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Research Article

SYNTHESIS AND ANTIMICROBIAL ACTIVITY OF TRIAZINOINDOLES

C.V Parwati[1]*, H. Ramesh[1], Patil Prakash[2], V. N sonar[3] and C.V Neelavati[4]
[1]Department of Pharmaceutical chemistry RRK'S College of Pharmacy, Bidar, India
[2]Department of Pharmacology, RRK'S College of Pharmacy, Bidar, India
[3]Department of Pharmaceutical chemistry, V L College of Pharmacy, Raichur, India
[4]Department of Pharmaceutical chemistry, Karnataka college of Pharmacy, Bidar, India

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*C.V Parwati, Asst. Prof, Department of Pharmaceutical Chemistry, RRK'S College of Pharmacy, Bidar-585401
E-Mail: parvathi1865@rediffmail.com

ABSTRACT
Several new 3,4-dihydro-4-oxo-1,2,4-triazino(4,5-a) indoles (3a-g) were synthesized string from ethyl substituted indole-2-carboxylates (1a-g) which were allowed to react with hydrazine hydrate (80%) in ethanol to furnish the corresponding indole-2-Carboxy hydrazine (2a-g) all the synthesized compounds were screened for their antimicrobial activity.
In continuation of our studies on the synthesis of bihetrocyclic compounds containing indole nucleus we report the synthesis of new triazinoindoles these bihetrocyclic were tested for their antimicrobial activity. The reaction sequence leading to the formation of 2-3 is outlined in the Scheme-1
Substituted indole -2-carboboxylate (1a-g) were treated with hydrazine hydrate to get the respective indole -7-Carboxy-hydrazides (2a-g) these hydrazides when reacted with ethyl orthoformate in DME good yielded 3,4-dihydro-4-oxo-1,24-triazino94,5-a) indoles (3a-g)
KEY WORDS: Triazinoindoles, antimicrobial activity

INTRODUCTION

The indole and its derivatives have occupied a unique place in the chemistry of nitrogen heterocyclic compounds. because of their varied biodynamic properties[1]. but, earlier derivatives of indole were known of their dyeing properties. Many compounds having structural resemblance to ancient dye indigo were known. Only after the beginning of twentieth century, a large number of naturally occurring compounds, like alkaloids, were found to possess indole nucleus. During this period the recognition of the plant growth hormone heteroauxin[2] and the essential amino acid tryptophan[3] as the derivatives of indole have added stimulus of this research.

The significant contribution of many derivatives of indole in the development of medicinal chemistry should be recognized. Serotoin, known for its vasoconstrictor principle[4]. Plays a vital role as neutransmitter and in psychosis. The discovery of psilocin and psilocybin[5]. as the important psychotomimetic indoles, have led to extensive research on derivatives of indole-3-ethylamine or tryptamine. Several derivatives of tryptamine are reported to be potent central nervous system depressants. The antiinflammatory[6] activity was found to be associated with many derivatives of indole viz., indomethacine.

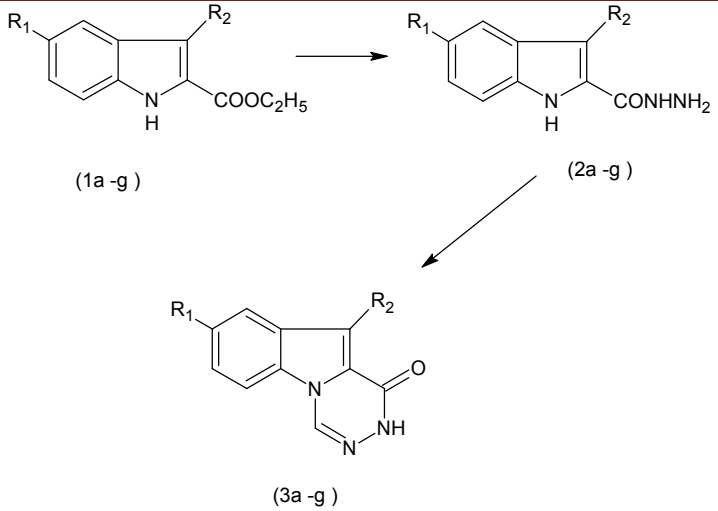
The spectroscopic data collected[7] on the newer derivatives of indole, isolated from various natural sources, have immensely helped in their structure elucidation, because of this, a good number of minor alkaloids containing indole nucleus are recorded in the literature. Today the scope of indole research is multifarious extending from rather simple parent molecule to highly complex molecules.

