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Synthesis of Chalcone Derivatives and its Biological Evaluations: An Overview

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Abstract: Chalcone heterocycles are important species because they are part of the keto-ethylenic, CO-CH=CH- moiety. Chalcone derivatives containing reactive functional groups are associated with favorable biological properties such as cytotoxicity, antiviral, antibacterial, antifungal, antimalarial, and pharmacological properties. The 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. Many chalcones are used in medicine to treat various illnesses, including parasites, inflammations, gastritis, bacterial infections, and stomach ulcers. They can also be found in nutritional supplements and cosmetics. Nonetheless, most of the therapeutic potential of chalcone remains unexplored. This work aims to provide an in-depth overview of chalcone synthesis, highlighting the significance of chalcone research and scientists' ongoing efforts to synthesize and investigate the biological features of pharmacologically active chalcones.

Keywords: chalcones; precursor; biological activities; Claisen–Schmidt condensation.

1. Introduction

Integrating heterocyclic moieties into the regular chemical structure using a biologically active scaffold is one of the most crucial procedures for creating pharmacologically effective candidates for the medication market. Heterocyclic scaffolds have been added to the synthesis process to produce a wide range of chalcones and their derivatives nowadays, especially those with heterocyclic moieties that demonstrate greater efficacy and promise for application in pharmaceutical industries as medications. This review will focus on the most recent advancements in synthetic techniques and the pharmacological characteristics of chalcone derivatives with N-heterocyclic moieties at either the A- or B-ring.

Heterocyclic organic compounds play a vital role in the functioning of living organisms in modern times, as these compounds are present in every element of the environment. This statement is true. The increasing number of living beings has created a scarcity of natural substances and pharmaceuticals containing heterocyclic compounds [1-6]. Thus, the need arises for novel heterocyclic compounds. The presence of a catalyst is necessary for the formation of such heterocycles. A wide range of heterocycles are created through different synthetic methods like cycloaddition, ultrasonication, etc. [1,2, 7-11]. Green catalysts are becoming more popular for heterocyclic synthesis due to rising awareness of the need to reduce pollution [3–7].

Chalcone derivatives are α, β -unsaturated carbonyl compounds formed from the alkenyl moiety of a reactive ketone, 1,3-diaryl-2-propen-1-one. It belongs to the flavonoid and isoflavonoid family. Chalcones are natural pigments found in edible plants. They are an important intermediate in flavonoid biosynthesis [8], Anti-inflammatory [9–15], antibacterial [16–19], anticholinergic [20], analgesic [21,22], anti-leishmania activity and properties [23], antiplatelet [24], antioxidant of chalcone derivatives [25,26], antidiabetic [27,28], anticancer, [29] estrogen [30] anticancer [31,32], immune modulation [33,34], aldose reductase inhibition [35], acetylcholinesterase inhibition [36].

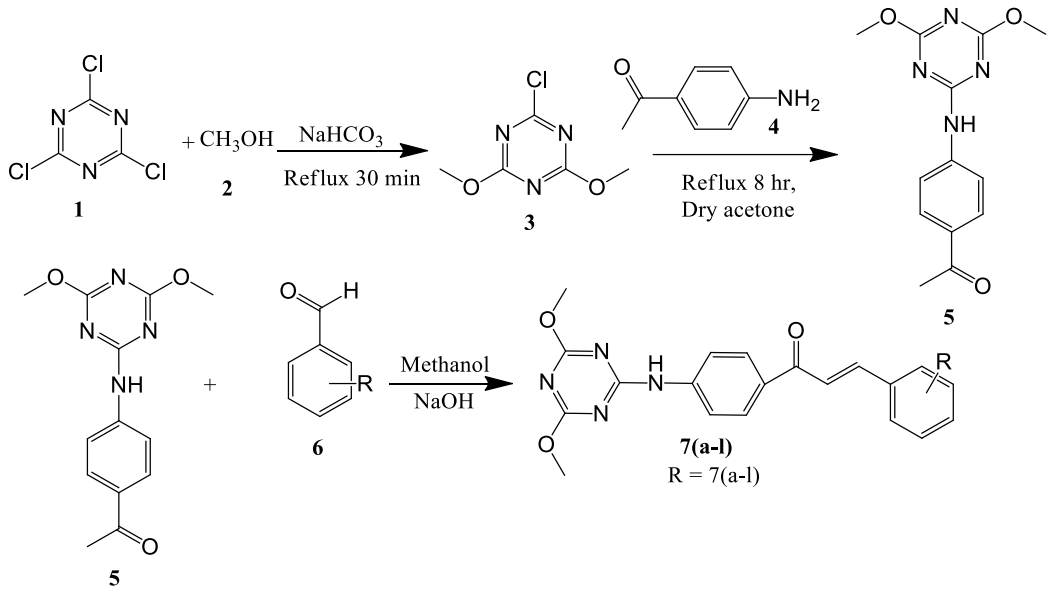
The chalcone derivatives also show antitubercular activity [37], antiproliferative agents [37], antimalarial activity [38], antiplatelet activity [39], carbonic anhydrase inhibitors [40] an inhibitor of microsomal enzyme glutathione-S-transferases [41], and CYP1 enzyme inhibitors [42], antitumor [43,44], antispasmodic [45], antiulcer [46, 47], cardiovascular [48], antiviral, [49], fungicidal [50–52], germicidal [53], herbicidal [54], insecticidal [55–57]. As a class of polyphenolic secondary metabolites, flavonoids have been shown to exhibit a wide range of biochemical properties, including antioxidant activity, inhibition of tyrosine kinases, cAMP phosphodiesterase, and stimulation of phase II metabolizing enzymes both in vitro and in vivo [58]. They are useful chemical reagents for the synthesis of new heterocyclic compounds. This review aims to analyze chalcone derivative synthesis, emphasizing the intricate details comprehensively.

Chalcones are very appealing compounds due to their straightforward structure, simplicity of synthesis, and potential biological uses. We outline the several synthetic routes utilized in recent years to create chalcone derivatives and their chemistry and biological properties.

Chalcones have found use not only in medicine and pharmaceuticals but also as light stabilizing agents, sweeteners, analytical reagents for amperometric copper estimation, spectrophotometric studies of germanium, and synthetic reagents for the synthesis of heterocyclic compounds with biodynamic behaviors [59,60].

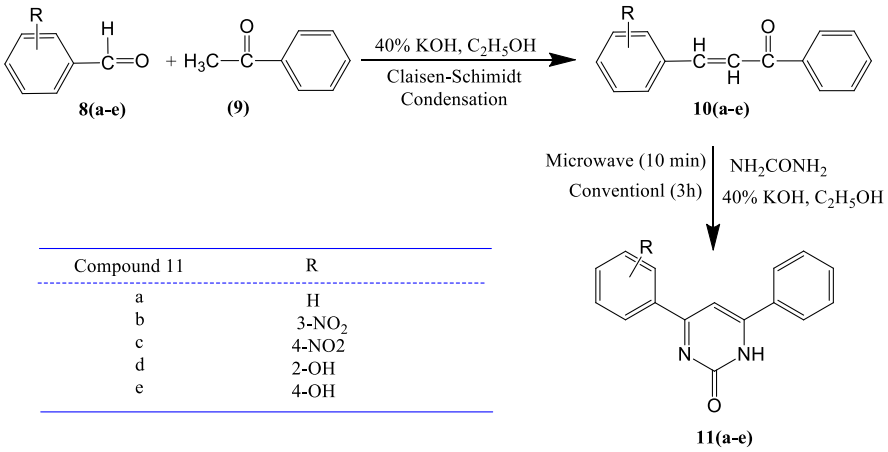
Shinde *et al*. conducted a study on triazinone (1-(4-(4,6-dimethoxy-1,3,5-triazin-2-ylamino) phenyl) ketene) (5) to assess its antioxidant and antioxidant properties. Prepared substituted benzaldehyde (6) using the Claisen-Schmidt condensation reaction in anhydrous methanol (as shown in Scheme 1) [61].

Sahoo *et al*. proposed a green process to combine chalcone 11(a-e) pyrimidine derivatives with pharmaceutical products, which is environmentally friendly, short-term, and has excellent results. In this work, chalcones 10(a-e) were reported by Claisen–Schmidt condensation of various substituted benzaldehydes 8(a-e) with acetophenones (9) in ethanol and basic 40% KOH. Use microwave heat as energy, react with urea in alkaline conditions, and irradiate for 7-10 minutes (Scheme 2) [62].



Compound 7	R
a	3, 4-dimethoxy 7g = 3,5-dimethoxy
b	4-benzyloxy 7h = 3-Methoxy
c	2-chloro 7i = 3,4-difluoro
d	Acetal 7j = 4-fluoro
e	2-chloro-3-methyl 7k = 3-fluoro
f	4-Methoxy 7l = 3-trifluoromethoxy

Scheme 1. Synthesis of triazine-based chalcones.

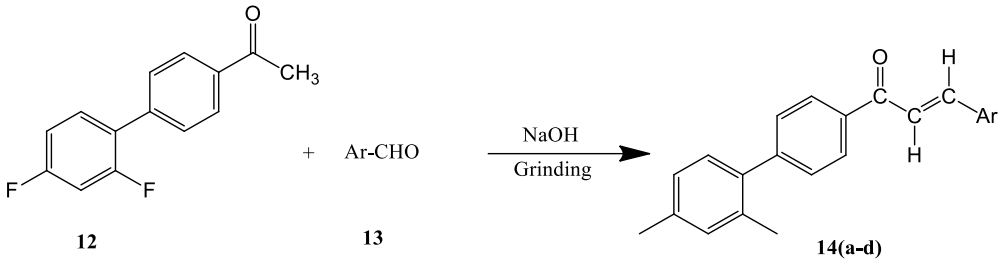


Compound 11	R
a	H
b	3-NO_2
c	4-NO2
d	2-OH
e	4-OH

Scheme 2. Synthesis of Chalcones derivatives of pyrimidine **11(a-e)**.

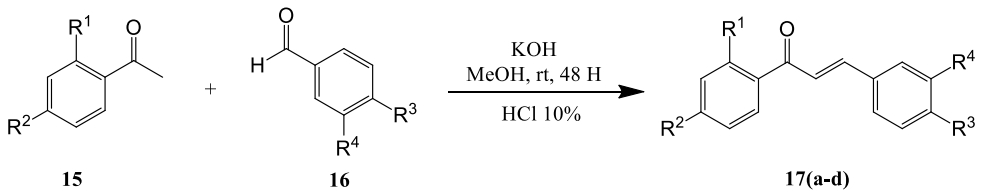
Fathimunnisa *et al*. Chalcones 14(a–d) was synthesized by solvent-free Claisen–Schmidt condensation of 1-(2,4-diflurobiphenyl-4-yl) ketene (12) and various substituted benzaldehydes (13) with a very good yield (Scheme 3) [63].

Chairil Anwar *et al*. Chalcone derivatives 17(a-d) were developed as targeting compounds and tested as anti-inflammatory agents in breast (T47D) and colon (WiDr) cell lines. Benzaldehyde derivatives can be combined at room temperature under alkaline conditions using methanol as the solvent with 4-hydroxyacetophenone. (Scheme 4) [64].



Compound 14	Ar
a	4-ClC_6H_4
b	4-BrC_6H_4
c	3-$NO_2C_6H_4$
d	2-Furyl

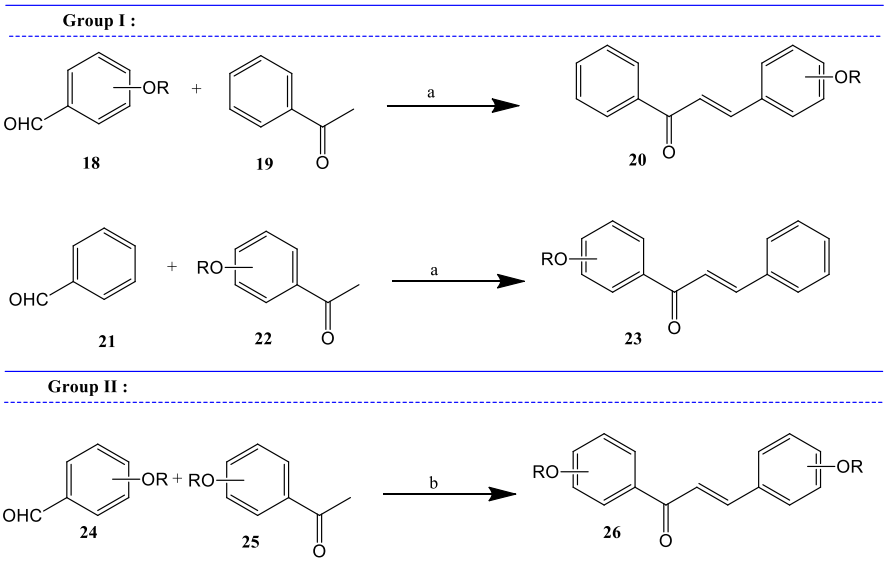
Scheme 3. Synthesis of (E)-1-(2',4'-Difluorobiphenyl-4-yl)-3-arylprop-2-en-1-ones.



Compound 17	R^1	R^2	R^3	R^4
a	H	OH	OCH_3	H
b	H	OH	OCH_3	OCH_3
c	H	OH	Cl	H
d	OH	OH	Cl	H

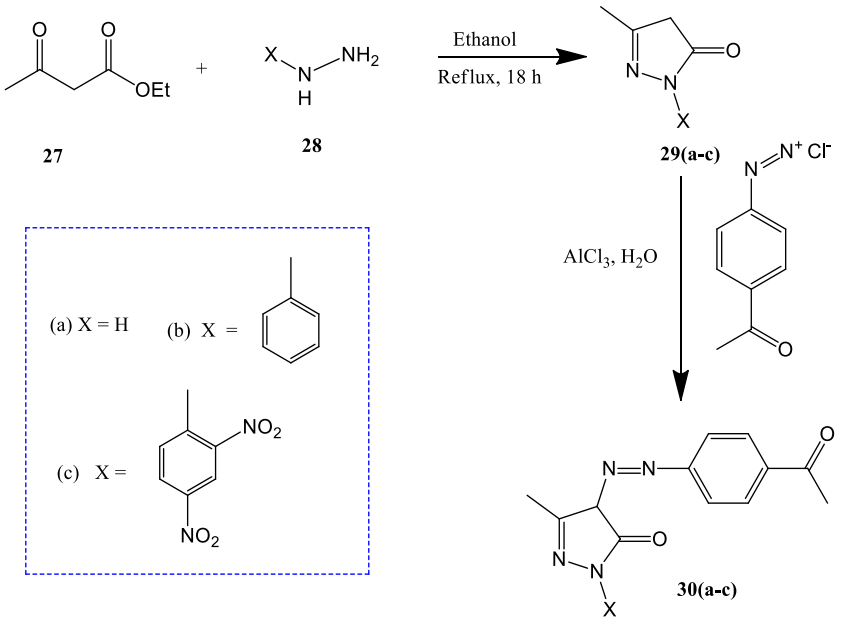
Scheme 4. Synthesis of chalcones **(17a-d).**

Bui *et al*. reported chalcone derivatives, acetophenone derivatives, and benzaldehyde derivatives are prepared by condensing them in methanol and potassium hydroxide by Claisen-Schmidt reaction and then irradiating them in an ultrasonic bath at 80°C for 8 hours and exhibiting xanthine oxidizing agent activity (Scheme 5) [65].

