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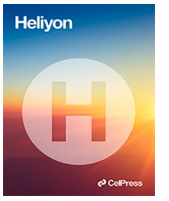

Review article

Phytochemicals as alternative fungicides for controlling plant diseases: A comprehensive review of their efficacy, commercial representatives, advantages, challenges for adoption, and possible solutions

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A R T I C L E I N F O

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A B S T R A C T

Fungal infections are responsible for about 70–80% of the losses in agricultural production brought on by microbial diseases. Synthetic fungicides have been employed to manage plant diseases caused by phytopathogenic fungi but their use has been criticized due to unfavorable side effects. As alternative strategies, botanical fungicides have caught the interest of many researchers in recent years. There are numerous experimental studies on the fungicidal activities of phytochemicals against phytopathogenic fungi, but there is not a thorough review article that summarizes these experimental studies. The purpose of this review is therefore to consolidate data from *in vitro* and *in vivo* studies on the antifungal activity of phytochemicals reported by various researchers. This paper describes antifungal activities of plant extracts and compounds against phytopathogenic fungi, approved botanical fungicides, their benefits, obstacles and mitigation strategies. Relevant sources were collected using online data bases such as Google Scholar, PubMed and Science Direct, and comprehensively reviewed for preparation of this manuscript. This review revealed that phytochemicals are effective to manage plant diseases caused by phytopathogenic fungi. Botanical fungicides are endowed with benefits such as resistance inhibition, being ecofriendly, effective, selective, and more affordable compared to synthetic fungicides. However, there are only small number of approved botanical fungicides due to the many challenges that hinder their adoption and utilization for a wider scale production. Farmers' reluctance, lack of standardized formulation techniques, strict legislation, rapid degradation, and other factors hinder their adoption and utilization. The ways to address these challenges include increasing awareness among farmers, conducting more research to identify potential plants with fungicidal properties, standardizing extraction and formulation techniques, implementing the idea of plant breeding to increase bioactive agents, identifying favorable environments for site-specific plant species production, discovering synthetic analogues of the active ingredient to maintain quality standards, establishing reasonable regulation procedures and price points for a quicker market introduction. To put all these into practice, we recommend collaboration of regulatory agencies and researchers from a variety of fields.

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1. Introduction

The eukaryotic organism fungi have numerous uses in the agricultural, medical, and industrial fields, from the generation of life-saving drugs to food supplements, but they are also responsible for significant crop losses around the world each year, which has a negative impact on the economy [1]. Fungal infections are responsible for about 70–80% of the losses in agricultural production brought on by microbial diseases. About 8000 different fungal species were known to cause around 100,000 different diseases of plants [2]. In recent years, the number of fungi known to cause plant diseases worldwide has been increased to over 19,000 [3].

One of the main infectious agents that affect plants, causing changes during the various stages of plant growth on the field, post-harvest, and even during storage, is phytopathogenic fungi. These fungi cause quality problems in cereals, fruits and vegetables, affecting their nutritional value, organoleptic characteristics and half-life [4]. They cause the death and extinction of the crop species by affecting various plant parts (roots, stems, leaves, fruits, tubers, etc.). They also secrete various types of toxic chemicals collectively called mycotoxins such as aflatoxins, ochratoxins, patulin, fumonisin, zearalenone, deoxynivalenol, and so on in the stored food products, resulting in postharvest losses of cereals, pulses, dry fruits, and spices [5]. Globally, mycotoxin contamination is a severe issue for the security and safety of food. These pollutants are responsible for significant economic losses in commerce and agricultural output, which are particularly pronounced in underdeveloped and developing nations. According to estimates, mycotoxins can infect between 60 and 80% of crops globally, causing huge economic losses [6]. Mycotoxins are also powerful disease causing chemicals in humans that can cause cancer, liver damage, kidney failure, and paralysis in addition to spoiling food [5].

For a long time, synthetic fungicides have been used to manage plant illnesses brought on by phytopathogenic fungus, although their usage has drawn criticism for many reasons. Continuous use leads to resistance, excessive use and improper handling of synthetic fungicides can have detrimental impacts on people, the environment, and non-target organisms, which has a negative influence on biodiversity. Due to their low biodegradability and high tendency to accumulate in the environment, constituent molecules of synthetic fungicides have been linked to chronic human illnesses in either intake or exposure scenarios in addition to ozone layer depletion [1,6,7].

To cope up with the mentioned problems of synthetic fungicides, a number of alternative techniques have been tried. Botanical fungicides are one of these methods and can be a viable and sustainable alternative to synthetic fungicides. Numerous studies have demonstrated that phytochemicals derived from plants have fungicidal effects [7]. Plants can be considered as a perfect laboratory with potential to supply organic substances which can be classified as primary metabolites (proteins, carbohydrates, and fats) or secondary metabolites (terpenes, steroids, anthocyanins, anthraquinones, phenols, alkaloids etc.) [8]. Due to a number of factors, the study of medicinal plants as potential natural sources of active compounds against phytopathogens has gained increased attention in recent years [9]. There are numerous experimental studies on the fungicidal activities of phytochemicals against phytopathogenic fungi, but there is not a thorough review article that summarizes these experimental studies. The aim of this review is therefore to compile information on the use of phytochemicals as substitutes for synthetic fungicides in the management of fungi-caused plant diseases. It includes investigations on the antifungal activity of crude extracts of plants and isolated compounds carried out in *in vitro* and *in vivo* models by various researchers. The review also discusses some representative commercial botanical fungicides, obstacles to the use of botanicals for managing plant diseases sustainably, and potential mitigating strategies. For simplicity and readers convenience, informations gathered from literatures were organized in tabular form with brief description of the scientific name of plants, plant parts used, extraction solvent and methods employed, fungi species tested along with the host plant disease, bioassay methods used and antifungal efficacy observed.

2. The review methodology

The relevant sources for this study were retrieved utilizing search engines including Google Scholar, PubMed, and Science Direct. For the purpose of finding relevant sources, several combinations of the terms and phrases such as antifungal phytochemicals, plant extracts, natural products, secondary metabolites, compounds, plant diseases, phytopathogenic fungi, and botanical fungicides were utilized. This review covered studies showing both *in vitro* and *in vivo* antifungal activity of plant extracts and compounds against pathogenic fungi that cause plant illnesses, but it excluded studies reporting such activities against pathogenic fungi that cause human diseases. Reports on antifungal effects of other derivatives, such as nanoparticles made from plant crude extracts or compounds were also disregarded. Studies that were published in languages other than English were not at all taken into account in this study. Following the collection of all sources, a rapid study of the sources' titles, abstracts, and conclusions was done to determine which ones met the qualifying requirements. The chosen sources were then carefully examined in order to prepare this review paper. The chemical structures of compounds were depicted using ChemDraw Ultra 8.0 software, while citations and references were provided using Mendeley Desktop software.

3. Crude extracts from plants as fungicides against phytopathogenic fungi

Crude extracts from numerous plant species have been discovered to be efficacious against a variety of phytopathogenic fungi without causing negative side effects, according to research being conducted worldwide to use botanicals in plant disease control [10]. There are a large number of papers published on an *in vitro* antifungal activity of crude extracts obtained from plants. Plant extracts have the benefit that they typically include a combination of compounds that may combine to suppress the growth of phytopathogenic fungus. Additionally, many plant extracts include many antifungal substances and a reduction in the emergence of resistance may result from the varied modes of action of these substances. Therefore, the usage of plant extracts may prevent the emergence of

Table 1
Antifungal activities of crude extracts from plants against phytopathogenic fungi that affect fruits and vegetables.

