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***ISSN-2394:3076***
***CODEN(USA) : JBPCBK***
**Journal of Biological Pharmaceutical And Chemical Research, 2023, 10(3): 31-39**

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# IN VITRO QUALITY ASSESSMENT OF FIVE DIFFERENT BRANDS OF CEFUROXIME AXETIL SUSPENSION SOLD IN AMASSOMA, NIGERIA

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## ABSTRACT

*Health professionals, regulatory agencies for drugs, drug users, and the general public are very worried about therapeutic failure as a result of increasing prevalence of utilizing fraudulent, contaminated, counterfeit, and inferior medications in Nigeria. This study's objective was to evaluate the in vitro efficacy of five different brands of cefuroxime axetil suspensions sold in Amassoma, Nigeria. They were physically evaluated for indications of manipulation or a broken seal on the primary containers' cap, as well as for their organoleptic qualities, pH, sedimentation volume, flow rate, viscosity, redispersibility and content of active ingredients/assay using approved protocols. Results revealed that the labels on the suspensions contained all the relevant information, and the containers had not been tampered with to get access to or alter the contents. For color variation, pH, viscosity, flow rate, sedimentation and redispersibility, every brand tested performed well. All of the brands adhered to the cefuroxime axetil content specifications stated on their labels (based on USP). Generally, all the brands are acceptable for distribution and consumption.*

**Keywords:** Quality Assessment, Suspensions, Cefuroxime Axetil.

## INTRODUCTION

A process of data gathering and analysis that determines the degree of compliance with established criteria can be referred to as quality assessment. It places emphasis on the standards for accepting or rejecting data. If the quality obtained through the procedure is subpar, attempts are made to identify the cause of the quality discrepancy. Following that, corrective measures are implemented, and the quality is then evaluated again after a reasonable amount of time (Nkemakolam et al.,2020). This is a rigorous process that enables ongoing review of the established standards and guidelines with the ultimate goal of raising the caliber of healthcare services. Pharmaceutical products or medication can be expressed as genuine, counterfeit or substandard (Akinyandenu et al.,2013 and Buowari et al.,2013). Genuine medications or drugs are those whose formulations have complied with the norms or requirements set by regulatory bodies for such items while authentic products that failed to meet

the standards of the quality testing processes already established for each product may be substandard medications or drugs. The World Health Organization (W.H.O) claims that counterfeit pharmaceuticals are those that have been purposefully or fraudulently mislabeled in terms of source and/or identity (W.H.O.,2018). Despite being a global issue, the problem of the distribution of fake, subpar, or counterfeit pharmaceuticals is especially prevalent in the third world nations, with Nigeria being one of them (Zulkifli et al.,2016). Poor storage circumstances, such as high temperatures and humidity, which stimulate chemical breakdown and alter the biopharmaceutical properties of the drugs that are stored before their estimated and labeled shelf lives, are often to blame for the integrity of pharmaceuticals supplied in tropical locations being compromised (Johnston et al.,2013).

When referring to dosage forms for pharmaceuticals, a suspension is a coarse dispersion made up of finely divided insoluble substance suspended in a liquid media (Ofoefule.,2002). Suspension systems typically consists of two phases, an internal phase and an external phase, and are heterogeneous and thermodynamically unstable systems. Most suspensions can be made stable by adding one or more suspending agents, which aid in keeping the insoluble dispersed materials suspended for long enough to allow for the administration of a consistent dosage when necessary (Bamiro et al.,2014).

The oral prodrug cefuroxime axetil contains the bactericidal cephalosporin antibiotic cefuroxime, which is effective against a variety of gram positive and gram-negative bacteria and is resistant to degradation by most β-lactamases. For paediatric illnesses such as upper respiratory tract infections, it is widely utilized (Vinod et al.,2013). Cefuroxime axetil has weak aqeous solubility and wettability, which makes it challenging to formulate pharmaceuticals for oral and parental distribution (BP.,2009). While brands of other suspensions sold in Nigeria have had their in vitro quality assessed, to our knowledge, no such study has been done on cefuroxime axetil suspension. To ensure that the cefuroxime axetil that health care professionals and consumers of these products have access to is advantageous and does not pose any risk to the end users, the aim of the present study is to examine various in vitro quality aspects of the suspension.

