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SYNTHESIS, CHARACTERIZATION AND BIOLOGICAL APPLICATIONS OF CHALCONES AND THEIR DERIVATIVES: A REVIEW

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ABSTRACT

Chalcone derivatives are considered valuable species because they possess a ketoethylenic moiety, −CO−CH=CH−. Due to the presence of a reactive α, β-unsaturated carbonyl group, chalcones and their derivatives possess a wide spectrum of antiproliferative, antifungal, antibacterial, antiviral, antileishmanial, and antimalarial pharmacological properties. Recent developments in heterocyclic chemistry have led to the synthesis of chalcone derivatives, which had been biologically investigated toward certain disease targets. Moreover, structural modifications provide various options and have been useful in developing more potent medications with reduced toxicity and advantageous pharmacological effects. Chalcones have a significant role in both industry and academia. Hence, present narrative review of literature study was conducted with the main purpose to describe and delineate on recent advances in synthesis, characterization and biological applications of chalcones and their derivatives.

Keywords: Chalcones, Derivatives, Synthesis, Characterization, Antidiabetic, Antibacterial

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INTRODUCTION

Chalcone is the absolute name for a simple chemical scaffold that is present in many compounds of natural origin, primarily in plants. The term chalcone is derived from the Greek word “chalcos”, which means bronze color, is the source of the term chalcone. This association is due to the yellow and orange color (like bronze) of plant tissues containing these compounds. Stanislaw Kostanecki and Joseph Tambor, who were the first scientists to synthesize these naturally occurring compounds with distinctive colors, first mentioned the term.[1] A pair of aromatic rings links an aliphatic chain of three carbon atoms, in this chemical.[2] It also has a ketone group and a notably reactive ketoethylenic group (-CO-CH=CH-).[3] A chalcone is a pigmented chemical with a chromophore (-CO-CH=CH-),[4] as illustrated in Figure 1.[5]

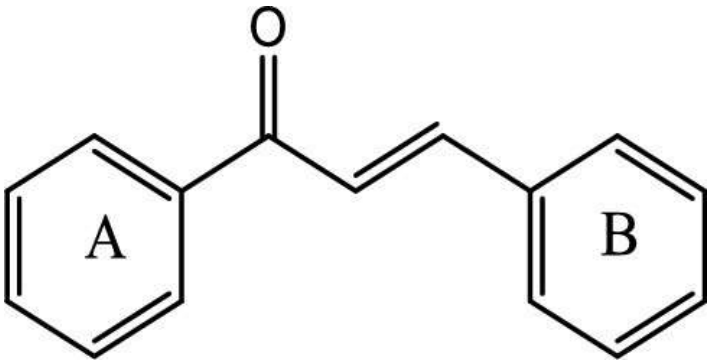

Figure 1. Structure of chalcone

Besides frequently offering effortless structural adaptation, organic materials can have the capacity to possess extraordinary biological or physical characteristics.[6] Among such belongs the group of chalcones and their by-products.[7] The remarkable properties of chalcone derivatives are normally attributed to the existence of the moiety of β, α-unsaturated.[8] A valuable structureactivity relationship can be made through the incorporation of diverse alternatives to the two aryl rings.[9] For this reason, these compounds have a broad spectrum of usages in industry and pharmacology.

10.48047/jocaaa.2024.33.06.194

Indeed, chalcones have been the object of several studies for different scopes, from nonlinear optics to a wide range of modulatory and cytoprotective activities.[10] They exhibit biological activity that has the potency to treat various disorders such as anti-inflammatory impacts,[11] anti-tuberculosis,[12] anti-cancer,[13] anti-leishmanial,[11] anti-microbial,[14] anti-malarial,[15] and antifungal properties,[16] as shown in Figure 2.[17]

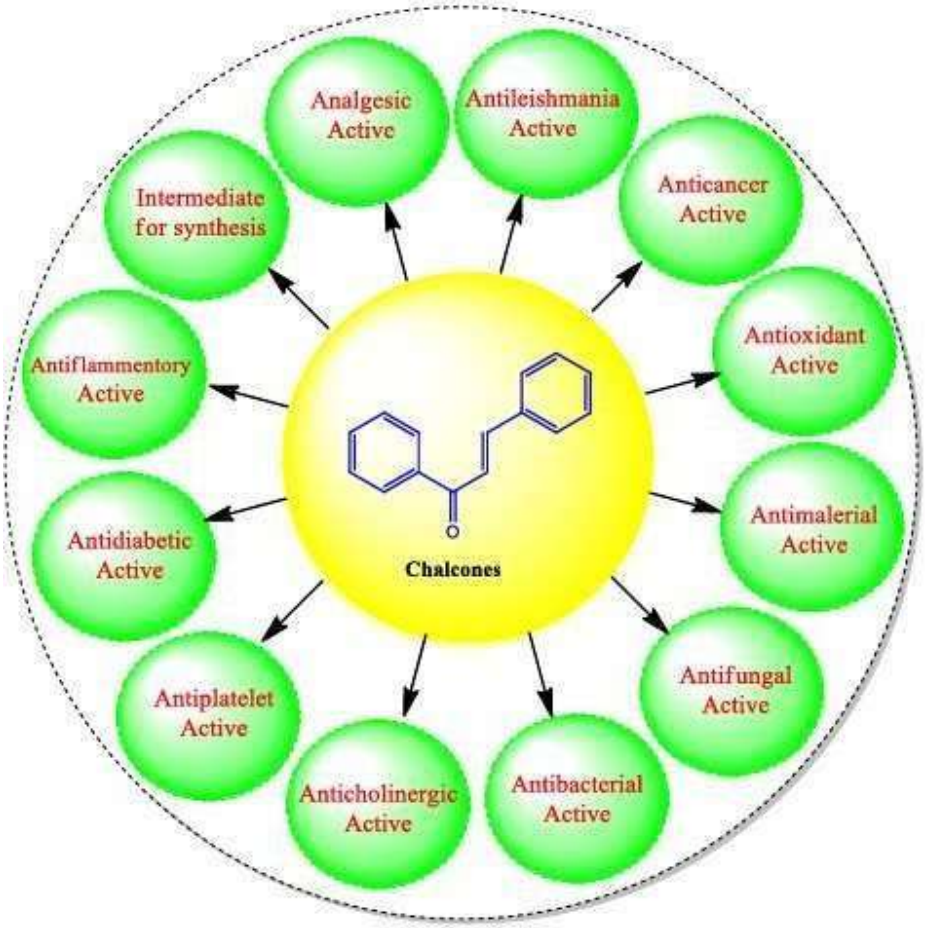

Figure 2. Biological activities of chalcones

Chalcones undergo many chemical reactions as well as being used to synthesize heterocyclic compounds. It is possible to synthesize a wide range of chalcone derivatives by treating aromatic aldehydes with aryl ketones in the presence of an appropriate amount of condensing agents.[18] By condensing aryl ketones with aromatic aldehydes and adding appropriate condensing agents, it is

10.48047/jocaaa.2024.33.06.194

possible to synthesize a wide range of chalcone derivatives. Chalcones are used in several biosynthetic pathways as initial intermediate structures in the production of flavonoids, isoflavonoids, and aurones.[19] A significant part of medicinal chemistry research in the 21st century has been focused on both natural and synthetic chalcones because of their various pharmacological potential.[11] Moreover, various researchers have attempted to grow new, successful antimicrobial reagents liberated from resistance and cost.[20] The Traditional micro sized fibers have applications especially in engineering fibers such as carbon, glass, and Kevlar fibers, is to be used as reinforcements in composite developments.[21] Furthermore, in the previous decade there has been a noticeable increment in the field of manufacture of nanoparticles with controlled morphologies and exceptional highlights making it a broad zone of research.[22]

With this background, present narrative review of literature study was conducted with the main purpose to describe and delineate on recent advances in synthesis, characterization and biological applications of chalcones and their derivatives.

SYNTHESIS AND CHALCONE DERIVATIVES

Synthesis of Chalcone Derivatives of 2-Acetyl Naphthalene Chalcones1a−g were constructed by treating 2-acetyl naphthalene with benzaldehyde and/or substituted benzaldehyde in methanol and potassium hydroxide, and the constructed derivatives exhibited antibacterial and antifungal activities (Scheme 1).[23]

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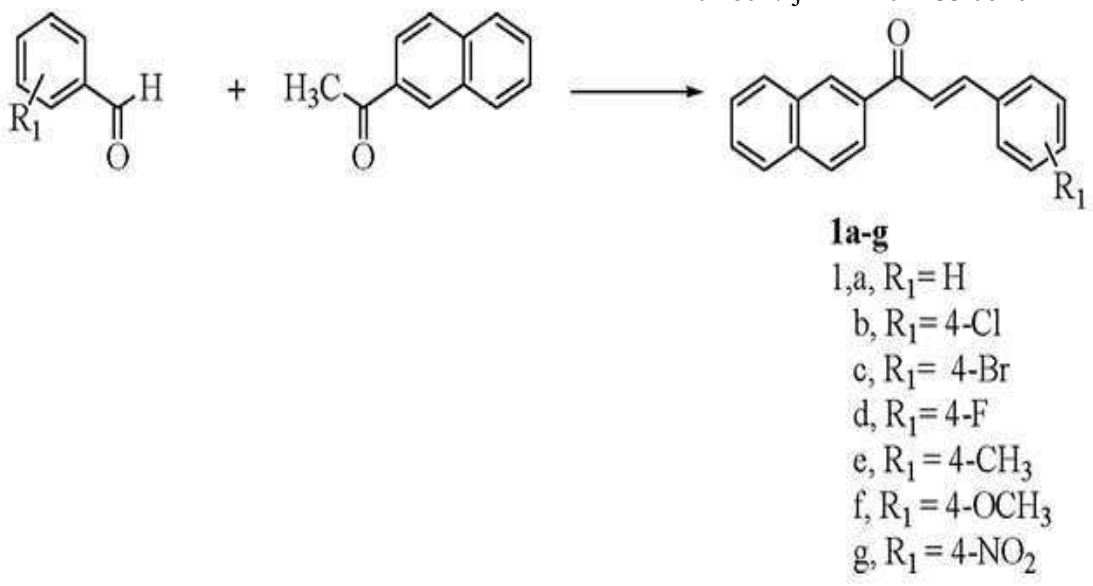

