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Evaluation of Therapeutic Equivalence of Different Antibiotics Brands

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ABSTRACT

Different antibiotics were selected, two local brands and one multinational brand for the same antibiotic so that comparison will be quite easy. Antibiotics used during the research work were Ofixime (Cebosh, Megnet, Fixitile), Paramycin (Nebra, Eyebrex, Tobracin), Emoxicillin (Supramox, Polyxil, Ospamox). These antibiotics were checked for their potential as antibacterial agents against some gram positive and gram negative bacterial strains, by agar well diffusion method. Antibacterial activity was deliberated against five bacterial strains i-e *Klebsiella pneumonia, E.Coli, Salmonella, Staphylococcus Aureus and Flavobacterium Aureus.*

Keywords: Antibacterial activity, Ofixime, Paramycin, Emoxicillin

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INTRODUCTION

An antibacterial is an agent that work in two ways that is either stop the growth of the bacteria or completely kills the bacteria.[1] The term antibacterial is mostly used interchangeably with antibiotic(s), but with the increase in the knowledge about the agents causing various infections, the term antibiotic gain much popularity and at present time it represent a broader class of antibacterial compounds that include antifungal and other as well as. The term antibiotic was first of all used by Selman Waksman and his collaborators in 1942. They describe antibiotic as a substance produced by one microorganism but is used against the growth of another microorganism.[2]

Antibiotic resistance has become a global public-health problem, thus it is necessary that new antibiotics continue to be developed. Antibacterial, Antifungal, Antitumor and Anticancer activity has been recognized and they are also active against a wide range of organisms e.g *C. Albicans, E. Coli, S. Aureus, B. Polymyxa, P. Viticola* etc. At present time, there are so many Antibiotics used against the infections caused by a large number of Bacteria or we can say that these antibiotics have great medical or clinical uses. Antibiotic resistance is a global health priority.[3]

The standard recommendation for treatment of young, febrile children with urinary tract infection has been hospitalization for intravenous antimicrobials. The availability of potent, oral, third-generation cephalosporin's as well as interest in cost containment and avoidance of nosocomial risks prompted evaluation of the safety and efficacy of outpatient therapy. Oral cefixime can be recommended as a safe and effective treatment for children with fever and urinary tract infection. Use of cefixime will result in substantial reductions of health care expenditures.[4] The emergence of multi drug-resistant Salmonella typhi (MDRST) in many developing countries including Pakistan, has led to a search for suitable alternatives to conventional therapy. Quinolones have been found to be an effective alternative for the treatment of MDRST, in adults as well as in children.[5]

The present study was concerned with the use of three antibiotics. The antibiotics Ofixime (Cebosh, Megnet, Fixitile), Paramycin (Nebra, Eyebrex, Tobracin), Emoxicillin (Supramox, Polyxil, Ospamox), were evaluated against the five bacterial strains i-e *Klebsiella Pneumonia, E.Coli, Salmonella, Staphylococcus Aureus and Flavobacterium Aureus.*

MATERIALS AND METHODS

Chemicals

All the studies were carried out at Kohat University of Science & Technology (KUST) Khyber Pukhtoonkhwa Pakistan. Chemicals used were Acetone, Nutrient agar(Muller-Hington agar). Antibiotics were purchased from market including Ofixime (Cebosh, Megnet, Fixitile), Paramycin (Nebra, Eyebrex, Tobracin), Emoxicillin (Supramox, Polyxil, Ospamox).

Apparatus used

Digital Balance, Beaker, Volumetric Flask, Oven(Oven Bescicking Loading Model 100-800 Memmert), Petri Dishes, Autoclave Digital Control Fuzzy System, Luminar Chamber, Cork Borer (6mm in diameter), Micropipette, Incubator.

Making Dilutions of Antibiotics

Dilutions of antibiotics were prepared according to the instructions provided on the label claim . Total 5 dilutions were prepared, so that concentration goes on decreasing from first to fifth.

Antibiotic Ofixime Dilutions

Three brands of Ofixime were used during research work i-e Cebosh (Bosch Pharmaceuticals), Megnet (Contenintal Pharmaceutical), Fixitile (Tabros Pharmaceuticals). These three antibiotics were mentioned 30ml after reconstitution. After reconstitution, 5ml suspension was taken and was mixed with 45ml distilled water so stock solution was prepared. Concentration of stock solution was 100mg/50ml. Now 25ml of suspension was taken from the stock solution and to this 25ml of distilled water was added and was labeled as first dilution. Same procedure was used to make the remaining dilutions.

