Impact of Chalcone on Agriculture and its Application: An Updated Review

Abstract

Chalcones, a distinctive group of natural compounds, have gained attention in agriculture due to their versatile biological activities. As a subclass of flavonoids, chalcones are known for their open-chain structure, contributing to their herbicidal, fungicidal, bactericidal, and antiviral properties. These attributes make chalcones promising candidates for sustainable agriculture, especially in light of increasing concerns about synthetic pesticides' environmental and health impacts. The European Green Deal 2030, which seeks to halve chemical pesticides, highlights the urgent need for alternatives like chalcones. Their synthesis has been refined over time, allowing for the development of compounds tailored to specific agricultural needs. Additionally, advanced analytical techniques, such as chromatography, are crucial in accurately identifying and characterizing chalcones, ensuring their efficacy and safety. As agriculture shifts towards more sustainable practices, chalcones are poised to become key players in reducing dependency on synthetic chemicals. They offer a natural and effective solution for pest and weed management. Their potential for broad application underscores the importance of continued research in this field.

Keywords: Chalcones; Preparation Techniques; Biological Activity, Insecticidal; Herbicidal; Analysis Techniques

Introduction

Chalcones distinguish themselves from the core flavonoid structure through their unique configuration. Unlike other flavonoids, chalcones are classified as open-chain flavonoids due to the absence of the C ring typically found in the basic flavonoid skeleton. These compounds are important secondary metabolites across the plant kingdom, contributing significantly to plant growth and defense against pathogens. Flavonoids, a broad family of phenolic compounds, are divided into 12 subgroups based on the presence of methyl or hydroxyl groups on the benzene ring and the oxidation state of their heterocyclic ring. Among these subgroups are chalcones, isoflavones, aurones, dihydroflavonols, flavanones, flavones, flavanols, leucoanthocyanidins, phlobaphenes, proanthocyanidins, and stilbenes.[1,2]

"Chalcone" is derived from the Greek word "chalcos," meaning bronze. Noteworthy chalcones include phloridzin, butein, phloretin, and chalconaringenin. These compounds are commonly found in strawberries, berries, wheat products, tomatoes, pears, apples, citrus fruits, and hops.[9,14,54]Chalcones and their derivatives have garnered significant interest due to their extensive range of nutritional and biological activities,[36,47] which include not just a few but a wide array of intriguing properties such as anti-inflammatory, antitumoral, antibacterial, antifungal, antimalarial, antitubercular, and anti-pigmentation properties, often demonstrating exceptional effectiveness.[9,14,54] Additionally, chalcones are valuable in weed control.[14,10] Remarkably, a single compound like isobavachalcone can have multiple biological activities, including chemopreventive, anticancer, antibacterial, and antifungal properties.[1,27] The structure of various chalconesis shown in **Figure 1.**

Chalcones have a long history of use in traditional medicine, and their natural forms are now being investigated for contemporary applications.[1] The European Union's Farm to Fork strategy aims to reduce synthetic pesticide use by 2030, driving a growing demand for biopesticides. These natural alternatives are preferred for their diverse mechanisms of action and greater environmental sustainability. This review offers a current and thorough examination of chalcones, covering their characteristics, properties, detection methods, and potential uses in agriculture.

Characteristics

Chemically speaking, chalcone molecules are α, β-unsaturated ketones of two aromatic rings (rings A and B) connected by a three-carbon alkenone unit.[23,54] The enzyme chalcone synthase (CHS, EC2.3.1.74) catalyzes the conversion of one p-coumaroyl-CoA molecule and three malonyl-CoA molecules into chalcones. In higher plants, this process synthesizes chalcones and orchestrates them. CHS is essential andsignificantly affects how plants grow and react to stressors, including UV rays, physical harm, herbivory, and microbial invasions. [23,54]CHS promotes and initiates the synthesis of secondary metabolites, such as phenolic compounds, in response to various stressors.
[11,24]

