Asian Journal of Chemistry; Vol. 30, No. 10 (2018), 2238-2240

ASIAN JOURNAL OF CHEMISTRY

https://doi.org/10.14233/ajchem.2018.21417

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

K. ANBARASU and K.K. ILAVENIL*

Department of Chemistry, Arignar Anna Government Arts College, Musiri-621 211, India

*Corresponding author: E-mail: illavenil81@gmail.com

Received: 27 April 2018; *Accepted*: 11 June 2018; *Published online*: 31 August 2018; AJC-19050

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 activites [1] . Many new drugs are synthesized using these moeities. The over practice of antimicrobial drugs have produced more impedance to the bacterias and fugi. As a result many infectious diseases have come to light. In order to prevent the spreading of these diseases, the pharmacisit 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 physiochemical 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], antiinflammatory [8], analgesic [9], ulcerogenic potential [10], antituberclosis [11], antimicrobial [12], antifungal, antioxidant, anticonvulsants [13], antiproliferative assay [14], serotonin activity [15], cytotoxic properties [16,17], antilipolytic activity [18], antidiabetic and antihistamines [19]. Several phenoxy derivatives illustrate antimycobacterial [20], antiviral [21], antituberclosis activity [22], hypolipidemic activity [23], antinociceptive [24], anti-inflammatory activity, antifungal activities [25], antioxidant activity [27], antidiabetic property [28].

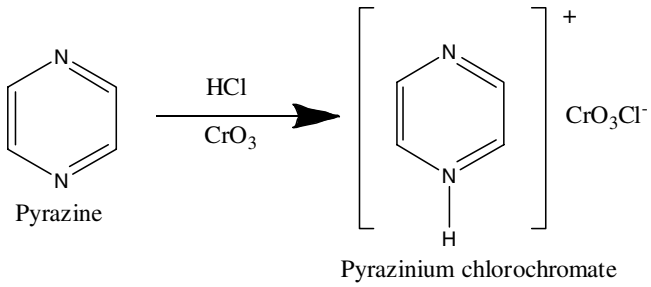
Aspergillus niger and *Fusarium* species are plant pathogens and they affect the plant growth. The mycotoxins [29] produced by these are proned to cause lung defilement, ear infections and has been disclosed in HIV patients [30]. Phenoxy acetic acid, pyrazinium chlorochromate compounds are screened for their biological activites towards few Gram-positive, Gram-negative bacterias 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 Lamda 365 make instrument.

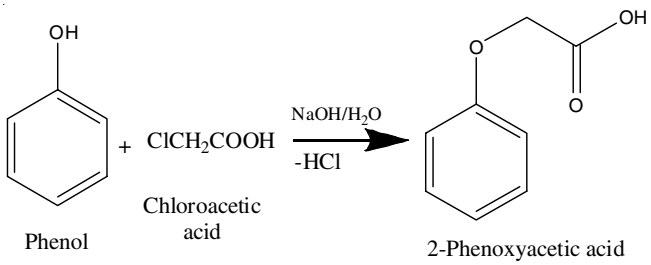
Synthesis of pyrazinium chlorochromate ($C_4N_2H_5CrO_3Cl$): An orange coloured solid was prepared by adding 1.30 mmol of chromium trioxide and 2.4 mmol of 12 M HCl in 2 mL of doubly distilled water with constant stirring to a solution of 2.24 mmol of pyrazine and 2.28 mmol of 12 M HCl in 4 mL of water, 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 acidifed 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 vacum 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, ν_{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, ν_{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 µL by dissolving in dimethy sulphoxide solvent.

Disc diffusion antibiotic sensitivity testing: The synthesized compounds were screened for antibacterial activity against *Streptococcus, Entrococcus, 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 µL 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 µL. 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 µL for (Gram-positive bacteria) *Mycobacterium tuberclosis*, *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 tuberclosis*, (Gram-negative bacteria) *Proteus vulgaris* and fungi as discussed above.

