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Antibacterial Activity of Some 4-*N*-Substituted Thiosemicarbazides and Thiosemicarbazones

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A series of synthesized 4-*N*-substituted thiosemicarbazides and thiosemicarbazones were screened for antibacterial activity. The compounds Ie and IIa were most active compounds of the series against *Staphylococcus aureus* and *Escherichia coli*.

Some new 1H indolo [3,2-c]isoquinolin-5-ylthiosemicarbazide and its derivatives were found to show antibacterial, anthelmintic, antiinflammatory and analgesic activity[1]. Copper and zinc chelates of 4-(4*n*) substituted thiosemicarbazones of 6-methyl-5-nitropyridine-2-carboxaldehyde showed good activity against both gram positive and gram negative bacteria[2]. Schiff and Mannich bases derived from isatin derivatives and *N*-[4-(4′-chlorophenyl)thiol-2-yl thiosemicarbazides were investigated for antimicrobial activity. Among the compound tested 1-[*N*,*N*-dimethylaminomethyl]-5-bromoisatin-3-{1′-4″-*p*-chlorophenyl)thiaxol-2″-yl} thiosemicarbazone showed significant antimicrobial activity[3]. New 4-acetyl-antipyrine-4-alkyl/aryl-3-thiosemicarbazones were tested for *invitro* antimicrobial activity[4]. A series of 3-benzylthiazolidine-2,4-dione-4-thiosemicarbazones was synthesized as potential antimicrobial agents[5]. In the view of these above compounds possessing antibacterial properties, a series of thiosemicarbazides (Ia-e) and thiosemicarbazones (IIa-e) were synthesized by using different isothiocyanates and screened for their antibacterial activity.

Equimolar quantity (0.1 mol) of cyclohexylisothiocyanate and hydrazine hydrate (2) was refluxed in ethanol for 1 h. The mixture was cooled, washed with pet. ether, dried and crystalized from ethanol to yield 4-*N*-cyclohexylthiosemicarbazide Ib. Equimolar quantity (0.05 mol) of 2-hydroxy acetophenone (1) and hydrazine hydrate (2) was stirred for 5-10 min. The yellow solid obtained as 2-hydroxyacetophenone hydrazone (3) was dissolved in 25 ml of ethanol and refluxed with cyclohexyl isothiocyanate in equimolar quantities (0.01 mol). The solid obtained was washed with pet. ether and recrystalized from a mixture of ethanol and acetone to give 2-[hydroxy] acetophenone-4-*N*-(cyclohexyl) thiosemicarbazone IIb (Scheme 1).

Two test strains of bacteria, *S. aureus* (NCTC 10418) and *E. coli* (NCTC 6571) were used. The standard drug used for comparison of test compounds were a disc of vancomycin (for *S. aureus*) and ofloxacin (for *E. coli*). A series of 4-*N* substituted thiosemicarbazides (Ia-e) and thiosemicarbazones (IIa-e) were synthesized and characterized by their melting point, TLC and IR data (Table 1). All the compounds were screened for their antibacterial activity against *S. aureus* and *E. coli* by filter paper disc technique[6]. The results are presented as in Table 2. The antibacterial activity of 4-*N*- substituted thiosemicarbazides and thiosemicarbazones was tested against *S. aureus* and *E.*

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TABLE 1: PHYSICAL CONSTANTS OF 4-*N*-SUBSTITUTED THIOSEMICARBAZIDES AND THIOSEMICARBAZONES.

