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Synthesis and Antimicrobial activity of Some Chalcone Derivatives.

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ABSTRACT

Para hydroxyacetophenones react with different aldehydes of Para nitro benzaldehyde (Ia) ,Ortho nitro benzaldehyde (Ib),4 hydroxy 3methoxy benzaldehyde (Ic) , 3, 4 dimethoxybenzaldehyde (Id) in the presence of aqueous solution of potassium hydroxide and ethanol at room temperature to form 1,3 Diaryl-2-propane-1-ones or chalcones. The synthesized compounds were characterized by means of their IR spectral data. All the compounds were tested for their antibacterial activities by the cup plate method *on E.coli ,Pseudomonasaeurgenosa, staphylococcus aeureous* .Screening results shows that Id compound shows better *antimicrobial activity against E.coli*

Keywords : Anti microbial agent, chalcone, synthesis.

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INTRODUCTION

Survival of the fittest is the basis for life and for the human beings also. The biggest threats for human beings are the various diseases and scientists and doctors are still fighting to find solutions with various forms of medications. Today's developed medicines are results of relentless effort made by human civilization time to time. When the era of synthetic drugs began, it opened thousand doors for the development of various synthetic molecules with potential action[1].

MICROBES:

Microbes are single celled organisms. Too small to be seen with the naked eye. They are found practically everywhere on earth. Also commonly known as bugs, germs and microbes. Generally divided into 3 different groups

- Bacteria
- Virus
- Fungi

Microbes are invisible to unaided eye, definitive knowledge about the them had to await development of microscope. Many microscopic microbes occur as single cell, other are multicellular still other such as viruses, do not have true cellular appearance .Some organisms called anaerobes are capable of carrying out vital function in absence of free oxygen, where as other organisms can be manufacture essential compounds for their physiological needs from atmospheric source of nitrogen, carbondioxide.

Other microbes like viruses and bacteria are totally dependent for their existence on cell of higher forms of life. Branch of science called microbiology embraces all of these properties of microbes and many more.

Fungi are the largest and most versatile of all microbes. Large plant like structures which lack chlorophyll need to absorb nutrients from whatever they are growing on. Fungi can be very helpful and humans have used them in .The food industry - brewing beer, making bread rise. They can also be harmful if they steal nutrients from another living organism. Examples include, mould on bread and athletes foot which is caused by a group of fungi known as dermatophytes. Fungi can be found in the air, on plants and in water[2].

Chalcones either natural or synthetic are known to exhibit various biological activities. They have been reported to possess antioxidant, antimalarial, antileishmanial, antiinflammatory, antitumor and antimicrobial activity[3].

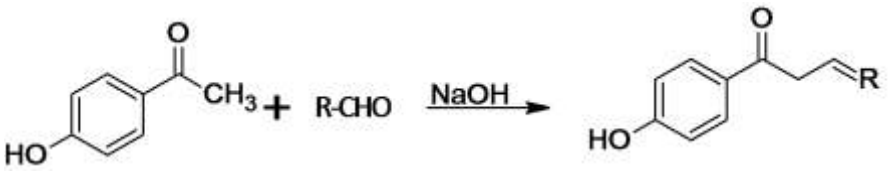
Chalcones or 1,3 Di-aryl-2-propane-1-ones are compounds belonging to the flavonoid family lacking of heterocyclic C ring. Chalcones are readily synthesised by condensation of base catalyzedclaizen Schmidt condensation of an aldehyde and an appropriate ketone in polar solvent like methanol. This method is versatile, convenient although yields may be variable. Chalcone and its derivatives have attracted particular interest during the last few decades due to the use of such ring same as the core structure on many substances covering wide range of antimicrobial application.

Therefore it is worthwhile to synthesize and investigate the compounds of chalcone derivatives for newer antimicrobial agents. The present work deals with the reaction of P-hyroxyacetophenone with different aromatic aldehydes to form chalcones and the compounds were screened for their antimicrobial activity[4].

