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Synthesis, Characterization and Antimicrobial Activities of Some Novel Derivatives of Phenol

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Phenolic compounds and benzaldehyde have undergone condensation with compounds containing active hydrogen atom like urea, thiourea, semicarbazide and thiosemicarbazide. The compounds thus synthesized (**I-XII**) were characterized by elemental analysis, molecular weight determination by Rast micro method, TLC and melting point and spectral methods such as IR, ^{1}H NMR, ^{13}C NMR and mass. The antimicrobial activities of synthesized compounds were also studied.

Key Words: Phenolic derivatives, Betti base, Mannich base.

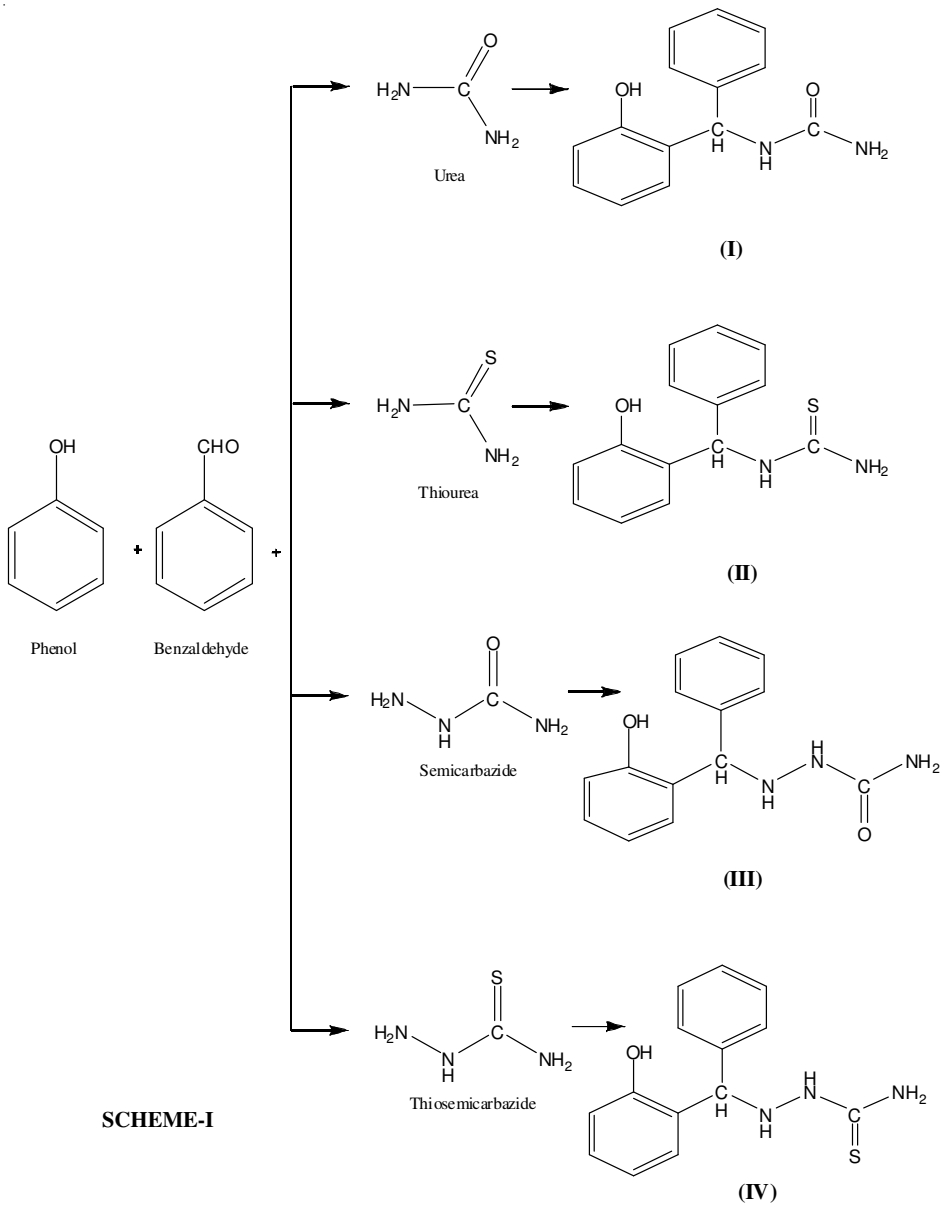
INTRODUCTION

The chemical reactions of aldehydes, amides and phenols are well known that the compounds containing amide moiety exhibit a wide range of biological activities[1-7]. In this view, the authors have synthesized the compounds **I-XII** by reacting benzaldehyde as a fixed component and varying amide component and phenolic compounds.

