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RESEARCH ARTICLE

Synthesis, and Biological Evaluation of Chalcone Scaffolds as Anti-Bacterial and Anti-oxidant

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Abstract: Chalcones, open-chain flavonoids with an α, β-unsaturated carbonyl system, are widely recognized for diverse biological activities, including antimicrobial and antioxidant effects. In the present study, ten chalcone derivatives (C1–C10) were synthesized using Claisen–Schmidt condensation and characterized by melting point, yield, and recrystallization profiles. Their antimicrobial activity was evaluated against Streptococcus pyogenes, Staphylococcus aureus, Pseudomonas aeruginosa, and Escherichia coli using the broth microdilution method, while antioxidant potential was determined by the DPPH radical scavenging assay. The antimicrobial results indicated that chalcones bearing electron-withdrawing substituents (–Cl, –Br, –CN, –NO_2) exhibited enhanced antibacterial effects. In contrast, derivatives with electron-donating groups (–OH, –OCH_3) displayed stronger antioxidant activity, as, C1, which demonstrated low IC_{50} values compared with the standard ascorbic acid. These findings establish a clear structure–activity relationship (SAR), suggesting that chalcones with electron-withdrawing groups are promising antibacterial agents, whereas those with electron-donating groups serve as potent antioxidants. Overall, the synthesized chalcone derivatives highlight the potential of structural modification in improving therapeutic efficacy and may serve as lead scaffolds for the development of novel antimicrobial and antioxidant agents.

Keywords: Chalcone derivatives; Claisen–Schmidt condensation; Antimicrobial activity; Antioxidant activity; Structure–activity relationship (SAR).

INTRODUCTION

1. Background of Chalcones

Chalcones represent an important group of organic molecules classified under the flavonoid family [1]. Structurally, they are open-chain precursors to flavonoids and isoflavonoids, characterized by an α, β-unsaturated carbonyl system connecting two aromatic rings (Fig.1.1). This unique framework makes chalcones highly reactive and versatile in medicinal chemistry. They are commonly found in various plants, including fruits, spices, vegetables, and medicinal herbs, where they play an essential role in plant defence mechanisms [2-4]. Chalcone shows a broad range of pharmacological actions, including antimicrobial, anti-inflammatory, antioxidant, anticancer, and anti-diabetic effects [2-3]. The ability of chalcones to interact with biological targets, such as enzymes and cellular receptors, makes them promising candidates for drug development. The presence of conjugated double bonds and a reactive carbonyl group in chalcones allows for modifications that can enhance their bioactivity [4]. Due to the rising resistance of pathogens to standard antibiotics and the escalating effects of oxidative stress on human health, chalcones are emerging as promising candidates for the development of new therapeutic agents [5].

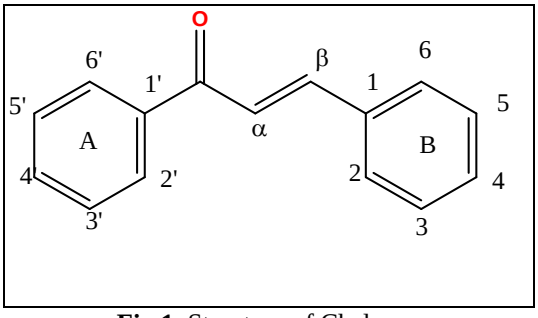


Fig 1. Structure of Chalcone

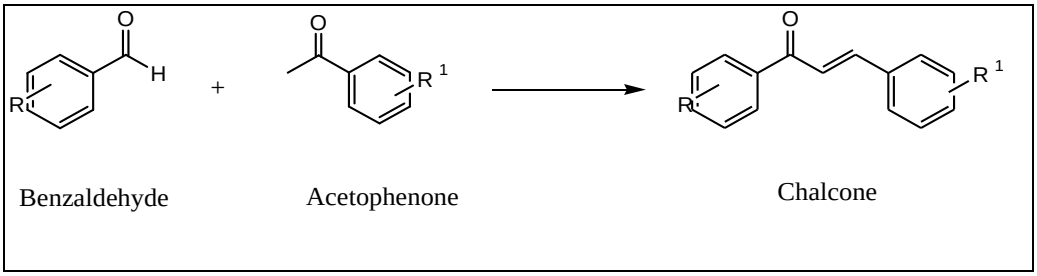
2. Methods of Synthesis of Chalcones:

The synthesis of chalcones has garnered significant attention in organic and medicinal chemistry due to their diverse biological activities and structural versatility. Over the years, numerous synthetic methods have been developed and refined to produce chalcones efficiently and sustainably [9-10]. These approaches vary in complexity, reaction conditions, and yields, allowing for the generation of a wide range of chalcone derivatives. The continuous advancement in synthetic

strategies reflects the growing demand for chalcones in pharmaceutical and chemical research, emphasizing their importance as key scaffolds in drug development and other industrial applications. Here are some commonly used synthesis methods for Chalcones can be synthesized using various methods that allow for precise structural modifications[9-10]. The most commonly used methods include:

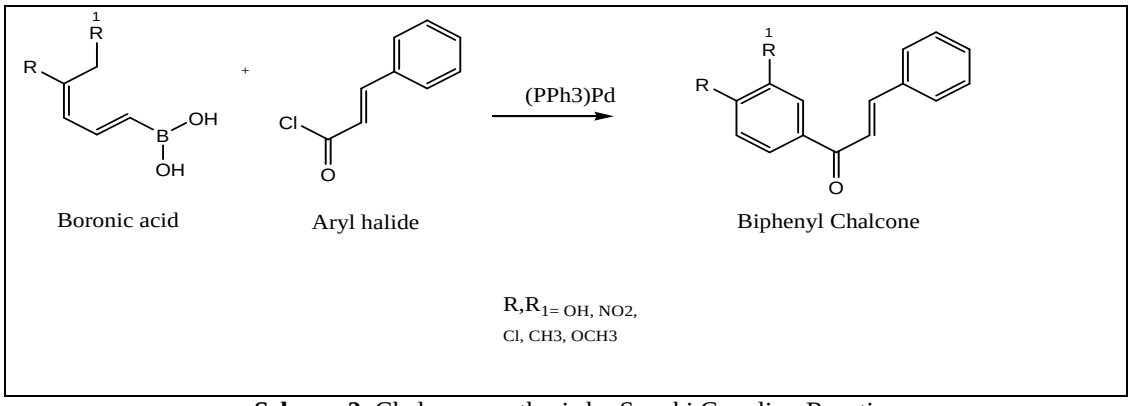
2.1 Claisen-Schmidt condensation:

The Claisen-Schmidt condensation is the most widely employed method for chalcone synthesis. It involves the reaction of an aromatic aldehyde with an aromatic ketone in the presence of bases (such as sodium, potassium or lithium hydroxide) or an acid catalyst (involves hydrochloric acid, sulfuric acid, or p-toluene (sulfonic acid). This reaction results in the formation of an α, β-unsaturated carbonyl system[9-11]. The reaction is typically carried out in a polar solvent like ethanol, methanol, or aqueous media to enhance solubility and reaction efficiency. The process generally follows an aldol condensation mechanism, where the enolate ion of the ketone attacks the carbonyl carbon of the aldehyde, forming a β-hydroxy ketone intermediate, which then undergoes dehydration to yield the final chalcone product. This method provides high yields, operational simplicity, and versatility in synthesizing diverse chalcone derivatives [11].



Scheme 1 Chalcone Synthesis by Claisen- Schmidt condensation

2.2 Suzuki coupling reaction: The reaction has been widely used to develop chalcones. The reaction is effective whether the reactant carry electron accepting or electron-releasing substituents, show that the electronic characteristics of the substituted group attached to the benzene rings exerts negligible infuence on the reaction outcome [15].



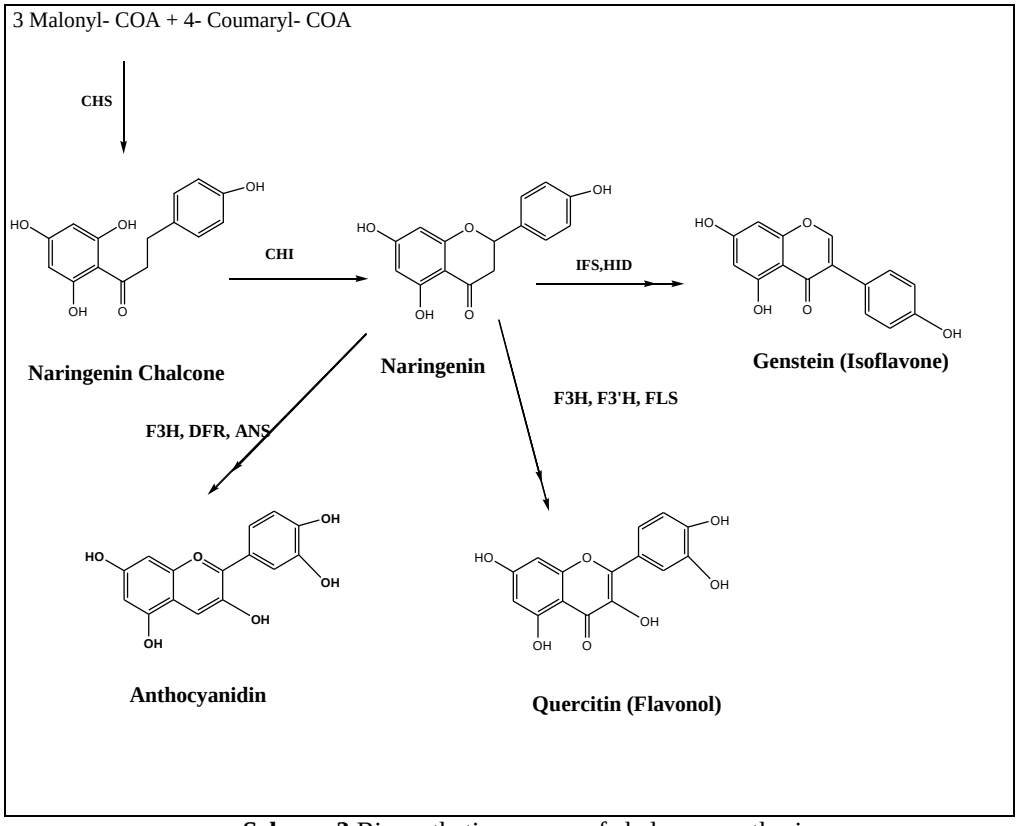
Scheme 2. Chalcone synthesis by Suzuki Coupling Reaction