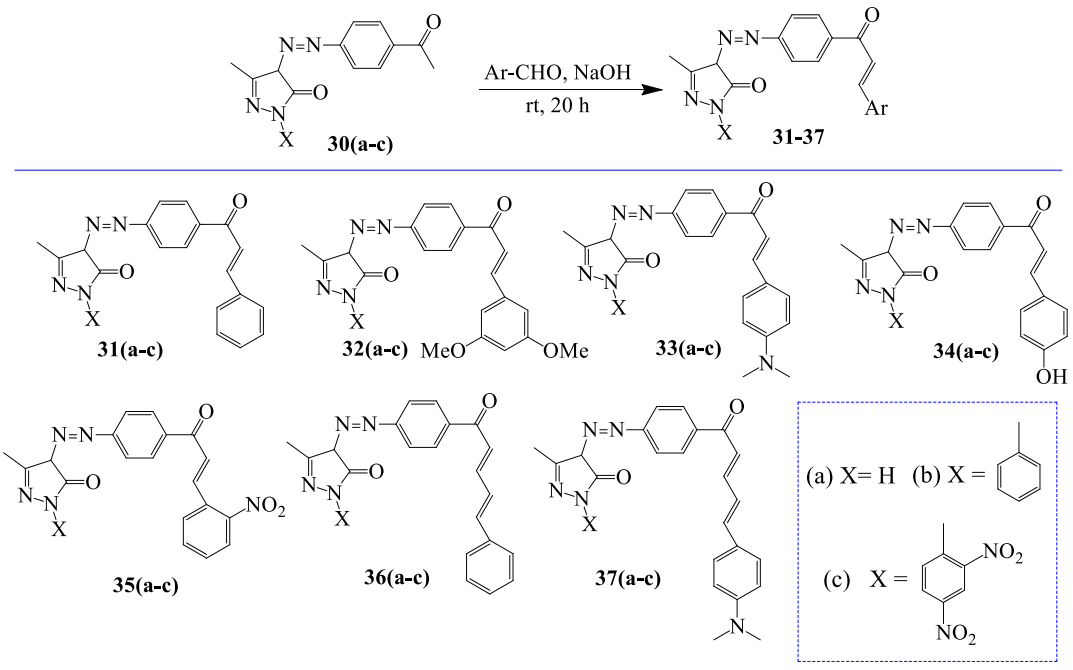


Scheme 5. Construction of chalcones derivatives.

Ahmed *et al*. synthesized a series of pyrazolone chalcones by condensing azo pyrazolone derivatives with various aromatic aldehydes, sodium hydroxide, and ethanol for 20 h at room temperature. Ethyl acetyl acetate and hydrazine derivatives were refluxed in ethanol for 8 hours to synthesize pyrazolone derivatives. Azo pyrazolinone derivatives were synthesized by the condensation of pyrazolinone with a freshly prepared solution of p-acetyl phenyl diazonium chloride in the presence of $AlCl_3$ (Schemes 6,7) [66].

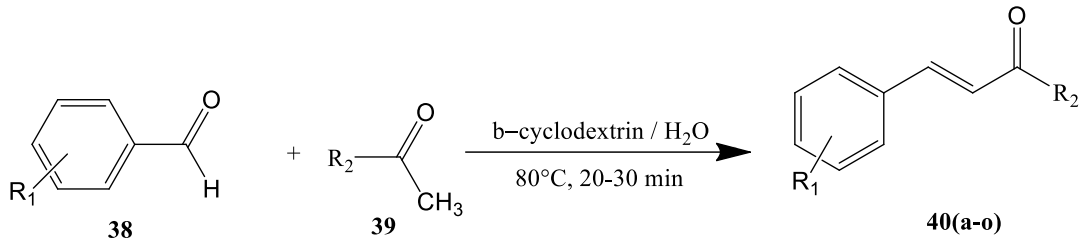


Scheme 6. Synthesis of pyrazolinone (**29a-c**) and azo pyrazolinone derivatives (**30a-c**).



Scheme 7. Synthesis of pyrazolinone chalcones **31-37B**.

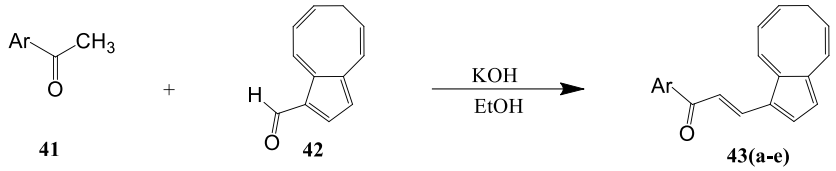
Bhadke *et al*. proposed an efficient, green, and environmentally friendly method to synthesize chalcones at 80°C by condensing benzaldehyde and acetophenone with 12 mol% β-cyclodextrin supramolecular catalyst in distilled water to obtain 94%. β-Cyclodextrin was successfully used in the following reaction with a yield of 90% (Scheme 8) [67].



40	(a) R_1 = H, R_2 = ph	(f) R_1 = 2-Cl, R_2 = 4-OH-ph	(k) R_1 = 4-OH, R_2 = 4-CH_3-ph
	(b) R_2 = 4-OH, R_2 = ph	(g) R_1 = H, R_2 = 4-CH_3-ph	(l) R_1 = H, R_2 = CH_3
	(c) R_1 = 2-Cl, R_2 = ph	(h) R_1 = H, R_2 = 3-NO_2-ph	(m) R_1 = 2-Cl, R_2 = CH_3
	(d) R_1 = 4NO_2, R_2 = ph	(i) R_1 = 2-Cl, R_2 = 4-CH_3-ph	(n) R_1 = 4-OH, R_2 =CH_3
	(e) R_1 = 4-OH, R_2 = 4-OHph	(j) R_1 = 4-NO_2, R_2 = 4-CH_3-ph	(o) R_1 = NO_2, R_2 = CH_3

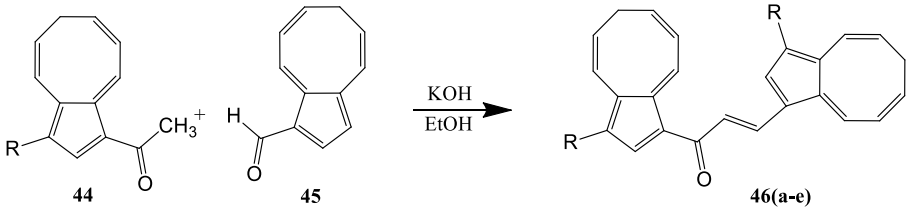
Scheme 8. Synthesis of chalcone using b-cyclodextrin.

Bala *et al*. Synthesis of azulene-containing chalcones by Claisen-Schmidt condensation of 1-azinylcarboxaldehyde with substituted aromatic methyl ketones and solid KOH in the presence of ethanol at room temperature (Schemes 9,10) [68].



Compound 43	Ar
a	Phenyl
b	4-OH-phenyl
c	4-NH_2-phenyl
d	1-Naphthyl
e	2-Naphthyl

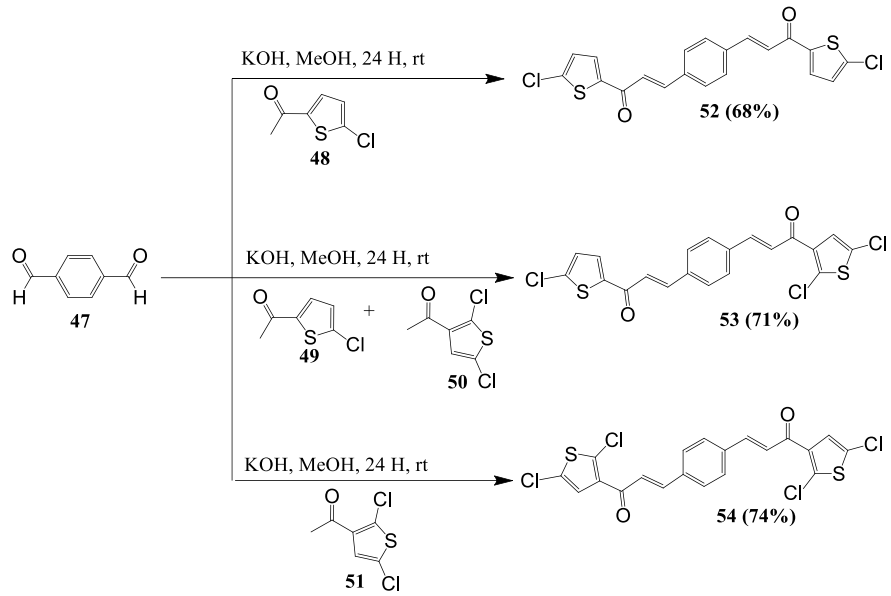
Scheme 9. Synthesis of Type I azulene-containing chalcone.



Compound 46	R	R'
a	H	H
b	H	Cl
c	H	Br
d	H	CH_3
e	CH_3	H

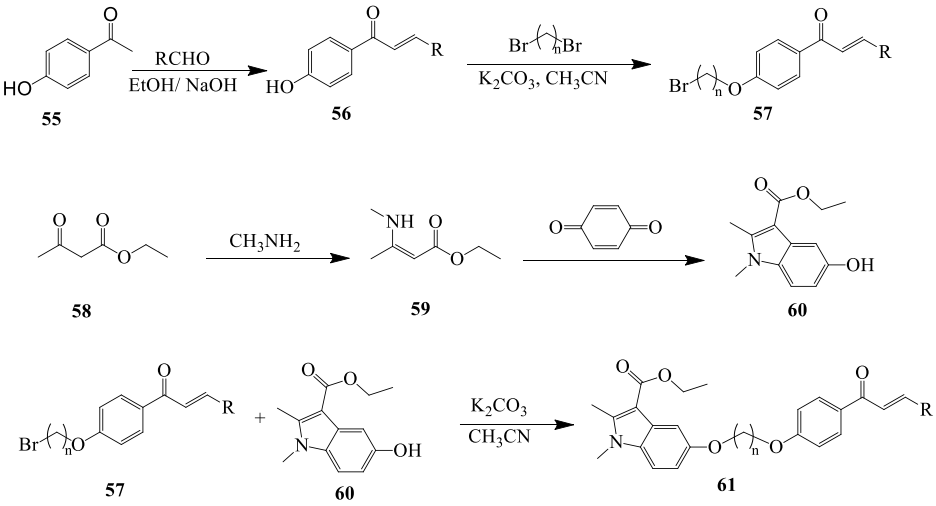
Scheme 10. Synthesis of Type II azulene-containing chalcone.

Alidmat *et al*. synthesized Bis-Chalcone derivatives as antibacterial agents through the reaction of 2-acetyl-5-chlorothiophene and terephtaldehyde in the presence of aqueous solution and methanol solution of potassium hydroxide left at room temperature for 24 hours (Scheme 11) [69].



Scheme 11. Synthesis of bis-chalcones derivatives.

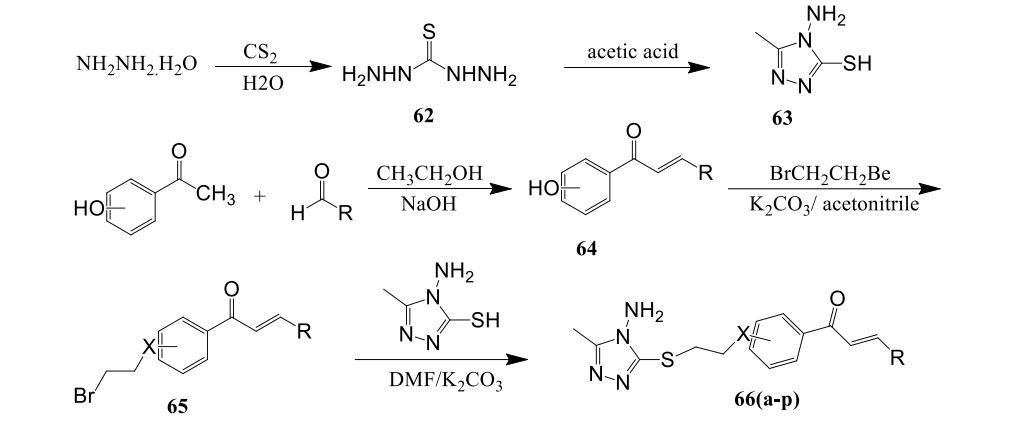
Hu *et al*. Synthesized bacterial inhibition activity of novel chalcones containing indole ring (61), condensation of intermediate (58), potassium carbonate, and CH3CN at 80°C for 1.0 hour, then intermediate (56) was added, and the reaction mixture heated at reflux temperature. Intermediates (57) and (58) were synthesized using a method found in the literature. An intermediate (57) was carefully prepared by slowly adding a solution of methylamine to ethyl acetoacetate and then keeping the reaction mixture at room temperature. The p-benzoquinone, acetone, and then intermediate (57) were added, and the reaction mixture was stirred at 30°C for 120 min. After concentration, it is then recrystallized from acetone to get intermediate (58) (Scheme 12) [70].



	n=3			n=4	
61	R=Ph	R=2-Thienyl	61	R=Ph	R=2-Thienyl
	R=3-F-Ph	R=4-OCH3-Ph		R=3-F-Ph	R=4-OCH3-Ph
	R=3-OCH3-Ph	R=4-F-Ph		R=3-OCH3-Ph	R=4-F-Ph
	R=3-CH3-Ph	R=4-Cl-Ph		R=3-CH3-Ph	R=4-Cl-Ph
	R=3-NO2-Ph	R=4-CH3-Ph		R=3-NO2-Ph	R=4-CH3-Ph
	R=3-Br-Ph	R=4-Br-Ph		R=3-Br-Ph	R=4-Br-Ph

Scheme 12. Synthesis of chalcones containing indole ring.

