

Review

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*Review*

# Chalcones—Features, Identification Techniques, Attributes and Application in Agriculture

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**Abstract:** This review provides a comprehensive and updated information on chalcones, presenting their sources, methods of identification and properties putting emphasis on applications in agricultural industry. Vast exploitation of synthetic pesticides led to the weed and pest resistance issue, causing economic loss but more importantly health risk due to pesticide overuse. Because one of the aim of the European Green Deal 2030 is the Farm to Fork strategy which targets on reducing by 50% the use of chemical pesticides by 2030, and push towards natural pesticides which are more environmentally friendly and restore natural resources, chalcones and their derivatives seem to fit perfectly. They have herbicidal, fungicidal, bactericidal and antiviral properties. Moreover, chalcones are naturally occurring substances, known for their favorable health effect for years, working on many areas. This review is complementary to the previous ones describing chalcones use in agriculture, updates them but additionally shows methods of detection.

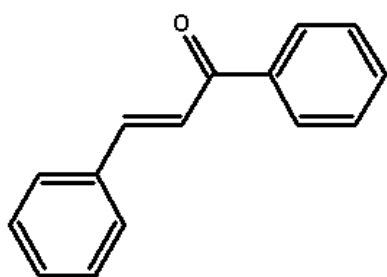
**Keywords:** chalcones; biopesticides; herbicides; insecticides; low risk active substances

## 1. Introduction

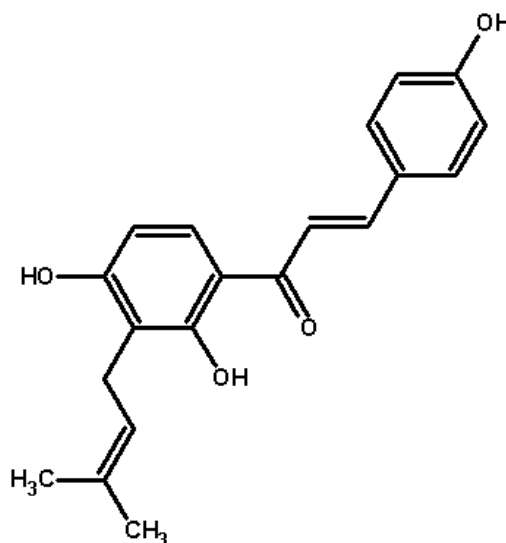
Chalcones are characterised by the absence of ‘C ring’ of the basic flavonoid skeleton structure (see Figure 1). Hence, they can also be referred to as open-chain flavonoids, which are well-known specialized (secondary) metabolites occurring ubiquitously in plant kingdom. They can be found in different parts of the plant supplying its growth and defence against pathogens. Flavonoids belong to a class of phenolic compounds and according to the degree of oxidation of the heterocyclic ring and the number of hydroxyl or methyl groups on the benzene ring, flavonoids can be divided into 12 subgroups: anthocyanins, aurones, chalcones, dihydroflavonols, flavanones, flavones, flavanols, isoflavones, leucoanthocyanidins, phlobaphenes, proanthocyanidins and stilbenes [1].

The term chalcone is originated from the Greek phrase “chalcos” which means bronze. Major examples of chalcones include phloridzin, butein, phloretin and chalco-naringenin. Chalcones can be found in considerable amounts in strawberries, berries, some wheat products, tomatoes, pears, apples, citrus fruit and hop plant. Because of numerous nutritional and biological benefits chalcones and their derivatives have gathered considerable attention [2–5]. Natural and synthetic chalcones have been reported to possess anti-inflammatory, antitumoral, antibacterial, antifungal, antimalarial, antitubercular and antipigmentation activities, not rarely with an excellent result [4,6–8]. Moreover, chalcones can be useful for weed control [9,10]. Interestingly, a single compound may exhibit several activities, for example isobavachalcone is known to have chemopreventive, anti-cancer, anti-bacterial and anti-fungal activities [11,12]. Naturally occurring chalcones have been used in traditional medicine for years, only now new applications appear [13]. Due to increased effort to reduce synthetic pesticides usage within Farm to Fork strategy from the European Union until 2030, biopesticides are

