Studying the Biological Activity of Some Oxazepine Derivatives Against Some $G^{(+)}$ and $G^{(-)}$ Bacteria.

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Abstract

The preliminary test of the compounds N [2– (3,4–dimethoxy nitrobenzene oxazepine–2,3–dihydro–4,7–dione]–5–mercupto–2–amino–1,3,4–thiadiazol [A] and N [2–anthralidene–5– (2–nitrophenyl) –1,3–oxazepine–4,7–dione–2–d](5–mercapto–1,3,4–thiadiazole–2–amin) [B] , showed that they possess high activity against some positive and negative bacteria , like *pseudomonas aeruginosa* (*pseudo*.), *Escherichia coli* (*E-coli*), *staphylococcus aureus* (*sta*.) and *Bacillus subtilis* (*Ba*.) and finally there is a study of the effect of some antibiotics like streptomycin (S), gentamycin (GN), chloramphenicol (C) and Nalitixic acid (NA) in order to compare the differences in effects.

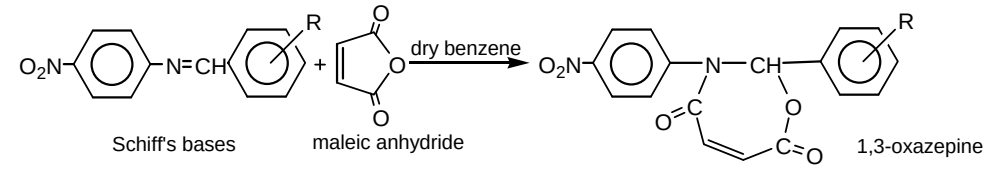
In the present study, results concerning the activity of oxazepines derivatives of compound [A] and [B] are reported.

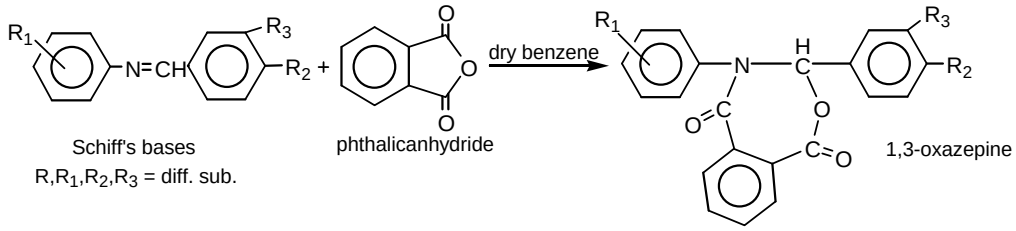
Key Words: activity of 1,3–Oxazepine , pseudomonas aeruginosa **,** E-coli, staphylococcus aureus**,** Bacillus subtilis., streptomycin**,** gentamycin, chloramphenicol**,** Nalitixic acid.

Introduction

The thiadiazole nucleus is important in compounds with antimicrobial and antitumer activity [1,2,3,4].

Preperation of oxazepine–dione from reaction of Schiff's bases with maleic or phthalic anhydride to give 3–aryl–2,3– dihydro–1,3–oxazepine–4,7–dione–2–yl in dry benzene, according to pericyclic reaction[5].





Oxazepine derivative is an antidepressant with a mild sedative component to it's action. The mechanism of its clinical action in man is not well understood. In animals, amoxapine reduced the uptake of noradrenaline and serotonine and blocked the response of dopamine receptors to dopamine[6].

The compounds N[2–(3,4–dimethoxy nitrobenzene oxazepine -2,3–dihydro–4,7–dione] –5–mercupto–2-amino–1,3,4–thiadiazol [A] and N[2–anthralidene–5–(2–nitrophenyl)–1,3–oxazepine–4,7–dione–2–(5–mercapto–1,3,4–thiadiazole–2–amine) [B] were investigated for their antibacterial activity as prepared and identified earler[7].These compounds are effective in inhibiting the growth of bacteria.

Heterocyclic rings are considered an important class of compounds having a wide range of biological activity , the heterocyclic compounds are well known for their antibacterial and antifungal activities[8].

Pseudomonas aeruginosa (Pseud.) is a gram negative rod, motile, non-spore forming. Pseudomonas aeruginosa is often a major cause of hospital acquired (non-social) infections. Infection can occur at many sites and can lead to urinary tract infections, sepsis, pneumonia, pharyngitis and wound infection[9] . These bacteria are clinically important because they are resistant to antibacterial agents and consequently are an important potential contaminant of pharmaceutical and cosmetic preparations.

Escherichia Coli (E-Coli) is a gram negative bacilli, non-motile, capsulated and non-spore forming. It is present in the respiratory tract and feces of about (5%) of normal individuals. It caused a small proportion about (1%) of bacterial pneumonias. It occasionally produces urinary tract infection and bacterium with focal lesions in debilitated patients[10].

