

Review

Chalcone: A Promising Bioactive Scaffold in Medicinal Chemistry

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Abstract: Chalcones are a class of privileged scaffolds with high medicinal significance due to the presence of an α,β -unsaturated ketone functionality. Numerous functional modifications of chalcones have been reported, along with their pharmacological behavior. The present review aims to summarize the structures from natural sources, synthesis methods, biological characteristics against infectious and non-infectious diseases, and uses of chalcones over the past decade, and their structure–activity relationship studies are detailed in depth. This critical review provides guidelines for the future design and synthesis of various chalcones. In addition, this could be highly supportive for medicinal chemists to develop more promising candidates for various infectious and non-infectious diseases.

Keywords: chalcones; natural sources; Claisen–Schmidt condensation; infectious diseases; non-infectious diseases; structure–activity relationship

1. Introduction

Molecular diversity is a crucial factor for any drug discovery program. The molecules of interest can be obtained through natural or chemical syntheses. Natural products remain a source of unexplored chemotypes (e.g., molecular scaffolds and pharmacophores) and offer many structural fragments for medicinal chemistry. Therefore, natural products are always considered to be invaluable sources of inspiration for drug discovery development. Recently, scientists have been attracted to smaller fragments or scaffolds (~300 Da) due to their unique properties, i.e., effective molecular interactions with the targeted biological receptors for pharmacological properties. These features are very crucial in the area of fragment-based drug design (FBDD). Such exceptional properties are found in flavonoids. Flavonoids are among the largest polyphenols that are widely distributed in fruits, vegetables, and the plant kingdom as secondary metabolites. Flavonoids are classified into chalcones, flavanones, flavones, isoflavones, aurones, neoflavones and biflavones. To date,

more than 7500 molecularly diverse flavonoids have been reported. Among flavonoids, chalcones play a prominent role and have been found to be a precursor for the biosynthesis of flavonoids.

Chalcones have an α,β -unsaturated system with three carbon units as its structural basis [1]. They are known as 1,3-diphenylprop-2-en-1-one, which is implicated in their hydrophobic/hydrophilic nature that has sparked much research—especially in the field of infectious and non-infectious diseases [2]. Chalcones occur in the cis or trans form, of which the trans isomer is more thermodynamically stable than the cis form. Chalcones have been reported to have biological properties such as anticancer [3] antimicrobial [4], antiviral [5], antioxidant [6], anti-Alzheimer's [7], antitumor [8], antidiabetic [9], anti-Parkinson's [10], anti-inflammatory [11], and anti-nociceptive [12] effects (Figure 1). After a careful literature search, it has been found that in the past decade many scientific developments took place in chalcone chemistry, which is scattered in nature. Furthermore, heterocyclic rings are known to be bioactive, and incorporating heterocyclic moieties in the structural framework of chalcones will further increase their bioactivity. In recent years, numerous research projects have been completed, and scientists have synthesized various chalcone analogs. Chalcones bearing heterocyclic rings—such as quinoline [13], pyrrole [14], pyridine [15], indole [16], pyrazole [17], benzofuran [18], coumarin [19], isoxazole [20], benzimidazole [21], and azulene [22]—have been reported in the literature. There have also been reports of metallocene-based chalcone analogs such as ruthenocenyl and ferrocenyl chalcones in the literature [23]. Chalcones can also be used for other optical applications, such as fluorescent probes [24]. With this view, the effort was taken to summarize the structure, synthesis, properties, and applications of chalcones over the past decade, and their structure–activity relationship (SAR) studies are described in detail in this review.

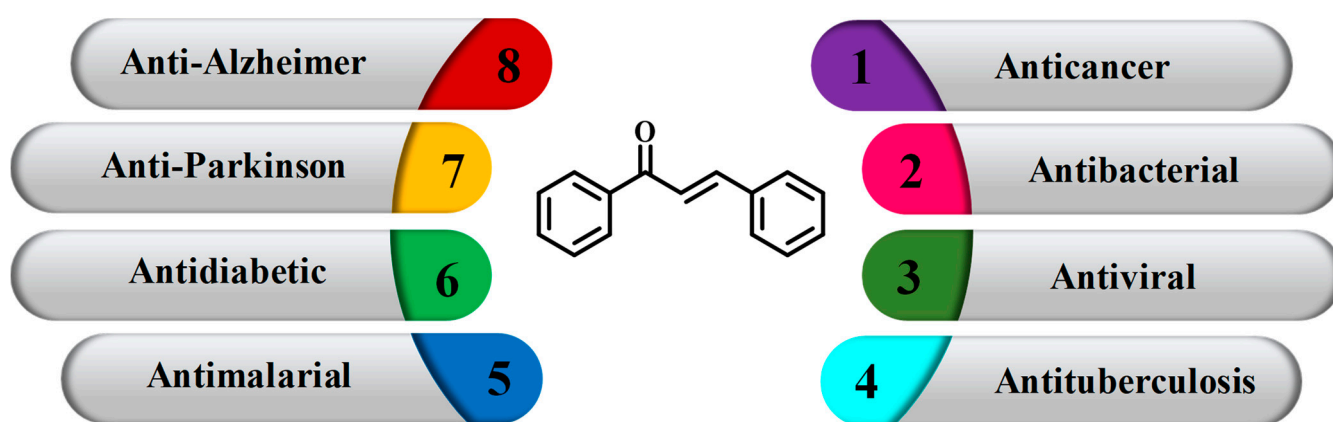


Figure 1. Structure of chalcone and its bioactivities (e.g., anticancer, antibacterial, antiviral, anti-tubercular).

2. Chalcones from Natural Sources

Chalcones can be biosynthesized by combining phenyl propane and acetate pathways through convergent syntheses. Coumaroyl-CoA is used for making phenylalanine in three enzymatic steps, and malonyl-CoA is synthesized by carboxylation of acetyl-CoA—a central intermediate in the Krebs tricarboxylic acid cycle. The chalcones are further classified based on their structure; for example, the compounds that usually occur in plants are commonly hydroxylated or methoxylated (Figure 2A); glycosylated and prenylated forms are found less frequently (Figure 2C), as are geranylated chromene-based derivatives (Figure 2B) and dihydroquinone-based chalcones (Figure 2D). Herbs that contain chalcones have been used as medicines in the past to treat a variety of illnesses. Chalcones can be found in large quantities in various plants, including *Butea monosperma*, *Desmodium gangeticum*, *Humulus lupulus*, *Helichrysum rugulosum*, *Neoraputia magnifica*, *Angelica keiskei*, *Piper hispidum*, *Tarenna attenuata*, and *Calythrops aurea* [12,25–57].

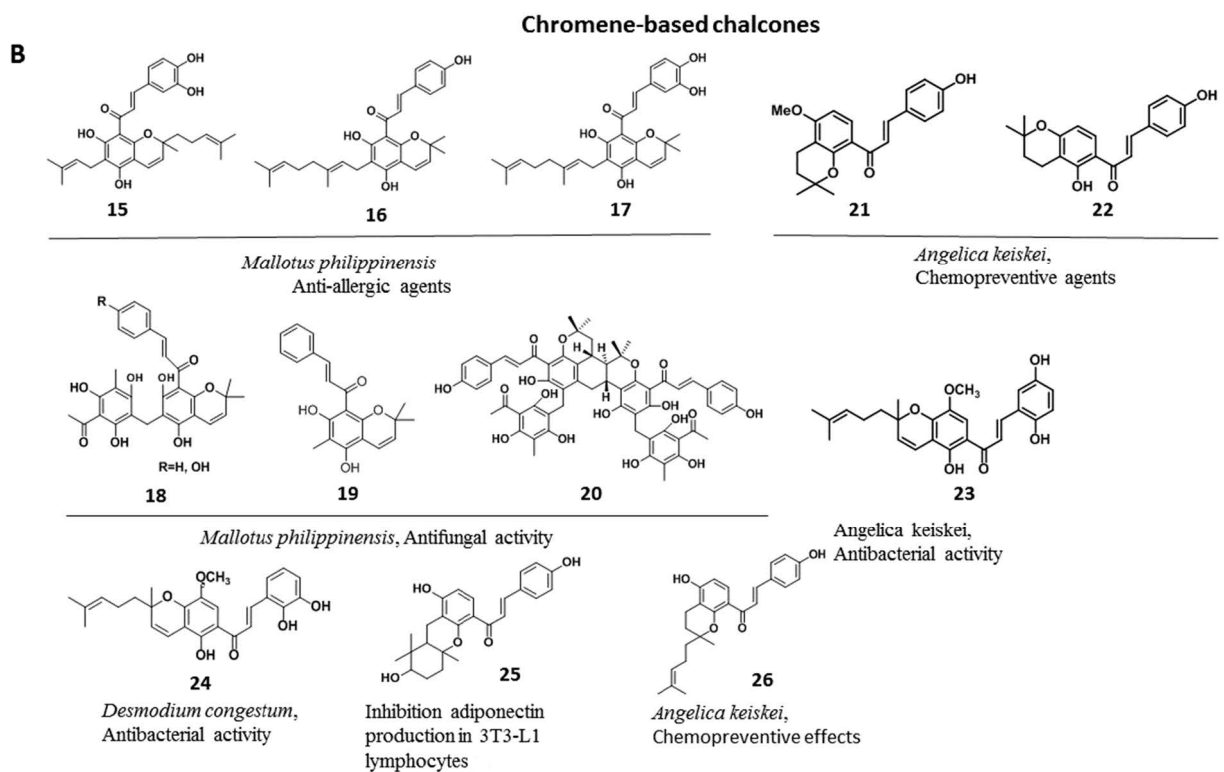
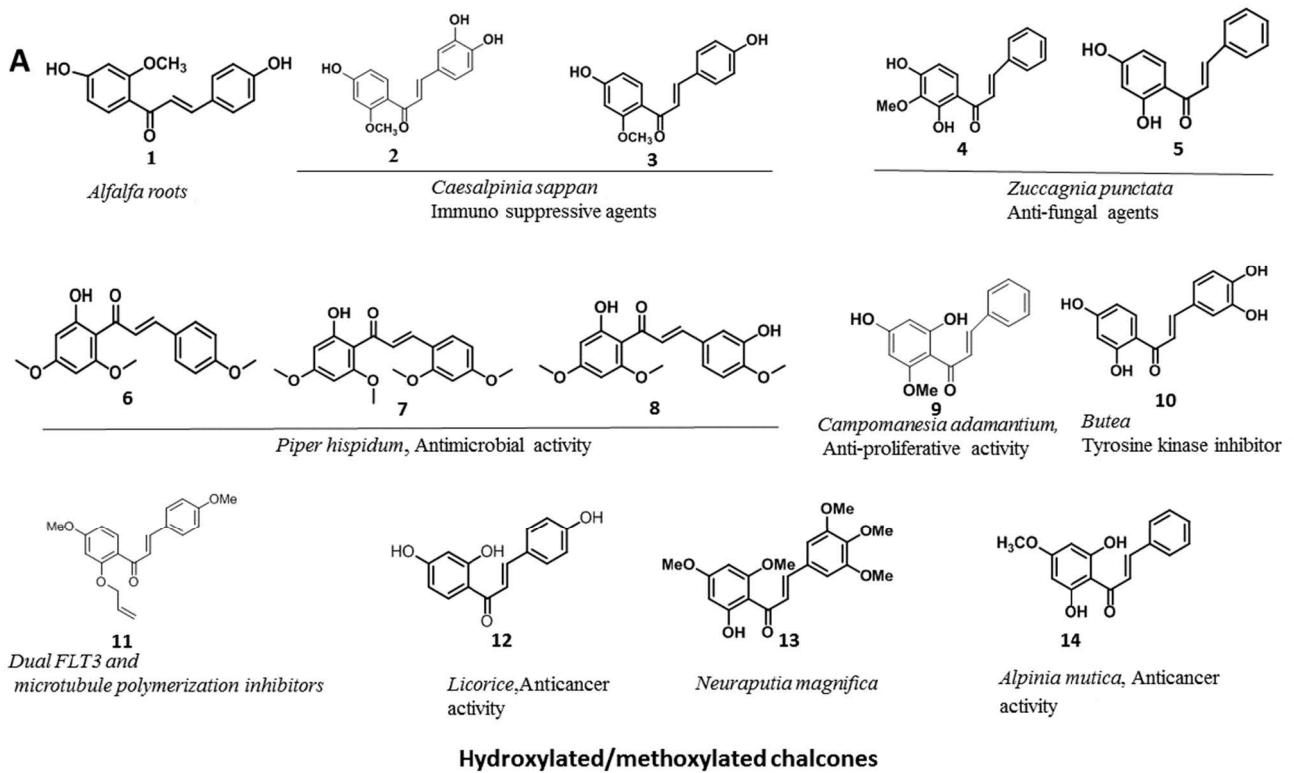


Figure 2. Cont.

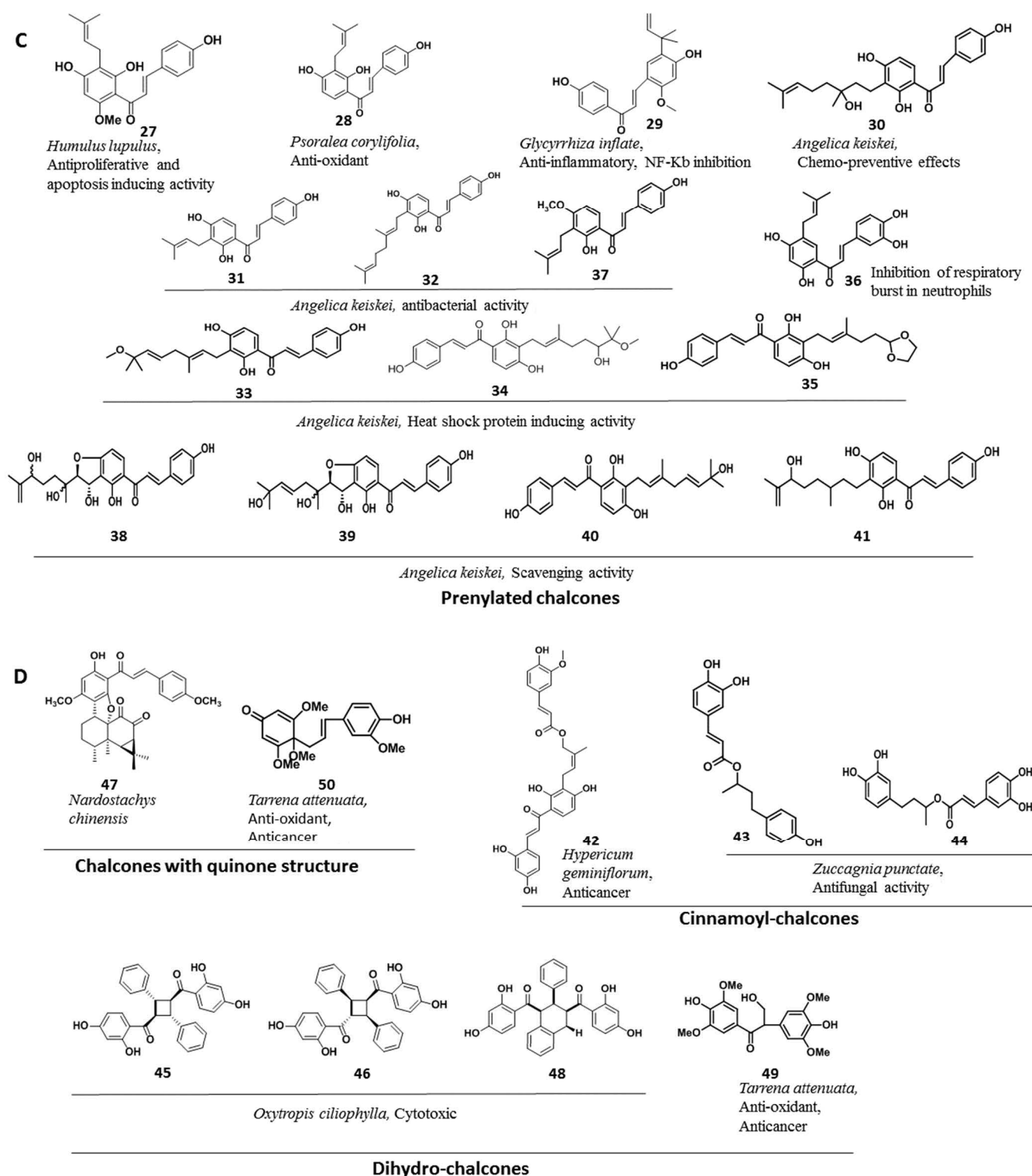


Figure 2. Naturally occurring chalcones: (A) hydroxylated and methoxylated chalcones; (B) chromene-based chalcones; (C) prenylated chalcones; (D) quinone-, cinnamoyl-, and dihydro-bearing chalcones.

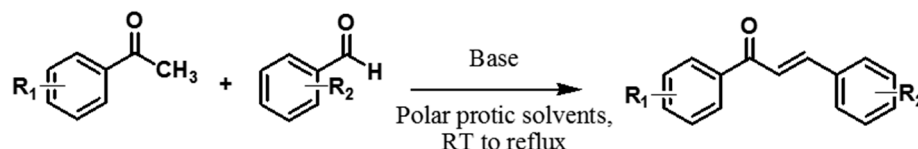
3. Synthesis of Chalcones

Chalcones possess an α,β -unsaturated ketone with a diphenyl substitution, and their other functionality makes them unique as a scaffold with multifunctional biological properties. Procurement of chalcones from natural sources often entails logistical problems. Thus, they are chemically synthesized through the following methods:

3.1. Conventional Synthesis of Chalcones

Generally, chalcones are synthesized from an aldehyde and acetophenone through Claisen–Schmidt condensation in the presence of an acid or base. Numerous conditions have been established for synthesizing chalcones, as detailed below.

In the Claisen–Schmidt condensation reaction (Scheme 1), different bases—such as NaOH, KOH, LiOH, Ba(OH)₂, and organic bases (i.e., piperidine and pyridine) have been used to facilitate the synthesis of chalcones. Likewise, acidic reagents such as HCl and AlCl₃ have also been established. In both conditions, the yield of chalcone is comparatively less, with an average yield of 50–60% based on the substitutions



Scheme 1. Chalcone synthesis via Claisen–Schmidt condensation.

Later, to increase the yield, different catalysts were also tried [58,59]. For example, materials such as chitosan [60], Al–Mg hydrotalcite [61], and Cs-pollucite nanozeolite modified with organosilane [62] have been used for the reaction. The acid-based catalyst, i.e., BF₃–Et₂O, has many advantages over others, with the yield of the chalcone increasing drastically, which is also helpful for the ease of production [2]. Similarly, other materials—such as activated carbons [63], nanoporous AISBA-15 [64], cesium salt of 12-tungstophoric acid [65], ionic liquids [66], protonated aluminate mesoporous silica nanomaterials [67,68], (MWCNTs)-COOH–CeO₂ hybrids [69], modified fluorapatite [68], Fe₃O₄-MOF core–shell magnetic microspheres [70], nanosized ZnWO₄ [71], and graphene-supported ZnO nanoparticles [72]—have also been established. BF₃-etherate can be used as a better catalyst for chalcone synthesis, as the products are obtained with higher yields—in the range of 75–96%. Using heterogeneous catalysts also yields chalcones in higher amounts, where the catalysts can be reused for many cycles of the reaction.

3.2. Greener Approaches for the Synthesis of Chalcones

3.2.1. Microwave-Assisted Method

Based on the disadvantages of the conventional methods, microwave-assisted synthesis has been developed for synthesizing chalcones. The main advantage of the microwave-assisted method is that the reaction is usually faster. For example, a few heteroaromatic chalcones can be yielded in 3–5 min without using solvents. Here, the catalysts (the conditions may be either acidic or basic) are combined with the starting materials to form a thick paste, from which the product can be isolated in a soluble form by the elution of catalysts. A series of chalcones have been synthesized using K₂CO₃ as a base along with microwave irradiation [73]. Furthermore, chalcones with pyrazoline moieties have been synthesized at higher yields under acidic conditions [74].

3.2.2. Ultrasound-Irradiated Synthesis

Similarly, another strategy—the ultrasound irradiation method—can also be established without solvents. The reaction rate is accelerated by ultrasonic irradiation, leading to the formation of the product in a much smaller amount of time and with a higher yield [75]. The completion of the reaction was shown in about 10 s during the synthesis of thiophene-based chalcones with cesium carbonate as a base [76]. Chalcones were also synthesized in the presence of a zeolite-based catalyst in solvent-free conditions, and the yield was greater than 95% [77].

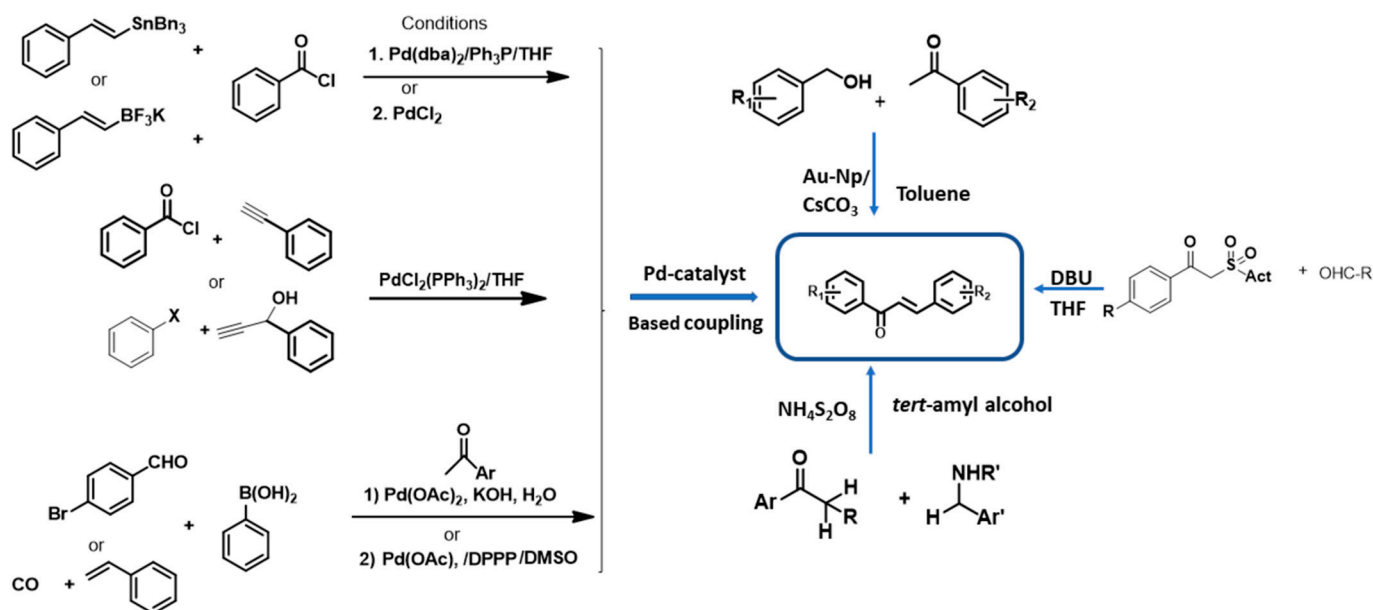
3.2.3. Grinding Technique

This technique provides an alternate way to synthesize chalcones without solvents. The equivalent quantities of aromatic aldehydes, acetophenone, and the reagent are mixed

and ground in a porcelain mortar for about 10 min. The desired product can be isolated after adding cold water through filtration [78]. A series of chalcones with different benzaldehydes and 2-acetyl-2-naphthol were synthesized using a grinding technique, and the products were obtained with a yield from 85 to 95% [79].

3.3. Coupling Reactions

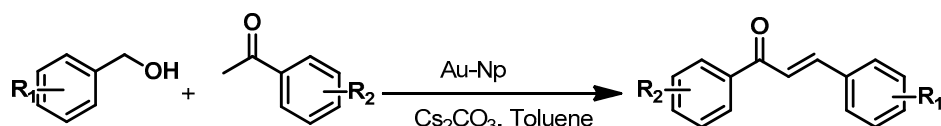
Although chalcones are obtained with a good yield through the greener approaches, they do not generally take the form of multi-substituted chalcones. On the other hand, a coupling reaction could be a good platform for developing chalcone synthesis. Some essential coupling reactions for preparing chalcones are described below (Scheme 2).