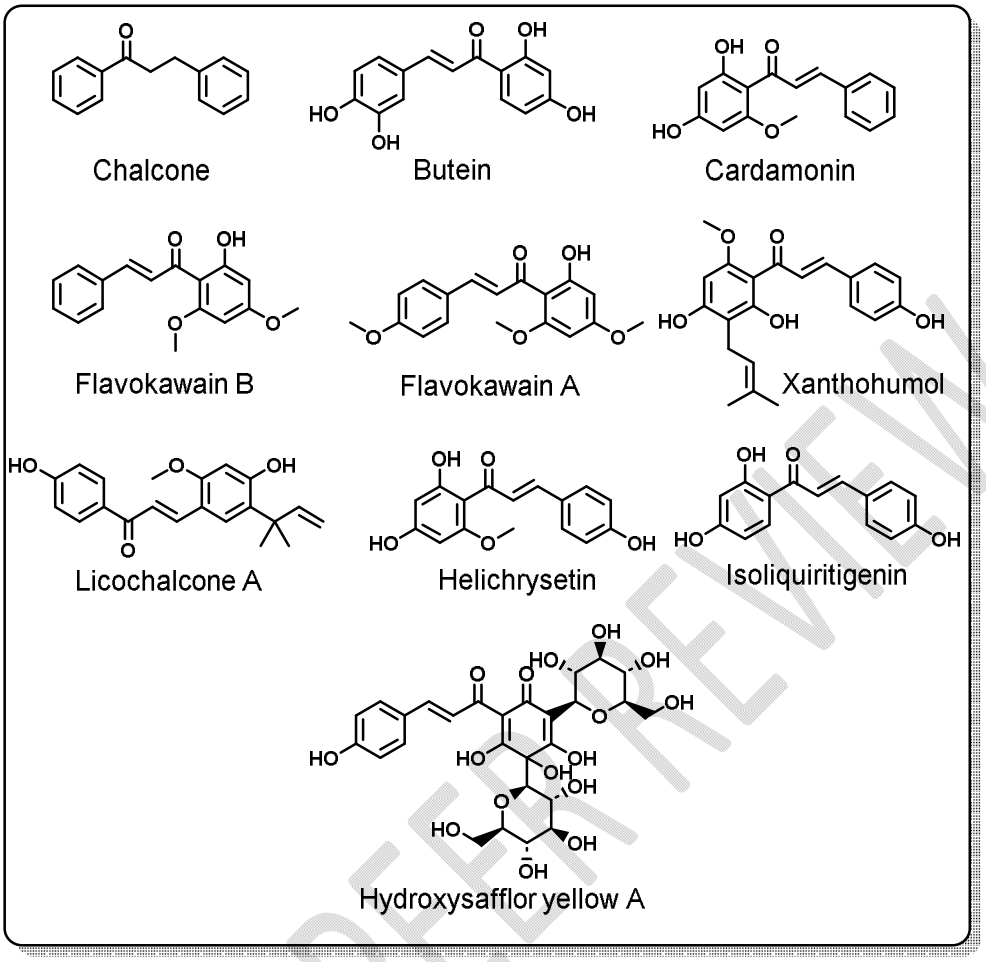

Figure 1: Chalcone and chalcone derived compounds

Although chalcones are found naturally and have a simple structural framework, several unique chalcone derivatives have been produced throughout time; bioactive chalcone derivatives have been improved for lesser toxicity by advances in synthetic chemistry,[54,55] opening up new applications in agriculture, food production, the chemical industry, and medicine.[39, 51] Extensive research has been conducted on synthetic chalcones since the early 1800s. For example, Kostanecki and Tambor were among the first to synthesize chalcones using alcoholic alkalis and o-acetoxychalcone dibromides.[30,54] The Claisen–Schmidt condensation with hydrochloric acid, the phosphonate carbanions synthesis, the microwave-assisted and solvent-free synthesis with biocatalysts, and the aldol condensation with hetero-aryl methyl ketones and 4-(benzyloxy) benzaldehyde are examples of standard synthetic techniques.[4,27,32]