Stock dilution concentration=100mg/50ml,

First dilution concentration=50mg/50ml,

Second dilution concentration=25mg/50ml,

Third dilution concentration=12.5mg/50ml,

Fourth dilution concentration=6.25mg/50ml,

Fifth dilution concentration=3.12mg/50ml.

Antibiotics Emoxicillin Dilutions

The dilutions of Emoxicillin were prepared by the same procedure as mentioned for Ofixime. Antibiotic Emoxicillin was 60ml after re-constitution. Five dilutions were prepared for amoxicillin as for Ofixime. And just like Ofixime, the concentration of Emoxicillin was 100mg/50ml.

Stock dilution concentration=100mg/50ml,

First dilution concentration=50mg/50ml,

Second dilution concentration=25mg/50ml,

Third dilution concentration=12.5mg/50ml,

Fourth dilution concentration=6.25mg/50ml,

Fifth dilution concentration=3.12mg/50ml.

Antibiotic Paramycin Dilution

Paramycin antibiotic was taken in injectable form. Five dilutions were prepared but with different concentration as compared to Ofixime, Emoxicillin and Paramycin.

First dilution concentration=7.5mg/5ml.

Second dilution concentration=3.75mg/5ml.

Third dilution concentration=1.87mg/5ml.

Fourth dilution concentration=0.93mg/5ml.

Fifth dilution concentration=0.46mg/5ml.

BIOASSAYS

Anti-Bacterial Assay

Anti-Bacterial activities mean to check the selected antibiotics that whether they show resistance against the selected bacteria or not. As these micro-organisms may affect us so to check anti-bacterial activities winter season is the best because during winter the growth of these micro-organisms is very slow so we will be able to carry out activities without any problem. Five bacterial strains were used to check the anti-bacterial activities of the selected antibiotics.[6] Anti-bacterial activities consist of following steps.

Preparation of Media

Nutrient Agar

28g of nutrient agar (Muller-Hington) was dissolved in one liter of distilled water in a volumetric flask(1L). The media was then autoclaved for 15 min at 121°C and then for 15-20 minutes, in order to sterilize the media, after sterilization the media is cooled to about 45°C in order to solidify the media.

Bacterial Growth

Bacterial strains used during the research work were i-e *Klebsiella Pneumonia, E.Coli, Salmonella, Staphylococcus Aureus and Flavobacterium Aureus*. Most important step involve in the anti-bacterial activities is the growth of Bacterial strains. These strains of bacteria were obtained from the Department of Pharmacy, Microbiology Laboratory KUST. In order to get fresh growth of bacterial strains, these were grown on Muller-Hington Agar plate and were placed in the oven for about 24hrs. So a fresh growth of the bacteria of the interest was obtained

and was used throughout the activities (bacterial strains refreshed). These were grown carefully so that to minimize the risks of contamination.

Preparation of plates

The plates were washed well, dried in an oven at 120°C, covered with aluminum foil, and sterilize in autoclave at 121°C for 40 minutes in order to kill the micro-organisms if any. And in order to avoid any contamination in plates, plates after sterilization were washed with ethanol. About 25ml of hot medium was poured in plates, while working in Luminar chamber. The plates were kept at rest for 5 minutes to cool and to solidify.

Boring of Wells

After preparing all the plates, a cork borer with diameter 6mm was taken, sterilized with a flame, and then cooled down and after cooling, a well was bored in the plate and marked with bacterium name, and antibiotic name and wells were numbered from 1 to 5 because of the five dilutions of each antibiotic already prepared.

Culturing of Bacteria

When media in the plates solidified completely, took one plate and at the time aluminum loop was sterilized in a flame until it become red-hot and then cooled in sterilized distilled water. The loop witted with distill water was put (touched) in the plate in which the test is to be carried out, for inoculation. The loop was then put in the plate having refreshed bacterial strains and then the bacteria were inoculated.

Injection of Samples

After inoculation, the samples were injected in the holes with the help of a micropipette. The capacity of a single hole is about 90-100 µL.

Development of Plates

After the completion of the process, the plates were then kept at room temperature, first, in order to evaporate the extra solvent then sealed and kept in an incubator at 37°C for about 24hrs. The zone of inhibition was noted after 24hrs and was measured.

