Plants and Phytocompounds as Natural Defenders Against Mycotoxin Contamination in Agriculture

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Abstract
Plants play a key role in preventing mycotoxin contamination in agriculture through both direct antifungal effects and indirect environmental modulation. This review explores how specific phytocompounds - especially those from aromatic and medicinal plants - can inhibit fungal growth and suppress mycotoxin production. Compounds such as phenolics, flavonoids, and essential oils from oregano (*Origanum vulgare*), thyme (*Thymus vulgaris*), and rosemary (*Rosmarinus officinalis*) have demonstrated both antifungal and anti-mycotoxigenic properties. The role of phytoalexins, synthesized by plants in response to pathogenic attacks, is also addressed as a rapid natural defense mechanism. By synthesizing recent experimental data, this review highlights the potential of plant-derived compounds to be integrated into sustainable agricultural practices as natural alternatives to synthetic fungicides. Although promising, the application of phytocompounds requires careful assessment of their efficacy, stability, and potential limitations under field conditions.

Keywords: antifungal activity, mycotoxins, phytocompounds, sustainable agriculture

Introduction

Contamination of food and feed with mycotoxin-producing fungal species is a major global concern, posing serious risks to public health even at low concentrations [1]. Mycotoxins, the toxic secondary metabolites produced by fungi such as *Aspergillus*, *Fusarium*, and *Penicillium*, can accumulate in crops, cereals, and animal-derived products like milk, meat, and eggs, leading to liver and kidney damage, immune suppression, and carcinogenic effects [2,3]. In developing countries, it is estimated that 60-80% of crops may be affected by fungal contamination, resulting in significant agricultural losses and increased healthcare costs [4].

Despite the use of chemical, physical, and microbiological decontamination methods, these approaches often fall short due to limitations in efficiency, safety, or affordability [5]. A promising solution is the use of phytocompounds-natural plant - derived substances with antimicrobial and antifungal activity [6]. These include essential oils, polyphenols, flavonoids, and phytoalexins, which can inhibit both fungal development and mycotoxin biosynthesis [7,8]. Their dual role supports sustainable agriculture and aligns with ecological farming principles [9]. This review aims to explore the natural defense mechanisms offered by plants, focusing on the antifungal and anti-mycotoxigenic effects of specific aromatic and medicinal species. The role of plant-induced compounds such as phytoalexins is examined in the context of natural pathogen resistance. Through the synthesis of recent experimental data, this study evaluates the potential of phytocompounds to serve as effective,

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environmentally friendly alternatives to chemical fungicides in mitigating mycotoxin contamination.

The Role of Phytocompounds in Preventing Fungal Contamination and Reducing Mycotoxins in Agriculture

Plants synthesize a wide range of chemical compounds as a defense mechanism against microorganisms, insects, and environmental stress [10]. These compounds, known as phytocompounds, are not essential from a nutritional standpoint but have numerous beneficial properties for human and animal health [11]. Among them are essential oils, polyphenols, flavonoids, terpenoids, and alkaloids, which are recognized for their antifungal, antioxidant, anti-inflammatory, and immunomodulatory activities [12]. Phytocompounds are considered promising agents for the development of new drugs and dietary supplements due to their structural and functional diversity. For example, flavonoids and carotenoids exert strong antioxidant effects, protecting cells from oxidative stress, while saponins and terpenoids demonstrate antimicrobial and anti-inflammatory activity [13]. These compounds play essential roles in both plant protection against pathogens and the prevention of chronic diseases in humans and animals. Studies show that phytocompounds contribute to immune response modulation, inhibition of carcinogenic processes, and a reduction in the risk of metabolic diseases [14]. Additionally, they can be used as adjuvants in conventional therapies or as active ingredients in nutraceutical products [15]. In the agricultural context, these biological benefits can be leveraged not only for plant protection but also for food chain safety by reducing early fungal contamination and, consequently, the risk of mycotoxin accumulation.

