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Review Article

# Phytochemicals from agricultural and agro-industrial waste: An alternative for the control of phytopathogenic bacteria and fungi

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## ABSTRACT

**Justification.** The use of chemical pesticides has been widespread for several decades, proving effective in controlling pests that reduce crop quality and productivity. However, due to their chemical nature, they present side effects that affect the health of the applicator, the consumer, and the environment. Therefore, the use of natural products is currently emerging as an alternative for controlling phytopathogenic diseases and pests. The objective of this research was to review and analyze the bactericidal and fungicidal effects of phytochemical-rich extracts obtained from agricultural and agro-industrial byproducts and waste.

**Theoretical and experimental framework.** A literature review was conducted using Scopus and Web of Science, focusing on English- and Spanish-language publications from the last 10 years. Only publications related to the extraction of phytochemicals from agricultural and/or agro-industrial byproducts and that investigated their effect against phytopathogenic organisms were considered. In this regard, the main phytochemicals with antibacterial and antifungal activity are phenolic compounds such as flavonoids and other derivatives. Likewise, hydrophobic compounds such as terpenes (essential oils) have demonstrated biocidal potential at concentrations similar to those currently marketed. The main modes and mechanisms of action are multi-target, meaning they affect more than one metabolic pathway and organelle. For example, they affect the cell membrane by inserting into the lipid bilayer, reduce biofilm formation, reduce ergosterol synthesis, and attenuate chitin synthesis in the cell wall.

**Conclusions and Perspectives.** Phytochemicals with potent bactericidal and fungicidal activity were identified, primarily phenolic compounds and essential oils (terpenes). These phytochemicals exhibited IC50 values and reduction percentages even higher than those of the chemical controls. Agricultural byproducts and biomass, which are undervalued resources, represent an important alternative for extracting value-added phytochemicals that can be used across multiple industries, including agriculture, to develop sustainable, non-toxic biopesticides.

**Keywords:** Natural products, Essential oils, Antibacterials, Antifungals, Green chemistry

## JUSTIFICATION

Agriculture is fundamental to humanity, providing more than 80% of the food consumed worldwide. Production methods have been optimized over time, overcoming challenges and conditions that have required adapting processes to achieve higher yields and productivity, with the aim of ensuring food availability for all people (FAO, 2017; Koul, 2023). In agriculture, the use of phytochemicals (FC) has been widely documented as biopesticides (De Benedetti *et al.*, 2021; Pacifico *et al.*, 2021), which have gained popularity in recent years due to their effectiveness, lower toxicity, and cost-efficiency. Agricultural residues are an important source of a wide variety of phytochemicals (FC), such as flavonoids, terpenes, alkaloids, and saponins, among others, which represent great potential for agriculture as potent fungicides and bactericides.

Mexico has a harvested agricultural area of more than 11,808,173.74 ha (SIAP, 2021), which also suggests significant production of by-products such as corn (*Zea mays*) stalks and leaves rich in ferulic acid (Tilay *et al.*, 2008), pepper (*Capsicum annuum*) leaves and stems rich in antioxidant flavonoids (Jiménez-Ortega *et al.*, 2024), and eggplant (*Solanum melongena*) leaves abundant in bioactive alkaloids (Germán-Soto *et al.*, 2024), among others. Numerous reports also indicate that the phytochemical content in agricultural by-products may be higher than that of fruits, due to the abiotic stress to which they are exposed (Anaya-Esparza *et al.*, 2021; Pacifico *et al.*, 2021).

Therefore, the aim of this study was to discuss the bactericidal and fungicidal activity of FC obtained from agricultural by-products. The sources, types, and extracts with the highest activity are described, and their advantages and potential applications as biopesticides are highlighted. It is worth noting that the valorization of agricultural and agro-industrial by-products may contribute to the development of circular economies that could, in the future, be established in the Mexican agricultural sector.

## THEORETICAL AND EXPERIMENTAL FRAMEWORK

The agroindustry plays an important role in the processing and preservation of perishable foods, as well as in the diversification of raw materials and finished products (Sadler *et al.*, 2021). Although the agricultural and agro-industrial sectors are essential for human nutrition, they generate large quantities of waste and residual by-products such as leaves, stems, roots, seeds, peels, bagasse, and pulps, which are often discarded or directed toward low–value applications. However, these residues are relevant due to their FC content; moreover, according to the valorization pyramid of agro-industrial waste and by-products (Figure 1), the extraction of bioactive compounds is the activity with the highest added value (Duque-Acevedo *et al.*, 2020).

In agriculture, the use of FC has been widely documented as biopesticides (De Benedetti *et al.*, 2021; Pacifico *et al.*, 2021), which have become increasingly popular in recent years due to their effectiveness, lower toxicity, and cost-efficiency. In contrast, chemical pesticides such as organophosphates and organochlorines, when used indiscriminately, can cause serious environmental damage by contaminating soil, water, and air. Health impacts have also been documented in mammals, insects, and other species inhabiting affected ecosystems.

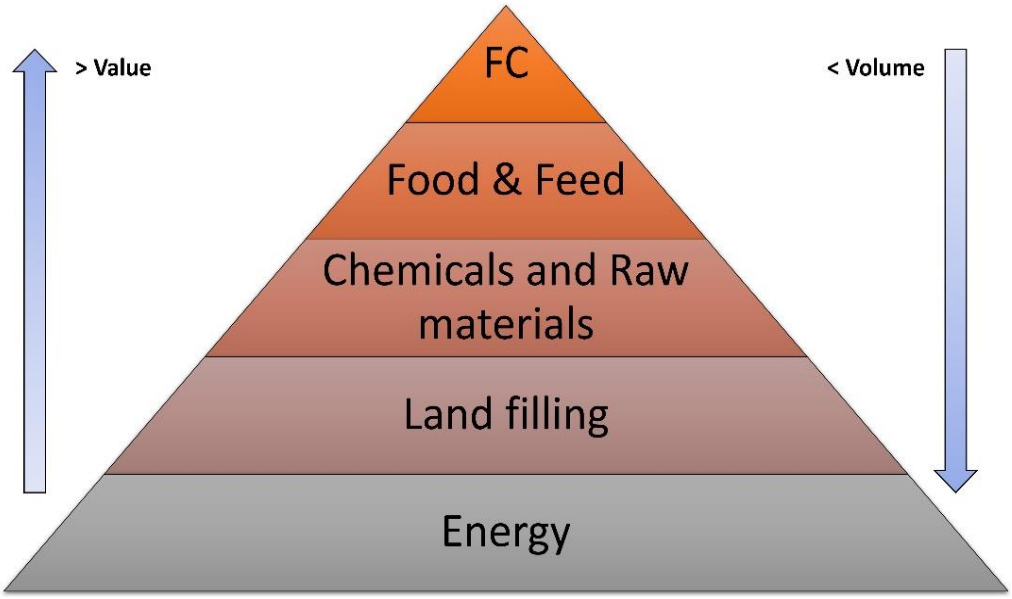


**Figure 1.** Valorization pyramid of biomasses and agricultural and agro-industrial by-products. FC (Phytochemicals).

Numerous studies support the toxic effects of pesticides on human health, particularly among field applicators, who are often not properly trained or lack adequate protective equipment. Acute exposure can cause death within hours due to systemic toxicity; chronic exposure can trigger the development of chronic-degenerative diseases such as cancer, as well as immunological and renal disorders, among others (Bapat *et al.*, 2022; Degrendele *et al.*, 2022; Dwivedi *et al.*, 2022; Vasseghian *et al.*, 2022). Nevertheless, chemical control remains the most efficient, cost-effective, and fast-acting method, making the search for new molecules and sustainable, non-toxic sources necessary. An alternative to chemical pesticides is FC. Because these are produced from natural resources (such as by-products) and applied at appropriate doses and with regulated applications during the recommended period, they have demonstrated greater effectiveness. Furthermore, their extraction can employ optimized techniques and safe, non-toxic solvents, with the aim of safeguarding green chemistry and human health.

