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REVIEW ARTICLE

Biological Potentials of Chalcones: A Review

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ABSTRACT

Chalcones and its derivatives are used in organic synthesis and they are used in evaluating new product that possesses different biological activities. This review article covers the most active chalcone derivatives that have shown considerable biological actions such as antimicrobial, anti-inflammatory, anticancer, anticonvulsant and antioxidant. Synthesis and biological evaluation of chalcone derivatives have been a topic of special interest to organic and medicinal chemists. The new structural classes of compounds may prove as lead molecules and good candidates for the future investigations.

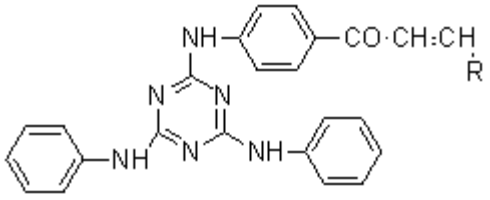
Key words: Chalcones , Antimicrobials and Anticonvulsants.

INTRODUCTION

Chalcones are well known intermediates for synthesizing various heterocyclic compounds. It constitute an important group of natural products.Chemically, they consist of open chain flavanoids in which the two aromatic rings are joined by a three carbon α, β unsaturated carbonyl system. The s-triazine based chalcones and their derivatives have been studied extensively because of their wide range of biological activity. They are found to be effective as local anaesthetics, antibacterial, antimalarial, antiprotozoal, antitubercular, anticancer and antifungal agents. These diverse properties of chalcones have prompted us to synthesize them in order to study their biological activities. Chalcones are products of condensation of simple or substituted aromatic with simple or substituted acetophenones in presence of alkali. Hence it was thought of modifying chemically benzofuran analogous of chalcones into isoxazole ring system so as to produce biheterocyclic Benzofuryl isoxazoles. α,β-Unsaturated ketones are biogenetic precursors of flavonoids in higher plants ,also known chemically as chalcones. Various chalcone derivatives are notable materials for their second harmonic generation (SHG). They are well known intermediates for synthesizing various heterocyclic compounds. Cyclization of chalcones, leading to thiazines, pyrimidines, pyrazline has been a developing field within the realm of heterocyclic chemistry for the past several years because of their ready accessibility and the broad spectrum of biological activity of the products as antibacterial, antifungal, antiprotozoal, anti-inflammatory substances.

ANTIMICROBIAL ACTIVITY

Synthesis of 2.4-bis-(phenylamino)-6-[4'-{3''-(4'''-substituted phenyl/2'''-furanyl/2'''-thienyl)-2''-propenon-1''-yl}phenylamino]-s-thriazines **(1)** were reported by Solankee *et al.*,[1] by base catalysed condensation of ketone 5 with different aldehydes.The synthesized compound on cyclization with hydrazine hydrate in the presence of glacial acetic acid, guanidine nitrate in the presence of alkali and malononitrile in the presence of ammonium acetate give the corresponding acetylpyrazolines , aminopyrimidines and cyanopyridines and tested for antibacterial activity.



(1)

R= 4-Nitrophenyl ,4-chlorophenyl ,2-furanyl ,2-thienyl ,2-methoxyphenyl

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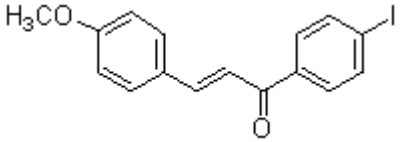
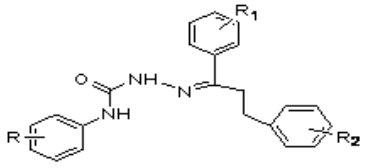
Synthesis of 3-(4-methoxyphenyl)-1-(4-iodophenyl)-2-propen-1-one **(2)** were reported by Chaudhary *et al.,*[2] by condensing benzaldehyde derivatives with acetophenone derivatives in dilute ethanolic sodium hydroxide solution at room temperature according to Claisen –Schmidt condensation. The synthesized compound showed excellent activity against *S. aureus* at both concentration i.e. 500µg/ml and1000 µg/ml.



(2)

Synthesis of chalconesemicarbazones **(3)** were reported Singhal *et al.,*[3] by paper disk diffusion method against two strains each of gram positive and gram negative bacteria. . The synthesized compound against gram negative bacteria. The choloro substitution in the aldehyde moiety and amino substitution in the aldehydic moiety and amino substitution in acetophenic moiety of chalcone exhibited better antibacterial activity against gram negative bacteria but lengthening of carbon chain does not favor antimicrobial activity.

