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Research Paper

Comparative Study of Quality of Some Brands of Oral Metronidazole Suspensions in Benin City, Nigeria

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ABSTRACT: *Poorly formulated pharmaceutical suspensions tend to pose a problem to the bioavailability of the drugs. This is against one of the purposes of formulating drugs in form of suspensions. Pharmaceutical suspensions may have the problem of stability which could be as a result of caking, viscosity changes, pH changes, color changes, change in flavor. This problem can make the drug loose its efficacy and as a result of this, the therapeutic effect would not be achieved and the drug may gain resistance and unwanted side effect can occur. The aim of this study is to evaluate and compare the quality of some commercially available brands of metronidazole oral suspensions in Benin City, Nigeria using standard methods to ensure that they meet the requirements of the pharmacopoeia. The suspensions were evaluated by assessing the organoleptic properties (color and taste),particle size and shape, determination of the pH and sedimentation volume, re-dispersibility test, and rheological assessment. From the research work all the suspensions were easily re-dispersed. The pH of all the suspension were not within the pharmacopoeia limit except MOS 10 and MOS 8 suspensions. All suspension formed sediment except MOS 2 and MOS 6 suspensions. From the comparative evaluation of the ten brands of Metronidazole suspension,it can be concluded that some of the brands did not meet up with standard pharmacopoeia requirement of a good suspension.*
KEYWORDS: *Suspension, metronidazole, stability, efficacy*

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I. INTRODUCTION

Suspension, a liquid dosage delivery system is a convenient way to administer insoluble or sparingly soluble drugs to pediatric and geriatric patients that have difficulty in swallowing tablets or capsules. It is employed to mask taste and to control absorption rate of the drug.

However, a major challenge in the formulation of suspension is that of physical stability on storage, the solid insoluble drug separates from the vehicle and settles to the bottom of the container. It is desirable that such formulations re-disperse easily upon shaking [1]. As a result, it is important to evaluate the properties of some suspension commercially available in Benin City, Nigeria. There are several brands of metronidazole suspensions available in pharmacy outlets in Benin City, Nigeria. Evaluation of these brands of suspensions is important for the assessment of certain properties that are common with the suspension such as organoleptic properties (color and taste), sedimentation volume, pH, rheological properties, re-dispersibility of the suspension, and particle size distribution.

Metronidazole is a nitro-imidazole derivative that has been synthesized in various laboratories throughout the world. It was first introduced as an antiprotozoal agent, but it is also active against anaerobic bacteria. Metronidazole is chemically (2-(2-methyl-5-nitro-1-H-imidazole-1-yl) ethanol). Metronidazole benzoate is chemically (2-(2-methyl-5-nitro-imidazole-1-yl) ethyl benzoate). Metronidazole benzoate is prepared as a suspension form which is indicated in the treatment of infections caused by a wide range of anaerobic bacteria, protozoa and bacteria. A suspension of metronidazole benzoate is often substituted for metronidazole in pediatric oral preparations because of the bland taste of the ester compared to the bitter taste of the free base. The main purpose of oral suspension is to deliver a certain and defined amount of drug to the human body through the gastro intestinal system [2,3].

The objectives of the study were to evaluate the physical properties of various brands of metronidazole suspension and to compare the values obtained with that of the pharmaceutical codex in order to ensure that they meet the required standard. The suspensions were evaluated by assessing the organoleptic properties (color and

taste), particle size and shape, determination of pH and sedimentation volume, re-dispersibility test, and rheological assessment.

II. MATERIALS AND METHODS

Metronidazole powder was a gift from Adels Crystal Lake Ltd. Osun State, Nigeria. Oral metronidazole suspensions were purchased from pharmacies in Benin City. For ethical reasons the products were coded MOS 1 to MOS 10 and listed in Table 1.

Table 1:Metronidazole suspensions used for the work

Brands	Volume (ml)	Manufacturing Date	Expiry Date
MOS 1	60 ml	07/19	07/22
MOS 2	60 mL	01/19, 03/19	12/21, 02/22
MOS 3	60 mL	01/19	01/22
MOS 4	60 mL	08/18	07/20
MOS 5	60 mL	10/18	10/21
MOS 6	60mL	10/19	09/22
MOS 7	60mL	01/19	12/21
MOS 8	60mL	08/19	07/22
MOS 9	60mL	04/17	04/20
MOS 10	60mL	08/18	07/21

NOTE: This research was conducted in 2020

2.1 Organoleptic properties

The sample of the different brands of metronidazole suspension was evaluated visually for its taste and color.