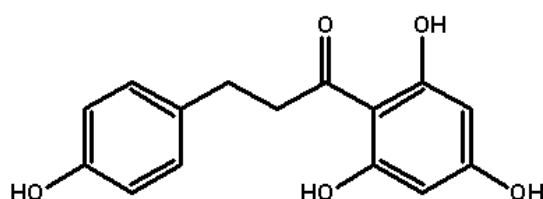
gaining popularity not only because of different mode of action but also, and more importantly, they are more environmentally friendly.



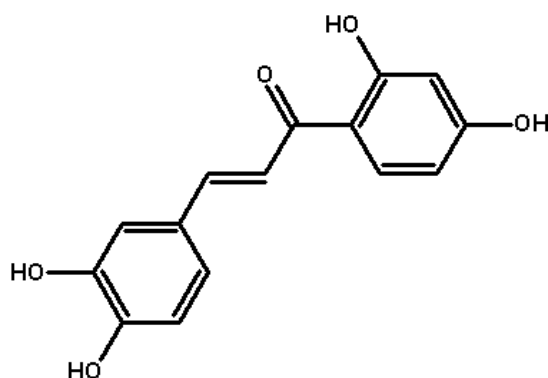
Chalcone



Isobavachalcone



Phloretin



Butein

Figure 1. Chalcones structures.

## 2. Characteristic

From the chemical point of view, chalcones are  $\alpha,\beta$  unsaturated ketones consisting of two aromatic rings (ring A and ring B) linked through a three-carbon alkenone unit [14]. In higher plants, chalcones are synthesized by the enzyme chalcone synthase (CHS, EC2.3.1.74) from one molecule of *p*-coumaroyl-CoA and three molecules of malonyl-CoA. CHS plays role not only in the development process in many plants but also is induced under stress conditions, like UV, wounding, herbivory and microbial pathogens, resulting in the production of secondary metabolites e.g. phenolic compounds [15,16]. Chalcone is a common simple scaffold found in many naturally occurring compounds but large number of new chalcone structures have been synthesized over the years [17]. A collection of bioactive synthetic chalcone derivatives, structurally improved to reduce their toxicity, allowed their use not only in medicine and chemical industry [14] but also in food production and agriculture sector [18].

Chalcones can be obtained either from natural sources or by chemical synthesis. From the beginning of 19th century, many researchers have developed synthetic chalcones, not to forget Kostanecki and Tambor experiment where they first obtained synthetic chalcone using o-acetoxychalcone dibromides with alcoholic alkali [14,19]. Among synthetic methods, the Claisen-Schmidt condensation, hydrochloric acid usage, chalcone synthesis from phosphonate carbanion, synthesis based on microwave and solvent-free conditions, involving biocatalysts or aldol condensation synthesis using (hetero)aryl methyl ketones and 4(benzyloxy)benzaldehyde are worth highlighting [12,20,21].

Native chalcone glycosides tend to transform to flavanone glycosides during extraction. Chalcones are by itself of restricted occurrence in food [3]. Mixtures of retrochalcones along with isomeric flavanones and chalcones (eg liquiritigenin and isoliquiritigenin) have been reported in licorice root (*Glycyrrhiza* spp) and some licorice-based traditional medicines [22]. Dihydrochalcones (DHC) are distinctive for apples and its products, with phloridzin being the most common [23]. Peeled fruits contain less DHCs, as they are removed together with the peel. Similarly, DHC content is 5-10 times higher in commercially produced juices and ciders not only because the whole fruit is used but also due to the thermal treatment which inactivates the enzymes that degrade DHC [24].