Scheme 1. Synthesis of Chalcones 1a−g

Synthesis of Chalcone Derivatives Bearing Triazine

The trisubstituted triazines 6a−f were constructed by treating aniline with cyanuric acid at 0−5 °C to yield monosubstituted triazine, which was reacted with substituted amine at RT to produce disubstituted triazine 4. Treating the latter 4 with 4-aminoacetophenone afforded the corresponding trisubstituted triazine 5, which was reacted with different aldehydes to provide chalcone derivatives 6a−f (Scheme 2).[24]

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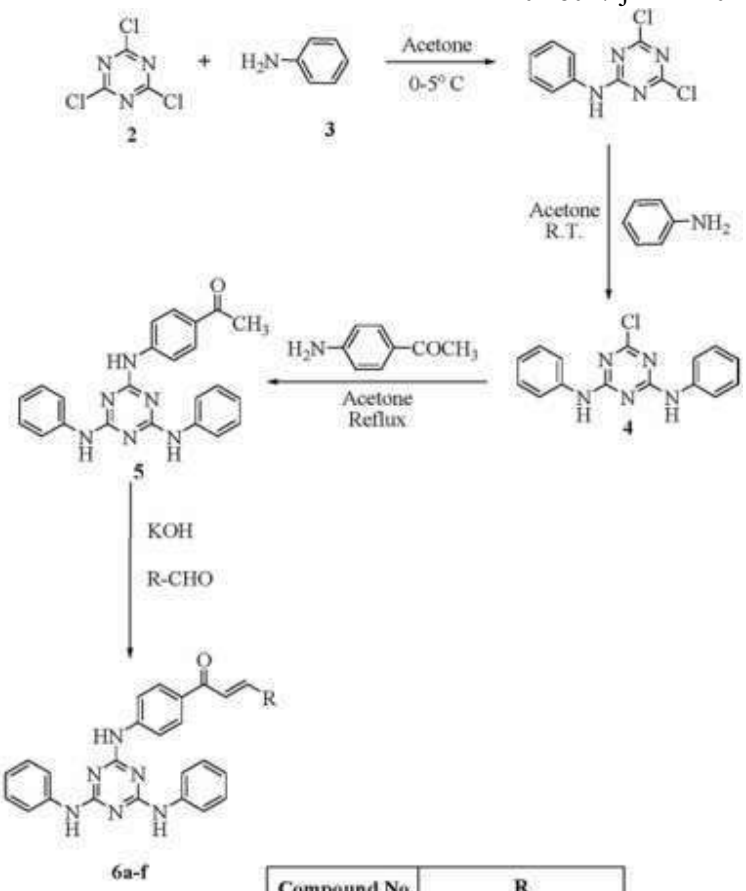

Compound No.	R
6a	5-methylfurfural
6b	3-nitrobenzaldehyde
6c	2-chlorobenzaldehyde
6d	2-bromobenzaldehyde
6e	3-bromobenzaldehyde
6f	4-bromobenzaldehyde

Scheme 2. Synthesis of Triazines 6a−f Containing Chalcone

Synthesis of Acetamido Chalcone Derivatives

Treatment of 4-acetamidoacetophenone (9) with substituted aldehydes in potassium hydroxide as the base in ethanol and sonication for 10−15 min using a water bath of ultrasonic cleaner afforded chalcone derivatives 10a−f (Scheme 3).[24]

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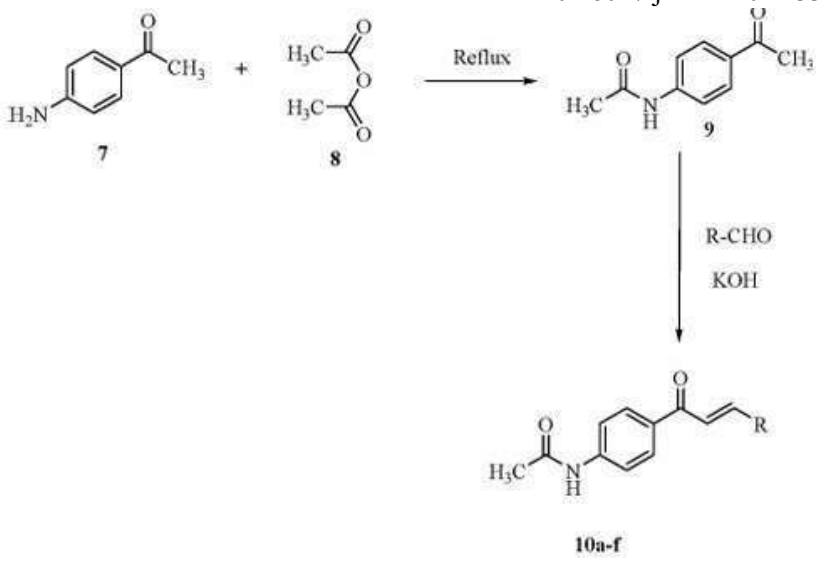

Compound No.	R
10a	5-methylfurfural
10b	3-nitrobenzaldehyde
10c	2-chlorobenzaldehyde
10d	2-bromobenzaldehyde
10e	3-bromobenzaldehyde
10f	2-methoxybenzaldehyde

Scheme 3. Synthesis of chalcones10a−f

Synthesis of Methoxyamino Chalcones

The chalcone derivatives 13−29 were synthesized via treatment of acetophenone derivative 11 and benzaldehyde derivative 12 in equal amounts using ethyl alcohol in 40% NaOH solution at 10°C and stirred for 1h and then at RT for 4h; the reaction proceeded via Claisen−Schmidt reactions (Scheme 4).[25]

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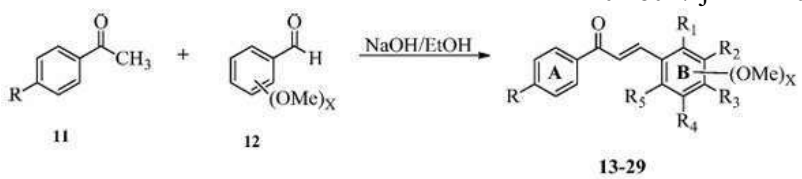

Compound	R	R_1	R_2	R_3	R_4	R_5
13	NH_2	OCH_3	H	H	H	H
14	NH_2	H	OCH_3	H	H	H
15	NH_2	H	H	OCH_3	H	H
16	NH_2	OCH_3	OCH_3	H	H	H
17	NH_2	OCH_3	H	OCH_3	H	H
18	NH_2	OCH_3	H	H	OCH_3	H
19	NH_2	H	H	H	H	H
20	H	OCH_3	H	H	H	H
21	H	H	H	OCH_3	H	H
22	H	H	H	OCH_3	H	H
23	H	OCH_3	OCH_3	H	H	H
24	H	OCH_3	H	OCH_3	H	H
25	H	OCH_3	H	H	OCH_3	H
26	Br	H	H	OCH_3	H	H
27	Br	OCH_3	H	OCH_3	H	H
28	Br	OCH_3	H	H	OCH_3	H
29	H	H	H	H	H	H

Scheme 4. Synthesis of chalcones derivatives 13−29

Synthesis of Sappanchalcone

Chalcone derivatives 32–44 were constructed via a Claisen–Schmidt reaction by treatment of benzaldehyde derivatives and acetophenone derivatives in methanol and potassium hydroxide and subject to ultrasonic irradiation for 8 h, utilizing a water bath at 80°C, and exhibited XO inhibitory activity (Scheme 5-7).[26]