During extraction, native chalcone glycosides can convert into flavanone glycosides, which limits their presence in food.[47] For example, licorice root and some traditional medicines based on licorice haveretro chalcones, isomeric flavanones, and chalcones such as liquiritigenin and isoliquiritigenin.[50]

Dihydrochalcones (DHCs), commonly found in apples and apple products, are predominantly represented by phloridzin.[6] The concentration of DHCs is higher in the fruit peel, meaning peeled apples have fewer DHCs. Conversely, commercially produced apple juices and ciders often have 5–10 times higher DHC content because they use the whole fruit and undergo thermal treatment that deactivates the enzymes responsible for DHC degradation.[45]

Preparation Techniques

Freeze-drying is one of the best techniques for sample preparation for chromatographic analysis, including UPLC-MS/MS. In this procedure, freeze-dried samples are ground for 1.5 minutes at 30 Hz using a mixer mill equipped with a zirconia bead. The resultant lyophilized powder is then dissolved in 1.2 mL of a 70% methanol solution to yield 100 mg. After six rounds of vortexing this combination for 30 seconds every 30 minutes, it is refrigerated at 4°C for the whole night. Following ten minutes of centrifugation at 12,000 rpm, the extracts are filtered, and then UPLC-MS/MS analysis is performed.[56]The crude product can be further purified using column chromatography. This method eliminates the target chemicals using a 3:1 volume ratio of petroleum ether to ethyl acetate (EtOAc).[8]

Solid-phase extraction-high-performance liquid chromatography (SPE-HPLC) is used in the pharmaceutical sector to analyze chalcones in different species and clones of Salix.[25] One gram of bark was dried and ground, then extracted for forty-five minutes at sixty degrees Celsius using three and a half milliliters of methanol. Next, at lower pressure, the mixed methanolic extracts were concentrated. For SPE, an aliquot containing 80 µL of the concentrated extract was dried off and then redissolved in 80 µL of 20% methanol.

Two new chalcone glycosides were among the bioactive chemicals the methanol recovered from the mint. The plant's aerial components were air-dried, powdered (1000 g), and then extracted four times at 40°C using methanol.[19] Following the solvent's vacuum evaporation, the crude

extract was diluted in water and separated into successive liquids using n-butanol, petroleum ether, chloroform, and ethyl acetate. A rotary evaporator evaporated each solvent layer at a lower pressure.[9]

Fructus psoralen powder was extracted using a methanol solution acidified with hydrochloric acid. The application of ultrasonication aided the extraction process. Following extraction, the mixture was centrifuged for 20 minutes at 3000 g, and the supernatant was saved for further examination. [8,52]

Two-Dimensional High-Performance Liquid Chromatography (2D-HPLC)

Pobłocka-Olech emphasized how quickly and effectively a two-dimensional high-performance liquid chromatography (2D-HPLC) system can be used for willow bark comparison analysis**(Figure 2)**. This technique used 54 reference materials in the chromatographic separation; they included salicin and catechin, as well as 29 phenolic acids and 21 flavonoids (of which there were nine flavonols, four flavones, four flavanones, two biflavones, and two chalcones). An online system was used in the separation process using a heart-cut method.[38, 41]

In the first dimension (I), a Supelcosil LC-18 column with gradient elution was used to progressively raise the methanol concentration in a methanol/water combination at a flow rate of 0.4 mL/min. In the second dimension (II), using isocratic elution with combinations of acetonitrile and water as eluents, a monolithic silica gel-packed Chromolith Performance RP18e column was utilized.[4,5,6]

Under these idealized circumstances, methanol extracts from the barks of Salix purpurea, S. daphnoides clone, and S. sachalinensis 'Sekka' were examined. The 2D-HPLC technology allows plant extracts to be analyzed without the need for previous purification, making finding secondary metabolites in various plant matrices possible.

