*IOSR Journal Of Pharmacy And Biological Sciences (IOSR-JPBS)*
*e-ISSN:2278-3008, p-ISSN:2319-7676. Volume 16, Issue 2 Ser. II (Mar. – Apr. 2021), PP 33-40*
*www.Iosrjournals.Org*

# Quality Assessment of Some Selected Brands of Amoxicillin Clavulanate from Pharmaceutical Stores in Kaduna Metropolis, Nigeria

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***Abstract***
***Background****: The quality parameters of different brands of Amoxicillin Clavulanate in terms of percentage composition of the Assay content, Karl Fischer, Dissolution, Hardness, Friability and Disintegration were determine using standard methods.*
***Materials and Methods****: Ten (10) different brands of amoxicillin/clavulanic acid tablets were used for this study. Five (5) expired amoxicillin clavulanic acid tablets were obtained from the Samples Reception Unit of NAFDAC Area Laboratory, Kaduna, while five (5) unexpired amoxicillin clavulanic acid tablets were purchased from reputable pharmaceutical stores within Kaduna metropolis.*
***Results****: The results showed that percentage composition of unexpired drugs ranged from 98.47% to 114.03%, expired ranged from 58.80% to 117.33% for Amoxicillin/Clavulanate. Percentage Karl Fischer of unexpired drugs ranged from 7.91% to 9.15% and expired ranged from 9.39% to11.46%, Percentage dissolution for unexpired drugs ranged from 82.04% to 120.34% and expired ranged from 34.29% to 106.62% Clavulanate/Amoxicillin at 37oC. Hardness for unexpired drugs ranged from 84.77N to 166.17N and for expired ranged from 111.80N to 228.67N, friability for unexpired drugs ranged from 0.45% to 0.87% and expired ranged from 0.02% to 0.23% and disintegration time of unexpired drugs ranged from 8.96mins to 13.90mins and expired ranged from 6.9mins to 11.87mins. The result of this research shows that all the tested parameters for unexpired drugs are within the USP monograph acceptable standard whereas only friability and disintegration for expired drugs are within the USP acceptable standard.*
***Conclusion:*** *This therefore showed that continuous consumption of expired drugs could pose potential damage to human's health and should be therefore avoided.*
***Keywords:*** *Amoxicillin clauvlanate, High performance Liquid Chromatography, Karl Fischer, Dissolution, Hardness, Friability.*

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Date of Submission: 22-03-2021 Date of Acceptance: 06-04-2021

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## I. Introduction

Antibiotics are very sensitive medicine and are used in the management of microbial infections. If not properly used as specified, the tendency that the microbes involved may develop resistance against them and render them ineffective (Dugal and Mamajiwala, 2011). Resistance towards the medicines can equally be developed in cases related to fake antibiotic products, where they are under-dosed. This has recently been observed in generic drugs related to Augmentin-like medicines, containing amoxicillin and clavulanic acid and it derivatives as the active ingredients: The low quality of the antimicrobial drugs cause increase in burden of disease, which lead to excess mortality and morbidity which result in various untoward clinical outcomes such as lack of effect, treatment failure, bacterial resistance and side effects (Kelesidis and Falagas, 2015). Amoxicillin and Clavulanic acid combinations are available in oral solid dosage form, powder for reconstitution as suspension and injectable. (Foulstone, 2001). These two drugs act synergistically to produce the desired therapeutic effect and the potency depends on content of the active moiety in these dosage forms. Thus the availability of very simple but highly sensitive and cost effective analytical methods to quantify the content of amoxicillin and clavulanic acid in liquid dosage forms and established the stability of both compounds under the temperature conditions in Nigeria which can go as high as 42˚C at certain times of the year is imperative if the synergistic efficacy of the two drugs is to be exploited in the treatment β-lactamase infections.

