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Quantification of the Content of Ten (10) Brands of Metronidazole Infusion Marketed in Abuja Metropolis by UV Spectroscopic Method

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Abstract

The proliferation of substandard drugs is a major public health challenge, especially in developing countries which lacks adequate resources to effectively monitor their prevalence. Currently, there are no reliable statistics on the level of incidence of fake drugs in Nigeria. The quality of medicines is an integral part in ensuring that pharmaceutical products are fit for their intended use, comply with requirements of marketing authorization and do not expose consumers to risks. For this to be achieved, there must be a system of quality assurance, which incorporates aspects including product development, manufacturing, distribution, and storage. This study aimed at quantifying the content of ten (10) brands of metronidazole infusion marketed in Abuja by UV-Spectroscopic method. Ten (10) brands of metronidazole were purchased in different pharmacies within the city of Abuja and were assayed using UV-Spectroscopic method as stated in British Pharmacopoeia 2017 edition. All the ten (10) brands of metronidazole that were assayed had a percentage content of 100.97% to 108.15%. From the study carried out, all the brands of metronidazole infusion complied with the content uniformity test as stated in the British Pharmacopeia.

Keywords: Metronidazole; UV- Spectroscopic method; Infusion; Percentage content.

1. Introduction

The quality of medicines is an integral part in ensuring that the pharmaceutical products are fit for their intended use, comply with the requirements for marketing authorization and do not expose consumers to risks. For this to be achieved, there must be a system of quality assurance, which incorporates aspects including product development, manufacturing, distribution, and storage [1]. In many of the developing countries, there are no effective means of monitoring the quality of generic products in the market. This is of a great challenge due to the fact that the lack of adequate means of monitoring quality of generic products can result to wide distribution of substandard drugs.

Quality of drugs is a source of concern in several developing countries. Available evidence suggests that there are high incidences of substandard pharmaceutical products [2]. Counterfeit pharmaceutical products comprise a significant problem in the health care system. Counterfeit medicines have been associated with therapeutic failure, antibiotic resistance, and death. Pharmaceutical counterfeiting is a pervasive problem, impacting nations of all sizes [3]. Available evidence suggest that the menace of counterfeit medicines is not restricted to developing countries alone, as Europe, USA and other developed nations are also having challenges of counterfeit medicines [4]. Production and sales of quality drugs is important in promoting good health in any population. A large number of ailments requires the use of drugs for treatment and as such, high quality drugs are necessary to prevent treatment failure and relapse [5]. In 2003, the World Health Organization (WHO) reported that fake drugs reported between 1999 and 2002 include analgesics and antipyretics (6%), antimalarials (7%), anti-asthma and anti-allergy (8%), antibiotics (28%), hormones and steroids (18%) and other therapeutic categories (33%). These problems above have resulted in a weak therapeutic efficiency and development of resistant strains of microorganisms.

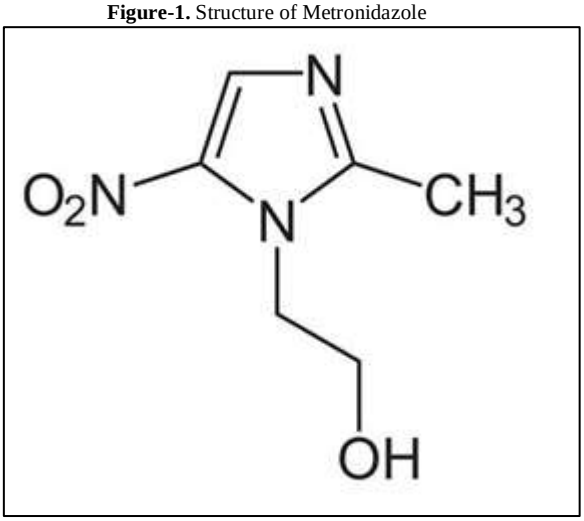
Metronidazole belong to nitroimidazole class, it inhibits nucleic acid synthesis by disrupting the DNA of microbial cell. This function only occurs when metronidazole is partially reduced, and because this reduction usually happens only in anaerobic bacteria and protozoans, it has relatively little effect upon human cells or aerobic bacteria [6].

