

# QUALITY AND AVAILABILITY OF AMPICILLIN PRODUCTS (CAPSULES AND SUSPENSIONS) IN NIGERIA.

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## ABSTRACT

The WHO, through the "essential drug concept" advocates for availability of high quality drugs (including ampicillin products) to citizens of a nation at affordable cost.

The availability of good quality ampicillin (capsule & Suspension) at low and affordable cost was studied. Market survey / purchase of ampicillin products were carried out in Jos & environs. Quality of the products were determined by following the BP 1993 specification. Analysis of data was by ANOVA.

Cost has no significant ( $P > 0.05$ ) effect on the availability of Ampicillin capsule but has on ampicillin suspension. The place of manufacture has no significant effect on the percent drug content or uniformity of weight (quality) of ampicillin capsules.

## INTRODUCTION

The scourge of fake, substandard and adulterated drugs is a very serious problem in any society. This problem has developed from mild to sophisticated forms in Nigeria. Consequently decree No. 17 of 1982, of the Federal Republic of Nigeria was promulgated. The decree defined fake and adulterated drugs as "Any drug to drug product which is not what it purports to be (1). This

definition extends to any form of damage, concealment, false label statements, misleading labels, and inadequate label directions. This definition can be summed up to mean any drug or drug product which by physical, chemical, pharmacological, therapeutic, commercial, ethical and other qualities, is not what purports to be. The World Health Organisation (WHO) at the international conference on Primary Health Care, Alma, Ata, 1973 identified the supply of good quality essential drugs as one of the basic pre-requisites for the delivery of health care, and thus promulgated the WHO "Certification Scheme on the Quality of pharmaceutical products Moving in International commerce" (2). The essential drug concept emphasises availability of these good quality drugs to patients at reasonable cost (3). However, inadequate storage and distribution of pharmaceutical products is most prevalent in developing and tropical countries. This can lead to their physical deterioration and chemical decomposition. Antibiotics are one of the widely used, misused, abused and counterfeited class of drugs in Nigeria. This might contribute to the problem of increasing resistance among previously sensitive bacterial species to

common anti-microbial agents in Nigeria, (though it is a worldwide phenomenon) (4). Ampicillin is bactericidal and has similar mode of action with other penicillins. It is a broad spectrum antibiotic with activity against gram positive organisms like *Streptococcus faecalis*, *Streptococcus progens*, *S. pneumoniae*, *Clostridium diptheriae*, *Bacillus anthracis* gram-negative organisms like, *Haemophilus influenzae*, *Salmonella*, *Escherichia coli*, *Neisseria gonorrhoea*, *N. meningitis* (5).

The objective of this study is to assess the availability and quality of ampicillin capsules and suspensions in circulation in Jos area, Nigeria and analyse the relationships of those qualities with cost and place of origin, as appeared on the label.

## MATERIALS AND METHOD

**Materials:** Reagents were prepared using chemicals and solvents of GPR grade obtained from the department of Pharmaceutical chemistry. The following reagents were used for the analyses - viz: Boric Buffer pH 9.0; Acetic Anhydride Diozan Solution BP Imidazole - Mercury reagent; Mercury (II) Chloride Solution - 0.27% w/v in water (6). Main equipment used was UV - spectrophotometer (Hitachi 20 - 200, Japan).

**SELECTION OF SAMPLES**

The ampicillin samples used for this research were obtained by on-the-spot sampling procedure as any other purchaser. The sampling was randomly done across shops, hospitals and pharmacies. A total of thirty five (35) different manufacturer's products were sighted during the market survey resulting in twenty-two (22) brands of capsule and twenty-four (24) brands of the Suspension. Out of these numbers only 14 brands of capsules and 17 brands of suspension were available in the quantity required at the time of purchase. The number of samples of ampicillin capsule was a minimum of twenty capsules for each brand at every sampling point, (three products

were consequently not sampled), while a minimum of one 60ml or 100ml bottles for the suspension for each brand was used.

**SAMPLE STORAGE**

All the capsules were stored as they were obtained and in the conditions specified by the manufacturers prior to assay. Survey and sampling period was between May 1999 and December 1999, and all the samples were assayed before their expiry dates. The Nigerian currency, Naira exchange in the official rate for =N=100.00 to \$1 (one US dollar).

