ORIGINAL RESEARCH

Comparative Quality of Different Brands of Metformin Tablet Marketed in Zaria, Nigeria.

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To cite this article: Yushau FM, Awwalu S and Musa A. Comparative Quality of Different Brands of Metformin Tablet Marketed in Zaria, Nigeria. Journal of Basic and Social Pharmacy Research, 2021;2(1):20-25
ISSN: 2705-3245

ABSTRACT

Background: Metformin tablets are oral anti hyperglycaemic agents that are used as the first line agent in the management of type 2 diabetes mellitus. The proliferation of many brands of metformin tablets in the market has led to availability of different types; some of which may be substandard or counterfeit. Thus, the need to determine the quality of the various brands marketed in Zaria.
Objective: To compare the quality of different brands of metformin tablets that are available in Zaria using British pharmacopoeia standards.
Method: Seven brands of metformin tablet (500 mg) were randomly sampled from various community pharmacies within Zaria and analysed with respect to identification, weight variation, friability, disintegration time, dissolution and drug content assay using Pharmacopoeial standards.
Results: Except for the dissolution and assay tests, the results of all the other parameters for the various brands were within the Pharmacopoeial limits. The percentage content of metformin in brand 2 was 89.90 % which is outside the official range (95 – 105 %). Furthermore, only 70.61, 75.34 and 70.58 % of metformin dissolved from brands 2, 4 and 7 respectively, after 30 minutes of the dissolution test.
Conclusion: It can be concluded that of the seven brands evaluated, only four brands are interchangeable with each other and can be substitutes of each other.

Keywords: metformin tablets; quality control; physicochemical parameters; dissolution; interchangeable.

INTRODUCTION

Metformin, chemically known as 1, 1-dimethylbiguanide hydrochloride, is a biguanide used as a first line anti-hyperglycemic drug in the management of type II diabetes mellitus[1]. It has fewer side effects and less likely to cause weight gain or rise in cholesterol levels when compared to other anti-diabetics[2].

There are several cheap brands of generic metformin tablets available in the market. As a result of this cost-saving incentive, end users are more likely to select these cheap generics over the more expensive innovator brand[3]. The selection of one product from a wide variety of drug products that appear to be equivalent for patient therapy poses a great concern to prescribers and pharmacists in developing countries; in part

because about 50% of drug products circulating in these countries are mostly counterfeits as reported by World Health Organization (WHO)[4,5].

Treatment failure and drug resistance that is prevalent in most developing countries are attributed amongst other things to inadequate routine monitoring of quality of drug products[6]. In view of this, the World Health Organization (WHO) issued guidelines for global standards and requirement for the registration, assessment, marketing, authorization and quality control of generic pharmaceutical products[7]. Multisource drugs must conform with quality standards, therapeutic equivalency and interchangeability with the innovator or comparator brand[7]. For drug products to be chemically and bio-pharmaceutically equivalent, they must be identical in strength, quality, purity, Active Pharmaceutical Ingredient(API), release profile, dosage form and route of administration[8]. Quality control ensures the identity, purity and safety of pharmaceutical products[9]. The aim of this research is to conduct comparative quality control assessment of available brands of metformin tablets marketed in Zaria metropolis.

MATERIALS AND METHODS

Materials

Seven brands of metformin tablet (500 mg) coded 1-7 were randomly sampled from different community pharmacies within Zaria. Metformin standard powder was purchased from Sigma Aldrich while analytical grade solvents were purchased from local vendors within Zaria.

Methods

The following physicochemical parameters were determined as follows:

Weight variation: Twenty (20) tablets from each brand were randomly selected, individually weighed using analytical balance and the average weight was calculated. Percent weight variation was then calculated and compared with the official limit[10]

Friability test: Ten (10) tablets from each brand were randomly selected and collectively weighed (W_1). They were then placed in friabilator and the machine was operated for four minutes at 25 revolutions per minute (rpm). The tablets were de-dusted, reweighed (W_2), and percent friability was then calculated[10]

$$\text{Friability (\%)} = \frac{(w1-w2)}{w1} \times 100$$

Disintegration test: One tablet was placed in each of the six baskets of the disintegration apparatus containing distilled water (one liter) maintained at temperature of 37 ± 0.5 ºC. The time taken for tablet granules to completely pass through the basket mesh was recorded. This process was repeated for all the other brands[10]

Dissolution test: This was done using the basket apparatus at 100 rpm in 900 ml of buffer solution at pH 6.8. The medium was maintained at 37 ± 0.5 ºC and the dissolution medium (10 ml) was withdrawn at 30 minutes, filtered and diluted to equal volume with the medium. Absorbance of the resulting solution was measured using double beam UV spectrophotometer at a wavelength 233 nm against the blank (media). Metformin concentration was calculated taking 806 as the value of *A* (1%, 1 cm).