## Agriculture and food security

Natural resources, key components in food production, have become increasingly limited. Therefore, it is urgently necessary to optimize production methods and agricultural inputs, such as pesticides and other agrochemicals, to ensure successful production and thereby safeguard food security for Mexico population (FAO, 2017). Mexico is characterized by its gastronomic diversity, with the following ingredients and raw materials standing out due to their high production volumes and yields: grain corn (*Zea mays*), beans (*Phaseolus vulgaris*), sorghum (*Sorghum* spp.), oats (*Avena sativa*), and forage corn. However, the crops that generate the greatest economic output are corn, green pepper, red tomato, sorghum, and beans (SIAP, 2021). It is worth noting that the states with the largest harvested agricultural area in 2024 were Zacatecas, Tamaulipas, Chiapas, Jalisco, and Puebla, while those generating the highest economic output were Sinaloa, Jalisco, Michoacán, Sonora, and Chihuahua (SIAP, 2026).

The slogan for the 2021 World Food Day, established by FAO, is: "Our actions are our future." By generating bioproducts obtained from the production chain of fruits and vegetables itself, it is possible to achieve a degree of sustainable, sufficient, and safe production, with adequate nutritional quality and accessible to all. It is important to consider all these factors to ensure sustainable agriculture; however, meeting all these objectives represents a major challenge (FAO, 2021).

Current figures indicate that around 690 million people worldwide suffer from hunger, representing nearly 9% of the global population, with a trend that continues to rise (UN, 2021). The growing world population is a challenge that puts agro-production systems to the test. It is estimated that by 2030, the population will reach 6 910 million in developed countries, while in developing countries, it will reach 381 million. By 2050, global population growth is projected to reach 9 322 million, with an annual increase of 0.6%; this means that 1.4% more agricultural food will be required to meet the daily caloric needs of an adult (3 050 kcal/capita/day). Therefore, it is necessary to implement efficient strategies for the production and management of insect and phytopathogenic pests, as they can cause losses of up to 20% of total production (CIPF, 2021). Although chemical pesticides are useful and effective for preventing and eradicating pests, they have, since their introduction, caused a series of serious environmental and public health impacts, in addition to inducing resistance in crops and contaminating groundwater and soil, among other effects documented in literature. Therefore, it is important to seek efficient alternatives that take environmental impact and toxicity into consideration (Bapat *et al.*, 2022; Moustafa *et al.*, 2021; Tang and Luo, 2021).

**Agro-industrial by-products as a source of value-added phytochemicals**

According to the Corporate Statistical Database of the Food and Agriculture Organization of the United Nations, the main agricultural products produced in 2024 were sugarcane (*Saccharum officinarum*) (1 939 782 021 t), maize (1 218 205 574 t), and rice (820 223 278 t) (Figure 2). The countries with the highest production volumes were China, Brazil, and the United States (FAO, 2026). These production volumes generate substantial quantities of by-products composed of fibers, peels, seeds, bagasse, roots, leaves, stems, and other lignocellulosic materials rich in phytochemicals, which have high value-added commercial implications (Nayak and Bhushan, 2019; Teigiserova *et al.*, 2019).

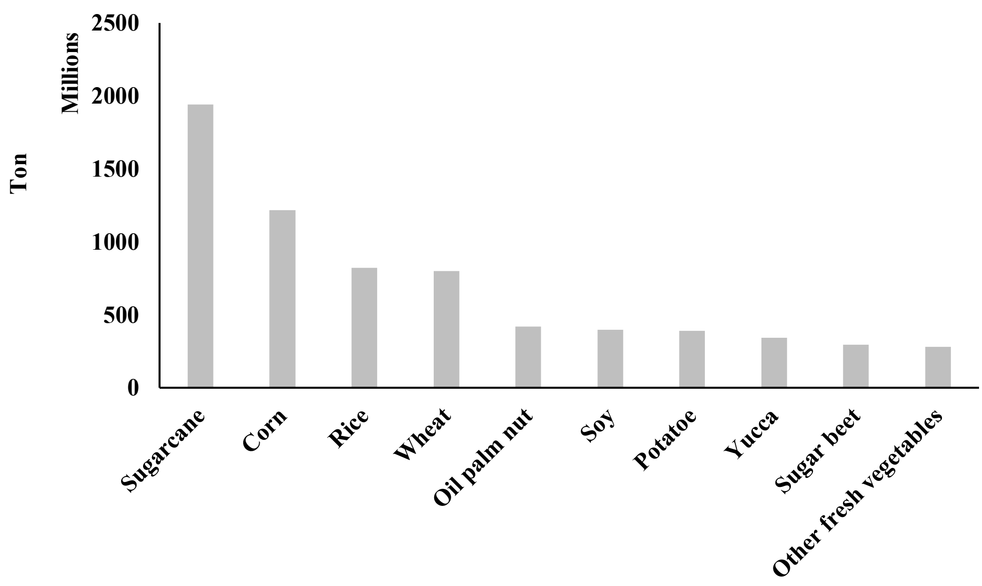


**Figure 2.** Major crops produced worldwide in 2024. Data obtained from FAO (2026).

FC derived from agro-industrial by-products, used as biopesticides, have been widely studied and exhibit a broad range of applications (Figure 3). For example, in the Web of Science (Clarivate) database, at least 931 original publications have been recorded in the last 10 years. However, most of these studies use medicinal plants or edible fruits as sources of FC. Among them, aromatic plants (rich in essential oils) lead chemical and biological research, mainly due to their bactericidal and antifungal activity.

On the other hand, the leading countries in this area of research are the United States, China, and India. It is worth noting that, only ≈588 documents on the extraction of phytochemicals from agro-industrial by-products, with Italy, Spain, and Portugal being the countries with the highest number of publications. Of these, only a small number focus on plant health, making it of interest to expand research to enhance the use of these underutilized resources for crop health and, consequently, for human and environmental health. In this context, incorporating practices such as the use of biopesticides as part of integrated management of major pests and diseases generates a circular economy model that produces biopesticides from crude extracts or purified metabolites obtained from crop-generated by-products, contributing to the shift from a linear to a circular economy and implementing differentiation strategies that support competitiveness in the agricultural sector (Campos *et al.*, 2020; Rojas Rojas *et al.*, 2021).