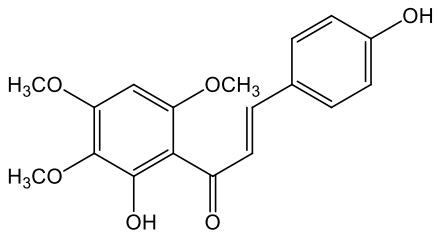
Chen, Y. *et al*. synthesized chalcones derivatives containing thioether triazole 66(a-p) from intermediate (63), potassium carbonate, and intermediate (65) in DMF at room temperature for 6-8 hours (Scheme 13) [71,52].



66 a:X= 2-O, R= thiophene-2-yl; b:X= 2-O, R= 4-F-Ph; c:X= 2-O, R=2,4-di-OCH_3-Ph; d:X= 2-O, R=3-NO_2-Ph; e:X= 2-O, R= 2-OCH_3-Ph; f:X= 2-O, R= 4-OCH_3-Ph; g:X= 2-O, R=4-methylthiazol-5-yl; h:X= 2-O, R=furan-2-yl; i:X= 2-O, R= 3,4-di-OCH_3-Ph; j:X= 2-O, R= 4-Br-Ph; k:X= 2-O, R=2,4-di-Cl-Ph; l:X= 2-O, R=3-Br-Ph; m:X= 2-O, R= 3-CF_3-Ph; n:X= 4-O, R= thiophene-2-yl; o:X= 4-O, R=4-Cl-Ph; p:X= 4-O, R=2-Cl-Ph

Scheme 13. Synthesis of chalcones derivatives containing thioether triazole.

Chromolaena odorata (L.) yields a compound known as 2',4-dihydroxy-3',4',6' trimethoxy chalcone (67) along with other chalcone analogs. The potential of its anti-inflammatory properties was investigated to mitigate lipopolysaccharide-induced inflammation in RAW 264.7 macrophages. The findings demonstrated a decrease in the production of NO and pro-inflammatory cytokines, including tumor necrosis factor-α, interleukin-1β, and IL-6, as a result of the combination. It effectively hinders NF-κB activation by preventing the initiation of inhibitory κB kinase α/β, breakdown of inhibitory κB (IκB) α, and movement of p65 NF-κB to the nucleus (Scheme 14) [72].

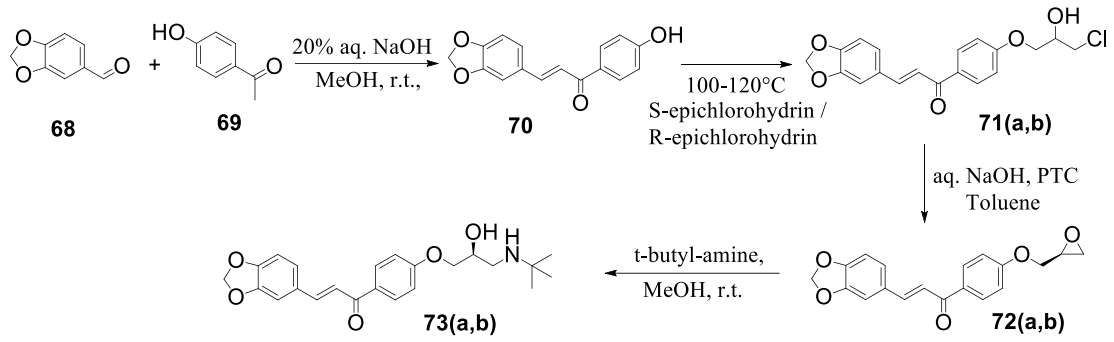


67

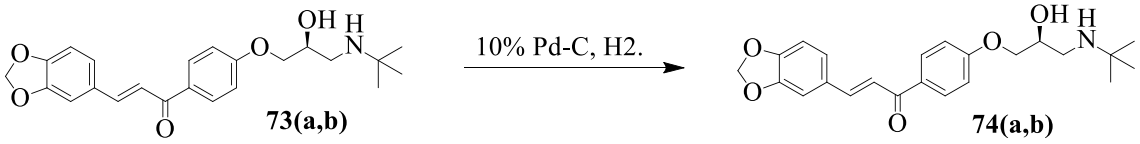
Scheme 14. Synthesis of 2',4-dihydroxy-3',4',6' trimethoxy chalcone derivatives.

A series of novel aryloxypropanolamine71(a, b), 72(a, b), 73(a, b), and 74(a, b) have been developed and evaluated as potent anti-inflammatory and anti-dyslipidaemias agents. The compound hydroxyl-chalcone (70) was synthesized through the reaction of 4-hydroxy-acetophenone (68) with piperonal (69) at a temperature range of 100–120°C. This reaction utilized either R- or S-epichlorohydrin, creating chlorohydrin intermediates 7a or 7b (Scheme 15). The intermediates underwent cyclization in the presence of basic conditions (aqueous NaOH and PTC in toluene) to yield epoxy chalcones. It is worth mentioning that the stereochemistry of the resulting epoxy-chalcones was reversed. Specifically, S-epichlorohydrin produced R-epoxy-chalcone (72a), whereas R-epichlorohydrin yielded S-epoxy-chalcone (72b). The optically active R- or S-isomer of epoxides were heated under reflux with 5–6

equivalents of tert-butyl amine in methanol to produce tert-butyl-aminocarbinols73a (R-isomer) and 73b (S-isomer) (Scheme 15) (Scheme 16) [73].

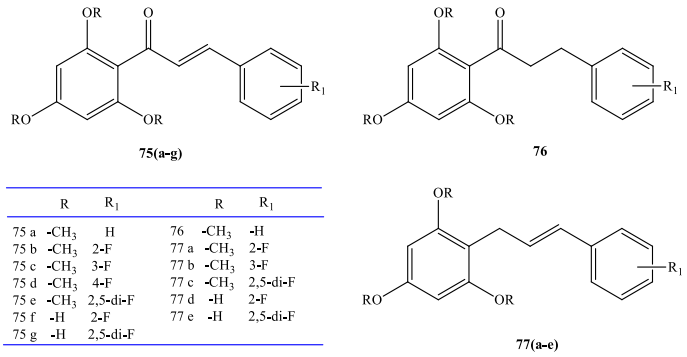


Scheme 15. Synthesis of Novel aryloxypropanolamine.



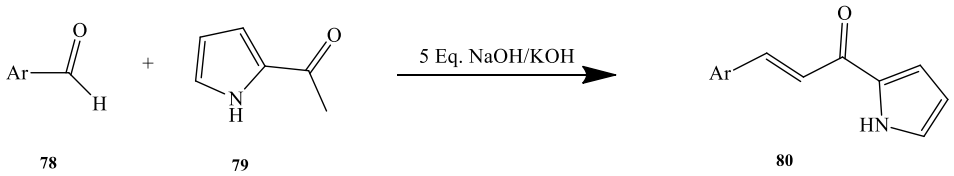
Scheme 16. Synthesis of Novel aryloxypropanolamine.

Some new fluorinated chalcones 75(a-g), 76, and 77(a-e) were synthesized and studied for their antibacterial activity against Mycobacterium Tuberculosis H37Rv and their antibacterial activity against bacteria and pathogenic bacteria (Scheme 17) [74].



	R	R_1		R	R_1
75 a	$-CH_3$	H	76	$-CH_3$	-H
75 b	$-CH_3$	2-F	77 a	$-CH_3$	2-F
75 c	$-CH_3$	3-F	77 b	$-CH_3$	3-F
75 d	$-CH_3$	4-F	77 c	$-CH_3$	2,5-di-F
75 e	$-CH_3$	2,5-di-F	77 d	-H	2-F
75 f	-H	2-F	77 e	-H	2,5-di-F
75 g	-H	2,5-di-F			

Scheme 17. Synthesis of fluorinated chalcones.



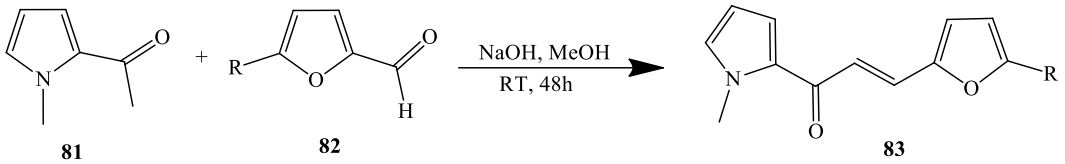
Ar =	Ph(3-OMe)	Cinnamyl(4-OMe)	Ph(2,4-di-OMe)	Ph(3-Br, 4-OMe)
	Ph(2,6-di-OMe)	Ph(4-$N(CH_3)_2$)	Cinnamyl	Furan-2-yl(5-Et)
	Ph(2-Cl, 5-NO_2)	Ph(4-OMe)	Ph(3,5-di-OMe)	Ph(3,4,5-tri-OMe)
	Ph(2,3-di-OMe)	Ph(2-Cl)	Ph(2-F)	Ph(4-OCF_3)
	Ph(3,4-Methylene-dioxy)	Ph(3-Br)	Ph(2-OMe)	Ph(4-COOH)
	Anthracen-9-yl	Ph(3-Cl)	Ph(4-Br)	

Scheme 18. synthesis of pyrrole-based chalcone derivatives.

A series of pyrrole-based chalcone derivatives were synthesized through the well-established Claisen-Schimdt condensation reaction. This compound has demonstrated efficacy

against CYP1 isoforms. In (Scheme18), the reaction under alkaline conditions yields a range of derivatives (80) by utilizing aromatic aldehyde derivatives (78) and pyrrole-based acetophenone (79) as the starting materials. 2-Pyrochalcone derivatives (80) can be synthesized through liquid or solid grinding, yielding excellent outcomes [75].

Ozdemir and his colleagues employed the Claisen-Schmidt condensation reaction to synthesize and document new pyrrolyl chalcone derivatives that effectively demonstrate impressive antibacterial and antifungal properties. Using the reference reaction method, the compounds 2-acetyl-1-methylpyrrole (81) and aryl-furfural (82) were added to a sodium hydroxide solution in methanol and stirred gently at room temperature for two days. After the reaction, the chalcone derivative (83) undergoes a meticulous purification process through recrystallization with ethanol. The resulting mixture is processed through filtration, washing, and drying to achieve a significant yield (Scheme 19) [76].

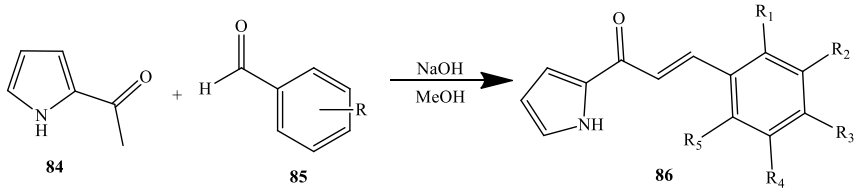


81 82 83

R			
	1-Methyl-4-nitro-benzene	1-Methyl-2-nitro-benzene	4-Chloro-1-methyl-2-nitro-benzene
	1-Chloro-2-methyl-benzene	1-Methyl-3-nitro-benzene	2,4-Dichloro-1-methyl-benzene
	1-Chloro-3-methyl-benzene	1,4-Dichloro-2-methyl-benzene	1-Chloro-4-methyl-benzene
	1,2-Dichloro-4-methyl-benzene		

Scheme 19. synthesis of pyrrolyl chalcone derivatives.

In a similar manner, Sharma and his colleagues accomplished the synthesis and reports of pyrrole-based chalcone derivatives. These derivatives were obtained through condensation reactions of 2-acetyl pyrrole-substituted benzaldehyde derivatives, carried out under specific conditions (86). As part of the process, a substituted benzaldehyde derivative (85) was introduced to a solution of 2-acetylpyrrole (84) in methanol. To facilitate the reaction, a 10% NaOH aqueous solution was incorporated, and the mixture was continuously stirred until the reaction reached completion. Following the completion of the reaction, the mixture was diluted with distilled water. The resulting precipitated product was then filtered and subjected to recrystallization from the EtOH/EtOAc solvent mixture, resulting in the formation of the chalcone derivative (86) (Scheme 20) [77].



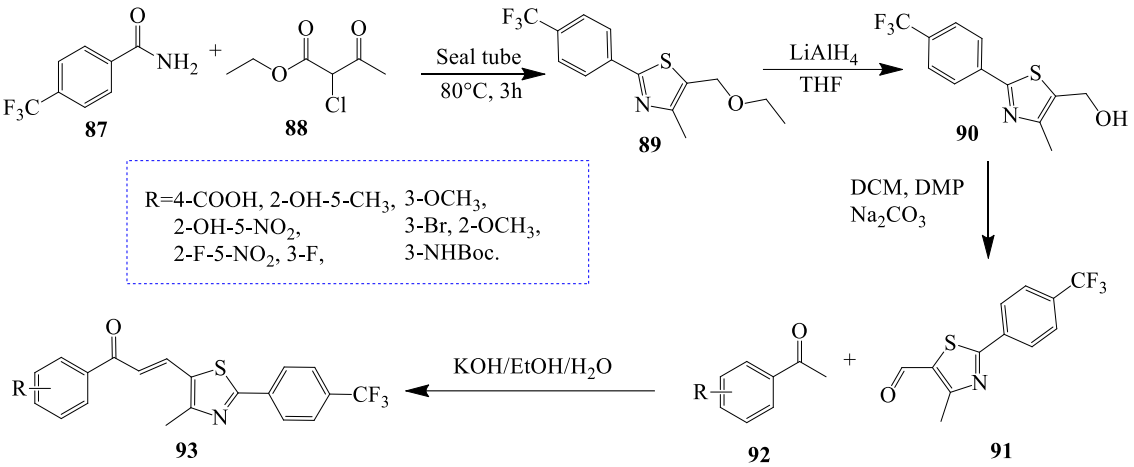
84 85 86

R_1	R_2	R_3	R_4	R_5
H	H	H	H	H
OCH_3	OCH_3	OCH_3	NO2	OCH_3
Cl	Cl	Cl		Cl
Br	NO_2	Br		
		NO_2		
		F		
		$N(OCH_3)_2$		

Scheme 20. General synthesis method of pyrrolyl chalcone derivatives.

