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Antimicrobial Activity Noveloxazolo- Pyridine Derivatives

Research Article

Sher Bahadur Mishra, Sandeep Patel, Alok Pal Jain
RKDF College of Pharmacy, SRK University, Bhopal, MP, India

Abstract

Synthesized oxazolopyridine derivatives (All five) were screened for *in vitro* antimicrobial activity against gram-positive bacteria *B. Subtilis* and gram-negative bacteria and *E. Coli*, cutaneous fungi *C. Albicans* and *A. Niger*.
Synthesized oxazolopyrine **OP-5** exhibited excellent antibacterial activity against *E. coli* in comparison to standard drug – Ciprofloxacin. Moreover, **OP-3** showed excellent antifungal activity against *A. Niger* in comparison to standard drug – griseofulvin. Gram-negative bacteria were found to be more sensitive towards the **OP-5** in comparison to gram-positive bacteria.
Analysis of the antifungal activity data concluded that OP-2 possessed significant bioactivity against both fungus *Candida Albicans* and *Aspergillus Niger* when compared to the reference drug griseofulvin. Also OP-4 and OP-5 possessed significant bioactivity against fungus *Aspergillus Niger*. OP-4 possessed significant antibacterial activity against *E. Coli***Keywords:** Ulcer healing, Symplocos Racemosa (SR), antioxidant, Indomethacin Ulcer

Introduction

A drug is considered as bacteriostatic or fungistatic when it inhibits the growth or multiplication of bacteria or fungi respectively and considered as bactericidal or fungicidal when it actually results in the death of bacteria or fungi. Drugs that are bactericidal under certain circumstances may have an apparent bacteriostatic effect at the other times. Important factors for the antimicrobial activity are size of the inoculums, metabolic state of organisms, pH, temperature and duration of interaction, concentration of the inhibitor and presence of interfering substance. In Vitro tests are used as screening procedure for new agents and for testing susceptibility of individual isolates from infections to determine which of the available drugs might be useful therapeutically. In general, minimum inhibitory concentration (MIC) and sensitivity tests are used to express the effectiveness of a compound as an antimicrobial agent. MIC is the smallest concentration of the substance required to inhibit the growth of a test organism under specified conditions. MIC can be determined by the tube dilution method. Sensitivity testing is done to determine the range of microorganisms that are susceptible to the compound under specified conditions.

* Corresponding Author
E.mail: vickyc.chourasia@gmail.com

This method is suitable for the organisms that grow well overnight such as most of the common aerobes and facultative anaerobes and rapidly growing fungi such as *Candida Albicans*. Several forms of disc diffusion methods have been advocated. Among this Kirby Bauer method is the official method of the USA Food & Drug Administration.[1-5]

Material and Methods-[6-13]

Preparation of the Nutrient Media

The following broths were used in the present work. Compositions of broths are as follows:

Table no.1: Composition of Nutrient broth

S. no.	Component	Amount
1	Peptone (bacteriological)	10 gm
2	Beef extract	10 gm
3	Sodium chloride	5 gm
4	Purified water	1000 ml
5	pH	7.2 ± 0.2

Table no. 2: Composition of Sabouraud's broth

S. no.	Component	Amount
1	Dextrose	20 gm
2	Peptone (mycological)	10 gm
3	Agar	15 gm
4	Purified water	1000 ml
5	pH	7.2 ± 0.2

The broths were prepared by dissolving the specified quantities of the dehydrated broth (Hi media) in purified water and were distributed 4 ml quantities in to each test tube. The tubes were closed with cotton plugs and sterilized by autoclaving at 121ºC for 15 minutes

Cultivation of Microorganisms:

The bacterial cultures were aseptically inoculated into nutrient broth and incubated under aerobic conditions at 37ºC for 24 h. Fungal cultures were inoculated into Sabouraud's broth and incubated under aerobic conditions at 25 ºC for 48 h. The following bacterial and fungal cultures were used for the study

Table no. 3: Different microbial cultures used

S. no.	Name of Microorganisms	Status
1	*Bacillius Subtilis*	Gram positive bacteria
2	*Escherichia Coli*	Gram negative bacteria
3	*Candida Albicans*	Fungi (yeast)
4	*Aspergillus Niger*	Fungi (mold)

The bacterial cultures were aseptically inoculated into nutrient broth and incubated under aerobic conditions at 37ºC for 24 h. fungal cultures were inoculated in to Sabouraud's broth and incubated under aerobic conditions at 25C for 48 h

Determination of Antimicrobial Activity

Modified Kirby-Bauer method, one of the official methods among disc diffusion methods, was used for the evaluation of antimicrobial activity of the synthesized compounds. Circular paper disks of 6 mm diameter was impregnated with the specific amount of the test sample and were placed on a suitable nutrient/sabraud's agar medium in a petri plate which was inoculated on its surface with one of the test organisms. After incubation, the plates were observed for the growth inhibition zones around the disks. The diameter of the zone of inhibition is proportional to the antimicrobial activity of the substance. The diameters of the zone of inhibition were compared with that produced by the standard antibiotics

Preparation of the Disks and Samples

Paper disks of 6 mm diameter and 2 mm thickness were used for the test. These disks were sterilized by autoclaving at 121 ºC (15 lb PSIG) for 15 minutes. Almost all samples were tested at 50 µg level. To obtain this, sample solutions containing 10 mg/ml were prepared in sterile dimethylformamide (DMF) and 5µl each of the solutions was added on each disk using a micropipette. All the solutions were added on each disk using a micropipette. All the solutions were prepared using aseptic precautions. Ciprofloxacin (10 µg/disk) was taken as standard antibiotics for the comparison of the antibacterial activity of the synthesized compounds and Clotrimazole (10 µg/disk) were used as standard drugs for antifungal activity studies.

