Antimicrobial Study against Seven Cycles Compounds Derivatives from Pyrimidine

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Abstract

The current study involves preparing newly pyrimidine derivative compound with seven membrane rings and used it to explain the antimicrobial activity of it against four isolates of four types of G+ & G– pathogenic bacteria (Staphylococcus aureus, Staphylococcus epidermidis, Escherichia coli and Klebsiella pneumonia) respectively, with two types of fungi (Aspergilus niger & Penicillium chrysogenum) by using four different concentrations (5, 10 , 15 & 20 mg/ml^{-1}). The characterizations and properties of this compound have biological and pharmacological functions through the inhibition the growth of many types of organisms.

Key words: *Antimicrobial activity, Schiff base, Pyrimidine.*

Introduction

Heterocyclic derivatives have effective antimicrobial, anti-inflammatory and anticancer activity with different pharmacological effects. Two atoms of imine group (two-membered component) was added to maleic or phthalic anhydrides (five-membered component) lead to form a seven-membered heterocyclic compound [1,14]. These products contain the seven rings with functional groups (R-N=N-R^{-}) the Schiff bases have aromatic azo group are colored therefore we used them as dyes that considered as an organic compound with many anti-microbial activity [2] . The seven membered rings are widely present in nature with nitrogen and oxygen atoms that have medicinal activity because of their structural similarities between them and natural substances. In the industrial field, they used in polymer processes and antioxidant [3,4].

Pyrimidine is a cyclic amine with a large group of heterocyclic compounds that plays an important role in many biological functions. It is found in nucleic acids, several vitamins, co-enzymes and purines [5] .

Azo dyes one of the important and the largest groups of synthetic organic dyes that mainly used as coloring agents for foods and cosmetics, besides to their applications in modern technology [1] .

These compounds have the ability to inhibit the replication of nucleic acid and protein synthesis that may be used against many of multidrug

resistant organisms among the world [6,14].

Objectives

This study was designed to determine the antibacterial and antifungal activities of a newly synthesized compound at different concentrations against four types of pathogenic bacteria with two types of fungi in vitro laboratory conditions.

Materials and Method

1- Chemical study:

We prepared A1 compound [-2, 6 diamino-5-((4-hydroxycyclohexyl) diazenyl) pyrimidin-4-ol] by dissolving (0.03 mol) from p- aminophenol in (0.03 ml) of concentrated HCl with (10 ml) of distilled water. Then we cooled the mixture to (0-5) ^{o}C in ice water bath. (0.03 mol) of sodium nitrate was dissolved in (10 ml) of cool distilled water and this solution was added to the mixture above step by step with continuous shaking for (15 min). The diazonium solution was added to solution contain (0.03 mol) from Pyrimidine that dissolved in (25 ml) of ethanol and sodium hydroxide the result was formation light purple solution at pH (6-7) then we left it for one

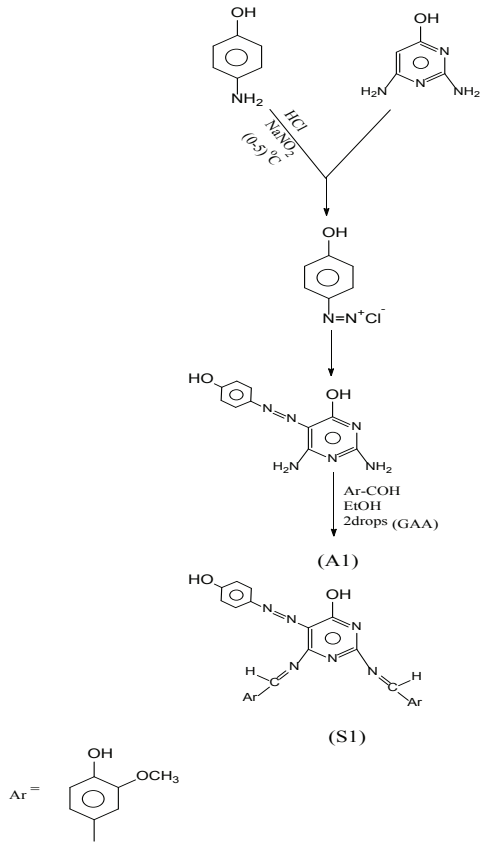
hour, filtrated the mixture and washed the precipitate with distilled water then we recrystallized from absolute ethanol.