EXPERIMENTAL

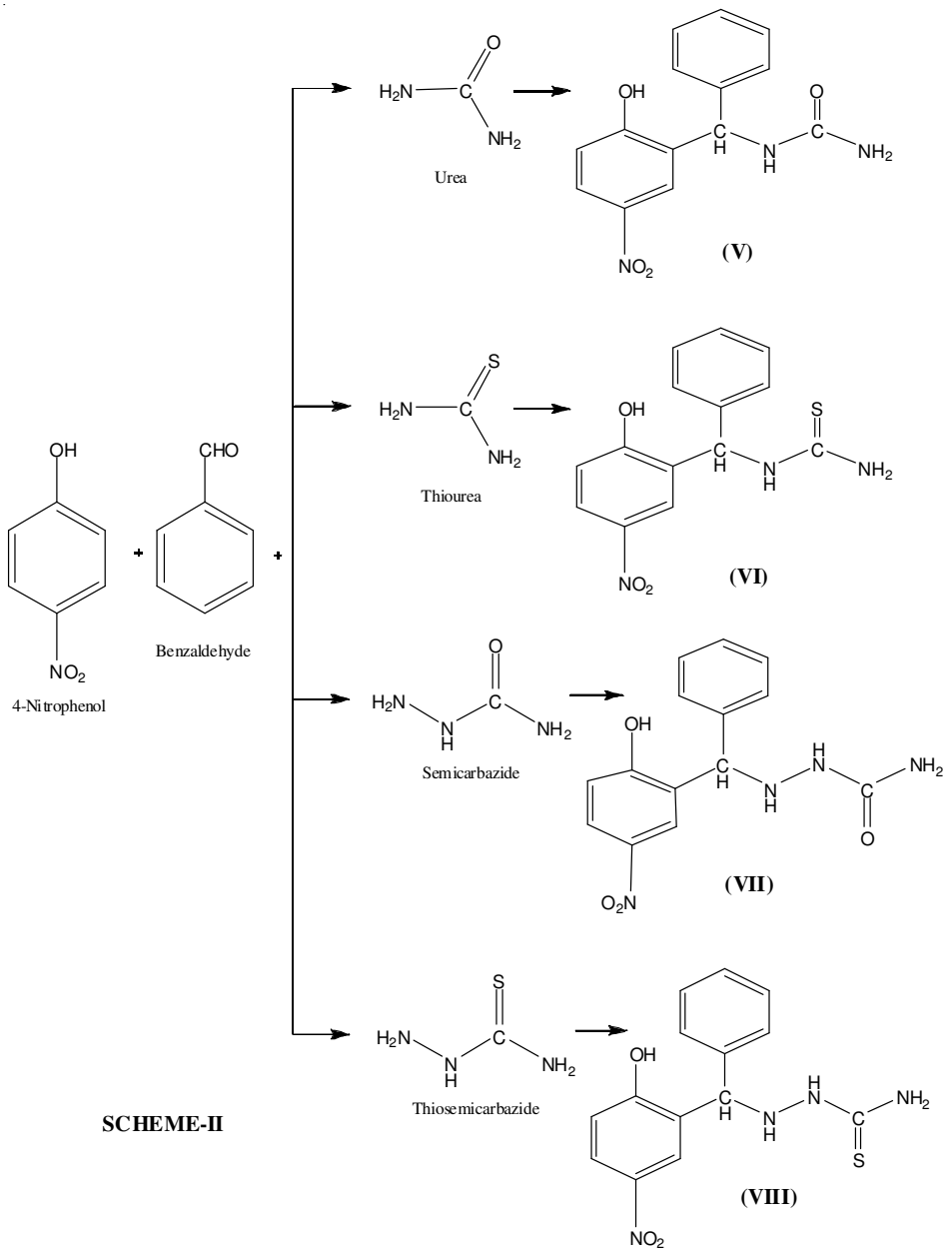
The melting points of the compounds was determined in open capillaries and are uncorrected. Purity of the compounds was checked by TLC using silica gel G coated glass plates with chloroform and ethyl acetate (1:1) as irrigant and iodine vapour as visualizing agent. The IR spectra were recorded in the ACIC at Trichy in KBr medium. The ^{1}H and ^{13}C NMR spectra of compound were recorded on a Brucker 300 MHz model in DMSO using tetramethyl silane as an internal standard. The elemental analyses were performed on a Perkin-Elmer series C, H, N and S analyzer-2000. Mass spectra were recorded on a Jeol-8X 102 (FAB).

