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Full Length Research Paper

Assessment of the efficacies, potencies and bacteriological qualities of some of the antibiotics sold in Calabar, Nigeria

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In this study, an assessment of the efficacies, potencies and qualities of 11 brands of 5 different antibiotics including 3 brands of ampiclox and 2 brands each of ciprofolxacin, gentamicin, rifampicin and tetracylcine sold in Calabar, South-South region of Nigeria was carried out using the agar diffusion technique (sensitivity testing). The efficacies, potencies and qualities of these antibiotics were tested against some clinical isolates which include *Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, Staphylococcus aureus* and *Streptococcus pyogenes in vitro*. The overall mean zones of inhibition for the test organisms ranged from 33.0 – 34.7 mm, with 33 mm for *E. coli*, 20.9 mm for *K. pneumoniae*, 34.7 mm for *P. aeruginosa*, 31.4 mm for *S. aureus* and 17.6 mm for S. *pyogenes.* The result showed that 3 (60%) of the antibiotics (alaclox, ciprofloxacin and rifampicin) tested showed lower potency against the test organisms compared with the standard controls. Alaclox produced significantly ($P < 0.05$) lower zones of inhibition compared to the other brands of ampiclox (superclox and vitaclox) on *S. aureus* and *S. pyogenes*. However, significant differences ($P = 0.007$, $P = 0.026$, $P = 0.050$, $P = 0.012$) were observed between the zones of inhibition of the test antibiotics and standard controls for the 3 brands of ampiclox tested on all the test organisms except for *K. pneumoniae.* There were also significant differences ($P = 0.038$, $P = 0.038$, $P = 0.049$, $P = 0.025$, $P = 0.032$) between the zones of inhibition observed for ciprofloxacin and their standard controls. Both brands of rifampicin (vitals and medifampi) produced significantly ($P = 0.020$, $P = 0.038$) lower zones of inhibition on *E. coli* and *S. pyogenes* compared to their standard controls. Our result also showed there were no significant differences ($P > 0.05$) between the observed zones of inhibition and standard controls of the brands of gentamicin (richem) and tetracycline. These overall and mean potencies of the test antibiotics showed differences in their efficacies, potencies and qualities. This confirmed that some brands of ampiclox, ciprofloxacin and rifampicin antibiotics sold in Nigeria do not contain the acclaimed quantity of active ingredients to exert bacteriocidal or bacteriostatic effect on common pathogens.

Key words: Antibiotics, assessment, bacteriological quality, efficacy, potency, zones of inhibition.

INTRODUCTION

The present day use of the term antibiotics was proposed by Naksman in 1945 as those chemical substances of microbial origin which in small amounts exert anti-microbial activity (Okonko et al., 2008). Antibiotics are usually of microbial origin but some have come from higher forms of life and chemotherapeutic agents made synthetically. Their selective toxicity means a low toxicity for host cells and high toxicity for parasites (Melmon and Morcelli, 1989). For an antibiotic to be effective, it exhibits selective toxicity and has a high therapeutic index. High therapeutic index implies a high ratio of maximum dose at which the antibiotics can be tolerated to a minimum dose required to cure infections. Such antibiotics do not eliminate the normal microbial flora of the host to avoid an upset of the balance of nature and prevent the readily development of resistant forms of these pathogens (Okonko et al., 2008).

In the last few decades, antibiotics have been increasingly exploited by workers in a number of disciplines. For example, their usefulness in agriculture as plant protecting agents or for the promotion of animal growth and metabolic activities; in food industries as preservatives and in basic biochemical research as specific inhibitors of metabolic pathways (processes) cannot be over emphasized (Florey, 1998). The major groups of antibiotics consist of families of chemically related substances with varying properties, some of which result from the natural manipulations of producing microbes and others from chemical alterations of the products of biosynthesis. The indiscriminate usage of these antibiotics influences its efficacy, resulting in resistance. It also leads to the growth of abnormal gut flora which inhibits proper digestion and assimilation of food. This undigested food putrefies and produces toxins that leads to the growth of yeast, fungal, bacterial and parasitic infections that damage the gut tissues. Amongst the more important beneficial bacterial destroyed by this indiscriminate usage include *lactobacillus, Acidophilus* and *Bifidobacterium bitidus.* It also affect many nutrients particularly the ones needed by the immune system to fight infection such as vitamins A and C. The sources in which antibiotics can be obtained include; microorganisms, synthesis and semi-synthesis. Thus, antibiotics can be obtained from the culture extracts and filtrates of fungi (example, penicillins and cephalosporins), bacteria-like *Streptomyces* spp., *Bacillus* spp., etc (example, rifampicin, aminoglycosides, chloramphenicol, erythromycin, tetracyclines).

As the predominance of either the gram-positive or gram-negative bacteria isolates is influenced by geographical location and changes in time; so also is their antibiotic susceptibility pattern influenced by location and time (Nwadioha et al., 2010). Most bacteria exhibit remarkable versatility in their behaviour towards antibiotics and its capacity to produce human diseases had not diminished even with the introduction of antibiotics (Obiazi et al., 2007). A number of literatures indicated a gradual increase in the emergence of antibiotic-resistant microorganisms in hospitals (Suchitra and Lakshmidevi, 2009). The changing patterns in the etiological agents of clinical pathogens and their sensitivities to commonly prescribed antibiotics are reported (Abubakar, 2009). High susceptibility of most pathogens to ampiclox and ciprofloxacin is an indication of effectiveness of the antibiotic against the bacteria (Doughari et al., 2007; Okonko et al., 2009a,b; Nkang et al., 2009a,b).

Multi-drug resistance to gentamicin, rifampicin and tetracycline in equal magnitude *in vitro* has been reported and, as such, these antimicrobials may not be suitable for treating case of nosocomial or community acquired infection in this locality (Okonko et al., 2009a,b; Nkang et al., 2009b). Ciprofloxacin and gentamicin-resistant *Pseudomonas* spp., *Klebsiella* spp. and *Escherichia coli* was reported in a study by Jamshidi et al. (2009) in a study on the antimicrobial resistance pattern among intensive care unit patients. A previous study combining the data from 25 UK hospitals has shown that this microorganism is resistant to ofloxacin and ciprofloxacin in 59 and 62% of the cases, respectively (Jamshidi et al., 2009). In their study, a change in the routine interventions used for empirical therapy of *Staphylococcus aureus* yielded a decline in resistance of this species against ciprofloxacin from 91.3 to 78.6%, suggesting that a modification of routine antimicrobial treatments can effectively alter the pattern of resistance of this pathogen to these drugs (Jamshidi et al., 2009). Resistance of intensive care unit (ICU)-acquired pathogens against ciprofloxacin can be attributed to its high usage in inpatient and outpatient settings (Jamshidi et al., 2009). *E. coli* sensitivity to ciprofloxacin and gentamycin was also reported by Nwadioha et al. (2010). *S. aureus* resistant to cloxacillin, penicillin, ampicillin and tetracycline was reported by Obiazi et al. (2007) in Benin City, Nigeria. Although, outbreaks of *S. aureus* resistant to beta-lactam antibiotics have been frequently associated with devastating nosocomial infections (Depardieu et al., 2007; Buhlmann et al., 2008), marked resistance to ampiclox which is a beta-lactam antibiotic by *S. auerus* has not been reported in recent studies (Obiazi et al., 2007; Nkang et al., 2009a). However, gentamycin, erthro-

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Abbreviations: ICU, Intensive care unit; **HAIs,** healthcare associated infections; **ESBL,** extended beta-lactamase; **NA,** nutrient agar, **MCA,** MacConkey agar; **MSA,** mannitol salt agar; **MICs,** minimal inhibitory concentrations; **GNB,** Gram-negative bacilli; **MDR,** multidrug resistant; **UTIs,** urinary tract infections; **GMP,** good manufacturing practices.

mycin and tetracycline among others with relatively higher susceptibility can be used for management of clinical conditions in our locality (Obiazi et al., 2007; Nkang et al., 2009a). Doughari et al. (2007) reported resistance rates of Salmonella isolates (92.3, 88.8, 79.6, 53.5 and 20%) to amoxicillin, ampicillin, chloramphenicol, cotrimoxazole and ciprofloxacin, respectively. The implication of this high percentage resistance recorded for the antibiotics is that only amoxicillin and ciprofloxacin will effectively treat *Salmonella typhi* infections (Doughari et al., 2007; Nkang et al., 2009a). Filioussis et al. (2008) in their study reported *Salmonella* isolates that were resistant to several antimicrobials (tetracycline, trimethoprim/sulfamethoxazole, ampicillin and amoxicillin/clavulanic acid), they found some susceptible to cefuroxime and ceftriaxone, as well as to nalidixic acid, ciprofloxacin and levofloxacin. A prominent reason for concern with regard to gastroenteritis-causing bacteria is the recognized emergence of antimicrobial resistance among key species.