Assay: Twenty tablets were selected at random, weighed together and then powdered. A quantity of the powdered tablets equivalent to 100 mg metformin was weighed and then placed in 100 ml volumetric flask containing water (70 ml). This was then shaken by mechanical means for 15 minutes and subsequently made up to volume with water. An amount of the filtrate (10 ml), after discarding the first 20 ml, was diluted to 100 ml with water. The resultant solution (10 ml) was further

diluted to 100 ml with water. Absorbance was then taken using the double beam UV spectrophotometer at 232 nm and subsequently metformin concentration in mg was calculated taking 798 as the value of *A* (1%, 1 cm).

Identification: Ten metformin tablets from each brand were weighed and size-reduced using mortar and pestle. A quantity of the powdered tablet containing an equivalent of 100 mg of metformin was taken and shaken with 10 ml of absolute ethanol (95 %) for 15 minutes, then filtered. The infrared absorption spectrophotometry of the dried residue was determined using FTIR analysis at 30 scans within the range of 4,000 - 650 cm^{-1} at eight resolutions and the spectrum was compared with metformin reference spectrum[10]

RESULTS

The superimposed FTIR spectra of the various brands of metformin tablet against the BP reference FTIR spectrum are shown in Figure 1. The results of weight variation, friability, dissolution and disintegration tests are presented in Tables 1-3 while