2.3 Biosynthesis

The process of biosynthesis Chalcone synthase, A common enzyme in higher plants is CHS, the first type I1 polyketide synthase (PKS) superfamily identified in the 1970s. A number of lesser plants, like the liverwort Marchantia polymorpha, have also been found to have CHS. The remaining members of this family are all classified as "CHS-like" enzymes. The biosynthesis of various chalcones is carried out by CHS[12]. The biosynthesis of a variety of secondary metabolites, such as flavonoids, stilbenes, and aurones, is linked to the CHS super family enzymes [12-13]. By crystallizing CHS from the legume Medicago sativa, Joseph P. Noel and colleagues created a crucial framework for the biosynthetic mechanism and revealed crucial structural details regarding chalcone production. CHS is a homodimer, with each monomer having a mass of about 42–45 kDa.81 Cys164.The essential active site residues, Cys164, Phe215, His303, and Asn336 have been conserved in all CHS members and CHS-like enzymes. The initial step in the production of chalcones by CHS_ is the transfer of the coumaroyl moiety from one 4coumaroyl-coenzyme A (CoA) to Cys164. Three malonyl-CoA thioesters then undergo a polyketide reaction to create an intermediate (Scheme 1.2). A regiospecific Claisen-type cyclization takes place following the formation of a thioester-linked tetrapeptide, creating a novel ring system that yields naringenin chalcone. Scheme 1. When chalcone reductase (CHR) and CHS are present, naringenin chalcone is changed into 6-deoxy-naringenin chalcone (is liquiritigenin, Table 1,). Using the appropriate catalytic enzymes, other plant secondary metabolites, including stilbenes,

phloroglucinols, resorcinol, and benzophenones, might be biosynthesised similarly. Naringenin Chalcones are used as the substrates by CHS and chalcone isomerase (CHI) to produce flavonoids and isoflavonoids. Naringenin chalcones are also serves as the building blocks for the biosynthesis of aurone compounds by a plant catechol oxidase, aurone synthase (AURS). These conversions from chalcones to flavanones or aurones could also be realized by chemical reactions, such as the Algar–Flynn–Oyamada reaction [12-13].

Chalcones serving as precursors have generated a range of plant metabolites, revealing interesting biological activities, which will be discussed in the following sections. Taking such experience from nature, simple chalcones have been synthetically hybridized with other templates, such as stilbenes.



Scheme 3 Biosynthetic process of chalcone synthesis

3. Antimicrobial Potential of Chalcones

The rising prevalence of antibiotic-resistant bacteria and fungi has built an urgent necessity for new antimicrobial agents. Chalcones have shown promising antibacterial and antifungal activity through different mechanisms:

- Disruption of Cell Membranes: Chalcones are capable of interacting with microbial cell membranes disruption, resulting in increased permeability and subsequent cell rupture.
- Inhibition of Essential Enzymes: They interfere with bacterial and fungal enzymes crucial for survival, such as DNA gyrase, topoisomerase, and β-lactamase.
- Efflux Pump Inhibition: Some chalcones prevent bacteria from expelling antibiotics, thereby enhancing the effectiveness of existing drugs.
- Inhibition of Biofilm Formation: Chalcones interfere with quorum sensing mechanisms, reducing the ability of bacteria to form protective biofilms, making them more susceptible to antibiotics [25-26].

4. Antioxidant Potential of Chalcones:

Oxidative stress due to an imbalance between reactive generation of reactive species (ROS) and the body's antioxidant defence. Chalcones have shown potent antioxidant activity through:

- Scavenging Free Radicals: Neutralizing ROS to prevent cellular damage.
- Inhibiting Lipid Peroxidation: Protecting cell membranes from oxidative degradation
- Chelating Metal Ions: Reducing metal-catalysed oxidative reactions [27-28].

These properties make chalcones potential candidates for treating diseases linked to oxidative damage, including neurodegenerative diseases, cardiovascular disorders, and various forms of cancer.

