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Research Article

Effect of Packaging and Storage Conditions on the Quality of Some Commercially Available Amoxicillin Oral Suspension in Benin City, Nigeria

Ibukun Olanrewaju ADELEKE*, Felix Ebitimi OMONI

Department of Pharmaceutics and Pharmaceutical Technology, College of Pharmacy, Igbinedion University Okada, Nigeria

Abstract

The clinical control of diseases frequently receives oral amoxicillin powder for reconstitution into suspension. Some of these suspensions are stored in bottles while some in plastic containers. There has been report of product instability which may be due to problem of reconstitution, storage condition or container used for storage. The aim of this work was to investigate possible instability of the suspension in plastic versus glass container, during the period of storage from the first to fourteenth day using standard methods. Parameters such as organoleptic properties, pH, sedimentation volume, rheological assessment as well as particle size and shapes were evaluated. Six brands of amoxicillin oral suspension were obtained from three local community pharmacies in Benin City, Nigeria. Three of them were packaged in bottle containers while the other three in plastic containers. The various brands were coded 1,2,3,4,5 and 6. They were then stored in the refrigerator during the period of study. From the study, it was found that those stored in plastic containers gave better results compared to those in glass containers. A significant caking was observed in three of the brands, namely 1,3 and 5. From the research work, it can be concluded that it is better to pack amoxicillin oral suspension in the plastic bottle.

Keywords: Amoxicillin oral suspension, plastic container, glass container, six brands

Article Info

***Corresponding Author**
Ibukun Olanrewaju ADELEKE
Department of Pharmaceutics and Pharmaceutical Technology, College of Pharmacy, Igbinedion University Okada, Nigeria

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CONTENTS

1. Introduction

Suspensions are two-phase systems in which the solid phase disperses in the liquid phase. The properties of this dosage form allow the incorporation of poorly soluble drugs, drugs that decompose rapidly in water, and excipients that alter the unpleasant taste of the antibiotic in order to increase the acceptability of such formulations [1]. Suspensions must have redispersion after shaking, constant particle size, homogeneous appearance and microbial resistance, as formulations with inappropriate

pharmaco-technics may alter the pharmacokinetics and pharmacodynamics of the drug. Amoxicillin suspensions are indicated for paediatric use due to their good palatability, ease and speed of use and low cost compared to cephalosporins. Amoxicillin is an antibiotic from the penicillin group with a common beta-lactam structure and antibacterial activity against susceptible infections such as actinomycosis, biliary tract infections, bronchitis, endocarditis, gastroenteritis, gonorrhoea, oral infections, pneumonia and others, as in the eradication of *Helicobacter pylori* [1].

These suspensions, which are usually packed in plastic and bottle containers, have to be kept under various conditions. For example, in the refrigerator at a certain temperature or at room temperature. In parts of Africa where there is no constant light, some patient care workers also store these suspensions in a bowl of water to achieve the required temperature for storage. Packaging is defined as a technique that allows a pharmaceutical product to be contained in a unit from the time it is manufactured until it is used. The role of pharmaceutical packaging is to package life-saving drugs, surgical devices, blood and blood products, powders, liquid dosage forms and other medicines [2].

Packaging of pharmaceuticals essentially provides containment, drugs safety, identity, convenience of handling and delivery. Pharmaceutical package has to balance lots of complex considerations, leaving behind relatively simple issue such as developing good designs and communicating with customers. Pharmaceutical packagers are concerned with more pressing concerns which fight with counterfeiting, encourage patient compliance, ensuring drug integrity or stability and balancing child-resistance and elderly accessibility. Issue of environmental safety is also an important consideration. Occasionally drugs have a limited shelf life irrespective of the pack used, but at the other extreme, some drug formulations are inherently stable and therefore a pack is needed only to prevent direct contamination, that is; dirt, dust, bacteria, etc. from atmosphere outside, and for containment. However, few pharmaceutical products can exist without the supporting role of a pack, as many of the above product factors are not only interdependent with the pack, but ultimately represent a compromise between these and other conflicting needs. Traditionally pharmaceutical products have aimed for a five-year shelf life where practical, or at least 3 years. General stability is currently supported through the International Conference on Harmonization (ICH) guidelines.

Studies have indicated different 'drug in – home' storage practices such as the keeping of drugs on dining tables, on top of refrigerators, inside first aid boxes, in bags, in the car, within closed cabinets, suit cases and the like as well as in the kitchen and bathroom. These practices may result in degradation [3].

The purpose of this study was to assess the stability of amoxicillin oral suspensions of six brands in the different storage containers, that is, glass and plastic bottles during their use after reconstitution.

2. Methodology

Six brands of amoxicillin oral suspension were obtained from three local community pharmacies in Benin City, Nigeria.