Scheme 2. Various methods to synthesize chalcones.

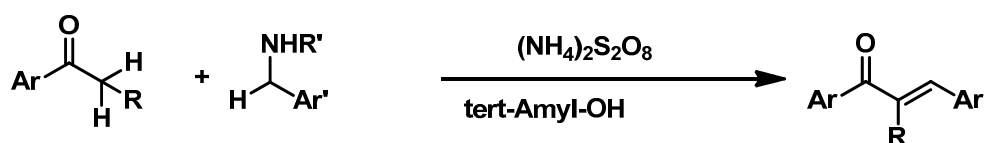
Palladium provides an excellent opportunity for developing cross-coupling reactions for synthesizing chalcones; for example, PdCl₂ is a suitable catalyst for preparing chalcones from potassium styryl trifluoroborates and benzoyl chlorides [80]. Chalcones have been synthesized via silver-catalyzed coupling of cinnamic acids with substituted α -keto acids [81]. In a similar vein, Sonogashira coupling has been utilized to prepare chalcones via the reaction of aryl halides bearing electron-withdrawing groups and prop-2-yl-1-ol [82]. Chalcone derivatives were synthesized using phenylacetylene and benzoyl chloride as starting materials; the reaction followed the same mechanism as Sonogashira coupling [83]. Subsequently, palladium acetate was effectively utilized for the generation of chalcones via the Suzuki reaction under basic conditions. Another method has been developed using palladium acetate through the oxidative carbonylation of boronic acid and styrene via a cross-coupling strategy [84].

Furthermore, the palladium dibutyl acetate derivative is utilized to develop chalcones through Stille coupling. The reaction involves C-C bond formation between organotin compounds and aryl halides. A new series of chalcones were synthesized by the reaction between organotin compounds and benzoyl chloride [85]. Three different types of coupling reactions have been reported in addition to the palladium coupling reactions. For example, a new series of chalcones were synthesized using gold nanoparticles via a coupling reaction between substituted methyl ketones and aryl alcohols (Scheme 3). The reported reaction is recyclable and gives a good yield of chalcones [86].



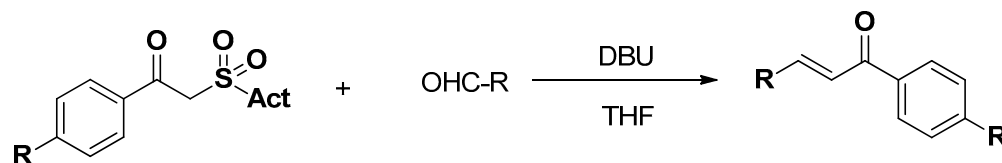
Scheme 3. Synthesis of chalcones by aerobic oxidative cross-coupling reaction.

Furthermore, a cross-dehydrogenative coupling reaction was developed for chalcones through an enamine-based strategy using a persulfate catalyst. New chalcone analogs were synthesized in 2009 using CDC in the presence of ammonium persulfate as an oxidant instead of metal-based catalysts (Scheme 4) [87].



Scheme 4. Synthesis of chalcones by cross-dehydrogenative coupling.

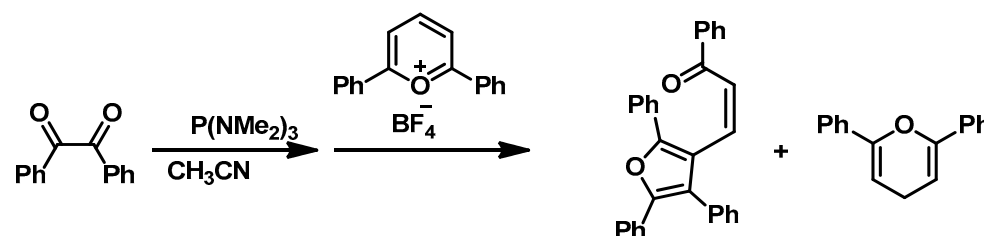
Further, Julia and Kocienski developed a coupling reaction involving C-C bond formation (Scheme 5). A series of *E*-enones were synthesized using this method, and the product formation was observed with higher yields [88]. The reaction involves β -ketosulfones and aldehyde in the presence of a base. The elimination of sulfur dioxide produces the chalcones.



Scheme 5. Synthesis of substituted chalcones through Julia-Kocienski olefination.

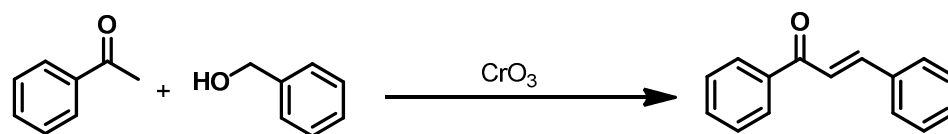
3.4. Miscellaneous Reactions

Due to their lower thermodynamic stability, *trans*-chalcones are synthesized more frequently than *cis*-chalcones. As a result of this phenomenon, *cis*-chalcones have not been subjected to many applications compared to *trans*-chalcones. *Cis*-chalcones containing furanyl rings were synthesized using reductive (3 + 2) annulation of pyrylium salts with benzil in the presence of $P(NMe_2)_3$ (Scheme 6) [89,90].



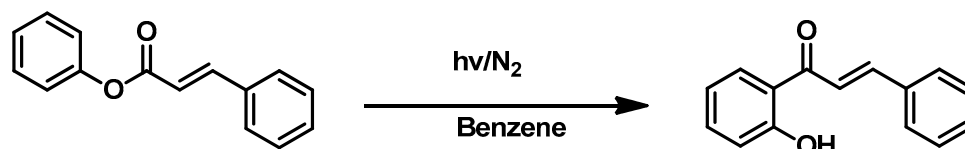
Scheme 6. Synthesis of *cis*-chalcones by reductive (3+2) annulation.

Furthermore, a one-pot reaction has been reported in which the starting materials are directly added to it in the presence of an oxidant. No purification is performed after a single step; thus, one-pot synthesis can be expedited. Phenyl methanol was oxidized into benzaldehyde in the presence of chromium trioxide, which further underwent a condensation reaction with acetophenone to produce chalcones with a good yield (Scheme 7) [90].



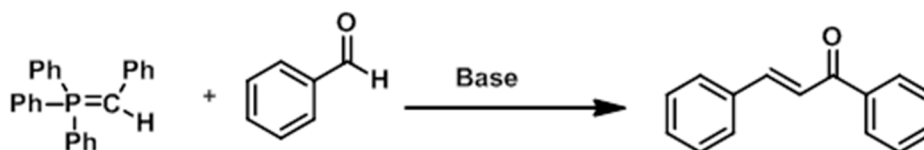
Scheme 7. One-pot synthesis of chalcones.

Furthermore, phenyl cinnamate undergoes rearrangement to produce hydroxy-group-bearing chalcones (Scheme 8). The reaction is performed under a nitrogen atmosphere using benzene as the solvent [91].



Scheme 8. Synthesis of chalcones via photo-Fries rearrangement.

Along the same line, the Wittig reaction (Scheme 9) has also been utilized to prepare chalcones. A series of chalcones were synthesized from aromatic aldehydes and arsonium salt in the presence of KF·2H₂O via the Wittig reaction using the grinding method [92]. The reaction of α -bromoylides with aldehydes in the presence of NBS results in bromo- α,β -unsaturated ketone [93].



Scheme 9. Wittig reaction for the synthesis of chalcones.

4. Chalcones against Infectious Diseases

Coronaviruses have affected millions of people across the world. Shigella bacterial infections have also been a significant threat in developing nations, and the mortality rate due to diseases such as TB and malaria is on the rise. Even though many medications are available to treat these diseases, the pathogens often resist them [94]. In recent years, there has been a significant advancement in the study of synthetic and medicinal organic chemistry. Chalcones are considered promising pharmaceuticals, and the following subsections detail their bioactivity against various infectious diseases.

4.1. Anti-Tubercular Activity

Tuberculosis (TB) is a contagious illness that primarily affects the lungs. It is ranked as the 7th leading global cause of rising mortality rates. Streptomycin, pyrazinamide, and rifampicin are just a few of the medications created to treat TB [95]. Many chalcone analogs have been tested for anti-tubercular activity, and there have been reports of chalcones with intense anti-tubercular activity [96–98] (Figure 3). Quinoline-based chalcone **51** showed anti-tubercular activity against the *M. tuberculosis* H37Rv strain, with better MIC values (10–80 μ M) than the standard drug rifampicin [99]. Chalcones with extended phenyl skeletons (**52** and **53**) showed good activity against *Mycobacterium tuberculosis*, with MIC values almost equal to those of standard drugs such as rifampicin and streptomycin. The docking and QSAR study results of these conformationally restricted chalcones also matched the MABA assay results [100,101]. The spirochrome chalcones (**54**) were tested for inhibitory activity against *M. tuberculosis*. Moreover, their docking studies were performed with protein phosphotyrosinase phosphatase B. Docking studies indicated that one of the spirochrome chalcones was bound to the protein at the same pocket region as the natural

ligand, and the MIC value indicated that it was more active than the standard drug used in the MABA assay [101].

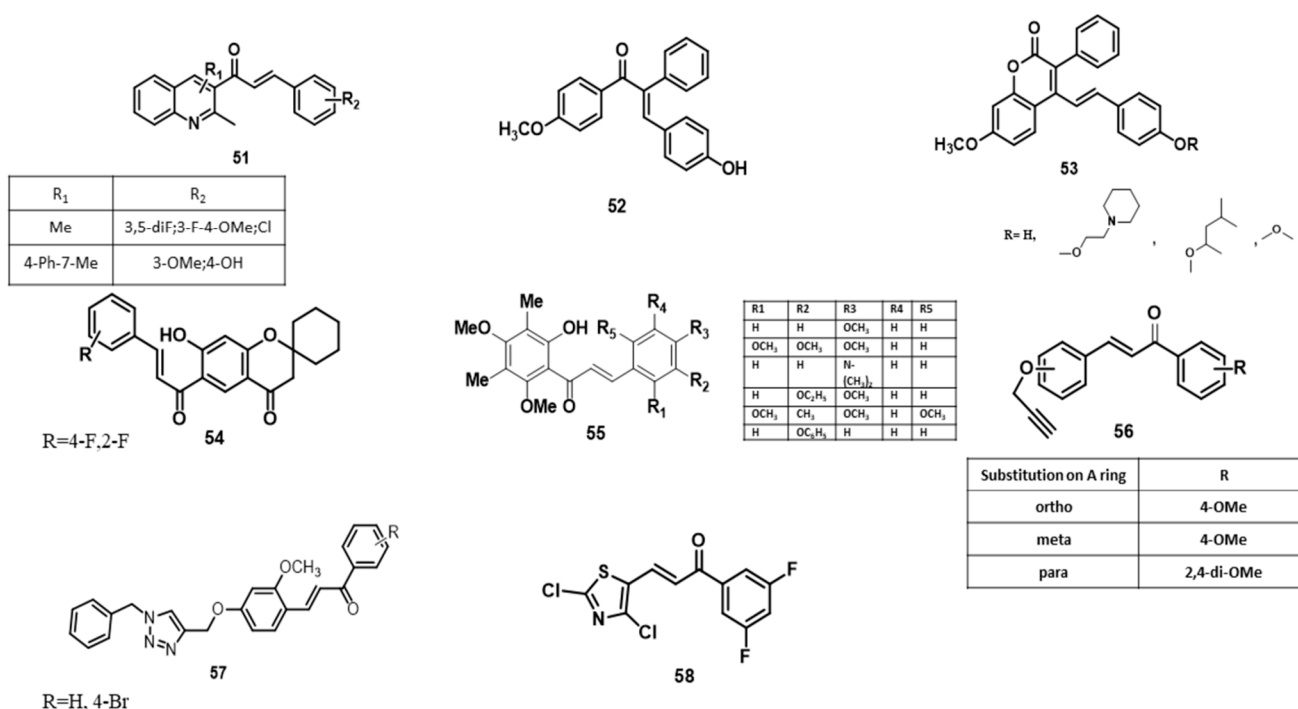


Figure 3. Structures of some chalcones showing anti-tubercular activity.

Seventeen new C-dimethylated chalcones of class 55 were tested for their anti-tubercular activity, and some of them in that class showed higher activity than streptomycin (MIC = 10.75 μ M) and ciprofloxacin (MIC = 9.43 μ M). The docking results with the *M. tuberculosis* protein tyrosinase phosphatase were analyzed, and compounds with 1,2,3-trimethoxy and 1,2,3,5-tetramethoxy substitutions in the aldehyde ring were more active, which was consistent with results from the MABA assay [102,103]. A class of acetylenic chalcones (56) were synthesized and studied for their anti-tubercular activity, with good MIC values (20–100 μ M) [103]. Twelve triazole-based chalcones were synthesized, and their activity was studied using the MABA assay and molecular docking (protein 4Y6U). The results indicated that structures (57) and scaffolds enhance the activity [96]. Thiazole-based chalcones (58) showed more promising activity than the standard drug pyrazinamide, with MIC values of 2.43 μ M [104].

4.2. Antiviral Activity

Numerous viral infections, including HIV and coronaviruses, cause serious health problems in people all over the world. Numerous plants that naturally contain chalcones have been used to treat viral infections since time immemorial. Some of these are listed in Section 2. The antiviral activity of numerous recently synthesized chalcones has been investigated, and most inhibit the activity of viruses [105–108]. The structures of some active chalcones are listed in Figure 4. Compound 59 has an EC₅₀ value of 51.65 μ g/mL, and its docking studies show that it forms four hydrogen bonds in the docking sites of TMV-CP (tobacco mosaic virus coat protein), indicating that it shows good activity against TMV [109]. Chalcone analogs containing purine units were synthesized, and among them, 60—with a nitro substitution on the para position and difluoro substitution on positions 2 and 4—showed activity against TMV [110]. Chalcone analogs that inhibit the activity of the hepatitis C virus have also been reported (category 61) [111]. Some natural chalcone derivatives (62) were screened for their activity against SARS-CoV-2, with satisfactory EC₅₀ values. The results matched the molecular docking studies with the protein RdRp, and the

threshold values were calculated [112]. Chalcone derivatives with the purine derivative (63) showed a better EC_{50} value than the standard drug ribavirin in inhibiting the tobacco mosaic virus [5]. A 1,2,3-triazine-containing chalcone (64) was reported to be active against TMV [113]. Chalcone 65 showed activity against CMV (cucumber mosaic virus) [114]. Chalcones 66 and 67, containing 1,3,4-oxadiazole and 1,3,4-thiadiazole units, showed efficient activity against TMV and were more effective than ribavirin [115]. Chalcone 68 with an O-benzyl substitution was reported to have anti-HIV activity [108]. Influenza A virus activity was inhibited by compound 69, which was synthesized via Hoveyda–Grubbs cyclization [116]. Compound 70—a chalcone derivative bearing malonate and pyrimidine units—showed significant activity against CMV [117]. The 4-thioquinazoline chalcone analog 71 showed potent activity against TMV, with EC_{50} values ranging from 138.1 μM to 154.8 μM , making it much more effective than ribavirin [118].

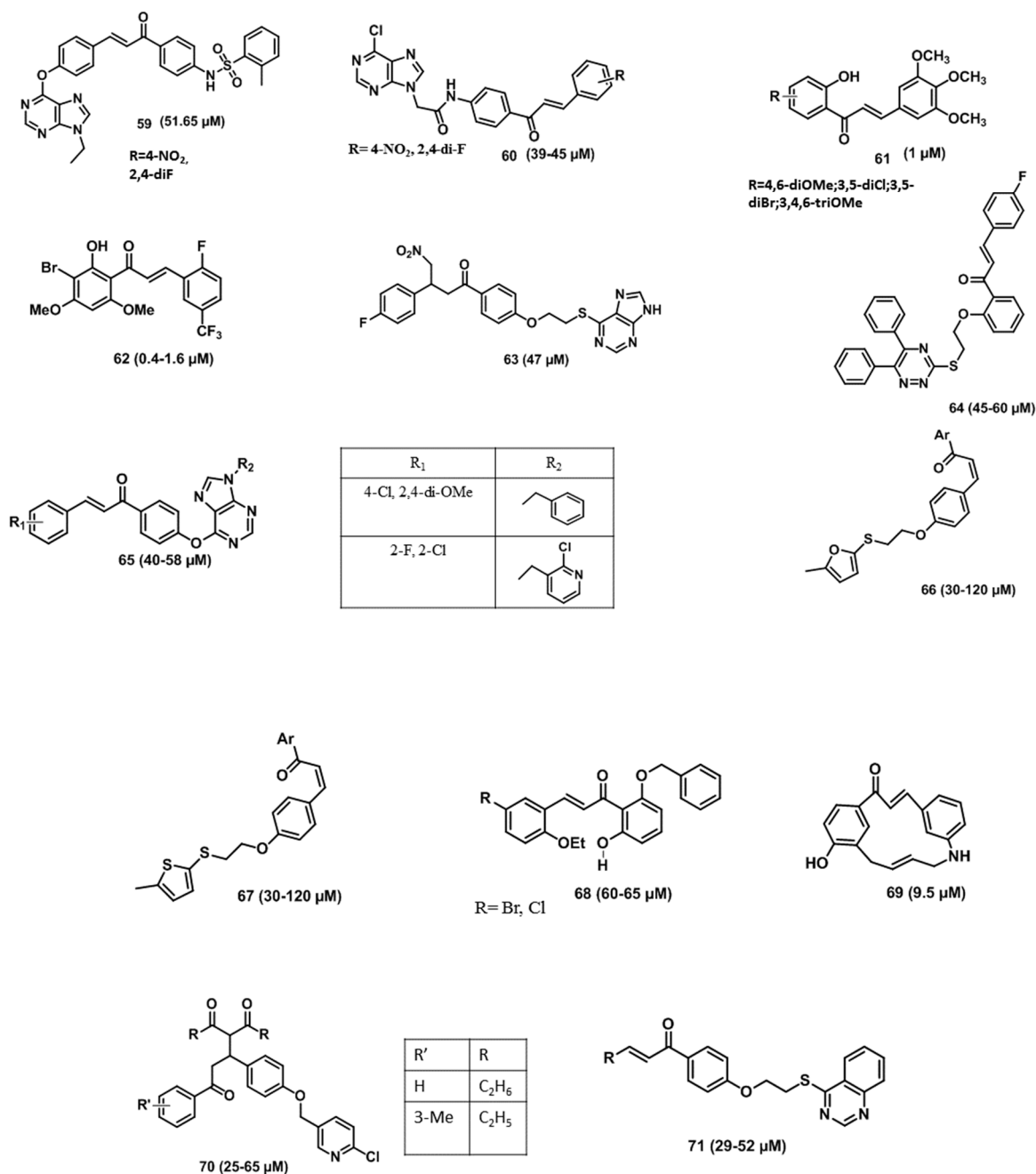


Figure 4. Chalcones with antiviral activity.

4.3. Antimalarial Activity

Malaria is caused by a parasite called *Plasmodium falciparum*, which is transmitted by mosquitoes. Antimalarial medications such as chloroquine and artemisinin are readily available. However, modern *P. falciparum* strains are resistant to available medications. Many chalcones that occur naturally have been used to treat malaria [119,120]. Additionally, a large number of synthetically developed chalcones have been tested for their efficacy against various parasite strains. Compound **72** (Figure 5), with a pyrimidine moiety, showed antimalarial activity, with an IC₅₀ value of 21.4 μM [121]. A sulfonyl-based 4-methoxychalcone (**73**) could be used as an efficient oral drug against malaria, with an IC₅₀ value of 2.06 μM; furthermore, the docking study indicated a comparatively high binding score of −7.3 Kcal/mol [122]. As expected, the imidazole group contributes to the activity, as indicated in compound **74**, which showed potent antimalarial activity, with an IC₅₀ value of 1.1 μM [123].

Since the quinolone group has already explored for its antiviral activity, the chalcone with the quinolone scaffold (**75**) showed an IC₅₀ value of 0.031 μM and high binding energy with the heme protein [124]. Similarly, another derivative (**76**) showed IC₅₀ values in the range of 44.06–59.37 μM and potency against the CQ-3D7 strain [125]. An unusual cyrhetrenyl chalcone (**77**) a derivative containing a ferrocene moiety—showed effective inhibition against strains CQ-3D7 and CQ-W2 [126]. Compound **78**—a chalcone extended with a pyrrolidine unit—was effective against the 3D7 strain. The docking results proved that the molecule shows H-bonding and aromatic interactions with the proteins 1J2I and 1J3K [127]. An azide–alkyne coupling can produce a triazole-bearing chalcone from the combination of quinolone and natural moieties, as in the case of **79**, which was found to be active against three different *P. falciparum* strains: CQ-D10, CQ-Dd2, and CQ-W2 [128]. A normal methoxylated chalcone possesses isopropyl ether linkage, as indicated in compound **80**, and can act as an excellent antimalarial agent with inhibitory activity against two parasitic strains [120,121,129]. Furthermore, chromene-based chalcones **81–84** have inhibitory activity against strains CQ-Dd2, 3D7, and KI [130,131]. Quinolone-based chalcone **85**, synthesized by MW irradiation, was proven to have inhibitory activity against *P. falciparum* [132]. Chalcone **86**, which contains an acridine unit in its structural framework, possesses high efficacy against malaria [133]. Similarly, prenylated chalcone **87** inhibits the activity of the CQ-3D7 strain of *P. falciparum* [134]. A 4-aminoquinolinyl chalcone amide in conjunction with the furano derivative (**88**) was active against two strains, with IC₅₀ values ranging from 0.004 μM to 0.07 μM [135]. Furthermore, **89** is an indole-moiety-containing chalcone that is active against malaria, with an IC₅₀ value of 2.5 μM [136].

4.4. Antibacterial Activity

One of the leading health problems affecting human populations is bacterial infection. Pathogens becoming more resistant to antibiotics have caused the effectiveness of current antibiotics to decline. Both natural and artificial chalcones have demonstrated activity against some Gram-positive and Gram-negative strains [137,138]. Biofouling is one of the significant problems in marine-based product development. The chalcones shown in Figure 6 are active against different bacterial strains. In one of the studies, the organism *V. natriegens* (MD6) and other marine strains (*P. fluorescens* and *B. flexus*) were taken for antibacterial studies. The compounds **90**, **91** (0.31–0.61 μM), and **92** (0.025–0.195 μM) were reported as having suitable microbial activities against all three organisms and could be used as anti-biofouling agents against marine microorganisms. [139]. Of these compounds, the thio-based chalcone (**90**) was more effective (0.058–0.22 μM) in inhibiting biofouling strains through cell membrane disruption. Chalcones **93**, **94**, and **95** were proven to have good activity, with MIC values in the range of 0.78–1.56 μM [140]. On the other hand, polyhydroxylated chalcones bearing hydroxy groups—**96–98**, **100** (62.5–250 μM), and **102** (6.25–25 μM)—were active against methicillin-resistant *Staphylococcus aureus* [141]. Another polyhydroxylated chalcone (**101**) showed enhanced inhibitory activity against Gram-positive organisms (0.1–0.717 μM) such as *Bacillus subtilis* and *Staphylococcus aureus*,

as well as the Gram-negative bacteria *Pseudomonas aeruginosa*, *Escherichia coli*, *Salmonella typhi*, and *Proteus vulgaris* [142]. The natural chalcone **102** was reported to be active against two Gram-positive bacteria [143].

