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A COMPARATIVE EVALUATION OF BRANDED AND GENERIC PRODUCTS OF METFORMIN TABLETS

K. P. R. Chowdary* and Ch. P. S. R. MadhuriVikas

Institute of Pharmaceutical Sciences, Nidigatla Road, Rajahmundry- 533103.

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***Correspondence**
For Author
Prof. K. P. R. Chowdary
Institute of Pharmaceutical Sciences, Nidigatla Road, Rajahmundry- 533103.

ABSTRACT

Metformin is a widely prescribed oral anti diabetic drug and is official in I.P 2014.Several brands of metformin tablets and generic metformin tablets are available in the market leading to a confusion of their quality and prices. The objective of the present study is to make a comparative evaluation of three metformin drug products (two branded, and one generic). The branded and generic products of metformin tablets procured from local pharmacies were evaluated for various physical parameters and *in vitro* dissolution rate as per official methods. The *in vitro* dissolution performance of the branded and generic products of metformin tablets is similar. No significant differences were observed in the dissolution parameters of the branded and generic products.. The differences observed in the dissolution characteristics of the three products tested as well as the trail variability are not significant ($P > 0.05$). All the three products of metformin tablets tested fulfilled the official (IP 2014) dissolution rate test specification of NLT 70% in 45 min.

KEYWORDS: Metformin tablets, Branded and generic products , Dissolution rate, Comparative study.

INTRODUCTION

Metformin is a widely prescribed oral anti diabetic drug and is official in I.P 2014. It is marketed as uncoated tablets of 500 mg strength. A dissolution rate test with a specification of NLT 70% dissolution in 45 minutes is prescribed in I.P 2014 to check the quality of market products. Several brands of metformin tablets as well as generic metformin tablets are available in the market leading to a confusion of their quality and prices.

A branded product contains,[1] a new drug that is discovered, developed and marketed by a pharmaceutical company over which the company has a patent to protect against other companies making copies and selling this drug. Developing a new drug involves many scientific studies and clinical studies to get approval from regulating authorities. The research and development cost along with marketing cost are the reasons for higher prices of the branded products. When the patent over a new drug developed expires, other manufactures can produce equivalent products called generic products and they are marketed by drug common scientific name. Generic products have less research and development cost since the original manufacturer had already done many studies to prove that the drug is safe. The branded products are costlier than generic products. The branded and generic products look different.[2] as they could have different sizes, shapes, colour, and markings, different names and also different cost. Because of the low cost the generic products are considered as less efficient and effective when compared to branded products though several studies,[3-7] proved that they are equally effective.

The objective of the present study is to make a comparative evaluation of three metformin drug products (two branded, and one generic). The branded and generic products of metformin tablets were evaluated for various physical parameters and in vitro dissolution rate as per official methods .The dissolution parameters of the three products tested are analysed as per ANOVA two way classification to evaluate their significance.

EXPERIMENTAL

MATERIALS

The following products of metformin tablets are procured from local pharmacies. Glyciphage (Branded metformin tablets), M/s FrancoIndian Pharmaceutical Pvt. Ltd., Batch No: GA14234, Mfg .Dt ., 09/2014 , Exp. Dt : 08/2017.

Okamet 500(Branded metformin tablets), M/s Cipla Ltd., Batch. No: AH4240, Mfg. Dt: June, 2014, Exp. Dt: May 2017.

Metformin hydrochloride tablets IP (generic metformin tablets) , M/s Biogenetics Drugs Pvt. Ltd ., Batch .No 45043 – BG138 ,Mfg. Dt: April ,2013 , Exp. Dt: Sept., 2015.

Metformin hydrochloride was a gift sample from M/s Natco Pharma Pvt.Ltd., Hyderabad. All other materials used were of pharmacopoeial grade.

METHODS

Estimation of Metformin

An UV Spectrophotometric method based on the measurement of absorbance at 233 nm in phosphate buffer of pH 6.8 was used for the estimation of metformin hydrochloride. The method was validated for linearity, accuracy, precision and interference. The method obeyed Beer's law in the concentration range of 1 – 10 µg/ ml. When a standard drug solution was repeatedly assayed (n=6), the relative error and coefficient of variance were found to be 0.6% and 1.40% respectively. No interference by the excipients used in the study was observed.

Evaluation of metformin Tablets

All the products of metformin tablets procured were evaluated for drug content, hardness, friability, disintegration time and dissolution rate as follows.

