ISSN: 2321-3760

Research Article

International Journal of Current Trends in Pharmaceutical Research

IJCTPR, 2014, Vol. 2(3): 477-482

www.pharmaresearchlibrary.com/ijctpr

Comparative Evaluation of Different Brands of Metformin Hydrochloride 500 mg Tablets Marketed in India

M. Siva Kumar Naik[1], M. Devendra[1], P. Mohan Babu[1], B. Mohammed Ishaq[1]*, E. Satheesh Kumar[1], Hindustan Abdul Ahad[1], Ramesh Dhani[2]

[1]Dept. of Pharmaceutical Analysis, Balaji College of Pharmacy, Anantapur–515001, A.P, India.
[2]Dept. of Pharmaceutical Chemistry, Ratnam Institute of Pharmacy, SPSR Nellore, Andhra Pradesh, India-524346

Received: 5 February 2014, Accepted: 1 May 2014, Published Online: 15 May 2014

Abstract

There are several generics of metformin hydrochloride tablets available within the drug delivery system globally. Availability of numerous brands of Metformin Hydrochloride tablets in Indian drug market today places health practitioners in a dilemma of generic substitution. The aim of the present study was the evaluation and comparison between ten different Metformin hydrochloride brands which are commercially available in the Indian market. The physicochemical equivalence of ten brands of Metformin hydrochloride tablets were determined through the evaluation of both official and non-official standards according to the Indian pharmacopoeia including uniformity of weight, friability, hardness, disintegration, dissolution rate and drug content (Assay) etc. All the brands complied with the official specifications for uniformity of weight, disintegration and dissolution tests. Few Brand had the highest and lowest crushing strengths. However, for the friability test, one of the ten brands failed to meet the Indian pharmacopoeia specification for friability. Seven brands had values within the range specified for assay in the IP while few brand failed the test. Of all the ten brands evaluated in this study, Indian government supply tablets could be regarded as being biopharmaceutically and chemically equivalent and therefore can be interchanged in the clinical practice.

Keywords: Metformin hydrochloride tablets, Indian pharmacopoeia, friability, hardness, disintegration, dissolution rate, Assay.

Contents

***Corresponding author**
B. Mohammed Ishaq
Balaji College of Pharmacy,
Anantapur–515001, A.P., India.
E-mail: bmdishaq@yahoo.com
Manuscript ID: IJCTPR2125

PAPER-QR CODE

1. Introduction

Metformin HCl (chemical structure was shown in figure 1) is an oral anti-diabetic drug from the biguanide class used mainly to treat type 2 diabetes mellitus. Metformin hydrochloride works by improving the body's sensitivity to insulin, allowing it to use glucose in the normal way. It is the first-line drug of choice for the treatment of type 2 diabetes, particularly in overweight and obese people and those with normal kidney function. Metformin hydrochloride is also being used increasingly in polycystic ovary syndrome (PCOS) which is a syndrome of ovarian dysfunction and hyperandrogenism [1]. Evidences suggest that insulin resistance and resulting hyper insulinaemia play a central role in the pathogenesis of the syndrome. Metformin, an insulin sensitizer, not only improves hyperandrogenism but also improves ovulation as well as pregnancy rates in patients with PCOS, nonalcoholic fatty liver disease (NAFLD) and premature puberty [2].

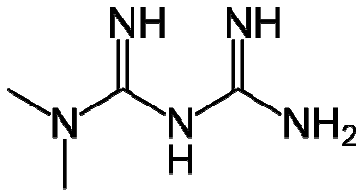

Figure 1. Chemical structure of Metformin HCl

Metformin was first described in the scientific literature in 1922, by Emil Werner and James Bell, as a product in the synthesis of N, Ndimethyl- guanidine free user [3]. French physician Jean Sterne published the first clinical trial of Metformin as a treatment for diabetes. It was introduced to the United Kingdom in 1958, Canada in 1972, and the United States in 1995. Metformin hydrochloride is now believed to be the most widely prescribed anti-diabetic drug in the world; in the United States alone, more than 48 million prescriptions were filled in 2010 for its generic formulations [4, 5].

