Design, synthesis, spectral characterization and in vitro antimicrobial activity of novel methoxy chromone chalcones

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ABSTRACT:

A novel method for the synthesis of Methoxy chromone chalcones (4a-i) have been introduced via Claisen-Schmidt synthesis by using recyclable PEG-400 as an alternative reaction medium. Different substituted methoxy chromone chalcones have been carried out by using 3-formyl 6- methoxy chromone and various different substituted tetralones , acetyl benziimidazole and acetyl ferrocene. It highlighten the chemical reactivity of 3-formyl chromones towards the synthesis of chromone chalcones. Bicyclic chromone moiety has been used as a privileged structure in the development of pharmacologically active compounds as scaffolds used as drug in medicinal chemistry. The structures of these compounds were confirmed on the basis of spectral data. Synthesized Novel methoxy Chromone Chalcones were screened for their antimicrobial activities against four pathogenic bacterial strains viz. Bacillus subtilis (Gram-positive), Escherichia coli (Gram-negative), Pseudomonas aeruginosa (gram-negative), Staphylococcus aureus (Gram-positive) and various antibiotics like Gentamicin, amoxycilin and streptomycin. Evaluation of the inhibitory influence of pathogenic bacterial growth of the synthesized methoxy chromone chalcones (4a-i) was carried out by Agar diffusion method. Their minimum inhibitory concentrations (MIC) were determined and the compounds 4d, 4f, 4g 4h and 4i shows good results of antimicrobial activity while compound 4a, 4b, 4c and 4e shows mild antimicrobial activity against standard B.subtilis, E.coli, P. aeruginosa and S.aureus bacteria and antibiotics like Gentamicin, amoxycilin and streptomycin.

KEYWORDS: Chromones, 3- formyl 6- methoxy chromones, Methoxy chromone chalcones, Vilsmeier – Haack reaction, Claisen-Schmidt synthesis , Antimicrobial Activity.

INTRODUCTION :

Chromone and their derivatives are the naturally occurring pharmacologically active compounds known so far as as oxygen-containing heterocyclic subcidaries.[1-2] The chromone moiety is an essential pharmacophore of a large number of bioactive molecules.[3] The biological activity of chromone derivatives includes antiviral [4], antioxidant [5-6], antibacterial [7] cytotoxic (anticancer)[8], antiallergic.[9] Due to their abundance in plants and their low mammalian toxicity, chromone derivatives are present in large amounts in the diet of humans. 3-Substituted chromones are very active substrates toward nucleophilic reagents . Among the 3-functionalized chromones, their 3-formyl derivatives are widely used in heterocyclic synthesis. Generally, chromones are synthesized by Vilsmeier-Haack formylation. The reactivity of 3-substituted chromones is extensively different depending upon the type of substitution present at the position 3 and the reaction conditions.

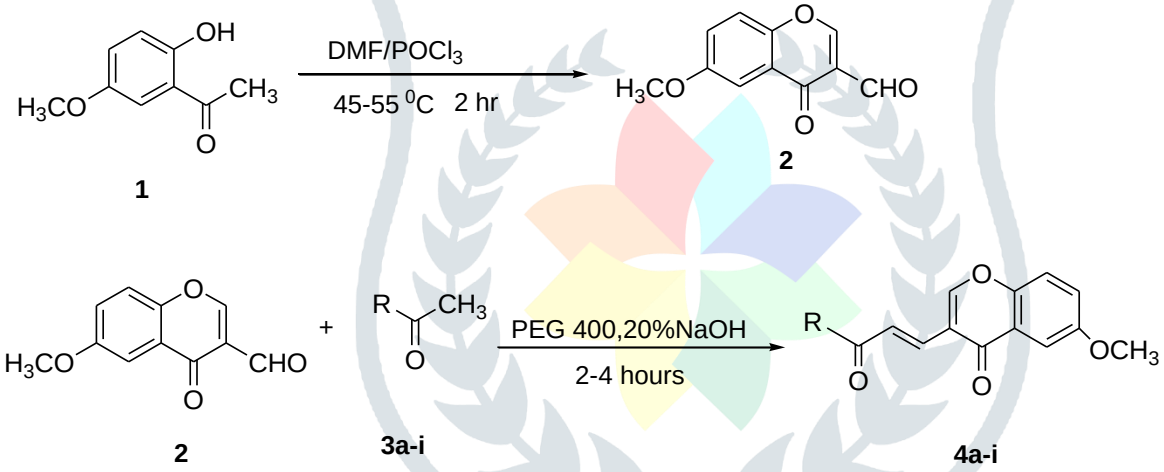
The aim of the study was to synthesize some different substituted derivatives of chromone chalcones using 3- formyl chromone aldehyde and different substituted tetralones as well as to assess them for their antimicrobial activity. Amalgamation of Chromone chalcone (4a-i) were carried out in PEG-400 as green solvent.[10-12] Till today number of various chalcones were prepared in various reaction medium under various medium like acidic (BF_3, B_2O_3), basic (Na_2CO_3) Water and ionic liquid.[13-15] We have intended to focus on green chemistry, using PEG-400 as an alternative reaction medium. PEG is an environmentally benign reaction solvent, non-toxic, inexpensive, potentially recyclable and water soluble,