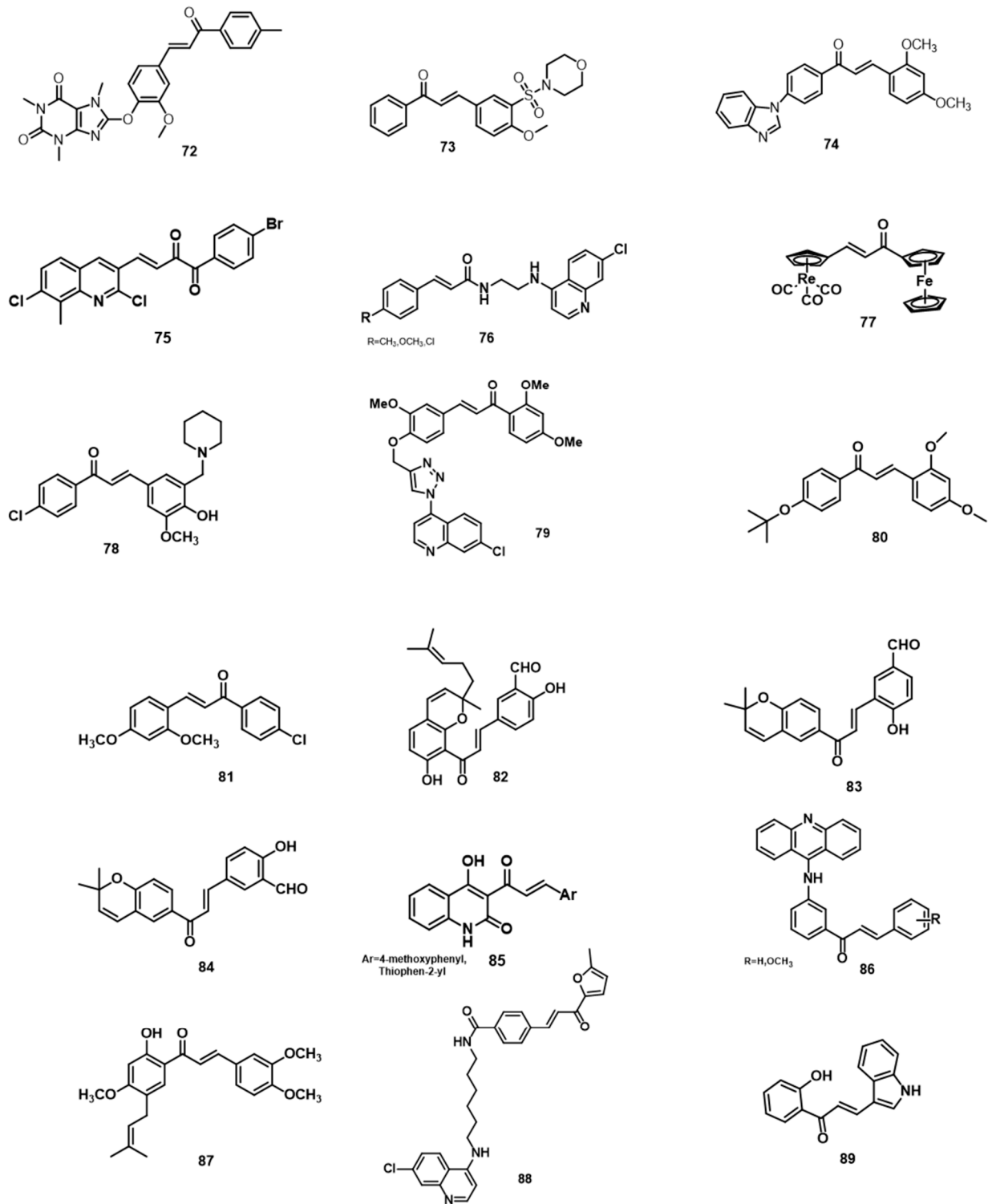


Figure 5. Structures of chalcones with antimalarial activity.

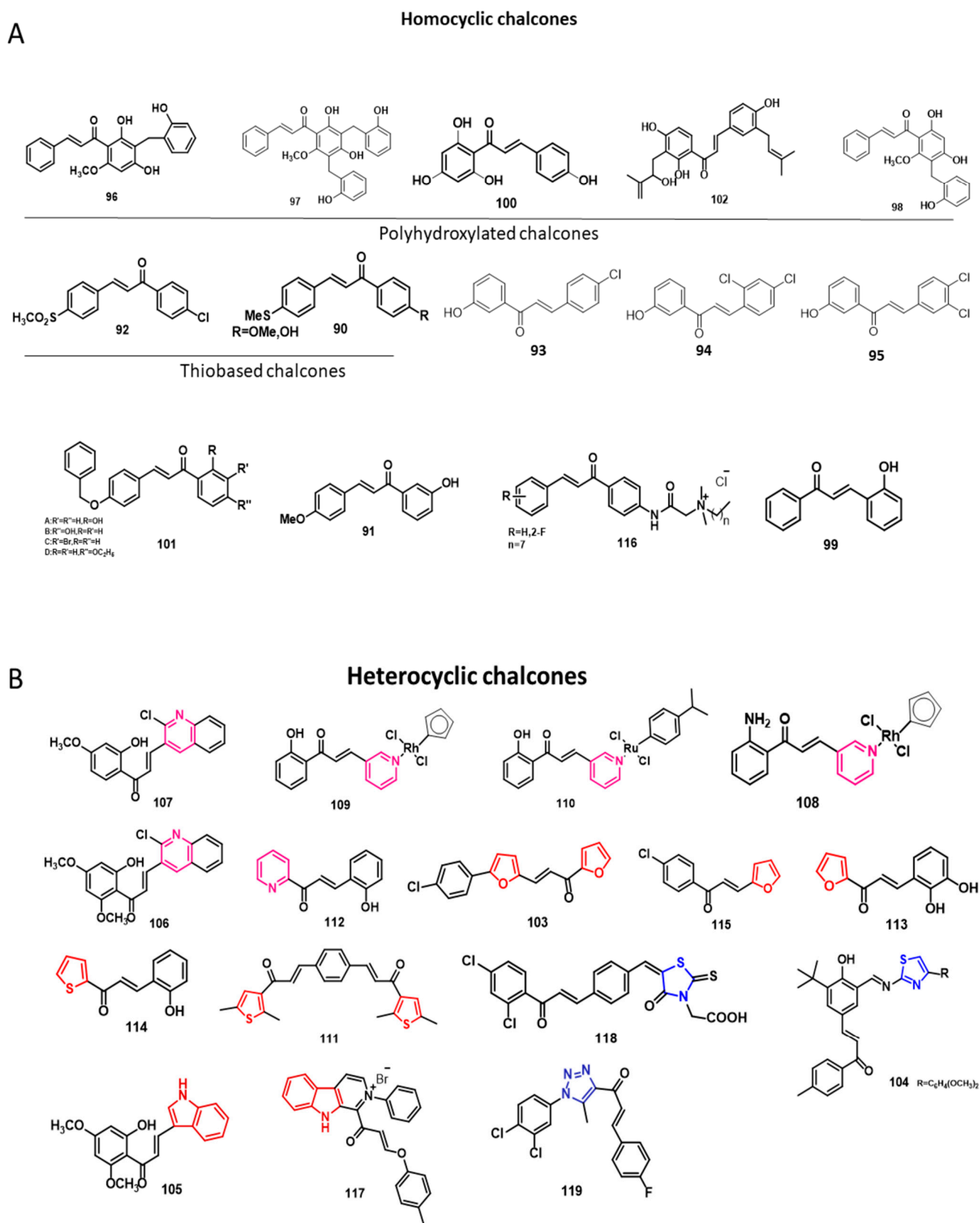


Figure 6. Chalcones with anti-bacterial activity: (A) homocyclic chalcones; (B) heterocyclic chalcones.

The extensive analysis of bacterial studies proves that heterocyclic chalcones are superior to homocyclic chalcones. The *trans*-chalcone containing a difurano ring (**103**) (28 μ M) potentially better inhibits the activity of *S. aureus* compared to the standard drug

amoxicillin [144]. The thiazole-containing chalcone **104** (1.4 μM) is similar to vancomycin against *S. aureus* [145]. Three nitrogen-heterocycle-bearing chalcones—**105**, **106**, and **107** (20 μM)—act against the Gram-negative bacterium *S. dysenteriae* and two Gram-positive bacteria (*S. Typhi* and *S. aureus*) [146]. Compounds **108**, **109**, and **110** are metal complexes formed by chalcones that show inhibitory activity against *E. coli*, *S. aureus*, and *K. pneumonia* (2–52 μM) [147]. Compound **111** is a bis-chalcone-bearing thiophene unit that shows an MIC value (10–12.5 μM) better than that of the standard [148]. Chalcones **112** (128 μM), **113** (128 μM), and **114** (32 μM) are active against *S. aureus* [149]. Compound **115**, with an MIC value of 2 μM , has an inhibitory activity similar to that of norfloxacin [150]. A cationic chalcone (**116**) inhibited the activity of *S. aureus* and MRSA strains, with MIC values ranging from 0.25 to 1 μM [151]. A β -carboline-linked chalcone (**117**) inhibited the activity of *S. aureus*, with an MIC of 440 μM and a ZOI of 15 mm [152,153]. A chalcone bearing a rhodamine-3-acetic acid unit (**118**) showed similar inhibitory activity (2 μM) to norfloxacin against *S. aureus* [153]. Compound **119** can be used as an efficient antibacterial agent with inhibitory activity against four different bacterial strains: *Pseudomonas aeruginosa* (44.06 mM), *Escherichia coli* (55.83 mM), *Staphylococcus aureus* (44.59 mM), and *Bacillus subtilis* (79.76 mM) [154].

5. Chalcones for Non-Infectious Diseases

Contact with an infected person does not result in the transmission of non-infectious diseases. They develop as a result of people's changing lifestyles. These illnesses are challenging to diagnose, and if they are not found at an early stage there are no highly effective medicines available to treat them. Chalcones exhibit activity against cancer, diabetes, and other non-contagious illnesses. In this section, a number of the data from the literature are thoroughly discussed.

5.1. Anti-Alzheimer's Activity

Alzheimer's disease is a neurological condition that causes memory loss in people—especially those over 65 years old. It also results in other behavioral problems and a decline in language and orientation abilities. The factors vital to its cause are oxidative stress, acetylcholinesterase (AChE), and A β 1-42 (amyloid beta) aggregation [155–160]. Compound **119a** (Figure 7) showed promising activity, inhibiting the aggregation of A β 1-42 [161,162]. The docking studies on newly synthesized chalcone-O-alkylamine analogs were performed with acetylcholinesterase, butyrylcholinesterase (BuChE), and A β 1-42. It was found that compound **120** was bound to the same pocket region as the natural ligand. Moreover, the in vitro analysis showed that it could cross the BBB and inhibit MAO-B and BACE-1 in the treatment of neurodegenerative disorders [162]. A naturally derived chalcone—L licochalcone B (compound **121**)—exhibits potent anti-Alzheimer's activity [7]. Butein (compound **122**) [163] and phloridzin (compound **123**) [164] are some chalcones or derivatives occurring in nature, showing anti-Alzheimer's activity as they induce oxidative stress.

5.2. Anticancer Activity

Cancer is one of the most serious illnesses and the leading cause of death worldwide. It is introduced by uncontrolled gene mutation or unregulated cell division in the body. Although drugs with minimal side effects have not yet been created, many chemotherapeutic drugs have been developed in recent years. Chalcones are pharmacologically significant molecules [165,166]. Numerous recently created chalcones exhibit activity against several cancer cell lines, such as MCF-7, A549, and PC3 [166–169].

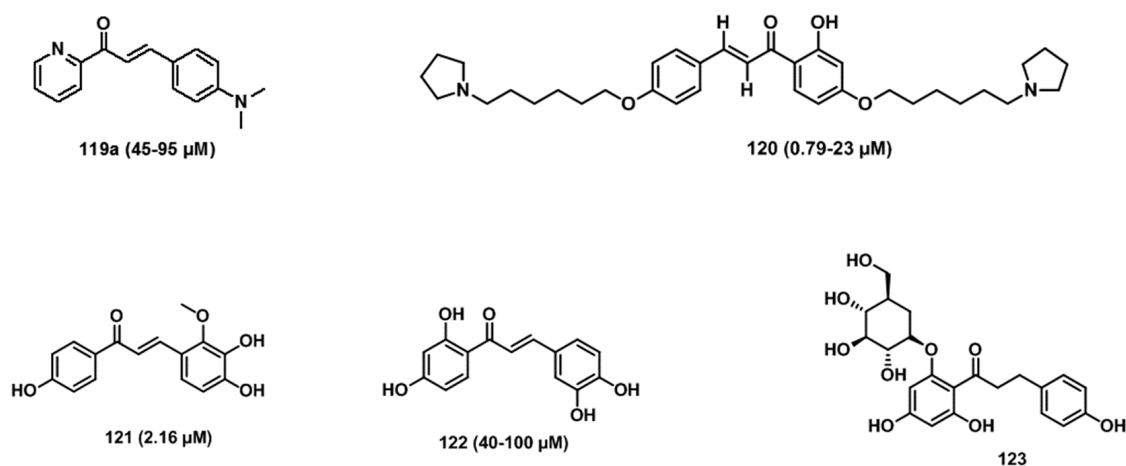


Figure 7. Chalcones for Alzheimer's disease.

5.2.1. Anti-Breast-Cancer Activity

Large numbers of chalcones (Figures 8 and 9; Table 1) have been studied for their anti-breast-cancer activities, mainly in MCF-7 cells. Based on their structures, they can be classified into two broad areas: homocyclic and heterocyclic chalcone derivatives. Furthermore, homocyclic chalcones can be divided into three classes: (i) hydroxylated, (ii) methoxylated, and (iii) chalcones with extended functionality. It has been found that chalcones with extended functionality show higher IC_{50} values when compared to other categories, of which the homocyclic chalcone **134** with electron-withdrawing groups such as nitro and trifluoro extensions showed the best IC_{50} value (0.03 μM).

Homocyclic-based chalcones

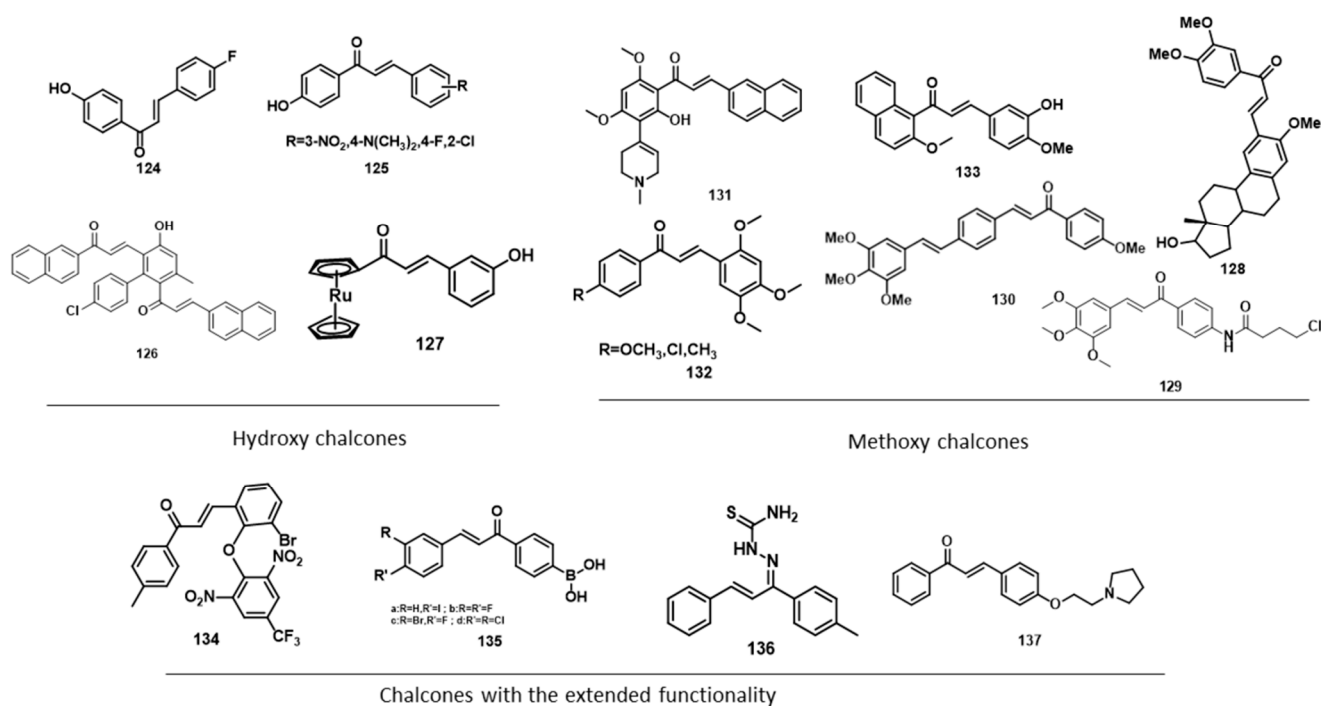
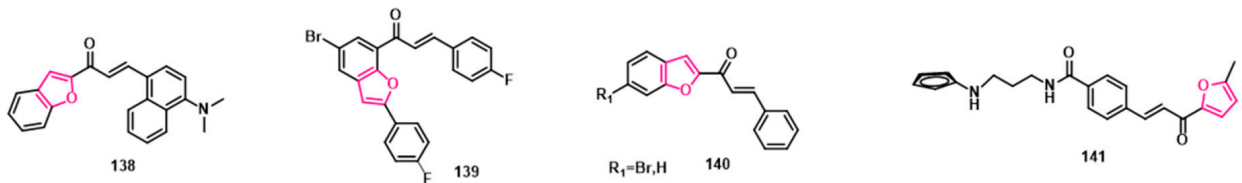
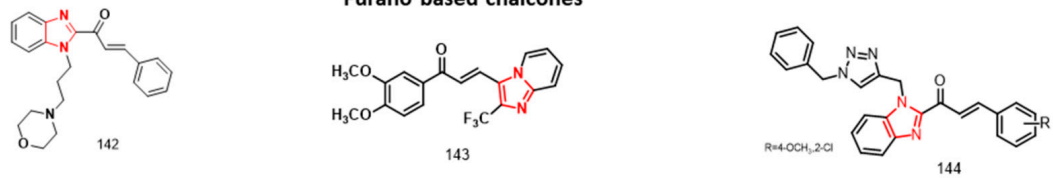


Figure 8. Homocyclic chalcones with anti-breast-cancer activity [170–183].

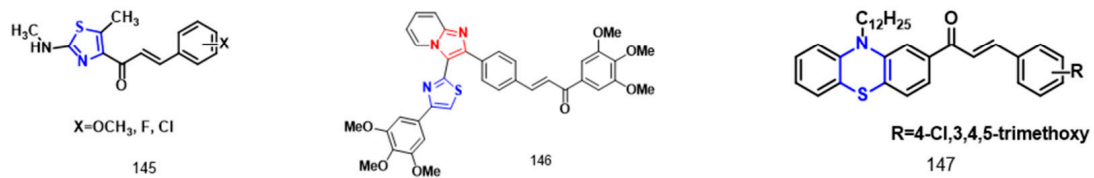
Heterocyclic-based chalcones



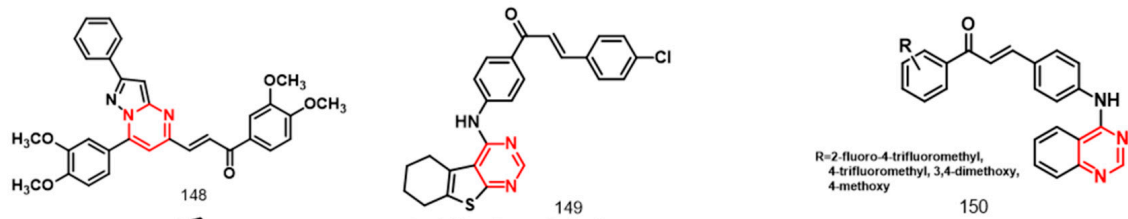
Furano based chalcones



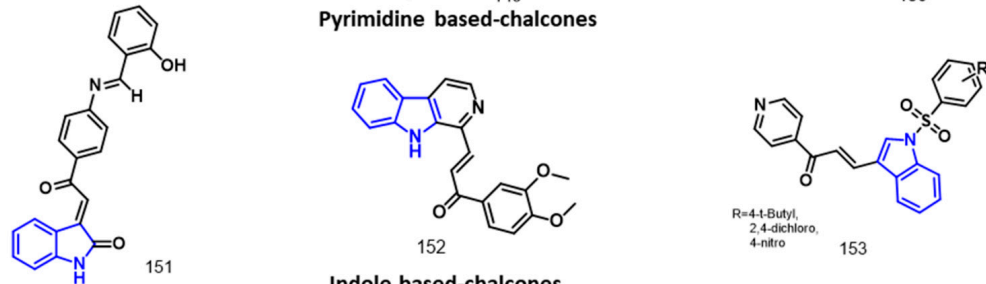
Imidazole based-chalcones



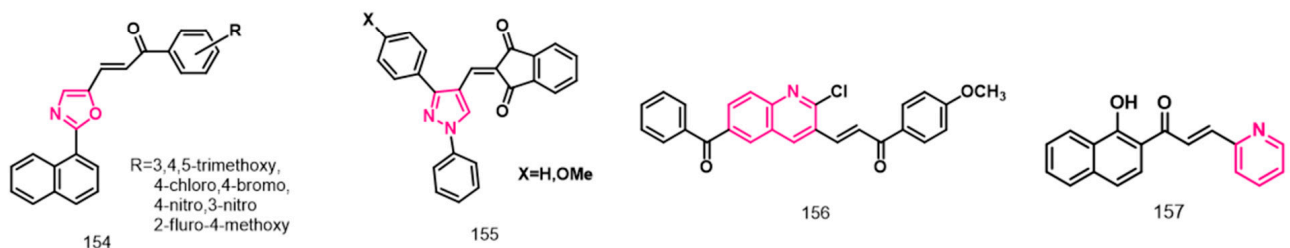
Thiazole based-chalcones



Pyrimidine based-chalcones



Indole based-chalcones



Oxazoline based-chalcones

Pyrazole based-chalcones

quinoline based-chalcones

pyridine based-chalcones

Figure 9. Heterocyclic chalcones with anti-breast-cancer activity [23,184–208].

Table 1. Chalcones with anti-breast-cancer activities.

Homocyclic chalcone derivatives (breast cancer cell lines; IC ₅₀ values in μM)					
Hydroxylated chalcones		Methoxylated chalcones		Chalcones with extended functionality	
124	1.37	128	7.3	134	0.03
125	-	129	2.54	135	3.5
126	4.4	130	30.55	136	-
127	91.4	131	23.45	137	<10
-	-	132	2.2	-	-
-	-	133	1.2	-	-
Heterocyclic chalcone derivatives (breast cancer cell lines; IC ₅₀ values in μM)					
Furano-based chalcones		Imidazole-based chalcones		Thiazole-based chalcones	
138	2.2	142	8.91	145	1.97
139	0.00035–0.59	143	0.56	146	0.18
140	1.45	144	5.89	147	12
141	1.8	-	-	-	-
Pyrimidine-based chalcones		Indole-based chalcones		Oxazoline/pyrazole/ quinoline/pyridine-based chalcones	
148	7.4	151	31.66	154	0.35
149	6.52	152	2.25	155	3.9
150	0.14	153	12	156	2.32
-	-	-	-	157	1.8

Similarly, heterocyclic chalcone derivatives are also categorized based on their functional derivatives. For example, a chalcone with a furano derivative (**139**) (IC₅₀ = 0.00035 μM) showed excellent inhibitory activity in the nanomolar range compared with other counterparts (i.e., **138**, **140**, and **141**). Furthermore, one representation from each of the categories—such as imidazole (**143**, IC₅₀ = 0.56 μM), thiazole (**146**, IC₅₀ = 0.18 μM), pyrimidine (**150**, IC₅₀ = 0.14 μM), and oxazoline (**154**, IC₅₀ = 0.35 μM) derivatives—showed inhibitory activity in the range of nanomolar concentrations. However, the indole/quinolone/pyridine classes showed comparatively less activity compared to derivatives **139**, **143**, **146**, **150**, and **154**. Of the listed compounds, heterocyclic derivatives showed comparatively higher anti-breast-cancer activity than homocyclic derivatives. The observation identified that furano derivative **139** with electron-withdrawing ability was the best inhibitor of breast cancer cell lines.

5.2.2. Anti-Lung-Cancer Activity

Furthermore, chalcones have been extended for their anti-lung-cancer activities. In the area, chalcones have been categorized in two ways: (i) chalcones with extended functionality, and (ii) heterocyclic chalcones. In the homocyclic category, compounds **160**, **163**, **165**, and **166** show inhibitory activities in the nanomolar range. In the heterocyclic category, unlike other inhibitory activities, only a few compounds (**168** and **169**) showed the best inhibitory activities in the nanomolar range. Amongst the compounds reported, the chalcones with extended heterocyclic functionality showed the best inhibitory activity, with IC₅₀ values of 0.33–2.07 nM (Figure 10) in the A549 and HLF cell lines.