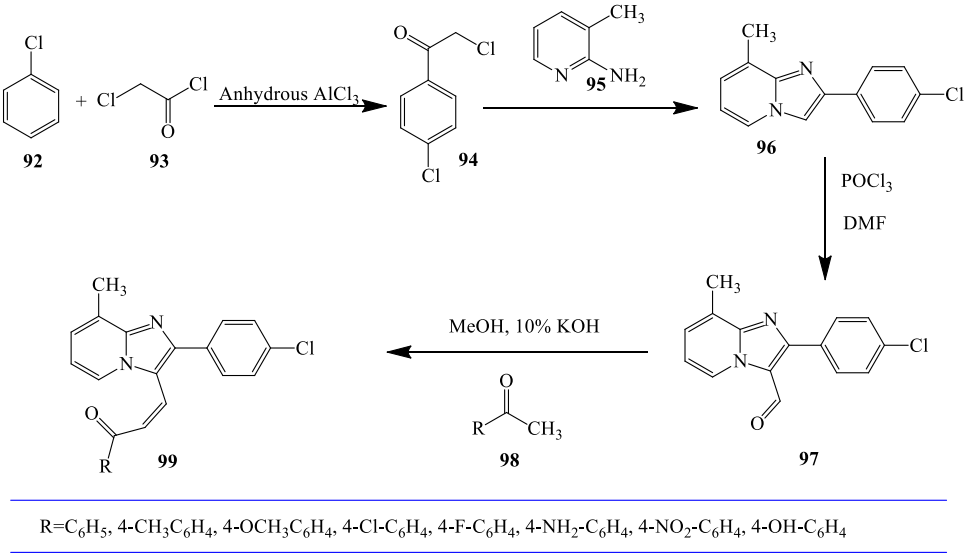
Kasetti and colleagues have reported the anticancer activity of thiazolyl chalcone derivatives (93). Thiazole carboxaldehyde (91) was successfully synthesized in three steps.

Initially, thiazole carboxylate (89) is generated through the reaction of benzamide (87) with 2-chloroacetate (88). The ester moiety of compound (89) was reduced to the alcohol compound (90) using LiAlH4, and then the target intermediate (91) was obtained through Dess Martin oxidation. The synthesized aldehyde (91) reacted with aryl methyl ketone (92) in ethanol, while KOH was gradually added to the mixture with continuous stirring. A yellow compound was obtained after completing the necessary steps of filtration, washing, and drying. Ethanol recrystallization was employed to ensure its purity, resulting in a high yield of a pure yellow thiazolyl chalcone derivative (93), as depicted in Scheme 21 [78].



Scheme 21. General Synthesis of thiazolyl chalcone derivatives.

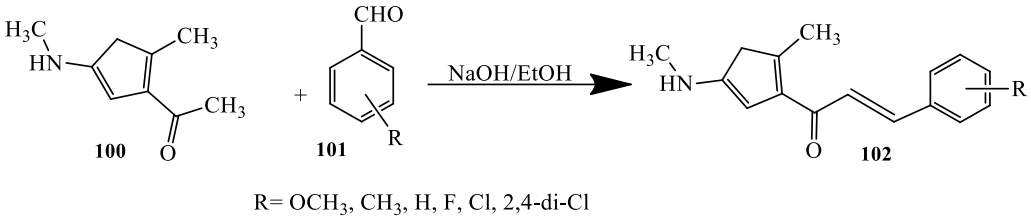
Rupala and colleagues have reported finding imidazopyridine derivatives formed by combining aryl methyl ketones with aryl aldehydes in an alkaline medium. The pyridine-3-carboxaldehyde (97) and ethanone (98) were subjected to reflux in methanol, and then NaOH was added as a catalyst. The unprocessed substance was cautiously placed into ice and then refined through recrystallization with dichloromethane, creating a compound (99) as illustrated in Scheme 22 [79].



Scheme 22. General Synthesis of imidazopyridine chalcone derivatives.

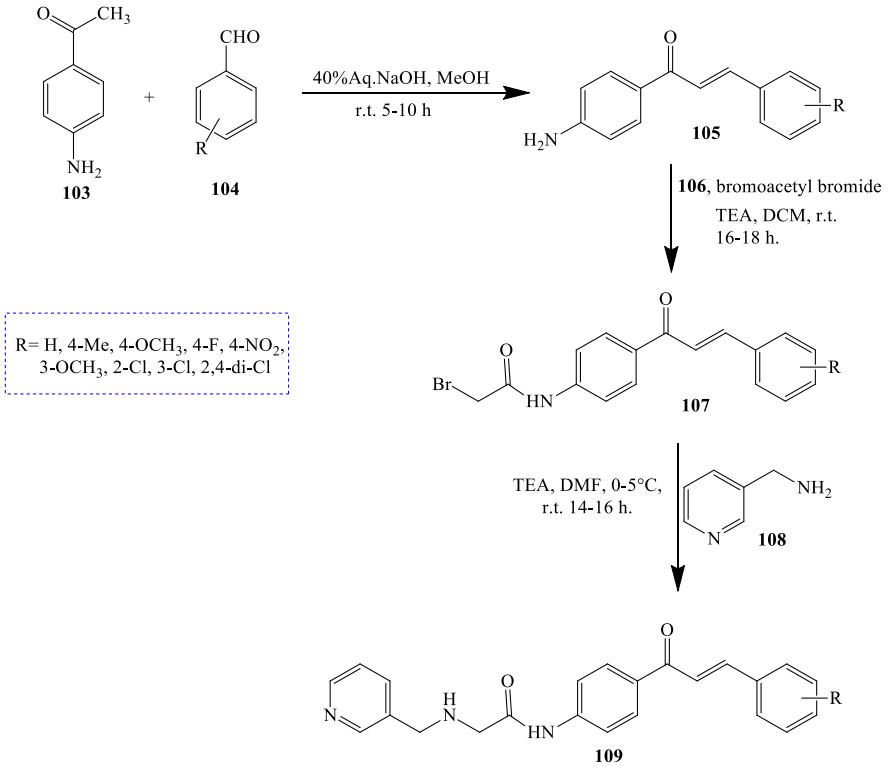
Farghaly *et al*. have made an intriguing discovery regarding the anticancer properties of chalcone derivatives containing thiazole. The mixture of 4-acetylthiazole (100) derivatives

was carefully combined with the aromatic aldehyde derivative (101) in pure ethanol. A solution containing sodium hydroxide was carefully added in small increments while thoroughly mixing the resulting liquid. The product was acquired through filtration and purified by recrystallization from a solvent mixture of ethanol and dioxane. The formation of a chalcone derivative based on thiazole, specifically compound (102), as shown in Scheme 23, was a significant outcome [80].



Scheme 23. General Synthesis of thiazole-containing chalcone derivatives.

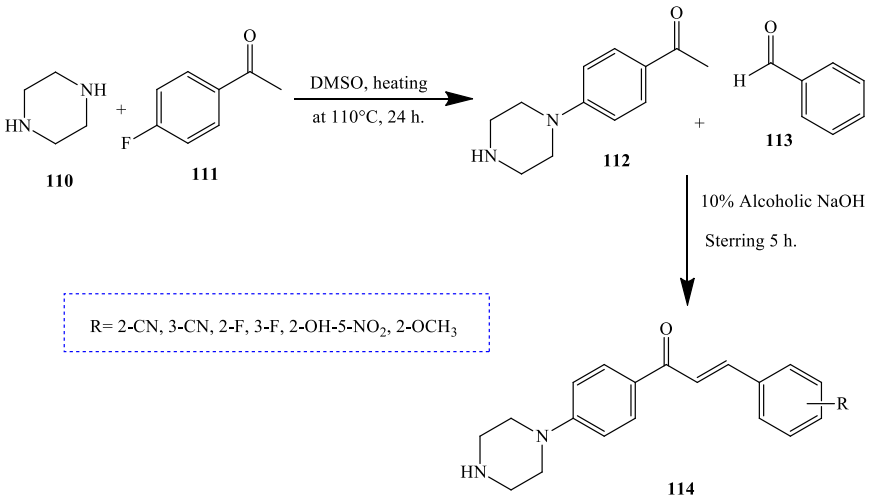
Durgapal and colleagues reported the synthesis of pyridyl chalcone derivatives with anticancer activity from 3-aminomethyl pyridine and 4-amino chalcone. The procedure involves 4-aminoacetophenone (103) reacting with aldehyde (104) in a simple reaction to obtain the 4-aminoacetophenone derivative (105). In addition, 4-aminochalcone (105) was acquired through a reaction with bromoacetate bromide (107) by combining them in the presence of DCM and TEA. Compound (107) underwent a reaction with 3-aminomethyl pyridine (108) in DCM using TEA base at room temperature, resulting in the formation of different pyridine-based chalcone derivatives (109), as depicted in Scheme 24 [81].



Scheme 24. General Synthesis of pyridyl chalcone derivatives.

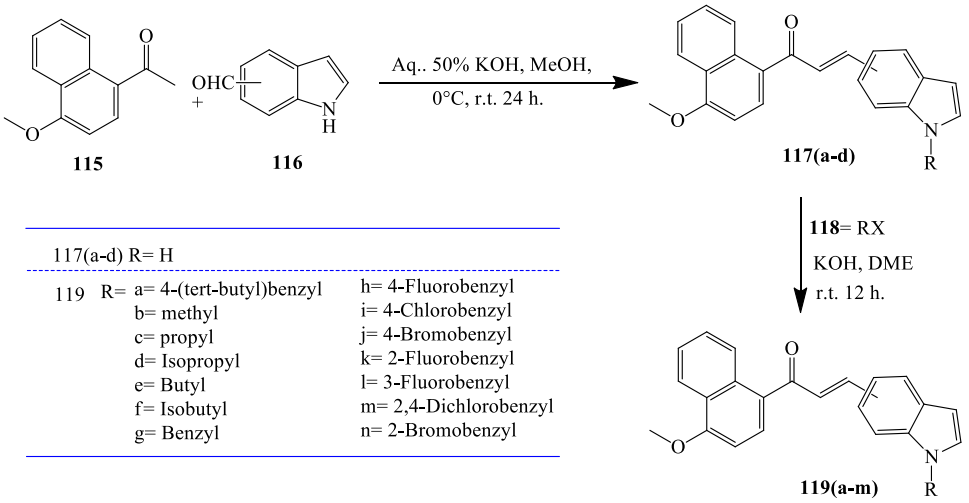
Ahmed and his colleagues have published a study on synthesizing piperazine-chalcone hybrid derivatives. These compounds show promise as inhibitors of vascular endothelial growth factor receptor 2 (VEGFR-2). A blend of the acetophenone derivative (112) and the corresponding aldehyde derivative (113) was dissolved in a solution of 10% sodium hydroxide

in alcohol and gently stirred at room temperature. Once the reaction has finished, the precipitate undergoes filtration, washing, drying, and recrystallization with ethanol to yield the desired compound (114) (Scheme 25) [82].



Scheme 25. Synthesis of pyridyl chalcone derivatives.

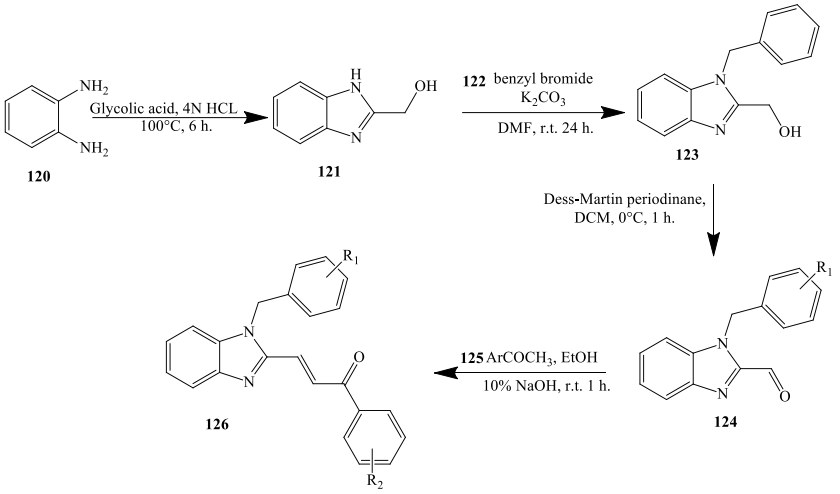
Recent reports have highlighted the anti-inflammatory properties of various chalcone derivatives containing indole and naphthalene components. Through Claisen-Schmidt condensation reactions, a range of indole-based chalcone derivatives 117(a–d) can be obtained with satisfactory yields using aromatic ketone derivatives (115) and commercially available indole aldehyde derivatives (116). The indole chalcone derivatives 117(a-d) react with alkyl halides (118) in the presence of a base, leading to the formation of N-alkylated indole chalcone derivatives 119(a-m) (Scheme 26) [83].



Scheme 26. Synthesis of chalcone derivatives containing indole and naphthalene moieties.

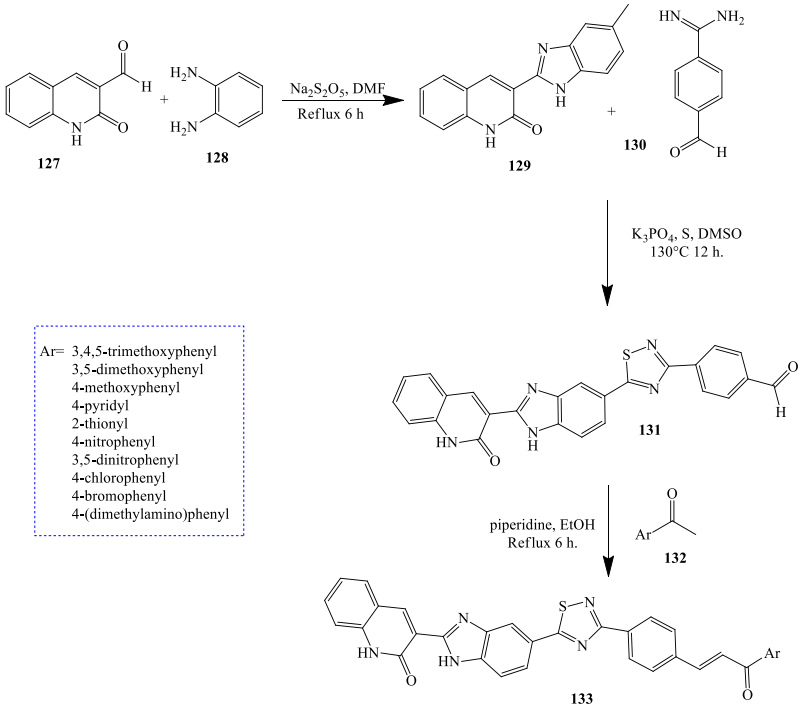
A group of benzimidazole-based chalcone derivatives were synthesized and evaluated as potential antibodies targeting Topo II using the Claisen-Schmidt reaction. The benzimidazole derivative (121) is synthesized through a reflux process involving O-phenylenediamine (120) and glycolic acid in the presence of HCl. A benzimidazole-2-methanol compound (123) was successfully synthesized by alkylating compound (121) with benzyl bromide in the presence of K2CO3. Substituted benzimidazole-2-carboxaldehyde derivatives (124) were obtained from (123) through oxidation using the Desmartin protocol. Compound

(123) is synthesized via the Claisen-Schmidt reaction (124) using an appropriate acetophenone derivative, as illustrated in Scheme 27 [84].



