A comparative study of antibacterial activity of antibiotics with different manufacturing origin

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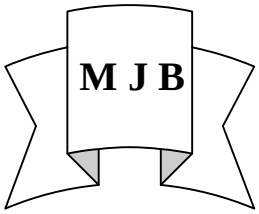

Abstract

This comparative study tested many antibiotics from different sources which were collected from local pharmacy in Iraq to determine their activities against some bacteria species. The antibiotics included in this study were 25 of 17 different origins from 5 countries against 5 types of bacteria .The Kirby-Bauer test has shown wide differences of inhibition zones of each origins of same antibiotics against same type of bacteria in vitro .

الخلاصة

قارنت الدراسة بين العديد من المضادات الحيوية الموجودة في الاسواق العراقية والمنتجة من مناشيء مختلفة لمعرفة الفروقات النوعية لتأثير تلك المناشيء على العديد من الانواع البكتيرية ، حيث استخدم 25 مضاد حيوي لـ 17 منشأ من 5 دول مختلفة . دُرس تأثير هذه الانواع من المضادات على خمس انواع من البكتريا وباستخدام طريقة Kirby-Bauer test تم تسجيل الفروقات النوعية للمناطق المثبطة حول مستعمرات البكتريا الناتجة من كل نوع من المناشيء المختلفة وكانت تلك الفروقات واضحة بين العديد من المناشيء على نفس النوع من البكتريا .

Introduction

An antibiotic is a drug that kills or slows the growth of bacteria. Antibiotics are one class of antimicrobials, a larger group which also includes anti-viral, anti-fungal, and anti-parasitic drugs. They are relatively harmless to the host, and therefore can be used to treat infections. The term, coined by Selman Waksman, originally described only those formulations derived from living organisms, in contrast to "Chemotherapeutic agents", which are purely synthetic. Recently the term "antibiotic" is also applied to synthetic antimicrobials, such as the sulfa drugs.(1)Antibiotics are small molecules with a molecular weight less than 2000 Dalton ,were labelled " Magic bullets " drugs which target disease without harming the host.(2)

Conventional individual antibiotics vary widely in their effectiveness on various types of bacteria. Antibiotics can be categorised based on their target specificity : 'narrow-spectrum' antibiotics target particular types of bacteria, such as gram-negative or gram-positive bacteria, while 'wide-spectrum' antibiotics affect a larger range of bacteria.The effectiveness of individual antibiotics also varies with the location of the infection, the ability of the antibiotic to reach the site of infection, and the ability of the bacteria to resist or inactivate the antibiotic. Some antibiotics actually kill the bacteria (bactericidal), whereas others merely prevent the bacteria from multiplying (bacteriostatic) so that the host's immune system can overcome

them(3).Antibiotics can also be classified by the organisms against which they are effective, and by the type of infection in which they are useful, which depends on the sensitivities of the organisms that most commonly cause the infection and the concentration of antibiotic obtainable in the affected tissue, but, what about the industrial differences of antibiotics from same origin to others ?

Materials and Methods

1-Antibiotics .

The antibiotics used in this study are shown in table 1, together with their potencies, trade name and origins of supplies .

2- Bacteria

The study elected five species of pathogenic bacteria ,represented by *Staphylococcus aureus* , *Escherichia coli* , *Klebsiella pneumonia*., *Proteus spp.* and *Pseudomonas aeruginosa,* these were diagnosed according to (4) .The density of bacteria was 10^6 cells /*ml* . They were cultured on Mueller-Hinton medium and incubated aerobically at 37°C for 24 h.

3-Antibiotics concentrations :

All antibiotics concentrations had been prepared as the following value :
weight(mg) / solvent (ml)

solvent was 10 ml from distilled water , and the weight according to their weight in capsules or vials. The concentrations of antibiotic can be seen in table 1

4 - Preparation of antibiotic disks :

Sterile filter paper disks 5 *mlm* in diameter were embedded about 30 min. in each antibiotic concentration , then dried by sterile filter paper , one disk of each antibiotic falls in a place on the culture media of each species of bacteria . Lightly touch each disc with sterile inoculating loop to make sure that it is properly contact with the agar surface. Incubate upside down at $37C^o$ for 24 h. (**5)** .