Application of Phytocompounds in Preventing Mycotoxin Contamination

Phytocompounds not only protect plants from pathogenic fungi but can also inhibit the development of mycotoxin-producing fungi and the biosynthesis of these toxic compounds in food and feed. Substances such as phenols, flavonoids, and terpenoids have proven effective in combating mycotoxin-producing fungal species from the genera *Aspergillus*, *Fusarium*, and *Penicillium* [16]. For example, lavender essential oil (*Lavandula angustifolia*), at concentrations of 200-400 µL/L, completely inhibited the growth of *Aspergillus flavus* and the synthesis of aflatoxin B_1 in stored corn samples [17]. Similarly, extracts of basil (*Ocimum basilicum*) and thyme (*Thymus vulgaris*), rich in thymol and carvacrol, demonstrated antifungal and anti-mycotoxigenic effectiveness against *Fusarium verticillioides*, significantly reducing fumonisin production [18]. The mechanisms of action of phytocompounds include: inhibition of key genes involved in mycotoxin biosynthesis, such as aflatoxins or trichothecenes; interference with fungal membrane integrity; disruption of cellular metabolism; and reduction of oxidative stress, which stimulates mycotoxin synthesis [19]. For instance, a study by Mossini et al. (2009) showed that neem leaf extract (*Azadirachta indica*) reduced ochratoxin A synthesis by up to 80% in *Penicillium verrucosum* cultures, depending on concentration and exposure time [20]. The application of plant extracts also contributes to extending the shelf life of agricultural products without affecting their nutritional quality. This ecological strategy reduces dependence on synthetic fungicides, supports sustainable agriculture, and provides a safe and accessible alternative for protecting human and animal health [21].

Antifungal and Anti-mycotoxigenic Effects of Aromatic and Medicinal Plants

Aromatic and medicinal plants, such as oregano (*Origanum vulgare*), thyme (*Thymus vulgaris*), and rosemary (*Rosmarinus officinalis*), are recognized not only for their culinary uses but also for their antifungal, antioxidant, and anti-inflammatory properties [20]. These plants contain active phytocompounds, such as carvacrol from oregano and thymol from thyme, which have proven effective against mycotoxin-producing fungi, especially species from the *Aspergillus* and *Penicillium* genera, commonly involved in the contamination of food and feed [22].
Table 1 provides an overview of the antifungal properties and uses of selected aromatic and medicinal plants, highlighting their effectiveness in combating fungal contamination and mycotoxin production.

Table 1. Antifungal Properties and Uses of Selected Aromatic and Medicinal Plants

Plant	Scientific Name	Active Compounds	Antifungal Properties	Uses	Reference
Oregano	*Origanum vulgare*	Carvacrol, Thymol	Inhibits the growth of pathogenic fungi, including Candida albicans	Food preservation, herbal treatments	23
Thyme	*Thymus vulgaris*	Thymol, Carvacrol	Strong antifungal activity against Aspergillus	Food protection, antiseptic in natural remedies	23
Rosemary	*Rosmarinus officinalis*	Rosmarinic acid, Carnosic acid	Reduces risks of contamination with mycotoxins	Culinary uses, cosmetics, aromatherapy	24
Garlic	*Allium sativum*	Allicin	Broad-spectrum antifungal effects	Food flavoring, natural antifungal treatments	23
Sage	*Salvia officinalis*	Camphor, Thujone	Antifungal properties against several fungi species	Culinary uses, traditional medicine	25
Peppermint	*Mentha × piperita*	Menthol, Menthone	Effective against certain fungal strains	Herbal teas, natural remedies	25
Clove	*Syzygium aromaticum*	Eugenol	Potent antifungal activity	Culinary spice, natural preservative	24
Lavender	*Lavandula angustifolia*	Linalool, Linalyl acetate	Antifungal effects, particularly against mold	Aromatherapy, cosmetics, natural cleaning	24
Basil	*Ocimum basilicum*	Eugenol, Linalool	Inhibits growth of various fungi	Culinary uses, pest deterrent	23

These plants can be effectively integrated into ecological and sustainable agricultural systems, serving as a natural alternative to chemical fungicides and thereby contributing to environmental protection and the production of safe food products [23]. Their application in agricultural practices-such as crop rotation or natural plant protection using botanical extracts-has demonstrated a significant reduction in mycotoxin contamination [24]. For instance, some studies have reported reductions of over 50% in *Aspergillus flavus* contamination in batches treated with aromatic plant extracts [25]. This sustainable approach offers an effective and eco-friendly solution for managing the risks associated with fungal and mycotoxin contamination. Moreover, recent studies have shown that oregano and rosemary extracts can inhibit the expression of genes involved in mycotoxin biosynthesis, thereby reducing their accumulation in agricultural products. For example, oregano essential oils reduced *Aspergillus flavus* growth by 70% at a concentration of 1.5 mg/mL [21]. Similarly, thyme oil completely inhibited aflatoxin B_1 production at a concentration of 2.0 mg/mL [22]. These findings support the use of aromatic plants as effective biofungicidal agents, not only by controlling fungal development but also by directly reducing mycotoxin synthesis.