Plant species (part used)	Fungi species (disease caused)	Efficacy observed	References
• *Lantana hirta* (leaf and flower) • *Argemone ochroleuca* (leaf-fruit and root) • *Adenophyllum Porophyllu* (leaf-stem and leaf)	• *Pestalotiopsis clavispora* • *Colletotrichum gloeosporioides* • *Lasiodiplodia pseudotheobromae* (Blueberry dieback)	• In an *in vitro* assay, ethyl acetate extracts of the listed plants obtained by maceration inhibited 100% of the mycelial growth of the fungal strains at a concentration of 5 mg/mL.	[12]
• *Cuminum cyminum* • *Zingiber officinale* • *Citrullus colocynthis*	• *Macrophomina phaseolina* (Okra seed rot and seedlings death)	• In an *in vitro* assay, *C. cyminum* 70% ethanol extract had a significant effect on the inhibition of the radial growth and dry weight of *M. phaseolina* followed by *Z. officinale* and *C. colocynthis.*	[13]
• *Acacia albida* (leaves) • *Azadirachta indica* (leaves) • *Argemone Mexicana* (leaves) • *Dovalis abyssinica* (leaves) • *Prosopis juliflora* (leaves) • *Vernonia amygdalina* (leaves)	• *Colletotrichum musae* (Banana anthracnose)	• *In vitro* assay using a paper disk and spore germination methods demonstrated that the methanol extracts have high to moderate antifungal activity. • *P. juliflora* methanol extract was the most effective in inhibiting mycelial growth of the test fungus (30.7 mm), followed by *A. albida* (19 mm). • *D. abyssinica, A. mexicana,* and *V. amygdalina* showed good antifungal activity (11.7, 11.0, and 9.7 mm, respectively). • Extracts from *D. abyssinica*, *P. juliflora* and *A. albida* reduced conidial germination to 0.5, 0.3 and 0.2%, respectively. • Aqueous extracts of *A. albida* showed the highest antifungal activity (18 mm), followed by *P. juliflora* (12.3 mm).	[14]
• *Thymus leptobotrys* (leaves and stems) • *Cistus villosus* (leaves and stems) • *Eucalyptus globulus* (leaves and stems) • *Peganum harmala* (seeds)	• *Penicillium digitatum* • *Penicillium italicum* • *Geotrichum candidum* (Citrus fruit decay)	• In an *in vitro* assay using agar plate method, all plants showed high antifungal activities against the tested pathogens. • The essential oil of *T. leptobotrys* (at 1.2 g/L) obtained by steam distillation had the highest fungistatic effect (100%), compared with the essential oils of *E. globulus, C. villosus* and *P. harmala*, where the growth inhibition was less than 40% on the tested fungal pathogens. • *T. leptobotrys* chloroform and methanol extracts obtained by soxhlet extraction exhibited a significant fungistatic activity, 100% inhibition of fungal growth by the chloroform extract at a concentration of 0.3% (w/v), and a 71–76% inhibition by the methanol extract at a concentration of 1.5% (w/v). • Chloroform and methanol extracts of *P. harmala* tested at a concentration of 1% and 2% (w/v), respectively, exhibited a pronounced activity against the tested pathogens. • *C. villosus* and *E. globulus* chloroform and methanol extracts showed relatively lower inhibitory effects.	[15]
• *Allium sativum* (bulb) • *Datura metel* (leaves) • *Dryopteris filix-mas* (aerial parts) • *Zingiber officinale* (rhizomes) • *Smilax zeylanica* (leaves) • *Azadirachta indica* (leaves) • *Curcuma longa* (rhizomes)	• *Pestalotiopsis theae* • *Colletotrichum camelliae* • *Curvularia eragrostidis* • *Botryodiplodia theobromae* (Tea leaf disease)	• *In vitro* assay using spore germination method revealed that ethanol and aqueous extracts of the listed plants have 100% inhibition of spore germination.	[16]
• *Acalypha subviscida* (aerial parts) • *Ipomoea murucoides* (leaves) • *Tournefortia densiflora* (aerial parts and roots) • *Lantana achyranthifolia* (aerial parts) • *Adenophyllum aurantium* (aerial parts and roots)	• *Alternaria alternata* • *Fusarium solani* (black molds in tomato ripe fruits and blight of pepper crops)	• In an *in vitro* assay using radial growth inhibition technique, methanol extracts of all plants inhibited fungal growth in the ranges of 0.76–56.17% against *F. solani* and 2.02–69.07% against *A. alternata.* • The extracts of *A. subviscida, I. murucoides, T. densiflora* and *L. achyranthifolia* showed MIC values between 5.77 and 12.5 mg/mL for at least one of the fungal species. • The best treatment *A. aurantium* exhibited a maximum inhibition for *F. solani* (56.17%, MIC = 7.78 mg/mL) and *A. alternata* (68.64%, MIC = 7.78 mg/mL).	[17]
• *Allium sativum* (cloves) • *Zingiber officinale* (rhizomes)	• *Phytophthora infestans* • *Alternaria solani* (early and late blight of tomato)	• In an *in vitro* assay using radial growth inhibition technique, the crude extracts obtained by maceration (using 95% methanol and ethanol) and the essential	[18]

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Table 1 (*continued*)

Plant species (part used)	Fungi species (disease caused)	Efficacy observed	References
• *Lantana camara* (leaves) • *Tagetes erecta* (leaves)		oils extracted by steam distillation portrayed some efficacy against the test pathogens. • *A. sativum* crude extracts were found to be the most effective. • Essential oils were more effective in restricting the pathogen growth than crude extracts. • *Z. officinale* and *A. sativum* oil was found to be as effective as the synthetic fungicide (Ridomil Gold®).	
• *Solanum indicum* (whole parts) • *Azadirachta indica* (young twigs with fruits) • *Oxalis latifolia* (aerial parts)	• *Fusarium oxysporum f. sp. lycopersici* (wilt disease of tomato)	• In an *in vitro* assay using poisoned food technique, the aqueous extracts of the plants obtained by maceration were proved to be potential in inhibiting the growth of the fungus viz., *S. indicum* (78.33%), *A. indica* (75.00%), and *O. latifolia* (70.33%).	[19]
• *Thespesia populnea var. acutiloba* (leaves) • *Chrysanthemum frutescens* (leaves)	• *Sclerotium rolfsii* (sugar beet damping-off)	• Laboratory experiments (*in vitro* assay) indicated that methanol extracts of both plants were effective against *S. rolfsii.* • *In vivo* results under greenhouse conditions confirmed that these plant extracts were effective against the damping-off pathogen, either by coating or soaking of sugar beet seeds.	[20]
• *Azadirachta indica* (seeds) • *Jatropha curcas* (seeds) • *Nicotiana tabacum* (leaves)	• *Colletotrichum gloeosporioides* (white yam anthracnose)	• The results of *in vitro* assay using poisoned food technique showed that aqueous extract of each plant obtained by maceration has significant inhibition on the mycelia growth of *C. gloeosporioide.* • The 75% concentration of the plant extracts exhibited the best inhibitory effect considering the percentage mycelial growth it recorded. • The results of the field trial (*in vivo* assay) revealed that each plant extract at 75% concentration significantly reduced the incidence and severity of the anthracnose disease.	[21]
• *Acacia nilotica* (leaves) • *Achillea fragrantissima* (leaves) • *Calotropis procera* (leaves)	• *Alternaria solani* (early blight of tomato)	• Aqueous or 80% ethanol extracts obtained by maceration of all tested plants reduced the mycelial growth and conidium germination of *A. solani* in an *in vitro* assay, ethanol extract being more effective. • Extract of *C. procera* exhibited more antifungal potential against the pathogen than other plant extracts. • In a plot experiment (*in vivo* assay), both types of extracts from *C. procera* reduced disease severity.	[22]
• *Mentha piperita* (leaves) • *Ocimum basilicum* (leaves) • *Eucalyptus camaldulensis* (leaves)	• *Fusarium oxysporum f.sp. lycopersici* (wilt of tomato)	• In an *in vitro* assay, all levels of concentration of aqueous extracts of the three test plants obtained by maceration significantly inhibited the growth of the fungus compared to the control treatment. • Over the course of the experiment, aqueous extracts of *E. camaldulensis* showed relatively high inhibition zone (44.1, 53.1 and 53.1%) followed by *O. basilicum* (36.8, 51.5, and 54.4%) and *M. piperita* aqueous extract as well (35.5, 39.6 and 39.6%), respectively.	[23]
• *Ocimum basilicum* (leaves) • *Azadirachta indica* (leaves) • *Eucalyptus chamadulonsis* (leaves) • *Datura stramonium* (leaves) • *Nerium oleander* (leaves) • *Allium sativum* (leaves)	• *Alternaria solani* (early blight disease of tomato)	• In an *in vitro* assay using poisoned food technique, the aqueous extracts of *D. stramonium, A. indica,* and *A. sativum* at 5% concentration caused the highest reduction of mycelial growth of *A. solani* (44.4, 43.3 and 42.2%, respectively) while *O. basilicum* at 1% and 5% concentration and *N. oleander* at 5% concentration caused the lowest inhibition of mycelial growth of the pathogen. • In greenhouse experiments (*in vivo* assay), the highest reduction of disease severity was achieved by the extracts of *A. sativum* at 5% concentration and *D. stramonium* at 1% and 5% concentration.	[24]
• *Anadenanthera colubrina* (bark) • *Artemisia annua* (leaves) • *Cariniana estrelensis* (leaves and barks) • *Ficus carica* (leaves) • *Ruta graveolens* (leaves and flowers)	• *Alternaria alternata* (Murcott tangor fruits brown spot disease)	• *A. colubrina* methanol extract obtained by maceration was the most active extract against *A. alternata* in *in vitro* assay while *A. annua, C. estrelensis, F. carica,* and *R. graveolens* presented moderate *in vitro* antifungal activity, but no effects were observed on the disease when the extracts were applied to fruits inoculated with the fungus. • In *in vivo* assay, only *A. colubrina* showed suppression of lesions caused by *A. alternata.*	[25]