General procedure for synthesis of compounds I-IV: To a mixture of phenol (0.05 mol) and benzaldehyde (0.05 mol), the compounds like urea, thiourea, semicarbazide and thiosemicarbazide in ethanol (0.05 mol) were added in drops and the reaction mixture was stirred in hot water bath maintained at 80 ºC with constant stirring for *ca.* 1 h. The solid separated on cooling was recrystalized from ethanol (**Scheme-I**). The analytical data of the synthesized compounds are given in Table-1.



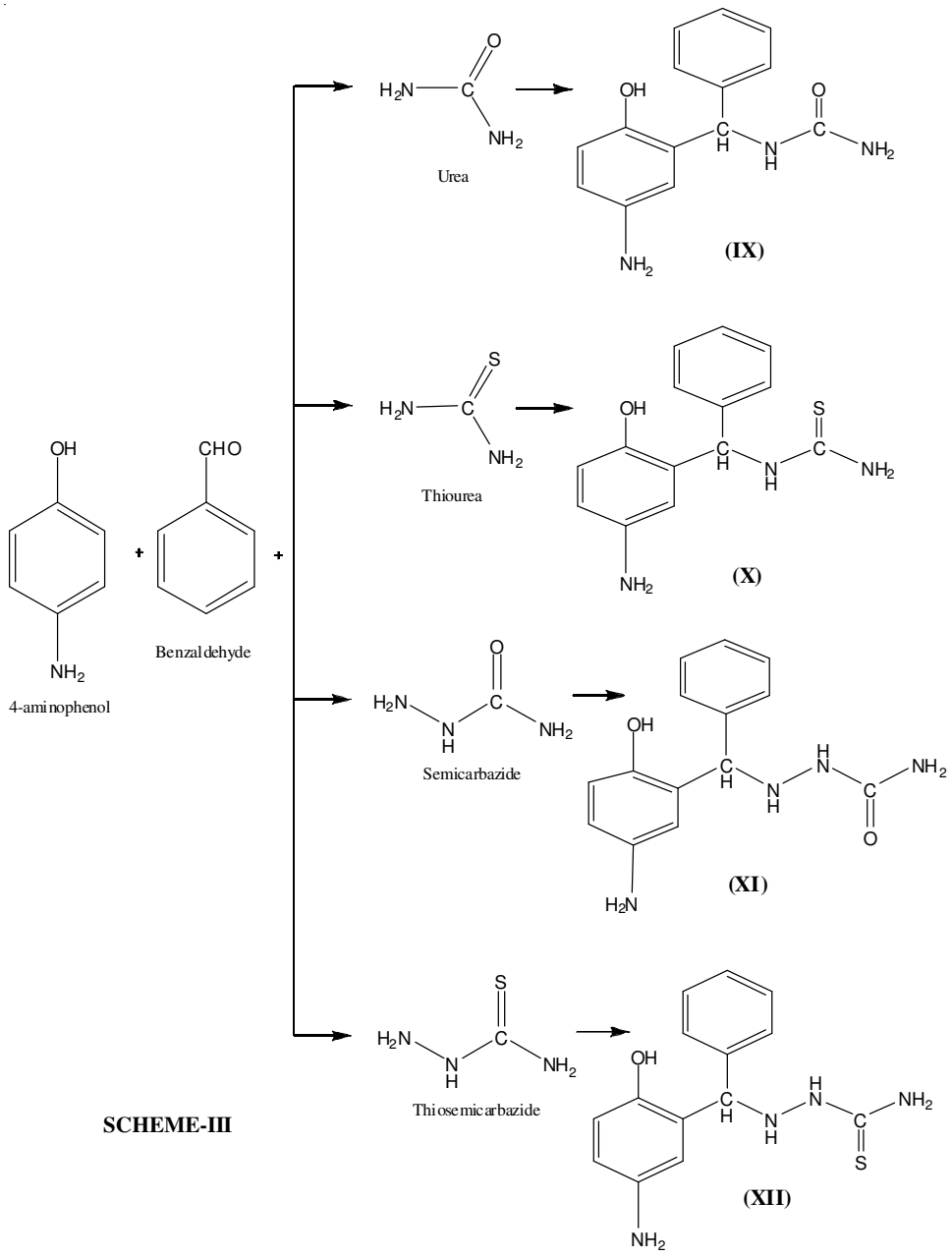
SCHEME-I

General procedure for synthesis of compounds V-VIII: To a mixture 4-nitrophenol (0.05 mol) and benzaldehyde (0.05 mol) compounds like urea, thiourea, semicarbazide and thiosemicarbazide in ethanol (0.05 mol) were added in drops and the reaction mixture was stirred well at room temperature for *ca.* 5 h. The colloidal formed was solution kept in a freezer for 24 h. The solid separated on cooling was washed with ether and recrystallized from ethanol (**Scheme-II**). The analytical data of the synthesized compounds are given in Table-1.



SCHEME-II

General procedure for synthesis of compounds IX-XII: To a mixture 4-aminophenol (0.05 mol) and benzaldehyde (0.05 mol) compounds like urea, thiourea, semicarbazide and thiosemicarbazide in ethanol (0.05 mol) were added in drops and the reaction mixture was stirred well for *ca.* 2 h in an ice path. The solid separated was washed with petroleum ether and recrystallized from ethanol (**Scheme-III**). The analytical data of the synthesized compounds are given in Table-1.



SCHEME-III