### 3. Chalkones Identification

#### *Sample Preparation*

One of the most efficient sample preparation methods before chromatographic analysis (i.e. UPLC-MS/MS) is freeze drying. In details: a mixer mill with a zirconia bead can be used for freeze-dried sample for 1.5 min at 30 Hz, then dissolve 100 mg of lyophilized powder with 1.2 mL 70% methanol solution, vortex for 30 s every 30 min, 6 times in total, and place the sample in a refrigerator at 4 °C overnight. Following centrifugation at 12,000 rpm for 10 min, the extracts should be filtered before UPLC-MS/MS analysis [25]. In order to purify the crude product, column chromatography can be used and eluted with (petroleum ether/EtOAc = 3:1, V/V) to give compounds of interest [4]. Krauze-Baranowska et al. [26] optimized the SPE-HPLC method for chalcones in some species and clones of *Salix* used for the pharmaceutical industry. The authors dried and pulverized 1 g of bark sample which was subsequently extracted with methanol (3 x 30 mL) for 45 min in 60°. The methanolic extracts were combined and concentrated under reduced pressure. Eighty µL of the extract was evaporated to dryness and re-dissolved in the same volume of 20% ACN. Next, the sample was subjected to a solid phase extraction (SPE) procedure. Also methanol was used as an extractant by Guvenalp et al. [27] for mint samples in order to isolate bioactive compounds, among which two new chalcone glycosides were reported. Air-dried and powdered aerial parts of the plant (1000 g) were extracted four times with MeOH at 40°C. After vacuum evaporation the crude extract was dissolved in water and subjected to liquid-liquid partitions successively with petroleum ether, CHCl<sub>3</sub>, EtOAc and n-butanol. Thereafter, the solvents were evaporated under reduced pressure in a rotary evaporator oven [28]. Chen et al. [28] extracted powdered fruit of *Fructus Psoreleae* using hydrochloric acid in methanol as an extraction solvent under ultrasonication. Afterwards, the sample was centrifuged at 3000 g for 20 minutes and the supernatant was collected.

#### *Liquid Chromatography Coupled with Absorbance Detectors*

There are two main absorption band in chalcones – band I and band II. Band I usually appears at 340-390 nm and band II usually appears at 220 – 270 nm.

According to Pobłocka-Olech [29] in order to perform qualitative and quantitative analysis of the mixture of five flavonoids: naringenin, naringenin (+) and (-)-5-O-glycosides, naringenin 7-O-glycoside, isosalipurposide and its *p*-coumaric ester using HPLC method, the chromatographic separation was carried out on reversed phases' system on Discovery C18 column, including the use of gradient elution in the mixture of acetonitrile / water+orthophosphoric acid. Identification was completed not only using the detector UV-Vis ( $\lambda = 280$  nm), but also the diode array detector (DAD). The SPE method was incorporated to speed up the analysis time [30]. Isosalipurposide also known

as phloridzin chalcone is a monosaccharide derivative that is trans-chalcone substituted by hydroxy groups at positions 4, 4' and 6 and a  $\beta$ -D-glucopyranosyloxy group at position 2' respectively. It has a role as a plant metabolite and an antioxidant [31].

According to Krauze-Baranowska et al. [26] the separation of chalcones from willow tree bark was performed using a Discovery C18 column (5  $\mu$ m, 150  $\times$  2.1 mm). The gradient elution was performed according 15 min; flow rate, 0.4 mL/min; Chalcones and flavanones were identified with UV-Vis DAD detection at 280 nm. The content of both compounds was determined by an external standardization with the use of isoliquiritigenin as a reference substance - a commercially available chalcone, and also isosalipurposide and its derivative, 6''-O-p-coumaroyl ester [27]. Chen et al. [28] performed HPLC - UV analyses using a DL-C<sub>18</sub> column (5.0  $\mu$ m, 250 mm 4.6 mm) with a flow rate of 0.5mL/min using acetonitrile (A) and 0.01M formic acid (B) as a mobile phase. Gradient elution was used and the detection wavelength was 246 nm.

