BIOLOGICAL SCREENING OF 1,2,3-TRIAZOLYL SUBSTITUTED CHROMEN-2-ONE DERIVATIVES

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Abstract - The increasing incidence of bacterial and fungal resistance to a large number of antimicrobial agents has prompted studies on the development of new 1,2,3-triazolyl substituted chromen-2-one derivatives potential antimicrobial as well as antibacterial compounds. The molecular manipulation of promising lead compounds is still a major line of approach to develop new drugs. In this paper we are discussing about the anti-bacterial activity as well as anti-fungal activity of newly synthesized compounds 4a-l by cup plate method using nutrient agar medium, whereas anti-fungal activity by using potato-dextrose-agar medium.

Keywords - 1,2,3-triazole, Chrome none, Biological activity.

I. INTRODUCTION

1,2,3-Triazole derivatives have a high potential for biological activity, such as an amine activity,¹ hericidal activity,² antimalarial activity,³ antiviral activity,⁴ anti-inflammatory activity,⁵ antibacterial activity,⁶ and antitumor activity.⁷–¹⁰ These are a class of important nitrogen containing heterocyclic compounds, and many of them displayed remarkable antibacterial activities.¹¹–¹⁴The 1,2,4-triazole fused chromen-2-one derivatives are valuable structural motifs present in a variety of functionalized molecules which have applied into organocatalysis and material science.¹⁵

The triazole fused chromene none derivatives are found to possess wide range of biological activities such as anti-bacterial,¹⁶–²⁶ anti-inflammatory,²⁷–²⁸ antiproliferative,¹ anti-cancer,²⁹ leishmanicidal agents,³⁰ antifungal,³¹ epilepsy,³² cycotic activity,³³ tyrosine kinase inhibitors,³⁴ and diuretic.³⁵

II. MATERIALS AND METHOD

The antibacterial activity of the newly prepared compounds 4a-l has been carried out with cup plate method³⁶ by using nutrient agar medium against Gram-positive bacteria Staphylococcus aureus, Streptococcus pyogenes and Gram-negative bacteria Pseudomonas aeruginosa, Escherichia coli. Ampicillin and Chloramphenicol were employed as references for antibacterial study. The test solution was prepared by dissolving 10 mg of compound in 10 ml of DMF. The nutrient agar medium (peptone-5.0 gm, sodium chloride-5.0 gm, beef extract-1.5 gm, yeast extract-1.5 gm, agar-15.0 gm, distilled water up to-1000 ml, pH-7.4 ± 0.2) s sterilized by autoclaving at 121 °C for 15 mins. The petri plates, tube and flasks plugged with cotton were sterilized in hot-air oven at 160 °C for 60 mins. The diameter of zone of inhibition surrounding each of the cups was measured after incubation of the plates at 37 ± 1 °C for 24 h. Each experiment was repeated thrice and the average of the three independent determinations was recorded. The zone of inhibition produced by each compound was measured in mm. Results are given in Table-1.

All the title compounds 4a-l were also screened for their antifungal activity against two fungal organism, C.albicans and A.clavatus with cup plate method³⁶ by using potato-dextrose-agar medium. Fluconazole has been employed as standard drug for the antifungal study. The test solution was prepared

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by dissolving the compound (10 mg) in DMF (10 ml). The potato-dextrose-agar medium was sterilized by autoclaving at 121 °C for 15 minutes. All the experiment was performed in triplicate in order to minimize the errors and the average of the three independent determinations was recorded. Diameter of zone of inhibition was measured for the plates in which the zone of inhibition in mm for each organism. The results are given in Table-2.

### III. RESULTS AND DISCUSSION

The results of antibacterial screening revealed that compounds 4a-l displayed good activity. The compounds 4c, 4d and 4f showed potent activity with Gram-positive bacteria *Staphylococcus aureus* and where as 4a and 4b active against *Streptococcus pyogenes*. The compounds 4e and 4j exhibited significant activity against Gram-negative bacteria *Escherichia coli* and 4a, 4b and 4d active against *Pseudomonas aeruginosa*. Zone of inhibition compared with standard drugs Ampicillin and Chloramphenicol for antibacterial study. However, the degree of inhibition varied both with test compound as well as with the bacteria used in the present investigation. These remarkable results may be due to the presence of 1,2,3-triazolyl substituted chromen-2-one derivatives. Some of the compounds may be used as bacteriocides after a detailed study.