RESULTS AND DISCUSSON

Antibacterial Activities

The antibiotics Ofixime (Cebosh, Megnet, Fixitile), Paramycin (Nebra, Eyebrex, Tobracin), Emoxicillin (Supramox, Polyxil, Ospamox) were evaluated against the five bacterial strains i-e *Klebsiella Pneumonia, E.Coli, Salmonella, Staphylococcus Aureus and Flavobacterium Aureus* (7).

Table 1: Zone of inhibition of antibiotic OFIXIME (CEBOSH)

Name of bacteria	Zone of inhibition(mm) Concentration of antibiotic(mg/50mL)				
	6.25	12.5	25	50	100
Salmonella	2mm	2mm	14mm	15mm	17mm
E.Coli	2mm	2mm	2mm	19mm	20mm
F.A	17mm	19mm	20mm	25mm	25mm
K.P	2mm	2mm	2mm	2mm	2mm
S.Aureus	2mm	2mm	2mm	15mm	16mm

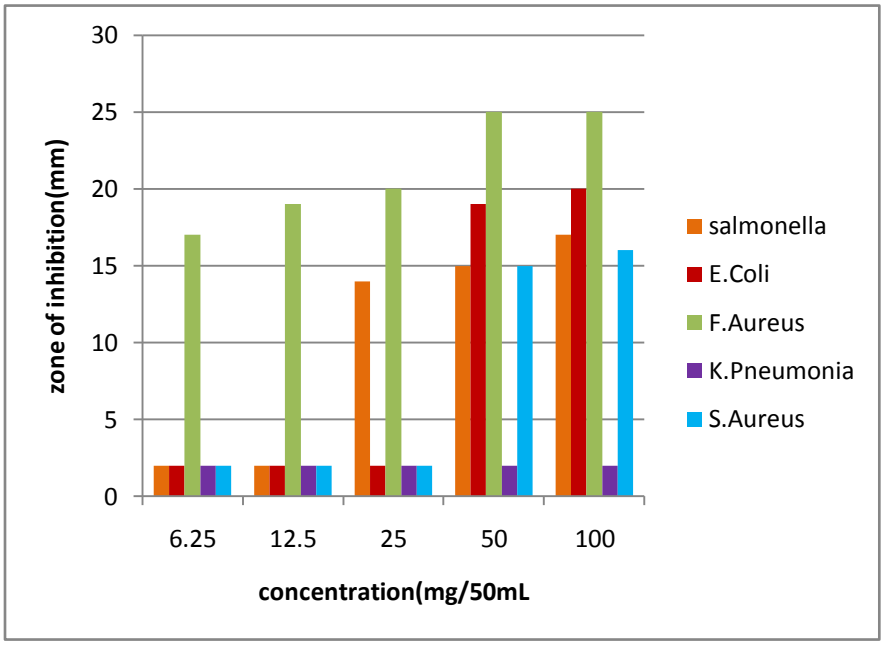

Figure 1: Graphical presentations for the zone of inhibition for Antibiotic OFIXIME (Cebosh)

It is obvious from the graph and table that at the concentration 25mg/50mL and below all the bacterial strains have no activity except *F.A* which has good activity even at low concentration that is 6.25mg/50mL. Ofixime (Cebosh) gives significant activity against *E.Coli* and *F.A* at concentration of 100mg/50mL. Ofixime (Cebosh) showing no activity against the bacterial strain *K.P* at all the concentration range studied.

Table 2: Zone of Inhibition for Antibiotic

Name of Bacteria	Zone of inhibition(mm) Concentration of Antibiotic(mg/50mL)				
	6.25	12.5	25	50	100
Salmonella	20mm	24mm	26mm	23mm	28mm
E.Coli	2mm	2mm	18mm	20mm	25mm
F.A	2mm	2mm	15mm	20mm	22mm
K.P	15mm	18mm	20mm	24mm	31mm
S.Aureus	2mm	17mm	19mm	21mm	25mm

OFIXIME (Magnet)