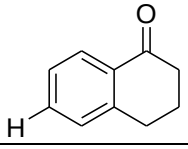
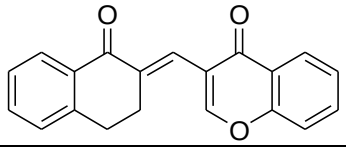
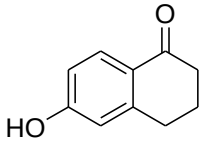
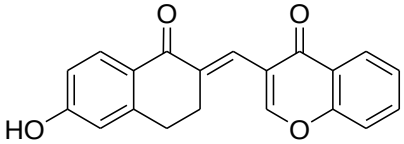
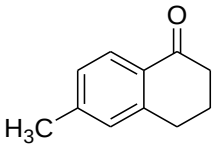
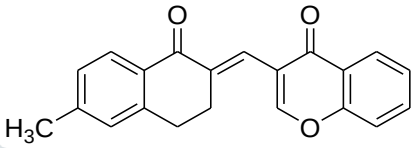
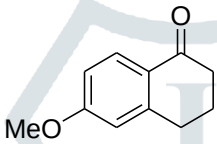
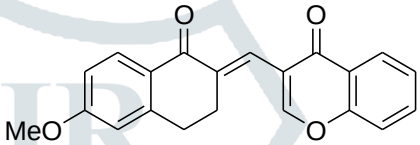
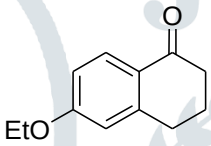
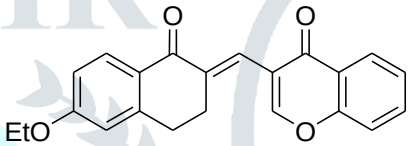
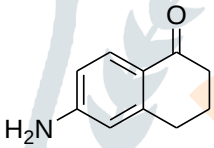
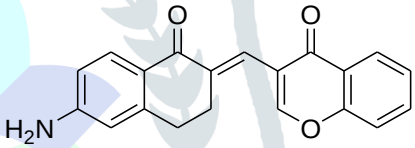
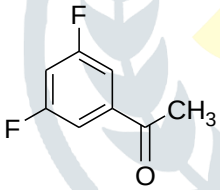
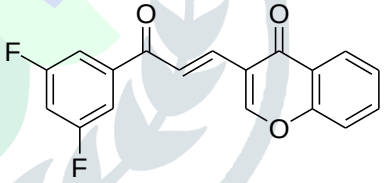
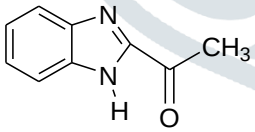
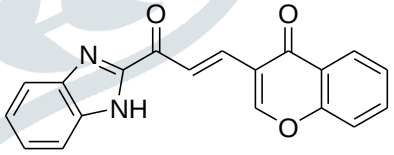
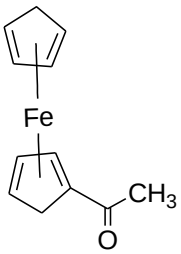
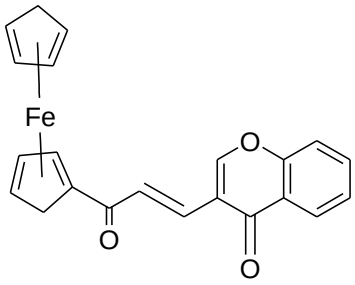
clean and product with excellent yield. Reaction occur in shorter reaction time and minimises the use of volatile organic compounds (VOCs). Also it is easier to remove the excess solvents from the reaction mixrure to get pure product. The structure of general chalcone is given as follows.

Figure 1 **:** General Structure of chalcone 1 and chromone chalcone 2

MATERIALS AND METHODS :

Scheme -1 : Synthesis Of Chromones Chalcone Compounds (4a-i) :



Sr.No.	Entry	Acetyl ketone (3a-i)	Entry	Methoxy Chalcone (4a-i)
1	**3a**		**4a**	
2	**3b**		**4b**	
3	**3c**		**4c**	
4	**3d**		**4d**	
5	**3e**		**4e**	
6	**3f**		**4f**	
7	**3g**		**4g**	
8	**3h**		**4h**	
9	**3i**		**4i**	

GENERAL

Instrumentation :

Melting points of the synthesized compounds were determined by using digital thermometer and were found to be uncorrected. IR spectra were recorded on FT-IR spectrometer (Perkin Elmer, Maharashtra, India) using KBr disk method. ^{1}HNMR spectra were recorded on ^{1}HNMR (Varian-NMR-mercury 300 MHz) spectrometer in $CDCl_3$ as solvent. All chemical shifts (δ) are quoted in parts per million downfield from TMS and coupling constants (J) are given in hertz. Abbreviations used in the splitting pattern were as

follows: s = singlet, d = doublet, t = triplet, q = quintet and m = multiplet. All the reagents and solvents were used of analytical grade and used as supplied unless otherwise stated. Thin layer chromatography was performed on silica gel coated plates for monitoring the reactions. The spots could be visualized easily under UV light.

