

1 **Plant extracts for the management of Black Shank and Fusarium Wilt of**  
2 **Tobacco: A Comprehensive review**

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19 **Abstract**

20 Tobacco (*Nicotiana tabacum* L.) is severely affected by soil-borne pathogens such as  
21 *Phytophthora nicotianae* and *Fusarium oxysporum* f. sp. *nicotianae*, causing major yield  
22 losses. Fungicide resistance and restrictions on synthetic pesticides necessitate eco-friendly  
23 alternatives. Plant extracts rich in compounds such as curcumin, allicin, and thymol exhibit  
24 antifungal and plant defense-inducing activity but face challenges of instability and  
25 variable field performance. Recent advances in nanotechnology, including chitosan- and  
26 lipid-based carriers, improve stability, bioavailability, and targeted delivery, while  
27 synergistic use with biocontrol agents (*Trichoderma*, *Pseudomonas*) enhances disease  
28 suppression. Despite these developments, regulatory hurdles, cost, and low farmer  
29 adoption limit large-scale application. This review highlights the potential of nano-  
30 formulated plant extracts and integrated biocontrol strategies for sustainable management  
31 of tobacco diseases and emphasizes the need for standardized protocols, farmer education,  
32 and supportive policies to enable commercialization. Integrating biotechnology and  
33 nanotechnology offers a promising path for long-term crop protection.

34 **Keywords:** *Phytophthora nicotianae*; *Fusarium oxysporum*; botanical fungicides; nano-  
35 encapsulation; sustainable agriculture

36 **1. Introduction**

37 Tobacco (*Nicotiana tabacum* L.) is a commercially significant crop cultivated widely across many  
38 regions of the world, and is valued mostly for its financial returns (Santos et al., 2025). However  
39 the production of *N. tabacum* meet major threats from soil-borne diseases, including Black Shank  
40 and Fusarium Wilt (Ping sun et al., 2025). According to (Gai & Wang, 2024), these soil borne

41 diseases not only affect the leaf quality but also reduce the overall yields leading to considerable  
42 economic losses for growers (Gai & Wang, 2024). In the past, chemical insecticides and soil  
43 fumigation have been key components of the control of these diseases, but these methods. There  
44 has been some degree of control thanks to these techniques, the limitations of traditional methods  
45 have been brought to light by increased environmental concerns, the advent of pesticide-resistant  
46 disease strains, and customer demand for tobacco products without residue (Abdullah & Zahoor,  
47 2023). In light of these challenges, there has been a growing interest in sustainable,  
48 environmentally friendly disease management strategies. Among these, the use of plant extracts  
49 has emerged as a promising alternative due to their bioactive properties, low environmental  
50 persistence, and biodegradability.

51 Black shank is still one of the most harmful tobacco diseases, and it is brought on by the oomycete  
52 pathogen *Phytophthora nicotianae* Breda de Haan (Cochran et al., 2024). Black lesions on the  
53 stems, drooping of the leaves, and eventually the collapse of the entire plant are the usual  
54 symptoms of the diseases (Han et al., 2024). The disease is particularly challenging to eradicate  
55 because *P. nicotianae* prefers warm, wet soil conditions and develops hardy oospores that can  
56 remain for long periods of time in the soil. Despite the use of cultural measures like crop rotation  
57 and the adoption of resistant cultivars, they have only partially succeeded, particularly in  
58 environments that are conducive to the development of disease (Pandey et al., 2025). Likewise,  
59 tobacco growers face a serious threat from Fusarium Wilt, which is brought on by *Fusarium*  
60 *oxysporum* f. sp. *nicotianae* (Xie et al., 2024). The symptoms of this disease including, vascular  
61 discoloration, leaf yellowing, wilting, and ultimately plant death (Vasić et al., 2025;Lucas, 1975).  
62 The Fusarium pathogen, like Black Shank, is showed remarkably resilient to environmental  
63 changes. It may live for years in plant debris and soil, and its ability to infect a huge variety of

64 plant hosts makes management attempts even more challenging (Naqvi et al., 2025). The efficacy  
65 of chemical control methods against Fusarium Wilt has only been average, and the development  
66 of strains resistant to fungicides makes controlling the disease more difficult (Fei et al., 2025).

67 Traditional chemical control methods have a number of drawbacks, even with their track record  
68 of efficacy (Akbar et al., 2024a; Akbar & Khan, 2021). Overuse of chemicals like metalaxyl,  
69 mefenoxam, and chloroneb has resulted in the selection of resistant disease strains, making  
70 treatments less and less effective over time (Akbar et al., 2024b) (Lucas et al., 2015). Furthermore,  
71 the pollution of the environment brought on by the application of pesticides has emerged as a major  
72 worldwide issue. Pesticide residues frequently find their way into water and soil systems, where  
73 they harmfully impact organisms that are not their intended targets and contribute to long-term  
74 ecological imbalances (Ali et al., 2021). Many countries are enforcing stricter laws for the use of  
75 pesticides in agricultural products, especially those intended for export markets, which restricts  
76 the variety of chemicals that growers can choose from (Sandeep et al., 2024). Last but not least,  
77 smallholder and resource-constrained farmers frequently cannot afford the high costs involved in  
78 the development, registration, and use of novel chemical fungicides (Khoza et al., 2025). These  
79 complex drawbacks highlight the pressing need for sustainable, alternative approaches to disease  
80 management that are safe for the environment.

81 Plant extracts are becoming more and more popular as a potential remedy for the issues posed by  
82 chemical pesticides (Akbar et al., 2022) . Several secondary metabolites, including phenolics,  
83 alkaloids, flavonoids, terpenoids, and essential oils, are produced by plants and many of them have  
84 strong antibacterial and antifungal qualities (Manzoor et al., 2025). Plant extracts, in contrast to  
85 synthetic fungicides, frequently contain several modes of action, which greatly minimize the  
86 possibility that diseases would become resistant (lawal et al., 2025). The antifungal effectiveness

87 of plant extracts against a variety of phytopathogens has been shown in several research. For  
88 example, extracts from turmeric (*Curcuma longa*), ginger (*Zingiber officinale*), garlic (*Allium*  
89 *sativum*), and neem (*Azadirachta indica*) have exhibited potent inhibitory effects on soil-borne  
90 fungus (Ali et al., 2025; Kim et al., 2024; Cao et al., 2024; Kapooria, 2024). Usually, these extracts  
91 cause spore germination inhibition, membrane integrity degradation, and disruption of fungal cell  
92 wall formation, which results in pathogen death (Zhang et al., 2024). Compared to traditional  
93 chemical fungicides, plant extracts have a various numbers of advantages. First of all, they  
94 decompose quickly in the environment without leaving behind harmful residues because they are  
95 biodegradable (Akbar et al., 2024). Secondly, it is in general accepted that plant-based pesticides  
96 are safer for non-target microorganism, humans, and other animals. This safety profile is in line  
97 with customer desires for agricultural goods that are residue-free and organic. Thirdly, integrated  
98 pest management (IPM) techniques are very compatible with plant extracts. Their application can  
99 be integrated with biological, mechanical, and cultural control techniques to produce  
100 comprehensive and long-lasting disease management programs. Given these qualities, there is  
101 increasing hope regarding the potential of plant extracts to manage tobacco disease in the future,  
102 especially in the fight against soil-borne diseases like *F. oxysporum* and *P. nicotianae*.

103 The results of previous research showed that the application of plant extracts against Fusarium  
104 Wilt and Black Shank infections have been promising. Both in laboratory and greenhouse tests,  
105 for example, extracts from *Azadirachta indica*, *Ocimum sanctum*, *M. micrantha*, *Senna alata*,  
106 *Datura metel*, and *Allium sativum* have been found to considerably lesser disease incidence (Haile,  
107 2025; Rifnas, 2025). Plant extracts may be a useful part of integrated disease management,  
108 according to these studies. However, several knowledge gaps remain in spite of the encouraging  
109 results. The majority of research to date has been carried out in carefully regulated lab settings,

110 and field applications are still difficult to move to. The efficacy of plant extracts in field conditions  
111 can be strongly impacted by variables like pathogen variety, environmental variability, and host  
112 plant reactions.

113 Moreover, there is a pressing need to better understand the specific modes of action of plant-  
114 derived compounds against *P. nicotianae* and *F. oxysporum*. Although broad mechanisms like  
115 membrane disruption have been suggested, there aren't enough in-depth molecular research.  
116 Standardizing extraction techniques is another important challenge. Variability in efficacy is  
117 frequently caused by variations in the plant components utilized, solvent systems, extraction  
118 methods, and quantities of active ingredients (Sharma et al., 2025). The commercialization of bio  
119 pesticides based on plant extracts is hampered by this lack of standardization. Furthermore, not  
120 enough research has been done on the possible phytotoxic effects of certain plant extracts on  
121 tobacco plants. For plant extracts to be successfully embraced by farmers, it is imperative that they  
122 do not adversely affect plant growth or production. Lastly, to optimize the effectiveness of plant  
123 extracts in actual agricultural contexts, practical elements of field application, such as the creation  
124 of stable formulations, efficient delivery systems, and suitable treatment schedules, must be  
125 methodically addressed.