Phytoalexins: Induced Plant Defenses Against Mycotoxin-Producing Fungi and Mycotoxins

Phytoalexins are a specialized class of phytocompounds synthesized by plants as a rapid response to stress, particularly during pathogenic attacks by fungi, bacteria, or viruses [25]. These substances are produced de novo immediately after the plant recognizes the pathogen and play a crucial role in protecting against fungal and bacterial infections [26,27]. Unlike phytocompounds that are constitutively present throughout the plant's life cycle, phytoalexins are synthesized exclusively under threat conditions and act as an active component of the plant's defense response [28]. Their mechanisms of action include inhibition of spore germination, disruption of fungal cell wall integrity, and blockage of metabolic pathways involved in mycotoxin biosynthesis [29]. Numerous studies have demonstrated that phytoalexins can reduce mycotoxin contamination, thereby providing protection to both the plant and the end consumer [30].

Relevant experimental examples include: glyceollin (from *Glycine max*, soybean), which reduced aflatoxin B_1 production by *Aspergillus flavus* by 70-95% at concentrations ranging from 6.25 to 62.5 μg/mL, while fungal growth was only marginally inhibited (11%) [31]. Arachidin-1 and arachidin-3, stilbenoid phytoalexins from infected peanuts, almost completely suppressed aflatoxin synthesis by *A. flavus* and *A. parasiticus* without significantly affecting mycelial development [32]. Capsaicin, an alkaloid from *Capsicum annuum*, reduced ochratoxin A production by over 50% in *Aspergillus carbonarius*, while also exhibiting antifungal activity against species in the *Nigri* section [33]. The essential oil of *Piper divaricatum*, rich in methyl eugenol (~75%) and eugenol (~10%), completely (100%) inhibited the growth of *Fusarium solani* f. sp. *piperis* at a concentration of 2.5 mg/mL. At concentrations ranging from 0.25 to 2.5 mg/mL, fungal growth was reduced by 18% to 100%, highlighting the strong antifungal action of these phenylpropenes in liquid culture [33]. Cinnamon (*Cinnamomum verum*) essential oil reduced the synthesis of aflatoxin B_1 and B_2 by up to 90% at concentrations of 0.125% (v/v) in stored cereals. The expression of key genes involved in mycotoxin biosynthesis (*aflR, nor-1*) was suppressed by over 94% [34]. Thyme (*Thymus vulgaris*) oil, rich in thymol and carvacrol, inhibited aflatoxin B_1 production by 60-79% at a concentration of 4% (v/v) in *A.flavus*-contaminated cashew kernels [35]. Essential oils of cumin, anise, and garden thyme demonstrated clear inhibition zones against *Penicillium spp.* at concentrations of 0.125-0.75 μL/mL (~125-750 ppm) in in vitro cultures [33]. Plant extracts rich in phytoalexins can act synergistically with other antimicrobial phytocompounds (e.g., flavonoids, essential oils), reducing the risk of fungal resistance and contributing to the preservation of agricultural products [27]. Moreover, phytoalexins may offer health benefits due to their antimicrobial, anti-inflammatory, and antioxidant properties [34]. However, the application of phytoalexins and similar phytocompounds in sustainable agricultural practices is limited by factors such as reduced stability under external conditions, high extraction and purification costs, and variable efficacy depending on concentration and fungal species [35]. To fully harness this potential, further research is needed to optimize formulations, assess consumer safety, and integrate these substances into ecological plant protection systems [36].

In recent years, research has highlighted the increased efficacy of plant extracts, essential oils, and nanoformulations derived from these compounds in combating mycotoxin-producing fungi. Table 2 summarizes the results of experimental studies on the antifungal effects of medicinal plants such as garlic, thyme, mint, chicory, and propolis, as well as essential oils and nanoformulations based on natural compounds.

Table 2. Antifungal effects of plant extracts, their compounds, and nanoformulations against mycotoxigenic fungi

Plant/Compound	Antifungal Effect	Target Mycotoxin Fungi	Application Form	Reference
Garlic *(Allium sativum)*	Inhibits fungal growth	*Aspergillus, Penicillium*	Extract, essential oil	36
Thyme *(Thymus vulgaris)*	Strong antifungal activity	*Aspergillus flavus, Fusarium spp.*	Extract, essential oil	36
Field Thyme *(Thymus serpyllum)*	Moderate antifungal effects	*Fusarium, Penicillium*	Extract, powder	37
Peppermint *(Mentha piperita)*	Antifungal activity	*Aspergillus, Fusarium spp.*	Extract, essential oil	37
Oregano Oil *(Origanum vulgare)*	Effective against fungi	*Aspergillus, Candida*	Essential oil	37
Propolis Extract	Variable antifungal effect	*Aspergillus, Penicillium*	Extract	38
Nanoformulations with Essential Oils	Enhanced antifungal efficacy	*Aspergillus, Fusarium spp.*	Nanoparticles with oils	38
Chicory *(Cichorium intybus)*	Moderate antifungal activity	*Aspergillus flavus*	Extract	36

These data suggest that nanoformulations can enhance the efficacy of active compounds, reducing the concentrations required to inhibit fungal growth or mycotoxin synthesis. Additionally, they may offer a sustainable solution for developing natural biofungicides that are more stable and effective in agricultural applications.