The antifungal activity results indicated that compounds 4a-l are significantly toxic towards both two fungi. The compounds 4e, 4h, 4j and 4l toxic against *C.albicans* and 4a, 4c, 4e, 4f, 4g and 4j toxic against the fungi *A.clavatus*. The antifungal activity of these compounds compared with the standard drug Fluconazole, which demonstrated that they have promising activity. In conclusion, almost all the series of compounds 4a-l are moderately toxic towards the fungi under investigation when comparison with standard Fluconazole. This may be due to the presence of 1,2,3-triazolyl substituted chromen-2-one derivatives.

### IV. CONCLUSION

All the synthesized compounds exhibited potent activity towards both gram positive and gram negative bacteria. Some of them were found to more active than standard reference drug. These compounds also showed significant antifungal activity against both the fungi.

Almost all the series of compounds 4a-l are moderately toxic towards the fungi under investigation when comparison with standard Fluconazole. This may be due to the presence of 1,2,3-triazolyl substituted chromen-2-one derivatives.

### Table-1. Antibacterial activity data of compounds 4a-4l

| Zone of inhibition (in mm) | Gram +ve | Gram –ve |
|---------------------------|----------|----------|
|                           | S. aureus | S.pyrogens | E. coli | P.aeruginosa |
| 4a                        | 16       | 19       | 16      | 19          |
| 4b                        | 16       | 18       | 14      | 18          |
| 4c                        | 18       | 17       | 16      | 15          |
| 4d                        | 18       | 17       | 15      | 19          |
| 4e                        | 12       | 15       | 21      | 15          |
| 4f                        | 18       | 17       | 17      | 13          |
| 4g                        | 17       | 09       | 16      | 08          |
| 4h                        | 14       | 15       | 10      | 06          |
| 4i                        | 15       | 10       | 08      | 12          |
Table-2. Antifungal activity results of compounds 4a-4l

|     | C. albicans | A. clavatus |
|-----|-------------|-------------|
| 4a  | 19          | 24          |
| 4b  | 21          | 19          |
| 4c  | 17          | 23          |
| 4d  | 18          | 16          |
| 4e  | 23          | 23          |
| 4f  | 14          | 23          |
| 4g  | 15          | 24          |
| 4h  | 25          | 16          |
| 4i  | 16          | 18          |
| 4j  | 22          | 24          |
| 4k  | 19          | 15          |
| 4l  | 25          | 17          |
| Fluconazole | 24      | 24          |

Structures of compounds 4a-4l

4-(2-(4-phenyl-1H-1,2,3-triazol-1-yl)ethoxy)-2H-chromen-2-one (4a):

![Structure of 4a](image)

4-(2-(4-(hydroxymethyl)-1H-1,2,3-triazol-1-yl)ethoxy)-2H-chromen-2-one (4b):

![Structure of 4b](image)

4-(2-(4-cyclopropyl-1H-1,2,3-triazol-1-yl)ethoxy)-2H-chromen-2-one (4c):

![Structure of 4c](image)
4-(2-(4-(trimethylsilyl)-1H,1,2,3-triazol-1-yl)ethoxy)-2H-chromen-2-one (4d):

1-((1-(2-((2-oxo-2H-chromen-4-yl)oxy)ethyl)-1H,1,2,3-triazol-4-yl)methyl)indoline-2,3-dione (4e):

4-(2-(4-heptyl-1H,1,2,3-triazol-1-yl)ethoxy)-2H-chromen-2-one (4f):

4-((1-(2-((2-oxo-2H-chromen-4-yl)oxy)ethyl)-1H,1,2,3-triazol-4-yl)methoxy)-2H-chromen-2-one (4g):

methyl ((1-(2-((2-oxo-2H-chromen-4-yl)oxy)ethyl)-1H,1,2,3-triazol-4-yl)methyl)
prolinate (4h):

Ethyl1-(2-((2-oxo-2H-chromen-4-yl)oxy)ethyl)-1H-1,2,3-triazole-4-carboxylate (4i):

4-(2-(4-(((tetrahydro-2H-pyran-2-yl)oxy)methyl)-1H-1,2,3-triazol-1-yl)ethoxy)-2H-chromen-2-one (4j):

4-(2-(4-((tert-butyldiphenylsilyl)oxy)ethyl)-1H-1,2,3-triazol-1-yl)ethoxy)-2H-chromen-2-one (4k):

4-(2-(4-(((3aR,6S,6aR)-5-((S)-2,2-dimethyl-1,3-dioxolan-4-yl)-2,2-dimethyltetrahydrofuro
[2,3-d][1,3]dioxol-6-yl)oxy)methyl)-1H-1,2,3-triazol-1-yl)ethoxy)-2H-chromen-2-one (4l):

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