General Procedure

Each Petri plate containing nutrient/ sabouraud's agar medium was inoculated with one bacterial/ fungal culture by spreading the suspension of the organism with a sterile cotton swap. Each plate was divided into six equal portions along the diameter. Each portion was used to place one disk. Four disks of each sample were placed on four portions, one disk with standard drug and a disk impregnated with the solvent (DMF). All the plates were kept in the refrigerator for 30 minutes to allow the diffusion of the sample in to the refrigerator for 30 minutes to allow the diffusion of the sample into the surrounding agar medium. Then the plates inoculated with bacterial cultures were incubated at 37 ºC for 18 h and those with incubated at 25 ºC for 48 h. Diameter of the zones of inhibition wherever produced were measured and the average diameter for each sample was calculated. The diameters obtained for the test samples were compared with that produced by the standard antibiotics, ciprofloxacin for antibacterial activity and clotrimazole for antifungal activity. The results of antibacterial and antifungal activity are given in Tables and figures.

Result and Discussion

Biological Evaluation of Synthesized Compounds

Table No. 8: Anti Bacterial Activity of all synthesized compound

Compounds	*B. subtilis*	*E. coli*
OP-1	12(6.25)[a]	10(12.5)
OP-2	8(12.5)	12(12.5)
OP-3	10(12.5)[a]	15(12.5)
OP-4	15(12.5)	18(12.5)
OP-5	17(25)	23(25)
Control	-	-
Ciproflaxacin	20(6.25)	20(12.5)

Antibacterial Activity of synthesized compounds

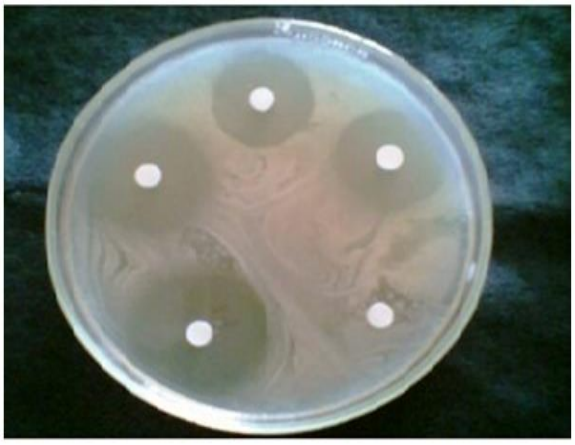

Fig :1Antibacterial Activity of synthesized compounds

Anti Fungal Activity

Table No. 2: Anti Fungal Activity of all synthesized compound

Compounds	*C. albicans*	*A. niger*
OP-1	11(6.25)[a]	16(6.25)
OP-2	13(6.25)	18(6.25)
OP-3	20(6.25)[a]	21(6.25)
OP-4	15(6.25)	18(6.25)
OP-5	10(25)	17(6.25)
Control	-	-
Griseofulvin	20(6.26)	19(6.25)

Antifungal Activity of synthesized compounds

Fig.2: Antifungal Activity of synthesized compounds

Synthesis of **oxazolopyridine & it 5 derivatives** was done and structure of synthesized oxazolopyridine & it 5 derivatives was confirmed using spectral as well as physical method data. Disappearance of absorption bands in synthetic derivatives at **3414(-NH_2** N-H **str.), 3260(-NH-** N-H **str.)** which is present in **OP-0**, and appearance of bands between 1640-1690 cm^{-1} of imine - **C=N-(Schiff base)** in FT-IR spectrum clearly indicated. This fact was further supported by ^{1}HNMR spectrum, disappearance of **NH_2** peak from different synthesized derivatives which was found in OP-0 at 6.95 ppm and peak at 8.43, 7.92 and 7.22 ppm was consistently appeared in all 5 synthesized derivatives. Moreover, synthesized compounds characterized by the TLC and melting point. In addition, by visual inspection synthesized compounds also characterized.

Discussion on biological activity of synthesized compounds:

Synthesized oxazolopyridine derivatives (All five) were screened for *in vitro* antimicrobial activity against gram-positive bacteria *B. Subtilis* and gram-negative bacteria and *E. Coli*, cutaneous fungi *C. Albicans* and *A. Niger.*

Synthesized oxazolopyrine **OP-5** exhibited excellent antibacterial activity against *E. coli* in

comparison to standard drug – Ciprofloxacin. Moreover, **OP-3** showed excellent antifungal activity against *A. Niger* in comparison to standard drug – griseofulvin. Gram-negative bacteria were found to be more sensitive towards the **OP-5** in comparison to gram-positive bacteria.

Analysis of the antifungal activity data concluded that **OP-2** possessed significant bioactivity against both fungus *Candida Albicans* and *Aspergillus Niger* when compared to the reference drug griseofulvin. Also **OP-4** and **OP-5** possessed significant bioactivity against fungus *Aspergillus Niger*. **OP-4** possessed significant antibacterial activity against *E. Coli.*

The analysis of bioactivity data, it is observed that **OP-2** and **OP-4** has moderate antifungal activity against *Candida Albicans.* Moreover, a moderate level of activity was observed against bacteria *B.subtilis* for the newly synthesized **OP-5**, in comparison to the standard drug ciprofloxacin.

However, **OP-1, OP-2** and **OP-3** had shown no significant or poor activity against neither Gram-positive nor Gram-negative bacteria. And **OP-4** had shown poor activity against Gram positive bacteria only.

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