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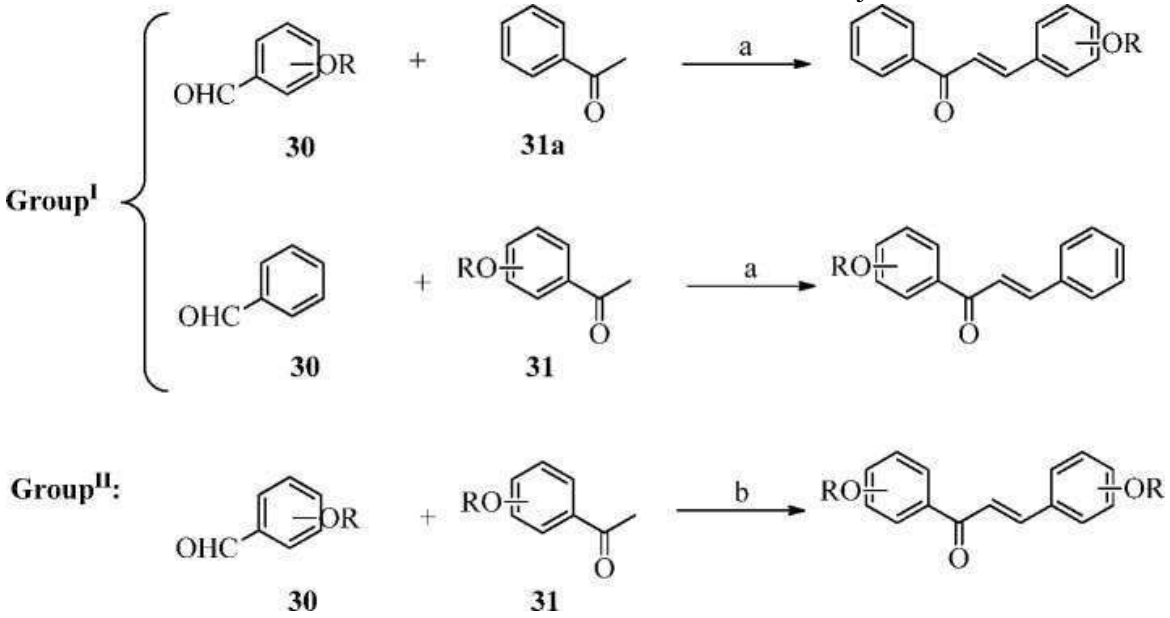
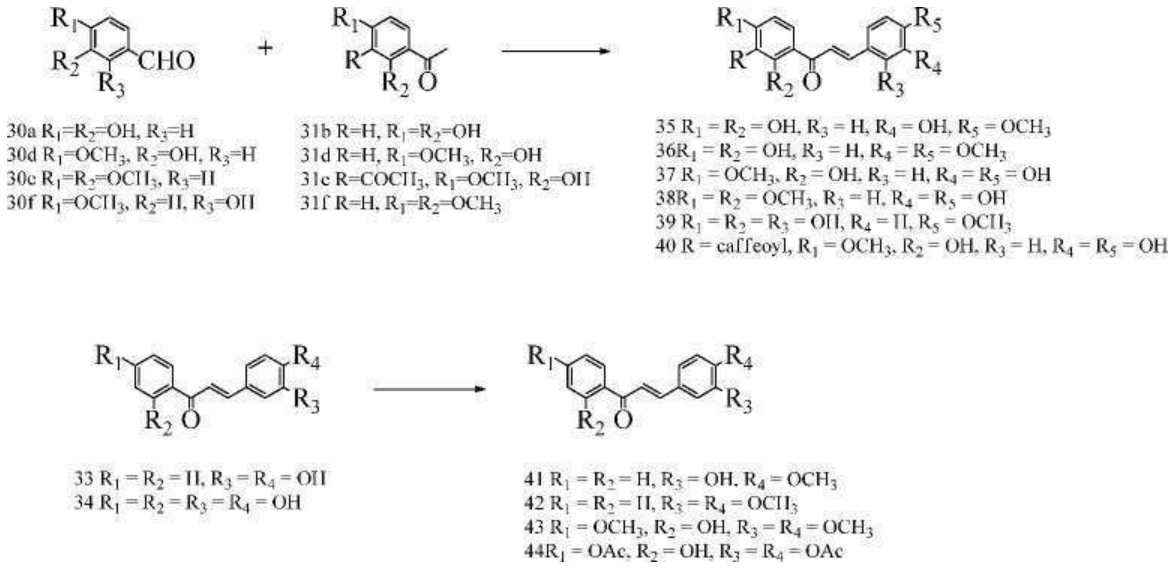
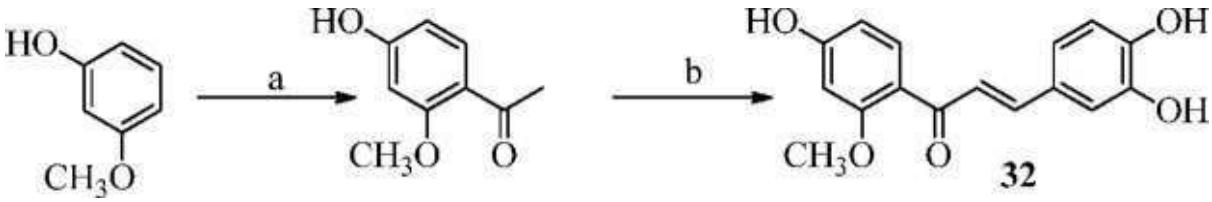


Scheme 5. Construction of Chalcone Derivatives

Reagents and conditions: (a) KOH_{aq}, MeOH, ultrasound-assisted; (b) KOH_{aq}, ultrasound-assisted



Scheme 6. Synthesis of Chalcone Derivatives 35–44



Scheme 7. Synthesis of Sappanchalcone 32

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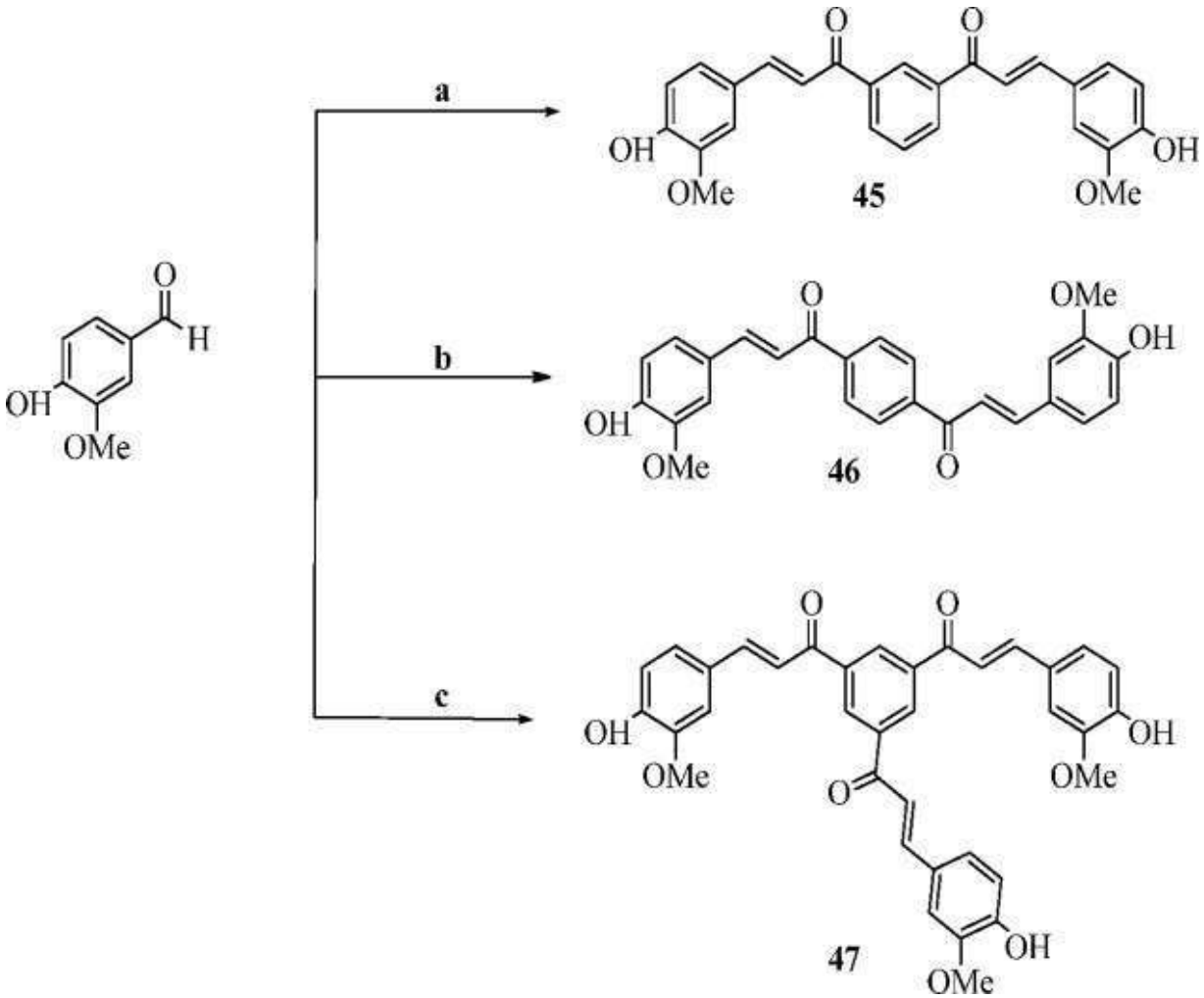
Reagents and conditions: (a) CH3COOH, polyphosphoric acid, 60°C, 30 min; (b) 2′,4′-dihydroxyacetophenone, 12 M KOH, ultrasound-assisted, 80°C, 8 h.