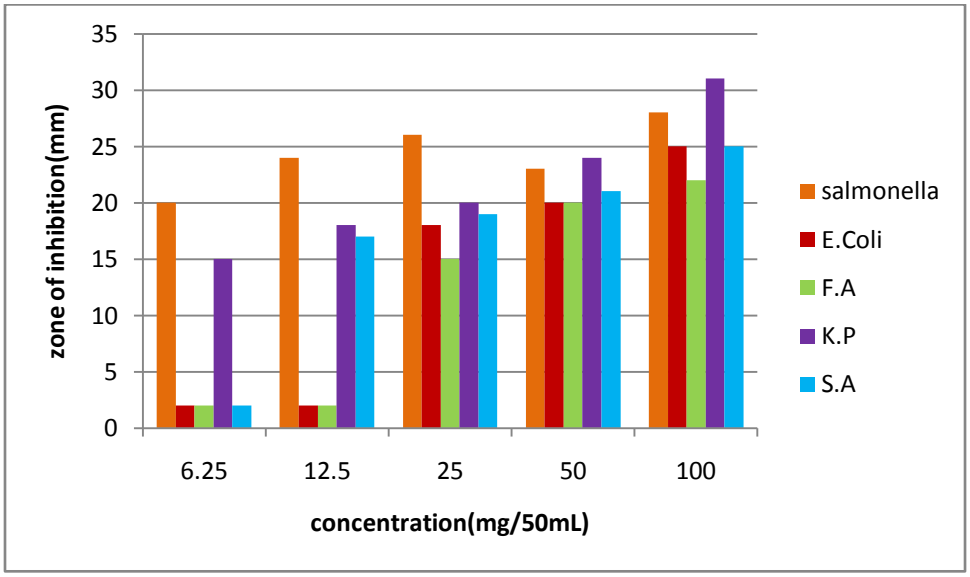

Figure 2: Presentation of the zone of inhibition for Antibiotic OFIXIME (Megnet)

It is obvious from the graph and table that antibiotic Ofixime (Magnet) shows significant activity against all the bacterial strains (*E.Coli*, *S.A*, *K.P*, *F.A*, *Salmonella*) at the concentration of 50mg/50mL and 100mg/50mL. *Salmonella* shows maximum activity even at low concentration i-e 6.25mg/50mL. *K.P*, *F.A* shows good activity at concentration of 25mg/50mL and 12.5mg/50mL. *F.A*, *E.Coli* and *S.A* shows no activity at the concentration of 12.5mg/50mL and 6.25mg/50mL.

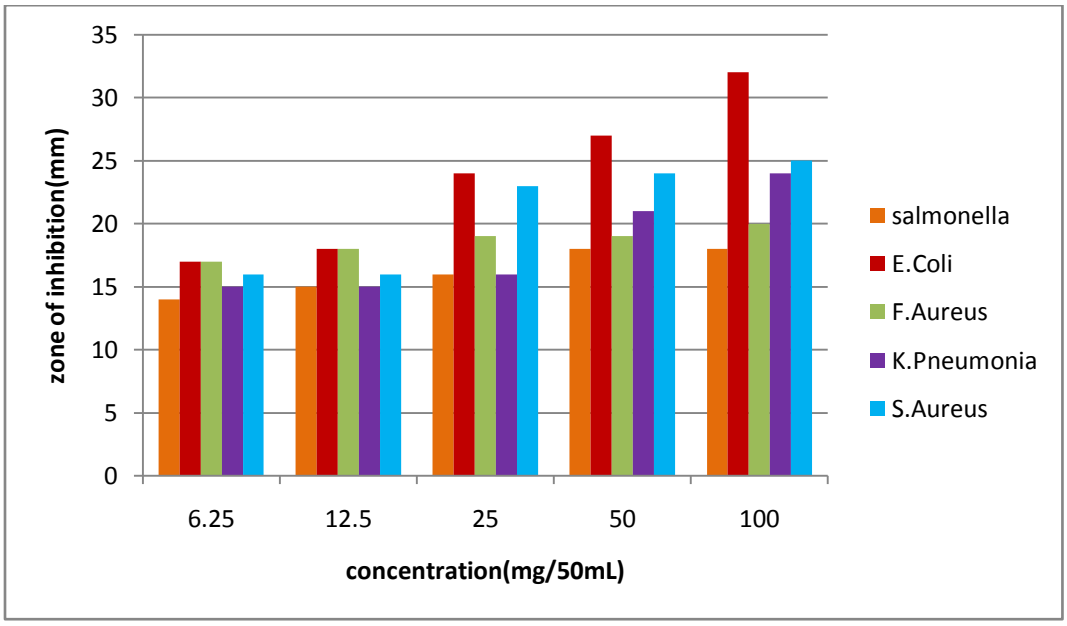

Figure 3: Graphical presentations for the zone of inhibition of Antibiotic OFIXIME (Fixitile)

