Comparative Study for Antibacterial Activity of Some Maleamic acid Derivatives with Some Commercial Antibiotic

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Abstract

Antibacterial activity of the following prepared compounds: Bis-Maleamic acid, Ethylene-Bis-Maleamic acid, 1,4-phenylene [2,2-diamino-Bis (1,3,4-thiadiazol-5-yl)] Maleamic acid, 4-N(2,3-dimethyl-1-phenyl pyrazolin-5-one-4-yl) Maleamic acid and 5-methyl-3-sulfanilamido Maleamic acid-isoxazde (Maleamic acid derivatives) were tested against five pathogenic bacterial species. These were*Pseudomonasaeruginosa*, *Escherichiacoli*, *Salmonellatyphimurium*, *Proteusmirabilis* (Gram negative) and *Staphylococcusaureus* (Gram positive). Results showed that all tested compounds have good antibacterial activities comparing with antibiotics Ampicillin, Gentamicin and Tetracycline. The highest growth inhibition zone diameter for the compounds were (30 mm) against *S. aureus* and *P. aeruginosa*, (28 mm) against *E. coli*, (23 mm) against *S. typhimurium* and (14 mm) against *P. mirabilis*.

Key words: Maleamic acid derivatives, antibacterial activity, ampicillin, gentamicin, tetracycline.

الخلاصة

اختبرت الفعالية المضادة للبكتريا بوساطة المركبات المحضرة التالية : بس– حامض المالميك، اثيلين– بس – حامض المالميك، 1، 4– فنيل [2، 2– د اي امين– بس (1، 3، 4– ثايودازول– 5– ايل)] حامض المالميك، 4–أن 2، 3– داي مثيل– 1– فنايل – بيرزانول –5 – اون–4 – ايل حامض المالميك و 5– مثيل –3– سلفن امايد اوكينازول حامض المالميك ضد خمسة أنواع من الجراثيمالمرضية وهي زوائف ايروجينوزا (*Pseudomonasaeruginosa*) ، ايشريا القولون (*Escherichiacoli*) ، سالمونيلا تايفي موريم (*Salmonellatyphimrium*) ، متقلبات ميرابلس (*Proteusmirabilis*) والمكورات العنقودية الذهبية(*Staphylococcusaureus*). أظهرت النتائج ان المركبات تمتلك فعالية تثبيطية عالية مقارنة بالمضادات الحيوية امبيسلين، جنتاميسين وتتراسايكلين.

الكلمات المفتاحية: مشتقات حامض المالميك، الفعالية التثبيطية للبكتريا، امبسلين، جنتاميسين، تتراسايكلين.

Introduction

Due to the occurrence of new disease and concomitant acquisition of bacterial and fungal resistance to currently drugs, therefore it becomes necessary to discover new antimicrobial agents [1, 2]. The biological effects of maleamic acid derivatives are quite different and have been investigated in many laboratories [3]. Maleimides are widely known as active electrophilic reagents to readily react with a variety of dien S and 1,3-dipoles including azomethine ylide, carbonylyide and nitorenes leading to various heterocycles [4]. We have explored the abundant synthetic potential of the new functionlize malleimdes which can effectively be converted to fused pyridazine derivatives [5] and polymethine dyes [6,7].

The aim of this study is testing the antibacterial activity of Bis-Maleamic acid, Ethylene-Bis-Maleamic acid, 1,4-phenylene [2,2-diamino-Bis(1,3,4-thiadiazol-5-yl)], 2,3-dimethyl-1-phenyl-pyrazolin-5-one-4-Maleamic acid and 5-methyl-3-sulfanilamido Maleamic acid isoxazole against *Pseudomonas aeruginosa*, *Escherichia coli*, *Proteus mirabilis*, *Salmonella typhimurium* (Gram negative) and *Staphylococcus aureus* (Gram positive).