Synthesis of Chalcone Derivatives from 1,3-Diacetylbenzene and 1,4-Diacetylbenzene Construction and biological potential of chalcone derivatives 45–47 were reported. These compounds were synthesized through acid-catalyzed one-step condensation of 1,3- and/or 1,4diacetylbenzene and 1,3,5-triacetylbenzene with 4-hydroxy-3-methoxybenzaldehyde in the presence of acids as acetic acid, concentrated hydrochloric acid, phosphoric acid, and concentrated sulfuric acid. The best result was achieved in case using concentrated sulfuric acid in ethanol (Scheme 8).[27]



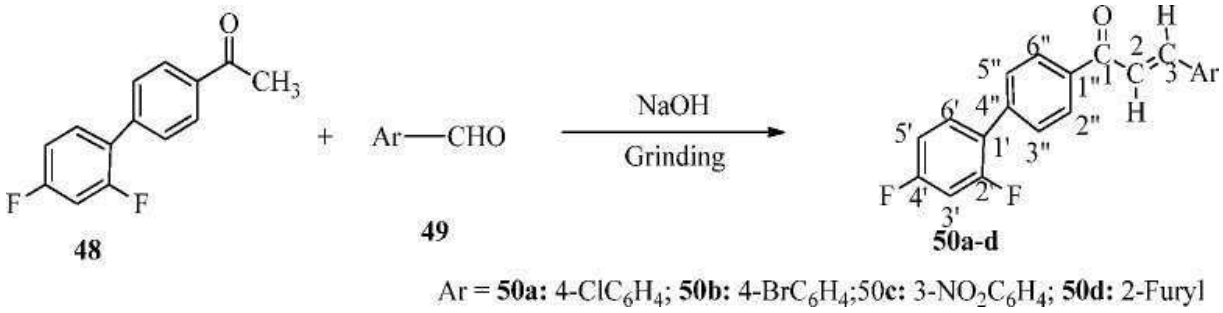
Scheme 8. Synthesis of Chalcone Derivatives from 1,3-Diacetylbenzene and 1,4Diacetylbenzene

Reagents and conditions: (a) H_2SO_4, 1,3-diacetylbenzene, ethyl alcohol, reflux, 3 h; (b) H2SO4, 1,4-diacetylbenzene, ethyl alcohol, reflux, 3 h; (c) H_2SO_4, 1,3,5-triacetylbenzene, reflux, 3 h.

10.48047/jocaaa.2024.33.06.194

Synthesis of Chalcone Derivatives from 1-(2′,4′-Difluorobiphenyl-4-yl)ethanone

The chalcone derivatives 50a–d were prepared in good yield via solvent-free Claisen–Schmidt condensation reaction of equal amounts of 1-(2′,4′-difluorobiphenyl-4-yl)ethanone with many aldehydes in 40% NaOH, leading to the formation of a sodium adduct which was neutralized by diluted HCl in cold water to afford the corresponding chalcone derivatives 50a–d (Scheme 9).[28]



Ar = **50a:** 4-ClC_6H_4; **50b:** 4-BrC_6H_4;**50c:** 3-$NO_2C_6H_4$; **50d:** 2-Furyl

Scheme 9. Synthesis of (E)-1-(2′,4′-Difluorobiphenyl-4-yl)-3-arylprop-2-en-1-ones

Synthesis of Chalcone from Acetophenone Derivatives

Treatment of hydroxyacetophenone 51 with benzaldehyde derivative 52 in 50% KOH provided the corresponding chalcones 53–56, and the highest yield of chalcones ranged from 93 to 97%.[29] On the other hand, chalcone 53 was prepared in a low 32% yield in the presence of KOH as the catalyst,[30] whereas chalcone B was synthesized with BF_3-Et_2O catalyst in a high yield 90%.[31] Reaction of veratraldehyde with 4-hydroxyacetophenone yielded chalcone 54 in a high 97% yield.

However, treatment of 2,4-dihydroxyacetophenone provided the corresponding chalcone 55 in 96% yield and 56 in 93% yield (Scheme 10).[29]

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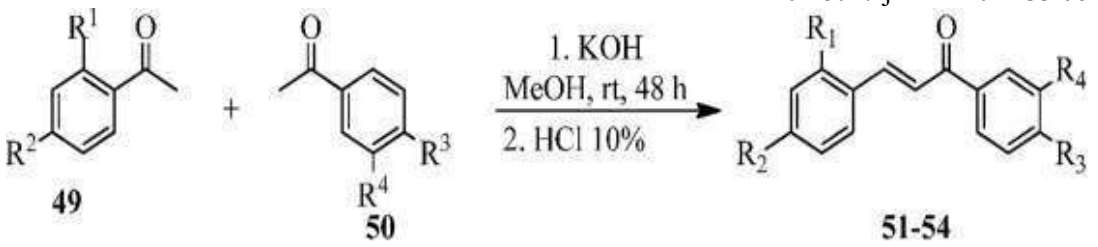
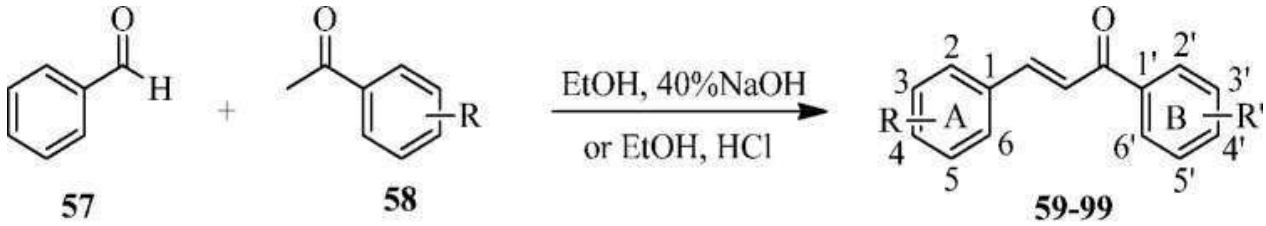


Chalcone 51: R_1= H; R_2= OH; R_3= OCH_3 ; R_4= H, 96%
Chalcone 52: R_1= H; R_2= OH; R_3= R_4= OCH_3, 97%
Chalcone 53: R_1= H; R_2= OH; R_3= Cl; R_4= H, 96%
Chalcone 54: R_1= R_2= OH; R_3= Cl; R_4= H, 93%

Scheme 10. Synthesis of Chalcones 53–56

Chalcone derivatives 59–99 were constructed by treating aldehyde 57 with acetophenone 58 in ethanol containing NaOH 40% or few drops of hydrochloric acid (Scheme 11 and Table 1).[32]



R,R' =Halogen, -NH_2, OCH_3, -OCH_2CH_3; Catalyst: 40% NaOH
R/R' = -OH; catalyst: HCl

Scheme 11. Construction of Chalcones 59–99

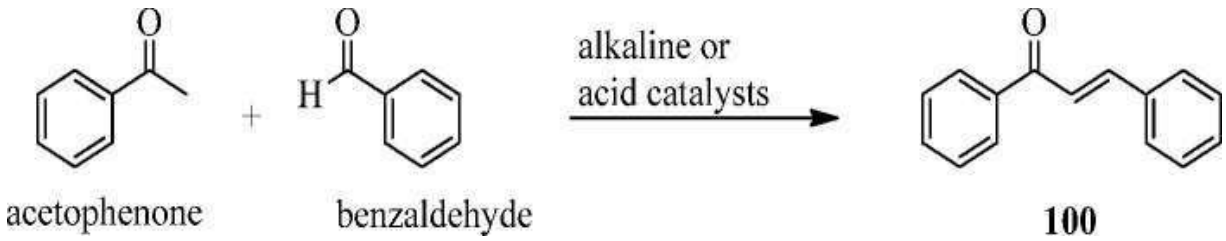
Reagents and conditions: ethyl alcohol, 40% NaOH or HCl, room temperature, 12–24 h

Table 1. Synthesis of Chalcone Derivatives 59–99

10.48047/jocaaa.2024.33.06.194

compound no.	R	R′	compound no.	R	R′
59	3,4-OH	3-OH	80	3,4-OCH_3	3,5-F
60	3,4-OCH_3	3-OH	81	4-OCH_3	3,4-OH
61	3,4-OH	4-NH_2	82	4-OCH_3	,4-OCH_3
62	3,4-OCH_3	4-NH_2	83	3-OH, 4-OCH_3	3,4-OH
63	3,4-OH	4-OCH_3	84	3-OH, 4-OCH_3	3,4-OCH_3
64	3,4-OCH_3	4-OCH_3	85	2,4-OCH_3	3,4-OH
65	3,4-OH	4-OCH_2CH_3	86	2,4-OCH_3	3,4-OCH_3
66	3,4-OCH_3	4-OCH_2CH_3	87	2-OCH_3	3,4-OH
67	3,4-OH	4-Cl	88	2-OCH_3	3,4-OCH_3
68	3,4-OCH_3	4-Cl	89	2,3-OCH_3	3,4-OH
69	3,4-OH	2-F	90	2,3-OCH_3	3,4-OCH_3
70	3,4-OCH_3	2-F	91	2,5-OCH_3	3,4-OH
71	3,4-OH	2-Cl	92	2,5-OCH_3	3,4-OCH_3
72	3,4-OCH_3	2-Cl	93	4-Cl	3,4-OH
73	3,4-OH	4-F	94	4-Cl	3,4-OCH_3
74	3,4-OCH_3	4-F	95	3,4-Cl	3,4-OH
75	3,4-OH	3,4-F	96	3,4-Cl	3,4-Cl
76	3,4-OCH_3	3,4-F	97	3,4,5-OCH_3	3,4,5-OCH_3
77	3,4-OH	3,4-OCH_3	98	3,4,5-OCH_3	3,4,5-OCH_3
78	3,4-OCH_3	3,4-OCH_3	99	3,4-OCH_3	3,4-OCH_3
79	3,4-OH	3,5-F			

