

## Synthesis, Characterization and Pharmacological Activity of Phenoxy Acetic Acid and Pyrazinium Chlorochromate

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This study describes the synthesis and antibacterial, antifungal activity of phenoxy acetic acid and pyrazinium chlorochromate. The compounds were characterized by infrared and ultra violet visible spectral data. These compounds were reviewed for antibacterial and antifungal activity against *Streptococcus*, *Entrococcus*, *Bacillus cereus*, *Proteus vulgaris*, *Mycobacterium tuberculosis*, *Azotobacter*, *E. coli*, *Pseudomonas aeruginosa*, *Candida albicans*, *A. niger*, *Fusarium* and *Trichoderma* by disc diffusion method.

**Keywords:** Phenoxy acetic acid, Pyrazinium chlorochromate, Biological activities.

### INTRODUCTION

The basic molecular structures of the heterocyclic system exhibit a broad range of biological and pharmacological activities [1]. Many new drugs are synthesized using these moieties. The over practice of antimicrobial drugs have produced more impedance to the bacteria and fungi. As a result many infectious diseases have come to light. In order to prevent the spreading of these diseases, the pharmacists are in the need to develop a unique, wide-ranging of antimicrobial agents [2-4]. The heterocyclic ring consisting of nitrogen or sulphur atoms are researched for their physicochemical properties. The sensitivity of these heterocyclic compounds towards the biological properties plays a key role in the kinetic study [5,6].

The literature survey reveals that the pyrazine derivatives displays numerous properties like antibacterial [7], anti-inflammatory [8], analgesic [9], ulcerogenic potential [10], antituberculosis [11], antimicrobial [12], antifungal, antioxidant, anticonvulsants [13], antiproliferative assay [14], serotonin activity [15], cytotoxic properties [16,17], antipolytic activity [18], antidiabetic and antihistamines [19]. Several phenoxy derivatives illustrate antimycobacterial [20], antiviral [21], antituberculosis activity [22], hypolipidemic activity [23], antinociceptive [24], anti-inflammatory activity, antifungal activities [25], antioxidant activity [27], antidiabetic property [28].

*Aspergillus niger* and *Fusarium* species are plant pathogens and they affect the plant growth. The mycotoxins [29] produced by these are prone to cause lung defilement, ear infections and has been disclosed in HIV patients [30]. Phenoxy acetic acid, pyrazinium chlorochromate compounds are screened for their biological activities towards few Gram-positive, Gram-negative bacteria and fungi.

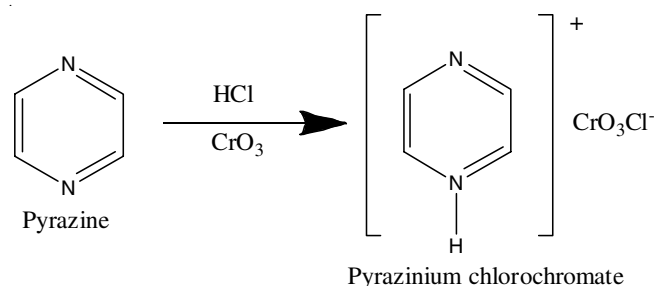
### EXPERIMENTAL

AnalaR grade reagents are used for the synthesis of phenoxy acetic acid and pyrazinium chlorochromate. The melting points of these two compounds were determined by Thomas Hoover capillary melting point instrument. The IR spectra were recorded on FTIR Bruker Alpha and UV-visible spectra were reported using PerkinElmer Lambda 365 make instrument.

#### Synthesis of pyrazinium chlorochromate ( $C_4N_2H_5CrO_3Cl$ ):

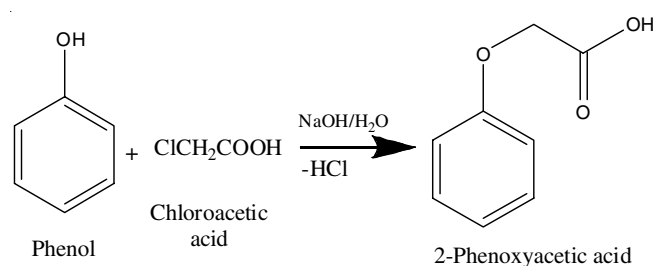
An orange coloured solid was prepared by adding 1.30 mmol of chromium trioxide and 2.4 mmol of 12 M HCl in 2 mL of doubly distilled water with constant stirring to a solution of 2.24 mmol of pyrazine and 2.28 mmol of 12 M HCl in 4 mL of water, in ice bath. After constant stirring for 2 h at 0 °C an orange coloured solid [31] obtained was filtered and then dried. The recrystallized solid (**Scheme-I**) from acidified water was used throughout the work (m.p. 148 to 150 °C).