In Nigeria, fixed dose combinations of amoxicillin and clavulanic acid is one of the first line medicines on the essential drug list of the National Health Insurance Scheme for the treatment of a wide range of bacterial

infections and post-operative prophylaxis (Standard Treatment Guideline, 2005). Among these bacterial infections are upper and lower respiratory tract infections, infections of the skin and other soft tissues. (Martin et al., 2009).Amoxicillin is chemically named or designated as (2-S,5R.6R)-6-[(2R)-2-amino-2-(4-hydroxyphenyl)acetyl]amino]-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid Trihydrate (US Pharmacopeia, 2007). The aim of this study is to assess the quality of Amoxicillin Clavulanate drugs within Kaduna metropolis and its environs.

## II. Material And Methods

**Sampling**

Ten (10) different brands of amoxicillin/clavulanic acid tablets were used for this study. Five (5) expired amoxicillin clavulanic acid tablets were obtained from the Samples Reception Unit of NAFDAC Area Laboratory, Kaduna, while five (5) unexpired amoxicillin clavulanic acid tablets were purchased from reputable pharmaceutical stores within Kaduna metropolis. The tablets were coded as follows: -

Expired; $Exp_1$, $Exp_2$, $Exp_3$, $Exp_4$, $Exp_5$

Unexpired; $UNE_1$, $UNE_2$, $UNE_3$, $UNE_4$, $UNE_5$

**Chemicals and Reagents**

All the reagents used were purchased from Merck Company. Amoxicillin clavulanate potassium, reference standards powder was manufactured by Sigma-Aldrich, USA. All other chemicals were used without further purification. Buffer solution of 4.4 pH**,**99% of Amoxicillin clavulanate potassium reference standard, Hydranal 1- composite 5 as titrant, Sodium tartrate as reference standard**,** Water –free methanol as Karl fischer solvent, 7.8 g Monobasic sodium phosphate**,** 85% Phosphoric acid of 1.170 density, 99 % Methanol (HPLC Grade).

**2.3 Materials and Equipment**

The materials and equipment used in the course of the analysis include; Mettle Toledo Analytical Balance (Max 120g, d=0.0001g), Millipore membranes (0.45) pH meter (Mettle Toledo GmbH CH-8902 Rudolf Switzerland, Karl Fischer Mettle Toledo Switzerland, CliSonicator (Nickel Electro Limited) and HPLC Chromatograph (LC 20AB Binary Pump- Schimadzu, SPD-20AB UV Detector, DGU-$20A_3$ Degasser, LC Solutions Software, ODS Column C18 Phenomenex 250x4.6mm(Ultracarb 5.0),Refrigerator, Desiccators, Distilled water, Volumetric Flask (10 ml,25 ml,50 ml,100 ml,250 ml,1000 ml), Transfer pipette ( 1.0 ml, 2.0 ml, 5.0 ml, 10.0 ml 25.0 ml), Beakers, Plastic Funnel, Hardness tester(Logan Instrument corp.HDT-300)Shaker(Stuart flash shakers SF1),Friability tester (Logan Instruments corp.FAB-2S), Disintegration tester (Logan instrument corp. DST-3), and Dissolution tester(ERWEKA DT-600 and DT-800).

**Physical/Visual Inspection:** The visual inspection of packaging and tablets were observed prior to the qualitative tests as a mean of checking the quality of the samples, the packaging was quickly check for legal labelling and for the active ingredient. The strength of the tablets, date markings, colours, size, country of origins, storage condition and as well as NAFDAC registration numbers if any, are observed as a quick check

**Uniformity of weight (Mass):** Twenty (20) tablets selected from each brand were weighed individually and the average weight calculated (USP, 2017).

$$Average\ weight = \frac{\sum(X1+X2\ldots Xn)}{n} \quad \text{..... Equation (1)}$$

Where X is the weight of each tablet; n is the total number of tablets

$$\%\ Deviation = \frac{\text{Decleared mass}}{100} \times \text{Average weight of tablets.}$$

**Preparation of the Buffer Solutions:** 7.8g of mono basic sodium phosphate was diluted in 900 ml of water. Adjusted with phosphoric acid to a pH of 4.4 ± 0.1 and was diluted with water to make up to 1000 ml (United State Pharmacopoeia, 2017).