Results and Discussions

Table 2 shows that there are some differences between each origin of the same antibiotic types.
. The figures 1,2,3,4,5 and 6 shown the qualitative differences among these origins of antibiotics . **Figure 1** shown the antibiotic Cefalexin from ANVAXX laboratory has a good ability to inhibit the different types of bacteria more than other types of Antibiotic origins ,for example , in the case of *Klebsiella* and *E . coli* the inhibition zone reached to 30 , 29 *mlm* respectively , but in other origins such as ACIA and INDIA did not reached to 20 *mlm* , and simple differences have been seen in the case of SDI (Samara Drug Industry), AJANTA and MICRO LAB. in each of *Klebsiella* . and *E .coli* . So in the case of *Pseudomonas* the distance between Cefalexin of ANVAXX laboratory and Cefalaxin of India was about 15 *mlm* , this difference is too much and may refer to activation of some origin to another,a similar result was obtained in the case of *Proteus* . In the case of *Staphylococcus aureus* in spite of some inhibition zone had been obtained but only ANVAXX origin with 19 *mlm* it was considered effective depending on standard sheet (6) .

In Erythromycin 250mg ,the four origins (ANHUI; ARBRO; S.D.I. and ACAI) are found in Iraqi market , so the study used these origins to compare with each other . In this case, SDI showed the best results against all types of bacteria them study than the other types of origins such as ANHUI and ARBRO ,but ACIA had shown a good result.

In case of Tetracycline, Flamingo had shown a good reaction against bacteria by 26 *mlm* in the case of *Klebsiella* , *25 mlm* against *Pseudomonas* , *25 mlm* against *E. coli* and 24 *mlm* in *Proteus* , but *S. aureus* resisted all origins in spite of

small inhibition zones had been obtained but these zones were under active ranges of antibiotic against these bacteria according to the standard sheet (6) .

SMITH KLINE Ampicillin had good distances for each other origin , simple distances had been seen with JULPHAPEN in each bacteria under study , but an important distance between SMITH KLINE and other origins such as MADEIN , SDI and ARBRO had shown , these distances in the case of *E. coli , Staphylococcus , Proteus ;Klebsiella , ,Pseudomonas* were 7,4,2*mlm*; 8 ,7,4*mlm*; 10,6,5 *mlm* ;7,3,3 *mlm* ;12,11,7*mlm* respectively . and other differences in the case of Amoxicillin can be seen in figure 5 .

In the case of Amoxillin , three different origins had been studied , the results shown some differences among the actions of these origins ,RAM PHARMA Amoxillin had a good ability to inhibit the bacteria under study with a simple distance with the later one LAB LIMITED ,and with an important difference with AJANTA origin .

In the case of Ceftriaxone (1g) ,SMITH LINK and FLAMINGO have a similar activation against bacteria with very simple differences can be seen in Figure 6 ,and RANBAXY and LABORATE have a similar activity ,but the difference between group one and group two is wide ,these result can be clearly observed in **table 2** and **figure 6** The results exposed some differences that have been present among the origins under study , and some origins have shown a similar activities against the same bacteria , such of these results have been got in ACAI and INDIA of Cefalexin against *Proteus* and *S. aureus* with 13,8 *mlm* respectively , and ANHUI and ACIA in the case of Erythromycin against *Klebsiella* and ARBRO and ACIA in the case of *S. aureus* , and others can be seen in **table 2** , this phenomenon may mean that some of the origins have a similar action against the same bacteria due to the similarity of manufacturing characters of these origins .

One of the many causes of different origins activities is the combination materials of these origins and all drug industries assist for this fact (7,8). The raw materials and others of these origins are kept as a mystery by these companies (8,9) .

Some investigates have studied the variation activities among different origins , a study (10) revealed the differences between 5 origins of Tetracycline , and this study observed a high variation among these five origins. By different references (4,7,8,9,10) , the companies of drugs used different origins of raw materials to produce the same Antibiotics ,this is the essential reason for the differences that have been obtained among the origins .