1-((2-Hydroxyphenyl)(phenyl)methyl)urea (compound-I): IR: (KBr, ν_{max}, cm^{-1}): 3504 (Ar-OH, stretching), 3247 (NH_2, stretching), 1635 (C=O), 1235 (CN). ^1H NMR (DMSO) δ: 11.8 (s, H, OH), 11.5 (s, 2H, NH_2), 8.27 (d, H, NH), 3.8 (q, H, NH), 2.9 (s, H, CH). ^{13}C NMR (DMSO) δ: 167 (C=O), 129 (Ar), 128 (Ar), 30 (CH). MS: m/z: 242.

TABLE-1
ANALYTICAL DATA OF THE SYNTHESIZED COMPOUNDS

Compd.	Yield (%)	m.w.	m.f.	m.p. (ºC)	Elemental analysis (%): Found (calcd.)			
					C	H	N	S
I	50	242	$C_{14}H_{14}N_2O_2$	136	69.41 (69.40)	5.82 (5.80)	11.56 (11.54)	-
II	50	258	$C_{14}H_{14}N_2OS$	186	65.09 (65.07)	5.46 (5.45)	10.84 (10.82)	12.41 (12.40)
III	50	257	$C_{14}H_{15}N_3O_2$	152	65.35 (65.33)	5.88 (5.86)	16.33 (16.32)	-
IV	50	273	$C_{14}H_{15}N_3OS$	220	61.51 (61.50)	5.53 (5.52)	15.37 (15.35)	11.73 (11.71)
V	62	287	$C_{14}H_{13}N_3O_4$	165	58.53 (58.52)	4.56 (4.55)	14.63 (14.61)	-
VI	71	303	$C_{14}H_{13}N_3O_3S$	240	55.43 (55.42)	4.32 (4.31)	13.85 (13.84)	10.57 (10.56)
VII	50	302	$C_{14}H_{14}N_4O_4$	206	55.63 (55.61)	4.67 (4.65)	18.53 (18.52)	-
VIII	60	318	$C_{14}H_{14}N_4O_3S$	258	52.80 (52.82)	4.47 (4.43)	17.63 (17.60)	10.09 (10.07)
IX	76	257	$C_{14}H_{15}N_3O_2$	218	65.30 (65.35)	5.82 (5.88)	16.30 (16.33)	-
X	72	273	$C_{14}H_{15}N_3OS$	253	61.48 (61.51)	5.52 (5.53)	15.35 (15.37)	11.71 (11.73)
XI	75	272	$C_{14}H_{16}N_4O_2$	209	61.72 (61.75)	5.91 (5.92)	20.54 (20.58)	-
XII	78	288	$C_{14}H_{16}N_4OS$	265	58.28 (58.31)	5.56 (5.59)	19.41 (19.43)	11.10 (11.12)

1-((2-Hydroxyphenyl)(phenyl)methyl)thiourea (compound-II): IR (KBr, ν_{max}, cm^{-1}): 3507 (Ar-OH, stretching), 3236 (NH_2, stretching), 1538 (C=S), 1232 (CN), ^1H NMR (DMSO) δ: 9.68 (S, aromatic C-OH), 9.53 (S, NH_2 thiourea), 5.19 (S, aromatic CH). ^{13}C NMR (DMSO) δ: 182.5 (CS, thiourea), 54.0 (aromatic CH). MS: m/z: 258.