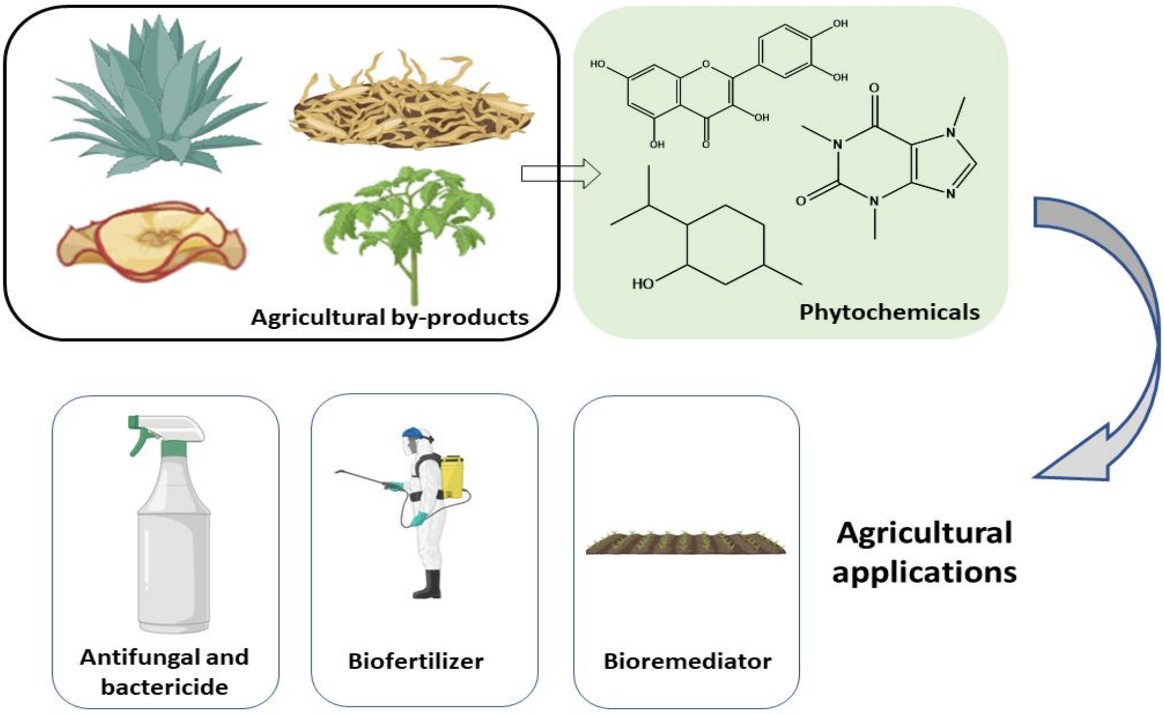


**Figure 3.** Industrial applications of phytochemicals isolated from agricultural by-products. Created with BioRender.

## Phytopathogenic organisms

The presence of phytopathogenic organisms and the diseases they cause can be influenced by biotic and abiotic factors during sowing, vegetative and productive stages, harvest, and postharvest of crops. Among the biotic factors, fungi, bacteria, viruses, protozoa, and nematodes stand out. However, the most abundant and economically significant phytopathogens are fungi, viruses, and bacteria, which are responsible for most phytosanitary problems worldwide and, consequently, for the greatest economic and food losses (Ravichandra, 2013). The bacterial genera associated with severe diseases that result in major crop losses and have the greatest economic relevance include: *Acidovorax*, *Agrobacterium*, *Bacillus*, *Burkholderia*, *Citrobacter*, *Clavibacter*, *Dickeya*, *Erwinia*, *Leifsonia*, *Pectobacterium*, *Pseudomonas*, *Ralstonia*, *Spiroplasma*, *Xanthomonas*, and *Xylella*, among others (Hernández-Díaz *et al.*, 2021; Setubal *et al.*, 2005). On the other hand, the most extensively studied fungal genera are *Alternaria*, *Botrytis*, *Colletotrichum*, *Fusarium*, *Drechslera* (Syn. *Helminthosporium*), *Aspergillus*, *Penicillium*, *Macrophomina*, *Neofusicoccum*, *Rhizoctonia*, *Sclerotinia*, *Curvularia*, *Mucor*, *Botryosphaeria*, *Diplodia*, *Sclerotium*, and *Phoma* (Di Canito *et al.*, 2021; Hernández-Díaz *et al.*, 2021; Xu *et al.*, 2021). Knowledge of these phytopathogenic agents allows for the effective study and application of biocontrol strategies.

**Pesticides: environmental and public health challenges**

Pest management is based on the principles of prevention, suppression, and/or eradication, and each of these can involve different strategies—biological, chemical, mechanical, cultural, genetic manipulation, among others (Zepeda-Jazo, 2018). Among the most widely used and effective tools against all types of pests are chemical pesticides; however, toxic side effects on humans, flora, fauna, and various ecosystems continue to be documented, as agrochemicals can migrate hundreds of kilometers and affect distant regions (Couvidat *et al.*, 2022; Degrendele *et al.*, 2022; Ding *et al.*, 2022). In response, governments are working to create alternatives that reduce or replace their use. In contrast, regarding the phytotoxicity of natural extracts, high doses may desiccate plants, but when applied at the doses recommended by producers, no toxic effects have been reported in humans or other mammals (Fenibo *et al.*, 2022).

**Phytochemicals (FC).** Phytochemicals (FC) are secondary metabolites synthesized through the shikimic acid, malonic acid, and mevalonic acid pathways, and it is estimated that more than 100,000 exist; however, those most extensively studied due to their bioactivities are flavonoids, terpenes, alkaloids, and saponins (Figure 4) (de la Rosa *et al.*, 2019; Khare *et al.*, 2020). The accumulation of phytochemicals in plants is generally associated with stress conditions caused by biotic and abiotic factors, which trigger a cascade of biochemical signals that primarily promote their synthesis as a defense mechanism (Marranzano *et al.*, 2018). Since ancient times, humans have used and commercialized FC for therapeutic purposes to treat a wide variety of diseases and ailments. With technological advances and increasing awareness of environmental protection, FC have been studied to demonstrate their biocidal potential against phytopathogens, among other applications, such as additives, pigments, and antioxidant agents. Phenolic compounds can exhibit a wide variety of structures and are therefore classified from simple phenolics to highly complex phenolics, depending on the number and position of hydroxyl groups attached to the phenolic ring (Chaudhary *et al.*, 2018; Singh *et al.*, 2017). Within this group of FC are flavonoids, phenolic acids, coumarins, lignins, and tannins. Flavonoids are recognized as the most important and widely distributed in plants, with more than 5,000 reported. These compounds are of low molecular weight; their structure contains two aromatic rings of phenolic nature linked by a three-carbon bridge (C6–C3–C6). They are divided into different subgroups, such as flavonols, flavanones, flavones, flavan-3-ols, isoflavones, catechin, leucoanthocyanidins, chalcones, and anthocyanins (Lattanzio, 2013; Medina-Meza and Ganjyal, 2017; Tsao, 2010).

