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Original Article

DESIGN, SYNTHESIS, CHARACTERIZATION AND BIOLOGICAL EVALUATION OF SOME NOVEL CINNOLO PIPERAZINE DERIVATIVES

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ABSTRACT

Objective: To design and synthesize a series of substituted 4-(p-amino piperazine) cinnoline-3- carboxamide derivatives and evaluate for anti-microbial activity.

Method: A novel series of substituted 4-(p-amino piperazine) cinnoline-3- carboxamide (4a-g) derivatives were synthesized by reacting substituted 4-amino cinnoline 3-carboxamide (3a-g) with DMF and p-chloro piperazine. Substituted 4-amino cinnoline 3-carboxamide (3a-g) were synthesized by reaction of substituted phenyl hydrazono cyano acetamide (2a-g) with anhydrous $AlCl_3$ and chlorobenzene in nitrogenous environment. Substituted phenyl hydrazono (cyano) acetamide was synthesized by reaction of substituted aniline diazonium chloride (1a-g) with CH_3COONa and ethanol. Substituted aniline diazonium chloride were synthesized by substituted aniline with conc HCl and sodium nitrite .The synthesized compounds were characterized by IR, NMR and Mass spectral data. The synthesized compounds were screened for their antibacterial and antifungal activity against 4 pathogenic bacteria and 2 pathogenic funguses.

Results: The compound 4a, 4c and 4g shows potent antimicrobial activity in comparison to standard drugs while other compounds showed moderate activity. Further all the compounds are obtained in good purity.

Conclusion: All the compounds synthesized were checked for their purity and spectral analysis shows their structural confirmation, some compounds shows potent antimicrobial activity.

Keywords: Cinnoline derivatives, Anti-bacterial, Anti-fungal.

INTRODUCTION

The main objective of organic and medicinal chemistry is the synthesis, characterization and pharmacological evaluation of molecules having highly therapeutic and efficacy in nature. Now a days increasing the resistance of many organisms, we have to synthesized the more active new molecules against the resistance microbes, particularly the bacteria, virus and fungus is the major area in the antimicrobial research. The aim of this research is to synthesize and characterize the biological active molecule for resistant bacteria and fungus [1]. The substituted cinnoline derivatives were reported for various pharmacological activities including antimicrobial, insecticidal [2], antitumor, and antifungal [3].

Microbial development of resistance, as well as economic incentives, has resulted in research and development in the search for new antibiotics in order to maintain a pool of effective drugs at all times. While the development of resistant strains is inevitable, the slack ways that we administer and use antibiotics has greatly exacerbated the process [4].In spite of the large number of antibiotics and chemotherapeutics available for medical use, the emergence of old and new antibiotic resistant bacterial strains in the last decades constitutes a substantial need for the new class of antibacterial agents [5].

The progress achieved in the synthesis of heterocyclic compounds with biological potential is due to improvement of methodological study of tested substances too. The progress achieved in the synthesis of heterocyclic compounds with biological potential is due to improvement of methodological study of tested substances too. Cinnoline ring is a versatile lead molecule [5] that has been investigated widely in medicinal chemistry due to its important pharmacological activities.

The nucleus gives out different biological activities as anti-microbial, anti-tubercular, anti-malarial, anti-hypertensive, antidepressant, anti-pyretic, analgesic, anesthetic etc. [6-10]

MATERIALS AND METHODS

All the melting points were determined by open capillary method and are uncorrected. The purity of compound was monitored by T.L.C on silica gel coating aluminium plate using U.V. light as visualizing agent. The I.R. spectra (KBr in cm^{-1}) were recorded on Perkin-Elmer Spectrophotometer in the range of 4000-400 cm^{-1}. The ^1H NMR Spectra were recorded on Varion 500 MHz NMR Spectrophotometer using DMSO-4f as a solvent and TMS as an internal standard (chemical shift in δ ppm. Mass spectra were obtained by MS (EI) JEOL GC MATE700 EV spectrometer.

Experimental procedure

Synthesis: Substituted Cinnolo piperazine were synthesized by three steps:

(1) synthesis of substituted phenyl hydrazono (cyno) acetamide (2a-g) then (2) synthesis of substituted 4-amino cinnoline-3-carboxamide (3a-g) and finally (3) synthesis of substituted 4-(p-amino piperazine) Cinnoline -3-carboxamide (4a-g).

General procedure for the preparation of substituted phenyl hydrazono (cyano) acetamide (2a-g):

The substituted aniline (0.195 mole) was dissolved a mixture of conc HCl (7.5ml), water (7.5ml) and cooled to 0 to 5 °C in an ice bath. To this a cold saturated solution of sodium nitrite (0.19 mole) was added slowly. Soon after the addition, the fumes of nitrous acid were liberated; a pinch of sulphamic acid / thiourea is added, stirred till the fumes were ceased. The diazonium salt thus formed was filtered in to a cooled solution of cyano acetamide (0.195 mole) in water (350ml) 10 gm CH_3COONa and 15 ml alcohol. The mixture was kept stirring up to 6 hrs at room temperature; the solid was collected and recrystallized from methanol. 1a-c 1-a M.P. 150°C (76.18%) R_f value 0.72, 1b- M.P. 182 °C (68.42%) R_f value 0.65, 1c - M.P. 164°C (72.16%) R_f value 0.54. 1d -M.P. 174°C (79.24%) R_f value 0.45, 1e- M.P. 150°C (70.28%) R_f value 0.62, 1f- M.P. 174°C (76.32%) R_f value 0.71, 1g- M.P. 132°C (80.22%) R_f value 0.53