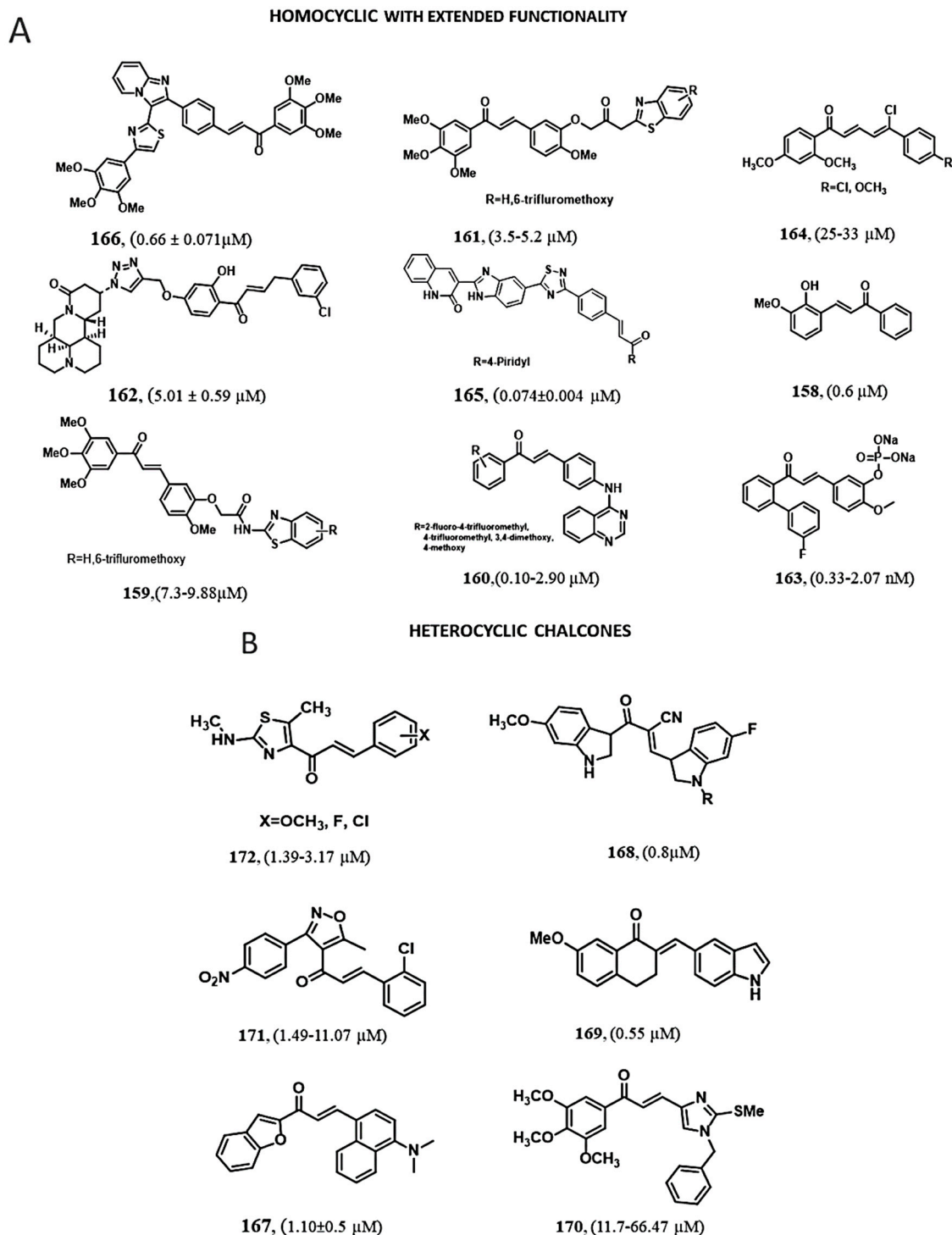


Figure 10. (A,B) Chalcones with anti-lung-cancer activity and their IC₅₀ values [187,193,200,209–217].

5.2.3. Chalcones with Broad-Spectrum Anticancer Activities

Some of the chalcones in Table 2 indicate a broad spectrum of anticancer activities on different cancer cell lines. The homocyclic chalcones—such as 174, 179, 182, 185, and 187—have broad-spectrum anticancer activities with moderate IC₅₀ values. Furthermore, heterocyclic chalcones (173, 175, 176, 181, and 184) showed lower to larger IC₅₀ values, and chalcones with extended hetero functionality (177, 178, 179, 182, 183, and 186) were found to be the best in the broad-spectrum cancer cell lines, as indicated in the table. Moreover, chalcones with nitrogen- and sulfur-containing heterocycles and with methoxy

substitutions have been reported to be active against microbes, leukemia, prostate cancer, and colon cancer [218–235].

Table 2. Chalcones with diverse anticancer activities.

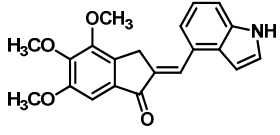
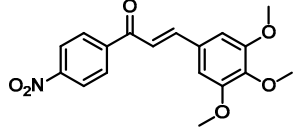
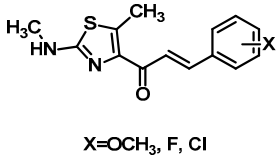
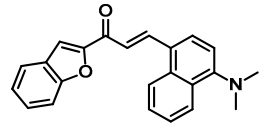
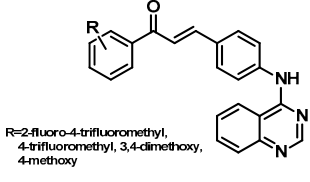
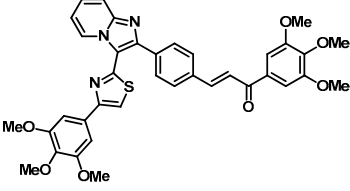
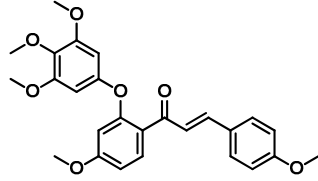
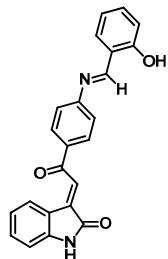
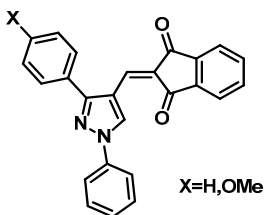
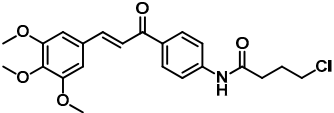
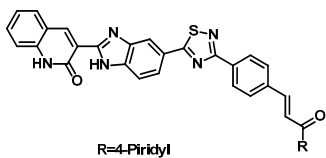
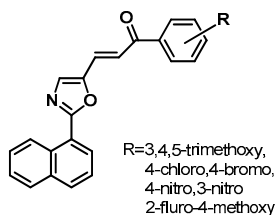
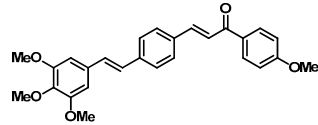
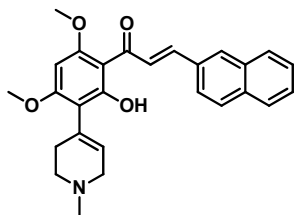
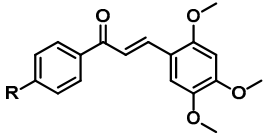
Compound Number	Structure of Chalcones	Types of Cancer
173		Cervical cancer ($0.027 \pm 0.01 \mu\text{M}$), prostate cancer ($0.031 \pm 0.05 \mu\text{M}$), leukemia ($0.031 \pm 0.12 \mu\text{M}$), lung cancer ($0.026 \pm 0.03 \mu\text{M}$) [236]
174		Lung cancer, colon cancer, renal adenocarcinoma, pancreatic carcinoma [237]
175	 X=OCH ₃ , F, Cl	Lung cancer (1.39–3.17 μM), breast cancer (1.97–4.14 μM), hepatocarcinoma (1.56–3.79 μM) [186]
176		Breast cancer ($2.2 \pm 0.3 \mu\text{M}$), prostate cancer ($0.9 \pm 0.5 \mu\text{M}$), lung cancer ($1.10 \pm 0.5 \mu\text{M}$), pancreatic carcinoma ($1.2 \pm 0.2 \mu\text{M}$) [187]
177	 R=2-fluoro-4-trifluoromethyl, 4-trifluoromethyl, 3,4-dimethoxy, 4-methoxy	Lung cancer (0.10–2.90 μM), breast cancer (0.14–0.17 μM), colon adenocarcinomas (0.13–2.89 μM) [189]
178		Lung cancer ($0.66 \pm 0.071 \mu\text{M}$), breast cancer ($0.18 \pm 0.094 \mu\text{M}$), prostate carcinoma ($1.03 \pm 0.45 \mu\text{M}$) [193]
179		Breast cancer ($3.44 \pm 0.19 \mu\text{M}$), liver carcinoma ($4.64 \pm 0.23 \mu\text{M}$), adenocarcinoma ($6.31 \pm 0.27 \mu\text{M}$) [171]
180		Colon cancer (11.78 μM), breast cancer (31.66 μM), liver cancer (13.95 μM) [194]

Table 2. Cont.

Compound Number	Structure of Chalcones	Types of Cancer
181	 <p>X=H,OMe</p>	Breast cancer (3.9–4.1 μM), liver cancer (3.8–5.0 μM), colorectal cancer (3.3 μM) [199]
182		Breast cancer (2.54 μM), colorectal cancer (1.83 μM), gastric carcinoma (1.52 μM) [178]
183	 <p>R=4-Pyridyl</p>	Breast cancer (0.012 \pm 0.007 μM), lung cancer (0.074 \pm 0.004 μM), colon cancer (0.074 \pm 0.004 μM), ovarian cancer (0.083 \pm 0.002 μM) [200]
184	 <p>R=3,4,5-trimethoxy, 4-chloro,4-bromo, 4-nitro,3-nitro 2-fluoro-4-methoxy</p>	Breast cancer (0.33–0.89 μM), melanoma (0.11–1.28 μM), lung cancer (0.34–7.56 μM) [238]
185		Ovarian carcinoma (6.66 μM), breast cancer (30.55 μM), lung cancer (36.35 μM) [181]
186		Colon carcinoma (33.31 μM), cervical carcinoma (21.80 μM), breast cancer (23.45 μM), lung cancer (4.28 μM) [206]
187	 <p>R=OCH₃,Cl,CH₃</p>	Breast cancer, synovial carcinoma, cervical carcinoma (2.2–4.5 μM) [183]

5.3. Antidiabetic Activity

Diabetes is a metabolic disorder characterized by high blood glucose levels. The inhibition of crucial enzymes—such as α -glucosidase, α -amylase, tyrosinase phosphatase, AMP-kinase, and aldose reductase—can cure hyperglycemia [9,239–241]. Compounds such as bischalcone **188** inhibit the activity of α -glucosidase, with an IC_{50} value of 23.7 μM [242]. Compound **189** (0.92 μM) is a trihydroxy chalcone that is effective against diabetes as it inhibits AMP-kinase activity [243]. A chalcone with an aryloxy propylamine unit (**190**) has been reported as an effective antidiabetic agent, inhibiting type 2 diabetes in rats [244]. Compound **191** shows good inhibitory activity against PTP1B [245]. Compound **192**,

with the presence of methoxy and halogen groups, exhibits activity against diabetes [238]. Chalcone **193** (0.5–2.5 μM) was active against type 2 diabetes even though its docking results were not high as expected [239]. Compounds **194** and **195** are aminochalcones, while **196** is a naturally derived hydroxychalcone showing inhibitory activity against the enzymes peptidase, α -glucosidase, and PPAR, which decrease the blood glucose levels [9]. A triazine-bearing chalcone (**197**) showed potent antidiabetic activity [246]. Compounds **198–202** (Figure 11) exhibit higher antidiabetic activity than the standards rosiglitazone and pioglitazone (250–300 mg/dL) [247]. Chalcone **203** shows inhibitory activity against α -glucosidase, with an IC_{50} value of 67.77 μM [248].

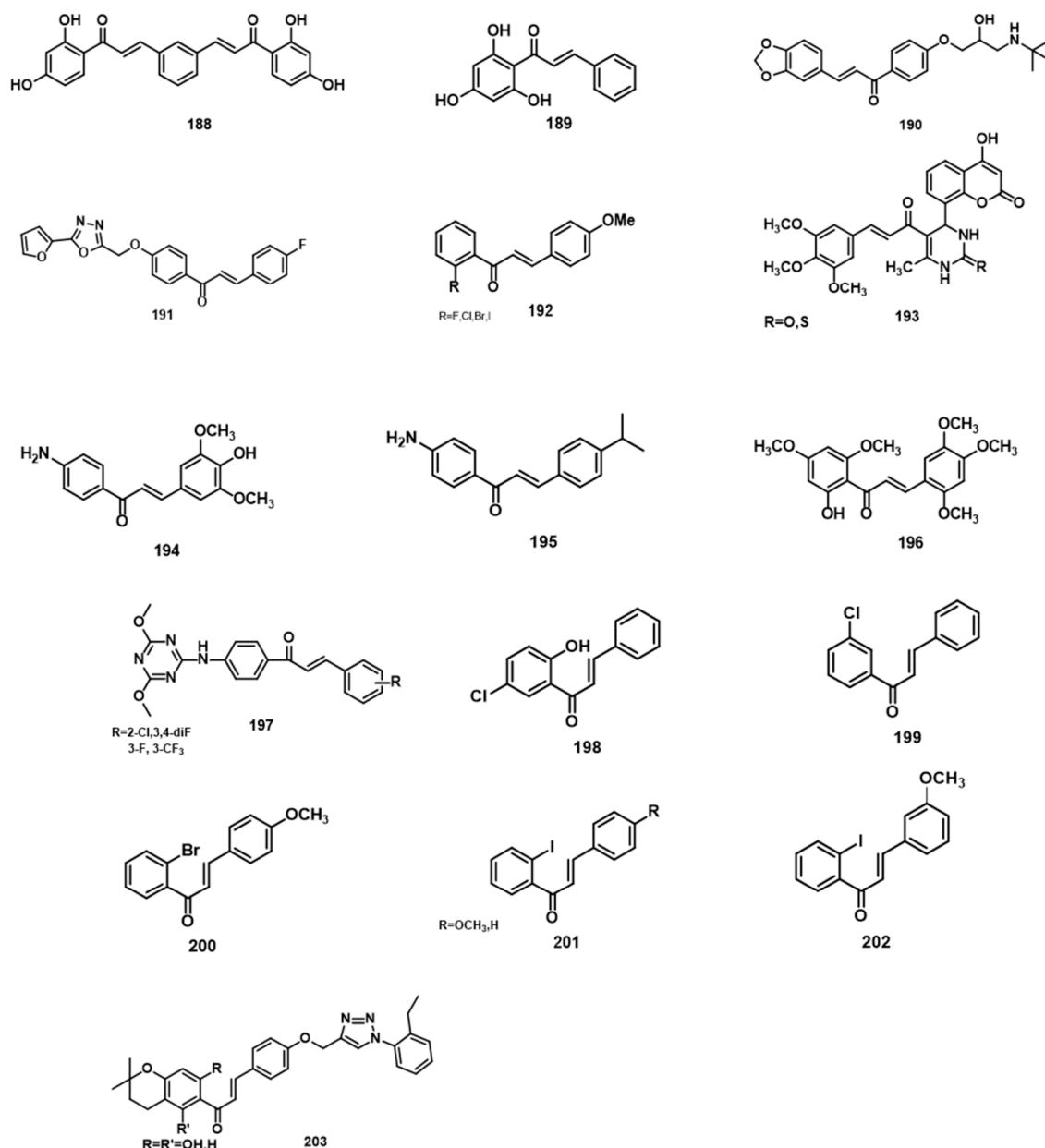


Figure 11. Structures of chalcones with antidiabetic activity.

5.4. Anti-Parkinson's Activity

Parkinson's disease is a neurological disorder involving the loss of dopamine neurons in the nigrostriatal pathway and decreased levels of neurotransmitters. Coordination, mental health, and mobility are all impacted by this. Chalcones have been found to inhibit MAO-B receptors in the literature (Figure 12) [10,249]. Compound **204** is an ethoxy-

lated chalcone that can bind reversibly with the MAO-B pocket site, with an IC_{50} value of $0.53 \mu\text{M}$ [10]. The trifluoromethyl-substituted chalcone **205** is a suitable hMAO-B inhibitor [250]. Compounds **206** and **207** are active against Parkinson's disease, with IC_{50} values of $0.29 \mu\text{M}$ and $0.087 \mu\text{M}$ [251]. Chalcone **208** can act as a good Parkinson's drug, with an IC_{50} value of $0.0044 \mu\text{M}$ [252]. Compounds **209** and **210** ($1\text{--}108 \mu\text{M}$) are potent MAO-B inhibitors [253]. Compound **211** ($1.20 \mu\text{M}$) is an indole-based chalcone that can easily cross the BBB, and the results have been analyzed via PAMPA assay [254]. An imidazole-containing chalcone, **212** ($20\text{--}100 \mu\text{M}$), acts as both an MAO-A and MAO-B inhibitor [255]. Chalcones bearing oxime ethers—**213** ($76.8 \mu\text{M}$) and **214** ($81.8 \mu\text{M}$)—and the thienyl chalcone **215** are active against diabetes, and their docking studies indicate that they bind efficiently at the pocket regions of hMAO-B [256].

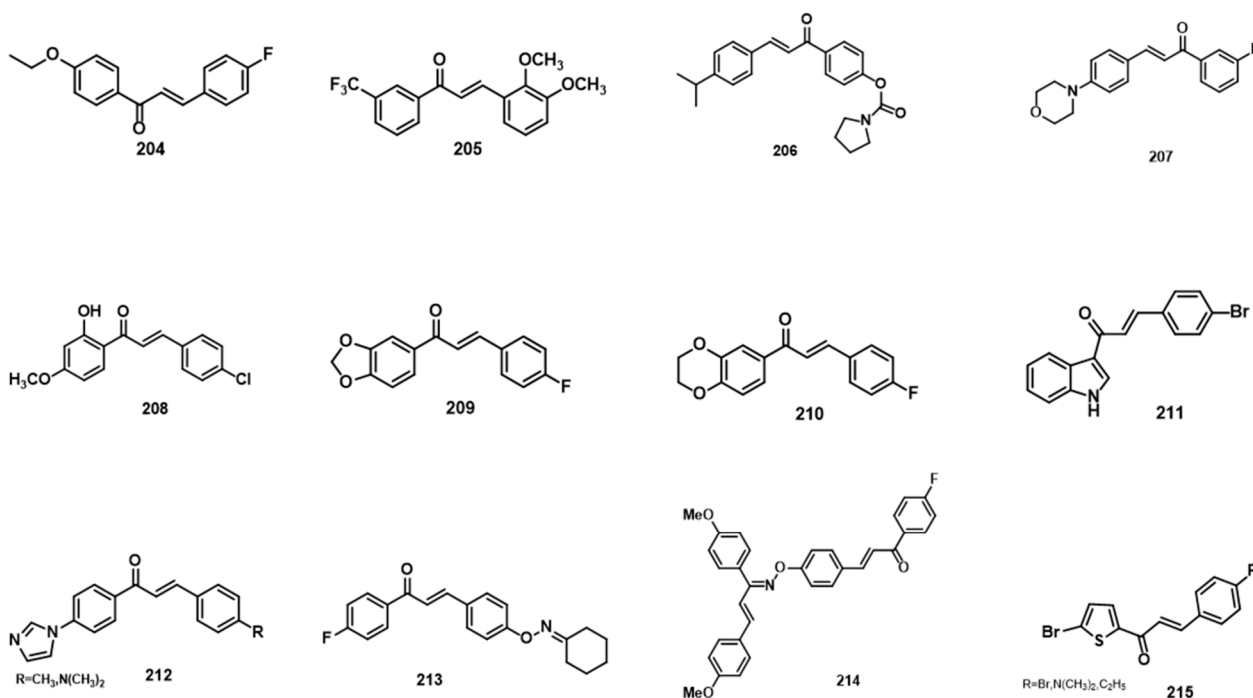


Figure 12. Chalcones showing anti-Parkinson's activity.

6. SAR Studies

The extensive search and analysis showed that chalcones possess outstanding biological properties with respect to infectious and non-infectious diseases. The first part of the study indicated that 60 new chalcones have been isolated from different families—mainly from Fabaceae, Euphorbiaceae, Cyperaceae, Piperaceae, Lecythidaceae, Annonaceae, Myrtaceae, Umbelliferae, Lauraceae, Rutaceae, Rubiaceae, Caprifoliaceae, and Zingiberaceae. The structures of the reported chalcones in the plants are hydroxylated, methoxylated, a combination of hydroxylated and methoxylated, prenylated, non-prenylated, glycosylated, cinnamoylated, dihydroformylated, and so on. Scarcity and chemotaxonomy lead to the synthesis of chalcones via chemical methods. With this in mind, many synthesis methods have been discovered and listed. However, extensive protection and de-protection strategies are necessary to prepare functional-based chalcones such as hydroxyl-, amino-, and thio-based compounds. Both synthetic (compounds **124** and **125**) and natural chalcones (compounds **1–14**) bearing hydroxyl functional groups demonstrate higher activity in breast cancer cell lines [257,258]. Similarly, halogenated synthetic chalcones and methoxylated chalcones derived from both natural and synthetic sources have proven to be highly active against liver, prostate, and lung cancer cell lines [259–262]. In addition, trihydroxylated and methoxylated chalcones showed higher activity than di- and mono-substituted ones [263–265].

From this report, it is very much clear that natural analogs of homocyclic chalcones with extended hetero functionality and heterocyclic chalcones possess excellent inhibitory activity against infectious and non-infectious diseases (Figure 13). In a similar vein, naturally occurring chalcones are poorly bioavailable molecules due to their decreased absorption in the intestine. However, the new chalcone categories are yet to be analyzed in terms of this particular property of interest. Similarly, the reported chalcones can be taken to the next level of studies, including animal studies, clinical trials, and much more.

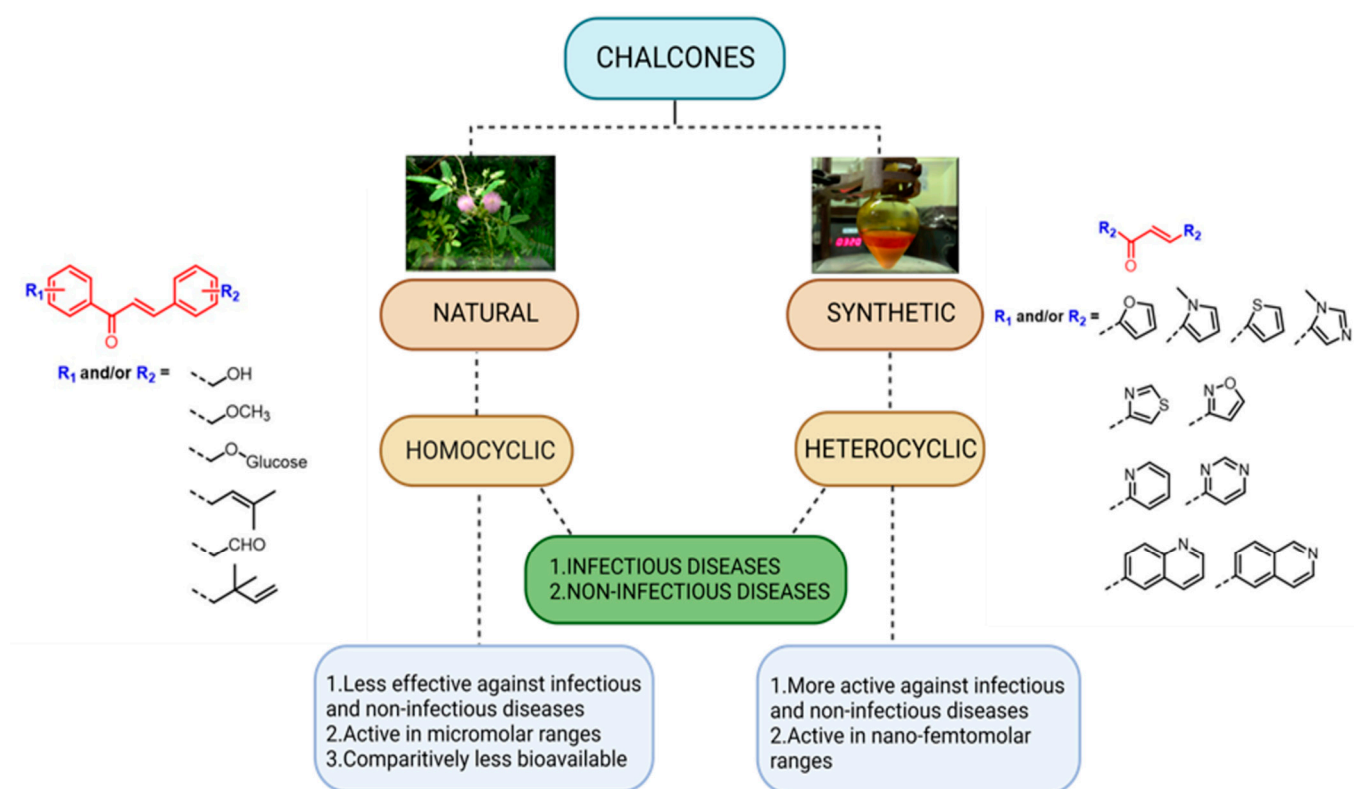


Figure 13. Flowchart depicting the structure–activity relationships of natural and synthetic chalcones.