**Preparation of Mobile Phase:** Methanol and buffer (1:19) that is, 50 ml of methanol was mixed with 950 ml of buffer in 1000ml volumetric flask.

**Preparation of 0.5mg/ml of Amoxicillin and 0.2mg/ml of Clavulanate Mixture:** 25 mg of the amoxicillin reference standard and 10 mg of clavulanate reference standard powder were weighed and transferred into 50 ml volumetric flask and make up to mark with distilled water to produce a concentration of 0.5 mg/ml of amoxicillin and 0.2 mg/ml of clavulanate (USP, 2017).

**Preparation of 10mg/ml of Amoxicillin and 2.5mg/ml of Clavulanate Mixture:** Ten tablets containing 500/125 mg (amoxicillin/clavulanate potassium) each were mixed and dissolved in a 500 ml volumetric flask with water using shaker to give concentration 10 mg/ml amoxicillin and 2.5 mg/ml clavulanate respectively (USP, 2017).

**Preparation of Sample Solution:** 1 ml of sample stock solution in combination (amoxicillin clavulanate potassium) was transferred into a 20 ml volumetric flask, mixed and made to volume with distilled water, given concentration of 0.5 mg/ml amoxicillin and 0.125 mg/ml of clavulanate. The solution was sonicated by using ultrasonic bath to remove air bubbles and kept in a vial bottle and injected in HPLC machine (United State Pharmacopeia, 2017).

**System Suitability Test:** System-suitability tests were performed accordingly to confirm the reproducibility of the instrument adequate for the analysis. The system suitability test was performed before analysis of every batch of sample to ensure the reproducibility of the chromatographic system. The HPLC system suitability test was perform by running six injections of Standard to establish the retention time and a baseline (United State Pharmacopeia, 2017).

The Formula used to calculate the active content and percentage content of the tablets using HPLC chromatogram is shown:

$$\text{Results} = (r_u/r_s) \times (C_s/C_u) \times 100 \quad \ldots\ldots (2)$$

Where:

$C_s$ = concentration of standard solution (mg/ml)

$C_u$ = nominal concentration of sample solution (mg/ml)

$r_u$ = peak area of samples solution

$r_s$ = peak area of standards solution.

**Test Summary on Karl Fischer:** A portion of the material to be analyzed is added to the titration vessel after the instrument has been standardized and stabilized. The sample is titrated automatically according to the parameters set by the user. The amount of the in the sample is usually reported on a percent weight/weight basis. The following equation describes the reaction of karlfischer reagent with water contained in liquid or solid materials:

$$CH_3OH + SO_2 + RN \rightarrow [RNH]SO_3CH_3$$

$$H_2O + I_2 + [RNH]SO_3CH_3 + 2RN \rightarrow [RNH]SO_4CH_3 + 2[RNH]I$$

*(RN=Base)*

**Determination of Drift:** The drift was determined which was below 25 microgram per minute, in line with the standards. (United State Pharmacopeia, 2017)

**Standardization of Karl Fischer Titrant:** When the drift is determined 0.10 g of karl standard (sodium tartrate) was weighed in a karlfischer using weighing boat and titrated using karlfischer titrant in determining the concentration of the titrant, hydranal 1-composite 5. The procedure was repeated twice. The average, standard deviation and percentage relative standard deviation were calculated automatically. An acceptance criterion for standardization is ±3 % of RSD NOT MORE THAN. (United State Pharmacopeia, 2017)

**Sample Titration:** 0.10 g each samples of amoxicillin clavulanic acid was weighed using a karlfischer weighing boat and titrated using titrant (hydranal 1- composite 5). The procedure was repeated twice, and the average, standard deviation and percentage relative standard deviation were calculated, and the acceptance claim for amoxicillin clavulanic mg/ tablet was as follows (USP, 2017).