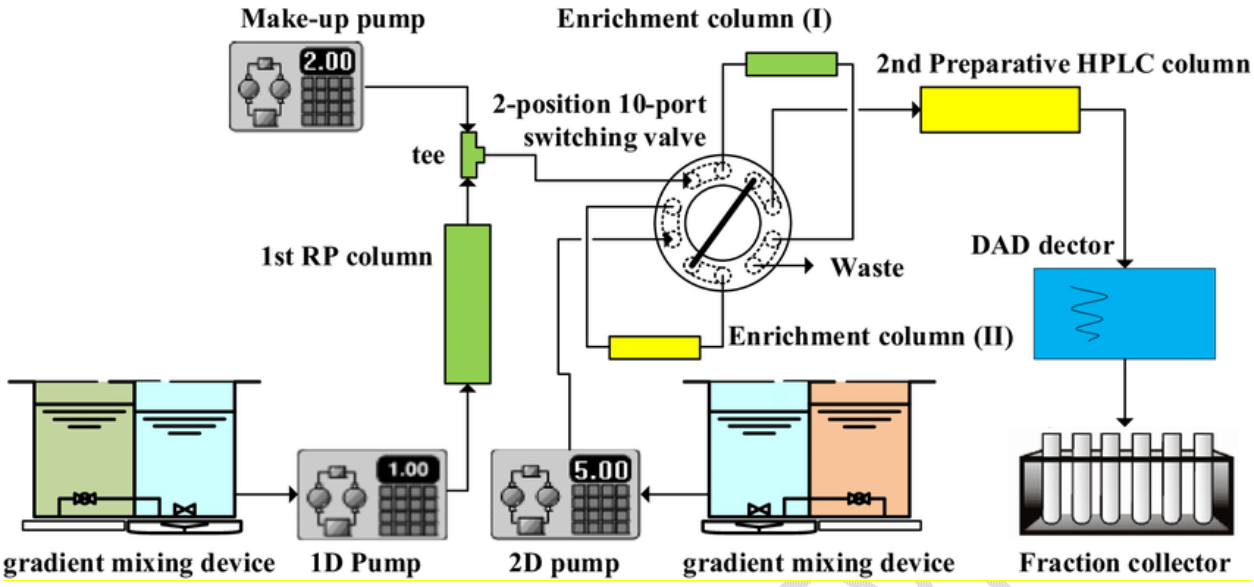

Figure 2: Two-Dimensional High-Performance Liquid Chromatography (2D-HPLC) (Source: Shimadzu)

Infrared Spectroscopy (FTIR) and Nuclear Magnetic Resonance(NMR)

Their molecular structure reveals the unique characteristics of Chalcones' infrared (IR) spectra. The aromatic C-H bonds' symmetric and asymmetric stretching vibrations are seen in the 3120–3080 cm^{-1} and 3060–3040 cm^{-1}, each distinguished by two low-intensity bands. Furthermore, at 3030–3010 cm^{-1}, the C–H stretching band of the =C–H group is visible. The in-plane deformation of the =C–H bond manifests as a wide weak band at 1460–1430 cm^{-1}, whereas vibrations linked to the aromatic rings are assigned to bands at 1610–1570 cm^{-1}. In the enones (=C–C=O), the carbonyl stretching vibrations range from 1650 to 1685 cm^{-1}.[9,13,20] Spectroscopic methods like proton nuclear magnetic resonance (1H NMR) and Fourier transform infrared spectroscopy (FTIR) can be used to investigate the different chalcone derivatives**(Figure 3)**.[9,13,20]

The FTIR spectra of these derivatives, according to Hassan et al., exhibit unique peaks that are related to the C=O stretching of carbonyl chalcone in 1708 and 1712 cm^{-1} and the C=C stretching of alkenes at 1612 and 1622 cm^{-1}. Protons of the aromatic ring are found between 7.5 and 6.6 ppm, protons of the amine group between 10.7 and 10.6 ppm, and protons linked to HC-S at five ppm, according to the 1H NMR study of derivative C. The protons of the amine group are located at 10.5 ppm in derivative D, whereas those of the aromatic ring are found between 7.7 and 6.8 ppm, HC-S protons are at 4.8 ppm, and methyl group protons are at 2.2 ppm.[9,13,20]

