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Microbiological Activity of A New Series of 1-Formamidino-(N-Substitutedthioamido)-5-Substituted -2-Thio-4-Imino Biurets.

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Abstract

Amidinothiocarbamides and their derivatives possess various pharmaceutical, industrial, medicinal and agricultural values. Intraction of different thiocarbamides and substituted cyanamides were carried out to synthesised respective substituted thiocarbamides, bis-foramidino sulphide, amidinothiocarbamides (salt) and their derivatives. Amidinothiocarbamides and their derivatives were successfully cyclised into respective Hector's bases, thiadiazines, dithiazines, thiadiazolidines, s-triazines and pyrimidines by using different reagent and different reaction conditions. So it was thought interesting to study of their antimicrobial activities by cup plate diffusion method to obtained new series of effective drugs. These compounds were screened against E.coli, S.typhi, A.aerogenes, S.aureus, and B.subtilis human pathogen. These compound shows effective drugs effect in medicinal and agricultural fields.

Keywords:
Amidinothiocarbamide,Synthesis, Antimicrobial activities, Pharmaceutical and Agricultural values

Introduction:

Thiocarbamides and their derivatives possess various pharmaceutical, agricultural, medicinal and values[1-4]. Intraction of different thiocarbamides and substituted cyanamides were carried out to synthesised respective substituted thiocarbamides, amidinothiocarbamides (salt) and their derivatives.[5-8] Amidinothiocarbamides and their derivatives were successfully cyclised into respective thiadiazines and s-triazines by using different reagent and different reaction conditions. [9-22] Dicyanamide has interesting to carry out the reaction with thiourea in presence of dil. hydrochloric acid in acetone medium to obtain 1,3-diformamidinothiocarbamide , having two amino groups at the terminal ends.

Intraction of phenylthiocarbamide were carried out with dicyanamide to obtain N"-phenylformamidinoformamidinothiocarbamide(1b). which were further reacted with different alkyl/arylisothiocyanate in 1:1 molar ratio in acetone medium to obtain series of 1-formamidino-(N-substitutedthioamido)-5-substituted -2-thio-4-iminobiuret. (2).

Experimental:

All chemicals used were of analar grade. Aryl/alkylisothiocyanate, Aryl/alkylisocyanodichlorides were prepared according to literature method[23] Melting points of all synthesized compounds were determined

in open capillary. IR spectra were recorded on Perkin-Elmer spectrometer in the range 4000-400 cm^{-1} in KBr pellets. PMR spectra were recorded with TMS as internal standard using $CDCl_3$ and DMSO-d_6. TLC checked the purity of the compounds on silica gel-G plates with layer thickness of 0.3 mm. All Synthesised compounds were screened for their antimicrobial activity using cup plate diffusion method.[24-25] The bacterial organisms used included both gram-positive and gram-negative strains viz. *S. aureus, B. subtilis, A. aerogenes, E. coli*, and *S. typhi.* The solvent used was DMF. The media plates were seeded with bacterial inoculums of 1×10^6 CIU/ml having well size 6 mm was loaded with 0.1 ml of test compound solution of variable concentration in DMF. The zone of inhibition was recorded after incubation for 24 h. using vernier calipers and result are cited in Table –I

Material and Methods:

"Any chemical moiety which inhibits the growth of microorganism or kill it is called as **Antimicrobial activity".**

All 1,3,5-thiadiazines compounds were screened for their antibacterial activity using cup plate diffusion method. Bacterial organisms used include both gram positive and gram negative strains like *S. aureus, S. typhi, A. aerogenes, E. coli* and *B. subtilis.*

The medium was prepared by dissolving 28 gm of ingredients in one liter of distilled water and was sterilized at 121°C temperature and 15 lbs/inch pressure in an autoclave for 15 minutes.

After sterilization it was cooled down to 50°C and poured into sterile petriplates and allowed to solidify. The media plates were then seeded with 24 hrs old active nutrient growth culture of the test organism in order to obtain lawn culture. The compounds were dissolved in 50% dimethylformamide (DMF) solvent at fix concentration 100 mg/ml to these added 2 drops of test solutions of synthesised compounds. Plane DMF solvent was used as control. The plates were then incubated at 37°C for 24 hrs. After incubation the zones of inhibition were recorded around the wells and result are cited in Table – I.

1-formamidino-(N-phenylthioamido)-5-phenyl -2-thio-4-iminobiuret. (2a).

Mixture of **(1b)** (0.05mol) phenylisothiocyanate (0.05 mol) and acetone (50ml) was refluxed for 12 h. on water bath in 1:1 molar ratio. The mixture was filtered and filtrate during distillation yielded the crystals of 2a.Yield (79%). m.p. 245 ^{0}c ; IR spectra of compound shows ν(N-H) 3453.9cm^{-1}**,** ν(C-H)(Ar) 3110.5cm^{-1}**,** ν(C=N) 1576.2cm^{-1}, ν(C-N) 1296.6cm^{-1} , ν(C=S) grouping 1135.3 cm^{-1}, ν(C=NH), grouping 1627.8cm^{-1}.The PMR spectra of compounds showed signals due to N-H protons at δ 3.4-4.7 ppm Ar-NH protons at δ 6.7 ppm, Ar-H protons at δ 5.7-6.3 and the signal at δ 3.5-3.7 ppm is due to moisture in DMSO-d_6. and δ1.5-2.1 ppm is due to DMSO. Found (Calc.) C = 51.79% (51.75%) H = 4.42% (4.58%) N = 26.31% (26.41%) S = 17.22% (17.25%).

Similarly others compounds (2b-2f) were synthesised by above mention method and were screened for their antimicrobial activity using cup plate diffusion method.

Result and Discussion:

All the bacterial organisms studied are human pathogens. The activity is compared with standard drug ciprofloxacine at the same concentration. From the Experimental data it has been observed that the compounds 2a, 2b, 2c & 2f shows highly activity against *S. typhi* and compounds 2e shows moderately activity while remaining compounds are inactive against same pathogen. Similarly compound 2d and 2f shows highly activity against *A.aerogenes* and compound 2a, 2b, and 2c shows moderately activity against same pathogen. In case of *E. coli* the compound 2b, 2d and 2e show moderately activity while compound 2c shows highly activity against the same bacteria. In case of Gram-positive bacteria like the compounds 2a, 2d and 2e shows highly activity against *S. aureus* while 2b and 2f shows moderately activity against *S. aureus* while the compound 2a and 2c were effective against the *B. subtilis* organisms. As newly thiocarbamides shows remarkable antimicrobial activity, these compounds can be easily used as alternative drugs for the treatment of diseases like typhoid.

Table-I *Physical data and antibacterial activity of the compounds [2a to 2f]

Compd.	Yield	m.p. (^{0}C)	Gram Positive		Gram Negative		
			S. aureus	*B. subtilis*	*A. aerogenes*	E. coli	*S. typhi*
[2a]	79	245	+++	+++	++	+	+++
[2b]	72	254	++	++	++	++	+++
[2c]	79	267	+	+++	++	+++	+++
[2d]	68	238	+++	+	+++	++	-
[2e]	73	234	+++	-	++	++	++
[2f]	62	261	++	+	+++	-	+++

* All Compounds gave satisfactory C, H, N, and S analysis.

(-) = Inactive (Less than 10 mm) (+) = Weakly Active (10-14 mm)

(++) = Moderately Active (15-18 mm) (+++) = Highly Active (19-35 mm)

Conclusion:

As outline in synthesis process, important novel iminobiuret have been synthesized. All the structure of the above compounds was in good agreement with Spectral and Analytical data. and also shows novel biological activity.

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