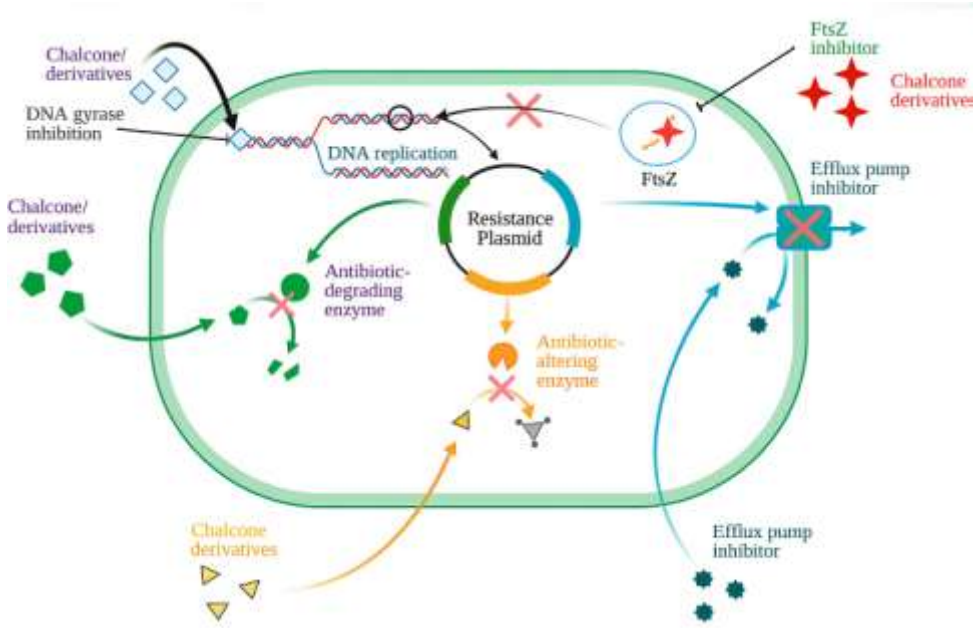


Fig 2. MOA of Chalcone as anti-microbials

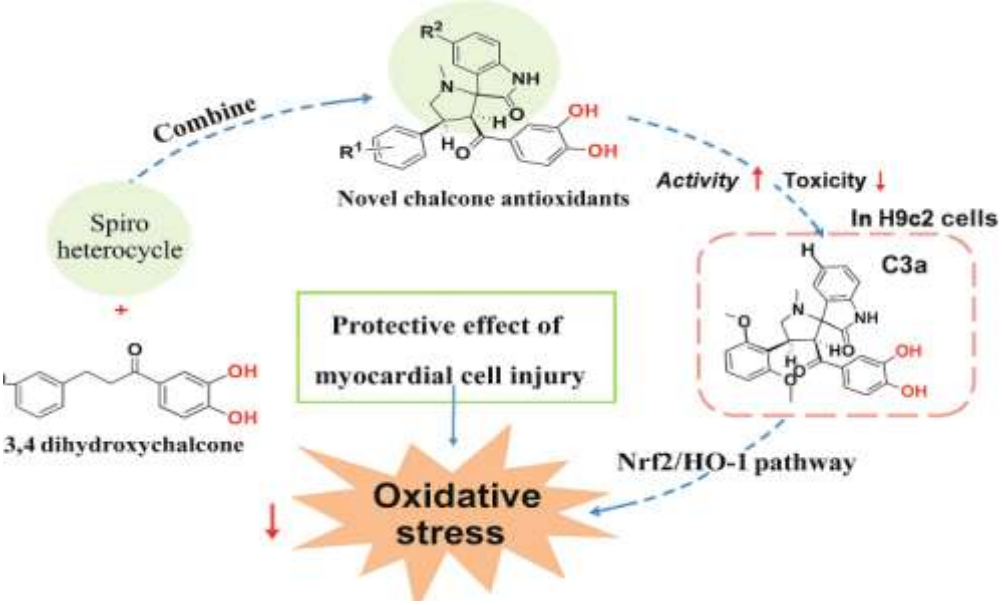


Fig 3. MOA of Chalcones as anti-oxidants

MATERIALS AND METHODS

5.2 Synthesis of Chalcone Derivatives (C1-C10)

5.2.1 Synthesis of (E)-1-(2,4-dihydroxyphenyl)-3-(4-chlorophenyl) prop-2-en-1-one (C1)

A mixture of each 2,4-dihydroxyacetophenone (0.01 mol) and 4-chlorobenzaldehyde (0.01 mol) was taken in a round bottom flask and dissolved in 20–25 mL of absolute ethanol. The reaction mixture was stirred magnetically, and 10 mL of 10% aqueous sodium hydroxide solution was added dropwise at room temperature (25–30°C). The solution was stirred for 4–5 hours. A precipitate gradually formed as the condensation progressed. To achieve pH ~6, upon completion, the solution was neutralized using dilute hydrochloric acid. After which the resulting solid was isolated via filtration, rinsed with cold water. The crude compound was then dried and recrystallized from ethanol to obtain the respective chalcone derivative.

5.2.2 Synthesis of (E)-1-(3,4,5-trimethoxyphenyl)-3-(4-nitrophenyl) prop-2-en-1-one (C2)

A mixture of each 3,4,5-trimethoxyacetophenone (0.01 mol) and 4-nitrobenzaldehyde (0.01 mol) was taken in a round bottom flask and dissolved in 20–25 mL of absolute ethanol. The reaction mixture was stirred magnetically, and 10 mL of 10% aqueous sodium hydroxide solution was added dropwise at room temperature (25–30°C). The solution was stirred continuously for 4–5 hours. A precipitate gradually formed as the condensation progressed. To achieve pH ~6, upon completion, the solution was neutralized using dilute

hydrochloric acid. After which the resulting solid was isolated via filtration, rinsed with cold water. The crude compound was then dried and recrystallized from ethanol to obtain the respective chalcone derivative.

5.2.3 Synthesis of (E)-1-(4-methylphenyl)-3-(2-thienyl) prop-2-en-1-one (C3)
A mixture of each 4-methylacetophenone (0.01 mol) and 2-thiophenecarboxaldehyde (0.01 mol) was taken in a round bottom flask and dissolved in 20–25 mL of absolute ethanol. The reaction mixture was stirred magnetically, and 10 mL of 10% aqueous sodium hydroxide solution was added dropwise at room temperature (25–30°C). The solution was stirred continuously for 4–5 hours. A precipitate gradually formed as the condensation progressed. To achieve pH ~6, upon completion, the solution was neutralized using dilute hydrochloric acid. After which the resulting solid was isolated via filtration, rinsed with cold water. The crude compound was then dried and recrystallized from ethanol to obtain the respective chalcone derivative.

5.2.4 Synthesis of (E)-1-(2-pyridyl)-3-(4-hydroxyphenyl) prop-2-en-1-one (C4)
A mixture of each 2-acetylpyridine (0.01 mol) and 4-hydroxybenzaldehyde (0.01 mol) was taken in a round bottom flask and dissolved in 20–25 mL of absolute ethanol. The reaction mixture was stirred magnetically, and 10 mL of 10% aqueous sodium hydroxide solution was added dropwise at room temperature (25–30°C). The solution was stirred continuously for 4–5 hours. A precipitate gradually formed as the condensation progressed. To achieve pH ~6, upon completion, the solution was neutralized using dilute hydrochloric acid. After which the resulting solid was isolated via filtration, rinsed with cold water. The crude compound was then dried and recrystallized from ethanol to obtain the respective chalcone derivative.

5.2.5 Synthesis of (E)-1-(2,3-dimethoxyphenyl)-3-(4-fluorophenyl) prop-2-en-1-one (C5)
A mixture of each 2,3-dimethoxyacetophenone (0.01 mol) and 4-fluorobenzaldehyde (0.01 mol) was taken in a round bottom flask and dissolved in 20–25 mL of absolute ethanol. The reaction mixture was stirred magnetically, and 10 mL of 10% aqueous sodium hydroxide solution was added dropwise at room temperature (25–30°C). The solution was stirred continuously for 4–5 hours. A precipitate gradually formed as the condensation progressed. To achieve pH ~6, upon completion, the solution was neutralized using dilute hydrochloric acid. After which the resulting solid was isolated via filtration, rinsed with cold water. The crude compound was then dried and recrystallized from ethanol to obtain the respective chalcone derivative.