Staphylococcus aureus (Sta.) is a gram positive cluster form, non-motile and non-spore forming. It is a leading cause of soft tissue infection, as well as toxic shock syndrome and scalded skin syndrome.

It has been found to be the causative agent in such illness as pneumonia, meningitis, boils, arthritis and osteomyelitis (chronic bone infection)[11].

Bacillus subtilis (Ba.) is a gram positive bacilli, motile with lateral flagella, spore forming non capsulated.

It is one of the commonest saprophytes in contaminant in foods, clinical specimens and laboratory cultures [12].

Experimental Part

Compounds were synthesized by the cyclization Schiff bases into the corresponding oxazepines (seven member ring) derivatives was accomplished by the reaction of the Schiff bases with maleic anhydride in dry benzene[13]. The structures of these compounds were characterized by usual methods (m.p and FT.IR spectrum)[7].

The in vitro antibacterial activity tests were performed using the agar plate diffusion method[14].

The test samples of required concentration [75mg/ml] in ethanol were added in their respective wells. Other wells were supplemented with reference drugs i:e. streptomycin (S), gentamycin (GN), chloramphenicol (C) and Nalitixic acid (NA) seving as the positive controls[15].

Experimental plates then incubated at 37°C for 24hrs. and zone of inhibition were measured in mm and compared with positive control.

The effect of ethanol (solvent) was tested on each bacteria, the effect of ethanol was negligible[15].

Results and Discussion

Compounds containing –N–C=S linkage are reported as antirritant agents and fungicides. This group is included in many basic structures of drugs either to be a part of an open chain, e:g. thio carbamates isothiocynates and thiosemicarbazides or involved in heterocyclic ring, e:g, mercapto derivatives of oxadiazoles[16].

The gram-positive bacteria and gram-negative bacteria utilized in the study were Staphylococcus aureus, Bacillus subtilis, Pseudomonas aerugiuosa and Escherichia Coli. In this study the effect of antibiotics were also studied, as shown in Table (1) and (2).

For Pseud.(G-),compound A showed more inhibition activity than compound B, that may be due to the presence of nitro group(with drawing group) while compound (B) containing alkyl groups or (donating group) which less active than nitro group.Besides ,the compound B containing aromatic ring fused with oxazepine ring while compound A doesn´t. While for E-coli and Bac. ,the compound B is more inhibition activity than A, but with Sta. (G+) both compounds exhibited the same activity in ethanol as shown in table (1).

In table (2), the effect of (chloramphenicol) is more against bacillus, while with staphylococcus, the effect of streptomycin is the strongest, while with E-Coli, the effect of gentamycin was more effective.

The results of the present study show that some of the prepared compounds have a relatively strong deactivating capacity against the spacimen of bacteria. Bacteria is known to be anti-toxic and enjoys a resistance to anti-biotic for blasma.

The lack of deactivation areas for compounds with E-coli may be due to the lack of the suitable carrier in the cell or the necessary energy to have access to the internal target[17] .on one hand. The results ,on the other hand, show that compounds have a good deactivating capacity against Staphylococcus aureus and Bacillus subtilis**.** This is due to the percentage of active material solved in the ethanol . Ethanol is known to be the most common solvent. It can solve many compounds.

The study showed also many evidences of other active anti-biotics that can be put to further use in the system of Bioresistense against the causes of several plant diseases inorder to avoid the excessive use of the chemical pasteyciedes that cause environumental problems and are very expensive**.**

References

1.Mishra, R.K; Tewri, R.K.(1991) Syntheses and biological activity of heterocycles derived from 3-methoxy-1-phenyl-1H-pyrazole-5-carboxylate, J.Indian chem..soc., 68: 110.

2.Tasaka.N.Tamura; Hatashi.R. and Itoh. K. (1993) Optically Active Antifungal Azoles. I. Synthesis and Antifungal Activity of (2R, 3R)-2-(2,4-Difluorophenyl)-3-mercapto-1-(1H-1,2,4-triazol-1-yl)-2-butanol and Its Stereoisomers, chemical and pharmaceutical Bulletin, 41(6): 1035-1042.

3.Abdon, N.A. and Amin, F.M. (1990) Synthesis and biological activity of certain 5-mercapto 3- [3-pyridyl] 4H-1,2,4-triazole derivatives, Mansoura J.pharma sci., 6(2): 9-25.

4. Khal, M.H. and Nizamuddin, H. (1997) Synthesis of e)-2,4'-(3'-Chloro-2'-Azetidinon)-1'-yl]-1,3,4-Oxa (thia) Diazoles and-(4'-Thiazolidinon)-3'-yl]-1,3,4- Oxa(thia) Diazoles as Antimicropial Agents, Indian J.chem. , 36B, 625-629.