Drug products that are biopharmaceutically and chemically equivalent must be identical in their quality, strength, purity and active ingredient release profile. They must to be in the same dosage form and intended for the same route of administration [6]. Dissolution testing of drug product is an important criterion in assessing the quality control to monitor batch to batch consistency of drug release [7]. The variations in the drug release among some generics indicate deficiency in the entire drug formulation and the delivery system. Dissolution rate determination used also for prediction of in-vivo bioavailability in most oral preparations [8, 9].

Metformin hydrochloride is the most popular anti-diabetic drug in India as well as all over the world. As reported by the annual statistical studies (Indian annual statistical book 2013) more than 25% of population is diabetic in India. Accordingly, the use of Metformin hydrochloride tablets needs to monitor and ensure the quality of the various brands commercially available in the Indian market in order to assess their quality control. Additionally, if these brands are interchangeable and patients can safely switch from one brand to another or not and which is the best economically. Numerous Metformin tablets brands in Indian drug market today make a problem of alternative generic brands for physician and the pharmacist. The present study aimed to evaluate and compare between different ten Metformin tablets brands applying both official and unofficial compendia method following the Indian pharmacopeia.

2. Materials and Methods

Materials

Metformin hydrochloride, having label strength of 500mg often different brands were purchased from registered pharmacies in Anantapur, Andhra Pradesh, India. The brand names and their manufacturing details were shown in table 1. Metformin HCL powder was a gift of (MSN pharmaceuticals, Hyderabad, India). The reagents used were potassium dihydrogen orthophosphate (Merck, Mumbai) and sodium hydroxide pellets (Merck, Mumbai). All reagents used were of analytical grade. Distilled water was used throughout the work.

Methods

Visual Inspection

The shape, size, and color of the different brands of tablets were examined visually. The diameter and thickness of 5 tablets from each brand were measured and the average was taken and standard deviation was calculated.

Uniformity of Weight

Sample tablets (20) of each brand were weighed together and average weight was determined. Each tablet was weighed individually on analytical balance and the percentage (%) deviation was determined [11-14].

Hardness Test

Sample tablets (10) of each brand were taken, a tablet was placed between the spindle of the Erwerka hardness tester machine and pressure was applied by turning the knurled knot just sufficiently to hold the tablet in position. The pressure was then increased as uniformly as possible until the tablet breaks and the pressure required to break the tablet was then read off the machine and recorded [11-13].

Friability Test

Twenty tablets of each brand were weighed and subjected to abrasion using a Roche friabilator at 100 revolutions for 4 min. The tablets were dedusted and weighed again then percent of weight loss was recorded. The friability of the tablets were then calculated using the following expression [11-13].

$$\textbf{\% Friability} = [(\text{Initial weight} - \text{Final weight})/\text{Initial weight}] \times 100$$

Disintegration Test

Tablet disintegration was determined at 37 °C using ERWAKA (Heusenstamm, Germany) disintegration apparatus. The disintegration time of randomly selected six tablets of each brand was determined in distilled water. The disintegration time was taken to be the time no granule of any tablet was left on the mesh [12-14].

Dissolution studies

Test was determined by using a 6-compartment dissolution test apparatus (Paddle type) containing 900ml of phosphate buffer pH 6.8, maintained at 37±0.5ºC with a fixed speed of 100 rpm. A tablet of each was put in each of the compartments and the machine operated at the intervals of 15, 30 and 45 minute. In the experiments of each sample, 5ml of the sample was withdrawn at specified intervals and replaced with a fresh 5ml dissolution medium to maintain the sink conditions. Each of the withdrawn samples was filtered with syringe filter 0.45µm, the filtrate diluted and its absorbance at 233nm was measured using UV-visible spectrophotometer. The concentration of Metformin hydrochloride dissolution medium was calculated According to Beer's-Lambert's law. From the concentration percentage (%) drug release was determined at specified time intervals [12-14].