**Dissolution Testing:** Two dissolution station apparatus: ERWEKA DT-600 and DT-800 were calibrated in the paddle mode and set to a temperature of 37˚C± 0.5˚C time duration of 30 minutes and a frequency of 75 rotations per minute (rpm). A set volume of 900 ml of dissolution medium, distilled water was accurately measured using a 1000 ml measuring cylinder and poured into each of the six glass vessels and maintained at a temperature of 37˚C± 0.5˚C Standard thermometers were placed in each vessel to crosscheck the temperature. One tablet each of the samples was drop in each of the vessels. This was repeated for all the samples available, hence, six tablets of the same brand were placed into the buffer/dissolution medium (distilled water) all at the same time. At the end of the run time, 10 ml was sampled from each vessel into a labeled beaker with a calibrated syringe for further analysis. The drug solutions were allowed to equilibrate to room temperature and portions filtered and transferred into Agilent HPLC vials. Three injections were made per sample.

**Hardness Test:** From each brand, ten tablets were taken, each placed between the spindles of Rework tablet hardness testing machine. By tuning the knurled knot, pressure applied to hold the tablet in place and was gradually increased until the tablet broke. The test for hardness of the tablet for each brand was conducted in triplicate and records were taken at the breaking points. Acceptance value 20 Newton to 200 Newton (United State Pharmacopeia, 2017).

**Friability Test:** Ten tablets from each brand were placed in a friabilator and were carefully dedusted prior to testing. Tablet samples were accurately weighed and place the friabilator's drum. The drum was rotated 100 times after which tablets were removed, dedusted and reweighed accurately again. A maximum mean weight loss from the three samples of not more than 1.0% is considered acceptable (USP, 2017).

$$\% \text{ Friability} = \frac{\% \ intialweight - finalweight}{initalweight} \text{ X } 10 \text{.....Equation (3)}$$

**Disintegration Test:** Randomly selected six tablets of each brand were placed in the plastic tubes of a multi-unit disintegration tester at 37$^{o}$C in distilled water. The apparatus was switched, with the vertical oscillatory motion, the tablets were left in the tubes and the disintegration time was taken to be the time no more granules from the tablets were left on the mesh. This experiment was carried out in triplicate. An acceptance value for uncoated tablets is 15minutes, coated tablets and capsules are 30minutes. (United State Pharmacopeia, 2017)

## III. Results and Discussion

**Average weight of tablets**

The average weight of unexpired and expired drugs ranges from (1.0092g to 1.2049g). The range meets standard uniformity of weigh in accordance to the official monograph which stated that sample complies with USP standard if no more than two tablets are outside the percentage derivation. As presented in Table 1 and 3 except for $UNE_{5.}$ The result is in accordance with the result obtained by Taddese *et al.,* (2016), and who reported the weight of the brand tablets in the range of 1.112g to 1.361g when compared. All the brands met the compendium specification for weight uniformity. Uniformity of weight of drugs is important because of the evenly distribution of the ingredients in the drugs, unevenly distribution may alter the dose in each individual drug and therefore causes a lot of problems like unable to reach the therapeutic range and toxic.

**Active Ingredient**

The content assay for unexpired drugs produced a good result. Amoxicillin active showed highest in UNE5 with a value of 114.03 ± 2.54% and lowest in UNE2 with value 98.47 ± 0.06% and all were significantly (*P*=0.05) different from each other, all the samples were within the acceptable limit for amoxicillin while clavulanate active was also within the acceptable limit for all the tablets, UNE1 and UNE2 were not significantly different (*P*=0.05) from each other while UNE3 had the highest value at 111.43 ± 2.72% which was significantly different (*P*=0.05) as shown in Table 3. The result is not in agreement with the results obtained by Henry *et al.,* (2014), who reported that all the tablets brands analyzed had at least 60% of either amoxicillin or Clavulanic acid which is below the acceptance range of 90-120% and thus failed the content assay test.