Material and Methods

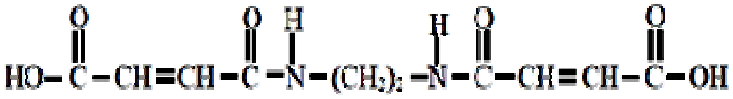
Preparation of compounds

All compounds used in this study were prepared according to [8]. Which showed in Fig (1).

Compound No.1

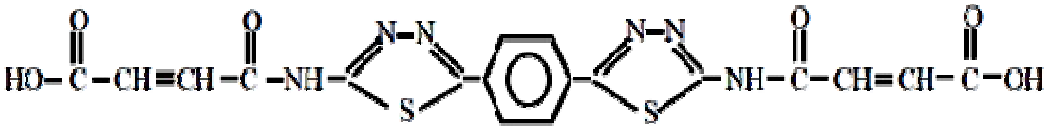
Bis- Maleamic acid [8]

Compound No. 2



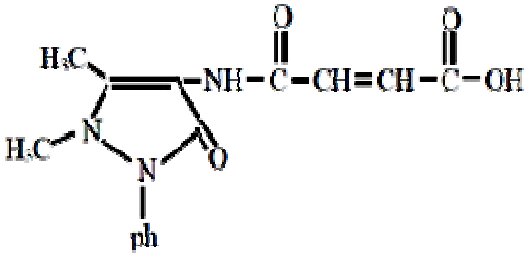
Ethylene-Bis-Maleamic acid [8]

Compound No. 3



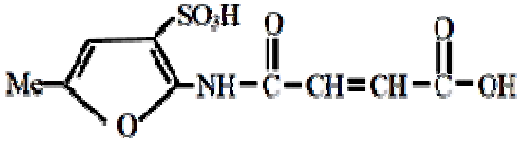
1,4- phenylene [2,2-diamino-Bis (1,3,4- thiadiazole-5-yl] Maleamic acid [8]

Compound No. 4



4-N (2,3- dimethyl-1-phenyl-pyrazolin-5-one-4-yl) Maleamic acid [8]

Compound No. 5



5-methyl-3-sulfanilamido isoxazole Maleamic acid [8]

Fig (1): Compounds of Maleamic acid derivatives [8].

Concentration of compounds

Concentrations of 10, 20 and 30 mg/ml (w/v) of each compound were prepared by using Dimethyl Sulfoxide (DMSO).

Bacterial cultures

Five species of pathogenic bacteria were used in this study as tested organisms. These are *Pseudomonas aeruginosa*, *Escherichiacoli*, *Proteus mirabilis*, *Salmonella typhimurium* (Gram negative) and *Staphylococcus aureus* (Gram positive).These bacterialspecieswere obtained from Al-Nahrain university research center for biochemistry.

Determination of antibacterial activity

The agar well diffusion method [9] was used to detect antibacterial activity for five prepared compounds of Maleamic acid derivatives. Fresh bacterial cultures suspension equivalent of 0.5 tube McFarland turbidity standards (10^8 cfu/ml) were spread on Muller-Hinton agar plates using sterile cotton swabs. Wells of 6mm diameter were cut in solidified agar and filled with 50 µl 0f each concentration. The Dimethyl Sulfoxide was also used as control. The plates were incubated aerobically at 37^0C for 24 hours, then inhibition zones diameter (mm) around wells were measured by rule. All testes were applied as triplicate.

Antibiotic sensitivity test

Antibiotic susceptibility of *P. aeruginosa*, *E. coli*, *S. typhimuriumP. mirabilis*, and *S. aureus*were determined also by the agar well diffusion method [9]. Antibiotics solutions were prepared by using DMSO. These antibiotics with their respective concentrations were Ampicillin (10 µg/50µl), Gentamicin (10 µg/50µl) and Tetracycline (30 µg/50µl).

