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E: ISSN NO.: 2455-0817 *Remarking An Analisation*

Synthesis of some new Derivatives of 4-[3'-iodo-4'-hydroxy-5'-methoxy]-2'-azetidinones with Possible Fungicidal Activity

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Abstract

The present study was conducted to evaluate the fungicidal activity, many phenols and compounds with phenolic groups have antifungal potency A large number of fungicides are formulated as wettable powders; this is the form most commonly used for spray mixes. They simply inhibit fungus growth temporarily.If the fungus is freed from such substance, it would revive. Such a chemical is called a ‘’fungistat” and the phenomenon of temporarily inhibiting the growth is ‘’fungistasis” .Some other chemicals, like certain phenanthrene derivatives and Bordeaux mixture, may inhibit spore production without affecting the growth of vegetative fungistate hyphae.These are called ‘’antisporulaaaaants’’. 2-amino 4-Phenyl thiazole is condensed with appropriate ethanol and piperidine aromatic was refluxed on water bath for 1 hr.Various. Obtaining gave benzal imine and azetidinones respectively and synthesized compounds showed moderate to good antifungal activity with respect to standard drugs.

Keywords: 2-amino 4-Phenyl Thiazole, Etoh, Anhydrous Zinc Chloride , Antifungal Activity

Introduction

The medicinal chemistry is the science which concerns essentially the understanding and explanation of mechanism of the action of drugs . For the chemist point of view it involves isolation .characterisation and synthesis of compounds, that can be used in medicines for the prevention , treatment and cure of diseases . Medicinal chemistry thus provides the chemical basis for the interdisciplinary field of therapeuties . The impact of the study of fundamental medicinal chemistry has given a new impectus to chemical , biological and engineering sciences . the approach to the study and design of the medicinal drug has centered primarily on the gross chemical structure of natural and synthetic compounds having established biological action . modification of the basis structure are obtained by chemical synthesis and the effect of these changes on biological response are used to compile structure activity relationship . These relationship are intended to serve as a guide in the interpretation of the structural features essential for a given typesof drug of new agents of similar biological activity . More commonly it is found that compounds are unrelated chemically may have the some action , and that compounds with the same functional group possess widly different biological activity . Such divergence from established structure activity relationship requires the synthesis of a large number of compounds before a useful agent can be found . A fungicide which kills on contact can check the growth of mycellum and limit the production of reproductive structures , such action delays or prevents the disease from spreading from infected plants t healthy ones near by , but the majority of successful non-systemic fungicides are most effective when applied prior to the arriaval of infection . Non systemic fungicides must therefore normally possess some degree of persistence and majiority of such fungicides are infected insoluble in water. In the present investigation synthesis of some new series Schiff bases derived from 2-Amino -4-phenyl thiazole with iodo vanillin is to be carried out which on cyclisation with corresponding thiazole derivative.

Material and Methods

Thiazoles are important class of natural and synthetic compounds. Thiazole derivatives display a wide range of biological activities such as cardiotonic, fungicidal, sedative, anesthetic, bactericidal and anti-inflammatory. The synthesis of thiazole derivatives is important of their wide range of pharmaceutical and biological properties .A large number of fungicides are Fungicide which is effective only if applied prior to fungal infection is called a protectant; caused infection and thereby ''curing" the plant, is called atherapeutant 8-quinolinol, antibiotics like Aureofungin, etc. Eradicants are those which remove pathogenic fungi from an infection court some chemicals do not kill fungi. The IR spectra were recorded on IR affinity-1, DRS-8000A, Shimadzu, Ptc. Ltd., Japan spectrophotometer. The 1H-NMR was recorded in DMSO on Bruker Advance II 400 MHz spectrometer using TMS as an internal standard. Melting points were determined in open capillary tubes and are uncorrected. The purity of the compounds was checked by TLC-using Silica gel-G (Merck). Column chromatography was performed on silica gel.