2-((2-Hydroxyphenyl)(phenyl)methyl)hydrazinecarboxamide (compound-III): IR: (KBr, ν_{max}, cm^{-1}): 3510 (Ar-OH, stretching), 3242 (NH_2, stretching), 1638 (C=O), 1237 (CN), ^1H NMR (DMSO) δ: 11.7 (s, H, OH), 11.6 (s, 2H, NH_2), 8.04 (d, H, NH), 3.4 (q, H, NH), 2.7 (s, H, CH). ^{13}C NMR (DMSO) δ: 187.5 (CS, thiourea), 56.0 (aromatic CH). MS: m/z: 257.

2-((2-Hydroxyphenyl)(phenyl)methyl)hydrazinecarbothioamide (compound-IV): IR: (KBr, ν_{max}, cm^{-1}): 3500 (Ar-OH, stretching), 3242 cm^{-1} (NH_2, stretching), 1534 (C=S), 1294 (CN), ^1H NMR (DMSO) δ: 11.4 (s, H, OH), 11.2 (s, 2H, NH_2), 8.04 (d, H, NH), 3.4 (q, H, NH), 2.5 (s, H, CH). ^{13}C NMR (DMSO) δ: 177 (C=S), 129 (Ar), 128 (Ar), 32 (CH). MS: m/z: 273.

1-((2-Hydroxy-5-nitrophenyl)(phenyl)methyl)urea (compound-V): IR: (KBr, ν_{max}, cm^{-1}): 3510 (Ar-OH), 3041 (CH, stretching), 1612 (NH_2), 1208 (C=O). ^1H NMR (DMSO) δ: 11.8 (s, H, OH), 11.1 (s, 2H, NH_2), 9.2 (d, H, NH), 7.6-7.8 (M,

2H, NH-NH) 2.7 (s, H, CH). ^{13}C NMR (DMSO) δ: 167 (C=O), 128 (Ar), 129 (Ar), 30 (CH), MS: m/z: 287.

1-((2-Hydroxy-5-nitrophenyl)(phenyl)methyl)thiourea (compound-VI): IR (KBr, ν_{max}, cm^{-1}): 3513 (Ar-OH), 3041 (CH, stretching), 1614 (NH_2), 1318 (C=S). ^{1}H NMR (DMSO) δ: 11.3 (s, H, OH), 11.2 (s, 2H, NH_2), 9.8 (d, H, NH), 7.8-8.0 (m, 2H, NH-NH), 2.4 (s, H, CH). ^{13}C NMR (DMSO) δ: 177 (C=S), 129 (Ar), 128 (Ar), 30 (CH). MS: m/z: 303.

2-((2-Hydroxy-5-nitrophenyl)(phenyl)methyl)hydrazinecarboxamide (compound-VII): IR: (KBr, ν_{max}, cm^{-1}): 1632 (C=O), 3518 (Ar-OH), 1617 (NH_2), 3048 (CH stretching). ^{1}H NMR (DMSO) δ: 8.08 (s, H, OH), 8.03 (s, H, NH_2), 7.7-7.9 (m, 2H, NH-NH). ^{13}C NMR (DMSO) δ: 30 (CH), 167 (C=O), 128 (Ar), 129 (Ar). MS: m/z: 302.

2-((2-Hydroxy-5-nitrophenyl)(phenyl)methyl)hydrazinecarbothioamide (compound-VIII): IR: (KBr, ν_{max}, cm^{-1}): 3408 (Ar-OH), 1599 (NH_2), 3148 (CH stretching), 1098 (C=S). ^{1}H NMR (DMSO) δ: 8.05 (s, H, OH), 8.0 (s, H, NH_2), 7.7-7.9 (m, 2H, NH-NH). ^{13}C NMR (DMSO) δ: 177 (C=S), 128 (Ar), 129 (Ar), 30 (CH). MS: m/z: 318.

1-((5-Amino-2-hydroxyphenyl)(phenyl)methyl)urea (compound-IX): IR: (KBr, ν_{max}, cm^{-1}): 3515 (Ar-OH), 3110 (CH, stretching), 1620 (NH_2), 1210 (C=O). ^{1}H NMR (DMSO) δ: 13.1 (s, 2H, NH_2), 12.8 (s, H, OH), 10.2 (d, H, NH), 8.6-8.8 (m, 2H, NH-NH) 3.5 (s, H, CH). ^{13}C NMR (DMSO) δ: 171 (C=O), 128 (Ar), 129 (Ar), 32 (CH), MS: m/z: 257.