Results and Discussion

Table (1) and Fig (2, 3, 4) showed results of antibacterial activity of Maleamic acid derivatives at 30 mg/ml against *E. coli*, *P. mirabilis*, *S. typhimurium*, *P. aeruginosa* and *S. aureus*. Bis-Maleamic acid exhibited the strongest antibacterial activity against *P. aeruginosa* (30 mm at 30 mg/ml). The ranking of antibacterial activity of Bis-Maleamic acid against the five bacterial species was *P. aeruginosa* > *E. coli* > *S. typhimurium* and *S. aureus* > *P. mirabilis*. The second compound was Ethylene-Bis-Maleamic acid exhibited maximum antibacterial activity against *S. aureus*(30 mm) at 30 mg/ml. The ranking of antibacterial activity of the second compound against the five bacterial species was *S. aureus* > *P. aeruginosa* > *S. typhimurium* > *E. coli* > *P. mirabilis*. The third compound 1,4- phenylene [2, 2-diamino-Bis (1, 3 ,4-thiadiazol-5-yl)] Maleamic acid exhibited the strongest antibacterial activity against *S. typhimurium* and S. aureus (19 mm at 30 mg/ml).The ranking of antibacterial activity of the third compound against the five bacterial species was *S. typhimurium* and *S. aureus* > *P. aeruginosa* > *E. coli* > *P. mirabilis*. While the fourth compound has maximum antibacterial activity against *E. coli* (24 mm at 30 mg/ml). The ranking of antibacterial activity of the fourth compound 4-N (2,3-dimethyl-1-phenyl-pyrazolin-5-one-4-yl) Maleamic acid was *E. coli* > *S. typhimurium* > *P. aeruginosa* > *S. aureus* > *P. mirabilis*.

Table (1): Antibacterial activity of Maleamic acid derivatives against five pathogenic Species.

Maleamic Acid Derivatives	Concentration (mg/ml)	Mean of Inhibition zone Diameter (mm)				
		P. aeruginosa	***E. coli***	***S. typhimurium***	***P. mirabilis***	***S. aureus***
Compound 1[A]	30	30	28	22	14	22
	20	18	18	14	11	17
	10	7	13	10	9	14
Compound 2[B]	30	27	18	19	13	30
	20	19	15	14	11	26
	10	7	13	11	8	24
Compound 3[C]	30	18	13	19	12	19
	20	7	9	12	9	15
	10	0.0	0.0	8	0.0	11
Compound 4[D]	30	19	24	23	9	18
	20	7	18	21	0.0	14
	10	0.0	17	18	0.0	10
Compound 5[E]	30	13	20	21	14	24
	20	9	18	16	8	18
	10	0.0	15	11	0.0	12
DMSO (Control)	100 %	0.0				

A: Bis-Maleamic acid; B: Ethylene-Bis-Maleamic acid; C: 1,4-phenylene [2,2-diamino-Bis(1,3,4-thiadiazol-5-yl)] maleamic acid; D: 4-N (2,3-dimethyl-1-phenyl-pyrazolin-5-one-4-yl) Maleamic acid; E:5-methyl-3-sulfanilamido Maleamic acid-isoxazole.