## MATERIAL AND METHODS

### Materials

Cefuroxime axetil (FDC Ltd Mumbai India), methanol (Tianjin China), sodium phosphate (dibasic/monobasic), sodium chloride, sodium azide and sodium hydroxide (Shinya Chem. Co.Ltd China), distilled water, five brands of cefuroxime axetil suspension (procured from different Pharmacies in Amassoma, Bayelsa State, Nigeria). This study was carried out between Jan-April 2021.

### Methods

### Collection of Samples

Ten bottles each of five different brands of cefuroxime axetil suspension were purchased from the major wholesale Pharmacy outlets in Amassoma, Bayelsa State, Nigeria. Selection of purchased brands was done randomly.

### Physical Inspection of Products Packaging

To determine if they had been tampered with, the physical inspection of the five different brands of cefuroxime axetil suspensions with the codes A to E was performed. This is important since the product was packaged in plastic bottles with screw-on tops that were designed to be tamper evident.

The label informations were also checked.

**Organoleptic Properties Determination**

Some organoleptic properties which includes the colour, odour and texture of the suspensions were observed using the appropriate sense organs and presented in table 2.

**pH Determination**: The pH of the five different brands of cefuroxime axetil suspension was determined using a pH meter (Hanna Italy). Replicate determinations were carried out.

**Flow Rate Determination:** It was calculated how long it took a 10ml sample of cefuroxime axetil suspension to pass through a 10ml pipette. For each brand, duplicate determinations were made, and the mean flow rate was computed using the following equation.

$$\text{Flow rate} = \frac{\text{volume of suspension (ml)}}{\text{Flow time (sec)}} \longrightarrow \text{Equation 1}$$

**Determination of Viscosity:** The viscosity of the suspension brands was determined using the Brooksfield viscometer at 100rpm. After each decision was made in triplicate, the data were reported as mean values.

**Determination of Sedimentation Volume/Ratio**

A 100ml volume of each of the cefuroxime axetil suspensions from the five different brands of cefuroxime axetil was poured into 100ml graduated glass measuring cylinder's after adequate shaking of the individual product container. Each measuring cylinder's mouth, which held the suspension, was sealed with cotton wool and kept uninterrupted on a flat surface under ambient conditions. This was completed for each brand in triplicates. The sedimentation ratio was computed using the equation below (Zhu et al.,2017).

$$F = Vt/Vo \longrightarrow \text{Equation 2}$$

Where F is the sedimentation ratio, Vt is the volume of sediment generated after a specific amount of time, while Vo is the initial volume of sediment at the moment the suspensions were put into the measuring cylinder.

**Redispersibility Determination:** On day 28, shortly after the last undisturbed sedimentation volume/height measurements were gathered and recorded, the redispersibility assessment was completed. The measuring cylinder's mouth was covered and held in place with the right palm, while the base was held in place with the left. The cylinder was rotated counterclockwise back to its initial position after being inverted clockwise through $180^0$ (Brhane et al.,2020). This was noted as one shake. The redispersion number was the number of shakes required by the suspensions to completely redisperse the sediment. When no sediments could be seen at the measuring cylinder's bottom, complete dispersion was thought to have occurred (Okoye et al.,2014). The test was carried out in triplicates.

**Standard Calibration Curve:** A 50mg quantity of cefuroxime axetil pure drug was dissolved in 100ml methanol to produce 500µg/ml stock solution. From the stock solution, 0.5ml is pipetted into a 100ml volumetric flask and phosphate buffer is added to make the volume equal (Amir et al.,2014). Additional dilutions were done to create various concentrations ranging from 2.5 – 20µg/ml. The absorbance of standard solutions was measured using an ultraviolet-visible spectrophotometer (UV –

Shimadzu 1800) set to 278nm. As a result of plotting the absorbance values against drug concentrations, a standard curve of cefuroxime axetil was created.

