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Short Communication

S-Triazines: As Alternative Drugs for the Treatments of Typhoid

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Abstract

1-substituted-2-thio-(1H)-4-[(2-imino-4-thiobiureto-5-yl) guanyl]-6-substitutedamino-1,2-dihydro-s-triazines [3a(i) to 3f(iv)] have been obtained by the isomerisation of 2-substitutedamino-4-(2-imino-4-thiobiureto-5-yl-carbamidino)-6-substitutedimino-1,3,5-thiadiazines [2a(i) to 2f(iv)] in presence of ethanolic sodium bicarbonate solution, which have been obtained by basification of their hydrochlorides [1a(i) to 1f(iv)] which are synthesized by the interaction of 1-formamidino-3-thioamido-N-substitutedformamidinothiocarbamides and N-aryl/alkylisocyanodichlorides. The latter were prepared initially by the condensation of N-aryl/alkylisothiocyanate and 1,3-Diformamidinothiocarbamide. The structure of all these compounds was established on the basis of elemental analysis and IR and NMR spectral data. All the synthesized compounds have been screened for their antimicrobial activity against both gram-positive and gram-negative human pathogens.

Keywords: S-triazine, antimicrobial activity.

Introduction

The literature survey reveals that the heterocyclic compounds containing nitrogen and nitrogen and sulphur have gain immense importance in human life due to their variety of applications in agricultural, medicinal, pharmacological and industrial value[1]. It has also been found that the heterocyclic compounds containing S-triazine in the nucleus have been successfully tested against several pathogens and found that they possess insecticidal, medicinal[2-3], industrial, pharmaceutical, agricultural and bactericidal properties. Some triazino compounds show remarkable biological activity[4-6] and help to find better alternative against drug.

Material and Methods

"Any chemical moiety which inhibit the growth of microorganism or kill it is called as Antimicrobial activity". All S-triazine compounds were screened for their antibacterial activity using cup plate diffusion method[7-8]. The 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 µg/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. Aryl/alkylisothiocyanate, Aryl/alkylisocyanodichlorides were prepared according to literature method[9]. Melting points of all synthesized compounds were determine 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.

Results 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 3a(i), 3a(iii), 3b(iii), 3d(i), 3c(ii) 3d(i), 3d(ii)and 3e(iv) shows high activity against *S. typhi* and compounds 3a(ii), 3a(iv), 3b(iv), 3c(iii), 3d(iv), 3e(i) and 3f(iv) shows moderate activity while remaining compounds are inactive against same pathogen. Similarly compound 3a(i), 3a(iv), 3b(iii),3b(iv), 3c(ii), 3c(iv), 3d(i), 3d(ii), 3d(iv), 3e(i),and 3e(iv) shows high activity while compound 3c(iii) and 3d(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), 3a(iv), 3d(i) and 3b(i), shows highly activity. The compound 3a(ii), 3a(iv),3b(iii), 3c(ii), 3d(iv) and 3f(iv) were effective against the *B subtilis* organisms.The compound 3a(iii) and 3b(iv) were effective against the *A. aerogenes* organisms. As newly s-triazines shows remarkable antimicrobial activity, these compounds can be easily used as alternative drugs for the treatment of various diseases such as typhoide.

Table-1
Physical Data and Antimicrobial Activity of the Compounds [3a(ii) to 3f(iv)]

Compd	R	R_1	m.p. (^{0}C)	Yield %	Gram Positive		Gram Negative		
					S. aureus	*B. subtilis*	*A. aerogenes*	E. coli	*S. typhi*
3a(i)	Phenyl	Phenyl	185	62	+	-	+ +	+ + +	+ + +
3a(ii)	Phenyl	*p*-Chloro-phenyl	191	59	+ + +	+ + +	+ +	+ + +	+ +
3a(iii)	Phenyl	Ethyl	179	71	+ +	+ +	+ ++	-	+ + +
3a(iv)	Phenyl	*t*-Butyl	167	69	+ + +	+++	+ +	+ + +	+ +
3b (iii)	Ethyl	Ethyl	174	69	+ +	+ + +	+ +	+ + +	+ + +
3b (iv)	Ethyl	*t*-butyl	159	71	-	++	+ + +	+ + +	++
3c (ii)	*p*-Chloro-phenyl	*p*-Chloro-phenyl	203	57	+ +	+ + +	+ +	+ + +	+ + +
3c (iii)	*p*-Chloro-phenyl	Ethyl	195	58	-	-	+	+ +	+ +
3c (iv)	*p*-Chloro-phenyl	*t*-Butyl	181	71	+	-	-	+ + +	+
3d (i)	*p*-Tolyl	Phenyl	194	79	+ + +	+ + +	+ +	+ + +	+ + +
3d (ii)	*p*-Tolyl	*p*-Chloro-phenyl	209	65	++	++	+	+ + +	+ + +
3d (iii)	*p*-Tolyl	Ethyl	191	59	-	-	+	+ +	-
3d (iv)	*p*-Tolyl	*t*-Butyl	172	72	+ +	+ + +	+	+ + +	++
3e (i)	Methyl	Phenyl	171	65	+ + +	+ +	+ +	+ + +	+ +
3e(iii)	Methyl	Ethyl	164	62	-	-	-	-	-
3e (iv)	Methyl	*t*-Butyl	174	68	++	+	-	+++	+++
3f (iv)	*t*-Butyl	*t*-Butyl	168	73	-	+++	+	-	++

(-) = Inactive (Less than 10 mm), (+) = Weakly Active (10-14 mm), (++) = Moderately Active (15-18 mm)
(+++) = Highly Active (19-35 mm)

Various1,3,5-thiadiazines derivatives **[3a(i) to 3f(iv)]** were prepared by the interaction of 1-formamidino-3-thioamido-N-substitutedformamidinothiocarbamides 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 bacteriocidal.

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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