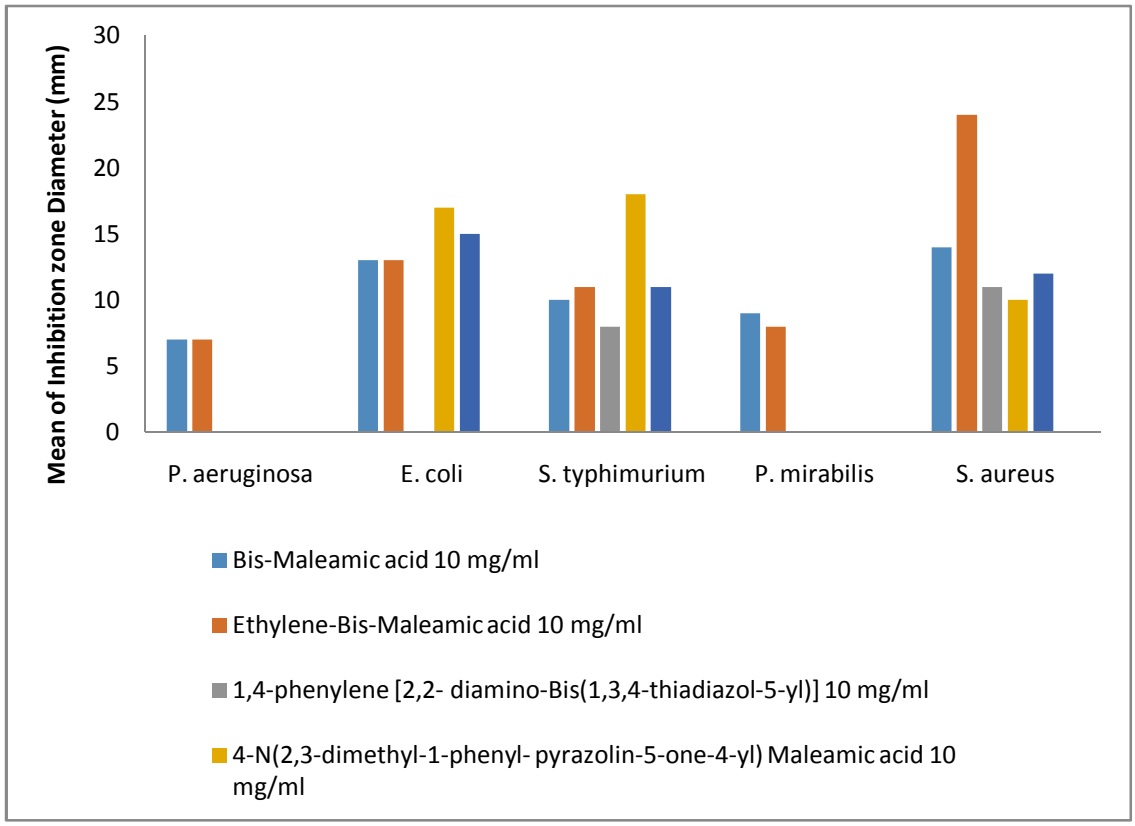


Fig (2): Antibacterial activity of Maleamic acid derivatives against five pathogenic Species at 10 mg/ ml.