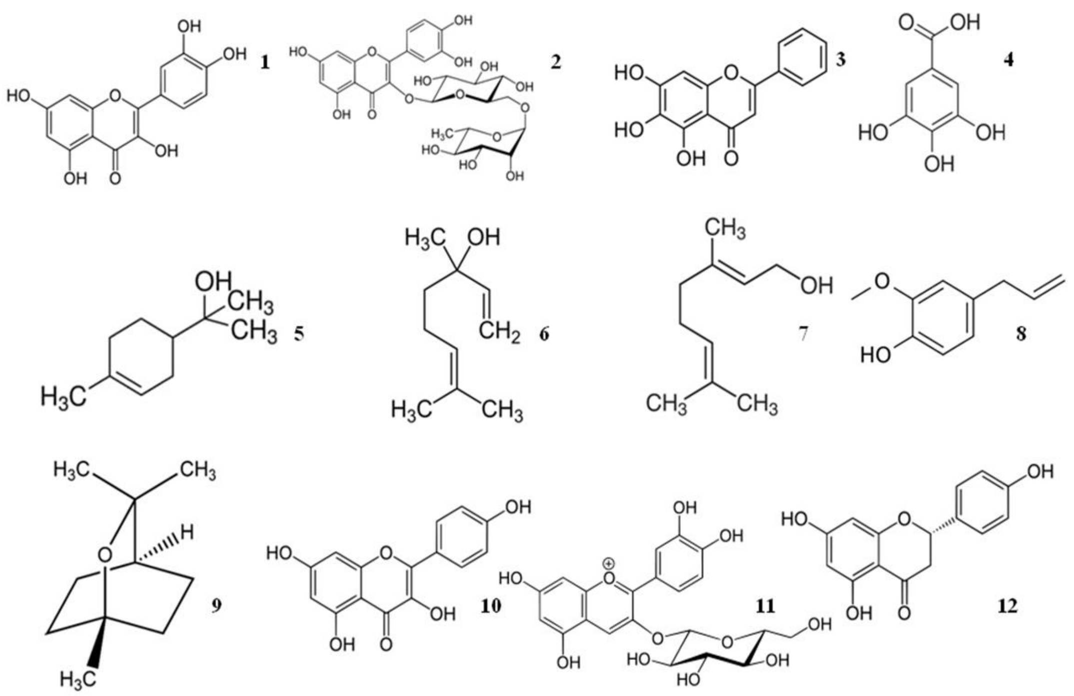

**Figure 4.** Molecular structures of antibacterial and antifungal phytochemicals identified in agricultural by-products. **1.** Quercetin. **2.** Rutin. **3.** Baicalein. **4.** Gallic acid. **5.** Terpineol. **6.** Linalool. **7.** Geraniol. **8.** Eugenol. **9.** Eucalyptol. **10.** Kaempferol. **11.** Cyanidin 3-O-glucoside. **12.** Naringenin.

On the other hand, terpenes are hydrophobic organic compounds derived from the condensation of isoprene (a five-carbon hydrocarbon). Based on this, they can be categorized as hemiterpenes (C5), monoterpenes (C10), sesquiterpenes (C15), diterpenes ($C_{20}$), sesterterpenes ($C_{25}$), triterpenes ($C_{30}$), tetraterpenes ($C_{40}$), and polyterpenoids ($C_{>40}$). Among the tetraterpenoids are the carotenoids; β-carotene, in particular, is highly relevant because it is the precursor of vitamin A. In this sense, some vitamins are considered terpenes, such as the fat-soluble vitamins D and K (Pichersky and Raguso, 2018).

**Methods for the extraction and purification of phytochemicals from agricultural and agro-industrial by-products.** Extraction methods for FC rely on their ability to degrade cellular structures, such as walls and membranes, and to subsequently solubilize the FC in the extraction solvent. Depending on the hydrophilicity or hydrophobicity of the molecules of interest, a solvent of similar polarity is used, following the solubility principle: "like dissolves like." Therefore, most FC are solubilized in organic solvents such as ethanol, methanol, or water. For example, flavonoids can be extracted with 70–80% hydroethanolic solutions, methanol, or acetone, whereas carotenoids and other nonpolar compounds, such as fats and oils, dissolve in hexane, toluene, and methylene chloride, among others (Jiménez-Ortega *et al*., 2024).

The extraction method will largely depend on the yield and purity of the compound. Currently, systems such as temperature-controlled maceration, ultrasonic baths, microwaves, supercritical fluids, ionic and eutectic solvents (DES), and hydrogenated solvents, among others, can be employed. Their advantage is that these techniques can be coupled, resulting in higher extraction yields while reducing energy consumption and operating time (Jiménez-Ortega *et al.*, 2024; Jiménez-Ortega *et al.*, 2023).

Once the crude extracts are obtained, they can be purified by column chromatography, using silica as the stationary phase and solvents of increasing polarity as the mobile phase to elute metabolites in fractions of different polarities. The effect of each fraction can then be evaluated and/or further purified to obtain pure crystals of the FC. Typically, the compound's retention factor is monitored by thin-layer chromatography (TLC); if crystals or precipitates are obtained, they can be analyzed using LC–MS/MS, GC–MS/MS, NMR, X-ray diffraction, FTIR, among other techniques (Patil *et al.*, 2023). Figure 5 shows the experimental protocol for obtaining FC from agricultural by-products, highlighting the unit operations involved.

**Phytochemicals from agricultural and agro-industrial by-products as biopesticides**

**Antibacterial activity.** Two of the most common mechanisms by which FC inhibit bacterial growth are: (1) molecular and genetic damage, and (2) disruption of cellular membranes. Genetic damage occurs when FC, such as alkaloids, interact with the nitrogenous bases of bacterial nucleic acids, altering the expression of genes responsible for flagellum production and thereby reducing bacterial motility. This results in decreased growth and a reduced capacity for infection (Dusane *et al.*, 2014).

On the other hand, damage or rupture of the bacterial cell membrane occurs through interactions with terpenoids, which partially or completely dissolve it, causing lysis and cell death (Yang *et al.*, 2020). Agricultural and agro-industrial by-products contain antibacterial FC; however, their effectiveness will depend on the type of FC, the extraction method, the concentration, and the type of bacterium, among other factors (Table 1).