Synthesis Of 3-formyl 6- Methoxy Chromen-4-One (2) :

In dry DMF (60 ml) in three neck flask, $POCl_3$ (37.5 ml) was added slowly with vigorous stirring at 50^0C. Heating and stirring was continued for 2 hrs at 45-55^0C. The solution of 2- hydroxyl 5-methoxy acetophenone (9.12 gm) in DMF (12.5 ml) was then slowly added with stirring at 50^0C and stirring was continued for 2 hrs. After cooling the mixture was kept overnight at room temperature and diluted slowly by adding ice cold water (250 ml) and was stirred for 6 hour. The red crystalline product separated was filtered and recrystallised from alcohol. [5-6,16]

Synthesis Of 6- Methoxy Chromone Chalcones (4a-i) :

A mixture of substituted 3- forrmly 6- methoxy chromone aldehyde 2 (1 mmol) and ubstituted tetrlones, 3a-i (1 mmol) was dissolved in 15 ml PEG-400. To this mixture, sodium hydroxide (20%, 1ml) was added and the reaction mixture was stirred at 40-50^0C temperature for 2-4 hours. The reaction mixture was then poured into 100 ml ice cold water. The product was separated out, it was filtered and processed out. The obtained products were recrystallised from ethanol to afford pure compounds [5-7 ,10] (4a-i).

The Spectral Data for Synthesized Compounds :

1H NMR (CDCl3, 300 MHz):

The spectral data of synthesized compounds (9a-i) :

4a : 3-[(*E*)-(1-oxo-3,4-dihydronaphthalen-2(1*H*)-ylidene)methyl]-4*H*-chromen-4-one

Tetralones ring :

δ 2.29 (t, 2H, C_3-H, δ 2.59 (t, 2H, C_4-H, Tetralone aomatic ring - δ 7.31 (d, 1H), C_5-H, δ 7.49 (d, 1H), C_6-H, ortho coupling ; δ 7.27 (d, 1H), C_7-H, - δ 7.76 (d, 1H), C_8-H, ortho coupling. Chalcone Trans Protons- δ7.48 (s 1H), J= 15.5 Hz. Chromones ring - δ 7.22 (s,1H) near to O, and C=C-C=O , C_3- H; δ 6.92 (d,1H) C_5- H; δ 3.73 (s,3H) Methoxy protons C_6-OMe; δ 7.01 (d,1H), C_7- H , δ 7.64 (d,1H), C_8- H .

4b : 3-[(*E*)-(6-hydroxy-1-oxo-3,4-dihydronaphthalen-2(1*H*)-ylidene)methyl]-4*H*-chromen-4-one

Tetralones ring :

δ 2.29 (t, 2H, C_3-H, δ 2.59 (t, 2H, C_4-H, Tetralone aomatic ring - δ 7.31 (d, 1H), C_5-H, δ 5.0 (s, 1H), C_6-OH (Hydroxy proton), ortho coupling ; δ 7.27 (d, 1H), C_7-H, δ 7.76 (d, 1H), C_8-H, ortho coupling. Chalcone Trans Protons- δ7.48 (s 1H), J= 15.5 Hz. Chromone ring - δ 7.22 (s,1H) near to O, and C=C-C=O , C_3- H; δ 6.92 (d,1H) C_5- H; δ 3.73 (s,3H) Methoxy protons C_6-OMe; δ 7.01 (d,1H), C_7- H , δ 7.64 (d,1H), C_8- H .

4c: 3-[(*E*)-(6-methyl-1-oxo-3,4-dihydronaphthalen-2(1*H*)-ylidene)methyl]-4*H*-chromen-4-one

Tetralones ring :

δ 2.29 (t, 2H, C_3-H, δ 2.59 (t, 2H, C_4-H, Tetralone aomatic ring - δ 7.31 (d, 1H), C_5-H; δ 2.35 (s, 1H) , methyl (CH_3) group C_6-CH_3 ortho coupling ; δ 7.27 (d 1H), C7-H, δ 7.76 (d, 1H), C_8-H, ortho coupling. Chalcone Trans Protons - δ7.48 (s 1H), J= 15.5 Hz. Chromones ring - δ 7.22 (s,1H) near to O, and C=C-C=O , C_2- H; δ 7.15 (d,1H) C_5- H; δ 3.73 (s,3H) Methoxy protons C_6-OMe; δ 6.81 (d,1H), C_7- H ; δ 6.88 (d,1H), C_8- H .