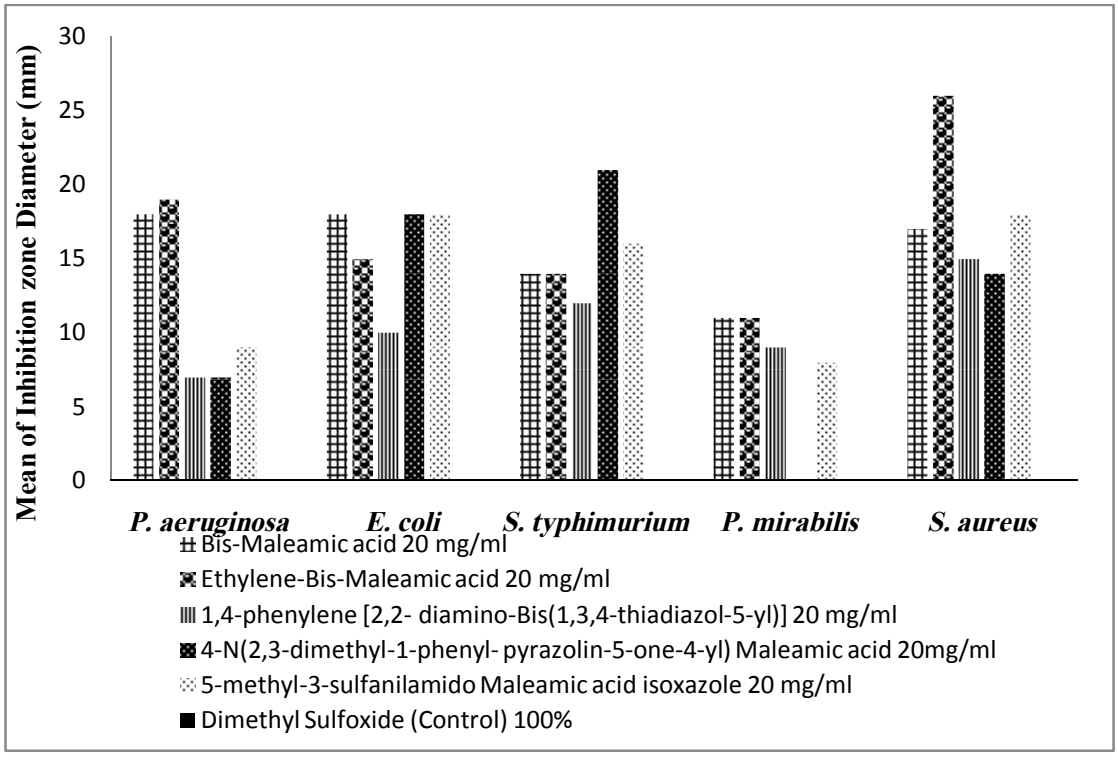


Fig (3): Antibacterial activity of Maleamic acid derivatives against five pathogenic Species at 20 mg/ ml.

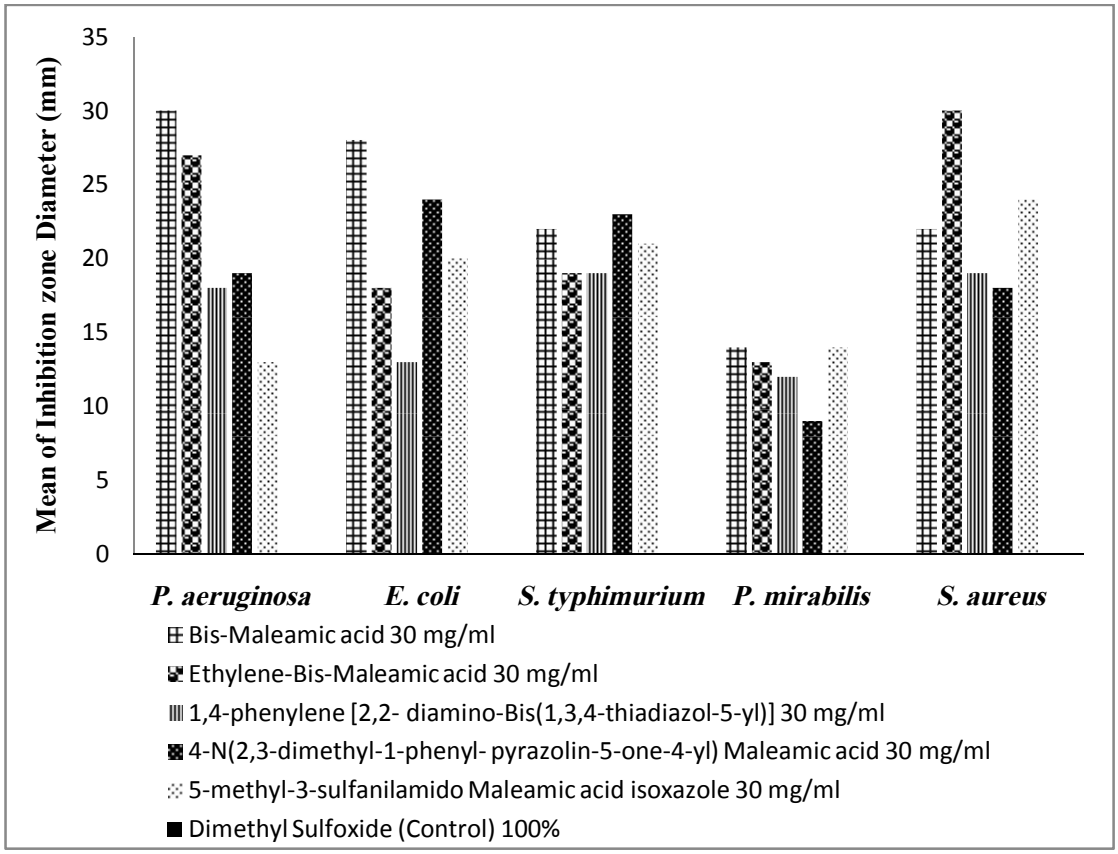


Fig (4): Antibacterial activity of Maleamic acid derivatives against five pathogenic Species at 30 mg/ ml.