7. Conclusions and Perspectives

Chalcones are well-known chemical compounds with high pharmacological importance. They can be of natural or synthetic origin. Many natural chalcones have been used as medicines since ancient times. Since the 1980s, research has been progressing in this particular area. Various routes have been developed for the synthesis of chalcones. The principal method used to synthesize chalcones is Claisen–Schmidt condensation. Other synthetic methodologies include coupling reactions in the presence of organometallic catalysts and rearrangement reactions. Light-enhanced synthesis methodologies have also been reported in the literature. Many studies have been conducted by varying the structural framework of chalcones by incorporating different heterocyclic moieties, and most showed different bioactivities. Metal-incorporated chalcones and their complexes have also been reported. Most chalcones are fluorescent and can be employed as fluorescent probes. Compared to synthetic chalcones, the extraction of natural chalcones often takes a long time and produces low yields. Chalcones obtained from natural sources are homocyclic, demonstrating lower bioactivity when compared to compounds synthesized with heterocyclic units. Many organic reactions have been reported in the literature to obtain a wide variety of substituted chalcones that are employed as anticancer, antidiabetic, antioxidant, antibacterial, anthelmintic, antiulcer, antiviral, insecticidal, and antiprotozoal agents. Therefore, the ability to structurally modify chalcones through synthesis has better advantages than natural chalcones, such as higher yields, easy handling, cost-effectiveness, and much more.

The literature indicates that chalcones are most active against cancerous disorders—mostly against breast cancer cell lines, and also against lung cancer. Furthermore, SAR studies indicate that they have good ADMET properties, making them efficient as drug molecules. From this point of view, it is clear that these molecules' research interest and importance will further increase in the coming years.

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References

1. Syam, S.; Abdelwahab, S.I.; Al-Mamary, M.A.; Mohan, S. Synthesis of Chalcones with Anticancer Activities. *Molecules* **2012**, *17*, 6179–6195. [[CrossRef](#)] [[PubMed](#)]
2. Narender, T.; Papi Reddy, K. A Simple and Highly Efficient Method for the Synthesis of Chalcones by Using Borontrifluoride-Etherate. *Tetrahedron Lett.* **2007**, *48*, 3177–3180. [[CrossRef](#)]
3. Constantinescu, T.; Lungu, C.N.; Jazvins'cak, M.; Jembrek, J. Anticancer Activity of Natural and Synthetic Chalcones. *Int. J. Mol. Sci.* **2021**, *22*, 11306. [[CrossRef](#)] [[PubMed](#)]
4. Mustafa, M.; Mostafa, Y.A. A Facile Synthesis, Drug-Likeness, and in Silico Molecular Docking of Certain New Azidosulfonamide-Chalcones and Their in Vitro Antimicrobial Activity. *Mon. Für Chem. Chem. Mon.* **2020**, *151*, 417–427. [[CrossRef](#)]
5. 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 Adv.* **2020**, *10*, 24483–24490. [[CrossRef](#)]
6. Osipova, V.P.; Polovinkina, M.A.; Telekova, L.R.; Velikorodov, A.V.; Stepkina, N.N.; Berberova, N.T. Synthesis and Antioxidant Activity of New Hydroxy Derivatives of Chalcones. *Russ. Chem. Bull.* **2020**, *69*, 504–509. [[CrossRef](#)]
7. Cao, Y.; Xu, W.; Huang, Y.; Zeng, X. Licochalcone B, a Chalcone Derivative from *Glycyrrhiza Inflata*, as a Multifunctional Agent for the Treatment of Alzheimer's Disease. *Nat. Prod. Res.* **2020**, *34*, 736–739. [[CrossRef](#)]
8. Zhou, W.; Zhang, W.; Peng, Y.; Jiang, Z.H.; Zhang, L.; Du, Z. Design, Synthesis and Anti-Tumor Activity of Novel Benzimidazole-Chalcone Hybrids as Non-Intercalative Topoisomerase II Catalytic Inhibitors. *Molecules* **2020**, *25*, 3180. [[CrossRef](#)]
9. Rammohan, A.; Bhaskar, B.V.; Venkateswarlu, N.; Gu, W.; Zyryanov, G.V. Design, Synthesis, Docking and Biological Evaluation of Chalcones as Promising Antidiabetic Agents. *Bioorg. Chem.* **2020**, *95*, 103527. [[CrossRef](#)]
10. Maliyakkal, N.; Saleem, U.; Anwar, F.; Shah, M.A.; Ahmad, B.; Umer, F.; Almoyad, M.A.A.; Parambi, D.G.T.; Beeran, A.A.; Nath, L.R.; et al. Ameliorative Effect of Ethoxylated Chalcone-Based MAO-B Inhibitor on Behavioural Predictors of Haloperidol-Induced Parkinsonism in Mice: Evidence of Its Antioxidative Role against Parkinson's Diseases. *Environ. Sci. Pollut. Res.* **2022**, *29*, 7271–7282. [[CrossRef](#)]
11. Hsieh, H.-K.; Tsao, L.-T.; Wang, J.-P.; Lin, C.-N. Synthesis and Anti-Inflammatory Effect of Chalcones. *J. Pharm. Pharmacol.* **2000**, *52*, 163–171. [[CrossRef](#)] [[PubMed](#)]
12. de Campos-Buzzi, F.; de Campos, J.P.; Tonini, P.P.; Corrêa, R.; Yunes, R.A.; Boeck, P.; Cechinel-Filho, V. Antinociceptive Effects of Synthetic Chalcones Obtained from Xanthoxylone. *Arch. der Pharm.* **2006**, *339*, 361–365. [[CrossRef](#)] [[PubMed](#)]
13. Abdullah, M.I.; Mahmood, A.; Madni, M.; Masood, S.; Kashif, M. Synthesis, Characterization, Theoretical, Anti-Bacterial and Molecular Docking Studies of Quinoline Based Chalcones as a DNA Gyrase Inhibitor. *Bioorg. Chem.* **2014**, *54*, 31–37. [[CrossRef](#)] [[PubMed](#)]
14. Özdemir, A.; Altıntop, M.D.; Sever, B.; Gençer, H.K.; Kapkaç, H.A.; Atli, Ö.; Baysal, M. A New Series of Pyrrole-Based Chalcones: Synthesis and Evaluation of Antimicrobial Activity, Cytotoxicity, and Genotoxicity. *Molecules* **2017**, *22*, 2112. [[CrossRef](#)]
15. Mojarrab, M.; Soltani, R.; Aliabadi, A. Pyridine Based Chalcones: Synthesis and Evaluation of Antioxidant Activity of 1-Phenyl-3-(Pyridin-2-Yl) Prop-2-En-1-One Derivatives. *Jundishapur J. Nat. Pharm. Prod.* **2013**, *8*, 125. [[CrossRef](#)]
16. Özdemir, A.; Altıntop, M.D.; Turan-Zitouni, G.; Çiftçi, G.A.; Ertorun, Ö.; Alataş, Ö.; Kaplancikli, Z.A. Synthesis and Evaluation of New Indole-Based Chalcones as Potential Antiinflammatory Agents. *Eur. J. Med. Chem.* **2015**, *89*, 304–309. [[CrossRef](#)]

17. Chavan, H.V.; Adsul, L.K.; Kotmale, A.S.; Dhakane, V.D.; Thakare, V.N.; Bandgar, B.P. Design, Synthesis, Characterization and in Vitro and in Vivo Anti-Inflammatory Evaluation of Novel Pyrazole-Based Chalcones. *J. Enzym. Inhib. Med. Chem.* **2015**, *30*, 22–31. [[CrossRef](#)]
18. Naik, N.; Kumar, V.H.; Dias, S.M.; Swami, R.J. Novel 4-methoxy-2-acetyl benzofuran based chalcones: A new perceptivity into their antioxidant potentials. *Int. J. Pharm. Pharm. Sci.* **2013**, *5*, 242–247.
19. Rajeshirke, M.; Sreenath, M.C.; Chitrabalam, S.; Joe, I.H.; Sekar, N. Enhancement of NLO Properties in OBO Fluorophores Derived from Carbazole-Coumarin Chalcones Containing Carboxylic Acid at the N-Alykl Terminal End. *J. Phys. Chem. C* **2018**, *122*, 14313–14325. [[CrossRef](#)]
20. Shaik, A.; Bhandare, R.R.; Palleepati, 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. [[CrossRef](#)]
21. Parikh, K.; Joshi, D. Antibacterial and Antifungal Screening of Newly Synthesized Benzimidazole-Clubbed Chalcone Derivatives. *Med. Chem. Res.* **2013**, *22*, 3688–3697. [[CrossRef](#)]
22. 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. [[CrossRef](#)]
23. Singh, A.; Rani, A.; Gut, J.; Rosenthal, P.J.; Kumar, V. Piperazine-linked 4-aminoquinoline-chalcone/ferrocenyl-chalcone conjugates: Synthesis and antiplasmodial evaluation. *Chem. Biol. Drug Des.* **2017**, *90*, 590–595. [[CrossRef](#)] [[PubMed](#)]
24. Liu, H.; Guo, C.; Guo, S.; Fan, J.; Wang, L.; Shi, D. Chalcone-Analogue Fluorescent Probes for Detecting Thiophenols in Seawater Samples. *Talanta* **2019**, *201*, 301–308. [[CrossRef](#)]
25. Malek, S.N.A.; Phang, C.W.; Ibrahim, H.; Wahab, N.A.; Sim, K.S. Phytochemical and Cytotoxic Investigations of *Alpinia Mutica* Rhizomes. *Molecules* **2011**, *16*, 583–589. [[CrossRef](#)]
26. Yang, X.W.; Wang, J.S.; Wang, Y.H.; Xiao, H.T.; Hu, X.J.; Mu, S.Z.; Yan-Lin, M.; Lin, H.; He, H.P.; Li, N.; et al. Tarenane and Tarenone, Two Novel Chalcone Constituents from *Tarenna Attenuata*. *Planta Med.* **2007**, *73*, 496–498. [[CrossRef](#)]
27. Liu, Y.; Zhang, X.; Kelsang, N.; Tu, G.; Kong, D.; Lu, J.; Zhang, Y.; Liang, H.; Tu, P.; Zhang, Q. Structurally Diverse Cytotoxic Dimeric Chalcones from *Oxytropis Chiliophylla*. *J. Nat. Prod.* **2018**, *81*, 307–315. [[CrossRef](#)] [[PubMed](#)]
28. Funakoshi-Tago, M.; Tanabe, S.; Tago, K.; Itoh, H.; Mashino, T.; Sonoda, Y.; Kasahara, T. Licochalcone A Potently Inhibits Tumor Necrosis Factor α -Induced Nuclear Factor- κ B Activation through the Direct Inhibition of κ B Kinase Complex Activation. *Mol. Pharm.* **2009**, *76*, 745–753. [[CrossRef](#)]
29. Tomazela, D.M.; Pupo, M.T.; Passador, E.A.P.; da Silva, M.F.D.G.F.; Vieira, P.C.; Fernandes, J.B.; Rodrigues Fo, E.; Oliva, G.; Pirani, J.R. Pyrano Chalcones and a Flavone from *Neoraputia Magnifica* and Their Trypanosoma *Cruzi* Glycosomal Glyceraldehyde-3-Phosphate Dehydrogenase-Inhibitory Activities. *Phytochemistry* **2000**, *55*, 643–651. [[CrossRef](#)]
30. Akihisa, T.; Tokuda, H.; Hasegawa, D.; Ukiya, M.; Kimura, Y.; Enjo, F.; Suzuki, T.; Nishino, H. Chalcones and Other Compounds from the Exudates of *Angelica Keiskei* and Their Cancer Chemopreventive Effects. *J. Nat. Prod.* **2006**, *69*, 38–42. [[CrossRef](#)]
31. Cui, Y.; Ao, M.; Li, W.; Hu, J.; Yu, L. Anti-Inflammatory Activity of Licochalcone a Isolated from *Glycyrrhiza Inflata*. *Z. Für Nat. Sect. C J. Biosci.* **2008**, *63*, 361–365. [[CrossRef](#)] [[PubMed](#)]
32. Pascoal, A.C.R.F.; Ehrenfried, C.A.; Lopez, B.G.C.; de Araujo, T.M.; Pascoal, V.D.B.; Gilioli, R.; Anheê, G.F.; Ruiz, A.L.T.G.; de Carvalho, J.E.; Stefanello, M.A.; et al. Antiproliferative Activity and Induction of Apoptosis in PC-3 Cells by the Chalcone Cardamonin from *Campomanesia Adamantium* (Myrtaceae) in a Bioactivity-Guided Study. *Molecules* **2014**, *19*, 1843–1855. [[CrossRef](#)] [[PubMed](#)]
33. Tuntipaleepun, M.; Chakthong, S.; Ponglimanont, C.; Plodpai, P.; Voravuthikunchai, S.P. Antifungal and Cytotoxic Substances from the Stem Barks of *Desmos Chinensis*. *Chin. Chem. Lett.* **2012**, *23*, 587–590. [[CrossRef](#)]
34. Liu, M.L.; Duan, Y.H.; Hou, Y.L.; Li, C.; Gao, H.; Dai, Y.; Yao, X.S. Nardoaristolones A and B, Two Terpenoids with Unusual Skeletons from *Nardostachys Chinensis* Batal. *Org. Lett.* **2013**, *15*, 1000–1003. [[CrossRef](#)] [[PubMed](#)]
35. Yang, E.B.; Zhang, K.; Cheng, L.Y.; Mack, P. Butein, a Specific Protein Tyrosine Kinase Inhibitor. *Biochem. Biophys. Res. Commun.* **1998**, *245*, 435–438. [[CrossRef](#)]
36. Ren, Y.; Yuan, C.; Qian, Y.; Chai, H.B.; Chen, X.; Goetz, M.; Kinghorn, A.D. Constituents of an Extract of *Cryptocarya Rubra* Housed in a Repository with Cytotoxic and Glucose Transport Inhibitory Effects. *J. Nat. Prod.* **2014**, *77*, 550–556. [[CrossRef](#)]
37. Rees, K.A.; Bermudez, C.; Edwards, D.J.; Elliott, A.G.; Ripen, J.E.; Seta, C.; Huang, J.X.; Cooper, M.A.; Fraser, J.A.; Yeo, T.C.; et al. Flemingian-Type Prenylated Chalcones from the Sarawak Rainforest Plant *Desmodium Congestum*. *J. Nat. Prod.* **2015**, *78*, 2141–2144. [[CrossRef](#)]
38. Inamori, Y.; Baba, K.; Tsujibo, H.; Taniguchi, M.; Nakata, K.; Kozawa, M. Antibacterial Activity of Two Chalcones, Xanthoangelol and 4-Hydroxyderricin, Isolated from the Root of *Angelica Keiskei* KOIDZUMI. *Chem. Pharm. Bull.* **1991**, *39*, 1604–1605. [[CrossRef](#)]
39. Costa, G.M.; Endo, E.H.; Cortez, D.A.G.; Nakamura, T.U.; Nakamura, C.V.; Dias Filho, B.P. Antimicrobial Effects of Piper *Hispidum* Extract, Fractions and Chalcones against *Candida Albicans* and *Staphylococcus Aureus*. *J. Mycol. Médicale* **2016**, *26*, 217–226. [[CrossRef](#)]
40. Wang, Z.; Wang, N.; Han, S.; Wang, D.; Mo, S.; Yu, L.; Huang, H.; Tsui, K.; Shen, J.; Chen, J. Dietary Compound Isoliquiritigenin Inhibits Breast Cancer Neovascularization via VEGF/VEGFR-2 Signaling Pathway. *PLoS ONE* **2013**, *8*, e68566. [[CrossRef](#)] [[PubMed](#)]

41. Agarkar, S.A.; Kulkarni, R.R.; Dhas, V.V.; Chinchansure, A.A.; Hazra, P.; Joshi, S.P.; Ogale, S.B. Isobutrin from Butea Monosperma (Flame of the Forest): A Promising New Natural Sensitizer Belonging to Chalcone Class. *ACS Appl. Mater. Interfaces* **2011**, *3*, 2440–2444. [[CrossRef](#)] [[PubMed](#)]
42. Wang, D.; Liang, J.; Zhang, J.; Wang, Y.; Chai, X. Natural Chalcones in Chinese Materia Medica: Licorice. *Evidence-Based Complement. Altern. Med.* **2020**, *2020*, 1–14. [[CrossRef](#)] [[PubMed](#)]
43. Malik, H.S.; Bilal, A.; Ullah, R.; Iqbal, M.; Khan, S.; Ahmed, I.; Krohn, K.; Saleem, R.S.Z.; Hussain, H.; Faisal, A. Natural and Semisynthetic Chalcones as Dual FLT3 and Microtubule Polymerization Inhibitors. *J. Nat. Prod.* **2020**, *83*, 3111–3121. [[CrossRef](#)] [[PubMed](#)]
44. Aoki, N.; Muko, M.; Ohta, E.; Ohta, S. C-Geranylated Chalcones from the Stems of Angelica Keiskei with Superoxide-Scavenging Activity. *J. Nat. Prod.* **2008**, *71*, 1308–1310. [[CrossRef](#)] [[PubMed](#)]
45. Kil, Y.S.; Choi, S.K.; Lee, Y.S.; Jafari, M.; Seo, E.K. Chalcones from Angelica Keiskei: Evaluation of Their Heat Shock Protein Inducing Activities. *J. Nat. Prod.* **2015**, *78*, 2481–2487. [[CrossRef](#)]
46. Daikonya, A.; Katsuki, S.; Kitanaka, S. Antiallergic Agents from Natural Sources 9. Inhibition of Nitric Oxide Production by Novel Chalcone Derivatives from Mallotus Philippinensis (Euphorbiaceae). *Chem. Pharm. Bull.* **2004**, *52*, 1326–1329. [[CrossRef](#)]
47. Fu, L.C.; Huang, X.A.; Lai, Z.Y.; Hu, Y.J.; Liu, H.J.; Cai, X.L. A New 3-Benzylchroman Derivative from Sappan Lignum (Caesalpinia Sappan). *Molecules* **2008**, *13*, 1923–1930. [[CrossRef](#)]
48. Phrutivorapongkul, A.; Lipipun, V.; Ruangrunsi, N.; Kirtikara, K.; Nishikawa, K.; Maruyama, S.; Watanabe, T.; Ishikawa, T. Studies on the Chemical Constituents of Stem Bark of Millettia Leucantha: Isolation of New Chalcones with Cytotoxic, Anti-Herpes Simplex Virus and Anti-Inflammatory Activities. *Chem. Pharm. Bull.* **2003**, *51*, 187–190. [[CrossRef](#)]
49. Svetaz, L.; Tapia, A.; López, S.N.; Furlán, R.L.E.; Petenatti, E.; Pioli, R.; Schmeda-Hirschmann, G.; Zacchino, S.A. Antifungal Chalcones and New Caffeic Acids Esters from Zuccagnia Punctata Acting against Soybean Infecting Fungi. *J. Agric. Food Chem.* **2004**, *52*, 3297–3300. [[CrossRef](#)]
50. Wang, J.P.; Tsao, L.T.; Raung, S.L.; Lin, C.N. Investigation of the Inhibitory Effect of Brousochalcone A on Respiratory Burst in Neutrophils. *Eur. J. Pharmacol.* **1997**, *320*, 201–208. [[CrossRef](#)]
51. Ohnogi, H.; Kudo, Y.; Tahara, K.; Sugiyama, K.; Enoki, T.; Hayami, S.; Sagawa, H.; Tanimura, Y.; Aoi, W.; Naito, Y.; et al. Six New Chalcones from Angelica Keiskei Inducing Adiponectin Production in 3T3-L1 Adipocytes. *Biosci. Biotechnol. Biochem.* **2012**, *76*, 961–966. [[CrossRef](#)] [[PubMed](#)]
52. Haraguchi, H.; Inoue, J.; Tamura, Y.; Mizutani, K. Antioxidative components of Psoralea corylifolia (Leguminosae). *Phytother. Res. Int. J. Devoted Pharmacol. Toxicol. Eval. Nat. Prod. Deriv.* **2002**, *16*, 539–544. [[CrossRef](#)] [[PubMed](#)]
53. Kulkarni, R.R.; Tupe, S.G.; Gample, S.P.; Chandgude, M.G.; Sarkar, D.; Deshpande, M.V.; Joshi, S.P. Antifungal Dimeric Chalcone Derivative Kamalachalcone e from Mallotus Philippinensis. *Nat. Prod. Res.* **2014**, *28*, 245–250. [[CrossRef](#)] [[PubMed](#)]
54. Strathmann, J.; Gerhauser, C. Anti-Proliferative and Apoptosis-Inducing Properties of Xanthohumol, a Prenylated Chalcone from Hops (*Humulus Lupulus* L.). In *Natural Compounds as Inducers of Cell Death*; Springer: Dordrecht, The Netherlands, 2012; Volume 1, pp. 69–93. [[CrossRef](#)]
55. McRae, J.M.; Yang, Q.; Crawford, R.J.; Palombo, E.A. Acylated Flavonoid Tetraglycoside from Planchonia Careya Leaves. *Phytochem. Lett.* **2008**, *1*, 99–102. [[CrossRef](#)]
56. Chung, M.-I.; Weng, J.-R.; Lai, M.-H.; Yen, M.-H.; Lin, C.-N. A New Chalcone, Xanthonones, and a Xanthonolignoid from *Hypericum geminiflorum*. *J. Nat. Prod.* **1999**, *62*, 1033–1035. [[CrossRef](#)]
57. Maxwell, C.A.; Hartwig, U.A.; Joseph, C.M.; Phillips, D.A. A Chalcone and Two Related Flavonoids Released from Alfalfa Roots Induce Nod Genes of Rhizobium Meliloti. *Plant Physiol* **1989**, *91*, 842–847. [[CrossRef](#)]
58. Nair, A.D.; Athira, C.K.; Manikandan, P.; Ramani, P. One-Pot Synthesis of Modified 4-Aryl-4H-Chromenes and Their Preliminary Anti-Cancer Studies. *J. Indian Chem. Soc.* **2019**, *96*, 19–22.
59. Pandurangan, N.; Bose, C.; Banerji, A. Synthesis and Antioxygenic Activities of Seabuckthorn Flavone-3-Ols and Analogs. *Bioorg. Med. Chem. Lett.* **2011**, *21*, 5328–5330. [[CrossRef](#)]
60. Hernawan; Purwono, B.; Triyono; Hanafi, M. The Use of Chitosan as a Solid Base Catalyst for the Chalcones Synthesis. *IOP Conf. Ser. Earth Environ. Sci.* **2020**, *462*, 2055. [[CrossRef](#)]
61. Climent, M.J.; Corma, A.; Iborra, S.; Velty, A. Activated Hydrotalcites as Catalysts for the Synthesis of Chalcones of Pharmaceutical Interest. *J. Catal.* **2004**, *221*, 474–482. [[CrossRef](#)]
62. Mohammad, S.A.G.; Khoerunnisa, F.; Rigolet, S.; Jean Daou, T.; Ling, T.C.; Ng, E.P. Hierarchical Cs–Pollucite Nanozeolite Modified with Novel Organosilane as an Excellent Solid Base Catalyst for Claisen–Schmidt Condensation of Benzaldehyde and Acetophenone. *Processes* **2020**, *8*, 96. [[CrossRef](#)]
63. Winter, C.; Caetano, J.N.; Araújo, A.B.C.; Chaves, A.R.; Ostroski, I.C.; Vaz, B.G.; Pérez, C.N.; Alonso, C.G. Activated Carbons for Chalcone Production: Claisen-Schmidt Condensation Reaction. *Chem. Eng. J.* **2016**, *303*, 604–610. [[CrossRef](#)]
64. Elamathi, P.; Chandrasekar, G.; Balamurali, M.M. Nanoporous AISBA-15 Catalysed Claisen–Schmidt Condensation for the Synthesis of Novel and Biologically Active Chalcones. *J. Porous Mater.* **2020**, *27*, 817–829. [[CrossRef](#)]
65. Rafiee, E.; Rahimi, F. A Green Approach to the Synthesis of Chalcones via Claisen-Schmidt Condensation Reaction Using Cesium Salts of 12-Tungstophosphoric Acid as a Reusable Nanocatalyst. *Mon. Für Chem. Chem. Mon.* **2013**, *144*, 361–367. [[CrossRef](#)]
66. Das, S.; Porashar, B.; Saikia, S.; Borah, R. Brønsted Acidic Ionic Liquids Catalysed Sequential Michael-Like Addition of Indole with Chalcones via Claisen-Schmidt Condensation. *ChemistrySelect* **2020**, *5*, 3041–3047. [[CrossRef](#)]

