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Original Article

QUALITY CONTROL EVALUATION OF BRANDS OF MEBENDAZOLE 100 mg TABLETS ON THE ILLEGITIMATE PHARMACY OUTLETS

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ABSTRACT

Objective: The objective of the present study is to assess physical properties and the quality control parameters of the marketed brands of Mebendazole 100 mg found in illegitimate pharmacy outlets

Methods: Five brands of mebendazole 100 mg were identified and purchased in February 2014. The tablets were evaluated for uniformity of weight, friability, hardness, disintegration and assay of active pharmaceutical ingredient according to established methods.

Results: Results obtained indicated that all brands comply with official requirements for uniformity of weight and hardness. One brand failed the friability test with more than 1% of weight loss. The disintegration test revealed that two brands disintegrate in less than 2 min while other brands in more than 1 hour. Titrimetric assay of mebendazole content showed only two brands containing not less than 90% (w/w) of labeled chemical content.

Conclusion: Brand MBZ3 showed better characteristics of chewable tablet. Consumers need to pay attention to the manufacturer information and chewable tablets have to be treated as such.

Keywords: Mebendazole, Illegitimate pharmacy outlet, Quality control, Chewable tablet.

INTRODUCTION

Helminths, roundworm and flatworm parasites are among the most widespread infectious agents that have affected and still affect human populations, particularly in the marginalized low-income and resource-constrained regions of the world [1]. It is estimated that over two billion people worldwide are infected with helminths with about 300 million suffering severe pathological manifestations associated with these diseases [2].

Helminths affect mostly school-age children from 1-14 years. In Cameroon and India more than two thirds of children at this age group are affected [3]. It is estimated that more than 610 million school-age children are at risk of contracting helminths [4]. The prevalence of these diseases in Cameroon and India is between 10-50% [3].

WHO recommends regular deworming as an effective way to reduce both morbidity due to these parasites and the occurrence of serious complications using the following drugs: praziquantel, albendazole, mebendazole and levamisole [5]. The benzimidazole drugs, albendazole and mebendazole are the most widely used drugs for the control of helminths.

Mebendazole, methyl (5-benzoyl-1H-benzimidazol-2-yl)carbamate is a highly effective broad-spectrum anthelmintic drug indicated for the treatment of nematode infestations (roundworm, whipworm, etc). Mebendazole inhibits the formation of the worms' microtubules and causes the worms' glucose depletion [6]. Mebendazole has low water solubility, limiting its oral absorption and resulting in a lower bioavailability [7]. With the proliferation of Generic Drugs, we are witnessing the emergence of pharmaceutical products of uncertain origin beyond the Standards of Quality and manufacture warranty [8]. In developing countries, counterfeit and substandard medicines are endemic particularly in the flourishing illegitimate pharmacy outlets or "street drugs" [9]. Recrudescence of helminth infections in low-income regions of the world is also related to the drug quality available for consumption.

They usually rely on cheap and retail able medicines available in illegitimate pharmacy outlets [10, 11]. It is estimated that 28% of antibiotics and other essential drugs as anthelmintic are counterfeit [12] and their use often leads to treatment failure and sometimes death [13].

The objective of this work was to assess physical properties and the quality control parameters of the marketed brands of Mebendazole 100 mg found in illegitimate pharmacy outlets, and to learn more about their quality, efficacy and safety.

MATERIALS AND METHODS

Materials

Pure mebendazole was obtained as gift sample from the National Laboratory of Drugs' Control, Yaounde, Cameroon. A survey was conducted in Yaounde city during February 2014 to take the census of all the different brands of mebendazole available on Cameroonian market. Illegitimate pharmacy outlets present in the two principal markets of that city, Central and Mokolo markets were scrupulously poll and five brands of mebendazole were identified and purchased (Table 1). All other chemicals and reagents used were of analytical grade

