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Green methods for the synthesis of chalcones: An overview with appraisal to sustainable development and bioactive compounds

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Abstract: In recent years, there has been a growing interest in developing green and sustainable synthetic strategies for chalcones, aiming to minimize waste, reduce the use of hazardous chemicals, and enhance the overall efficiency of the reactions. This review provides an overview of various green synthesis approaches for chalcones and their derivatives, emphasizing environmentally friendly techniques such as solvent-free reactions, microwave-assisted synthesis, ultrasound-assisted synthesis, and enzyme-catalytic methods. Additionally, the biological activities of chalcones synthesized via green methods are explored, underscoring their potential in drug development and therapeutic applications.

Keywords: Chalcones; green synthesis; biologically active compounds.

1. Introduction

Chalcones, characterized by their α, β-unsaturated ketone structure (Fig.1), have received significant attention in medicinal chemistry due to their diverse pharmacological properties. Chalcones exhibit potent antioxidant activity [1-6], crucial in combating oxidative stress-related diseases such as cancer, cardiovascular disorders, and neurodegenerative diseases. Their ability to scavenge free radicals and inhibit oxidative damage makes them promising candidates for therapeutic intervention. Many chalcones possess anti-inflammatory properties[7-11], which can help alleviate inflammation associated with various conditions like arthritis, asthma, and inflammatory bowel diseases. By modulating inflammatory pathways, chalcones offer potential for developing new anti-inflammatory drugs. Chalcones have demonstrated antimicrobial activity [12-16] against a wide range of pathogens, including bacteria, fungi, and viruses. This antimicrobial efficacy makes them valuable for developing novel antibiotics, antifungal agents, and antiviral drugs, especially in the face of growing antimicrobial resistance.

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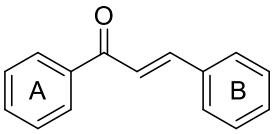


Figure 1. General structure of chalcone

Chalcones exhibit promising anticancer [17-21] properties by interfering with multiple cellular pathways in cancer development and progression. They can induce apoptosis (programmed cell death), inhibit cell proliferation, and suppress tumor growth by targeting various molecular targets implicated in carcinogenesis. Additionally, some chalcone derivatives have shown selectivity towards cancer cells while sparing normal cells, highlighting their potential as cancer therapeutics with reduced side effects. Certain chalcones possess antidiabetic properties [22-25] by modulating glucose metabolism, improving insulin sensitivity, and protecting pancreatic β-cells from damage. These compounds promise to develop new strategies for managing diabetes and its complications.

Chalcones exhibit neuroprotective effects [26] by attenuating neuronal damage, reducing oxidative stress, and inhibiting neuroinflammation. These properties make them potential candidates for the treatment of neurodegenerative disorders such as Alzheimer's disease and Parkinson's disease. Chalcones can inhibit angiogenesis, the formation of new blood vessels, essential for tumor growth and metastasis. By targeting angiogenic pathways, chalcones hold promise as anti-cancer agents to suppress tumor angiogenesis and metastasis. Chalcones also demonstrate a range of other pharmacological activities, including anti-allergic, antiviral [27-30], analgesic [31-32], and hepatoprotective effects, indicating their versatility and potential for addressing various health conditions. The diverse pharmacological properties of chalcones underscore their importance in medicinal chemistry. Their multifaceted activities make them valuable scaffolds for drug discovery and development, with the potential to yield novel therapeutic agents for a wide range of diseases.

Green chemistry principles advocate for the design, development, and implementation of chemical processes that minimize environmental impact while maximizing efficiency and sustainability. Aqueous medium synthesis aligns well with these principles by utilizing water as a green solvent, which offers numerous advantages over traditional organic solvents. Water is inherently safer than many organic solvents commonly used in chemical synthesis. It is non-toxic, non-flammable, and readily available, reducing the risk of environmental contamination and potential health hazards to workers. Aqueous medium synthesis minimizes the generation of hazardous waste by utilizing water as the primary solvent. Unlike organic solvents that often require extensive purification and disposal procedures, water-based reactions typically produce less waste, contributing to pollution prevention and waste reduction efforts.

Many reactions conducted in aqueous medium can be performed under milder conditions, such as ambient temperature and pressure, leading to energy savings compared to high-temperature reactions often necessitated by organic solvents. Lower energy requirements translate to reduced greenhouse gas emissions and overall energy consumption, aligning with sustainability goals. Aqueous medium synthesis often employs catalytic processes, which enhance reaction efficiency, selectivity, and atom economy. Catalysts facilitate reactions under mild conditions, reducing energy input and minimizing the formation of undesired by-products. Additionally, catalysts can be recovered and reused, further enhancing process sustainability. Water is readily biodegradable, offering environmental advantages over persistent organic solvents that can accumulate in ecosystems and pose long-term environmental risks. Aqueous medium synthesis promotes the development of biodegradable processes that minimize environmental persistence and toxicity.

Some aqueous medium synthesis routes utilize renewable feedstocks derived from biomass or waste streams, contributing to utilizing sustainable resources and reducing reliance on fossil fuels. By integrating renewable feedstocks into chemical processes, aqueous medium synthesis promotes circular economy principles and resource efficiency. Green chemistry emphasizes the importance of

maximizing atom economy and minimizing waste generation. Aqueous medium synthesis often enables high atom economy by facilitating selective reactions that minimize the formation of by-products. Selective transformations reduce the need for purification steps and increase the overall efficiency of the synthesis process. Aqueous medium synthesis embodies key principles of green chemistry by prioritizing safety, efficiency, resource conservation, and environmental sustainability. By utilizing water as a green solvent and implementing innovative synthetic strategies, aqueous medium synthesis contributes to the advancement of sustainable chemical practices and the development of greener, more environmentally friendly processes. Top of Form.

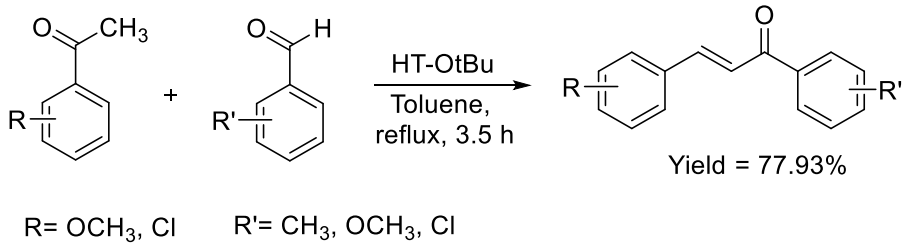
2. Conventional Methods of Chalcone Synthesis

Traditional methods of chalcone synthesis have been foundational in organic chemistry and have paved the way for developing more modern and efficient approaches. Some traditional methods are illustrated below.

2.1. Claisen-Schmidt Condensation

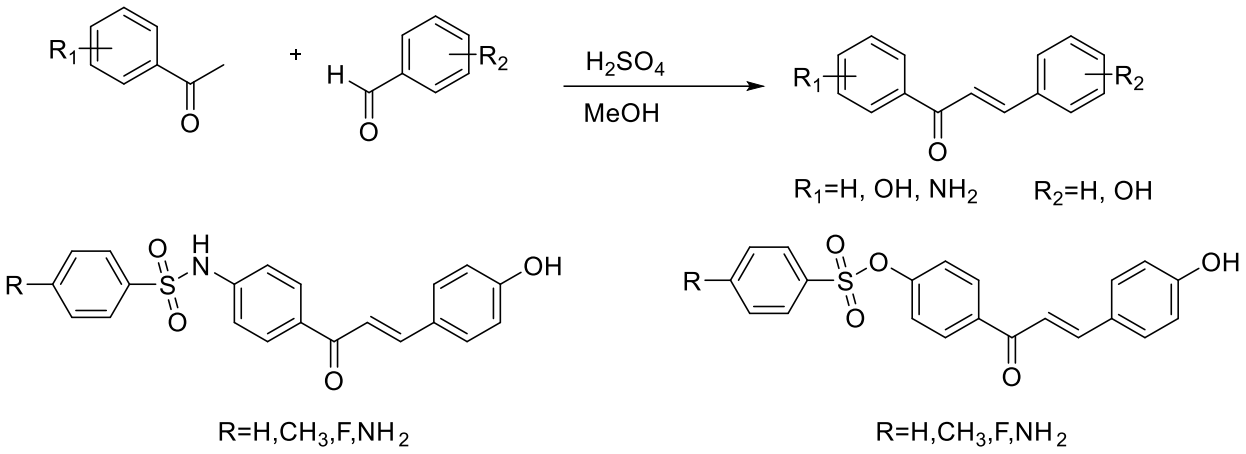
This classic method involves the condensation of an aromatic aldehyde with a ketone or another aldehyde containing an α-hydrogen atom in the presence of a base. The reaction proceeds via the formation of an enolate ion from the α-hydrogen of the ketone/aldehyde, followed by a nucleophilic attack on the carbonyl carbon of the aromatic aldehyde. The resulting β-hydroxy ketone undergoes dehydration to yield the chalcone product.

Kantam et al.[33] To synthesize substituted chalcones in a straightforward work-up, a heterogeneous solid base catalyst Mg−Al-OtBuhydrotalcite (HT-OtBu) was devised for CSC between arylaldehydes and ketones. A comparative analysis was conducted using the hydrotalcite catalysts Mg-Al-F, Mg-Al-NO_3, and Mg-Al-CO_3, demonstrating that HT-OtBu is the most active catalyst in CSC, among other catalysts. Using HT-OtBu as a catalyst, the CSC of benzaldehyde and acetophenone in toluene produced a high yield of chalcone (98%) in 3.5 hours. The reaction produces large yields quickly (Scheme 1)



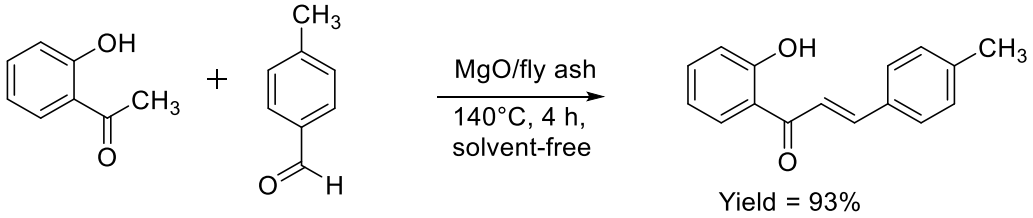
Scheme 1. CSC reactions catalyzed by the HT-OtBu catalyst

Eun-jin et al and co-workers.[34] The synthesis of substituted chalcones was carried out using a catalytic amount of H_2SO_4 in methanol. The method was extended to synthesize some sulfonamide–N–chalcones and sulfonate-O-chalcones. Further, their biological activities were studied. (Scheme 2)



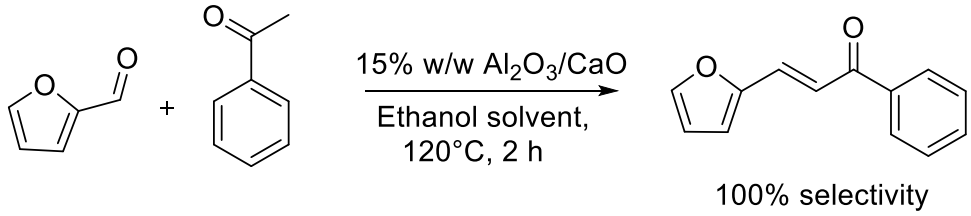
Scheme 2. Synthesis of substituted chalcones using H_2SO_4

Jain et al. [35] synthesized chalcones by using chemically activated fly ash with 50 wt % NaOH as a catalyst for a solventless liquid phase reaction of 4-methylbenzaldehyde with 1-(2-hydroxyphenyl)ethan-1-one. The reaction was conducted using fly ash-supported solid base MgO, yielding a 93 % yield of (E)-1-(2-hydroxyphenyl)-3-(p-tolyl)prop-2-en-1-one (Chalcone) and an 86 % conversion of 4-methylbenzaldehyde (Scheme 3).