**Karl Fisher**

The range are 7.91 % to 9.15 % of unexpired drugs, $UNE_5$ showed lowest at 7.91 ± 0.56 while UNE3 had the highest value at 9.15 ± 0.68, all the tablets were within the acceptable limit. The result is in accordance with the result obtained by Nagaraju and Kaza, 2008, who reported that all the sample water content present are in the range 5.95% - 9.09% which are within the acceptable limit of not more than 11% showed in Table 3.

**Dissolution**

Both Amoxicillin and Clavulanate were within the acceptable limits of Not Less Than (NLT) 85% and 80% respectively with the $UNE_5$ sample having the least amount for both as shown in Table 3. The result is in accordance with the result obtained by Henry *et al.,* 2014, who reported that all the brands studies passed the dissolution with the exception of a sample (DT-E) which contained an average of 3.36% of amoxicillin and 7.30% of clavuanic acid and this may be attributed to factors that may have influenced the dissolution of the active pharmaceutical ingredient from the dosage form.

**Hardness**

The range for hardness is 84.70 Newton to 166.17 Newton which shows a good results, UNE4 had the highest with a value of 166.17 ± 11.86 Newton which is significantly different(*P*= 0.05) from the others while UNE1 had the lowest with a value of 84.77 ± 46.62Newton as shown in Table 3, all the tablets were within the acceptable limit. The result is not in agreement with the result obtained by Taddese *et al.,* 2016, who reported the crushing strength/ hardness of the tablets in the range of 230.60 Newton to 337.83Newton which surpassed the compendium specification of not more than 200 Newton and thus failed the hardness test.

**Friability**

The friability of all the brands ranges between 0.02% and 0.87%. The result of friability shows that all the tablets were strong enough to withstand abrasion as none of them has a friability value of more than the

specified. The accepted compendium specification for friability test is 1.0%. The result is in accordance with the result obtained by Odulaja *et al.,* 2012, who reported that the friability result shows that all the tablets were strong enough to withstand abrasion as none of them has a friability value of more than the specified. The friability of all the brands ranges between 0.27% and 0.60% which did not surpass the compendium specification of 1% and thus passed the friability test.

**Disintegration**

The range are 8.96 to13.90 minutes the disintegration test results show that $UNE_5$ had the lowest disintegration value at 8.96 ± 0.46 minutes which was statistically similar with UNE3 whereas UNE4 showed the highest disintegration time at 13.90 ± 0.71mins as shown in Table 3, all the tablets were within the acceptable limit. The result is in agreement with the result obtained by Henry *et al.*, (2014) who report that all the tablets analyzed passed the disintegration test of not more than 15 minutes for uncoated tablets with the highest disintegration time of 15 minutes and the lowest disintegration time of 6 minutes.

**Table: 1 Average Weight of Unexpired Drugs**

| Code Unexpired Drugs | Batch Numbers | Average Weights (g) | Percentage Derivation (%) | Upper Limit | Lower Limit |
|---|---|---|---|---|---|
| $UNE_1$ | 180902 | 1.0427 | 0.05214 | 1.09484 | 0.999056 |
| $UNE_2$ | 1801004-1 | 1.0325 | 0.05163 | 1.08413 | 0.98088 |
| $UNE_3$ | SEBPT 0080 | 1.0209 | 0.05105 | 1.07195 | 0.96986 |
| $UNE_4$ | NMBBV0062 | 1.0925 | 0.05463 | 1.14713 | 1.03788 |
| $UNE_5$ | B2418 | 1.2049 | 0.06025 | 1.26515 | 1.14466 |

