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Antimicrobial Study of 4-(substituted Phenyl)-1H-Imidazol-2(5H)-One/ Thione /Imine

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ABSTRACT

The antimicrobial activity of the synthesized heterocyclic viz4-(substituted phenyl)-1H-imidazol-2(5H)-one/thione/imine compounds have been tested against *Staphylococcus aureus, Escherichia coli, Salmonella typhi, Proteus vulgaris* using cup-plate methodand their minimum inhibitory concentration (MICs) were determined using broth macrodilution method Also these compounds were tested against seed germination study.

Keywords: Antimicrobial study, cup plate method, seed germination study.

INTRODUCTION

The increasing resistance of human pathogens to current antimicrobial agents is a serious medical problem. Microbial infections are being recognized with increasing frequency as an important cause of both morbidity and mortality. The immune system resists bacterial and fungal infections. Many of the drugs currently available have undesirable effects and might be toxic. Considering the fact that the available antimicrobial agents originate from a limited number of sources, and that most of them have similar modes of activity, it is very important to explore additional sources for substances with potential antimicrobial activity, which could possibly have different modes of activity or affect different sites in the bacterial and fungal cells. In view of wide spread of resistant strains of microorganism there is an urgent need for the development of new antimicrobial agents to treat the patients infected with multidrug-resistant bacteria and fungi.

Imidazole and its derivatives are of great significance due to their important roles in biological systems. Unlike pyrrole (a proton donor) and pyridine (a proton acceptor), 1*H*-imidazole has proton donor and acceptor properties [1,2]. Imidazole derivatives possess a broad spectrum of pharmacological activities such as anticonvulsant [3] antiparkinson [4,5] anthelmintics[6], anticancer and anti-HIV agents[7,8] antiviral [9], CNS depression [10]

MATERIALS AND METHODS

General procedure for the synthesis of 4-(substituted phenyl)-1H-imidazol-2(5H)-one/thione/ imine

2-Bromo-1-(substituted phenyl) ethanone (IIa-c) (0.02 M) dissolved in ethanol and substituted amide/imidine (0.02 M) in water using TEBA (0.05 M) as catalyst were irradiated under microwave for 3.5 min at 700 W. The reaction mixture was allowed to cool and triturate it. Add ice-cold water and neutralize with sodium acetate. The product thus separated out was filtered and crystallized from ethanol as 4-(substituted phenyl)-1H-imidazol-2(5H)-one/thione/imine (IIIa-i) in 60 to 80% yield. The products were confirmed by IR and ^{1}H NMR spectra and melting point.

Spectral data of principal compound

Synthesis of 4-(2'-hydroxy-5'-methylphenyl)-1H-imidazol-2(5H)-thione (IIIb)

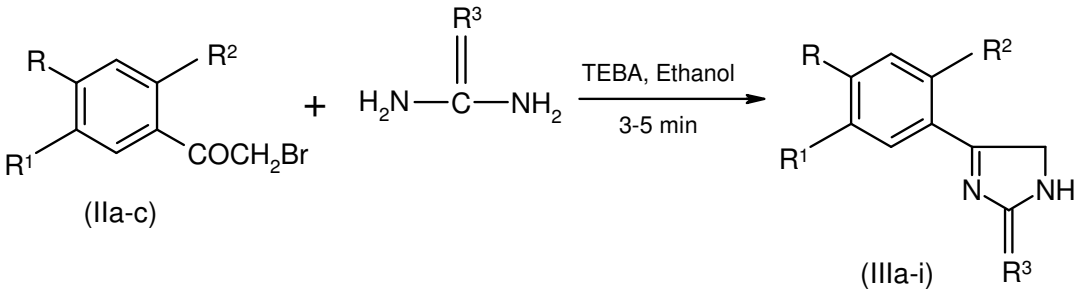
IR (KBr) : 3172 (vb,OH), 3032 (s,-C-H), 1631(s,-C=C), 1481(s, –C=N), 1006 (s,-C-N) cm^{-1}. ^{1}H NMR $CDCl_3$,300 MHz , δ, ppm): 2.1(s,3H, -CH_3) 2.3 (s,1H, NH),4.2 (s, 2H, -CH_2) 7.4 - 7.7(m, 3H, Ar-H) 12.1(s, 1H,-OH)

Synthesis of 4-(4'-chloro phenyl)-1H-imidazol-2(5H)-one (IIId)