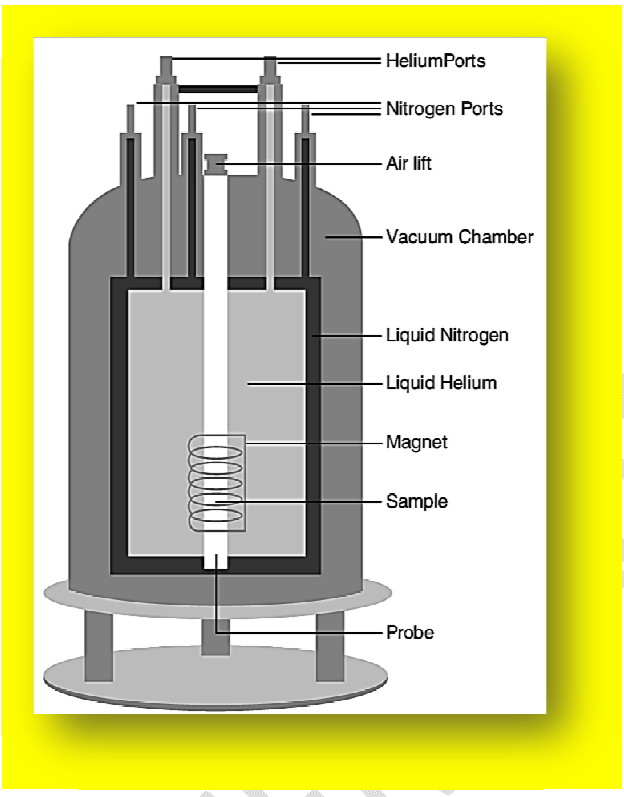

Figure 3: Nuclear Magnetic Resonance (Source: Wikipedia)

Liquid Chromatography (LC)

When examined with absorbance detectors, chalcones have two prominent absorption bands: Band I, usually observed between 340 and 390 nm, and Band II, between 220 and 270 nm. A combination of flavonoids, including naringenin, its glycosides (both (+) and (-)-5-O-glycosides), naringenin 7-O-glycoside, isosalipurposide, and its p-coumaric ester, were subjected to both qualitative and quantitative HPLC analysis.[38] Gradient elution was used in this research on a Discovery C18 column. Water and acetonitrile comprised the mobile phase, and orthophosphoric acid was added to balance the pH. A diode array detector (DAD) and a UV–vis detector set at 280 nm were used to expedite identification. This method was most effective with solid-phase extraction (SPE) procedures.[13] A particular derivative of trans-chalcone, which is substituted with hydroxyl groups at the 4, 4′, and 6 positions and a β-D-glucopyranosyloxy group at the 2′ position, acts as both a plant metabolite and an antioxidant.[20]

The separation of chalcones from willow tree bark using a Discovery C18 column (5 µm, 150 × 2.1 mm).[25] They used a 15-minute gradient elution with a 0.4 mL/min flow rate. Detection was performed using UV–vis DAD at 280 nm, and chalcones and flavanones were quantified through external standardization, employing isoliquiritigenin and its derivative, the 6″-O-p-coumaroyl ester, as reference standards.[19]

Additionally, Chen et al. conducted HPLC–UV analyses using a DL-Cl8 column (5.0 µm, 250 mm, and 4.6 mm) with a 0.5 mL/min flow rate. Using gradient elution, the mobile phase included acetonitrile (A) and 0.01 M formic acid (B). Detection was set at 246 nm, offering detailed insights into chalcones' chromatographic properties and related compounds.[8]

Liquid Chromatography Coupled with Mass Spectrometry (LC-MS)