126 A thorough analysis of the body of research on the application of plant extracts to the control of  
127 Fusarium Wilt and Black Shank in tobacco is urgently needed in light of these factors. A review  
128 of this kind can synthesize existing knowledge, pinpoint important research gaps, and offer tactical  
129 guidance for upcoming studies. Hence, the goals of this review are to: (1) summarize the major  
130 findings about the use of plant extracts against Fusarium Wilt and Black Shank of tobacco, (2)  
131 examine the mechanisms of action behind the antifungal activities of plant extracts, (3) discuss  
132 about the difficulties and restrictions related to their practical application, and (4) determine the

133 future research directions required for the creation of efficient plant extract-based disease  
134 management strategies.. Through this comprehensive synthesis, we aim to contribute valuable  
135 insights into the promising but underutilized domain of plant-based disease management strategies  
136 for tobacco. By highlighting the potential and limitations of plant extracts, this review aspires to  
137 support the broader goal of promoting sustainable agricultural practices that are both  
138 environmentally sound and economically viable.

139 **2. Major Diseases of Tobacco: Black Shank and Fusarium Wilt**

140 **2.1 Black Shank (Caused by *Phytophthora nicotianae*)**

141 **Black Shank of Tobacco**

142 One of the most significant and dangerous diseases affecting tobacco (*Nicotiana tabacum* L.)  
143 plants is black shank (Pandey, 2023). It is brought on by the fungus *Phytophthora parasitica* var.  
144 Nicotianae, which is found in most areas where tobacco is grown (Zhang et al., 2024; Zhang et al.,  
145 2003). *P. nicotianae* belongs to the Kingdom Chromista, phylum Oomycota, class Oomycetes, and  
146 order Peronosporales. Ten different clades were found within the genus *Phytophthora* in recent  
147 studies that used genetic markers like beta-tubulin, elongation factor 1 alpha, enolase, heat shock  
148 protein 90, 60S ribosomal protein L10, 28S ribosomal DNA, and tigA (Yan et al., 2024). The white  
149 hyphae (filaments) of *P. nicotianae* are branched and range in diameter from 3 to 11 micrometers  
150 (Pandey, 2023). The hyphae may appear fluffier and turn pale yellow as they mature. Although  
151 the hyphae lack septa, or partitions, older cultures may produce pseudosepta, or seeming partitions.  
152 As they age, the hyphae develop oil globules and turn granular (Gupta & Chugh, 2022). The  
153 sporangia (structures that produce spores) of this fungus are oval, lemon-shaped, pear-shaped,  
154 sympodial (occurring in pairs), and span between 18 and 61 by 14 and 39 micrometers. Sporangia

155 are pale yellow to transparent and develop from the hyphae on short pedicels (Mondal et al., 2020).  
156 With an apical papilla, these sporangia can generate five to thirty zoospores, which are tiny, mobile  
157 spores that range in size from seven to eleven micrometers (Delmas et al., 2014). There are several  
158 varieties of spores seen in *P. nicotianae*. The concave side of biflagellate zoospores has flagella  
159 attached to it (Kasteel et al., 2023). Typically measuring 30  $\mu\text{m}$  in diameter and ranging from 14  
160 to 43  $\mu\text{m}$  in length, chlamydospores are spherical or ovoid in shape and non-papillate (Scanu et  
161 al., 2021). At first, they have thin walls and are hyaline, but as they become older, they thicken  
162 and change from yellow to brown. Perpendicular to the vegetative hyphae, chlamydospores  
163 develop on short lateral hyphae. Oospores, which are spherical to pyriform and hyaline to pale  
164 yellow in appearance, have been observed in laboratory settings but do not have a strong  
165 environmental record (Nam et al., 2022). The structures that surround the oosphere are called  
166 oogonia, and they are hyaline to pale yellow in color. The developing oospore, which is normally  
167 23–30  $\mu\text{m}$  in diameter, is the result of fertilization (Tsai & Thines, 2025).

168 One type of plant pathogen that is frequently seen in tropical and subtropical areas with high  
169 humidity and warm temperatures is *P. nicotianae* (Bahadur & Dutta, 2023). Temperatures  
170 between 28 and 32°C and pH values between 5.7 and 7.0 are usually ideal for their growth. For  
171 optimal infection, they also need a temperature of at least 20°C (Pandey, 2023). When there is  
172 enough oxygen and water in the environment, sporangia can grow and form; the ideal temperature  
173 range is between 24 and 28°C. Within 48 hours of the mycelium developing, sporangia may  
174 emerge (Benigno et al., 2025). When sporangia germinate, they will create secondary sporangia  
175 at the same temperature. A tiny projection known as a papilla will allow kidney-shaped zoospores  
176 with two flagella to emerge from the sporangia (Crouch et al., 2022). Within 72 hours of landing  
177 on a host's tissue, these zoospores will swim in circles and germinate to generate new sporangia,

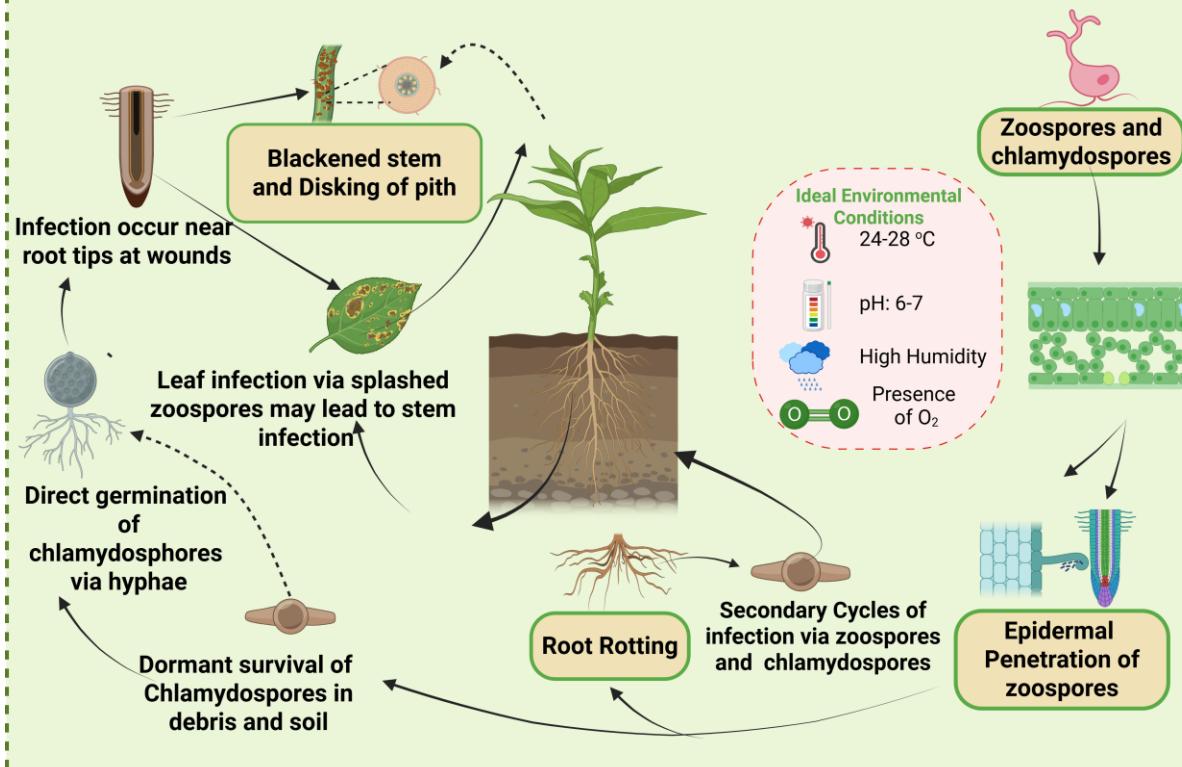
178 which will then produce another generation of zoospores (Moreira et al., 2023). Plant pathogen *P.*  
179 *nicotianae* is a polycyclic disease-causing agent that mostly targets the roots of its host plant but  
180 can also infect leaves and flowers (Volynchikova & Kim, 2022). Its classification as a  
181 hemibiotrophic pathogen indicates that, throughout its disease cycle, it undergoes both biotrophic  
182 (living off a host) and necrotrophic (producing death in the host) stages (Rajarammohan, 2021).  
183 The pathogen *P. nicotianae* first establishes a mutually advantageous association with its host. But  
184 after a while, it kills the host cells and goes into a phase when it feeds on the dead host tissue. The  
185 necrotrophic phase is the term for this stage (Singh et al., 2024). The amount of zoospores in soil  
186 is correlated with the severity of the infection, which occurs when asexually generated, multi-  
187 nucleated sporangia release zoospores, which are mobile and lack a cell wall (Del Castillo-  
188 González et al., 2024). The zoospores attract to certain compounds in the soil and go to the root  
189 tissue, where they develop into a cyst on the plant. The development of a germ tube, which  
190 ultimately becomes an appressorium, is crucial to the *P. nicotianae* disease cycle (Legrifi et al.,  
191 2023). The pathogen may penetrate and infect host cells thanks to these structures, which causes  
192 the host cells to die. Additionally, *P. nicotianae* can persist in the soil for long periods of time as  
193 chlamydospores, which can infect subsequent growth seasons (Bag et al., 2023). To try to stop this  
194 infection from spreading, management techniques frequently focus on the development of germ  
195 tubes (Delai et al., 2024).