The S1 Schiff base [4,4'-((1Z,1'Z)-((6-hydroxy-5-((4-hydroxycyclohexyl) diazenyl) pyrimidine2,4diyl) bis (azaneylylidene)) bis (methaneylylidene)) bis (2-methoxycyclohexan-1-ol)] was prepared as following: 0.03 moles of vanillin (3-methoxy-4-hydroxy benzes aldehyde) was dissolved in (25 ml) in absolute ethanol, then we added 1-2 drops of Glacial acetic acid with continuous shaking for (20 min) on magnetic stirrer. Then, we treated it with (0.03 mole) from A1 compound gradually to complete the process at 70 °C in 7 hr. The mixture was evaporated and dried the solution for recrystallized from absolute ethanol as in scheme (1).

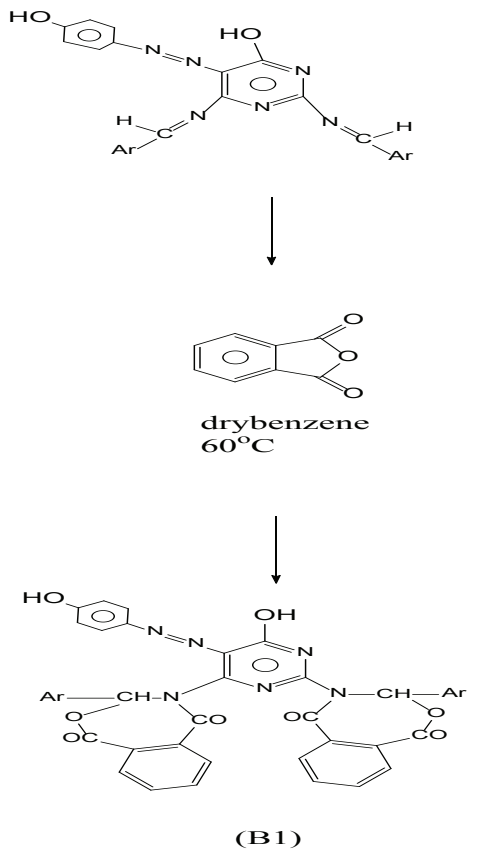
The B1 compound [4,4'-(6-hydroxy-5-((4-hydroxycyclohexyl) diazenyl) pyrimidine-2,4-diyl) bis(3-(4-hydroxy-3-methoxycyclohexyl) octahydrobenzo[e][1,3]oxazepine-1,5-dione)] was prepared by dissolved of 0.03 mol from Schiff bases (S1) in (25 ml) dry benzene with continuous shaking to complete solving . Then we added (0.03 mol) from phathalic anhydride gradually to complete the process at 65 °C in 15 hr. The solution was dried for recrystallized by absolute ethanol as in scheme (2).

2- Microbiological study:

The antimicrobial activity of the newly synthesized compound was examined by using 4 isolates of four types of G+ & G– pathogenic bacteria that include the following (S. aureus, S. epidermidis, E. coli and K. pneumonia) respectively, with two types of fungi A. niger & P. chrysogenum at four different concentrations (5, 10 , 15 & 20 mg/ml^{-1}) after dissolving these compounds in DMSO as solvent as in[7, 8,9]. The antimicrobial activity was measured by minimum inhibitory concentrations in (mm).



Scheme (1): Preparation of A1 And S1 compounds



Scheme (2): Synthesis of B1 compound

Results and Discussion:

In this study we prepared B1 compound from the S1 Schiff base that was confirmed by IR & HNMR as in scheme (2) to determine the antibacterial and antifungal activities of it against G+ & G– bacteria with fungi by measuring the minimum inhibitory concentration (MIC) in (mm) at four different concentrations (5, 10 , 15 & 20 mg/ml^{-1}) as in table (1) and figure (1).