Some studies have shown *Pseudomonas aeruginosa* was 100% resistant to gentamicin, which was one of the antibiotics used for antimicrobial prophylaxis (Suchitra and Lakshmidevi, 2009). *P. aeruginosa* resistance to rifampicin and tetracycline has also been reported (Nkang et al., 2009b; Okonko et al., 2009a). *P. aeruginosa* and enterobacteriaceae species are the major cause of healthcare associated infections (HAIs), associated with significant morbidity and mortality (Jamshidi et al., 2009). They are also subjected to multi-drugs resistance (Jamshidi et al., 2009). Approximately, 2 - 10% of *P. aeruginosa* are resistant to all available treatments (Babay, 2007; Jamshidi et al., 2009). Reish et al. (1993) reported resistance of 55.6% to tetracycline by *Klebsiella* spp. Outbreak of multi-resistance *Klebsiella* was reported in neonatal intensive care unit in a hospital in Israel, *Klebsiella* isolates were resistant to gentamycin among others, but sensitive to quinolenes (Aiyegoro et al., 2007). *Klebsiella pneumoniae* isolates showed resistance to ciprofloxacin and amoxicillin/clavulanic acid was reported to be 55 and 12.5% in a study by Amin et al. (2009). There are reports covering high levels of resistance of *K. pneumoniae* towards these antibiotics in many countries. Moreover, limited use of these antibiotics is one of low levels of resistance towards *K. pneumoniae* (Amin et al., 2009). Hsu et al. (2007) reported *K. pneumoniae* and *E. coli* to be resistant to ciprofloxacin in their study on antimicrobial drug resistance in Singapore Hospitals. Susceptibility to tetracycline by *E. coli* was reported by Aiyegoro et al. (2007) and Nkang et al. (2009b).

In the last three decades, there have been a lot of reports in the scientific literature on the inappropriate use of antimicrobial agents and the spread of bacterial resistance among microorganisms causing infections (Abubakar, 2009). The emergence of antibiotic resistance in the management of most infections are serious public health issue, particularly in the developing world where apart from high level of poverty, ignorance and poor hygienic practices, there is also high prevalence of fake and spurious drugs of questionable quality in circulation. Much of the current discourse on infectious disease and drug resistance as it affects sub-Saharan Africa is limited to the pressing problems associated with emerging- and re-emerging resistant organisms. Resistance, however, equally compromises the management of acute respiratory infections, sexually transmitted diseases and diseases spread by the fecal-oral route, such as typhoid fever, cholera, dysentery and other diarrheal diseases (Okeke et al., 2007; Okonko et al., 2009b).

The negative health and socioeconomic impact of indiscriminate usage of antibiotics and of fake drugs cannot be over emphasized. It is a common knowledge that some infections in Nigeria are becoming increasingly difficult to treat with the available antibiotics meant for it. These poor quality or sub standard drugs could be responsible for the increasing number of resistant strains of microorganisms in the country. The general concept here is that the active ingredients in these antibiotics may be less than what is indicated on the drugs and it calls for serious concern, because the quality of a drug is dependent on the correctness of its active ingredient (Immaculata and Abraham, 1990). The potencies of these antibiotics could also be affected by deterioration of the active ingredients due to expiration of the drugs and or storage conditions (Nnela and Cox, 1988). Further implication is that many bacterial and parasitic diseases that could, until recently, be treated with inexpensive antimicrobial agents, has recently been made more expensive and less successful by the emergence and spread of resistant organisms (Okeke et al., 2007; Okonko et al., 2009a,b). Bacterial resistance to beta-lactam antibiotics is primarily due to the production of beta-lactam ring of the antibiotics rendering them inactive (Akpan, 1992). Resistance by microorganisms to antibiotics may be an indication of the presence of resistance factors such as R plasmids and enzymes such as beta-lactamases and of recent, extended beta-lactamase (ESBL) (Doughari et al., 2007). The widespread use of broad-spectrum antibiotics has led to the emergence of nosocomial infections caused by drug resistant microbes (Chikere et al., 2008). Multidrug resistance and the presence of several virulence factors in the strains of many pathogens responsible for different diseases pose an increasing threat to the successful management of disease scourge. Also, the rising prevalence of drug resistance such as penicillin-resistant pneumococci worldwide, mandates selective susceptibility testing and epidemiological investigations during outbreaks (Okonko et al., 2008). However, strategies for addressing antimicrobial drug resistance stress the need for new drugs (WHO, 2001) and yet the rate of drug development is in decline (Metlay et al., 2006).

Knowledge of etiological agents of infections and their sensitivities to available drugs is of immense value to the

rational selection and use of antimicrobial agents and to the development of appropriate prescribing policies. The changing spectrum of microorganisms causing infections and the emerging resistance to many of the older and cheaper antibacterial agents require continuous monitoring (Abubakar, 2009). We believe that regular monitoring of the pattern of resistance of common pathogens in the hospitals and the assessment of the efficacies, potencies and qualities of antibiotics sold in a particular area is critical in planning the best routines for empirical treatment of infectious patients. This study therefore, reports the assessment of the efficacies, potencies and qualities of some of the antibiotics sold in Calabar, South-South region of Nigeria based on their brands or manufacturers; using their measured zones of inhibition on the test organisms.

MATERIALS AND METHODS

Study area

The study area was Calabar, Cross River State, South-South region of Nigeria. Calabar is one of the most ancient, colonial and cosmopolitan cities in Nigeria.

Test organisms

All the chemicals and reagents used were of analytical grade, obtained from Sigma chemical co. Ltd, England. Media used in this study included: Nutrient agar (NA), Mac Conkey agar (MCA), blood agar, Mueller-Hinton Agar and Mannitol salt agar (MSA). All media were prepared according to the manufacturer's specification and sterilized at 121°C for 15 min at 15 lb pressure. Clinical isolates used in this study were obtained from Microbiology Section of the Sufat Medical Laboratories, Ishie, Calabar; the Microbiology laboratory of the University of Calabar Teaching Hospital (UCTH) and the Department of Microbiology, University of Calabar, respectively. Isolations were also made from the clinical samples such as blood (for blood culture), urine, pus swab, wound swab and sputum collected from the above laboratories. All the samples and the test organisms were replicated on different media and the plates were then incubated at 37°C for 24 - 48 h.

Discrete colonies were sub-cultured into fresh agar plates aseptically to obtain pure cultures of the isolates. Colonies identifiable as discrete on the Mueller Hinton agar were carefully examined macroscopically for cultural characteristics. All isolates were gram stained to determine their gram reaction. Biochemical tests were carried out as described by Jolt et al. (1994). The isolates were identified by comparing their characteristics with those of known taxa, as described by Jolt et al. (1994), Cheesbrough (2006) and Oyeleke and Manga (2008).

