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QUALITY CONTROL ASSESSMENT OF FOUR BRANDS OF TINIDAZOLE TABLET MARKETED WITHIN KADUNA CITY, NIGERIA

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ABSTRACT

Like most drugs, various brands of tinidazole tablets are available in Nigeria and therapeutically equivalent products are being selected for various reasons. The aim of the study was to quarantine the different tablets brands that are commonly used, accessible and prescribed to see if the conform to the official standard and the specifications set by the regulatory agencies. The weakness of our regulatory agencies, rising incidence of fake and counterfeiting of drugs, increase in number of generic substitutes of tinidazole tablets in the market in addition to increase prescription and usage of tinidazole tablets in our society due to Parasitic and bacterial infections of the gastrointestinal responsible for significant morbidity and mortality worldwide with substantial increase of *trichomoniasis* infection among African women warrant this study. Four tablet brands of tinidazole sourced from the major pharmacies within Kaduna metropolis were identified, assayed and evaluated for uniformity of weight, friability, disintegration time, uniformity of dosage units and dissolution following standard BP procedure. The four generic brands of tinidazole were identified using their IR spectra and melting points which were found to be within the range of (125 to 128 °C) specified limits for tinidazole and passed the uniformity of weight and friability tests with the range of less than 1%. The absolute drug content of tinidazole in two of the four brands was however outside the specified range. Three of the four brands passed the disintegration tests within the disintegration time frame of less than 15 minutes. The four brands of tinidazole tablets marketed in Kaduna city vary in quality and so their use interchangeably should be carefully considered.

Keywords: Tinidazole tablets, Quality Control, Bioequivalence, Nigeria

INTRODUCTION

The provision of good quality medicines and pharmaceutics is the backbone of every healthcare system. This is dependent on the administration of right medicament containing the amount of active medicament at the right time[1]. Brand to brand as well as batch to batch equivalence of pharmaceutical dosage forms is very important so as to guaranteed their quality, efficacy, predictability and consistency [2,1,3]. This has been integrated into the contemporary pharmaceutical quality control and good manufacturing practices[4]. Non-compliance to quality specifications considered essential can have serious medico-legal implications[5].The implication of which may range from lack of effectiveness in the treatment due to therapeutic sub-doses to toxic effects caused by therapeutic over-doses and, consequently, lack of patient adherence to treatment[5].

The contents of active pharmaceutical ingredients and other physicochemical and

pharmaceutical equivalence of different tablets brands and product batches have been shown to vary from one region to the other[6]. For example, at Benin, south-southern Nigeria, there has been report of variation in the pharmaceutical quality of various brands of ibuprofen tablets[6]. This is more important in antibiotics where the amount of active pharmaceutical ingredient in the dispensed drugs is a very sensitive parameter. The administration of substandard drugs containing less than minimum inhibitory concentration of the active ingredients may result in therapeutic failure and generously triggers the manifestation of resistance[5]. Tinidazole, a synthetic nitroimidazole, is a structural analogue of metronidazole and a second generation 2-methyl- 5-nitroimidazole derivative with antibacterial and antiprotozoal property[7]. It has been widely used with established efficacy and acceptable tolerability for the treatment of *trichomoniasis, giardiasis, amoebiasis,* and *amoebic liver abscess.* Oral delivery has become a widely accepted route of administration.[1, 2]

In Nigeria and other developing countries, assessment of quality of circulating medicines is barely possible due to limited laboratory capacity, weak analytical infrastructure and chaotic distribution logistics[4]. Considering the porosity of Nigerian drug market with high circulation of substandard medicine, quality control assessment of the different tablet brands is necessary. This study was designed to investigate the quality control parameters of different tablet brands of tinidazole in Kaduna, Nigeria with a view to ascertain the quality and interchangeability of the different brands of the tablets.

MATERIALS AND METHODS

Acquisition of Tinidazole Tablets and Standard Powder

The tinidazole tablets used in this study were purchased from the major pharmacies in Kaduna metropolis, Kaduna-Nigeria. The tablets were code named as Samples A, B, C and D. The addresses of manufacturers, batch numbers, manufacturing dates and expiry dates were recorded for all the samples and only products within its shelf life were used (Table 1). The standard tinidazole powder used for this study was provided by the Department of Pharmaceutical Chemistry, Faculty of Pharmaceutical Sciences, University of Lagos, Nigeria. All other reagents were of analytical grade and water double distilled.

Table 1: Label Information of four different samples of tinidazole tablets

S/No	Product code	Batch No	Mfg. Date	Exp. Date
1	Sample A	A063E1005	Oct-11	Dec 2015
2	Sample B	12TNX07	Aug-12	Jul 2016
3	Sample C	N-4001	Jun-14	Feb- 2016
4	Sample D	J3044	Feb-13	Oct- 2016

Identification Test

The identification of the tinidazole standard powder was done according to the standard guideline in the Pharmacopeia[8]. In brief, three tablets were randomly picked from each tablet brand and powdered using a porcelain pestle and mortar. A quantity of the powder equivalent to 0.5 g of the tinidazole was weighed and extracted with 20 mL acetone; the extract was then heated on a water bath and allowed to dry. Two separate portions were taken for Melting point determination and FTIR spectral analysis.