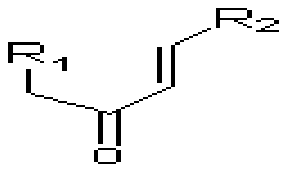


(Z)-4-phenyl-1-(1,3-diphenylpropylidene)semicarbazide

(3)

R = 2-CH_3, 4-CH_3; R_1 = H, p-NH_2 ; R_2 = p-Cl, H, Cinnamaldehyde

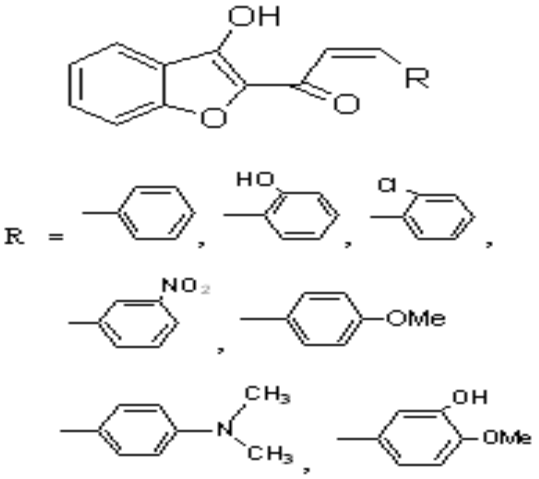
Synthesis of chalcones **(4)** were reported by Tiwari *et al.,*[4] by Claisen-Schmidt condensation of appropriate acetophenones with appropriate aromatic aldehydes in the presence of aqueous solution of potassium hydroxide and ethanol at room temperature. The synthesized compounds were characterized by means of their IR, ^{1}H-NMR spectral data and tested for antimicrobial activity screened for their in vitro antimicrobial activity against *Escherichia coli, Pseudomonas aeruginosa* by measuring the zone of inhibition in mm. The antimicrobial activity was performed by filter paper disc plate method at concentration 100 µg/mL.



(4)

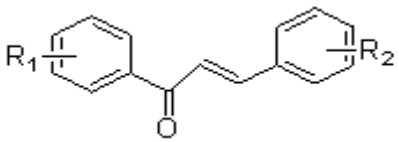
R_1 = 4-F C_6H_4 , 4-NO_2 C_6H_4; R_2 = 3-OH C_6H_4 , 3-$NO_2C_6H_4$, 3-Cl C_6H_4 ,4-F C_6H_4 , 4-$CH_3C_6H_4$, 3, 4-$OCH_3C_6H_4$.

Synthesis of 3-hydroxy benzofuran substituted chalcones**(5)** were reported by Swamy *et al.,*[5] by reaction of 2-Acetyl-3-hydroxy benzofuran with different aromatic aldehydes . The synthesized compounds were screened for antimicrobial activity against both gram positive *S.aureus* and gram negative *E.coli* bacteria . Streptomycin and Gresofulvin were used as standard for comparison of antibacterial activity.



(5)

Synthesis of chalcones **(6)** were reported by Doan *et al.,*[6] by the Claisen-Schmidt condensation and by the reaction of respective chalcones and hydrazine hydrate. The synthesized compounds were tested for their in vitro antimicrobial properties against the Gram-positive bacteria Methicillin-resistant Staphylococcus aureus (MRSA), Methicillin-sensitive Staphylo- coccus aureus (MSSA), Streptococcus faecalis, the Gram-negative bacteria Es- cherichia coli, Pseudomonas aeruginosa .

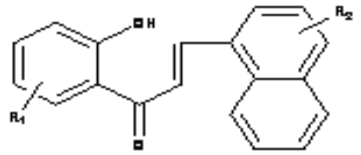


(6)

R_1 = 2-OH ,4 –OCH_3 , 4-NO_2 , 2-OH.

R_2 = 3-OCH_3, 4-OCH_3 ,4-$N(CH_3)_2$,2-OCH_3 ,4-OCH_3.

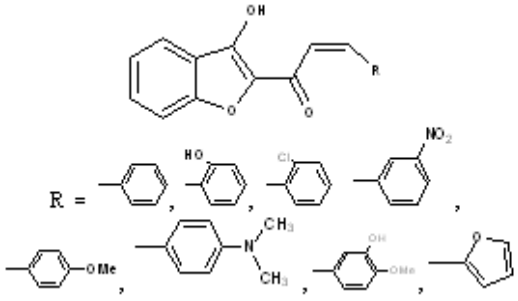
Synthesis *of* chalcones containing substitued naphthalene nucleus **(7)** were reported by Zangade *et al.,*[7] the synthesized compounds were screened for antibacterial activity against *Escherichia coli*and *Stahylococcus aureus* . by disc diffusion method, using tetracycline antibiotic for comparision of activity. Compounds and tetracycline 100 µg/ml were dissolved in 5 % aqueous DMF and used. It was found that the compounds with chloro subtituents have shown remarkable inhibition against *E. coli* and *S. aureus.*