Table 3 : Zone of Inhibition for Antibiotic OFIXIME (Fixitile)

Name of Bacteria	Zone of inhibition(mm) Concentration of Antibiotic(mg/50mL)				
	6.25	12.5	25	50	100
Salmonella	14mm	15mm	16mm	18mm	18mm
E.Coli	17mm	18mm	24mm	27mm	32mm
F.A	17mm	18mm	19mm	19mm	20mm
K.P	15mm	15mm	16mm	21mm	24mm
S.Aureus	16mm	16mm	23mm	24mm	25mm

Similarly the graph and table that Ofixime (Fixitile) show significant activity against *E.Coli, K.P, S.A and F.A* at concentration of 25mg/50mL, 50mg/50mL and 100mg/50mL. While showing good activity against *E.Coli, S.A, F.A* and *K.P* at concentration of 25mg/50mL, 12.5mg/50mL. *Salmonella* shows low activity against the applied antibiotic at concentration of 6.25mg/50mL.

Table 4 : Zone of inhibition for antibiotic EMOXICILLIN (supramox)

Name of Bacteria	Zone of inhibition(mm) Concentration of antibiotic(mg/50mL)				
	6.25	12.5	25	50	100
Salmonella	19mm	20mm	30mm	31mm	33mm
E.Coli	2mm	2mm	2mm	2mm	2mm
F.A	2mm	2mm	2mm	2mm	2mm
K.P	2mm	2mm	2mm	2mm	2mm
S.Aureus	2mm	2mm	2mm	2mm	2mm

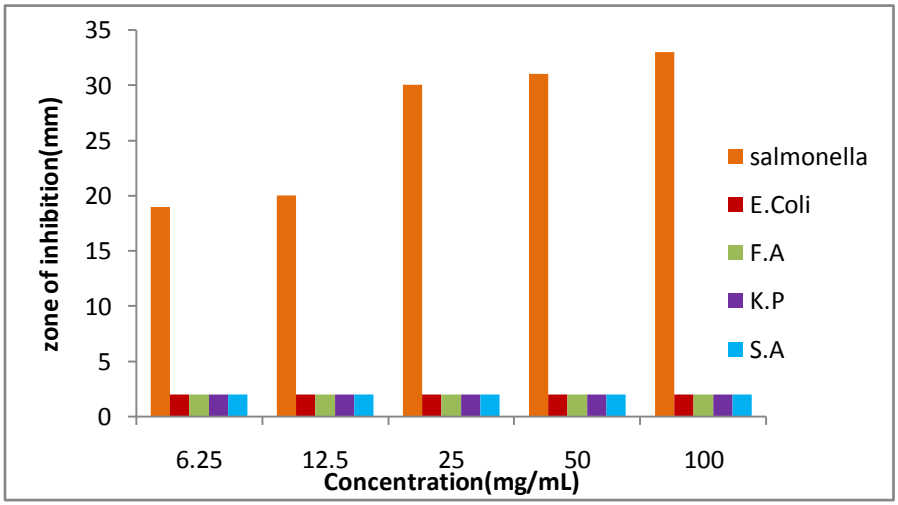

Figure 4 :Graphical presentations for the zone of inhibition of Antibiotic EMOXICILLIN (Supramox)

It is obvious from table and graph that *Salmonella* shows larger zone of inhibition. While Emoxicillin (Ospamox) has showing no activity for the bacterial strains e.g *E.Coli, F.A, K.P* and

S.A at all the concentration range studied, means showing no zone of inhibition. In term of activity, the applied antibiotic shows significant activity against *Salmonella*. While at low concentration i-e 6.25mg/50mL, it shows good activity against the same strain of bacterium.