5.2.6 Synthesis of (E)-1-(4-nitrophenyl)-3-(4-methoxyphenyl) prop-2-en-1-one (C6) A mixture of each 4-cyanoacetophenone (0.01 mol) and 4-methoxybenzaldehyde (0.01 mol) was taken in a round bottom flask and dissolved in 20–25 mL of absolute ethanol. The reaction mixture was stirred magnetically, and 10 mL of 10% aqueous sodium hydroxide solution was added dropwise at room temperature (25–30°C). The solution was stirred continuously for 4–5 hours. A precipitate gradually formed as the condensation progressed. To achieve pH ~6, upon completion, the solution was neutralized using dilute hydrochloric acid. After which the resulting solid was isolated via filtration, rinsed with cold water. The crude compound was then dried and recrystallized from ethanol to obtain the respective chalcone derivative.

5.2.7 Synthesis of (E)-1-(4-aminophenyl)-3-(3,4-dimethoxyphenyl) prop-2-en-1-one (C7)
A mixture of each 4-aminoacetophenone (0.01 mol) and 3,4-dimethoxybenzaldehyde (0.01 mol) were dissolved in 20–25 mL of absolute ethanol. The reaction mixture was stirred magnetically, and 10 mL of 10% aqueous sodium hydroxide solution was added dropwise at room temperature (25–30°C). The solution was stirred continuously for 4–5 hours. A precipitate gradually formed as the condensation progressed. To achieve pH ~6, upon completion, the solution was neutralized using dilute hydrochloric acid. After which the resulting solid was isolated via filtration, rinsed with cold water. The crude compound was then dried and recrystallized from ethanol to obtain the respective chalcone derivative.

5.2.8 Synthesis of (E)-1-(naphthalen-2-yl)-3-(4-methoxyphenyl) prop-2-en-1-one (C8)
A mixture of each 2-acetylnaphthalene (0.01 mol) and 4-methoxybenzaldehyde (0.01 mol) was taken in a round bottom flask and dissolved in 20–25 mL of absolute ethanol. The reaction mixture was stirred magnetically, and 10 mL of 10% aqueous sodium hydroxide solution was added dropwise at room temperature (25–30°C). The solution was stirred continuously for 4–5 hours. A precipitate gradually formed as the condensation progressed. To achieve pH ~6, upon completion, the solution was neutralized using dilute hydrochloric acid. After which the resulting solid was isolated via filtration, rinsed with cold water. The crude compound was then dried and recrystallized from ethanol to obtain the respective chalcone derivative.

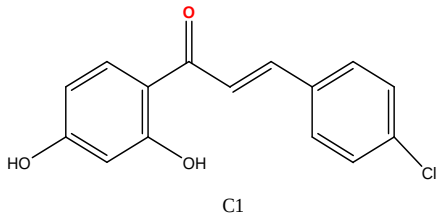
5.2.9 Synthesis of (E)-1-(3,5-dibromophenyl)-3-(4-hydroxyphenyl) prop-2-en-1-one (C9)

A mixture of each 3,5-dibromoacetophenone (0.01 mol) and 4-hydroxybenzaldehyde (0.01 mol) was taken in a round bottom flask and dissolved in 20–25 mL of absolute ethanol. The reaction mixture was stirred magnetically, and 10 mL of 10% aqueous sodium hydroxide solution was added dropwise at room temperature (25–30°C). The solution was stirred continuously for 4–5 hours. A precipitate gradually formed as the condensation progressed. To achieve pH ~6, upon completion, the solution was neutralized using dilute hydrochloric acid. After which the resulting solid was isolated via filtration, rinsed with cold water. The crude compound was then dried and recrystallized from ethanol to obtain the respective chalcone derivative.

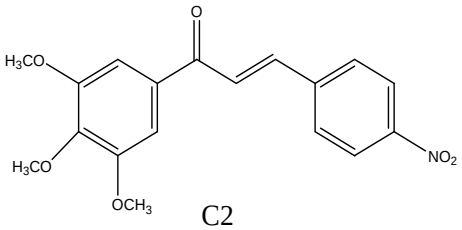
5.2.10 Synthesis of (E)-1-(4-sulfamoylphenyl)-3-(4-hydroxyphenyl) prop-2-en-1-one (C10)

A mixture of each 4-sulfamoylbenzaldehyde (0.01 mol) and 4-hydroxyacetophenone (0.01 mol) was taken in a round bottom flask and dissolved in 20–25 mL of absolute ethanol. The reaction mixture was stirred magnetically, and 10 mL of 10% aqueous sodium hydroxide solution was added dropwise at room temperature (25–30°C). The solution was stirred continuously for 4–5 hours. A precipitate gradually formed as the condensation progressed. To achieve pH ~6, upon completion, the solution was neutralized using dilute hydrochloric acid. After which the resulting solid was isolated via filtration, rinsed with cold water. The crude compound was then dried and recrystallized from ethanol to obtain the respective chalcone derivative.