The studies (9,10,11) had observed clearly variations between different antibiotic origins and conceived more reasons that accumulate to give these facts , starting from raw material and it's purity ,to the company's work and cheat of some industries ,flow methods of the these industries, concentration of effect material of antibiotics and adulteration ,storage methods and carriage methods of antibiotics (12) According to these results ,in all cases where SDI had been tested , the activity of SDI was more active against some of others origins .

The study had been done in vitro, and the results of different activities were studied out of body without view of body activities and exchanging of material by body fluids or enzymes or other processes that may change the activities of drugs (13, 14) .

References

1- Langevelde P.v , Dissel J. T., Ravensbergen E., Appelmelk B. J., Schrijver I. A., and.Groeneveld P. H. Antimicrobial Agents and Chemotherapy, December 1998, Vol. 42, p. 307-314.

2-Sharon J. Gardiner and Evan J. Begg ,Antibiotics - Magic bullets, Pharmacol Rev , 2006, Vol . 58 pp.521-590

3- Bell S.M., Gatus B.J., Pham J.N. and Rafferty D.L., Classification of Antibiotics ,2003,pp.123-129 .

4-Wistreich MD. and Lechtman D., Laboratory exercises in microbiology, 1980,3rd ed , Vol 1,Glencoe publishing Co.,Inc, p.200 ,312,401.

5- Williamson R ; Le Bouquenec C ; Gutmann L and Horaud T , Techniques in Microbiology: Antimicrobial Susceptibility Testing,1985, Vol.2 ,pp.45-46,87.

6- Ericsson H M and Sherris J C, Antibiotic Sensitivity Testing , Microbiology. Scand ,1999,Vol 22 ,pp.34-36 .

7-Acar J. F. and Goldstein F. W., Antibiotics in laboratory medicine ,1996, pp. 28-32., 4th ed. The Williams & Wilkins Co., Baltimore, Md.

8- Thompson C. ; Fink D. and Nguyen L. , Using of drug materials and herbs in industries , J. Microbiol. 2002, Vol. 131, 1933-40.

9-Evans M E , and Pollack M . Effects of antibiotic class and concentration against different types of bacteria. J. Infect. Dis. ,1993,Vol 167:1336-1343 .

10- White RL and Hancock R E ,Comparative Activity of tetracycline Against 16 Clinical Isolates of bacteria in the United States During 1999-2000. Diag Microbiol Infect Dis. 2007;43:207]

11- Adham A S.; Jams R Y. and Ajfer A D ,Variations between different antibiotic origins against isolate of *Staphylococcus aureus* , J. Saudi Arabic ,2006,Vol.43,pp.23-26 .

12- Tomasz A. and Waks S. The effectiveness of bad storage and carriage to foods and drugs , 1997, FAO articles , Vol.3, pp.212

13- World Health Organization ,2002 Interaction of body mechanisms and drugs and value of drug intake

14- Labro, M T, Interference of Antibacterial Agents with Phagocyte Functions: Immunomodulation or "Immune-Fairy Tales",2000. Clin. Microbiol. Rev. 13: 615-650