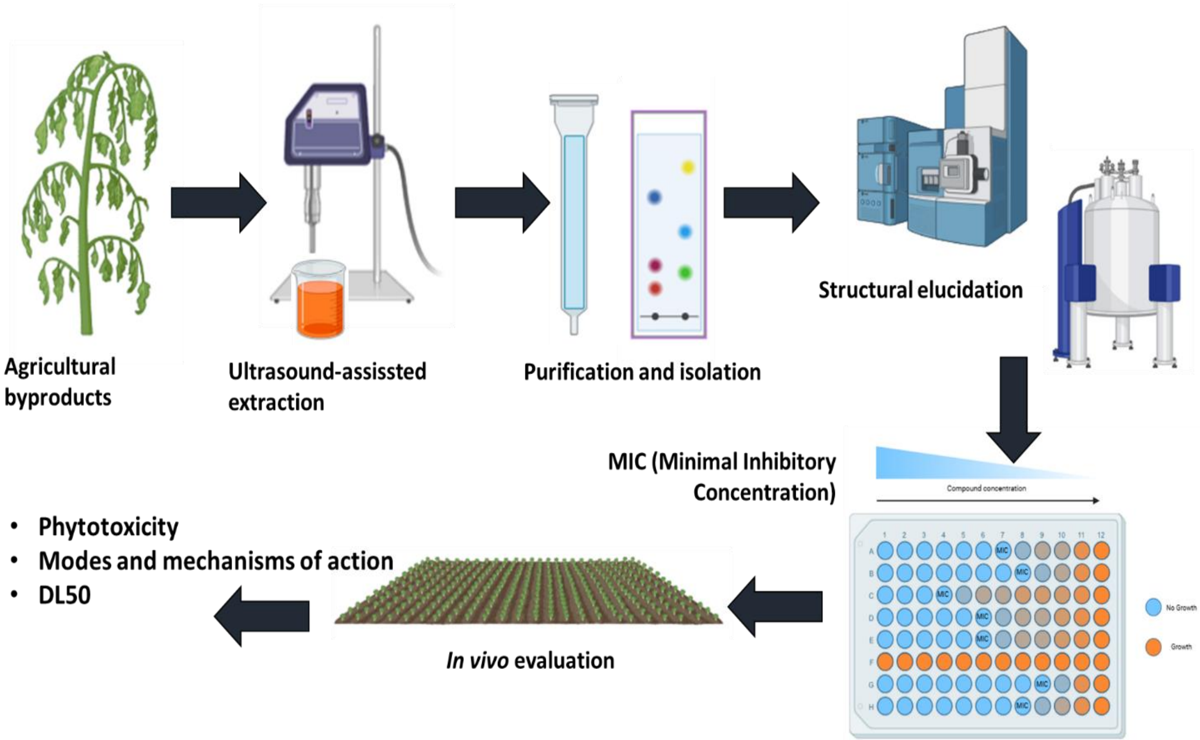


**Figure 5.** Process for obtaining phytochemicals from agricultural biomasses and scaling them to an industrial level for the generation of biopesticides potentially applicable to the crops. Created with BioRender.

Terpenes can cause irreversible damage to bacterial cell membranes and walls, leaving them without adequate protection against other toxic agents. Polyphenols, on the other hand, can inhibit bacterial growth by decreasing the activity of key enzymes involved in essential biological functions (Yang *et al.*, 2020).

Some outstanding examples include the study by Do *et al.* (2021), who evaluated the antibacterial activity of crude root extracts of *Scutellaria baicalensis* and purified baicalein (BAI). The authors observed that the bacterium *Ralstonia solanacearum* was more susceptible to BAI, showing greater inhibition than the control group treated with chloramphenicol (MIC of 0.019 mg $mL^{-1}$ and 0.000044 mg $mL^{-1}$, respectively). This is attributed to the presence of hydroxyl groups in BAI, which may be responsible for the inhibition. Likewise, BAI was more effective than the crude extract (up to 105-fold).

Currently, science and technology are developing new methods to maximize the extraction of FC from by-products, as these compounds are often bound to lignified polymeric structures (in stems and roots) composed of cellulose, hemicellulose, and lignin, making their extraction particularly challenging. To release them, it is necessary to break the cell wall and the ester and ether bonds between FC and the polymers so that they can dissolve in the solvent. In such cases, acidic and alkaline processes must be used, coupled with emerging extraction methods such as ultrasound–microwave techniques, among others (Santos-Zea *et al.*, 2018; Wang *et al.*, 2020).

**Table 1.** Agricultural and agro-industrial by-products with antibacterial activity.

| By-product | Extract | Phytochemical | Phytopathogen | MIC | Inhibition (%) | Reference |
|---|---|---|---|---|---|---|
| *Scutellaria* roots | Ethanolic | Baicalein | *A. avenae* subsp. *cattlyae*<br>*A. tumefaciens*<br>*B. glumae*<br>*C. michiganensis* subsp. *michiganensis*<br>*P. carotovara* subsp. *carotorova*<br>*D. chrysanthemi*<br>*P. syringae* pv. *lachrymans*<br>*X. arboricola pruni*<br>*P. syringae* pv. *actinidiae* KW11<br>*R. solanacearum* | 19 µg $mL^{-1}$ | 75–94 | Do *et al*., 2021 |
| Date palm | Aqueous | Protocatechuic acid<br>Tyrosol<br>Vanillic acid<br>*p*-Coumaric acid<br>Syringic acid<br>Gallic acid | *X. campestris*<br>*E. amylovora*<br>*E. toletana*<br>*C. michiganensis* subsp. *michiganensis*<br>*C. michiganensis* subsp. *insidiosus*<br>*R. radiobacter*<br>*P. savastanoi*<br>*P. syringae* | 3.13 mg $mL^{-1}$ | 100 | Mrabet *et al*., 2017 |
| Pomegranate peel | Aqueous | Flavonoids and tannins | *X. campestris*<br>*C. michiganensis* | 5 mg $mL^{-1}$ | 100 | Elshafie *et al*., 2021 |
| Banana pseudostem and marigold leaves | Aqueous | α-Terthienyl<br>Polyacetylenes<br>Polythienyls<br>Coumarins | *P. syringae* pv. *spinacae*<br>*P. syringae* pv. *Tomato* | 100 mg $mL^{-1}$ | 37–40 | Mitra & Paul, 2016 |
| Pine and olive bark, and leaves | Acetone | Terpenes<br>Caryophyllene<br>β-Cubenene<br>Cembrene<br>Thunbergol | *A. tumefaciens*<br>*E. carotovora*<br>*C. fascians*<br>*P. solanacearum* | 0.41 mg $mL^{-1}$ | 100 | Badawy & Faraj, 2019 |

On the other hand, if the by-products are leaves, pulps, or bagasse, they can be extracted directly through hydrothermal treatments, since phenolic compounds and terpenes are typically located in vacuoles and trichomes, respectively. For example, thermal pretreatments can increase the extraction yield of FC. In date palm (*Phoenix dactylifera*), the release of polyphenols is facilitated. Extraction temperature plays a fundamental role, as higher temperatures release greater amounts of compounds such as hydroxymethylfurfural and, consequently, in most cases, greater inhibition of phytopathogens is observed. Likewise, it was reported that increasing the temperature from 140 to 160 °C reduced the MIC by up to 50% against *Xanthomonas campestris*, *Erwinia amylovora*, *Clavibacter michiganensis* subsp. *michiganensis*, *C. michiganensis* subsp. *insidiosus*, *Rhizobium radiobacter*, *Pseudomonas savastanoi*, and *Pseudomonas syringae* (Mrabet *et al.*, 2017). Additionally, it has been observed that the aqueous extract of pomegranate peel (*Punica granatum*), rich in flavonoids and tannins, exhibited activity against *X. campestris* and *C. michiganensis*, with an MIC of 5 mg $mL^{-1}$. This concentration produced nearly 100% inhibition in both bacteria, similar to the controls treated with kanamycin (0.05 mg $mL^{-1}$) and tetracycline (0.16 mg $mL^{-1}$) (Elshafie *et al.*, 2021).

