IJPT
1735-2657/08/72-165-167
IRANIAN JOURNAL OF PHARMACOLOGY & THERAPEUTICS

IJPT 7:165-167, 2008

RIDR

RESEARCH ARTICLE

Evaluation of Antibacterial and Antifungal Activity of some 1, 3, 4 Oxadiazoles

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Received August 26, 2007; Revised March 1, 2008; Accepted March 19, 2008

This paper is available online at *http://ijpt.iums.ac.ir*

ABSTRACT

In the last three decades investigations in the field of oxadiazoles have been intensified due to their diverse therapeutic uses. Oxadiazole are well known to have a wide range of therapeutic activities namely anti-inflammatory, analgesic, antipyretic, anticonvulsant, antiparasitic, antimicrobial etc. In this study, we have evaluated the antimicrobial activity of some carboxymethyl derivatives of oxadiazole-2-thiones, the antimicrobial effects of which have not yet been evaluated till date. The synthesized compounds showed significant antibacterial activity against *Staphylococcus aureus* and *Escherichia coli,* as well as antifungal activity against *Aspergillus niger* and *Candida albicans*. The activity was significant in comparison to the positive antibacterial and antifungal control of Ofloxacin (5µg/ml) and Miconazole nitrate (40µg/ml), respectively. Hence, it can be concluded that the oxadiazole derivatives are important molecules in the field of developing promising antimicrobial compounds. The present study can help and stimulate the researcher for further exhaustive study in exploiting oxadiazole compounds to develop newer useful antimicrobial agents.

Keywords: *1, 3, 4 oxadiazole, Antimicrobial activity*

In an era of increasing bacterial resistance to classical antibacterial agents, it has been postulated that the development of resistance to known antibiotics could be overcome by identifying new drug targets via genomic, improving existing antibiotics and most importantly by identifying new antibacterial agents [1] with novel structures and mode of action. Following in this vein, it was apparent that oxadiazoles have received considerable attention because of their effective properties as antimicrobial agents. Although oxadiazoles have been known for about ninety years, it is only in the last three to four decades that investigations in this field have been intensified. This is due to the large number of uses of oxadiazoles in the most diverse areas, for example in drug synthesis, scintillation materials and the dye industry. 1, 3, 4-Oxadiazoles are well known to have a wide range of biological activities such as anti-inflammatory [2], antiparasitic [3], antihyperglycemic [4], apoptosis-inducing [5], antiproliferation [6], antitumor [7], antitrypanosomal [8] and antimicrobial activities [9].

Various oxadiazoles have been shown to be active against a wide range of bacteria such as Bacillus subtilis, Staphylococcus aureus, Escherichia coli, Pseudomonas aeruginosa, Mycobacterium tuberculosis and fungi such as Candida albicans, Candida krusei and Candida parapsilosis [1, 10-15].

In the present investigation, some substituted 1, 3, 4-oxadiazole derivatives were synthesized and evaluated for their potential antibacterial and antifungal activity.

MATERIALS AND METHODS

Chemicals

All the chemicals and reagents used were of analytical grade and obtained from E-Merck. Ofloxacin and Miconazole nitrate were used as standards.

Synthesis of Compounds

Carboxymethyl derivatives of para substituted/unsubstituted oxadiazole-2-thione were synthesized by ring closure reaction with appropriate acid hydrazide following conventional refluxing method [16-19]. The synthesized compounds (Table 1) were characterized by IR and ^{1}HNMR studies and evaluated for potential antimicrobial activity. The compounds synthesized were 2-carboxymethylthio-5-phenyl-1,3,4-

Table 1. Antibacterial and antifungal activity of the tested compounds.

Compound*	Gram positive	Gram negative	Fungi	
	S. aureus	*E. coli*	*C. albicans*	*A. niger*
A	+++	+	++	+
B	+++	+	+++	++
C	+++	++	+++	++
D	+++	+	+++	++
E	+++	+	++	+
Ofloxacin	+++	+++	-	-
Miconazole nitrate	-	-	+++	+++

*All compounds were dissolved in DMSO.
-Values (mean of three replicates) are diameter of zone of inhibition (mm);
-Key to symbols: Highly active = +++ (inhibition zone > 18 mm); Moderately active = ++ (inhibition zone 10 - 18 mm); Slightly active = + (inhibition zone 5 - 9 mm); Inactive = - (inhibition zone < 5 mm)

oxadiazole (A), 2-carboxymethylthio-5-(4-hydroxyphenyl)-1,3,4-oxadiazole (B), 2-carboxymethylthio-5-(4-chloro phenyl)-1,3,4-oxadiazole (C), 2-carboxymethylthio-5-(4-nitrophenyl)-1,3,4-oxadiazole (D), 2-carboxymethylthio -5-(4-aminophenyl)-1,3,4-oxadiazole (E). The structures of the compounds synthesized and evaluated for antimicrobial activity are given in Fig 1.