[i]Synthesis of 2-Amino -4- Phenyl Thiazole

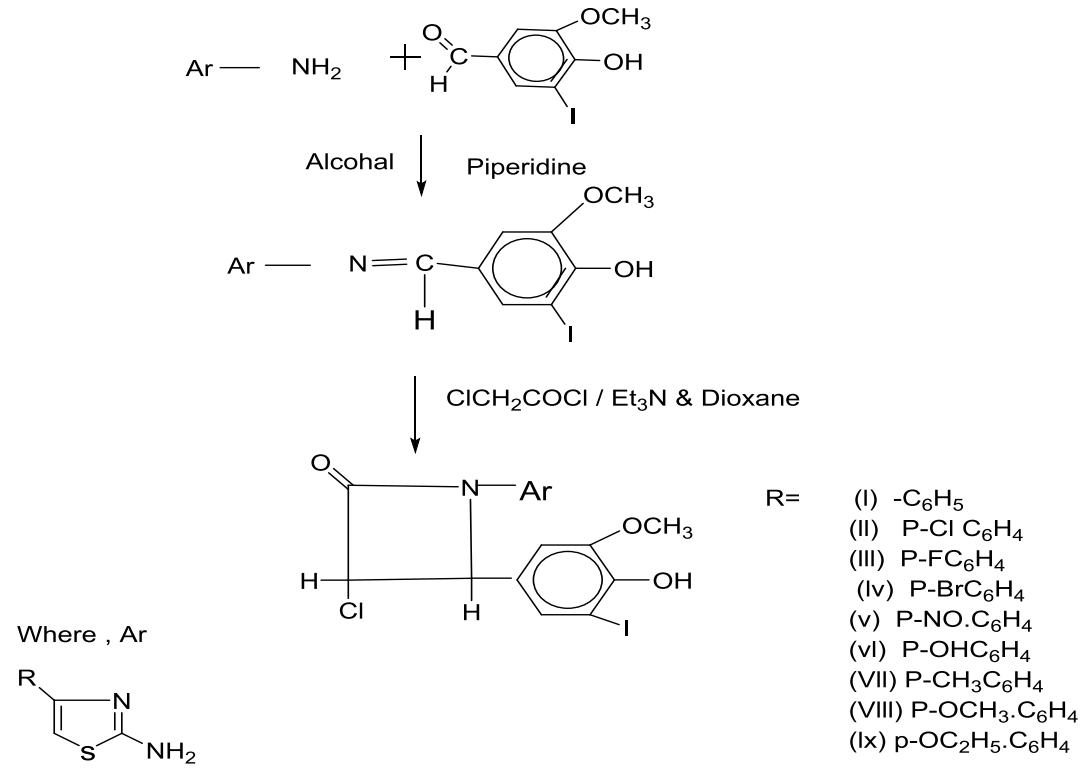
A mixture of acetophenone (12.0 gm , 0.1 mol.) thiourea 15.2 gm.0.2 mol.) and iodine25.4 gm.0.1 mol) was heated for 10 hrs on a steam ath . The crude reaction mixture are cooled and repeatedly extracted with ether to remove unreacted acetophenone and iodine. The reduse was then dissolved in hot water & filtered to remove sulphur and other impurities. The solution was then moderately cooled and madealkaline with concentrate ammonia.2-amino-4-phenyl thiazole, thus precipitated was collected and re-crystallised from dilute ethanol as long colourless , Yeld :65 5 , M.p: 149^{0}C% of N and S Calculated 16.27 % and 37.20% ,% of N and S found 16.20 and 36.20%16.27 % and 37.20% . The compound have been characterized on the basis of I.R spectra and the purify of the compound was checked by T.L.C.

[ii] Synthesis of N-(4-Phenyl-2-thiazolyl)-2-imino-(3-iodo-4'-Hydroxy-5'-methoxy benzalimine)

A mixture of 2-Amino-4-phenyl thiazole (0.01 mol) and vanillin 0.01 moles in ethanol 30 ml and piperidine 3-4 drops was refluxed on water bath for 1 hours. The reaction mixture was cooled and the sol separated was filtered and recrystallised from ethanol. Yield: (92%), m.p. 160^{0}C , IR(KBr) = 1210-1220 cm- 1 (due toC-O-c). Eradicants are those which remove pathogenic fungi from an infection court some chemicals do not kill fungi. The IR spectra were recorded on IR affinity-1, DRS-8000A, Shimadzu, Ptc. Ltd., Japan spectrophotometer. The 1H-NMR was recorded in DMSO on Bruker Advance II 400 MHz spectrometer using TMS as an internal standard. Melting points were determined in open capillary tubes and are uncorrected.The purity of the compounds was checked by TLC-using Silica gel-G (Merck). Column chromatography was performed on silica gel. All the compounds were tested for thei, 1665-1670 cm-1 ,(C=N) , 1590 -1595 cm-1 (C=C), 3000-3110 cm-1 (due to -OH) ,1640-1625 cm-1 and 1250 cm-1 (due to C=N and C-N) , PMR = δ 4.0-4.2(3H,s.OCH3) , δ 7.1-7.6(8H, m, ArH) , δ 8.2-8.5(1H,s =CH), δ 9.5-.9.7(1H, s,-OH) Similarly, various N-[4-(P-subst/un-subst)-Phenyl-2- thiazolyl]-2-imino(3-iodo-4'-Hydroxy-3'-methoxy benzylidine were prepared byusing similar reaction procedure and their analytical data are incorporated in the table (l) respectively.

