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COMPARATIVE PHYSICO-CHEMICAL STUDY OF SOME DIFFERENT BRANDS OF DRUGS CONTAINING METFORMIN HYDROCHLORIDE

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ABSTRACT

Metformin hydrochloride (MF.HCL) is an anti diabetic agent of biguanide class used for treating type2 diabetes there are several generics of MF.HCL tablets available within the drug delivery system globally. Numerous brands tablets in India drug market today place health practitioners in a tight spot of generic substitution. The present study was aimed to evaluating the physicochemical equivalence of five brands of MF.HCL tablets marketed in India using in vitro tests. The official and non-official standards such as uniformity of weight, friability, hardness, L.O.D., Sulphated ash Assay and dissolution rate.

All the brands complied with the official specifications for uniformity of weight, and dissolution tests. Brand M2 and M3 had the highest and lowest crushing strength respectively. five brands had values within the range specified for assay in the IP while Brand M3 failed the test of all the five brands evaluated in this study, only four brands could be regarded as being physicochemical equivalence and therefore can be interchanged in the clinical practice.

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INTRODUCTION

Metformin (N-N-dimethylimidodi carbonimidic HCl,) is an oral antidiabetic drug (1,2) MF.HCL is formulated as tablet form. This drug was approved by FDA in dec. 1994 MF.HCL reduce hyperglycemia by decreasing hepatic glucose production, intestinal absorption of glucose and improve sensitivity by increasing peripheral glucose uptake and utilization (3). In patient suffering from type 2 diabetes. MF.HCL is also being used increasingly in polycystic ovary syndrome (pcos)(4) non alcoholic fatty liver disease(5) and premature puberty (6) . the benefit of MF.HCL in NAFLD has not been extensively studied & may be only temporary (7) evidence suggested that it may be the best choice for people with heart failure (8). MF.HCL is one of only two oral antidiabetic in the who model list of essential medicines (second is

glibenclamide) (9) MF.HCL is also official in IP(10) BP(11) and USP(12) a literature survey revealed it.

According to who India account for nearly 35% of world counterfeit drug market. According to who bogus in relation to medicinal product means the deliberate and fraudulent mislabeling with respect to the identity composition or source of finished medicinal product or ingredient for the preparation of a medicinal product. Counterfeiting may be applicable to both generic and branded product as well as traditional remedies. Counterfeit product include product with correct ingredient (containing insufficient quantity of active ingredient or expired ingredient) wrong ingredient, without active ingredient or with false packaging (WHO 1999) several generic of met are available within the drug delivery system in India as well in global market. Most of the generic have much lower prices than the innovator product which raise the issue of unequal performance of this generic product. The first stage is establishing the therapeutic equivalence of any drug product involving ascertaining the chemical and biopharmaceutical equivalence (olaniyi et al 2001). In the bioavailability classification system met is classified as a class third drug because of its high water solubility one part of met dissolving in two part of water (bretnall & Clarke 1998).

MATERIAL AND METHODOLOGY

All The samples of METFORMIN HCL having the level strength of 500 mg were purchased from registered pharmacies M1 (USV ltd.) M2 (acme formulation pvt. Ltd.) M3 (omega biotech ltd.) M4 (aristo pharmaceutical ltd) M5 (Sandoz pharmaceutical ltd) in Vidisha (M.P.) and the study was performed within product expiration date. all the chemicals of analytical grade and Freshly prepared distilled water, for preparing the solutions, were used throughout the research work. .

Hardness test

Sample tablets (10) of each brand were taken, a tablet was placed between the spindle of the Erwerka hardness tester machin 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 tablets breaks and the pressure required to break the tablet was then read off the machine and recorded (15)

Friability:

The sample of tablets equal to 6.5g of tablets was taken (equals to 10) Sample was weighed and placed in the drum of friabilator and subjected to 100 revolutions, the tablets were than dusted and weighed and %loss was calculated. The sample passes the test if %loss is not more than 1% of the weight of the tablet tested (16)

Weight variation:

Twenty tablets were selected randomly and weighed individually. The average weight was calculated and individual weight was compared to the average weight. The tablet passes the test according to Indian Pharmacopeia if not more than two of the individual weights deviate from the average weight by ± 5% and none deviates by ± 10 % [16].