IR (KBr) : 3369(s,NH),3170 (s,-C-C), 1697(s,-C=O), 1487(s, –C=N), 1010 (s,-C-N), 777 (s,-C-Cl) cm^{-1}. ^{1}H NMR $CDCl_3$,300 MHz , δ, ppm): 0.91(s,1H, NH tautomeric) 1.2(s,1H, NH), 4.3 (s, 2H, -CH_2) 4.6(s,1H,=CH tautomeric) 7.3 (d,J=9Hz, 2H, Ar-H) 7.9(d,J=9Hz, 2H, Ar-H)

Synthesis of 4-(4'-chloro phenyl)-1H-imidazol-2(5H)-imine (IIIf)

IR (KBr) : 3360 (s,-NHstreach), 1697 (s,-C=C), 1485(s,-C=N), 1093(s, –C- N), 817 (s,-C-Cl)559(s,-C=C-N) cm^{-1}. ^1H NMR $CDCl_3$,300 MHz , δ, ppm): 1.50(s, 1H,-NHtautomeric) 1.60(s,1H,-NH) 3.50(s,1H=NHtautomeric) 4.66(s,2H, $-CH_2$) 7.75(d,J=9Hz, 2H, Ar-H) 7.91(d,J=9Hz, 2H, Ar-H)



Scheme-1: Synthesis of 4-(substituted phenyl)-1H-imidazol-2(5H)-one/thione/imine (IIIa-i) from 2-Bromo-1-(substituted phenyl) ethanone (IIa-c) and substituted amide.

Table-1: Synthesis of 4-(substituted phenyl)-1H-imidazol-2(5H)-one/thione/imine

Expt. No.	α-halocarbonyl compound	4-(substituted phenyl)-1H-imidazol-2(5H)-one/thione/imine	m.p. (°C)	M.F.	M.W. Yield (%)
1	2-Bromo-1-(2-hydroxy-5-methyl phenyl) ethanone (IIa)	4-(2-Hydroxy-5-methyl phenyl)-1H-imidazol-2(5H)-one (IIIa)	96	$C_{10}H_{10}N_2O_2$	78
2	(IIa)	4-(2-Hydroxy-5-methyl phenyl)-1H-imidazol-2(5H)-thione (IIIb)	50	$C_{10}H_{10}N_2OS$	60
3	(IIa)	4-(2-Hydroxy-5-methyl phenyl)-1H-imidazol-2(5H)-imine (IIIc)	100	$C_{10}H_{11}N_3O$	65
4	2-Bromo-1-(4-chloro phenyl) ethanone (IIb)	4-(4-chlorophenyl)-1H-imidazol-2(5H)-one (IIId)	90	$C_9H_7ClN_2O$	70
5	(IIb)	4-(4-chlorophenyl)-1H-imidazol-2(5H)-thione (IIIe)	110	$C_9H_7ClN_2OS$	75
6	(IIb)	4-(4-chlorophenyl)-1H-imidazol-2(5H)-imine (IIIf)	160	$C_9H_8ClN_3$	68
7	2-Bromo-1-(4-nitro phenyl) ethanone (IIc)	4-(4-nitrophenyl)-1H-imidazol-2(5H)-one (IIIg)	132	$C_9H_7N_3O_3$	78
8	(IIc)	4-(4-nitrophenyl)-1H-imidazol-2(5H)-thione (IIIh)	98	$C_9H_7N_3O_2S$	63
9	(IIc)	4-(4-nitrophenyl)-1H-imidazol-2(5H)-imine (IIIi)	48	$C_9H_8N_4O_2$	75

Screening for antimicrobial activity

The antimicrobial activity of the synthesized 4-(Substituted Phenyl)-1H-Imidazol-2(5H)-One/Thione/Imine heterocyclic compounds have been tested against *Staphylococcus aureus, Escherichia coli, Salmonella typhi, Proteus vulgaris* using cup-plate method [11]and their minimum inhibitory concentration (MICs) were determined using broth macrodilution method.

The sterilized nutrient agar medium was poured into the petridishes and allowed to solidify. The lawn of the culture was prepared by spreading the microbial suspension on the surface of the medium with the help of sterilized triangular loop. Petridishes were allowed to remain for 10 min, after which excess of nutrient broth

cultures were taken out aseptically using pasture pipettes. Standard 8 mm size cups were prepared in the solidified medium with the help of per-sterilized steel cylinder of 8 mm diameter. The wells were then filled with the 0.5 ml stock solution of the test compounds and standard drug Chloramphenicol (200 µg/ml). Controls were run using only DMF solvent. All the plates were incubated at 37 ± 2°C 24 ± 2 hours. The zones of inhibition were recorded by using vernirecalipers. The zone of inhibition is recorded including the well diameters of 8mm.MIC values of all the synthesized compounds against various organisms have been recorded The test compounds were dissolved in DMF.