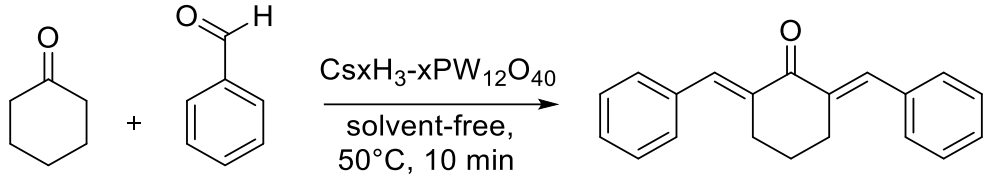
Scheme 3. Condensation of 4-methylbenzaldehyde with 1-(2-hydroxyphenyl)ethan-1-one by using chemically activated fly ash

Yadav and Yadav [36] using the sol-gel method, a 5–15% w/w Al_2O_3/CaO catalyst was produced, and it was thoroughly described. The most effective solid super base catalyst, 15% w/w Al_2O_3/CaO in ethanol solvent at 120°C, was used for the liquid phase CSC of furfuraldehyde with acetophenone. This resulted in 100% selectivity of 3-(furan-2-yl)-1-phenylprop-2-en-1-one and 98.5 % conversion of furfural for two hours. The activity of different prepared catalysts with different Mg:Al ratios, such as 15% w/w Al_2O_3 supported on MgO, CaO, and SrO, calcined hydrotalcite, and hydrated hydrotalcite, was investigated. In two hours, Al_2O_3/CaO produced 98.5 % of the maximum furfural conversion, while $Ca(OH)_2$ produced 88.5 %. Extremely little furfural was converted by other catalysts (Scheme 4).



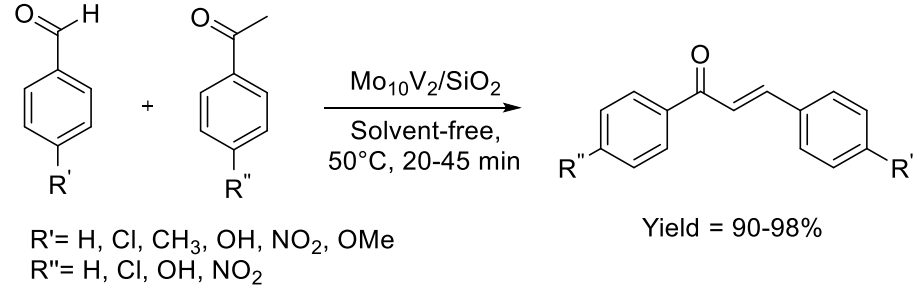
Scheme 4. Cross condensation of 2-furfural with acetophenone over Al_2O_3/CaO

The agrochemical, fragrance, and pharmaceutical industries employ 2,6-dibenzylidenecycloalkanones as an intermediate. It is produced by CSC, which uses an acid or base catalyst to combine cycloalkanones with aldehydes. The synthesis of 2,6-dibenzylidenecycloalkanones [37] has been accomplished by a number of described techniques, including heterogeneous catalysis, metal salt catalysis, microwave assistance, and ionic liquid catalysis. Previous study by Rafiee and Rahimi used heterogeneous solid acid catalyst $CsxH_3$-$xPW_{12}O_{40}$ as a highly active super acid catalyst in CSC of benzaldehyde with cyclohexanone for chalcone at 50 °C for 10 min under solventless conditions (Scheme 5).



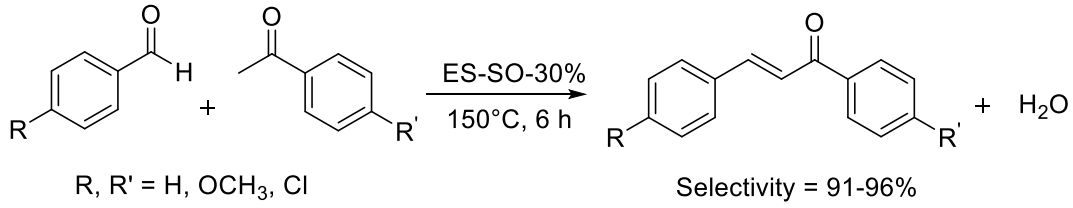
Scheme 5. CSC of benzaldehyde with cyclohexanone using $CsxH_3$-$xPW_{12}O_{40}$ acid catalyst

Rafiee et al.[38] studied the effect of $H_5PMo_{10}V_2O_{40}$ supported on SiO_2 as a solid acid-supported catalyst in a solvent-free, clean acid-based condensation of aldehydes with various ketones at 50°C. The results showed excellent product yields with no byproducts (Scheme 6).



Scheme 6. $H_5PMo_{10}V_2O_{40}$ supported on SiO_2 as a solid acid catalyst for Claisen-Schmidt condensation

Shylesh et al.[39] In the condensation of benzaldehyde with acetophenone, the catalytic activity of MCM-41, which is functionalized with sulfonic acid and ethane-bridged mesoporous organosilica, was examined. The greater surface area and bigger pore channels of mesoporous organosilica provide easy reactant accessibility and thermal stability. By functionalizing mesoporous materials with sulfonic acids, solid acid catalysts with varying acidic strengths can be produced. After six hours of reaction at 150°C, 72% of the acetophenone was converted and 95% of the chalcone was selectively produced (Scheme 7).

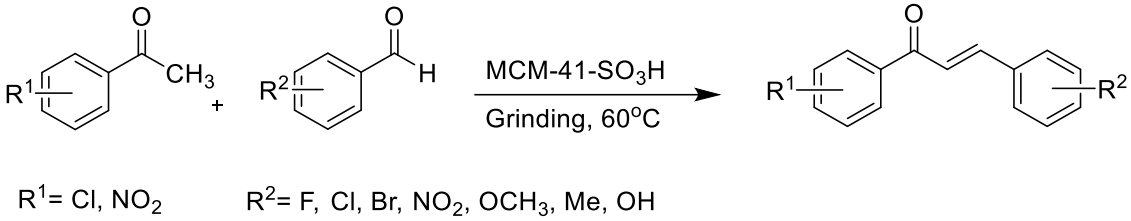


Scheme 7. Claisen-Schmidt condensation reaction using solid acid catalyst ES-SO-30%

2.2. Aldol Condensation

The aldol condensation involves the condensation of two molecules of an aldehyde or a ketone in the presence of a base to form aβ-hydroxy aldehyde and β-hydroxy ketone, which subsequently undergoes dehydration to yield the chalcone product. This method can also be extended to the crossed aldol condensation between different aldehydes/ketones to produce chalcones.

E. Neyestani-Naeeni and M.R. Naimi-Jamal.[40] studied the applicability of nanoporous MCM-41-SO3H catalyst in organic reactions. In continuation of this, they studied the usefulness of solvent-free grinding in organic reactions. They reported MCM-41-SO_3H as a heterogeneous catalyst for the synthesis of chalcones and dibenzylidenealkanones via the aldol condensation reaction by grinding in a solvent-free and efficient method without the formation of any by-products (Scheme 8).

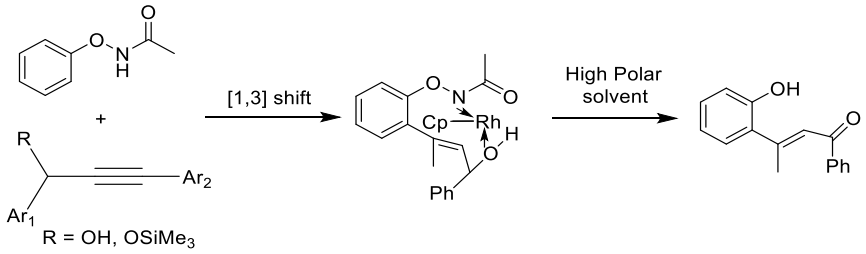


Scheme 8. The aldol condensation reaction catalyzed by MCM-41-SO_3H

When catalyst used is Al-MCM-41 and catalyst loading is 10 mg time required for the reaction to complete is 90 min the yield of the product obtained was 25% Similarly when catalyst used is MCM-41-SO_3H and catalyst loading is 5mg time required for the reaction to complete is 90 min the yield of the product obtained was 70% Maximum yield is obtained when catalyst used is MCM-41-SO_3H and catalyst loading is 10mg time required for this reaction for completion is only 15 min with 98% yield.

2.3. Meyer-Schuster Rearrangement

Meyer–Schuster involves the synthesis of chalcones from reactants such as propargyl alcohol. This rearrangement is employed by using bases such as trimethylamine, KOH, and Rh(III) catalyst, which results in the synthesis of chalcone with a yield of 81-84% [41].



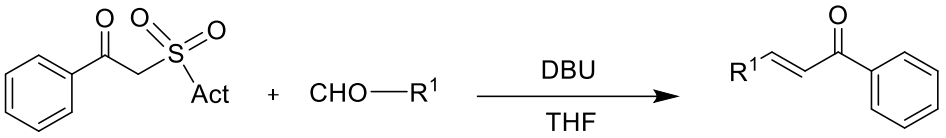
Scheme 9. The aldol condensation reaction catalyzed by Rh(III) catalyst

2.4. Chalcone Synthesis via Coupling Reaction

Chalcones' coupling reaction results in a C-C and C-heteroatom covalent bond via oxidative addition-reductive elimination, which is tabulated below (Table 1).

2.5. Synthesis via Julia-Kocienski Olefination

The modified Julia reaction, also known as Julia-kocienski olefination, involves directly coupling heteroaryl sulfones with carbonyl compounds in a single-step protocol [48-49]. Atulkumar et al. [50] synthesized chalcones via Julia-kocienski olefination by taking benzaldehyde and reacting it with different coupling reagents. Several bases were used, such as DBU, LiHMDS, t-BuOK, and DABCO, to optimize the reaction conditions. DBU was the most efficient base among all the bases used (Scheme 10).



R1= Ar, Ar-OMe, Ar-F, Naphthelene, Ar-Cl, Ar-NHAc, Ar-OAc, Ar-Me

Scheme 10. DBU mediated synthesis of E-enones by coupling of BT-sulfones and benzaldehyde derivatives in THF

2.6. Other Methods for Chalcone synthesis

In addition to the classical methods mentioned, chalcones can be synthesized through various other traditional approaches, such as the Claisen rearrangement, the Knoevenagel condensation, and the Reformatsky reaction. These methods offer versatility in chalcone synthesis and have been extensively utilized in organic synthesis.