196 *P. nicotianae* reproduces mostly asexually, while it can occasionally reproduce sexually by fusing  
197 male and female gametangia (Berbeć, 2024). Both A1 and A2 mating types must be present for  
198 sexual reproduction to produce thick-walled oospores (Babarinde et al., 2024). But the uneven  
199 distribution of these mating types in the environment raises the possibility that oospore production  
200 may not play a major role in the pathogen's life cycle and that worries about virulence and

201 pathogenicity changes brought on by sexual reproduction may be exaggerated (Meng et al., 2014).  
202 At any stage of growth, the virus can infect the tobacco plant's roots, stems, and leaves, among  
203 other areas. This may drastically lower the tobacco crop's output and quality (Sun et al., 2024).  
204 Tobacco plants may become stunted and fall before their leaves are developed enough to be  
205 harvested if they contract Black Shank disease early in the growing season (Bahadur & Dutta,  
206 2023). *P. nicotianae* can infect tobacco plants at any stage of growth, although it usually affects  
207 plants between 6 and 8 weeks of age (He et al., 2022). According to Tong et al. (2024), Within 48  
208 hours of the pathogen being introduced, black shank signs can be seen, and the plant may die  
209 within a week of infection. Its main symptoms include root and crown rot, consistent wilting, and  
210 chlorosis of the leaves, which result in water-soaked lesions on stem tissue that are 15 to 20  
211 centimeters above the soil line (Sapkota et al., 2022). Root necrosis may also be seen as the  
212 condition progresses (Zhou et al., 2023). The defining signs of black shank are brown to black  
213 vascular disking and pith necrosis (Cochran et al., 2024). On older foliage, a large, concentric,  
214 round, dark-brown lesion that is 7 to 8 cm in diameter may also develop as a result of the inoculum  
215 being dispersed by rain splash (Cochran et al., 2024). Since other tobacco diseases like Fusarium  
216 Wilt and Granville Wilt might exhibit similar symptoms, the macroscopic symptoms mentioned  
217 above should be utilized in concert with microscopic inspection and molecular characterisation to  
218 accurately detect *P. nicotianae* infection. Plant tissue exhibiting signs of illness, water, or soil can  
219 all harbor *P. nicotiana* as shown in **Figure 1**. *Ageratina adenophora*, *Ageratum houstonianum*,  
220 *Parthenium hysterophorus*, and *Xanthium strumarium*, these invasive species demonstrated  
221 antifungal activity against *Phytophthora capsici* (Han et al., 2024). While not specifically tested  
222 against *Phytophthora nicotianae*, their potential to inhibit *Phytophthora* species suggests they could  
223 be further investigated for black shank management. The methanolic extracts of these plants

224 generally exhibit stronger inhibitory effects compared to aqueous extracts(Han et al., 2024),  
225 indicating that the active compounds are more soluble in organic solvents. *Ipomoea carnea*:  
226 Although tested against different fungal pathogens (*Fusarium solani*, *Alternaria*  
227 *solani*,and*Colletotrichum circinans*)(Tao et al., 2021), the antifungal properties of*Ipomoea*  
228 *carnea*suggest potential for broader applications, warranting further research against*P. nicotiana*e.  
229 *Parthenium hysterophorus*: Whole plant is used for organic and inorganic pollutant removal and  
230 Cr(VI) remediation(Zhu et al., 2024). *Prosopis juliflora*and*Leucaena leucocephala*: These  
231 invasive plants, commonly found in Egypt, have shown antifungal activity against*Fusarium*  
232 *solani*, *Alternaria solani*,and*Colletotrichum circinans*(Tao et al., 2021). Their water-based extracts  
233 exhibited antifungal properties, suggesting a readily accessible method for potential application.  
234 Further research is often needed to optimize their use in integrated disease management  
235 strategies(Naqvi et al., 2024) as shown in **Table 1**.

### Black shank (*Phytophthora nicotianae*) life cycle in tobacco



236

237 **Figure 1:** Life cycle and pathogenesis of *P. nicotianae* causing Black Shank disease in tobacco.

239 **Table1.** List of plant species used against Black Shank of Tobacco

S. No	Plant	Active ingredients	Mechanism	Reference
1	<i>Sophora flavescens</i>	Matrine and oxymatrine	Part of a mixed plant extract that, combined with fungicides, successfully controlled black shank in greenhouse experiments.	Alsarhan et al. (2014)
2	<i>Forsythia suspense</i>	forsythiaside A, arctigenin	Part of a mixed plant extract that, combined with fungicides, successfully controlled black shank in greenhouse experiments.	Alsarhan et al. (2014)
3	<i>Nicotiana plumbaginifolia</i>	Nicotine	Contains the <i>NpPP2-B10</i> gene, which, when transferred to <i>Nicotiana tabacum</i> , promotes resistance to <i>P. nicotianae</i> .	Deaton et al. (1982)
4	<i>Tagetes erecta L.</i> )	lutein, $\beta$ -carotene	Rotation with marigold reduces disease incidence in continuously cropped tobacco fields, influencing soil microbial communities.	Boro et al. (2024)
5	<i>Sophora flavescens, Forsythia suspense,</i>	Oxymatrine, sophocarpine	Induces PR proteins (PR-1, PR-4, and PR-5) in tobacco plants, enhancing resistance against black shank and tobacco. The extract, alone or combined with fungicides, shows successful disease control in both non-continuously and continuously cropped land.	Wang et al. (2018)
6	<i>Syringa oblata</i>	syringic acid, caffeic acid derivative	Inhibits mycelial growth of <i>P. nicotianae</i> in a dose-dependent manner, disrupting extracellular pH and electrolyte leakage. Minimum inhibitory concentration (MIC) of eugenol is 200 $\mu$ g/mL.	Zhu et al. (2024)

7	<i>Zanthoxylum bungeanum</i> Maxim.	berberine, chelerythrine	Increases soil organic matter, hydrolysable nitrogen, available potassium, and total phosphorus while decreasing pH, promoting plant growth (increased plant height, root length, and dry weight. Acts as a bio-fumigation material against tobacco black shank.	Dhuldhaj et al. (2023)
8	<i>Azadirachta indica</i>	azadirachtin, nimbin, nimbiden	Disrupts fungal membrane integrity; inhibits mycelial growth and spore germination.	Mahmoud et al. (2011)
9	<i>Allium sativum</i>	Allicin	Increases mycelial membrane permeability; causes cell death in <i>P. nicotianae</i>	Wang et al. (2019)
10	<i>Syzygium aromaticum</i>	Eugenol, $\beta$ -Caryophyllene	Damages mycelial membranes, inhibiting growth & spore germination	Jing et al. (2017)

241 **2.2 Fusarium Wilt (Caused by *Fusarium oxysporum* f. sp.*nicotianae*)**

242 In many countries throughout the world, Fusarium wilt, a disease brought on by the *F. oxysporum*  
243 species complex, causes significant damages (Engalycheva et al., 2024). In 1916, Maryland had  
244 the first documented incidence of the disease in the United States. In the states of Connecticut and  
245 Massachusetts, it had developed into the most serious and destructive disease affecting broadleaf  
246 cigar wrapper tobacco by the 1980s and early 1990s (Pandey, 2023). About 20% of the tobacco  
247 producing areas were affected by the disease, which caused significant damage and led to the  
248 removal of badly infected fields from tobacco production (Liang et al., 2024). The three species of  
249 *F. oxysporum* f. sp. *nicotianae*, f. sp. *batatas*, and f. sp. *vasinfectum* are the fungus that causes wilt  
250 in tobacco plants (Berruezo et al., 2021). These species were distinguished by their effects on  
251 cotton, sweet potatoes, and tobacco, among other hosts. It was discovered that four races of the  
252 fungus *F. oxysporum* were harmful to tobacco (Berruezo et al., 2018). According to recent studies  
253 using cluster analysis, the pathogen consists of at least three different isolate groups, which may  
254 show distinct lineages from tobacco and sweet potatoes (Paul et al., 2020). All isolates that were  
255 initially discovered in tobacco are included in one of these clusters, *F. oxysporum* f. sp. *Nicotianae*  
256 (Rahman et al., 2021). Sweet potato isolates from North Carolina and Louisiana (Race 0) or  
257 California (Race 1) make up the second and third clusters of *F. oxysporum* f. sp. *batatas*. No  
258 disease was caused by Race 0 of *F. oxysporum* f. sp. *batatas* in flue-cured tobacco or resistant  
259 sweet potatoes, however Race 1 caused wilt in resistant sweet potatoes but had no effect on  
260 tobacco. This shows the variability of the tobacco wilt pathogen. The symptoms of Fusarium wilt  
261 in tobacco plants include leaf yellowing, drying, and death. These symptoms can occur in a vertical  
262 pattern, usually on one side of the plant or the mid vein of the leaf (Wang et al., 2022). The vascular  
263 tissue of the plant becomes characteristically chocolate-brown discolored due to the disease, and