"*Paeoniadelavayi* var. lutea extracts were examined by Zou et al. utilizing a Shimadzu UPLC-ESI-MS/MS system. An Agilent SB-C18 (1.8 µm, 2.1 × 100 mm) UPLC column was utilized, and the mobile phase comprised acetonitrile and clean water combined with 0.1% formic acid".[56]"The samples were put through a gradient program using an injection volume of 4 µL, and an ESI-triple quadrupole-linear ion trap (QTRAP)-MS was used to collect the effluent. Similar to this, Ma et al. created an internal standard (IS) of neobavaisoflavone to measure isobavachalcone (IBC) in rat plasma using selective high-performance liquid chromatography-mass spectrometry (LC-MS/MS)" [60]. "Isomatic elution separated the analytes on a Kinetex C18 column using acetonitrile (60:40, v/v) as the mobile phase".[18,29,37]"An electrospray ionization (ESI) source was employed, worked in the negative ion mode, and quantification was achieved through multiple reactions monitoring (MRM). This method showed good linearity within the concentration range of 3.79–484.5 ng/mL for IBC in rat plasma. Furthermore, Chen et al. detected significant constituents, including bakuchiol, bavachin, bavachinin, and isobavachalcone in Fructus psoraleae using HPLC coupled with UV, MS, and electrochemical detectors (ECD) **(Figure 4)**. The MS analysis was conducted in negative ion mode using selected ion monitoring (SIM), offering high selectivity and sensitivity for deciding the constituents within a mass range of 50–1000 m/z".[8,9,40]

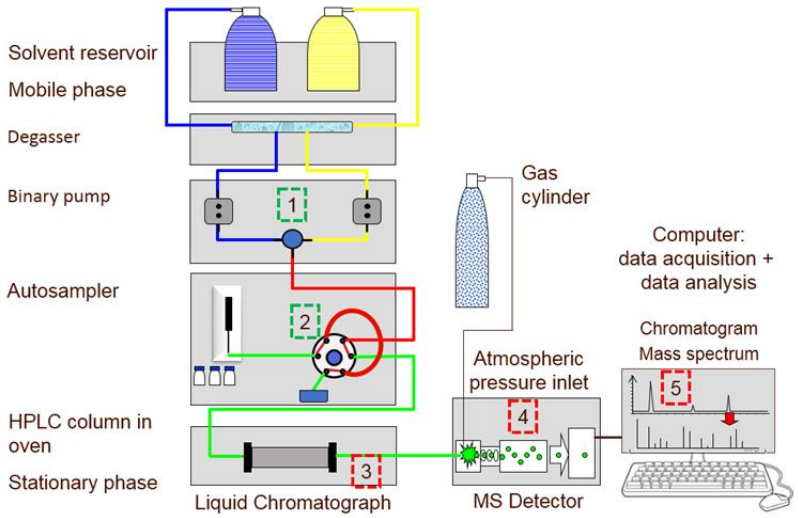

Figure 4: LC-MS (Source: Technology Networks)

MALDI Technique

"Krittanai et al. reported that liquid chromatography coupled with UV detection lacks sensitivity in finding licochalcone A (LicoA), a compound commonly found in the root of Chinese licorice (Glycyrrhiza inflata Batalin). Consequently, they developed an enzyme-linked immunosorbent assay (ELISA) using a specific antibody to measure LicoA quantitatively. This assay showed high specificity to LicoA with minimal cross-reactivity to structurally similar substances. Upon method optimization, the detection limit was determined to be 4.32 ng/mL, with a quantification range of 6.84–107.21 ng/mL. The newly developed assay successfully measured LicoA concentration in raw licorice and commercially available products**(Figure 5)"**.[9,26]