While traditional methods of chalcone synthesis have been widely employed and are well-established, they often suffer from limitations such as poor atom economy, harsh reaction conditions, and limited substrate scope. Modern synthetic approaches, including those utilizing aqueous medium, enzymatic catalysis, and green chemistry principles, have emerged to address these challenges and offer more sustainable and efficient alternatives for chalcone synthesis. Organic solvent-based synthesis methods come with several challenges, including environmental, health, and economic concerns.

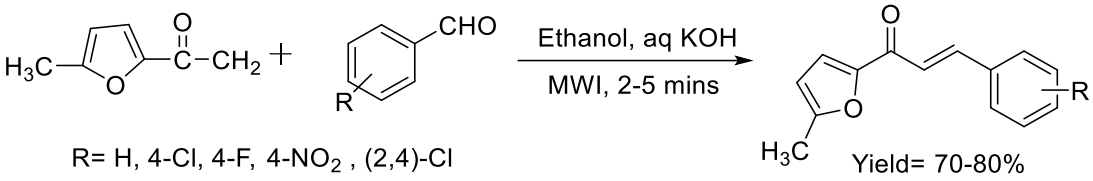
Table1. Various coupling reactions for chalcone synthesis

Name of reaction	Reactants	Catalyst	Yield (%)	Reference
Suzuki coupling	phenylboronic acid and *N*-acylsaccharins	$Pd(PPh_3)_2Cl_2$	87	[42]
	N-Vinylpyridinium and -trialkylammonium tetrafluoroborate salts	$Pd_2(dba)_3$	88	[43]
Heck coupling	Allylic alcohol	$O_2/Pd(OAc)_2)$/ Dmphen	97	[44]
Still coupling	benzoyl chloride and alkenylstannanes	$Pd_2(dba)_3/PPh_3$	91	[45]
Decarboxylative cross-coupling	cinnamic acid and benzoylformic acid	$FeCl_2$/ $K_2S_2O_8$	62-83	[46]
Julia type olefination /Cu-oxidativecoupling	phosphorous ylides and sulfones	$CuCl_2/Ph_3P=S$	45-72	[47]

3. Methodologies for Chalcone Synthesis through a Green Approach

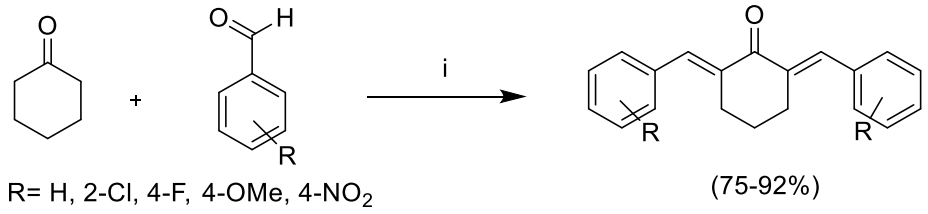
3.1. Microwave-Assisted Synthesis

Microwave-assisted organic synthesis (MAOS) is a valuable technique in green chemistry, known for significantly reducing reaction times while enhancing product yields. This method offers an efficient and energy-saving alternative to conventional heating [51]. Microwave irradiation has accelerated chalcone synthesis in aqueous medium. Mohammed Rayees Ahmad et al. [52] reported the synthesis of chalcone derivatives using microwave irradiation. Equimolar amounts of the corresponding aldehydes and 2-acetyl heterocyclic derivatives were combined and dissolved in the least amount of alcohol. Aqueous potassium hydroxide solution was gradually added and combined. A 70–80% yield was achieved after the reaction mixture was microwave-irradiated for two to five minutes at a power of 180 watts. It uses microwave irradiation to get a decent yield in a shorter reaction time (Scheme 11).



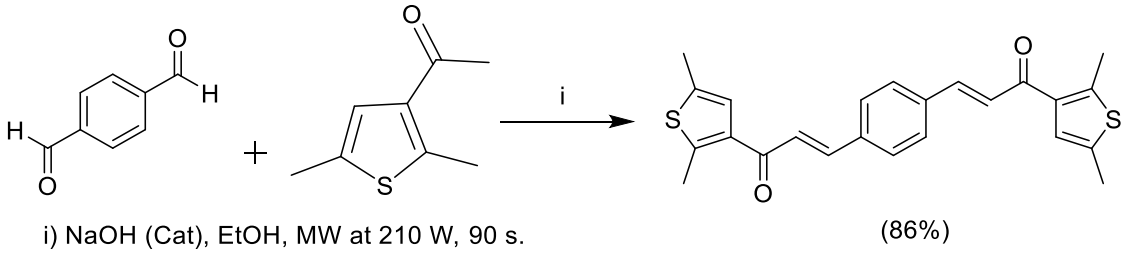
Scheme 11. Microwave assisted synthesis of chalcones from aldehydes and 2-acetyl heterocyclic derivatives

Tupare et al. [53] used a microwave to facilitate acid-catalyzed condensation of aromatic aldehydes with cyclohexanone to synthesize a number of mono and bis-chalcone analogues. Under microwave radiation, the reaction was carried out using catalytic quantities of Eaton's reagent (1 mmol) for 3 mmol of reactants in a brief length of time (2-4 min) and with high yields, without the production of byproducts. The stability of the acid catalyst in these settings is one benefit of using microwave irradiation with this technique (Scheme 12).



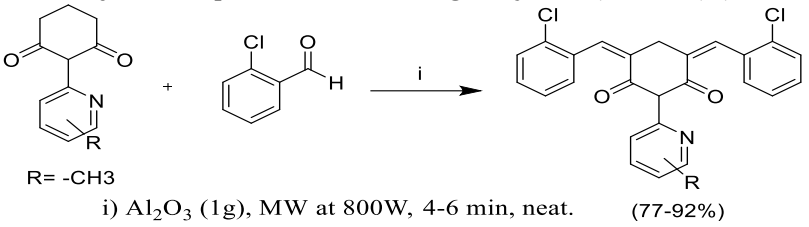
Scheme 12. Synthesis of bis-chalcone by using Eaton's reagent

Asiri et al. [54] used microwave irradiation and basic catalysis to create a new bis-chalcone analogue with a thiophene moiety by aldol condensation of terephthalaldehyde with 3-acetyl-2,5-dimethylthiophene (Scheme 13).



Scheme 13. Synthesis of bis-chalcone with thiophene moiety via aldol condensation

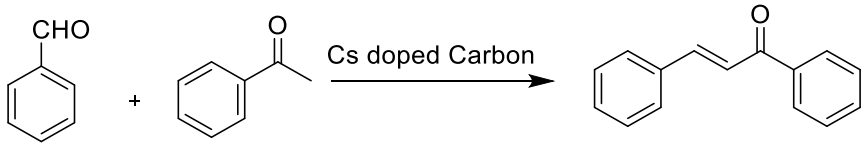
Chaudhari et al. [55] Beginning with N-phenylpyrrolidine-2,5-dione and N-phenylpiperidone-2,5-dione, reported the synthesis of a series of N-phenylpyrrolidine and N-phenylpiperidone-based bis-chalcone analogues. Utilizing neutral Al_2O_3 (a solid support) and microwave heating, they completed the reaction in just a couple of minutes with good yields (77–92%) (Scheme 14).



Scheme 14. Synthesis of bis-chalcone analogues using Al_2O_3 as a solid support under microwave heating

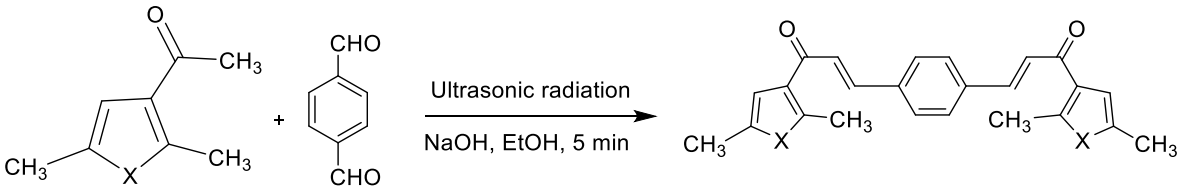
3.2. Ultrasound-Assisted Synthesis

Ultrasound irradiation has emerged as an effective tool for chalcone synthesis in aqueous medium. The use of ultrasound can overcome mass transfer limitations and promote efficient mixing of reactants, facilitating chalcone formation. Calvino,[56] and team synthesized chalcones via Claisen-schmidt under sonochemical irridation(ultrasound). The reaction between benzaldehyde and acetophenone was carried out using two basic activated carbons (Na and Cs-Norit) as a catalyst. The effect of ultrasound activation has been studied. A substantial enhancing effect in the yield was observed when the carbon catalyst was activated under ultrasound. This green method has been generally used in the synthesis of chalcones having antibacterial properties. Cs-doped carbon act's as optimum catalyst giving excellent activity for this kind of condensation (Scheme 15).



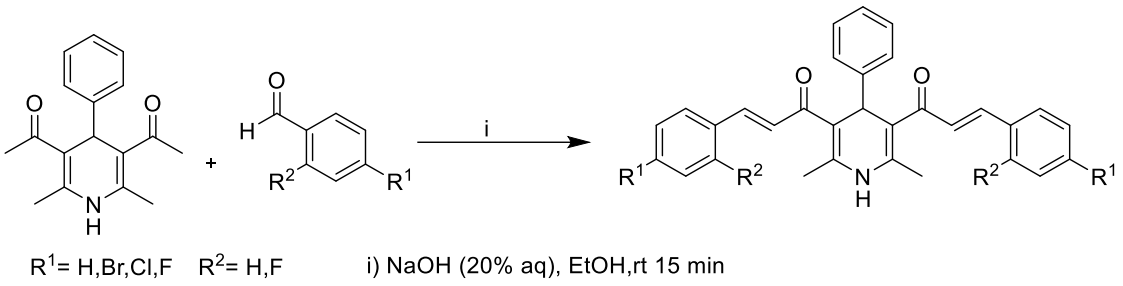
Scheme 15. Claisen-Schmidt condensation between benzaldehyde and acetophenone in the presence of basic activated carbons as a catalyst to yield the chalcone

Khan et al. [57] conducted the green synthesis of bis-chalcones via ultrasonic radiation. They synthesized the chalcones by ultrasonic radiation-aided aldol condensation reaction between 3-acetyl-2,5-dimethylthiophene/3-acetyl-2,5-dimethylfuran and terephthalaldehyde (Scheme 16).