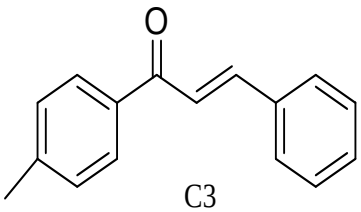
RESULTS AND OBSERVATIONS:



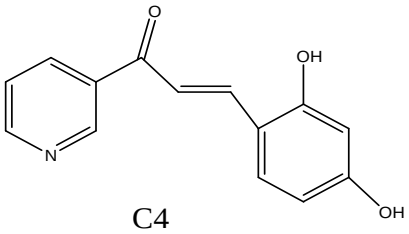
C1



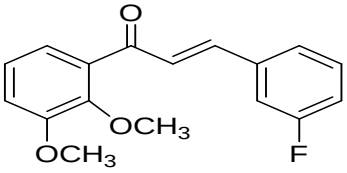
C2



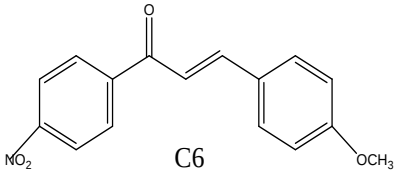
C3



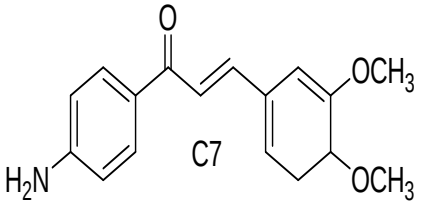
C4



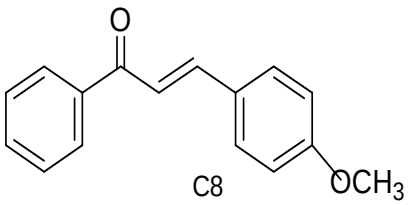
C5



C6



C7



C8

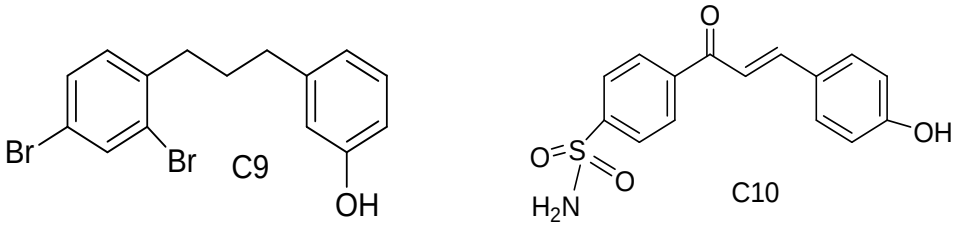


Fig 5. Structures of Synthesized Chalcone derivatives

Table 2: Physical Characterization Data of Chalcone Derivatives (C1–C10)

Compound	Substituents (Ar1 - Ar2)	Molecular Formula	Melting Point (°C)	Yield (%)	Color
C1	2,4-dihydroxy - 4-chlorophenyl	$C_{15}H_{11}ClO_3$	182–185	85	Yellow
C2	3,4,5-trimethoxy - 4-nitrophenyl	$C_{16}H_{15}NO_5$	168–170	82	Light Yellow
C3	4-methyl - 2-thienyl	$C_{14}H_{12}OS$	125–127	80	Orange
C4	2-pyridyl - 4-hydroxyphenyl	$C_{14}H_{11}NO_2$	176–178	79	Pale Yellow
C5	2,3-dimethoxy - 4-fluorophenyl	$C_{16}H_{13}FO_3$	160–163	83	Light Orange
C6	4-cyano - 4-methoxyphenyl	$C_{16}H_{11}NO_2$	189–191	86	Yellow
C7	4-amino - 3,4-dimethoxyphenyl	$C_{16}H_{15}NO_3$	162–165	88	Bright Yellow
C8	naphthalen-2-yl - 4-methoxyphenyl	$C_{18}H_{14}O_2$	192–195	84	Golden Yellow
C9	3,5-dibromo - 4-hydroxyphenyl	$C_{15}H_{10}Br_2O_2$	198–201	78	Deep Yellow
C10	4-sulfamoyl - 4-hydroxyphenyl	$C_{15}H_{13}NO_4S$	214–217	81	Yellowish Brown

5.3 Evaluation of Biological Activities

5.3.1 Anti-Bacterial Screening Method:

The antibacterial screening was performed against the microbial strains are Streptococcus pyogenes (MTCC 443), Staphylococcus aureus (MTCC 96), Pseudomonas aeruginosa (MTCC 2488), Escherichia coli (MTCC 442). P. aeruginosa, E. coli (Gram-negative bacteria) and S. pyogenes, S. aureus (Gram-positive bacteria) was screened for antibacterial effect. Mueller-Hinton broth and Saburou's broth were served as nutritional media for both gram-positive and gram-negative bacteria, respectively. Ampicillin served as standard for antibacterial activity.

The broth microdilution method (Monga et al., 2014; Balouiri et al., 2016) was employed for antibacterial susceptibility testing. DMSO was used to prepare dilutions of test compounds. To evaluate the antibacterial activity of the chalcones (compounds C-1 to C-10), we used the Minimum Inhibitory Concentration (MIC) method. MIC is the lowest concentration of a compound that completely prevents the growth of bacteria after overnight incubation. It's a widely used technique to test how effective a compound is against bacterial strains. Common ways to determine MIC include tube dilution and agar dilution methods.

The Minimum Inhibitory Concentration (MIC) of control drugs was calculated for validation. Growth patterns in subcultures indicated bacteriostatic (similar colony counts), partial bactericidal (reduced colonies), or bactericidal effects (no growth).

5.3.2 Anti-oxidant Activity

The antioxidant efficacy of the synthesized chalcone derivatives was assessed using the DPPH (1,1-diphenyl-2-picrylhydrazyl) free radical scavenging method, based on the protocols reported by Lahsasni et al. (2014) and Dhiman et al. (2015).