MATERIALS AND METHIOD

Chemistry:

General Procedure For Chalcone Preparation:



(I_a-I_d)

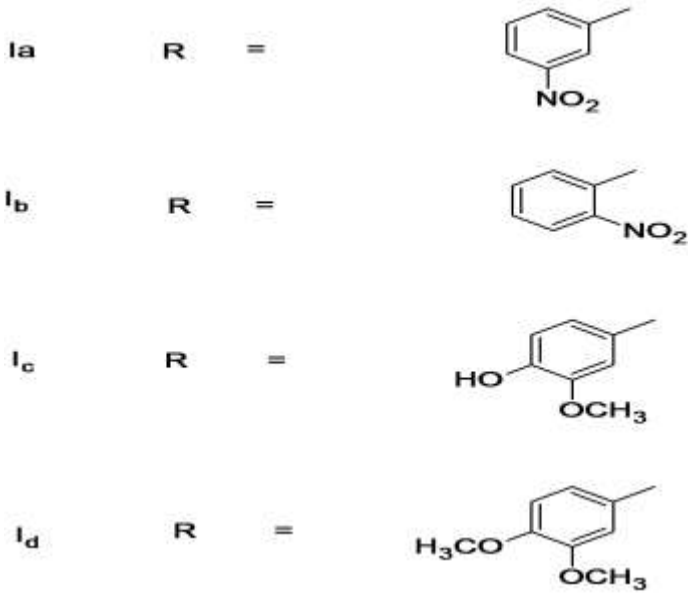


Figure 1. Synthetic pathway of Chalcones

Compounds Ia to Id were obtained by reactions of appropriate acetophenone (0.01M) and benzaldehyde (0.01M) in presence of 10% NaOH and ethanol and the following procedure was

adapted to synthesize individual compounds. The mixture was stirred for 2 hrs until entire mixture become very cloud. Then the mixture was poured slowly in to 400ml of water with constant stirring and kept in refrigerator for 24 hrs. The products obtained were filtered, washed and recrystallized from ethanol. The reaction was manipulated by TLC (Benzene: Ethyl acetate)[5].

Melting points were determined with Lab line melting point (Science house, Chennai) apparatus and are uncorrected[6]. Infra-Red spectra were recorded on a Shimadzu 8400-s spectrophotometer using KBr pellets.**IR (Cm-1, KBr)** :Ia –886 (C-H) 1976.14 (C =C) 3328 (O-H)Ib -843.88 (C-H) 1985.78 (C =C) 3369.75 (O-H)Ic – 1767 (C=O) 629.78(C-H) 1666.55 (C=C) Id - 1720 (C=O) 630 (C-H) 1694 (C=C)[7]. The reactions were monitored by thin layer chromatography (TLC) using silica gel-G (benzene: ethylacetate, 9:1)[8].

Antimicrobial activity:

Cup plate method using Mueller-Hinton agar medium was employed to study the preliminary antibacterial activity of **(I_a-I_d)** against *E.coli*. and*S.aureus.* The agar medium was purchased from HI media Laboratories Ltd., Mumbai, India. Preparation of nutrient broth, subculture, base layer medium, agar medium and peptone water was done as per the standard procedure. Each test compound (5 mg) was dissolved in 5 mL of dimethyl formamide (1000 µg/mL). Concentration of 50µg and 100µg of each compound were used for testing.

The cups each of 9mm diameter were made by scooping out medium with a sterilized cork borer in a Petri dish which was streaked with the organisms. The solutions of each test compound (50µg and 100µg) were added separately in the cups and petri dishes were subsequently incubated. Penicillin and Streptomycin were used as standard reference drugs (200 & 500 µg/mL respectively) and dimethyl formamide as a control which did not reveal any inhibition. Zone of inhibition produced by each compound was measured in mm and the results are presented in Table 2[2,9,11].