Limitations of Using Phytocompounds as Biofungicides

Although phytocompounds and plant extracts have shown significant efficacy in controlling the growth of mycotoxin-producing fungi and in reducing the synthesis of these toxic metabolites, their large-scale application remains limited by several technical, biological, and economic factors. These limitations must be analyzed in detail to understand the real challenges of integrating such substances into sustainable agricultural practices [39]. One of the main obstacles is the compositional variability of plant extracts. The content of active compounds such as thymol, carvacrol, eugenol, or flavonoids varies significantly depending on plant species, cultivar, soil and climate conditions, harvest period, and extraction method [40]. For example, comparative studies on oregano (*Origanum vulgare*) essential oil have shown that the carvacrol concentration can range from 20% to over 70%, leading to inconsistent antifungal efficacy in practical applications. Thus, the lack of rigorous standardization of plant extracts limits their use as commercial biofungicides, as dosage and results are difficult to reproduce under field conditions [41]. Another important aspect is the low stability of active phytocompounds under external conditions. Many of these compounds are sensitive to light, oxygen, temperature, or pH, resulting in rapid degradation during storage or after application on crops [42]. Essential oils, for instance, may undergo oxidation processes that reduce their biological activity and generate potentially irritating or toxic by-products. This instability impacts field efficacy and requires special formulation and preservation methods, which increase production costs [43]. In addition to instability, the antifungal effectiveness of phytocompounds often depends on high concentrations to achieve significant effects against mycotoxigenic fungi. For instance, to fully inhibit aflatoxin B_1 synthesis by *Aspergillus flavus*, thyme essential oil had to be used at concentrations of 2-4% (v/v) in experimental media-levels that are difficult to apply on a large scale due to cost and the potential impact on the organoleptic properties of treated products [44]. Moreover, natural compounds may exhibit selective efficacy, acting only against certain fungal species or strains while being ineffective against others. This narrow spectrum of action limits their universal applicability as biofungicidal agents [45]. An additional challenge is the lack of long-term toxicological and safety studies, both for human consumption and for agricultural ecosystems. Although phytocompounds are often considered safer than synthetic pesticides, this is not always the case [46]. Some essential oils may have cytotoxic or irritant effects at high doses or with repeated exposure, and their impact on beneficial soil microorganisms or pollinators remains insufficiently documented [47].

Furthermore, integrating phytocompounds into crop protection strategies requires complex technological adaptations. Effective application demands specialized formulations (e.g., nanoencapsulation, stable emulsions), controlled-release systems, and compatible equipment - all of which imply significant initial investments. Although certain nanoformulations have demonstrated improved efficacy and stability of phytocompounds, research is still in early stages, and regulations concerning their use in agriculture are often unclear or restrictive [48].

Finally, it is important to note that phytocompounds primarily act preventively by inhibiting fungal development and mycotoxin biosynthesis but are not effective for detoxifying already contaminated food [49]. Once mycotoxins are produced, they are extremely chemically stable and difficult to eliminate, meaning that phytocompounds must be implemented as part of a prevention system, not as a curative solution. Therefore, early monitoring, timely application, and integration into integrated pest management (IPM) programs are essential to ensure the effectiveness of this strategy [50].

Overall, although phytocompounds offer a promising and eco-friendly alternative to synthetic fungicides, limitations related to standardization, stability, selective efficacy, potential toxicity, and technological challenges must be carefully evaluated. Advances in biotechnology, green chemistry, and nanoformulation may help overcome these barriers; however, until then, the large-scale use of phytocompounds as biofungicides remains a valuable yet constrained option that requires rigorous further research [51].

Conclusions

Phytocompounds represent a promising solution for the prevention of mycotoxin contamination due to their ability to inhibit fungal growth and reduce toxin synthesis. The mechanisms involved - such as disruption of fungal cell membrane integrity, induction of oxidative stress, and inhibition of specific signaling pathways - have been demonstrated in numerous experimental studies. Moreover, the use of plant - derived compounds as biocontrol agents offers a sustainable alternative to conventional chemical methods, contributing to reduced environmental and human health impact. However, the practical application of phytocompounds remains limited by factors such as low stability, reduced bioavailability, and the lack of standardized extraction and application protocols. Therefore, further research is needed to optimize formulations, dosages, and delivery methods, as well as to assess their effectiveness under real storage and food processing conditions on a larger scale. In conclusion, although phytocompounds cannot fully replace current mycotoxin prevention strategies, they have the potential to become a key component of an integrated control system, making a significant contribution to global food safety.

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