Common adverse effects associated with systemic metronidazole therapy include the following: diarrhea, nausea, vomiting, headache, dizziness, weight loss, abdominal pain, headache, and metallic taste in the mouth. The administration of metronidazole intravenously is commonly associated with thrombophlebitis. Infrequent adverse reaction includes the following: stomatitis, dark urine, paraesthesia, and hypersensitivity reactions [7]. The use of metronidazole in high dose and long-term systemic treatment are associated with the development of leucopenia,

neutropenia, increased risk of peripheral neuropathy, and central nervous system toxicity. The use of metronidazole has been found to be associated with cancer in animal studies [8]. Metronidazole has also demonstrated some mutagenic effects in bacterial cultures. However, the relationship between exposure to metronidazole and human cancer is unclear Bendesky, *et al.* [9]. Available evidence suggest that metronidazole is a possible carcinogen [10]. Metronidazole interact with alcohol to cause disulfiram-like reaction which results to the following effect: nausea, vomiting, flushing of the skin, tachycardia, and shortness of breath [11]. Patients on metronidazole therapy are therefore advised not to drink alcohol during metronidazole therapy and for at least 48 hours after treatment has been completed [7]. Some studies have however call into question the mechanism of interaction of alcohol and metronidazole [12-14]. Karamanakos, *et al.* [15], has suggested a possible central toxic serotonin reaction for the alcohol intolerance. Metronidazole is also thought to inhibit the liver metabolism of propylene glycol; thus, propylene glycol may potentially have similar interaction effects with metronidazole. Metronidazole also inhibits CYP2C9, and therefore, the drug may interact with medications metabolized by CYP2C9 of which examples include lomitapide, warfarin.

Metronidazole is a widely used anti-infective agent, a literature search has shown that no study has been carried out to assay metronidazole samples distributed across Nigeria. In view of the rate of circulation of fake and counterfeit medicines, there is need to continuously assess the samples medicines available to the public. This study aimed at quantifying the content of ten (10) brands of metronidazole infusion marketed in Abuja by UV-Spectroscopic method.

Figure-1. Structure of Metronidazole



2. Materials and Methods

2.1. Materials

The UV – Spectrophotometer used to analyze the metronidazole infusions was Jenway 6505 (series No-2115 UK), other materials include; beakers, pipette, test tubes, test tube holder, micropipette, volumetric flask, measuring cylinders, Hydrochloric Acid, and distilled water.

2.2. Samples

Ten (10) commercial brands of metronidazole infusions were purchased from pharmacies within the city of Abuja. The infusion samples were claimed to contain 0.5g per 100ml (0.5%w/v) of the metronidazole active pharmaceutical ingredient. Before purchased, all the infusions were checked for physical requirements for packaging and labeling which include the presence NAFDAC registration and batch number, manufacturing date, and expiration date. The infusions were randomly coded (Sample A, Sample B, Sample C, Sample D, Sample E, Sample F Sample G, Sample G, Sample H, Sample I, and Sample J).

2.3. Preparation of 0.1 M Hydrochloric Acid

Exactly 8.29mL of 37% concentrated hydrochloric acid was accurately measured using measuring cylinder. Some quantity of distilled water was transferred into 1000ml volumetric flask, the acid was added in little quantity while shaking the solution so as to ensure homogenous mixing until all the acid was added. The volumetric flask was then made up to 1000ml mark.

2.4. Sample Preparation and Percentage Content Assay

The method as described in British Pharmacopoeia, 2017 was used. A volume of the infusion containing 0.05g of metronidazole was diluted to 100ml with 0.1M hydrochloric acid. 10mL of the resulting solution was diluted to 250mL with 0.1M hydrochloric acid. The absorbance of the resulting solution was then measured at 277nm, after which the percentage content of metronidazole was calculated. The value of A (1%, cm) was taken as 375 at maximum at 277nm. This procedure was done for all the samples and the samples were analyzed by UV-Spectrophotometer. The readings were taken in triplicates while 0.1M hydrochloric acid was used as blank for the

spectrophotometric assay. The acceptance limit was 95.0% – 110.0%. Table 1 below shows labelling description of analyzed metronidazole infusion.

Table-1. Labelling description of analyzed metronidazole infusion

Code	Country of Manufacture	Claimed strength(g/100ml)	Date of manufacture	Expiry date
A	India	0.5	DEC 2016	NOV 2019
B	Nigeria	0.5	DEC 2018	NOV 2021
C	India	0.5	JULY 2016	JUNE 2019
D	Nigeria	0.5	MAY 2017	MAR 2021
E	Nigeria	0.5	APRIL 2018	MAR 2021
F	Nigeria	0.5	APRIL 2018	MAR 2020
G	China	0.5	OCT 2017	SEPT 2020
H	China	0.5	JAN 2018	DEC 2020
I	China	0.5	OCT 2017	SEPT 2020
J	Nigeria	0.5	OCT 2018	SEPT 2021

3. Results and Discussion

All the ten (10) brands were within their shelf life as at the time of the assay and they were all registered with the National Agency for Food Administration and Control (NAFDAC). The strength of the various brands of metronidazole infusion was 0.5g per 100mL All the samples passed the physical requirements for packaging and labeling

The absorbance, actual concentration, and percentage content for each of the samples are shown in table 2 and table 3 below.