It is worth mentioning that extracts from banana pseudostem (*Musa paradisiaca*) and marigold leaves (*Tagetes erecta*) showed *in vivo* inhibitory activity against *P. syringae*, reducing disease severity in tomato (*S. lycopersicum*), spinach (*Spinacia oleracea*), cucumber (*Cucumis sativus*), and barley (*Hordeum vulgare*). A 38% reduction in disease was observed at a concentration of 100 mg $mL^{-1}$. Although application of the extracts did not completely reduce disease severity, it did contribute to treatment when used synergistically with another extract of higher activity (Mitra and Paul, 2016). This suggests that plant extracts may serve as potential biocidal products *in vivo*; therefore, further research on phytotoxicity, dosage, and treatment regimens is recommended.

On the other hand, hydrophilic extracts from pine leaves and bark (*Pinus* spp.) and olive (*Olea europaea*) were shown to be rich in monoterpenes, steroids, diterpenes, sesquiterpenes, resins, and polyphenols. These extracts exhibited inhibitory activity against *Agrobacterium tumefaciens*, *Erwinia carotovora*, *Corynebacterium fascians*, and *P. solanacearum*. The most effective extract across all bacteria was olive bark, which showed the lowest MIC against *C. fascians* (0.41 mg $mL^{-1}$) (Badawy and Faraj, 2019). Extracts from wine industry by-products, such as grape pomace and seeds (*Vitis vinifera*), obtained through emerging methods, inhibited *P. syringae* pv. *syringae* with an MIC > 1 mg $mL^{-1}$, lower than that of the control (dithianon), which is attributed to the presence of anthocyanins and fatty acids (Tacchini *et al.*, 2019).

**Antifungal activity.** Antifungal activity is evaluated using different techniques, such as inhibition of sporulation (%), inhibition of mycelial growth (%), minimum inhibitory concentration (MIC), and minimum fungicidal concentration (MFC). As in bacteria, the mechanism by which FC inhibits fungi is also related to disruption of the fungal membrane; when it is dissolved or ruptured, internal organelles become exposed, triggering a series of cell-death pathways and leading to growth inhibition. Another mechanism occurs once FC cross the fungal membrane: they negatively affect mitochondrial cellular respiration, causing metabolic imbalance. With reduced energy availability, fungi are unable to carry out vital metabolic functions, which consequently diminishes their growth and propagation. Other mechanisms include inhibition of efflux pumps that remove intracellular toxic substances; inhibition of protein and genetic material synthesis; promotion of mitochondrial dysfunction; and inhibition of cell division (Al Aboody and Mickymaray, 2020; Peng *et al.*, 2012).

**Agricultural by-products for fungal management**

**Wine industry by-products.** Grape pomace extracts are rich in anthocyanins, polyphenols, and fatty acids. However, their effectiveness depends on the extraction method (Mendoza *et al.*, 2013; Tacchini *et al.*, 2019). For example, grape seed extracts obtained by ultrasound contained higher amounts of FC and were effective against *Sclerotinia minor* and *S. sclerotiorum*, with an MIC > 15 µg mL$^{-1}$ for both fungi (Tacchini *et al.*, 2019).

***Solanum lycopersicum* by-products.** Hydrophilic extracts from tomato leaves and stems showed *in vivo* inhibition against *Colletotrichum coccodes*, *Fusarium oxysporum* f. sp. *lycopersici*, *Glomerella cingulata*, and *Rhizoctonia solani*. The leaf extract exhibited inhibition against *R. solani*, with an MIC < 0.31 mg mL$^{-1}$ (Kim *et al.*, 2019). On the other hand, hydroethanolic extracts from tomato leaves were effective against *Aspergillus niger* (MIC 0.90 mg mL$^{-1}$) and *Penicillium funiculosum* (MIC 0.45 mg mL$^{-1}$). The inhibition was attributed to the presence of flavonoids and phenolic acids, which are abundant in polar solvents such as ethanol. The strongest effect was observed against *P. funiculosum*, with an MIC lower than that of ketoconazole (MIC 2.50 mg mL$^{-1}$) (Añibarro-Ortega *et al.*, 2020).

***Jatropha curcas* by-products.** It is well known that *Jatropha* is an important source of fats and oils for various industries. One of its main by-products is the seed, a structure that is resilient to conventional extraction treatments; however, it contains antifungal FC. For example, Haq *et al.* (2021) evaluated the methanolic extract of defatted *J. curcas* seeds against *C. coccodes*, *R. solani*, *Bipolaris oryzae*, and *Fusarium fujikuroi*. Among the fungi tested, *B. oryzae* was the most susceptible, with an MIC of 1.5 mg mL$^{-1}$, being even more effective than the control (amphotericin B). This activity is attributed to the presence of flavonoids, which may interact with fungal genetic material, affecting the synthesis of physiologically important proteins and reducing growth. On the other hand, *Lasiodiplodia theobromae*, *Curvularia lunata*, *Fusarium semitectum*, *C. capsici*, and *C. gloeosporioides* were found to be susceptible to the ethanolic extract of defatted *Jatropha* seed, with an MIC of 500 mg mL$^{-1}$ (Saetae and Suntornsuk, 2010).

***Punica granatum* by-products.** Pomegranate is a fruit highly valued by consumers; however, during its ripening period, large quantities of by-products such as leaves, pomace, and peels are generated, which, due to their composition, have demonstrated antifungal capacity. For example, ethanolic extract from pomegranate peel applied against *F. oxysporum*, *A. niger*, *F. graminearum*, *F. culmorum*, and *A. alternata* showed an MIC of 0.31 mg mL$^{-1}$, with flavonoids and tannins identified as the compounds responsible for the bioactivity (Hlima *et al.*, 2019). In contrast, aqueous extracts exhibited lower activity against *F. oxysporum* and *P. digitatum*, with an MIC of 10 mg mL$^{-1}$, which may be due to the lower extraction efficiency of water, a more polar solvent than ethanol (Elshafie *et al.*, 2021).

Other extracts obtained from pomegranate by-products and evaluated against *P. italicum*, *B. cinerea*, and *R. stolonifer* showed mycelial growth inhibition (MGI) of 28.46% for *P. italicum* and 42.50% for *B. cinerea* and *R. stolonifer*. Regarding spore germination inhibition (SGI), *P. italicum* exhibited 17.86% inhibition, while *B. cinerea* and *R. stolonifer* showed 30.5% inhibition. With respect to the type of by-product, leaves, seeds, and peels showed SGI values of 32.16, 38.60, and 43%, and MGI values of 17.13, 29.93, and 32.25%, respectively. For the concentrations tested—500, 1,000, and 1,500 ppm—SGI values were 40.99, 49.20, and 61.78%, and MGI values were 27.05, 33.86, and 45%, respectively (Tehranifar *et al.*, 2011). On the other hand, aqueous extraction (microwave-assisted) of pomegranate peel combined with avocado peel and seed, evaluated against *P. expansum* and *A. niger*, showed an MIC of 25 mg $mL^{-1}$ (Skenderidis *et al.*, 2021).

