviation
IP	USP	
130 or less	80 or less	±10
130 to 324	80 to 250	±7.5
324 or more	250 or more	±5

**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. 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/cm<sup>2</sup>

**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:

$$\text{Friability} = \frac{(\text{Initial wt} - \text{Final wt})}{\text{Initial wt}} \times 100$$

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 p<sup>H</sup>- 6.8 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.

TABLE 4. Disintegration testing condition and interpretation (IP).

S. No	Type of tablets	Medium	Temperature	Limits
1.	Uncoated	Water/Buffer	37°±2°C	15 min as per individual monograph
2.	Film coated	Water	37°±2°C	30 min as per individual monograph
3.	Sugar coated	Water /0.1N Hcl	37°±2°C	60 min as per individual monograph
4.	Dispersible Tablets	Water	25°±1°C	03 min as per individual monograph
5.	Effervescent Tablets	Water	25°±5°C	0.5 min as per individual monograph
6.	Enteric Coated Tablets	0.1M Hcl mixed phosphate buffer pH 6.8	37°±2°C	02 hour in Hcl: no disintegration 60 minutes in buffer: disintegrate
7.	Soluble Tablets	Water	20°±5°C	03 min

**Content Uniformity**

**(a) Content uniformity for Ranitidine**

Weigh and powder 20 tablets .Weigh accurately a quantity of the powder containing about 0.1gms of Ranitidine, shake with 70ml of water for 15minutes, dilute to 100ml with water and filter. Dilute 10ml of the filtrate to 100ml with water. Further dilute 10ml to 100ml with water and measure the absorbance of the resulting solution at the maximum at about 322nm.calculate the absorbance at 322nm.

**(b) Content uniformity for Metformin HCl**

Weigh and powder 20 tablets .Weigh accurately a quantity of the powder containing about 0.1gms of Metformin Hydrochloride, shake with 70ml of water for 15minutes, dilute to 100ml with water and filter. Dilute 10ml of the filtrate to 100ml with water. Further dilute 10ml to 100ml with water and measure the absorbance of the resulting solution at the maximum at about 232nm.calculate the absorbance at 232nm.

To Calculate the Content uniformity by using the following formula

$$\text{Assay} = (A_t/A_s) \times C_s \times (D_t/W_d) \times 100$$

Where  $A_t$  is the Sample (test) absorbance.

$A_s$  is the Standard absorbance,  $C_s$  is the standard concentration of drug,  $D_t$  is the dilution factor,  $W_d$  is the Weight of the drug

*In-Vitro Drug Release study*

*Dissolution studies*

The drug release rate of Ranitidine and Metformin HCl tablets were determined by using United States Pharmacopeia (USP) dissolution testing apparatus type 2 (paddle method). The dissolution test was performed by using 900 ml of Dissolution medium at  $37 \pm 0.5^\circ \text{C}$  and 50 rpm. In specified time intervals an aliquot of 5ml samples of the solution were withdrawn from the dissolution apparatus and with replacement of fresh fluid to dissolution medium. The samples were filtered through filter paper of 0.45  $\mu\text{m}$ . Absorbance of these solutions were measure at  $\lambda_{\text{max}}$  322 nm for Ranitidine and 232nm for Metformin HCl by using UV/Visible Spectrophotometer. The drug release of tablet was plotted against time to determine the release profile of selected generic and branded drugs.

The % drug release of the formulation can be calculated by

$$\% \text{ drug release} = (A_t/A_s) \times C_s \times (D_t \times V_m/W_d \times 1000) \times 100$$

Where  $A_t$  is the Sample (test) Absorbance.

$A_s$  is the Standard Absorbance,  $C_s$  is the standard concentration of drug,  $D_t$  is the Dilution factor,  $W_d$  is the Weight of the drug,  $V_m$  is the volume of the dissolution medium.

TABLE 5. Dissolution parameters.

Dissolution Parameters	For Ranitidine	For Metformin HCl
Dissolution medium	0.1N HCl	Phosphate Buffer- pH 6.8
Dissolution medium volume	900ml	900ml
Apparatus	USP-II (Paddle type)	USP-II (Paddle type)
Speed	50 rpm	50 rpm

of rotation		
Temperature	$37 \pm 0.5^\circ \text{C}$	$37 \pm 0.5^\circ \text{C}$
Volume of Samples withdrawn	5ml	5ml
Sampling time interval(min)	5,10,15,20,25,30,40,50,60	5,10,15,20,25,30,40,50,60
Measurement of absorbance	322nm	232nm

*In-Vitro Release Kinetics Studies*

The analysis of drug release mechanism from a pharmaceutical dosage form is Important but complicated process and is practically evident in the case of matrix systems. The order of drug release from was described by using zero order kinetics or first order kinetics.