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Table 1 (*continued*)

Plant species (part used)	Fungi species (disease caused)	Efficacy observed	References
• *Curcuma longa* • *Zingiber officinale* • *Cymbopogon citratus* • *Garcinia mangostana* • *Hibiscus sabdarifa* • *Syzygium aromaticum*	• *Neopestalotiopsis* and *Pseudopestalotiopsis* species (fruit diseases: jackfruit, rose apple, mangosteen, plum, snake fruit, rambutan,strawberry, and avocado)	• Ethanol extracts of all plants obtained by maceration could inhibit the growth of *Neopestalotiopsis* and *Pseudopestalotiopsis* species in an *in vitro* assay except *G. mangostana.*	[26]
• *Lantana camara* (leaves) • *Salvadora persica* (bark) • *Thymus vulgaris* (leaves) • *Zingiber officinale* (rhizomes) • *Ziziphus spina-christi* (leaves)	• *Fusarium oxysporum* • *Pythium aphanidermatum* • *Rhizoctonia solani* (tomato damping-off diseases)	• In an *in vitro* assay, *T. vulgaris* and *Z. officinale* methanol extracts obtained by maceration were strongly active and showed fungistatic and fungicidal activities against the phytopathogenic fungi with minimal inhibitory concentration (MIC of 4 mg/mL) and minimal fungicidal concentrations (MFC of 8 mg/mL) except *F. oxysporum* which was less sensitive and its MFC reached to 16 mg/mL of *Z. officinale* extract. • *S. persica* extract showed a moderate antifungal activity while *L. camara* and *Z. spina-christi* were not effective against tomato phytopathogenic fungi except *P. aphanidermatum* which was completely inhibited at 10 mg/mL of *L. camara* extract.	[27]
• *Plantago major* • *Rosmarinus officinalis*	• *Alternaria* species (Carrot leaf blight and black rot)	• In an *in vitro* assay, *R. officinalis* extract obtained by liquid carbon dioxide subcritical extraction had an apparent reducing effect on fungal growth that was dose-dependent while *P. major* was found to be less effective.	[28]
• *Oxalis barrelieri* (leaves) • *Stachytarpheta cayennensis* (leaves) • *Euphorbia hirta* (leaves)	• *Fusarium oxysporumf. sp. vasinfectum* • *Alternaria solani* • *Rhizoctonia solani* (tomato diseases)	• Aqueous and 70% ethanol extracts of the plants obtained by maceration inhibited fungal growth *in vitro* at 1.25–20 mg/mL and ethanol extracts were more effective (80–100% inhibition) than water extracts (<62%). • In greenhouse experiments (*in vivo* assay), spraying *E. hirta* ethanol extract on tomato plants infected by *R. solani* reduced disease severity up to 80%, when compared to non-sprayed plants.	[29]
• *Curcuma longa* (rhizomes) • *Allium sativum* (bulbs) • *Zingiber officinale* (rhizomes)	• *Fusarium oxysporum f. sp. lycopersici* • *F. solani* (wilt and root rot of tomato)	• *In vitro* assay revealed that mycelial growth and spore germination was inhibited significantly with all aqueous extracts of the plants obtained by maceration. • *A. sativum* completely reduced the mycelial growth of *F. oxysporum f. sp. lycopersici* and *F. solani* at highest concentration. • *Z. officinale* showed moderate inhibition ranging from 37.77 to 48.47% against *F. solani* and 30.33–44.49% against *F. oxysporum f. sp. lycopersici.* • *C. longa* exhibited moderate inhibition of *F. oxysporum f. sp. lycopersici,* whereas, least inhibition was observed against *F. solani.* • Conidial germination of test fungi was almost completely reduced by *A. sativum* extract.	[30]
• *Citrus sinensis* (fruit peel) • *Ananas comosus* (fruit peel) • *Anacardium occidentale* (fruit peel) • *Musa* species (fruit peel)	• *Aspergillus niger* • *Alternaria alternata* (fruits spoilage)	- Results of *in vitro* assay showed that *A. niger* had its respective inhibition zones with *C. sinensis*, *A. occidentale*, *A. comosus* and *M.* species peel extracts as 0.33 ± 0.33, 0.40 ± 0.30, 0.60 ± 0.20 and 0.87 ± 0.33 cm while inhibition zones of *A. alternata* with the peels in the same order were 0.50 ± 0.50, 0.60 ± 0.35, 0.87 ± 0.43 and 1.37 ± 0.67 cm. • The order of antifungal activity of the peel extracts against the tested fungi was *M.* species > *A. comosus* > *A. occidentale* > *C. sinensis.*	[31]
• *Ageratum conyzoides* (whole plant) • *Bidens pilosa* (whole plant) • *Callistemon citrinus* (leaves) • *Cymbopogon citratus* (leaves) • *Erigeron floribundus* (whole plant) • *Ocimum gratissimum* (whole plant)	• *Phythopthora infestans* (late blight disease of potato and tomato)	• Essential oils obtained by hydrodistillation exhibited the best control of the pathogen, followed by ethanol extracts obtained by maceration in *in vitro* assay. • Total inhibition of pathogens growth was obtained with essential oils of *C. citratus* at 300 ppm, *O. gratissimum* at 400 ppm, and *C. citrinus* at 5000 ppm. • The ethanol extracts of *A. conyzoides* and *C. citrinus* totally inhibited the pathogen at 5000 ppm, and that of *O. gratissimum* at 10,000 ppm.	[32]

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Table 1 (*continued*)