Table 5: Zone of inhibition for Antibiotic EMOXICILLIN (polyxil)

Name of Bacteria	Zone of inhibition(mm) Concentration of Antibiotic(mg/50mL)				
	6.25	12.5	25	50	100
Salmonella	20mm	24mm	30mm	32mm	40mm
E.Coli	2mm	2mm	2mm	2mm	2mm
F.A	20mm	25mm	25mm	30mm	32mm
K.P	2mm	2mm	2mm	2mm	2mm
S.Aureus	2mm	2mm	2mm	2mm	2mm

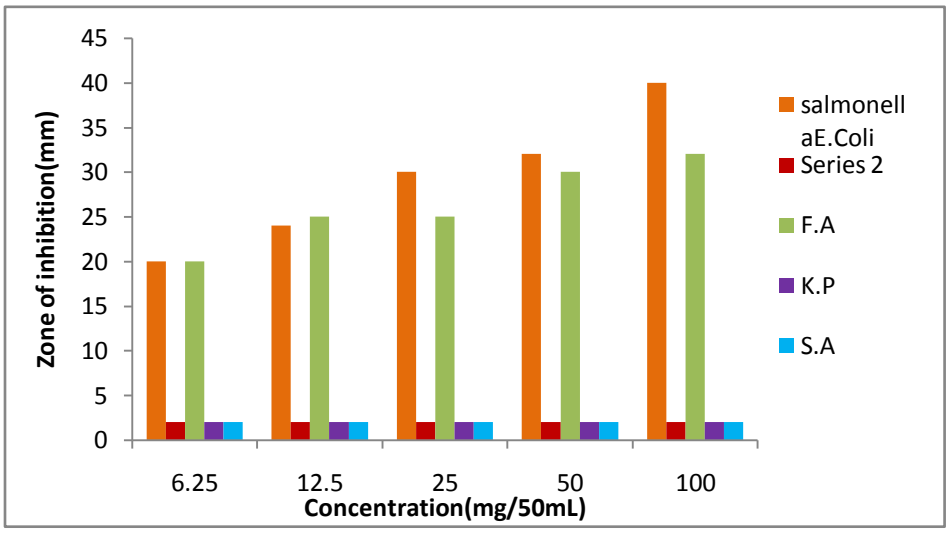

Figure 5: Graphical presentations for the zone of inhibition of Antibiotic EMOXICILLIN (Polyxil).

According to the graph and table that at concentration 6.25mg/50mL, *Salmonella* and *F.Aureus* has good activity, while at high concentration 50mg/50mL and 100mg/50mL it shows significant activity. Emoxicillin (Polyxil) showing no activity for the bacterial strains i-e *E.Coli*, *K.P* and *S.A* at all concentration range studied.

Table 6: Zone of inhibition for antibiotic *EMOXICILLIN* (ospamox)

Name of Bacteria	Zone of inhibition(mm) Concentration of Antibiotic(mg/50mL)				
	6.25	12.5	25	50	100
Salmonella	24mm	25mm	29mm	30mm	30mm
E.Coli	2mm	2mm	2mm	2mm	2mm
F.A	25mm	25mm	26mm	28mm	30mm
K.P	2mm	2mm	2mm	2mm	2mm
S.Aureus	20mm	22mm	30mm	35mm	35mm

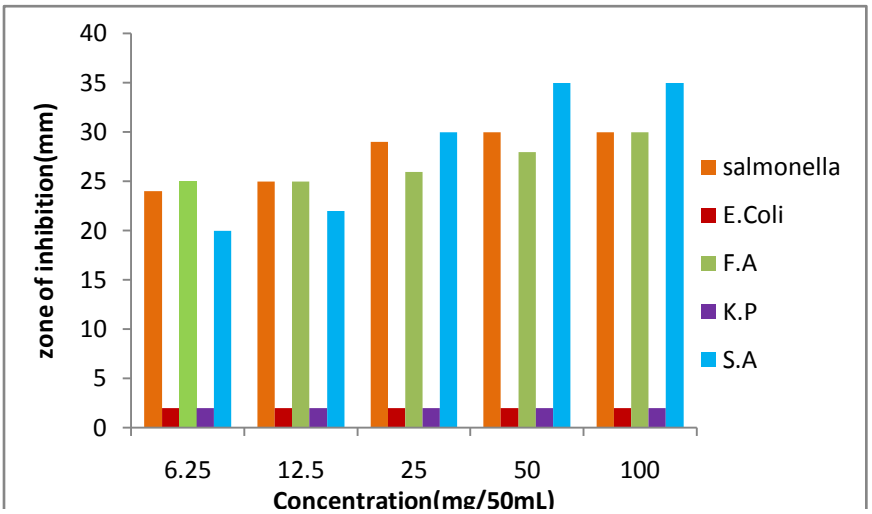

Figure 6: Graphical presentations for the zone of inhibition of Antibiotic EMOXICILLIN (Ospamox)

It is obvious from the graph and table that Emoxicillin (Ospamox) shows significant activity against *Salmonella, F.Aureus, S.Aureus* at all concentration range studied. While *E.Coli* and *K.P* showing no activity at all the concentration range studied.