**Assay/Content of Cefuroxime axetil determination**

The method of (Hadi Valizadeh et al.,2011) was used with slight modifications at 278nm wavelength.

**Statistical Analysis:** Microsoft Excel 2016 was used. The mean and standard deviation were computed for each data generated.

## RESULT AND DISCUSSION

The products were intact and the suspension bottles of the five distinct brands of cefuroxime axetil suspensions with the codes A-E had not been tampered with, according to evaluation results of the packaging and label information. The cefuroxime axetil suspension brands had the label claim, volume content, batch numbers, manufacturing dates, expiry dates, NAFDAC registration numbers, manufacturers name and distributors name.

**Table 1:** Package informations of the cefuroxime axetil suspensions used

| Brand name | Label claim | Volume (ml) | Batch No | Man. Date | Exp. Date | NAFDAC REG NO. | MANUFACTURER | DISTRIBUTORS |
|---|---|---|---|---|---|---|---|---|
| Aquatce®/A | 125mg/5ml | 100 | TPNAE9048 | Dec 2019 | May 2022 | BA-9543 | FINECURE PHARM. LTD INDIA | PINNACLE HEALTH PHARM. LAGOS |
| Oxisper®/B | 125mg/5ml | 70 | ZED0230 | May 2020 | April 2022 | BA-8954 | ZEE LAB, INDIA | DONY-TRIUMPH LTD, ONITSHA |
| Fidson®/C | 125mg/5ml | 70 | DAAW0014A | July 2020 | June 2022 | A4-0677 | THE MADRAS PHARM. INDIA | FIDSON HEALTH CARE PLC LAGOS |
| Plumocef®/D | 125mg/5ml | 100 | M905 | Dec 2019 | Nov 2021 | B4-4327 | ZIM LAB. LTD. INDIA | GENEITH PHARM LTD. LAGOS |
| Pocco®/E | 125mg/5ml | 70 | 0330Z004 | Jan 2020 | Dec 2022 | B4-9555 | SCOH-EDIL ADVANCE RES.LAB LTD INDIA | FIRST J. POCCO PHARM LTD. ASABA |

Table 2 lists and displays the findings of some organoleptic characteristics of cefuroxime axetil suspension:

**Table 2:** Organoleptic characteristics of cefuroxime axetil suspension

| BRAND NAME/CODE | COLOUR | TEXTURE | ODOUR |
|---|---|---|---|
| Aquatce®/A | Cream | Coarse | Lemon flavor |
| Oxisper®/B | White | Coarse | Lemon flavor |
| Fidson®/C | White | Coarse | Banana flavor |
| Pulmocef®/D | Cream | Coarse | Banana flavor |
| Pocco®/E | Cream | Coarse | Pineapple flavor |

Table 3 displays the pH measurement findings for each brand of cefuroxime axetil suspension. The suspensions were all slightly acidic, which is in accordance with the compendia standards of 5.0 – 6.5 (B P.,2012). The pH levels did not significantly alter during the 28-day research period. This demonstrates that the suspensions were stable and were neither chemically nor microbiologically degraded.

Table 3 displays the cefuroxime axetil suspension flow rate values. The flow rate for brand A suspension was the highest, whereas brand E had the lowest flow rate. The flow rates of all the brands examined were less than 1.0ml/sec. The viscosity of the suspensions is indicated by the flow rate, which demonstrates how easily a suspension can be poured from its container. The suspension will be easier to pour from the container at a higher flow rates. All the five brands were easily pourable from their containers.

Table 3 displays the results of the viscosity assessment. Brand A had the lowest viscosity compared to the other brands, whereas brand E had the highest viscosity and could not be easily poured out of the product container. As a result of the findings, brand E would be least pourable, least flowable, and most stable of the suspensions because its particles would be suspendable for the longest period of time before sedimentation, whereas brand A's particles would sediment at the fastest pace. The type and quantity of polymer employed as a suspending agent in the formulation will determine the degree of viscosity experienced (Oraeluno et al.,2021).