RESULTS AND DISCUSSION

Chemistry:

The scheme Figure 1 shows the general synthesis procedure employed for the chalcone derivatives. The compounds were generally obtained in good yields (50-60%). The compounds have low solubility in common solvents. All the synthesized compounds were characterized by TLC, melting point and IR and the results were shown in Table 1.

Antimicrobial activity:

All these chalcones were screened for their antimicrobial activities against *E.coli* and *S.aureus* by cup plate method using Penicillin and Streptomycin antibiotics for comparison of activity. Compounds were dissolved in 5 % aqueous DMF and used[2,10].

Compounds I_a, I_c, I_d have shown remarkable activity against *E.coli* and compound I_b has shown lesser activity against *E.coli* when compared to streptomycin. Similarly, compounds I_a, I_b, I_c have shown better activity against *S.aureus* but compound I_d has shown lesser activity against *S.aureus*. Therefore o-nitro substitution decreases the activity against *E.coli* and dimethoxy substitution reduces the activity against *S.aureus.*

Table 1: Synthesis of Substituted Chalcones[5]

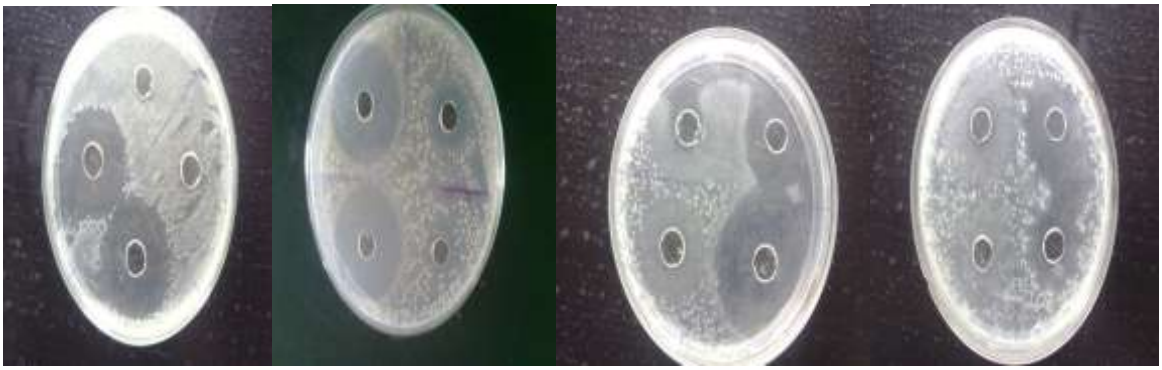
S.No	Compound	Solubility	Molecular Formula	M.P ^{O}c	% Yield	R_f Value
1	I_a	Alcohol	$C_{15}H_{11}NO_4$	66-70	60.09	0.833
2	I_b	Alcohol	$C_{15}H_{11}NO_4$	78-82	59.97	0.905
3	I_c	Alcohol	$C_{16}H_{14}O_4$	88-94	52.58	0.857
4	I_d	Alcohol	$C_{17}H_{16}O_4$	83-85	49.25	0.895

Table 2: Antimicrobial activity of synthesized compound[11].

S.No	Compound	*Mean* Zone of inhibition (in mm)			
		E.coli		*S.aureus*	
		50µg	100µg	50µg	100µg
1	Penicillin	15	17	21	25
2	Streptomycin	21	24	20	21
3	I_a	19	20	17	19
4	I_b	16	18	19	22
5	I_c	20	22	16	19
6	I_d	20	23	11	12