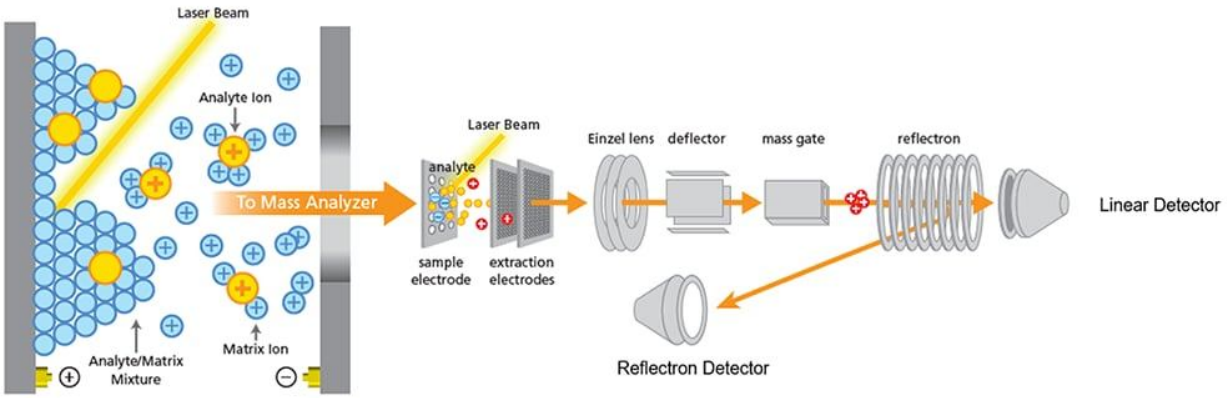

Figure 5: MALDI Technique (Source: Shimadzu)

Chalcones Biological Activities and Their Applications in Agriculture

Chalcones are versatile compounds highly regarded in agriculture for their essential role in managing weeds and pests. As environmentally friendly pesticides, they exhibit various biological activities, effectively targeting various organisms.[16] The biological effectiveness of chalcones is primarily determined by their structural features, such as the positioning of substituents like hydroxyl groups and the presence of the α, β double bond.[9] By modifying the structure of chalcones through the addition of specific functional groups, their desired biological activities can be enhanced, making them valuable intermediates in the synthesis of therapeutically beneficial compounds.[48] Chalcones demonstrate significant potential in agricultural applications, offering a broad spectrum of activities, including phytotoxic, bactericidal, antifungal, antiviral, antihelmintic, insecticidal, and antifeedant properties.

Nematicides

Chalcones and their derivatives show promising nematocidal activity against plant-parasitic nematodes, including economically significant species like *Meloidogyne* spp.[7,31,32,42] Studies have found chalcone analogs with superior nematocidal activity to commercial nematicides, offering potential alternatives for nematode control in agriculture.[7,42] Mechanistic investigations suggest that chalcones inhibit crucial nematode enzymes, contributing to their nematocidal activity.[7,42] Additionally, the polarity and planarity of chalcones influence their effectiveness against nematodes, highlighting the importance of structural characteristics in their nematocidal activity.[2,7]

Fungicides

Chalcones are renowned for their antifungal properties against human and plant pathogens. They inhibit crucial fungal enzymes in cell wall synthesis, making them effective against various pathogens. For example, chalcones derived from *Zuccagnia punctata* have shown potent activity against soybean pathogens like *Phomopsis longicollaand Colletotrichum truncatum*.[46] Similarly, plant-origin chalcones have proved inhibitory effects on fungi such as *Alternaria sp*., *Fusarium spp*., and *Botrytis sp*., which cause significant agricultural losses.[3,34] Synthetic chalcone derivatives have been developed with enhanced antifungal properties, offering

promising alternatives to conventional fungicides.[54] These derivatives disrupt fungal cell membranes and inhibit fungal growth through diverse mechanisms, highlighting their potential as future fungicides.[56,57,58]

Antiviral Agents

Chalcones and their derivatives have appeared as promising antiviral agents against various viruses, including plant viruses like the tobacco mosaic virus (TMV) and cucumber mosaic virus (CMV). Structural modifications of chalcones have led to compounds with potent antiviral activity against TMV and CMV.[17,53] Mechanistic studies have revealed their ability to inhibit viral replication by targeting essential viral proteins like coat proteins.[53] Recent research has also focused on enhancing the antiviral activity of chalcones through structural modifications, offering new avenues for combating viral infections in crops.