Assay of the Tablets

According to Indian pharmacopoeia, dissolve 0.200g in 10 ml of 0.01 M hydrochloric acid previously cooled in iced water and titrate immediately, drop wise, with 0.05 M iodine. Before each addition of 0.05 M iodine dissolve the precipitate by swirling. At the end of the titration add 2 ml of starch solution and titrate until the blue color of the solution persists for at least 2 minutes temperature of the solution during the titration must not exceed 10ºC. (1 ml of 0.05 M iodine is equivalent to 16.67 mg of metformin HCl).

Table 1. Brand names and their manufacturing details

Name of the Brand	Manufacturer	Batch Number	Manufactured date
Glycomet	USV Limited	28008854	Dec 2013
Okamet	Cipla Limited	AH2138	Apr 2012
Gluconorm	Lupin Limited	I300766	March 2013
Metadoze	Biocon Limited	BPTP13089	Sep 2013
Metafort	Eris Life sciennces, Pvt. Ltd.	ERSAB3013	July 2013
Glyciphage	Franco-Indian Pharmaceutical Pvt. Ltd.	239432	Oct 2012
X Met	Glenmark limited	05121542	Jun 2012
Bigomet	Aristo Pharmaceutical Ltd	001153	Oct 2013
Walaphage	Wallage Life science	WER3033	
Government supply tablets	Biogenetic Drug Pvt. Ltd.	53043-BG138	Apr 2013

3. Results and Discussion

Ten different brands of Metformin hydrochloride tablets which are commercially available in India were subjected to a number of quality control tests in order to assess their biopharmaceutical equivalence. The assessments involved the evaluation of uniformity of Weight, friability, hardness, disintegration, potency test and dissolution tests. All the brands used were within their shelf life as at the time of study. The weight uniformity for the ten brands of Metformin hydrochloride tablets gave values that comply with the IP specification with a deviation less than 5% from the mean value.Using hardness tester, the strength of the tablets was tested. Ten brand tablets allow this official test according to IP specifications (4-6 kg). Glycomate had the maximum hardness. Hardness values of Glycomate ws 13.38 kg but which was within the IP specification. (Table 1) The friability test is mostly important criteria for uncoated tablets (during and after manufacture) to examine that the tablets have a good withstand strength for transportation, packaging, shipping and coating. All the tested brands in this study were film coated tablets. The

friability was also tested for these coated tablets for all brands. The friability was less than 1% for all the brands. The values of <1% are considered to be highly satisfactory evaluation characteristics Table 1.

Table 2. The evaluated physical characteristics of Metformin tablet

Brands	Sample Weight uniformity Deviation (%)	Friability (%)	Thickness (mm)	Average Hardness (kg)
Glycomate	0.585±0.01	0.51±0.01	8.1±0.4	13.38±0.11
Okamet	0.526±0.01	0.38±0.02	8.1±0.5	13.24±0.12
Gluconorm	0.962±0.02	0.83±0.02	8.2±0.7	9.58±0.05
Metadoze	0.784±0.01	0.77±0.01	8.2±0.7	8.08±0.02
Metafort	0.750±0.02	0.53±0.02	8.1±0.6	13.26±0.01
Glyciphage	0.547±0.01	4.38±0.01	8.1±0.5	6.92±0.02
X met	0.656±0.02	5.03±0.02	8.1±0.5	11.16±0.11
Bigomet	0.682±0.01	1.02±0.01	8.2±0.7	11.80±0.12
Walaphage	0.526±0.02	2.09±0.02	8.3±0.6	10.42±0.12
Govt.tablets	0.731±0.01	0.27±0.01	8.1±0.5	12.30±0.13
All values were mentioned as mean± S.D: number of trials (n)=5				

The results obtained from the assessment, the percentage content of active ingredient of seven brands of Metformin hydrochloride tablets showed values within the monograph specification 95% to 105% of stated amount of Metformin HCl as demonstrated in table 2. When a drug is administered orally in the form of the tablet, the absorption of the tablet depends upon how fast it goes into solution i.e. absorption of a drug is totally dependent upon the dissolution of the tablet. Dissolution of a tablet is influenced largely by the pH of the absorption site as well as pKa factor of a drug. Some factors directly affect dissolution.