Conclusion

At higher concentration (100 µL) 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 µL added and zone of inhibition (mm/mL)				
		25 µL	75 µL	50 µL	100 µL	Control
Streptococcus	Gram-positive bacteria	10	12	14	16	30
Bacillus cereus	Gram-positive bacteria	12	14	16	18	20
Entrococcus	Gram-positive bacteria	10	12	14	16	20
Proteus vulgaris	Gram-negative bacteria	10	12	14	16	15
Micrococcus	Gram-positive bacteria	10	11	13	16	30
Mycobacterium tuberclosis	Gram-positive bacteria	12	15	18	20	22
Azotobacter	Gram-negative bacteria	12	14	16	18	25
E. coli	Gram-negative bacteria	10	12	14	16	25
Pseudomonas aeruginosa	Gram-negative bacteria	12	15	18	20	25
Candida albicans	Fungi	12	14	16	19	32
A. niger	Fungi	–	10	11	12	12
Fusarium	Fungi	11	13	16	18	12
Trichoderma	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
Streptococcus	Gram-positive bacteria	10	12	14	16	28
Bacillus cereus	Gram-positive bacteria	12	14	16	18	22
Entrococcus	Gram-positive bacteria	12	15	18	20	22
Proteus vulgaris	Gram-negative bacteria	14	17	21	25	15
Micrococcus	Gram-positive bacteria	–	10	11	12	20
Mycobacterium tuberclosis	Gram-positive bacteria	14	16	18	20	20
Azotobacter	Gram-negative bacteria	10	12	14	16	25
E. coli	Gram-negative bacteria	12	14	16	18	25
Pseudomonas aeruginosa	Gram-negative bacteria	10	11	13	15	23
Candida albicans	Fungi	12	15	18	21	30
A. niger	Fungi	10	11	12	14	12
Fusarium	Fungi	–	10	11	12	12
Trichoderma	Fungi	10	12	14	16	14

cereus, Proteus vulgaris, Mycobacterium tuberclosis, Aspergiullus niger, Fusarium, Trichoderma and pyrazinium chlorochromate were resistant towards *Entrococcus, Proteus vulgaris, Mycobacterium tuberclosis, Aspergiullus niger* and *Fusarium, Trichoderma*.