4d : 3-[(*E*)-(6-methoxy-1-oxo-3,4-dihydronaphthalen-2(1*H*)-ylidene)methyl]-4*H*-chromen-4-one

Tetralones ring :

δ 2.29 (t, 2H, C_3-H, δ 2.59 (t, 2H, C_4-H, Tetralone aomatic ring - δ 7.31 (d, 1H), C_5-H; δ 3.35 (s, 1H) , methoxy (OCH_3) group C_6-OCH_3, ortho coupling; δ 7.27 (d, 1H), C_7-H, δ 7.76 (d, 1H), C_8-H, ortho coupling. Chalcone Trans Protons - δ7.48 (s 1H), J= 15.5 Hz. Chromones ring - δ 7.22 (s,1H) near to O, and C=C-C=O , C_2- H; δ 7.15 (d,1H) C_5- H; δ 3.73 (s,3H) Methoxy protons C_6-OMe; δ 6.81 (d,1H), C_7-H ; δ 6.88 (d,1H), C_8- H .

4e: 3-[(*E*)-(6-ethoxy-1-oxo-3,4-dihydronaphthalen-2(1*H*)-ylidene)methyl]-4*H*-chromen-4-one

Tetralones ring :

δ 2.29 (t, 2H, C_3-H, δ 2.59 (t, 2H, C_4-H, Tetralone aomatic ring - δ 7.31 (d, 1H), C_5-H; δ 2.35 (q, 2H) & δ 1.2 (t,3H) , ethoxy (OCH_2CH_3) group C_6-OCH_2CH_3, ortho coupling ; δ 7.27 (d, 1H), C_7-H ; δ 7.76 (d, 1H), C_8-H, ortho coupling. Chalcone Trans Proton - δ 7.48 (s 1H), J= 15.5 Hz. Chromones ring - δ 7.22 (s,1H) near to O, and C=C-C=O , C_2- H; δ 7.15 (d,1H) C_5- H; δ 3.73 (s,3H) Methoxy protons C_6-OMe; δ 6.81 (d,1H), C_7- H ; δ 6.88 (d,1H), C_8- H .

4f: 3-[(*E*)-(6-amino-1-oxo-3,4-dihydronaphthalen-2(1*H*)-ylidene)methyl]-4*H*-chromen-4-one

Tetralone ring :

δ 2.29 (t, 2H, C_3-H, δ 2.59 (t, 2H, C_4-H, Tetralone aomatic ring - δ 6.51 (d, 1H), C_5-H; δ 4.0 (s, 2H) , amino (NH_2) group; δ 6.47 (d,1H), C_7-H, δ 7.51 (d, 1H), C_8-H, ortho coupling. Chalcone Trans Protons δ7.48 (s 1H), J= 15.5 Hz.

Chromones ring - δ 7.20 (s,1H) near to O, and C=C-C=O , C_2- H; δ 7.15 (d,1H) C_5- H; δ 3.73 (s,3H) Methoxy protons C_6-OMe; δ 6.81 (d,1H), C_7- H ; δ 6.88 (d,1H), C_8- H .

4g : 3-[(1*E*)-3-(3,5-difluorophenyl)-3-oxoprop-1-en-1-yl]-4*H*-chromen-4-one

Aromatic difluoro benzene ring :

δ 7.29 (d, 1H), C_2-H, δ 7.29 (d, 1H, C_5-H, near to F; δ 6.96 (d, 1H), C_7-H; near to F. Chalcone Trans Protons- δ 7.22 (d, 1H), δ 6.35 (d, 1H) J= 15.5 Hz. Chromone ring - δ 7.20 (s,1H) near to O, and C=C-C=O , C_2- H; δ 7.15 (d,1H) C_5- H; δ 3.73 (s,3H) Methoxy protons C_6-OMe; δ 6.81 (d,1H), C_7- H ; δ 6.88 (d,1H), C_8- H .

4h: 3-[(1*E*)-3-(1*H*-benzimidazol-2-yl)-3-oxoprop-1-en-1-yl]-4*H*-chromen-4-one

Benzaimidazole ring :

δ 5.0 (s, 1H), N-H, δ 7.70 (d, 1H) , C_5-H; δ 7.70 (d, 1H) C_6-H; δ 7.26 (d, 1H) C_7-H; δ 7.26 (d, 1H) C_8-H; Chalcone Trans Protons- - δ7.48 (s 1H), J= 15.5 Hz. Chromone ring - δ 7.20 (s,1H) near to O, and C=C-C=O , C_2- H; δ 7.15 (d,1H) C_5- H; δ 3.73 (s,3H) Methoxy protons C_6-OMe; δ 6.81 (d,1H), C_7- H ; δ 6.88 (d,1H), C_8- H .

