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Synthesis of 4–(2'–substituted benzothiazoles)–5–mercapto–3–(substituted)-1,2,4-traizole derivatives for possible Antimicrobiological activities

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ABSTRACT

Benzothiazoles and traizoles have proven to be good antimicrobial agents certain 4-(2'-substituted benzothiazoles)-5-mercapto-3-(substituted)-1,2,4-traizoles. The condensation of 2-Hydrazino benzothiazoles (Part-I) with potassium dithiocarbazinate suspension (Part-II), the result in compounds (A_1-A_6) were prepared and have been characterized by melting point, TLC, UV, IR, ^{1}H-NMR spectral studies. All the compounds were evaluated for antibacterial and antifungal activities.

Keywords: Hydrazinobenzothiazoles, potassium dithiocarbazinate, 1,2,4 traizoles, antimicrobial activities.

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INTRODUCTION

Benzothiazoles and traizoles are important heterocyclic systems with varied biological activities. Hydrazinobenzothaizole[1] exhibit antibacterial[2] antituberculer[3] antidiabetic[4] and anti inflammatory[5] activities. Traizoles also posses antibacterial [6] antifungal [7] anti inflammatory[8] activities. In view of this we planned to synthesize some new 4-(2'-substituted benzothiazoles)-5-mercapto-3-(substituted)-1,2,4-traizoles (A_1-A_6) containing both benzothaizole and traizole moieties to get more potent compounds.

The title of the compounds prepared by the scheme 2-hydrazinobenzothaizoles (I),(II),(III) were prepared from appropriate hydrazides by the reaction of potassium thaiocyanate, acetic acid and bromine. Then compounds (I-III) were refluxed with potassium bio carbonate when profuse evolution to hydrogen sulphate and reaction mixture is cooked on acidification the resolutions compounds are separated out and screened for antimicrobial activities.

MATERIALS AND METHODS

Chemicals and Reagents

Phenyl hydrazine, Benzoyl benzoate, Ethyl benzoate, Hydrazine hydride, Potassium thiocyanate, Glacial acetic acid, Bromine, Isonicotinic acid hydrazide, Metyl salicylate, Carbondisulphide, Alchoholic potassium hydroxide,Conc.Hydrochloric acid.

Experimental section

Part – I: General method for synthesis of 2 hydrazinobenzothaizoles [9] [10].

Various hydrazines was treated with potassium thiocynate in presence of glacial acetic acid and bromine to get 2 hydrazinobenzothaizoles (I) (II) (III).

Part – II: General method for preparation of potassium dithiocarbozinate [11].

Acid hydrazides and potassium hydroxide in absolute alcohol was refluxed with carbon disulphide for 6 hr then the mixture was used directly for next step.

An equimolar amounts of hydrazinobenzothaizoles and potassium dithiocarbozinate were dissolved in alcohol and refluxed for 6hr when profuse evolution of hydrogen disulphide was observed the contents were cooled and poured into crushed ice an acidification with 10ml hydrochloric acid and the resulting compounds which separated out was filtered washed with water dried and recrystalized by using ethanol.

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Identification and Characterization

Melting pointes were determined in open capillary and are uncorrected. IR spectra (KBr pellet technique) were recorded using a Perkin – Elmer 237 Spectrophotometer. ^{1}H NMR Spectra were recorded on Bruker AM 400 instrument (at 400 MHz) using tetramethyl silane (TMS) as an internal standard and DMSO-d6 as a solvent. Chemical shifts are given in parts per million (ppm). All the synthesized compounds was monitored on pre-coated TLC plates and visualizing the spots in ultraviolet light.

4-(2'-amino benzothiazoles)-5-mercapto-3-(pyridine)-1,2,4-traizole(A_1). Yield 63%; mp 181^{o}c; IR (KBr)v(cm^{-1}); 3403(NH);2926(Ar-CH);2635(SH);1594(C=C);1234(N-N=C);691(CS); ^{1}H-NMR($CDCl_3$):δ8.8(1H-SH); 7.9(1H-NH); 7.6-7.8(4H-pyridyl);7.4-7.6(4H-Ar).

4-(2'-amino-1,4- benzothiazine)-5-mercapto-3-(pyridine)-1,2,4-traizole(A_2).
Yield 74%;mp 198^{o}c; IR (KBr)v(cm^{-1}); 3430(NH);3063(Ar-H);2624(SH);1632(C=C); 1217(N-N=C);687(CS);^{1}H-NMR($CDCl_3$);δ10.14(2H,1H-NH); 8.9(1H-NH); 7.6-7.9 (4H-pyridyl); 7.4-7.6(4H-Ar).

4-(2'-carboxamido benzothiazole)-5-mercapto-3-(pyridine)-1,2,4-traizole(A_3).
Yield 77%;mp 207^{o}c; IR (KBr)v(cm^{-1}); 3429(NH);3073(Ar-CH);2630(SH);1632(C=O); 685(CS).^{1}H-NMR($CDCl_3$):δ10.2(1H-SH);8.8(1H-NH); 7.6-7.9 (4H-pyridyl);7.4-7.6(4H-Ar).

4-(2'- amino benzothiazoles)-5-mercapto-3-(phenol)-1,2,4-traizole(A_4). Yield 55%;mp 203^{o}c; IR (KBr)v(cm^{-1}); 3406(NH);3210(OH);2915(Ar-CH);2646(SH);1228(N-N=C);685(CS).^{1}H-NMR($CDCl_3$):δ14.1(1H-SH);10.2(1H-NH);8.01(1H-OH);6.8-7.9(8H-Ar).