Table-2. Absorbance for different samples of the Metronidazole Infusion using UV-Spectrophotometric method

Sample	1st Absorbance	2nd Absorbance	3rd Absorbance
A	0.747	0.7526	0.7722
B	0.7449	0.7668	0.7879
C	0.7900	0.7861	0.777
D	0.8032	0.776	0.8067
E	0.7847	0.7787	0.7711
F	0.7831	0.7729	0.7711
G	0.7821	0.7779	0.767
H	0.7915	0.7569	0.7678
I	0.7769	0.7791	0.8415
J	0.8091	0.8307	0.7935

Table-3. Actual concentration, and percentage content for different samples of the Metronidazole Infusion using UV-Spectrophotometric method

Sample	Dilution factor	Actual Conc. (g/100mL)			Mean Actual Conc. (g/100mL) ±SD	Theoretical Conc. (g/100mL)	% Content	Remarks (B.P, 2017)
		1st	2nd	3rd				
A	250	0.4980	0.5017	0.5148	0.5048±0.0088	0.5	100.97	Passed
B	250	0.4966	0.5112	0.5253	0.5110±0.0143	0.5	102.20	Passed
C	250	0.5267	0.5241	0.5180	0.5229±0.0044	0.5	104.58	Passed
D	250	0.5355	0.5173	0.5378	0.5302±0.0112	0.5	106.04	Passed
E	250	0.5231	0.5191	0.5141	0.5188±0.0045	0.5	103.76	Passed
F	250	0.5221	0.5153	0.5130	0.5168±0.0047	0.5	103.36	Passed
G	250	0.5214	0.5186	0.5113	0.5171±0.0052	0.5	103.42	Passed
H	250	0.5277	0.5046	0.5119	0.5147±0.0118	0.5	102.94	Passed
I	250	0.5179	0.5194	0.5610	0.5328±0.0245	0.5	106.56	Passed
J	250	0.5394	0.5538	0.5290	0.5407±0.0125	0.5	108.15	Passed

A literature search revealed that no work has been done relating to quantitative assessment of metronidazole marketed in Abuja and Nigeria as a whole. Abuja is the capital city of Nigeria located within the Federal Capital Territory. Abuja became the capital of Nigeria on 12th of December 1991 and its population was 776,298 as at 2006 census. However, as at 2016, the population of Abuja was estimated to be six million. Abuja is one of the fastest growing cities in the world with an annual growth of 35%. It is therefore important to assess the quality of medicines being circulated within a capital city such as Abuja.

Drug products having more than three generics require analysis for their biopharmaceutical and chemical equivalency. These methods ensure that any of the generic products can be used interchangeable [16]. There is grave danger in using a substandard metronidazole which is an anti-infective agent that is used to manage a number of bacterial and protozoal infections. The use of anti-infective agent that contain lower amount of the stated drug can

result to treatment failure and resistance while a situation where the drug contain higher amount of the stated content will lead to higher toxicity of the drug. Although it is a difficult task to trace illness and death to counterfeit or substandard medicines, evidence has however shown that poor quality medicine poses significant threats to consumers as they cause adverse reactions, lack of successful treatment and possibly death [17].

The ten (10) brands were assayed according to the method outline in British Pharmacopoeia, 2017. In the British Pharmacopoeia, it is stated that metronidazole infusions should contain not less than 95.0% and not more than 110.0% of the stated amount. As seen in table 3, all the various brands of metronidazole infusions passed according to the British Pharmacopoeia specification. The highest content was found in sample J (108.15%) while the lowest content was found in sample A (100.97%). This finding suggest that the quality of metronidazole sold across different pharmacies in Abuja are of high quality. However, there is need for this study to also be carried out across different states in Nigeria. It is important that continuous quantification of drugs consumed by patients be carried out, this is to guarantee the safety and efficacy of drugs administered to patients.

4. Conclusion

The study was carried out to quantify the content of ten (10) brands of metronidazole infusions marketed in community pharmacies within the city of Abuja by UV-Spectroscopic method. From the study carried out, it was observed that all the ten (10) brands complied with the British Pharmacopoeia specification described for content uniformity test for metronidazole infusion. British Pharmacopeia specify 95.0% to 110.0% for content uniformity test of metronidazole infusion and from the assay carried out, sample A, B, C, D, E, F, J, H, I, and J had a content uniformity of 100.97%, 102.20%, 104.58%, 106.04%, 103.76%, 103.36%, 103.42%, 102.94%, 106.56%, and 108.15 respectively.

5. Limitation of the Study

This study is all about quantification of samples of metronidazole infusion marketed within Abuja city, there is however the need to carry out further qualitative assessment of the various brands of metronidazole infusion which was not done due to financial constraint. Carrying out qualitative assessment will help ascertain if these samples are safe for patient consumption.

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