Plant species (part used)	Fungi species (disease caused)	Efficacy observed	References
• *Tephrosia vogelii* (whole plant)			
• *Vitis vinifera* (leaves) • *Zizyphus spina-christi* (leaves) • *Punica granatum* (leaves) • *Ficus carica* (leaves)	• *Alternaria solani* • *Botrytis cinerea* • *Fusarium oxysporum* • *Fusarium solani* (potato, tomato, and artichoke diseases)	• *F. oxysporum* and *F. solani* were the most resistant fungi against all methanol extracts tested.	[33]
• *Azadirachta indica* (leaves) • *Ocimum sanctum* (leaves) • *Allium sativum* (bulbs)	• *Alternaria solani* (tomato early blight disease)	• Aqueous extracts of *A. indica, A. sativum* and *O. sanctum* showed signifcant antifungal activity at all tested concentrations in both *in vitro* and *in vivo* (greenhouse and field) assays. • *A. indica* extracts reduced disease incidence to 62.32%, in the greenhouse assay while in the field experiment, *A. sativum* showed highest reduction in disease incidence to 77.42%.	[34]
• *Artemisia annua* (leaves)	• *Sclerotinia sclerotiorum* • *Botrytis cinerea* • *Phytophthora infestans* • *Verticillium dahliae* (foliar and soil-borne fungal diseases of tomato)	• *S. sclerotiorum* was found to be highly sensitive to volatile and contact phase of the essential oil obtained by steam distillation in *in vitro* assay. • Minimum fungicidal concentrations of the volatile phase of the essential oil for *S. sclerotiorum, B. cinerea, P. infestans* and *V dahliae* were 1.6, 2.4, 2.4 and 4.4 μg/mL, respectively. • The essential oil in the contact phase showed minimum fungicidal concentration ranging from 6.4 μg/mL to 51.2 μg/mL. • Volatile and contact phase of the essential oils, at 2.4 and 51.2 μg/mL concentrations completely inhibited the conidial germination and germ tube elongation of the tested fungal pathogens.	[35]
• *Phyllostachys pubescens* (leaves)	• *Phytophthora capsici* • *Fusarium graminearum* • *Valsa mali* • *Botryosphaeria dothidea* • *Venturia nashicola* • *Botrytis cinerea* (pepper phytophthora blight)	• The extract obtained by 95% ethanol showed good anti-fungal activity to *P. capsici, F. graminearum, V. mali, B. dothidea, V. nashicola,* and *B. cinerea* with inhibitory rate of 100.00%, 75.12%, 60.66%, 57.24%, 44.62%, and 30.16%, respectively in *in vitro* assay. • In *in vivo* (greenhouse) assay, the formulated extract (10% emulsion in water) had a control effect of 85.60% on pepper phytophthora blight.	[36]
• *Cupressus benthamii* (leaves) • *Pachypodanthium staudtii* (bark) • *Dracaena deisteliana* (leaves) • *Erigeron floribundus* (leaves) • *Vetiveria zizanioides* (roots) • *Croton macrostachyus* (leaves) • *Lantana camara* (leaves) • *Hymenodictyon floribundum* (leaves) • *Bryophyllum pinnatum* (leaves)	• *Phytophthora infestans* (tomato late blight disease)	• *C. benthamii* and *V. zizanioides* extracts obtained by dichloromethane: methanol (1:1) were the most effective preparations, leading to 23% and 35% inhibition of sporangial germination, respectively in *in vitro* assay, and to 86% and 77% disease reduction in *in vivo* (greenhouse) assay. • Preparations made from the remaining plants showed moderate to low efficiency.	[37]
• *Ricinus communis* • *Chromolaena odorata*	• *Alternaria solani* (early blight diseases of tomato)	• The radial growth results revealed that aqueous extract of *R. communis* at 100% concentration has the lowest radial growth rates of 1.43 cm, 2.00 cm and 2.72 cm at 24, 48 and 72 h respectively in *in vitro* assay.	[38]
• *Lantana camara* (fruits, leaves and stem)	• *Colletotrichum gloeosporioides* (Mango anthracnose)	• The results of *in vitro* experiment revealed that higher concentration of methanol extract of fruits (5%) obtained by maceration significantly reduced the biomass *C. gloeosporioides* up to 66%. • The trials also showed that 0.5% concentration of *n*-hexane fraction of methanol extract of fruits caused the highest reduction (45%) in the radial colony growth of the test fungus.	[39]

antimicrobial chemical resistance [2].

Plant extracts are substances obtained from the roots, barks, seeds, shoots, leaves, fruits, flowers, cloves, rhizomes, or stems of plants which have a long therapeutic history and chosen for their natural defense mechanisms. The process of obtaining plant extracts typically entails macerating the plant material with various organic solvents, and may be followed by the purification of the resulting crude extracts using chromatographic techniques to acquire specific chemicals, which ultimately results in the isolation of the metabolites in pure form. Additionally, it has been noted that the method and solvent used to get the final material (extract) of this procedure affect the quantity and variety of chemicals or secondary metabolites thought to have antifungal properties. As a result, the extracts' antifungal effects may be influenced by different compounds present in the extracts or by the same compounds present in varied concentrations [4]. The intended bioactive chemicals and their concentration within the subject plant part will determine which plant part is employed. The allelopathic effect of botanical fungicides on crops varies depending on the source plant and the amounts utilized. Their effectiveness depends on the type of the source plant, whether it is dried or fresh, the extraction solvents and the extraction techniques employed. The common bioactive compounds in botanical pesticides are majorly secondary metabolites that possess fungicidal and many other biological activities [11].

A given plant species are efficient against a particular class of pests because of the specific chemicals found in those species. Botanical fungicides contain secondary metabolites that are poisonous to the cell membranes, organelles, and walls of fungi. These metabolites prevent the germination of spores, the growth of mycelium, the lengthening of germ tubes, delayed sporulation, as well as the production of critical enzymes, DNA, and proteins. Additionally, they cause structural changes in the hypha and mycelia, which prevent some fungi such as *Aspergillus* spp. and *Fusarium* spp. from producing toxic compounds like aflatoxin and fumonisin respectively. As a result, mycotoxin-producing fungal infections are less pathogenic [11].

3.1. Crude extracts from plants as fungicides against phytopathogenic fungi that affect fruits and vegetables

Many plant extracts have been extensively studied for controlling fruits and vegetable diseases including blueberry dieback, okra seed rot and seedlings death, banana anthracnose, citrus fruit decay, tea leaf disease, black molds in tomato ripe fruits and blight of pepper crops, early and late blight of tomato, wilt disease of tomato, sugar beet damping-off, white yam anthracnose, murcott tangor fruits brown spot disease, tomato damping-off diseases, carrot leaf blight and black rot, root rot of tomato, late blight disease of potato, artichoke diseases, pepper phytophthora blight, and mango anthracnose which are caused by pythopathogenic fungi as indicated in Table 1. Among these, the fungal diseases of tomato are the most widely studied one. Most of the tested plant extracts showed promising antifungal activity in *in vitro* and *in vivo* assays in controlling the mentioned fungal diseases of fruits and vegetables as described in Table 1.

As it can be seen from Table 1, different parts of plants including roots, rhizomes, bulbs, stem, barks, leaves, flowers, fruits, peels, and seeds, were studied on different phytopathogenic fungi in *in vitro* and *in vivo* models and the leaf part is the most frequently studied plant part. The method of extraction used for obtaining the crude extract involves maceration, steam distillation, soxhlet extraction, liquid carbon dioxide subcritical extraction, and hydrodistillation, maceration being the most frequently used one. In most cases, the crude extract were used directly for antifungal activity study, while partitioning into different fractions using solvents of different polarity is also applied in some cases. The solvents employed for extraction involve ethyl acetate, ethanol, methanol, water (aqueous), chloroform, liquid carbon dioxide, and dichloromethane: methanol (1:1 v/v) as presented in Table 1. Among these solvents, ethanol, methanol and water constitute the three most commonly used extractants. Majority of the studies presented in Table 1 involve *in vitro* assays while *in vivo* models (including both greenhouse and field trials) were rarely used. The antifungal assays used generally involve inhibition of mycelial growth, radial growth, spore germination, conidial germination, germ tube elongation, and sporangial germination, the first being the most frequently applied approach.

In some *in vivo* studies under greenhouse and/or field conditions, the tested extracts showed no phytotoxicity to the host plant [20,29], and increased fruit yield after treatment [22,24,29,34]. In some of the studies presented in Table 1, identification of phytochemical constituents of the crude extract was carried out using GC-MS analysis [12,20,27,35,39], and phytochemical screening tests [22,30–34]. However, they did not involve identification of the active compound in the crude extract. All studies also lack mechanisms by which the crude extract showed its antifungal activity against phytopathogenic fungi.

3.2. Crude extracts from plants as fungicides against phytopathogenic fungi that affect cereals and pulses

Different solvent extracts of many plants were also studied for their antifungal activity against pathogenic fungi that cause diseases of cereals and pulses including wheat blast disease, rice blast, rice sheath blight, wheat leaf rust, sorghum grains disease, barley seeds disease, maize seeds spoilage, milkvetch yellow dwarf and root-rot, chocolate spot of broad bean, rust and anthracnose of soybean leaf, bean and cowpea anthracnose, peanut rust, and so on in *in vitro* and *in vivo* assays and promising efficacy were observed as indicated in Table 2.

4. Compounds isolated from plants as fungicides against phytopathogenic fungi

There are numerous reports of plant compounds with antifungal properties. Higher plants provide an abundant source of bioactive secondary metabolites that have been shown to have antifungal effects in *in vitro* assay. In order to achieve a sustainable control of phytopathogenic fungi and to lessen the heavy reliance on synthetic fungicides used to control them, secondary metabolites with antifungal activity constitute an alternative mechanisms. These compounds can be utilized directly or as a starting point for developing

Table 2
Antifungal activities of crude extracts of plants against phytopathogenic fungi affecting cereals and pulses.