*Zero Order Release Kinetics*

It defines a linear relationship between the fractions of drug released versus time.

$$Q = k_0 t$$

Where,  $Q$  is the fraction of drug released at time  $t$ .

$k_0$  is the zero order release rate constant.

A plot of the fraction of % of drug released against time (min) will be linear if the release obeys zero order release kinetics.

*First Order Release Kinetics*

Wagner assuming that the exposed surface area of a tablet decreased exponentially with time during dissolution process suggested that the drug release from most of the slow release tablets could be described adequately by the first-order kinetics. The equation that describes first order kinetics is

$$\text{Log } C = \text{Log } C_0 - kt/2.303$$

Where  $C$  is the amount of drug dissolved at time  $t$ ,

$C_0$  is the amount of drug dissolved at  $t=0$  and

$k$  is the first order rate constant

A graph of log cumulative of log % drug remaining Vs time yields a straight line. It will be linear if the release obeys the first order release kinetics.

III. RESULTS & DISCUSSION

TABLE 6. Branded and generic drug characteristics.

S.NO	Drug Code	Colour	Odour	Thickness in mm (mean $\pm$ S.D)	Diameter in mm (mean $\pm$ S.D)	Shape
1	C1	Orange	Characteristic	$2.86 \pm 0.11$	$3.14 \pm 0.09$	Round
2	C2	Brick Red	Characteristic	$2.90 \pm 0.02$	$3.14 \pm 0.06$	Round
3	C3	White	Characteristic	$4.60 \pm 0.10$	$12.57 \pm 0.11$	Oblong/Capsule
4	C4	White	Characteristic	$4.80 \pm 0.14$	$12.57 \pm 0.02$	Oblong/Capsule

*Standard Calibration Curves*

TABLE 7. Standard calibration curve data of ranitidine.

S.No	Concentration( $\mu\text{g/ml}$ )	Absorbance at 322 nm
1	0	0
2	2	$0.101 \pm 0.0003$
3	4	$0.196 \pm 0.0012$
4	6	$0.28 \pm 0.0004$
5	8	$0.372 \pm 0.0006$
6	10	$0.471 \pm 0.0011$

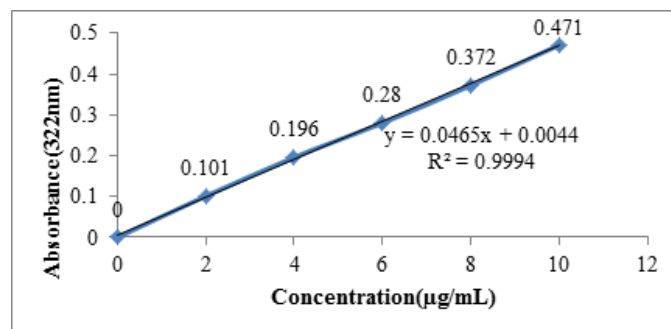


Fig. 1. Standard calibration curve of ranitidine.

TABLE 8. Standard calibration curve data of metformin HCl.

S.No	Concentration( $\mu\text{g/ml}$ )	Absorbance at 232 nm
1	0	0
2	2	0.011 $\pm$ 0.0017
3	4	0.023 $\pm$ 0.0008
4	6	0.034 $\pm$ 0.0014
5	8	0.045 $\pm$ 0.0004
6	10	0.057 $\pm$ 0.0007

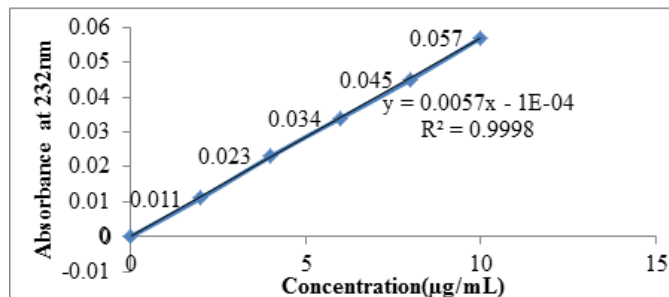


Fig. 2. Standard calibration curve of metformin HCl.

I. EVALUATION TESTS FOR TABLETS

All the Branded and Generic tablets were evaluated for thickness, drug content, hardness, friability and disintegration time and *In - Vitro* dissolution studies.

TABLE 9. Evaluation of branded and generic tablets.