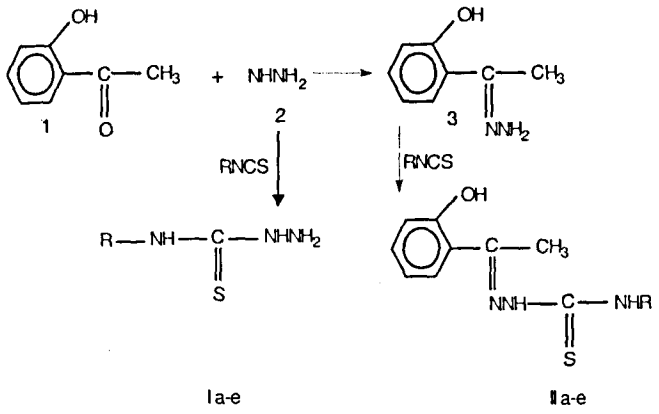
Comp. No.	R	m.p.°	Yield %	Mol. Form.	R_f Value	IR (νcm^{-1})				
						CS	CN	NH	NH_2	OH
Ia	*p*-Br.C_6H_4	166	69	$C_7H_8N_3SBr$	0.73	1536	-	3183	3291	-
Ib	C_6H_{11}	148	84	$C_7H_{15}N_3S$	0.56	1529	-	3147	3299	-
Ic	C_4H_9	184	78	$C_5H_{13}N_3S$	0.69	1545	-	3282	3391	-
Id	C_2H_5	170	62	$C_3H_9N_3S$	0.48	1521	-	3195	3282	-
Ie	CH_3	106	45	$C_2H_7N_3S$	0.54	1562	-	3282	3330	-
IIa	*p*-Br.C_6H_4	182	75	$C_{15}H_{14}N_3OSBr$	0.80	1530	1650	3150	-	3160
IIb	C_6H_{11}	162	80	$C_{15}H_{21}N_3OS$	0.66	1538	1630	3121	-	3317
IIc	C_4H_9	120	72	$C_{13}H_{19}N_3OS$	0.72	1527	1620	3223	-	3406
IId	C_2H_5	220	66	$C_{11}H_{15}N_3OS$	0.55	1542	1673	3231	-	3413
IIe	CH_3	180	55	$C_{10}H_{13}N_3OS$	0.60	1542	1607	3233	-	3413

R_f values were determined in toluene, ethyl acetoacetate, formic acid (TEF, 5:4:1), IR spectra were recorded in KBr on Hitachi IR-spectrophotometer 270-30.

TABLE 2: ANTIBACTERIAL ACTIVITY OF 4-*N*-SUBSTITUTED THIOSEMICARBAZIDES AND THIOSEMICARBAZONES.

Comp. No.	R	Diameter of zone of inhibition(mm)			
		S. aureus		*E. coli*	
		100 µg/disc	25 µg/disc	100 µg/disc	25 µg/disc
Ia	*p*-Br.C_6H_4	18	12	18	16
Ib	C_6H_{11}	12	12	18	16
Ic	C_4H_9	16	14	16	16
Id	C_2H_5	16	12	18	16
Ie	CH_3	20	16	18	16
IIa	*p*-Br.C_6H_4	22	16	26	20
IIb	C_6H_{11}	20	16	20	20
IIc	C_4H_9	20	16	18	16
IId	C_2H_5	18	16	18	16
IIe	CH_3	16	12	14	14
Vancomycin	-	25	20	-	-
Ofloxacin	-	-	-	27	21

Solvent= dimethyl formamide (No zone of inhibition), Vancomycin= 30 µg/disc (17 mm zone of inhibition), Ofloxacin = 5 µg/disc (15 mm zone of inhibition).



Ia-e IIa-e

R= *p*-BrC_6H_5, C_6H_{11}, C_4H_9, C_2H_5, CH_3

Scheme 1: Synthesis of thiosemicarbazides and thiosemicarbazones.

coli. The results show that in series Ia-e the compound having methyl substitution (Ie) was most active compound. The replacement of methyl group with *p*-Br.Ph., butyl, ethyl and cyclohexyl groups decreases the activity while in series IIa-e the compound having *p*-Br.Ph. substituent (IIa) was most active compound and replacement of this group with cyclohexyl, butyl, ethyl and methyl groups decreases the activity.

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Antiinflammatory Effect of *Ocimum sanctum* Linn. and its Cultures

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Callus cultures from stem of *Ocimum sanctum* were induced on slightly modified Murashige and Skoog's medium and supplemented with 2,4-dichlorophenoxyacetic acid (2ppm) and kinetin (1ppm). Different extracts of stem, leaf and stem calli of *O. sanctum* were tested for antiinflammatory activity using carrageenan-induced rat paw oedema model in comparison with the standard indomethacin. The ethanol extract of callus tissue exhibited maximum significant antiinflammatory activity out of all extracts studied followed by ethanol extracts of leaves of *O. sanctum*.

Ocimum sanctum Linn. (Labiatae, *Tulsi*) is a widely grown plant. In herbal medicine it has been included as a general health promotor[1] and most of its activities that include antistress[2], adaptogenic[3], anticancer[4], antiinflammatory[5-6], antihyperlipidemic[7], antihypercholesteremic[8], hepatoprotective[9], radioprotective[10] and antimicrobial[11] have been investigated scientifically. No investigations to determine the antiinflammatory activity of the tissue culture samples of *O. sanctum* or the stem extracts of this plant have been carried out even though antiinflammatory effect has been reported with the leaf[12] and seeds[13] of *O. sanctum*. Hence in the present study, an attempt has been made to determine the antiinflammatory effect of cultured tissues and stems of *O. sanctum*.

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O. sanctum herb was collected from cultivated plants