**Table: 2: Average weights of expired drugs**

| Codes Expired Drugs | Batch Numbers | Average Weights (g) | Percentage Derivation (%) | Upper Limit | Lower Limit |
|---|---|---|---|---|---|
| $EXP_1$ | ET1600415 | 1.0305 | 0.05153 | 1.08205 | 0.97899 |
| $EXP_2$ | SEBPT 0010 | 1.0092 | 0.05046 | 1.05966 | 0.95869 |
| $EXP_3$ | BE404 | 1.1667 | 0.05834 | 1.22506 | 1.10838 |
| $EXP_4$ | 664313 | 1.0713 | 0.05357 | 1.12489 | 1.01776 |
| $EXP_5$ | 668897 | 1.0612 | 0.05306 | 1.11426 | 1.00814 |

**Table 3: Physico-chemical Analysis of the Unexpired Drugs**

| Code | Amoxicillin (%) | Clavulanate (%) | Karl fisher (%) | Dissolution (Amoxicillin) (%) | Dissolution (Clavulanate) (%) | Hardness (n) | Friability (%) | Disintegration (Mins) |
|---|---|---|---|---|---|---|---|---|
| UNE1 | 110.27±0.35$^{c}$ | 99.47±3.58$^{a}$ | 8.99±0.24$^{b}$ | 120.34±0.12$^{c}$ | 85.70 ± 1.32$^{c}$ | 84.77± 46.62$^{a}$ | 0.87% | 13.00 ± 0.50$^{bc}$ |
| UNE2 | 98.47±0.06$^{a}$ | 99.40±0.00$^{a}$ | 8.79±0.37$^{ab}$ | 115.60±1.34$^{b}$ | 85.03 ±0.19$^{bc}$ | 155.63±31.18$^{ab}$ | 0.56% | 12.75 ± 0.44$^{b}$ |
| UNE3 | 102.80±0.87$^{b}$ | 111.43±2.72$^{c}$ | 9.15±0.68$^{b}$ | 115.76±1.34$^{b}$ | 84.21 ±0.21$^{bc}$ | 120.83±41.82$^{ab}$ | 0.45% | 9.03 ± 0.32$^{a}$ |
| UNE4 | 104.47±0.06$^{b}$ | 104.70±2.04$^{b}$ | 8.69±0.75$^{ab}$ | 114.96±0.36$^{b}$ | 83.55 ± 1.16$^{b}$ | 166.17±11.86$^{c}$ | 0.55% | 13.90 ± 0.71$^{c}$ |
| UNE5 | 114.03±2.54$^{d}$ | 107.50±0.36$^{b}$ | 7.91±0.56$^{a}$ | 111.36±1.12$^{a}$ | 82.04 ± 0.05$^{a}$ | 136.87±57.17$^{ab}$ | 0.78% | 8.96 ± 0.46$^{a}$ |
| | **90-120 %** | | **11 %** | **NTL 85-80 %** | | **200 N** | **1%** | **15%** |

Values are mean ± standard deviation of triplicate analysis.

Values with different superscripts down the column are significant (P<0.05) different.

UNE= Unexpired Drugs

USP= United StatesPharmacopeia

For Expired Drugs, $EXP_1$ had the lowest amoxicillin content at value of 103.03 ± 0.23% while $EXP_3$ showed the highest value at 119.37 ± 0.41% and was significantly (*P*=0.05) different from the others as shown in Table 4, all the tablets fall within the acceptable limit. Clavulanate was found to be highest in $EXP_2$ with value of 117.33 ± 0.55% whereas $EXP_3$ showed the lowest value; $EXP_3$ and $EXP_5$ were not within the acceptable limit and failed analysis based on clavulanate content as shown in Table 4. $EXP_3$ and $EXP_5$ had Karl