**Preparation of phenoxy acetic acid ( $C_8H_8O_3$ ):** To 11.47 mmol of sodium hydroxide 5 mmol of phenol was added and



Scheme-I: Synthesis of pyrazinium chlorochromate (PzCC)

diluted. 6 mmol of chloroacetic acid was dissolved in warm water and added to the above mixture and stirred constantly for 2 h at 60 to 80 °C. 35 % Hydrochloric acid was added and vacuum fractionated using benzene as solvent. The white coloured solid obtained (**Scheme-II**) was recrystallized using water and ethanol mixture (m.p. 98.2 to 98.9 °C) [32].



Scheme-II: Synthesis of phenoxy acetic acid

**Phenoxy acetic acid:** m.f.  $C_8H_8O_3$ , m.p. 98.2-99.0 °C, m.w. 152.15, Yield 98.5 %. IR (KBr,  $\nu_{max}$ ,  $cm^{-1}$ ) 3300, 2467.70, 859.16, 3000, 1441.72, 3120, 1607.11, 1172.25, 1348.95, 1235.27 1043.36. The UV-visible spectrum showed absorbance peaks at 216.85 nm (s), 268.70 nm (w), transmittance peaks at 216.85 nm (s), 268.70 nm (s).

**Pyrazinium chlorochromate:** m.f.  $C_4N_2H_5CrO_3Cl$ , m.p. 148-154 °C, Yield 61%. IR (KBr,  $\nu_{max}$ ,  $cm^{-1}$ ) 3113, 3049, 2955, 2768, 2700, 2085, 1614, 1490, 1373, 608, 1160, 770. The UV-visible spectrum showed peaks at 312 nm (m,b), 267 nm (s), transmittance peaks at 260.05 nm (s), 350.45 nm (b), 772.80 nm (w).

**Determination of biological potential:** The solution of the phenoxy acetic acid and pyrazinium chlorochromate were

prepared in various concentrations like 25, 50, 75 and 100  $\mu L$  by dissolving in dimethyl sulphoxide solvent.

**Disc diffusion antibiotic sensitivity testing:** The synthesized compounds were screened for antibacterial activity against *Streptococcus*, *Enterococcus*, *Bacillus cereus*, *Proteus vulgaris*, *Mycobacterium tuberculosis*, *Azotobacter*, *E. coli*, *Pseudomonas aeruginosa*, *Candida albicans*, *A. niger*, *Fusarium* and *Trichoderma* using the agar disc diffusion method [33-36].

Bacterial inoculums containing approximately  $10^5$ - $10^6$  colony forming units (CFU)/mL were used at 37 °C. The culture medium (Agar medium) was composed of peptone 5 g/L, NaCl-5 g/L, Agar-15 g/L, Beef extract-3 g/L, Yeast extract-1.5 g/L. The pH was maintained to be neutral at 7. All the materials were diluted in doubly distilled water and the medium was sterilized at 121 °C for 20 min at pressure 15 psi. The solutions of the chemical compounds were prepared at the concentration of 25, 50, 75 and 100  $\mu L$  in DMSO.

The agar plate was incubated for 20 to 28 h at 37-38 °C for bacteria and 25 °C for fungi by following the standard procedure. Ciprofloxacin was selected as the standard and the zone of inhibition were measured and compared with the controls. Bacterial cultures were obtained from Eumic analytical Lab and Research Institute, Tiruchirappalli. Bacterial strains were maintained on Nutrient agar slants (Hi media) at 4 °C.

## RESULTS AND DISCUSSION

As the concentration of phenoxy acetic acid and pyrazinium chlorochromate increased from 25 to 100  $\mu L$ . The lethal zone of the bacteria and fungi also increased (Tables 1 and 2). The inhibition for the organic compound phenoxy acetic acid was high at 100  $\mu L$  for (Gram-positive bacteria) *Mycobacterium tuberculosis*, *Proteus vulgaris* (Gram-negative bacteria) and fungi, *Aspergillus niger*, *Fusarium* and *Trichoderma* than the control of standard drug ciprofloxacin. Likewise for heterocyclic pyrazinium chlorochromate compound the impedance was more for (Gram-positive bacteria) *Mycobacterium tuberculosis*, (Gram-negative bacteria) *Proteus vulgaris* and fungi as discussed above.