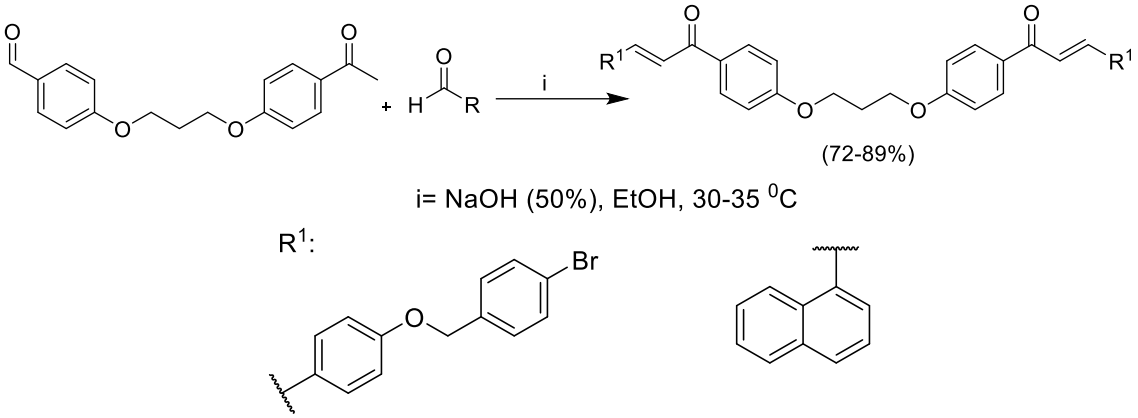
Scheme 16. Synthesis of bischalcones via ultrasonic radiation

Ganesan et al., [58] have effectively produced a novel range of bis-chalcone analogues by employing the 1,4-dihydropyridine derivative along with a variety of aromatic aldehydes. This reaction was conducted in ethanol with an ultrasonic generator in a water bath that was about room temperature, and NaOH 20% as the catalyst. Without raising the temperature, the ultrasonic waves aided the reaction, saving time and boosting yields to 83–87% (Scheme 17).



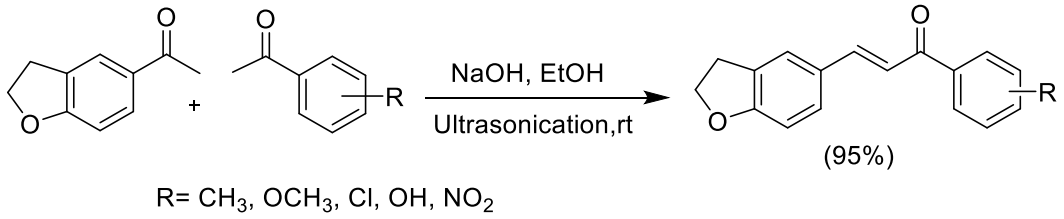
Scheme 17. Synthesis of bis-chalcone analogues by using 1,4-dihydropyridine derivatives

Liargkova et al,[59] synthesized new bis-chalcone ethers, which have the potential to be pleiotropic agents. They achieved this by combining ultra-sound with basic catalysis, which speed up the reaction time and increased the yields. The influence of the ultrasound on the reaction's shortening is unclear, however, as the reaction times for the synthesis of the bis-chalcone analogs were not clear (Scheme 18).



Scheme 18. Synthesis of bis-chalcone ethers using ultrasound with a basic catalyst

Adole et al, [60] reported the first synthesis method for obtaining (E)-3-(2,3-dihydrobenzofuran-5-yl)-1-(aryl)prop-2-en-1-one derivatives under ultrasound irradiation. Simplifying the work-up procedures was their aim. The optimal reaction conditions were found when substituted acetophenones and 2,3-dihydrobenzofuran-5-carbaldehyde reacted in ethanol with sodium hydroxide present and under ultrasound radiation at room temperature (Scheme 19).



Scheme 19. Synthesis of(E)-3-(2,3-dihydrobenzofuran-5-yl)-1-(aryl)prop-2-en-1-one derivatives

3.3. Enzyme-Catalyzed Synthesis

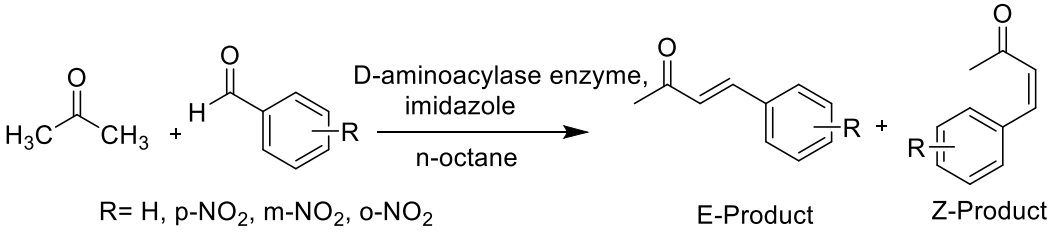
Biocatalytic approaches for chalcone synthesis have also been explored, utilizing pure enzymes, crude enzyme extracts, subcellular fractions, or whole-cell suspensions of eukaryotic organisms[61]. Enzymes, such as lipases and proteases, have been employed as catalysts

for chalcone synthesis in aqueous medium. Enzymes can facilitate the regio- and stereoselective synthesis of chalcones, enabling the production of specific chalcone derivatives.

For the first time, an extremely highly stereoselective enzyme-catalyzed process produced E-chalcone. Given the significance of these chemicals as formula ingredients in the food, pharmaceutical, and cosmetic industries, a "green" approach to their production is desirable.

Only the lipase from the hog pancreas showed promiscuity among the lipases under study, activating the Claisen-Schmidt condensation when imidazole was present as a promoter. Under the same reaction conditions, acylase from Aspergillus melleusalso showed activity in the synthesis of E-chalcone. This acylase also catalyzed the reaction between acetophenone and p-nitrobenzaldehyde, together with the recombinant D-aminoacylase. More research will be done to shed further light on imidazole's mechanism of action. The best conditions for achieving high yields and selectivity in the biocatalytic synthesis of differently substituted chalcones should be determined using the use of molecular modelling, protein engineering, and process engineering methods.[62]

While looking for the appropriate reaction conditions, X. Chen, B.-K. Liu, H. Kang, X.-F. Lin, and J. Mol identified a way to implement a heterogeneous enzyme-catalyzed aldol condensation. In this reaction, acetone (R = CH_3) and aromatic aldehydes were employed. Imidazole and recombinant D-aminoacylase were used to create the arylbut-3-en-2-ones, which had good yields (74%), as well as high E-selectivity (245:1).[63] (Scheme 20).

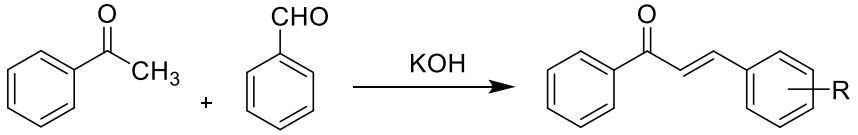


Scheme 20. Enzyme catalyzed synthesis of chalcones

3.4. Solvent-Free Synthesis of Chalcone

This method describes the eco-friendly, solvent-free synthesis of chalcones via condensation between substituted acetophenone and benzaldehyde in the presence of a suitable base catalyst such as NaOH or KOH. The reaction is carried out under grinding to enhance yield and reaction efficiency. In traditional methods, organic solvents such as ethanol, methanol, or acetone are used as reaction media. However, solvent-free synthesis eliminates their use, reducing environmental pollution, health hazards, and cost.

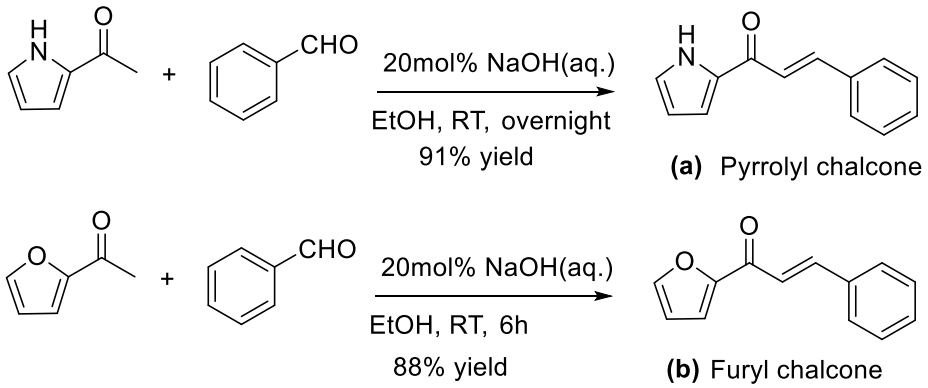
Raghav and Malik [64] reported the solvent free synthesis of chalcones. The synthesis was accomplished by mixing acetophenone, substituted benzaldehyde and KOH in pestle mortar. The mixture first went into solution and thereafter solidified. The solid was washed properly with water to obtain the chalcones(Scheme 21).



Scheme 21. Synthesis of chalcones in solvent-free conditions by using KOH as a catalyst

3.5. Heteroaromatic Hybrid Chalcone Synthesis

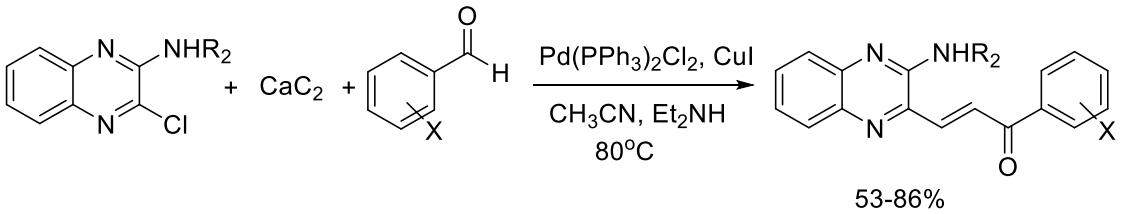
This section presents a range of conventional and green synthetic methods used to prepare hybrid chalcones featuring a heteroaromatic moiety. The heteroaromatic units incorporated into the chalcone framework include both single-ring systems (such as furan, pyrrole, thiazole, thiophene, pyridine, and pyrimidine) and fused-ring systems (including indole, benzimidazole, benzothiazole, benzofuran, pyrazolopyridine, and quinoline) [65].



Scheme 22. Synthesis of Hybrid Chalcone by using NaOH as a catalyst

3.6. One-Pot synthesis via Claisen-Schmidt Condensation

One-pot reactions involve performing multiple sequential synthetic steps within a single reaction vessel, eliminating the need to isolate or purify intermediate compounds. This streamlined approach enables the efficient formation of multiple chemical bonds in a single operation, often leading to the synthesis of structurally complex molecules. Considered a green chemistry strategy, one-pot procedures minimize solvent use and chemical waste, reduce the need for harsh reaction conditions, and enhance the overall efficiency and sustainability of synthetic pathways. The chalcone chemical scaffold may be synthesized by classical one-pot Claisen-Schmidt condensation, where the desired aldehyde and ketone mixed under basic conditions render final chalcones [66].



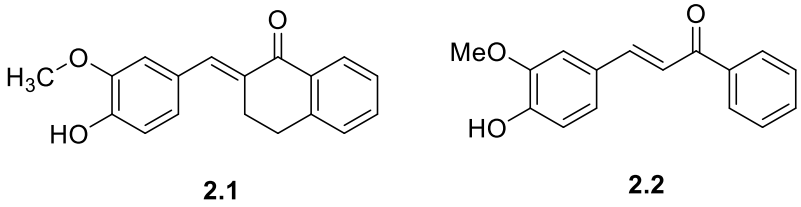
Scheme 23. One-Pot synthesis of chalcones under basic conditions

3.7. Nano Catalyst in Chalcone Synthesis

Nanocatalysts are regarded as next-generation catalysts owing to their exceptional efficiency, sustainability, and ability to significantly accelerate chemical reactions compared to traditional catalysts. They combine the recoverability of heterogeneous catalysts with the high activity of homogeneous systems. Moreover, nanocatalysts are considered environmentally friendly, as they often deliver near-quantitative yields of the desired product with minimal or no side products. Their high catalytic efficiency also means they are required in smaller amounts, further contributing to their green credentials.