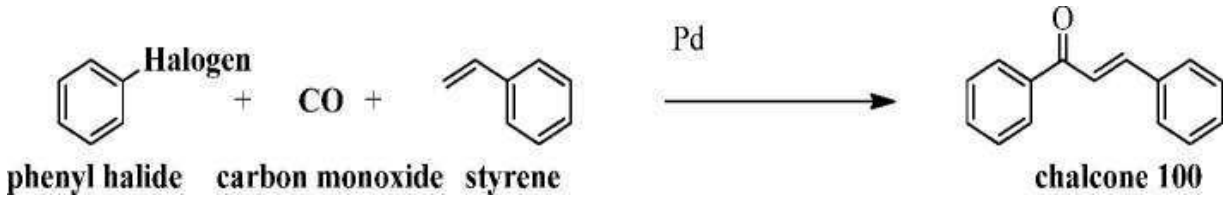
Treatment of benzaldehyde and acetophenone derivatives in acid catalyst or alkaline conditions at 50–100°C in presence of liquid solvent led to 100 (Scheme 12).[33,34]



Scheme 12. Claisen–Schmidt Condensation

Synthesis of Chalcone from Phenyl Halide

Chalcone 100 was prepared by reaction of phenyl halide and styrene in carbon monoxide and pd catalyst (Scheme 13).[35]



Scheme 13. Construction of Chalcone Derivative 100

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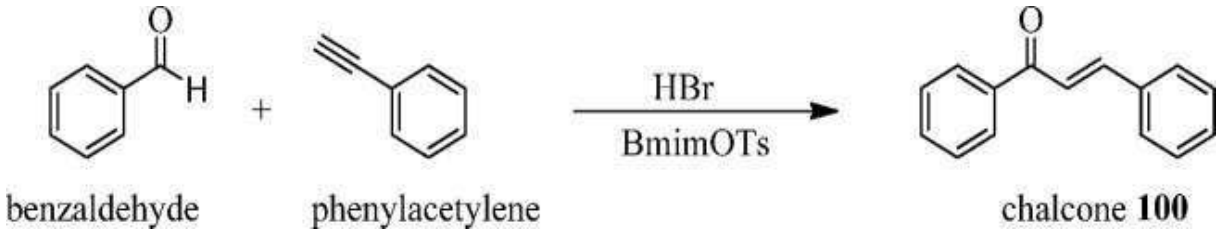
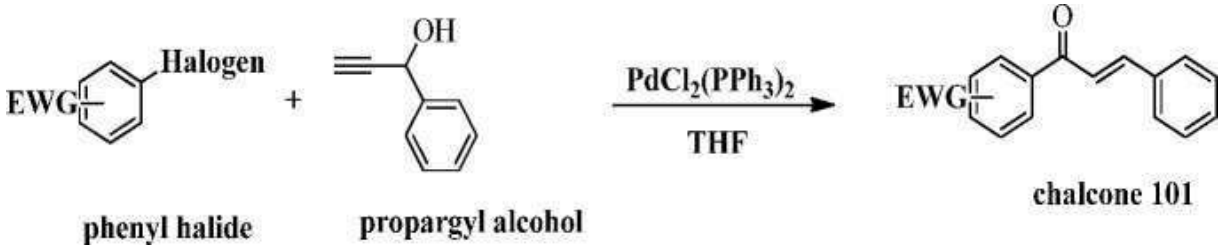
Treatment of phenylacetylene with benzaldehyde in and HBr at 100 °C for 12 h provided the corresponding chalcone 99. The reaction proceeds via a coupling reaction (Scheme 14).[36]



Scheme 14. Synthesis of Chalcone 100 via a Coupling Reaction

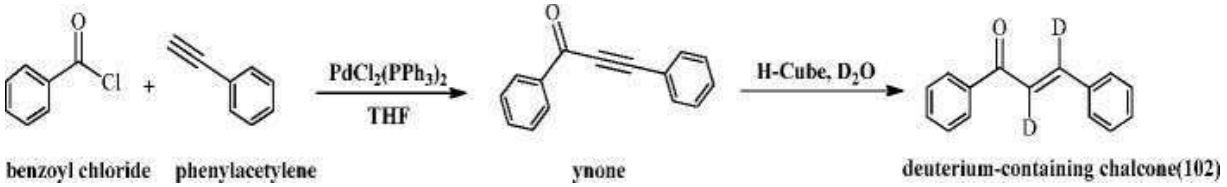
Chalcone derivative 101 was constructed from the reaction of propargyl alcohol and phenyl halide using microwave irradiation utilizing $PdCl_2(pph_3)_2$ in THF (Scheme 15).[37]



Scheme 15. Synthesis of Chalcone 101

Synthesis of Chalcone Derivatives from Benzoyl Chlorides

Ynones were synthesized by reaction of benzoyl chlorides and phenylacetylenes using Sonogashira conditions described in a literature procedure. Ynones undergo deuterations using the H-Cube system using D_2O instead of water (Scheme 16).[38]



Scheme 16. Synthesis of Chalcone 102 via Continuous-Flow Deuteration Reaction

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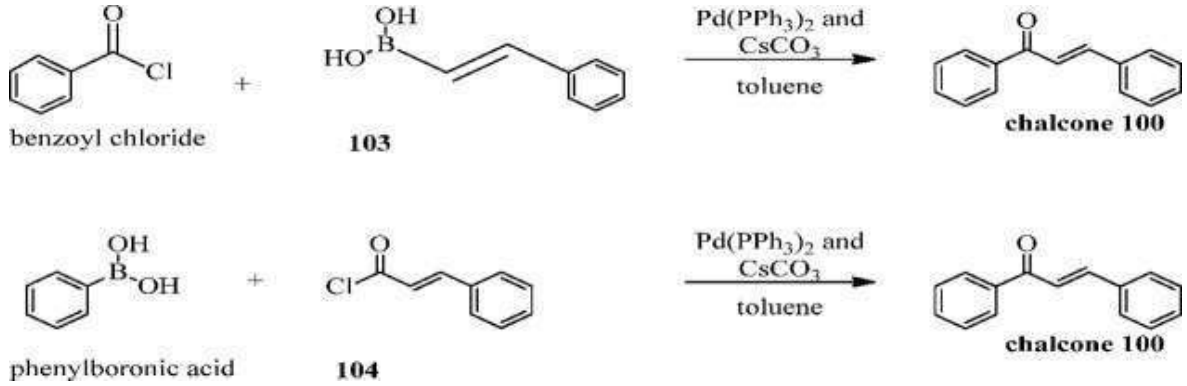
Chalcone 100 was synthesized by reaction of benzoyl chloride with styrylboronic acid 103 in anhydrous toluene and in presence of $Pd(PPh_3)_4$ and $CsCO_3$. Also, from the reaction of cinnamoyl chloride 104 and phenylboronic acid in anhydrous toluene and in the presence of

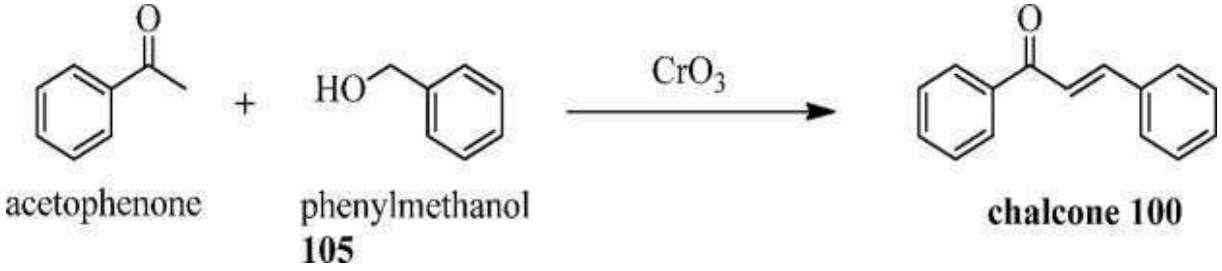
$Pd(PPh_3)_4$ and $CsCO_3$, the reaction proceeds via the Suzuki–Miyaura coupling reaction (Scheme 17).[39]



Scheme 17. Synthesis of Chalcone 100 through Suzuki–Miyaura Coupling Reaction

Synthesis of Chalcone via One-Pot Synthesis

Treatment of phenylmethanol 105 and acetophenone using CrO_3 as the oxidizing agent provided chalcone derivative 100 (Scheme 18).[33]



Scheme 18. One-Pot Synthesis of Chalcone 100

Treatment of benzaldehyde and phenylacetylene under microwave irradiation using heterogeneous acid in a catalytic amount in 1,2-dichloroethane as solvent provided the corresponding chalcone 100 (Scheme 19).[40]