4i : 3-[(1*E*)-3-(1*H*-ferrocene-2-yl)-3-oxoprop-1-en-1-yl]-4*H*-chromen-4-one

Ferrocene ring :

δ 2.90 (d,2H) similarly corresponding 2 protons, δ 6.40 (d,1H) similarly corresponding 2 protons, δ 6.50 (d,2H) similarly corresponding 2 protons, δ 7.53 (d,2H) similarly corresponding 2 protons, Chalcone Trans Protons- - δ7.48 (s 1H), J= 15.5 Hz. Chromone ring - δ 7.20 (s,1H) near to O, and C=C-C=O , C_2- H; δ 7.15 (d,1H) C_5- H; δ 3.73 (s,3H) Methoxy protons C_6-OMe; δ 6.81 (d,1H), C_7- H ; δ 6.88 (d,1H), C_8- H .

BIOLOGICAL STUDY :

ANTIMICROBIAL ACTIVITY :

The antimicrobial activity was screened against four pathogenic bacterial strains viz. They were tested against four species of bacteria namely, Bacillus subtilis (Gram-positive), Escherichia coli (Gram-negative), Pseudomonas aeruginosa (gram-negative), Staphylococcus aureus (Gram-positive).[16-18] The functionlised role of each bacteria and remedies of the antibiotics is as follows.

Generally E. coli bacteria lives in intestines and found in the gut of some animals. Mostly large numer of forms of E. coli are harmless and useful in keeping digestive tract healthy. Eating of contaminated food or drink polluted water, some strains can cause diarrhea. E. coli associating with food poisoning, you can also get pneumonia and urinary tract infections. Near about, 75% to 95% of urinary tract infections are caused by E. coli. Some versions of E. coli make you sick by making a toxin called Shiga. This toxin damages the lining of your intestine. The strains of E. coli that make the toxin are

sometimes called STEC, which is short for "Shiga toxin-producing E. coli." One especially bad strain can make very sick. It causes abdominal cramps, vomiting, and bloody diarrhea.

Staphylococcus aureus is a Gram-positive, round-shaped bacterium that is a member of the Firmicutes, and it is a usual member of the microbiota of the body, frequently found in the upper respiratory tract and on the skin. It is often positive for catalase and nitrate reduction and is a facultative anaerobe that can grow without the need for oxygen. The emergence of antibiotic-resistant strains of S. aureus such as methicillin-resistant S. aureus (MRSA) is a worldwide problem in clinical medicine.

Pseudomonas aeruginosa is a common encapsulated, Gram-negative, rod-shaped bacterium that can cause disease in plants and animals, including humans that can cause disease in plants and animals, including humans. P. aeruginosa is a multidrug resistant pathogen recognized for its ubiquity, its intrinsically advanced antibiotic resistance mechanisms, and its association with serious illnesses.

Bacillus subtilis, is a Gram-positive, catalase-positive bacterium, found in soil and the gastrointestinal tract of ruminants and humans. A member of the genus Bacillus, B. subtilis is rod-shaped, and can form a tough, protective endospore, allowing it to tolerate extreme environmental conditions. Bacterial Strain" which is a certain biological form of the influenza or "flu" virus and therefore it is an absolutely essential part of bacterial identification. The brief information about the all used antibiotics is described as follows.

Gentamicin injection is used to prevent or treat a wide variety of bacterial infections. Gentamicin belongs to a class of drugs known as aminoglycoside antibiotics. It works by stopping the growth of bacteria. Gentamicin, sold under brand name Garamycin among others, is an antibiotic used to treat several types of bacterial infections. This may include bone infections, endocarditis, pelvic inflammatory disease, meningitis, pneumonia, urinary tract infections, and sepsis among others.

Amoxicillin is an antibiotic often used for the treatment of a wide variety of bacterial infections. This medication is a penicillin-type antibiotic. It works by stopping the growth of bacteria. These include middle ear infection, strep throat, pneumonia, skin infections, and urinary tract infections among others. It will not work for viral infections to cure common cold and flu. It is taken by mouth, or less commonly by injection. Amoxicillin is also used with other medications to treat stomach/intestinal ulcers caused by the bacteria H. pylori and to prevent the ulcers from returning. Amoxicillin is used to treat a wide variety of bacterial infections. This antibiotic treats only bacterial infections. Unnecessary use or misuse of any antibiotic can lead to its decreased effectiveness.