Recently, Elamathi et al. reported the use of a heterogeneous AlSBA-15 mesoporous solid acid catalyst under non-conventional, environmentally friendly conditions for the synthesis of vanillin-based chalcones and their derivatives. Among the tested catalysts, AlSBA-15 with an nSi/nAl ratio of 41 (AlSBA-15 (41)) demonstrated superior catalytic efficiency, achieving 98% conversion of 1-tetralone and 100% selectivity for compound **2.1**, with a 91% yield in just 120 minutes (Figure 2). This enhanced performance, compared to AlSBA-15 (129) and AlSBA-15 (210), is likely attributed to the higher density of acidic sites and better accessibility of reactants due to the larger pore size (54 Å) of AlSBA-15 (41). The newly synthesized chalcone derivatives also exhibited notable antioxidant

activity, with some outperforming both the parent chalcone (compound **2.2**) and the standard antioxidant, curcumin [67].



2.1 **2.2**

Figure 2. chalcone derivatives exhibited notable antioxidant activity

4. Applications of Synthesized Chalcones

Chalcones, are a class of bioactive compounds with a broad spectrum of pharmacological activities. They have been investigated for their potential as anticancer, antidiabetic, anti-HIV, antioxidant, antimalarial, antitubercular, antiviral, anti-inflammatory, and antidiuretic agents. Additionally, certain chalcones have been identified as inhibitors of key biological targets such as lipoxygenase, β-secretase (BACE1), acetylcholinesterase (AChE), butyrylcholinesterase (BChE), cyclooxygenase, peroxisome proliferator-activated receptor gamma (PPARγ), and Yersinia enterocolitica tyrosine phosphatase [68]. Some biological properties of chalcones are presented below. (Figure 3)

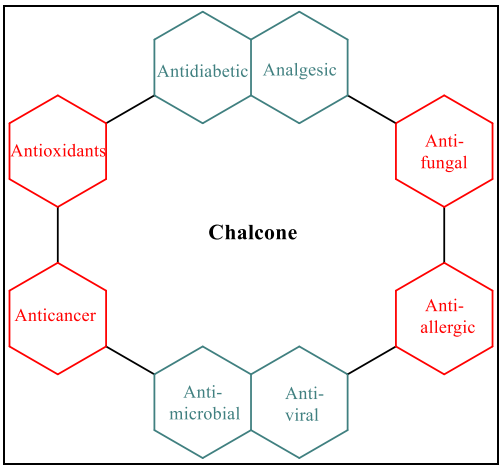


Figure 3. Biological properties of chalcones

4.1. Anticancer Agents

Chalcones exhibit significant anticancer activity by interfering with various cellular pathways in tumor growth and metastasis. Aqueous medium synthesized chalcones have shown promise as lead compounds for developing novel anticancer drugs with improved efficacy and reduced toxicity. Some anticancer drugs used include Dabrafenib (used for skin cancer) and Dasatinib (used for bone marrow) as anticancer treatment (Figure 4).

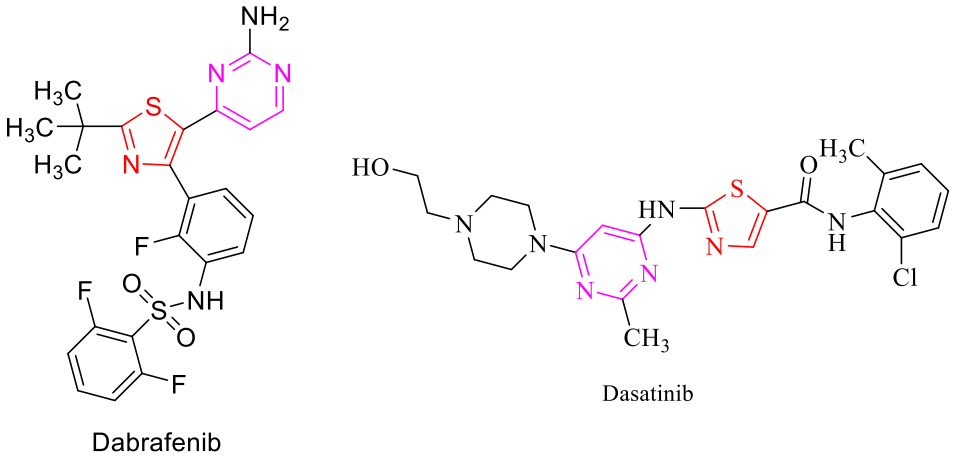


Figure 4. Anticancer drugs containing chalconesmoity

4.2. Antimicrobial Agents

Chalcones possess antimicrobial properties against bacteria, fungi, and viruses, making them potential candidates for developing new antibiotics, antifungal agents, and antiviral drugs. Aqueous medium-synthesized chalcones have been investigated for their antimicrobial activity and potential applications in infectious disease management. Cloxacillin, Dicloxacillin, and Sulfisoxazole are examples of antimicrobial agents (Figure 5).

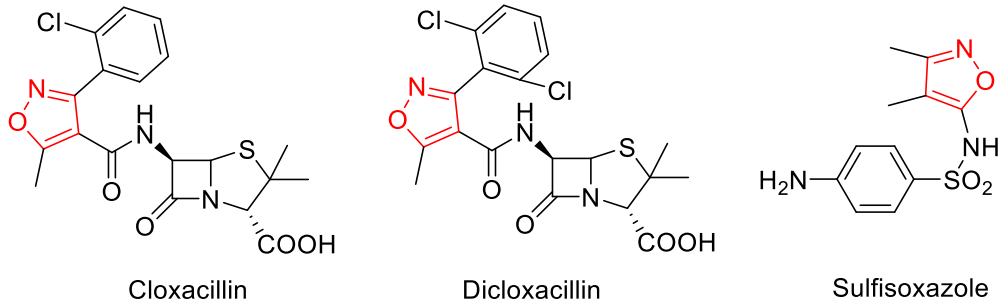
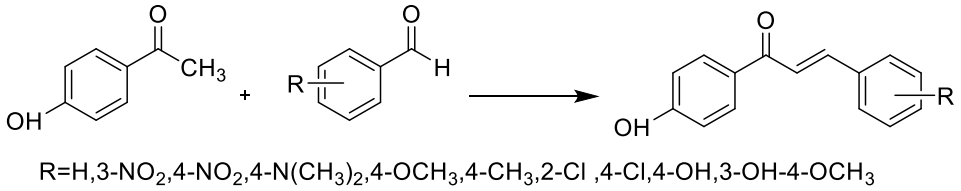


Figure 5. VariousChalcones containing molecules as a antimicrobial agent

4.3. Anti-inflammatory Drugs

Chalcones exhibit anti-inflammatory effects by modulating inflammatory pathways and reducing inflammation associated with various diseases such as arthritis, asthma, and inflammatory bowel diseases.

Visagaperumal et al. [69] produced 4-hydroxychalcones using traditional and microwave-aided synthesis techniques. Three to four drops of concentrated sodium hydroxide were added to equimolar amounts of substituted benzaldehydes and 4-hydroxyacetophenones dissolved in alcohol. After stirring the mixture for two to three hours and refrigerating it overnight, chalcones were produced. All required to accomplish the microwave assisted synthesis was to expose the reaction mixture to 160–320 W radiation for 60–120 seconds. When the anti-inflammatory activity of the chalcones was evaluated, it was discovered that all of them had a negligible anti-inflammatory effect, with edema inhibition ranging from 4.6 to 8.05 %, compared to indomethacin's 74.71 %. (Scheme 24).



Scheme 24. Synthesis of chalcone exhibiting anti-inflammatory property

Five chalcone derivatives were synthesized by Yadav et al. [70] and subjected for anti inflammatory properties. The -F/-Cl groups of the molecule, 4-fluoro/4-chloro chalcone, reportedly gave it more activity than the usual medication, indomethacin. Therefore, electron-withdrawing groups (EWG) on the chalcone moiety improved the anti-inflammatory action of chalcone derivatives. Butein and sappanchalcones are few examples of anti-inflammatory agents (Figure 6).

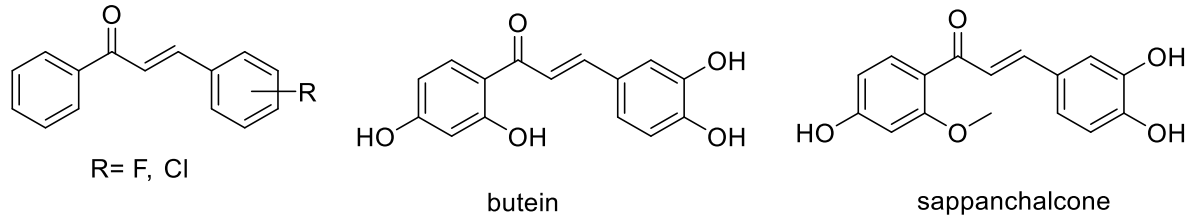


Figure 6. Chalcone exhibiting anti-inflammatory property

4.4. Anti-tuberculosis Drugs

Tuberculosis is disease generally having highest cases occurring in Africa and Asia. The drugs for the treatment of tuberculosis have been available for nearly 50 years but still patients of TB are dying nearly two million people each year.[71-72] Tuberculosis is caused by Mycobacterium tuberculosis, which is facultative intracellular bacillus, this is the world's number one killer among the infectious disease and leading cause of the death among women of reproductive age. [73] Chalcones like compound have been demonstrated the most significant anti-TB activity among all the compounds evaluated Y.-M. Lin et al,[74] studied Anti-tuberculosis activity of chalcones-like compounds. As presented in the table below, compounds 1,2,3 and 4 show inhibition of 96,97,96 and 98% growth respectively, of Mtb H37Rv at a drug concentration of 12.5 mg/mL. (Table 2)

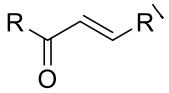


Table 2. Various chalcone-like compounds show Anti-tuberculosis activity

Compound	R	R'	Activity % inhibition at 12.5 mg/mL
1	Pyridin-3-yl-	Phenanthren-9-yl-	96
2	3-Hydroxyphenyl-	Phenanthren-9-yl-	97
3	Furan-2-yl-	3-Phenyl-	96
4	4-Fuorophenyl-	Pyridin-3-yl-	98

Solankee and Tailor [75] described a new series of chalcones with a 1,3,5-triazine group **(**Figure 7). These were synthesized using the traditional Claisen-Schmidt condensation of a substituted ketone with the matching substituted aldehydes. All of the recently created compounds' in vitro antitubercular properties were assessed using a Lowenstein-Jensen medium against the Mycobacterial tuberculosis H37Rv strain compared to the reference medications rifampicin and isoniazid.