Assay of Tinidazole in Tablet Brands and Standard Powder

The methods outlined in the monograph was followed [8]. For the standard tinidazole powder, 0.150 g of the standard powder was weighed

and dissolved in 25 mL of anhydrous acetic acid and two drops of crystal violet indicator was added. This was then titrated with 0.1 M perchloric acid.

For assay of the tablets, a quantity equivalent to 0.150 g of tinidazole was weighed and dissolved in 25 mL of anhydrous acetic acid and two drops of crystal violet indicator was added then titrated with 0.1 M perchloric acid. End-point was determined by yellowish green coloration. Each 1 mL of 0.1 M perchloric acid consumed is equivalent to 24.73 mg of $C_8H_{13}N_3O_4S$.

Uniformity of Weight

This was done accordance to BP guideline [9]. Twelve (12) tablets from each sample were individually weighed on an analytical balance. The mean and standard deviation were calculated and the percentage deviation was determined.

Disintegration Test

From the four brands of tinidazole tablets, six (6) tablets were randomly selected and respectively placed in the six basket units of Eureka disintegration machine containing 0.1 N HCl solution and operated a temperature of 37 ±0.5 ^{0}C. The time taken for all the tablet particles in each unit to pass through the mesh was recorded. The mean time for the six tablets was taken as the disintegration time[9].

Friability Test

Roche friabilator machine was used to carry out the friability test. This was performed by subjecting ten randomly selected tablets from each sample to abrasions in a friabilator operated at 25 rpm for four (4) minutes. The tablets were then de-dusted, re-weighed and the difference in tablet weight determined. The percentage friability was calculated as follows:

$$Friability = \frac{W1 - W2}{W1} * 100$$

Where, W1 = original weight and, W2 = final weight

Dissolution Test

The *in vitro* bioavailability of each sample of tinidazole tablets was studied by determining its dissolution rate at 37 ^{0}C in simulated gastric pH (0.1 N HCl), simulated intestinal pH (phosphate buffer pH 6.8) and simulated blood pH (phosphate buffer 7.4) as previously described[10]. The Erweka (England) dissolution apparatus was maintained at 37± 0.5^{0}C and at a speed of 100 rpm. At successive 10 minutes interval, 5 mL samples were withdrawn and replaced with 5 mlof the same solvent. The solution of tinidazole samples collected was spectrophotometrically analyzed to obtain the concentration of tinidazole in the solution. All measurements were conducted in triplicates and the mean of the three-reading recorded as the concentration (mg/mL)

RESULTS

Identification and assay parameters of four brands of tinidazole tablets is presented in Table 2. The results of the quality control test on the four brands of tinidazole tablets and the standard powder is presented in Table 3. The extracted portion of the different tablet samples alongside the pure standard tinidazole powder were identified by determining their melting points. The result of the melting point analysis revealed that none of the four brands of tinidazole tablets used in this study passed the test as the melting point of the four tested brands was outside the official BP (2009) specified melting point range for tinidazole.

The percentage content of tinidazole in two of the four tested brands was outside the acceptable range of 95-105%. Though not within the range, it was however approximately the acceptable lower limit.

All the samples passed the weight variation test as their percentage mean deviation was less than 5%.

All the samples passed the friability test with percentage friability of less than 1 % weight difference. A total of three of the four brands tested passed the disintegration test. Samples A and D have similar disintegration time with sample B completely disintegrating only after 28.5 minutes.

Table 2: Identification and Assay parameters of four brands of tinidazole tablets

Samples	**Melting Temp. (^{0}C)**	**% Content**	Remark
A	127-130	101	passed
B	126-129	94.56	passed
C	124 -127	100.7	passed
D	126-129	94.56	passed
Standard powder	124-127	98.1	passed

Note:

The melting point range of tinidazole is between 125 to 128 °C (BP 2009)

Table 3: Quality control parameters of four brands of tinidazole tablets

Samples	**% Mean Weight Deviation**	**Friability (%)**	**Disintegration time (min.)**
A	0.045	0	4.456±0.06
B	0.015	0	28.5±11.88
C	0.005	0.296	9.94±3.14
D	0.006	0	3.78±0.55

Note:

- Acceptable limit of weight uniformity test is less than 5 % of the mean percentage deviation
- Normal friability value for uncoated tablets is less than 1 % of the tablet initial weight
- Normal disintegration time for uncoated tablets is less than 15 minutes

The dissolution profiles of tinidazole tablets in the simulated gastric, intestinal and blood pH are shown in the Figures 1, 2 and 3.