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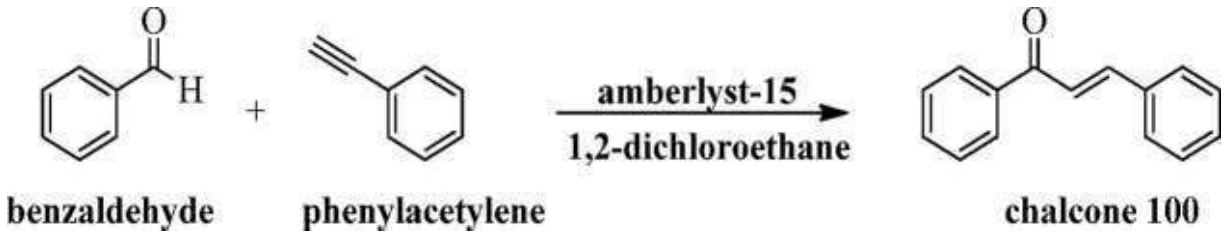

Scheme 19. Synthesis of Chalcone Using Solid Acid Catalyst

Chalcones from Natural Product

Chalcones occur in natural products derived from plant species, such as Macaranga denticulata, which contains compound 106.[41] Also, Uvaria siamensis roots contain compound 107;[42] compound 108 is derived from Stevia lucida,[43] and compound 109 is found in Pongamia pinnata (L.).[44] Hydroxychalcone-based sugar functionalities 110–112 were separated from Coreposis lanceolata flowers (Scheme 20).[45]

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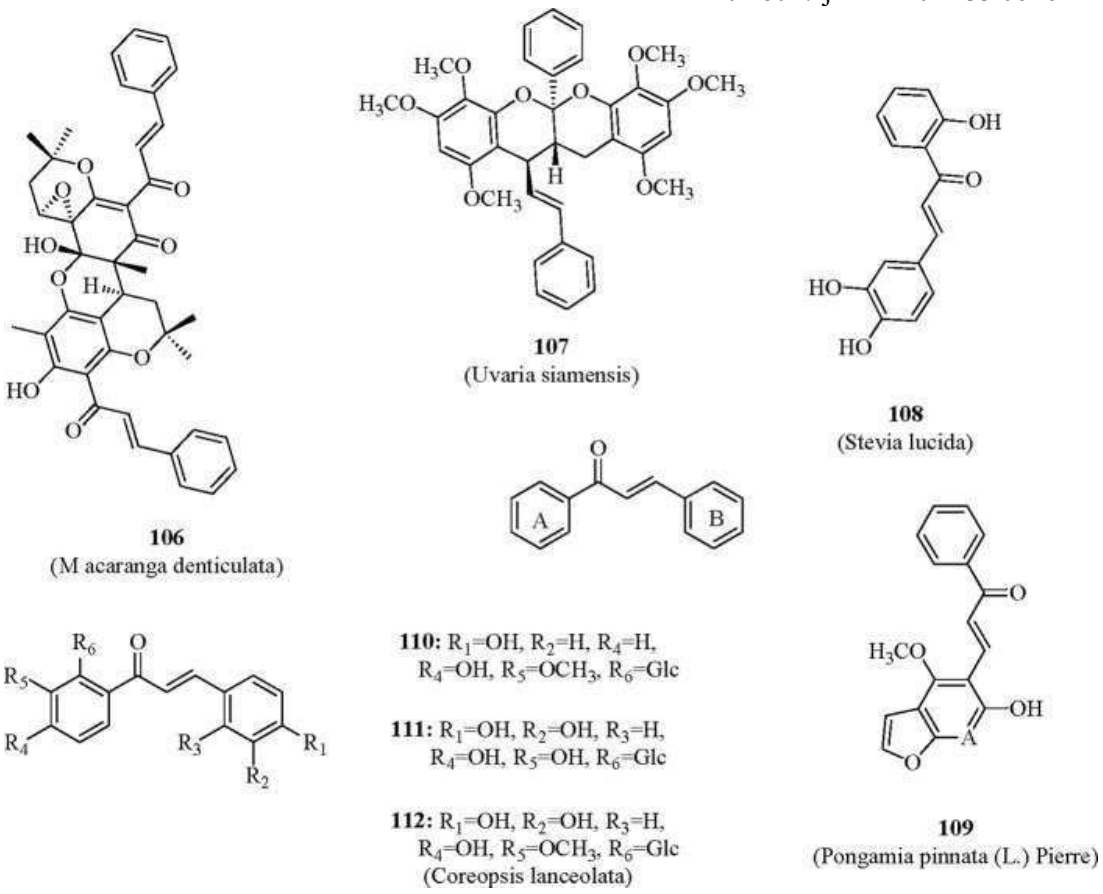


Scheme 20. Chalcones from natural products

CHARACTERIZATION OF CHALCONE DERIVATIVES

Chalcones are an important class of flavonoid precursors characterized by an α,β-unsaturated carbonyl bridge connecting two aromatic rings. These compounds have attracted considerable attention because of their diverse pharmacological activities, including anticancer, antimicrobial, anti-inflammatory, and antioxidant properties. Accurate characterization is essential for confirming structural integrity and establishing relationships between chemical structure and biological activity.[11,46,47]

Literature reports evidenced that the synthesized nanofibers were further characterized by employing the standard techniques such as FTIR, SEM and X-RD for Chemical, Morphological and

10.48047/jocaaa.2024.33.06.194

for Structural studies, respectively.[21] Also, the nanoparticles were characterized using UVVisble, Fourier transform infrared spectroscopy (FTIR), X-ray diffraction (XRD), and Scanning electron microscopic (SEM) methods.[22] Fourier-transform infrared (FT-IR) spectroscopy is widely employed for the preliminary characterization of chalcones and their derivatives. The presence of a conjugated carbonyl group is typically indicated by absorption bands around 1650–1680 cm^{-1}, while aromatic C=C stretching vibrations further support the chalcone framework. Ultravioletvisible (UV-Vis) spectroscopy also provides valuable information regarding electronic transitions associated with the conjugated π-system.[48,49]

Nuclear magnetic resonance (NMR) spectroscopy remains the most definitive analytical technique for structural elucidation. In ^{1}H NMR spectra, trans-olefinic protons generally exhibit coupling constants of approximately 15–16 Hz, confirming the E-configuration of the α,βunsaturated system. Complementary ^{13}C NMR and two-dimensional NMR experiments facilitate detailed assignment of carbon and proton environments in substituted chalcone derivatives.[6,49] Mass spectrometry (MS), liquid chromatography-mass spectrometry (LC-MS), which can isolate and analyze compounds in a single step using a mass detector and available GC–MS libraries,[50] and high-performance liquid chromatography (HPLC) are routinely utilized to determine molecular mass, purity, and fragmentation patterns. Previously GC-MS technique was for employed for the characterization of plant secondary metabolites.[51] Also, these techniques are particularly useful in the characterization of newly synthesized chalcone analogues and in monitoring synthetic transformations during drug development studies.[6,52]

Recent advances have incorporated single-crystal X-ray diffraction, density functional theory (DFT), molecular docking, and electrochemical analyses to investigate molecular geometry, electronic properties, and structure–activity relationships. Such multidisciplinary characterization

10.48047/jocaaa.2024.33.06.194

approaches have significantly enhanced the understanding of chalcone derivatives and facilitated their applications in medicinal chemistry, materials science, and chemical sensing technologies.[49,53-55]

BIOLOGICAL ACTIVITIES OF CHALCONE DERIVATIVES

The main role of antimicrobial agents is to lessen the burden of infectious illnesses worldwide.[56] But, because there are fewer, or occasionally no, effective antimicrobial treatments available for the illness caused by pathogenic bacteria, the rise and spread of multi-drug resistance (MDR) strains in pathogenic bacteria have grown to be a serious concern to public health .[57] Finding novel antimicrobial drugs is therefore of utmost relevance in view of the evidence of the fast worldwide spreading of resistant clinical isolates.[58]

Antibacterial activity

Chalcone derivatives and their heterocyclic structures form the basis for antibiotic development. Shaik and his colleagues reported the synthesis of a new bioactive isoxazolyl chalcone and its derivative dihydropyrazole. Every synthetic product undergoes testing to determine its antibacterial efficacy against a mixture of Staphylococcus aureus and Pseudomonas aeruginosa. Every chemical demonstrates antibacterial action. The medication containing the 2,4,6trimethoxyphenyl ring (150) exhibited greater antibacterial activity than ciprofloxacin.

