A comparative evaluation of the quality & price of generic medicine with their branded counterparts

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ABSTRACT

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 present study aims to evaluate and compare the quality of generic medicine with their branded counterparts as per Indian Pharmacopoeial standards and other validated methods on a commonly used type 2 diabetes drug (Metformin). The qualitative as well as quantitative studies were performed as per IP 2010. The official test performed includes uniformity of weight, disintegration, dissolution, assay and friability. Non official test includes hardness test and assay by HPLC using validated methods. The study revealed that branded as well as generic metformin tablets comply with the standards provided in IP 2010 and generic metformin was found to be 111.52% lesser in cost per tablet as compared to costliest branded version of metformin.

Keywords: generics, branded medicine, metformin, quality of generics, *Jan Aushadhi.*

INTRODUCTION

A baguette brand bag costs more because of its good quality as compared to a non-branded bag, although it is not the same in the case of quality of low cost generics or non-branded medicines when compared to their branded counterparts. Generic medicines are equally effective and safe in terms of quality to their costly branded counterpart. A study reported by US FDA of the evaluation of the results of 38 published clinical trials that compared cardiovascular generic medicines to their branded counterparts revealed no evidence that brand-name heart drugs worked any better than generic heart drugs [1].

According to World Health Organization (W.H.O.) "a generic drug is a pharmaceutical product, usually intended to be interchangeable with an innovator product that is manufactured without a license from the innovator company and marketed after the expiry date of the patent or other exclusive rights" [2].

When it comes to prescribing a generic medicine most of the doctors in India and several other countries are found to be reluctant in prescribing generic medicine due to cynical about the quality, safety and efficacy of generic medicine. Medical Council of India, Code of Ethics Regulations regarding the use of Generic names of drugs says *"Every physician should, as far as possible, prescribe drugs with generic names and he / she shall ensure that there is a rational prescription and use of drugs"* [3]. Prescribing medicine with generic name was also recommended by Parliamentary Standing Committee (PSC) for Health and Family Welfare to the 'Rajya Sabha' on August 4, 2010 [4]. Several studies conducted worldwide raise the issue of myths and prejudice regarding the 'quality' of generic medicine in the minds of patients, healthcare professionals and even the medical specialists.

A study conducted to evaluate perceptions of physician about generic medicine in USA in 2011 revealed that out of 506 physicians surveyed more than 23% of physicians expressed negative perceptions about efficacy of generic drugs, almost 50% reported negative perceptions about quality of generic medications and more than one quarter do not choose to use generics as first-line medications for themselves or for their families [5].

Similarly a study in Malaysia revealed that majority of physicians was positive about generics substitution but doubtful about their quality in terms of efficacy and safety for some drug categories [6]. According to a survey report conducted on 500

doctors in Haryana, India reveals that 40% of doctors in private as well as in public facilities never prescribe a generic medicine [7]. There are several similar studies worldwide by Jamshed *et al.* [8], Yousefi *et al.* [9], Kumar *et al.* [10] and Gupta *et al.* [11], which describe the misconception in minds of physician as well as patient about the quality of generic medicine.

A generic medicine costs less from that branded medicine because a brand name medicine has to go through 10-15 years of research and testing in animals and clinical trials in proving that it is safe and effective before it can be sold to the public. The testing can cost over $1 billion. Once the new drug is approved, the company that made and tested it files for patent protection and as it receives a patent, that company is only the sole manufacturer of that medicine. When a patent for a brand name medicine expires, any other company can copy the medicine and sell a generic version. These other companies are required to only prove that their product is the same as the brand name medicine through Bioavailability/Bioequivalence studies [12]. This means that generic drug companies do not have to spend as much time and money because they do not have to conduct clinical trials. Since there are ample of companies manufacturing the generic medicine, due to competition the price is lowered even farther.

Skyrocketing cost of medicine has always been a matter of great concern to the health authorities providing health care to mankind. Efforts are made globally to provide quality medicine at affordable prices to the public at large. Generic medicines provide the same medical benefits to the suffering mankind as these are certified to be perfect substitute for the innovator branded product and its use can reduce the healthcare expenditure to a great extent. The effective use of generic products saved the U.S. health system nearly $1.5 trillion over the past 10 years (2004-2013) as per the IMS Institute for Healthcare Informatics [13]. As per US-FDA data nearly 8 in 10 prescriptions filled in the United States are for generic drugs (2014) [14].

In India due to the prejudice in the minds of physicians regarding the safety and efficacy of generics, their use is hindered and further as per law pharmacist cannot substitute the brand name with generic [15] so consumer has to buy costly branded medicine even though the equivalent low cost generic medicines are available.