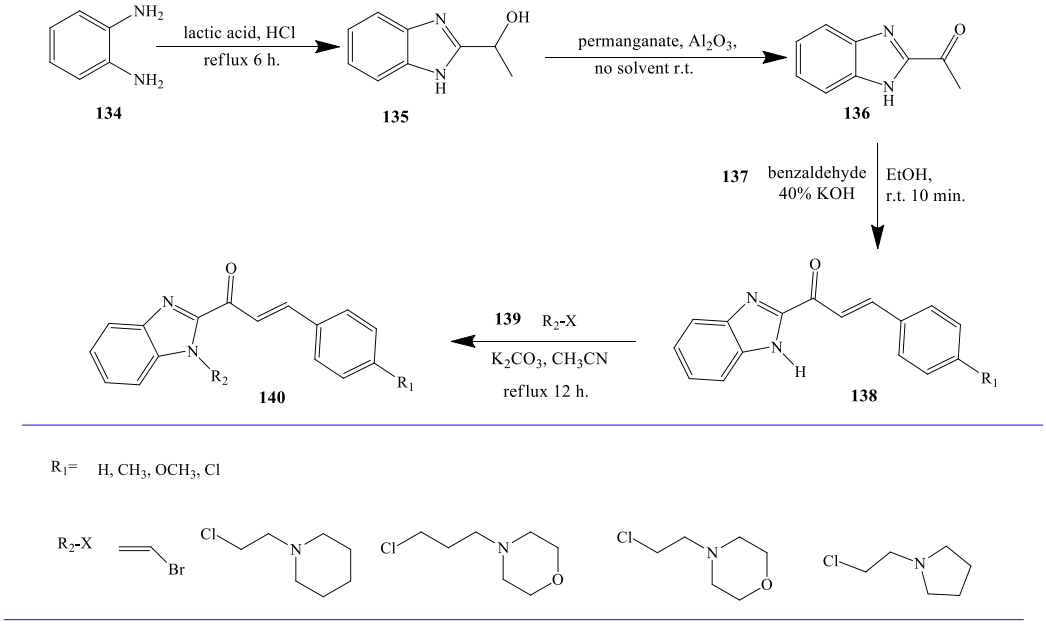
Scheme 27. Synthesis of benzimidazole-based chalcone derivatives.

Using aldol condensation processes, Pragathi and colleagues studied antibacterial benzimidazole-based chalcones attached to quinoline-benzimidazole-thiadiazole heterocyclic scaffolds. Compound (129) is formed through two condensation processes between 1,2-dihydro-2-oxoquinoline-3carboxaldehyde (127) and benzene-1,2-diamine (128). The intermediate (129) is then treated with 4-methanoylbenzamidine hydrochloride (130), yielding the derivative (131). Compound (131) is further aldol condensation reaction with acetophenone derivative (132) to obtain benzimidazolyl chalcones derivative (133) as shown in (Scheme 28) [85].

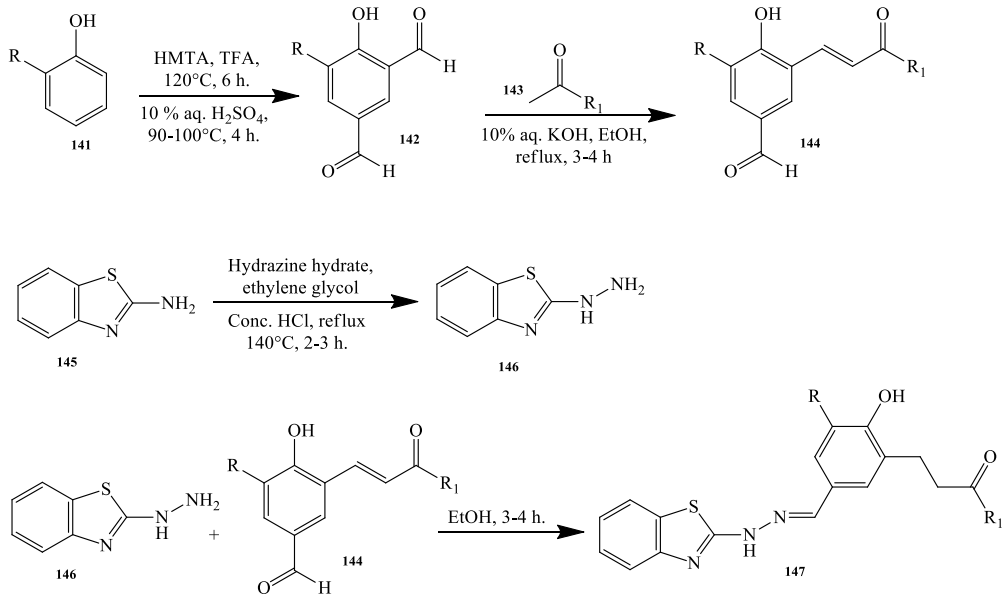


Scheme 28. Synthesis of quinoline-benzimidazole-thiadiazole heterocyclic scaffolds.

Hsieh and co-workers discovered new N-substituted benzimidazolyl chalcone derivatives with the potential as anti-inflammatory drugs. These compounds were synthesized by combining benzimidazole and aromatic aldehyde derivatives under alkaline conditions. The compound was obtained through a reflux reaction, where the O-phenylenediamine (134) reaction with lactic acid in HCl was utilized. Subsequently, the oxidation reaction occurred in the presence of the strong oxidant potassium permanganate and solid alumina. (134). Aldol condensation led to the synthesis of benzimidazolyl-aryl chalcone derivatives (138). In addition, compound (138) underwent a methylation reaction using the appropriate reagent to yield compound (140), as outlined in Scheme 29 [86].



Scheme 29. Synthesis of N-substituted benzimidazolylne chalcone derivatives.



Scheme 30. Synthesis of benzothiazole-based chalcones derivatives.

Several benzothiazole-based chalcones have been found to exhibit promising inhibitory activity against the thymidylate kinase (BmTMK) enzyme. Various phenol and hexamethylenetetramine derivatives were dissolved in TFA at 120°C while continuously stirred, resulting in the successful production of a compound (142) with a high yield. A compound (142) and various ketone derivatives (143) were dissolved in 10% KOH and ethanol. The resulting solution was then refluxed to yield a compound (144). The ortho-substituted chalcone derivative (144) and 2-hydrazinobenzothiazole (146) mixture were dissolved in ethanol and thoroughly blended. Allow the mixture to sit undisturbed for 3–4 hours until the desired benzothiazole-based chalcone derivative (145) is formed, as illustrated in Scheme 30 [87].

2. Chalcones Derivatives and its Biological Activities

The synthesis section provides a concise overview of chalcone derivatives that incorporate heterocyclic scaffolds, including pyrrole, imidazole, thiazole, pyridine, piperazine, indole, benzimidazole, benzothiazole, and quinoline. The section also describes the diverse range of biological activity these derivatives exhibit. This section will discuss the potential, biological activities, and treatment challenges of chalcone derivatives that incorporate N-heterocyclic scaffolds in medicinal chemistry. The chemical names are stimulating, and published data illustrate the significance of the α, β-unsaturated carbonyl group for medication use and biological efficacy [88]. Both natural and synthetic compounds that include N-heterocyclic scaffolds demonstrate diverse therapeutic properties, including antibacterial, antifungal, and anti-leishmania activity (Figure 1, 2) [89].

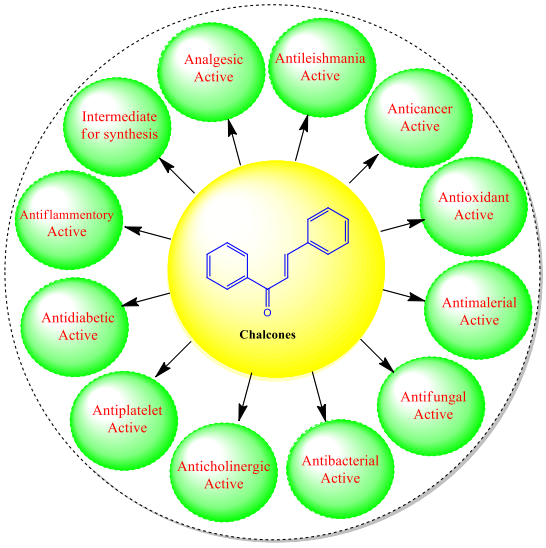


Figure 1. Chalcones biological evaluation.

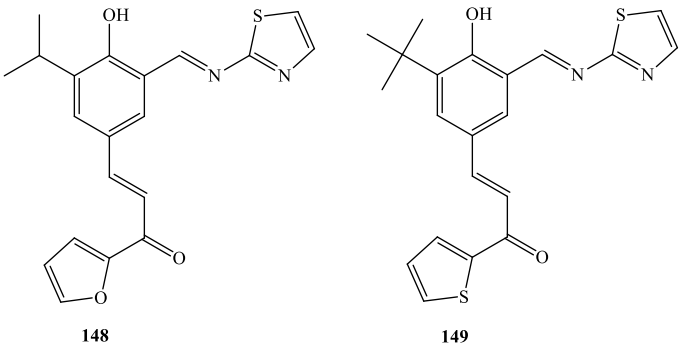
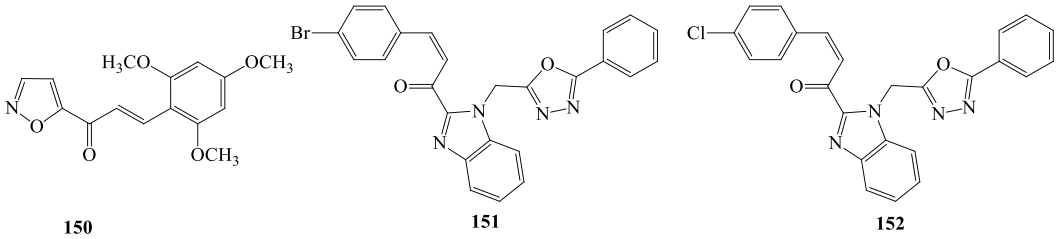


Figure 2. Biological active chalcones.

3. Chalcones with 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 2,4,6-trimethoxyphenyl ring (150) exhibited greater antibacterial activity than ciprofloxacin (Figure 2). Furthermore, the produced compounds have antifungal, antioxidant, and anticancer properties [90-92].

In a study conducted by Meshram and colleagues, 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 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 are incorporated into the molecule [93].



150 151 152

Figure 3. Antibacterial active chalcones.

4. Chalcones with Antifungal Activity

Osmaniye and colleagues 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. Similarly, Sunitha and her colleagues 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 were combined with nystatin (75) and tested at 100 μg/mL concentration. Compounds (153), (154), (155), and (156) were found to have the highest anti-inflammatory properties and also showed strong anti-inflammatory properties (Figure 4) [94, 95].

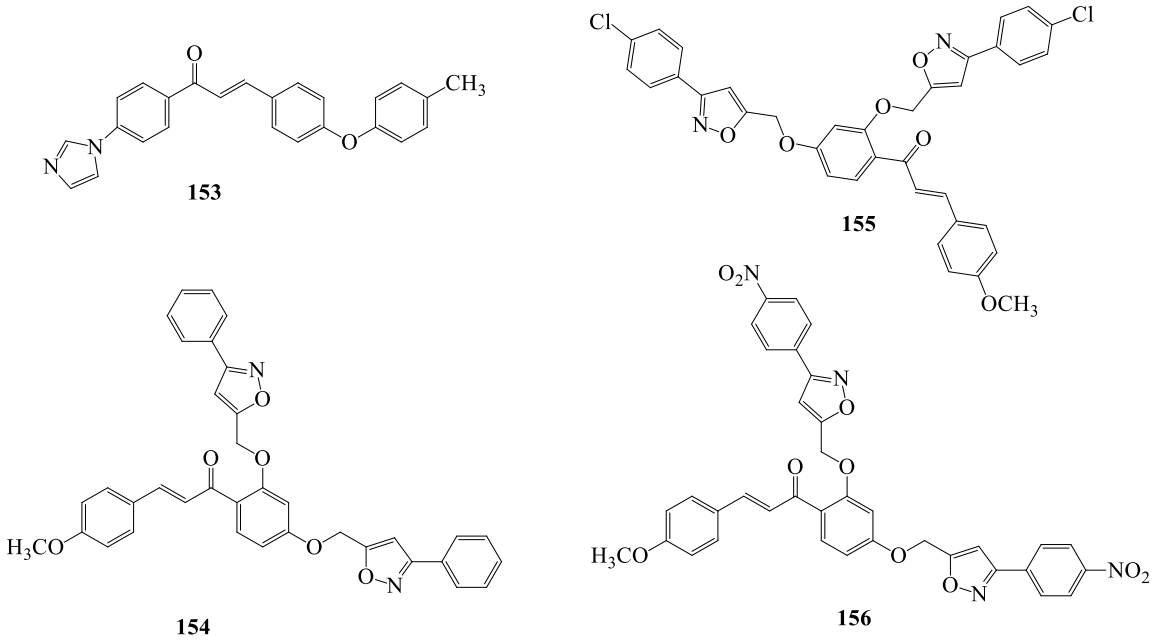


Figure 4. Antifungal active chalcones.