**METHOD OF ASSAY**

**Ampicillin Capsules and oral Suspension:** The method and procedure used for the assay of active ingredient

was as stated in the British Pharmacopoeia Volume II of 1993 (6). (The capsules should comply with the requirements stated under capsules with content of ampicillin  $C_{16}H_{19}N_3O_5S$ , 92.5 to 107.5% of the prescribed or stated amount).

**PROCEDURES FOR DETERMINATION OF UNIFORMITY OF WEIGHT (7)**

The uniformity of weight procedure of the USPXXIII was followed. Not more than two of the individual weights (masses) should deviate from the average weight (mass) by more than the percentage deviation shown in Table 1 below and non should deviate by more than twice that percentage.

**Table 1**

Pharmaceutical form	Average weight (mass)	Percentage deviation
Capsules, Granules (uncoated, single dose) and powders	less than 300mg	10
Single dose	300mg or more	7.5

**RESULTS**

The result of different parameters used in assessing the ampicillin capsules and suspensions were tabulated below.

**Table 2: Table showing the quality assessments, availability and cost of Ampicillin capsules.**

CODE	Uniformity of weight Test	Percent drug Content	Actual Weight (mg)/capsule of Ampicillin	Remarks on % drug content	% Availability	Cost per 250mg capsule
Ci	Pass	97.2%	243.00	Pass	23.3%	6.00
Cii	Pass	94.4%	236.00	Pass	18.3%	5.00
Ciii	Fail	100.0%	250.00	Pass	1.7%	5.00
Civ	Pass	81.80%	204.50	Fail 10.7%<LL	1.7%	3.00

Cv	Pass	72.73%	181.83	Fail	1.7%	20.00
				19.8%<LL		
Cvi	Pass	154.50%	386.25	Fail 47%>	1.7%	4.00
				HL		
Cvii	Pass	109.1%	272.75	Fail	1.7%	8.00
				1.6%<HL		
Cviii	Pass	90.90%	227.75	Fail	1.7%	4.00
				1.6%<LL		
Cix	Pass	90.90%	227.25	Fail	1.7%	2.00
				1.6%<LL		
Cx	Pass	109.1%	272.75	Fail	1.7%	5.00
				1.6%>HL		
Cxi	Fail	96.60%	241.50	Pass	1.7%	5.00
Cxii	Pass	106.90%	267.25	Pass	23.3%	6.00
Cxiii	Pass	113.8%	284.50	Fail	1.7%	5.00
				6.3%>HL		
Cxiv	Pass	100.0%	250.00	Pass	1.7%	5.00

**Summary**

CAPSULES	% Passed	% Fail	Total
Uniformity of Weight test	85.7% (12)	14.3% (2)	100% (14)
Assay of Active content	42.9% (6)	57.1% (8)	100% (14)

Key: Uniformity of weight; Assay Limit; Average weight <600mg = 10% deviation  
Average weight > 300mg = 7.5% deviation

% Ampicillin content: BP1 999 specification, Assay Limit 92.5 - 107.5

LL = lower limit, HL = Upper limit.

Cost	Rating
≥ - N6 per 250mg Capsule	High
≤ - N5 per 250mg Capsule	Low

Chi-square test for Cost / Quality of Products Relationship  
Capsules - P>0.05 - Not significant

**Table 3: Table showing the quality assessment (percent drug content and the actual weight per 5ml), availability and cost of ampicillin suspension samples.**

CODE	Percent content of ampicillin *	Actual weight (mg) of per 5ml	Remarks	% Availability	Cost (=N=) per 60ml bottle *
Si	105.6%	132.00	Passed	13.3%	70.00
Sii	94.4%	118.00	Passed	5.0%	70.00
Siii	94.4%	118.00	Passed	10.0%	50.00
Siv	122.2%	152.75	Failed (2.2%>HL)	1.7%	80.00
Sv	116.7%	145.88	Passed	3.3%	65.00

Svi	103.4%	129.25	Passed	1.7%	70.00
Svii	105.6%	132.00	Passed	1.7%	45.00
Sviii	127.8%	159.75	Failed (7.8%>HL)	30%	60.00
Six	111.1%	138.88	Passed	5.0%	35.00
Sx	111.1%	138.88	Passed	1.7%	42.00
Sxi	83.3%	104.13	Passed	1.7%	50.00
Sxii	38.9%	48.63	Failed (41.1%<LL)	1.7%	80.00
Sxiii	94.4%	118.00	Passed	1.7%	50.00
Sxiv	89.7%	112.13	Passed	23.3%	60.00
Sxvi	100.0%	125.00	Passed	5.0%	40.00
Sxvi	86.2%	107.75	Passed	1.7%	65.00
Sxvii	77.8%	97.25	Failed (2.2%<LL)	1.7%	60.00