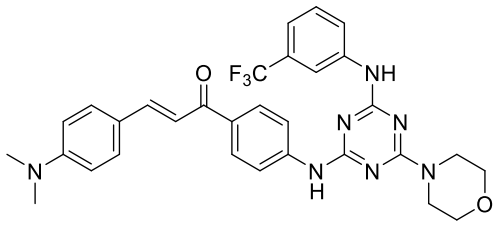


Figure 7. Chalcone with triazine group as antitubercular agent

4.5. Herbicides

Chalcones have been investigated for their herbicidal activity against weeds and unwanted plant species. Aqueous medium synthesized chalcones may offer environmentally friendly alternatives to conventional herbicides with reduced environmental impact and toxicity.

Weeds are becoming more and more resistant to herbicides, and they pose a threat to the world's food production. Nguyen, et al. [76] have identified chalcones as selective inhibitors of phosphoenolpyruvate carboxylase (PEPC), a key enzyme for carbon fixation in the C_4 photosynthetic pathway of many of the world's most damaging weeds. In contrast, many of the most important crop plants use C_3 photosynthesis. Computational screening using the feedback inhibitor binding pockets of C_4 PEPC from F. trinervia (PDB ID 3ZGE) and C_3 PEPC from F. pringlei (PDB ID 3ZGB) as models indicated that the plant polyphenol butein could be a potential inhibitor against the C_4 over the C_3 Isomers.

Butein is a chalcone containing two hydroxyl groups on rings A and B. If ring A contains only two hydroxyl groups, ring B must have at least two hydroxyl groups for a good inhibitory effect. The $IC_{50,\ C3value}$ of butein, robetin are ~ 2.5 μM. This result indicates that the hydroxyl group at position 3' of ring A or positions 3,4 of ring B in butein & robetin which is necessary to increase inhibition of C_4 PEPC. Examples of a few herbicides are Butein and Robtein **(**Figure 8).

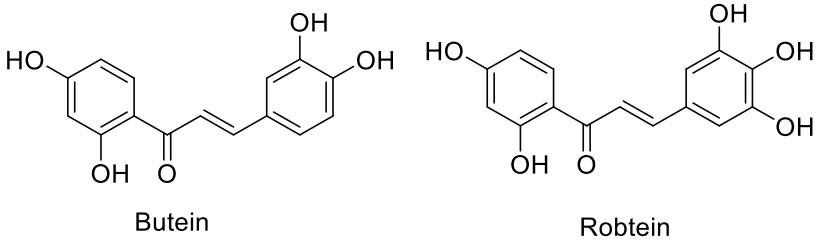


Figure 8. Butein and Robteinas chalcones as a herbicides

4.6. Cosmetics

Chalcones possess antioxidant properties that can help protect the skin from oxidative damage and premature aging. Aqueous medium synthesized chalcones have applications in cosmetic formulations, including skincare products, sunscreens, and anti-aging creams. chalcone derivatives with skin-lightening properties have been developed for use in cosmetic products aimed at reducing hyperpigmentation and improving skin tone.

Aqueous medium synthesis allows for producing chalcone derivatives with desirable cosmetic properties and formulation compatibility. Over the past few years, dermatologists have explored using chalcone derivatives to extract the most active ingredient for treating or preserving skin health. Xanthohumol, isoliquiritigenin, and licochalcone A are a few well-known chalcone derivatives that have minimal side effects and low toxicity when used to treat illnesses and skin conditions. It has been discovered that chalcone, along with other bioactive substances like hesperidin methyl chalcone and lipochalcone A, can lessen the harmful effects of UV radiation.[77] Some examples of chalcones used in cosmetics are Xanthohumol and isoliquiritigenin (Figure 9).

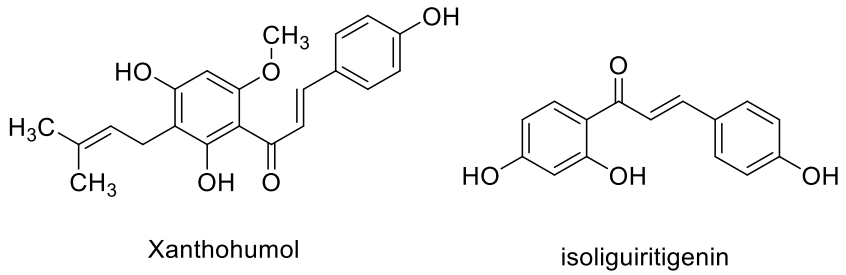
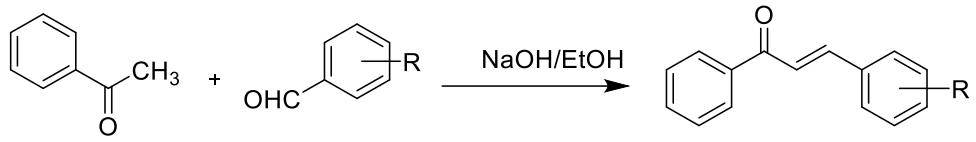


Figure 9. Xanthohumol andisoliquiritigenin chalcones used in cosmetics

4.7. Antioxidant Activity

Reactive oxygen species and free radicals cause aging, and oxidative damage is linked to a number of clinical processes, including cancer. Because they can scavenge free radicals, antioxidants are substances that stop oxidative damage. [78] In chalcones this ability is attributed to phenolic –OH group attached to the ring structures. [79]

Sandip et al. [80] synthesized chalcone compounds with antioxidant properties by employing traditional Claisen-Schmidt condensation. Substituted benzaldehydes and acetophenones were used in the presence of methanol and sodium hydroxide at room temperature for 45 minutes to achieve their synthesis (Scheme 25). Isoliguiritigenin and isoprenylchalcone are some example of antioxidant chalcones. (Figure 10)



Scheme 25. Substituted chalcones having antioxidant property

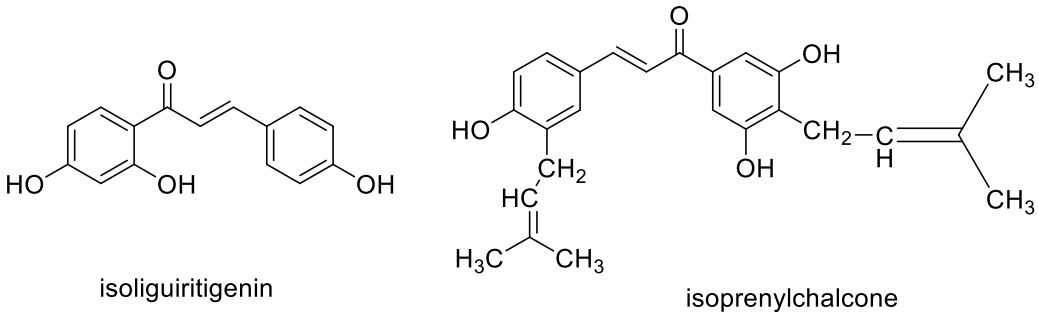


Figure 10. Soliguiritigenin and isoprenylchalconeas an antioxidant agent

4.8. Antifungal Activity

Chalcones appear to be a potential class of antifungal drugs. It has been demonstrated that they prevent the growth of various fungi and yeasts, including members of the Candida species [81]. It is well established that the chalcones' route of antifungal action involves inhibiting the fungal cell wall. The reactive enone moiety is mostly responsible for their antimicrobial activity, especially the antifungal action. [82]

Lopez etal.[83] Using the agar dilution method, chalcones were evaluated against a panel of human opportunistic pathogenic fungi and found that the most active compound did not have an electron-withdrawing group in the para-position of ring A (Figure 11). As well as did not have substituents in ortho-position but showed strong antifungal activities against fungi such as Microsporumgypseum (MIC=1.5µg/mL), *Trichophyton mentagrophytes* (3 µg/mL), Microsporumcanis (25 µg/mL), trichophyton rubrum (3 µg/mL) and Epidemophytonfloccosum (0.5 µg/mL). Isobavachalcone and chinendihydrochalcone are few examples of anti-fungal agents.

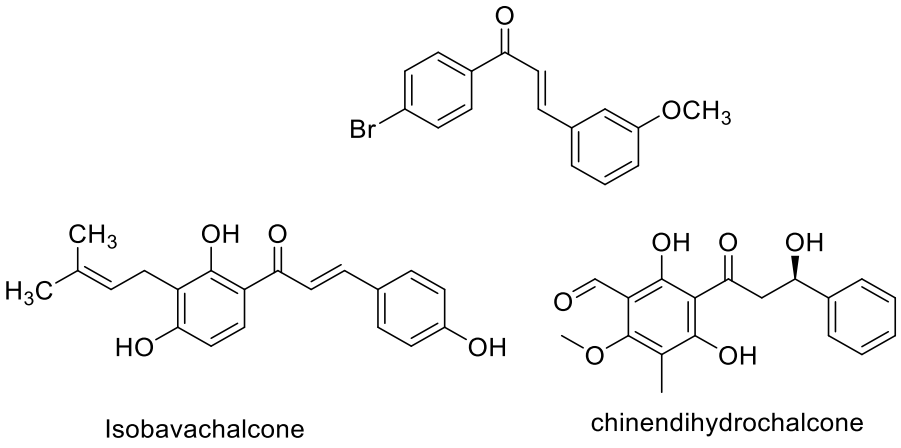


Figure 11. Various anti-fungal agents having substituted Chalcone moiety

5. Challenges and Future Directions

Despite the promising advantages, there are several challenges associated with the green methods for the synthesis of chalcones: While green synthesis methods may work efficiently on a small scale in laboratories, scaling them up to industrial levels can present difficulties. This includes challenges in maintaining reaction efficiency, yield, and reproducibility in large-scale production. Some green methods require the use of specialized equipment, catalysts, or solvents that can increase production costs compared to traditional synthetic methods.

Certain substrates or complex reactions may require more specific conditions that may not be achievable through green methods. Green methods often involve the use of non-toxic, environmentally friendly reagents, but optimizing reaction conditions such as temperature, pressure, and time to achieve high yields can still be a challenge. While green chemistry aims to minimize harmful impacts, some new materials or reagents used in the synthesis may still have unintended ecological effects or require energy-intensive processes for their production and disposal. The introduction of new green solvents, catalysts, or reagents often faces regulatory scrutiny.

6. Conclusion

The green methods for the synthesis of chalcones present a promising approach to enhance both the efficiency and sustainability of chemical processes. These environmentally friendly techniques, which utilize renewable resources, non-toxic solvents, and energy-efficient processes, align well with the principles of green chemistry. Furthermore, chalcones themselves exhibit significant biological activity, making them valuable compounds in the development of pharmaceuticals and other bioactive materials. The integration of green synthesis methods not only reduces the environmental impact of chemical production but also contributes to the sustainable development goals by promoting eco-friendly practices in the chemical industry. Continued research and development in this area will likely lead to even more efficient and scalable green processes, enhancing the accessibility of chalcones as bioactive compounds and supporting the transition toward a more sustainable and health-conscious future.

