International Journal of Pharmaceutical Research and Development (IJPRD)
Platform for Pharmaceutical Researches & Ideas
www.ijprd.com

SYNTHESIS OF N'-(3Z)-2-OXO-1,2-DIHYDRO-3H-INDOL-3-YILDENE) (1,3) THIAZOLE (5,4-B) PYRIDINE-2-CARBOHYDRAZIDE DERIVATIVE FOR POSSIBLE ANTI-MICROBIOLOGICAL ACTIVITIES

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ABSTRACT
Isatin have proven to be good Anti-microbiological Activities agents certain N'-(3z)-2-Oxo-1,2-Dihydro-3h-Ind0l-3-Yildene) Thiazole (5,4-B) Pyridine-2-Carbohydrazide Derivative were prepared by the reaction of thiazolo pyridine 2- carbohydrazide with different aryl substituted isatins in ethanol. The newly synthesized compounds were characterized on the basis of melting point, TLC, IR, H-NMR and mass spectra. All the synthesized compounds were tested for their anti-bacterial and anti-fungal activities.

KEYWORDS: *Isatin, Antibacterial, Antifungal etc.*

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INTRODUCTION

The synthesis of a newer class of anti-bacterial and anti fungal agents is in need of time, especially against drug resistant, bacteria and fungi, which are responsible for a number of serious infections in the acute and chronic care units in hospital. The search of new anti-microbial agents with reduced toxicity and lower side effects is of continuous process. One of the most frequently encountered heterocyclic in medicinal chemistry is isatin and its derivatives. Istain (2,3-dioxindole) is an endogenous compound with a long history and wide range of pharmacological actions. Isatins are reflected by their use as antimicrobial[1-6], anti-inflammatory[7], activities. In view of this we planned to synthesize N'-(3z)-2-Oxo-1,2-Dihydro-3h-Ind0l-3-Yildene) Thiazole (5,4-B) Pyridine-2-Carbohydrazide Derivative.

The title of the compounds prepared by scheme-I thiazolo 2- Carbohydrazide were prepared by the reaction of INH with potassium thiocynate, acetic acid and bromine. These compounds were refused with aryl substituted isatins in alcohol. The chemical structures were confirmed by IR, H-NMR and mass spectroscopy. These compounds were screened for their antibacterial activity and anti fungal activity.

MATERIAL AND METHODS:

INH, Bromine, alcohol, glacial acetic acid, ammonia solution, isatin, Potassium-thiocyanate alcohol, hydrochloric acid, substituted anilines.

EXPERIMENTAL SECTION:

STEP-1: General method for synthesis of Thiazolo pyridine-2-carbohydrazide [8]

Isonicotinic acid was treated with potassium thiocyanate in presence of glacial acetic acid and bromine to get thiazolo pyridine-2-carbohydrazide

STEP-2: General method for synthesis of substituted isatins [9]

Substituted isatins was prepared by treating aniline derivatives with chloral hydrate and anhydrous sodium sulphate to form substituted isonitroso acetanilide, then this intermediate undergoes to cyclization with sulphuric acid to form substituted isatins.

STEP-3: General method for synthesis of isatin substituted (1, 3)-thiazolo (5, 4-b) pyridine-2-carbohydrazide derivatives [10]

An equimolar quantities of thiazolo pyridine 2-carbohydrazide and different aryl substituted isatins were dissolved in alcohol, refluxed for 6hr, then the contents were cooled and poured into crushed ice and the resulting compounds which separated out was filtered washed with water dried and recrystalized by using ethanol.

RESULTS: SPECTRAL DATA

Melting points were determined in open capillary and IR spectra of the compound were recorded on FTIR-4200 Spectrophotometer. H^1NMR spectra were recorded on Brucker AM 400 instrument at 400MHZ using DMSO-d6 as a solvent and mass spectra on a Varian atlas CH-7 mass spectrophotometer at 70ev. Chemical shifts are given in parts per million (ppm)

N'-(3z)-2-Oxo-1,2-Dihydro-3h-Ind0l-3-Yildene) (1,3) Thiazole (5,4-B) Pyridine-2-Carbohydrazide(III_A) yield 68%, m.p:182^oC; IR(KBr)v (cm^{-1}); 3184(NH): 2922(Ar-CH); 1679(C=N); 1215(N-N=C); 765(CS); H^1NMR (DMSO); 7.2-7.3(4H-Ar); 7.0(2H-NH); EI-MS 324(M+1)