With a view to adjudge and compare the quality of generic medicines with that of their costly branded counterparts, a comparative quality evaluation study was undertaken on commonly used drug for type 2 diabetes i.e. Metformin. India has more diabetics than any other country in the world, as per the International Diabetes Foundation the estimate of the actual number of diabetics in India is around 40 million (2014) [16]. So a commonly prescribed medicine (metformin) was selected and their existed remarkable price difference between generic and branded metformin.

MATERIAL AND METHODS

Materials:

Standard Metformin was procured as a gift sample from Mankind Pharma. The three branded marketed formulation of Metformin was purchased from authorized dealer (Glycomet®, Gluformin® and Glyciphage®) and generic version was obtained from *Jan Aushadhi* store, Shastri Bhawan, New Delhi. All of the samples purchased were containing 500 mg of Metformin and all of them were in tablet dosage form. The efforts were made to procure these test samples having almost identical dates of manufacturing to rule out the possibility of difference in assay of the samples bearing different dates of manufacturing. The chemicals Acetonitrile, O-phosphoric acid were of HPLC grade and Sodium Hydroxide, Potassium di-hydrogen phosphate were of analytical grade. Milli-Q-Water was used for preparing all HPLC solutions and rest procedure distilled water was used.

Methods:

1. OFFICIAL TESTS

The following official tests were performed on all the three branded and generic metformin. Identification of Standard metformin was done as per IP 2010 through Infrared Spectroscopy. The IR spectrum of standard metformin is provided in Figure 1.3.

(i) Uniformity of weight: 20 tablets selected randomly weighed individually (using Mettler Toledo weighing balance) 20 units and average weight was calculated.

(ii) Dissolution: Dissolution study was performed using the IP Apparatus 2 (Lab India DS 8000-basket type) in 900 ml phosphate buffer pH 6.8, maintained at 37±0.5°C with paddle speed at 100 rpm for 45 minutes. 5 milliliters of samples were withdrawn at specified time intervals. The volume of dissolution fluid was adjusted to 900 ml, by replacing each 5 ml aliquot withdrawn with 5 ml of phosphate buffer pH 6.8, pre-warmed at 37±0.5°C. Samples withdrawn were filtered through whatmann filter paper (no.41), suitably diluted with phosphate buffer pH 6.8, and analyzed at 233 nm, using UV-Visible double beam spectrophotometer (UV-Visible spectrophotometer 3000, Lab India). The content of $C_4H_{11}N_5.HCl$ was calculated in the medium taking 806 as the specific absorbance at 233 nm. The percentage drug release is depicted in Figure 1.1.

(iii) Disintegration Test: Disintegration was performed using basket rack assembly (IP 2010) maintained at 37±2°C. One tablet was introduced into each of 6 tubes and, a disc was added on each tube. The assembly was suspended in the beaker containing distilled water and operated for the specified time.

(iv) Assay: 20 tablets were weighed and powdered. The exact amount of powder was weighed containing about 0.1 g of Metformin Hydrochloride; it was shaken with 70 ml of distilled water for 15 minutes, diluted to 100.0 ml and filtered. 10.0 ml of this filtrate diluted to 100.0 ml with distilled water. Further diluted 10.0 ml of above solution to 100.0 ml with distilled water and measured the absorbance of the resulting solution at the maximum at about 232 nm. The content of $C_4H_{11}N_5.HCl$ was calculated taking 798 as the specific absorbance at 232 nm.

(v) Friability: A sample of whole tablets (11 tablets) corresponding to about 6.5 g weight was taken. The tablets were placed in drum and rotated it 100 times at 25 rpm. Tablets were removed and any loose dust from them also discarded and weighed. Dedusted the tablets carefully and weighed accurately.

2. UNOFFICIAL TESTS
The assay of metformin was also performed by HPLC through modified method [17].

(i) Assay: Accurately weighed 100 mg of standard metformin and dissolved in mobile phase; Acetonitrile:Water acidified to pH 3 by O.P.A (30:70). This solution was filtered through whatmann filter (No.41) and 7 dilutions were made and assay was performed using HPLC (Agilent 1200 series) by Agilent ODS column (250 mm x 4.6 mm i. d., 5 µm particle size). Flow rate of mobile phase was set to 1 ml/min and injection volume was 20 µl. The wavelength for detection used was 250 nm and column compartment temperature was 30ºc. The standard plot of Metformin by HPLC is depicted in Figure 1.2. Similarly the samples were examined in triplicate. 20 tablets were weighed individually and average weight was calculated and powdered. Exact amount of powder was weighed containing 100 mg of metformin and dilution was made in mobile phase, filtered and examined in same conditions as that of standard.