Zone of inhibition of I_a

S-standard **O-organism** **O-*S.aureus*** **O-*E.coli***



S-penicillin ***S*-Streptomycin** **S-penicillin** ***S*-Streptomycin**

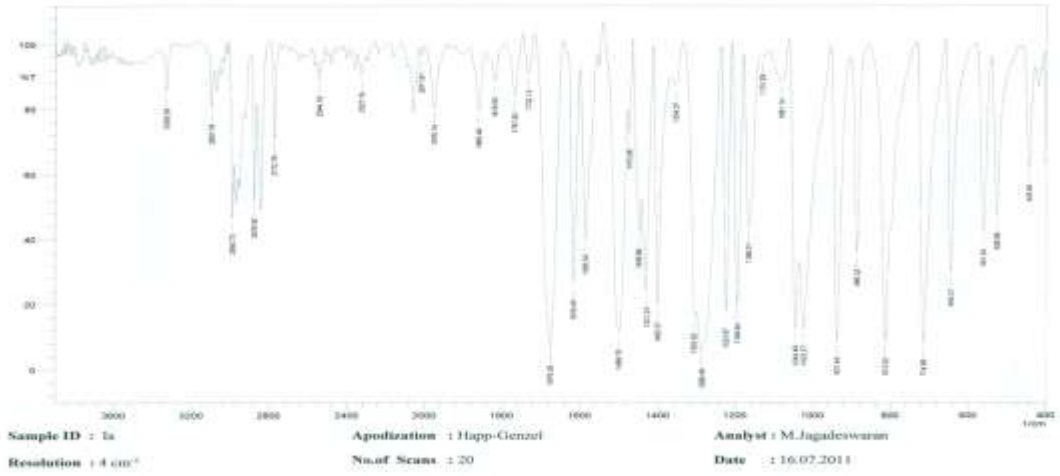
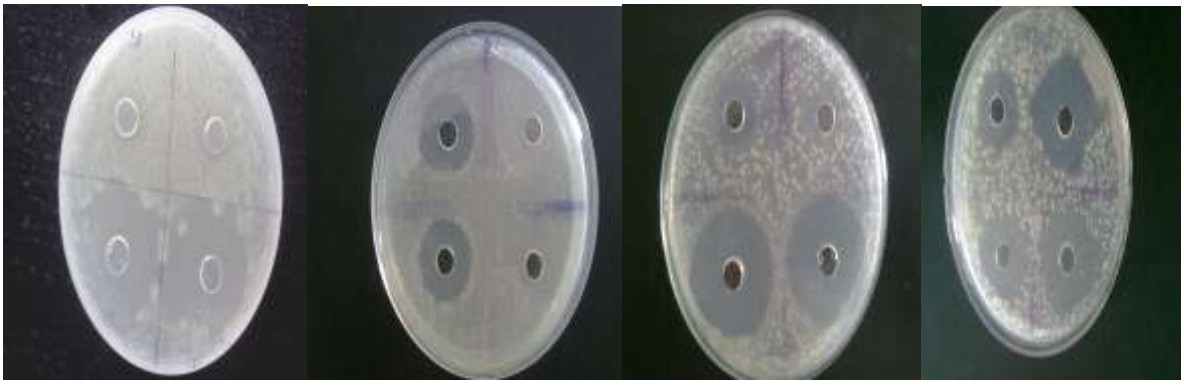