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

According to Poblócka-Olech [29] the rapid comparative analysis of the willows' bark was possible using the system of two dimensional high performance liquid chromatography (2D-HPLC). 52 standard substances were applied in the separation system, including 29 phenolic acids and 21 flavonoids: 9 flavonols, 4 flavones, 4 flavanones, 2 biflavones, and 2 chalcones, and salicin, catechin as well. The separation was performed using the on-line system by heart-cut technique. The Supelcosil column LC-18 was used at first (I) dimension as well as the gradient elution of the increasing methanol concentration in the mixture of methanol/ water with the flow rate of mobile phase 0,4 ml/min. At the second (II) dimension it was filled up with monolithic silica gel on the column of Chromolith Performance RP18e, and isocratic elution with the use of the acetonitrile and water mixtures as eluents. In this conditions the methanol extracts from barks of *Salix purpurea*, *S. daphnoides* clone and *S. sachalinensis* 'Sekka' were analyzed. The 2D-HPLC method enables to analyze the plant extracts avoiding the purifying process. It can be successfully used for the secondary metabolites identification from different plant matrices.

#### *Infrared Spectroscopy, FTIR and HNMR*

The IR spectra of chalcones asymmetric and symmetric stretching vibrations of the aromatic C-H bonds are seen at 3120 – 3080 cm<sup>-1</sup> and 3060 – 3040 cm<sup>-1</sup> ranges with two low intensity bands. C-H stretching band of the =C-H group is observed at 3030 – 3010 cm<sup>-1</sup>. The bands at 1610 - 1570 cm<sup>-1</sup> are assigned to the vibrations of the aromatic ring. The inplane deformation of the=C-H bond appears as broad weak band at 1460 – 1430cm<sup>-1</sup>. The carbonyl stretching vibrations for the enones (=C-C=O) can be found between 1650 and 1685cm<sup>-1</sup>. [30]

A mixture of chalcone derivatives can also be evaluated via spectroscopic techniques, such as FTIR and <sup>1</sup>HNMR [4,31]. According to Hassan et al., the FTIR spectrum showed the appearance of compounds by the carbonyl chalcone C=O stretching in 1708 and 1712 cm<sup>-1</sup> and the C=C of alkene detected at 1612 and 1622 cm<sup>-1</sup>. The <sup>1</sup>HNMR for derivative C showed the protons of the amine group that were detected at 10.7 ppm and 10.6 ppm, the protons of the aromatic ring detected at a range of 7.5 – 6.6 ppm, and protons of HC-S detected at 5 ppm. In derivative D the protons of the amine group were detected at 10.5 ppm, the aromatic ring 094–101 protons detected at a range of 7.7 – 6.8 ppm, and the protons of HC-S were detected at 4.8 ppm, and protons of the methyl group were detected at 2.2 ppm. [31].

#### *Liquid Chromatography Coupled with Mass Spectrometry*

According to Zou et al. [25], the *Paeonia delavayi* var. *lutea* sample extracts were analyzed using an UPLC-ESI-MS/MS Shimadzu system under the above analytical conditions: UPLC: column, Agilent SB-C18 (1.8  $\mu$ m, 2.1  $\times$  100 mm); the mobile phase consisted of pure water with 0.1% formic acid and acetonitrile with 0.1% formic acid. Sample measurements were performed with a gradient program and the injection volume was 4  $\mu$ L. The effluent was alternatively connected to an ESI-triple