Antibiotic susceptibility testing

The test antibiotics used in this study were 3 brands of ampiclox (10 mcg), and 2 brands each of ciprofloxacin (10 mcg), gentamicin (10 mcg), rifampicin (10 mcg) and tetracylcine (25 mcg) as shown in Tables 1 to 6. The test antibiotics were bought from reputable pharmacy stores located within Calabar metropolis. Standard antibiotic sensitivity disks were also purchased from scientific supply stores in the Calabar metropolis. Whatman No.1 filter papers were obtained and disks of about 5.25 mm were cut out from the filter papers.

These were wrapped in foil paper and sterilized in the oven at 160°C for 1 h. The sensitivity disks were prepared to the National Committee for Clinical Laboratory Standards and guidelines (NCCLS, 2002) to contain the concentrations 25 and 10 mcg equivalent to the standards. The different brands of the antibiotics were diluted to obtain the concentrations of the commercial standard disks using sterile distilled water. In order to get 25 mcg from 250 mg of the antibiotic, 250 mg of the antibiotic was converted to 250000 mcg. This was dissolved in 10 ml of sterile distilled water. This gave 25000 mcg and a 1: 10 dilution was prepared which gave 2500 mcg concentration. The 100 sensitivity disks already sterilized were put into the above solution. Each disk will absorb 25 mcg of the drug. In order to get 10 mcg from 500 mg of the antibiotic, 500 mg was converted to 500,000 mcg. This was also dissolved in 5 ml of sterile distilled water which gave 100,000 mcg concentrations and a 1: 100 dilution was prepared to give 1000 mcg. One hundred disks were each soaked with 1 ml containing 10 mcg of the antibiotic.

Activities of the antibiotics against the test organisms

The antibiotic susceptibility patterns of the isolates to common antibiotics sold in Calabar were evaluated using the Kirby Bauer disc diffusion technique (Bauer et al., 1996) and 0.5 MacFarland's 10^8/ml employed in inoculum suspensions preparation according to the recommendations of the National Committee for Clinical Laboratory Standards (NCCLS) and Clinical and Laboratory Standards Institute (CLSI) (NCCLS, 2002; CLSI, 2006; Okonko et al., 2009a, b). Mueller-Hinton agar (Difco Laboratories, Michigan, USA) is the NCCLS recommended medium for sensitivity analysis. It is an ideal medium for routine antimicrobial susceptibility tests since it shows good batch-to-batch uniformity and is low in tetracycline and sulfonamide inhibitors (Cheesbrough, 2006). Trypticase soy broth (BBL™ Trypticase™ Soy Broth, BIOTECH) was prepared. Five discrete colonies of the different identified isolates were inoculated into 5 ml of the broths and incubated at 35°C for 4-6 h. The inoculum for primary sensitivity testing was prepared from a broth that has been incubated for 4-6 h. The density of the suspension was adjusted by adding the bacterial suspension to a sterile saline tube to match the density of the desired 0.5 McFarland standard. Each of the isolates was uniformly and aseptically inoculated into a different Mueller-Hinton agar plates by spread plate method using sterile cotton wool.

These discs include ampiclox, ciprofloxacin, gentamicin, rifampicin and tetracylcine and were tested against the isolates. The antibiotic sensitivity test was performed by disc diffusion technique using commercially available discs on Mueller Hinton agar plates (Iroha et al., 2009). The appropriate antibiotic discs were aseptically placed on the agar using sterile forceps. The plates were then incubated at 37°C for 24 h. Interpretation of results was done using the zones of inhibition sizes (Cheesbrough, 2006; Okonko et al., 2009a, b).

Preparation of the control sensitivity disks

The method described by Pratt and Fekety (1986) was used. In this method, the sterilized filter paper disks were impregnated with the various dilutions (l0 and 25 mcg) of the test antibiotics in duplicates. With the aid of a sterile forceps, the impregnated disks were carefully placed on the inoculated plates and firmly pressed unto the agar with the sterile forceps to ensure complete contact with the agar. The disks were distributed evenly at 24 mm distance and in a manner as to be no closer than 15 mm from the edge of the Petri dish. The standard antibiotic disks were also placed on separate plates seeded with the test organisms. The plates were covered with the tops, inverted and incubated immediately at 37°C for 24 h. The standard positive commercial disks included gram positive,

Table 1. Activities of the different brands of ampiclox against test organisms and their zones of inhibition.

Code	Test organism	Brand	Zones of inhibition (mm)			Test statistics	
			Test antibiotics	Standard controls	Mean + SE (n = 3)	t- value	P value
I	*E. coli*	Alaclox (10 mcg)	32.0	40.0	34.0 ± 1.15	-5.196	0.007*
		Superclox (10 mcg)	36.0	40.0			
		Vitaclox (10 mcg)	34.0	40.0			
II	*K. pneumoniae*	Alaclox (10 mcg)	22.0	27.0	24.7 ± 1.45	-1.606	0.184
		Superclox (10 mcg)	27.0	27.0			
		Vitaclox (10 mcg)	25.0	27.0			
III	*P. aeruginosa*	Alaclox (10 mcg)	34.5	44.0	37.5 ± 1.89	-3.434	0.026*
		Superclox (10 mcg)	41.0	44.0			
		Vitaclox (10 mcg)	37.0	44.0			
IV	*S. aureus*	Alaclox (10 mcg)	17.0	25.0	20.2 ± 1.74	-2.778	0.050*
		Superclox (10 mcg)	23.0	25.0			
		Vitaclox (10 mcg)	20.5	25.0			
V	*S. pyogenes*	Alaclox (10 mcg)	17.5	27.0	20.5 ± 1.50	-4.333	0.012*
		Superclox (10 mcg)	22.0	27.0			
		Vitaclox (10 mcg)	22.0	27.0			

*Significant at 0.05 level; SE = standard error of mean.

Table 2. Activities of the different brands of ciprofloxacin against test organisms and their zones of inhibition.

Code	Test organism	Brand	Zones of inhibition (mm)			Test statistics	
			Test antibiotics	Standard controls	Mean + SE (n = 2)	t- value	P value
I	*E. coli*	Ciprocin (10 mcg)	38.0	47.0	39.5 ± 1.50	-5.000	0.038*
		Ciproxcin (10 mcg)	41.0	47.0			
II	*K. pneumoniae*	Ciprocin (10 mcg)	31.5	33.0	31.8 ± 0.25	-5.000	0.038*
		Ciproxcin (10 mcg)	32.0	33.0			
III	*P. aeruginosa*	Ciprocin (10 mcg)	43.0	51.0	44.5 ± 1.50	-4.333	0.049*
		Ciproxcin (10 mcg)	46.0	51.0			
IV	*S. aureus*	Ciprocin (10 mcg)	40.0	50.5	38.0 ± 2.00	-6.250	0.025*
		Ciproxcin (10 mcg)	36.0	50.5			
V	*S. pyogenes*	Ciprocin (10 mcg)	30.0	39.0	28.0 ± 2.00	-5.500	0.032*
		Ciproxcin (10 mcg)	26.0	39.0			

*Significant at 0.05 level; SE = standard error of mean.

gram negative and broad spectrum disks while the negative control disks were impregnated with sterile distilled water. After incubation, the zones of clearance of organisms around the disks were also measured and recorded (NCCLS, 2002; Cheesbrough, 2006; Okonko et al., 2009a, b). An isolate was considered multi-drug resistant if it was resistant to at least three of the antibiotics tested (Santo et al., 2007). Quality control on the susceptibility discs were performed using laboratory strains of *E. coli, P. aeruginosa, S. aureus* and *Streptococcus faecalis* of known sensitivity.

Statistical analyses

Data were analyzed using the general linear model procedure, analysis of variance (ANOVA) and independent t-test to compare the level of significant difference between the test antibiotics and the standard controls. Indicator of statistical significance is $P \leq 0.05$.