2.2 pH Determination

The pH of the different brands of metronidazole suspension was determined in triplicate using the pH meter at day 1,3,5,7, and 9. The pH meter electrode was allowed to stay in the 5 ml suspension of each brand for 30 seconds before the reading was obtained.

2.3 Rheological Assessment

The time to empty 10 mL of the suspension from a 10 mL pipette was carried out in triplicate.The flow rate then calculated as follows:

Flow rate= volume of pipette (mL) / flow time (s)

2.4 Re-dispersibility Test

A 5 ml suspension from each brand was poured into three test tubes. These were stored at room temperature for 1, 3, 5, 7, 9 days. At the end of the storage period, each tube was hand shaken at constant moderate rate of 30 shakes to observe if the suspension has re-dispersed.

2.5 Determination of Sedimentation Volume

A 10 mL suspension of each brand of suspension was stored in 10 mL measuring cylinder at room temperature in triplicate, left undisturbed and labeled properly. The sediment volume was observed and noted at 1, 3, 5, 7, and 9 days. The sedimentation volume was calculated using the equation.

$F=V_u/V_o$ ---------- Equation 1

The Sedimentation volume is denoted by F, while V_u is the ultimate volume of the sediment and V_o is the original volume of the suspension.

2.6 Particle Size and Shape Analysis

The particle size and shape of the suspended particles in each brand of metronidazole suspension were determined by using optical microscope (LEIC Galen 111 Research Microscope, USA) equipped with an integrated camera (Celestron digital microscope imager, model 44421, USA) on 300 particles randomly selected from the optical field. The photomicrographs taken were analyzed using Image-J software (Model 1.48v, Wayne Rasband, USA). The size and shape descriptors used in this study are defined below:

$\text{Aspect ratio}=\frac{b}{l}$ ---------- Equation 2

$\text{Elongation ratio}=\frac{l}{b}$ ---------- Equation 3

$\text{Roundness}=\frac{4\pi A}{p^2}$ ---------- Equation 4

$\text{Irregularity}=\frac{p}{l}$ ---------- Equation 5

$\text{Equivalent circle diameter}=2\sqrt{A/\pi}$ ---------- Equation 6

Where:

b=length of minor axis (minimum ferret diameter)

l=length of major diameter (maximum ferret diameter)

A=projected area of particle

P=perimeter of the particle

III. RESULTS AND DISCUSSION

3.1 Organoleptic Property

There was no change in the colour and taste of the suspension during storage is as shown in Tables 2 and 3. Overtime, it was seen that the colour of the drug became darker than usual which could be due to exposure to light. Metronidazole suspension darkens on exposure to light [3].

Table 2: Taste of Metronidazole suspension

Suspension	Day_1	Day_3	Day $_5$	Day $_7$	Day_9
MOS 1	++	++	++	++	++
MOS 2	+++	++	++	+++	+++
MOS 3	+++	+++	+++	+++	+++
MOS 4	+++	+++	++	++	++
MOS 5	++	++	++	++	++
MOS 6	++	++	++	++	++
MOS 7	+++	+++	+++	++	+++
MOS 8	+++	+++	+++	++	++
MOS 9	+++	+++	+++	+++	+++
MOS 10	++	++	++	++	++

++ means sweet taste
+++ means very sweet taste

Table 3: Colour of Metronidazole suspension

Suspension	Colour	Day_1	Day_3	Day $_5$	Day $_7$	Day_9
MOS 1	Milk	++	++	++	++	++
MOS 2	Light yellow	++	++	++	++	++
MOS 3	Bright Yellow	++	++	++	++	++
MOS 4	Milk	++	++	++	++	++
MOS 5	Pale yellow	++	++	++	++	++
MOS 6	Orange	++	++	++	++	++
MOS 7	Milk	++	++	++	++	++
MOS 8	Pale yellow	++	++	++	++	++
MOS 9	Light yellow	++	++	++	++	++
MOS 10	Milk	++	++	++	++	++

++ means steady

3.2 pH

The pH of the metronidazole suspensions is as shown in Table 4 and Figure 1, the pH values was found to be within the range of 3.48to 5.16 on the first day while it was within the range of 3.15 to 5.04 on the ninth day. Change in the pH of the brands of metronidazole suspension may be due to temperature change and microbial degradations of the polymer of suspending agent with time.