(7)

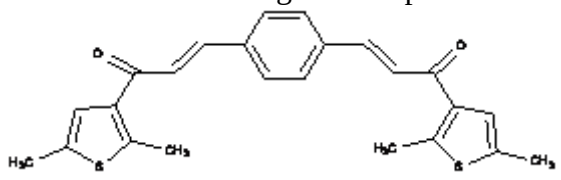
R_1 = 2-OH , 5-Br , 3,5-Cl , 5-Cl ,3-I, 5-CH_3 ,3-I , 4-CH_3 , 3-Br.
R_2 = 4-Br , 2-OCH_3.

Synthesis of 3-Hydroxy Benzofuran Chalcones **(8)** were reported by Swamy *et al*.,[8] by the reaction of 2-acetyl-3-hydroxybenzofuran with different aromatic aldehydes in the presence of a strong base, cyclocondensation of 3-Hydroxy benzofuran with hydroxlaminehydrochloride resulted in the formation of various Isoxazolines bearing hydroxyl benzofuran. The synthesized compounds were screened for antimicrobial activity against both gram positive S.aureus and gram negative E.coli bacteria at a concentration of 0.005 mole/ml.



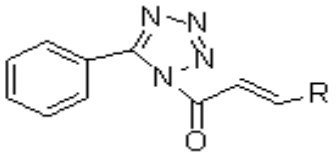
(8)

Synthesis of Chalcones **(9)** were reported by Abdullah *et al*.,[9] by the reaction of terephthalaldehyde with 3-acetyl-2, 5-dimethylthiophene. The synthesized compound have been characterized by IR, 1H-NMR, 13C-NMR, GC-MS and elemental analyses. The anti-bacterial activity of these compounds were first tested *in vitro* by the disk diffusion assay against two Grampositive and two Gram-negative bacteria, and then the minimum inhibitory concentration(MIC) was determined with the reference of standard drug chloramphenicol.



(9)

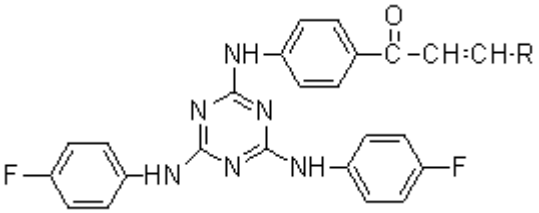
Synthesis of 5-phenyl tetrazole 1- substituted chalcones **(10)** were reported by Popat *et al.*, [10] by the reaction of 5-phenyl 1-acetyl tetrazole react separately with different aromatic aldehydes in presence of alkaline medium. The synthesized compound were identified by spectral data and screened evaluated for *in vitro* antimicrobial activity. The results of antibacterial screening, it is evident that most of the compounds are very weakly active and few are moderately active against *S. aureus* and *E. coli*



(10)

R = C_6H_5 , 2-Cl-C_6H_5 , 4-Cl-C_6H_5 , 4-Br-C_6H_5 , 4-OCH_3-C_6H_5 , 2-NO_2-C_6H_5 , 4-NO_2-C_6H_5 , 4-(CH3)N-C_6H_5 , 4-CH_3-C_6H_5

Synthesis of Chalcones, 2,4-bis-(4'-fluorophenylamino)-6-[4'-{3''-(phenyl /4'''-substituted phenyl)-2''-propenon-1'-yl} phenylamino]-s-triazine **(11)** were reported by Solankee *et al* .,[11] were prepared by according to Claisen-Schmidt condensation.The synthesized compound have been characterized on the basis of their IR and ^{1}H NMR spectral data and have been screened for their antibacterial activities.

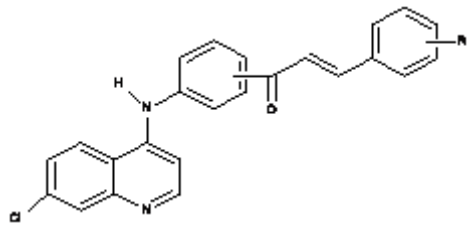


(11)

R =Phenyl ,4-chlorophenyl,4-ethoxyphenyl,4-flourophenyl, 4-N,N-dimethylaminophenyl,4-methoxyphenyl

ANTICANCER ACTIVITY

Synthesis of [(7-Chloroquinolin-4-yl) amino]chalcone derivatives **(12)** were reported by Ferrer *et al*.,[12]derived from the corresponding 3- or 4-[(7-chloroquinolin-4-yl)amino]acetophenone were synthesized and evaluated for *in vitro* anticancer activity. The most active compounds displayed inhibitory values against heme cristallization in the range of 93.14 ± 1.74 – 94.93 ± 1.50 %.

