Synthesis of Novel Isoniazid And Fused Isoniazid Derivatives And Its Anthelmintic Activity

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Abstract- *The objective of this work is to synthesize novel isoniazid and fused isoniazid derivatives 4-substituted isonicotinamide (S1-S4) as a key intermediate. The structure of newly synthesized compound was characterized using IR, 1HNMR, mass spectroscopy and elemental analysis.*

Methods: *The target compound were synthesized starting from N-[4-(sulfamoyl)-phenyl]- pyridine 4-carboxamide (S1-S4) which prepared from the appropriate 4-substituted isonicotinamides. several synthetic pathway were be used for the preparation of the targets.*

Results: *Compound 4S was the most active against worms when compared with piperazine citrate as a standard.*

Keywords- Isoniazid, sulphonamide, anthelmentic activity.

I. INTRODUCTION

Sulphonamides were the 1st antimicrobial drug and the way for antibiotic revolution in medicine. Isoniazid is the 1st line antitubercular medication used in treatment and prevention of tuberculosis. Novel isoniazid derivatives was characterized by spectral method like IR, 1H ?NMR and mass spectra. Synthesized compound were screened for anthelmintic activity and compared with known standard.

II. EXPERIMENTAL

General procedure for the synthesis of 4-substituded Isoniazid (S1-S4)

To sulphonamide (0.003mole) in dry benzene (15ml) was added to Isoniazid (0.003mole) in dry benzene (15ml) and the reaction mixture was refluxed for 3hours. The product was then cooled, filtered and dried. The procedure was repeated with different sulphonamides.

Equipement: Melting points of synthesized compound were determine in open capillary tubes and uncorrected the IR spectroscopy was performed by BRUKER ALPHA ATR Infrared Spectrophotometer software used- OPUS. The 1H-NMR spectra of synthesized compound were recorded on a bruker avance III HD 500MHz NMR spectrophotometer in DMSO. The mass spectra was recorded on Bruker Compass data analysis instrument impact HD. the homogenecity of all newly synthesized compounds were checked by TLC on silica gel using chloroform: methanol as a eluent and visualized in UV chamber.

Anthelmintic activity: Indian adult earthworms (pheretima posthuma) were used to study anthelmintic activity. The earthworms (collected from the water logged area of soil) were wash with normal saline to remove all fecal materials. The earthworm 4-5cm in length and 0.1-0.3cm in width were used for all experimental procedures. The newly synthesized compound were tested for anthelmintic activity prepared minimal quantity of water and diluted to prepare two concentrations therefore, 0.1% w/v and 0.5%w/v by using piperazine citrate as a standard drug. The paralyzing and dead times are recorded and their mean was calculated. The time taken for worm to become motionless was noted as a paralysis time and to ascertain death, each worm was frequently applied with external stimuli which stimulates and induce movement in earthworms, if alive.

Procedure: The synthesized compounds are screened for anti-helminthic activity by using earthworms. six earthworm nearly of equal size were placing in standard drug solution, normal saline used as a control. The standard drug and test compound were dissolve in minimal quantity of water and diluted to prepare two concentrations therefore, 0.1% w/v and 0.5%w/v by using piperazine citrate as a standard drug. The paralyzing and dead times are recorded and their mean was calculated. The time taken for worm to become motionless was noted as a paralysis time and to ascertain death, each worm was frequently applied with external stimuli which stimulates and induce movement in earthworms, if alive. The mean lethal time and paralysis time of earthworm for different test compound and standard drugs are tableted below as:

Concentration 0.1%

Table no. 1

Sr. no.	Sample	Pin pinch in minute	For paralysis in minute	For death in minute
1.	S1	0.18	0.30	4.75
2.	S2	0.55	1.15	18.49
3.	S3	1.10	1.55	21.24
4.	S4	1.20	1.75	21.39
5.	Piperazine citrate (std.)	0.20	0.45	19.90