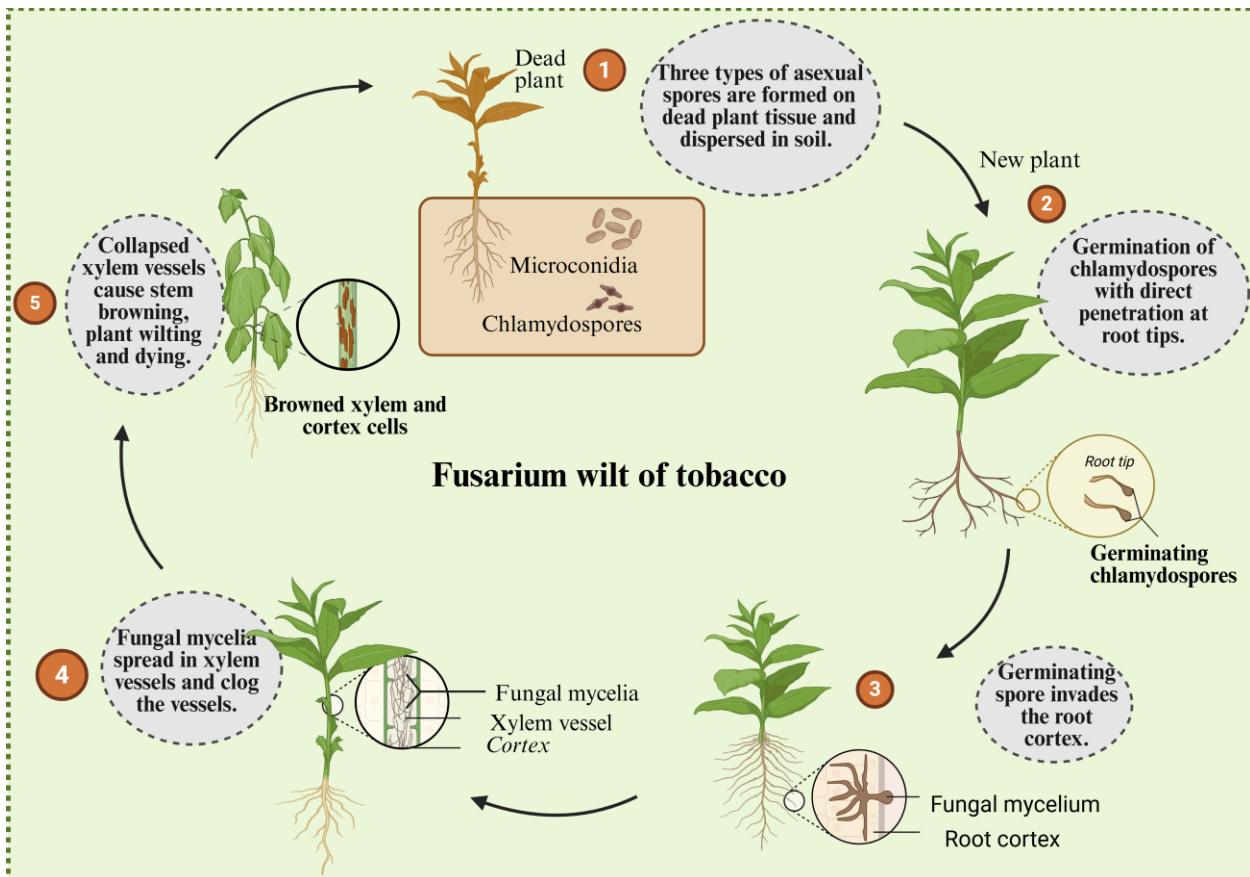
264 this discoloration may extend to the top of the plant (Dell'Olmo et al., 2023). The outside of the  
265 green stem gradually shows similar darkening. The leaves will curl on the stalk rather than rot,  
266 which will cause the stalk to bend over at the bud and give it a characteristic "crookneck" look  
267 (Pandey, 2023). The plant will eventually become dry and necrotic as a whole. Sandy loam soils  
268 and warm weather increase the disease's severity (Abbas et al., 2022). Plant resistance, cleanliness,  
269 crop rotation, nutrition, nematode control, and fumigation or bio fumigation are some of the  
270 strategies used to prevent Fusarium wilt in tobacco. But not all approaches work the same way  
271 (Haruna et al., 2024). According to El-Aswad et al. (2023), recently there are no chemical  
272 management for *F. oxysporum*. f. sp. *nicotianae* in soil that are completely effective. The quality  
273 and look of wrapper leaves are negatively impacted by the phase-out of the most effective  
274 fumigants, methyl bromide and chloropicrin (Villarino et al., 2021), but fumigation of soil may  
275 result in a little decrease in the severity of disease. Moreover, fumigation with metam sodium does  
276 not reduce cotton wilt induced by soil borne Fusarium or *F. oxysporum* f. sp. *Vasinflectum*  
277 (McDonald et al., 2021). In the crop residue Chlamydospores may also resistant to fumigation. In  
278 Connecticut, fumigation has produced mixed outcomes, especially when tobacco is planted in the  
279 same area over time. However, it may indirectly limit disease manifestation by affecting plant  
280 parasitic nematodes. The recent study by (Lal et al., 2024), The development and broad use of  
281 tobacco cultivars resistant to Fusarium wilt has shown to be the most effective strategy for  
282 managing the disease on a global scale. The broadleaf cigar wrapper varieties including 'B2' and  
283 'C9' resistant to Fusarium wilt pathogen were introduced in Connecticut (LaMondia, 2013). This  
284 resistance is caused by several genes building up for increased effectiveness (Sadeghpour et al.,  
285 2024). These resistant cultivars may still exhibit wilt signs in severe environments since they are  
286 not totally immune to Fusarium infection (Lal et al., 2024). Broadleaf tobacco resistant to wilt has

287 often been found to contain *F. oxysporum*, and this resistance has been found to be associated with  
288 the pathogen's slower migration inside the plant's vascular tissues. Moreover, within 24 hours of  
289 inoculation, resistant plants exhibited rapid reactions, such as the development of vesicles to block  
290 xylem, the deposition of callose, and the production of lipoidal material (Chen et al., 2024;  
291 LaMondia, 2013). Chlamydospores spread through soil on agricultural equipment that moves  
292 between fields, and the habit of utilizing tobacco stalks for fertilizer and rubbish disposal are two  
293 of the many factors contributing to the pathogen's rapid spread. Studies have revealed that *F.*  
294 *oxysporum* is resistant to composting, in contrast to many other plant diseases (Bouchtaoui et al.,  
295 2024). These days, tobacco stalks are either buried or dispersed in non-tobacco areas rather than  
296 remaining on tobacco fields. By implementing sanitation procedures, such as removing soil clumps  
297 from field equipment before moving it to another field, the wilt pathogen and other soil-borne  
298 illnesses, like tobacco cyst nematodes, can be prevented throughout their spread as shown in  
299 **Figure 2.** Despite these precautions, *F. oxysporum* continues to spread between farms more rapidly  
300 and extensively than expected (Ismaila et al., 2023); (Wichuk et al., 2011). Wounding roots  
301 through close cultivation, hoeing, or drip tape irrigation creates holes for infection and increases  
302 Fusarium wilt (Bhumarkar et al., 2021). Reducing injury lowers the incidence and severity of wilt.  
303 Beyond merely generating new infection sites from wounds, tobacco cyst nematodes (*Globodera*  
304 *tabacum*) and root knot worms (*Meloidogyne* spp.) also create Fusarium wilt (Khan & Sharma,  
305 2020). Prior to fungal exposure, plants with nematode infestations showed higher rates and severity  
306 of wilt than those exposed concurrently. It was discovered that an infestation of *G. tabacum* caused  
307 more wilt than an equivalent amount of *Meloidogyne hapla*. In field tests, early season nematode  
308 control reduced the frequency and intensity of Fusarium wilt in tobacco (Makunde et al., 2023).  
309 By modifying the pH and nitrogen levels of the soil, several Fusarium wilt infections have

310 successfully managed (Habte & Dobo, 2025). The incidence and severity of the diseases in  
311 tomatoes and chrysanthemums have been related to factors such soil pH, lime, calcium, and  
312 nitrogen sources (Valenzuela, 2024). Calcium was the most successful nutritional component  
313 studied for controlling Fusarium wilt in tobacco, according to (Okiro et al., 2025). Since calcium  
314 controls the synthesis of callose, a plant defense mechanism against vascular wilt pathogens, its  
315 deficiency has been connected to the onset of the diseases. Calcium is thought to be the most easily  
316 manipulated nutrient in Connecticut broadleaf tobacco cultivation (Daunoras et al., 2024)  
317 (LaMondia, 2015). Although fusarium wilt can develop in soil with varying pH values, the illness  
318 may be affected if the pH is raised to above 6.4. However, soils with a pH of 5.6 to 6.0 might  
319 develop severe black root rot (Šišić et al., 2025). Although Fusarium wilt in susceptible broadleaf  
320 tobacco can be suppressed by applying substantial amounts of gypsum to the soil, this effect was  
321 minimal at low disease incidence levels. The 13,400 kg/ha of gypsum needed to minimize wilt is  
322 far more than tobacco growers typically use (340–560 kg/ha), and it may have detrimental  
323 agronomic impacts like slower crop growth (LaMondia, 2015). Without a vulnerable host, the  
324 fungus in a field lasts for several years. Based on the chlamydospores' survival, crop rotation's  
325 ability to reduce the density of Fusarium wilt pathogens in the soil varies widely (Garzón-Nivia et  
326 al., 2025; Obiazikwor et al., 2025) and the pathogen's capacity to infect other plant species that are  
327 not impacted as well as the roots of resistant crops (Nowicki et al., 2025). It is necessary to assess  
328 how resistant plants and rotation crops affect the soil's pathogen populations over time for each  
329 unique pathosystem and crop..