(ii) Hardness Test: Hardness was tested using Pfizer Hardness Tester. The tablet was placed between two platens and compressed and the value of the hardness is measured (kg/cm2). The platens should be parallel and their faces should be polished smooth and precision-ground perpendicularly to the direction of movement.

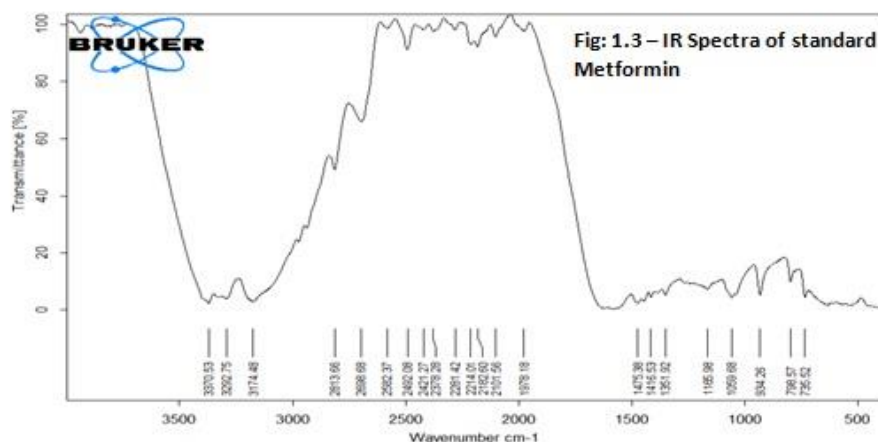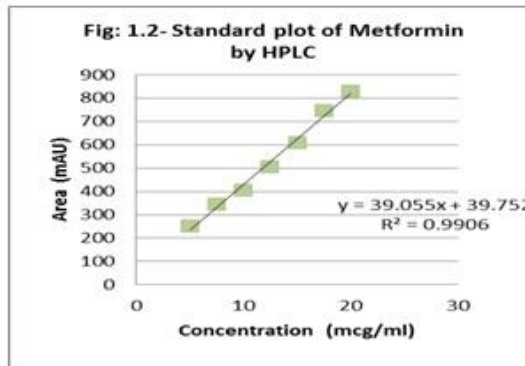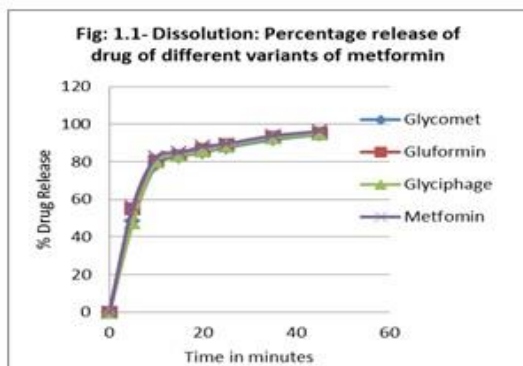## PRICE VARIATION OF BRANDED MEDICINE TO THAT OF GENERIC MEDICINE
Out of all the three branded metformin formulation from USV- Glycomet®, Abbott- Gluformin® and Franco Indian- Glyciphage® and one generic version from *Jan Aushadhi* contained the same labeled amount of metformin i.e. 500mg but the price per tablet varied. The per tablet price of Glycomet®, Gluformin® and Glyciphage® were Rs.1.69, Rs.1.63 and Rs.1.46 while that of generic was Rs.0.48 per tablet. This shows a price variation of 111.52% as compared to branded version. This data suggest that switching the prescription from branded to generic drug can result to a huge amount cost saving and cutting down the health care expenditure without compromising with the safety, quality and efficacy of medicinal product. The trade name, price, batch number, strength and manufacturer is depicted in Table 1 (b) and Figure 1.4 shows the percent variation in price of 4 variants.

RESULTS AND DISCUSSIONS

In this research work, the quality of generic Metformin (Jan Aushadhi Store) was compared to that of branded Metformin (Glycomet®, Gluformin®, and Glyciphage®), using pharmacopoeial and other tests. It was found that the generic Metformin was of "similar" pharmacopoeial standards, as that of branded Metformin, although the generic Metformin was much cheaper than the branded Metformin (111.52 % cheaper than costliest branded counterpart). The branded and generic variant showed comparable results. The assay was found to be more than 95% and less than 105% as per IP 2010, of all the branded (100.37%, 99.74%, 99.24%) and generic medicine (99.87%). (The results of the entire tests performed is depicted in Table 1 (a)) Hence, the general notion and doubt regarding the quality of the generic version of medicines needs to be expunged and government must campaign to promote generics about their quality and efficacy.

