Special Chalcones and their novel Antimicrobial Activities

Arpita Desai1*, K.B. Vyas2, Rajiv A. Shah3, Rajarshi N. Patel3 and K.S.Nimavat4

1 Pacific Academy of Higher Education and Research University Udaipur, Rajasthan, India
2 Department of Chemistry, Sheth .L.H. Science Collage, Mansa Gujarat, India
3 Department of Chemistry, APMS, Anand, Gujarat, India.
4 Department of Chemistry, Government Science Collage– Gandhinagar., Gujarat, India

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

INTRODUCTION:

Chalcone (1) are the compounds were aromatic substitutes are introduced in to the terminal position of system C==C==, So chalcone are characterized by their position of a Ar(A)-CO-CH = CH-Ar(8) 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 pyrimidene 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 synthesize a novel compound that can be used for formulation of anticancer drugs.

**REACTION SCHEME**

**Scheme 1: Chalcone derivative**

Where R as :
- (3a) -H
- (3b) -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$_3$)$_2$

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

**Scheme 2: Chalcone derivative**

A mixture of (E)$-1$-$(4$-$(1$H-imidazol-$1$-yl)phenyl)$-3$-phenylprop-$2$-en-$1$-one (0.45 g, 0.002 mol) and NH$_2$CSNH$_2$ (0.09 gm, 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) $4$-$(4$-$(1$H-imidazol-$1$-yl)phenyl)-6-$(4$-methoxyphenyl)-5,6-dihydropyrimidine-2(1H)-thione:

**Scheme 3: Chalcone derivative**

A mixture of (E)$-1$-$(4$-$(1$H-imidazol-$1$-yl)phenyl)$-3$-$(4$-methoxyphenyl)prop-$2$-en-$1$-one (0.45 g, 0.002 mol) and NH$_2$CSNH$_2$ (0.09 gm, 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$_3$ / 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

<table>
<thead>
<tr>
<th>No.</th>
<th>Code No.</th>
<th>R</th>
<th>Molecular Formula</th>
<th>Molecular Weight (g/m)</th>
<th>Yield (%)</th>
<th>M.P. °C</th>
<th>C %</th>
<th>H %</th>
<th>N %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3a</td>
<td>H</td>
<td>C_{19}H_{16}N_{4}S</td>
<td>332.11</td>
<td>66</td>
<td>169</td>
<td>68.65</td>
<td>4.85</td>
<td>16.85</td>
</tr>
</tbody>
</table>

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 | - | ✓ |

**Compoun d code:** 3a  
**Molecular formula:** C_{19}H_{16}N_{4}S  

**1H 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).  

**13C 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 ppm.  

**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: ^1^3^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.

ACKNOWLEDGEMENTS

The authors are thankful to Dr. Rajarshi N. Patel for providing research facilities. They are also grateful to and the Department of Biosciences, Sardar Patel University, Vallabh Vidyanagar, for screening the newly synthesized compounds for their antimicrobial activities, for scanning the IR spectra and 1H NMR spectra of newly synthesized compounds.

REFERENCES

11. Patel. RN, Patel PV, Patel DS, Vyas KB, Synthesis of 2-methyl-5-nitro-n-(4-(3-(3-phenylquinoxalin-2-yl) methyl) phenoxy) phenyl


19. Patel RB, Patel RN, Patel KS, Desai AP Chemical Study of Ground Water Taken From Highly Polluted Pond (Goya Talav) of Anand District (Gujarat), *Journal Club for Applied Sciences (JCAS), 2015*, 2, 5-10