Table-2: Antimicrobial activity of 4-(substituted phenyl)-1H-imidazol-2-(5H)-one/thione/imine (III a-i)

Compd. No.	Compounds	Inhibition zone in mm (MIC in µg/ml)			
		P. vulgaris	*S. aureus*	*E. coli*	*S. typhi*
IIIa	4-(2-Hydroxy-5-methyl phenyl)-1H-imidazol-2(5H)-one	17 (125)	15 (500)	18 (250)	22 (250)
IIIb	4-(2-Hydroxy-5-methyl phenyl)-1H-imidazol-2(5H)-thione	22 (250)	20 (125)	20 (250)	22 (250)
IIIc	4-(2-Hydroxy-5-methyl phenyl)-1H-imidazol-2(5H)-imine	22 (250)	15 (250)	16 (250)	7(250)
IIId	4-(4-chlorophenyl)-1H-imidazol-2(5H)-one	21 (250)	17 (250)	15 (250)	21 (250)
IIIe	4-(4-chlorophenyl)-1H-imidazol-2(5H)-thione	23 (250)	16(250)	16 (250)	14(250)
IIIf	4-(4-chlorophenyl)-1H-imidazol-2(5H)-imine	20 (250)	18 (250)	17 (250)	18 (500)
IIIg	4-(4-nitrophenyl)-1H-imidazol-2(5H)-one	21 (250)	17 (500)	16 (500)	7(250)
IIIh	4-(4-nitrophenyl)-1H-imidazol-2(5H)-thione	20 (250)	17 (250)	16 (500)	12 (250)
IIIi	4-(4-nitrophenyl)-1H-imidazol-2(5H)-imine	22 (500)	12 (250)	18 (500)	8 (500)
	Chloramphenicol	28 (12.5)	24 (12.5)	27 (25)	26 (50)

Effect on seed germination

The technique of applying chemicals such as plant hormones, insecticidesandfungicides to dry seeds in organic solvent have been described by several workers[12-17] We therefore, thought worthwhile to undertake the study of newly synthesized heterocycles such as 4-(substituted phenyl)-1H-imidazol-2(5H)-one/thione/imine in the context of seeds germination effect (cytotoxicity) by paper towel (between paper) technique[18].

The experimental setup of the proposed study divided into following two parts-

i. Seed infusion
ii. Lab experiment

Seed infusion

For seed infusion, ten dry seeds of each *Trititicum durum* (wheat), *Sorghum bicolor* (jowar) and vegetable crops like *Abelmoschusexculentus* (L) moenchi (Bhendi) and *Trigonellafonumgraecum* (Methi) were immersed for four hrs. in two solvents, DMF and DMSO, containing the synthesized compounds which were designated as treated. Similarly ten dry seeds each of *Trititicum durum* (wheat), *Sorghum bicolor* (jowar) and vegetable crops like *Abelmoschusexculentus* (L) moenchi (Bhendi) and *Trigonellafonumgraecum* (Methi) were immersed for four hrs in water respectively (control seeds). The concentration of solutions used for these experiments was 15 mg/ml.

Lab experiment

Pre-germinated quality seeds of *Trititicum durum* (wheat), *Sorghum bicolor* (jowar) and vegetable crops like *Abelmoschusexculentus* (L) moenchi (Bhendi) and *Trigonellafonumgraecum* (Methi)were procured from KrishiVigyan Kendra, Durgapur, Bandenra, District Amravati (M.S.) India. The information pertaining to tested sample is written on the mid portion of the paper towel prior to its proper moistening with water. Moist towel is

stretched on a clean table and on the other side of the paper towel 10 seeds are arranged on it half portion containing two rows each of 10 seeds about 3 cm space is left on lower and right side of the paper towel. Seeds are covered with another paper and the right and lower portion is folded upward to close both the ends. The paper towel is rolled from the right end wrapped in a wax paper and the ends are tightened with rubber bands. This paper towel is placed vertically in a seed germinator with upper direction of open end. Average length of radicles and plumules were observed after 24 hrs., 48 hrs. (2 days), 72 hrs. (3 days), 96 hrs. (4days), 120 hrs (5 days), 144 hrs (6days) and 168 hrs. (7days). Observed data was recorded in tablesThe data obtained was subjected to analysis of percentage germination and growth parameters.