The suspensions measured viscosities and flow rates may be correlated (Table 3). The flow rate that was seen in the cefuroxime axetil suspension increased with deceasing viscosity values.

Figure 1 displays the results of the sedimentation volume or ratio of each of the insoluble components suspended over the duration of a 28-day observation period. All of the particles were initially suspended in the measuring cylinder with sedimentation ratio of one (Nkemakolam et al.,2020). When the particles were left undisturbed on the shelf for the course of the investigation, different volumes /ratios of the sediments of the particles were observed. For all of the suspensions, the sedimentation ratio generally reduced as the number of days increased, while brands E and D saw the least amount of change. The sedimentation volume or ratio can be related to the viscosity of the individual suspensions (Alok et al.,2010). In comparison to lower viscosities, higher viscosities kept their particles suspended in the suspensions for a longer period of time. This happens as a result of a decrease in rate of particle sedimentation brought on by the viscous environment. Since none of the suspensions particles formed a cake at the base of the measuring cylinder, all of them were flocculated. The capacity of the particles to stay suspended within the suspension long enough after agitation to enable the removal of a constant dose each time the formulation is to be supplied was used to evaluate the suspension's stability. Whenever the sedimentation value approaches one (Bhurat et al.,2012), an oral suspension is seen more stable and acceptable. Generally, the suspension is less stable when the regression line is steeper. The order of stability is brand E>D.>C>B>A.