Table 4: pH of Metronidazole suspension

Suspension	Day_1	Day_3	Day $_5$	Day $_7$	Day_9
MOS 1	4.82	4.89	4.93	3.45	3.47
MOS 2	4.86	3.79	4.24	4.58	4.61
MOS 3	4.90	4.82	4.77	4.86	4.86
MOS 4	5.13	4.94	5.10	5.02	5.04
MOS 5	4.81	4.89	4.82	4.64	4.57
MOS 6	4.20	4.64	4.54	4.74	4.75
MOS 7	4.59	5.03	4.96	4.87	4.88
MOS 8	5.16	5.05	5.08	5.00	5.00
MOS 9	3.48	3.39	3.40	3.08	3.15
MOS 10	4.39	4.61	4.54	4.83	4.79

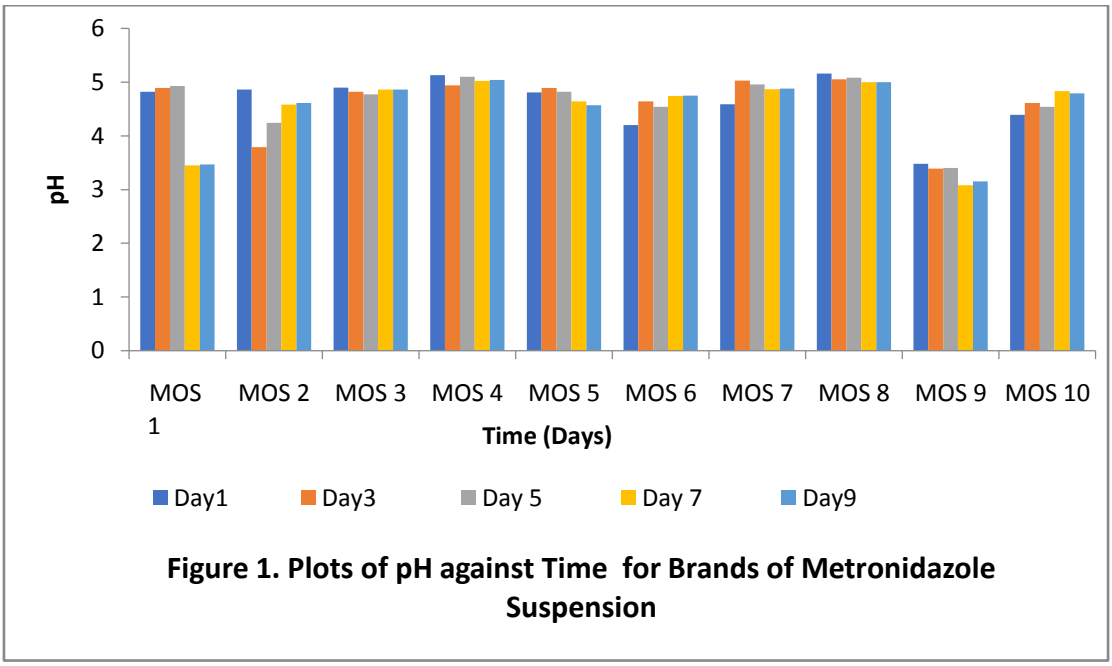

Figure 1. Plots of pH against Time for Brands of Metronidazole Suspension

3.3 Rheological Assessment

A comparative study in Table 5 and Figure 2 showed a fluctuation in the flow rate of the suspensions. The result showed a steady increase in their flow rate. It was observed that there was an increase in flow rate of the suspension with reduced viscosity.