Table 1: Brands of mebendazole used in this study

Code	Brand Name	Lot Number	Manufacturer Country	Fabrication – Expiration Date
MBZ1	Mebendazole Pharmaquick	9500	Benin	01/2014 - 01/2017
MBZ2	Mebavard-100	MC-196	India	07/2011 - 06/2015
MBZ3	Diameb	MG13072	India	03/2013 - 02/2017
MBZ4	Surelife Mebendazole	004	Nigeria	02/2014 - 01/2017
MBZ5	Mebendazole	AX0303	India	07/2013 - 06/2016

Evaluation of Tablets

Visual inspection and identification

The general appearance of all tablets is essential for consumer acceptance. The five brands of tablets bought were evaluated for size, shape and color. The diameter and thickness of the tablets were measured by using micrometer screw gauge. Mebendazole samples were identified using thin layer chromatography. Powdered samples of the tablets including the pure sample were dissolved in a mixture of chloroform-formic acid (10/1 v/v), spotted on the plate and immersed in the development solvent system chloroform: formic acid: methanol (92/5/3 v/v/v) contained in the chromatank. The plates were removed when the solvent had moved three-fourths of the length of the plate. The solvent front was then marked, allowed to evaporate from the plate and examined under short-wavelength U.V light.

Weight variation

Twenty tablets of each formulation were selected at random and weighed individually. The weight of individual tablets was noted. Average weight was calculated and the individual weights were compared with the average weight.

Hardness test

Hardness is a force required to break a tablet across the diameter. The hardness of a tablet is an indication of its strength. The hardness was measured using Schleuniger-2E Hardness tester. The values were expressed in Newton (N).

Friability test

The friability of tablets was determined by using ERWEKA TA Friabilator. Ten tablets were weighed and placed in the friabilator and rotated at 25 rpm for 4 minutes. Then the tablets were taken out, dusted and reweighed. The percentage friability of the tablets were calculated by the formula, Percentage Friability = [(Initial Weight – Final Weight)/ Initial Weight] × 100. Three trials per brand were performed.

Disintegration Time

Disintegration test was carried out by using ERWEKA ZT 3 Disintegration test apparatus. One tablet is placed in each tube, and the basket rack was positioned in a 1-litre beaker of distilled water, at 37°C ±2°C. A standard motor-driven device is used to move the basket assembly containing the tablets up and down through a distance of 5 to 6 cm at a frequency of 32 cycles per minutes. The time taken for the tablet to disintegrate completely was noted.

Drug content estimation

Weighed accurately 250 mg of drug then dissolve in 3 ml of anhydrous formic acid and 30 ml of anhydrous glacial acetic acid and titrate with 0.1 M perchloric acid. The end point was potentiometrically determined (1 ml of 0.1 M perchloric acid = 29.53 mg of $C_{16}H_{13}N_3O_3$).

RESULTS AND DISCUSSION

The formulations were evaluated for various physical parameters such as diameter, thickness, hardness, friability, uniformity of the weight, disintegration time and drug content. The results are presented in Table 2.

From the identification test, the result of thin layer chromatography indicated that all the sample were mebendazole. A retention factor value of 0.33 was recorded for all brands. The effect of transporting the tablets from the factory to the point of sale or consumption is evaluated through the friability test. No sample is expected to lose more than 1% of its weight after the test.

This was true for all the brands except for brand MBZ5 which lose 1.74% of its weight after the test. However, even if MBZ4 passed the friability test, visual inspection showed powder residue in blister after removal of tablet as well as some tablets joined to blister. Lose of weight of more than 1% as well as the precedent visual inspection remarks are signs that tablets are not adapted for rough handling and for transportation through potholed roads.