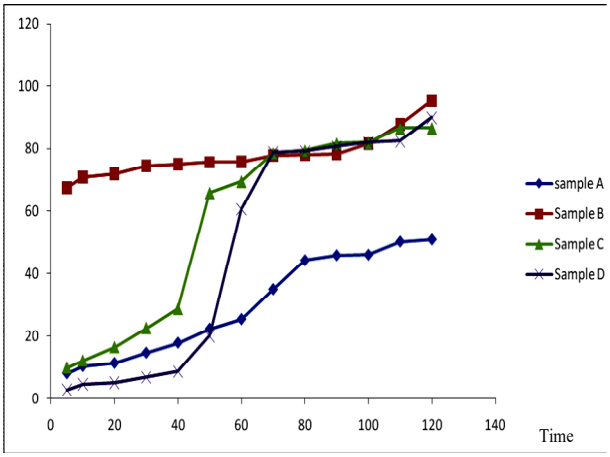

Figure 1: Dissolution profile of the different tablet samples of tinidazole in simulated gastric pH

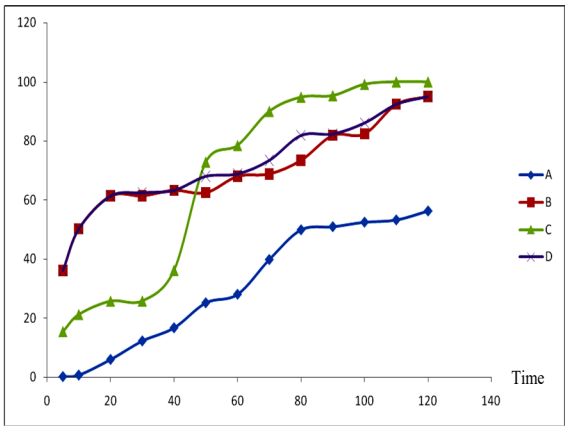

Figure 2: Dissolution profile of samples of tinidazole tablets in phosphate buffer 6.8 (Simulated intestinal pH)

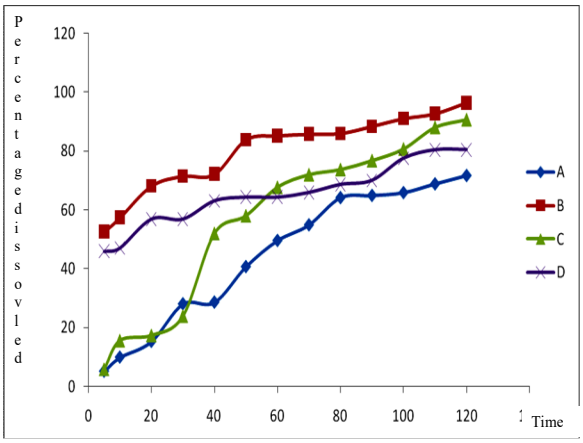

Figure 3: Dissolution profile of different tablet samples of tinidazole in phosphate buffer 7.4 (Simulated blood pH)

DISCUSSION

Quality control assessments are often conducted based on the general assumption that "if the physical and chemical integrity of a drug product was assured, satisfactory pharmacologic or therapeutic performance will be obtained"[2]. The result of melting point analysis of standard tinidazole powder and the entire test samples though similar, was out of range of melting point specified for tinidazole in the monograph[8]. This concurs with a previous report on the melting point analysis of tinidazole powders before recrystallization[11]. All the samples passed the weight uniformity test as none deviated from the mean weight by more than 5%, the acceptable limit of weight variation for tablets weighing 250 mg or more [1,8]. This is a good indication of content uniformity as the tablets containing more than the labeled amount may predispose the patients to adverse effect of the drug while the one weighing less than the labelled amount may lead to treatment failure[5]. This may be due to adherence to good manufacturing practice (GMP) during granulation and compression stages of the tableting[2]. This finding concurs with the result of a similar study conducted on four different brands of aspirin in Brazil where similarly all the tested tablet brands passed the uniformity of weight test [5].

An important parameter for evaluating the ability of tablets to withstand abrasion during handling is the friability. The loss of less than 1% of the weight of all the four brands of the tablets after friability is an indication that the tablets will be capable of withstanding the rigors of transportation without undergoing chipping at the edges[2,5]. Since tinidazole tablets are mostly prepared uncoated, the disintegrate time is expected to be less than 30 minutes[8,9]. In this study, only three of the four samples including the innovator product (sample C) disintegrated in less than 15 minutes. However, sample B showed a non-uniformpattern of disintegration with only one out of the five tested tablets disintegrating in < 15 minutes. This may affect the bioavailability of the sample because tablets must disintegrate before they get absorbed and have their active ingredient available systemically[2,5,1]. The disintegration of three of the four tested tablets within the monograph specified time is an indication of the use of good disintegrants that ensure good penetration of aqueous liquid during the tablet formulation[2].

According tollomuanya *et al.,* (2015), "the study of dissolution *in vitro* is considered a fundamental requirement in the pharmaceutical industry in order to assure the quality of solid pharmaceutical dosage forms for oral use, guarantee the quality from batch to batch, orientate the development of new formulations and secure the uniformity in quality and performance of the drug even after modifications"[9]. The release profile of the drug in gastric and intestinal pH was remarkable with more than 60% of the drug released in less than 60 minutes and 40 minutes respectively in simulated gastric and intestinal pH. Therefore, a greater proportion of drug absorption is expected to occur in the intestine[2].

CONCLUSION

The findings of this study revealed that the four brands of tinidazole tablet sourced from Kaduna metropolis vary in quality and so their use interchangeably should be carefully considered.

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