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Special Chalcones and their novel Antimicrobial Activities

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ABSTRACT:

Chalcones have been the center of attraction for researchers from several decades due to nits innumerous therapeutic application, Efforts have been done in my research to synthesized chalcones and their derivatives that further reacts with various substituted aldehyde to give corresponding substituted chalcone derivatives .Now these derivatives on condensation with Guanidine nitrate gives the vast range of phenyl pyrimidine amine Derivatives. Structure elucidation of synthesized compound had been made on the basis of element analysis, 1H NMR Spectra studies. The microbial activity of the synthesized compounds has been studied against the species bacillus subtillis, staphylococcus aureus, Escherichia coli, and salmonella typhi.

Key words: Synthesis, heterocyclic substituted chalcone derivatives, Pyrimidine derivatives, Chalcones

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INTRODUCTION:

Chalcone (1) are the compounds were aromatic substitutes are introduced in to the terminal position of system C═C-C═, So chalcone are characterized by their position of a Ar(A)-CO-CH ═ CH-Ar(B) Structure in which two aromatic ring are linked by an aliphatic three carbon chain (2), thus chalcones are phenyl-styryl ketones containing reactive ketoethylenic group –C-CO═CH- .

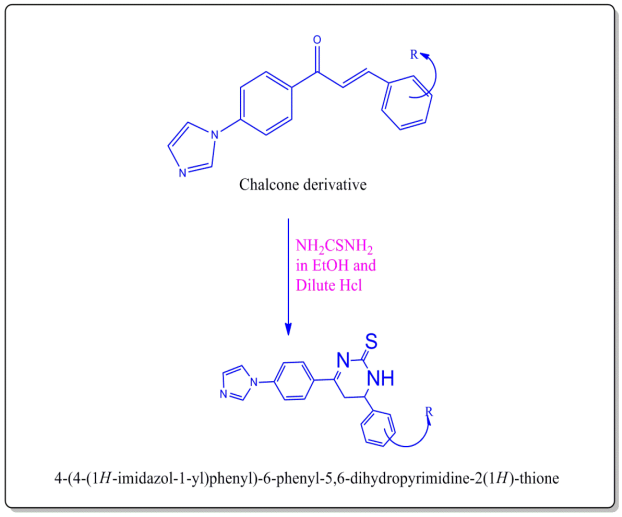
Pyrimidines have chemical and biological importance, as the pyrimidine ring system has associated with the valuable pharmacological activity(3-5). The simple pyrimidine compounds were prepared by the. cyclization of aliphatic raw materials, ..Polysubstituted Pyrimidines compound were synthesized from acyclic compounds in a similar manner to..Chemistry of the benzenoid. The NH2CSNH2 group act as an antithyroid..compound (6-9), with the same actions and uses as thiouracil. Numerous derivative of NH2CSNH2 are valuable in the treatment of leprosy.

Mostly NH2CSNH2 derivatives show cytotoxic activity(10-11) along with antithyroid activity. NH2CSNH2 also shows some..anti-inflammatory, antimicrobial and antifungal activities. The diverse medicinal uses and biological activities of pyrimidine are reported earlier(12-15).

Here a series of thioxo tetrahydro pyrimidine derivatives are synthesized to evaluate their antibacterial and antifungal activities

All effort are done in the research is to synthesized a novel compound that can be used for formulation of anticancer drugs.

REACTION SCHEME

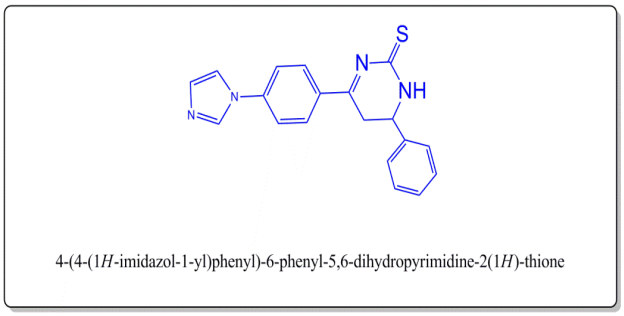


Scheme 1: Chalcone derivative

Where R as : (3a) -H (3b) 4-OCH_3 (3c) 2- OCH_3 (3d) 2-OH (3e) 2-Cl (3f) 4-Cl
(3g) 2-NO_2 (3h) 3-Br (3i) 3,4-$(OCH_3)_2$ (3j) 3,4,5-$(OCH_3)_2$

EXPERIMENTAL:

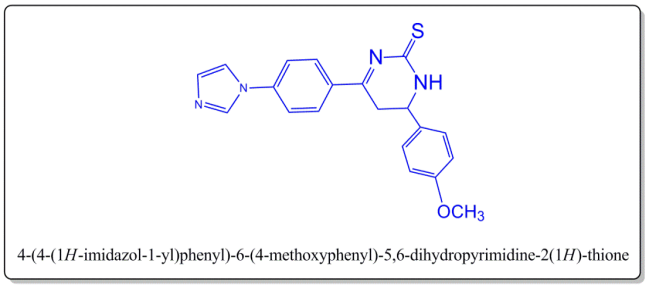
(3a) Synthesis of 4-(4-(1H-imidazol-1-yl)phenyl)-6-phenyl-5,6-dihydropyrimidine-2(1H)-
thione:



Scheme 2: Chalcone derivative

A mixture of (E)-1-(4-(1H-imidazol-1-yl)phenyl)-3-phenylprop-2-en-1-one (0.45 g, 0.002 mol) and NH_2CSNH_2 (0.09gm, 0.002 mol) in the presence of ethyl alcohol (40 ml) and con. HCl (25 ml) was refluxed for 2 hours.. The crude product was filtered when it was hot, let the reaction cooled and neutralized by using KOH. Wash the solid with water and then follow crystallization by solvent.

(3b) 4-(4-(1H-imidazol-1-yl)phenyl)-6-(4-methoxyphenyl)-5,6-dihydropyrimidine-2(1H)-
thione:



Scheme 3: Chalcone derivative

A mixture of (E)-1-(4-(1H-imidazol-1-yl)phenyl)-3-(4-methoxyphenyl)prop-2-en-1-one (0.45 g, 0.002 mol) and NH_2CSNH_2 (0.09gm, 0.002 mol) in the presence of ethyl alcohol (40 ml) and con. HCl (25 ml) was refluxed for 2 hours. .The crude product was filtered when it was hot, let the reaction cooled and neutralized by using KOH. Wash the solid with water and then follow crystallization by solvent.

RESULTS AND DISCUSSIONS

Melting points

All melting points were determined in open capillaries in a liquid paraffin bath and are uncorrected[16]. The IR spectra were recorded with KBr pellets on Perkin - Elmer - 783 spectrophotometer and 1H NMR spectra were recorded on a Varian Geminy 200 MHz spectrophotometer with CDC_{l3} / $DMSOd_6$ as a solvent using tetramethylsilane (T.M.S.) as an internal standard; the chemical shift values are in d ppm. The purity of the compounds was checked by thin layer chromatography (T.L.C.) on silica gel coated glass plates .

Antimicrobial activity

Antimicrobial activity of newly synthesized compounds was studied against gram-positive bacteria *Staphylococcus aureus* and gram-negative bacteria *Escherichia coli* (for antibacterial activity) and against the culture "Candela albicans" (for antifungal activity). The antimicrobial screening was carried out by cup - plate method[17-19] at a concentration of 50 $mg.mL^{-1}$ in solvent D.M.F. The zone of inhibition was measured in mm. The antimicrobial activity of the synthesized compounds was

compared with standard drugs Ampicillin, Penicillin and Tetracycline at the same concentration.

Table 1 Analytical and physical parameters Compound

No.	Code No.	R	Molecular Formula	Molecular Weight (g/m)	Yield (%)	M.P. °C	C %	H %	N %
							Found		
1	3a	H	$C_{19}H_{16}N_4S$	332.11	66	169	68.65	4..85	16.85
2	3b	4-OCH_3	$C_{20}H_{18}N_4OS$	362.12	79	168	64.28	5.03	15.46
3	3c	2-OCH_3	$C_{20}H_{18}N_4OS$	362.12	79	168	64.28	5.03	15.46
4	3d	2-OH	$C_{19}H_{16}N_4OS$	348.42	78	144	65.47	4.63	16.06
5	3e	2-Cl	$C_{19}H_{15}ClN_4S$	366.87	69	110	60.09	4.54	16.17
6	3f	4-Cl	$C_{19}H_{15}ClN_4S$	366.87	69	110	60.09	4.54	16.17
7	3g	2-NO_2	$C_{19}H_{15}N_5O_2S$	377.42	78	162	63.71	4.15	16.26
8	3h	3-Br	$C_{19}H_{15}BrN_4S$	410.02	74	150	61.91	4.98	16.93
9	3i	3,4-$(OCH_3)_2$	$C_{21}H_{20}N_4O_2S$	392.13	65	103	63.04	4.45	15.78
10	3j	3,4,5-$(OCH_3)_2$	$C_{22}H_{22}N_4O_3S$	422.14	73	161	64.02	5.13	15.69