Table 1 : The Antibiotics ,their potencies and sources

	Type of antibiotics (Conc. In *mg*)	Trade name	The origin	Industry	mg/ml
1	Ampicillin as trihydrate-250mg	-----	India	Maiden Pharmaceuticals Limited(500mg)	33
2	Ampicillin as trihydrate-250mg		Iraq	S.D.I. IRAQ (300mg)	30
3	Ampicillin as trihydrate–250mg	-----	Netherland	ARBRO PHARMACEUTICAL LIMITED (350mg)	35
4	Ampicillin as trihydrate 250mg	Ampicin	India	JULPHAPEN (300mg)	30
5	Ampicillin as trihydrate 250 mg	Penbitin	India	Smithkline Beecham pharmaceutical (275mg)	27.5
6	Amoxillin 250 mg	Moxiram	Jordan	Ram pharma (380mg)	38
7	Amoxillin 250 mg	Amox	India	Ajanta (320mg)	32
8	Amoxicillin 250mg	Brumox	India	LAB. LIMITED (340mg)	34
9	Cefalexin 250 mg	Apkef	India	Ajanta pharma . limited (430mg)	43
10	Cefalexin 250 mg	Cefex	India	Micro labs limited (320mg)	32
11	Cefalexin 250 mg	Cefix	India	India (360 mg)	36
12	Cephalexin 250 mg	Cefixime	Iraq	ACAI (330 mg)	33
13	Cefalexin 250 mg	Cefixin	USA	Anvaxx lab. (340mg)	34
14	Cefalexin 250 mg	Cephalexin	Iraq	S.D.I. (300mg)	30
15	Ceftriaxone -1g	Oframax	India	Ranbaxy lab. limit.industries(1g)	100
16	Ceftriaxone -1g	Cefxone	India	Laborate pharmaceutical(1 g)	100
17	Ceftriaxone -1g	Glocef	India	Smithkline Beecham pharmaceutical	100
18	Ceftriaxone -1g	Ceftaxone	India	Flamingo pharmaceutical limited	100
19	Erythromycin 250mg	Erythrocyn	India	ANHUI WELCOME FOREIGN TRADE CO.,LTD. (300mg)	30
20	Erythromycin 250mg	ErythroX	India	ARBRO PHARMACEUTICAL LIMITED (340 mg)	34
21	Erythromycin 250mg	Erythrosam	Iraq	S.D.I. IRAQ (300 mg)	30
22	Erythromycin 250mg	Acamycin	Iraq	ACAI (300 mg)	50
23	Tetracycline 250mg	Apcycline	India	Ajanta pharma . limited (300mg)	30
24	Tetracycline 250mg	Samacycline	Iraq	SDI IRAQ (350 mg)	35
25	Tetracycline 250mg	Tetcyclin	India	Flamingo pharmaceutical limited(280mg)	28

Table 2 : The inhibition zones (*mlm*) of antibiotic origins against Bacteria

	Type of antibiotics	The origin	*E coli*	*S. aureus*	*Pr. mirabilis*	*Kl .*	*Ps. aeroginosa*
1	Cefalexin - 250 mg	Ajanta pharma . limited (430mg)	22	10	22	25	17
2	Cefalexin -250 mg	Micro labs limited (320mg)	24	14	25	25	20
3	Cefalexin 250	India (560 mg)	16	8	13	18	8
4	Cephalexin 250	ACAI (530 mg)	18	8	13	19	12
5	Cefalexin 250	Anvaxx laboratory USA	29	19	26	30	24
6	Cefalexin -250 mg	S.D.I. IRAQ (300mg)	23	13	23	24	17
7	Erythromycin-250mg	Anhui Welcome Foreign Trade CO.,LTD. (300mg)	18	15	20	22	20
8	Erythromycin-250mg	Arbro Pharmaceutical Limited	16	12	23	20	14
9	Erythromycin-250mg	S.D.I. IRAQ (300 mg)	22	17	29	23	26
10	Erythromycin-250mg	ACAI (300 mg)	20	12	22	22	21
11	APA- Tetracycline-250mg	Ajanta pharma . limited (300mg)	20	9	20	20	20
12	Tetracycline-250mg	SDI IRAQ	24	11	20	23	21
13	Tetracycline-250mg	Flamingo pharmaceutical limited(500mg)	25	14	24	26	25
14	Ampicillin as trihydrate250mg	Maiden Pharmaceuticals Limited(500mg)	21	10	20	22	13
15	Ampicillin as trihydrate250mg	S.D.I. IRAQ (300mg)	24	11	24	24	14
16	Ampicillin as trihydrate 250mg	Arbro Pharmaceutical Limited(550mg)	26	13	25	24	18
17	Ampicillin as trihydrate 250mg	Julphapen (300mg)	26	14	28	25	25
18	Ampicillin as trihydrate 250mg	Smithkline Beecham pharmaceutical (275mg)	28	18	30	29	25
19	Amoxillin 250 mg	Ram pharma (580mg)	19	16	23	20	18
20	Amoxillin 250 mg	Ajanta(550mg)	10	13	15	12	12
21	Amoxillin 250mg	LAB. LIMITED (450mg)	13	12	22	20	17
22	Ceftriaxone -1g	Ranbaxy laboratories limited industrial areas	22	12	22	18	14
23	Ceftriaxone -1g	Laborate pharmaceutical .	20	11	22	17	10
24	Ceftriaxone -1g	Smithkline Beecham pharmaceutical	28	17	26	24	17
25	Ceftriaxone -1g	Flamingo pharmaceutical limited	28	16	25	22	19