Table-3: Effect of newly synthesized compounds on seed germination *Trititicum durum* (wheat)

Compounds	In DMSO			In DMF		
	Germination(%)	Avg. radicle length (cm)	Avg. plumule length(cm)	Germination (%)	Avg. radicle length (cm)	Avg. plumule length (cm)
Control	50	2.49	2.61	30	1.03	5.76
IIId	80	5.78	5.57	90	2.16	.47
IIIe	90	7.19	5.74	90	6.53	4.36

Table-4: Effect of newly synthesized compounds on seed germination *sorghum bicolor* (jowar)

Compounds	In DMSO			In DMF		
	Germination(%)	Avg. radicle length (cm)	Avg. plumule length(cm)	Germination(%)	Avg. radicle length (cm)	Avg. plumule length (cm)
Control	80	2.69	4.16	50	2.16	2.27
IIId	90	9.52	8.06	100	8.43	7.21
IIIe	100	10.39	6.78	90	14.24	10.52

Table-5: Effect of newly synthesized compounds on seed germination *Abelmoschusexculentus* (L) moenchi (Bhendi)

Compounds	In DMSO			In DMF		
	Germination(%)	Avg. radicle length (cm)	Avg. plumule length (cm)	Germination(%)	Avg. radicle length (cm)	Avg. plumule length (cm)
Control	30	1.22	1.82	60	2.57	3.13
IIId	20	1.02	1.75	100	4.16	12.4
IIIe	30	1.46	1.06	30	1.17	1.13

Table-6: Effect of newly synthesized compounds on seed germination *Trigonellafonumgraecum* (Methi)

Compounds	In DMSO			In DMF		
	Germination(%)	Avg. radicle length (cm)	Avg. plumule length (cm)	Germination(%)	Avg. radicle length (cm)	Avg. plumule length (cm)
Control	70	2.7	6.33	60	2.53	4.2
IIId	90	3.32	2.72	90	1.07	.09
IIIe	100	5.29	5.32	100	4.24	4.56

RESULTS AND DISCUSSION

All the compounds exhibited appreciable activity against *P. vulgarius*. Every test compound of imidazole (IIIa-i) showed more than 20 mm inhibition zone against *P. vulgarius*. The results have indicated that *P. vulgarius* is sensitive to all the synthesized heterocycles.

The compounds (IIIa-i) showed less activity against *S. aureus.* The results indicate that the *S. aureus* is less sensitive to the synthesized heterocycles.Theimidazoles have been found to show good activity against *E. coli*, It shows average acyivity against *S. typhi*.
Effect of test compound (IIId, IIIe) is more than control. In control average germination, radicle and plumule length was less than the treated one.

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REFERENCES

1. Foster E.J., Lavigueur C.K.E., Williams V.E., Journal of Material Chemistry, **37** (2005) 4062.
2. Brunsveld L., Zong H., Glasbeek M.E.W., Meijer E. W., Journal of American Chemical society, **122** (2000)6175.
3. Upadhyay P.S., Joshi H. D., Baxi A. J., Parikh A.R., Intrnational Journal of Heterocyclic Chemistry, **1** (1991) 71.
4. D.K. Naithani., V.K.Srivastava., J.P. Barthwal., A.K. Saxena., T.K. Gupta., K. Shanker., I. J. Chem., **28** (1989) 990.
5. Miyachi H., Kiyota H., Egawa M.,Bioorganic & Medicinal Chemistry Letter, **8** (1998) 1807 .
6. Imtiaz H. M., Kumar V., Indian Journal of Chemistry, **31** (1992) 285.
7. Shah B.R., Bhatt J.J., Patel H.H., Undavia N.K., Trivedi P.B., Desai N.C., Indian Journal of Chemistry, **34** (1995) 201.
8. Krezel I., Farmacolgy **53** (1998) 342.
9. Sharma D., Narasimhan B., Kumar P., Judge V., Narang R., De Clercq E., Balzarini .,Europian Journal of Medicinal Chemistry, **44** (2009) 2347.
10. Meenakshi S., Reena K., Renu S., Dixit K.S., Nath C., Barthwal J.P., Indian Journal of Chemistry, **29** (1990) 85.
11. Seelay H. W., Van Dnmark., Microbes in action ., A Laboratory Manual of microbiology, **55** (1975) 80.
12. Anderson J. D., Science, **179** (1973) 94-95.
13. Ellis M. A., Foor S.R., Sinclair J.B., Phytopathology, **66** (1976) 149-1251.
14. Khan A.A., Tao K.L., Roe C.H., Plant Physiology, **52** (1973) 79-81.
15. Meyer H., Meyer A.M., Science, **171**, 583-584.
16. Milborrow B.V., Nature., **199** (1963)716-717.
17. G.C. Papvizas ., Lewis J.A., Plant Dis Rep, **60** (1976) 484-488.
18. Dhirendra Khare., Mohan S., Bhale., A Textbook of Agriculture Botany (2000) 64.

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