67. Sazegar, M.R.; Mahmoudian, S.; Mahmoudi, A.; Triwahyono, S.; Jalil, A.A.; Mukti, R.R.; Nazirah Kamarudin, N.H.; Ghoreishi, M.K. Catalyzed Claisen–Schmidt Reaction by Protonated Aluminate Mesoporous Silica Nanomaterial Focused on the (E)-Chalcone Synthesis as a Biologically Active Compound. *RSC Adv.* **2016**, *6*, 11023–11031. [[CrossRef](#)]
68. Jioui, I.; Dânoun, K.; Solhy, A.; Jouiad, M.; Zahouily, M.; Essaid, B.; Len, C.; Fihri, A. Modified Fluorapatite as Highly Efficient Catalyst for the Synthesis of Chalcones via Claisen–Schmidt Condensation Reaction. *J. Ind. Eng. Chem.* **2016**, *39*, 218–225. [[CrossRef](#)]
69. Heidarzadeh, T.; Nami, N.; Zareyee, D. Preparation of (MWCNTs)-COOH/CeO₂Hybrid as an Efficient Catalyst for Claisen–Schmidt Condensation. *J. Appl. Chem. Res.* **2021**, *15*, 44–57.
70. Ke, F.; Qiu, L.G.; Zhu, J. Fe₃O₄@MOF Core-Shell Magnetic Microspheres as Excellent Catalysts for the Claisen–Schmidt Condensation Reaction. *Nanoscale* **2014**, *6*, 1596–1601. [[CrossRef](#)]
71. Paul, A.; Devi, M.; Dhar, S.S. Incorporation of Nanosized ZnWO₄ and Fe₃O₄ on Graphitic Carbon Nitride to Fabricate a Novel, Highly Active Magnetically Recoverable Catalyst in Claisen–Schmidt Condensation. *J. Phys. Chem. Solids* **2020**, *136*, 109117. [[CrossRef](#)]
72. Li, Z.; Zhao, H.; Han, H.; Liu, Y.; Song, J.; Guo, W.; Chu, W.; Sun, Z. Graphene-Supported ZnO Nanoparticles: An Efficient Heterogeneous Catalyst for the Claisen–Schmidt Condensation Reaction without Additional Base. *Tetrahedron Lett.* **2017**, *58*, 3984–3988. [[CrossRef](#)]
73. Srivastava, Y.K. Ecofriendly Microwave Assisted Synthesis of Some Chalcones. *Rasayan J. Chem.* **2008**, *1*, 884–886.
74. Farooq, S.; Ngaini, Z.; Mortadza, N.A. Microwave-Assisted Synthesis and Molecular Docking Study of Heteroaromatic Chalcone Derivatives as Potential Antibacterial Agents. *Bull. Korean Chem. Soc.* **2020**, *41*, 918–924. [[CrossRef](#)]
75. Calvino, V.; Picallo, M.; López-Peinado, A.J.; Martín-Aranda, R.M.; Durán-Valle, C.J. Ultrasound Accelerated Claisen–Schmidt Condensation: A Green Route to Chalcones. *Appl. Surf. Sci.* **2006**, *252*, 6071–6074. [[CrossRef](#)]
76. Perozo-Rondón, E.; Martín-Aranda, R.M.; Casal, B.; Durán-Valle, C.J.; Lau, W.N.; Zhang, X.F.; Yeung, K.L. Sonocatalysis in Solvent Free Conditions: An Efficient Eco-Friendly Methodology to Prepare Chalcones Using a New Type of Amino Grafted Zeolites. *Catal. Today* **2006**, *114*, 183–187. [[CrossRef](#)]
77. Homerin, G.; Nica, A.S.; Farce, A.; Dubois, J.; Ghinet, A. Ultrasounds-Mediated 10-Seconds Synthesis of Chalcones as Potential Farnesyltransferase Inhibitors. *Bioorg. Med. Chem. Lett.* **2020**, *30*, 127149. [[CrossRef](#)]
78. Kumar, S.; Lamba, M.S.; Makrandi, J.K. An Efficient Green Procedure for the Synthesis of Chalcones Using C-200 as Solid Support under Grinding Conditions. *Green Chem. Lett. Rev.* **2008**, *1*, 123–125. [[CrossRef](#)]
79. Yeshwant, S.M.; Nanded, M.; Nalwar, Y.; Zangade, S.; Mokle, S.; Vibhute, A.; Vibhute, Y. An Efficient and Operationally Simple Synthesis of Some New Chalcones by Using Grinding Technique. *Chem. Sci. J.* **2009**, *2011*, 13.
80. Al-Masum, M.; Ng, E.; Wai, M.C. Palladium-Catalyzed Direct Cross-Coupling of Potassium Styryltrifluoroborates and Benzoyl Chlorides—A One Step Method for Chalcone Synthesis. *Tetrahedron Lett.* **2011**, *52*, 1008–1010. [[CrossRef](#)]
81. Diana, E.J.; Kanchana, U.S.; Mathew, T.V.; Anilkumar, G. Recent Developments in the Metal Catalysed Cross-Coupling Reactions for the Synthesis of the Enone System of Chalcones. *Appl. Organomet. Chem.* **2020**, *34*, e5987. [[CrossRef](#)]
82. Braun, R.U.; Ansorge, M.; Müller, T.J.J. Coupling-Isomerization Synthesis of Chalcones. *Chemistry* **2006**, *12*, 9081–9094. [[CrossRef](#)]
83. Hsieh, C.T.; Ötvös, S.B.; Wu, Y.C.; Mándity, I.M.; Chang, F.R.; Fülöp, F. Highly Selective Continuous-Flow Synthesis of Potentially Bioactive Deuterated Chalcone Derivatives. *ChemPlusChem* **2015**, *80*, 859–864. [[CrossRef](#)] [[PubMed](#)]
84. Rao, M.L.N.; Venkatesh, V.; Jadhav, D.N. A Palladium Catalyzed Atom-Efficient Cross-Coupling Reactivity of Triarylbiomeths with α,β -Unsaturated Acyl Chlorides. *J. Organomet. Chem.* **2008**, *693*, 2494–2498. [[CrossRef](#)]
85. Yamakawa, T.; Kinoshita, H.; Miura, K. Synthetic Utility of Tribenzyltin Hydride and Its Derivatives as Easily Accessible, Removable, and Decomposable Organotin Reagents. *J. Organomet. Chem.* **2013**, *724*, 129–134. [[CrossRef](#)]
86. Kim, S.; Bae, S.W.; Lee, J.S.; Park, J. Recyclable Gold Nanoparticle Catalyst for the Aerobic Alcohol Oxidation and C–C Bond Forming Reaction between Primary Alcohols and Ketones under Ambient Conditions. *Tetrahedron* **2009**, *65*, 1461–1466. [[CrossRef](#)]
87. Li, C.J. Cross-Dehydrogenative Coupling (CDC): Exploring C–C Bond Formations beyond Functional Group Transformations. *Acc. Chem. Res.* **2009**, *42*, 335–344. [[CrossRef](#)] [[PubMed](#)]
88. Kumar, A.; Sharma, S.; Tripathi, V.D.; Srivastava, S. Synthesis of Chalcones and Flavanones Using Julia–Kocienski Olefination. *Tetrahedron* **2010**, *66*, 9445–9449. [[CrossRef](#)]
89. Tan, P.; Wang, S.R. Reductive (3 + 2) Annulation of Benzils with Pyrylium Salts: Stereoselective Access to Furyl Analogues of Cis-Chalcones. *Org. Lett.* **2019**, *21*, 6029–6033. [[CrossRef](#)] [[PubMed](#)]
90. Mahapatra, D.K.; Bharti, S.K.; Asati, V. Anti-Cancer Chalcones: Structural and Molecular Target Perspectives. *Eur. J. Med. Chem.* **2015**, *98*, 69–114. [[CrossRef](#)] [[PubMed](#)]
91. Ramakrishnan, V.T.; Kagan, J. The Photochemical Synthesis of 2'-Hydroxychalcones from Phenyl Cinnamates. *J. Org. Chem.* **1970**, *35*, 2901–2904. [[CrossRef](#)]
92. Wang, C.Q. Solvent-Free Stereoselective Synthesis of Chalcones via Wittig Reaction of Arsonium Ylide by Grinding. In *Advanced Materials Research*; Trans Tech Publications Ltd.: Wollerau, Switzerland, 2014; Volume 864, pp. 2132–2135.
93. Huang, Z.; Wang, L.; Huang, X. Stereoselective Synthesis of α -Bromo- α,β -Unsaturated Ketones via Wittig Reaction. *Synth. Commun.* **2006**, *33*, 757–762. [[CrossRef](#)]
94. Baker, R.E.; Mahmud, A.S.; Miller, I.F.; Rajeev, M.; Rasambainarivo, F.; Rice, B.L.; Takahashi, S.; Tatem, A.J.; Wagner, C.E.; Wang, L.F.; et al. Infectious Disease in an Era of Global Change. *Nat. Rev. Microbiol.* **2021**, *20*, 193–205. [[CrossRef](#)] [[PubMed](#)]

95. Sahoo, B.M.; Banik, B.K.; Mahato, A.K.; Shanthi, C.N.; Mohantad, B.C. Microwave-assisted synthesis of antitubercular agents: A novel approach. In *Green Approaches in Medicinal Chemistry for Sustainable Drug Design*; Elsevier: Amsterdam, The Netherlands, 2020; pp. 779–818. [[CrossRef](#)]
96. Kaur, H.; Singh, R.; Kant, R. Synthesis, Molecular Docking, and Evaluation of Triazole and Chalcone Conjugate as Antitubercular Agent. *Res. Sq.* **2021**. [[CrossRef](#)]
97. Bhoot, D.; Khunt, R.C.; Parekh, H.H. Synthesis and Biological Evaluation of Chalcones and Acetyl Pyrazoline Derivatives Comprising Furan Nucleus as an Antitubercular Agents. *Med. Chem. Res.* **2012**, *21*, 3233–3239. [[CrossRef](#)]
98. Muradás, T.C.; Abbadi, B.L.; Villela, A.D.; Macchi, F.S.; Bergo, P.F.; de Freitas, T.F.; Sperotto, N.D.M.; Timmers, L.F.S.M.; de Souza, O.N.; Picada, J.N.; et al. Pre-Clinical Evaluation of Quinoxaline-Derived Chalcones in Tuberculosis. *PLoS ONE* **2018**, *13*, e0202568. [[CrossRef](#)]
99. Rao, N.S.; Shaik, A.B.; Routhu, S.R.; Hussaini, S.M.A.; Sunkari, S.; Rao, A.V.S.; Reddy, A.M.; Alarifi, A.; Kamal, A. New Quinoline Linked Chalcone and Pyrazoline Conjugates: Molecular Properties Prediction, Antimicrobial and Antitubercular Activities. *ChemistrySelect* **2017**, *2*, 2989–2996. [[CrossRef](#)]
100. Yadav, D.K.; Ahmad, I.; Shukla, A.; Khan, F.; Negi, A.S.; Gupta, A. QSAR and Docking Studies on Chalcone Derivatives for Antitubercular Activity against M.Tuberculosis H37Rv. *J. Chemom.* **2014**, *28*, 499–507. [[CrossRef](#)]
101. Mujahid, M.; Yogeewari, P.; Sriram, D.; Basavanag, U.M.V.; Díaz-Cervantes, E.; Córdoba-Bahena, L.; Robles, J.; Gonnade, R.G.; Karthikeyan, M.; Vyas, R.; et al. Spirochromone-chalcone conjugates as antitubercular agents: Synthesis, bio evaluation and molecular modeling studies. *RSC Adv.* **2015**, *5*, 106448–106460. [[CrossRef](#)]
102. Anandam, R.; Jadav, S.S.; Ala, V.B.; Ahsan, M.J.; Bollikolla, H.B. Synthesis of New C-Dimethylated Chalcones as Potent Antitubercular Agents. *Med. Chem. Res.* **2018**, *27*, 1690–1704. [[CrossRef](#)]
103. Hans, R.H.; Guantai, E.M.; Lategan, C.; Smith, P.J.; Wan, B.; Franzblau, S.G.; Gut, J.; Rosenthal, P.J.; Chibale, K. Synthesis, Antimalarial and Antitubercular Activity of Acetylenic Chalcones. *Bioorg. Med. Chem. Lett.* **2010**, *20*, 942–944. [[CrossRef](#)]
104. 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. [[CrossRef](#)]
105. Trivedi, J.C.; Bariwal, J.B.; Upadhyay, K.D.; Naliapara, Y.T.; Joshi, S.K.; Pannecouque, C.C.; de Clercq, E.; Shah, A.K. Improved and Rapid Synthesis of New Coumarinyl Chalcone Derivatives and Their Antiviral Activity. *Tetrahedron Lett.* **2007**, *48*, 8472–8474. [[CrossRef](#)]
106. Elkhalfi, D.; Al-Hashimi, I.; Al Moustafa, A.E.; Khalil, A. A comprehensive review on the antiviral activities of chalcones. *J. Drug Target.* **2021**, *29*, 403–419. [[CrossRef](#)] [[PubMed](#)]
107. Onyilagha, J.C.; Malhotra, B.; Elder, M.; French, C.J.; Towers, G.N. Comparative studies of inhibitory activities of chalcones on tomato ringspot virus (ToRSV). *Can. J. Plant Pathol.* **1997**, *19*, 133–137. [[CrossRef](#)]
108. Cole, A.L.; Hossain, S.; Cole, A.M.; Phanstiel, O. Synthesis and Bioevaluation of Substituted Chalcones, Coumaranones and Other Flavonoids as Anti-HIV Agents. *Bioorg. Med. Chem.* **2016**, *24*, 2768–2776. [[CrossRef](#)] [[PubMed](#)]
109. Zhou, D.; Xie, D.; He, F.; Song, B.; Hu, D. Antiviral Properties and Interaction of Novel Chalcone Derivatives Containing a Purine and Benzenesulfonamide Moiety. *Bioorg. Med. Chem. Lett.* **2018**, *28*, 2091–2097. [[CrossRef](#)] [[PubMed](#)]
110. Gan, X.; Wang, Y.; Hu, D.; Song, B. Design, Synthesis, and Antiviral Activity of Novel Chalcone Derivatives Containing a Purine Moiety. *Chin. J. Chem.* **2017**, *35*, 665–672. [[CrossRef](#)]
111. Mateeva, N.; Eyunni, S.V.K.; Redda, K.K.; Ononuju, U.; Hansberry, T.D.; Aikens, C.; Nag, A. Functional Evaluation of Synthetic Flavonoids and Chalcones for Potential Antiviral and Anticancer Properties. *Bioorg. Med. Chem. Lett.* **2017**, *27*, 2350–2356. [[CrossRef](#)]
112. 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. *Int. J. Clin. Pract.* **2021**, *75*, e14846. [[CrossRef](#)]
113. Tang, X.; Su, S.; Chen, M.; He, J.; Xia, R.; Guo, T.; Chen, Y.; Zhang, C.; Wang, J.; Xue, W. Novel chalcone derivatives containing a 1, 2, 4-triazine moiety: Design, synthesis, antibacterial and antiviral activities. *RSC Adv.* **2019**, *9*, 6011–6020. [[CrossRef](#)]
114. Wang, Y.J.; Zhou, D.G.; He, F.C.; Chen, J.X.; Chen, Y.Z.; Gan, X.H.; Hu, D.Y.; Song, B.A. Synthesis and Antiviral Bioactivity of Novel Chalcone Derivatives Containing Purine Moiety. *Chin. Chem. Lett.* **2018**, *29*, 127–130. [[CrossRef](#)]
115. Gan, X.; Hu, D.; Chen, Z.; Wang, Y.; Song, B. Synthesis and Antiviral Evaluation of Novel 1,3,4-Oxadiazole/Thiadiazole-Chalcone Conjugates. *Bioorg. Med. Chem. Lett.* **2017**, *27*, 4298–4301. [[CrossRef](#)] [[PubMed](#)]
116. Bizzarri, B.M.; Fanelli, A.; Piccinino, D.; De Angelis, M.; Dolfa, C.; Palamara, A.T.; Nencioni, L.; Zippilli, C.; Crucianelli, M.; Saladino, R.; et al. Synthesis of stilbene and chalcone inhibitors of influenza A virus by SBA-15 supported Hoveyda-Grubbs metathesis. *Catalysts* **2019**, *9*, 983. [[CrossRef](#)]
117. 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. *Arab. J. Chem.* **2019**, *12*, 2685–2696. [[CrossRef](#)]
118. Wan, Z.; Hu, D.; Li, P.; Xie, D.; Gan, X. Synthesis, antiviral bioactivity of novel 4-thioquinazoline derivatives containing chalcone moiety. *Molecules* **2015**, *20*, 11861–11874. [[CrossRef](#)]
119. Awasthi, S.K.; Mishra, N.; Kumar, B.; Sharma, M.; Bhattacharya, A.; Mishra, L.C.; Bhasin, V.K. Potent Antimalarial Activity of Newly Synthesized Substituted Chalcone Analogs in Vitro. *Med. Chem. Res.* **2009**, *18*, 407–420. [[CrossRef](#)]

120. 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. *Eur. J. Med. Chem.* **2020**, *193*, 112215. [[CrossRef](#)]
121. Insuasty, B.; Ramírez, J.; Becerra, D.; Echeverry, C.; Quiroga, J.; Abonia, R.; Robledo, S.M.; Vélez, I.D.; Upegui, Y.; Muñoz, J.A.; et al. An Efficient Synthesis of New Caffeine-Based Chalcones, Pyrazolines and Pyrazolo[3,4-b][1,4]Diazepines as Potential Antimalarial, Antitrypanosomal and Antileishmanial Agents. *Eur. J. Med. Chem.* **2015**, *93*, 401–413. [[CrossRef](#)]
122. De Oliveira, M.E.; Cenzi, G.; Nunes, R.R.; Andrighetti, C.R.; Valadão, D.M.D.S.; Dos Reis, C.; Simões, C.M.O.; Nunes, R.J.; Junior, M.C.; Taranto, A.G.; et al. Antimalarial activity of 4-metoxychalcones: Docking studies as falcipain/plasmeprin inhibitors, ADMET and lipophilic efficiency analysis to identify a putative oral lead candidate. *Molecules* **2013**, *18*, 15276–15287. [[CrossRef](#)]
123. Yadav, N.; Dixit, S.K.; Bhattacharya, A.; Mishra, L.C.; Sharma, M.; Awasthi, S.K.; Bhasin, V.K. Antimalarial Activity of Newly Synthesized Chalcone Derivatives In Vitro. *Chem. Biol. Drug Des.* **2012**, *80*, 340–347. [[CrossRef](#)]
124. Hameed, A.; Masood, S.; Hameed, A.; Ahmed, E.; Sharif, A.; Abdullah, M.I. Anti-Malarial, Cytotoxicity and Molecular Docking Studies of Quinoliny Chalcones as Potential Anti-Malarial Agent. *J. Comput. Mol. Des.* **2019**, *33*, 677–688. [[CrossRef](#)] [[PubMed](#)]
125. Gayam, V.; Ravi, S. Cinnamoylated Chloroquine Analogues: A New Structural Class of Antimalarial Agents. *Eur. J. Med. Chem.* **2017**, *135*, 382–391. [[CrossRef](#)] [[PubMed](#)]
126. Arancibia, R.; Biot, C.; Delaney, G.; Roussel, P.; Pascual, A.; Pradines, B.; Klahn, A.H. Cyrhretrenyl Chalcones: Synthesis, Characterization and Antimalarial Evaluation. *J. Organomet. Chem.* **2013**, *723*, 143–148. [[CrossRef](#)]
127. Syahri, J.; Nasution, H.; Nurohmah, B.A.; Purwono, B.; Yuanita, E.; Zakaria, N.H.; Hassan, N.I. Design, synthesis and biological evaluation of aminoalkylated chalcones as antimalarial agent. *Sains Malays.* **2020**, *49*, 2667–2677. [[CrossRef](#)]
128. Guantai, E.M.; Ncokazi, K.; Egan, T.J.; Gut, J.; Rosenthal, P.J.; Smith, P.J.; Chibale, K. Design, Synthesis and in Vitro Antimalarial Evaluation of Triazole-Linked Chalcone and Dienone Hybrid Compounds. *Bioorg. Med. Chem.* **2010**, *18*, 8243–8256. [[CrossRef](#)]
129. Gutteridge, C.E.; Thota, D.S.; Curtis, S.M.; Kozar, M.P.; Li, Q.; Xie, L.; Zhang, J.; Melendez, V.; Asher, C.O.; Luong, T.T.; et al. In Vitro Biotransformation, in Vivo Efficacy and Pharmacokinetics of Antimalarial Chalcones. *Pharmacology* **2011**, *87*, 96–104. [[CrossRef](#)]
130. Kumar, R.; Mohanakrishnan, D.; Sharma, A.; Kaushik, N.K.; Kalia, K.; Sinha, A.K.; Sahal, D. Reinvestigation of Structure–Activity Relationship of Methoxylated Chalcones as Antimalarials: Synthesis and Evaluation of 2,4,5-Trimethoxy Substituted Patterns as Lead Candidates Derived from Abundantly Available Natural β -Asarone. *Eur. J. Med. Chem.* **2010**, *45*, 5292–5301. [[CrossRef](#)]
131. Tadigoppula, N.; Korthikunta, V.; Gupta, S.; Kancharla, P.; Khaliq, T.; Soni, A.; Srivastava, R.K.; Srivastava, K.; Puri, S.K.; Raju, K.S.R.; et al. Synthesis and Insight into the Structure-Activity Relationships of Chalcones as Antimalarial Agents. *J. Med. Chem.* **2013**, *56*, 31–45. [[CrossRef](#)]
132. Sarveswari, S.; Vijayakumar, V.; Siva, R.; Priya, R. Synthesis of 4-Hydroxy-2(1h)-Quinolone Derived Chalcones, Pyrazolines and Their Antimicrobial, in Silico Antimalarial Evaluations. *Appl. Biochem. Biotechnol.* **2015**, *175*, 43–64. [[CrossRef](#)]
133. Tomar, V.; Bhattacharjee, G.; Kamaluddin; Rajakumar, S.; Srivastava, K.; Puri, S. Synthesis of new chalcone derivatives containing acridinyl moiety with potential antimalarial activity. *Eur. J. Med. Chem.* **2010**, *45*, 745–751. [[CrossRef](#)]
134. Syahri, J.; Rullah, K.; Armunanto, R.; Yuanita, E.; Nurohmah, B.A.; Aluwi, M.F.F.M.; Kok, L.; Wai, B.P. Synthesis, biological evaluation, QSAR analysis, and molecular docking of chalcone derivatives for antimalarial activity. *Parasite* **2016**, *4*, 8. [[CrossRef](#)]
135. Smit, F.J.; N'Da, D.D. Synthesis, in vitro antimalarial activity and cytotoxicity of novel 4-aminoquinoliny-chalcone amides. *Bioorg. Med. Chem.* **2014**, *22*, 1128–1138. [[CrossRef](#)] [[PubMed](#)]
136. 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. *Nat. Prod. Res.* **2021**, *35*, 3261–3268. [[CrossRef](#)] [[PubMed](#)]
137. Mouzié, C.M.; Guefack, M.-G.F.; Kianfé, B.Y.; Serondo, H.U.; Ponou, B.K.; Siwe-Noundou, X.; Teponno, R.B.; Krause, R.W.M.; Kuete, V.; Tapondjou, L.A. A New Chalcone and Antimicrobial Chemical Constituents of *Dracaena Stedneuri*. *Pharmaceuticals* **2022**, *15*, 725. [[CrossRef](#)]
138. Lagu, S.B.; Yejella, R.P.; Bhandare, R.R.; Shaik, A.B. Design, Synthesis, and Antibacterial and Antifungal Activities of Novel Trifluoromethyl and Trifluoromethoxy Substituted Chalcone Derivatives. *Pharmaceuticals* **2020**, *13*, 375. [[CrossRef](#)]
139. Sivakumar, P.M.; Prabhawathi, V.; Doble, M. Antibacterial Activity and QSAR of Chalcones against Biofilm-Producing Bacteria Isolated from Marine Waters. *SAR QSAR Environ. Res.* **2010**, *21*, 247–263. [[CrossRef](#)]
140. Satokata, A.A.C.; Souza, J.H.; Silva, L.L.O.; Santiago, M.B.; Ramos, S.B.; de Assis, L.R.; Theodoro, R.D.S.; e Oliveira, L.R.; Regasini, L.O.; Martins, C.H.G. Chalcones with potential antibacterial and antibiofilm activities against periodontopathogenic bacteria. *Anaerobe* **2022**, *76*, 102588. [[CrossRef](#)]
141. Moreira Osório, T.; Delle Monache, F.; Domeneghini Chiaradia, L.; Mascarello, A.; Regina Stumpf, T.; Roberto Zanetti, C.; Bardini Silveira, D.; Regina Monte Barardi, C.; de Fatima Albino Smânia, E.; Viancelli, A.; et al. Antibacterial Activity of Chalcones, Hydrazones and Oxadiazoles against Methicillin-Resistant *Staphylococcus Aureus*. *Bioorg. Med. Chem. Lett.* **2012**, *22*, 225–230. [[CrossRef](#)]
142. Sivakumar, P.M.; Ganesan, S.; Veluchamy, P.; Doble, M. Novel Chalcones and 1,3,5-Triphenyl-2-Pyrazoline Derivatives as Antibacterial Agents. *Chem. Biol. Drug Des.* **2010**, *76*, 407–411. [[CrossRef](#)]
143. Li, Y.; Sun, B.; Zhai, J.; Fu, L.; Zhang, S.; Zhang, J.; Liu, H.; Xie, W.; Deng, H.; Chen, Z.; et al. Synthesis and Antibacterial Activity of Four Natural Chalcones and Their Derivatives. *Tetrahedron Lett.* **2019**, *60*, 151165. [[CrossRef](#)]