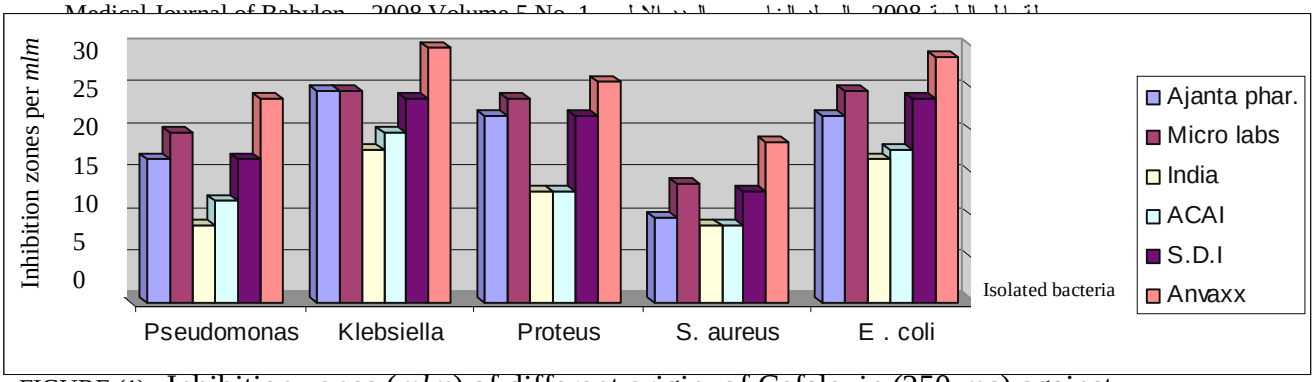

FIGURE (1) : Inhibition zones (*mlm*) of different origin of Cefalexin (250 *mg*) against different types of Bacteria

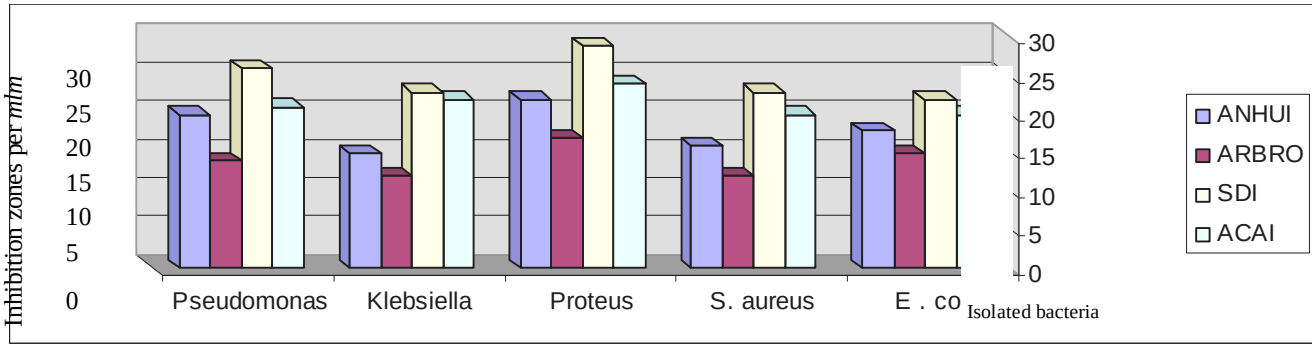

FIGURE (2): Inhibition zones (*mlm*) of different origin of Erythromycin (250 *mg*) against types of Bacteria