330 Recent studies as shown in **Table 2**, have demonstrated the efficacy of various plant extracts in  
331 controlling *Fusarium* wilt pathogens across different crops. *Datura metel* leaf extract completely  
332 inhibited mycelial growth of *F. oxysporum* f. sp. *cubense* in banana at 10% concentration (Hassan

333 et al., 2022). For tomato pathogens, *Aloe vera* extracts significantly inhibited growth and  
334 sporulation of *F. oxysporum* f. sp. *Lycopersici* (FOL) under both laboratory and greenhouse  
335 conditions (Al-Gallas et al., 2021), while clove (*Syzygium aromaticum*) essential oils reduced  
336 fungal growth and spore populations (He et al., 2021). Extracts from *Eucalyptus camaldulensis*,  
337 *Chromolaena odorata*, *Bidens pilosa*, and *Wedelia trilobata* also showed effective control of *F.*  
338 *oxysporum* in tomatoes (Al-Gallas et al., 2021). In chickpea, neem (*Azadirachta indica*)  
339 suppressed *F. oxysporum* f. sp. *ciceri* activity *in vitro* (Meena et al., 2021), and garlic (*Allium*  
340 *sativum*) induced physiological and biochemical defenses against *Fusarium* wilt in both chickpea  
341 and tomato (Selva Amala et al., 2024). Other effective botanicals included resins  
342 from *Commiphora swynnertonii* and latex from *Synadenium glaucescens* against tomato wilt  
343 (Fenollosa & Munné-Bosch, 2020), as well as *Monsonia burkeana* and *Moringa oleifera* extracts  
344 (Jamil et al., 2021). *Xanthium strumarium* demonstrated efficacy against *F. oxysporum* in  
345 pomegranate (Powell et al., 2024), while combined neem and willow (*Salix babylonica*) extracts  
346 reduced tomato wilt severity by inducing antioxidant enzymes (Farag Hanaa et al., 2011). These  
347 findings highlight the potential of plant-derived solutions for integrated *Fusarium* wilt  
348 management.



350 **Figure 2:** Disease cycle and pathogenesis of *Fusarium* wilt in tobacco.

**Table 2:** Antifungal effects of plant extracts against *Fusarium oxysporum* pathogens in different crops.

Plant Extract Source	Target Crop	Pathogen	Observed Effect	References
<i>Datura metel</i> (leaf extract)	Banana	<i>F. oxysporum</i> f. sp. <i>cubense</i>	Complete inhibition of mycelial growth at 10% concentration.	Hassan et al. (2022)
<i>Aloe vera</i>	Tomato	<i>F. oxysporum</i> f.sp. <i>lycopersici</i>	Inhibited growth and sporulation of FOL under laboratory and greenhouse conditions.	Al-Gallas et al. (2021)
<i>Syzygium aromaticum</i> )	Tomato	<i>F. oxysporum</i> f.sp. <i>lycopersici</i>	Essential oils from clove also significantly reduced growth and spore population	He et al. (2021)
<i>Eucalyptus camaldulensis, Chromolaena odorata, Bidens pilosa, Wedelia trilobata</i>	Tomato	<i>F. oxysporum</i>	Effective control of <i>F. oxysporum</i> in vitro and in tomatoes.	Al-Gallas et al. (2021)
<i>Azadirachta indica</i> (Neem)	Chickpea	<i>F. oxysporum</i> f. sp. <i>ciceri</i>	Suppressed activity of <i>F. oxysporum</i> f. sp. <i>ciceri</i> under in-vitro conditions.	(Meena et al. (2021)
<i>Allium sativum</i>	Chickpea, Tomato	<i>F. oxysporum</i> f. sp. <i>ciceri</i> , <i>F. oxysporum</i> f. sp. <i>lycopersici</i>	Used as inducers on physiological and biochemical activities in tomato against <i>Fusarium</i> wilt.	Selva Amala et al. (2024)

<i>Commiphora swynnertonii</i> (resins), <i>Syn adenium glaucescens</i> (	Tomato	<i>F. oxysporum</i> f. sp. <i>Lycopersici</i>	Extracts were effective against <i>F. oxysporum</i> f. sp. <i>Lycopersici</i>	Fenollosa & Munné-Bosch (2020)
<i>Monsonia burkeana</i> , <i>Moringa oleifera</i>	Tomato	<i>F. oxysporum</i> sp. <i>Lycopersici</i>	f. Extracts were effective against <i>F. oxysporum</i> f. sp. <i>Lycopersici</i>	Jamil et al. (2021)
<i>Xanthium strumarium</i>	Pomegranate	<i>F. oxysporum</i>	Effective against pomegranate isolated pathogenic fungi.	Powell et al. (2024)
<i>Neem</i> ( <i>Azadirachta indica</i> ) and <i>willow</i> ( <i>Salix babylonica</i> )	Tomato	<i>F. oxysporum</i>	Reduced Fusarium wilt disease in tomato seedlings, induced antioxidant defensive enzymes.	Farag Hanaa et al. (2011)

354 **3. Current Management Strategies**

355 Current tobacco management of Fusarium Wilt and Black Shank depends on an integrated strategy  
356 that combines biological, cultural, and chemical control techniques. Still, each approach has  
357 important drawbacks that jeopardize sustainability and long-term effectiveness. According to  
358 Sapkota et al. (2023), fungicides continue to be the main line of defense against these debilitating  
359 diseases. Metalaxyl and fosetyl-Al are frequently applied to manage Black Shank, while  
360 benzimidazoles (like carbendazim) and triazoles (like tebuconazole) are used to manage Fusarium  
361 Wilt. But there are concerning trends in resistance as a result of the overuse of these fungicides.  
362 More than 60% of *P. nicotianae* populations in important tobacco-growing regions are resistant to  
363 metalaxyl, according to recent surveys, making the fungicide useless in many places (Clement et  
364 al., 2025; Van Jaarsveld et al., 2002). Also, benzimidazole resistance has grown widely in *F.*  
365 *oxysporum* f. sp. *nicotianae*, with resistance frequencies above 80% reported in China and Brazil  
366 (El-Nagar et al., 2023). In addition to their resistance, chemical fungicides can contaminate soil  
367 and water, harm beneficial microorganisms without their intended target, and threaten the health  
368 of farmers. The EU's prohibition on methyl bromide and impending limitations on phosphonates  
369 are just two examples of how regulatory bodies are regulating synthetic fungicides more and more,  
370 which further reduces the range of alternatives (Nader et al., 2020). Crop rotation and resistant  
371 cultivars are examples of cultural methods that provide some partial solutions but are difficult to  
372 apply. Although switching tobacco to non-host crops (such maize or sorghum) can decrease the  
373 pathogen burden, this strategy is compromised by the long-term survival of *F. oxysporum*  
374 chlamydospores (decades) and *P. nicotianae* (up to 5 years in soil) (Ristaino et al., 2021). Although  
375 resistant tobacco cultivars have been developed (such as Black Shank's "K 326"), resistance  
376 frequently breaks off in 5–10 years due to pathogen adaptation (McCorkle et al., 2018). According

377 to Mavroeidis et al. (2024), resistant cultivars may degrade leaf quality, which is essential for  
378 commercial viability. *Trichoderma harzianum* and *Pseudomonas fluorescens* are biological agents  
379 showed promising results in laboratory condition but they exhibit different results in field, this is  
380 due to environmental sensitivity and competition with native microbiota (Ayaz et al., 2023).  
381 Although *Trichoderma spp.* can lower the incidence of Black Shank by 30 to 50% in greenhouse  
382 experiments, their effectiveness is greatly diminished in field condition with varying moisture and  
383 temperature (Naorem et al., 2023). Similarly, efficacy rates for Bacillus-based bio fungicides vary  
384 from 20% to 70% depending on the location, and they frequently fall short of commercial-scale  
385 consistency (Barros-Rodríguez et al., 2024).

386 **3.1 Plant Extracts as Sustainable Alternatives: A Path toward Eco-Friendly Disease  
387 Management**

388 Research on plant-derived antimicrobials as sustainable substitutes for traditional disease  
389 management techniques has increased due to the rising limitations of these methods for preventing  
390 *Fusarium* Wilt and Black Shank in tobacco (Deressa & Diriba, 2023). Plant extracts contain  
391 complex combinations of bioactive compounds that attack pathogens through several processes  
392 concurrently, greatly minimizing the possibility of resistance development, in contrast to  
393 manufactured fungicides that target single metabolic pathways (Ayaz et al., 2019). Alkaloids,  
394 flavonoids, terpenoids, and phenolic compounds are among the hundreds of secondary metabolites  
395 that have been discovered by recent developments in phytochemical research to have strong  
396 antifungal effects against both *Fusarium oxysporum* and *Phytophthora nicotianae* (Deressa &  
397 Diriba, 2023). For example, *P. nicotianae* zoospores' cell membrane viability is damaged by  
398 curcumin from turmeric (*Curcuma longa*), which also prevents mycelial growth by interfering  
399 with mitochondrial activity (Wang et al., 2019). Plant extracts' mechanisms of action go beyond

simply suppressing pathogens; they can also cause tobacco plants to develop systemic resistance (Yang et al., 2024). Plants are primed for improved immune responses by compounds like thymol from thyme (*Thymus vulgaris*) and allicin from garlic (*Allium sativum*), which have been demonstrated to activate the salicylic acid defense system and upregulate pathogenesis-related (PR) proteins (Anisimova et al., 2021). Because plant extracts have both direct antibacterial activity and host defense potentiation, they are very useful for integrated disease management. Field experiments in China's main tobacco-growing regions showed that neem (*A. indica*) kernel extract and chitosan together decreased the incidence of Black Shank by 68–72%, which is similar to synthetic fungicides but without the hazards of resistance (Ibrahim et al., 2023). Plant extract formulations have historically presented difficulties that are being addressed by recent technological advancements. Utilizing biodegradable carriers like as lignin and chitosan, nanoencapsulation strategies have greatly increased the stability and bioavailability of volatile chemicals (Deng et al., 2023). Oregano (*Origanum vulgare*) essential oil Nano emulsions, for example, retained 85% antifungal activity after 30 days of field exposure, but unformulated oil only exhibited 35% (Hosny et al., 2021). Additionally, developments in extraction methods, including supercritical fluid extraction and ultrasound-assisted extraction, have reduced processing time and energy usage while increasing active compounds yields (Khadhraoui et al., 2021).