Hardness

The hardness of the prepared tablets was determined by using Monsanto hardness tester and measured in terms of kg/cm^2.

Friability

The friability of the tablets was measured in a Roche friabilator using the formula

Friability (%) = [(Initial weight- Final weight) / (Initial weight)] x 100

Drug Content

Five tablets were weighed in each case and powdered in a glass mortar with a pestle. An accurately weighed quantity of tablet powder equivalent to 25 mg of metformin was taken into 25 ml volumetric flask, methanol was added and mixed to dissolve the drug. The solution was made upto 25 ml with methanol. The solution was then suitably diluted with phosphate buffer of pH 6.8 and assayed for metformin at 233 nm.

Disintegration time

Disintegration time of the tablets was determined using single unit disintegration test apparatus (Make: Paramount) employing water as test fluid.

Dissolution Rate Study

Dissolution rate of metformin from various products of metformin tablets was studied employing eight station dissolution rate test apparatus (LABINDIA, DS 8000) using paddle stirrer at 50 rpm and at a temperature of 37°C ± 1°C. Phosphate buffer of pH 6.8 (900 ml)

was used as dissolution fluid. One tablet containing 500 mg of metformin was used in each test. Samples of dissolution fluid (5 ml) were withdrawn through a filter at different time intervals and assayed for metformin at 233 nm. The sample of dissolution fluid withdrawn at each time was replaced with fresh drug free dissolution fluid and a suitable correction was made for the amount of drug present in the samples withdrawn in calculating percent dissolved at various times. Each dissolution experiment was run in triplicate (n=3).

Analysis of Data

The dissolution data were analyzed as per zero order and first order kinetic models. Dissolution efficiency (DE_{30}) values were estimated as suggested by Khan.[8] The dissolution parameters of the three products tested were also analysed as per ANOVA two- way classification to evaluate their significance.

RESULTS AND DISCUSSION

Metformin is a widely prescribed oral anti diabetic drug and is official in I.P 2014.Several brands of metformin tablets and generic metformin tablets are available in the market leading to a confusion of their quality and prices. The objective of the present study is to make a comparative evaluation of three metformin drug products (two branded, and one generic). The branded and generic products of metformin tablets were evaluated for various physical parameters and *in vitro* dissolution rate as per official methods.

The physical parameters of metfromin products tested are given in Table 1. Hardness of the tablets was in the range of 4.0 – 5.5 kg/sq.cm with all the three products. Weight loss in the friability test was less than 0.98 % with all the three products. All the tablets tested were disintegrated with 2 min10 sec. Metformin content of all the three brands of tablets tested was within 100 ± 3% of the labeled content. As such all the three products of metformin tablets tested fulfilled the official (IP 2014) requirements of uncoated tablets with regard to hardness, friability, D.T and drug content.

Dissolution rate of metformin tablets tested was studied in phosphate buffer of pH 6.8 as prescribed in IP 2014. Variations were observed in the dissolution characteristics of the three products tested. The dissolution profiles of the products tested are shown in Fig.1. The dissolution parameters are summarized in Table 2. Based on PD_{10} (percent dissolved in 10 min) and DE_{30} (dissolution efficiency up to 30 min), the order of dissolution performance of the products tested was Glyciphage > Okamet > Metformin tablets. The dissolution of

metformin from all the products tested followed first order kinetics with R^2 (coefficient of determination) values greater than 0.940. The corresponding first order dissolution rates (K_1) are given in Table 2. The dissolution parameters, PD_{10} and DE_{30} of various products tested are analyzed by ANOVA two-way classification to find out the significance of the observed differences in the dissolution parameters of the three products tested and also the significance of the trail variability. The results of ANOVA are given in Tables 3- 4.The results of ANOVA of dissolution parameters indicated no significant differences in the dissolution characteristics of the three products tested ($P > 0.05$).ANOVA also indicated that the trail variability is also not significant ($P > 0.05$).All the three products tested fulfilled the official (IP 2014) dissolution rate test specification of NLT 70% in 45 min.