Streptomycin is an aminoglycoside Antibacterial and Antimycobacterial antibiotic used to treat a number of bacterial infections by killing the organisms that cause the infection. This includes tuberculosis, Mycobacterium avium complex, endocarditis, brucellosis, Burkholderia infection, plague, tularemia, and rat bite fever typically used for treatment of active tuberculosis, It inhibites the initiation and elongation processes during protein synthesis. All the synthesized nine Methoxy chromone chalcones MCC (4a-i) purified and characterized and screened for their qualitative antimicrobial activity, were found to possess good antimicrobial activity against all four strains bacterial taken by developing a zone of inhibition in the range of 16-26 mm. (Table 1).

Evaluation of the inhibitory influence of pathogenic bacterial growth of the synthesized chromone chalcones compounds (4a-i) was carried out by Agar diffusion method.[17-19] The minimal inhibitory concentration (MIC) was assessed by the soup containing meat and vegetable cooked stock of liquid medium nutrients for culture of bacteria by microdilution method at the concentration level of 100µg/ml. Gentamycin, Amoxicillin and Streptomycin was used as standard drug at the concentration level of 100µg/ml. Specified quantity of beef extract, peptone & agar were accurately weight, dissolved in distilled water and sterlised by autoclaving at 121^0C for 15 minutes. The plates were prepared with the assay media was cooled to 50 ^{0}C. It was then inoculated with the test organisms. Four bores per plate were made using sterile cork borer. The above operation was carried out under asceptic condition to prevent contamination from pathogens and to prevent from harmful bacteria in sterile area. Everywhere there is bacteria out of these some are good for us while others are harmful bacteria The following Table-1 indicates the antimicrobial activity of the test compounds synthesized.

TABLE 2 : Zone of Inhibition (MM) of Active compounds against pathogenic bacteria test strains using Ampiciline as positive control

Entry	Concentration Ul/ml	Zone of Inhibition (MM)			
		Escherichia Coli	Staphylococcus aureus	Pseudomonas aeruginosa	Bacillus subtilis
4a	100	17	18	17	16
4b	100	18	17	18	17
4c	100	19	19	18	18
4d	100	24	23	22	21
4e	100	19	18	17	17
4f	100	20	20	21	19
4g	100	22	22	21	20
4h	100	25	24	23	22
4i	100	26	25	24	23
Gentamicine	100	**31**	**32**	**31**	**30**
Amoxycillin	100	**35**	**32**	**29**	**28**
Streptomycin	100	**27**	**25**	**24**	**26**

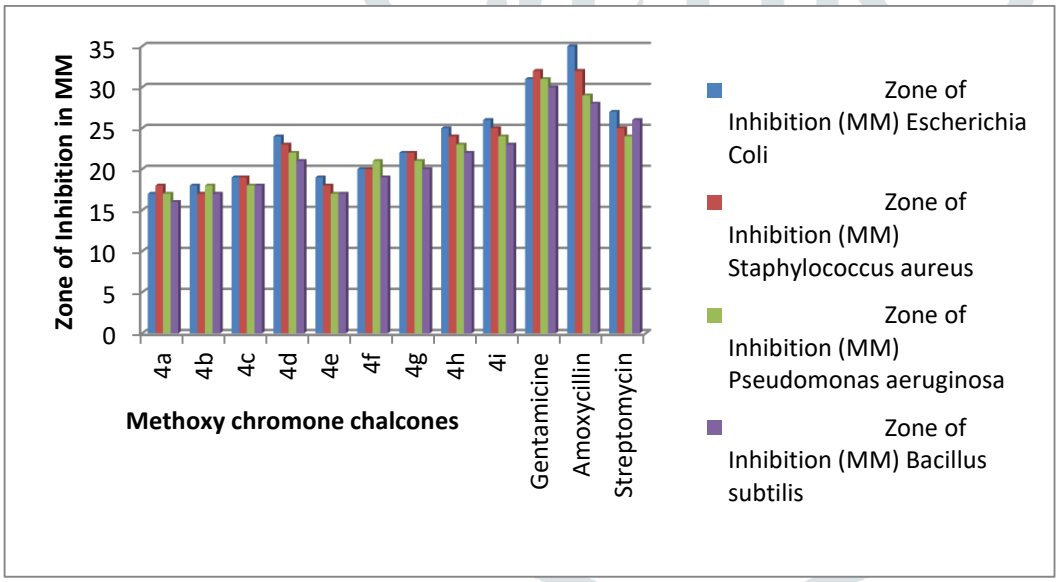


Figure-1: In vitro of antimicrobial activity - Zone of Inhibition in mm against pathogenic bacteria