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References

[1] Jankovic, T.; Turkovic, N.; Stevuljevic, J. K.; Vujic, Z.; Ivkovic. B. Differences in antioxidant potential of chalcones in human serum: In vitro study. *Chem. Biol. Interact.***2020**, *324*, 109084.
[2] Cuendet, M.; Potterat, O.; Salvi, A.; Testa, B.; Hostettmann, K. A stilbene and dihydrochalcones with radical scavenging activities from *Loiseleuria procumbens*. *Phytochemistry* **2000**, *54*, 871–874.
[3] Weber, W. M.; Hunsaker, L. A.; Abcouwer, S. F.; Deck, L. M.; van der Vliet. J. Anti-oxidant activities of curcumin and related enones. *Bioorg. Med. Chem.* **2005**, *13*, 3811–3820.
[4] Jung, J.-C.; Lee, Y.; Min, D.; Jung, M.; Oh, S. Practical synthesis of chalcone derivatives and their biological activities. *Mol.* **2017**, *22*(*11*), 1872.
[5] Bale, A. T.; Salar, U.; Khan, K. M.; Chigurupati, S.; Fasina, T.; Ali, F.; Ali, M.; Nanda, S. S.; Taha, M.; Perveen, S. Chalcones and bischalcones analogs as DPPH and ABTS radical scavengers. *Lett. Drug Des. Discov.* **2021**, *18(3)*, 249–257.
[6] Ünver, Y.; Tuluk, M.; Kahriman, N.; Emirik, M.; Bektas, E.; Direkel, Ş. New chalcone derivatives with Schiff base-thiophene: synthesis, biological activity, and molecular docking studies. *Russ. J. Gen. Chem.* **2019**, *89*(4), 794–799.
[7] Mahapatra, D. K.; Bharti, S. K.; Kumar, S.; Asati, V. Chalcone derivatives: anti-inflammatory potential and molecular targets perspectives. *Curr. Top. Med. Chem.* **2017**, *17(28)*, 3146–3169.
[8] Rashid, H.; Xu, Y.; Ahmad, N.; Muhammad, Y.; Wang, L. Promising anti-inflammatory effects of chalcones via inhibition of cyclooxygenase, prostaglandin E2, inducible NO synthase and nuclear factor κB activities. *Bioorg. Chem.* **2019**, *87*, 335–365.
[9] Nowakowska, Z. A review of anti-infective and anti-inflammatory chalcones. *Eur. J. Med. Chem.* **2007**, *42(2)*, 125–137.
[10] Rajendra, P.; Srinivasa, R. A.; Rambabu, R. Synthesis of some 4′-amino chalcones and their anti-inflammatory and antimicrobial activity. *Asian J. Chem.* **2009**, *21*, 907–914.
[11] Fu, Z. Y.; Jin, Q. H.; Qu, Y. L.; Guan, L. P. Chalcone derivatives bearing chromen or benzo[f]chromen moieties: design, synthesis, and evaluations of anti-inflammatory, analgesic, selective COX-2 inhibitory activities. *Bioorg. Med. Chem. Lett.* **2019**, *29(15)*, 1909–1912.
[12] Okolo, E. N.; Ugwu, D. I.; Ezema, B. E.; Ndefo, J. C.; Eze, F. U.; Ezema, C. G.; Ezugwu, J. A.; Ujam, O. T. New chalcone derivatives as potential antimicrobial and antioxidant agents. *Sci. Rep.* **2021**, *11*, 21781.
[13] Tratrat, C.; Haroun, M.; Xenikakis, I.; Liaras, K.; Tsolaki, E.; Eleftheriou, P.; Petrou, A.; Aldhubiab, B.; Attimarad, M.; Venugopala, K. N.; Harsha, S.; Elsewedy, H. S.; Geronikaki, A.; Sokovic, M. Design, synthesis, evaluation of antimicrobial activity and docking studies of new thiazole-based chalcones. *Curr. Top. Med. Chem.***2019**, *19*(*5*), 356–375.
[14] Nielsen, S. F.; Boesen, T.; Larsen, M.; Schønning, K.; Kromann, H. Antibacterial chalcones—bioisosteric replacement of the 4′-hydroxy group. *Bioorg. Med. Chem.***2004**, *12*, 3047–3054.
[15] Selvakumar, N.; Kumar, G. S.; Azhagan, A. M.; Rajulu, G. G.; Sharma, S.; Kumar, M. S.; Das, J.; Iqbal, J.; Trehan. S. Synthesis, SAR and antibacterial studies on novel chalcone oxazolidinone hybrids. *Eur. J. Med. Chem.***2007**, *42*, 538–543.
[16] Tomar, V.; Bhattacharjee, G.; Kamaluddin, A. K. Synthesis and antimicrobial evaluation of new chalcones containing piperazine or 2,5-dichlorothiophene moiety. *Bioorg. Med. Chem. Lett.***2007**, *17*, 5321–5324.
[17] Syam, S.; Abdelwahab, S. I.; Al-Mamary, M. A.; Mohan, S. Synthesis of chalcones with anticancer activities. *Mol.* **2012**, *17*(6), 6179–6195.
[18] Ferrari, S. M.; Materazzi, G.; Baldini, E.; Ulisse, S.; Miccoli, P.; Antonelli, A.; Fallahi, P. Antineoplastic effects of PPARγ agonists, with a special focus on thyroid cancer. *Curr. Med. Chem.***2016**, *23*, 636–649.
[19] Karthikeyan, C.; Moorthy, N. S.; Ramasamy, S.; Vanam, U.; Manivannan, E.; Karunagaran, D.; Trivedi, P. Advances in chalcones with anticancer activities. *Recent Pat. Anticancer Drug Discov.***2015**, *10*, 97–115.

[20] León-González, A. J.; Acero, N.; Muñoz-Mingarro, D.; Navarro, I.; Martín-Cordero, C. Chalcones as promising lead compounds on cancer therapy. *Curr. Med. Chem.***2015**, *22*, 3407–3425.
[21] Madhavi, S.; Sreenivasulu, R.; Jyotsna, Y.; Raju, R. R. Synthesis of chalcone incorporated quinazoline derivatives as anticancer agents. *Saudi Pharm. J.***2016**.
[22] Adelusi, I.; Du, L.; Chowdhury, A.; Xiaoke, G.; Lu, Q.; Yin, X. Signaling pathways and proteins targeted by antidiabetic chalcones. *Life Sci.***2021**, *284*, 118982.
[23] Kahssay, S. W.; Hailu, G. S.; Desta, K. T. Design, synthesis, characterization and in vivo antidiabetic activity evaluation of some chalcone derivatives. *Drug Des. Dev. Ther.***2021**, *15*, 3119–3129.
[24] Rocha, S.; Ribeiro, D.; Fernandes, E.; Freitas, M. A systematic review on antidiabetic properties of chalcones. *Curr. Med. Chem.* **2020**, *27*, 2257–2321.
[25] 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.
[26] Pérez-González, A.; Chávez-Arriaga, R.; Guzmán-López, E. G.; Hernández-Ayala, L. F.; Galano, A. Chalcone derivatives with a high potential as multifunctional antioxidant neuroprotectors. *ACS Omega* **2022**, *7*(*43*), 38254–38268.
[27] Ben Lagha, A.; Haas, B.; Grenier, D. Tea polyphenols inhibit the growth and virulence properties of *Fusobacterium nucleatum*. *Sci. Rep.* **2017**, *7*, 44815.
[28] Cheenpracha, S.; Karalai, C.; Ponglimanont, C.; Subhadhirasakul, S.; Tewtrakul, S. Anti-HIV-1 protease activity of compounds from *Boesenbergiapandurata*. *Bioorg. Med. Chem.* **2006**, *14*, 1710–1714.
[29] Deng, J.; Kelly, J. A.; Barchi, J. J.; Sanchez, T.; Dayam, R.; Pommier, Y.; Neamati, N. Mining the NCI antiviral compounds for HIV-1 integrase inhibitors. *Bioorg. Med. Chem.* **2006**, *14*, 3785–3792.
[30] Wu, J. H.; Wang, X. H.; Yi, Y. H.; Lee, K. H. Anti-AIDS agents 54: A potent anti-HIV chalcone and flavonoids from genus *Desmos*. *Bioorg. Med. Chem. Lett.* **2003**, *13*, 1813–1815.
[31] Lakshminarayanan, B.; Kannappan, N.; Subburaju, T. Synthesis and biological evaluation of novel chalcones with methanesulfonyl end as potent analgesic and anti-inflammatory agents. *Int. J. Pharm. Res. Biosci.* **2020**, *11*(10), 4974–4981.
[32] Higgs, J.; Wasowski, C.; Marcos, A.; Jukic, M.; Paván, C. H.; Gobec, S.; de Tezanos Pinto, F.; Colettis, N.; Marder, M. Chalcone derivatives: synthesis, in vitro and in vivo evaluation of their antianxiety, anti-depression and analgesic effects. *Heliyon* **2019**, *5*(3), 01376.
[33] Kantam, M. L.; Prakash, B. V.; Reddy, C. V. Efficient synthesis of chalcones by a solid base catalyst. *Synth. Commun.* **2005**, *35*, 1971–1978.
[34] Kim, E.-J.; Ryu, H. W.; Curtis-Long, M. J.; Han, J.; Kim, J. Y.; Cho, J. K.; Kang, D.; Park, K. H. *Bioorg. Med. Chem. Lett.***2010**, *20*, 4237–4239.
[35] Jain, D.; Khatri, C.; Rani, A. *Fuel* **2011**, *90*, 2083–2088.
[36] Yadav, G. D.; Yadav, A. R. Novelty of Claisen-Schmidt condensation of biomass-derived furfural with acetophenone over solid super base catalyst. *RSC Adv.* **2014**, *4*, 63772–63778.
[37] Kang, L. Q.; Cai, Y. Q.; Wang, H.; Li, L. H. Solvent-free catalytic preparation of 2,6-dibenzylidenecycloalkanones using 2-hydroxyethylammonium acetate ionic liquid as catalyst. *Monatsh. Chem.* **2014**, *145*, 337–340.
[38] Rafiee, E.; Rahimi, F. Synthesis of biologically active chalcone analogues via Claisen–Schmidt condensation in solvent-free conditions: supported mixed addenda heteropoly acid as a heterogeneous catalyst. *J. Chil. Chem. Soc.* **2013**, *58*, 1926–1929.
[39] Shylesh, S.; Samuel, P. P.; Srilakshmi, C.; Parischa, R.; Singh, A. P. Sulfonic acid functionalized mesoporous silicas and organosilicas: synthesis, characterization and catalytic applications. *J. Mol. Catal. A* **2007**, *274*, 153–158.
[40] Neyestani-Naeeni, E.; Naimi-Jamal, M. R. Nanoporous MCM-41-SO_3H as an efficient catalyst for chalcones and dibenzylidenealkanones synthesis via solvent-free aldol-condensation reaction. *Sci. Iranica* **2015**, *22*(*6*), 2282–2289.
[41] Yi, W.; Chen, W.; Liu, F.-X.; Zhong, Y.; Wu, D.; Zhou, Z.; Gao, H. Rh(III)-Catalyzed and solvent-controlled chemoselective synthesis of chalcone and benzofuran frameworks via synergistic dual directing groups enabled regioselective C–H functionalization: a combined experimental and computational study. *ACS Catal.* **2018**, *8*(*10*), 9508–9519.
[42] Wu, H.; Li, Y.; Cui, M.; Jian, J.; Zeng, Z. Suzuki coupling of amides via palladium-catalyzed C–N cleavage of N-acylsaccharins. *Adv. Synth. Catal.* **2016**, *358*(*23*), 3876–3880.