Table 1: Brands of Amoxicillin Suspension used for the Study

Brand Code	Volume (ml)	Package	Manufacturing Date	Expiry Date
1 (Ref)	100	Glass	08/2016	07/2021
2	100	Glass	14/12/2016	11/2018
3	100	Glass	08/16	08/2019
4	100	Plastic	05/2016	04/2019
5	100	Plastic	01/2017	01/2020
6	100	Plastic	11/2015	08/2018

Note: This research was conducted in 2017

Sample Collection

Six brands of amoxicillin oral suspension were purchased from three local community pharmacies in Benin City. Three of them were packaged in bottle containers while the other three in plastic containers. The various brands were coded 1 (Glass), 2 (Glass), 3 (Glass), 4 (Plastic), 5 (Plastic) and 6 (Plastic).

Reconstitution of Oral Suspension

The method of Nwokoye (2012) was adapted [4]. Six brands of amoxicillin powder for oral suspension (125 mg/5 ml) were freshly reconstituted to 100 ml using table water. The reconstituted preparations were labelled 1 to 6. The pH of the various brands was then measured using a pH meter (HM DIGITAL pH -200; USA).

Organoleptic Properties

The samples were examined for their colours. They were also tested by six different persons on the 1st 2nd 3rd 4th 5th 10th and 14th day to determine the taste of the various suspensions.

Rheological Assessment

The method of Aremu and Oduyela (2015) was adapted [5]. 5 ml of each of the various brands of amoxicillin suspension were drawn into a 5 ml pipette. The time taken to empty the 5 ml pipette was noted and recorded. This was repeated on day 2, 3, 4, 5, 10 and day 14. The flow rate and share rate were then calculated using the formula shown below:

$$\text{Flow rate} = \frac{\text{Volume of Pipette (ml)}}{\text{Flow time(s)}} \quad \ldots\ldots\ldots\ldots\ldots\ldots (1)$$

Share rate = $\frac{\text{Flow Rate (ml/s)}}{\text{Volume of pipette (ml)}}$ …… (2)

pH of Suspension

The method of Aremu and Oduyela (2015) was adapted [5]. The pH of the various suspensions was determined using a pH meter, (HM DIGITAL pH -200; USA). This was done by pouring 10 ml of each brand of the suspension into a 15 ml measuring cylinder and the pH was measured. This was repeated on day 2, 3, 4, 5, 10 and 14.

Sedimentation Volume

The method of Nwokoye (2012) was adapted [4]. The sedimentation volume of the suspensions was carried out by introducing 20 ml of each of the brands of suspension into a 50 ml measuring cylinder and kept undisturbed in a refrigerator. The sedimentation volume, F, was calculated, using the formula below:

$F = V_u / V_o$ …… (3)

Where;

F = sedimentation volume (ml)

V_u= final volume (ml)

V_o = original volume (ml)

This procedure was done in triplicate and repeated on the on day 2, 3, 4, 5, 10 and 14.

Determination of Particle Size and shape

The particle size and shape of brands of amoxicillin powder in the various suspensions were determined using optical microscopy (LEICA Galen III Research Microscope, USA; 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:

$$\text{Aspect ratio} = \frac{b}{l} \quad (4)$$

$$\text{Elongation ratio} = \frac{l}{b} \quad (5)$$

$$\text{Roundness} = 4\pi A/p2 \quad (6)$$

$$\text{Irregularity} = \frac{p}{l} \quad (7)$$

$$\text{Equivalent circle diameter} = 2\sqrt{A/\pi} \quad (8)$$

where:

b= Length of minor axis (minimum Feret diameter)

l= Length of major diameter (maximum Feret diameter)

A= Projected area of the particle

P=Perimeter of the particle

3. Results and Discussion

Tables 2 and 3 shows the taste and colour of various brands of amoxicillin suspension respectively.

Table 2: Taste of various Brands of Amoxicillin Suspension

Suspension	Day 1	Day 5	Day 10	Day 14
1	+	+	+	+
2	++	++	++	++
3	++	++	++	++
4	++	++	++	++
5	++	++	++	++
6	++	++	++	++

Table 3: Colour of various Brands of Amoxicillin Suspension

Suspension	Colour	Day 1	Day 5	Day 10	Day 14
1	Lemon	++	++	++	++
2	Light orange	++	++	++	++
3	Orange	++	++	++	++
4	Sunset yellow	++	++	++	++
5	Cream	++	++	++	++
6	Yellow	++	++	++	++

There was really no significant change in the colour and taste of the suspension with respect to storage time, in both plastic and glass container. This implies that the length of time of storage in the glass or plastic container did not affect its colour and taste.