Furthermore, the produced compounds have antifungal, antioxidant, and anticancer properties.[59-61]

In a study conducted by Meshram and Vala, they investigated the synthesis of chalcone derivatives that incorporated the oxadiazole moiety using the Claisen-Schmidt condensation reaction. An assessment was conducted to determine the compound's effectiveness against various

10.48047/jocaaa.2024.33.06.194

bacteria, including Staphylococcus aureus, Streptococcus pyogenes, E. coli, and Pseudomonas aeruginosa. Antimicrobial agents and bacterial microdilution methods were employed for this evaluation. While all the compounds that were evaluated had a strong anti-inflammatory effect, compounds (151) and (152) demonstrated the highest potency (Figure 3). The antibacterial activity of chalcone derivatives is increased when they contain an oxadiazole ring and a benzimidazole skeleton since these heterocyclic moieties.[62]

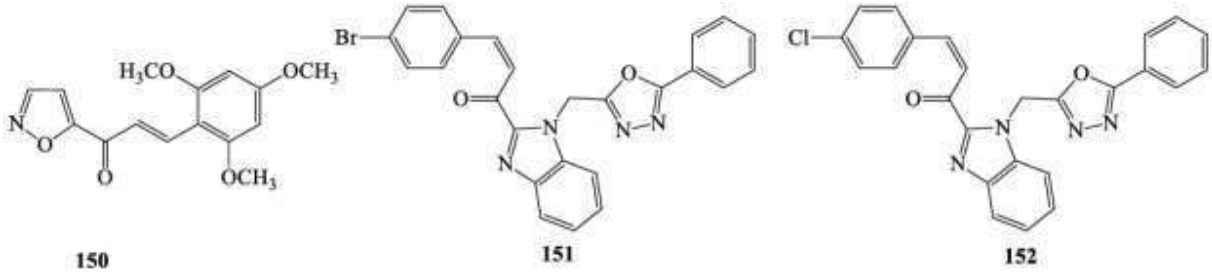


Figure 3. Antibacterial active chalcones

Antifungal activity

Osmaniye et al., conducted a study on the synthesis of imidazolyl chalcones. These chalcones were composed of 4-substituted benzaldehyde derivatives of imidazole acetophenone and were created via the Claisen-Schmidt condensation procedure. The efficacy of the synthesized drug was evaluated against four strains of Candida, namely Candida albicans (ATCC 24433), Candida krusei (ATCC 6258), Candida parapsilosis (ATCC 22019), and Candida glabrata (ATCC 90030). The study also included comparing the medication with acute ketoconazole and ketoconazole in combination with pesticide data. Fluconazole. Compound (148) was shown to be effective against all Candida species as an antibiotic versus ketoconazole and was evaluated as the most effective compound in the series.[63] Similarly, Sunitha et al., described the production of biscisoxazole compounds combined with chalcone compounds. Various synthetic antibiotics were evaluated for their effectiveness against Microsporumcanis, Microsporum gypsum, and Epidermophyton floccosum. The antibiotics

10.48047/jocaaa.2024.33.06.194

were combined with nystatin (75) and tested at 100 μg/mL concentration. Compounds (153), (154), (155), and (156) were found to have the highest antiinflammatory properties and also showed strong anti-inflammatory properties (Figure 4).[64]

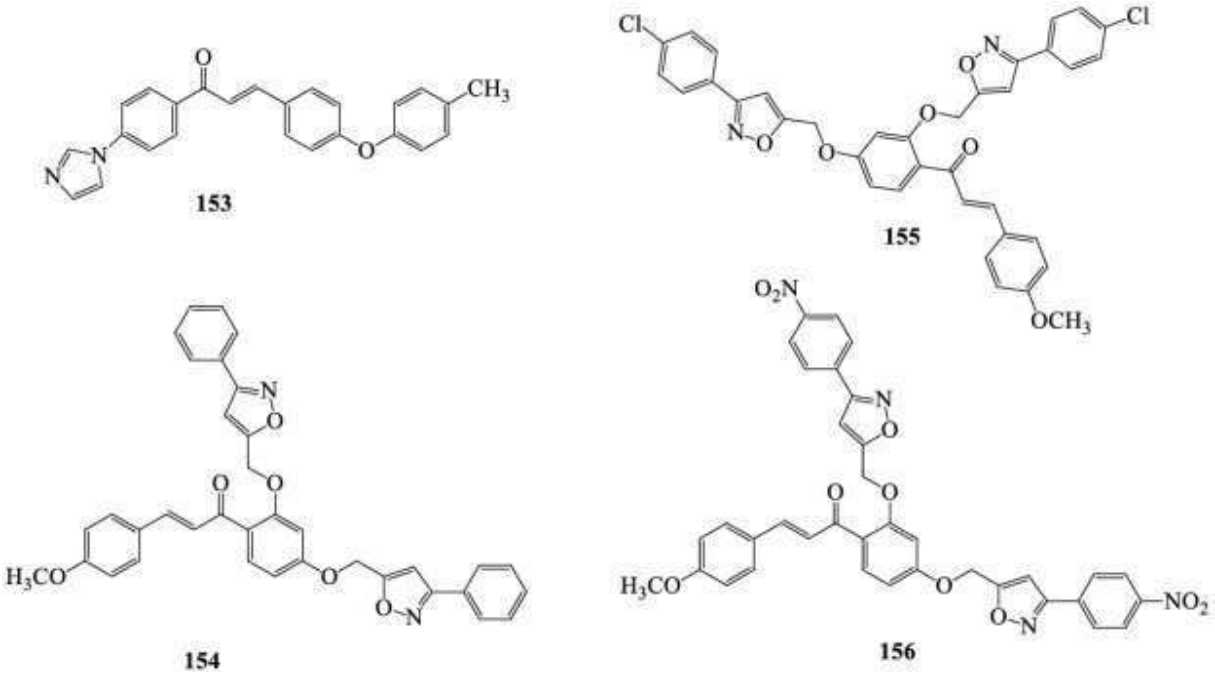


Figure 4. Antifungal active chalcones

Antioxidant activity

A recent study by Bhat et al., unveiled a novel collection of bioactive chalcone derivatives that incorporate 1,2,3-triazolyl groups. The synthesis of these derivatives was accomplished by the Claisen−Schmidt reaction. The antioxidant capabilities of these compounds were subsequently evaluated using the ABTS antioxidant test technique, which quantifies the capacity of a chemical to eliminate free radicals. The assessment of the antioxidant activity demonstrated that most of the examined compounds exhibited a range of moderate to outstanding DPPH and ABTS radical scavenging capabilities compared to the positive control, ascorbic acid. Two distinct compounds, (157) and (158), exhibited exceptional efficacy and potency. Compound (157) featured a 3,4dimethyl phenyl group, whilst compound (158) possessed a 1,3-(biphenyl)-1Hpyrazole group

10.48047/jocaaa.2024.33.06.194

connected to the third position of the chalcone moiety. These compounds exhibited notable DPPH radical scavenging capacity, with IC_{50} values of 15.33 and 14.48 μM, respectively, compared to ascorbic acid, which had an IC_{50} value of 12.27 μM. Moreover, the ABTS assay method verified the antioxidant activity of compounds (157) and (158), exhibiting inhibition percentages of 80.4% and 81.8%, respectively, compared to the positive control ascorbic acid, which displayed 88.5% inhibition.[65]

A study by Kumari et al., found that the arylic substitutions with pyrazolic chalcones, synthesized through Claisen−Schmidt condensation, showed strong antimicrobial and antioxidant properties. The antioxidant potential of these compounds was assessed using the DPPH method, with ascorbic acid as the standard reference. Compound (159) exhibited significant radical scavenging activity with an IC_{50} value of 88.04 μg/mL, whereas the standard drug ascorbic acid demonstrated a 48 μg/mL value. Overall, these findings emphasize the impressive antioxidant activities of the synthesized chalcone derivatives and their wide range of potential applications in various fields (Figure 5).[66]

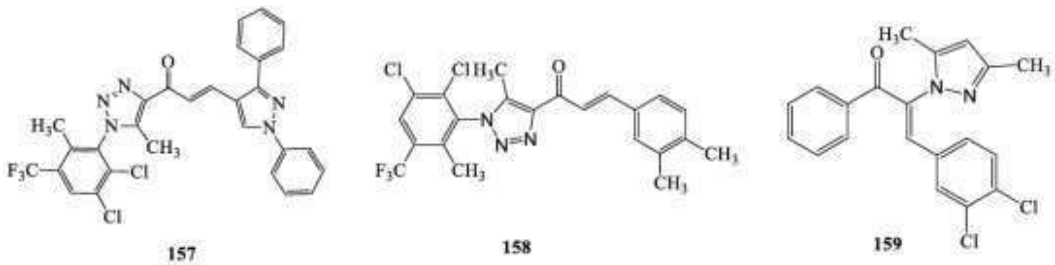


Figure 5. Antioxidant active chalcones

Antimalarial activity

Numerous antimalarial drugs, such as artemisinin derivatives, are currently in use. However, the development of resistance to these drugs is a significant concern, as it contributes to the widespread malaria epidemic and undermines efforts to control the disease. To address this issue, it is crucial to

10.48047/jocaaa.2024.33.06.194

develop new vaccines, particularly targeting the Plasmodium falciparum virus responsible for causing severe malaria.[67] Jyoti et al., have recently published a study on synthesizing indolyl chalcone derivatives and their evaluation for in vitro antibacterial activity against the Plasmodium falciparum NF54 strain. Compound (160) demonstrated exceptional efficacy against Plasmodium, exhibiting an impressive IC_{50} value of 2.1 mM/L. In previous studies, molecular hybrids were created using suitable linkers by combining the quinoline moiety with different chalcone derivatives.[68] The effectiveness of these molecular hybrids was evaluated against the drugsusceptible P. falciparum strain (NF54). Compounds (161), (162), and (163) demonstrated the highest potency against Plasmodium activity. When focusing on multidrug-resistant P., specifically Plasmodium falciparum, compounds (161) and (162) showed limited effectiveness against K1 (Figure 6).[69]