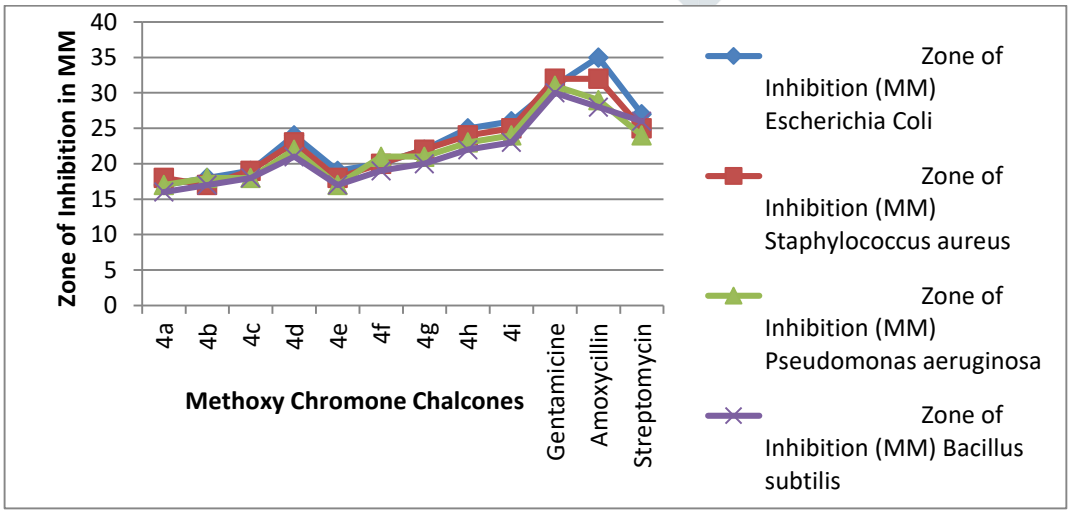


Figure-2: Antimicrobial screening comparision zone of inhibition in mm against pathogenic bacteria

RESULTS AND DISCUSSION :

CHEMISTRY

In the present investigation, in our laboratory, the Chromone chalcones (4a-i) have been prepared by the Claisen-Schmidt condensation of 3- formyl chromone aldehyde and different substituted tetralones using sodium hydroxide in PEG-400 as a alternative reaction medium as shown in above (Scheme 1). All the compounds were obtained in good to excellent yields. The 3- formyl 6 methoxy chromone aldehyde is prepared by the Vilsmeir-Haack reaction using DMF/$POCl_3$ by using 2- hydroxy 5-methoxy acetophenone. The reaction was simple and efficient and yields the title compounds almost in pure form. However the resultant compounds were purified by recrystallization in ethanol solvent. The structures of the synthesized compounds were confirmed by IR, ^1H NMR. The IR spectra of final compounds showed an absorption band at 3300-3600 cm^{-1} indicates the presence of -OH stretching. The compounds with methoxy substitution exhibited absorption band in the region of 1033 – 1016 cm^{-1} stretching vibration. The NMR spectra of title compounds showed singlets in the region of δ 6.9 - 7.4 due to the protons of phenolic hydroxyl group. In compound the spectra of the compounds showed singlets in the region of δ 3.3 - 3.8 indicative of methyl protons. In the compounds containing methoxy group exhibited characteristic signals in the region of δ 3.8 -3.9 δ, 6.4 -8.2 aromatic protons in all the NMR spectra of final compounds confirm the structures of title compounds.

All the synthesized compounds have been evaluated for their antimicrobial activity against Gram positive and Gram negative organisms. Compound 4d, 4f, 4g, 4h and 4i showed significant antimicrobial activity against all test organisms. Compounds 4a, 4b, 4c and 4e showed moderate antimicrobial activity against test organisms. This research work reveals that the chromone chalcone possess overall good antimicrobial activity.

CONCLUSION :

An eco-friendly and easy method has been used to synthesize the title compounds. The method includes mild reaction conditions, use of recyclable PEG solvent and easy work-up procedure for the separation of products. The reaction lead to the expected products with high yield and in all most all cases the products obtained in pure form.

Methoxy chromone chalcones have been synthesized and characterized on the basis of analytical and spectral data. All of the new synthesized compounds were screened for their antimicrobial activity against four pathogenic bacterial strains. All tested compounds have shown good antimicrobial activity against all the tested strains with zone of inhibition in mm.

From the antimicrobial screening data it was concluded that the compounds 4d, 4f, 4g, 4h and 4i showed activity against both gram positive and gram negative bacteria and were found to have zones of inhibition value at 24 mm, 20 mm, 22 mm, 25 and 26 mm respectively against E. Coli, 23mm, 20mm, 22mm, 24mm, and 25 mm respectively against Staphylococcus aureus, 22 mm 21 mm, 21 mm, 22 mm and 23 mm respectively against Pseudomonas aeruginosa, 21mm, 19 mm, 20 mm, 22 mm, 23 mm respectively against Bacillus subtilis as shown in the experimental studies.

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CONFLICT OF INTEREST:

The authors confirm that this article content has no conflict of interest.