N'-(3z)-5-Bromo-2-Oxo-1,2-Dihydro-3h-Ind0l-3-Yildene) (1,3) Thiazole (5,4-B) Pyridine-2-Carbohydrazide(III_B) yield62%, m.p:178^oC; IR(KBr)v (cm^{-1}); 3093 (NH): 2918 (Ar-CH); 1614 (C=N); 1218 (N-N=C); 747 (CS); H^1NMR (DMSO); 7.8-(2H,S); 7.58(4H-M);6.84(2H,M)

N'-(3z)-5-NITRO-2-Oxo-1,2-Dihydro-3h-Ind0l-3-Yildene) (1,3) Thiazole (5,4-B) Pyridine-2-Carbohydrazide(III_C) yield66%, m.p:165^oC; IR(KBr)v (cm^{-1}); 3421.08 (NH): 2254.02 (C=O); 1613.61 (C=N); 1248.22 (N-N=C); 750.18 (CS);1492.17($N0_2$): H^1NMR (DMSO); 10.25(1H,S); 8.13(3H,d J=8.851);7.54 (1H,S): EI-MS 368(M+1)

N'-(3z)-5-Chloro-2-Oxo-1,2-Dihydro-3h-Ind0l-3-Yildene) (1,3) Thiazole (5,4-B) Pyridine-2-Carbohydrazide(III_D) yield70% m.p:172^oC; IR(KBr)v (cm^{-1}); 3429.09 (NH): 1617.82 (C=N); 1219.16 (N-N=C); 708.63.18 (CS);748.47.17(Cl): H^1NMR (DMSO);11.05(1H,S);.69(1H,S),7.46(4H,dJ=6.9); 6.90(2H,dJ=7.911): EI-MS 358(M+1)

N'-(3z)-7-Nitro-2-Oxo-1,2-Dihydro-3h-Ind0l-3-Yildene) (1,3) Thiazole (5,4-B) Pyridine-2-Carbohydrazide(III_E) yield72% m.p:168^oC; IR(KBr)v (cm^{-1}); 3421.08 (NH): 2254.02 (C=O); 1613.61 (C=N); 1248.22 (N-N=C); 750.18 (CS);1492.17($N0_2$): H^1NMR (DMSO); 10.26(1H,S); 7.52(1H,S),8.10.(3H,dJ=8.851), 7.95(3H,dJ=8.851)

N'-(3z)-2-Oxo-3-[2-(1,3-thiazolo[5,4-b]pyridine-2ylcarbonyl) hydrazinylidene]-2,3-dihydro-1H-indole-5-carboxylic acid(III_F) yield 55%,m.p 185^oC

ANTIBACTERIAL ACTIVITY [11]

The synthesized compounds were screened for their antibacterial activity against two microorganisms, i.e *Escherichia coli* and *Staphylococcus aureus* by cup plate method in nutrient agar medium with on incubation for 24hr at 37^{o}c. All the compounds exhibited promising antibacterial activity at 100mg/ml concentrations when compared to standard norfloxacin as a positive control.