Plant-based disease management has significant positive effects on the environment. According to life cycle assessments, botanical pesticides decompose entirely in soil in 2-4 weeks and have carbon footprints that are three to five times lower than those of synthetic counterparts (Yin et al., 2023; Ristaino et al., 2021). In response to the increased consumer demand for "clean label" products, this quick degradation removes residual problems in cured tobacco leaves. Most significantly, local production of plant extract formulations employing native species in tobacco-

423 growing countries can open up new business prospects for smallholder farmers (Ouma, 2024).  
424 Considering these benefits, there are still issues with obtaining regulatory permissions, maximizing  
425 application timing, and standardizing extract potency. Next-generation botanical fungicides are  
426 being developed more quickly, though, because to the fusion of traditional ethnobotanical  
427 knowledge with contemporary analytical methods (such as metabolomics and machine learning).  
428 Plant extracts have the potential to evolve from additional treatments to essential elements of  
429 sustainable tobacco production systems across the globe as resistance to traditional fungicides  
430 keeps growing and regulatory demands increase.

431 **3.2 Modes of action of plant extracts**

432 Plant extract or botanicals act against microorganisms are even less known. These mechanisms  
433 rely on the composition of botanicals, which is multifactor dependent (Radulovic et al., 2013). A  
434 few studies reveal that the major components are mainly responsible for the biological activity of  
435 botanicals, but others conclude that several components act in synergy (Amenu, 2014;  
436 Chaachouay, 2025). Furthermore, as botanicals contain a mixture of diverse components, their  
437 antifungal activity is probably not attributable to a single mechanism. The main mechanisms  
438 reported so far are membrane disruption, metal chelation, interaction with DNA, and induction of  
439 plant defense reactions (Redondo-Blanco et al., 2020). Several studies report that EO or some of  
440 their components are able to disrupt cell wall and membrane integrity and to easily penetrate into  
441 the cells (Yap al., 2021). This disruption causes mitochondrial membrane damage, which induces  
442 changes in the electron transport chain. Consequently, free radicals are produced, and they oxidize  
443 and damage lipids, proteins, and DNA. In contact with reactive oxygen species (ROS), EO  
444 phenolic compounds are oxidized and release reactive phenoxy radicals (Hajam et al., 2023). The  
445 induction of plant defenses by EO has also been investigated as shown in **Figure 3**. Thyme oil

446 application on tomato roots efficiently triggered peroxidase accumulation in roots, which are well-  
447 known to be part of the plant defense mechanisms (Saltos-Rezabala et al., 2022). Similarly, Farooq  
448 et al. (2024) found evidence of the induction of plant defense responses against *F. oxysporum* f.  
449 sp. *lycopersici* using different plant extracts. Although the antimicrobial mechanisms of action of  
450 botanicals have been carefully studied for their pharmaceutical or food preservative uses, less  
451 information is available concerning their use to control plant pathogenic microorganisms (Oulahal  
452 et al., 2012

### 453 **3.3 Molecular Modes of Action of Plant Extracts**

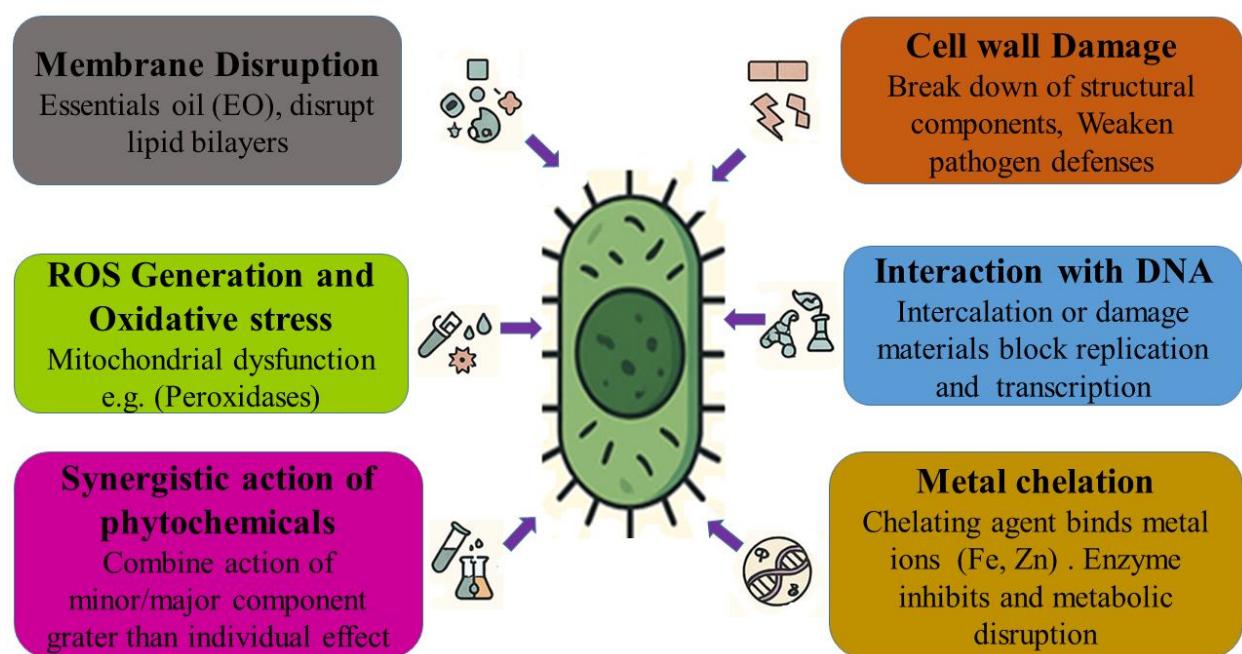
454 Plant extracts possess inherent complexity, making it difficult to attribute their bioactivity to a  
455 single mechanism; yet, growing evidence highlights both particular molecular targets and  
456 synergistic interactions among their phytochemical components. Principal molecules frequently  
457 dictate primary function; nevertheless, minor components can substantially enhance effectiveness  
458 through synergistic interactions (Amenu, 2014; Chaachouay, 2025). A fundamental antibacterial  
459 process involves the degradation of microbial cell membranes. Terpenoids, such as carvacrol (from  
460 oregano) and thymol (from thyme), integrate into lipid bilayers due to their lipophilic properties,  
461 causing destabilization of plasma membranes, ion leakage ( $K^+$ ,  $H^+$ ), ATP depletion, and ultimately  
462 cell lysis (Bakkali et al., 2008; Yap et al., 2021).

463 This membrane disruption frequently impacts organelles, particularly mitochondria, hence  
464 disrupting the electrochemical gradient and impairing the electron transport chain (ETC). The  
465 resultant surplus of reactive oxygen species (ROS), including superoxide anions ( $O_2^-$ ) and  
466 hydrogen peroxide ( $H_2O_2$ ), exceeds microbial antioxidant defenses such as catalase and  
467 glutathione, resulting in lipid peroxidation, protein carbonylation, and DNA strand breaks (Camele

468 et al., 2019). Phenolics exacerbate this stress by generating phenoxy radicals by microbial  
469 oxidation, hence perpetuating oxidative chain damage (Hajam et al., 2023).

470 Besides these broad harmful effects, plant metabolites significantly influence microbial  
471 physiology. Flavonoids and tannins chelate essential metals such as  $\text{Fe}^{2+}$  and  $\text{Zn}^{2+}$ , thereby  
472 inhibiting pathogens from acquiring crucial cofactors for their enzymes (Miklańska-Majdanik et  
473 al., 2018). Alkaloids, including berberine, directly intercalate with DNA, obstructing replication  
474 and transcription. Conversely, thiol-reactive compounds, such as allicin (derived from garlic),  
475 irreversibly inhibit cysteine-dependent enzymes. Plant extracts possess direct antibacterial  
476 properties and enhance the body's defenses against infections. For instance, the application of  
477 thyme oil to tomato roots induced systemic resistance by enhancing the expression of  
478 pathogenesis-related proteins (PRs) and activating critical defense enzymes such as peroxidase  
479 (POD) and phenylalanine ammonia-lyase (PAL), which promote phytoalexin biosynthesis (Saltos-  
480 Rezabala et al., 2022). Farooq et al. (2024) similarly demonstrated that plant extracts can prime  
481 defense mechanisms to combat *Fusarium oxysporum* f. sp. *lycopersici*. While several processes  
482 have been explored in food preservation, their implementation in agricultural disease management  
483 remains an insufficiently studied yet highly prospective research domain (Oulahal et al., 2012).