[43] Buszek, K. R.; Brown, N. N-vinylpyridinium and ammonium tetrafluoroborate salts: new electrophilic coupling partners for Pd(0)-catalyzed Suzuki cross-coupling reactions. *Org. Lett.* **2007**, *9*, 707–710.

[44] Vellakkaran, M.; Andappan, M. M. S.; Nagaiah, K. Oxygen as single oxidant for two steps: base-free one-pot Pd(II)-catalyzed alcohol oxidation & arylation to halogen-intact β-aryl α,β-enones. *RSC Adv.* **2014**, *4*(*85*), 45490–45494.

[45] 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.

[46] Jiang, Q.; Jia, J.; Xu, B.; Zhao, A.; Guo, C.-C. Iron-facilitated oxidative radical decarboxylative cross-coupling between α-oxocarboxylic acids and acrylic acids: an approach to α,β-unsaturated carbonyls. *J. Org. Chem.***2015**, *80*(*7*), 3586–3596.

[47] Shyam, P. K.; Lee, C.; Jang, H.-Y. Copper-catalyzed oxidative olefination of thiols using sulfones and phosphorous ylides. *Bull. Korean Chem. Soc.***2015**, *36*(*7*), 1824–1827

[48] Rinu, P. X. T.; Radhika, S. & Anilkumar, G. Recent applications and trends in the Julia-Kocienski olefination. *ChemistrySelect*, **2022**, *7*(31), e202200760.

[49] Baudin, J. B.; Hareau, G.; Julia, S. A.; Ruel, O. A direct synthesis of olefins by reaction of carbonyl compounds with lithio derivatives of 2-[alkyl- or (2′-alkenyl)- or benzyl-sulfonyl]-benzothiazoles. *Tetrahedron Lett.* **1991**, *32(9)*, 1175-1178.

[50] Kumar, A.; Sharma, S.; Tripathi, V. D.; Srivastava, S. Synthesis of chalcones and flavanones using Julia–Kocienski olefination. *Tetrahedron* **2010**, *66*(*48*), 9445–9449.

[51] Ahmed, H. S.; Green synthesis of chalcones under microwave irradiation, *Int.J. ChemTech Res.* **2016**, *9(2)*, 36-39.

[52] Ahmad, M. R.; Sastry, V. G.; Bano, N.; Anwar, S. Synthesis of novel chalcone derivatives by conventional and microwave irradiation methods and their pharmacological activities. *Arabian J. Chem.* **2016**, *9*, 931–935.

[53] Tupare, S. A.; Nalage, S. V.; Bobe, S. R.; Hallale, S. N.; Bhosale, S. V.; Vyawahare, S. K.; Dake, S. A.; Bhosale, S. V.; Pawar, R. P. Revisit: Eaton's reagent catalyzed synthesis of mono and bis-chalcone derivatives. *Lett. Org. Chem.* **2012**, *9*, 526–529.

[54] Asiri, A. M.; Khan, S. A. Synthesis, characterization and optical properties of mono and bis-chalcone. *Mater. Lett.* **2011**, *65*, 1749–1752.

[55] Chaudhari, P. P.; Rajput, S. S. Clean synthesis and antimicrobial interpretation of azo (dipyrano) and bis-chalcones derivatives. *Heterocycl. Lett.* **2018**, *8*, 133–144.

[56] Calvino, V.; Picallo, M.; Lopez-Peinado, A. J.; Martin-Aranda, R. M.; Duran-Valle, C. J. Ultrasound accelerated Claisen–Schmidt condensation: a green route to chalcones. *Appl. Surf. Sci.* **2006**, *252*, 6071–6074.

[57] Khan, S. A.; Asiri, A. M.; Marwani, H. M.; Alamry, K. A.; Al-Amoud, M. S.; El-Daly, S. A. *Int. J. Electrochem. Sci.* **2014**, *9*, 799–809.

[58] Ganesan, R.; Avupati, V. R.; Shabi, M. M. Ultrasonic synthesis and in vitro evaluation of some bischalcones as potential cytotoxic agents. *Indo Am. J. Pharm. Sci.* **2017**, *4*, 670–687.

[59] Liargkova, T.; Hadjipavlou-Litina, D. J.; Koukoulitsa, C.; Voulgari, E.; Avgoustakis, C. Simple chalcones and bis-chalcone ethers as possible pleiotropic agents. *J. Enzyme Inhib. Med. Chem.* **2016**, *31*, 302–313.

[60] Adole, V. A.; Jagdale, B. S.; Pawar, T. B.; Sagane, A. A. Ultrasound-promoted stereoselective synthesis of 2,3-dihydrobenzofuran appended chalcones at ambient temperature. *S. Afr. J. Chem.* **2020**, *73*, 35–43.

[61] Gonçalo, P. R.; Ana, M. L.; Mariado, C. B; Diana, C. G. A. Chalcone: A Valuable Scaffold Upgrading by Green Methods, *ACS Sustainable Chem. Eng*. **2017**, 5, 9, 7467–7480.

[62] Mitrev, Y. N.; Mehandzhiyski, A. Y.; Batovska, D. I.; Liese, A.; Galunsky, B. Original enzyme-catalyzed synthesis of chalcones: utilization of hydrolase promiscuity. *J. Serb. Chem. Soc.* **2016**, *81*, 1231–1237.

[63] Chen, X.; Liu, B.-K.; Kang, H.; Lin, X.-F. A tandem aldol condensation/dehydration co-catalyzed by acylase and N-heterocyclic compounds in organic media. *J. Mol. Catal. B: Enzym.* **2011**, *68*, 71–76.

[64] Raghav, N.; Malik, P. Solvent free synthesis of some chalcones and their effect on bovine serum albumin. *Adv. Appl. Sci. Res.* **2011**, *2*(*5*), 410–415.

[65] Mallia, A.; Sloop, J. Advances in the synthesis of heteroaromatic hybrid chalcones. *Molecules* **2023**, *28*, 3201.

[66] Marotta, L.; Rossi, S. ; Ibba, R.; Brogi, S.; Calderone, V.; Butini, S.; Campiani, G.; Gemma, S., The green chemistry of chalcones: Valuable sources of privileged core structures for drug discovery, *Frontier. Chem.* **2022**, *10*, 988376.

[67] Jain, S. ; Kumar, S. ; Lamba, B. Y. ; Patra, J. ; Mahindroo, N. Nanocatalysts: applications in synthesis of chalcones- a review. *Synth. Comm.*, **2020,** *51*(*1*), 1–12.

[68] Ugwu, D.I.; Ezema, B.E.; Okoro, U.C.; Eze, F.U.; Ekoh, O.C.; Egbujora, M.C. and Ugwuja,D.I. Syntheses and pharmacological applications of chalcones : a review, *int. J. Chem. Sci.* **2015**, *13*(*1*), 459-500

[69] Visagaperumal, D.; Revathi, R.; Ratna Sree, C.; Jayakumar, R.; Anbalagan, N. Microwave assisted synthesis and biological activity of certain 4-hydroxy chalcones. *Pharmacophore* **2013**, *4*(*2*), 59–69.

[70] Yadav, H.; Gupta, P.; Pawar, P. S.; Singour, P. K. *Med. Chem. Res.* **2010**, *19*, 1–8.

[71] Khasnobis, S.; Escuyer, V. E.; Chatterjee, D. Emerging therapeutic targets in tuberculosis: post-genomic era, *Expert Opin. Ther. Targets* **2005**, *6*, 21–40.

[72] Kaufmann, S. H. E. How can immunology contribute to the control of tuberculosis? *Nat. Rev. Immunol.* **2001**, *1*, 20–30.

[73] Lopez, A. In *Disease Control Priorities in Developing Countries*; Jamison, D. T.; Mosely, W. H., Eds.; Oxford University Press: New York, **1993**; p 35.

[74] Lin, Y. M.; Zhou, Y.; Flavin, M. T.; Zhou, L. M.; Nie, W.; Chen, F. C. Chalcones and flavonoids as anti-tuberculosis agents. *Bioorg. Med. Chem.* **2002**, *10*, 2795–2802.

[75] Solankee, A.; Tailor, R. An efficient synthesis of some new chalcone, acetyl pyrazoline and amino pyrimidine bearing 1,3,5-triazine nucleus as potential antimicrobial and antitubercular agents. *Chem. Int.***2016**, *2*(*4*), 189–200.

[76] Nguyen, G. T. T..; Erlenkamp, G.; Jack, O.; Küberl, A.; Bott, M.; Fiorani, F.; Gohlke, H.; Groth, G. Chalcone-based selective inhibitors of a C4 plant key enzyme as novel potential herbicides. *Sci. Rep.***2016**, *6*, 27333.

[77] Jumina, J.; Harizal, H.; Kurniawan, Y. S. Beauty–cosmetic science, cultural issues and creative developments. In: *London: IntechOpen* **2020**. E-Book ISBN: 978-1-83962-449-0. doi:10.5772/intechopen.77628

[78] Velavan, S.; Nagulendran, K.; Mahesh, R.; Begum, V. In vitro antioxidant activity of *Asparagus racemosus* root. *Pharmacogn. Mag.* **2007**, *3*(*9*), 26–33.

[79] Okawa, M.; Kinjo, J.; Nohara, T.; Ono, M. DPPH (1,1-Diphenyl-2-Picrylhydrazyl) Radical Scavenging Activity of Flavonoids Obtained from Some Medicinal Plants, *Biol. Pharm. Bull.* **2001**, *24*(10), 1202–1205.

[80] Sen, S.; Eashwari, T. S.; Farooqui, N. A.; Mahashwari, S.; Kumar, R. In vitro antimicrobial and antioxidant activity of substituted chalcones. *Der Pharm. Lett.***2012**, *4*(*3*), 986–992.

[81] Opletalová, V.; Sediv, D. Chalcones and their heterocyclic analogs as potential antifungal chemotherapeutic agents. *Ceska Slov. Farm.* **1999**, *48*, 252–255.

[82] Boeck, P.; Leal, P. C.; Yunes, R. A.; Filho, V. C.; Lopez, S.; Sortino, M.; Escalante, A.; Furlan, R. L. E.; Zacchino, S. Antifungal activity and studies on mode of action of novel xanthoxyline-derived chalcones. *Arch. Pharm. Chem. Life Sci.***2 005**, *338*, 87–95.

[83] Lopez, S.N.; Castelli, M.V.; Zacchino, S.A.; Dominguez, J.N.; Lobo, G.; Jaime, C.C.; Cortes, J.C.G.; Ribas, J.C.; Devia, C.; Ana, M.R.; Ricardo, D.E. In vitro antifungal evaluation and structure–activity relationships of a new series of chalcone derivatives and synthetic analogues, with inhibitory properties against polymers of the fungal cell wall, *Bioorg. Med. Chem.* **2001**, *9*, 1999–2013.