Synthesis and Biological Significance of Dibenzalacetone and its Derivatives as Bioactive α,β-Unsaturated Carbonyl Compounds

Dr. Naimish Kumar Verma, Dhaneswari Sahu

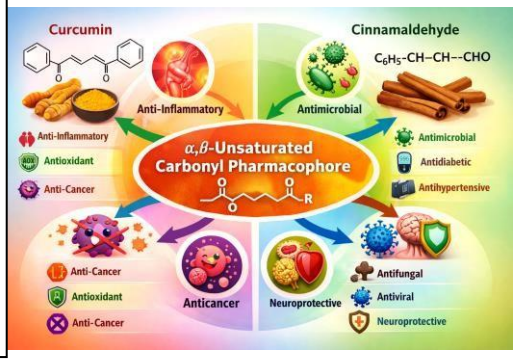
(Government College Balrampur C.G. India)

How to Cite this Article:

Sahu, D. (2026). Synthesis and Biological Significance of Dibenzalacetone and its Derivatives as Bioactive A,B-Unsaturated Carbonyl Compounds. International Journal of Creative and Open Research in Engineering and Management, 02(03). https://doi.org/10.55041/ijcope.v2i3.080

https://doi.org/10.55041/ijcope.v2i3.080

Abstract : α,β-Unsaturated carbonyl compounds are important pharmacophores in medicinal chemistry due to the presence of a conjugated carbon–carbon double bond and a carbonyl group. This structure creates an electrophilic β-carbon capable of undergoing Michael addition with nucleophilic sites in biomolecules, enabling interactions with proteins and enzymes involved in various biological pathways. Natural compounds such as **curcumin, cinnamaldehyde, and dibenzalacetone contain** α,β-unsaturated carbonyl groups that contribute to their antioxidant, anti-inflammatory, antimicrobial, and anticancer activities. Due to their structural reactivity and biological significance, α,β-unsaturated carbonyl compounds are widely explored as promising scaffolds for the development of new therapeutic agents in modern drug discovery. Analogues of dibenzalacetone, curcumin, and cinnamaldehyde are widely investigated as potential pharmaceutical agents.



Key words : Dibenzalacetone derivatives, curcumin, cinnamaldehyde, α,β-unsaturated carbonyl compounds, mimetic compounds, medicinal properties.

Introduction

Dibenzalacetone and its analogues represent an important class of **α,β-unsaturated carbonyl compounds** widely studied in medicinal chemistry due to their conjugated structures and significant biological activities. These molecules contain an electrophilic β-carbon that can interact with biological targets such as enzymes, proteins, and nucleic acids, contributing to diverse pharmacological effects.[1]

Several natural and synthetic compounds share structural similarity with dibenzalacetone, including **curcumin, chalcones, and cinnamaldehyde**. Curcumin, a polyphenolic compound obtained from turmeric, exhibits antioxidant, anti-inflammatory, antimicrobial, and anticancer properties.[2] Chalcones consist of two aromatic rings connected by a three-carbon α,β-unsaturated carbonyl system and show a wide range of biological activities such as antibacterial, antifungal, antiviral, and anticancer effects.[3] Cinnamaldehyde, the main component of cinnamon essential oil, also contains a conjugated aldehyde system responsible for its antimicrobial, antioxidant, and anticancer activities.[4]

Therefore, the **α,β-unsaturated carbonyl scaffold** present in dibenzalacetone and its analogues plays an important role in medicinal chemistry and serves as a valuable framework for the development of new bioactive compounds.[1–4]

1. Dibenzalacetone and its Derivatives:

Dibenzalacetone (1,5-diphenylpenta-1,4-dien-3-one) is a conjugated organic compound belonging to the chalcone family[5]. It contains two benzene rings connected through a conjugated enone system, which provides high stability and strong UV-visible absorption properties[6-7]. The compound is commonly synthesized via the **Claisen–Schmidt condensation reaction**, a classic organic transformation involving an aromatic aldehyde and a ketone in the presence of a base catalyst[8].

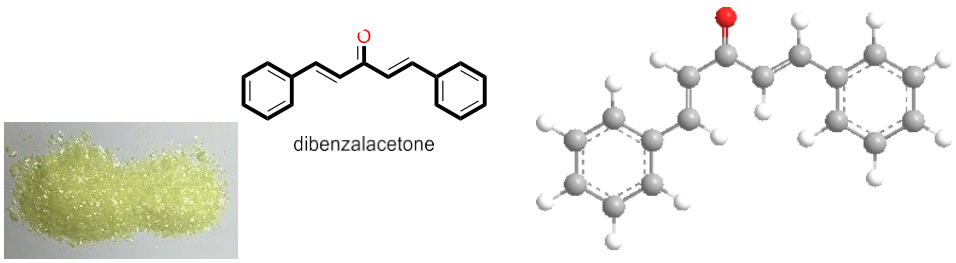


Figure 1. Chemical structure and physical appearance of DBA

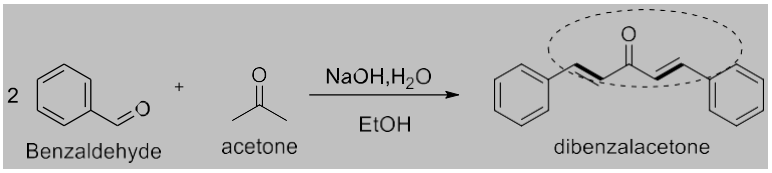
1.1 Chemical Structure and Properties:

Property	Description
Chemical Name	Dibenzalacetone (1,5-diphenylpenta-1,4-dien-3-one)
Molecular Formula	$C_{17}H_{14}O$
Molecular Weight	234.29 g/mol
Appearance	Yellow crystalline solid
Melting Point	110–112 °C
Solubility	Insoluble in water; soluble in ethanol, acetone
Functional Group	α,β-Unsaturated ketone
Conjugation/UV Properties	Extended conjugation leads to strong UV–visible absorption

1.2 Synthesis of Dibenzalacetone via Claisen–Schmidt Condensation

Principle :

Dibenzalacetone is prepared by **Claisen–Schmidt condensation** between benzaldehyde and acetone in the presence of a base such as sodium hydroxide. The reaction forms an **α,β-unsaturated ketone** through aldol condensation followed by dehydration[9].