484



485

486 **Figure 3:** Mode of action of Plant extracts against pathogenic microorganisms

487 **3.4 Recent research on plant extract interactions with pathogen resistance genes**

488 Recent research has improved our understanding of how plant extracts influence disease  
 489 resistance by interacting with microbial virulence factors and host defense pathways.  
 490 Xanthomonas species employ type III effectors (T3Es), including Xop proteins, to suppress host  
 491 immunity. Recent studies indicate that phytochemicals can modify these interactions, hence  
 492 diminishing pathogen pathogenicity (Medina et al., 2017). Plant extracts assist plants in managing  
 493 oxidative stress caused by heavy metals, so safeguarding them from environmental stressors and  
 494 enhancing their resilience (Mirkov et al., 2020). Pathogenic fungi face oxidative stress from plants  
 495 during infection and must maintain redox balance to develop disease, highlighting a critical  
 496 vulnerability that can be targeted by bioactive phytochemicals (Park & Son, 2024). Terpenoids,  
 497 the primary constituents of essential oils, alter the integrity of lipid bilayers, hence compromising  
 498 fungal and bacterial membranes (Konuk & Ergüden, 2020). Moreover, their efficacy can be

499 augmented by synergistic combinations, as demonstrated by the conjunction of oregano oil and  
500 blue light, which amplifies bactericidal activity against multidrug-resistant *Pseudomonas*  
501 *aeruginosa* by targeting both planktonic and biofilm cells (Lu et al., 2022). The antifungal  
502 effectiveness of terpenoids is markedly linked to phenolic –OH groups that induce membrane  
503 instability (Konuk & Ergüden, 2020).

504 Besides their antibacterial effects, plant metabolites also influence the host's stress response  
505 and the body's ability to combat infections. Thymol enhances the salt tolerance of Chinese cabbage  
506 seedlings by augmenting their antioxidant capacity, maintaining redox equilibrium (AsA/DHA  
507 and GSH/GSSG ratios), and activating crucial ROS-scavenging enzymes such as SOD, CAT,  
508 APX, and POD (Sun et al., 2024). This mechanism prevents oxidative damage and sustains  
509 seedling growth during salt stress. Extracts of *Borreria verticillata* and silver nanoparticles exhibit  
510 nematicidal properties against *Meloidogyne incognita* in tomatoes, presenting a sustainable  
511 alternative to chemical nematicides (Fabiyi & Olatunji, 2024). Hydrocarbons and plant-derived  
512 compounds are detrimental to membranes since they accumulate in lipid bilayers, disrupt normal  
513 cellular functions, and alter microbial food degradation processes (Sikkema et al., 1995). These  
514 findings jointly highlight that plant extracts function as both direct antimicrobials and modulators  
515 of pathogen resistance genes, host oxidative stress responses, and environmentally viable crop  
516 protection strategies. This expanding body of research indicates their potential utility in integrated  
517 disease management and sustainable agriculture.

518  
519 **4. Challenges and Future Perspectives**

520 **4.1 Limitations of Plant Extracts**

521 For the management of Black Shank and Fusarium Wilt diseases in tobacco, plant extracts have  
522 gained attention as environmentally friendly alternatives (X. ping Sun et al., 2025). However, a  
523 number of restrictions hindered them from being used in practice. The chemical composition of  
524 plant extracts varies greatly depending on the plant species, growth conditions, harvesting time,  
525 and extraction techniques, making this one of the main problems (Raudone & Savickiene, 2024).  
526 Because of this inconsistency, antifungal efficacy is frequently unpredictable, which makes it  
527 challenging to standardize therapies for trustworthy disease management (Tang et al., 2012).  
528 Furthermore, many plant extracts have comparatively weaker direct toxicity against soil-borne  
529 infections such as *Fusarium oxysporum* and *Phytophthora nicotianae* than synthetic fungicides,  
530 which can limits their efficacy, particularly when disease pressure is high (Mirmajlessi et al.,  
531 2024). Since variables like pH, moisture, microbial community dynamics, and organic matter  
532 content can change the stability, bioavailability, and activity of bioactive chemicals in plant  
533 extracts, the intricate interactions within the soil environment also have an impact on their  
534 performance (Adeniji et al., 2024). The sustainable sourcing of raw plant materials, preserving the  
535 stability and shelf-life of extracts, and creating affordable formulations appropriate for large-scale  
536 agricultural use are additional logistical and financial challenges associated with scaling up the  
537 production of plant extracts (Lisboa et al., 2024). Considering their typically good safety profiles,  
538 careful assessment of any non-target and environmental consequences is necessary to guarantee  
539 sustainable use (Punniyakotti et al., 2024). These problems showed the need for more study to  
540 improve formulation stability, refine extraction methods, comprehend soil-plant-pathogen  
541 interactions, and successfully incorporate plant extracts into all-encompassing tobacco cultivation  
542 disease management programs.

543

544 **4.2 Emerging Technologies to Enhance Efficacy**

545 The effectiveness of plant extracts in controlling Fusarium Wilt and Black Shank infections in  
546 tobacco is being quickly improved by emerging technologies, which is viable, eco-friendly  
547 substitutes for traditional agrochemicals (Ahmad et al., 2024). According to Dewi et al. (2022),  
548 nanotechnology is essential because it enhances the stability, transport, and bioavailability of plant  
549 extracts. Polymeric nanoparticles, particularly those based on chitosan, are useful for the targeted  
550 use and regulated release of bioactive substances, which improves systemic plant resistance and  
551 antifungal activity (Zhou et al., 2024). In addition to directly inhibiting pathogens like  
552 *Phytophthora nicotianae* and *Fusarium oxysporum*, metal and metal oxide nanoparticles, like  
553 copper oxide (CuO) and silver nanoparticles, have built-in antimicrobial qualities that trigger plant  
554 defense mechanisms by producing reactive oxygen species (ROS) and activating antioxidant  
555 enzymes (Chen et al., 2022). Sensitive bioactive chemicals are kept safe from environmental  
556 stresses by nanoencapsulation and microencapsulation procedures, which enhance their functional  
557 stability and regulated release in the field (Guía-García et al., 2022). By changing plant immune  
558 signaling pathways (salicylic acid, ethylene, and hypersensitive response) and reshaping the  
559 rhizosphere microbial community to suppress pathogen abundance, synergistic strategies that  
560 combine plant extracts, nanocarriers, and beneficial microbes such as the co-application of  
561 chitooligosaccharides with *Bacillus* strains have shown increased control efficacy. By providing  
562 antioxidants and strengthening plant structural defenses at the same time, advanced formulations  
563 such as silicon-stabilized hybrid lipid nanoparticles functionalized with quercetin act as  
564 nanobiostimulants that increase plant resistance (Gutsch et al., 2023). Early disease detection and  
565 the timing and dosage of plant extract applications are optimized by precision agriculture  
566 technologies that use UAV-borne hyperspectral remote sensing and machine learning algorithms,

567 maximizing their efficacy while minimizing inputs (Padhiary et al., 2024). By improving the  
568 stability, bioavailability, targeted distribution, and effectiveness of plant extracts, decreasing  
569 reliance on chemical fungicides, and advancing environmental health, these integrated  
570 technologies work together to enhance sustainable tobacco disease control (Ashraf et al., 2021).  
571 By improving efficacy through regulated and sustained release mechanisms, emerging  
572 technologies such as nano-encapsulation are transforming drug delivery systems (Ayyaril et al.,  
573 2023). In order to prevent premature drug degradation and guarantee targeted administration,  
574 active pharmacological ingredients are encapsulated into nanoscale carriers such liposomes,  
575 polymeric nanoparticles, or dendrimers (Petrovic et al., 2024).

576 A promising strategy to improve sustainable agriculture and disease management is the coupling  
577 of nano-encapsulation with biocontrol agents, such as *Trichoderma* fungus and plant extracts  
578 (Saberi-Riseh et al., 2021). According to Zhou et al. (2024), nano-encapsulation can shield these  
579 delicate biological agents from environmental deterioration, guaranteeing their stability and long-  
580 term effectiveness. To maintain a steady inhibitory impact against infections, for example,  
581 *Trichoderma* spores or plant-derived bioactive chemicals can be encapsulated in polymeric  
582 nanoparticles or lipid-based carriers for gradual and regulated release (Zafar et al., 2024). In  
583 addition to increasing the biocontrol agents' field performance and shelf life, this synergistic  
584 strategy lessens the requirement for frequent applications (Teixidó et al., 2022). Furthermore, to  
585 maximize these compounds' antibacterial and growth-promoting properties, nano-formulations  
586 can improve their adherence and targeted distribution to plant roots or foliar surfaces (Mahmood  
587 et al., 2024). Farmers can minimize their reliance on chemical pesticides and achieve more  
588 efficient, environmentally friendly crop protection by combining nanotechnology with biocontrol  
589 techniques (Jaiswal et al., 2022).