5. Chalcones with Antioxidant Activity

A recent study by Bhat and their colleagues 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 3,4-dimethyl phenyl group, whilst compound (158) possessed a 1,3-(biphenyl)-1Hpyrazole group connected to the third position of the chalcone moiety. These compounds exhibited notable DPPH radical scavenging capacity, with IC50 values of 15.33 and 14.48 μM, respectively, compared to ascorbic acid, which had an IC50 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 [96].

A study by Kumari and their colleagues 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) [97].

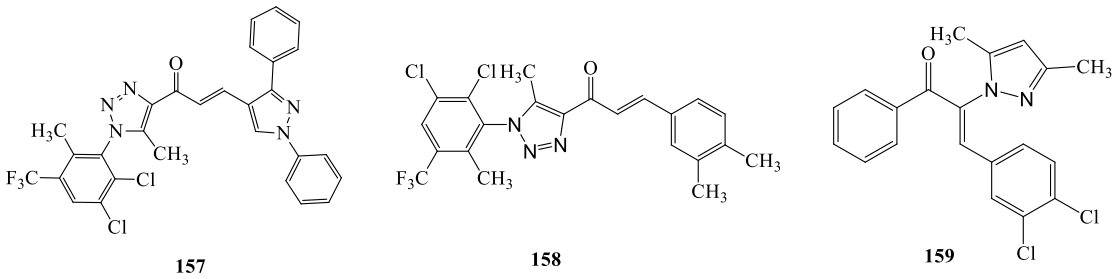


Figure 5. Antioxidant active chalcones.

6. Chalcones with 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 develop new vaccines, particularly targeting the Plasmodium falciparum virus responsible for causing severe malaria [98]. Jyoti and co-workers 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 IC50 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.[100] The effectiveness of these molecular hybrids was evaluated against the drug-susceptible 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) [100].

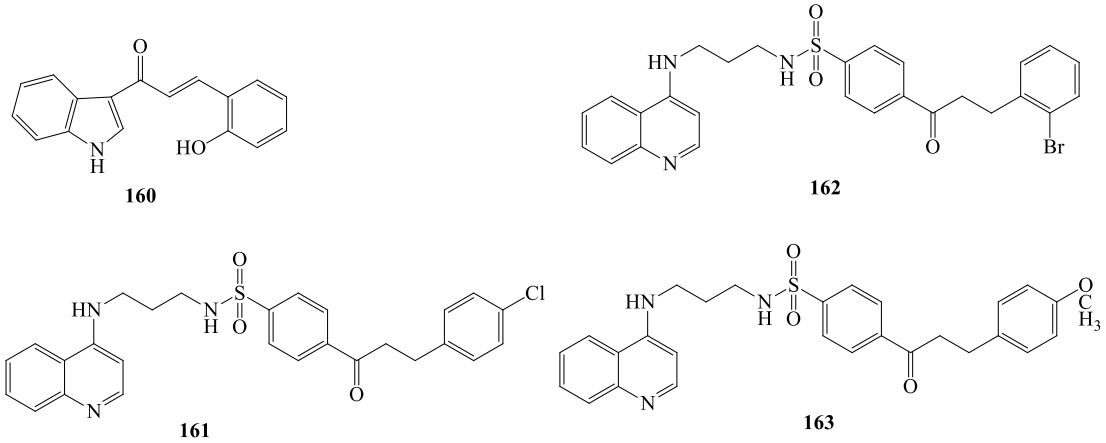
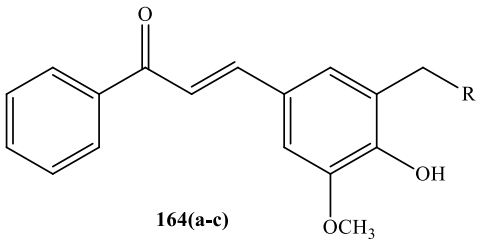


Figure 6. Antimalarial Active chalcones.

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. 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) [101].



164(a-c)

Compound	R
a	Morpholine
b	Piperidine
c	Diethylamine

Figure 7. Derivatives of antimalarial active chalcones.

7. Chalcones with 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) [102].

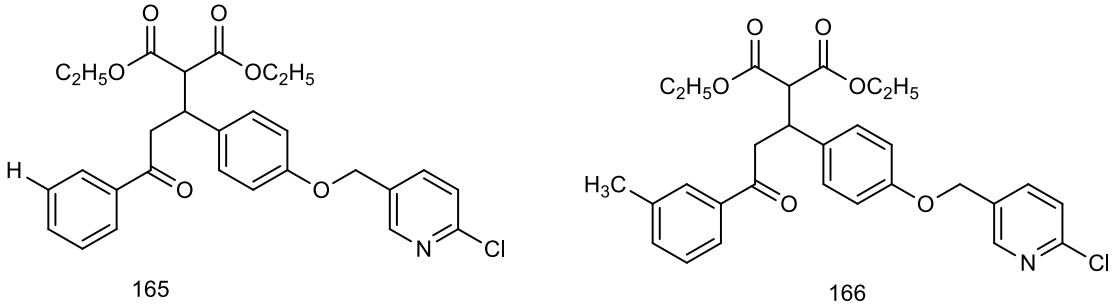


Figure 8. Chalcones with antiviral properties.

4. Conclusions

The chalcone compound holds significant importance within the realm of organic heterocycles. We have completed a review on this topic. During our extensive research for this review, it became evident that 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 presents a study conducted by researchers on chalcone derivatives. This review will be valuable for researchers looking to develop chalcones and other pharmacologically active drugs.

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Conflicts of Interest

The authors declare no conflict of interest.

References

1. Sharma, S.; Monga, Y.; Gupta, A.; Singh, S. 2-Oxindole and related heterocycles: synthetic methodologies for their natural products and related derivatives. *RSC Advances* **2023**, *13*, 14249–14267, https://doi.org/10.1039/D3RA02217J.
2. Jena, S.; Chanda, K. Copper-Catalyzed Synthesis of Heterocyclic Molecules via C–N and C–O Bond Formation under Microwaves: A Mini-Review. *ACS Omega* **2023**, *8*, 23240–23256, https://doi.org/10.1021/acsomega.3c02041.
3. Jain, S.; Kumar, S.; Lamba, B.Y.; Patra, J.; Mahindroo, N. Nanocatalysts: Applications in the synthesis of chalcones – a review. *Synthetic Communications* **2021**, *51*, 1–12, https://doi.org/10.1080/00397911.2020.1817941.
4. Abu-Dief, A.M.; Nassar, I.F.; Elsayed, W.H. Magnetic $NiFe_2O_4$ nanoparticles: an efficient, heterogeneous and reusable catalyst for the synthesis of acetylferrocene chalcones and their antitumor activity. *Applied Organometallic Chemistry* **2016**, *30*, 917–923, https://doi.org/10.1002/aoc.3521.
5. Jadhav, S.; Farooqui, M.; Chavan, P.; Hussain, S.; Rai, M. $ZnFe_2O_4$ Nano-Catalyzed One-Pot Multi-Component Synthesis of Substituted Tetrahydropyranoquinoline under Neat Ultrasonic Irradiation. *Polycyclic Aromatic Compounds* **2022**, *42*, 2067–2075, https://doi.org/10.1080/10406638.2020.1825005.
6. Sonawane, H.R.; Deore, J.V.; Chavan, P.N. Reusable Nano Catalysed Synthesis of Heterocycles: An Overview. *ChemistrySelect* **2022**, *7*, e202103900, https://doi.org/10.1002/slct.202103900.
7. Bangale, S.; Jondhale, V.; Pansare, D.; Chavan, P. Reusable $ZnCr_2O_4$ Nano Catalyzed One Pot Three-Component Cycloaddition Reaction for Synthesis of Azetidine Derivatives under Ultrasound Irradiation. *Polycyclic Aromatic Compounds* **2022**, *42*, 6398–6410, https://doi.org/10.1080/10406638.2021.1983617.
8. Alam, M.S.; Rahman, S.M.M.; Lee, D.-U. Synthesis, biological evaluation, quantitative-SAR and docking studies of novel chalcone derivatives as antibacterial and antioxidant agents. *Chemical Papers* **2015**, *69*, https://doi.org/10.1515/chempap-2015-0113.
9. Rashid, H.; Xu, Y.; Ahmad, N.; Muhammad, Y.; Wang, L. Promising anti-inflammatory effects of chalcones via inhibition of cyclooxygenase, prostaglandin E2, inducible NO synthase and nuclear factor κb activities. *Bioorganic Chemistry* **2019,** *87*, 335–365, https://doi.org/10.1016/j.bioorg.2019.03.033.
10. Nurkenov, O.A.; Ibraev, M.K.; Schepetkin, I.A.; Khlebnikov, A.I.; Seilkhanov, T.M.; Arinova, A.E.; Isabaeva, M.B. Synthesis, Structure, and Anti-Inflammatory Activity of Functionally Substituted Chalcones and Their Derivatives. *Russian Journal of General Chemistry* **2019**, *89*, 1360–1367, https://doi.org/10.1134/S1070363219070028.
11. Ibrahim, T.S.; Moustafa, A.H.; Almalki, A.J.; Allam, R.M.; Althagafi, A.; Md, S.; Mohamed, M.F.A. Novel chalcone/aryl carboximidamide hybrids as potent anti-inflammatory via inhibition of prostaglandin E2 and inducible NO synthase activities: design, synthesis, molecular docking studies and ADMET prediction. *Journal of Enzyme Inhibition and Medicinal Chemistry* **2021**, *36*, 1067–1078, https://doi.org/10.1080/14756366.2021.1929201.
12. Fu, Y.; Liu, D.; Zeng, H.; Ren, X.; Song, B.; Hu, D.; Gan, X. New chalcone derivatives: synthesis, antiviral activity and mechanism of action. *RSC Advances* **2020**, *10*, 24483–24490, https://doi.org/10.1039/D0RA03684F.
13. Alsafi, M.A.; Hughes, D.L.; Said, M.A. First COVID-19 molecular docking with a chalcone-based compound: synthesis, single-crystal structure, and Hirshfeld surface analysis study. *Acta Crystallographica Section C Structural Chemistry* **2020**, *76*, 1043–1050, https://doi.org/10.1107/S2053229620014217.
14. Duran, N.; Polat, M.F.; Aktas, D.A.; Alagoz, M.A.; Ay, E.; Cimen, F.; Tek, E.; Anil, B.; Burmaoglu, S.; Algul, O. New chalcone derivatives as effective against SARS-CoV-2 agent. *International Journal of Clinical Practice* **2021**, *75*, e14846, https://doi.org/10.1111/ijcp.14846.
15. Kalirajan, R. Activity of Some Novel Chalcone Substituted 9-anilinoacridines against Coronavirus (COVID-19): A Computational Approach. *Coronaviruses* **2020**, *1*, 13–22, https://doi.org/10.2174/2666796701999200625210746.

16. Okolo, E.N.; Ugwu, D.I.; Ezema, B.E.; Ndefo, J.C.; Eze, F.U.; Ezema, C.G.; Ezugwu, J.A.; Ujam, O.T. New chalcone derivatives as potential antimicrobial and antioxidant agent. *Scientific Reports* **2021**, *11*, 21781, https://doi.org/10.1038/s41598-021-01292-5.
17. Henry, E.J.; Bird, S.J.; Gowland, P.; Collins, M.; Cassella, J.P. Ferrocenyl chalcone derivatives as possible antimicrobial agents. *The Journal of Antibiotics* **2020**, *73*, 299–308, https://doi.org/10.1038/s41429-020-0280-y.
18. Benouda, H.; Bouchal, B.; Challioui, A.; Oulmidi, A.; Harit, T.; Malek, F.; Riahi, A.; Bellaoui, M.; Bouammali, B. Synthesis of a Series of Chalcones and Related Flavones and Evaluation of their Antibacterial and Antifungal Activities. *Letters in Drug Design & Discovery* **2018**, *16*, 93–100, https://doi.org/10.2174/1570180815666180404130430.
19. Tupare, S.D. Synthesis and characterization of some nitrogen-containing heterocyclic derivatives via novel chalcones. *World Journal of Pharmaceutical Research* **2021**, *10*, 1203–1213, http://dx.doi.org/10.20959/wjpr202114-22403.
20. Murtaza, S.; Mir, K.Z.; Tatheer, A.; Ullah, R.S. Synthesis and Evaluation of Chalcone and its Derivatives as Potential Anticholinergic Agents. *Letters in Drug Design & Discovery* **2019**, *16*, 322–332, https://doi.org/10.2174/1570180815666180523085436.
21. Lakshminarayanan, B.; Kannappan, N.; Subburaju, T. Synthesis and biological evaluation of novel chalcones with methane-sulfonyl end as potent analgesic and anti-inflammatory agents. *International Journal of Pharmaceutical Sciences and Research* **2020**, *11*, 4974–4981, https://doi.org/10.13040/IJPSR.0975-8232.11(10).4974-81.
22. Higgs, J.; Wasowski, C.; Marcos, A.; Jukič, M.; Paván, C.H.; Gobec, S.; de Tezanos Pinto, F.; Colettis, N.; Marder, M. Chalcone derivatives: synthesis, in vitro and in vivo evaluation of their anti-anxiety, anti-depression and analgesic effects. *Heliyon* **2019**, *19*, e01376, https://doi.org/10.1016/j.heliyon.2019.e01376.
23. Escrivani, D.O.; Charlton, R.L.; Caruso, M.B.; Burle-Caldas, G.A.; Borsodi, M.P.G.; Zingali, R.B.; Arruda-Costa, N.; Palmeira-Mello, M.V.; de Jesus, J.B.; Souza, A.M.; Abrahim-Vieira, B. Chalcones identify cTXNPx as a potential antileishmanial drug target. *Plos neglected tropical diseases* **2021**, *15*, e0009951, https://doi.org/10.1371/journal.pntd.0009951.
24. Fakhrudin, N.; Pertiwi, K.K.; Takubessi, M.I.; Susiani, E.F.; Nurrochmad, A.; Widyarini, S.; Sudarmanto, A.; Nugroho, A.A.; Wahyuono, S.A. geranylated chalcone with antiplatelet activity from the leaves of breadfruit (Artocarpus altilis). *Pharmacia* **2020**, *67*, 173–180, https://doi.org/10.3897/pharmacia.67.e56788.
25. Bale, A.T.; Salar, U.; Khan, K.M.; Chigurupati, S.; Fasina, T.; Ali, F.; Ali, M.; Nanda, S.S.; Taha, M.; Perveen, S. Chalcones and Bis-Chalcones Analogs as DPPH and ABTS Radical Scavengers. *Letters in Drug Design & Discovery* **2021**, *18*, 249–257, https://doi.org/10.2174/1570180817999201001155032.
26. Al Zahrani, N.A.; El-Shishtawy, R.M.; Elaasser, M.M.; Asiri, A.M. Synthesis of Novel Chalcone-Based Phenothiazine Derivatives as Antioxidant and Anticancer Agents. *Molecules* **2020**, *25*, 4566, https://doi.org/10.3390/molecules25194566.
27. Welday K.S.; Hailu, G.S.; Taye D.K. Design, Synthesis, Characterization and in vivo Antidiabetic Activity Evaluation of Some Chalcone Derivatives. *Drug Design, Development, and Therapy* **2021**, *15*, 3119–3129, https://doi.org/10.2147/DDDT.S316185.
28. Jain, A.; Jain, D.K. Synthesis, characterization and biological evaluation of some new heterocyclic derivatives of chalcone as antihyperglycemic agents. *International Journal of Pharmaceutical Sciences and Research* **2021**, *10*, 5700–5706, https://doi.org/10.13040/IJPSR.0975-8232.10(12).5700-06.
29. Qin, H.-L.; Zhang, Z.-W.; Lekkala, R.; Alsulami, H.; Rakesh, K.P. Chalcone hybrids as privileged scaffolds in antimalarial drug discovery: A key review. *European Journal of Medicinal Chemistry* **2020**, *193*, 112215, https://doi.org/10.1016/j.ejmech.2020.112215.
30. Shah, H.H.; Patel, S.G.; Patel, M.M.; Gandhi, K. Identification of chalcone derivatives as putative non-steroidal aromatase inhibitors potentially useful against breast cancer by molecular docking and ADME prediction. *Indian Journal of Chemistry Section B* **2020**, *59*, 283–293, https://doi.org/10.56042/ijcb.v59i2.27865.
31. Ouyang, Y.; Li, J.; Chen, X.; Fu, X.; Sun, S.; Wu, Q. Chalcone Derivatives: Role in Anticancer Therapy. *Biomolecules* **2021**, *11*, 894, https://doi.org/10.3390/biom11060894.
32. Čižmáriková, M.; Takáč, P.; Spengler, G.; Kincses, A.; Nové, M.; Vilková, M.; Mojžiš, J. New Chalcone Derivative Inhibits ABCB1 in Multidrug Resistant T-cell Lymphoma and Colon Adenocarcinoma Cells. *Anticancer Research* **2020**, *39*, 6499–6505, https://doi.org/10.21873/anticanres.13864.