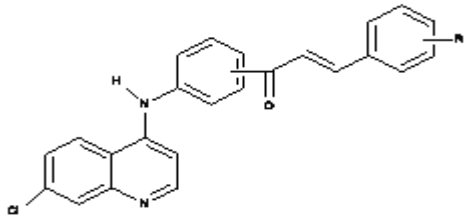


(12)

R = 4-OCH_3 , 4-$N(CH_3)_2$, 4-Cl , 4-F , 4-OCH_3 ,3-OCH_3 , 2-OCH_3 , 4-$N(CH_3)_2$, 3-Cl , 2-Cl ,4- F , 3-F , 2-F , H

Synthesis of copolyester chalcone derivatives **(13)** were reported by Selvi *et al*.,[13] were synthesised from 1, 3-bis (4-hydroxy-3-methoxyphenyl) propenone (BHMPP) and 1- (3, 5-dihydroxyphenyl)-3-(4-methoxyphenyl) propenone (DHPMPP) with adipoyl, suberoyl, azeloyl and sebacoyl chlorides by phase

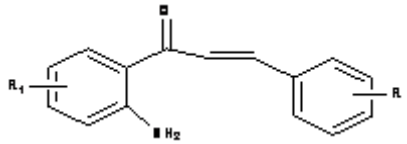
transfer catalysed polycondensation method.The synthesized compound are the microstructure of the repeating unit was confirmed by IR, ^{1}H and ^{13}C NMR,these copolyesters are evaluated for anticancer activity. These chalcone derivatives showed good activity against HepG2 cells with IC50 values.



(13)

R = $-(CH_2)_4-$, $-(CH_2)_6-$, $-(CH_2)_7-$, $-(CH_2)8-$

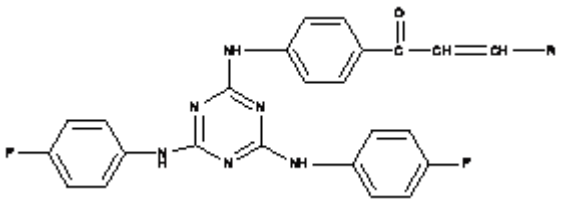
Synthesis of 4',5',2,3,4-substituted 20-amino chalcones **(14)**were reported by Xia *et al*.,[14] were synthesized and evaluated for cytotoxicity against a panel of human tumor cell lines. Several compounds displayed significant cytotoxicity. The synthesized compound had high activity toward multi-drug resistant KB-VIN, and ovarian 1A9 cell lines. 2'- Amino chalcones demonstrated signicantly increased anti- tumor activity compared with the corresponding chalcones, while, the epoxide derivatives generally showed greatly reduced activity.



(14)

R = 2-CH_3 , 3-OCH_3 , 2-F , 3-OCH_3 , 4-F,
R' = OCH_2O

Synthesis of Chalcones, 2,4-bis-(4'-fluorophenylamino)-6-[4'-{3"-(phenyl / 4"'-substituted phenyl)-2"-propenon-1'-yl} phenylamino]-s-triazine **(15)**were reported by Solankee *et al*.,[15] have been prepared according to Claisen-Schmidt condensation. The synthesized compounds have been characterized on the basis of their IR and ^{1}H NMR spectral data. The synthesized compounds have been screened for their anticancer activities.

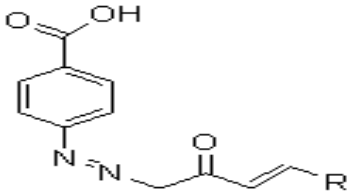


(15)

R= Phenyl , 4-chlorophenyl , 4-ethoxyphenyl , 4-fluorophenyl , 4-N,N-dimethylaminophenyl , 4-methoxyphenyl .

ANTI- INFLAMMATORY ACTIVITY

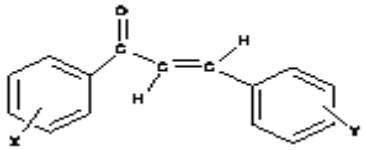
Synthesis of series of chalcone **(16)** were reported by Bukhari *et al*.,[16] were synthesized and used as precursor for the synthesis of novel series of pyrimidines. The synthesized com pounds have been evaluated for their effects on the cyclooxygenases (COXs) that are imperative enzymes in the genesis of prostaglandin H2, which is an antecedent for the biosynthesis of prostaglandins, thromboxanes and prostacyclins and are very active inhibitors.