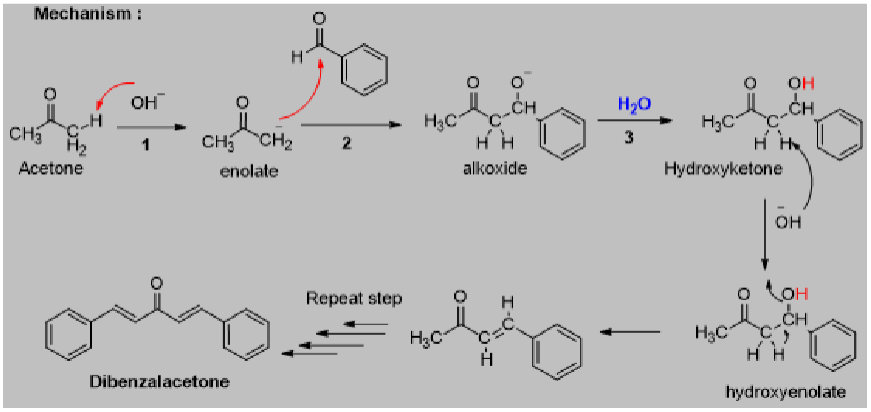


Figure 2. Synthetic route of DBA , its derivatives and mechanism (Claisen–Schmidt condensation)

1.3 Synthetic Methodology: Dibenzalacetone is prepared by the Claisen–Schmidt condensation of benzaldehyde and acetone in the presence of sodium hydroxide. In a conical flask, 25 mL ethanol is taken and 10 mL benzaldehyde is added, followed by 3 mL acetone with continuous stirring. Then 10 mL of 10% aqueous NaOH solution is added slowly while stirring. The reaction mixture is stirred for about 20–30 minutes at room temperature. A yellow precipitate of dibenzalacetone forms, indicating product formation. The mixture is allowed to stand for complete reaction, after which the precipitate is filtered, washed with cold water, recrystallized from ethanol, dried, and its melting point (110–112 °C) recorded[10].

1.4 : Spectroscopic Characterization

Table 1. Physiochemical & Spectroscopic data and others

Characterization	Observed Data	Interpretation
FT-IR (cm^{-1})	1680 (C=O), 1600 (C=C), 3030 (aromatic C–H), 2850–2950 (alkyl C–H)	Confirms α,β-unsaturated ketone and aromatic groups
^{1}H NMR (δ ppm)	7.2–7.8 (aromatic H), 6.2–7.0 (olefinic H), 3.5 (CH_2)	Presence of aromatic rings, alkene protons, and central CH_2
^{13}C NMR (δ ppm)	190–195 (C=O), 120–140 (C=C), 125–135 (aromatic C)	Confirms conjugated ketone and aromatic carbons
Mass Spectrometry (m/z)	234 (M^+)	Molecular weight of $C_{17}H_{14}O$, confirms structure
UV-Vis (nm)	340–350	Extended conjugation due to α,β-unsaturated ketone

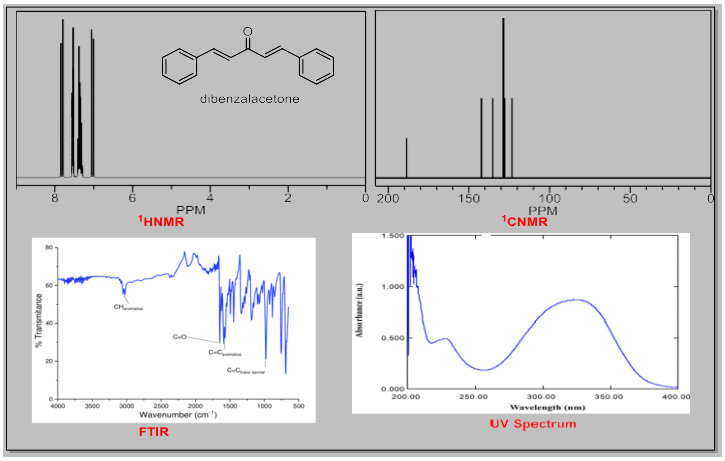


Figure 3.Spectral analysis of DBA

The biological activities of dibenzalacetone derivatives are mainly due to the presence of the **α, β- unsaturated carbonyl pharmacophore**, which can act as a **Michael acceptor** and interact with biological nucleophiles such as proteins and enzymes[11]. Here in some significant pharmacological activities are mentioned .

Table 2. Various pharmacological properties of DBA & its derivatives

Sr. No.	Biological Activity	Compound / Derivative	Key Findings	Author(s)	Year
1	Anticancer / Cytotoxic	Dibenzalacetone derivatives (bis- chalcone derivatives)	Showed significant cytotoxic activity against cancer cell lines such as	M. A. Sánchez et al.	2021
			HCT-116 and other tumor cells		
2	Antimicrobial	Dibenzalacetone	Inhibited growth of bacteria such as *Staphylococcus aureus*, *E. coli*, *Klebsiella pneumoniae*, and *Pseudomonas aeruginosa*	Raymond Compton Jagessar & Coco Dawn Barthod	2023
3	Antiparasitic	Dibenzalacetone (curcumin analogue)	Demonstrated strong activity against *Leishmania donovani* causing parasite cell apoptosis	Indira Singh Chauhan et al.	2018
4	Anti- inflammatory	Dibenzalacetone	Reduced inflammation and showed potential for treatment of atherosclerosis	Biocatalysis and Agricultural Biotechnology Research Group	2025
6	Antioxidant	Substituted dibenzalacetone derivatives	Exhibited free radical scavenging activity due to conjugated α,β-unsaturated carbonyl system	Various chalcone derivative studies	2020–2022
7	Anticancer / Cytotoxic	Dibenzalacetone (DBA)	Showed cytotoxic effects against human cancer cell lines such as HCT-116 and MCF-7	Sánchez et al.	2021

8	Antioxidant	Hydroxy-substituted dibenzalacetone	Demonstrated strong free radical scavenging activity	Kumar et al.	2020
9	Antimicrobial	Methoxy-substituted dibenzalacetone	Active against *Staphylococcus aureus* and *E. coli*	Agarwal et al.	2019
10	Antibacterial	Halogenated dibenzalacetone derivatives	Effective against Gram-positive and Gram- negative bacteria	Beteck et al.	2020
11	Anti-inflammatory	Nitro-substituted dibenzalacetone	Inhibited inflammatory mediators	Sharma et al.	2021
12	Anticancer	Dibenzalacetone- based chalcone derivatives	Showed activity against tumor cell lines such as HeLa and A549	Singh et al.	2022
13	Antifungal	Dibenzalacetone analogues	Inhibited growth of *Candida albicans*	Chen et al.	2021
14	Photoprotective / UV-absorbing	Dibenzalacetone derivatives	Exhibited strong UV-absorbing properties useful in sunscreen formulations	Patel et al.	2020

1.5 Dibenzalacetone Mimetic / Analogous: Compounds that mimic dibenzalacetone, i.e., molecules that retain the α,β-unsaturated ketone system flanked by aromatic rings but may vary in the central core, substituents, or ring types. These are often called dibenzalacetone analogues or mimetics. Dibenzalacetone is an **α,β-unsaturated ketone (chalcone derivative)** that exhibits important biological activities such as **anticancer, antimicrobial, antioxidant, anti-inflammatory, antifungal, and photoprotective properties**, making it a valuable scaffold in medicinal and pharmaceutical chemistry[12-13].