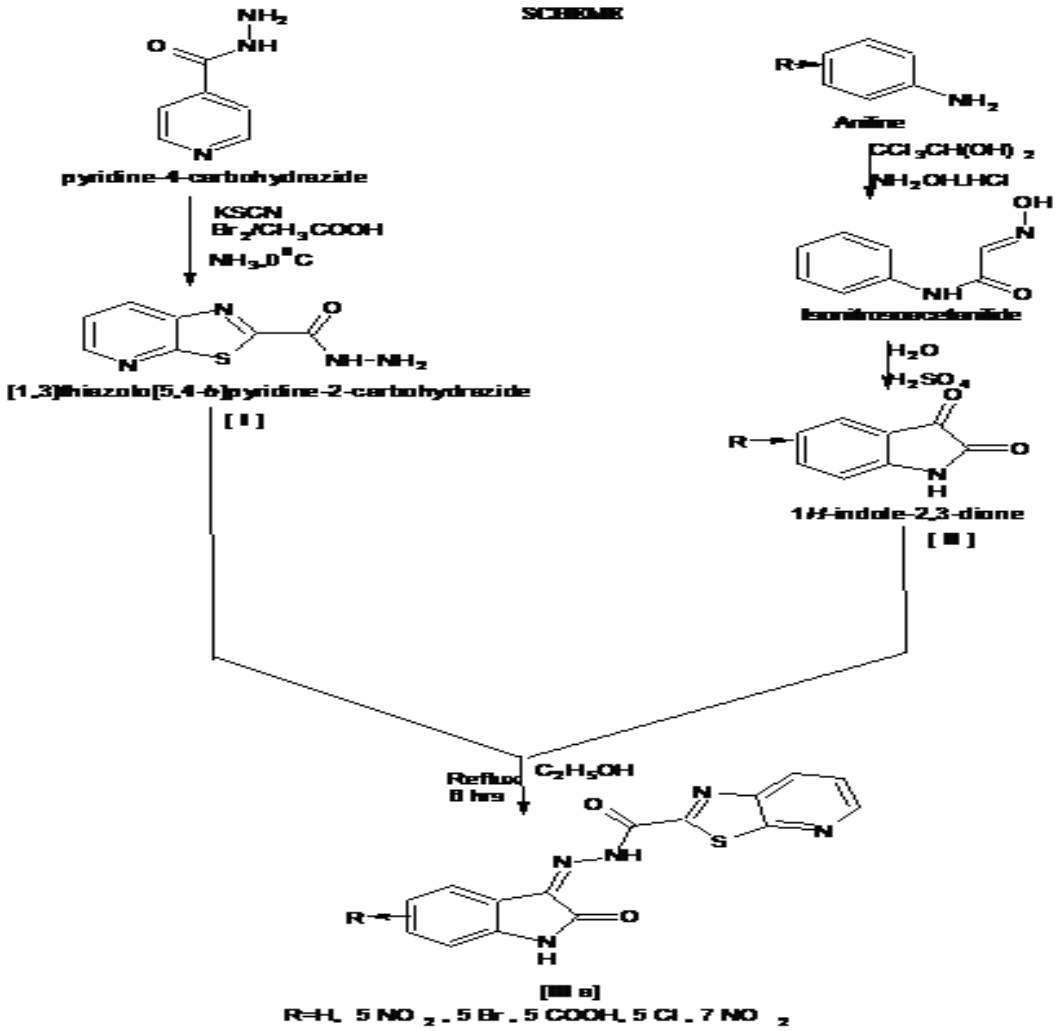
ANTIFUNGAL ACTIVITY [12]

The synthesized compounds were screened for their antibacterial activity against two microorganisms, i.e *Canada albicans* and *aspergillus niger* by cup plate method in sabourands dextrose agar medium with on incubation for 48hr at 28^{o}c. All the compounds exhibited promising antibacterial activity at

100mg/ml concentrations when compared to standard Griseofulvin as a positive control.

Table-1: Antibacterial and antifungal activity of synthesized compounds (III_a-III_f)

SL NO.	Compound	Zone of inhibition (in mm) 100 µg/ml			
		S. Aureus	E. Coli	C. Albicans	A. Niger
1	III_a	15	16	15	17
2	III_b	21	22	23	22
3	III_c	20	21	24	25
4	III_d	18	17	16	17
5	III_e	20	21	25	24
6	III_f	19	20	17	19
Std	Norfloxacin	22	23	----	----
Std	Griseofulvin	---	---	27	26



RESULTS AND DISCUSSION:

The synthesized compounds were subjected to antibacterial, antifungal activities by the standard methods. All the compounds were screened antibacterial activity, compounds III_c& III_e have shown promising and compounds III_c & III_f have shown excellent antibacterial & antifungal activity compared to standard drugs norfloxacin & griseofulvin.

ACKNOWLEDGEMENT:

The authors are thankful to shri. Shekhar reddy secretary & correspondent scient educational society, ranga reddy for providing necessary facilities through the principal, scient institute of pharmacy, ranga reddy to carry out this work.

CONCLUSION:

The title of the compounds proposed work as given out any antibacterial and antifungal activities. Some of the compounds have shown moderate activities, these compounds with suitable modification can be explored better for their therapeutic activities in future. Hence further extension of the work in this direction may be possible.

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