The last compound 5-methyl-3-sulfanilamido Maleamic acidisoxazole has maximum antibacterial activity against *S. aureus* (24 mm at 30mg/ml). The ranking of antibacterial activity of the last compound against the five bacterial species was *S. aureus* > *S. typhimurium* > E. coli> *P. mirabilis* > *P. aeruginosa.* The strongest compound which has the largest inhibition activity was compound No.1, it has the highest inhibition activity against *P. aeruginosa* and *E. coli*. While compound No.2 has the best inhibition activity against *S. aureus*. Compound No.3 has the highest activity against *S. typhimurium*. All the compounds have the same inhibition activity against *P. mirabilis* except compound No.4 which has a weak inhibition activity.

The structures for all compound showed in figures 1-5. While table (2) and fig (5) showed the results of sensitivity test for five bacterial species to traditional antibiotics Ampicillin, Gentamicin and Tetracycline.

All the Maleamic acid derivatives were found chemically stable and active biological [3]. The Maleamic acid compounds stabilizer are reasonable biological activity due to presence of either –NH or – C=O groups in its structure [10]. The cell wall structural nature of gram negative enteric bacteria may be responsible for the observed susceptibility. For instance, the cell wall of gram negative bacteria contains 15-20 % polysaccharides and 10-20% lipid, whereas that of gram positive bacteria contain 35-60% polysaccharides and only 0-2% lipid [11]. The polysaccharides and the lipid contents of the cell wall affect the permeability of allicin and porrum constituents, and thus the observed susceptibility to porrum by the diarrheagenic organisms [12, 13]. The effect of Maleamic acid derivative was due to interfering with the structure of bacteria cell wall or by stopping bacteria multiplying [14]. The antibacterial activity of Maleamic acid derivatives were compared with antibiotics Ampicillin, Gentamicin and Tetracycline which considered popular for treatment of diseases caused by those five pathogenic bacterial species. The effect of Maleamic acid compounds reached to that of antibiotics without serious allergy which may be caused by antibiotics.

Table (2):Inhibition zone diameter (mm) of three antibiotics against five pathogenic bacterial Species.

Antibiotic	Concentration (µg/50 µl)	Inhibition zone Diameter (mm)				
		Pseudomonas aeruginosa	*Escherichia coli*	*Salmonella typhimurium*	*Proteus mirabilis*	*Staphylococcus aureus*
Ampicillin	10	0.0	0.0	0.0	0.0	11
Gentamicin	10	15	19	11	16	25
Tetracycline	30	0.0	25	12	15	18
Dimethyl Sulfoxide (Control)	100 %	0.0				