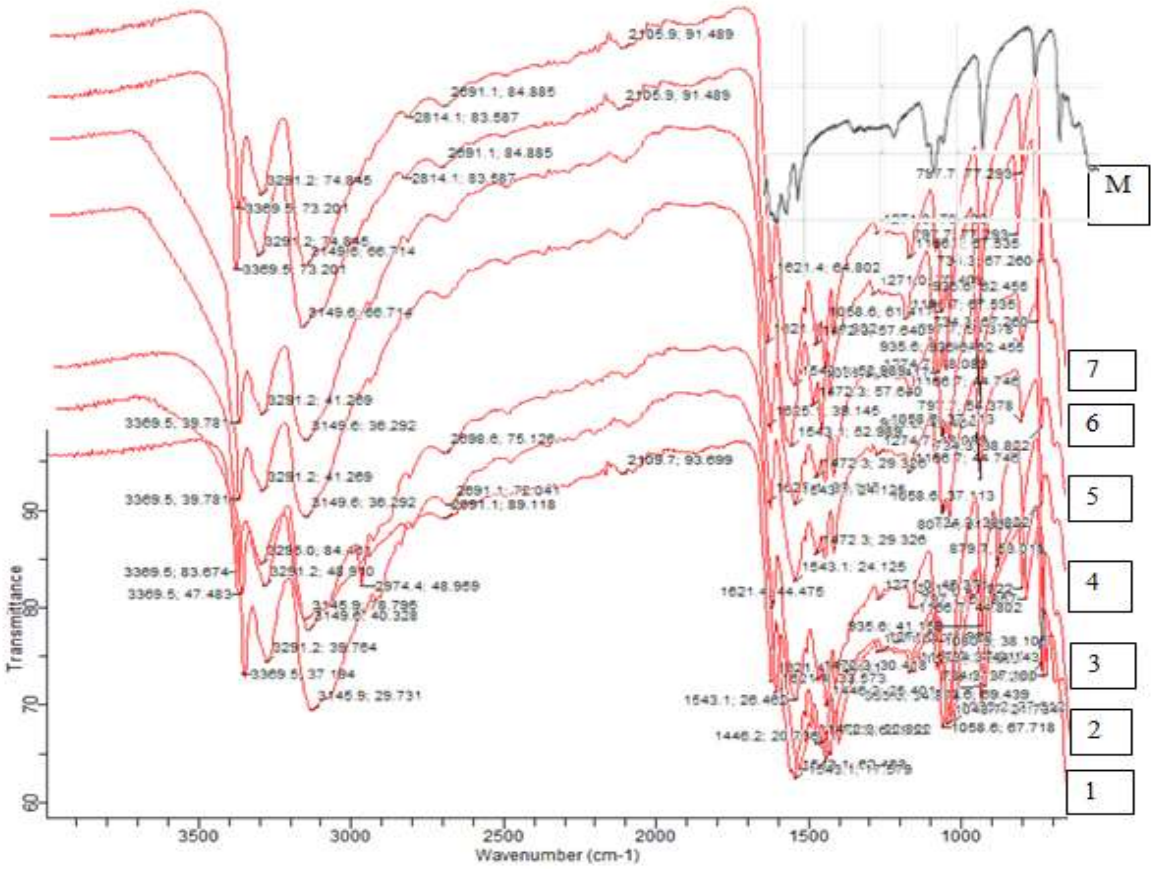

Fig. 1: FTIR spectra of the brands against BP reference spectra

Key: *M: metformin BP reference FTIR; 1-7: Brands*

Table 1: Weight variation result of metformin tablet brands

Brand	Mean ± S.D (g)	Percentage deviation from the mean
1	0.533 ± 0.014	0.131-2.572
2	0.618 ± 0.020	0.146-3.059
3	0.563 ± 0.010	0.000-1.776
4	0.619 ± 0.022	0.016-1.955
5	0.673 ± 0.023	0.052-2.921
6	0.523 ± 0.005	0.038-1.185
7	0.510 ± 0.517	0.078-1.253

**BP 2009 limit: 5 % for tablets above 324 mg*

Table 2: Assay, friability and dissolution results of metformin tablet brands

Brand code	Assay (%) *	Friability (%) **	Dissolution (%) ***
1	98.93	0.20	99.19
2	89.90	0.47	70.61
3	95.23	0.53	83.81
4	98.43	0.08	75.34
5	97.89	0.07	85.43
6	98.76	0.06	84.69
7	99.71	0.70	70.58

**BP 2009 limit for content of metformin in tablets is 95 – 105 %*
***BP 2009 limit for friability is 1%*
****BP 2009 limit for percent drug release is 80% in 30 minutes*

Table 3: Disintegration time result

Disintegration time (min)	Brands						
	1	2	3	4	5	6	7
1	7.08	4.35	10.33	5.55	11.50	6.00	4.50
2	7.23	4.46	10.37	10.37	11.80	6.10	5.09
3	8.10	4.52	10.42	6.05	12.12	6.15	5.00
4	8.15	4.58	10.50	6.07	12.40	7.00	5.15
5	13.15	5.90	11.15	6.32	13.20	7.05	5.30
6	13.40	5.13	11.41	6.45	13.35	7.30	5.50

BP 2009 limit for disintegration of film coated tablets is 30 minutes

DISCUSSION

The brands (1-7) contain metformin hydrochloride as indicated by their completely superimposed FTIR spectra, within the finger print region, against the metformin BP reference FTIR spectrum (Fig. 1). With the exception of brand 2, all the brands were found to contain metformin hydrochloride within BP, 2009 official range (95-105 %) as shown in Table 2. Hence, the strength of metformin indicated on the product label was ascertained except for brand 2 which was significantly below the official range. This implies that a patient taking brand 2 may not get the required amount of metformin to elicit the desired pharmacological action.

A failed weight variation test implies inconsistency in the concentration of API which could lead to unpredictable clinical outcomes, inefficacy and toxicity[11]. All the brands passed the weight variation test (table 1), as no tablet brand differs from the

average weight by up to 5 % as stipulated by the BP, 2009. This indicated adherence to good manufacturing practices (GMP) during tablet manufacturing. Akinleye *et al.* evaluated eight brands of metformin (500 mg) tablets marketed in Lagos, Nigeria and reported that all the brands passed the weight variation test[4]. A study by Oliveira *et al.* (2012) evaluated three brands (850 mg) in Brazil and reported that all passed the weight variation test[12].

The percent friability of all the brands (Table 2) was below the 1 % BP official limit. Hence, the brands will be able to resist chipping and wearing during packaging, shipping, transportation and storage and will reach the end users in an intact dose[6]. Akinleye *et al.* reported a failed friability test in one of the eight brands studied[4].

The disintegration test reveals that all the brands rapidly disintegrated in less than 30 minutes as required by BP (2009) for immediate release tablets. Hence, the metformin will be available for absorption in the gastrointestinal tract.