Table 4: Flow Rate of Various Brands of Amoxicillin Suspension

		Share Rate (S^{-1})						
Suspension	**Container**	**Day 1**	**Day 2**	**Day 3**	**Day 4**	**Day 5**	**Day 10**	**Day 14**
1	Glass	0.25	0.22	0.29	0.30	0.31	0.33	0.35
2	Glass	0.27	0.28	0.23	0.25	0.33	0.34	0.38
3	Glass	0.15	0.11	0.16	0.16	0.17	0.34	0.38
4	Plastic	0.24	0.04	0.04	0.05	0.05	0.08	0.10
5	Plastic	0.15	0.08	0.09	0.13	0.17	0.18	0.22
6	Plastic	0.014	0.016	0.02	0.02	0.02	0.03	0.03

Table 5: Share Rate of Various Brands of Amoxicillin Suspension

		Share Rate (S^{-1})						
Suspension	**Container**	**Day 1**	**Day 2**	**Day 3**	**Day 4**	**Day 5**	**Day 10**	**Day 14**
1	Glass	0.25	0.22	0.29	0.30	0.31	0.33	0.35
2	Glass	0.27	0.28	0.23	0.25	0.33	0.34	0.38
3	Glass	0.15	0.11	0.16	0.16	0.17	0.34	0.38
4	Plastic	0.24	0.04	0.04	0.05	0.05	0.08	0.10
5	Plastic	0.15	0.08	0.09	0.13	0.17	0.18	0.22
6	Plastic	0.014	0.016	0.02	0.02	0.02	0.03	0.03

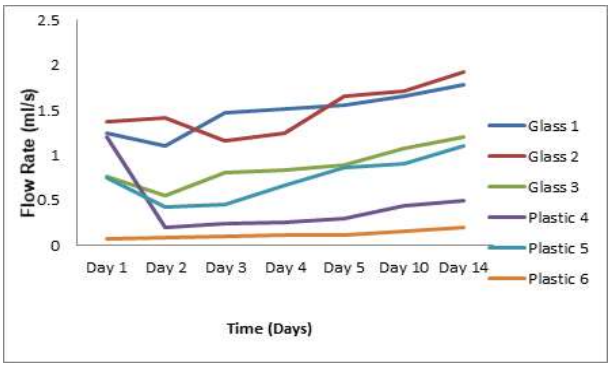

Figure 1: Plots of Flow Rate of Various Brands of Amoxicillin Oral Suspension against Time

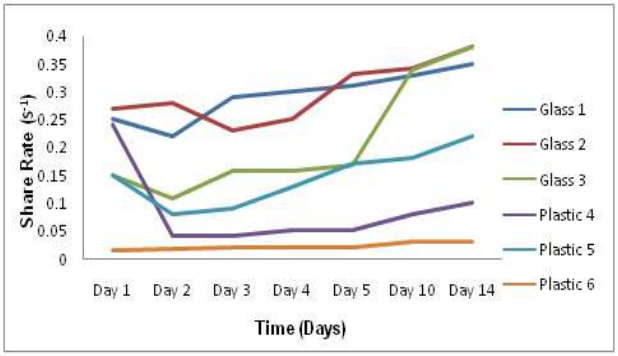

Figure 2: Plots of Share Rate of Various Brands of Amoxicillin Oral Suspension against Time

The higher the viscosity of a suspension, the lower the flow rate. Comparing the flow rate of the various suspensions stored in the plastic container with that of the glass container, it was found that the flow rate of the content in the glass container increased progressively during the period of storage meaning that, the viscosity was reduced with storage. However, for the plastic containers, there was a fluctuation in the flow rate, it slightly increased and then decreased with storage but the increase and decrease were insignificant. The decrease in viscosity may be due to depolymerization of the polymer suspending/ thickening agent due to the storage time.

Table 6: pH of Suspension of Various Brands of Amoxicillin Suspension

		pH Values						
Suspension	**Container**	**Day 1**	**Day 2**	**Day 3**	**Day 4**	**Day5**	**Day10**	**Day 14**
1	Glass	6.76	7.33	7.39	7.42	7.58	7.85	7.98
2	Glass	6.83	7	7.11	7.26	7.47	7.64	7.83
3	Glass	7.36	7.67	7.74	7.79	7.9	8.1	8.28
4	Plastic	7.24	7.4	7.56	7.72	7.74	7.83	7.99
5	Plastic	6.61	6.28	6.46	6.96	6.99	7.1	7.25
6	Plastic	6.97	7.27	7.32	7.52	7.63	7.75	8.38