1-((5-amino-2-hydroxyphenyl)(phenyl)methyl)thiourea (compound-X): IR (KBr, ν_{max}, cm^{-1}): 3513 (Ar-OH), 3041 (CH, stretching), 1614 (NH_2), 1318 (C=S). ^{1}H NMR (DMSO) δ: 11.3 (s, H, OH), 11.2 (s, 2H, NH_2), 9.8 (d, H, NH), 7.8-8.0 (m, 2H, NH-NH), 2.4 (s, H, CH). ^{13}C NMR (DMSO) δ: 177 (C=S), 129 (Ar), 128 (Ar), 30 (CH), MS: m/z: 273.

2-((5-Amino-2-hydroxyphenyl)(phenyl)methyl)hydrazinecarboxamide (compound-XI): IR: (KBr, ν_{max}, cm^{-1}): 1632 (C=O), 3518 (Ar-OH), 1617 (NH_2), 3048 (CH stretching). ^{1}H NMR (DMSO) δ: 8.08 (s, H, OH), 8.03 (s, H, NH_2), 7.7-7.9 (m, 2H, NH-NH). ^{13}C NMR (DMSO) δ: 167 (C=O), 128 (Ar), 129 (Ar), 30 (CH). MS: m/z: 272.

2-((5-Amino-2-hydroxyphenyl)(phenyl)methyl)hydrazinecarbothioamide (compound-XII): IR: (KBr, ν_{max}, cm^{-1}): 3408 (Ar-OH), 3148 (CH stretching), 1599 (NH_2), 1098 (C=S). ^{1}H NMR (DMSO) δ: 8.05 (s, H, OH), 8.0 (s, H, NH_2), 7.7-7.9 (m, 2H, NH-NH). ^{13}C NMR (DMSO) δ: 177 (C=S), 128 (Ar), 129 (Ar), 30 (CH). MS: m/z: 288.

Antimicrobial activity: The synthesized compounds (**I-XII**) were screened for antibacterial and antifungal activity against certain pathogenic bacteria by disc diffusion method at concentration of 10 μg/mL in DMSO using both gram positive *S. aureus, B. substilis*, gram negative *E. coli, P. aeruginosa* and antifungal activity against *C. albicans*. The zone of inhibition was measured in mm and the activity was compared with ciprofloxacin 1 μg/disc for bacteria, clotrimazole 10 μg/disc for fungi as standard drugs. The compound posses appreciable antibacterial activity against selected organism when compared with the standard.

RESULTS AND DISCUSSION

Phenol, benzaldehyde and the compounds like urea, thiourea, semicarbazide and thiosemicarbazide in equimolar afford compounds **I-IV**. 4-Nitrophenol, benzaldehyde and the compounds like urea, thiourea, semicarbazide and thiosemicarbazide in equimolar afford compounds **V-VIII**. 4-Aminophenol, benzaldehyde and the compounds like urea, thiourea, semicarbazide and thiosemicarbazide in equimolar afford compounds **IX-XII**. All the compounds are characterized by means of physical methods (melting point, elemental analysis, molecular weight determination by Rast micro method and TLC) and spectral methods (IR, ^{1}H NMR, ^{13}C NMR and mass). All the compounds **I-XII** were screened for antibacterial and antifungal activity against certain organisms. All compounds possess appreciable activity against selected organisms. The zone of inhibition values are presented in Table-2.

TABLE-2
ANTIMICROBIAL ACTIVITIES OF THE SYNTHESIZED COMPOUNDS

Compd.	Diameter zone of inhibition (mm)				
	Gram Positive		Gram Negative		Fungi
	S. aureus	*B. subtilis*	*E. coli*	*P. aeruginosa*	*C. albicans*
I	10	16	14	11	09
II	16	15	13	NI	10
III	10	13	NI	08	07
IV	12	12	12	NI	15
V	15	08	10	09	13
VI	14	18	17	NI	14
VII	11	15	12	07	13
VIII	15	12	13	10	17
IX	13	11	10	12	10
X	15	13	09	12	08
XI	12	17	15	16	10
XII	10	NI	17	18	13
Standard	20	19	16	19	12
Solvent	NI	NI	NI	NI	NI

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