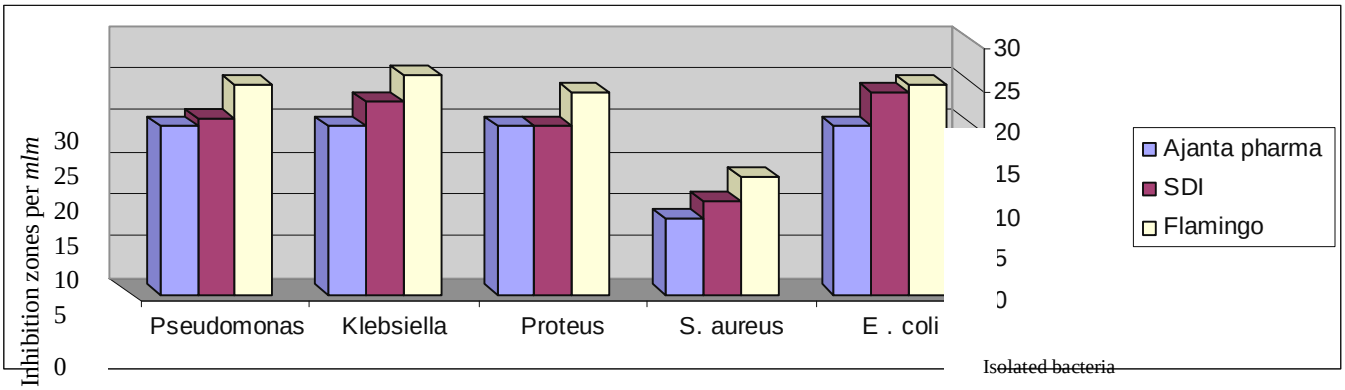

FIGURE (3): Inhibition zones (*mlm*) of different origin of Tetracycline (250 *mg*) against different types of Bacteria

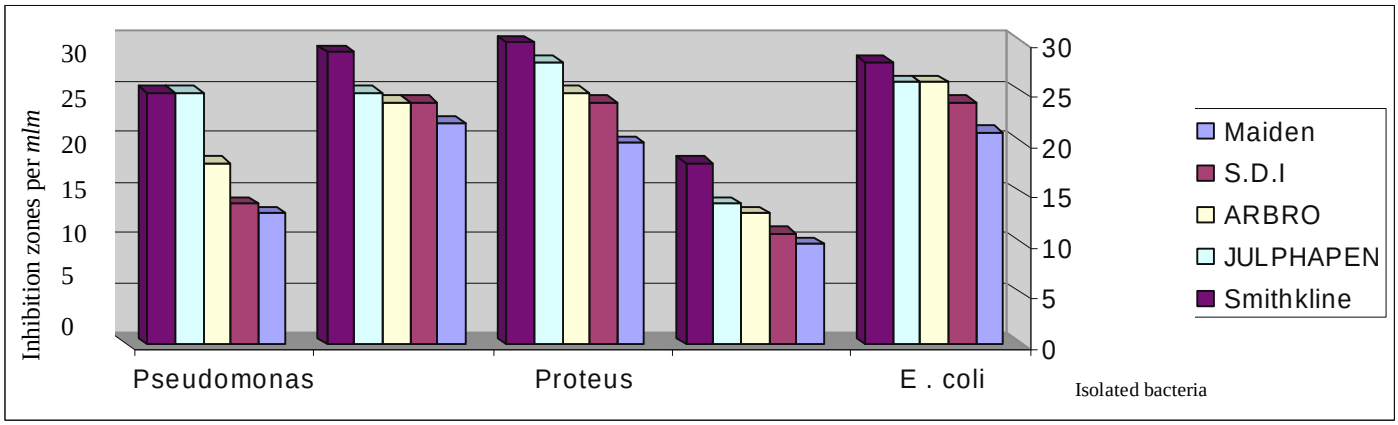

FIGURE (4): Inhibition zones(*mlm*) of different of Ampicillin (250 *mg*) against different types of Bacteria