Insecticides

Both natural and synthetic chalcones exhibit potent insecticidal activity against a wide range of insect pests. Compounds like xanthohumol and isoxanthohumol derived from hop plants have shown significant insecticidal activity.[44]Synthetic chalcones have been synthesized and evaluated for their pesticidal properties, with structural modifications influencing their efficacy against insect pests. Mechanistic studies have elucidated the mode of action of chalcones, suggesting their potential in developing novel insecticides for pest management in agriculture.[12,21,28]

In conclusion, chalcones represent a versatile class of compounds with immense potential in agriculture. Their diverse biological activities and structural modifiability make them valuable assets in developing eco-friendly pesticides, herbicides, fungicides, nematicides, and insecticides. Continued research into chalcone derivatives and their mechanisms of action holds promise for addressing agricultural challenges and ensuring sustainable crop production.

Herbicides

Chalcones are increasingly recognized for their phytotoxic properties, paving the way for developing novel herbicides. Research shows that many chalcones exhibit potent herbicidal effects while keeping low crop toxicity.[15,16] Their activity varies based on the substituents on

their structural rings A and B, the concentrations applied, and the specific plant species targeted. Derivatives holding functional groups such as phenoxyacetic acid, 4-(N, N-dimethylamino) phenyl, N-methylpyrrole, and especially thiophenyl have shown significant inhibitory effects.[9,5,10,1] For instance, flavokawains, derivatives of xantoxyline, effectively inhibited the growth of Chinese amaranth and barnyard grass.[10] Further studies have highlighted the inhibitory effects of chalcones on key plant enzymes such as coenzyme A ligase (4CL) and phosphoenolpyruvate carboxylase (PEPC), which are crucial for plant growth and metabolism.[33,49] Additionally, chalcones like trans-chalcone have been shown to induce programmed cell death (PCD) in plant seedlings, suggesting their potential as plant growth regulators.[38] Selectivity studies have revealed differential effects of chalcones on the growth of crops and weeds, further emphasizing their potential in weed management.[15,16] Furthermore, dihydrochalcones like phloretin have shown significant growth-retarding effects on Arabidopsis seedlings, highlighting the broad applicability of chalcones in plant growth regulation and weed control.[35,43]

Conclusions

Chalcones are both naturally occurring and synthetically derived compounds and are recognized for their complexity and diversity. These compounds exhibit various biological activities, including herbicidal, fungicidal, antiviral, insecticidal, and plant-growth regulatory properties. Despite their long history of use in traditional medicine and agriculture, the full extent of their potential remains largely unexplored and insufficiently understood. This review provides an in-depth analysis of the various applications of chalcones, focusing on their effectiveness in different biological contexts and the innovative detection methods that have emerged from recent research. One significant challenge is the limited natural production of chalcones and their short half-life in plants, which makes direct extraction from nature difficult. These challenges have prompted substantial efforts to develop synthetic methods for producing chalcones and improving their stability and efficacy. To fully capitalize on the potential of chalcones, extensive research is necessary to uncover their mechanisms of action, validate their practical effectiveness in agricultural settings, and assess their safety for both the environment and human health. Addressing these critical areas will be crucial for optimizing the use of chalcones and ensuring their safe and practical application in agriculture.

Data availability statement

The data supporting this study's findings are available in Google Scholar at https://scholar.google.com/.

Because this work is a review, the data supporting the findings of this study are available online on various websites. All references (Doi) are reported in the references section. The dataset that supports the findings of this review is included in the article.

Availability of data and materials

The data was collected from various websites and search engines, such as Science Direct, Taylor and Francis, Google Scholar, etc.

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Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc) and text-to-image generators have been used during writing or editing of manuscripts.

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