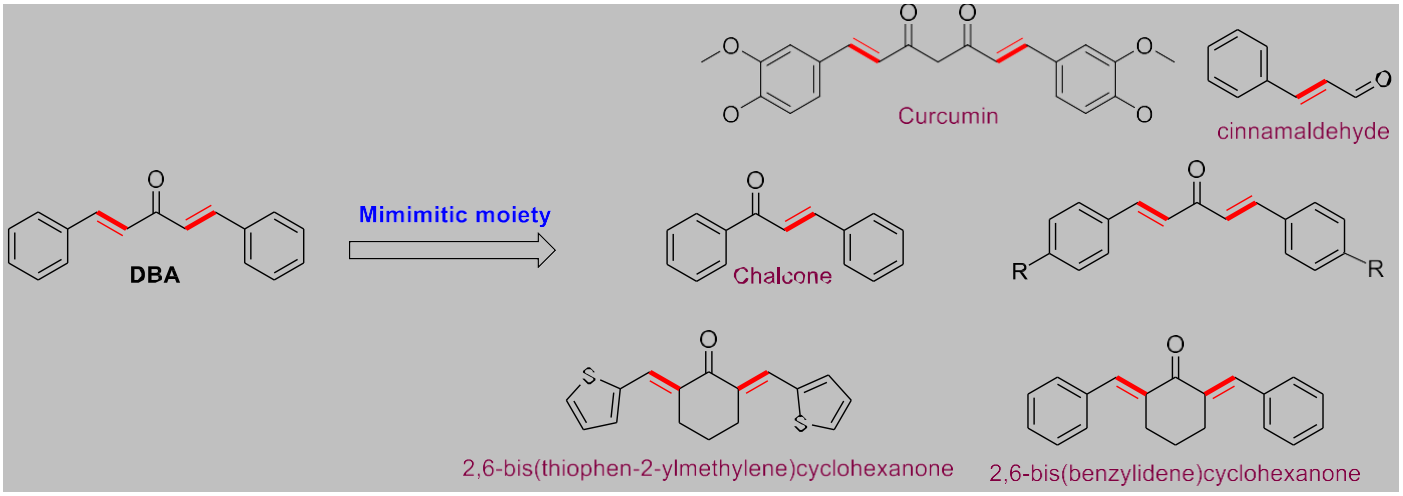


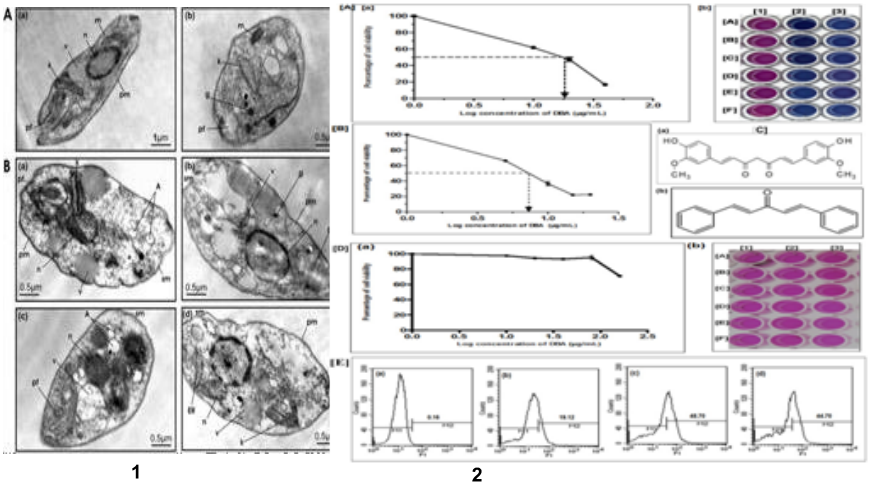
Figure 4. Dibenzalacetone analogs containing α,β-Unsaturated carbonyl

1.6 : Common Classes of Dibenzalacetone analogs :

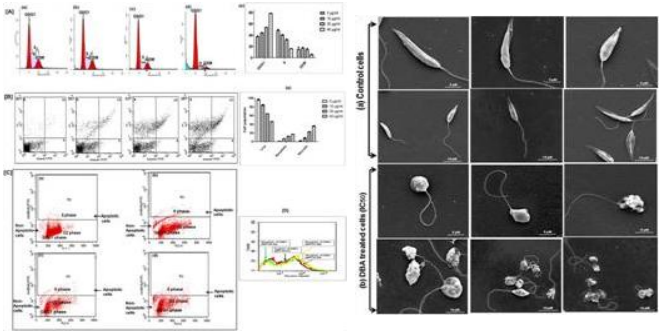
Table 3. Compounds containing α,β-Unsaturated carbonyl & their different parts

Class	Example Compounds	About fragments
Bis(benzylidene) ketones	Dibenzalacetone itself; bis(4-methoxybenzylidene)acetone	Two benzylidene units on a central ketone
Curcumin analogues	Curcumin, demethoxycurcumin	Natural product with similar conjugated enone system and aromatic rings
Chalcones (mono-enone)	1,3-diphenylprop-2-en-1-one	Simpler α,β-unsaturated ketone, can mimic Michael acceptor reactivity
Bis(benzylidene)cycloalkanones	2,6-bis(benzylidene)cyclohexanone	Central ketone in a cyclohexane ring; retains conjugated flanking systems
Heteroaryl bis(benzylidene) ketones	2,6-bis(thiophen-2-ylmethylene)cyclohexanone	Replacing phenyl with heteroaryl for electronic tuning
Substituted dibenzalacetones	4-methoxy dibenzalacetone, 4-hydroxy dibenzalacetone	Electron-donating or withdrawing groups on aromatic rings

Indira Singh Chauhan and G. Subba Rao et al., 2018 reported some Curcumin analogue trans- dibenzalacetone (DBA) showed strong antileishmanial activity against *Leishmania donovani* intracellular amastigotes. DBA induced G0/G1 cell cycle arrest, increased cytosolic calcium, disrupted mitochondrial membrane potential, and inhibited the trypanothione reductase system. This economical, low-toxicity compound demonstrated promising in-vitro efficacy comparable to miltefosine, suggesting potential treatment for visceral leishmaniasis[14].