Loss on drying

Take a L.O.D. bottle and clean it, dry it and cool in desiccators containing silica gel. Now weigh 1.000gm of sample using calibrated balance. It was then taken out with stopper enclosed in the oven at specified condition like temp., vacuum and time. When the sample is dried it is taken out, stopper is closed. The L.O.D. bottle is cooled in desiccators and weighed

Determination of sulphated ash

Heat the crucible to the redness for 10 minutes, allow cooling in a desiccators and weighing. Transfer to crucible 1 gm. of the substance being examined and weigh the crucible and the contents accurately. Ignite; gently at firstly, unit the substance is thoroughly charred. Cool, moisten the residue with 1 ml. of sulphuric acid, heat gently until the black, particles have disappeared. Conduct the ignition in a place drop of sulphuric acid and heat. Ignite before; allow cooling and weighing repeat the operation until two successive weighing do not differ by more than 0.5 mg.

Dissolution:

Dissolution is a process in which drug from solid dosage form gets dissolved in the surrounding dissolution fluid. The process of dissolution is a prerequisite for the absorption of drug across biological barrier. In-vitro dissolution test studies the factors affecting the bioavailability of drug from the solid dosage form. During dissolution, drug passes into solution. In dissolution testing the amount of drug passing into solution is studied as a function of time thus describing the overall rate of drug release from solid dosage form. Dissolution testing was carried out using IP Dissolution apparatus No: 2 (basket rack assembly) and the medium for dissolution was 900ml of a 0.68%w/v solution of potassium dihydrogen phosphate after adjusting its pH to 6.8 with 1M sodium hydroxide.900ml Potassium dihydrogen phosphate pH6.8 was transferred into six dissolution flasks and Each was allowed to equilibrate to 37±0.5°C.Then 6 MF.HCL tablets were placed in each basket and it was lowered in the vessels and rotated at 100rpm for 45 minutes After pre-determined interval of 5, 15, 25, 35 and 45 min 5ml of sample was withdrawn and replaced with 5ml of fresh phosphate buffer pH 6.8 to maintain the volume of dissolution fluid constant. The sample was suitably diluted and the absorbance was measured at 233nm.The amount of drug dissolved was calculated using Beer's Lambert law as shown.

Assay:

Tablet contain specific amount of active ingredient (drug) with allowable variable limit. Assay of tablet ensures the amount of active ingredient which is indicative of its efficacy and stability of product. Twenty tablets were weighed, powdered and powdered sample was weighed equivalent to 0.1g of MF.HCL, and was shaken with 70ml of water for 15minutes

and then diluted to 100ml with water and filtered. From this dilute 10ml to100ml with water and measure absorbance at 232 nm .% drug content was calculated taking A1% as 798.

RESULT & DISCUSSION

Table 1 represents the dissolution profile of all the five Brands while figure 1 represents the dissolution profiles of all the five Brands. Table 2 show the evaluated physicochemical parameters. All The brands used were within their shelf life as at the time of study. five different brands of MF.HCL tablets obtained From different retail pharmacy outlets within their shelf life as at the time of study Were subjected to a number of pharmacopoeial tests in order to Assess their biopharmaceutical equivalence. The assessments Involved the evaluation, hardness test friability test, weight variation, L.O.D. sulphated ash dissolution and active ingredient test., the strength of the tablets was tested. All the tablets showed good strength, which is necessary for safe transportation Assay values of all MF.HCL tablets were within the range of 95% to 105% of stated amount of MF.HCL only one(M3) of the five brand fail to meet specification for assay test. The dissolution test was carried out using IP Dissolution apparatus No: 2 (basket rack assembly) under specified test conditions. From the data, it was interesting to note that more than 90% drug released from all the brands in eight hours which exhibit their good *in vivo* bioavailability. Crushing strength test shows the ability of tablets to withstand pressure or stress during handling, packaging and transportation. It is a property of a tablet that is measured to assess its resistance to permanent deformation.