RESULTS

The different test organisms used in this study for assessment of efficacies, potencies and bacteriological qualities of some of the antibiotics sold in Nigeria include *E. coli, K. pneumoniae*, *P. aeruginosa*, *S. aureus* and *Streptococcus pyogenes* and the results presented in Tables 1 through 6. This indicated that efficacies, potencies and bacteriological qualities of these antibiotics sold in Nigeria differed depending on their brands or manufacturers. The sensitivity testing of the sensitivity

Table 3. Activities of the different brands of gentamicin against test organisms and their zones of inhibition.

Code	Test organism	Brand	Zones of inhibition (mm)			Test statistics	
			Test antibiotics	Standard controls	Mean + SE (n = 2)	t- value	P value
I	*E. coli*	Richem (10 mcg)	35.5	37.0	34.3 ± 1.25	-2.200	0.159
		Shanghai (10 mcg)	33.0	37.0			
II	*K. pneumoniae*	Richem (10 mcg)	53.5	56.0	51.8 ± 1.75	-2.249	0.136
		Shanghai (10 mcg)	50.0	56.0			
III	*P. aeruginosa*	Richem (10 mcg)	49.0	57.0	47.5 ± 1.50	-6.333	0.024*
		Shanghai (10 mcg)	46.0	57.0			
IV	*S. aureus*	Richem (10 mcg)	45.0	49.0	44.0 ± 1.00	-5.000	0.038*
		Shanghai (10 mcg)	43.0	49.0			
V	*S. pyogenes*	Richem (10 mcg)	06.0	10.0	04.0 ± 2.00	-3.000	0.095
		Shanghai (10 mcg)	02.0	10.0			

*Significant at 0.05 level; SE = standard error of mean.

Table 4. Activities of the different brands of rifampicin against test organisms and their zones of inhibition.

Code	Test organism	Brand	Zones of inhibition (mm)			Test statistics	
			Test antibiotics	Standard controls	Mean + SE (n = 2)	t- value	P value
I	*E. coli*	Vitals (10 mcg)	20.0	23.0	19.5 ± 0.50	-7.000	0.020*
		Medifampi (10 mcg)	19.0	23.0			
II	*K. pneumoniae*	Vitals (10 mcg)	43.0	45.0	41.8 ± 1.25	-2.600	0.122
		Medifampi (10 mcg)	40.5	45.0			
III	*P. aeruginosa*	Vitals (10 mcg)	09.0	12.0	07.0 ± 2.00	-2.500	0.130
		Medifampi (10 mcg)	05.0	12.0			
IV	*S. aureus*	Vitals (10 mcg)	18.0	20.0	17.5 ± 0.50	-5.000	0.038*
		Medifampi (10 mcg)	17.0	20.0			
V	*S. pyogenes*	Vitals (10 mcg)	27.0	29.5	26.0 ± 1.00	-3.500	0.073
		Medifampi (10 mcg)	25.0	29.5			

*Significant at 0.05 level; SE = standard error of mean.

Table 5. Activities of the different brands of tetracycline against test organisms and their zones of inhibition.

Code	Test organism	Brand	Zones of inhibition (mm)			Test statistics	
			Test antibiotics	Standard controls	Mean + SE (n = 2)	t- value	P value
I	*E. coli*	Tetracap (25 mcg)	35.0	44.0	37.5 ± 2.50	-2.600	0.122
		Tetrim (25 mcg)	40.0	44.0			
II	*K. pneumoniae*	Tetracap (25 mcg)	04.0	08.0	05.0 ± 1.00	-3.000	0.095
		Tetrim (25 mcg)	06.0	08.0			
III	*P. aeruginosa*	Tetracap (25 mcg)	35.5	41.0	36.8 ± 1.25	-3.400	0.077
		Tetrim (25 mcg)	38.0	41.0			
IV	*S. aureus*	Tetracap (25 mcg)	35.0	44.0	37.5 ± 2.50	-2.600	0.122
		Tetrim (25 mcg)	40.0	44.0			
V	*S. pyogenes*	Tetracap (25 mcg)	08.0	13.0	09.3 ± 1.25	-3.000	0.095
		Tetrim (25 mcg)	10.5	13.0			

SE = Standard error of mean.

Table 6. Multiple responses of test organisms to different test antibiotics.

Dependent variable	(I) Brand grp	(J) Brand grp	Mean difference (I-J) + SE	Significance
E. coli	Ampiclox	Ciprofloxacin	-5.50 ± 1.99*	0.033
		Gentamicin	-.250 ± 1.99	0.904
		Rifampicin	14.50 ± 1.99*	0.000
		Tetracycline	-3.50 ± 1.99	0.130
	Ciprofloxacin	Ampiclox	5.50 ± 1.99*	0.033
		Gentamicin	5.25 ± 2.18	0.053
		Rifampicin	20.00 ± 2.18*	0.000
		Tetracycline	2.00 ± 2.18	0.395
	Gentamicin	Ampiclox	0.25 ± 2.18	0.904
		Ciprofloxacin	-5.25 ± 2.18	0.053
		Rifampicin	14.75 ± 2.18*	0.001
		Tetracycline	-3.25 ± 2.18	0.187
	Rifampicin	Ampiclox	-14.50 ± 1.99*	0.000
		Ciprofloxacin	-20.00 ± 2.18*	0.000
		Gentamicin	-14.75 ± 2.18*	0.001
		Tetracycline	-18.00 ± 2.18*	0.000
	Tetracycline	Ampiclox	3.50 ± 1.99	0.130
		Ciprofloxacin	-2.00 ± 2.18	0.395
		Gentamicin	3.25 ± 2.18	0.187
		Rifampicin	18.00 ± 2.18*	0.000
K. pneumoniae	Ampiclox	Ciprofloxacin	-7.08333*	0.008
		Gentamicin	-27.08 ± 1.82*	0.000
		Rifampicin	-17.08 ± 1.82*	0.000
		Tetracycline	19.66667*	0.000
	Ciprofloxacin	Ampiclox	7.08 ± 1.82*	0.008
		Gentamicin	-20.00 ± 2.00*	0.000
		Rifampicin	-10.00 ± 2.00*	0.002
		Tetracycline	26.75 ± 2.00*	0.000
	Gentamicin	Ampiclox	27.08 ± 2.00*	0.000
		Ciprofloxacin	20.00 ± 2.00*	0.000
		Rifampicin	10.00 ± 2.00*	0.002
		Tetracycline	46.75 ± 2.00*	0.000
	Rifampicin	Ampiclox	17.08333*	0.000
		Ciprofloxacin	10.00 ± 2.00*	0.002
		Gentamicin	-10.00 ± 2.00*	0.002
		Tetracycline	36.75 ± 2.00*	0.000
	Tetracycline	Ampiclox	-19.66667*	0.000
		Ciprofloxacin	-26.75000*	0.000
		Gentamicin	-46.75 ± 2.00*	0.000
		Rifampicin	-36.75 ± 2.00*	0.000
P. aeruginosa	Ampiclox	Ciprofloxacin	-7.00 ± 2.40*	0.027
		Gentamicin	-10.00 ± 2.40*	0.006
		Rifampicin	30.50 ± 2.40*	0.000
		Tetracycline	0.75 ± 2.40	0.766

Table 6. contd.