Physicochemical properties of the drug: Partition coefficient, dissociation constant, particle size, crystal habit and crystal structure, polymorphism, hydration state etc.
Formulation Factors: Binder, lubricant, compression force and nature of the dissolution medium and also depend on temperature of the medium, intensity of agitation of the drug.

The observed disintegration times for all the brands of Metformin hydrochloride was less than the 30-min limit prescribed by the official compendium (Table 2). A comparison of the dissolution of the different brands of metformin tablets were shown in the fig. 2. All tablets of the different brands passed the disintegration test. The fastest disintegrated tablets were of brand Government supply tablets and Glyciphage, while the slowest one was Gluconorm even though their active drug release pattern and potency 96.24%, 99.24% and 87.02 % respectively. From above analyzed cleared that all branded samples within the standard but small variation in strength of tablets, it was might be while handling active powders .Dissolution of drug from oral solid dosage forms is an important aspect for drug bioavailability (i.e., the drug must be solubilized in the aqueous environment of the gastrointestinal tract to be absorbed). Accordingly, dissolution testing of solid oral drug products has emerged as one of the most important control tests for assuring product uniformity and batch-to-batch equivalence.

Table 3. The evaluated chemical characteristics of Metformin tablet

Brand	Disintegration time (minute)	Drug Released (%) after			Assay %	Potency (500mg tablet with excipient)
		30 min	45 min	60 min		
Glycomate	8.50±0.10	45.00±0.02	85.00±0.2	88.00±0.2	99.85±3.5	499.25±3.5
Okamet	9.05±0.11	35.10±0.02	66.33±0.2	74.21±0.2	99.99±6.5	499.95±5.6
Gluconorm	45.00±0.11	29.89±0.02	76.344±0.2	87.026±0.5	100.02±5.2	500.11±6.6
Metadoze	30.00±0.21	29.34±0.02	59.289±0.2	80.736±0.4	100.45±6.5	502.25±8.5
Metafort	26.76±0.21	37.45±0.02	89.82±0.2	95.67±0.4	98.46±2.6	492.31±3.5
Glyciphage	4.86±0.01	34.56±0.02	84.24±0.2	96.24±0.5	99.56±3.6	497.82±8.6
X met	5.50±0.01	30.05±0.02	72.45±0.2	83.05±0.5	99.04±3.6	495.23±9.6
Bigomet	9.00±0.02	42.78±0.02	107.66±0.2	123.88±0.4	100.04±4.6	500.22±3.6
Walaphage	5.50±0.02	41.04±0.02	83.44±0.2	90.34±0.2	97.65±5.6	488.25±5.6
Govt.tablets	3.50±0.01	48.21±0.02	85.66±0.02	99.24±0.02	100.01±7.6	500.05±6.6
All values were mentioned as mean± S.D: number of trials (n)=5						