5. Abdullatieef, M. (2010) ph.D.thesis, College of Education for Pure Science Ibn-AL-Haitham, Baghded University.

6.Huan-M ing chen and Ramachandra S.Hosmane (2000) 6-amino-2-phenylimidazo[4,5-e][1,3]diazepine-4,8(1H,5H)-dione, J.Molecules, 5:M164.

7. Saoud, S.A.(2007) Msc.Thesis, College of Education For Pure Science AL-Haitham, Baghded University.

8.Hassan, S.S. (2006) Msc.Thesis, College of Science, AL-Nahrain University.

9.AL-Jobonry, N.R.(1987) Msc.Thesis, College of Pharmacy, Baghdad university.

10.Dart, J. K. and Seal, D. V. (1988) Pathogenesis and therapy of Pseudomonas aeruginosa keratitis, Eye, 2 :46-55.

11.Lowy, F.D.(1998) Staphylococcus aureus Infections, N.Engl J.Med., 339(6): 520-539.

12.Cacic, M.; Trkovnik, M.; Cacic, F. and Has-Schon, E. (2006) Synthesis and Antimicrobial Activity of Some Derivatives of (7-Hydroxy-2-oxo-2H-chromen-4-yl)-acetic Acid Hydrazide, Molecule,11:134-137.

13.Hussein, F.A.;Mahmoud, M.J. and Tawfig, M. T.(2006) Synthesis of substituted 1,3-oxazepine-4,7-diones via Schiff bases (Part 1),Al– Mustansirya J. Sci., 17 (1).

14.Dutta, M.M.;Goswami, B.N. and Kateky, J.S. (1986) Studies on biologically active heterocycles. Part I. Synthesis and antifungal activity of some new aroyl hydrazones and 2,5-disubstituted-1,3,4-oxadiazoles, J.Heterocyclic chem., 23,793.

15.Gunav, V.I;Mikhailopulo, I.A.; Ovechkina, L.F. and Zavyalov, S.I., Chem.Abst., 67, 5497, 1967.

15.ATTO, A.T.;Mahmoud, M.J. and Ayad.S.Homeed (2000) Synthesis , Spectroscopy and studyof Some New 1,3,4-O xadiazole Derivatives, Iraqi.J.of chem., 26,1:86-93.

16.Wilson and Gisold,s. (Textbook of organic medical and pharmaceutical chemistry) Tenth Edition , Lppincott Williams & wilkins P 444 - 446 .

Table No.(1): Diameters of deactivation of Bacteria by using compound A and B

	Diameters of deactivation mm		
	Compound A [con. 75mg/ml]	**Compound B [con. 75mg/ml]**	**Ethanol**
Psend.	20	12	5
Sta.	24	24	5
E-coli.	12	14	5
Bac.	20	25	5

Psend.= psendomonas aerugiuosea G^{-ve}
Sta. = staphylococcus aureus G^{+ve}
E-coli = Escherichia coli G^{-ve}
Bac. = bscillus subtilis G^{+ve}

Table No. (2): Diameters of deactivation of Bacteria by using some antibiotic

	Diameters of deactivation mm			
	C [con. 75mg/ml]	**GN [con. 75mg/ml]**	**S [con. 75mg/ml]**	**NA [con. 75mg/ml]**
Bac.	30	24	25	22
Stap.	25	28	28	20
E-coli.	22	12	12	16

C= chloromphenicol
GN= gentamycin
S= streptomycin
NA= nalitixic acid

دراسة الفعالية البايولوجية لبعض مشتقات الاوكسازبين ضد بعض انواع البكتريا الموجبة(+G) والسالبة(-G)

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الخلاصه

من الدراسات الاولية للمركبين N][2-(4,3- ثنائي ميثوكسي نايتروبنزين-3,1- اوكسازبين -3,2- ثنائي هايدرو-7,4-دايون]-5- مركبتو-2- امينو-4,3,1-ثايادايزول [1] & N][2- انثرالدين-5-(2- نايتروفنيل)-3,1- اوكسازبين-7,4-دايون-2-(5- مركبتو-4,3,1- ثايادايزول-2- امين)] [2] .بينت لها فعالية مضادة لبعض انواع البكتريا الموجبة (G^+) والسالبة (G^-) مثل:(staphylococcus , Escherichia coli(E-coli), pseudomonas aeruginosa(pseudo.) aureus(sta.) و Bacillus subtilis(Ba.) وقورنت فعاليتها البايولوجية مع فعالية بعض المضادات الحيوية مثل: chloramphenicol(C), gentamycin(GN), streptomycin(S) و Nalitixic acid(NA) .

وتم التركيز في هذه الدراسة على فعالية مشتقات الاوكسازبين [2,1].

الكلمات المفتاحية: فعالية 3,1-أوكسازبين , .pseudo ,E-coli , sta. , Ba. , S, GN ,C ,NA .