Plant species (part used)	Fungi species (disease caused)	Efficacy observed	References
• *Artemisia indica* (leaves and stems) • *Persicaria orientalis* (leaves and stems) • *Clerodendrum indicum* (leaves and stems)	• *Magnaporthe oryzae* (wheat blast disease)	• *In vitro* assay using disk diffusion method revealed that methanol extracts of *A. indica, P. orientalis* and *C. indicum* obtained by maceration possess significant antifungal properties (29.6 ± 01.5 mm, 25.1 ± 01.0 mm and 20.0 ± 02.0 mm) zone of inhibition, respectively at 5 mg/disk against the tested fungus.	[40]
• *Artemisia herba* (aerial parts) • *Cotula cinerea* (aerial parts) • *Asphodelus tenuifolius* (aerial parts) • *Euphorbia guyoniana* (aerial parts)	• *Fusarium graminearum* • *Fusarium sporotrichioides* (wheat disease)	- *In vitro* assay using poisoned food method revealed that aqueous extracts obtained by maceration from all plants are effective at concentrations of 10% and 20% for the *Fusarium* mycelia growth inhibition. - In particular, *A. tenuifolius* extract is effective against *F. graminearum*, whereas *F. sporotrichioides* mycelium growth is strongly affected by *E. guyoniana* 20% extract.	[41]
• *Eugenia aromatica* (seeds) • *Piper guineense* (seeds) • *Garcinia kola* (nuts)	• *Pyricularia oryzae* (Rice blast)	• *In vitro* assay using poisoned food technique revealed that hexane extracts of all plants obtained by soxhlet extraction reduced the growth of *P. oryzae* at all tested concentrations. • Highest mycelial growth inhibitions of 100%, 98% and 97.3% were achieved by *E. aromatica*, *P. guineense* and *G. kola*, respectively at 100% concentrations. • All extracts at 100% concentration also showed significant inhibition on sporulation of *P. oryzae*.	[42]
• *Datura metel* (leaves) • *Jatropha carcus* (leaves) • *Ruellia tuberosa* (leaves)	• *Pycularia grisea* (Rice blast) • *Rhizoctonia solani* (Rice sheath blight)	• The results of *in vitro* assay using poisoned food technique showed that the 95% ethanol extract of *D. metel* and *J. carcus* obtained by maceration has the highest antifungal activity at 100% concentration against isolated pathogen causing sheath blight having 98.611 ± 1.589 and 98.588 ± 1.589% of mycelial inhibition, respectively. • *J. carcus* and *R. tuberosa* has highest antifungal property against rice blast having 97.436 ± 0.555% and 97.115 ± 0.96% respectively.	[43]
• *Lawsonia inermis* (leaves) • *Lantana camara* (leaves) • *Acalypha wilkesiana* (leaves) • *Melia azedarach* (leaves) • *Punica granatum* (fruit peel)	• *Puccinia triticina* (Wheat leaf rust)	• In an *in vitro* experiment using spore germination technique, all methanol extracts inhibited the germination of the fungus spores by 100%, while aqueous extracts were less effective. • In an *in vivo* experiment (greenhouse assay), all plant extracts decreased the disease severity of wheat leaf rust.	[44]
• *Olea europaea* (leaves) • *Capsicum annuum* (fruits)	• Seed borne fungi (sorghum grains disease)	• Aqueous extract obtained by maceration of *O. europaea* leaf and *C. annuum* fruit were found effective in reducing incidence of seed-borne fungi.	[45]
• *Eucalyptus globulus* (leaves) • *Calotropis procera* (leaves) • *Melia azedarach* (leaves) • *Datura stramonium* (leaves) • *Acalypha indica* (leaves)	• *Alternaria alternata* • *Rhizopus spp.* • *Mucor spp.* • *Fusarium moniliforme* • *Aspergillus flavus* • *Aspergillus niger* • *Penicillium spp.* • *Drechslera australiensis* • *Curvularia lunata* • *Cladosporium spp.* • *Stemphylium spp.* • *Ulocladium spp.* (barley seeds disease)	• The results revealed that aqueous extracts of all plants significantly inhibited the mycelial growth of *A. alternata* in an *in vitro* assay using poisoned food technique. • Leaf extract of *E. globulus* at 20% concentration caused highest inhibition of mycelial growth of *A. alternata* (52.6%) followed by *C. procera* (50.88%), *M. azedarach* (48.21%) and *D. stramonium* (47.42%), whereas the lowest inhibition (37.52) of mycelial growth was recorded at 5% leaf extract concentration in case of *A. indica*. • Seed treatment at 20% concentration of all the tested plant extracts was also found to be effective in eliminating majority of fungi and reducing the relative frequency of seed-borne fungi occurring on the seeds and also resulted in percent germination increase in both standard blotter and agar plate methods.	[46]
• *Alpinia galangal* (rhizomes) • *Curcuma longa* (rhizomes) • *Zingiber officinale* (rhizomes)	• *P. oryzae* (rice blast disease)	• In *in vitro* assay, *A. galangal* hexane crude extract exhibited strong inhibitory effect against *P. oryzae* with the highest percentage of inhibition (52.9%), followed by *C. longa* hexane crude extract with 49.1% and *Z. officinale* methanol crude extract with 43.5% inhibition.	[47]
• *Combretum erythrophyllum* (leaves) • *Quercus acutissima* (leaves) • *Melia azedarach* (leaves)	• *Fusarium proliferatum* • *F. oxysporum* • *F. subglutinans* • *F. verticilloides* • *F. semitectum* • *F. chlamydosporum* • *F. solani* • *F. equisite* • *F. graminearum* (maize seeds spoilage)	• In *in vivo* assay, *M. azedarach* acetone extract obtained by ultrasonic extraction showed strong antifungal activity (97% inhibition) against *F. proliferatum* while combined acetone extracts from *C. erythrophyllum* and *Q. acutissima* exhibited 96%, 67% and 56% inhibition against *F. verticilloides*, *F. proliferatum* and *F. solani*, respectively.	[48]

(*continued on next page*)

Table 2 (*continued*)

Plant species (part used)	Fungi species (disease caused)	Efficacy observed	References
• *Saposhnikovia divaricata* (roots) • *Allium sativum* (bulb) • *Juglans regia* (green husks)	• *Embellisia astragali* (Standing milkvetch yellow dwarf and root-rot)	• In *in vitro* assay using poisoned food technique, extracts of the three plants obtained by 95% ethanol totally inhibited mycelial growth of *E. astragali* and significantly inhibited spore germination with inhibition rates ranging from 86% to 88%.	[49]
• *Vitis vinifera* (leaves) • *Zizyphus spina-christi* (leaves) • *Punica granatum* (leaves) • *Ficus carica* (leaves)	• *Botrytis fabae* (chocolate spot disease of broad bean)	• In *in vitro* assay, the methanol extract of *Z. spina-christi* leaves obtained by maceration had the greatest inhibitory effect on mycelial growth of *B. fabae* by 95.56% at 4 mg/mL. • Also, extract of *P. granatum* caused remarkable reduction on the fungal growth (94.44%) of *B. fabae* at 4 mg/mL, while *F. carica* extract caused 91.11% inhibition against the same fungus at the same concentration.	[33]
• *Morinda citrifolia* (fruits and leaves)	• *Phakopsora pachyrhizi* • *Colletotrichum truncatum* (Asian rust and anthracnose diseases of soybean leaf)	• Foliar application of aqueous extracts and essential oil obtained by hydrodistillation did not differ from fungicide in Asian rust and anthracnose control in *in vivo* experiments.	[50]
• *Ipomoea batatas* (leaves) • *Carica papaya* (leaves) • *Allium sativum* (bulbs) • *Syzygium cordatum* (fruits) • *Chlorophytum comosum* (whole plant) • *Agapanthus caulescens* (whole plant)	• *Colletotrichum lindemuthianum* • *Colletotrichum dematium* (bean and cowpea anthracnose)	• Extracts of the listed plants were active on both fungi in *in vitro* assay and effectively reduced the incidence and severity of bean and cowpea anthracnose disease in the greenhouse (*in vivo* assay).	[51]
• *Ageratum conyzoides* • *Amaranthus spinosus* • *Cyperus rotundus*	*Puccinia arachidis* (peanut rust disease)	• Applications of 5% *A. conyzoides* and 5% *C. rotundus* methanol extracts obtained by maceration suppressed the spore germinations by 78–80% and 76–80%, respectively in *in vitro* assay. • *A. conyzoides* extract also suppressed the germination and the growth of rust disease in greenhouse experiments (*in vivo* assay).	[52]
• *Vernonia amydgalina* (leaves) • *Azadirachta indica* (leaves)	• *Candida spp.* • *Pythium spp.* • *Rhizopus stolonifera* • *Trichoderma spp.* • *Aspergillus niger* (seed-borne fungal disease of cowpea)	• Aqueous extract obtained by maceration of *A. indica* had better inhibitory effect on *Pythium spp.* in *in vitro* assay at concentrations of 1.95 mg/mL and 1.43 mg/mL. • *V. amydgalina* at 1.45 mg/mL inhibited *A. niger* and *C. spp.* by 83.75% and 87.5% respectively.	[53]

