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Synthesis and biological evaluation of newly synthesized Flavones

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Abstract: **- Flavones are bioactive substances, essential for human growth and development. It is naturally available in cereals and herbs. It is synthesized in excellent yield by Baker-Venkataraman reaction for formation of 1, 3-diketone by using substituted acetophenone and benzoyl chloride in presence of dry pyridine. The structures of newly synthesized compounds have been confirmed on the basis of elemental analysis, UV, IR, H-NMR spectral data and evaluated for biocidal activity on the basis of inhibition of growth of bacteria and fungus compared with a standard drug.**

Index Terms: 4-chlorophenol, flavones, conventional method, Biocidal activity.

INTRODUCTION

In general large group of compounds constitutes Flavones as natual products which is used for human growth and development. Flavones and their derivatives which are newly synthesized has attracted considerable attention due to their significant biocidal[1-3], pharmaceutical[4-7], anti-oxidant[8-11], anti-anxiolytic[12], anti-cancer[13] and anti-inflammatory effects. Due to which major research area is going on flavones derivatives and their biological activity is been studied. This paper reports the synthesis of 7-chloro flavones from their corresponding diketones and its characterization by elemental analysis,UV,IR,H1NMR spectroscopic techniques is done.The synthesized flavones derivatives are been tested for antimicrobial and antifungal activity against various bacterial and fungal strains viz.,E.Coli, S.aureus, A.niger, F.oxysporium. The present study was carried out to investigate the biocidal properties of the above flavones and diketones with the view of adding new and potent antimicrobial agent used against resistant organisms as well as other highly infectious lethal diseases.

MATERIAL AND METHODS

This paper represents synthesis and biocidal activity of newly synthesized flavones derivative viz., 7-chloro flavones. In this synthesis chemicals and reagents analytical grade of Sigma-Aldrich Corporation, Richman Chemical Inc., Merck and Alfa Aesar Company Ltd. The synthesized substituted 7-chloro flavone characterized by elemental analysis, UV characterized from Lab India 3000+ spectrophotometer, IR spectra characterized from Cary 60-FTIR (Agilent Technologies), ^{1}H-NMR spectral data characterized from Bruker Avance II 400-MHz NMR Spectrometer using $CDCl_3$ as a solvent and TMS as an internal standard, and evaluated for their biocidal activities for the inhibition of growth of bacteria and fungus. The purity of all the compounds was checked by thin layer chromatography and were recrystallised from hot ethanol. The melting points were measured by open capillary method and they are uncorrected.

PROCEDURE

Firstly 3-chloro phenol was refluxed with acetic anhydride in presence of dry sodium acetate for 1.5 hr and then it was allowed to cool followed by decomposition in water separated and lower layer by means of separating funnel and further distilled . The resultant product undergone through Fries rearrangement with anhydrous $AlCl_3$ then decomposed in 10% ice cold Hcl,which was filtered and crystallised using glacial acetic acid. The prepared substituted acetophenone shaken with benzoyl chloride and dry pyridine for 18-20 minutes. The reaction mixture which becomes warm and poured over crushed ice with HCl (1M). The separated product is filtered, washed with ice-cold methanol and then water. The resultant product obtained is 2-benzoyloxy 6-chloro acetophenone which is heated with KOH (powder form) and pyridine at 50^0C for 15 minutes and acidified with 10% glacial acetic acid resulting in the formation of substituted diketone viz.,1-(6'-chloro-2'-hydroxy phenyl)3-phenyl propan-1,3-dione (Baker-Venkataraman rearrangement)[10-11] product. Further addition of conc. H_2SO_4 with continuous stirring in glacial acetic acid. The reaction mixture is allowed to be heated on a water bath for 1hr followed with occational stirring and poured over crushed ice. The separated flavones are washed with water and stirred at 50^0C and crystallized from petroleum ether.
The reaction scheme for substituted flavone synthesis is-(figure-1)

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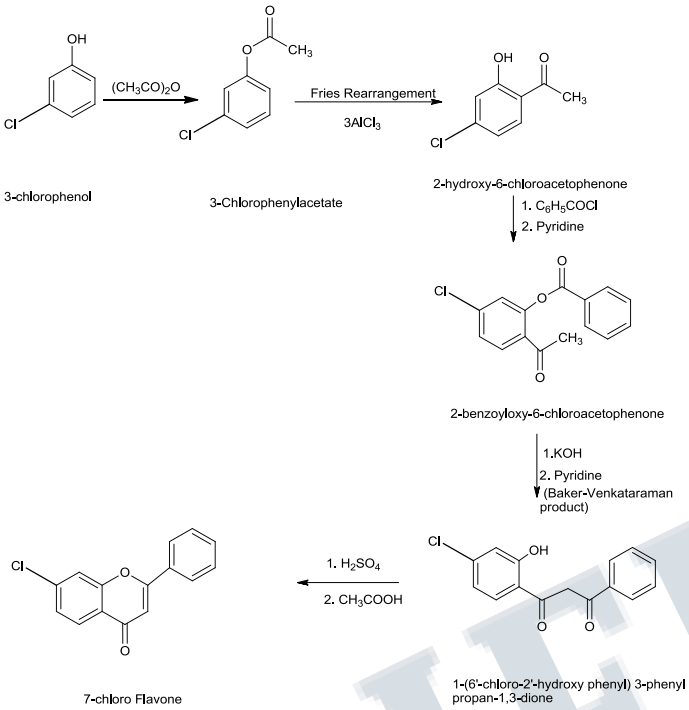
Figure - 1