33. Bhoj, P.; Togre, N.; Bahekar, S.; Goswami, K.; Chandak, H.; Patil, M. Immunomodulatory Activity of Sulfonamide Chalcone Compounds in Mice Infected with Filarial Parasite, Brugia malayi. *Indian Journal of Clinical Biochemistry* **2019**, *34*, 225–229, https://doi.org/10.1007/s12291-017-0727-5.
34. Mohd F.N.; Lee, J.S.; Abbas Bhukari, S.N. Effects of chalcone derivatives on players of the immune system. *Drug Design, Development and Therapy* **2015**, *9*, 4761, https://doi.org/10.2147/DDDT.S86242.
35. Reddy, M.R.; Aidhen, I.S.; Reddy, U.A.; Reddy, G.B.; Ingle, K.; Mukhopadhyay, S. Synthesis of 4- C -β-D-Glucosylated Isoliquiritigenin and Analogues for Aldose Reductase Inhibition Studies. *European Journal of Organic Chemistry* **2019**, *24*, 3937–3948, https://doi.org/10.1002/ejoc.201900413.
36. Aljohani, G.; Al-Sheikh Ali, A; Alraqa, S.Y.; Itri Amran, S.; Basar, N. Synthesis, molecular docking and biochemical analysis of amino alkylated naphthalene-based chalcones as acetylcholinesterase inhibitors. *Journal of Taibah University for Science* **2021**, *15*, 781–797, https://doi.org/10.1080/16583655.2021.2005921.
37. Kasetti, A.B.; Singhvi, I.; Nagasuri, R.; Bhandare, R.R.; Shaik, A.B. Thiazole–Chalcone Hybrids as Prospective Antitubercular and Antiproliferative Agents: Design, Synthesis, Biological, Molecular Docking Studies and In Silico ADME Evaluation. *Molecules* **2021**, *26*, 2847, https://doi.org/10.3390/molecules26102847.
38. Atukuri, D.; Vijayalaxmi, S.; Sanjeevamurthy, R.; Vidya, L.; Prasannakumar, R.; Raghavendra, M. M. Identification of quinoline-chalcones and heterocyclic chalcone-appended quinolines as broad-spectrum pharmacological agents. *Bioorganic Chemistry* **2020**, *105*, 104419, https://doi.org/10.1016/j.bioorg.2020.104419.
39. Maatougui, A. El; Yáñez, M.; Crespo, A.; Fraiz, N.; Coelho, A.; Raviña, E.; Laguna, R.; Cano, E.; Loza, M. I.; Brea, J.; Gutiérrez de Terán, H.; Sotelo, E. 3-Oxopyridazin-5-yl-Chalcone Hybrids: Potent Antiplatelet Agents That Prevent Glycoprotein IIb/IIIa Activation. *ChemistrySelect* **2017**, *2*, 4920–4933, https://doi.org/10.1002/slct.201700243.
40. Tugrak, M.; Gul, H.I.; Akincioglu, H.; Gulcin, I. New Chalcone Derivatives with Pyrazole and Sulfonamide Pharmacophores as Carbonic Anhydrase Inhibitors. *Letters in Drug Design & Discovery* **2021**, *18*, 191–198, https://doi.org/10.2174/1570180817999201001160414.
41. Joseph, M.; Alexander, S. Design, Synthesis, and Characterization of Thiophene Substituted Chalcones for Possible Biological Evaluation. *Journal of Pharmaceutical Research International* **2021**, *33*, 55–79, https://doi.org/10.9734/jpri/2021/v33i49B33341.
42. Horley, N.J.; Beresford, K.J.M.; Kaduskar, S.; Joshi, P.; McCann, G.J.P.; Ruparelia, K.C.; Williams, I.S.; Gatchie, L.; Sonawane, V.R.; Bharate, S.B.; Chaudhuri, B. (E)-3-(3,4,5-Trimethoxyphenyl)-1-(pyridin-4-yl)prop-2-en-1-one, a heterocyclic chalcone is a potent and selective CYP1A1 inhibitor and cancer chemopreventive agent. *Bioorganic & Medicinal Chemistry Letters* **2017**, *27*, 5409–5414, https://doi.org/10.1016/j.bmcl.2017.11.009.
43. Pinto, P.; Machado, C.M.; Moreira, J.; Almeida, J.D.P.; Silva, P.M.; Henriques, A.C.; Soares, J.X.; Salvador, J.A.; Afonso, C.; Pinto, M.; Bousbaa, H. Chalcone derivatives targeting mitosis: Synthesis, evaluation of antitumor activity and lipophilicity. *European Journal of Medicinal Chemistry* **2019**, *184*, 111752, https://doi.org/10.1016/j.ejmech.2019.111752.
44. Abbas, A.; Naseer, M.M.; Hasan A.; Hadda, T.B.; Mater, J. Synthesis and Cytotoxicity Studies of 4-Alkoxychalcones as New Antitumor Agents. *Environ. Sci*. **2014**, *5*, 281-292.
45. Nagai, H.; He, J.X.; Tani, T.; Akao, T. Antispasmodic activity of licochalcone A, a species-specific ingredient of Glycyrrhiza inflata roots. *Journal of Pharmacy and Pharmacology* **2007**, *59*, 1421-1426, https://doi.org/10.1211/jpp.59.10.0013.
46. Shibata, S. Anti-tumorigenic chalcones. *Stem cells* **1994**, *12*, 44-52, https://doi.org/10.1002/stem.5530120109.
47. Takahashi, M.; Maeda, S.; Ogura, K.; Terano,A.; Omata. M. The possible role of vascular endothelial growth factor (VEGF) in gastric ulcer healing: effect of sofalcone on VEGF release in vitro. *J. Clin. Gastroenterol*. **1998**, *27*, 178-182, https://doi.org/10.1097/00004836-199800001-00029.
48. Mahapatra, D.K.; Bharti, S.K. Therapeutic potential of chalcones as cardiovascular agents. *Life sciences* **2016**, *148*, 154-172, https://doi.org/10.1016/j.lfs.2016.02.048.
49. Elkhalifa, D.; Al-Hashimi, I.; Al Moustafa, A.E.; Khalil, A.A comprehensive review on the antiviral activities of chalcones. *Journal of Drug Targeting* **2021**, *29*, 403-419, https://doi.org/10.1080/1061186X.2020.1853759.

50. Mellado, M.; Espinoza, L.; Madrid, A.; Mella, J.; Chávez-Weisser, E.; Diaz, K.; Cuellar, M. Design, synthesis, antifungal activity, and structure–activity relationship studies of chalcones and hybrid dihydrochromane–chalcones. *Molecular diversity* **2020**, *24*, 603-615, https://doi.org/10.1007/s11030-019-09967-y.
51. Zheng, Y.; Wang, X.; Gao, S.; Ma, M.; Ren, G.; Liu, H.; Chen, X. Synthesis and antifungal activity of chalcone derivatives. *Natural product research* **2015**, *29*, 1804-1810, https://doi.org/10.1080/14786419.2015.1007973.
52. Chen, S.; Zhang, M.; Feng, S.; Gong, C.; Zhou, Y.; Xing, L.; He, B.; Wu, Y.; Xue, W. Design, synthesis and biological activity of chalcone derivatives containing pyridazine. *Arabian Journal of Chemistry* **2023**, *16*, 104852, https://doi.org/10.1016/j.arabjc.2023.104852.
53. Parmar, V.S.; Jain, S.C.; Bisht, K.S.; Sharma, N.K.; Gupta, S.; Prasad, A.K.; Jha, A.; Malhotra, S.; Sharma, S.K.; Bracke, M.E. Synthesis and anti-invasive activity of novel 1, 3-diarylpropenones. *Indian. J. Chem. B.* **1998**, *37B*, 628-643.
54. Duarte, V.S.; Paula, R.L.; Custodio, J.M.; D'Oliveira, G.D.; Borges, L.L.; Pérez, C.N.; Perjesi, P.; Oliver, A.G.; Napolitano, H.B. A new quinolinone-chalcone hybrid with potential antibacterial and herbicidal properties using in silico approaches. *Journal of Molecular Modeling* **2022**, *28*, 176, https://doi.org/10.1007/s00894-022-05140-9.
55. Modi, S. R.; Naik, H. B. Synthesis and Antibacterial Activity of Some Chalcones and Isoxazoles. *Orient J. Chem*. **1994**, *10*, 85-86.
56. Cheng, W.; Xiao, T.; Qian, W.; Lu, T.; Zhang, T.; Tang, X. Design, synthesis and insecticidal activity of novel semicarbazones and thiosemicarbazones derived from chalcone. *Natural product research* **2021**, *35*, 3801-3809, https://doi.org/10.1080/14786419.2020.1739679.
57. Middleton, E.; Kandaswami,Jr., C.; Theoharides, C. The effects of plant flavonoids on mammalian cells: implications for inflammation, heart disease, and cancer. *Pharmacol. Rev*. **2000**, *52*, 673-751.
58. Ugwu, D.I.; Ezema, B.E.; Okoro, U.C.; Eze, F.U.; Ekoh, O.C.; Egbujor, M.C.; Ugwuja, D.I. Synthesis and pharmacological applications of chalcones: A review. *Int. J. Chem. Sci*. **2015**, *13*, 459-500.
59. Bhuva, V.V. Studies on some Heterocyclic Compounds of Therapeutic Interest. Thesis PhD, Saurashtra University, Gujarat, India, **2009**.
60. Purohit, D.H. Studies on Medicinally Interesting Chemical Entities. Thesis PhD, Saurashtra University, Gujarat, India, **2006**.
61. Shinde, R.S.; Salunke, S.D. Facile synthesis of some triazine-based chalcones as potential antioxidant and anti-diabetic agents. *Journal of Chemical and Pharmaceutical Research* **2015**, *7*, 114–120.
62. Sahoo, B.M.; Rajeswari, M.; Jnyanaranjan, P.; Binayani, S. Green Expedient Synthesis of Pyrimidine Derivatives via Chalcones and Evaluation of their Anthelmintic Activity. *Indian Journal of Pharmaceutical Education and Research* **2017**, *51*, s700–s706, https://doi.org/10.5530/ijper.51.4s.101.
63. Fathimunnisa, M.; Manikandan, H.; Sivakumar, D. An Efficient, Solvent-Free Synthesis of Some Chalcone Derivatives and Their Biological Evaluation. *Asian Journal of Chemistry* **2018**, *30*, 807–810, https://doi.org/10.14233/ajchem.2018.21016.
64. Anwar, C.; Prasetyo, Y.D.; Matsjeh, S.; Haryadi, W.; Sholikhah, E.N.; Nendrowati, N. Synthesis of chalcone derivatives and their in vitro anticancer test against breast (T47D) and colon (WiDr) cancer cell line. *Indonesian Journal of Chemistry* **2018**, *18*, 102, https://doi.org/10.22146/ijc.26864.
65. Bui, T.H.; Nguyen, N.T.; Dang, P.H.; Nguyen, H.X.; Nguyen, M.T.T. Design and synthesis of chalcone derivatives as potential non-purine xanthine oxidase inhibitors. *Springer Plus* **2016**, *5*, 1789, https://doi.org/10.1186/s40064-016-3485-6.
66. Noser, A.A.; Shehadi, I.A.; Abdelmonsef, A.H.; Salem, M.M. Newly Synthesized Pyrazolinone Chalcones as Anticancer Agents via Inhibiting the PI3K/Akt/ERK1/2 Signaling Pathway. *ACS Omega* **2022**, *7*, 25265–25277, https://doi.org/10.1021/acsomega.2c02181.
67. Bhadke, P.K.; Pahelkar, A.R.; Gadkari, Y.U.; Naik, J.M.; Telvekar, V.N. Eco-Friendly and Efficient Greener Process for the Synthesis of Chalcones and Pyrazolones Using the Supramolecular Catalyst β-Cyclodextrin. *Organic Preparations and Procedures International* **2022**, *54*, 363–369, https://doi.org/10.1080/00304948.2022.2034462.
68. Bala, D.; Jinga, L.-I.; Popa, M.; Hanganu, A.; Voicescu, M.; Bleotu, C.; Tarko, L.; Nica, S. Design, Synthesis, and Biological Evaluation of New Azulene-Containing Chalcones. *Materials* **2022**, *15*, 1629, https://doi.org/10.3390/ma15051629.