[III]Synthesis of [l]N-(4-Phenyl-2-thiazolyl)-2-imino-(3-iodo-4'-Hydroxy-5'-methoxy benzalimine) :

To a mixture of compound first (0.01 moles) andmercaptoacetic acid 0.001 mole) dissolved in dioxane (20ml) apinch of anhydrous zinc chloride was added and the mixture was refluxed for eight hours on cooling the separated solid was washed with dilute sodium bicarbonate was crystallized from ethanol .Yield 47 , M.P 148^{0}c IR(KBr) = 3100 cm-1 (due to OH) , 1640-1625 cm-^{1} AND 1250 ,(C=N) , 1590 - 1595 cm^{-1} (C=C) , 3000-3110 cm-1 (due to -OH) , 1640-1625 cm^{-1} and 1250 cm^{-1} (due to C=N and C-N) , 1210-1220 CM^{-1}(due to C-O-C) , 1660-1670 cm^{-1} (due to C-S-C) 1685 cm^{-1} (due to cyclic > c=o), PMR = δ 3.82-3.86(3H,s.OCH_3) , δ 9.85(1H, s,OHm) , δ 4.15-(2H,s CH_2S) , δ6.5-6.8(1H, s,-CH), δ6.5-7.4(8H, M,-Ar-H) , Similarly , various N-[4-(P-subst/un-subst)-Phenyl-2-thiazolyl]-2-imino-(-3'-iodo4'-Hydroxy-3'-methoxyphenyl)-4´´thiazlidone were prepared by using similar reaction procedure and their analytical data are incorporated in the table(ll)respectivily.



2-Amino-4-(P-subst / Un-subst)-phenyl thiazole

Table_I : Analytical data of N-[4-(P-subst/un-subst)-Phenyl-2-thiazolyl] -2-imino-(-3-iodo-4'-Hydroxy-3'-methoxy benzylidine

S. N.	Nature of Ar	Molecular Formula	Yield %	M.P. °C	ELEMENTAL ANALYSIS			
					% of N		% of S	
					Cald	Fond	Cald	Found
Ia	2-Amino-4-phenyl thiazole	$C_{17}H_{13}N_2O_2Sl$	42	138	9.03	09.00.	10.32	10.25
Ib	2-Amino-4(p-chloro)-phenyl thiazole	$C_{17}H_{12}N_2O_2ClSl$	50	140	19.92	19.86	22.77	22.69
Ic	2-Amino-4(p-fluoro)-phenyl thiazole	$C_{17}H_{12}N_2O_4SFl$	52	145	08.53	08.50	09.75	09.70
Id	2-Amino-4(p-bromo)-phenyl thiazole	$C_{17}H_{12}N_2O_4SBrl$	48	106	07.21	07.11	08.24	08.20
Ie	2-Amino-4(p-nitro)-phenyl thiazole	$C_{17}H_{12}N_3O_4Sl$	47	148	11.83	11.76	09.01	08.93
If	2-Amino-4(p-hydroxy)-phenyl thiazole	$C_{18}H_{15}N_2O_3Sl$	48	165	08.53	08.49	09.75	09.73
Ig	2-Amino-4(p-methyl)-phenyl thiazole	$C_{20}H_{16Cl}N_2O_3Sl$	52	226	08.64	08.60	09.87	09.80
Ih	2-Amino-4(p-methoxy)-phenyl thiazole	$C_{17}H_{13}N_2O_2Sl$	53	246	08.23	08.20	09.41	09.35
Ii	2-Amino-4(p-ethoxy)-phenyl thiazole	$C_{20}H_{16}N_2O_3Sl$	50	250	07.90	07.80	09.03	09.00

Table-II
Analytical Data of N-[4-(P-Subs/Un-Subst)Phenyl-2-Thiazolyl]-3¯Chloro-4-[3'-Iodo4'-Hydroxy-5-Methoxy)-2'-Aazetidinone