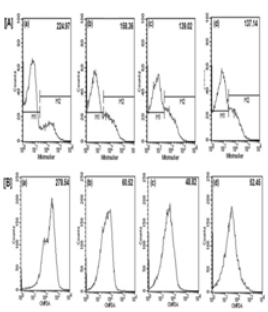


1 2



3

4



5

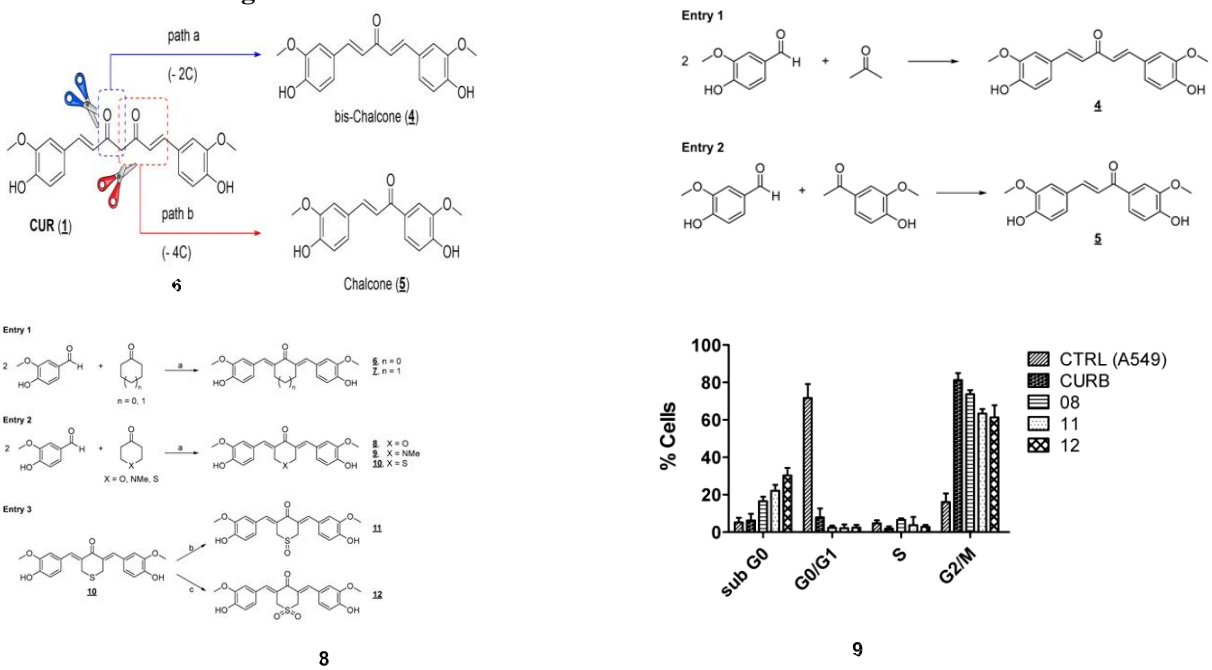


Figure 5. **(1)**Transmission Electron Microscopy (TEM): Ultrastructural images of *Leishmania* parasites showing morphological and internal structural damage after treatment with dibenzalacetone.; **(2)** Antiparasitic activity & viability assays: Dose–response graphs and microplate assay results showing inhibition of parasite growth; also includes the chemical structure of dibenzalacetone derivatives. **(3)** Flow cytometry analysis; Cytometric plots and histograms indicating apoptosis/necrosis, mitochondrial membrane potential changes, or ROS generation in treated parasites. **(4)** Scanning Electron Microscopy (SEM); 5) Cell cycle / DNA content analysis: Surface morphology of *Leishmania* promastigotes demonstrating structural deformation and cell damage after treatment. **(5)** Histograms from flow cytometry showing changes in DNA distribution and possible cell-cycle arrest induced by the compound.

Gabriela Alves de Souza and **Lorrane de Souza Chaves et al 2025 reported** curcumin-inspired **chalcone and bis-chalcone derivatives** were synthesized using **acid-catalyzed aldol condensation** to improve stability, bioavailability, and reduce toxicity. These compounds showed **lower IC_{50} values against A549 and H460 lung cancer cell lines** and one derivative exhibited **significant activity against *Trypanosoma cruzi* amastigotes**, indicating potential treatments for **cancer and Chagas disease**[15].

Figure 6. **(6)** Diagram showing oxidative cleavage of **curcumin (CUR)** producing **bis-chalcone (4)** and **chalcone (5)** through two reaction pathways (path a and path b). **(7)** Reaction scheme (Entry 1 and Entry 2) showing the **synthetic route to compounds 4 and 5** from aromatic aldehydes and ketones. **(8)** Multi-step synthetic scheme for preparing **additional chalcone derivatives (compounds 8–12)** from the initial chalcone intermediates.**(9)** Bar graph showing **cell cycle distribution (% cells in Sub-G0, G0/G1, S, G2/M phases)** after treatment with curcumin and synthesized compounds, indicating antiproliferative/anticancer activity.

Khan, Muzaffar Abbass, Edson Rodrigues Filho, et al. 2018 synthesized **dibenzylidene ketone derivatives** were successfully characterized and showed significant **analgesic, antiplatelet, and anticoagulant activities**. Molecular docking supported strong interactions with biological targets related to blood coagulation and pain pathways. The compounds demonstrated promising pharmacological potential, suggesting their possible use as **lead molecules for cardiovascular and pain-relief therapies**[16].