**Other by-products.** Extracts obtained with various solvents—such as dichloromethane, ethyl acetate, acetone, and methanol—from hop by-products generated by the brewing industry were evaluated against *F. culmorum*, *F. equiseti*, *F. semitectum*, *F. oxysporum*, *P. purpurogenum*, *B. cinerea*, *Mucor hiemalis*, and *A. ochraceus*. Notably, *F. culmorum* showed the lowest MIC across all extracts (0.5 mg $mL^{-1}$) (Bartmańska *et al.*, 2018).

On the other hand, wastewater and oil-free solid residues derived from lavender (*Lavandula angustifolia*) contained phenolic compounds and terpenes. Ethanolic extracts of both by-products exhibited antifungal activity against *A. niger*, *A. alternata*, and *P. chrysogenum*, with MIC values of 0.08 µg $mL^{-1}$ (wastewater) and 0.50 µg $mL^{-1}$ (solid residue). Notably, both extracts showed lower MICs than lavender essential oil (0.75 µg $mL^{-1}$), and the wastewater extract displayed lower MIC values than synthetic antifungals such as caspofungin (0.24 µg $mL^{-1}$) and kanamycin (Ciocarlan *et al.*, 2021). The study suggests that the wastewater from essential oil distillation exhibits broad bactericidal activity, likely due to its high content of hydrophobic (terpenes) and hydrophilic (flavonoids) compounds.

Papaya seeds and leaves (*Carica papaya*) contain saponins, flavonoids, and carotenoids, which have demonstrated activity against *Fusarium* spp. and *C. gloeosporioides*. Ethanolic extracts of papaya leaves showed an MIC of 0.625 mg $mL^{-1}$ against *Fusarium* spp. and >10 mg $mL^{-1}$ against *C. gloeosporioides* (Chávez-Quintal *et al.*, 2011). Citrus peel extracts obtained by hydrodistillation were evaluated against *R. solani*, *C. lunata*, *F. oxysporum*, *Helminthosporium oryzae*, *A. niger*, *Cladosporium herbarum*, and *Trichoderma viride*, with the lowest MIC observed against *A. niger* (6.25 µL $mL^{-1}$) (Vasudeva and Sharma, 2012). Table 2 presents additional examples of the antifungal activity of FC from agricultural and agro-industrial by-products.

**Sustainability, toxicity, and scalability of phytochemical-based bactericides and fungicides**

According to the 12 principles of green chemistry (Anastas and Eghbali, 2010), the production of biopesticides can be considered green, as energy consumption is minimal, waste generation is reduced, and the final products are not hazardous. Likewise, biorational products provide protection against microorganisms and insects and are effective at low concentrations. They are biodegradable and leave no residues, in contrast to chemical pesticides (Fenibo *et al.*, 2022). Before being marketed, it is necessary to evaluate their phytotoxicity to determine appropriate doses and routes of application. However, biorational products do not exhibit toxicity in mammals when applied at the recommended concentrations. In addition, their commercialization requires compliance with strict health and safety regulations. The biorational products industry is continually growing. Some commercial successes include Aza-Direct, which contains azadirachtin; Timorex Gold, based on tea tree oil; and Regalia MAXX, formulated with *Reynoutria sachalinensis* extract, among others.

**Table 2.** Agricultural and agro-industrial by-products with antifungal activity.

| By-product | Extract | Phytochemical | Phytopathogen | MIC | Inhibition (%) | Reference |
|---|---|---|---|---|---|---|
| Tomato leaves and stems | Hexane, dichloromethane, acetone, methanol | Linolenic acid<br>Caffeic acid | *C. coccodes*<br>*F. oxysporum* f. sp. *lycopersici*<br>*G. cingulata*<br>*R. solani* | < 0.31 mg mL⁻¹ | 51.2–69.8 | Kim *et al*., 2019 |
| *J. curcas* seed oils and extracts | Aqueous, hexane, methanol | Flavonoids<br>Saponins<br>Tannins<br>Steroids<br>Glycosides | *C. coccodes*<br>*R. solani*<br>*B. oryzae*<br>*F. fujikuroi* | 1.5 mg mL⁻¹ | 80 | Haq *et al*., 2021 |
| *J. curcas* seeds | Ethanolic | Phorbol esters | *F. oxysporum*<br>*L. theobromae*<br>*C. lunata*<br>*F. semitectum*<br>*C. capsici*<br>*C. gloeosporioides* | 500 mg L⁻¹ | 50 | Saetae and Suntornsuk, 2010 |
| Pomegranate peel (*P. granatum*) | Ethanolic | Flavonoids<br>Anthocyanins | *F. oxysporum*<br>*A. niger*<br>*F. graminearum*<br>*F. culmorum*<br>*A. alternata* | 0.312 mg mL⁻¹ | 100 | Hlima *et al*., 2019 |
| Pomegranate peel (*P. granatum*) | Aqueous | Tannins<br>Flavonoids<br>Polysaccharides | *F. oxysporum*<br>*P. digitatum*<br>*B. cinerea* | 10 mg mL⁻¹ | 42 | Elshafie *et al*., 2021 |
| Spent hops | Dichloromethane; Ethyl acetate; Acetone; Methanol | Flavonoids | *F. culmorum*<br>*F. equiseti*<br>*F. semitectum*<br>*F. oxysporum*<br>*P. purpurogenum*<br>*B. cinerea*<br>*M. hiemalis*<br>*A. ochraceus* | 0.5 mg mL⁻¹ | 50 | Bartmańska *et al*., 2018 |
| Avocado and pomegranate peel and seed | Aqueous | Procyanidin<br>Catechins<br>Quercetin<br>Caffeoylquinic acid<br>Coumaric acid | *P. expansum*<br>*A. niger* | 25 mg mL⁻¹ | 100 | Skenderidis *et al*., 2021 |
| Lavender | Aqueous | Eucalyptol<br>Linalool<br>Linalool oxide<br>Terpinen-1-en-4-ol<br>α-Terpineol | *A. niger*<br>*A. alternata*<br>*P. chrysogenum* | 0.08 µg mL⁻¹ | 100 | Ciocarlan *et al*., 2021 |
| Pomegranate peel, leaves, and seeds | Aqueous; methanolic | Punicalagin<br>Ellagic acid | *P. italicum*<br>*B. cinerea*<br>*R. stolonifer* | 500 ppm | 40.99 | Tehranifar *et al*., 2011 |
| Grape pomace | Methanolic; ethanolic | Gallic acid<br>Protocatechuic acid<br>Vanillic acid<br>Ellagic acid<br>Quercetin<br>Kaempferol<br>*p*-Coumaric acid<br>Syringic acid<br>Epicatechin<br>Catechin | *B. cinerea* | 35.7 µg mL⁻¹ | 50 | Mendoza *et al*., 2013 |
| Spent grape pomace and grape seed | Ethanolic | Anthocyanins<br>Malvidin-3-*O*-glucoside<br>Delphinidin-3-*O*-glucoside<br>Cyanidin-3-*O*-glucoside | *S. minor*<br>*S. sclerotiorum* | >15 µg mL⁻¹ | 50 | Tacchini *et al*., 2019 |
| Tomato leaves and stems | Hydroethanolic | *p*-Coumaric acid hexoside<br>5-*O*-Caffeoylquinic acid<br>5-*p*-Coumaroylquinic acid, 5-*O*-Feruloylquinic acid, Quercetin-pentosyl-rutinoside<br>Rutin, Quercetin-deoxyhexosyl-hexoside<br>Kaempferol-3-*O*-rutinoside | *P. funiculosum*<br>*A. niger* | 0.45 mg mL⁻¹ | 100 | Añibarro-Ortega *et al*., 2020 |