This compound had good activity against all types of bacteria and fungi that used in this study with a significant increased against G+ especially S. aurous at (20 mg/ml^{-1}) concentration compared with others microorganisms and this is may be occurring due to their ability to damage the cell wall of the microorganisms and inhibit their function or stopping microbial replication and these results were agreements with many researches [10,11,12,13].

The presences of central ring separator play an important role in the noncovalent DNA cooperation through intermolecular interaction as formation of hydrogen bonds, which can increase the antimicrobial activity and that depend on the nature of hetero atoms in their structures and the presence of phenyloxy moiety with NH_2 as an electron releasing group[6, 11,13].

Table (1) Antibacterial and antifungal activity against B1 compound at four different concentrations (5, 10, 15 &20 mg/ml^{-1})

Isolates number	Concentrations (mg/ml-1)	G+ bacteria Inhibition zone(mm)		G– bacteria Inhibition zone(mm)		Fungi Inhibition zone(mm)	
		S. aureus	S. epidermidis	E. coli	K. pneumonia	A. niger	P. chrysogenum
1	5	9	8	6	7	-	-
	10	15	10	9	8	6	-
	15	22	17	13	12	10	8
	20	29	19	15	14	15	11
2	5	9	9	7	8	3	-
	10	14	11	11	7	7	-
	15	20	19	14	13	9	11
	20	30	22	15	13	14	12
3	5	8	9	8	8	-	-
	10	15	11	10	9	4	2
	15	22	17	12	13	12	9
	20	32	20	17	15	14	11
4	5	10	9	7	9	2	-
	10	16	11	11	9	6	4
	15	22	18	14	14	11	11
	20	32	20	17	15	13	12

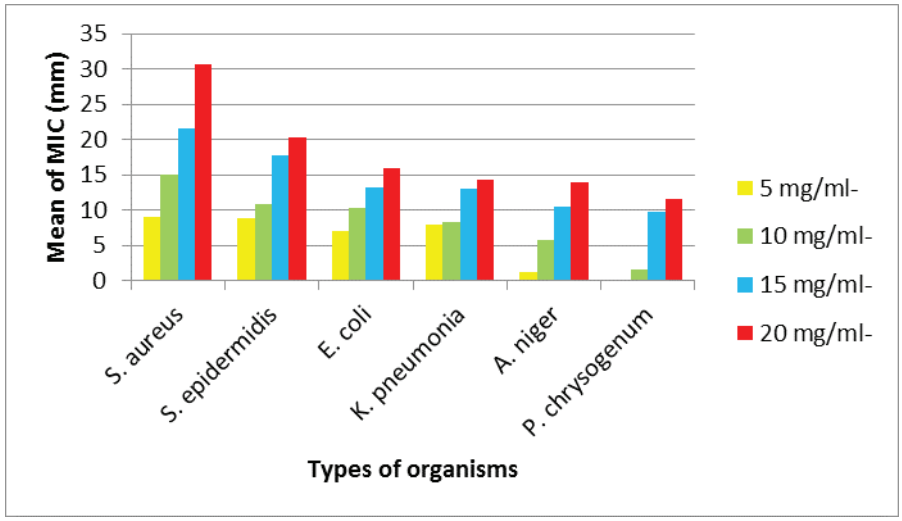


Figure (1) Mean of inhibition zone (mm) of antibacterial and antifungal activity against B1 compound at different concentrations

Conclusions

The present research focused on the synthesis of novel chemical derivatives to explain their antibacterial and antifungal activity that be safely used in future towered many infectious diseases.

Financial Disclosure: There is no financial disclosure.

Conflict of Interest: None to declare.

Ethical Clearance: All experimental protocols were approved under the College of Pharmacy, Iraq and all experiments were carried out in accordance with approved guidelines.

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