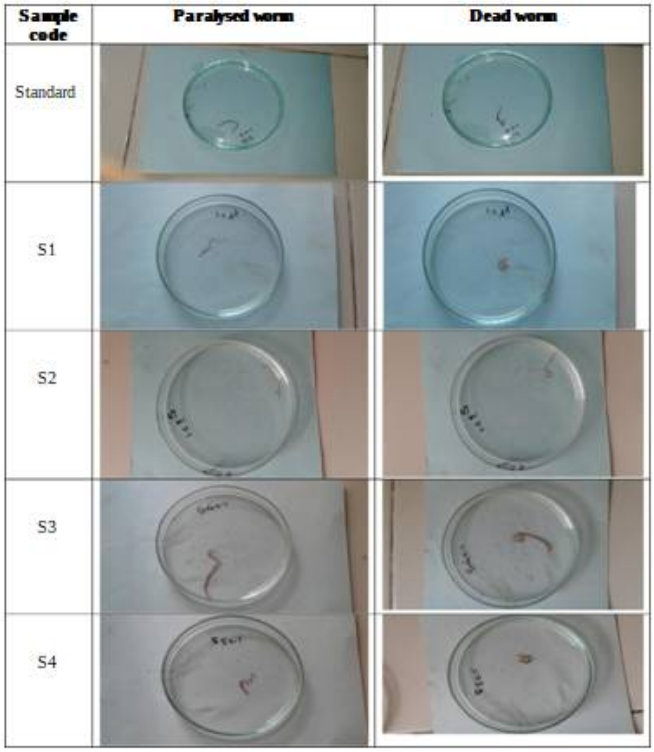
Concentration 0.5%

Table No.2

Sr. no.	Sample	Pin pinch in minute	For paralysis in minute	For death in minute
1.	S1	1.01	1.15	7.52
2.	S2	1.02	1.46	10.49
3.	S3	0.20	0.36	7.45
4.	S4	0.30	0.75	7.32
5.	Piperazine citrate (std.)	0.10	0.15	2.25

Concentration 0.1%

Table No. 3



Concentration 0.5%

Table No. 3

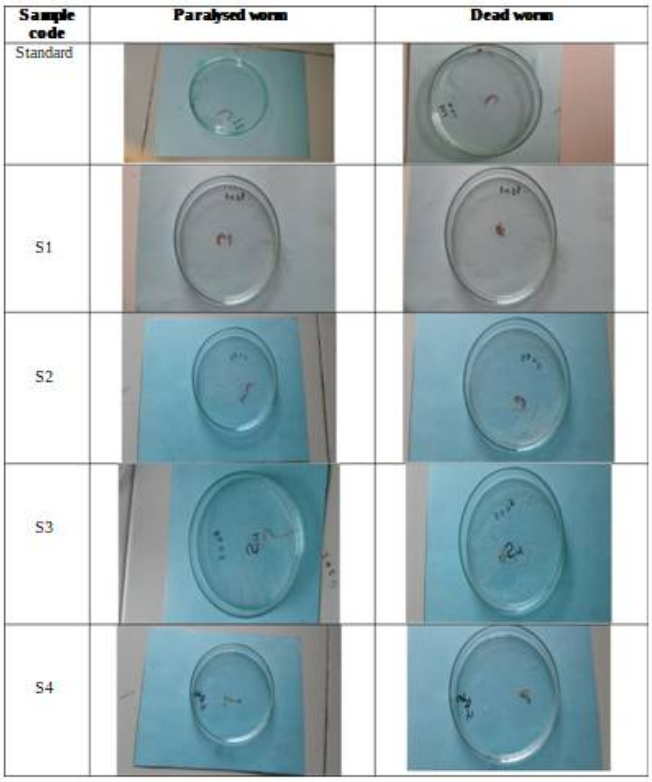


Table No. 4

Sr. no.	Sample	Mol. Formula	Mol. Wt.(gm)	solubility	% yield	Melting point (c)
1.	S1	$C_{13}H_{13}N_3O_4S$	319.08	DMSO, methanol water	85.98%	125
2.	S2	$C_{16}H_{13}N_5O_4S$	355.08	DMSO, methanol water	95.28%	155
3.	S3	$C_{17}H_{12}ON_4S$	344.08	DMSO, methanol water	96.02%	134
4.	S4	$C_{17}H_{17}ON_3S$	291.08	DMSO, methanol water	95%	110

The spectral data of all the title compound (S1-S4)

S1= N[4-(acetylsulfamoyl)phenyl]pyridine-4-carboxamide.