Dependent variable	(I) Brandgrp	(J) Brandgrp	Mean difference (I-J) + SE	Significance
P. aeruginosa	Ciprofloxacin	Ampiclox	7.00 ± 2.40*	0.027
		Gentamicin	-3.00 ± 2.63	0.298
		Rifampicin	37.50 ± 2.63*	0.000
		Tetracycline	7.75 ± 2.63*	0.026
	Gentamicin	Ampiclox	10.00 ± 2.40*	0.006
		Ciprofloxacin	3.00 ± 2.63	0.298
		Rifampicin	40.50 ± 2.63*	0.000
		Tetracycline	10.75 ± 2.63*	0.006
	Rifampicin	Ampiclox	-30.50 ± 2.63*	0.000
		Ciprofloxacin	-37.50 ± 2.63*	0.000
		Gentamicin	-40.50 ± 2.63*	0.000
		Tetracycline	-29.75 ± 2.63*	0.000
	Tetracycline	Ampiclox	-0.75 ± 2.63	0.766
		Ciprofloxacin	-7.75000*	0.026
		Gentamicin	-10.75 ± 2.63*	0.006
		Rifampicin	29.75 ± 2.63*	0.000
S. aureus	Ampiclox	Ciprofloxacin	-17.83 ± 2.39*	0.000
		Gentamicin	-23.83 ± 2.39*	0.000
		Rifampicin	2.67 ± 2.39	0.307
		Tetracycline	-17.33 ± 2.39*	0.000
	Ciprofloxacin	Ampiclox	17.83 ± 2.39*	0.000
		Gentamicin	-6.00 ± 2.61	0.062
		Rifampicin	20.50 ± 2.61*	0.000
		Tetracycline	0.50 ± 2.61	0.855
	Gentamicin	Ampiclox	23.83 ± 2.39*	0.000
		Ciprofloxacin	6.00 ± 2.61	0.062
		Rifampicin	26.50 ± 2.61*	0.000
		Tetracycline	6.50 ± 2.61*	0.048
	Rifampicin	Ampiclox	-2.67 ± 2.39	0.307
		Ciprofloxacin	-20.50 ± 2.61*	0.000
		Gentamicin	-26.50 ± 2.61*	0.000
		Tetracycline	-20.00 ± 2.61*	0.000
	Tetracycline	Ampiclox	17.33 ± 2.39*	0.000
		Ciprofloxacin	-0.50 ± 2.61	0.855
		Gentamicin	-6.50 ± 2.61*	0.048
		Rifampicin	20.00 ± 2.61*	0.000
S. pyogenes	Ampiclox	Ciprofloxacin	-7.50 ± 2.19*	0.014
		Gentamicin	16.50 ± 2.19*	0.000
		Rifampicin	-5.50 ± 2.19*	0.046
		Tetracycline	11.25 ± 2.19*	0.002
	Ciprofloxacin	Ampiclox	7.50 ± 2.19*	0.014
		Gentamicin	24.00 ± 2.40*	0.000
		Rifampicin	2.00 ±2.40	0.437
		Tetracycline	18.75 ± 2.40*	0.000

Table 6. contd.

Dependent variable	(I) Brandgrp	(J) Brandgrp	Mean difference (I-J) + SE	Significance
S. pyogenes	Gentamicin	Ampiclox	-16.50 ± 2.19*	0.000
		Ciprofloxacin	-24.00 ± 2.40*	0.000
		Rifampicin	-22.00 ± 2.40*	0.000
		Tetracycline	-5.25 ± 2.40	0.072
	Rifampicin	Ampiclox	5.50 ± 2.19*	0.046
		Ciprofloxacin	-2.00 ± 2.40	0.437
		Gentamicin	22.00 ± 2.40*	0.000
		Tetracycline	16.75 ± 2.40*	0.000
	Tetracycline	Ampiclox	-11.25 ± 2.19*	0.002
		Ciprofloxacin	-18.7 5± 2.40*	0.000
		Gentamicin	5.25 ± 2.40	0.072
		Rifampicin	-16.75 ± 2.40*	0.000

*The mean difference is significant at the 0.05 level. Analysis was carried out using ANOVA and least significant difference (LSD).

testing of the test antibiotics were compared with that of the standardized commercial sensitivity disks which was analyzed using *E. coli, S. aureus, P. aeruginosa*, *K. pneumoniae* and *S. pyogenes* as presented in Tables 1 to 6, respectively. The results obtained were interpreted using the measured diameter of the zones of inhibition shown by these antibiotics against the pathogens used. From Tables 2, 3, 4 and 5, there were no significant differences (P > 0.05) between the zones of inhibition and standard controls for the drugs tested against the test organisms.

Activities of the different brands of ampiclox against test organisms and their zones of inhibition are shown in Table 1. It can be deduced that superclox showed a higher potency followed by vitaclox and alaclox when compared with the standard control. The result also showed that 1 (33.3%) of the ampiclox (alaclox) tested showed lower potency against the test organisms. In the same vein, superclox produced significantly (P < 0.05) higher zones of inhibition compared to the other brands of the drug (alaclox and vitaclox) on all test organisms except for S. *pyogenes*, in which superclox (22 mm) showed similar zones of inhibition with vitaclox (22 mm). Alaclox produced significantly (P < 0.05) lower zones of inhibition compared to the other drugs (superclox and vitaclox) on S. *aureus* and S. *pyogenes*. However, significant differences (P = 0.007, P = 0.026, P = 0.050, P = 0.012) were observed between the zones of inhibition of the test antibiotics and standard controls for the 3 brands of ampiclox tested on all the test organisms except for *K. pneumoniae. K. pneumoniae* showed significantly (P = 0.184) high sensitivity to ampiclox comparable to the standard controls.

Table 2 shows the activities of the different brands of ciprofloxacin against test organisms and their zones of inhibition. Ciproxcin produced significantly (P < 0.05) higher zones of inhibitions compared to ciprocin on all test organisms except for *S. aureus* (36 mm) and *S. pyogenes* (26 mm). Ciprocin produced significantly (P < 0.05) higher zones of inhibition on *S. aureus* (40 mm) and *S. pyogenes* (30 mm). However, there were significant differences (P = 0.038, P = 0.038, P = 0.049, P = 0.025, P = 0.032) between the zones of inhibition of the test antibiotics and standard controls tested against the test organisms.

Table 3 shows the activities of the different brands of gentamicin against test organisms and their zones of inhibition. Richem produced significantly (P < 0.05) higher zones of inhibitions compared to shanghai on all test organisms. However, there were no significant differences (P = 0.159, P = 0.136, P = 0.095) between the zones of inhibition and standard controls against the test organisms except for *P. aeruginosa* and *S. aureus*.

Both brands produced significantly (P = 0.024, P = 0.038) lower zones of inhibition on *P. aeruginosa* and *S. aureus* compared to the standard control.

In Table 4, the activities of the different brands of rifampicin against test organisms and their zones of inhibition are shown. It can be deduced that vitals showed a higher efficacy than medifampi. Vitals produced higher zones of inhibition compared to medifampi on all test organisms, though it was not significant (P > 0.05). However, there were no significant differences (P = 0.122, P = 0.130, P = 0.073) between the zones of inhibition and standard controls for the drugs tested against the test organisms except for *E. coli* and *S. pyogenes*. Both brands produced significantly (P = 0.020, P = 0.038) lower zones of inhibition on *E. coli* and *S. pyogenes* compared to the standard controls.

The activities of the different brands of tetracycline against test organisms and their zones of inhibition are shown in Table 5. It can also be inferred that tetrim showed a higher efficacy than tetracap on all the test organisms. However, there were no significant differences

(P = 0.122, P = 0.095, P = 0.077, P = 0.122, P = 0.095) between the zones of inhibition and standard controls of the drugs tested against the test organisms.

Table 6 shows the overall multiple responses of organisms of the test organisms to different test antibiotics. The overall mean zones of inhibition for the test organisms ranged from 33.0 – 34.7 mm, with 33 mm for *E. coli*, 20.9 mm for *K. pneumoniae*, 34.7 mm for *P. aeruginosa*, 31.4 mm for *S. aureus* and 17.6 mm for *S. pyogenes.* The multiple responses (LSD) of the test organisms to different antibiotics in terms of the effectiveness/efficacies of each test antibiotics compared with each other is shown in Table 6.