TABLE 1: drug dissolution profile of tablets containing MF.HCL

Time(hr)					**%drug release**
	M1	**M2**	**M3**	**M4**	**M5**
0	0	0	0	0	0
1	49.2	48.5	45.3	43	40
3	66.7	65	57.6	58	58.9
6	90.6	85	88.3	83.8	80.8
9	100	98	98.1	96.7	92.6

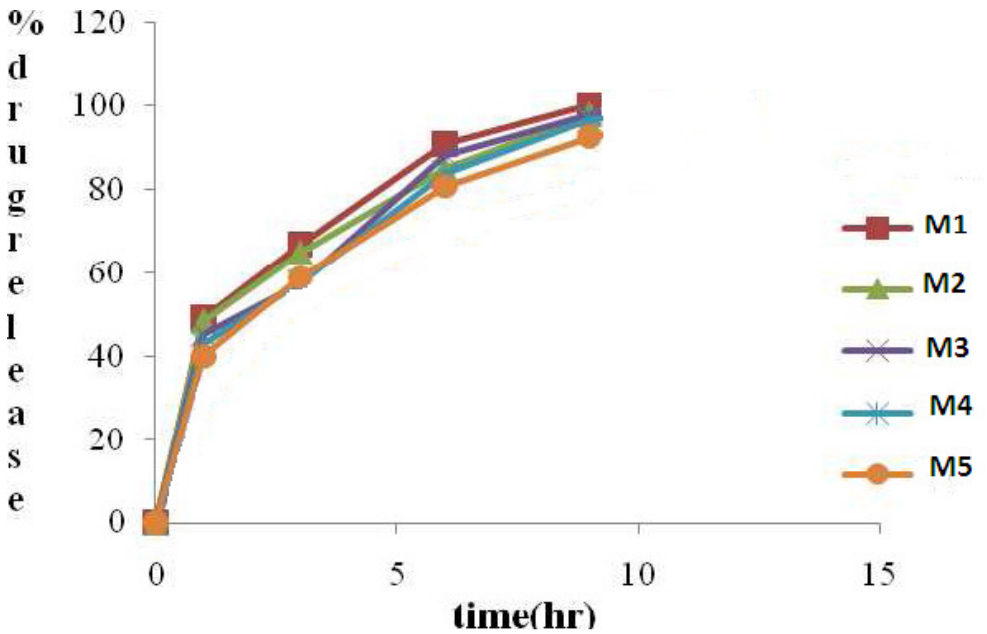

Figure 1: drug dissolution profile of tablets containing MF.HCL

Table 2: the evaluated physico chemical parameter of metformin hydrochloride tablets

S.No.	Code No	Hardness (Kg/Cm^2)	% Friability:	Weight variation	%Loss on drying	sulphated ash	%Assay
01	M1	14.65±0.14	0.28	0.179±1.59	0.22	0.03	99.3%
02	M2	15.75±0.23	0.18	0.184±1.28	0.14	0.05	96.2%
03	M3	12.59±0.04	0.10	0.188±2.28	0.28	0.06	108%
04	M4	14.34±0.16	0.36	0.174±1.63	0.36	0.02	101%
05	M5	14.78±0.18	0.59	0.191±1.18	0.14	0.02	103%

CONCLUSION-

It can be concluded from the study that all the five brands evaluated in the study only four brands M1 M2 M4 M5 passed IP limit test, and their dissolution and API curve were similar thus could be considered physico chemically equivalent and therefore can be substituted with the innovator product in principle practice.

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