more effective fungicidal chemicals [54]. Numerous plant secondary metabolites have been examined for their antifungal properties [55]. Table 3, below describes *in vitro* and *in vivo* studies conducted on antifungal activity of compounds isolated from plants (structures given on Fig. 1) in controlling plant diseases caused by phytopathogenic fungi. The tested compounds belong to different classes of secondary metabolites including sesquiterpenoids (**1, 20–25**), triterpenoid (**18**), triterpene glycosides or triterpenoid saponins (**3–7**), isoquinoline alkaloids (**8–13**), lignans (**2, 14-16**), flavone (**17**), and steroidal lactone (**19**) as shown on Fig. 1.

5. Commercialized botanical fungicides

New classes of natural plant protection products have recently been developed, approved, and successfully integrated into agricultural practice with the help of organizations empowered to market these products and this has been a real success for commerce. Some examples are jojoba essential oil (commercial names: Detur, E-Rasem, Eco E-Rase, Permatrol, Erase™), rosemary essential oil (commercial names: Ecotrol™, Sporan™, Ecosmart), and others [8]. Table 4, below lists a few cutting-edge plant products that have been successfully marketed as fungicides to treat plant diseases.

6. Advantages of using botanical fungicides for controlling plant diseases

Botanical fungicide development could lessen the drawbacks of synthetic fungicides, such as resistance and environmental contamination. Botanical fungicides may be less hazardous to the environment, effective, selective, and biodegradable in this regard [70]. The finest defense against any form of infection, pathogenesis, or disease protection issues is a product from nature. They are the primary alternatives that agriculturalists and plant biologists utilize to prevent fungal disease due to their degradability in nature [1]. Plant extracts have benefits like multiple action mechanisms because there are so many active ingredients in each mixture, low toxicity to non-target organisms, including humans, relatively straightforward and inexpensive production processes, and reduced health risks during application because of low residue toxicity [8]. Botanicals are more affordable and more environmentally friendly than synthetic fungicides in agriculture [71]. They are enzymatically biodegradable with, typically, short half-lives, they have selectivity and specificity in how they affect the target species, they can be combined in ways that reduce the amount of active ingredients needed to achieve an effect, they come from a variety of chemical families, and by expanding the range of molecules that are available, they help to diversify the biochemical and molecular targets that are directed at fungi and thus limit or delay the resistance phenomenon [72].

Table 3
Activity of compounds isolated from plants against phytopathogenic fungi of fruits, vegetable, and cereals.

Plant species (part used)	Fungi species (disease caused)	Efficacy observed	References
Efficacy against pathogenic fungi of fruits and vegetables			
• *Curcuma longa* (roots)	• *Podosphaera xanthii* (cucumber powdery mildew)	• The EC_{50} value of (+)-(S)-*ar*-turmerone (**1**) isolated from petroleum ether fraction of ethanol extract was found to be 28.7 μg/mL and the compound was proved to have a curative effect in *in vivo* (greenhouse) assay.	[56]
• *Caryodaphnopsis baviensis* (leaves and stems)	• *Alternaria porri* (purple blotch diseases of *Allium* plants)	• Magnolol (**2**), a neolignan compound isolated from *n*-hexane and ethyl acetate fractions of methanol extract showed a significant inhibitory activity against the spore germination and mycelial growth of *A. porri* with IC_{50} values of 4.5 and 5.4 μg/mL, respectively in *in vitro* assay. • When magnolol was sprayed onto onion plants at a concentration of 500 μg/mL, it showed more than 80% disease control efficacy for the purple blotch diseases in *in vivo* (greenhouse) assay.	[57]
• *Trevesia palmata* (aerial parts)	• *Alternaria porri* • *B. cinerea* • *C. coccodes* • *F. oxysporum* • *P. infestans* (tomato and pepper diseases)	- In an *in vitro* assay, disease control values against tomato gray mold, and tomato late blight were 82 and 88 respectively when the plants were treated with hederagenin-3-*O*-β-D-glucopyranosyl-(1→3)-α-L-rhamnopyranosyl-(1→2)-α-L-rhamnopyranosyl-(1→2)-α-L-arabinopyranoside (**3**) (500 μg/mL), a triterpene glycoside isolated from n-butanol and ethyl acetate fractions of methanol extract obtained by reflux.	[58]
• *Corydalis ternata* (tubers)	• *Botrytis cinerea* (tomato gray mold) • *Phytophthora infestans* (tomato late blight) • *Colletotrichum coccodes* (pepper anthracnose)	• Isoquinoline alkaloids (dehydrocorydaline (**8**), stylopine (**9**), and corydaline (**10**)) isolated from chloroform fraction of methanol extract exhibited *in vivo* antifungal activity against *C. coccodes.*	[59]
• *Coptis japonica* (roots)	• *Botrytis cinerea* • *Phytophthora infestans* • *Rhizoctonia solani* (cucumber gray mold, tomato late blight)	• Berberine chloride (**11**), an isoquinoline alkaloid isolated from chloroform fraction of methanol extract had an apparent LC_{50} value of approximately 190 mg/L against *B. cinerea* in *in vivo* assay. • Coptisine chloride (**13**), another isoquinoline alkaloid isolated from butanol fraction of methanol extract had an LC_{50} value of 210 mg/L against *B. cinerea*.	[60]
• *Myristica fragrans* (seeds)	• *Alternaria alternata* • *Colletotrichum coccodes* • *C. gloeosporioides* (tomato gray mold and tomato late blight).	• In *in vitro* assay, the listed fungi were relatively sensitive to *erythro*-austrobailignan-6 (**14**), *meso*-dihydroguaiaretic acid (**15**) and nectandrin-B (**16**), lignans isolated from ethyl acetate and n-butanol combined fractions of methanol extract with varied activity. • Nectandrin-B was highly active against the development of tomato late blight.	[61]
Efficacy against pathogenic fungi of cereals			
• *Combretum erythrophyllum* (leaves) • *Withania somnifera* (leaves)	• *Fusarium oxysporum* • *F. verticilloides* • *F. subglutinans* • *F. proliferatum* • *F. solani* • *F. graminearum* • *F. semitectum* • *F. chlamydosporum* (maize disease)	• In *in vitro* assay, compounds isolated from acetone and ethyl acetate extracts (5-hydroxy-7,4′-dimethoxyflavone (**17**) maslinic acid (**18**) and withaferin A (**19**)) showed good antifungal activity with minimum inhibitory concentrations (MIC) less than 1.0 mg/mL against one or more of the tested *Fusarium* pathogens.	[62]
• *Drimys winteri* (barks)	• *Gaeumannomyces graminis var. tritici* (take-all disease of the roots of cereals such as wheat).	• In *in vitro* assay, drimane sesquiterpenoids isolated from ethyl acetate extract obtained by maceration (drimenin (**20**), drimenol (**21**), polygodial (**22**), isodrimeninol (**23**), valdiviolide (**24**) and drimendiol (**25**)) showed high antifungal activity against the fungus. • Polygodial and isodrimeninol were the more effective with an activity of LC_{50} between 7 and 10 μg/L and higher fungal lipid peroxidation.	[63]
• *Trevesia palmata* (aerial parts)	• *B. graminis f. sp. hordei* • *M. oryzae* (wheat, rice and barley diseases)	• An *in vitro* antifungal bioassay revealed that except for ilekudinoside D (**7**) with $IC_{50} > 256$ μg/mL, compounds isolated from n-butanol and ethyl acetate fractions of methanol extract obtained by reflux including hederagenin-3-*O*-β-D-glucopyranosyl-(1→3)-α-L-rhamnopyranosyl-(1→2)-α-L-rhamnopyranosyl-(1→2)-α-L-arabinopyranoside (**3**), 3-*O*-α-L-rhamnopyranosyl asiatic acid (**4**), macranthoside A (**5**), and α-hederin (**6**) exhibited strong antifungal activities against *M. oryzae* with IC_{50} values ranging from 2 to 5 μg/mL. • In particular, when the plants were treated with compound **3** (500 μg/mL), disease control values against rice blast and wheat leaf rust were 84 and 70%, respectively.	[58].