Test microbes

Escherichia coli (ATCC 9837, gram negative bacteria), *Staphylococcus aureus* (ATCC 6538, gram positive bacteria) and *Candida albicans* (ATCC, 10231), *Aspergillus niger* (ATCC 16404) were used to evaluate antibacterial and antifungal activity respectively. The bacterial and fungal stock cultures were maintained on Muller Hinton agar slants, which were stored at 4ºC.

Antibacterial and antifungal activity

The antibacterial and antifungal activity of the compounds was tested by the disk diffusion method [20] against 'Gram positive' bacteria (*Staphylococcus aureus*), 'Gram negative' bacteria (*Escherichia coli*) and fungi (*Candida albicans* and *Aspergillus niger*). Whatman No. 1 filter paper disk of 5 mm diameter were sterilized by autoclaving for 15 min at 121°C. Agar plates were surface inoculated uniformly from the broth culture of the tested microorganisms. The concentration of bacterial suspensions was adjusted to 10^8 colony forming units (10^8cfu/ml) in Mueller Hinton Agar. Sterile discs were then impregnated with 10 µl of each of the test compounds (250µg/ml). The impregnated disks were placed on the medium suitably spaced apart and the plates were then incubated at 5°C for 1 hour to permit good diffusion and then were transferred to an incubator at 37°C for 24 hours for bacteria, and at 28 °C for 72 hours for fungi. The diameters of zone of inhibition were measured after incubation for 24 hours at 37°C. All data on antimicrobial activity are the average of triplicate analyses. Ofloxacin (5µg/ml) and Miconazole nitrate (40µg/ml) were used as standard antibacterial and antifungal compounds respectively.

RESULTS

The antibacterial and antifungal activity of the tested

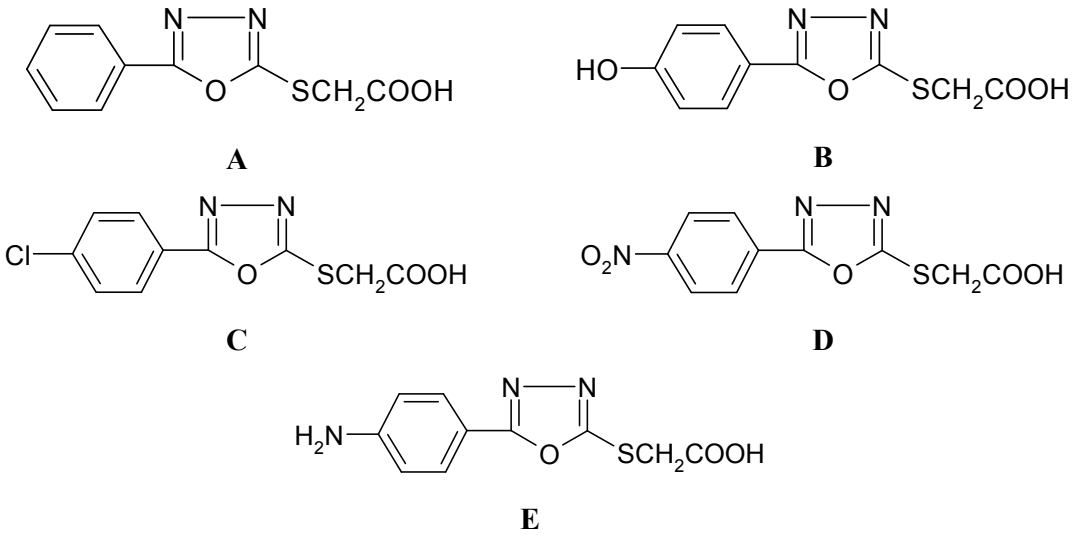

Fig 1. Structure of compounds synthesized and evaluated for antibacterial and antifungal activity

compounds evaluated by measuring the zone of inhibition are summarized in Table 1.

DISCUSSION

The results of the present study revealed that all of the synthesized compounds (250 µg/ml) showed significant antimicrobial activity against *Staphylococcus aureus*. The activity was comparable to that of the positive control Ofloxacin (5µg/ml). Against *Escherichia coli*, compounds A, B, D and E showed less activity except compound C which showed moderate activity as compared to Ofloxacin. Compounds B, C, D showed significant activity against *Candida albicans* whereas moderate activity against *Aspergillus niger* as compared to Miconazole nitrate (40µg/ml). Compounds A and E showed moderate activity against *Candida albicans* whereas slight activity was observed against *Aspergillus niger* as compared to Miconazole nitrate (40µg/ml).

The importance of developing new antibacterial active compounds need not be emphasized, especially if one considers the problem of resistance and multi resistance properties arising continuously among pathogenic bacteria. Thus, from the present study, it can be concluded that the synthesized oxadiazole compounds can be potentially be developed into useful antimicrobial agents that can prompt future researcher to synthesize a series of oxadiazole derivatives containing wide varieties of susbstituent with the aim of obtaining some novel heterocyclic systems with enhanced antimicrobial properties.

ACKNOWLEDGEMENT

Authors are grateful to Jadavpur University for providing the necessary facilities to carry out this research work and also to the University Grant Commission for providing fellowship.

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