Table 7: Zone of inhibition for antibiotic PARAMYCIN (Nebra)

Name of bacteria	Zone of inhibition(mm) Concentration of Antibiotic(mg/5mL)				
	0.46	**0.93**	**1.87**	**3.75**	**7.5**
Salmonella	23mm	25mm	26mm	29mm	36mm
E.Coli	15mm	19mm	20mm	21mm	25mm
F.Aureus	19mm	20mm	20mm	25mm	30mm
K.Pneumoniae	19mm	19mm	24mm	25mm	25mm
S. Aureus	2mm	15mm	19mm	20mm	25mm

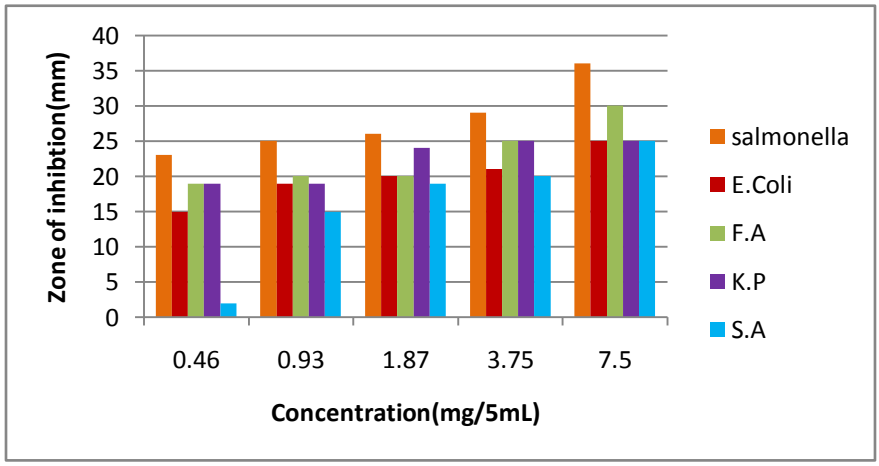

Figure 7: Graphical presentations for the zone of inhibition of Antibiotic PARAMYCIN (Nebra)

Graph and table shows that, at low concentration (0.46mg/5mL), *E.Coli* has good activity and *Salmonella* showing no activity. At concentration 0.93mg/5mL, *Salmonella* shows good activity. While at high concentration that is beyond 0.93mg/5mL, all the bacterial strains(*Salmonella, E.Coli, K.P, F.A and S.A*) give significant activity.

Table 8: Zone of inhibition for antibiotic PA*RAMYCIN* (Eyebrex)

Name of Bacteria	Zone of inhibition(mm) Concentration of Antibiotic(mg/5mL)				
	0.46	**0.93**	**1.87**	**3.75**	**7.5**
Salmonella	17mm	19mm	20mm	27mm	29mm
E.COLI	14mm	17mm	17mm	20mm	25mm
F.Aureus	2mm	2mm	20mm	24mm	29mm
K.Pneumoniae	2mm	2mm	20mm	24mm	26mm
S.Aureus	2mm	2mm	20mm	20mm	25mm

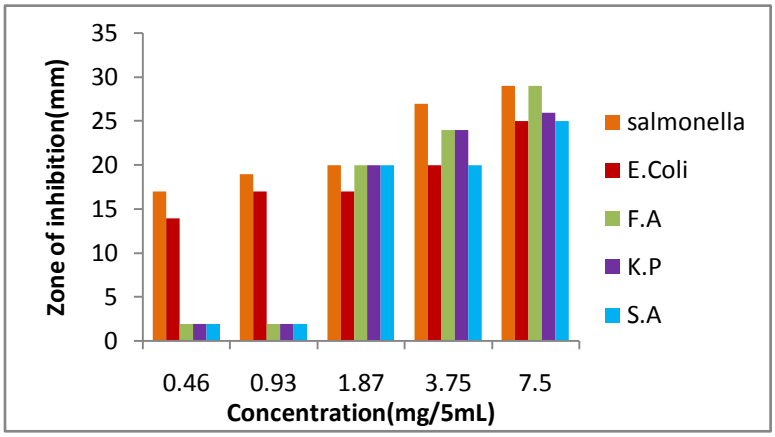

Figure 8 Graphical presentations for the zone of inhibition of Antibiotic PARAMYCIN (Eyebrex)

According to the graph and table *Salmonella* shows good activity at concentration 0.46mg/50mL while *E.Coli* at the same concentration shows low activity. *S.A, K.P and F.A* has no activity at concentration 0.46mg/5mL and 0.93mg/5mL. Paramycin(Eyebrex) give a significant against *Salmonella, S.A, K.P, F.A ans E.Coli* at concentration 1.87mg/5mL, 3.75mg/5mL and 7.5mg/5mL.