Codes	Weight variation (mg)	Thickness in mm (mean $\pm$ S.D)	Hardness in kg/cm <sup>2</sup> (mean $\pm$ S.D)	Friability in % (mean $\pm$ S.D)	Assay in % (mean $\pm$ S.D)	Disintegration time in min (mean $\pm$ S.D)
C1	Pass	2.86 $\pm$ 0.11	4.23 $\pm$ 0.02	0.66 $\pm$ 0.03	100.28 $\pm$ 0.10	5.2 $\pm$ 0.05
C2	Pass	2.90 $\pm$ 0.02	4.61 $\pm$ 0.08	0.75 $\pm$ 0.05	98.23 $\pm$ 0.13	8.45 $\pm$ 0.07
C3	Pass	4.60 $\pm$ 0.10	4.82 $\pm$ 0.02	0.63 $\pm$ 0.02	99.64 $\pm$ 0.10	6.5 $\pm$ 0.03
C4	Pass	4.80 $\pm$ 0.14	5.25 $\pm$ 0.06	0.60 $\pm$ 0.08	99.13 $\pm$ 0.07	8.6 $\pm$ 0.08

TABLE 10. Disintegration time of branded and generic tablets.

S.No	Code	Disintegration Time in min
1	C1	5.2 $\pm$ 0.05
2	C2	8.45 $\pm$ 0.07
3	C3	6.5 $\pm$ 0.03
4	C4	8.6 $\pm$ 0.08

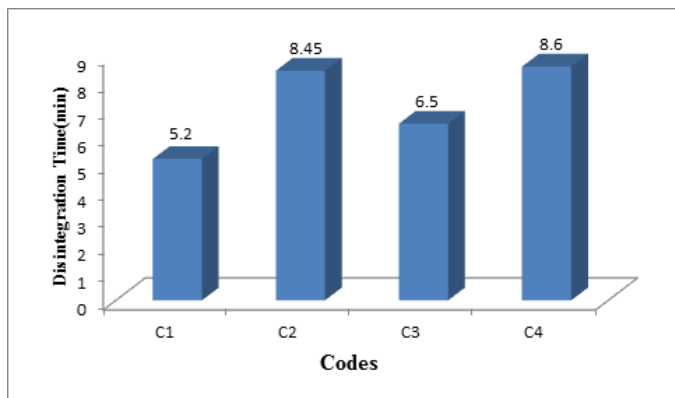


Fig. 3. Disintegration time of branded and generic tablets.

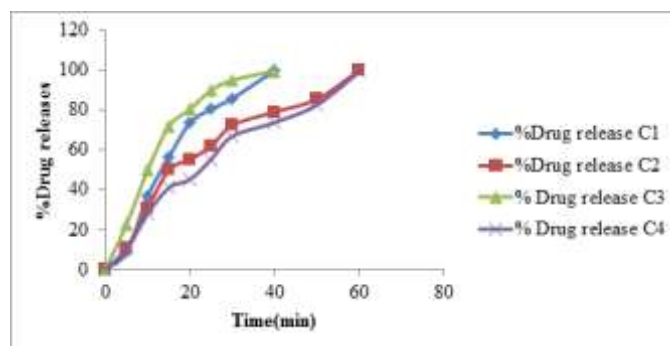


Fig. 4. Dissolution profile of branded and generic tablets (C1 to C4).

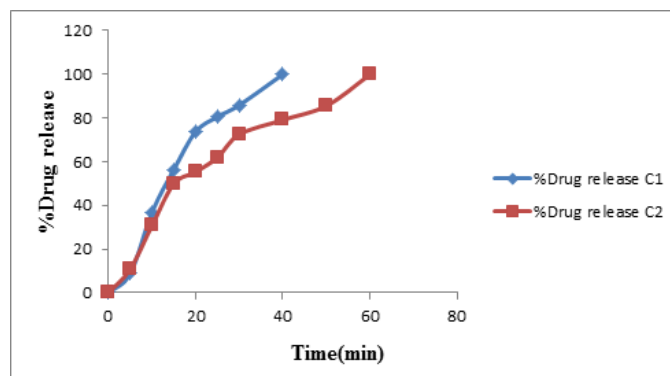


Fig. 5. Dissolution graph of C1 & C2.

*In - Vitro* Dissolution Studies

TABLE 11. Dissolution profile of branded and generic tablets (C1to C4)

S.No	Time in min	% Drug Release			
		C1	C2	C3	C4
1	0	0	0	0	0
2	5	8.79 $\pm$ 0.09	10.87 $\pm$ 0.08	22.76 $\pm$ 0.06	10.15 $\pm$ 0.05
3	10	36.9 $\pm$ 0.11	30.81 $\pm$ 0.10	49.88 $\pm$ 0.09	28 $\pm$ 0.08
4	15	56.34 $\pm$ 0.13	49.88 $\pm$ 0.12	71.81 $\pm$ 0.08	41.11 $\pm$ 0.09
5	20	73.69 $\pm$ 0.15	55.33 $\pm$ 0.14	80.5 $\pm$ 0.11	45.27 $\pm$ 0.12
6	25	80.5 $\pm$ 0.014	61.9 $\pm$ 0.07	90 $\pm$ 0.04	55.33 $\pm$ 0.11
7	30	85.87 $\pm$ 0.16	72.45 $\pm$ 0.09	94.98 $\pm$ 0.12	66.88 $\pm$ 0.12
8	40	99.93 $\pm$ 0.17	79.1 $\pm$ 0.15	99.66 $\pm$ 0.17	73.8 $\pm$ 0.14
9	50		99.04 $\pm$ 0.17		82.62 $\pm$ 0.17
10	60				99.21 $\pm$ 0.11