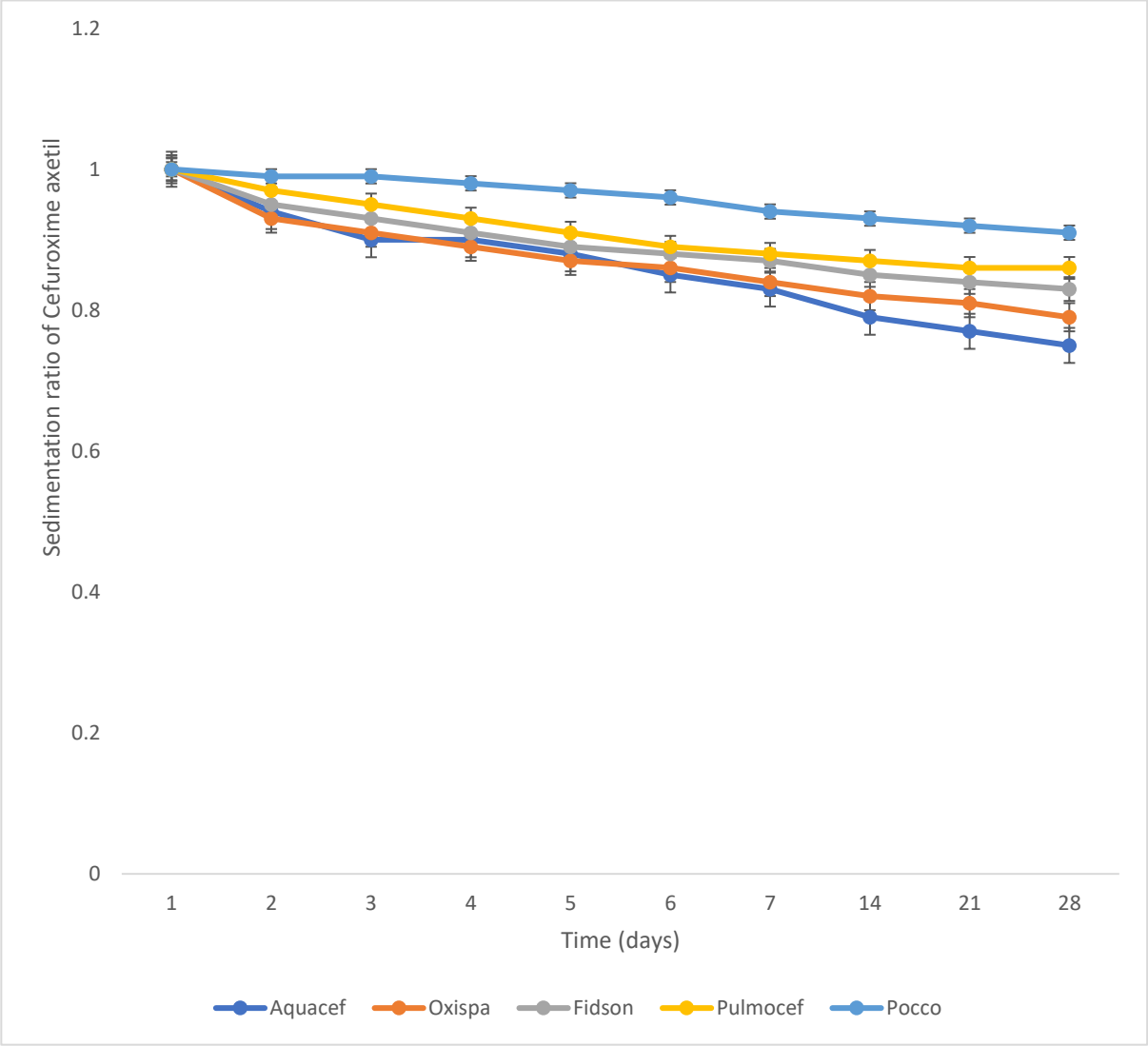


**Figure 1:** Sedimentation ratio of Cefuroxine Suspension

Table 3 displays the redispersibility numbers attained from testing the various brands of cefuroxime axetil suspensions. After 28 days on the shelf, all of the suspensions were re-dispersible. Their level of redispersibility, however, differed from one brand to another.

In order to ensure that provided doses of medication are uniform after shaking, a good suspension should display quick redispersibility (Oraeluno et al.,2021).

**Table 3:** pH, flow rate, viscosity and redispersibility of cefuroxime axetil suspensions.

| Brand | pH | Flow rate ml/s | Viscosity (P) | Redispersibility Number |
|---|---|---|---|---|
| A | 5.2 ± 0.10 | 0.12 ± 0.00 | 1.18 ± 0.00 | 5.0 ± 0.01 |
| B | 5.5 ± 0.11 | 0.089 ± 0.02 | 3.28 ± 0.02 | 8.0 ± 0.10 |
| C | 5.4 ± 0.09 | 0.070 ± 0.00 | 4.48 ± 0.01 | 9.0 ± 0.02 |

| | | | | |
|---|---|---|---|---|
| D | 5.9 ± 0.12 | 0.062 ± 0.01 | 5.98 ±0.05 | 12.0 ± 0.05 |
| E | 6.0 ± 0.08 | 0.054 ± 0.02 | 6.25 ± 0.05 | 13.0 ± 0.05 |