REFERENCES :

1. 1.Ibrahim, M , Ali T. Mohamed G. Azak M. 2013. 3-Formylchromones as diverse building blocks in heterocycles synthesis. European Journal of Chemistry, 4 (3): 311-328.
2. Tyrrell E., Tesfa K. Greenwood A. Mann, 2008. The synthesis and biological evaluation of range of novel functionalised benzopyran. Bioorg. Med. Chem. Lett., 18: 1237–1240.
3. Hatzade, K. Taile, V. Gaidhane, V. Umare, A. Haldar, G. Ingle, N. 2009. Synthesis and biological activities of new 7-o--D-glucopyranosyloxy-3-(3-oxo-3-arylprop-1-enyl)-chromones. Indian J. Chem. *48B:* 1548-1557.
4. Kaur R. N. Taheam N., Sharma A., and R. Kharb R. 2013. Important Advances on Antiviral Profile of Chromone Derivatives. Research Journal of Pharmaceutical, Biological and Chemical Science, 4 (2): 81.
5. Sonawane, V. 2013. Design, Synthesis, Characterization and In vitro Antioxidant screening of Novel Chromone Chalcones. Review Of Research, 3 (2) 1-8.
6. Sonawane, V. 2016. Design, Synthesis, Chracterization And Antioxidant valuation Of Novel Asymmetrical Methoxy Curcumin Analogues Containing Chromone Moiety. Review Of Research, 5 (9): 1-17.
7. Sonawane V. 2017. Synthesis, Characterization And Antibacterial Screening Of Some Novel Chalcone Derivatives Containing Imidazo [1,2-A]-Pyridine Moiety. Science Park International Research Journal, 4 (38): 1-9.
8. Koniezny, M. Konieczny, W. Sabisz, M. Skladanowski, A. Wakiec, R. 2007. Augustnowicz Kopec E. And Zwolska Z., Acid-catalyzed synthesis of oxathiolone fused chalcones. Comparison of their activity toward various microorganisms and human cancer cells line European J.Medicinal Chem. 42(5): 729-733.
9. Nohara, A. Kuriki, H. Saijo, T. Ukawa, K. Murata, T. Kanno, M. Sanno, Y. 1975. Antianaphylactic agents. Synthesis and structure-activity relations of 3-(4-oxo-4H-1-benzopyran-3) acrylic acids, a new series of antiallergic substances and some related compounds. J. Med. Chem. 18 : 34-37.
10. Jadhav, S. Bhosale, R. Shirame, S Sonawane, V. Hublikar, M. Sonawane, K. Shaikh, R. 2013. Synthesis and biological evaluation of fluoro-hydroxy substituted pyrazole chalcones as anti-inflammatory, antioxidant and antibacterial agents. International journal of pharm. biosciences, 4 : 390– 39.
11. J. Chen, S. Spear, K. Huddlestn, J. and Roggers, R. 2005. Polyethylene glycol and solutions of polyethylene glycol as green reaction, Green chem. 7 : 64-82.
12. Jayapal, M. Sreenivasa, P and Sreedhar, N. 2010. Synthesis and Characterization of 2,6- Dihydroxy Substituted Chalcones Using PEG-400 as a Recyclable Solvent. J Pharm. Sci & Res., 2(8) : 450-458.
13. Petrov O., Ivanova,Y.and Gerova M., 2008. $SOCl_2$/EtOH: Catalytic system for synthesis of chalcones. Catalysis Communications, 9(2): 315-316.
14. Perozo-Rondon E., Martin-Aranda, R. Casal, B. Duran-Valle, C. Lau, W. Zhang, X. Yeung K. 2006. Sonocatalysis in solvent free conditions: An efficient eco-friendly methodology to prepare chalcones using a new type of amino grafted zeolites. Catalysis Today, 114 2(3): 183-187.
15. Craig, M. Comisar, P. and Savage, Green Chem. 2006. An Efficient and Operationally Simple Synthesis of Some New Chalcones by Using Grinding Technique Chemical Sciences Journal. Chemical Sciences Journal, 2011 (13) : 227-231.
16. Patil, R. Sawant, S. Thombare, P, 2007. Design, Synthesis and Pharmacological Evaluation of Chromenones and Related Analogues International Journal of PharmTech Research 4(1): 375-381.
17. Lacova, M. Loos, D. Matulova, M. Hafez, M. Shaaer, El.1998. Synthesis and Reactions of New 4-Oxo-4H-benzopyran-3-carboxaldehydes containing hydroxy groups or 2- Oxopyran Cycles, Molecules 3 : 149-158.
18. Anjum, N. Abdul, A. Nayeem, N. Asdaq, S. 2011. Synthesis and antibacterial activity of substituted 2-phenyl-4-chromones. Scholars Research Library Der Pharma Chemica, 3 (5): 56-62.
19. Savita Chahal, S. Selwal, K. Sonia, N. 2017. Synthesis and antibacterial studies of 3-substituted chromone derivatives, Integrated Research Advances . 4(1): 14-17.