quadrupole-linear ion trap (QTRAP)-MS [25]. Ma et al. [32] have developed a simple and selective specific high-performance liquid chromatography-tandem mass spectrometry (LC-MS/MS) method for determination of isobavachalcone (IBC) in rat plasma. Neobavaisoflavone was used as an internal standard (IS) and together with the analyte were separated on a 2.6  $\mu\text{m}$  Kinetex C18 column (100 mm $\times$ 2.1 mm i.d., Phenomenex) by isocratic elution with acetonitrile:water (60:40, v/v) as the mobile phase at a flow rate of 0.2 mL/min. An electrospray ionization (ESI) source was applied and operated in the negative ion mode. Multiple reactions monitoring (MRM) mode was used for quantification, and the target fragment ions  $m/z$  323.0 $\rightarrow$ 118.9 for IBC and  $m/z$  321.1 $\rightarrow$ 265.0 for the IS were chosen. Good linearity was observed in the concentration range of 3.79–484.5 ng/mL for IBC in rat plasma [32]. Chen et al. [28] carried out the detection of four major constituents including bakuchiol, bavachin, bavachinin and isobavachalcone in *Fructus Psoraleae* using HPLC coupled with UV, MS and electrochemical detectors (ECD). MS provided a high selectivity and sensitivity for determination of bavachin, isobavachalcone, and bavachin in negative-ion mode using selected ion monitoring (SIM) for the listed compounds in mass range 50 – 1000  $m/z$ .

#### MALDI Technique

According to Krittanai et al. [33] liquid chromatography coupled with UV detection has poor sensitivity to detect licochalcone (LicoA), which is found in the root of Chinese licorice (*Glycyrrhiza inflata* Batalin), therefore enzyme-linked immunosorbent assay (ELISA) was developed for the quantitative determination of LicoA using a constructed antibody. The assay validation results were highly specific for the target compound, but minimally cross-reactive with the structure-related substances. After method optimization, the detection limit was 4.32 ng/mL and the quantification limit was 6.84–107.21 ng/mL. The developed technique was applied to determine the concentration of LicoA in raw licorice and marketed samples.

## 4. Properties

### *Chalcones Biological Activities and Their Applications in Agriculture*

Chalcones are highly bioactive substances that are of great concern for agriculture in terms of controlling weeds and pests. Eco-friendly pesticides and weed control agents have far-reaching biological effects and can be used to combat many organisms [6].

The structure of chalcones is a key factor that determines their biological activity. In this regard, the number and position of various substituents, mainly hydroxyl groups and the  $\alpha,\beta$ -double bond are important [13]. Moreover, chalcones can be modified by the addition of specified moieties to obtain the desired activities. Thanks to their specific structure, they have been used as intermediate for the preparations of compounds having therapeutic value [34]. Chalcones have been found to be effective for controlling weeds and pests by exhibiting phytotoxic, bactericidal, antifungal, antiviral, antihelminthic, insecticidal, and antifeedant activities.

### *Herbicides and Plant Growth Regulators*

From the agricultural point of view, very important is the chalcones' phytotoxic activity, which may be used in the process of developing new herbicides. As evidenced by studies, many chalcones are able to exhibit strong herbicidal activity with low toxicity for crops [6,9]. The activity depends on the groups added to rings A and B that are part of their structure, the applied concentrations, plant species, and organs. Derivatives containing phenoxyacetic acid, 4-(N,N-dimethylamino)phenyl, N-methylpyrrole, or especially thiophenyl functional groups have shown promising inhibitory activity. [10,13].

Chotsaeng, et al. [10] have shown that flavokawains, which are chalcone-related derivative of xanthoxylone, can greatly suppress the growth of Chinese amaranth and barnyardgrass. Among 45 synthesized chalcones, (E)-2-(2-(3-Oxo-3-(thiophen-2-yl)prop-1-en-1-yl)phenoxy)acetic acid was found as the most potent, thanks to the thiophenyl group on ring A and phenoxyacetic acid group on ring B.

Perera et al. [35] proved that other three chalcones derivatives, salsolol A and B are effective against *Lemna pausicotata* with IC<sub>50</sub> values of 261, 275, and 251  $\mu$ M, respectively.