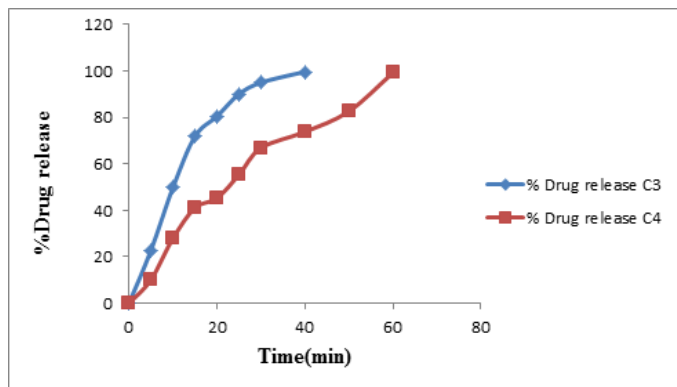


Fig. 6. Dissolution graph of C3&C4.

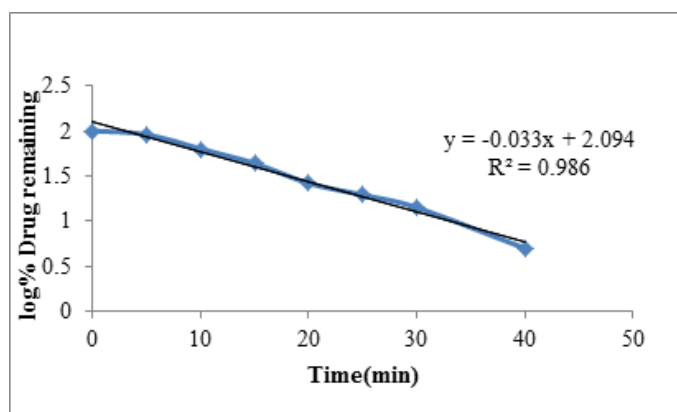


Fig. 7. First order kinetic of C1.

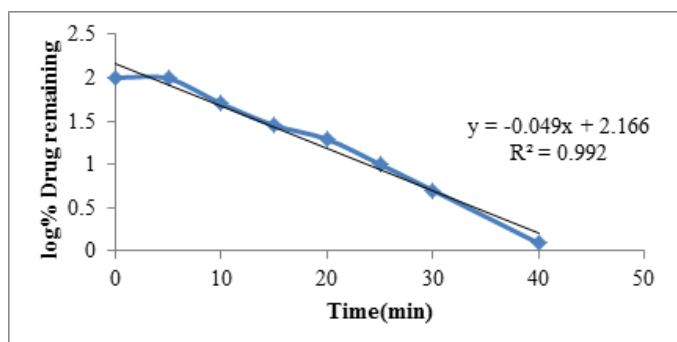


Fig. 9. First order kinetics of C3.

## II. CONCLUSION

The present study was aimed to compare the Branded and Generic tablets based on the Price and Evaluation tests of tablets. For this study we have selected two fast moving drugs i.e. Ranitidine & Metformin which are anti histaminic & anti diabetic drugs respectively. It was observed that the Weight variation, Hardness, Friability, Thickness, Disintegration and Assay results showed better for Branded drugs compared to Generic drugs, but both the values were found to be within the limits. Based on the *In-Vitro* dissolution studies, Drug Release Rate kinetics and Correlation coefficient value the Branded

drugs showed better drug release compared to generic drugs. The mechanism of drug release was followed to be First order kinetics for Branded and Generic drugs.

Both Branded and Generic tablets of the two “paired” medicines had identical quality and they fulfilled all the criteria prescribed by the Indian pharmacopoeia. Hence, the general notion and doubt regarding the quality of the Generic medicines needs to be erased conducting more such studies and publishing them widely. The economic benefits of the use of Generic medicines cannot be denied; and in many countries their use is essential to control healthcare spending. Suitable changes in the drug price policy may be made to have lower prices for Generic medicines. Transparency in fixing the MRP by the manufacturer and clear guidelines for mark-ups at least for Generics is required in pharmaceutical trade. The government and healthcare professionals must take up generic promotional schemes, general awareness programs on quality of generics to build confidence among prescribers, pharmacists, and consumers.

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