Figure 1: IR spectra of I_a

Zone of inhibition of I_b

O-*S.aureus* **O-*E.coli***



S-penicillin ***S*-Streptomycin** **S-penicillin** ***S*-Streptomycin**

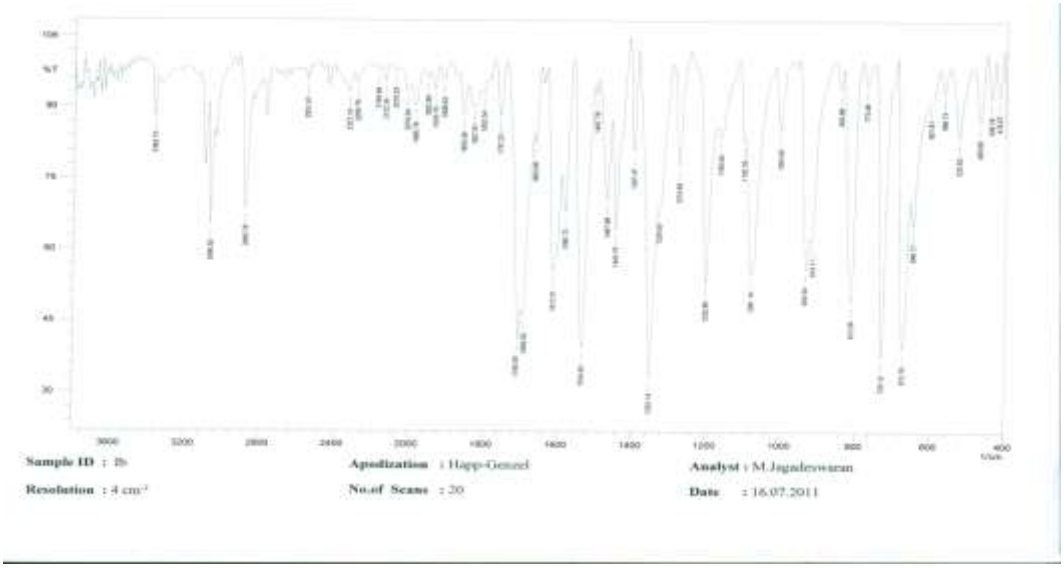


Figure 2: IR spectra of I_b

Zone of inhibition of I_c:

O-*S.aureus* **O-*E.coli***

S-penicillin ***S*-Streptomycin** **S-penicillin** ***S*-Streptomycin**

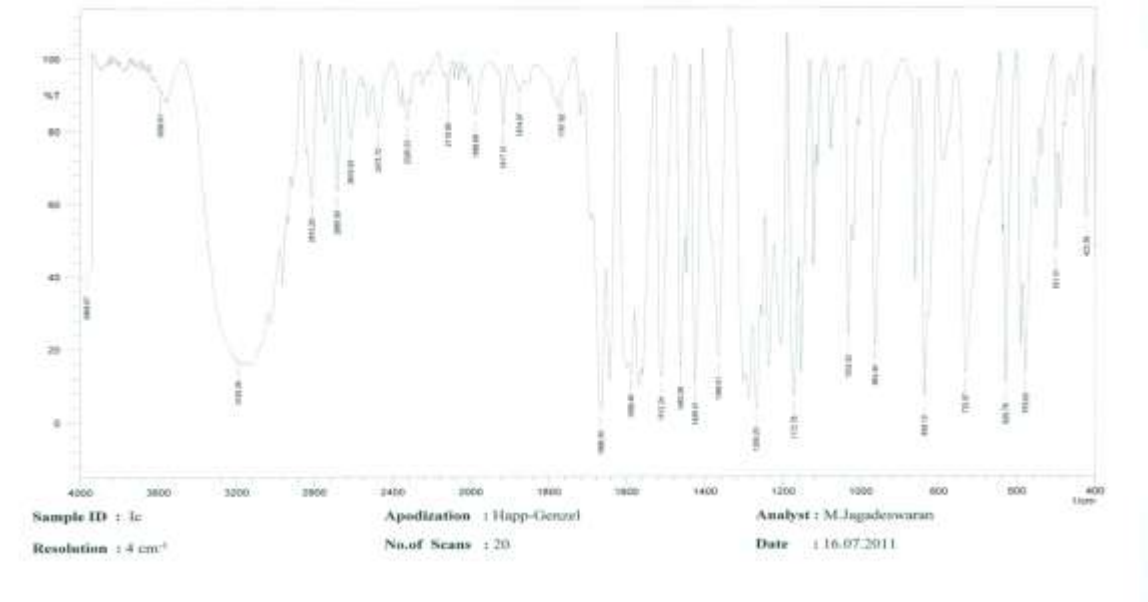
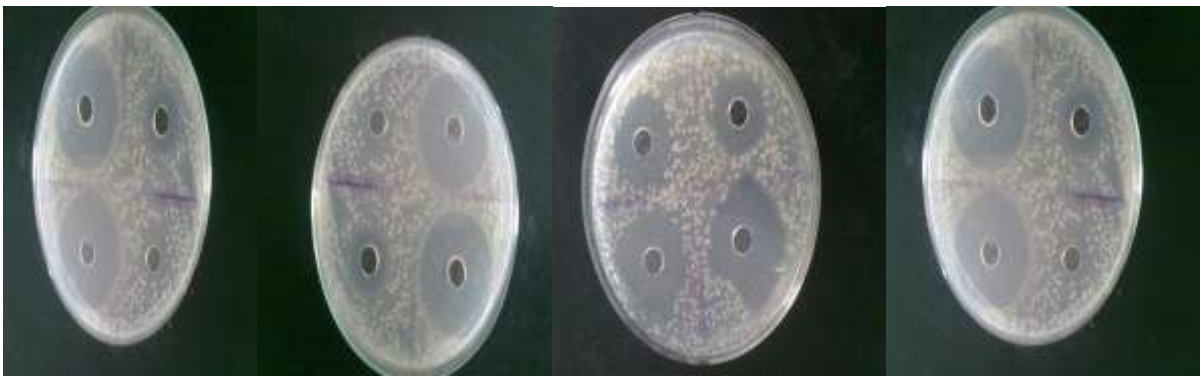