## Conclusion

At higher concentration (100  $\mu L$ ) the phenoxy acetic acid exhibited good resistant towards the organisms like *Bacillus*

TABLE-1  
INHIBITION ZONE FOR PHENOXY ACETIC ACID

| Organisms                         | Gram stain             | Control 100 $\mu L$ added and zone of inhibition (mm/mL) |            |            |             |         |
|-----------------------------------|------------------------|----------------------------------------------------------|------------|------------|-------------|---------|
|                                   |                        | 25 $\mu L$                                               | 75 $\mu L$ | 50 $\mu L$ | 100 $\mu L$ | Control |
| <i>Streptococcus</i>              | Gram-positive bacteria | 10                                                       | 12         | 14         | 16          | 30      |
| <i>Bacillus cereus</i>            | Gram-positive bacteria | 12                                                       | 14         | 16         | 18          | 20      |
| <i>Enterococcus</i>               | Gram-positive bacteria | 10                                                       | 12         | 14         | 16          | 20      |
| <i>Proteus vulgaris</i>           | Gram-negative bacteria | 10                                                       | 12         | 14         | 16          | 15      |
| <i>Micrococcus</i>                | Gram-positive bacteria | 10                                                       | 11         | 13         | 16          | 30      |
| <i>Mycobacterium tuberculosis</i> | Gram-positive bacteria | 12                                                       | 15         | 18         | 20          | 22      |
| <i>Azotobacter</i>                | Gram-negative bacteria | 12                                                       | 14         | 16         | 18          | 25      |
| <i>E. coli</i>                    | Gram-negative bacteria | 10                                                       | 12         | 14         | 16          | 25      |
| <i>Pseudomonas aeruginosa</i>     | Gram-negative bacteria | 12                                                       | 15         | 18         | 20          | 25      |
| <i>Candida albicans</i>           | Fungi                  | 12                                                       | 14         | 16         | 19          | 32      |
| <i>A. niger</i>                   | Fungi                  | —                                                        | 10         | 11         | 12          | 12      |
| <i>Fusarium</i>                   | Fungi                  | 11                                                       | 13         | 16         | 18          | 12      |
| <i>Trichoderma</i>                | Fungi                  | 10                                                       | 11         | 12         | 14          | 12      |

TABLE-2  
INHIBITION ZONE FOR PYRAZINIUM CHLOROCHROMATE

| Organisms                         | Gram stain             | Control 100 µL added and zone of inhibition (mm/mL) |       |       |        |         |
|-----------------------------------|------------------------|-----------------------------------------------------|-------|-------|--------|---------|
|                                   |                        | 25 µL                                               | 75 µL | 50 µL | 100 µL | Control |
| <i>Streptococcus</i>              | Gram-positive bacteria | 10                                                  | 12    | 14    | 16     | 28      |
| <i>Bacillus cereus</i>            | Gram-positive bacteria | 12                                                  | 14    | 16    | 18     | 22      |
| <i>Enterococcus</i>               | Gram-positive bacteria | 12                                                  | 15    | 18    | 20     | 22      |
| <i>Proteus vulgaris</i>           | Gram-negative bacteria | 14                                                  | 17    | 21    | 25     | 15      |
| <i>Micrococcus</i>                | Gram-positive bacteria | –                                                   | 10    | 11    | 12     | 20      |
| <i>Mycobacterium tuberculosis</i> | Gram-positive bacteria | 14                                                  | 16    | 18    | 20     | 20      |
| <i>Azotobacter</i>                | Gram-negative bacteria | 10                                                  | 12    | 14    | 16     | 25      |
| <i>E. coli</i>                    | Gram-negative bacteria | 12                                                  | 14    | 16    | 18     | 25      |
| <i>Pseudomonas aeruginosa</i>     | Gram-negative bacteria | 10                                                  | 11    | 13    | 15     | 23      |
| <i>Candida albicans</i>           | Fungi                  | 12                                                  | 15    | 18    | 21     | 30      |
| <i>A. niger</i>                   | Fungi                  | 10                                                  | 11    | 12    | 14     | 12      |
| <i>Fusarium</i>                   | Fungi                  | –                                                   | 10    | 11    | 12     | 12      |
| <i>Trichoderma</i>                | Fungi                  | 10                                                  | 12    | 14    | 16     | 14      |

*cereus*, *Proteus vulgaris*, *Mycobacterium tuberculosis*, *Aspergillus niger*, *Fusarium*, *Trichoderma* and pyrazinium chlorochromate were resistant towards *Enterococcus*, *Proteus vulgaris*, *Mycobacterium tuberculosis*, *Aspergillus niger* and *Fusarium*, *Trichoderma*.

### CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this article.

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