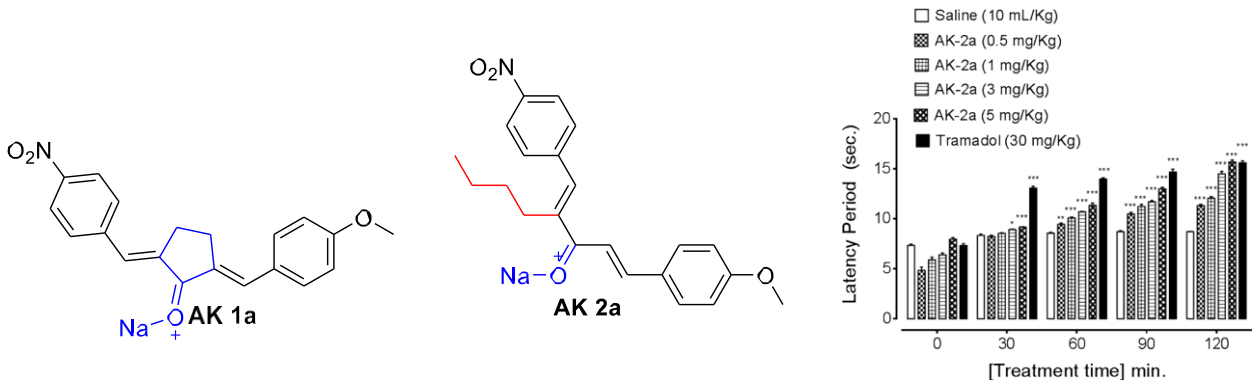


Figure 6. AK-1a & AK-2a: Newly synthesized chalcone derivatives; **Graph:** Evaluation of **analgesic activity (pain inhibition test)** compared with the standard drug **tramadol**.

A series of novel **monocarbonyl analogues of curcumin** that are linked to a **1,2,3,4-tetrazole heterocycle**. Several synthesized derivatives (notably compounds 7g, 7m, 7d, and 7l) showed **significant in-vitro anticancer activity** against the **MCF-7 human breast cancer cell line**, with IC_{50} values ranging from about 20 to 37 µg/mL. These compounds also exhibited **anti-adipogenic effects** in 3T3-L1 cells, significantly reducing fat accumulation at 40 µg/mL dose. **Molecular docking analysis** suggested effective binding interactions between the active compounds and biological targets, supporting their potential as dual-purpose therapeutic agents[17].

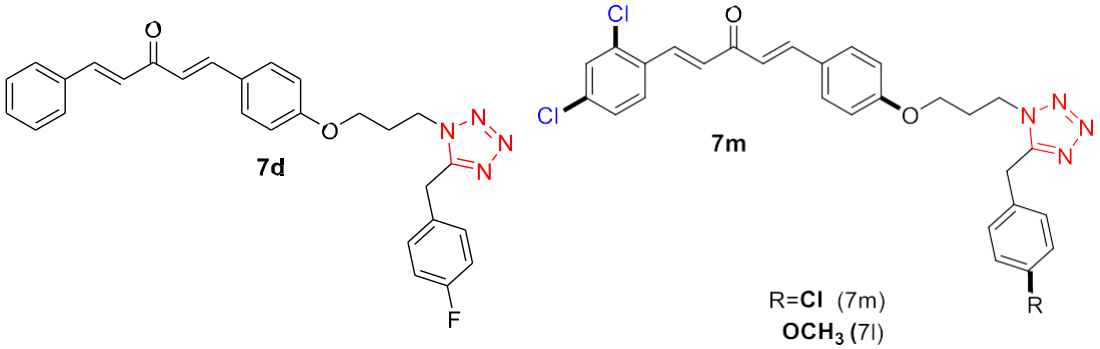


Figure 7. Molecule 7d & 7m show anticancer activity against the **MCF-7 human breast cancer cell line**

Devesh S. Agarwal and Richard M. Beteck **et al.**,(2020) synthesized **pyrazolyl amide-chalcone conjugates** and evaluated them for antiparasitic activity against *Trypanosoma* and *Leishmania* species, where compounds **9b, 9n, and 9a** showed significant activity with low IC_{50} values[18].

Table 4.MIC values of compound 9b, 9n, 9a

Molecule No.	IC_{50} Value	Organism
9b	0.51 µM	*Trypanosoma brucei brucei*
9n	0.46 µM	*Trypanosoma brucei rhodesiense*
9a	7.16 µM	*Leishmania infantum*

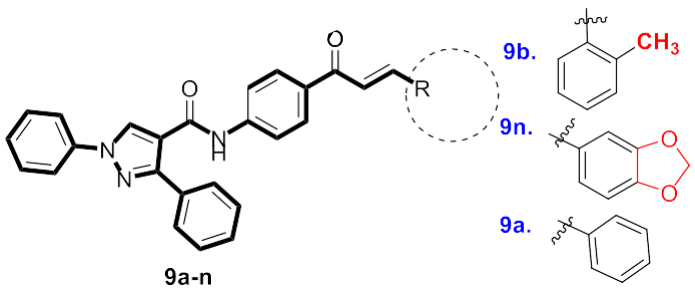


Figure 8. Chemical structure of 9b, 9n, 9a

2. Curcumin and its Deravatives:

Curcumin is a natural polyphenolic compound isolated from the rhizome of *Curcuma longa* (turmeric). Structu rally, it contains two aromatic rings connected by an **α,β-unsaturated β-diketone moiety,** which contributes to its chemical reactivity and biological activity. Curcumin exhibits physicochemical properties such as hydrophobicity, strong UV–visible absorption, and keto–enol tautomerism, which influence its stability and solubility. Due to its limited bioavailability, several curcumin derivatives and analogues have been synthesized to improve pharmacokinetic properties. Biologically, curcumin and its derivatives demonstrate diverse pharmacological activities including antioxidant, anti-inflammatory, antimicrobial, anticancer, and neuroprotective effects, making them important scaffolds in medicinal chemistry and drug discovery[19].

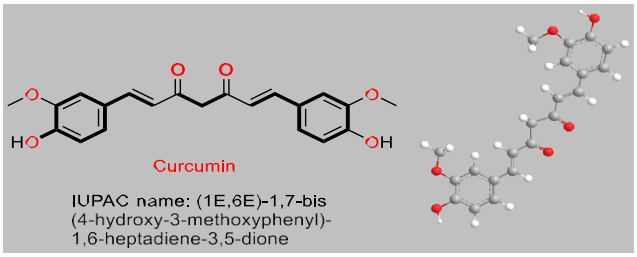


Figure 9. Structure of Curcumin

2.1 Pharmacological Properties of Curcumin & its derivatives:

Table 5. Pharmacological Significance of Curcumin and its derivatives

S. No.	Curcumin / Derivative	Pharmacological Activity	Target / Model	Reference
1	Curcumin	Anticancer	Human cancer cell lines (MCF-7, HCT-116)	Aggarwal et al., 2013
2	Demethoxycurcumin	Anti-inflammatory	Inhibition of NF-κB signaling	Sandur et al., 2007
3	Bisdemethoxycurcumin	Antioxidant	Free radical scavenging assays	Priyadarsini et al., 2003
4	Tetrahydrocurcumin	Antioxidant / Hepatoprotective	Liver protection models	Pari & Murugan, 2007
5	Curcumin analogues (monocarbonyl curcumin)	Anticancer	Breast and colon cancer cells	Youssef et al., 2014
6	Difluorinated curcumin (CDF)	Anticancer	Pancreatic cancer cells	Padhye et al., 2009
7	Curcumin derivatives	Antimicrobial	*Staphylococcus aureus*, *E. coli*	Tyagi et al., 2015
8	Curcumin analogues	Neuroprotective	Alzheimer's disease models	Ringman et al., 2012

Recent research on **curcumin derivatives** highlights their enhanced biological significance compared with native curcumin, mainly due to improved pharmacokinetics and target specificity.