MATERIAL AND METHODS

Anti-microbial activity

The Compounds 3a-g were screened for their antibacterial activity against staphylococcus- aureus, Escherichia coli, proteus valgaris and Bacillus pumilis. The filter paper disc method 2 was employed using DME solution of the compounds at 100µ/ml and 200µ/ml Concentrations.

Pencillin was used as a reference drug. Antibacterial activity were tested against S.aureus , B. Pumilis, E-coli, P.Vulgaris.



Spectral data

2f IR NH_2 /NH and C=O at 3325 & 1620cm^{-1} PMR

3f IR nh, C=O and c=N at 3200/3100, 1680 & 1630 cm^{-1} PMR singlet at 3.8 S OCH_3 Protons Ar Protons 7.1 to 8.1 δ for 4 Proteins. 9.0 δ for moiety, for amide 11.7 δ

Experimental

Melting po0IRints were determined in open Capillaries and are uncorrected. Shimadzu FT-IR 8000 series spectrometer was used to record the IR spectra by using KBr disc and PMR spectra in DMSO-d6 on 270 and Gemini-200 MHZ spectrometer using TMS as internal standard (chemical shifts in δ ppm)

Ethyl 5-methoxyindole-2-carboxylate (1f) obtained from P-anisidine, was reacted with hydrazine hydrate (88%) in ethanol to yield 5-methoxy indole-2-carboxyhydrazide (2f)

(which exhibited NH_2 /NH and C=O absorptions at 3325 and 1620 cm^{-1} , respectively in it's IR spectrum) Compound 2f was reacted with ethyl 1-orthoformate in presence of DMF. The mixture was refluxed for 4 hours, solvent was removed in vaccuo and the residue crystallized with dioxane producing spongy white rystals of 3,4-dihydro-7-methoxy-4-oxo-1,2,4 triazino (4,5-a) indole (3f) (the IR Spectrum of 3f exhibited absorptions due to NH, C=O an C=N at 3200/3100, 1680 and 1630 cm^{-1} respectively the solid that separated was collected.

RESULTS AND DISCUSSION

On the basis of the results obtained during the present screening of various compounds for microbiological activity the following conclusion could be made.

Activity against Gram-Positive Organism

Among the various substituted 3, 4-dihydro-4-oxo1,2,4-triazinol(4,5-a) indoles (3a-g) the compounds 3a, 3c are highly active and 3b, 3f are moderately active and 3d, 3e and 3f showed weak activity against S. aureus. The compounds 3f, 3g are highly active and 3a, 3b, 3c, 3d showed weak activity against B.Pumilis.

Activity against Gram-negative Organism

The compounds 3a, 3g, 3c exhibit high activity and compounds 3f shows moderate activity and remaining compounds show weak activity against E. coli.

The compound 3f exhibits high activity and 3a shows moderate activity and 3c, 3d, 3e showed weak activity against gram negative organism P. Vulgaris.

Antifungal Activity

The compounds 3f, 3c exhibit high activity 3a, 3b, 3e, 3d are weakly active against A.niger the compounds 3g, 3f, 3c show high activity and 3a, 3b, 3c show moderate activity against p.vulgaris.

CONCLUSION

The various substituted 3,4-dihydro-4-oxo-1,2,4-trizino[4,5-a] indoles (3a-g) some compounds were highly active against gram positive organism and gram negative organism. Some compounds also shows antifungal activity.

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Table 1

Compounds	Substituents		M P 0^0 C
	R_1	R_2	
3a	Cl	H	184
3b	Cl	CH_3	238
3c	Cl	C_6H_5	240
3d	Br	H	225
3e	Br	C_6H_5	250
3f	OCH_3	H	58
3g	OCH_3	CH_3	262

Table 2: Antimicrobial evaluation data of the compounds

Compounds			Antibacterial activity					
			S.aureus		B.Pumilis		E-coli	
	R_1	R_2	100µg	200µg	100µg	200 µg	100µg	200µg
3a	Cl	H	18	20	10	14	18	20
3b	Cl	CH_3	16	18	10	12	--	--
3c	Cl	C_6H_5	18	22	12	14	16	18
3d	Br	H	10	12	--	10	12	14
3e	Br	C_6H_5	12	14	10	12	14	16
3f	OCH_3	H	16	18	12	16	16	18
3g	OCH_3	CH_3	14	16	12	14	18	20
Encillin Standard			18	20	14	16	20	24
Methyl formide			--	--	--	--	--	--

a) Zone of inhibition in (mm) 10-14 weakly active
b) Zone of inhibition in (mm) 15-18 Moderately active.
c) Zone of inhibition in (mm) 19-22 highly active

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