One of the mechanisms of phytotoxicological action of chalcones were presented by Yun et al. [36]. The authors proved that chalcone efficiently suppress the growth of several annual plant species by inhibition the activity of coenzyme A ligase (4CL), one of the key enzymes in the biosynthesis of lignin monomers. The mechanizm of inhibition of key enzyme is used also by Nguyen et al. [37], who identified chalcones as selective inhibitors of phosphoenolpyruvate carboxylase (PEPC), a key enzyme for carbon fixation and biomass increase in the C<sub>4</sub> photosynthetic pathway of many of the world's most damaging weeds.

The results of the study of Diaz-Tielas et al. [38], highlighted the mode of action of transchalcone as programmed cell death (PCD) inducer, through the probable mechanism of action based on the modification of mitochondrial function with the subsequent depolarization of the membrane and the release of factors, which trigger PCD in these cells. These results confirmed the phytotoxic activity of chalcone on *Arabidopsis* seedlings and support its potential use as plant-growth regulator.

In addition, Diaz-Tielaz et al. (2014) [9] evaluated if the phytotoxic effect obtained after the chalcone treatment can be selective and work differently for crops and associated weeds. Moreover, they have investigated two forms of herbicide application – spraying and watering on the growth of the model plant – adult *Arabidopsis* and found that trans-chalcone is harmful to the germination and/or early root growth of certain weeds and crops (though apparently beneficial for others), and likewise is detrimental to the development of adult *Arabidopsis* plants. These results support the role of chalcone as a plant growth regulator.

In other studies, one of the most known dihydrochalcone, phloretin exhibited significant dose-dependent growth retardation, severe morphological abnormalities and agravitropic behavior in *Arabidopsis* seedlings [39].

### Fungicides

Chalcones are well known from their antifungal properties against many fungal pathogens of humans. The mechanizm of action is inhibition of  $\beta$ (1,3)-glucan and chitin synthases, enzymes, that catalyze the biosynthesis of  $\beta$ (1,3)-glucan and chitin polymers of the fungal cell wall, respectively [40].

However, there are also many research results proving the effectiveness of chalcones against plant pathogens responsible economic losses of arable land worldwide.

The study of Svetaz et al. (2004) [41] have proven significant sensitivity *Phomopsis longicolla* to action of chalcones derived from *Zuccagnia punctata*. The chloroformic fractrion of ethanolic extract from this plant consisting of 2',4'-dihydroxy-3'-methoxychalcone and 2',4'-dihydroxychalcone displayed very good activities against *P. longicolla* Hobbs CE117 (MIC = 6.25 and 3.12 mg ml<sup>-1</sup>, respectively), as well as against *Colletotrichum truncatum* CE175 (MIC = 6.25 mg). Both fungi species cause of the most soybean diseases, reduction of seed quality and yields, due to their high incidence and persistence. Badaracco et al. [42] found that chalcone of plant origin 1,3-difenylo-2propen-1on was characterized by the inhibition of *Alternaria* sp., *P. longicolla*, *Fusarium proliferatum*, and *Fusarium Subglutinans*, the causal agents of pathologies in agronomic and food crops of agronomic and food importance. Minimum inhibitory concentrations (MIC) were from 62.5 to 125  $\mu$ g ml<sup>-1</sup>. Regarding fungicidal activity, the compound was effective only on *Alternaria* sp. and *P. longicolla* at minimum fungicidal concentrations (CFM) of 125 and 250  $\mu$ g ml<sup>-1</sup>, respectively. Oleszek et al. [43] tested antifungal activity of methanolic extract from apple pomace. The fraction rich in phloridzin, one of the most known chalcones, exhibited the strongest antifungal properties against *Botrytis* sp., *Fusarium oxysporum*, *Petriella setifera*, and *Neosartorya fischeri*.