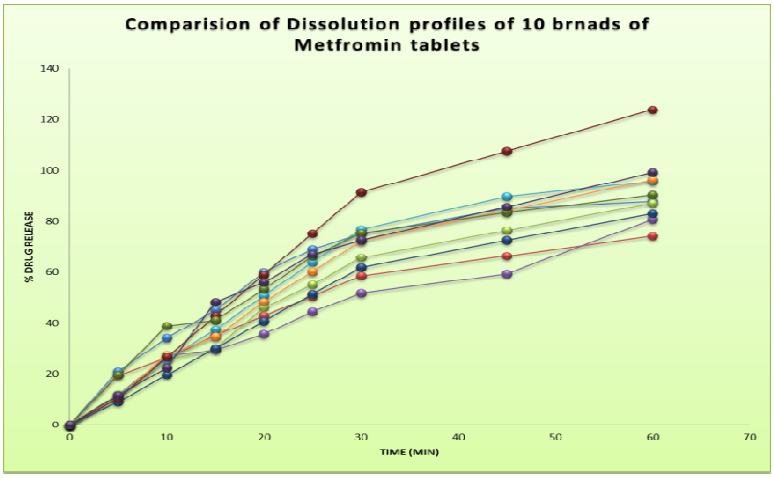

Figure 2. Comparison of Dissolution of different brands of metformin HCl tablets

4. Conclusion

It can be concluded that of all the ten brands evaluated in this study, Government supply tablets passed both pharmacopoeial limit tests and their dissolution curves were similar thus could be considered biopharmaceutically and chemically equivalent and therefore they can be substituted with the innovator product in clinical practice. According to the present study patients can safely switch from one brand to another but with consulting them of the possibility of some minor GIT complications that may occur after the treatment with new alternative brand. Pharmacists have to be informed which Metformin hydrochloride brands in the Indian are alternative to each other.

5. Acknowledgement

Authors were thankful to MSN pharmaceuticals, Hyderabad, India for providing gift sample of Metformin.

6. References

1. International Diabetes Federation, clinical Guideline Task Force. Glucose control: Oral therapy, Global Guidelines for Type 2 Diabetes Brusseles. **2005**, 35-8.
2. Giovanna C, Francesca M, Marzia C, Naima Z, Poala M. Development and evaluation of an in vitro method for prediction of human drug absorption II demonstration of the method suitability. European. **2005**, 27:354-362.
3. Werner E, Bell J. The preparation of methyl guanidine, and of ββ-dimethylguanidine by the interaction of dicyanodiamide, and methyl ammonium and dimethyl ammonium chlorides respectively. J Chem Soc, Transactions. **1921**, 121:1790–5.
4. Bailey CJ, Day C. Metformin: its botanical background. Practical Diabetes International. **2004**, 21(3):115–7.
5. Alan D. The use of Medicines in the United States. IMS Institute for Healthcare Informatics, **2011**, 28.
6. Adegbolagun OA, Ololade OA, Osamah SE. Comparative evaluation of biopharmaceutical and chemical equivalence of some commercially evaluable brands of ciprofloxacin hydrochloride tablets. Tropical journal of pharmaceutical research. **2007**, 6:737-745.
7. Awofisayo OS, Oladoja AA, Nse E, Imo EU. Comparative Assessment of the quality control measurements of multisource ofloxacin tablets marketed in Nigeria. Dissolution Technologies, **2010**, 6:20-25.
8. Esiomone CO, Okoye FBC, Onah BU, Nworu CS, Omeje EO. In-vitro bioequivalence study of nine brands of artesunate tablets marketed in Nigeria. J.Vector Borne Dis, **2008**. 45:60-65.
9. Pamula RB, Surender G, Reddy KVS, Ujwala P, Jyosthna G, Kumar RM. Comparative in vitro evaluation of commercial metformin HCL tablets. JITPS, **2010**, 1:152-157.
10. USP/NF. Physical Tests: Disintegration (701). 22/17 ed. Rockville, MD: United States Pharmacopeial Convention Inc, **1990**.
11. Lachman L, Liberman H, Kanig J, The theory and practice of industrial Pharmacy, Varghese Publishing House, Mumbai , 3rd edition, **1987**, 171-195, 293-345.

12. Naresh Gorantla, Hindustan Abdul Ahad, Rajesh Pawan A, Formulation and Characterization of Effervescent Floating Tablets of Esomeprazole Drugs, Int. J. Chem. and Life Sciences, **2013**, 02 (03), 1136-1139.
13. Sravanthi B, Hindustan Abdul Ahad, Sreeramulu Jadi, Naresh babu G, Effect of polymers in release rate of Metoprolol succinate in Pulsatile release tablets, Int. J. Chem. Pharm. Sci., **2013**, 1(3), 224-231.
14. Goutham Dev, Hindustan Abdul Ahad, Sreeramulu J, Sanjay Kumar M, Rajesh Pawan A, Formulation and evaluation of Gastro retentive floating tablets of Cefixime, Int. J. Chem. Pharm. Sci., **2013**, 1(3): 215-223