Table 5: Flow rate of Metronidazole suspension

	Flow rate (ml/sec)				
Suspension	Day 1	Day 3	Day 5	Day 7	Day 9
MOS 1	0.5	0.480769	0.526316	0.478469	0.47619
MOS 2	0.188679	0.2	0.190476	0.194932	0.188324
MOS 3	0.232558	0.231911	0.232558	0.227273	0.224215
MOS 4	0.294118	0.285714	0.289855	0.297442	0.284495
MOS 5	1	0.947867	0.854701	0.909091	0.847458
MOS 6	0.30003	0.302939	0.302024	0.307503	0.305717
MOS 7	1.25	1.215067	1.218027	1.175088	1.233046
MOS 8	0.825764	0.812348	0.833333	0.839631	0.816327
MOS 9	0.999001	0.95057	0.98912	0.970874	0.97561
MOS 10	0.54615	0.554939	0.554324	0.553403	0.549149

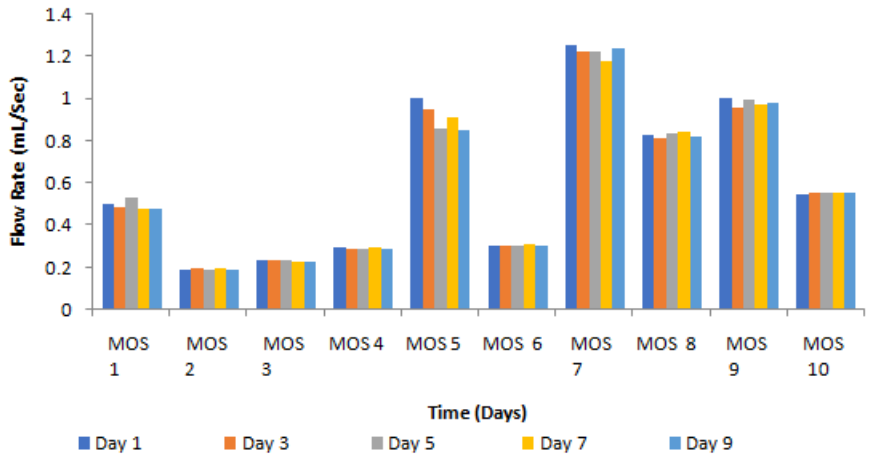

Figure 2. Plots of Flow Rate against Time for Brands of Metronidazole Suspension

3.4 Re-dispersibility

The re-dispersibility ability of the suspension is shown in Table 6. It was observed that all the suspensions had a degree of re-dispersibility ranging from excellent to moderate. This showed that the suspensions possessed a good ability to re-disperse the particle sufficiently and efficiently. It was observed that the degree of re-dispersibility of MOS 4 and MOS 8 suspensions decreased with increase in storage time.

Table 6: Re-dispersibility of Metronidazole suspension

Suspension	Day_1	Day_3	Day_5	Day_7	Day_9
MOS 1	+++	+++	+++	+++	+++
MOS 2	+++	++	++	+++	+++
MOS 3	+++	+++	+++	+++	+++
MOS 4	+++	+++	++	++	++
MOS 5	+++	+++	+++	+++	+++
MOS 6	+++	+++	+++	+++	+++
MOS 7	+++	+++	+++	++	+++
MOS 8	+++	+++	+++	++	++
MOS 9	+++	+++	+++	+++	+++
MOS 10	+++	+++	+++	+++	+++

+++ = Excellent, ++ =Moderate, + =Poor

3.5 Sedimentation Volume

The results obtained for average sedimentation volume is shown in Table 7 and Figure 3. The result showed that the suspended particles in the samples settled to form sediments at one time or the other except for MOS 3 and 4. This is probably due to the interaction between the suspended particles which eventually led to generation of energy. This is in conformity with observations of Tabibi and Rhodes [4]. Sedimentation took place with time but tend to re-disperse by shaking. The result showed that all the particles formed sediment except MOS 3 and 4.

Table 7: Sedimentation volume of Metronidazole suspension

	Sedimentation volume				
Suspension	Day_1	Day_3	Day_5	Day_7	Day_9
MOS 1	1	0.52	0.4	0.33	0.3
MOS 2	1	0.34	0.12	0.08	0.07
MOS 3	1	1	1	1	1
MOS 4	1	1	1	1	1
MOS 5	1	0.07	0.04	0.04	0.03
MOS 6	1	0.22	0.2	0.2	0.18
MOS 7	1	0.04	0.04	0.04	0.04
MOS 8	1	0.8	0.8	0.7	0.63
MOS 9	1	0.2	0.08	0.08	0.06
MOS 10	1	0.04	0.04	0.04	0.04