CONCLUSION

All the four variants of metformin tablets confirmed with the limits provided in IP 2010, in term of Uniformity of weight, Disintegration, Dissolution, Assay and Friability. This confirms that the generic medications are of equivalent and comparable quality of the costlier branded medicines available in the market. The government should therefore expand the scheme of opening *Jan Aushadhi* stores and promoting generics throughout the country to provide quality medicine at affordable prices to larger section of its population. There is also dire necessity of expanding the scope of the study to entire range of generic medicines available at different centers to eradicate the myth about quality and safety of generic medicines. Creating public awareness by advertisements in print as well as electronic media to instill confidence in the minds of patients and physician regarding quality and efficacy of such drugs and also to propagate that patient ask their doctors to prescribe medicines in generic name rather than the brand name /trade name through which the benefit of the scheme can be finally be availed.
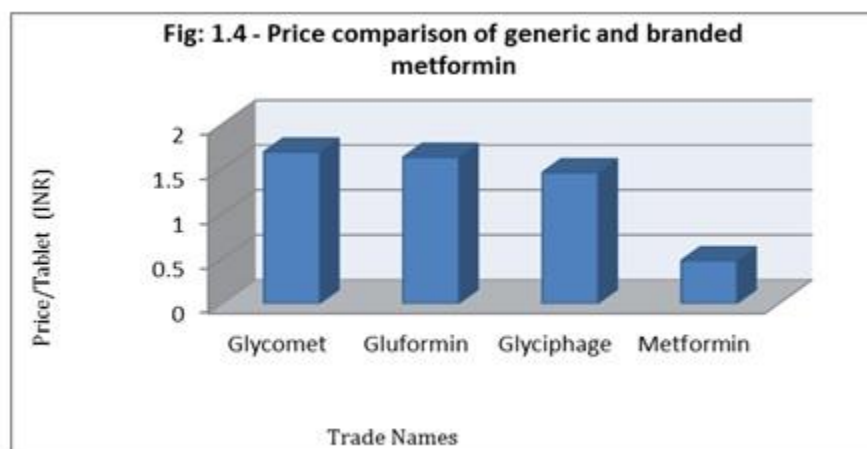

Fig: 1.1- Dissolution: Percentage release of drug of different variants of metformin

Fig: 1.2- Standard plot of Metformin by HPLC

$y = 39.055x + 39.752$
$R^2 = 0.9906$

Fig: 1.3 – IR Spectra of standard Metformin

Fig: 1.4 - Price comparison of generic and branded metformin

Table 1 (a): Results of tests performed.

	TRADE NAME	GLYCOMET	GLUFORMIN	GLYCIPHAGE	GENERIC-
	TEST				METFORMIN
Uniformity of Weight	Observations (Average Weight of 20 tablets in mg)	586.15	596.02	549.54	628.94
	Limits (As per I.P. 2010)	556.75- 615.36	566.22- 625.82	522.06- 577.02	597.52-660.31
	Results	All the 20 tablets comply with the test and were found within the above range.			
Dissolution	Observations (% Amount of Drug Release after 45 minutes)	94.43%	95.02%	94.75%	96.25%
	Limits (As per I.P. 2010)	Not less than 70% of the label claimed			
	Results	Complies			
Disintegration	Observations (Average time of 6 tablets on minutes)	12.11	4.25	3.38	3.32
	Limits (As per I.P. 2010)	Not more than 15 minutes			
	Results	Complies			
Assay	Observations (% of drug content)	100.37%	99.74%	99.24%	99.87%
	Limits (As per I.P. 2010)	Not less than 95% and not more than 105%			
	Results	Complies			
Friability	Observations (% weight lost after friability)	0.46	0.31	0.15	0.29

Hardness Test	**Limits** (As per I.P. 2010)	Not more than 1%			
	Results	Complies			
	Observations	10 kg/cm^2	8 kg/cm^2	7.5 kg/cm^2	6.5 Kg/cm^2
	Limits	5-10 Kg/cm^2			
	Results	Complies			
Assay by HPLC	**Observations** (AUC)	414.56	405.25	395.07	394.72
	Limits (As per IP 2010)	385.84 to 426.46			
	Results	Complies			

Table: 1. (b) Branded and Generic Metformin.

Trade Name	Company	IIN Name & Strength	Price (Rupees)	Packing	Price/Tab (Rupees)
GLYCOMET	USV	Metformin-500mg	16.95	1*10	1.69
GLUFORMIN	Abbott	Metformin-500mg	16.38	1*10	1.63
GLYCIPHAGE	Franco-Indian Pharmaceuticals Ltd.	Metformin-500mg	29.20	1*20	1.46
METFORMIN	*Jan Aushadhi*	Metformin-500mg	4.80	1*10	0.48

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