DISCUSSION

The potency or activity per milligram of a chemotherapeutic agent is usually expressed on the basis of the lowest concentration of minimal inhibitory concentrations (MICs) or higher zones of inhibition (Nnela and Cox, 1988). In this study, an assessment of the efficacies, potencies and bacteriological qualities of 11 brands of 5 different antibiotics sold in Nigeria was carried out including 3 brands of ampiclox and 2 brands each of ciprofolxacin, gentamicin, rifampicin and tetracylcine. From the results, the overall mean zones of inhibitions for the test organisms ranged from 33.0 – 34.7 mm, with 33 mm for *E. coli*, 20.9 mm for *K. pneumoniae*, 34.7 mm for *P. aeruginosa*, 31.4 mm for *S. auras* and 17.6 mm for *S. pyogenes.* In this study, the potency of the standard drugs when compared to test antibiotics and the mean potency of the antibiotic on the organisms determined showed differences in efficacy and quality of the various brands of antibiotics sold in Nigeria. From our study, there were no significant differences (P > 0.05) between the zones of inhibitions of the test antibiotics and standard controls for some of the drugs tested against the test organisms while significant differences (P < 0.05) were observed between the zones of inhibitions of the test organisms and the standard controls for some other drugs tested against the test organisms.

Our result showed there were no significant differences (P > 0.05) between the zones of inhibitions and standard controls for the brands of gentamicin (richem) and tetracycline. Gentamycin, a relatively cheap and an easily available antibiotic, is effective against the gram-negative bacilli (GNB) (*E. coli* and *K. pneumonia*) except for *P. aeruginosa* and effective against the grampositive cocci (GPC) [*S. pyogenes*] except for *S. aureus* in the study. This is similar to a study done in Calabar claiming 80% effectiveness (Martins et al., 2005) and a study done in Kano claiming 70.7 and 76.7% effectiveness against GNB and GPC, respectively (Nwadioha et al., 2010). Chikere et al. (2008) reported the sensitivities of GNB to gentamycin to be 100% and GPC to be 93.3%. This is also comparable to our findings. However, the higher zones of inhibitions reported for gentamicin and tetra-cycline in this study is contrary to the findings of some previous studies (Okonko et al., 2009b; Abubakar, 2009; Nkang et al., 2009a, b; Adedeji and Abdulkadir, 2009; Ullah et al., 2009).

Tetracycline is an antibiotic that inhibits bacterial growth. They are bacteristatic and widely used as a broad-spectrum antibiotic with activity against Gram- positive and Gram- negative bacteria. Resistance to tetracycline is common and this is further confirmed from the results obtained in a study by Adedeji and Abdulkadir (2009). Resistance to tetracycline has developed because it is readily available in the country and has been widely misused (Adedeji and Abdulkadir, 2009). Tetracycline resistant *K. pneumoniae* and *S. pyogenes* has been reported in our previous study (Nkang et al., 2009a, b). Okonko et al. (2009b) reported 100% resistance to gentamicin and tetracycline by *K. pneumoniae*, *P. aeruginosa*, *E. coli*, *S. aureus* and *S. pyrogenes* in a similar study. Abubakar (2009) reported high rate of resistance to tetracycline and gentamicin in their study. Tetracycline-resistant *S. enterica* Serovar Typhimurium and Eenteritidis was reported by Halawani and Shohayeb (2008). Recently, an epidemic multi-drug have emerged, presumably due to the extensive use of resistant strain serovar Typhimurium phage type 104 antimicrobial agents both in humans and animals (Halawani and Shohayeb, 2008).

Aminoglycosides have good activity against clinically important gram negative bacilli (Ullah et al., 2009). The aminoglycoside antibiotics include gentamcin, kanamycin, amikacin etc. These act by inhibiting bacterial protein synthesis. Among the non-β-lactams, gentamicin showed good activity with 48% isolates found susceptible in a study by Ullah et al. (2009), which is more than 29% recorded in Israel and 36% recorded in India (Colodner et al., 2007).This may be due to increased use of gentamicin in India and Israel as compared to Pakistan. Gentamycin is routinely used synergistically with a beta-lactam antibiotic or vancomycin for empirical therapy in infective endocarditis (Nwadioha et al., 2010). According to Ullah et al. (2009), pattern of resistance to aminoglycosides is affected by selective pressure in different regions. Ako-Nai et al. (2005) presented a report in which 70.2% of staphylococcal isolates were resistant to tetracycline and 1.8% to gentamycin in a study in Ibadan, Nigeria. Similar resistance profiles were presented among *S. epidermidis* in some hospitals in Turkey to be resistant to tetracycline (Abubakar, 2009). Gentamicin is the most commonly used aminoglycoside for serious urinary tract infections (UTIs) but it could have serious side effects such as damage to hearing, sense of balance and kidneys (Adedeji and Abdulkadir, 2009). The highest efficacy of gentamicin in the treatment of UTIs has also been reported by Al Sweih et al. (2005).

The potency of the standard drugs when compared to test antibiotics and the mean potency of the antibiotic on

the organisms determined showed differences in efficacy and quality of the various brands of antibiotics sold in Nigeria. It also showed that 3 (60%) of the antibiotics (alaclox, ciprofloxacin and rifampicin) tested showed lower potency against the test organisms compared with the standard controls. This may reflect the fact that these are the most commonly prescribed antibiotics in the hospital and also the most easily available in the community without prescription and because they are also very cheap in terms of cost and so subject to abuse and misuse (Abubakar, 2009). The lower zones of inhibition reported for these 3 antibiotics in this study are contrary to what has been previously reported. Okonko et al. (2009b) reported 100% sensitivity to ciprofloxacin by *K. pneumoniae*, *P. aeruginosa*, *E. coli*, *S. aureus* and *S. pyrogenes*. Ciprofloxacin was 82.9% effective across all the bacterial isolates tested *in vitro* in a study by Nwadioha et al. (2010). Chikere et al. (2008) reported the sensitivities of GNB to ciprofloxacin to be 63.6%. Aiyegoro et al. (2007) reported 77.8% sensitivity to ciprofloxacin. This is contrary to our present findings in which lower zones of inhibition was reported for ciprofloxacin.

Ampiclox is a broad-spectrum penicillin, which is active against Gram- positive bacteria such as *Streptococcus sp*. and *S. aureus* but inactive against *E. coli* in up to 25% of cases. It is very clear from the results obtained in this study as well as in similar studies in Kuwait (Al Sweih et al., 2005) that most pathogens have acquired resistance to this antibacterial agent. Zones of inhibition shown by rifampicin tested against *E. coli* and *S. aureus* isolates were significantly lower. This is a clear indication that the isolated organisms have developed resistance to the antibiotic. Resistance of *S. aureus* to rifampicin has also been reported in Calabar (Nkang et al., 2009b). Fluoroquinolones are antibiotics which act by inhibiting the activity of DNA gyrase and topoisomerase, enzymes essential for bacterial DNA replication. These include ciprofloxacin, ofloxacin, enoxacin, sparfloxacin etc (Ullah et al., 2009). Ciprofloxacin is a member of the quinolones which are effective against a wide range of organisms (Cheesbrough, 2006). At the present time, the cost of obtaining this antibiotic is quite high and because of this, fewer number of people have access to it, thus, diminishing the chances of its misuse and of organisms developing resistance to it. Ciprofloxacin has been recommended as first line therapy in urinary tract infection (Ullah et al., 2009). Ciprofloxacin is not routinely recommended for pediatric use except in special cases where the benefits out – weigh the short term risk of joint toxicity, such as in cystic fibrosis (Nwadioha et al., 2010). But resistance to flouroquinolones is increasing throughout the world. The observed resistance in *E. coli* to ciprofloxacin was 62% in a study by Ullah et al. (2009). Higher percentages have been reported in other studies from Palestine, Canada, USA and Turkey (Yuksel et al., 2006).