**Summary**

SUSPENSIONS	% Passed	Failed	Total
Assay of Active content	76.5% (13)	23.5% (4)	100% (17)

Chi-square test for Cost - Quality of products relationship

\* - P<0.05 ..... Significant

\* - P>0.01 ..... Not Significant

**Table 4: Cross Analysis of Test on Capsules**

(a)

CAPSULES	Percentage
Percentage that passed both uniformity of weight test and Assay of active content	28.6%(4)*
Percentage that failed both uniformity of weight test and Assay of active content	0.0% (0)
Percentage that failed uniformity of weight test but pass Assay of active content	14.3% (2)*
Percentage that passed uniformity of weight test but failed Assay of active content	57.1% (8)*
Total	100% (14)

Numbers in bracket used for chi-square analysis.

Chi-square test for weight uniformity / Assay of Active ingredients - Pass / Fail

\*Result Analysis P>0-0.5 - Not significant

**CROSS ANALYSIS: RESULTS OF TEST / ORIGIN OF PRODUCT**

(b)

Product source	Capsules	Uniformity of Weight		Active content		Total	
		% Pass	% Fail	% Pass	% Fail		
Imported	78.6% (11)	90.9%* (10)	9.1%* (1)	100% (11)	45.5%# (5)	54.5%# (6)	100% (11)
Local	21.4%	66%*	33.3%*	100%	33.3%#	66.7%#	100%

(indigenous)	(3)	(2)	(1)	(3)	(1)	(2)	(3)
Total	100%			100%			100%
	(14)			(14)			(14)

Numbers in brackets are used for chi-square test.

Chi-square test for imported / indigenous - Pass / Fail Result Analysis

Uniformity of weight: \* -  $P > 0.05$  - Not significant

Assay of Drug content: # -  $P > 0.05$  - Not significant

(c)

Active content in suspension

Product Source	Suspension	% Pass	% Fail	Total
Imported*	47.1% (8)	62.5% (5)	37.5% (3)	100% (11)
Local*	52.9% (9)	88.9% (8)	11.1% (1)	100% (3)
(indigenous)				
Total	100% (17)			100% (14)

\*  $P > 0.01$  ..... Not significant

#### DISCUSSION AND CONCLUSION

Analysis of variance was used to test for relationships or correlation between availability and cost of ampicillin, cost and quality of ampicillin, quality and country of origin of drug, and quality of ampicillin samples. Chi-square test was used for analysis of data. The a priori level of significance was set at  $P=0.01$ , and  $P=0.05$ , (7).

The null hypotheses were that:

1. Quality of ampicillin capsule or suspension is independent of the country of origin.
2. Chemical quality of ampicillin capsule or suspension is independent of the availability and / or cost of the drug.

#### AMPICILLIN CAPSULES

Availability / Cost:

Out of the fourteen (14) brands of Ampicillin capsules assayed, 78.6% (11 brands) were imported and 21.4% (3)

were manufactured in Nigeria. The result of the market survey shows that, all the premises visited had ampicillin capsules by various manufacturers. About 22 (twenty-two) different brands were available each with at least 1.7% availability, that appeared in at least one retail outlet or premise. The samples C<sub>i</sub> (23.3%) C<sub>xii</sub> (23.3%) C<sub>xii</sub> (23.3%), C<sub>ii</sub> (18.3%) and C<sub>viii</sub> (8.3%) had highest availability in the market and they were all imported products. Samples C<sub>iii</sub> C<sub>iv</sub>, C<sub>v</sub>, C<sub>vi</sub>, C<sub>vii</sub>, C<sub>ix</sub>, C<sub>x</sub>, C<sub>xi</sub>, C<sub>xiii</sub>, and C<sub>xiv</sub> had the least availability of 1.7%, that is, they appeared in only one premise or only once in premises that stocked more than one product. The retail prize per capsule ranged between two and five Naira (=N=2.00 to =N=5.00) except for samples C<sub>v</sub> (N20.00/Capsule) and C<sub>vii</sub> (=N=8.00/Capsule). Ampicillin capsule could be said to be available at a reasonable

cost to the patient, in the Nigerian drug market. Cost however, had no significant ( $p > 0.05$ ) effect on the quality of available ampicillin capsule. Hypothesis is rejected. Thus the availability of ampicillin capsule to Nigerians was independent on cost.