Fisher values which were above the acceptable limit. Dissolution for Amoxicillin were within the acceptable limit of NLT 85% with $EXP_1$ sample having the lowest amount whereas Dissolution for Clavulanate were not within the acceptable limits of NLT 80% with the $EXP_2$ sample having the least amount as shown in Table 4.$EXP_3$ had the least hardness with a value of 111.80 ± 4.95N while $EXP_2$ had the highest at 228.67 ± 15.93N; $EXP_2$ was above the acceptable limit for hardness while the rest fall within the limit as shown in Table 4. All the tablets had disintegration time within the acceptable limits where $EXP_5$ had the highest value at 11.87 ± 1.11mins while $EXP_1$ showed the lowest value but was significantly (*P*= 0.05) different from $EXP_3$, $EXP_4$ and $EXP_5$ except $EXP_2$ as shown in Table 4. It could be observed from the literature that expired drugs have not been worked upon which served as a novelty in this experiment and intended to established the fact that some drug marketers with respect to identity indulge in re-labeling of fake/expired drugs to represent new/unexpired in their packaging. PhRMA considers a "genuine product that has expired and then has been fraudulently relabelled" to be counterfeit (Rago, 2002).

**Table 4: Physio-chemical Analysis of the Expired Drugs**

| CODE | Amoxicillin (%) | Clavulanate (%) | Karl Fisher | Dissolution (Amoxicillin) (%) | Dissolution (Clavulanate) (%) | Hardness (N) | Friability (%) | Disintegration (Mins) |
|---|---|---|---|---|---|---|---|---|
| EXP1 | 103.03±0.23$^{a}$ | 104.20±0.00$^{c}$ | 9.39±0.27$^{a}$ | 99.49 ± 1.17$^{a}$ | 58.60 ± 0.16$^{d}$ | 189.80±13.78$^{bc}$ | 0.02% | 8.45 ± 0.13$^{a}$ |
| EXP2 | 106.67±2.48$^{b}$ | 117.33±0.55$^{e}$ | 9.78±0.44$^{a}$ | 103.61 ±0.37$^{b}$ | 34.29 ± 0.18$^{a}$ | 228.67±15.93$^{c}$ | 0.03% | 6.94 ± 1.17$^{a}$ |
| EXP3 | 119.37±0.41$^{d}$ | 58.80 ± 0.00$^{a}$ | 11.08±0.40$^{b}$ | 105.30±0.29$^{cd}$ | 58.02 ± 0.19$^{d}$ | 111.80 ±4.95$^{a}$ | 0.23% | 10.95 ± 1.14$^{b}$ |
| EXP4 | 113.70±0.20$^{c}$ | 106.20±0.17$^{d}$ | 10.97±1.13$^{b}$ | 106.62 ±1.38$^{d}$ | 52.40 ± 1.43$^{c}$ | 156.77±55.21$^{ab}$ | 0.12% | 11.47 ± 0.19$^{b}$ |
| EXP5 | 108.80±1.60$^{b}$ | 85.73 ± 0.56$^{b}$ | 11.46±0.56$^{b}$ | 103.89±0.11$^{bc}$ | 50.04 ± 0.02$^{b}$ | 112.73 ±6.15$^{a}$ | 0.02% | 11.87 ± 1.11$^{b}$ |
| | **90-120 %** | **11%** | **NTL 85-80 %** | | **200N** | **1 %** | **15** | |

Values are mean ± standard deviation of triplicate analysis.
Values with different superscripts down the column are significant (P<0.05) different.
EXP= Expired Drugs
USP=United States Pharmacopoeia

**Relationship between the Unexpired and Expired Drugs**

The independent sample t-test is an inferential statistical test that determines whether there is a statistically significant difference between the means in two unrelated groups. From Table 5, Amoxicillin, Clavulanate, Disintegration and Hardness had significance of 0.055, 0.094, 0.055 and 0.139 respectively which were greater than p-value of 0.05, thus; there is no statistically significant (p<0.05) difference of these parameters between the unexpired and expired drugs. Whereas, Karl fisher had a t-test value of 0.000 which is less than p-value of 0.005, hence, the unexpired drugs were significantly (p<0.05) different.