Table 2: Evaluation of mebendazole Tablets

Code	Color	Diameter (mm)	Thickness (mm)	Weight variation(mg)	Hardness (N)	Friability %	Disintegration time (min)	Drugs content%
MBZ1	pink	8.04±0.12	3.10±0.00	177.7±3.46	54.8±6.34	0.09±0.03	1.07±0.07	65.97±4.44
MBZ2	orange	9.51±0.02	3.25±0.00	301.8±4.24	91.0±6.13	0.01±0.00	179.33±12.9	33.3±2.66
MBZ3	orange	10.1±0.00	3.09±0.03	313.9±4.20	45.8±3.82	0.26±0.03	0.36±0.14	92.36±2.66
MBZ4	pink	8.67±0.05	3.09±0.1	226.8±13.65	70.2±20.6	0.73±0.93	107.33±16.92	109.44±0.71
MBZ5	beige	9.49±0.02	3.56±0.05	361.2±5.95	62.4±5.31	1.74±0.25	145.67±21.19	64.08±1.77

Considering the average weight per tablet for each brand of drug and for twenty tablets selected at random, no two tablets should deviate by 7.5% and no single tablet by 15% for brands MBZ1 and MBZ4 while for brands MBZ2, MBZ3 and MBZ5, no two tablets should deviate by 5% and no single tablet by 10%. All brands passed the uniformity of weight test.

Complete disintegration is defined as that state in which any residue of the unit, except fragments of insoluble coating or capsule shell, remaining on the screen of the test apparatus is a soft mass having no palpable firm core. Chewable tablets are exempted from disintegration test according to British and India Pharmacopoeia while in the US Pharmacopoeia, the disintegration time for chewable tablets should not exceed 4 hours. There were differences in the disintegration time for the various brands of mebendazole (Figure 1).

Samples MBZ1 and MBZ3 recorded fastest disintegration times of 64 seconds and 21.57 seconds respectively. The disintegration time values recorded for the three other brands were found to be in the range of 1 to 3 hours: MBZ2, 2h59min, MBZ4, 1h47min and MBZ5, 2h25min. Though disintegration times for tablets do not bear a direct correlation with dissolution, Chapman et al demonstrated that tablets with long disintegration times might not show good bio-availability [14]. Poor disintegration time values could mean that the manufacturing process such as compression force, dwell time as well as tablet composition needs to be reviewed

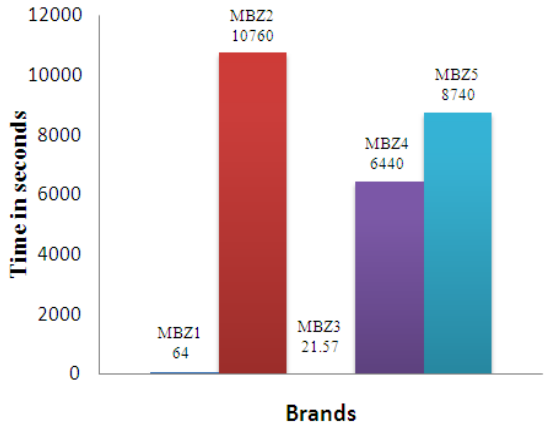

Fig. 1: **Time of disintegration for brands of mebendazole**

The hardness was found to be in the range of 45 to 91 N for all the brands indicating good mechanical strength. It can easily be seen from table 2 that the disintegration time seems to be related to hardness. The more a tablet is hard, the more its disintegration time is long. Titrimetric analysis of the brands yielded results out of range of some pharmacopoeia. According to the standard of the USP, upon essay of a product of mebendazole, between 90 to 110% of the claim label should contain the active ingredient [15]. By this standard, brands MBZ3 and MBZ4 were found to contain active ingredient within the accepted limit: 92.35% and 109.44% (w/w) respectively. By the standard of the international pharmacopoeia, mebendazole tablet should contains not less than 98% and not more than 102% of active ingredient, calculated with reference to the dried substance[16]: on this basis, only brand MBZ3 passed the test for the active ingredient content.

CONCLUSION

Brand MBZ3 showed better characteristics of chewable tablets. Consumers need to pay attention to the manufacturer information and to treat chewable tablets as such. "Street drugs" as seen in this study, do not always contain the amount of active principle necessary for their efficacy. The fight against helminths should include effective quality control of anthelmintic drugs and urgent control regulations in the marketing of pharmaceutical products.

CONFLICT OF INTERESTS

Declared None

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