Table 8: Zone of inhibition for antibiotic PA*RAMYCIN* (*Tobracin*)

Name of Bacteria	Zone of inhibition (mm) Concentration of Antibiotic(mg/5mL)				
	0.46	**0.93**	**1.87**	**3.75**	**7.5**
Salmonella	2mm	22mm	23mm	25mm	35mm
E.Coli	2mm	2mm	2mm	2mm	2mm
F.Aureus	2mm	2mm	2mm	25mm	30mm
K.Pneumoniae	17mm	17mm	19mm	20mm	25mm
S.Aureus	25mm	27mm	27mm	30mm	35mm

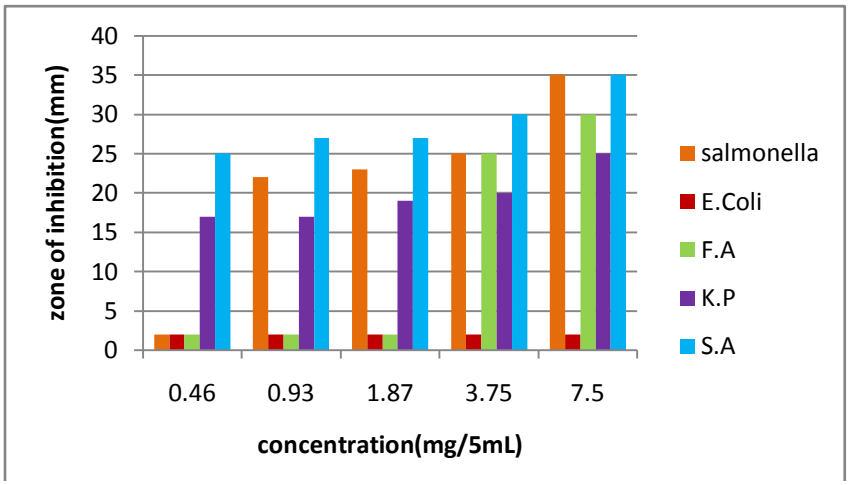

Figure 9 Graphical presentations for the zone of inhibition of Antibiotic PARAMYCIN (Paracin)

According to the graph and table at concentration 0.46mg/5mL, K.P shows good activity and S.A gives significant activity while *Salmonella* and *F.A* shows no activity at the same concentration. when the concentration increases, *Salmonella, K.P, S.A and F.A* shows significant activity. Tobramycin (Tobracin) has showing no activity against the bacterial strain *E.Coli* at all the concentration range studied.

CONCLUSION

It is found that the Antibiotic OFIXIME (all brands namely Cebosh (Bosch Pharmaceuticals), Megnet (Continental Pharmaceuticals), Fixitile (Tabros Pharmaceuticals). are active against both the rods and rounded shaped (cocci) bacteria equally. Antibiotic EMOXICILLIN shows variations in activity that is most of the strains (rods , cocci) are resistant to two brands supramox (Bosch Pharmaceuticals) and polyxil (Polyfine Chempharma) but not for ospamox (Novartis Pharma) which is due to the fact that this brand (ospamox) has higher pharmaceutical properties so more activity than other two against the bacterial strains used(*E.Coli, Salmonella, Staphylococcus Aureus, Flavobacterium Aureus, Klebsiella Pneumonia*). Antibiotic PARAMYCIN is found active against both gram positive, gram negative, rods and cocci. Brand Eyebrex is most active against all the five strains (*E.Coli, Salmonella, S.A, F.A, K.P*) and even at low concentration against *Salmonella* and *E.Coli* as compared to Nebra and Paracin that may be due to the more purity or best formulation of Paramycin (Eyebrex). Except OFIXIME and PARAMYCIN, *E.Coli* is resistant to all other antibiotics or showing no activity.

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