**Table 5: Independent Sample T Test**

| | Unexpired drugs | Expired drugs | t-Test sig. (2 tailed) |
|---|---|---|---|
| Amoxicillin (%) | 106.01 | 110.31 | 0.055 |
| Clavulanate (%) | 104.50 | 94.45 | 0.094 |
| Karl Fisher | 8.71 | 10.54 | 0.000 |
| Disintegration (mins) | 11.52 | 9.94 | 0.055 |
| Hardness(N) | 132.85 | 159.95 | 0.139 |

**Correlation Matrices for the Unexpired and Expired Drugs**

For the unexpired drugs, clavulanate and disintegration had a negative correlation at $p<0.01$ which implies that as one increases the other decreases. Whereas, the others had no correlation at both $p<0.01$ and $p<0.05$ as shown in Table 6. For the expired drugs, all the parameters were correlated at both levels of $p<0.01$ and $p<0.05$. Amoxicillin had a positive correlation with Karl Fisher and Disintegration. Clavunalate also had a positive correlation with hardness. Whereas, Amoxicillin had a negative correlation with Clavunalate and Hardness. Also, Clavunalate had a negative correlation with Amoxicillin, Karl Fisher and Disintegration as shown in Table 7.

**Table 6: Correlation Matrix for Unexpired drugs**

| | Amoxicillin (%) | Clavulanate (%) | Karl Fisher | Disintegration (Mins) | Hardness (N) |
|---|---|---|---|---|---|
| Amoxicillin (%) | 1 | 0.152 | -0.337 | -0.313 | -0.209 |
| Clavulanate (%) | 0.152 | 1 | -0.003 | -0.764** | 0.217 |
| Karl Fisher | -0.337 | -0.003 | 1 | 0.185 | 0.030 |
| Disintegration (mins) | -0.313 | -0.764** | 0.185 | 1 | 0.102 |
| Hardness(N) | -0.204 | 0.217 | 0.030 | 0.102 | 1 |

** Correlation is significant at the 0.01 level (2 tailed)

*Correlation is significant at the 0.05 level (2 tailed)

**Table 7: Correlation Matrix for expired drugs**

| | Amoxicillin (%) | Clavulanate (%) | Karl Fisher | Disintegration (mins) | Hardness (N) |
|---|---|---|---|---|---|
| Amoxicillin (%) | 1 | -0.712** | 0.607* | 0.599* | -0.560* |
| Clavulanate (%) | -0.712** | 1 | -0.519* | -0.561* | 0.771** |
| Karl Fisher | 0.607* | -0.519* | 1 | 0.780** | -0.772** |
| Disintegration (mins) | 0.599* | -0.561* | 0.780** | 1 | -0.748** |
| Hardness(N) | -0.560* | 0.771** | -0.772** | -0.748** | 1 |

** Correlation is significant at the 0.01 level (2 tailed)

*Correlation is significant at the 0.05 level (2 tailed)

## IV. Conclusion

The findings showed that all the unexpired drug samples analyzed were within limits set forth by USP and were therefore considered to be of good qualities and safe for treatments. Although, some of the expired drugs were within the specified limits, which was due to the nature of the active ingredients used for the formulation and improved quality of the packaging materials utilized. While most of the expired drug failed the Karl Fischer test, as a result of level of moisture absorption and temperature conditions at the storage sites. It is therefore necessary to ensure regular quality control and routine checks of drugs from the time of manufacture till they get to the consumers.

## References


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A.O. Aliyu, et. al. "Quality Assessment of Some Selected Brands of Amoxicillin Clavulanate from Pharmaceutical Stores in Kaduna Metropolis, Nigeria)." *IOSR Journal of Pharmacy and Biological Sciences (IOSR-JPBS)*, 16(2), (2021): pp. 33-40.