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Short Communication

Biological Evaluation of 1, 3-Bis-(2- Substitutedamino-6-Substitutedimino-1, 3, 5- Thiadiazin- 4- yl)-Thiourea Derivatives as Antimicrobial agents

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Abstract

A series of 1,3-bis (2- substitutedamino-6-substituted-imino-1,3,5-thiadiazin- 4- yl)-thiourea [3a(i) to 3f (iii)] have been obtained by basification of their hydrochlorides [2a(i) to 2f (iii)].The latter were synthesized by the interaction of 1,3-bis (N-substitutedamidinothiocarbamido)- thiourea (1) and N-aryl/alkylisocyanodichlorides in 1:2 molar ratio. The compound (1) was prepared initially by the condensation of aryl/alkylisothiocyanate and 1,3-diformamidinothiourea in 1:2 molar ratios. The structure of all these compounds was established on the basis of IR and NMR spectral data. All the synthesized compounds have been assayed for their antibiological activity against both gram-positive and gram-negative human pathogens and found that they possess insecticidal, and bacteriocidal. Some 1,3,5-thiadiazine compounds show remarkable biological activity.

Keywords: Thiourea, 1, 3, 5-thiadiazine, antimicrobial activity.

Introduction

The literature survey reveals that the thiourea and its derivatives having 1,3,5-thiadiazine nucleus enhanced pharmaceutical, agricultural and industrial values[1]. So, the medicines containing thiadiazines nucleus are now used extensively in medical, biomedical and biotechnological faculties. It has been shown to posses industrial[2], medicinal[3-4] fungicidal, insecticidal[5-7], values. The synthetic applications of N-aryl/alkylisocyanodichlorides[8-10] have been investigated and shown to have enough potential in the synthesis of nitrogen and sulphur containing heterocyclic compounds, thus with an aim to synthesize 1,3,5-thiadiazine, reaction of N-aryl/alkylisocyanodichlorides have been carried out with different 1,3-bis (N-substitutedamidinothiocarbamido) thiourea (1) in 1:2 molar ratios.

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.[8-10] 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 – 1.

Experimental: All chemicals used were of analar grade. N-aryl/alkylisocyanodichlorides were prepared according to literature method[7]. Melting point of all synthesized compounds was determined in open capillary and uncorrected; 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 0.3mm.

The parent compound 1,3-bis (N-substitutedamid-inothiocarbamido) thiourea (1a-f) was prepared by refluxing the mixture of 1,3-diformamidinothiourea[11] with aryl/ alkylisothiocyanate in 1:2 molar ratio in acetone ethanol medium for 12 h. on water bath.

Results and Discussion

Various thiourea derivatives [3a(i) to 3f(iii)] were prepared using 1,3-bis (N-substitutedamidinothiocarbamido)- thiourea and N-aryl/alkylisocyanodichlorides. All the compounds synthesized were adequately characterized by their elemental analyses and spectral IR, UV and H-NMR. All the synthesized compounds have been assayed for their antibiological activity against both gram-positive and gram-negative human pathogens and found that they possess insecticidal, and bactericidal

Table-1
Physical Data and Antimicrobial Activity of the Compounds [3a (i) to 3f (iii)].

Compd	R	R_1	Yield %	m.p. (^{0}C)	Gram Positive		Gram Negative		
					S. aureus	*B. subtilis*	*A. aerogenes*	E. coli	*S. typhi*
[3a(i)]	Phenyl	Phenyl	60	254	+	++	+++	++	+++
[3a(ii)]	Phenyl	*p*-Chloro-phenyl	58	257	+++	++	++	-	+
[3a(iii)]	Phenyl	Ethyl	64	242	+	+++	-	+	++
[3b(i)]	*p*-Chlorophenyl	Phenyl	71	252	++	+	+	++	+++
[3b(ii)]	*p*-Chlorophenyl	*p*-Chloro-phenyl	69	264	++	+	++	+	++
[3b(iii)]	*p*-Chlorophenyl	Ethyl	73	272	+	+	++	-	++
[3c(i)]	*p*-Tolyl	Phenyl	62	268	+++	++	++	+	+++
[3c(ii)]	*p*-Tolyl	*p*-Chloro-phenyl	58	257	++	+++	++	-	++
[3c(iii)]	*p*-Tolyl	Ethyl	63	256	++	-	+	+	+++
[3d(i)]	Ethyl	Phenyl	67	261	+++	+	+++	++	-
[3d(ii)]	Ethyl	*p*-Chloro-phenyl	72	272	++	-	+	-	++
[3d(iii)]	Ethyl	Ethyl	58	242	+	-	++	++	+++
[3e(i)]	Methyl	Phenyl	62	232	++	++	+++	-	+++
[3e(ii)]	Methyl	*p*-Chloro-phenyl	59	227	++	+	++	++	++
[3e(iii)]	Methyl	Ethyl	61	231	+	++	-	-	+++
[3f(i)]	*t*-Butyl	Phenyl	67	242	+	+	+	+	-
[3f(ii)]	*t*-Butyl	*p*-Chloro-phenyl	69	251	+++	-	++	++	+++
[3f(iii)]	*t*-Butyl	Ethyl	73	237	-	++	+++	++	+

* 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)

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 3a(i), 3b(i), 3c(i), 3c(iii), 2d(iii), 3e(i), 3e(iii) and 3f(ii) shows high activity against *S. typhi* and compounds 3a(iii), 2b(ii), 3b(iii), 3e(ii), 3d(ii), and 3e(ii) shows moderate activity while remaining compounds are inactive against same pathogen. Similarly compound 3a(i), 3b(i), 3d(i), 3d(iii), 3e(ii), 3f(ii) and 3f(iii) shows moderate activity and remaining compounds shows inactivity against *E. coli* .

In case of Gram-positive bacteria like *S. aureus* the compound 3a(ii), 3e(ii), 3d(i) and 3f(ii) shows highly activity while compound 3b(i), 3b(ii), 3c(ii), 3c(iii), 3d(ii), 3e(i) and 3e(ii) shows moderately activity against the same bacteria. The compound 3a(iii) and 3c(ii) were effective against the *B. subtilis* organisms. As newly thiadiazines shows remarkable antimicrobial activity, these compounds can be easily used as alternative drugs for the treatment of various diseases.

Conclusion

As outline in synthesis process, important novel thiourea 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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