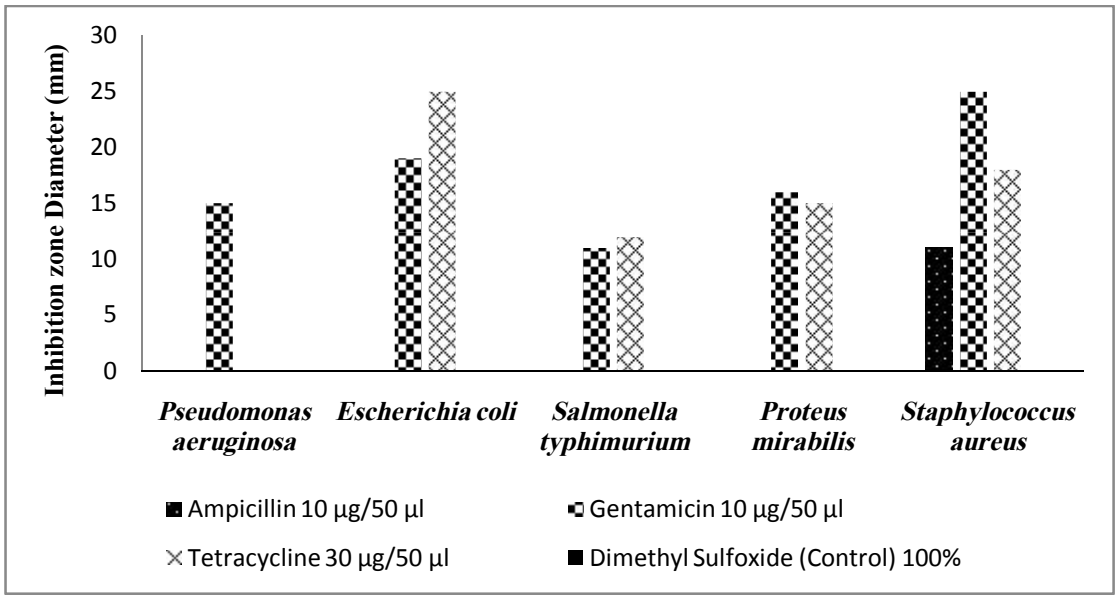
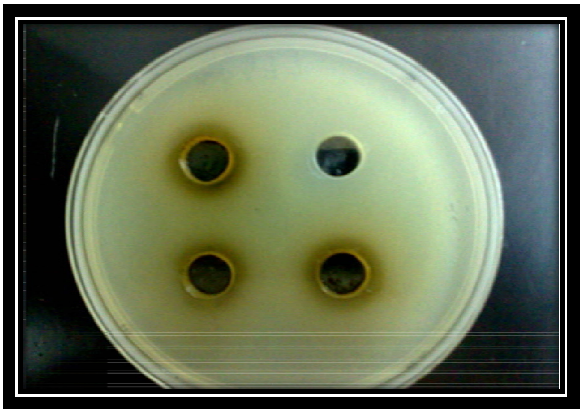
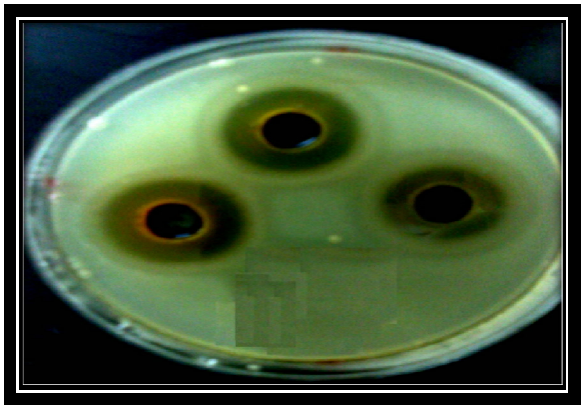


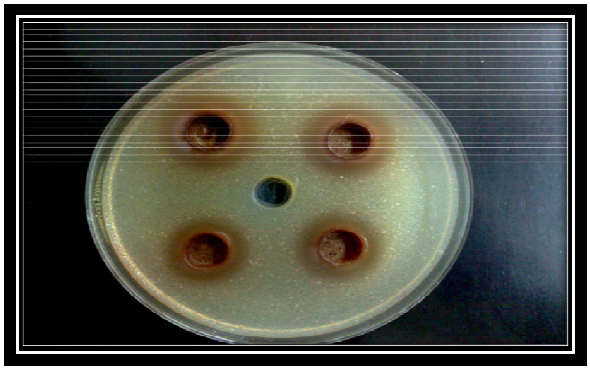
Fig (5):Inhibition zone diameter (mm) of three antibiotics compounds against five pathogenic bacterial species at 50 µg/50 µl).