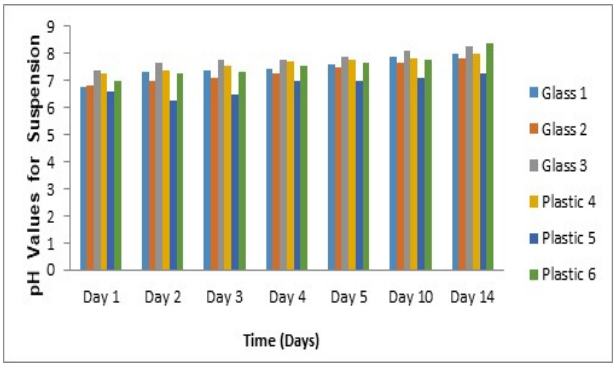

Figure 3: Plots of pH of Various Brands of Amoxicillin Oral Suspension against Time

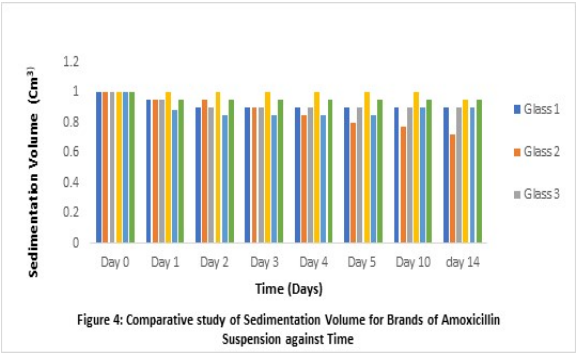

Figure 4: Comparative study of Sedimentation Volume for Brands of Amoxicillin Suspension against Time

The pH of the amoxicillin suspension in the glass and plastic containers was found to beapproximately neutral. The pH of all suspension in the containers progressed towards alkaline as storage progresses. Changes in pH of a product can occur depending on whether acidic or basic metabolites are released, and become so modified as to permit secondary attack by other microbes previously inhibited by the initial product pH [6].

Table 7: Sedimentation Volume of Various Brands of Amoxicillin Suspension

	Sedimentation volume (ml)							
	Day							
Drug	0	1	2	3	4	5	10	14
1	1.00	0.95	0.90	0.90	0.90	0.90	0.90	0.90
2	1.00	0.95	0.95	0.9	0.85	0.8	0.77	0.72
3	1.00	0.95	0.90	0.90	0.90	0.90	0.90	0.90
4	1.00	1.0	1.0	1.0	1.0	1.0	1.0	0.95
5	1.00	0.88	0.85	0.85	0.85	0.85	0.90	0.90
6	1.00	0.95	0.95	0.95	0.95	0.95	0.95	0.95

Suspension tends to settle with time and thus are designed to redisperse by gentle shaking, resulting in homogenous suspension. Redispersibility depends on the size of the particles and the nature of the suspension formed. Since suspensions sediment on storage, it must readily be dispersed so as to allow uniformity of the dose. Comparing the sedimentation volume of the various brands of suspension in both the plastic and the bottle container, it was observed that there was significant caking in containers 2, 3 and 5. Both 2 and 3 were plastic containers while 5 was glass container. This may be due to the size of the particles in the suspension.

Table 8: Amoxicillin Particle Size and Shapes

Suspension	Equivalent Circle Diameter (µm)	Aspect Ratio	Roundness	Irregularity	Elongation Ratio
1	7.026	0.5689	0.244	4.247	1.75
2	6.664	0.5890	o.285	4.275	1.69
3	6.978	0.6031	0.380	4.019	1.66
4	7.124	0.5785	0.137	4.312	1.72

Discussion:

Drug particle size is an important factor influencing product appearance, settling rate, drug solubility, in-vivo absorption, resuspendability and overall stability of pharmaceutical product. Sedimentation of particles in a suspension may also depend on the particle size [5]. Larger particles tend to sediment faster than smaller particles, making it difficult for removal of accurate doses if not

removed immediately after shaking. From the particle size analysis shown in result table above, it was discovered that; sample 1 and 4 have larger particles than others; hence, will settle faster thus affecting pourability of accurate dose.

Information on particle shape is important in order to understand the behaviour of suspension during storage. The particle shape of a suspended particle may have an impact on the packing sediment (e.g. packing density and settling characteristics) and thus product resuspendability and stability. Packing density is defined as the weight to volume ratio of the sediment at equilibrium. The symmetrical barrel shaped particles of calcium carbonate were found to produce stable suspensions without caking upon storage, while asymmetric needle shaped particle forms a tenacious sediment cake which could not be easily re-dispersed [7].

From the results shown in Table 8 on particle size and shape of amoxicillin powder, the brand which showed the least roundness (Plastic 4) gave a value of 0.137, but was not quick to cake or sediment unlike (Glass 3), which shows a higher roundness with value of 0.380, but was found to cake or sediment faster.

4. Conclusion

From the comparative study of the various brands of amoxicillin oral suspension obtained from the three local community pharmacies in Benin City, it can be concluded that amoxicillin suspension stored in plastic containers gave better results compared to those in glass containers.

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