4-(2'-amino-1,4- benzothiazine)-5-mercapto-3-(phenol)-1,2,4-traizole(A_5). Yield 74%;mp 195^{o}c; IR (KBr)v(cm^{-1}); 3435(NH);3221(OH);3041(Ar-CH);2630(SH);1211(N-N=C);685(CS).^{1}H-NMR($CDCl_3$):δ10.9(1H-SH);10.3(1H-thiazine-NH); 8.05(1H-OH); 7.9(1H-1H)6.9-7.6(8H-Ar).

4-(2'-carboxamido benzothiazole)-5-mercapto-3-(phenol)-1,2,4-traizole(A_6).
Yield 75%;mp 183^{o}c; IR (KBr)v(cm^{-1}); 3431(NH);3057(Ar-CH);2657(SH);1631(C=O); 1280(N-N=C);694(CS).^{1}H-NMR($CDCl_3$):δ14.3(1H-SH);9.94(1H-OH);7.0-7.9(8H-Ar);6.8(1H-NH);

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Antimicrobial activity

Antibacterial activity [13]

The synthesized compounds (A_1-A_6) were screened for their antibacterial activity against two micro organisims, i.e. *Escherichia coli* and *Staphylococus 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 100 mcg/ml concentrations when compared to standard norfloxacin as a positive control. The zone of inhibition was measured in mm and DMF was used as negative control. (Table No.1)

Antifungal activity [14]

The synthesized compounds (A_1-A_6) were screened for their antifungal activity against two fungal strains, i.e. *Candida albicins* 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 antifungal activity at 100 mcg/ml concentrations when compared to standard Griseofulvin as a positive control. The zone of inhibition was measured in mm and DMF was used as negative control. (Table No.1)

RESULTS AND DISCUSSION

The synthesized compounds were subjected to antibacterial, antifungal activities by the standard methods. All the compounds were screened antibacterial activity, compounds A_2 & A_4 have shown promising and compounds A_3, A_5 & A_6 have shown excellent antibacterial activity when compared to standard drug norfloxacin.

All the compounds were also screened for antifungal activity, however compound A_2 have shown promising and compounds A_3,A_5 & A_6 have shown excellent antifungal activity when compared to standard drug griseofulvin.

CONCLUSION

The title of the compounds proposed work as given out any active 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.

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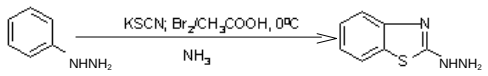
Table – 1: Antibacterial and Antifungal activity of synthesized compounds (A_1 - A_6)

SL. No.	Compd.	Zone of Inhibition (in mm) 100 µg/ml			
		S.Aureus	E.coli	C.albicans	A.niger
1.	**A_1**	15	16	15	17
2.	**A_2**	19	18	18	20
3.	**A_3**	20	21	24	25
4.	**A_4**	18	17	16	15
5.	**A_5**	21	22	23	25
6.	**A_6**	20	21	27	26
standard	Norfloxacin	22	23	----	----
standard	Griseofulvin	---	---	27	26

SCHEME

Part-I



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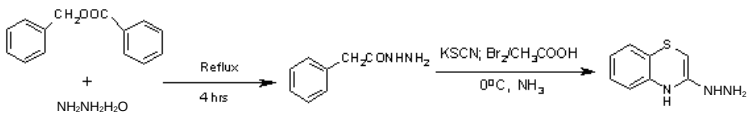

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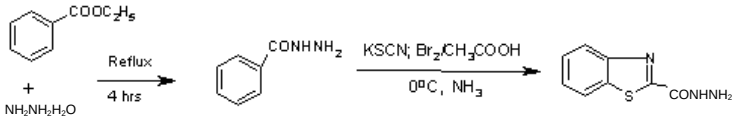

III

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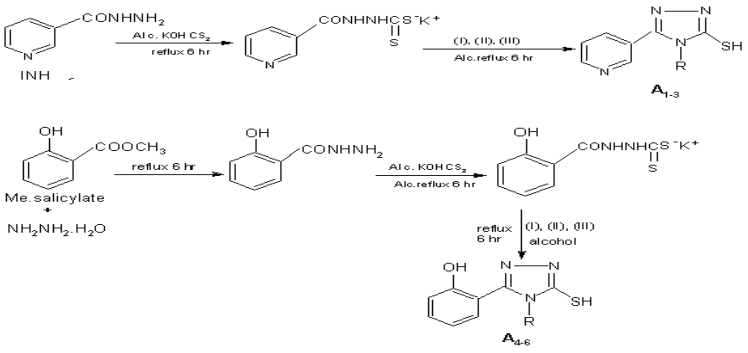
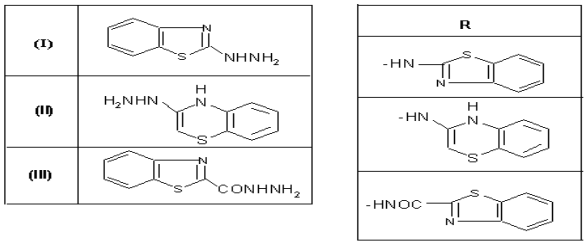
Part-II





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