Naturally occurring chalcones became the inspiration of scientists for design and synthesis of new synthetic chalcones with antifungal properties. Hence, the latest research largely concerns synthetic compounds. Chen et al. (2023) [4] tested a series of chalcone derivatives containing pyridazine against nine fungi: *Rhizoctonia solani*, *Botrytis cinerea*, *Phomopsis* sp., *Colletotrichum acutatum*, *Botryosphaeria dothidea* (Bd), *Fusarium graminearum* (FG), *Colletotrichum gloeosporioides*,

*Sclerotinia sclerotiorum* (SS) and *Phytophthora capsica*. The results showed that most of tested compounds exhibited stronger antifungal activity than azoxystrobin, positive control agent. Therefore, they have the potential to become fungicides, due to the ability to disruption the cell membrane of the mycelium and thus inhibition of the fungus growth.

Other research on the synthetic derivatives of chalcones was conducted by Zhou et al. [44], who tested chalcone derivatives containing a piperazine against *Rhizoctonia solani* and *Colletotrichum gloeosporioides*. The mechanism of action was induction irregular and shrivelled growth of mycelium and rupture of the mycelium surface.

#### Antiviral Agents

Chalcones and their derivatives has been investigated also as antiviral agents. Chalcones show significant antiviral activity against tomato ringspot virus (ToRSV). In one of the first study conducted on *Chenopodium quinoa*, 2-hydroxychalcone was found weak inhibitor of ToRSV infection [45]. Onyilagha et al. [46] investigated 21 different chalcones activity against ToRSV. This study proved that the antiviral properties was increased by hydroxylation of the A-ring at 2',3',4' positions and B-ring at C-4', and decreased by hydroxylation at C-5' and methoxylation of the B-ring.

In the newest literature related to agriculture, most information refer to the issue of tobacco mosaic virus (TMV), which were diminished by the application of chalcone type-compounds. Substituents and structure moieties as well as their positions in chalcone molecule are most important for the potency of antiviral activity of chalcones.

Dong et al. [47] synthesized and tested a series of novel chalcone derivatives containing 1,1-dichloropropene moiety, and stated that most of the tested compounds exhibited moderate to good antiviral activity. Particularly one of them possessed excellent inactivation activity against TMV similar to that of ningnanmycin, commercially available antiviral agent.

Zhou et al. [48] stated that presence of purine and benzenesulfonamide moieties in chalcone molecule resulted in effective antiviral activity both against TMV, and also cucumber mosaic virus (CMV), which are two significant plant viruses causing serious economic problem in crops production. In particular, one of tested compounds proved to be indubitable effective against both viruses, thanks to electron-donating group at the 2-position of benzenesulfonamide aromatic rings, and with low steric hindrance group. This compound demonstrated the strongest binding capacity and affinity for coat protein (CP) of TMV, which is key functional protein of the TMV, involved in translation of mRNAs, transcription of tRNA, elongation, and self-assembly of TMV. The hydrogen bond plays an important role in the stabilization of interactions of compound with TMV-CP, and their number determines antiviral activity.

One of the newest studies conducted by Zhang et al. [49] proved anti-TMV activity of chalcone derivatives containing other nitrogenous base: pyrimidine. As regards of curative activity, the EC<sub>50</sub> value of four tested chalcones derivatives were much lower than ningnanmycin, commercial agent. The curative and protective activity of the target compounds depended on the type, location and carbon chain length of the substituent.

#### Nematicides

Plant-parasitic nematodes pose a major threat to crop protection. With the increasing resistance to nematicides and the lack of new modes of action, there is a growing need for novel nematicides. The most publications about nematicidal activity of chalcones concern *Meloidogyne* genus, the most economically important phytopathogens. To find new nematicidal leads, a series of fused ring compounds were obtained by utilizing a ring closure design strategy based on the structure of chalcone. These compounds were further modified and their nematicidal activity against *M. incognita* was evaluated.