(16)

R = phenyl , 2-Hydroxyphenyl , 4-Hydroxyphenyl , 2-Nitrophenyl , 4-Methoxyphenyl , 3- Nitrophenyl , 2-Chlorophenyl

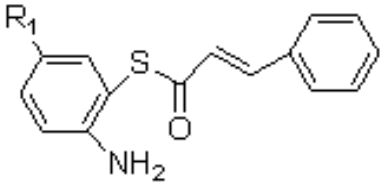
Synthesis of 1,3-diaryl propen-1-ones (chalcones) **(17)** were reported by okunrobo *et al*., [17] by the Claisen-Schmidt condensation between acetophenones and benzaldehydes in potassium hydroxide /methanol medium at room temperature which were evaluated for anti-inflammatory activity at doses of 20, 40 and 80mg/kg. The synthesized compounds were found to be effective inhibitors of carrageenan-induced rat paw edema in Wistar rats and this activity was dose dependent and increased between the third and fourth hour and were found to have anti-inflammatory activities.



(17)

X =4-NO_2 , 4-OCH_3 , 2,4-OH , 4-NO_2
Y = 2,4,6-OCH_3 , 3-Br , 2,4,6-OCH_3 , H , 4-Cl

Synthesis of Chalcones, 1, 3-Thiazines **(18)** and 1, 3-Pyrimidines derivatives were reported by Dabholkar *et al*.,[18] and were studied by IR, NMR and Mass spectroscopy. The synthesized compounds showed anti-inflammatory activities.

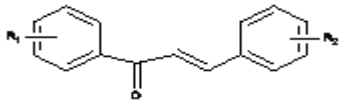


(18)

R_1 =H , CH_3

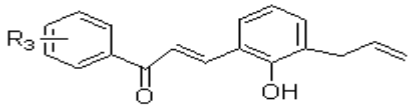
ANTIOXIDANT ACTIVITY

Synthesis of chalcones **(19)** and allylicchalcones **(20)** were reported by Doan *et al*.,[19] were prepared by the Claisen-Schmidt condensation. The structures of the compounds were confirmed by spectral data (infrared spectroscopy and 1H nuclear magnetic resonance).The synthesized compound have been tested for their antioxidant activities (1,1-biphenyl-2-picrylhydrazyl free radical scavenging method).



(19)

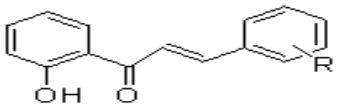
R_1 =2'-OH , 4'-OCH_3 , 4'-NO_2 , 2'-OH.
R_2 = 3-OCH_3, 4-OCH_3, 4-N $(CH_3)_2$, 2-OCH_3, 4-OCH_3



(20)

R_3 = 2'-OH ,5'-CH_3 , 4'-NO_2

Synthesis of series of chalcone **(21)** were reported by Singh *et al*.,[20] by the reaction of 2-hydroxyacetophenone and substituted aldehyde. The synthesized compound was elucidated by melting point, retention factor, I.R. spectroscopic technique, ^{1}H NMR and elemental analysis and showed the most potent anti-oxidant activity and the other derivatives showed mild anti-oxidant activity.

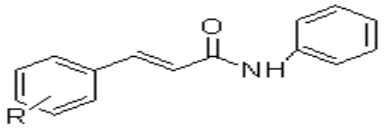


(21)

R = F ,Cl , OCH_3 ,NO_2

ANTICONVULSANT ACTIVITY

Synthesis of a series of chalcones of anilide and their corresponding product 1-[(4,5-dihydro-5-phenyl-3-(phenylamino)pyrazol-1-yl)]ethanone derivatives**(22)** were reported by Singh *et al*.,[21].The synthesised compound was evaluated for their anticonvulsant activity against electric shock induced convulsion method in rat at a dose of 125 mg/kg and 250 mg/kg intraperitonially.Their pharmacophoric groups are similar and the possible structure of suitable fused heterocyclic could be accepted to give anti convulsant activity.



(22)

R = $C_{19}H_{22}N_4O$,$C_{17}H_{16}N_4O_3$
$C_{17}H_{16}N_3OCl$,$C_{17}H_{17}N_3O$
$C_{17}H_{15}N_3OCl_2$,$C_{17}H_{17}N_3O_2$

CONCLUSION

The present study revealed that all mentioned chalcones and their derivatives, under this review showed promising biological activities. Thus, the quest to explore many more modifications on chalcone moiety needs to be continued.

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