Dissolution result revealed that only four (1, 3, 5 and 6) out of the seven brands studied passed the dissolution test. Brand 2 failed the assay test (89.90 %) which may partly explain why it also failed the dissolution test (70.61 %). For a drug in immediate release tablet dosage form to pass the dissolution test 85% of API should be released in 30 minutes[10]. Brands 4 and 7 have percentage drug release below the BP (2009) acceptable range despite their excellent disintegration time and percentage content of metformin. This can be due to the type of excipients added which hinders the release of the API or may be due to poor manufacturing practice. Effectiveness of a drug in a tablet dosage form depends on its release from a dosage form, dissolution in the gastrointestinal fluid and absorption at the site of action[13].

For a tablet brand to be used as substitute with an innovator brand or reference brand, it must pass all the compendial quality control parameters set aside for the tablet. A failure in any of the quality parameters disqualifies a brand for interchangeability.

CONCLUSION

With the exception of brands 2, 4 and 7, all the other brands passed the quality control test and hence can be interchangeable with each other. Only four brands can be taken by patient to give the desired glycaemic control (anti-hyperglycaemic effect). Thus, there should be routine quality control testing of metformin tablets in the local markets and community pharmacies by regulatory bodies to ensure that end users have maximum benefit from the use of these drug products.

ACKNOWLEDGEMENTS

Special thanks to the staff of the Department of Pharmaceutical and Medicinal Chemistry, Ahmadu Bello University, Zaria for their support during the course of this research. The authors declare no conflict of interest during the course of this research.

REFERENCES

1. Sweetman SC, Paul BS, Alison B, Julie MM, Gail CN AVP. Martindale: The Complete Drug Reference. Thirty-six. editor. Vol. 3, Royal Pharmaceutical Society of Great Britain. London: Pharmaceutical Press; 2009. 3709 p.
2. Alhadramy MS. Diabetes and oral therapies A review of oral therapies for diabetes mellitus. J Taibah Univ Med Sci [Internet]. 2016;11(4):317–29. Available from: http://dx.doi.org/10.1016/j.jtumed.2016.02.001
3. Glass BD. Counterfeit drugs and medical devices in developing countries. Dove Press J Res Reports Trop Med. 2014;11–22.
4. Akinleye OM, Adelaja AI, Odulaja OJ. Comparative evaluation of physicochemical properties of some

commercially available brands of metformin Hcl tablets in Lagos, Nigeria. J Appl Pharm Sci. 2012;2(2):41–4.
5. World Health Organization. WHO Global Surveillance and Monitoring System. World Health Organization 2017. 2017. 64 p.
6. Ajala T, Adebona A. and Bamiro O. The Pharmaceutical Quality of Brands of Metformin Tablets in Ogun-State, Nigeria. African J Biomed Res. 2014;17:43–8.
7. World Health Organization. Multisource (generic) pharmaceutical products: Guidelines on registration requirements to establish interchangeability. WHO Tech Rep Ser [Internet]. 2006;(937):17–9. Available from: http://apps.who.int/prequal/info_general/documents/TRS937/WHO_TRS_937__annex7_eng.pdf
8. Oyetunde OO, Tayo F, Akinleye MO and Aina BA. In vitro equivalence studies of generic metformin hydrochloride tablets and propranolol hydrochloride tablets under biowaiver conditions in Lagos State, Nigeria. Dissolution Technol. 2012;19(4):51–5.
9. WHO. Quality Assurance of Pharmaceuticals: a compendium of guidelines and related materials. Second. World Health Organization. India: World Health Organisation 2007; 2007. 418 p.
10. British Pharmacopoeia. Volume III. London: Stationery Office; 2009. Metformin; p. 1- 10952
11. Kassahun H, Asres K and Ashenef A. In vitro quality evaluation of metformin hydrochloride tablets marketed in Addis Ababa. Bangladesh J Sci Ind Res. 2019;54(2):169–76.
12. Oliveira CL, Souza EF, Guimaraes LL, Sampaio PG, Soares VCG, Francesconi EMS, *et al.* Half Uniformity dosage of Metformin hydrocloride in tablets of different brands. Scientific Electronic Archives, 9(2), 92–101. https://doi.org/10.36560/922016263
13. Chandrasekaran AR, Jia CY, Theng CS, Muniandy T, Muralidharan S and Dhanaraj SA. Invitro studies and evaluation of metformin marketed tablets-Malaysia. J Appl Pharm Sci. 2011;1(5):214–7.