IR (zinc selenium, cm-1): 1539.42(C=C), 1645.63(C=O), 1645.63(C=N), 3092.35(N-H)
1131.46(C-O), 1076.19(SO), 1261.93(SO NH), 996.49(C-N).
H-NMR(ð ppm): 6-9-aromrtic H, 5-9-R(CO)NH, 2.1-2.9-CH-CONH, 2.2-2.9R(CO)N-CH, 3.2-3.8-ROCH, 3-5-ArNH. MS: mol. Wt.-320.0712.

S2= N[4-(pyrimidin-2yl sulfamoyl)phenyl]pyridine-4-carboxamide.

IR (zinc selenium, cm-1): 1422.22(C=C), 1745.92(C=O), 1641.48(C=N), 3219.83(N-H), 1135.14(C-O), 1073.50(SO), 1300.45(SO NH), 966.12(C-N).1H-NMR(ð ppm): 6-9-aromrtic H, 5-9-R(CO)NH, 2.1-2.9-CH-CONH, 2.2-2.9R(CO)N-CH, 3-5-ArNH. MS: mol.Wt.-355.0712.

S3= N[4-(isoxazole-3yl sulfamoyl)phenyl]pyridine-4-carboxamide.

IR (zinc selenium, cm-1): 1469.05(C=C), 1613.76(C=O), 1603.79(C=N), 3127.10(N-H),1140.38(C-O), 1086.69(SO), 1361.11(SO NH), 924.13(C-N).1H-NMR(ð ppm): 6-9-aromrtic H, 5-9-R(CO)NH, 2.1-2.9-CH-CONH, 2.2-2.9R(CO)N-CH, 3-5-ArNH. MS: mol.
Wt.-344.02.

S4= N[4-(benzyl lsulfamoyl)phenyl]pyridine-4-carboxamide.

IR (zinc selenium, cm-1): 1527.63(C=C), 1774.39(C=O), 1687.81(C=N), 3107.54(N-H), 1147.55(C-O), 1077.98(SO), 1314.04(SO NH), 980.52(C-N). H-NMR(ð ppm): 6-9-aromrtic H, 5-9-R(CO)NH, 2.1-2.9-CH-CONH, 2.2-2.9R(CO)N-CH, 3-5-ArNH. MS: mol.Wt.-292.0164.

Conclusion: The compound S posses good anthelmintic activity and also other synthesized derivatives posses moderate anthelmintic activity.

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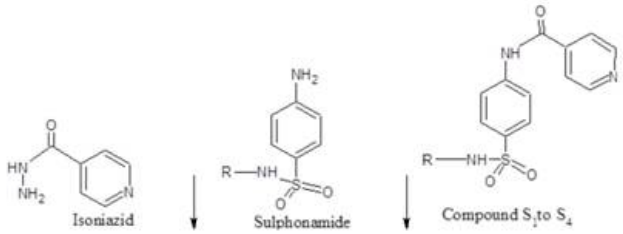
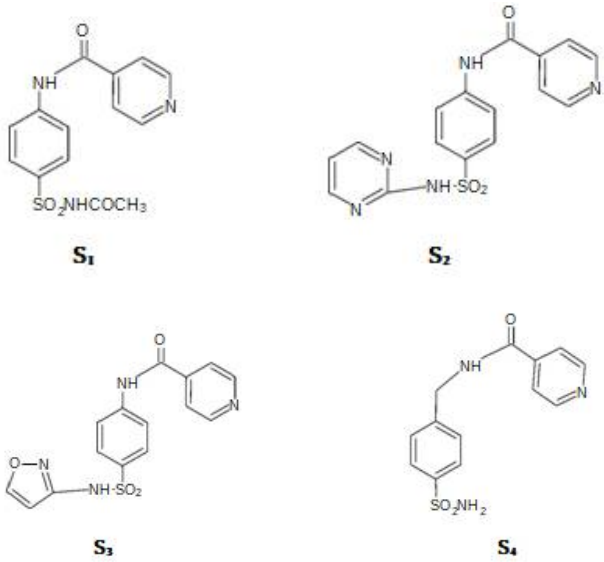
Synthesis Scheme for sulphonamide derivatives:



Structures of sulphonamide derivatives:



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