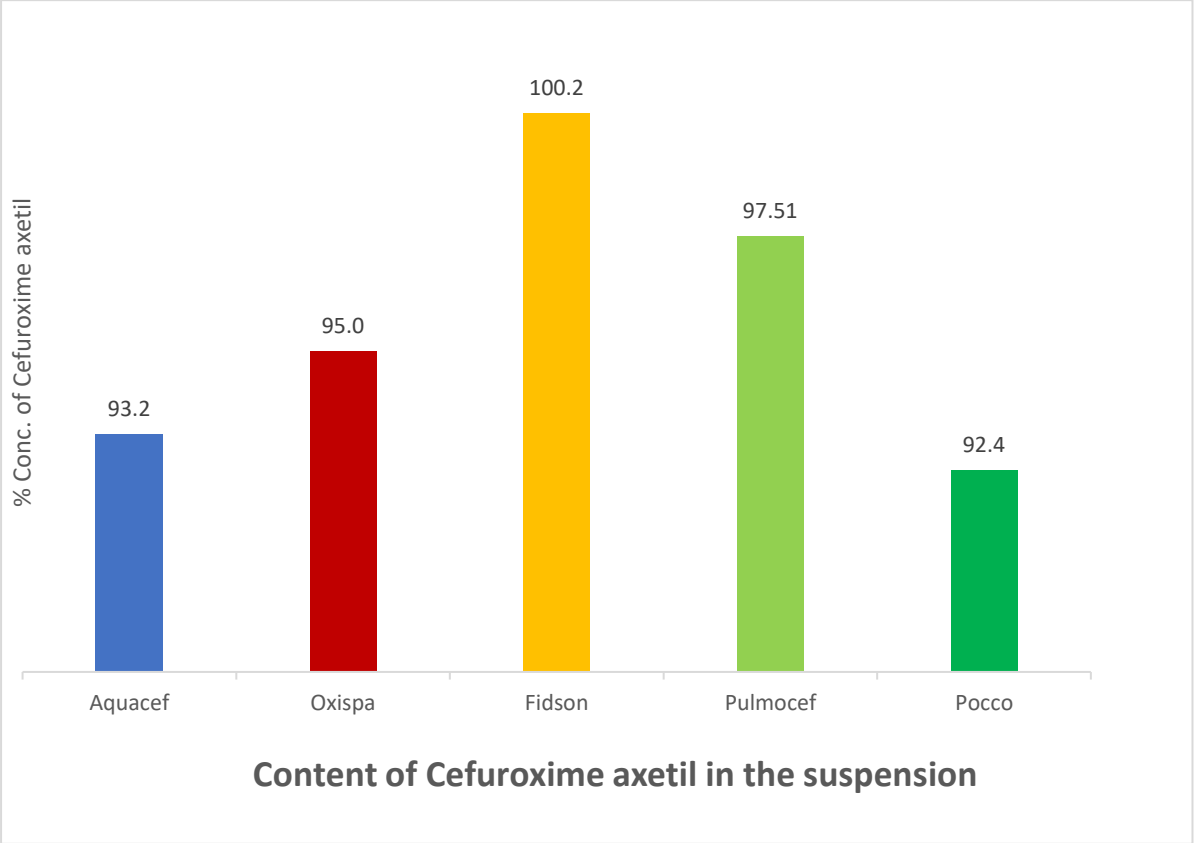


Figure 2 displays the outcomes of the test/content of cefuroxime axetil suspension found in the brands of commercial suspension. Brand E had the lowest value of cefuroxime axetil

(92.4%) while brand C had the greatest concentration (100.2%). All the brands met with the label claims. As a result, the five brands assessed met the USP requirements for the assay/content of active component test (USP.,2009). According to the USP, suspensions containing cefuroxime axetil should contain not less than 91.00% or more than 106.00% of cefuroxime axetil.

## CONCLUSION

Physical evaluation of the cefuroxime axetil suspension containers revealed that the seals on the bottles that served as the main containers had not been compromised, confirming the integrity of the products as intended by the manufacturer. The labels for each of the five suspension brands contained the necessary information about the product. All of the drugs were produced in India, registered by NAFDAC, and distributed by Pharmaceutical firms with offices in Nigeria.

Based on established assessment criteria, such as pH, the cefuroxime axetil suspensions were found to be mildly acidic (pH 4-6), suggesting that they should be compatible with active pharmaceutical components that have pH values in this range.

The products stability was also supported by the flow rate and viscosity. All of the brands were pourable from the container and viscous enough to keep the formulations insoluble particles suspended for long enough to allow for an adequate and consistent withdrawal of these particles in a uniform dose following shaking and redispersing the suspensions sediments.

The sedimentation volume or ratio was typically less than 1, and the particles settled in a way that made it simple for the vehicle to move through the floccules, enabling quick loosening and complete redispersibility within a short period of time.

The results of the assay for cefuroxime axetil revealed that all the brands met the label claims for cefuroxime axetil. As a result, it is clear from the findings that the majority of commercial brands of cefuroxime axetil suspensions being marketed in Amassoma are of high quality and capable of inducing the anticipated therapeutic response when used as directed.

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