144. Abdula, A.; Abdula, A.M. Synthesis, Characterization and Antibacterial Activity of (E)-Chalcone Derivatives. *Eur. J. Chem.* **2013**, *4*, 207–210. [[CrossRef](#)]
145. Sashidhara, K.V.; Rao, K.B.; Kushwaha, P.; Modukuri, R.K.; Singh, P.; Soni, I.; Shukla, P.K.; Chopra, S.; Pasupuleti, M. Novel Chalcone-Thiazole Hybrids as Potent Inhibitors of Drug Resistant Staphylococcus Aureus. *ACS Med. Chem. Lett.* **2015**, *6*, 809–813. [[CrossRef](#)]
146. Venkatesan, P.; Sumathi, S. Piperidine Mediated Synthesis of N-heterocyclic Chalcones and Their Antibacterial Activity. *J. Heterocycl. Chem.* **2009**, *47*, 81–84. [[CrossRef](#)]
147. Dkhar, L.; Banothu, V.; Pinder, E.; Phillips, R.M.; Kaminsky, W.; Kollipara, M.R. Ru, Rh and Ir Metal Complexes of Pyridyl Chalcone Derivatives: Their Potent Antibacterial Activity, Comparable Cytotoxicity Potency and Selectivity to Cisplatin. *Polyhedron* **2020**, *185*, 114606. [[CrossRef](#)]
148. Asiri, A.M.; Khan, S.A. Synthesis and anti-bacterial activities of a bis-chalcone derived from thiophene and its bis-cyclized products. *Molecules* **2011**, *16*, 523–531. [[CrossRef](#)]
149. Tran, T.-D.; Nguyen, T.-T.; Do, T.-H.; Huynh, T.-N.; Tran, C.-D.; Thai, K.-M. Synthesis and antibacterial activity of some heterocyclic chalcone analogues alone and in combination with antibiotics. *Molecules* **2012**, *17*, 6684–6696. [[CrossRef](#)] [[PubMed](#)]
150. Zheng, C.J.; Jiang, S.M.; Chen, Z.H.; Ye, B.J.; Piao, H.R. Synthesis and Anti-Bacterial Activity of Some Heterocyclic Chalcone Derivatives Bearing Thiofuran, Furan, and Quinoline Moieties. *Arch. der Pharm.* **2011**, *344*, 689–695. [[CrossRef](#)]
151. Chu, W.C.; Bai, P.Y.; Yang, Z.Q.; Cui, D.Y.; Hua, Y.G.; Yang, Y.; Yang, Q.Q.; Zhang, E.; Qin, S. Synthesis and Antibacterial Evaluation of Novel Cationic Chalcone Derivatives Possessing Broad Spectrum Antibacterial Activity. *Eur. J. Med. Chem.* **2018**, *143*, 905–921. [[CrossRef](#)] [[PubMed](#)]
152. 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. *Bioorg. Med. Chem. Lett.* **2018**, *28*, 1278–1282. [[CrossRef](#)] [[PubMed](#)]
153. Chen, Z.H.; Zheng, C.J.; Sun, L.P.; Piao, H.R. Synthesis of New Chalcone Derivatives Containing a Rhodanine-3-Acetic Acid Moiety with Potential Anti-Bacterial Activity. *Eur. J. Med. Chem.* **2010**, *45*, 5739–5743. [[CrossRef](#)] [[PubMed](#)]
154. Santosh, R.; Selvam, M.K.; Kanekar, S.U.; Nagaraja, G.K. Synthesis, Characterization, Antibacterial and Antioxidant Studies of Some Heterocyclic Compounds from Triazole-Linked Chalcone Derivatives. *ChemistrySelect* **2018**, *3*, 6338–6343. [[CrossRef](#)]
155. Rani, A.; Singh, A.; Kaur, J.; Singh, G.; Bhatti, R.; Gumede, N.; Kisten, P.; Singh, P.; Kumar, V. 1H-1, 2, 3-triazole grafted tacrine-chalcone conjugates as potential cholinesterase inhibitors with the evaluation of their behavioral tests and oxidative stress in mice brain cells. *Bioorg. Chem.* **2021**, *114*, 105053. [[CrossRef](#)] [[PubMed](#)]
156. Mathew, B.; Haridas, A.; Uçar, G.; Baysal, I.; Joy, M.; Mathew, G.E.; Lakshmanan, B.; Jayaprakash, V. Synthesis, Biochemistry, and Computational Studies of Brominated Thieryl Chalcones: A New Class of Reversible MAO-B Inhibitors. *ChemMedChem* **2016**, *11*, 1161–1171. [[CrossRef](#)] [[PubMed](#)]
157. Rampa, A.; Montanari, S.; Pruccoli, L.; Bartolini, M.; Falchi, F.; Feoli, A.; Cavalli, A.; Belluti, F.; Gobbi, S.; Tarozzi, A.; et al. Chalcone-Based Carbamates for Alzheimer's Disease Treatment. *Futur. Med. Chem.* **2017**, *9*, 749–764. [[CrossRef](#)]
158. Thapa, P.; Upadhyay, S.P.; Suo, W.Z.; Singh, V.; Gurung, P.; Lee, E.S.; Sharma, R.; Sharma, M. Chalcone and Its Analogs: Therapeutic and Diagnostic Applications in Alzheimer's Disease. *Bioorg. Chem.* **2021**, *108*, 104681. [[CrossRef](#)]
159. Zhang, X.; Rakesh, K.P.; Bukhari, S.N.A.; Balakrishna, M.; Manukumar, H.M.; Qin, H.L. Multi-Targetable Chalcone Analogs to Treat Deadly Alzheimer's Disease: Current View and Upcoming Advice. *Bioorg. Chem.* **2018**, *80*, 86–93. [[CrossRef](#)]
160. Cong, L.; Dong, X.; Wang, Y.; Deng, Y.; Li, B.; Dai, R. On the Role of Synthesized Hydroxylated Chalcones as Dual Functional Amyloid- β Aggregation and Ferroptosis Inhibitors for Potential Treatment of Alzheimer's Disease. *Eur. J. Med. Chem.* **2019**, *166*, 11–21. [[CrossRef](#)]
161. Wang, X.Q.; Zhou, L.Y.; Tan, R.X.; Liang, G.P.; Fang, S.X.; Li, W.; Xie, M.; Wen, Y.H.; Wu, J.Q.; Chen, Y.P. Design, Synthesis, and Evaluation of Chalcone Derivatives as Multifunctional Agents against Alzheimer's Disease. *Chem. Biodivers.* **2021**, *18*, e2100341. [[CrossRef](#)]
162. Bai, P.; Wang, K.; Zhang, P.; Shi, J.; Cheng, X.; Zhang, Q.; Zheng, C.; Cheng, Y.; Yang, J.; Lu, X.; et al. Development of Chalcone-O-Alkylamine Derivatives as Multifunctional Agents against Alzheimer's Disease. *Eur. J. Med. Chem.* **2019**, *183*, 111737. [[CrossRef](#)]
163. Lee, D.S.; Jeong, G.S. Butein Provides Neuroprotective and Anti-neuroinflammatory Effects through Nrf2/ARE-dependent Haem Oxygenase 1 Expression by Activating the PI3K/Akt Pathway. *Br. J. Pharmacol.* **2016**, *173*, 2894. [[CrossRef](#)]
164. Bhullar, K.S.; Rupasinghe, H.P.V. Polyphenols: Multipotent Therapeutic Agents in Neurodegenerative Diseases. *Oxid. Med. Cell. Longev.* **2013**, *2013*, 891748. [[CrossRef](#)] [[PubMed](#)]
165. Singh, M.; Kaur, M.; Silakari, O. Flavones: An Important Scaffold for Medicinal Chemistry. *Eur. J. Med. Chem.* **2014**, *84*, 206–239. [[CrossRef](#)] [[PubMed](#)]
166. Quattrocchio, F.; Baudry, A.; Lepiniec, L.; Grotewold, E. The regulation of flavonoid biosynthesis. In *The Science of Flavonoids*; Springer: New York, NY, USA, 2006; pp. 97–122. [[CrossRef](#)]
167. Nijveldt, R.J.; Van Nood, E.L.S.; Van Hoorn, D.E.; Boelens, P.G.; Van Norren, K.; Van Leeuwen, P.A. Flavonoids: A review of probable mechanisms of action and potential applications. *Am. J. Clin. Nutr.* **2001**, *74*, 418–425. [[CrossRef](#)] [[PubMed](#)]

168. Thomas, N.; Zachariah, S.M.; Ramani, P. 4-Aryl-4H-Chromene-3-Carbonitrile Derivates: Synthesis and Preliminary Anti-Breast Cancer Studies. *J. Heterocycl. Chem.* **2016**, *53*, 1778–1782. [[CrossRef](#)]
169. Doroghazi, J.R.; Albright, J.C.; Goering, A.W.; Ju, K.S.; Haines, R.R.; Tchalukov, K.A.; Labeda, D.P.; Kelleher, N.L.; Metcalf, W.W. A Roadmap for Natural Product Discovery Based on Large-Scale Genomics and Metabolomics. *Nat. Chem. Biol.* **2014**, *10*, 963–968. [[CrossRef](#)]
170. Kim, S.H.; Lee, E.; Baek, K.H.; Kwon, H.B.; Woo, H.; Lee, E.S.; Kwon, Y.; Na, Y. Chalcones, Inhibitors for Topoisomerase I and Cathepsin B and L, as Potential Anti-Cancer Agents. *Bioorg. Med. Chem. Lett.* **2013**, *23*, 3320–3324. [[CrossRef](#)]
171. Wang, G.; Liu, W.; Gong, Z.; Huang, Y.; Li, Y.; Peng, Z. Design, Synthesis, Biological Evaluation and Molecular Docking Studies of New Chalcone Derivatives Containing Diaryl Ether Moiety as Potential Anticancer Agents and Tubulin Polymerization Inhibitors. *Bioorg. Chem.* **2020**, *95*, 103565. [[CrossRef](#)]
172. Wang, G.; Liu, W.; Gong, Z.; Huang, Y.; Li, Y.; Peng, Z. Synthesis, Biological Evaluation, and Molecular Modelling of New Naphthalene-Chalcone Derivatives as Potential Anticancer Agents on MCF-7 Breast Cancer Cells by Targeting Tubulin Colchicine Binding Site. *J. Enzym. Inhib. Med. Chem.* **2020**, *35*, 139–144. [[CrossRef](#)] [[PubMed](#)]
173. Mokale, S.N.; Dube, P.N.; Bhavale, S.A.; Sayed, I.; Begum, A.; Nevase, M.C.; Shelke, V.R.; Mujahed, A. Synthesis, in-Vitro Screening, and Docking Analysis of Novel Pyrrolidine and Piperidine-Substituted Ethoxy Chalcone as Anticancer Agents. *Med. Chem. Res.* **2015**, *24*, 1842–1856. [[CrossRef](#)]
174. Khanapure, S.; Jagadale, M.; Bansode, P.; Choudhari, P.; Rashinkar, G. Anticancer Activity of Ruthenoceny Chalcones and Their Molecular Docking Studies. *J. Mol. Struct.* **2018**, *1173*, 142–147. [[CrossRef](#)]
175. Zhang, H.; Liu, J.J.; Sun, J.; Yang, X.H.; Zhao, T.T.; Lu, X.; Gong, H.B.; Zhu, H.L. Design, Synthesis and Biological Evaluation of Novel Chalcone Derivatives as Antitubulin Agents. *Bioorg. Med. Chem.* **2012**, *20*, 3212–3218. [[CrossRef](#)] [[PubMed](#)]
176. Reddy, P.B.; Reddy, M.B.M.; Reddy, R.; Chhajed, S.; Gupta, P.P. Molecular Docking, PKPD, and Assessment of Toxicity of Few Chalcone Analogues as EGFR Inhibitor in Search of Anticancer Agents. *Struct. Chem.* **2020**, *31*, 2249–2255. [[CrossRef](#)]
177. Sharma, A.; Chakravarti, B.; Gupt, M.P.; Siddiqui, J.A.; Konwar, R.; Tripathi, R.P. Synthesis and Anti Breast Cancer Activity of Biphenyl Based Chalcones. *Bioorg. Med. Chem.* **2010**, *18*, 4711–4720. [[CrossRef](#)]
178. Lu, C.-F.; Wang, S.-H.; Pang, X.-J.; Zhu, T.; Li, H.-L.; Li, Q.-R.; Li, Q.-Y.; Gu, Y.-F.; Mu, Z.-Y.; Jin, M.-J.; et al. Synthesis and biological evaluation of amino chalcone derivatives as antiproliferative agents. *Molecules* **2020**, *25*, 5530. [[CrossRef](#)] [[PubMed](#)]
179. Kumar, S.K.; Hager, E.; Pettit, C.; Gurulingappa, H.; Davidson, N.E.; Khan, S.R. Design, synthesis, and evaluation of novel boronic-chalcone derivatives as antitumor agents. *J. Med. Chem.* **2003**, *46*, 2813–2815. [[CrossRef](#)] [[PubMed](#)]
180. Ngameni, B.; Cedric, K.; Mbaveng, A.T.; Erdoğan, M.; Simo, I.; Kuete, V.; Daştan, A. Design, Synthesis, Characterization, and Anticancer Activity of a Novel Series of O-Substituted Chalcone Derivatives. *Bioorg. Med. Chem. Lett.* **2021**, *35*, 127827. [[CrossRef](#)]
181. Kumar, D.; Raj, K.K.; Malhotra, S.V.; Rawat, D.S. Synthesis and anticancer activity evaluation of resveratrol–chalcone conjugates. *MedChemComm* **2014**, *5*, 528–535. [[CrossRef](#)]
182. Saxena, H.O.; Faridi, U.; Kumar, J.K.; Luqman, S.; Darokar, M.P.; Shanker, K.; Chanotiya, C.S.; Gupta, M.M.; Negi, A.S. Synthesis of Chalcone Derivatives on Steroidal Framework and Their Anticancer Activities. *Steroids* **2007**, *72*, 892–900. [[CrossRef](#)]
183. Shenvi, S.; Kumar, K.; Hatti, K.S.; Rijesh, K.; Diwakar, L.; Reddy, G.C. Synthesis, Anticancer and Antioxidant Activities of 2,4,5-Trimethoxy Chalcones and Analogues from Asaronaldehyde: Structure–Activity Relationship. *Eur. J. Med. Chem.* **2013**, *62*, 435–442. [[CrossRef](#)]
184. 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. [[CrossRef](#)]
185. Kamal, A.; Reddy, J.S.; Ramaiah, M.J.; Dastagiri, D.; Bharathi, E.V.; Sagar, M.V.P.; Pushpavalli, S.N.C.V.L.; Ray, P.; Pal-Bhadra, M. Design, synthesis and biological evaluation of imidazopyridine/pyrimidine-chalcone derivatives as potential anticancer agents. *MedChemComm* **2010**, *1*, 355–360. [[CrossRef](#)]
186. Farghaly, T.A.; Masaret, G.S.; Muhammad, Z.A.; Harras, M.F. Discovery of Thiazole-Based-Chalcones and 4-Hetarylthiazoles as Potent Anticancer Agents: Synthesis, Docking Study and Anticancer Activity. *Bioorg. Chem.* **2020**, *98*, 103761. [[CrossRef](#)] [[PubMed](#)]
187. Qin, H.L.; Shang, Z.P.; Jantan, I.; Tan, O.U.; Hussain, M.A.; Sher, M.; Bukhari, S.N.A. Molecular Docking Studies and Biological Evaluation of Chalcone Based Pyrazolines as Tyrosinase Inhibitors and Potential Anticancer Agents. *RSC Adv.* **2015**, *5*, 46330–46338. [[CrossRef](#)]
188. Sankappa Rai, U.; Isloor, A.M.; Shetty, P.; Pai, K.S.R.; Fun, H.K. Synthesis and in Vitro Biological Evaluation of New Pyrazole Chalcones and Heterocyclic Diamides as Potential Anticancer Agents. *Arab. J. Chem.* **2015**, *8*, 317–321. [[CrossRef](#)]
189. Madhavi, S.; Sreenivasulu, R.; Yazala, J.P.; Raju, R.R. Synthesis of Chalcone Incorporated Quinazoline Derivatives as Anticancer Agents. *Saudi Pharm. J.* **2017**, *25*, 275–279. [[CrossRef](#)]
190. Mirzaei, S.; Hadizadeh, F.; Eisvand, F.; Mosaffa, F.; Ghodsi, R. Synthesis, Structure-Activity Relationship and Molecular Docking Studies of Novel Quinoline-Chalcone Hybrids as Potential Anticancer Agents and Tubulin Inhibitors. *J. Mol. Struct.* **2020**, *1202*, 127310. [[CrossRef](#)]
191. Kamal, A.; Srinivasulu, V.; Nayak, V.L.; Sathish, M.; Shankaraiah, N.; Bagul, C.; Reddy, N.V.S.; Rangaraj, N.; Nagesh, N. Design and Synthesis of C3-Pyrazole/Chalcone-Linked Beta-Carboline Hybrids: Antitopoisomerase I, DNA-Interactive, and Apoptosis-Inducing Anticancer Agents. *ChemMedChem* **2014**, *9*, 2084–2098. [[CrossRef](#)]

