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Biological activity of newly synthesized substituted Dihydropyrimidinone and Thione

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Abstract: The screening of newly synthesized compounds through condensation of ethylacetoacetate, Urea/thiourea and different aldehyde was carried for the antifungal activity against two fungal species i.e. A. niger and C. albicans. The comparison shows that all the synthesized compounds are significantly active. Out of which thione compounds showed more activity than pyrimidinone compounds
Keywords: - Pyrimidinones, thiones, biological activity, standard drug.

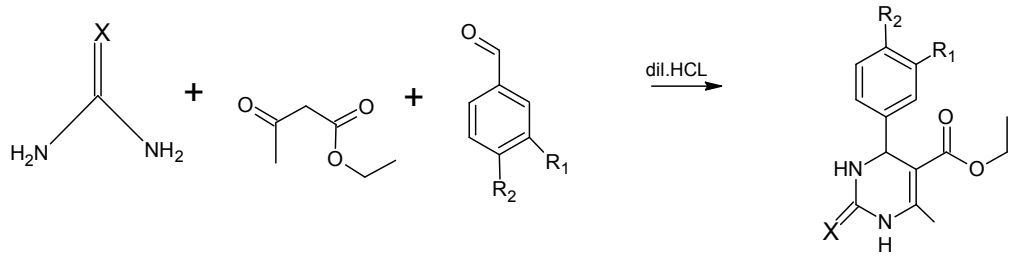
Introduction

Nitrogen heterocycles are of special interest as they constitute an important class of natural and non-natural products, many of which exhibit useful biological activities[1]. In Nitrogen containing heterocyclic compounds dihydropyrimidinone and their sulphur analogue have been reported to possess diverse range of pharmacological activity[2] such as anticancer,anti HIV,antibacterial,antimalarial,antihypertensive,sedative,hypnotics,anticonvulsant, antithyroid,antihistaminic agents and antibiotics[3-8].They are mostly used as calcium channel blockers[9-11] alpha-antagonista[12] and neuropeptide-antagonists. Alkaloids containing the dihydro pyrimidine structure have been isolated from various marine source which have been shown some interesting biological properties[13] Most important among these alkaloids was batzelladine, which was found to be potent HIV-gp-120-CD_4 inhibitors[14-15]. Because of these efficient applications of the above compound our interest in synthesis of Dihydropyrimidinone and their thioanalogue is increasing tremendously and we have synthesized earlier a series[Ref.-16] of dihydropyrimidinone/thione by three component condensation of Urea/thiourea, ethylacetoacetate and substituted aldehydes. These compounds have been screened for their antifungal activity against A. niger and C. albicans.

Experimental

The chemicals used for the synthesis were of analytical grade (BDH, E.Merck and Spectrochem.) and were used as received. The solvents were used after double distillation. All the analyses were carried out at RSIC, CDRI, Lucknow.

These compounds were prepared by refluxing a mixture of urea/thiourea and substituted aldehyde in equimolar ratio with slightly higher ratio of acetoacetic ester and catalytic amount of acid was refluxed for required period of time. After the completion of reaction the reaction mixture was kept in refrigerator overnight. The solid separated out was filtered, washed with suitable solvent and crystallized by appropriate solvent or solvent system. The filtrate was again refluxed for few hours to check further precipitation. These compounds were characterized by MPs, elemental analysis and spectral studies (IR, ^1H &^{13}C NMR.



Comp. No.	X	R1	R2
1, 8	O, S	H	H
2, 9	O, S	H	Me
3, 10	O, S	H	OMe
4, 11	O, S	NO_2	H
5, 12	O, S	H	Cl
6, 13	O, S	H	N $(Me)_2$
7, 14	O, S	OMe	OMe

Biological activity

The cultures were obtained from National Chemical Laboratory (NCL), Pune and preserved at 4°C. Subculturing was done once a month to maintain their viability and to check for their purity. . Then the newly synthesized compounds were screened for their antifungal activity by Agar well diffusion method. The funguses employed were *A. niger* and *C. albicans.* The screening results indicated that the tested compounds showed significant activity against both funguses. They were active at very low concentration compared with the standard employed ciclopiroxolamine. The results showed that thiones are more active antifungal compounds than pyrimidinones.

Table 1*

Comp. No.	Conc. (µg/ml)	Radial growth in (mm) A. niger		Radial growth in (mm) C. albicans	
		Pyrimidinones	Thiones	Pyrimidinones	Thiones
1,8	20	11	14	10	12
	40	10	16	12	14
	60	12	17	14	16
2,9	20	-	12	-	10
	40	-	10	-	12
	60	-	-	11	14
3,10	20	10	13	-	-
	40	11	15	10	12
	60	13	16	13	15
4,11	20	12	-	-	10
	40	10	13	10	13
	60	11	14	13	14
5,12	20	10	13	10	11
	40	12	15	12	13
	60	11	13	14	15
6,13	20	-	12	12	14
	40	10	14	13	14
	60	12	16	14	16
7,14	20	-	11	-	-
	40	10	13	10	11
	60	11	14	12	13
Standard Drug		20	20	20	20

Result and Discussion

The reaction between substituted aldehydes, urea/thiourea and ethylacetoacetate in presence of catalytic amount of acid yield the required products in good yield[16].

These newly synthesized compounds were screened for their antifungal activity against the fungi A. niger and C. albicans using agar well diffusion method. The screening results indicates that among the compounds tested ( ) show significant activity against both the microorganism. They were found to be more active at low concentration compared to standard employed for ciclopiroxolamine. It was further noticed that thione products were more active than pyrimidinones.

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