**Continuation of the Table 2.**

| By-product | Extract | Phytochemical | Phytopathogen | MIC | Inhibition (%) | Reference |
|---|---|---|---|---|---|---|
| Papaya leaves and seeds | Ethanolic | Triterpenes<br>Flavonoids<br>Alkaloids<br>Saponins | *Fusarium* spp.<br>*C. gloeosporioides* | 0.625 mg mL$^{-1}$ | 50 | Chávez-Quintal *et al*., 2011 |
| Citrus peel | Aqueous | Essential oils<br>D-Limonene<br>(±)-Linalool<br>β-Myrcene<br>α-Pinene<br>Sabinene<br>δ-3-Carene | *R. solani*<br>*C. lunata*<br>*F. oxysporum*<br>*H. oryzae*<br>*A. niger*<br>*C. herbarum*<br>*T. viride* | 6.25 µg mL$^{-1}$ | 100 | Vasudeva and Sharma, 2012 |
| Pine and olive bark, and leaves | Acetone | Terpenes<br>Caryophyllene<br>β-Cubenene<br>Cembrene<br>Thunbergol | *B. cinerea* | 0.071 mg mL$^{-1}$ | 50 | Badawy and Faraj, 2019 |

Regarding their toxicity, these molecules have a high $LD_{50}$, but being of natural origin does not mean they are non-toxic. Phytochemicals with generally higher toxicity profiles include essential oils and alkaloids in their pure state. Even commercial derivatives such as spinosad, azadirachtin, thujone, pulegone, thymol, menthol, among others, are toxic when administered at high concentrations.

The market for natural products continues to grow, and this trend is expected to continue. For example, since the 1990s, pesticide consumption in Europe has reached 460 000 t, while in the United States it has exceeded 406,000 t (Rufo *et al.*, 2024). This suggests a constant increase in the sector, indicating that the profitability and scalability of producing biopesticides derived from agricultural by-products could represent a sound technical–industrial option.

A process that minimizes resource use and maximizes extraction yields uses response surface optimization designs, which generate quadratic equations for ANOVA analysis and comparison of treatment levels such as temperature, time (min), solid–liquid ratio, and other process variables. The analysis identifies the temperature, time, and solid–liquid ratio that hypothetically maximize FC extraction; to confirm this, it is necessary to evaluate the extraction yield under these conditions.

## Status of phytochemicals in Mexico

Most agrochemicals on the market are chemical pesticides belonging to the organochlorine, organophosphate, carbamate, and pyrethroid families. There are also some commercially manufactured products derived from natural sources—mainly essential oils or nutraceuticals—that have proven to be equally or even more effective than conventional products. However, these natural-origin products can be more expensive, which limits their use. Therefore, it is necessary to identify new, cost-effective, and readily available sources of FC, such as agricultural and agro-industrial by-products.

In Mexico, the volumes of waste generated are extremely large, as it is one of the leading producers of crops such as pepper, corn, avocado, agave, and tomato, which generate seeds, peels, fibers, leaves, and stems. From a commercial standpoint, their high availability in the region can create competitive advantages. For this reason, within a circular economy framework, the goal is to recover these by-products and subsequently obtain functional molecules for agriculture (Gopinath *et al.*, 2018). It is worth noting that traditional disposal practices for agricultural by-products (field burning, effluent contamination, and pollution of water bodies) do not generate added value; rather, they can harm the environment and the health of workers (Koul, 2023). Mexico is one of the countries with the highest agricultural production, and thus it can take advantage of this asset to develop new industries that process residues and isolate and purify FC. However, this requires the scientific sector to promote, evaluate, and disseminate information in order to attract the attention of the private sector and enable the corresponding technology transfer for the production of biorational products.

Without a doubt, FC extracted from natural sources such as agricultural and agro-industrial residues can become sustainable and optimizable resources. Therefore, it is recommended to continue exploring new agricultural materials—such as peels and seeds—rich in phenolic compounds, primarily flavonoids, and in terpenes, whose use as potential biofungicides and biobactericides has been suggested by various studies and may support the development of commercial applications (Duque-Acevedo *et al.*, 2020).

## CONCLUSIONS AND PERSPECTIVES

The analysis of the literature shows that agricultural and agro-industrial by-products represent an abundant, diverse, and still underexploited source of phytochemicals with bactericidal and fungicidal activity against phytopathogenic organisms of agricultural relevance. In particular, phenolic compounds—mainly flavonoids and phenolic acids—as well as terpenes and essential oils have demonstrated multiple effective mechanisms of action, including disruption of cellular membranes, enzymatic inhibition, and interference with essential metabolic processes in bacteria and fungi. In numerous cases, these metabolites exhibit inhibitory concentrations comparable to or even greater than those of conventional chemical pesticides, confirming their technological and industrial potential.

From a frontier-of-knowledge perspective, the valorization of agricultural residues through the extraction of phytochemicals aligns with the principles of the circular economy and green chemistry, offering a dual strategy that, on the one hand, mitigates the environmental impact associated with the inadequate disposal of by-products and, on the other, generates biorational inputs with added value for sustainable agriculture. Current trends point to the use of more efficient and sustainable extraction methods—such as ultrasound, microwaves, supercritical fluids, and natural deep eutectic solvents—as well as to the design of optimized processes through statistical methodologies, representing a research avenue with high potential for technological development.

Nevertheless, several understudied areas still require attention. These include the systematic evaluation of synergistic or cooperative effects among phytochemicals present in complex extracts, the detailed elucidation of structure–activity relationships, and the validation of biocidal efficacy under *in vivo* conditions and at greenhouse or field scales. Likewise, the integration of sustainability, toxicity, and industrial scalability analyses remains limited in many studies, hindering the transition of these systems from the laboratory to commercial applications. In this context, future research should focus on closing these gaps, consolidating phytochemicals derived from agricultural by-products as viable, safe, and competitive alternatives for integrated pest management in the Mexican agricultural sector.

**Limitations.** The present review manuscript has certain limitations inherent to the methodological framework adopted. First, the review was restricted to publications indexed in scientific databases with academic access, which may have excluded relevant information contained in technical reports, patents, theses, or industrial documents not publicly available. Likewise, the temporal period considered, although sufficient to identify recent trends, may have limited the inclusion of pioneering studies or very recent technological developments that have not yet been indexed.

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