192. Alswah, M.; Bayoumi, A.H.; Elgamal, K.; Elmorsy, A.; Ihmaid, S.; Ahmed, H.E. Design, synthesis and cytotoxic evaluation of novel chalcone derivatives bearing triazolo [4,3-a]-quinoxaline moieties as potent anticancer agents with dual EGFR kinase and tubulin polymerization inhibitory effects. *Molecules* **2017**, *23*, 48. [[CrossRef](#)]
193. Suma, V.R.; Sreenivasulu, R.; Rao, M.V.B.; Subramanyam, M.; Ahsan, M.J.; Alluri, R.; Rao, K.R.M. Design, Synthesis, and Biological Evaluation of Chalcone-Linked Thiazole-Imidazopyridine Derivatives as Anticancer Agents. *Med. Chem. Res.* **2020**, *29*, 1643–1654. [[CrossRef](#)]
194. Ammar, Y.A.; Fayed, E.A.; Bayoumi, A.H.; Ezz, R.R.; Alsaid, M.S.; Soliman, A.M.; Ghorab, M.M. New Chalcones Bearing Isatin Scaffold: Synthesis, Molecular Modeling and Biological Evaluation as Anticancer Agents. *Res. Chem. Intermed.* **2017**, *43*, 6765–6786. [[CrossRef](#)]
195. Bagul, C.; Rao, G.K.; Makani, V.K.K.; Tamboli, J.R.; Pal-Bhadra, M.; Kamal, A. Synthesis and biological evaluation of chalcone-linked pyrazolo [1,5-a] pyrimidines as potential anticancer agents. *MedChemComm* **2017**, *8*, 1810–1816. [[CrossRef](#)] [[PubMed](#)]
196. Nelson, G.; Alam, M.A.; Atkinson, T.; Gurrupu, S.; Sravan Kumar, J.; Bicknese, C.; Johnson, J.L.; Williams, M. Synthesis and Evaluation of P-N,N-Dialkyl Substituted Chalcones as Anti-Cancer Agents. *Med. Chem. Res.* **2013**, *22*, 4610–4614. [[CrossRef](#)]
197. 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. [[CrossRef](#)] [[PubMed](#)]
198. Peerzada, M.N.; Khan, P.; Ahmad, K.; Hassan, M.I.; Azam, A. Synthesis, Characterization and Biological Evaluation of Tertiary Sulfonamide Derivatives of Pyridyl-Indole Based Heteroaryl Chalcone as Potential Carbonic Anhydrase IX Inhibitors and Anticancer Agents. *Eur. J. Med. Chem.* **2018**, *155*, 13–23. [[CrossRef](#)]
199. Mohamed, M.F.; Mohamed, M.S.; Shouman, S.A.; Fathi, M.M.; Abdelhamid, I.A. Synthesis and Biological Evaluation of a Novel Series of Chalcones Incorporated Pyrazole Moiety as Anticancer and Antimicrobial Agents. *Appl. Biochem. Biotechnol.* **2012**, *168*, 1153–1162. [[CrossRef](#)]
200. 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. *Chem. Data Collect.* **2020**, *30*, 100556. [[CrossRef](#)]
201. Chauhan, S.S.; Singh, A.K.; Meena, S.; Lohani, M.; Singh, A.; Arya, R.K.; Cheruvu, S.H.; Sarkar, J.; Gayen, J.R.; Datta, D.; et al. Synthesis of Novel β -Carboline Based Chalcones with High Cytotoxic Activity against Breast Cancer Cells. *Bioorg. Med. Chem. Lett.* **2014**, *24*, 2820–2824. [[CrossRef](#)]
202. Gurrupu, N.; Praveen Kumar, E.; Kolluri, P.K.; Putta, S.; Sivan, S.K.; Subhashini, N.J.P. Synthesis, Biological Evaluation and Molecular Docking Studies of Novel 1,2,3-Triazole Tethered Chalcone Hybrids as Potential Anticancer Agents. *J. Mol. Struct.* **2020**, *1217*, 128356. [[CrossRef](#)]
203. Coşkun, D.; Tekin, S.; Sandal, S.; Coşkun, M.F. Synthesis, Characterization, and Anticancer Activity of New Benzofuran Substituted Chalcones. *J. Chem.* **2016**, *2016*, 7678486. [[CrossRef](#)]
204. Djemoui, A.; Naouri, A.; Ouahrani, M.R.; Djemoui, D.; Lahcene, S.; Lahrech, M.B.; Boukenna, L.; Albuquerque, H.M.T.; Saher, L.; Rocha, D.H.A.; et al. A Step-by-Step Synthesis of Triazole-Benzimidazole-Chalcone Hybrids: Anticancer Activity in Human Cells+. *J. Mol. Struct.* **2020**, *1204*, 127487. [[CrossRef](#)]
205. Dong, J.; Huang, G.; Zhang, Q.; Wang, Z.; Cui, J.; Wu, Y.; Meng, Q.; Li, S. Development of benzochalcone derivatives as selective CYP1B1 inhibitors and anticancer agents. *MedChemComm* **2019**, *10*, 1606–1614. [[CrossRef](#)] [[PubMed](#)]
206. Jayashree, B.S.; Patel, H.H.; Mathew, N.S.; Nayak, Y. Synthesis of Newer Piperidinyl Chalcones and Their Anticancer Activity in Human Cancer Cell Lines. *Res. Chem. Intermed.* **2016**, *42*, 3673–3688. [[CrossRef](#)]
207. Khan, N.S.; Khan, P.; Ansari, M.F.; Srivastava, S.; Hasan, G.M.; Husain, M.; Hassan, M.I. Thienopyrimidine-Chalcone Hybrid Molecules Inhibit Fas-Activated Serine/Threonine Kinase: An Approach to Ameliorate Antiproliferation in Human Breast Cancer Cells. *Mol. Pharm.* **2018**, *15*, 4173–4189. [[CrossRef](#)] [[PubMed](#)]
208. Mphahlele, M.J.; Maluleka, M.M.; Parbhoo, N.; Malindisa, S.T. Synthesis, Evaluation for Cytotoxicity and Molecular Docking Studies of Benzo[c]Furan-Chalcones for Potential to Inhibit Tubulin Polymerization and/or EGFR-Tyrosine Kinase Phosphorylation. *Int. J. Mol. Sci.* **2018**, *19*, 2552. [[CrossRef](#)]
209. Tatsuzaki, J.; Bastow, K.F.; Nakagawa-Goto, K.; Nakamura, S.; Itokawa, H.; Lee, K.H. Dehydrozingerone, Chalcone, and Isoeugenol Analogues as in Vitro Anticancer Agents. *J. Nat. Prod.* **2006**, *69*, 1445–1449. [[CrossRef](#)]
210. Wan, M.; Xu, L.; Hua, L.; Li, A.; Li, S.; Lu, W.; Pang, Y.; Cao, C.; Liu, X.; Jiao, P. Synthesis and Evaluation of Novel Isoxazolyl Chalcones as Potential Anticancer Agents. *Bioorg. Chem.* **2014**, *54*, 38–43. [[CrossRef](#)]
211. Kumar, D.; Maruthi Kumar, N.; Tantak, M.P.; Ogura, M.; Kusaka, E.; Ito, T. Synthesis and Identification of α -Cyano Bis(Indolyl)Chalcones as Novel Anticancer Agents. *Bioorg. Med. Chem. Lett.* **2014**, *24*, 5170–5174. [[CrossRef](#)]
212. Rahimzadeh Oskuei, S.; Mirzaei, S.; Reza Jafari-Nik, M.; Hadizadeh, F.; Eisvand, F.; Mosaffa, F.; Ghodsi, R. Design, Synthesis and Biological Evaluation of Novel Imidazole-Chalcone Derivatives as Potential Anticancer Agents and Tubulin Polymerization Inhibitors. *Bioorg. Chem.* **2021**, *112*, 104904. [[CrossRef](#)]
213. Bandgar, B.P.; Gawande, S.S. Synthesis and Biological Screening of a Combinatorial Library of β -Chlorovinyl Chalcones as Anticancer, Anti-Inflammatory and Antimicrobial Agents. *Bioorg. Med. Chem.* **2010**, *18*, 2060–2065. [[CrossRef](#)]
214. Kamal, A.; Mallareddy, A.; Suresh, P.; Shaik, T.B.; Lakshma Nayak, V.; Kishor, C.; Shetti, R.V.C.R.N.C.; Sankara Rao, N.; Tamboli, J.R.; Ramakrishna, S.; et al. Synthesis of Chalcone-Amidobenzothiazole Conjugates as Antimitotic and Apoptotic Inducing Agents. *Bioorg. Med. Chem.* **2012**, *20*, 3480–3492. [[CrossRef](#)]

215. Zhao, L.; Mao, L.; Hong, G.; Yang, X.; Liu, T. Design, Synthesis and Anticancer Activity of Matrine–1H-1,2,3-Triazole–Chalcone Conjugates. *Bioorg. Med. Chem. Lett.* **2015**, *25*, 2540–2544. [[CrossRef](#)] [[PubMed](#)]
216. Wang, Y.; Hedblom, A.; Koerner, S.K.; Li, M.; Jernigan, F.E.; Wegiel, B.; Sun, L. Novel Synthetic Chalcones Induce Apoptosis in the A549 Non-Small Cell Lung Cancer Cells Harboring a KRAS Mutation. *Bioorg. Med. Chem. Lett.* **2016**, *26*, 5703–5706. [[CrossRef](#)] [[PubMed](#)]
217. Zhu, C.; Wang, R.; Zheng, W.; Chen, D.; Yue, X.; Cao, Y.; Qin, W.; Sun, H.; Wang, Y.; Liu, Z.; et al. Synthesis and Evaluation of Anticancer Activity of BOC26P, an Ortho-Aryl Chalcone Sodium Phosphate as Water-Soluble Prodrugs in Vitro and in Vivo. *Biomed. Pharmacother.* **2017**, *96*, 551–562. [[CrossRef](#)] [[PubMed](#)]
218. Park, S.; Kim, E.H.; Kim, J.; Kim, S.H.; Kim, I. Biological Evaluation of Indolizine–Chalcone Hybrids as New Anticancer Agents. *Eur. J. Med. Chem.* **2018**, *144*, 435–443. [[CrossRef](#)]
219. Jain, U.K.; Bhatia, R.K.; Rao, A.R.; Singh, R.; Saxena, A.K.; Sehar, I. Design and Development of Halogenated Chalcone Derivatives as Potential Anticancer Agents. *Trop. J. Pharm. Res.* **2014**, *13*, 73–80. [[CrossRef](#)]
220. de Vasconcelos, A.; Campos, V.F.; Nedel, F.; Seixas, F.K.; Dellagostin, O.A.; Smith, K.R.; de Pereira, C.M.P.; Stefanello, F.M.; Collares, T.; Barschak, A.G. Cytotoxic and Apoptotic Effects of Chalcone Derivatives of 2-Acetyl Thiophene on Human Colon Adenocarcinoma Cells. *Cell Biochem. Funct.* **2013**, *31*, 289–297. [[CrossRef](#)]
221. Gupta, S.; Maurya, P.; Upadhyay, A.; Kushwaha, P.; Krishna, S.; Siddiqi, M.I.; Sashidhara, K.V.; Banerjee, D. Synthesis and Bio-Evaluation of Indole-Chalcone Based Benzopyrans as Promising Antilipase and Antiproliferative Agents. *Eur. J. Med. Chem.* **2018**, *143*, 1981–1996. [[CrossRef](#)]
222. Wu, J.-Z.; Cheng, C.-C.; Shen, L.-L.; Wang, Z.-K.; Wu, S.-B.; Li, W.-L.; Chen, S.-H.; Zhou, R.-P.; Qiu, P.-H. Synthetic chalcones with potent antioxidant ability on H₂O₂-induced apoptosis in PC12 cells. *Int. J. Mol. Sci.* **2014**, *15*, 18525–18539. [[CrossRef](#)]
223. Singh, A.; Fong, G.; Liu, J.; Wu, Y.-H.; Chang, K.; Park, W.; Kim, J.; Tam, C.; Cheng, L.W.; Land, K.M.; et al. Synthesis and preliminary antimicrobial analysis of isatin–ferrocene and isatin–ferrocenyl chalcone conjugates. *ACS Omega* **2018**, *3*, 5808–5813. [[CrossRef](#)]
224. Kurt, B.Z.; Ozten Kandas, N.; Dag, A.; Sonmez, F.; Kucukislamoglu, M. Synthesis and Biological Evaluation of Novel Coumarin-Chalcone Derivatives Containing Urea Moiety as Potential Anticancer Agents. *Arab. J. Chem.* **2020**, *13*, 1120–1129. [[CrossRef](#)]
225. Xu, F.; Li, W.; Shuai, W.; Yang, L.; Bi, Y.; Ma, C.; Yao, H.; Xu, S.; Zhu, Z.; Xu, J. Design, Synthesis and Biological Evaluation of Pyridine-Chalcone Derivatives as Novel Microtubule-Destabilizing Agents. *Eur. J. Med. Chem.* **2019**, *173*, 1–14. [[CrossRef](#)] [[PubMed](#)]
226. Stanojković, T.; Marković, V.; Matić, I.Z.; Mladenović, M.P.; Petrović, N.; Krivokuća, A.; Petković, M.; Joksović, M.D. Highly Selective Anthraquinone-Chalcone Hybrids as Potential Antileukemia Agents. *Bioorg. Med. Chem. Lett.* **2018**, *28*, 2593–2598. [[CrossRef](#)] [[PubMed](#)]
227. Reddy, M.V.R.; Pallela, V.R.; Cosenza, S.C.; Mallireddigari, M.R.; Patti, R.; Bonagura, M.; Truongcao, M.; Akula, B.; Jatiani, S.S.; Reddy, E.P. Design, Synthesis and Evaluation of (E)- α -Benzylthio Chalcones as Novel Inhibitors of BCR-ABL Kinase. *Bioorg. Med. Chem.* **2010**, *18*, 2317–2326. [[CrossRef](#)]
228. Ferrer, R.; Lobo, G.; Gamboa, N.; Rodrigues, J.; Abramjuk, C.; Jung, K.; Lein, M.; Charris, J.E. Synthesis of [(7-Chloroquinolin-4-Yl)Amino]Chalcones: Potential Antimalarial and Anticancer Agents. *Sci. Pharm.* **2009**, *77*, 725–742. [[CrossRef](#)]
229. Kumar, D.; Kumar, N.M.; Akamatsu, K.; Kusaka, E.; Harada, H.; Ito, T. Synthesis and Biological Evaluation of Indolyl Chalcones as Antitumor Agents. *Bioorg. Med. Chem. Lett.* **2010**, *20*, 3916–3919. [[CrossRef](#)]
230. Szliszka, E.; Czuba, Z.P.; Mazur, B.; Sedek, L.; Paradysz, A.; Krol, W. Chalcones enhance TRAIL-induced apoptosis in prostate cancer cells. *Int. J. Mol. Sci.* **2009**, *11*, 1–13. [[CrossRef](#)] [[PubMed](#)]
231. Kamal, A.; Reddy, V.S.; Santosh, K.; Bharath Kumar, G.; Shaik, A.B.; Mahesh, R.; Chourasiya, S.S.; Sayeed, I.B.; Kotamraju, S. Synthesis of Imidazo[2,1-b][1,3,4]Thiadiazole–Chalcones as Apoptosis Inducing Anticancer Agents. *Medchemcomm* **2014**, *5*, 1718–1723. [[CrossRef](#)]
232. Wu, C.M.; Lin, K.W.; Teng, C.H.; Huang, A.M.; Chen, Y.C.; Yen, M.H.; Wu, W.B.; Pu, Y.S.; Lin, C.N. Chalcone derivatives inhibit human platelet aggregation and inhibit growth in human bladder cancer cells. *Biol. Pharm. Bull.* **2014**, *37*, 1191–1198. [[CrossRef](#)]
233. Gargantilla, M.; López-Fernández, J.; Camarasa, M.J.; Persoons, L.; Daelemans, D.; Priego, E.M.; Pérez-Pérez, M.J. Inhibition of XPO-1 Mediated Nuclear Export through the Michael-Acceptor Character of Chalcones. *Pharmaceuticals* **2021**, *14*, 1131. [[CrossRef](#)]
234. Muchtaridi, M.; Syahidah, H.N.; Subarnas, A.; Yusuf, M.; Bryant, S.D.; Langer, T. Molecular Docking and 3D-Pharmacophore Modeling to Study the Interactions of Chalcone Derivatives with Estrogen Receptor Alpha. *Pharmaceuticals* **2017**, *10*, 81. [[CrossRef](#)]
235. Alam, M.J.; Alam, O.; Perwez, A.; Rizvi, M.A.; Naim, M.J.; Naidu, V.G.M.; Imran, M.; Ghoneim, M.M.; Alshehri, S.; Shakeel, F. Design, Synthesis, Molecular Docking, and Biological Evaluation of Pyrazole Hybrid Chalcone Conjugates as Potential Anticancer Agents and Tubulin Polymerization Inhibitors. *Pharmaceuticals* **2022**, *15*, 280. [[CrossRef](#)] [[PubMed](#)]
236. Chen, J.; Yan, J.; Hu, J.; Pang, Y.; Huang, L.; Li, X. Synthesis, Biological Evaluation and Mechanism Study of Chalcone Analogues as Novel Anti-Cancer Agents. *RSC Adv.* **2015**, *5*, 68128–68135. [[CrossRef](#)]
237. Bandgar, B.P.; Gawande, S.S.; Bodade, R.G.; Totre, J.V.; Khobragade, C.N. Synthesis and Biological Evaluation of Simple Methoxylated Chalcones as Anticancer, Anti-Inflammatory and Antioxidant Agents. *Bioorg. Med. Chem.* **2010**, *18*, 1364–1370. [[CrossRef](#)]

238. Venkatarao, V.; Kumar, L.; Jha, A.; Sridhar, G. Synthesis and Biological Evaluation of Chalcone Fused Quinoline Derivatives as Anticancer Agents. *Chem. Data Collect.* **2019**, *22*, 100236. [[CrossRef](#)]
239. Konidala, S.K.; Kotra, V.; Danduga, R.C.S.R.; Kola, P.K. Coumarin-Chalcone Hybrids Targeting Insulin Receptor: Design, Synthesis, Anti-Diabetic Activity, and Molecular Docking. *Bioorg. Chem.* **2020**, *104*, 104207. [[CrossRef](#)]
240. Adelusi, T.I.; Du, L.; Chowdhury, A.; Xiaoke, G.; Lu, Q.; Yin, X. Signaling Pathways and Proteins Targeted by Antidiabetic Chalcones. *Life Sci.* **2021**, *284*, 118982. [[CrossRef](#)] [[PubMed](#)]
241. Kaushal, R.; Kaur, M. Bio-Medical Potential of Chalcone Derivatives and Their Metal Complexes as Antidiabetic Agents: A Review. *J. Coord. Chem.* **2021**, *74*, 725–742. [[CrossRef](#)]
242. Cai, C.Y.; Rao, L.; Rao, Y.; Guo, J.X.; Xiao, Z.Z.; Cao, J.Y.; Huang, Z.S.; Wang, B. Analogues of Xanthonones—Chalcones and Bis-Chalcones as α -Glucosidase Inhibitors and Anti-Diabetes Candidates. *Eur. J. Med. Chem.* **2017**, *130*, 51–59. [[CrossRef](#)]
243. Shin, J.; Jang, M.G.; Park, J.C.; Koo, Y.D.; Lee, J.Y.; Park, K.S.; Chung, S.S.; Park, K. Antidiabetic Effects of Trihydroxychalcone Derivatives via Activation of AMP-Activated Protein Kinase. *J. Ind. Eng. Chem.* **2018**, *60*, 177–184. [[CrossRef](#)]
244. Shukla, P.; Satyanarayana, M.; Verma, P.C.; Tiwari, J.; Dwivedi, A.P.; Srivastava, R.; Rehuja, N.; Srivastava, S.P.; Gautam, S.; Tamrakar, A.K.; et al. Chalcone-based aryloxypropanolamine as a potential antidiabetic and antidyslipidaemic agent. *Curr. Sci.* **2017**, *112*, 1675–1689. [[CrossRef](#)]
245. Mahapatra, D.K.; Asati, V.; Bharti, S.K. Chalcones and Their Therapeutic Targets for the Management of Diabetes: Structural and Pharmacological Perspectives. *Eur. J. Med. Chem.* **2015**, *92*, 839–865. [[CrossRef](#)] [[PubMed](#)]
246. Shinde, R.S.; Salunke, S.D. Facile synthesis of some triazine based chalcones as potential antioxidant and anti-diabetic agents. *J. Chem. Pharm.* **2015**, *7*, 114–120. [[CrossRef](#)]
247. Hsieh, C.T.; Hsieh, T.J.; El-Shazly, M.; Chuang, D.W.; Tsai, Y.H.; Yen, C.T.; Wu, S.F.; Wu, Y.C.; Chang, F.R. Synthesis of Chalcone Derivatives as Potential Anti-Diabetic Agents. *Bioorg. Med. Chem. Lett.* **2012**, *22*, 3912–3915. [[CrossRef](#)] [[PubMed](#)]
248. Chinthala, Y.; Thakur, S.; Tirunagari, S.; Chinde, S.; Domatti, A.K.; Arigari, N.K.; Srinivas, K.V.N.S.; Alam, S.; Jonnala, K.K.; Khan, F.; et al. Synthesis, Docking and ADMET Studies of Novel Chalcone Triazoles for Anti-Cancer and Anti-Diabetic Activity. *Eur. J. Med. Chem.* **2015**, *93*, 564–573. [[CrossRef](#)] [[PubMed](#)]
249. Tarozzi, A.; Króllicka, E.; Kie, K.; Ła, D. Chalcones as Potential Ligands for the Treatment of Parkinson's Disease. *Pharmaceuticals* **2022**, *15*, 847. [[CrossRef](#)]
250. Hammuda, A.; Shalaby, R.; Rovida, S.; Edmondson, D.E.; Binda, C.; Khalil, A. Design and Synthesis of Novel Chalcones as Potent Selective Monoamine Oxidase-B Inhibitors. *Eur. J. Med. Chem.* **2016**, *114*, 162–169. [[CrossRef](#)]
251. Mathew, B.; Parambi, D.G.T.; Mathew, G.E.; Uddin, M.S.; Inasu, S.T.; Kim, H.; Marathakam, A.; Unnikrishnan, M.K.; Carradori, S. Emerging Therapeutic Potentials of Dual-Acting MAO and AChE Inhibitors in Alzheimer's and Parkinson's Diseases. *Arch. Pharm. Chem. Life Sci.* **2019**, *352*, 1900177. [[CrossRef](#)]
252. Hitge, R.; Smit, S.; Petzer, A.; Petzer, J.P. Evaluation of Nitrocatechol Chalcone and Pyrazoline Derivatives as Inhibitors of Catechol-O-Methyltransferase and Monoamine Oxidase. *Bioorg. Med. Chem. Lett.* **2020**, *30*, 127188. [[CrossRef](#)]
253. Parambi, D.G.T.; Saleem, U.; Shah, M.A.; Anwar, F.; Ahmad, B.; Manzar, A.; Itzaz, A.; Harilal, S.; Uddin, M.S.; Kim, H.; et al. Exploring the Therapeutic Potentials of Highly Selective Oxygenated Chalcone Based MAO-B Inhibitors in a Haloperidol-Induced Murine Model of Parkinson's Disease. *Neurochem. Res.* **2020**, *45*, 2786–2799. [[CrossRef](#)]
254. Sasidharan, R.; Manju, S.L.; Uçar, G.; Baysal, I.; Mathew, B. Identification of Indole-Based Chalcones: Discovery of a Potent, Selective, and Reversible Class of MAO-B Inhibitors. *Arch. Pharm.* **2016**, *349*, 627–637. [[CrossRef](#)]
255. Sasidharan, R.; Baek, S.C.; Sreedharannair Leelabaiamma, M.; Kim, H.; Bijo, M. Imidazole Bearing Chalcones as a New Class of Monoamine Oxidase Inhibitors. *Biomed. Pharmacother.* **2018**, *106*, 8–13. [[CrossRef](#)] [[PubMed](#)]
256. Oh, J.M.; Rangarajan, T.M.; Chaudhary, R.; Singh, R.P.; Singh, M.; Singh, R.P.; Tondo, A.R.; Gambacorta, N.; Nicolotti, O.; Mathew, B.; et al. Novel class of chalcone oxime ethers as potent monoamine oxidase-B and acetylcholinesterase inhibitors. *Molecules* **2020**, *25*, 2356. [[CrossRef](#)] [[PubMed](#)]
257. Padhye, S.; Ahmad, A.; Oswal, N.; Dandawate, P.; Rub, R.A.; Deshpande, J.; Swamy, K.V.; Sarkar, F.H. Fluorinated 2'-Hydroxychalcones as Garcinol Analogs with Enhanced Antioxidant and Anticancer Activities. *Bioorg. Med. Chem. Lett.* **2010**, *20*, 5818–5821. [[CrossRef](#)]
258. Kim, S.Y.; Lee, I.S.; Moon, A. 2-Hydroxychalcone and Xanthohumol Inhibit Invasion of Triple Negative Breast Cancer Cells. *Chem. Interact.* **2013**, *203*, 565–572. [[CrossRef](#)] [[PubMed](#)]
259. Gul, H.I.; Yamali, C.; Gunesacar, G.; Sakagami, H.; Okudaira, N.; Uesawa, Y.; Kagaya, H. Cytotoxicity, apoptosis, and QSAR studies of phenothiazine derived methoxylated chalcones as anticancer drug candidates. *Med. Chem. Res.* **2018**, *27*, 2366–2378. [[CrossRef](#)]
260. Prabhakar, V.; Balasubramanian, R.; Sathe, P.; Krishna, C.M.; Juvekar, A. In Vitro Anticancer Activity of Monosubstituted Chalcone Derivatives. *Int. J. Tumor Ther.* **2014**, *3*, 1–9. [[CrossRef](#)]
261. Schmitt, F.; Draut, H.; Biersack, B.; Schobert, R. Halogenated naphthochalcones and structurally related naphthopyrazolines with antitumor activity. *Bioorg. Med. Chem. Lett.* **2016**, *26*, 5168–5171. [[CrossRef](#)]
262. Mai, C.W.; Yaeghoobi, M.; Abd-Rahman, N.; Kang, Y.B.; Pichika, M.R. Chalcones with Electron-Withdrawing and Electron-Donating Substituents: Anticancer Activity against TRAIL Resistant Cancer Cells, Structure–Activity Relationship Analysis and Regulation of Apoptotic Proteins. *Eur. J. Med. Chem.* **2014**, *77*, 378–387. [[CrossRef](#)]

-
263. Echeverria, C.; Santibañez, J.F.; Donoso-Taouda, O.; Escobar, C.A.; Ramirez-Tagle, R. Structural Antitumoral Activity Relationships of Synthetic Chalcones. *Int. J. Mol. Sci.* **2009**, *10*, 221–231. [[CrossRef](#)]
 264. Zhuang, C.; Zhang, W.; Sheng, C.; Zhang, W.; Xing, C.; Miao, Z. Chalcone: A Privileged Structure in Medicinal Chemistry. *Chem. Rev.* **2017**, *117*, 7762–7810. [[CrossRef](#)]
 265. Rammohan, A.; Reddy, J.S.; Sravya, G.; Rao, C.N.; Zyryanov, G.V. Chalcone Synthesis, Properties and Medicinal Applications: A Review. *Environ. Chem. Lett.* **2020**, *18*, 433–458. [[CrossRef](#)]