69. Alidmat, M.M.; Khairuddean, M.; Salhimi, S.M.; Al-Amin, M. Docking studies, synthesis, characterization, and cytotoxicity activity of new bis-chalcones derivatives. *Biomedical Research and Therapy* **2021**, *8*, 4294–4305, https://doi.org/10.15419/bmrat.v8i4.668.
70. Hu, D.; Zhang, N.; Zhang, Y.; Yuan, C.; Gong, C.; Zhou, Y.; Xue, W. Design, synthesis and biological activity of novel chalcone derivatives containing indole. *Arabian Journal of Chemistry* **2023**, *16*, 104776, https://doi.org/10.1016/j.arabjc.2023.104776.
71. Chen, Y.; Li, P.; Chen, M.; He, J.; Su, S.; He, M.; Wang, H.; Xue, W. Synthesis and antibacterial activity of chalcone derivatives containing thioether triazole. *Journal of Heterocyclic Chemistry* **2020**, *57*, 983–990, https://doi.org/10.1002/jhet.3755.
72. Dhar, R.; Kimseng, R.; Chokchaisiri, R.; Hiransai, P.; Utaipan, T.; Suksamrarn, A.; Chunglok, W. 2′,4-Dihydroxy-3′,4′,6′-trimethoxychalcone from Chromolaena odorata possesses anti-inflammatory effects via inhibition of NF-κB and p38 MAPK in lipopolysaccharide-activated RAW 264.7 macrophages. *Immunopharmacology and Immunotoxicology* **2018**, *40*, 43–51, https://doi.org/10.1080/08923973.2017.1405437.
73. Shukla, P.; Satyanarayana, M.; Verma, P.C.; Tiwari, J.; Dwivedi, A.P.; Srivastava, R.; Rehuja, N.; Srivastava, S.P.; Gautam, S.; Tamrakar, A.K.; Dwivedi, A.K.; Kushwaha, H.N.; Gautam, N.; Singh, S.K.; Srivastava, M.; Nath, C.; Raghubir, R.; Srivastava, A.K.; Pratap, R. Chalcone-Based Aryloxypropanolamine as a Potential Antidiabetic and Antidyslipidaemic Agent. *Current Science* **2017**, *112*, 1675, https://doi.org/10.18520/cs/v112/i08/1675-1689.
74. Burmaoglu, S.; Algul, O.; Gobek, A.; Aktas Anil, D.; Ulger, M.; Erturk, B.G.; Kaplan, E.; Dogen, A.; Aslan, G. Design of potent fluoro-substituted chalcones as antimicrobial agents. *Journal of Enzyme Inhibition and Medicinal Chemistry* **2017**, *32*, 490–495, https://doi.org/10.1080/14756366.2016.1265517.
75. Williams, I.S.; Joshi, P.; Gatchie, L.; Sharma, M.; Satti, N.K.; Vishwakarma, R.A.; Chaudhuri, B.; Bharate, S.B. Synthesis and biological evaluation of pyrrole-based chalcones as CYP1 enzyme inhibitors, for possible prevention of cancer and overcoming cisplatin resistance. *Bioorganic & Medicinal Chemistry Letters* **2017**, *27*, 3683–3687, https://doi.org/10.1016/j.bmcl.2017.07.010.
76. Özdemir, A.; Altıntop, M.D.; Sever, B.; Gençer, H.K.; Kapkaç, H.A.; Atlı, Ö.; Baysal, M. A New Series of Pyrrole-Based Chalcones: Synthesis and Evaluation of Antimicrobial Activity, Cytotoxicity, and Genotoxicity. *Molecules* **2017**, *22*, 2112, https://doi.org/10.3390/molecules22122112.
77. Sharma, P.; Kumar, S.; Ali, F.; Anthal, S.; Gupta, V.K.; Khan, I.A.; Singh, S.; Sangwan, P.L.; Suri, K.A.; Gupta, B.D.; Gupta, D.K.; Dutt, P.; Vishwakarma, R.A.; Satti, N.K. Synthesis and biologic activities of some novel heterocyclic chalcone derivatives. *Medicinal Chemistry Research* **2013**, *22*, 3969–3983, https://doi.org/10.1007/s00044-012-0401-7.
78. Kasetti, A.B.; Dwivedi, J.; Nagasuri, R. Antioxidant Studies of Thiazole Ring Bearing Chalcone Derivatives. *Journal of Pharmaceutical Research International* **2021**, *33*, 355–359, https://doi.org/10.9734/jpri/2021/v33i59A34280.
79. Rupala, R.G.; Kundariya, D.S.; Patel, P.K. Synthesis, Characterization and Biological Evaluation of Some Novel Chalcone Derivatives Containing Imidazo[1,2-a] Pyridine Moiety. *Journal of Chemistry, Environmental Sciences and Its Applications* **2014**, *1*, 23–32, https://doi.org/10.15415/jce.2014.11003.
80. Farghaly, T.A.; Masaret, G.S.; Muhammad, Z.A.; Harris, M.F. Discovery of thiazole-based-chalcones and 4-hetarylthiazoles as potent anticancer agents: Synthesis, docking study and anticancer activity. *Bioorganic Chemistry* **2020**, *98*, 103761, https://doi.org/10.1016/j.bioorg.2020.103761.
81. Durgapal, S.D.; Soni, R.; Umar, S.; Suresh, B.; Soman, S.S. 3-Aminomethyl pyridine chalcone derivatives: Design, synthesis, <scp>DNA</scp> binding and cytotoxic studies. *Chemical Biology & Drug Design* **2018**, *92*, 1279–1287, https://doi.org/10.1111/cbdd.13189.
82. Ahmed, M.F.; Santali, E.Y.; El-Haggar, R. Novel piperazine–chalcone hybrids and related pyrazoline analogs targeting VEGFR-2 kinase; design, synthesis, molecular docking studies, and anticancer evaluation. *Journal of Enzyme Inhibition and Medicinal Chemistry* **2021**, *36*, 308–319, https://doi.org/10.1080/14756366.2020.1861606.
83. Wang, G.; Peng, Z.; Li, Y. Synthesis, Anticancer Activity and Molecular Modeling Studies of Novel Chalcone Derivatives Containing Indole and Naphthalene Moieties as Tubulin Polymerization Inhibitors. *Chemical and Pharmaceutical Bulletin* **2019**, *67*, 725–728, https://doi.org/10.1248/cpb.c19-00217.
84. Zhou, W.; Zhang, W.; Peng, Y.; Jiang, Z.-H.; Zhang, L.; Du, Z. Design, Synthesis and Antitumor Activity of Novel Benzimidazole-Chalcone Hybrids as Non-Intercalative Topoisomerase II Catalytic Inhibitors. *Molecules* **2020**, *25*, 3180, https://doi.org/10.3390/molecules25143180.

85. Pragathi, Y.J.; Veronica, D.; Anitha, K.; Rao, M.V.B.; Raju, R.R. Synthesis and biological evaluation of chalcone derivatives of 1,2,4-thiadiazol-benzo[d]imidazol-2-yl)quinolin-2(1H)-one as anticancer agents. *Chemical Data Collections* **2020**, *30*, 100556, https://doi.org/10.1016/j.cdc.2020.100556.
86. Hsieh, C.Y.; Ko, P.W.; Chang, Y.J.; Kapoor, M.; Liang, Y.C.; Chu, H.L.; Lin, H.H.; Horng, J.C.; Hsu, M.H. Design and Synthesis of Benzimidazole-Chalcone Derivatives as Potential Anticancer Agents. *Molecules* **2019**, *24*, 3259, https://doi.org/10.3390/molecules24183259.
87. Sashidhara, K.V.; Avula, S.R.; Doharey, P.K.; Singh, L.R.; Balaramnavar, V.M.; Gupta, J. Misra-Bhattacharya, S.; Rathaur, S.; Saxena, A.K.; Saxena, J.K. Designing, synthesis of selective and high-affinity chalcone-benzothiazole hybrids as Brugia malayi thymidylate kinase inhibitors: In vitro validation and docking studies. *European Journal of Medicinal Chemistry* **2015**, *103*, 418–428, https://doi.org/10.1016/j.ejmech.2015.09.004.
88. Kumar, V.; Dhawan, S.; Girase, P.S.; Awolade, P.; Shinde, S.R.; Karpoormath, R.; Singh, P. Recent Advances in Chalcone-Based Anticancer Heterocycles: A Structural and Molecular Target Perspective. *Current Medicinal Chemistry* **2021**, *28*, 6805–6845, https://doi.org/10.2174/0929867328666210322102836.
89. Venkataramireddy, V.; Shankaraiah, M.; Tejeswara Rao, A; Kalyani, C.; Lakshmi Narasu, M.; Varala, A.; Jayashree, A. Synthesis and anti-cancer activity of novel 3- aryl thiophene-2-carbaldehydes and their aryl/heteroaryl chalcone derivatives. *Rasayan J. Chem*. **2016**, *9*, 31–39.
90. Venkataramana Reddy, P.O.; Hridhay, M.; Nikhil, K.; Khan, S.; Jha, P.N.; Shah, K.; Kumar, D. Synthesis and investigations into the anticancer and antibacterial activity studies of β-carboline chalcones and their bromide salts. *Bioorganic & Medicinal Chemistry Letters* **2018**, *28*, 1278–1282, https://doi.org/10.1016/j.bmcl.2018.03.033.
91. Khan, S.A.; Asiri, A.M.; Al-Ghamdi, N.S.M.; Asad, M.; Zayed, M.E.M.; Elroby, S.A.K.; Aqlan, F.M.; Wani, M.Y.; Sharma, K. Microwave assisted synthesis of chalcone and its polycyclic heterocyclic analogues as promising antibacterial agents: In vitro, in silico and DFT studies. *Journal of Molecular Structure* **2019**, *1190*, 77–85, https://doi.org/10.1016/j.molstruc.2019.04.046.
92. Shaik, A.; Bhandare, R.R.; Palleapati, K.; Nissankararao, S.; Kancharlapalli, V.; Shaik, S. Antimicrobial, Antioxidant, and Anticancer Activities of Some Novel Isoxazole Ring Containing Chalcone and Dihydropyrazole Derivatives. *Molecules* **2020**, *25*, 1047, https://doi.org/10.3390/molecules25051047.
93. Meshram, G.A.; Vala, V.A. Synthesis, characterization, and antimicrobial activity of benzimidazole-derived chalcones containing 1,3,4-oxadiazole moiety. *Chemistry of Heterocyclic Compounds* **2015**, *51*, 44–50, https://doi.org/10.1007/s10593-015-1653-1.
94. Osmaniye, D.; Kaya Cavusoglu, B.; Saglik, B.; Levent, S.; Acar Cevik, U.; Atli, O.; Ozkay, Y.; Kaplancikli, Z. Synthesis and Anticandidal Activity of New Imidazole-Chalcones. *Molecules* **2018**, *23*, 831, https://doi.org/10.3390/molecules23040831.
95. Sunitha, V.; Kumar, A.K.; Mahesh, M.; Shankaraiah, P.; Jalapathi, P.; Lincoln, Ch. A. Synthesis and Antimicrobial Evaluation of Bis-3,5-disubstituted Isoxazoles Based Chalcones. *Russian Journal of General Chemistry* **2018**, *88*, 1904–1911, https://doi.org/10.1134/S1070363218090232.
96. Bhat, M.; Nagaraja, G.K.; Divyaraj, P.; Harikrishna, N.; Biswas, S.; Peethamber, S.K. Design, synthesis, characterization of some new 1,2,3-triazolyl chalcone derivatives as potential antimicrobial, antioxidant and anti-cancer agents via a Claisen–Schmidt reaction approach. *RSC Advances* **2016**, *6*, 99794–99808, https://doi.org/10.1039/C6RA22705H.
97. Kumari, S.; Paliwal, S.K.; Chauhan, R. An Improved Protocol for the Synthesis of Chalcones Containing Pyrazole with Potential Antimicrobial and Antioxidant Activity. *Current Bioactive Compounds* **2018**, *14*, 39–47, https://doi.org/10.2174/1573407212666161101152735.
98. Thillainayagam, M.; Pandian, L.; Murugan, K.K.; Vijayaparthasarathi, V.; Sundaramoorthy, S.; Anbarasu, A.; Ramaiah, S. In silico analysis reveals the antimalarial potential of quinolinyl chalcone derivatives. *Journal of Biomolecular Structure and Dynamics* **2015**, *33*, 961–977, https://doi.org/10.1080/07391102.2014.920277.
99. Jyoti, Gaur, R.; Kumar, Y.; Cheema, H.S.; Kapkoti, D.S.; Darokar, M.P.; Khan, F.; Bhakuni, R.S. Synthesis, molecular modelling studies of indolyl chalcone derivatives and their antimalarial activity evaluation. *Natural Product Research* **2021**, *35*, 3261–3268, https://doi.org/10.1080/14786419.2019.1696788.
100. Vinindwa, B.; Dziwornu, G.A.; Masamba, W. Synthesis and Evaluation of Chalcone-Quinoline Based Molecular Hybrids as Potential Antimalarial Agents. *Molecules* **2021**, *26*, 4093, https://doi.org/10.3390/molecules26134093.

101. Syahri, J.; Nasution, H.; Nurohmah, B.A.; Purwono, B.; Yuanita, E. Novel aminoalkylated chalcone: Synthesis, biological evaluation, and docking simulation as potent antimalarial agents. *Journal of Applied Pharmaceutical Science* **2020**, *10*, 1–5, https://doi.org/10.7324/JAPS.2020.10601.
102. Chen, Z.; Li, P.; Hu, D.; Dong, L.; Pan, J.; Luo, L.; Zhang, W.; Xue, W.; Jin, L.; Song, B. Synthesis, antiviral activity, and 3D-QSAR study of novel chalcone derivatives containing malonate and pyridine moieties. *Arabian Journal of Chemistry* **2019**, *12*, 2685–2696, https://doi.org/10.1016/j.arabjc.2015.05.003.