Figure 3: IR spectra of I_c

Zone of inhibition of I_d:

O-*S.aureus* **O-*E.coli***



S-penicillin ***S*-Streptomycin** **S-penicillin** ***S*-Streptomycin**

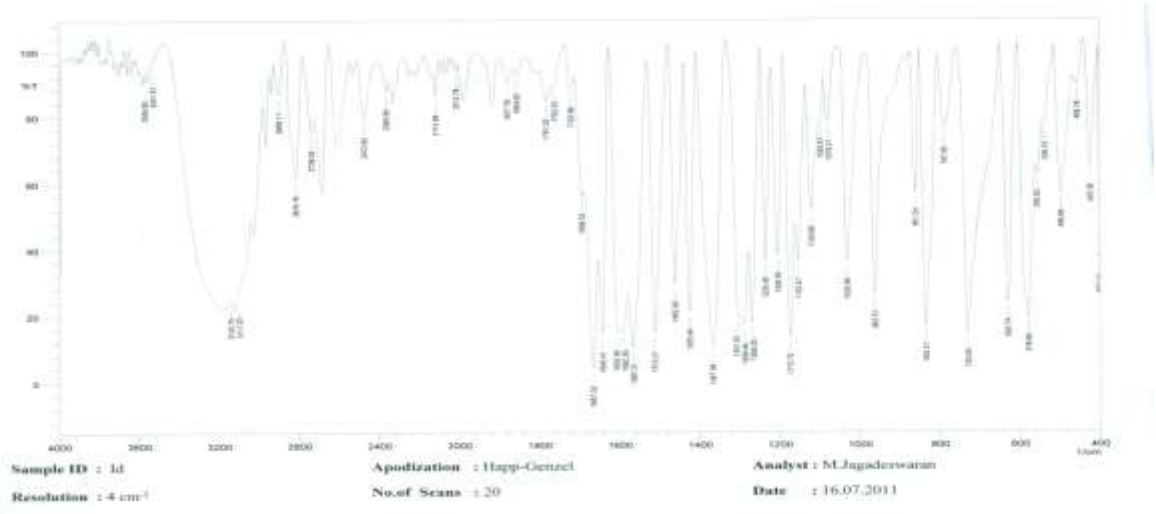


Figure 4: IR spectra of I_d

CONCLUSION

The screening results revealed that the compounds with nitro, hydroxy and methoxy substituents have shown significant antimicrobial activity against *E.coli* and *S.aureus* which are comparable to that of standard drugs penicillin and streptomycin. In this study dimethoxy substituted chalcone (I_d) is more active against *E.coli*. But the same compound does not show significant antimicrobial activity against *S.aureus.* Dinitro or dihydroxy substitution of the chalcones may be more active than the synthesised chalcones or may not be. This has to be proved further by synthesis with that substitution and by antimicrobial evaluation.

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