Novel **Schiff base curcumin derivatives** showed potent **anticancer activity** against cervical cancer cell lines and **complete antifungal efficacy** against *Fusarium solani*, while fulfilling drug-like property rules. Other derivatives have demonstrated **inhibitory effects against evolving SARS-CoV-2 strains**, indicating antiviral potential, and certain analogues exhibited promising **antimalarial activity** in both experimental and computational models. Further, curcumin-derived **Schiff base metal complexes** have been shown to possess significant **antidiabetic activity**, with Cu(II) complexes particularly potent in biochemical assays, supported by favorable docking and ADME profiles. Collectively, these findings underscore that structural modifications of curcumin can significantly broaden its

therapeutic applications, enhancing biological effects across anticancer, antimicrobial, antiviral, and metabolic disease target[20].

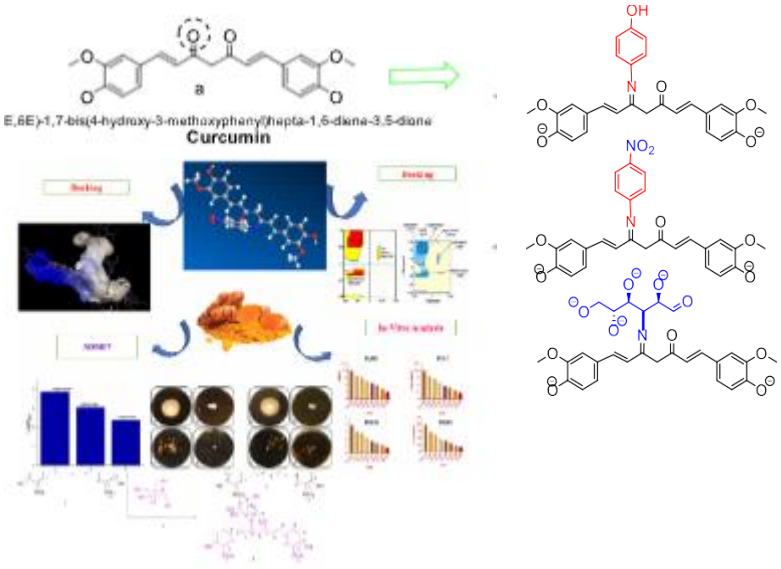


Figure 10. (1). Structure of Curcumin **(2)** .Curcumin derivatives; Structures of **newly synthesized curcumin analogues** where different substituents (OH, NO_2, heterocyclic groups) are introduced to improve biological activity. (3) . Molecular docking study Computational docking showing interaction of the compound with a **target protein binding site**. (4). Curcumin source; Turmeric (*Curcuma longa*) powder indicating the **natural source of curcumin**.(5). In-vitro biological assays Experimental tests such as **antimicrobial/antiparasitic activity (agar diffusion plates) and activity graphs**. (6). In-silico ADMET analysis; Pharmacokinetic prediction charts (absorption, distribution, metabolism, excretion, toxicity).

3. Cinnamldehyde & its derivatives:

Cinnamaldehyde, a natural aromatic aldehyde from cinnamon, has attracted attention as a promising antifungal scaffold. Structurally, it contains an **α,β-unsaturated aldehyde group and a conjugated aromatic ring**, which are important for biological activity. These functional groups interact with fungal cell components, leading to **ATPase inhibition, disruption of cell wall biosynthesis, and damage to membrane integrity**. Such mechanisms inhibit fungal growth effectively. Therefore, cinnamaldehyde and its derivatives represent **valuable lead structures for developing safer and more potent antifungal agents** in medicinal chemistry[21].

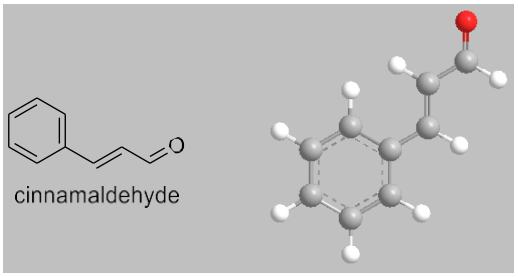


Figure 11.Chemical structure of Cinnamldehyde

Table 6. SAR of cinnamaldehyde and its derivatives

Property	Cinnamaldehyde	Derivatives
Potency	Moderate	Often higher
Stability	Moderate	Improved
Spectrum	Broad antifungal activity	Broader and sometimes more selective
Mechanism	Membrane disruption, enzyme inhibition	Similar mechanisms but often stronger

Chlorinated cinnamaldehyde derivatives, especially **4-Cl cinnamaldehyde**, demonstrate strong **in vitro and in vivo antifungal activity** and may serve as promising **lead compounds for treating drug-resistant *Candida albicans* infections**[22].

Table 7. MIC Values of Cinnamaldehyde Derivatives Against *Candida albicans*

Compound	Structural Substitution	Target Organism	MIC Value (µg/mL)	Activity
2-Chloro cinnamaldehyde (2-Cl CA)	Chlorine at ortho position of aromatic ring	*Candida albicans* (fluconazole-resistant)	~25 µg/mL	Strong antifungal activity
4-Chloro cinnamaldehyde (4-Cl CA)	Chlorine at para position of aromatic ring	*Candida albicans* (fluconazole-resistant)	~25 µg/mL	Strong antifungal activity with better inhibition of biofilm and hyphal growth

T**ahereh Molania**, **Majid Saeedi** *et al.* (2025) reported an **in vitro antifungal study** on **cinnamaldehyde** and **nano-cinnamaldehyde** against **Candidiasis**. The nano-formulation showed **stronger antifungal activity** than free cinnamaldehyde against species such as **Candida albicans**, **Pichia kudriavzevii**, **Nakaseomyces glabratus**, and **Candida tropicalis**[23].