S. No.	Nature of Ar	Molecular Formula	Yield %	M.P. °C	Elemental Analysis			
					% of N		% of S	
					Cald	Fond	Cald	Found
IIa	2-Amino-4-phenyl thiazole	$C_{19}H_{13}N_2O_3ClI$	52	179	07.09	07.05	16.24	16.22
IIb	2-Amino-4(p-chloro)-phenyl thiazole	$C_{19}H_{12}N_2O_3SCl_2I$	53	190	06.50	06.45	14.93	14.90
IIc	2-Amino-4(p-fluoro)-phenyl thiazole	$C_{19}H_{12}N_2O_3SFClI$	50	185	06.54	06.50	15.05	15.00
IId	2-Amino-4(p-bromo)-phenyl thiazole	$C_{19}H_{12}N_2O_3S_2BrClI$	42	186	05.93	05.88	13.55	13.52
IIe	2-Amino-4(p-nitro)-phenyl thiazole	C19H12N3O5SClI	50	225	09.56	09.49	14.97	14.55
IIf	2-Amino-4(p-hydroxy)-phenyl thiazole	$C_{20}H_{14}N_2O_4S_2$	42	148	06.82	06.78	15.60	15.55
IIg	2-Amino-4(p-methyl)-phenyl thiazole	C2oH15N2O4ClI	51	144	06.86	06.81	15.68	15.60
IIh	2-Amino-4(p-methoxy)-phenyl thiazole	$C_{20}H_{15}N_2O_4ClI$	50	141	06.60	06.55	15.09	14.55
IIi	2-Amino-4(p-ethoxy)-phenyl thiazole	$C_{21}H_{17}N_2O_4SCl L$	54	145	06.39	06.20	14.61	14.02

Antifungal Screening

The newly synthesized compounds were evaluated against *Fusarium solani* fungus at optimum temperature of 28± 1oC (after 7 days incubation) was observed . After inoculation , All the petridishes were incubated at (25 ± 20C) for 7 days , the efficiency of varios ant-fungal was recorded by measuring the radial growth of the fungal colony(in mm). The percentage inhibition of fungus mycelia growth was calculated by the equation

$$\% \text{ of Inhibition} = \frac{[(C- T) \times 100]}{C}$$

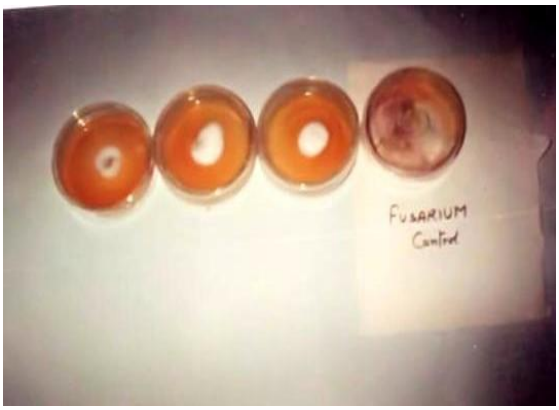
Where C and T are average colony diameters (in mm) of the fungal colony in control © and treated (T) plates respectively and their Antifungal screening data are incorporated in the table(lll) data are incorporated in the table(lll) respectively.

Table (lll)
Effect of Some Newly Synthesised Antifungal Compounds against *Alternaria alternata* at optimum temperature (After 7 days incubation)

Compound	Dose	Average colony diameter (in mm) in PDA medium	% Inhibition
Control		**60.88**	
Ia	0.20	2.8	95.39
Ib	0.20	3.2	94.73
Ic	0.20	4.0	93.42
Id	0.20	1.9	96.87
Ie	0.20	2.7	95.55
If	0.20	2.8	95.39
Ig	0.20	9.9	83.71
Ih	0.20	3.0	95.06
Ii	0.20	3.2	94.73
IIa	0.20	3.1	94.90
IIb	0.20	2.7	95.55
IIc	0.20	4.1	93.25
IId	0.20	3.5	94.24
IIe	0.20	3.2	94.73
IIf	0.20	2.8	95.39
IIg	0.20	2.4	96.05
IIh	0.20	1.7	97.20
IIi	0.20	2.8	95.39
BAVISTIN (Std drug)	0.20	0.22	99.65

Results And Discussions

In the present section thediscussions have made regarding the method used for determing the antifungal activity and the pharmalogical screening result of various compounds synthesized are given in the present investigation. A few azetidinones was evaluated for fungicidal activity by food and poison and *Fusarium solani* fungas is taken. effect of newly synthesized anti-fungal compounds against *Fusarium solani f*ungasat optimum temperature of 28±1^{0}with substitution p-Chloro (compound-1 &-6 shown good antibacterial activity against Bavistin(Std drug), in the range of 125-250 µg/ml. While rest of all derivatives are poor against *Fusarium solani*



Conclusion

It is evident from fungal screening data that all the newly synthesized compound tested were found satisfactorially superior over control but inferior to that of standard antifungal (Bavistin) compound mostly synthesized compound showed marked of the fungal growth in vitro test . It can also be concluded from the result that mostly synthesized compound are good antifungal and showed significant level of antifungal activity and .compound No(lg) showed moderate activity.

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