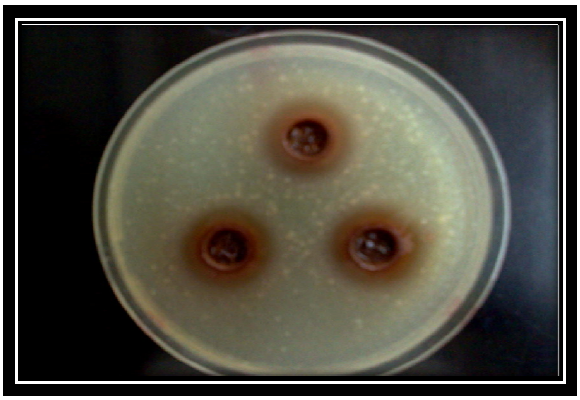
Compound No.1 against *Proteus mirabilis*



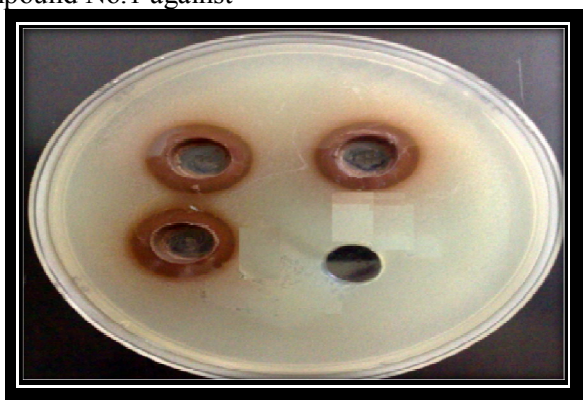
Compound No.1 against *Pseudomonas aeruginosa*



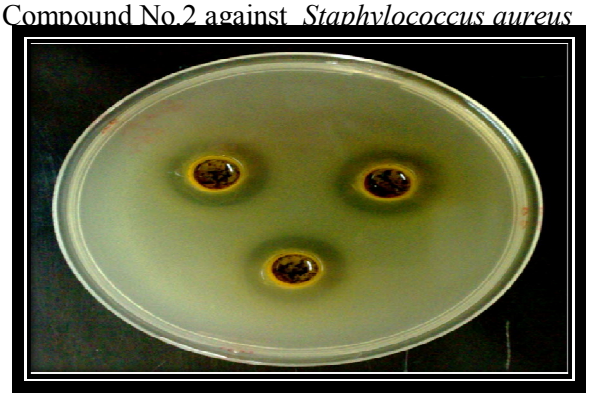
*Escherichia coli*Compound No.1 against



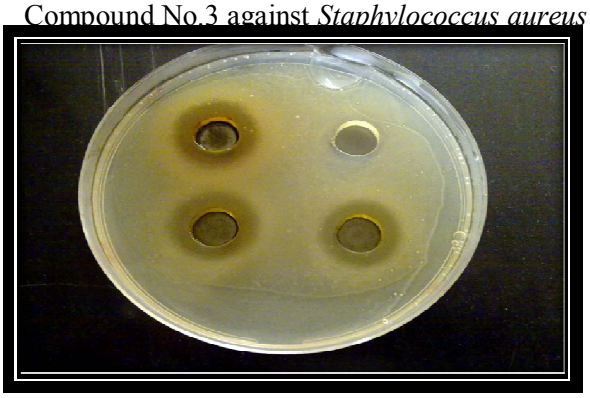
Compound No.2 against *Staphylococcus aureus*



Compound No.3 against *Staphylococcus aureus*



Compound No. 4 against *Salmonella typhimurium*



Compound No. 5 against *Proteus mirabilis*

Fig (6): Inhibition zone diameter of compounds against some species of bacteria.

Conclusion

According to the results, biological activity data showed that reported compounds have a significant antibacterial activity against *E. coli*, *P. mirabilis*, *S. typhimurium*, *P. aeruginosa* and *S. aureus* especially compound No.1 (Bis-Maleamic acid) and No.2 (Ethylene-Bis-Maleamic acid) has highly significant antibacterial activity.

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