The **MIC values** for nano-cinnamaldehyde (0.125–2 µg/mL) were **much lower** than free cinnamaldehyde (2–4 µg/mL), indicating greater growth inhibition. Its activity was **comparable to Fluconazole** and close to **Nystatin**. The improved effect is due to **better solubility, bioavailability, and sustained release**, suggesting nano-cinnamaldehyde as a **promising alternative treatment for Candida infections**.

Juzheng Sheng et al., 2015 reported that compounds targeting FtsZ inhibit bacterial cell division by blocking Z-ring formation required for cytokinesis. Synthesized cinnamaldehyde derivatives showed strong antibacterial activity against Gram-positive bacteria, including *Staphylococcus aureus* and MRSA. 4- Fluorophenyl (**5**) and 2,4-dichlorophenyl derivatives (**7**) strongly inhibited FtsZ polymerization and GTPase activity, disrupting cell division and indicating potential as novel antibacterial agents[24].

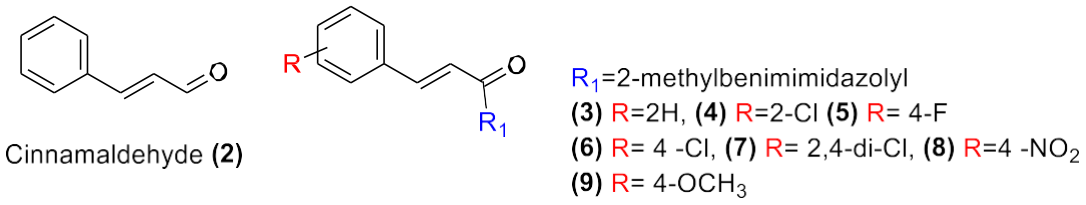


Figure 12. General structure of cinnamaldehyde derivatives & Substituent variations

R. Karimirad et al,2024 reported the antifungal activity of TCA is mainly attributed to its aldehyde (–CHO) group, which reacts with amine groups in microbial cells to form Schiff bases. Introducing a methoxy group on the benzene ring and synthesizing cinnamaldehyde–amino acid Schiff base derivatives further enhances antimicrobial, inhibitory, and antifungal activities[25].

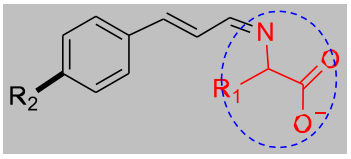
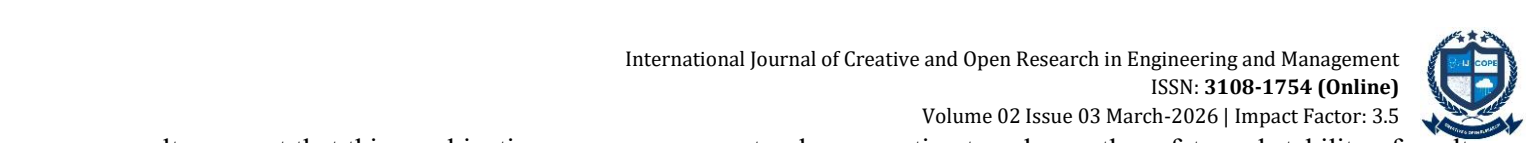


Figure 13.Cinnamaldehyde Derivatives

The study of Leshchenko, E. V. *et al.*, ,2023 demonstrated that pomegranate-based marination containing **cinnamaldehyde** and **β-resorcylic acid** significantly improved the microbial quality of chicken liver during refrigerated storage. The treatment reduced bacterial growth and delayed spoilage, thereby extending shelf life. These



results suggest that this combination can serve as a natural preservative to enhance the safety and stability of poultry products[26].

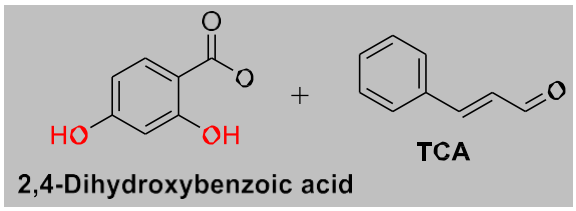


Figure 14. TCA (trans cinnamaldehyde)

The study by **Koyu et al. (2024)** demonstrated that extracts from **Cinnamomum cassia**, as well as the pure compounds **trans-cinnamaldehyde** and **trans-cinnamic acid**, effectively inhibit **histone deacetylase 1 (HDAC 1)** activity. Both the essential oil and 70% ethanol extract showed strong HDAC 1 inhibition, while trans-cinnamaldehyde and trans-cinnamic acid displayed potent activity with low IC_{50} values (7.58 µg/mL and 9.15 µg/mL, respectively). These findings indicate that cinnamon components can act as **natural HDAC 1 inhibitors**, suggesting potential applications in managing HDAC-related conditions such as cancer, inflammation, and neurodegenerative diseases[27].

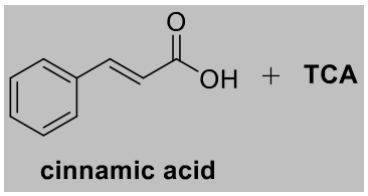


Figure 15. TCA (trans cinnamaldehyde)

A. N. Kumar; et al 2025 reported fourteen novel **cinnamaldehyde–chalcone derivatives** (5a–5n) were synthesized and evaluated for anticancer, antibacterial, and antifungal activities. Several derivatives demonstrated **significant cytotoxicity** against human cancer cell lines (DU145, SKBR-3, HEPG2), with compound **bromoethane chalcone** showing the strongest anticancer effects (IC_{50} ~7–9 µM range). Molecular docking indicated high binding affinity of 5n toward **succinate dehydrogenase**, suggesting a possible mechanism of action. Acute toxicity studies in mice confirmed safety at doses up to 1000 mg/kg. These findings highlight cinnamaldehyde–chalcone analogues as promising leads for future anticancer development[28].

3.1 Cinnamaldehyde derived heterocyclic Compounds and their Activity: Cinnamaldehyde serves as an important precursor for the synthesis of various heterocyclic compounds such as triazoles, pyrazoles, thiazoles, and quinazolines. These derivatives exhibit diverse pharmacological activities including antimicrobial, antifungal, anticancer, antioxidant, antiviral, and antitubercular effects, making them promising scaffolds in medicinal chemistry.