Our result also showed that alaclox brand of the ampiclox tested showed lower potency against the test organisms, though, superclox and vitaclox showed a higher potency when compared with the standard controls. Alaclox produced significantly ($P < 0.05$) lower zones of inhibitions compared to the other drugs (superclox and vitaclox) on S. *aureus* and S. *pyogenes*. However, significant differences ($P = 0.007$, $P = 0.026$, $P = 0.050$, $P = 0.012$) were observed between the zones of inhibitions of the test antibiotics and standard controls for the 3 brands of ampiclox tested on all the test organisms except for *K. pneumoniae. K. pneumoniae* showed significantly ($P = 0.184$) high sensitivity comparable to the standard controls. There were also significant differences ($P = 0.038$, $P = 0.038$, $P = 0.049$, $P = 0.025$, $P = 0.032$) between the zones of inhibitions of test ciprofloxacin and standard controls and in the same vein, both brands of rifampicin (vitals and medifampi) produced significantly ($P = 0.020$, $P = 0.038$) lower zones of inhibitions on *E. coli* and *S. pyogenes* compared to the standard controls. This indicates that some of the ampiclox, ciprofloxacin and rifampicin sold in Calabar, Nigeria may be fake or adulterated and may not have contained the required ingredients needed to exert bacteriocidal or bacteriostatic (inhibitory) activity on the pathogens (Adejoh, 2000), which is a reflection of what goes on in many developing countries; in particular, in sub-Saharan Africa it is considerable and, within those countries, economically disadvantaged persons are most likely to contract communicable diseases and least likely to access appropriate treatment (Okeke et al., 2007; Okonko et al., 2009a, b).

The overall multiple responses of the organisms of the test organisms to different test antibiotics showed that for *E. coli* there were significant differences between the effectiveness/efficacy of ampiclox and ciprofloxacin ($P = 0.033$), ampiclox and rifampicin ($P = 0.000$), ciprofloxacin and rifampicin ($P = 0.000$), gentamicin and rifampicin ($P = 0.001$) and tetracycline and rifampicin ($P = 0.0001$). For *K. pneumoniae*, there were significant differences ($P < 0.05$) between the mean zones of inhibitions showed by all the test antibiotics. *P. aeruginosa* responses in terms of their mean zones of inhibitions, showed significant differences ($P < 0.05$) between the effectiveness/efficacy of each antibiotics compared except between ampiclox and tetracycline ($P = 0.766$) as well as ciprofloxacin and gentamicin ($P = 0.298$) that showed comparable efficacies. In the same vein, for *S. aureus,* there were significant differences ($P < 0.05$) between the effectiveness/efficacy of ampiclox and other antibiotics except rifampicin ($P = 0.307$) as well as, between ciprofloxacin and other test antibiotics except gentamicin ($P = 0.062$) and tetracycline ($P = 0.855$). In the case of *S. pyogenes*, there were significant ($P < 0.05$) differences between the effectiveness/ efficacy of each antibiotics compared except between ciprofloxacin and rifampicin ($P = 0.437$) and between gentamicin and tetracycline ($P = 0.072$).

Similar observations have been made in a previous study

by other scholars (Nwanze et al., 2007; Abubakar, 2009). In a study by Abubakar (2009), *S. faecalis* had a profile of 70.7% susceptibility to ofloxacin and a susceptibility of less than 50.0% to gentamycin and tetracycline similar to the data presented by Nwanze et al. (2007). In a similar study by Kebira et al. (2009), 80% of the isolates were susceptible to gentamycin and ciproxin®. Adedeji and Abdulkadir (2009) reported gentamicin and ofloxacin to be the most active antibiotics against *E. coli*, *S. saprophyticus*, *K. aerogenes*, *S. aureus*, *P. aeruginosa* and *S. faecalis*. Their results of the antibiotic susceptibility tests showed that the isolates were generally highly susceptible to gentamicin (89%) and ofloxacin (60%). Also in a study by Abubakar (2009), *P. aeruginosa* had a susceptibility profile of 31.6% to ofloxacin, but not susceptible to gentamycin and tetracycline. *P. aeruginosa* maintains antibiotic resistance plasmids and are able to transfer these genes by bacterial processes of transduction and conjugation (Nwanze et al., 2007). Occurrence of multidrug resistant (MDR) *P. aeruginosa* from chronically infected patients has been a major reason for ultimate failure of antibiotic treatments. Early studies had shown that it is the environment in the lungs and the virulence factors that are the major reason for the MDR nature of this opportunistic pathogen. However, recent investigations have proved that it is the ability of increasing the rate of mutations that allow this organism to adapt to the heterogeneous and dynamic atmosphere of the lungs. These insights into the survival strategy of this organism will open ways to newer targets that are susceptible to new methods and allow us to tackle these infections (Seshadri and Chhatbar, 2009).

Major concern however, in the case of *P. aeruginosa*, is the combination of its inherent resistance and ability to acquire resistance via mutations to all treatments leading to increasing occurrence of multi drug resistant strains (Henrichfreise et al., 2007b). Ability of *P. aeruginosa* to escape the effects of antibiotics is attributed by its capability of growing in microaerophilic environment as biofilms both of which reduce the efficiency of many antibiotics (Seshadri and Chhatbar, 2009). Resistance towards antimicrobial agents to survive in the lungs during frequent and prolonged treatments also requires great adaptive skills. Development of acquired resistance to antibiotics of different classes during antimicrobial therapy, which is rarely observed in acute infections, is a marked feature of chronic *P. aeruginosa* infections (Seshadri and Chhatbar, 2009). Our worst nightmare may even be more dreadful, with the occurrence of “panresistant” strains that arise due to the accumulation of multiple mechanisms of antibiotic resistance and are resistant to all antibiotics except polymyxins (Bonomo and Szabo, 2006; Seshadri and Chhatbar, 2009).

The observations documented in current literature were compared and correlated with changes at the genetic level and it is clearly visible that *P. aeruginosa* adapts to the conditions in the lungs of chronically infected patients and major part of this adaptation comes from the mutations that take place in the genome of bacteria inside the lungs of the patients only (Henrichfreise et al., 2007b; Seshadri and Chhatbar, 2009). However, the important role played by the selective pressure should not be neglected as it this condition which selects only those cells who have adapted to the conditions. This sequential continuous process of mutation and selection gives rise to the highly adapted strains so much so that sometimes the ability to survive in primary environment such as soil or distilled water is lost (Hogardt et al., 2007). Intrinsic antibiotic resistance of *P. aeruginosa* accompanied by its ability to acquire resistance via mutations and adaption to the heterogeneous and dynamic environment of chronically infected lungs are major threats and reasons for the ultimate failure of the current antibiotic therapies in eradicating the infection from lungs (Seshadri and Chhatbar, 2009). New insights at molecular levels in the process of accumulating such beneficial mutations at faster rates, termed as hyper-mutation have allowed us to understand the high acquired resistance of this opportunistic pathogen. Also, these understandings will allow us to develop new therapeutic strategies to combat chronic infections (Seshadri and Chhatbar, 2009).

E. coli, worldwide, have developed resistance to antimicrobial agents and the phenomenon is increasing both in outpatients and hospitalized patients (Akram et al., 2007; Garcia et al., 2007). Among members of the enterobacteriaceae family, resistance to β-lactams has been reported to be associated with ESBL, which hydrolyze oxyimino beta-lactams like cefotaxime, ceftriaxone, ceftazidime and monobactams but have no effect on cephamycins, carbapenems and related compounds (Ullah et al., 2009). ESBL producing *E. coli* in this part of the world has been observed by several workers; its prevalence was variously reported from 28 to 67% (Akram et al., 2007; Hammer et al., 2007; Mehrgan and Rahbar, 2008). Production of ESBL is frequently plasmid encoded and bears clinical significance. Plasmids responsible for ESBL production frequently carry genes encoding resistance to other drug classes also. Therefore, antibiotic options in the treatment of ESBL producing organisms are extremely limited (Paterson and Bonomo, 2005). Detection of ESBL production is important. One major concern is the spread of ESBL positive bacteria within hospitals, which may lead to outbreaks or to endemic occurrence (Ullah et al., 2009). Another concern is failure to treat infections caused by ESBL positive organisms, as therapeutic choices are limited (Paterson and Bonomo, 2005). It is necessary to investigate the prevalence of ESBL positive strains in hospitals so as to formulate a policy of empirical therapy in high risk units where infections due to resistant organisms are much higher (Ullah et al., 2009).