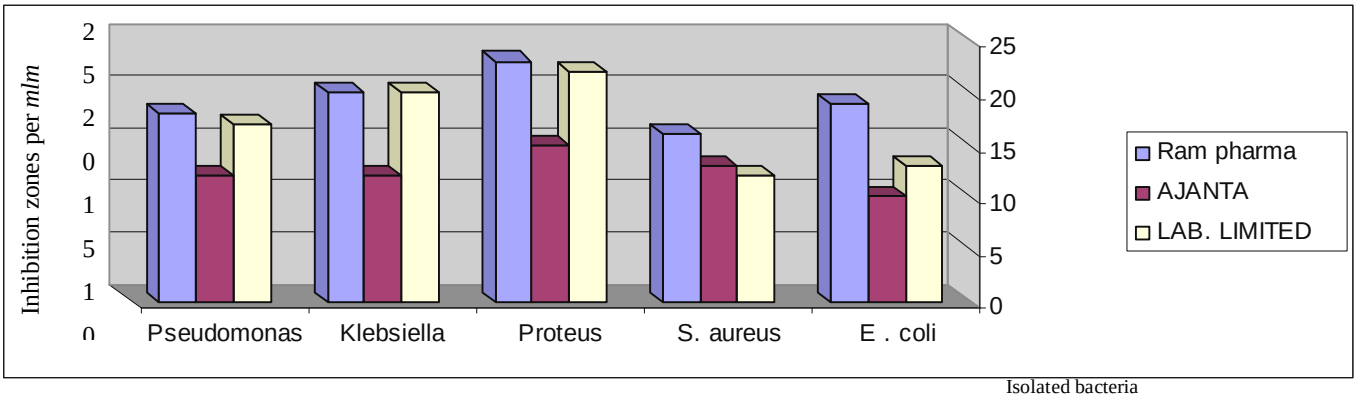

FIGURE (5): Inhibition zones (*mlm*) of different of Amoxillin (250 *mg*) against different types of Bacteria

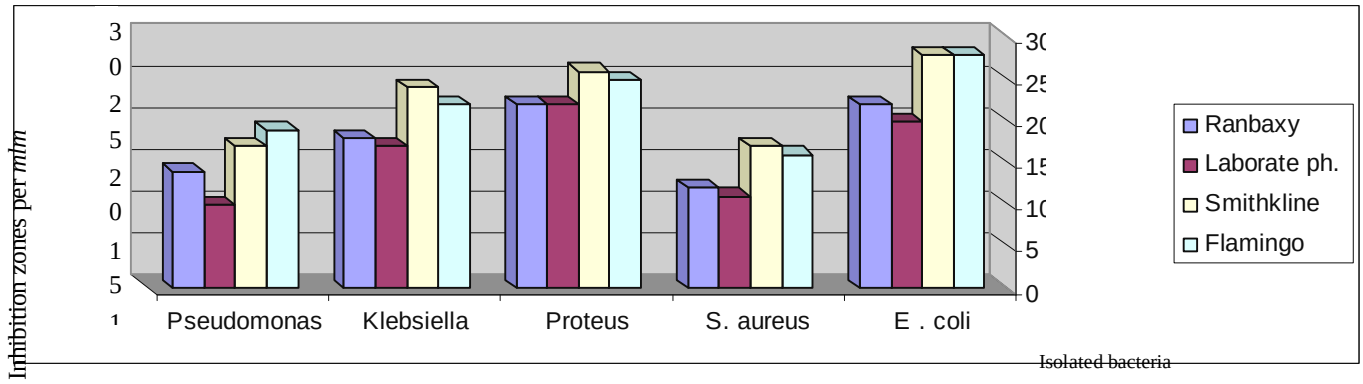

FIGURE (6): Inhibition zones (*mlm*) of different of Ceftriaxone (1g) against different types of Bacteria