Silva et al. [50] stated that (1E,4E)-1,5-di(4-nitrophenyl)-2-butylpenta-1,4-dien-3-one, one of twelve tested synthesized chalcone analogues poses greater activity than commercial nematicide Carbofuran®, exhibiting lower LC<sub>50</sub>. This compounds is able to reduce of 51% and 68% of galls and



eggs, respectively, when applied to infected tomatoes. The mechanism of action based on the inhibition of P450 enzyme associated with the oxidation of several substances in the nematode.

The bioassay conducted by Cao et al. [51] revealed that modified chalcones-like compounds containing 2-carbonyl tiophene exhibited excellent nematocidal activity. The most active compound showed significant bioactivity with an  $LC_{50}$  / 72h value of 3.20 mg/L in vitro and an inhibition rate of 100.00% at 40 mg/L in the matrix.

Attar et al. [52] reported that polarity as well as planarity of chalcones compounds play important role in their activity of against nematode *Caenorhabditis elegans*. Tested organic chalcones were found to be less polar than synthesized ferrocenyl (Fc) analogues, and simultaneously, they were much more active. It is associated with chalcone's ability to pass through the organism's cell walls.

### Insecticides

Many studies proved effectiveness of both natural and synthesized chalcones against insects. Among naturally occurring chalcones, xanthohumol and isoxanthohumol isolated from hop (*Humulus lupulus* L.) should be mentioned as good example of insecticides. Their effective insecticidal activity has been proven against the peach-potato aphid (*Myzus persicae*) [53].

Shakil and Saxena [54] isolated new chalcone cordifolin from woody stem of Giloe (*Tinospora cordifolia*), and determined its activity against larvae of *Spodoptera litura*. The results showed that cordifolin caused pupation delay, prolonged pupal period and decreased pupal weight.

Many studies were conducted on the synthesis and development new chalcones and its derivatives with insecticidal properties. The works consisted of the modification of chalcones structure and selection of substituents.

Hidalgo et al. [55] conducted study on bis and mono chalcones as insecticides against *Spodoptera frugiperda*. The results showed that two monochalcones containing bromines and hydroxyl groups in ring A and N-N dimethyl group in ring B killed 40 and 60 % larvae, when incorporated to the larval diet at 100 mg per g of diet (40 and 60%, respectively). Bis-chalcones did not exhibit such activity. Contradictory results were obtained by Devi et al. [56], where bis-chalcones showed more toxicity than mono-chalcones. The study of Kumar et al. [8] is the first report on the pesticidal activity of chalcones against *Plutella xylostella*, wherein series of chalcones were synthesized under microwave irradiation. Electron-withdrawing ring A of chalcone was found crucial for pesticidal activity, meanwhile ring B can bear either electron-withdrawing or electron-releasing substituents. Particularly, Cl substitution and its positions on ring A as well as on ring B were found vital. Compound 1,3-Bis(4-chlorophenyl)prop-2-en-1-one showed the maximum activity with  $LC_{50}$  value of 170.24  $\mu\text{g mL}^{-1}$ . The results of the study provide the foundations for further modification of potent units and the design of novel chalcone-based pesticidal agents against *P.xylostella* and related insect pests.

## 5. Conclusions

To sum up, chalcones, both these of natural origin and chemically synthesized, form a diverse and sophisticated group of molecules with a wide spectrum of biological potential. They are known for centuries but collecting data on their use is still ongoing. Much of the pharmacological potential of chalcones is still not utilized and not clearly understood. For that reason, they are of great interest amongst the scientists. The herbicidal, fungicidal, antiviral, insecticidal and plant growth regulator-type activities of various chalcones are presented in this review together with their overall description and methods of detection for the first time based on the most up to date literature.

Because plants do not accumulate chalcones in larger quantities, obtaining them from natural sources is difficult. Another challenge could be their short half-life. It is the reason for the intensive studies on their synthesis and development.

Moreover, further intensive investigation is needed to understand the mode of action of reactive chalcones, their effectiveness in the field, as well as the safety of their possible use for the environment and humans.

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