(*continued on next page*)

Table 3 (*continued*)

Plant species (part used)	Fungi species (disease caused)	Efficacy observed	References
• *Corydalis ternata* (tubers)	• *Puccinia triticina* (wheat leaf rust) • *Blumeria graminis f. sp. hordei* (barley powdery mildew)	• The isoquinoline alkaloids isolated from chloroform fraction of methanol extract (dehydrocorydaline (**8**), stylopine (**9**), and corydaline (**10**)) exhibited *in vivo* antifungal activity against *P. triticina*.	[59]
• *Coptis japonica* (roots)	• *Erysiphe graminis* • *Phytophthora infestans* • *Puccinia recondite* • *Pyricularia grisea* (rice blast, rice sheath blight, wheat leaf rust, and barley powdery mildew)	• Berberine chloride (**11**) had an apparent LC_{50} value of approximately 80, and 50 mg/L against *E. graminis*, and *P. recondita*, respectively in *in vivo* assay. • Coptisine chloride (**13**) had an LC_{50} value of 20, 180, and 290 mg/L against *E. graminis, P. recondita,* and *P. grisea*, respectively. • Palmatine iodide (**12**) had an LC_{50} value of 160 mg/L against *P. grisea*.	[60]
• *Myristica fragrans* (seeds)	• *Magnaporthe grisea* • *Agrobacterium tumefaciens* • *Acidovorax konjaci* • *Burkholderia glumae* (rice blast, rice sheath blight, wheat leaf rust and barley powdery mildew).	• In *in vitro* assay, the listed fungi were relatively sensitive to isolated lignans (*erythro*-austrobailignan-6 (**14**), *meso*-dihydroguaiaretic acid (**15**) and nectandrin-B (**16**)) with varied activity. • In *in vivo* assay, all three compounds effectively suppressed the development of rice blast and wheat leaf rust. • Compound **14** was highly active against the development of barley powdery mildew. • Both **15** and **16** also moderately inhibited the development of rice sheath blight.	[61]

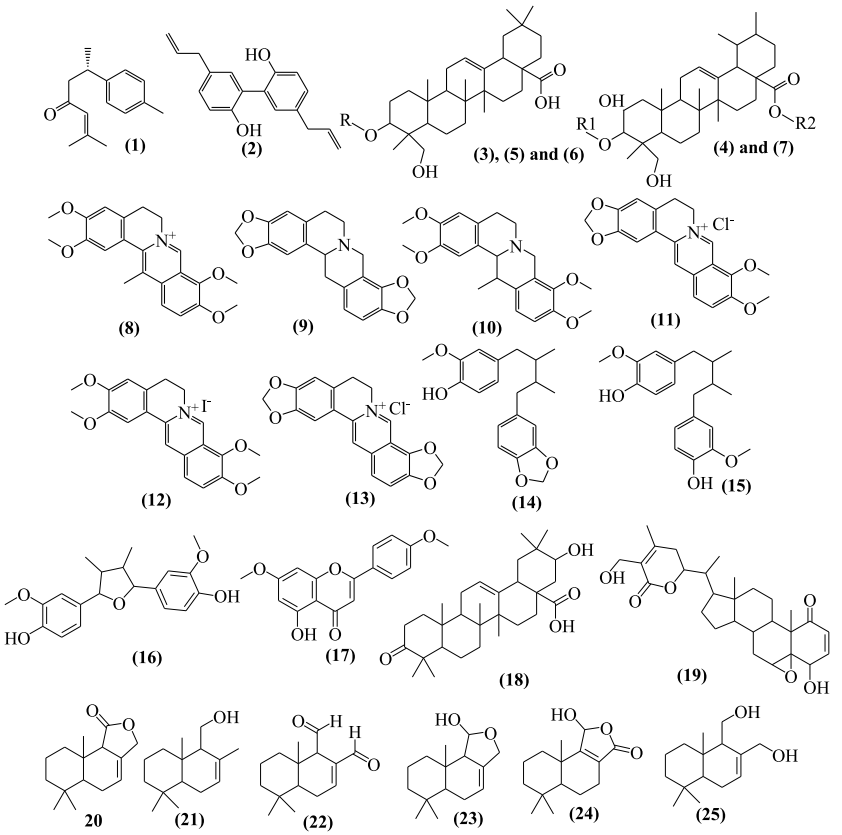

Fig. 1. Chemical structures of antifungal compounds isolated from plants. In structures 3–7, R, R1 & R2 stands for the following substituents. (**3**). R = β-D-glucopyranosyl-(1→3)-α-L-rhamnopyranosyl-(1→2)-α-L-rhamnopyranosyl-(1→2)-α-L-arabinopyranoside. (**4**). R1 = α-L-rhamnopyranosyl, R2 = H. (**5**). R = β-D-glucopyranosyl-(1→3)-α-L-rhamnopyranosyl-(1→2)-α-L-arabinopyranoside. (**6**). R = α-L-rhamnopyranosyl-(1→2)-α-L-arabinopyranoside. (**7**). R1 = α-L-arabinopyranosyl, R2 = β-D-glucopyranosyl

Table 4
Plant products commercialized as effective fungicides for controlling plant diseases.

Trade names	Descriptions on botanical sources, uses, efficacy, application method and mechanism of action	References
• Regalia® (formerly formulated as Milsana®)	• Botanical source: *Reynoutria sachalinensis* • Uses: Used to control powdery mildew of cucurbits, downy mildew of lettuce (*Bremia lactucae*), *Botrytis* of grapes and strawberries, bacterial spot of tomatoes and peppers (*Xanthomonas campestrispv vesicatoria*), Cercospora on soybeans (*Cercospora kikuchii*) and bacterial canker on citrus (*Xanthomonas axonopodis pv. citri*), amongst others. • Efficacy: Extensive tests have been conducted in the laboratory, glasshouse and field on multiple crop-disease systems to evaluate its efficacy for disease control. Test results demonstrated the efficacy of Regalia® applied as a foliar spray in controlling a wide range of fungal and bacterial diseases mentioned above. • Application methods: Multiple delivery methods can be used, such as seed treatment, soil drenches, irrigation applications, and dipping seedlings prior to transplanting. • Mechanism of action: Induces plant resistance: increases the activity of chalcone synthase and chalcone isomerase in the phenylpropanoid pathway and induces the production and accumulation of phytoalexins. Simple phenolic compounds, which are fungitoxic, also accumulate. It increases the papillae formation at pathogen penetration sites as well as the liginification of plant cell walls. Activities of pathogenesis-related protein (PR-proteins) such as chitinase, glucanase, and peroxidase are also increased.	[64]
• EcoSwing®	• Botanical source: *Swinglea glutinosa* • Application method: Applied in a regularly scheduled preventative spray program. Ground applications, aerial applications, chemigation applications are possible. • Mechanism of action: It has a unique mode of action, 0-day pre-harvest interval, and exemption from tolerances, making it an essential tool in any integrated pest management (IPM) program. EcoSwing has a multi-site mode of action, and may be used to delay or prevent the development of resistance to single site fungicides.	[65]
• Timorex Gold®	• Botanical source: *Melaleuca alternifolia* (tea tree) • Efficacy: Effective against a broad spectrum of ascomycete and bacterial plant diseases like powdery mildew, early blight, *Botrytis* and more, in a wide range of vegetable and fruit crops. Used for a wide variety of high value fruit and vegetable crops, including grapes, leafy vegetables, fruiting vegetables, berries, vines, tree nuts, tropicals and cucurbits. • Application method: Ground and drench applications • Mechanism of action: Multiple modes of actions that disrupt the fungal cell membrane and destroy the cell walls. Impacts the plant's defense processes, reducing the energy required to build its defense response. When a plant is attacked by disease, it activates its immune system, building crystalline structures inside cell walls. When Timorex Gold® is used, an attacked plant can divert energy to growth and yield instead of defense processes.	[66]
• Fracture®	• Botanical source: Cotyledons of lupine plants • Uses: A broad-spectrum, biological fungicide labeled for the prevention and control of powdery mildew, botrytis and brown rot blossom blight on almonds, grapes, strawberries and tomatoes. • Application method: Foliar applications • Mechanism of action: It works on contact by deforming and inhibiting fungal cell production, ultimately tearing apart the cell wall and disrupting the fungal cell membrane.	[67]
• Sporan® EC2	• Botanical source: Rosemary, Clove, Thyme, and Peppermint • Uses: It controls diseases such as *Botrytis* gray mold of strawberries, powdery mildews of grapes andgerbera daisies, *Phytophthora* late blight of tomatoes, etc. • Application method: Foliar spray (aerial applications) • Mechanism of action: Destroys pathogen cell walls, interferes with fungus attaching to plant.	[68]
• Thyme Guard®	• Botanical source: Thyme (*Thymus vulgaris*) • Uses: Used for controlling *Botrytis*, *Fusarium*, powdery mildew, downy mildew, citrus canker, citrus greening-HLB, fire blight, and many others. • Application method: Aerial application • Mechanism of action: With plant pathogens, it attacks and breaches their cellular membranes, causing their death.	[69]