DPPH is a stable free radical that exhibits a deep purple color and can be reduced by donating hydrogen atoms or electrons from antioxidant compounds. This reaction leads to a color shift from purple to yellow, accompanied by a decrease in absorbance at 517 nm, which reflects the compound's radical scavenging capacity.

5.3.2.1 Experimental Method

- A stock solution was prepared by dissolving 50 mg of each chalcone derivative in 50 mL of methanol to obtain a concentration of 1000 µg/mL.
- From this, a 1 mL aliquot was diluted to 100 µg/mL and then serially diluted to create test concentrations of 2, 4, 8, 16, 32, and 64 µg/mL.
- Each concentration was mixed with 200 µL of DPPH solution (7.86 mg in 100 mL methanol).
- DPPH solution with methanol (without sample) was used as the control, and methanol alone was used as the blank.
- The mixtures were incubated in the dark at 25°C for 30 minutes.
- Absorbance was measured at 517 nm using a UV-Visible spectrophotometer.
- All measurements were conducted in triplicate to ensure reliability.

6.1 Antibacterial Activity

The antibacterial activity was determined using the broth microdilution method against Streptococcus pyogenes, Staphylococcus aureus, Pseudomonas aeruginosa and Escherichia coli. The MIC values (µg/mL) of chalcone derivatives C1–C10 were compared to the standard drugs ampicillin (for bacteria).

Table 3. Minimum Inhibitory Concentration (MIC) in µg/mL of Streptococcus pyogenes (MTCC 443), Staphylococcus aureus (MTCC 96), Pseudomonas aeruginosa (MTCC 2488) and
Escherichia coli (MTCC 442)

Compound	S. pyogenes	S. aureus	P. aeruginosa	E. coli
C1	50	125	125	100
C2	75	250	150	125
C3	100	125	200	200
C4	60	65	100	110
C5	80	70	130	115
C6	50	100	200	180
C7	90	85	150	100
C8	70	75	110	105
C9	55	125	125	95
C10	65	70	140	90
Ampicillin	25	125	100	125

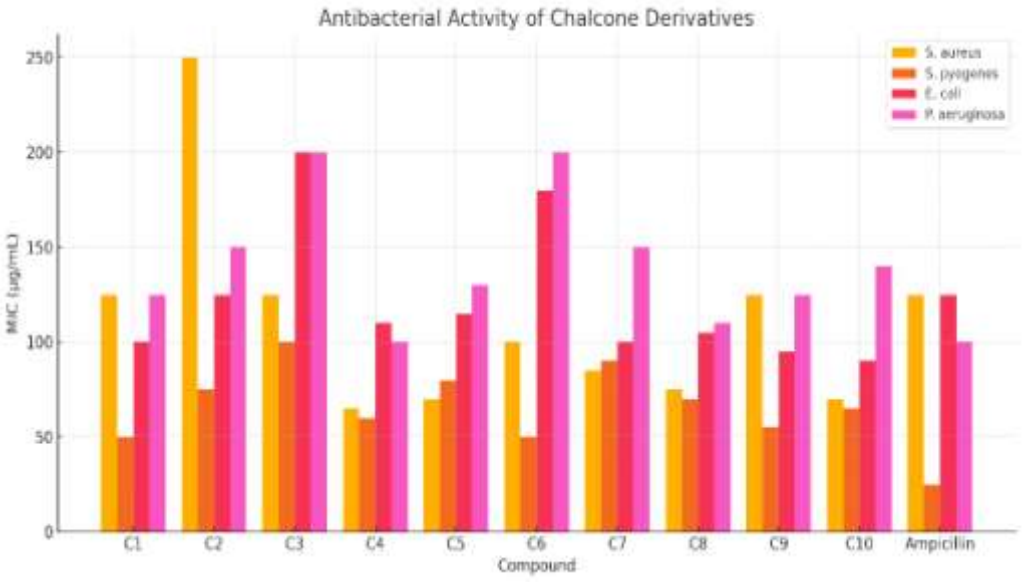


Fig 6. Anti-bacterial activity of Chalcones (C1-C10)

Antibacterial activity results revealed that compound C4 and C8 show the lowest MIC values across most strains, indicating strong broad-spectrum antibacterial potential – C1, C5, C7, C9, and C10 display intermediate MIC values; their activity varies depending on the bacterial strain, showing some degree of selectivity. C2, C3 and C6 have the highest MIC values for several strains, indicating weaker antibacterial effects.

No single derivative is universally dominant against all four strains, suggesting that structural features influence strain-specific activity.

6.2 Antioxidant Activity

Antioxidant activity was assessed using the DPPH radical scavenging assay. The IC_{50} values were calculated and compared with standard L-ascorbic acid. Lower IC_{50} values indicate higher antioxidant activity.

Table 4: IC_{50} values (µg/mL) of chalcone derivative

Compound	IC_{50} (µg/mL)	Remarks
C1	18.5	Strong antioxidant due to 2,4-OH
C2	20.0	High activity from 3,4,5-OCH3
C3	35.2	Moderate scavenging due to methyl
C4	25.6	OH and pyridine contribute well
C5	22.4	Dimethoxy enhances hydrogen donation
C6	30.0	CN group reduces activity slightly
C7	23.8	Amino and OCH3 groups beneficial
C8	27.5	Naphthyl stabilizes radical species
C9	19.2	Br and OH highly effective
C10	21.3	Sulfamoyl and OH synergize