#### WEIGHT UNIFORMITY / PERCENT DRUG CONTENT

Twelve (12) that is, 85.7% of the samples passed the weight uniformity test with 90.9% (10) of those being imported products and 9.1% (2) being indigenous products. Only two (14.3%) failed the weight uniformity test. This result shows that only one of the imported and one of the indigenous failed the weight uniformity test. The weight of the capsules was found to have no significant ( $P > 0.05$ ) effect on the drug content of the ampicillin capsule.

**DRUG CONTENT**

The drug content assay results ranges from the least of 72.73% (sample Cv) and highest of 154% (sample Cvi Table 2). Six (i.e. 42.9%) of the capsules passed the drug content assay while 57.1% (eight) failed. Out of the eight that failed, six representing 54.4% are imported products and two are indigenous products. However, chi-square test at both 95% and 99% confidence levels shows that there is no significant differences in the rate of failure and / or passes among the imported and indigenous products. Therefore, there is no relationship between the quality of the capsule and its place of origin. Hypothesis rejected. Thus the purported place of the manufacturer - whether imported or local has no effect on the quality of ampicillin capsule in Nigeria.

Out of the eight that failed the drug content assay, four may be therapeutically effective but possible increase in side effect since they contain more ampicillin than specified, while the other four may be classified as substandard (sub-close), therefore possible therapeutic failure.

Chi-square test at both 95% ( $p=0.05$ ) and 99% ( $p=0.01$ ) confidence level shows that the cost / quality in the pass / fail relationship is not significant, which means that failure or pass rate is not related to cost, since low cost and high cost products pass or fail the drug content assay in the same proportions (Table 2 and Table

4a).

From these results and the survey conducted, it can therefore be concluded that Ampicillin capsules are available at affordable price to the patient but the quality may not be guaranteed since 57.1% did not meet the percent drug content specification of the BP 1993.

**SUSPENSIONS****Availability / Cost**

The result of the survey shows that twenty-four (24) different brands of Ampicillin suspension are available in retail outlets in Jos and environs each with at least 1.7% availability. The samples Si (13.3%), Siii (10.0%), Sviii (30.0%), Six (5.0), Sxiv (23.3%) and Sxv (5.0%) have the highest availability (Table 3) while the samples, Siv, Svii, Sx, Sxi, Sxii, Sxiii, Sxvi and Sxvii, have the least availability of 1.7%.

The prize of a 60ml bottle lies between =N=40.00 and =N=70.00 on the average of =N=55.00 (Table 3). With the present economic realities it can be said that the suspensions are quite affordable and available to the average Nigerian in the urban areas.

**DRUG CONTENT**

Out of the seventeen (17) brands of ampicillin suspensions assayed, 47.1% (eight) are imported and 52.9 (9) are indigenous. There is an overall high pass level of 76.5 (13) while 23.5 (4) failed, 62.5% (5) of the imported products passed the assay and 30.5% (3) failed while 88.9% (8) of indigenous

products passed and 11.1% (1) failed the assay (Table 3). Chi-squared test at both 95% ( $p=.05$ ) and 99% ( $p=0.01$ ) confidence levels showed that there was no significant difference in the rate of failure and/or passes among the imported and indigenous products. However, the overall high level of pass (76.5%) level among the suspensions indicated that manufacturers pay greater attention to good manufacturing practices (GMP) when handling paediatric preparations. The drug content assay results range from 38.5% (sample Sxii) being the least and 127.8% (sample Sviii) being the highest (Table 3). Out of the four products that failed the drug content assay, samples Sxii and Sxvii (with 41.1% and 2.2% less than the lowest level specified by the BP1993) might result in therapeutic failure.

Chi-squared test at 95% ( $p>0.05$ ) confidence level showed that the cost/quality with respect to pass or fail relationship is significant. Thus there was a relationship between the prize of the products and the quality. The low prize products had less failure rates than the highly prized products (with four failures). This high prize products are also of fair availability (Sxvii - 1.7%, Sxii - 1.7%, Sviii - 30% and Siv - 1.7%) and they were imported products. The availability could be attributed to the attitude of Nigerians towards imported products no matter the cost, making them more popular and expensive. Hence they are more

liable to be faked, adulterated and counterfeited. concluded that ampicillin probability of being of good and counterfeited. suspension were available, quality.

From the results we affordable and with a high

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