ANTIBACTERIAL ACTIVITY

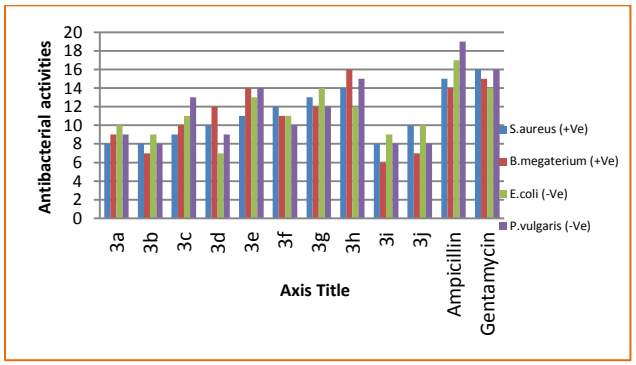
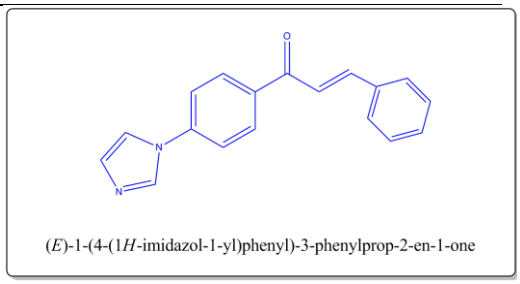


Figure 1: MIC chart of compound

Results: (Comparison of Thioxo Tetrahydro Pyrimidine Derivatives against standard Drugs)

Organisms	Compounds	Ampicillin	Gentamycin
S.aureus	3-Br	✓	-
B. megaterium	4-Cl and 2-Cl	✓	✓
E.coli	2-OH	-	✓
P. vulgaris	3-Br	-	✓

Compound code: 3a	 (*E*)-1-(4-(1*H*-imidazol-1-yl)phenyl)-3-phenylprop-2-en-1-one
Molecular formula: $C_{19}H_{16}N_4S$	
^{1}H NMR (400 MHz, $CDCl_3$) δ ppm:	1.66-1.91 (2H, dd), 2.34 (3H, s), 4.9 (1H, s), 6.86-7.40 (17H, Ar-H, m), 8 (1H, s).
^{13}C NMR (100 MHz, $CDCl_3$) δ ppm:	20.5, 39.2, 52.6, 117.5, 118.8, 120.9, 121.2, 127.5, 128.1, 129.3, 130.1, 131.4, 131.9, 143.6, 151.8, 153.6, 155.1, 151.8, 162.6
IR cm-1 (KBr):	3545, 3049, 1644, 1614, 1592, 1569, 744
Mass (M+1):	332.11

IR Spectral Studies

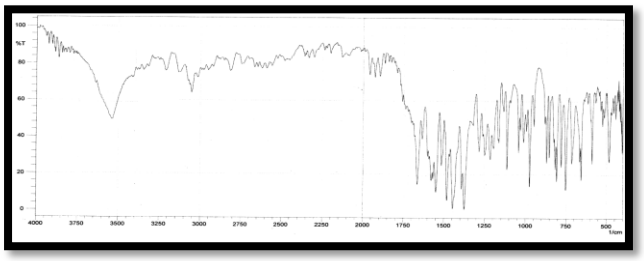


Figure 2: IR Spectra of 3a

^{1}H NMR Spectral Studies:

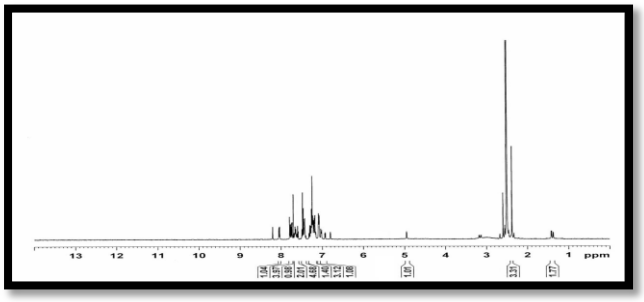


Figure 3: ^{1}H NMR Spectra of 3a

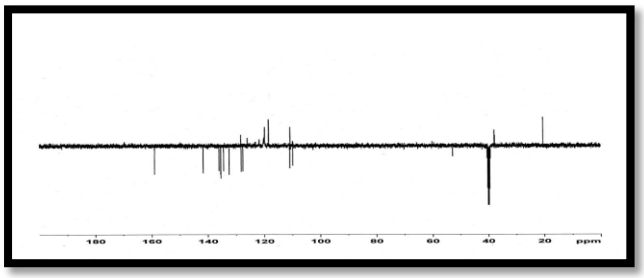


Figure 4: ^{13}C NMR of compound 3a

CONCLUSION

The screening results revealed that the compounds (i) showed significant antimicrobial activity. In particular compounds (h) and (j) showed moderate to considerable antibacterial and antifungal activities against all the organisms employed at a conc. of 1000 _g/mL (0.1ml dose level) Comparable to that of standard drugs Ampicillin and Gentamycin.

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