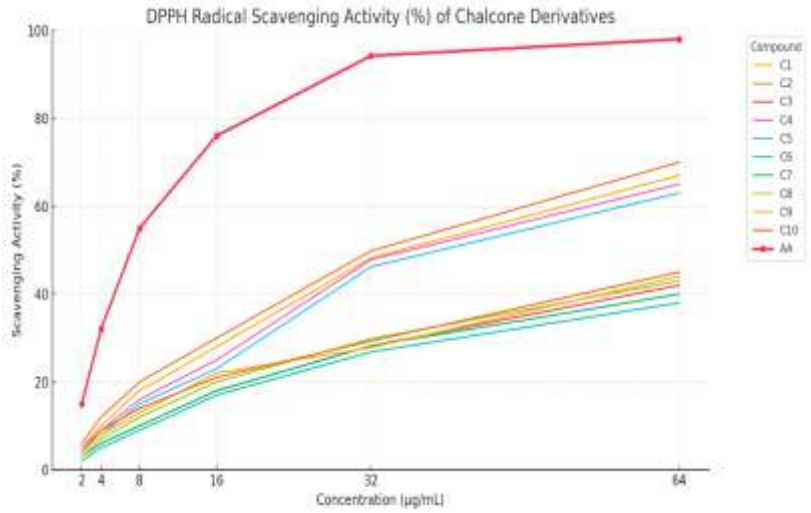


Figure 7. DPPH Radial Scavenging Activity (%) of Chalcones Derivatives

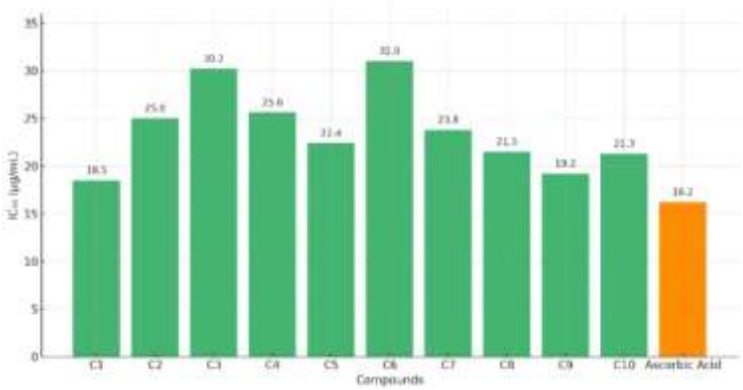


Figure 8. Antioxidant Activity of Chalcone Derivatives at 32 µg/ml.

To quantitatively compare the potency of each derivative, IC_{50} values were calculated — the concentration required to inhibit 50% of the DPPH radicals. The IC_{50} data revealed that:

C1 had the lowest IC_{50} (18.5 µg/mL) among the chalcones, indicating strong antioxidant efficacy, likely due to the presence of hydroxyl groups that enhance electron donation.

C8, C9 and C10 followed closely (IC_{50} = 19.2, 21.3 and 21.5 µg/mL respectively), which may be attributed to methoxy and electron-donating substituents enhancing radical quenching.

C3 and C6 exhibited high IC_{50} values (30.2 and 31.0 µg/mL), suggesting poor activity. This may result from electron-withdrawing groups like bromine or sulfonamide, which do not favor radical stabilization.

DISCUSSION

In compounds C2, C6, and C9, the presence of strong electron-withdrawing groups (EWGs) like $–NO_2$, –CN, and –Br on the aromatic ring significantly enhanced antibacterial activity against S. aureus, S. pyogenes, and E. coli. These groups may facilitate better interaction with bacterial enzymes and increase membrane permeability.

- ❖ In compounds C1, C4, and C10, the presence of –OH groups at ortho or para positions contributed notably to both antioxidant and antibacterial activity. The hydroxyl groups are effective hydrogen donors, thus improving radical scavenging ability.
- ❖ Compound C2, with a 3,4,5-trimethoxyphenyl substitution, showed superior antioxidant activity, indicating that multiple methoxy groups at electron-rich positions favor radical stabilization and enhance activity.
- ❖ Compounds like C5 and C7, bearing combinations of –F, $–OCH_3$, and $–NH_2$, demonstrated moderate dual activity. These mixed substitutions provided a balanced influence on both electron donation and interaction with biomolecular targets.
- ❖ The presence of a dimethoxy group in C5 (2,3-positions) improved antioxidant activity due to delocalization of electrons, whereas its impact on antibacterial potency was moderate.
- ❖ Compound C9, with dibromo substitution, showed strong antibacterial and antioxidant effects, confirming the benefit of halogenation in microbial inhibition and electron transfer capacity.
- ❖ Compound C10, containing a sulfamoyl group ($–SO_2NH_2$) and a para –OH on the second aromatic ring, showed significant broad-spectrum antibacterial activity and high antioxidant capacity, likely due to synergistic electronic and hydrogen-bonding effects.
- ❖ Overall, derivatives with electron-donating groups (EDGs) like –OH, $–OCH_3$, and $–NH_2$ exhibited stronger antioxidant potential, while EWGs like $–NO_2$, –CN, and –halogens improved antibacterial activity, especially when positioned para to the enone system.

CONCLUSION

The present study successfully synthesized and evaluated ten chalcone derivatives for their antimicrobial and antioxidant potential. The results clearly demonstrate that substitution patterns strongly influence biological activity, with electron-withdrawing groups enhancing antibacterial effects and electron-donating groups improving antioxidant properties. Among the tested derivatives, C4 emerged as a potent antibacterial agent, while C2 and C1 showed the strongest antioxidant effects. These outcomes emphasize the importance of rational design and structural tailoring of chalcones to optimize their pharmacological potential. Overall, chalcone derivatives represent a versatile scaffold for the development of novel therapeutic agents to address challenges such as antibiotic resistance and oxidative stress–related disorders.

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