It is also well documented that gram negative bacilli

habour series of antibiotic resistant genes which can be transferred to other bacteria horizontally (Depardieu et al., 2007; Leavitt et al., 2007; Lockhart et al., 2007). Epidemiologic surveillance of antimicrobial resistance is indispensable for empirically treating infections, implementing resistance control measures and preventing the spread of antimicrobial-resistant microorganisms. The worldwide escalation in both community- and hospital-acquired antimicrobial-resistant bacteria is threatening the ability to effectively treat patients, emphasizing the need for continued surveillance, more appropriate antimicrobial prescription, prudent infection control and new treatment alternatives (Zhanel et al., 2008; Chikere et al., 2008). The worldwide trend of empirically treating infections may not work well in Nigeria, because decreased susceptibility rates have been documented for majority of the common pathogens in various parts of the country. Some studies explained the higher resistance rates in tertiary hospitals especially where both inpatients and outpatients are used to collect data, as is the case in this study, to be due to those patients having more complicated UTIs and thus, exposed to more resistant flora, or may have failed previous therapy, all of which may account for the increased resistance observed (Abubakar, 2009). In a recent study in Lancet in 2001, out of 581 samples of 27 different drugs from pharmacies in Lagos and Abuja analyzed, 279 (48%) were found not to comply with the set pharmacopedia limits. Although some preparations contained no active ingredients, samples with either too much or too little of the active drug contents were identified and the manufacturers were from Belgium, China, Pakistan, Egypt, Germany, Switzerland, United Kingdom and Nigeria. Also, one of the cankerworms plaguing our country, Nigeria, in recent times is the menace of the sales of fake adulterated and substandard drugs which has eaten deep into the fabric of our society like a bad ulcer (Popoola, 2001).

This study showed that the efficacy of antibiotics sold in Nigeria is poor with reference to the active ingredients used. In this study, the observed efficacy and quality of some of the antibiotics sold in Nigeria differ in their efficacy or potency according to their brands or manufacturers. Some show a higher efficacy and some a low efficacy when compared to the standards used. In accordance with the assertion of Abubakar (2009), some of the drugs were sensitive, but a good number have also lost their usefulness. These differences in efficacy among brands of some antibiotics constitute a grave danger to health. This study has also shown that about 20% of the brands of antibiotics studied had reduced potency against the test bacteria used in this study. The data presented in this investigation are similar to those obtained in other Nigerian cities of Kano, Yola, Jos, Lafia, Abuja, Enugu, Port-Harcourt, Calabar, Abeokuta, Lagos and Ibadan and have shown the changing pattern in the types of organisms causing infections and their resistance to many of the commonly available antibiotics, thus leading to the use of newer and more costly agents (Ako-Nai et al., 2005; Nwanze et al., 2007; Kolawale et al., 2009; Okesola and Oni, 2009; Abubakar, 2009; Okonko et al., 2009a,b; Nkang et al., 2009a, b). Indiscriminate use and under dosage have resulted in the emergence of drug resistant strains in Nigeria (Akpan, 1992; Okonko et al., 2009a, b). Resistance due to over use and adulteration of the antibiotics has also been reported. Misuse of drugs in a hospital can influence further misuse outside the hospital. All the isolates in this study showed resistance to at least 1-3 different antibiotics, indicating the presence of strong selective pressures from the antibiotics in the community. The use of antibiotics within the hospital has also become a cause for concern as they are commonly prescribed without sound justification thus, calling to question the professional competences of the attending healthcare givers (Fehintola, 2009). Most hospitals in Nigeria lack guidelines for the use of antibiotics and the country lacks any antibiotics and indeed any drug policy (Fehintola, 2009).

Previous studies have reported that horizontal gene transfer is a factor in the occurrence of antibiotic resistance in clinical isolates and suggested that the high prevalence of resistance to a particular antibiotic does not always reflect antibiotic consumption as previously suggested by other scholars (Ako-Nai et al., 2005; Nwanze et al., 2007; Abubakar, 2009). Notwithstanding the knowledge of contribution of misuse of antibacterial agents to the development and spread of drug resistance, there appears to be total lack of efforts at controlling the use of this life-saving medication amongst the general populace particularly in Nigeria and many other countries of Africa (Fehintola, 2009). Rational and optimal use of antibiotics should be predicated on the right information with respect to epidemiology; ensuring the training and retraining of prescribers with respect to proper orientation to the use of antibiotics; provision of essential laboratory facilities for bacteriological diagnosis and controlling information and marketing in such way as to ensure promotion and availability of the essential antibiotics. The unbridled advertisement, promotion and sale of antibiotics as currently practiced in Nigeria can only encourage antibacterial drug resistance and the attendant threat from bacteria (Akande and Ologe, 2007; Fehintola, 2009). The zones of inhibitions shown by these brands of antibiotics against the test organisms indicate their potencies (Cheesbrough, 2006). The potencies of course have to do with the active ingredients contained in each of the antibiotics since the test were compared to the standards. In line with the assertions of Winstanley et al. (1997) and Abubakar (2009), even though susceptibility pattern shown in this study emphasizes the need for *in vitro* sensitivity reports before initiation of antibiotic therapy, it must not be forgotten that *in vitro* antimicrobial sensitivity reports serve only as guide and that conditions *in vivo* may be quite different. The data presented in this and in previous studies may be of immense value for use to

determine trend in antimicrobial sensitivities, to formulate local antibiotic policies to compare local with national and international data and above all, to assist clinicians in the rational choice of antibiotic therapy and to prevent misuse, or over use of antibiotics. The data obtained in this study shows that the bacteria causing most community and nosocomial infections are still susceptible to anti-microbial agents routinely used in the hospital though this is changing. Although the disc diffusion method was used to assess sensitivity and resistance and can be correlated clinically, further investigations employing the MIC method will be needed to obtain more reliable results (Abubakar, 2009).

Other factors, though not tested in this study, that could have affected their potencies include storage procedure, temperature, adulteration, humidity, expiring dates, pathophysiological state of the patient, natural history of the infection, presence of R-factor, age of patient, etc. Also, the widespread counterfeiting of these antibiotics, excessive decomposition of active ingredient as a result of exposure to high temperature and humidity, and poor quality assurance during manufacturing which are not exceptions, were not investigated; however, the differences in efficacy among brands of the antibiotics constitute a grave danger to health. There is therefore an urgent need for all pharmaceutical products manufacturers to make sure that the manufacturing of antibiotics is undertaken in accordance with the basic principles of good manufacturing practices (GMP). They should be sold and distributed by pharmaceutical medical representatives. The pharma-ceutical inspectorate division of the Federal Ministry of Health in conjunction with National Agency for Food and Drug Administration and Control (NAFDAC) should be empowered to arrest and prosecute hoodlums and inspect these antibiotics accordingly. The label on the package and the leaflets in the package should provide instruction for the use of the antibiotic and its potential adverse reactions. The antibiotic should indicate the name dosage of the product, date of manufacture, identification number, formulation, batch number, quality assurance and control provisions, name of manufacturer and supplier (Immaculata and Abraham, 1990).

Moreover, the application of some industrial and good manufacturing practices should be applied (Connor and Berlin, 2000). These include that: (1) all equipment, including sterilizers, air filtration and water treatment systems should be subject to planned maintenance, validation and monitoring; (2) the industrial environment should be cleaned frequently and thoroughly in accordance with the written programme approved by the quality control department; (3) the use of nutrient media that support microbial growth in trials to stimulate aseptic' operations (Sterile media fills, "broth fills") is a valuable part of the overall validation of an aseptic process and should be employed; (4) the microbiological contamination of starting materials should be minimal and the "bioburden" should be monitored before sterilization and (5) each heat sterilization cycle should be recorded by appropriate equipment with suitable accuracy and precision.

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