CONFLICT OF INTEREST

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

REFERENCES

1. A.P. Taylor, R.P. Robinson, Y.M. Fobian, D.C. Blakemore, L.H. Jones and O. Fadeyi, *Org. Biomol. Chem.*, **14**, 6611 (2016); https://doi.org/10.1039/C6OB00936K.
2. R. Chawla, U. Sahoo, A. Arora, P.C. Sharma and V. Radhakrishnan, *Acta Pol. Pharm. Drug Res.*, **67**, 55 (2010).
3. A.R. Katritzky, *Chem. Rev*., **104**, 2125 (2004); https://doi.org/10.1021/cr0406413.
4. M.E. Azab, M.M. Youssef and E.A. El-Bordany, *Molecules*, **18**, 832 (2013); https://doi.org/10.3390/molecules18010832.
5. K.G. Sekar and G. Manikandan, *Oxid. Commun.*, **35**, 577 (2012).
6. B.H. Asghar, *Arab. J. Chem.*; https://doi.org/10.1016/j.arabjc.2015.04.006.
7. H. Foks, D. Pancechowska-Ksepko, A. Kedzia, Z. Zwolska, M. Janowiec and E. Augustynowicz-Kopec, *II Farmaco*, **60**, 513 (2005); https://doi.org/10.1016/j.farmac.2005.05.002.
8. E. Abignente, *Actual Chim. Ther.*, **18**, 193 (1991).
9. P. Gund and T.Y. Shen, *J. Med. Chem.*, **20**, 1146 (1977); https://doi.org/10.1021/jm00219a007.
10. E. Abignente, P. de Caprariis, M.G. Rimoli, L. Avallone, L. Gomez Paloma, F. Rossi, M. D'Amico, V. Calderaro and C. Parrillo, *Eur. J. Med. Chem.*, **28**, 337 (1993); https://doi.org/10.1016/0223-5234(93)90150-D.
11. M.V. Baldwin, D.A. Sonia, T.J. Sindhu, C. Meena, A.R. Bhar and K. Krishnakumar, *World J. Pharm. Pharm. Sci.*, **3**, 1124 (2014).
12. M. Gür, N. Sener, H. Muglu, M.S. Çavus, O.E. Özkan, F. Kandemirli and I. Sener, *J. Mol. Struct.*, **1139**, 111 (2017); https://doi.org/10.1016/j.molstruc.2017.03.019.
13. K. Nishie, A.C. Waiss Jr. and A.C. Keyl, *Toxicol. Appl. Pharmacol.*, **17**, 244 (1970); https://doi.org/10.1016/0041-008X(70)90149-3.
14. L. Racané, S. Kraljevic Pavelic, I. Ratkaj, V. Stepanic, K. Pavelic, V. Tralic-Kulenovic and G. Karminski-Zamola, *Eur. J. Med. Chem.*, **55**, 108 (2012); https://doi.org/10.1016/j.ejmech.2012.07.005.
15. B.V. Clineschmidt, J.C. McGuffin and A.B. Pflueger, *Eur. J. Pharmacol.*, **44**, 65 (1977); https://doi.org/10.1016/0014-2999(77)90117-0.
16. N. Dias, U. Jacquemard, B. Baldeyrou, A. Lansiaux, J.-F. Goossens, C. Bailly, S. Routier and J.-Y. Mérour, *Eur. J. Med. Chem.*, **40**, 1206 (2005); https://doi.org/10.1016/j.ejmech.2005.07.003.
17. R.S. Kumar, I.A. Arif, A. Ahamed and A. Idhayadhulla, *Saudi J. Biol. Sci.*, **23**, 614 (2016); https://doi.org/10.1016/j.sjbs.2015.07.005.
18. P.P. Lovisolo, G. Briatico-Vangosa, G. Orsini, R. Ronchi, R. Angelucci and G. Valzelli, *Pharmacol. Res. Commun.*, **13**, 151 (1981); https://doi.org/10.1016/S0031-6989(81)80016-1.
19. C.P. Meher, A.M. Rao and Md. Omar, *Asian J. Pharm. Sci. Res.*, **3**, 43 (2013).
20. M. Shahar Yar, A.A. Siddiqui and M.A. Ali, *Bioorg. Med. Chem. Lett.*, **16**, 4571 (2006); https://doi.org/10.1016/j.bmcl.2006.06.021.
21. M. Shahar Yar, M.A. Bakht, A.A. Siddiqui, M.M. Abdullah and E. De Clercq, *J. Enzym. Inhib. Med. Chem.*, **24**, 876 (2009); https://doi.org/10.1080/14756360802447917.
22. M.A. Ali, M.S. Yar, M. Kumar and G.S. Pandian, *Nat. Prod. Res.*, **21**, 575 (2007); https://doi.org/10.1080/14786410701369367.
23. S.N. Mokale, M.C. Nevase, N.S. Sakle, P.N. Dube, V.R. Shelke, S.A. Bhavale and A. Begum, *Bioorg. Med. Chem. Lett.*, **24**, 2155 (2014); https://doi.org/10.1016/j.bmcl.2014.03.030.
24. G. Turan-Zitouni, L. Yurttas, Z.A. Kaplancikli, Ö.D. Can and Ü. Demir Özkay, *Med. Chem. Res.*, **24**, 2406 (2015); https://doi.org/10.1007/s00044-014-1309-1.
25. A. Iqbal, H. Siddiqui, C. Ashraf, M. Ahmad and G. Weaver, *Molecules*, **12**, 245 (2007); https://doi.org/10.3390/12020245.
26. M. Urban, J. Sarek, M. Kvasnica, I. Tislerova and M. Hajduch, *J. Nat. Prod.*, **70**, 526 (2007); https://doi.org/10.1021/np060436d.
27. M. Kucerova-Chlupacova, M. Dosedel, J. Kunes, M. Soltesova-Prnova, M. Majekova and M. Stefek, *Monatsh. Chem.*, **149**, 921 (2018); https://doi.org/10.1007/s00706-018-2146-6.
28. X. Wang, T. Zhao, B. Yang, Z. Li, J. Cui, Y. Dai, Q. Qiu, H. Qiang, W. Huang and H. Qian, *Bioorg. Med. Chem. Lett.*, **23**, 132 (2015); https://doi.org/10.1016/j.bmc.2014.11.016.
29. A. Ghafoor and S.A.J. Khan, List of Diseases of Econonomic Plants in Pakistan, Ministry of Food and Agriculture, Islamabad, Pakistan, pp. 26 (1976).
30. I. Rzewnicki, E. Olszewska and D. Rogowska-Szadkowska, *Med. Sci. Monit.*, **18**, RA17 (2012); https://doi.org/10.12659/MSM.882505.
31. G.L. Gard, H.B. Davis, R.M. Sheets, J.M. Brannfors and W.W. Paudler, *Heterocycles*, **20**, 2029 (1983); https://doi.org/10.3987/R-1983-10-2029.
32. C.F. Koelsch, *J. Am. Chem. Soc.*, **53**, 304 (1931); https://doi.org/10.1021/ja01352a042.
33. Atta-ur-Rahman, M.I. Choudhary and W.J. Thomsen, Bioassay Techniques for Drug Dtwelopment, Harwood Academic Publishers, The Netherlands, p. 16 (2001).
34. K.M. Khan, Z.S. Saify, M.Z. Khan, Zia-Ullah, M.I. Choudhary, Atta-ur-Rahman, S. Perveen, Z.H. Chohan and C.T. Supuran, *J. Enzym. Inhib. Med. Chem.*, **19**, 373 (2004); https://doi.org/10.1080/14756360409162453.