Table 1: Physical Parameters of Branded and Generic Tablets of Metformin

Product	Hardness (Kg/sq cm)	Friability (% wt loss)	D.T (min- sec)	Drug Content (%)
Glyciphage	4.0	0.85	1-40	96.8
Okamet	4.5	0.92	1-50	98.2
Metformin	5.5	0.98	2-10	99.2

Table 2: Dissolution Parameters of Branded and Generic Tablets of Metformin

Product	T_{50} (min)	PD_{10} (%)	DE_{30} (%)	K_1 (min^{-1})
Glyciphage	6.0	54.3	55.8	0.0435
Okamet	15.0	43.2	52.5	0.0318
Metformin	18.0	42.8	44.73	0.0360

Table 3: ANOVA 0f (PD_{30}) values for Metformin Tablets

Source of variation	Degrees of freedom	Sum of squares	Mean Sum of squares	F ratio
Total	8	430.34	53.79	
Treatment				
Product	2	196.21	98.1	1.99
Trail	2	37.21	18.60	2.7
Error	4	196.58	49.14	

$F_{(0.05)}$ (4, 2) = 19.24, $F_{(0.05)}$ (2, 4) = 6.94

Table 4: ANOVA of (DE_{30}) values for Metformin Tablets :

Source of variation	Degrees of freedom	Sum of squares	Mean Sum of squares	F ratio
Total	8	692.01	86.5	
Treatment Product Trail	 2 2	 149 131.8	 74.5 65.9	 1.37 1.55
Error	4	411.2	102.8	

$F_{(0.05)}(4, 2) = 19.24$

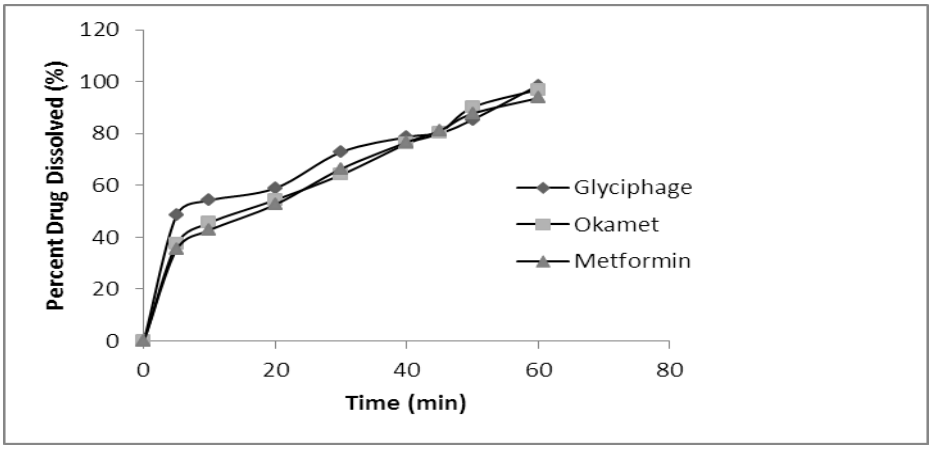

Fig.1: Dissolution Profiles of Branded and Generic Products of Metformin Tablets

CONCLUSIONS

1. The *in vitro* dissolution performance of the branded and generic products of metformin tablets is similar. No significant differences were observed in the dissolution parameters of the branded and generic products.

2. The differences observed in the dissolution characteristics of the three products tested as well as the trail variability are not significant ($P > 0.05$).

3.All the three products of metformin tablets tested fulfilled the official (IP 2014) dissolution rate test specification of NLT 70% in 45 min.

REFERENCES

1. FDA Web site at www.fda.gov/cder/ogd/index.html.
2. Davit BM, Nwakama PE, Buehler GJ, . Comparing generic and innovator drugs: a review of 12 years of bioequivalence data from the United States Food and Drug Administration. Ann Pharmacother., 2009; 43(10): 1583-1597.
3. McCormack J, Chmelicek JT. Generic versus brand name: the other drug war, Can Fam Physician., 2014; 60(10): 911.

4. Generics and Biosimilars Initiative. Quantitative evaluation of bioequivalence , available from: www.gabionline.net/Biosimilars/Research/Quantitative-evaluation-of-bioequivalence
5. Kesselheim AS, Misono AS, Lee JL, Stedman MR, Brookhart MA, Choudhry NK, Clinical equivalence of generic and brand-name drugs used in cardiovascular disease: a systematic review and meta-analysis. JAMA., 2008; 300(21): 2514-26.
6. Dentali F, Donadini MP, Clark N, Crowther MA, Garcia D, Hylek E, . Brand name versus generic warfarin: a systematic review of the literature, Pharmacotherapy. 2011; 31(4): 386-93.
7. Generics and Biosimilars Initiative. Generic substitution causing confusion, available from: www.gabionline.net/Generics/Research/Generic-substitution-causing-confusion Khan, K.A. *J. Pharm. Pharmacol.*, 1975; 27: 48- 49.