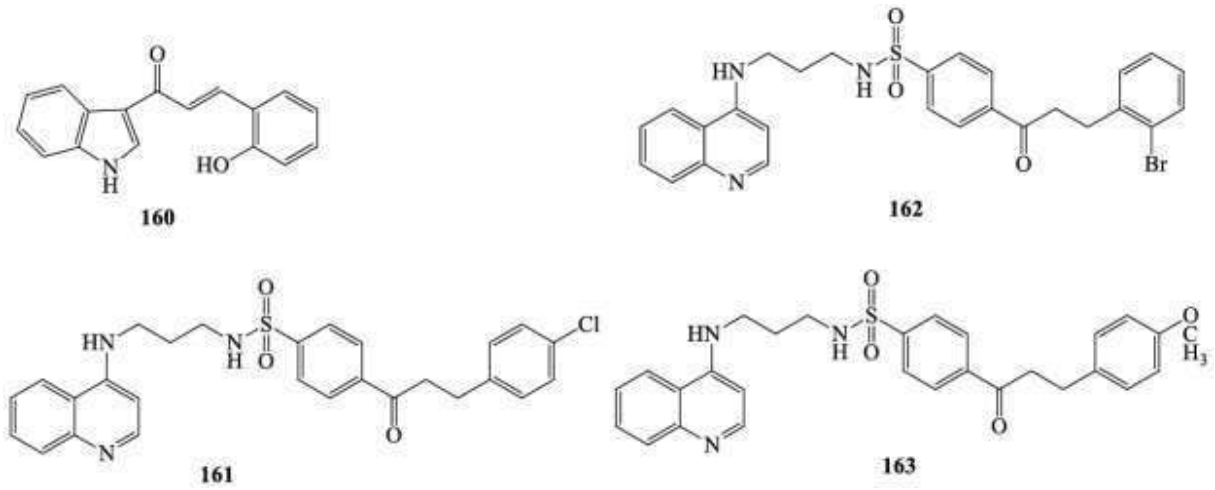
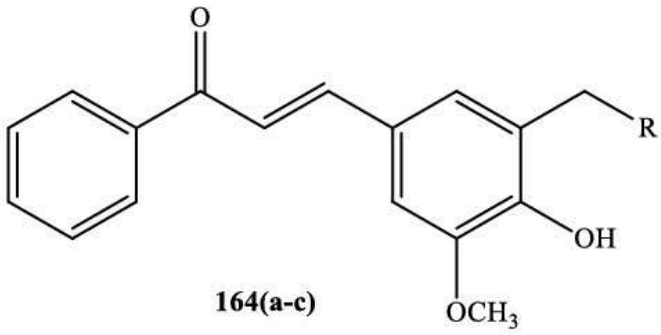


Figure 6. Antimalarial active chalcones

Three chalcone derivatives 164(a-c) were synthesized through the Claisen-Schmidt condensation reaction of chloroacetophenone and vanillin. After this reaction, the amine group is added through the Mannich reaction. The compound's antimalarial activity was tested against the P.

10.48047/jocaaa.2024.33.06.194

falciparum strain (3D7), and molecular docking was conducted. Based on molecular docking and biological testing, it was determined that the 164(b)-component exhibited superior synthetic properties (Figure 7).[70]



164(a-c)

Compound	R
a	Morpholine
b	Piperidine
c	Diethylamine

Figure 7. Derivatives of antimalarial active chalcones

Antiviral activity

A series of chalcone derivatives with pyridine were synthesized, and chemical analysis was performed to assess their antibacterial effectiveness. Many newly created medications have antibodies targeting the cucumber mosaic virus (CMV). Several drugs have been scientifically proven to have anti-inflammatory properties. Chalcone derivatives (165) exhibit therapeutic, inactivating, and anti-inflammatory properties. In addition, chalcone (166) demonstrated impressive effectiveness against CMV, as shown in (Figure 8).[71]

10.48047/jocaaa.2024.33.06.194

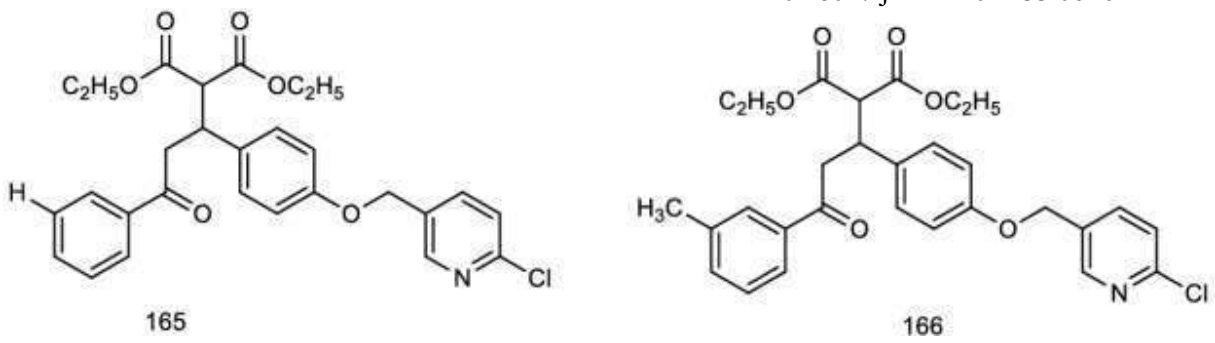


Figure 8. Chalcones with antiviral properties

Antidiabetic activity

Diabetes is an important human ailment afflicting many from various walks of life in different countries. Diabetes mellitus is a complex and a diverse group of disorders that disturbs the metabolism of carbohydrate, fat and protein.[72] According to the International Diabetes Federation (IDF), a total of 387 million people were diagnosed with diabetes worldwide in 2014, with the figure expected to rise to 592 million by 2035.[73] Chalcones 65 was synthesized (Figure 9) and evaluated for their antidiabetic activity through an oral glucose tolerance test to gain preliminary information regarding the antihyperglycemic effect in normal Swiss albino male mice. The derivatives showed a significant blood glucose lowering effect. The compounds were selected for in-vivo antidiabetic activity and found to be potential candidates for the treatment of diabetes.[74]

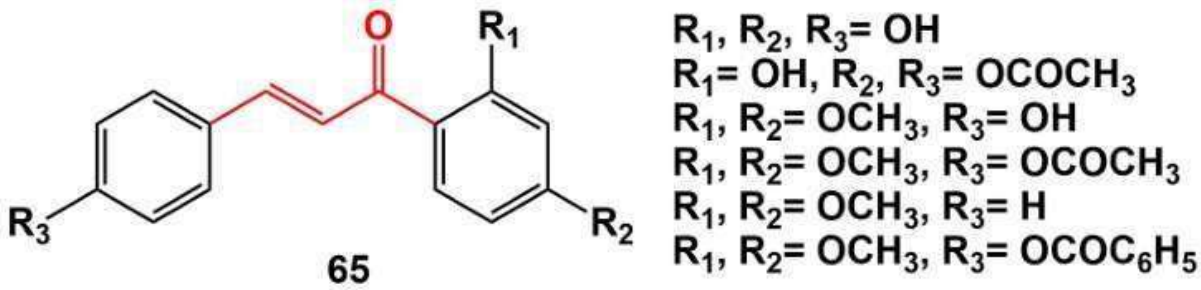


Figure 9. Chalcones 65 possess anti-diabetic activity

Anti-tubercular activity

10.48047/jocaaa.2024.33.06.194

Chalcone 63 having antimycobacterial activity. Furthermore, a new fluorine-substituted chalcone analog 64 was synthesized (Figure 10), and its antitubercular efficacy was evaluated against the strain of Mycobacterium tuberculosis H37Rv.[75]

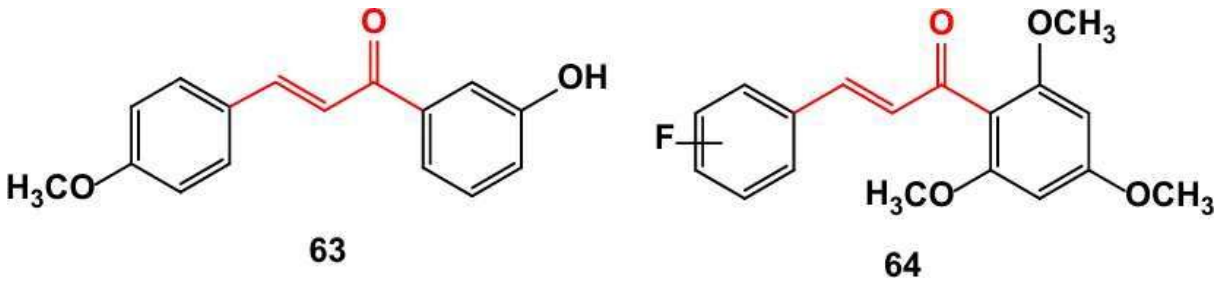


Figure 10. The two chalcones 63 and 64 possess anti-tubercular activity

CONCLUSION

Chemically, chalcones are easily modified and synthesized to create a variety of compounds with different structures. It is because of these properties that these compounds are very attractive as basic building blocks for the development of molecule-targeting agents. The chalcone compound holds significant importance within the realm of organic heterocycles. Chalcone inhibitors serve as highly reliable indicators of biological activity. Chalcones exhibit many activities, including antibacterial, antifungal, antioxidant, antiviral, and antimalarial properties. It is highly regarded as a valuable tool for synthesizing novel organic heterocyclic compounds. This review will be valuable for researchers looking to develop chalcones and other pharmacologically active drugs.

FUTURE PERSPECTIVES

A large number of preclinical studies have not completely established the mechanism of action of chalcone derivatives. Despite being relatively easy to synthesize, novel methods of synthesis must be developed in the future. This will enable the study of new biological properties, the study of molecular mechanisms of action, and, most importantly, the identification of their targets.

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