7. Challenges in adoption and utilization of botanical fungicides for controlling plant diseases

Despite the fact that plant products are effective substitutes for synthetic fungicides and have a strong track record, their extensive practical applicability is still constrained by farmers' resistance to using natural products as biofungicides and the paucity of research in this field. Developing efficient stabilization processes (such as microencapsulation), simplifying complicated and expensive authorization requirements for the use of natural plant protection products, and optimizing plant growth conditions and extraction processes leading to a homogenous chemical composition are the main challenges for future research, according to an analysis of the main strengths and weaknesses that arise from the use of plant extracts as natural plant protection products [8].

The main causes of their low adoption for production at a commercial scale are a lack of adequate information and extension services at the farmer's level and sluggish results compared to synthetic fungicides. Farmers are discouraged from using botanical fungicides since they are less effective than chemical fungicides and are not readily available on the market when needed. Farmers themselves can make botanical fungicides but they tend to choose chemical fungicides since the creation of botanical fungicides necessitates the use of specialized plants and takes a lot of time and effort. Furthermore, the widespread use of botanical fungicides is hindered by rigorous regulations, less lasting or quick degradation, and variations in the active ingredient composition with plants

growing in various climatic situations. Large biomass of chosen plants is needed for the commercial manufacture of botanical fungicides. Their manufacturing and adoption are hindered by the bulkiness issue during collection, production, and application. Plant products for the production of fungicides have limited market range. Less market demand of such products and increasing demand of food crops hinder the commercial production of botanical fungicides [7].

The need to develop formulations, the presence of some chemical compounds that are harmful to people and plants, the lack of standardized extraction methods, rapid degradation, inadequate *in vivo* studies, less effectiveness, and limited availability of formulations are additional barriers to the use of botanicals in the management of plant diseases [71].

Additionally, there are a number of variables that affect the industrial development of formulations incorporating plant components, including the accessibility and availability of the raw material. The supply of vegetable biomass must be constant, abundant, and easily renewable, which excludes species with slow development, like the woody species, if they are not cultivated. Other considerations include the standardization and refinement of the plant commercial product, which is susceptible to variation in its chemistry due to geographic, genetic, and climatic factors; the products put on the market must be of uniform and consistent quality; the difference in procedures of regulatory approval processes in different countries, as well as the protection of technologies and formulations, which will ensure companies exclusivity in the market through the protection granted by patents. Due to toxicologic and ecotoxicologic standards, fungicide registration is extremely expensive for businesses planning to market their products in industrialized nations. The current issue is that few appropriate and acceptable test procedures have been created for biofungicides and regulators are unsure of the best course of action as a result [72].

8. Possible solutions for mitigating the challenges of adoption and utilization of botanical fungicides

For the production on a small scale, farmers need to have access to extension services about botanical fungicide identification, preparation methods, and application. They should get subsidies in order to promote the creation and use of botanical fungicides. It is important to raise awareness about the advantages of natural fungicides over synthetic ones. Focus should be placed on sustainable agriculture and organic farming because these concepts can draw customers to such goods. None of the producers are willing to take risk in their production and thus, market for the botanical fungicides should be made secured. It would be preferable if the government set the prices in accordance with the goods' quality. Legislation regarding their import and export must be made simple. Taxes on these goods ought to be decreased, although they might be raised on chemical fungicides. For large-scale production, the government must make loans with low interest rates available to the producers. It is important to investigate prospective plants with fungicidal qualities. By using plant breeding methods, the percentage of bioactive compounds in such plants can be raised. In order to retain high quality, extraction and processing techniques should be improved. By undertaking a number of studies, particular climatic requirements for the site-specific production of plant species should be discovered [7].

These factors are particularly significant for the industrial future of plant-derived products. In order to meet the quality requirements of the marketed products, companies that produce botanical fungicides strive to improve formulations by stabilizing extracts and maintaining a consistent chemical compositions. These requirements could be resolved with the marketing of synthetic molecules that are exact replicas of natural molecules in all aspects (i.e., organoleptic properties, degree of purity, and absence of residual solvents) [72].

The data needed for the biocontrol agents, such as plant extracts and allelochemicals, should be decided by expert committees. To construct reasonable regulatory procedures and speed up market introduction, regulators, industrial, and academic employees should come together to develop suggestions that take the risk assessment into account [72]. Therefore, it is now more important than ever for academics, decision-makers, business people, and farmers to work together to explore, legalize, properly market, and widely utilize botanical fungicides. Focus should be placed on botanical fungicides if methods like integrated pest management (IPM), organic farming, and sustainable agriculture need to be expanded [7].

9. Conclusion

Phytochemicals are effective fungicides against a wide range of fungal species that cause pre- and post-harvest illnesses of plants. Reviewing available literatures on efficacy of plant products against phytopathogenic fungi causing diseases of economically important crops such as cereal grains, pulses, fruits and vegetables revealed that plant extracts and isolated compounds have significant antifungal activity in *in vitro* and *in vivo* assays. Botanical fungicides inhibit development of resistance, are ecofriendly, effective, selective, and more affordable compared to synthetic fungicides. However, their number in the market is very small because of many factors that hinder wide scale production at commercial scale. Challenges of adoption and utilization of botanical fungicides at commercial level for wide scale production may be caused by a variety of issues, including farmers' resistance to using natural products as biofungicides, lack of standardized extraction and formulation techniques, slow results in comparison to chemical fungicides, strict legislation, rapid degradation, and variations in the active ingredient composition with plants grown in various climatic conditions. The ways to address these challenges include increasing awareness among farmers, conducting more research to identify potential plants with fungicidal properties, standardizing extraction and formulation techniques, implementing the idea of plant breeding to increase bioactive agents, identifying favorable environments for site-specific plant species production, discovering synthetic analogues of the active ingredient to maintain quality standards, establishing reasonable regulation procedures and price points for a quicker market introduction. Numerous researchers have recommended isolating and characterizing the active antifungal compounds in the crude extract, conducting *in vivo* experiments in controlled greenhouse settings and open fields to practically evaluate the use of these extract in the context of an Integrated Pest Management system, determining the precise mechanism of action by which these

extracts work, the use of multiple plant extracts in combination to increase effectiveness, conducting phytotoxicity research, analyzing the number and timing of applications to determine the efficacy of the extract to prevent disease in the field, investigating potential toxicity on humans or livestock, as well as the stability of the extracts during grain storage treatment, and the use of plant extracts in conjunction with other well-established disease control practices for effective control. In addition to these recommendations, the authors of this article suggest collaboration of regulatory agencies and researchers from a variety of fields, including chemistry, biology, agriculture, environmental science, engineering, and so on in order to put all these plans into practice.

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