BIOCIDAL ACTIVITY

The synthesized substituted 7-chloro flavone derivative is been tested for their biocidal activities on the basis of their potential to inhibit the growth of bacteria and fungus like *Escherichia coli, Staphylococcus aureus, Aspergillus niger, Fusarium oxysporum* by using agar well diffusion method. The preparation of petridish for anti-bacterial and anti-fungal activities as follows-

The Petridish for inoculation of organism were sterilized.

1) Upto 5 mm wells were formed by cork bearer.
2) The compound dissolved in DMSO and form solution of conc. 1mg/ml.
3) Inoculated it in wells.
4) The particulate get dry, sealed and petriplates placed in incubation chamber for 3-4 days at 370C and diameters of zones of inhibition measured in millimeter.
5) Compare the potential of synthesized substituted flavone with standard Streptomycin.

RESULTS AND DISCUSSION

The data of synthesized substituted 7-chloro flavone compound (i.e. compounds name, molecular formula, molecular weights and melting point) given in table-1. U.V., FTIR and H^1-NMR spectroscopic data illustrated in table 2, 3 and 4 resp., and spectra shows in figure 2, 3 and 4 resp. The result for potential of biocidal activity of synthesized substituted flavones over different pathogens and comparison against standard streptomycin at 500mcg/disc illustrated in table 5-8.

Table-1

Compounds name, molecular formulae, molecular weights and melting points of synthesized substituted flavone.

Name of synthesized substituted Compound	Molecular Formula	Molecular Weight	Melting point
7-Chloro Flavone	$C_{15}H_9O_2Cl$	256.5***gm/mol***	98^0C

Table-2

UV interpretation of compound as follows-

The molecular extinction coefficient was found to be more than 200 shows extended conjugation.

Calculated Lambda max value
(Via Woodward-Fisher Rule) : 354nm

Observed Lambda max value
(Via Spectrophotometer) : 367 nm

Table-3

The IR spectrum important peaks as under.

Literature Value (cm^{-1})	Absorption observed (cm^{-1})	Assignment
785-540	769.96	C-Cl stretching
1300-1000	1164.59	C-O linkage
1600-1475	1565.03	C=C Aromatic
1725-1705	1685.66	C=O stretching
3100-3000	3081.05	C-H Alkene stretching
3150-3050	3081.05	C-H Aromatic stretching

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Table-4

The ^{1}H-NMR spectrum important shifts as under.

Peak observed (∂ value in ppm)	Multiplicity	No of protons	Assignment
6.89	s	1H	Ar-H
7.26	s	5H	Ar-H
7.3-7.4	m	1H	Ar-Ph
7.9-8.2	s	2H	Ar-H

Table -5

Anti-bacterial activities at 500mcg/disc

Name of Bacteria	Std. Streptomycin	Substituted Flavone
E.coli	20mm	12mm
S.aureus	26mm	11mm

Table-6

Anti-fungal activities 500mcg/disc

Name of Fungus	Std. Streptomycin	Substituted Flavone
A.niger	No Effect	No Effect
F.oxysporum	Minimum growth	Minimum growth

Zone Of Inhibition of E.Coli by Synthesized Compound and Comparison against Std. Streptomycin-

Std. Streptomycin

Substituted 6-chloro flavones

Std. Streptomycin on E.coil shows zone of inhibition 20mm at 25mcg/disc and 500mcg/disc, synthesized flavone shows 9mm and 12mm at 25mcg/disc and 500mcg/disc resp.

Zone Of Inhibition of A.Niger by Synthesized Compound and Comparison against Std. Streptomycin-

Std. Streptomycin

Substituted 6-chloro flavone

Std. Streptomycin on A.niger not shows zone of inhibition at 25mcg/disc and 500mcg/disc, synthesized flavone also not shows any effect

CONCLUSION

The current investigation proves that, the laboratory synthesized newly substituted 7-chloro flavones derivative inhibits both anti-bacterial as well as anti-fungal activities but shows more activity against bacteria as compare to fungus. As the concentration increases, its activity also increases against the bacteria , whereas no effect over fungal strain used.

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