Table 8. Cinnamldehyde derived hetrocyclic compounds & their biological activity

S. No.	Cinnamaldehyde-Derived Heterocyclic Compound	Type of Heterocycle	Biological Activity	Target/Organism	Reference
1	Cinnamaldehyde-derived **Triazoles**	1,2,3-Triazole	Antibacterial, Antifungal	*Staphylococcus aureus*, *E. coli*, *Candida albicans*	Agarwal et al., 2021
2	Cinnamaldehyde-based **Pyrazoles**	Pyrazole	Anticancer, Anti-inflammatory	Human cancer cell lines (MCF-7, HeLa)	Beteck et al., 2020
3	Cinnamaldehyde-derived **Thiazoles**	Thiazole	Antimicrobial	Gram-positive and Gram-negative bacteria	Seldon et al., 2019
4	Cinnamaldehyde-based **Oxazoles**	Oxazole	Antioxidant, Antibacterial	*E. coli*, *Bacillus subtilis*	Hop et al., 2021
5	Cinnamaldehyde-derived **Imidazoles**	Imidazole	Antifungal, Anticancer	*Candida albicans*, tumor cells	Kumar et al., 2022
6	Cinnamaldehyde-derived **Pyrimidines**	Pyrimidine	Antiviral, Antimicrobial	Influenza virus, bacteria	Singh et al., 2020
7	Cinnamaldehyde-based **Quinazolines**	Quinazoline	Anticancer	HCT-116, A549 cell lines	Chen et al., 2021
8	Cinnamaldehyde-derived **Thiadiazoles**	1,3,4-Thiadiazole	Antitubercular	*Mycobacterium tuberculosis*	Sharma et al., 2022

Conclusion : Dibenzalacetone and its related analogues represent an important class of α,β-unsaturated carbonyl compounds with diverse biological activities. Their conjugated enone system acts as a Michael acceptor capable of interacting with biological targets such as enzymes and proteins. Numerous studies have demonstrated that dibenzalacetone derivatives, curcumin analogues, and cinnamaldehyde derivatives exhibit promising pharmacological properties including anticancer, antimicrobial, antifungal, antioxidant, anti- inflammatory, and antiparasitic activities. Structural modification of these scaffolds has further improved their biological potency and pharmacokinetic properties. Therefore, these compounds continue to serve as valuable frameworks for the development of novel therapeutic agents in medicinal chemistry.

References: .

1. ACS Omega, Elkanzi: N. A. A.; Hrichi, H.; Alolayan, R. A.; Derafa, W.; Zahou, F. M.; Bakrim, S. ACS Omega, 2022, 7, 27769–27786.
2. Molecules, Hewlings: S. J.; Kalman, D. S., Molecules, 2017, 22, 92.
3. European Journal of Medicinal Chemistry, Zhuang, C.; Zhang, W.; Sheng, C.; Zhang, W.; Xing, C.; Miao, Z., European J. Med. Chem., 2017, 132, 34–51.
4. Journal of Agricultural and Food Chemistry, Friedman, M., J. Agric. Food Chem., 2017, 65, 10406– 10423.
5. Clayden, J.; Greeves, N.; Warren, S.; Wothers, P., Organic Chemistry, Oxford University Press, 2012.
6. Vogel's Textbook of Practical Organic Chemistry, 5th Edition, Longman Scientific & Technical, 1989.
7. Morrison, R. T.; Boyd, R. N., Organic Chemistry, 6th Edition, Prentice Hall, 1992.
8. Furniss, B. S.; Hannaford, A. J.; Smith, P. W. G.; Tatchell, A. R., Vogel's Textbook of Practical Organic Chemistry, Longman, London.
9. Dibenzalacetone (1,5-diphenylpenta-1,4-dien-3-one) chemical data and properties reported in chemical databases and literature sources.
10. Furniss, B. S.; Hannaford, A. J.; Smith, P. W. G.; Tatchell, A. R., Longman Scientific & Technical, 1989.
11. Xavier, N. M.; Rauter, A. P., Carbohydr. Res., 2008, 343(10–11), 1523–1539.
12. Nowakowska, Z., Eur. J. Med. Chem., 2007, 42, 125–137.
13. DOI: 10.1016/j.ejmech.2006.09.019.
14. Chauhan, I. S.; Rao, G. S.; Shankar, J.; Chauhan, L. K. S.; Kapadia, G. J.; Singh, N., Parasitol. Int., 2018, 67(5), 627–636.
15. Gabriela Alves de Souza; Lorrane de Souza Chaves; Velez, A. S. M. M.; Lacerda, J. L. F.; Pitasse- Santos, P.; Santos, J. C. C., et al., Pharmaceuticals, 2025, 18(4), 456.

16. Khan, M. A.; Rodrigues Filho, E., et al., Bioorg. Chem., 2018, 80, 123–134.
17. Nagaraju, B., J. Heterocycl. Chem., 2025.
18. Agarwal, D. S.; Beteck, R. M.; Mabille, D.; Caljon, G.; Legoabe, L. J., Naunyn-Schmiedeberg's Arch. Pharmacol., 2025, 398(4), 4199–4210.
19. Anand, P.; Kunnumakkara, A. B.; Newman, R. A.; Aggarwal, B. B., Mol. Pharm., 2007, 4(6), 807– 818.
20. Srivastava, S.; Srivastava, A.; Singh, G.; Parveen, S.; Kumar, S.; Banerjee, M.; Gaurav, H., J. Mol. Struct., 2025, 1339, 142164.
21. Zalivatskaya, A. S.; Zakusilo, D. N.; Vasilyev, A. V., Mini Rev. Org. Chem., 2021, 18(8), 992–1011.
22. Long, Y.; Xu, J.; Hu, Z.; Fan, X. Y.; Wang, H., Microb. Pathog., 2024, 195, 106877.
23. BMC Oral Health, 2025, 25, 1432.
24. Juzheng Sheng; Guihua Huang; Ruixin Ma; Fengxin Yin; Di Song; Can Zhao; Shutao Ma, Eur. J. Med. Chem., 2015, 97, 32–41.
25. Jaramillo Jimenez, B. A.; Awwad, F.; Desgagné Penix, I., 2024.
26. Poultry Sci., 2024, 103(2), 103285.
27. Halil Koyu; Huseyin Istanbullu; Sinem Ezgi Turunc Ozoglu; Tijen Kaya Temiz, Food Funct., 2024, 15(17), 8689–8699.
28. Kumar, A. N.; Soumya, G.; Kanchana, V.; Singh, K.; Maurya, N.; Kumar, S.; Singh, A.; Kotesh Kumar, J. K.; Srinivas, K. V. N. S.; Chanda, D.; Luqman, S.; Misra, S.; Meena, A.; Balakishan, B., RSC Adv., 2025, 15, 30627–30638.