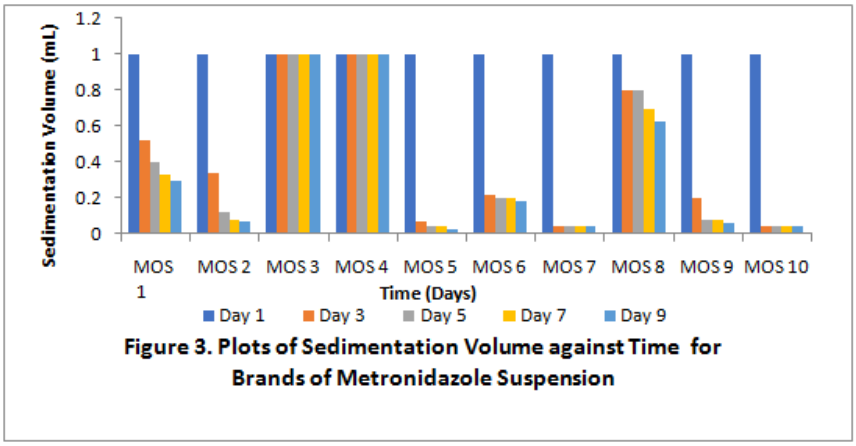

Figure 3. Plots of Sedimentation Volume against Time for Brands of Metronidazole Suspension

3.6 Particle Size and Shape Analysis

Table 8: Particle size analysis of Metronidazole suspension

Suspension	Elongation Ratio	Aspect Ratio	Irregularity	Roundness	Equivalent Circle Diameter
MOS 1	1.25	0.8	2.497	1.048	4.068
MOS 2	1.235	0.809	2.525	0.984	4.652
MOS 3	1.599	0.625	2.103	0.976	3.742
MOS 4	1.536	0.651	2.283	0.881	3.909
MOS 5	2.800	0.399	2.166	0.536	3.568

Drug particle size is an important factor influencing the drug appearance, settling rates, drug solubility and stability of pharmaceutical suspension. The larger the diameter of the suspended particle, the faster such particles sediments thereby leading to a shorter suspending time and consequently results into caking. The smaller the particle diameter, the slower the sedimentation rate and the longer the suspending time. These results in a better suspension as re-dispersibility is easy and accurate dosage can be withdrawn [5].

Larger particles will settle faster at the bottom of the container while small particles easily form hard cake at the bottom of the container. The particle size distribution data of metronidazole is shown in table 10 above and it shows that MOS 2 has the larger particle seize while MOS 5 has the least particle size.

Drug particle size is an important factor influencing product appearance, settling rates, drug solubility in vivo absorption, re-suspendability and overall stability of pharmaceutical suspension [5].

IV. CONCLUSION

It can be concluded that from the comparative evaluation of the ten brands of Metronidazole suspension, some of the brands did not meet up with standard pharmacopoeia requirement of a good suspension.The suspensions were easily re-dispersed. The pH of all the suspension were not within the pharmacopoeia limit except MOS 10 and MOS 8 suspensions. The various brands of metronidazole suspension formed sediment except MOS 2 and MOS 6.

REFERENCES

[1]. Musilin O. A., Emmanuel O. O., and Edidiong L. A. Comparative Evaluation of metronidazole suspensions formulated with Raphia Africana Hydrocolloid and other natural Polymers. Journal of Applied Pharmaceutical Science, 2017; 7 (6):121-126.

[2]. Wubayehu K, Ayenew A. Research article on comparative quality evaluation of some metronidazole tablets and metronidazole benzoate oral suspension available in retail outlets of Addis Ababa, Ethiopia. International Journal of Pharmaceutical Science and Research, 2013; 4(4):1384-1391.

[3]. Oga E.F and Ochekpe N.A. Effect of heating on the chemical stability of two brands of metronidazole suspension. African Journal of Pure and Applied Chemistry, 2009; 3(8): 135-139

[4]. Tabibi E S, Rhodes C T. Disperse system in: Gilbert S B and Christopher T R. Modern Pharmaceutics. New York Mercel Dekker, 1995; 310-314.

[5]. Aremu, O.I, Oduyela, O.O. Evaluation of Metronidazole Suspension. African Journal of Pharmacy and Pharmacology, 2015;9(12): 439-450.