590 A new method for improving the absorption and effectiveness of bioactive extracts used in  
591 pharmaceuticals and agriculture is the genetic engineering of tobacco plants (Padhiary et al., 2024).  
592 Researchers can maximize tobacco's capacity to absorb, produce, and store advantageous  
593 substances like antibacterial agents or growth-promoting phytochemicals by altering important  
594 genes involved in metabolic pathways (Sun et al., 2024). For example, the potency of the plant  
595 extract may be increased by overexpressing transporter proteins or enzymes that promote the  
596 accumulation of particular secondary metabolites (Shitan, 2016). Furthermore, CRISPR-Cas9  
597 gene editing may be used to inhibit opposing pathways, focusing greater resources on the synthesis  
598 of the targeted chemical (Jiang et al., 2021). These genetically modified tobacco extracts may  
599 allow for more effective and prolonged delivery of biocontrol chemicals when paired with nano-  
600 encapsulation, further enhancing crop protection and production (Chadha, 2020). There is a lot of  
601 potential for creating next-generation bio pesticides and plant-based medicines with this creative  
602 combination of genetic engineering and nanotechnology. We have compiled examples from  
603 contemporary literature about the nano-encapsulation of plant extracts for antifungal applications,  
604 highlighting nanocarrier type, particle size, loading/encapsulation efficiency, and asserted efficacy (Table  
605 3).

606

607 Table 3. A comparative investigation of nanocarriers utilized for the transport of plant extracts in  
608 relation to fungal diseases.

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Nano carrier type	Plant extract / compound	Particle size (nm)	Encapsulation / Loading efficiency (%)	Antifungal target / efficacy	Reference
Chitosan nanoparticles	Thyme essential oil	80–150 nm	65–85%	Suppressed growth of <i>F. oxysporum</i> and reduced mycelial biomass.	Salem et al., 2020
Liposomes	Clove oil	100–200 nm	70–90%	Enhanced stability, prolonged release, and robust activity against <i>Candida albicans</i> .	Fathi et al., 2021
Solid lipid nanoparticles (SLNs)	Curcumin extract	120–180 nm	75–92%	Inhibited the germination of <i>Aspergillus flavus</i> spores, hence reducing aflatoxin synthesis.	Ghosh et al., 2021
Polymeric nanoparticles (PLGA)	Garlic extract (allicin)	150–250 nm	60–80%	More efficacious against <i>Botrytis cinerea</i> than the free extract	Li et al., 2022
Nanoemulsions	Oregano essential oil	50–120 nm	80–95%	cts against <i>Alternaria alternata</i> and improves absorption and penetration throughout the body.	Ahmad et al., 2022
Silica nanoparticles	Eucalyptus oil	90–200 nm	70–85%	Reduced <i>Rhizoctonia solani</i> infection in tomato seedlings	Mahmoud et al., 2023
Zeolite-based carriers	Cinnamon oil	100–250 nm	65–78%	Prolonged release improved antifungal effectiveness against <i>Penicillium expansum</i> .	Hassan et al., 2023

610 **4.3 CRISPR-Cas9 applications in enhancing plant extract efficacy**

611 CRISPR-Cas9 is an excellent method for enhancing the efficacy of plant extracts through precise  
612 genomic modifications. It can enhance crops, increasing their resilience to stress and illnesses.  
613 (Gan & Ling, 2022). By targeting critical biosynthetic genes, it can enhance the production of  
614 secondary metabolites in medicinal plants. This is typically executed in conjunction with multi-  
615 omic approaches to achieve optimal quantity and quality of metabolites (Jeyaraj et al., 2024).  
616 CRISPR-Cas9 exhibits superior accuracy and efficiency compared to TALENs and ZFNs. This  
617 enables the enhancement of beneficial molecules while reducing undesirable metabolites (Angon  
618 and Habiba, 2022). Moreover, altering stress-response and immune genes improves plant  
619 resilience to biotic and abiotic stressors, ensures consistent extract production, and fosters  
620 sustainable agriculture (Bhattacharjee et al., 2022). Innovative delivery technologies, including  
621 virus-based systems and nanoparticles, facilitate the modification of plant genes to enhance their  
622 resistance to diseases (Gan & Ling, 2022; Zhou et al., 2023).

623 CRISPR-Cas9 possesses significant potential; yet, it is also associated with challenges like as off-  
624 target mutations, delivery obstacles, regulatory concerns, and ethical dilemmas (Mohamed et al.,  
625 2024). Researchers are developing methods to enhance the selectivity and efficiency of guide  
626 RNAs, ribonucleoprotein complexes, novel promoters, and transformation protocols [Bortesi &  
627 Fischer, 2015]. Research indicates that crops can endure higher salinity, modify their lignin and  
628 pectin synthesis, and enhance disease resistance (Ly et al., 2024). The integration of CRISPR-Cas9  
629 with sustainable methodologies presents a promising approach to enhance the efficacy of plant  
630 extracts, elevate crop quality, and bolster food security (Borrelli et al., 2018).

631

632

633 **4.3 Regulatory and Commercialization Hurdles**

634 Significant regulatory obstacles remain in the way of the commercialization of botanical  
635 pesticides, such as genetically modified plant extracts and nano-encapsulated biocontrol agents,  
636 especially the requirement for approvals from organizations like the Food and Drug  
637 Administration (FDA) and the U.S. Environmental Protection Agency (EPA) (Waidyanatha et al.,  
638 2024). These products must pass extensive safety, efficacy, and environmental impact evaluations  
639 because they are made from natural sources but may also contain innovative delivery systems or  
640 genetic alterations (Aware et al., 2022). Under the Federal Insecticide, Fungicide, and Rodenticide  
641 Act (FIFRA), the EPA controls pesticides and requires comprehensive information on toxicity,  
642 impacts on non-target organisms, and residual levels (Dietz-Pfeilstetter et al., 2021). In the  
643 meanwhile, the FDA may impose further measures to guarantee the safety of humans and animals  
644 if the product has pharmaceutical applications (Dietz-Pfeilstetter et al., 2021). Small and medium-  
645 sized businesses frequently face difficulties due to the drawn-out and expensive approval  
646 procedure. Furthermore, different international legislation and public opinion make market entry  
647 much more difficult. Stakeholders must make significant investments in preclinical and clinical  
648 research, interact with regulatory agencies early on, and guarantee open information regarding the  
649 dangers and advantages of the product in order to get beyond these obstacles. Adoption of creative,  
650 sustainable pest management techniques may be accelerated by streamlining these procedures  
651 through legislative lobbying and standardized international standards. Farmers' awareness and  
652 adoption of nano-encapsulated agrochemicals and biocontrol agents continue to be major obstacles  
653 to their widespread commercialization, despite the potential advantages of these products (Vishnu  
654 et al., 2024). Due to a lack of knowledge about these cutting-edge technology, many farmers  
655 especially those in developing nations are skeptical or reluctant to abandon traditional methods

656 (Kuhl, 2020). Misconceptions regarding safety, cost-effectiveness, and application techniques may  
657 also arise due to the intricacy of nanotechnology and genetically modified solutions (Saleh &  
658 Hassan, 2023).

659 Furthermore, small-scale farmers frequently have limited resources, which makes it challenging  
660 for them to invest in more expensive nano-formulated products in the absence of convincing proof  
661 of long-term advantages (Yadav et al., 2023). In order to overcome these obstacles, focused  
662 education and extension initiatives are required to highlight the benefits of slow-release nano-  
663 encapsulation, including decreased labor costs, increased crop yields, and less chemical usage.  
664 Governments, agribusinesses, and research organizations working together can help to further  
665 support adoption through pilot programs, farmer training, and subsidies. The full potential of these  
666 cutting-edge technologies may go untapped in actual agricultural systems in the absence of  
667 efficient outreach and financial incentives.

668 **5. Conclusion and Recommendations**

669 In tobacco, plant-derived extracts have shown great promise in the fight against soil-borne diseases  
670 such as *Fusarium oxysporum* (Fusarium wilt) and *Phytophthora nicotianae* (Black Shank),  
671 providing a sustainable substitute for synthetic fungicides. According to research, bioactive  
672 substances found in neem, garlic, turmeric, and other therapeutic plants have immune-stimulating  
673 and antifungal qualities that lower pathogen viability and increase plant resilience. Their broad  
674 usage is hampered by issues such uneven efficacy, deterioration in field settings, and low farmer  
675 uptake.

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679 **Recommendations for Improved Implementation:**

- 680 • To improve stability, gradual release, and targeted distribution, research should concentrate  
681 on standardizing plant extract quantities and creating formulations that are  
682 nanoencapsulated.
- 683 • Integration with Biocontrol Agents: Through synergistic effects, combining plant extracts  
684 with helpful microorganisms (*Trichoderma, pseudomonas*) may enhance disease  
685 suppression.
- 686 • Genetic enhancement of tobacco, CRISPR-based breeding, or transgenic methods may be  
687 investigated to create tobacco cultivars that demonstrate increased sensitivity to  
688 treatments with plant extracts.
- 689 • Support for Farmer Education and Policy, to boost adoption among smallholder farmers,  
690 governments and agricultural organizations should raise awareness through field  
691 experiments, subsidies, and training initiatives.
- 692 • Future research should focus on developing standardized extraction and preparation  
693 methods to ensure the consistency, reproducibility, and comparability of studies  
694 evaluating the efficacy of plant extracts.
- 695 • To guarantee adherence to organic agricultural laws, more research on residual effects  
696 and environmental safety is required.

697

698 **Credit authorship contribution statement**

699 **R A and J S:** Writing-original draft, Visualization, Validation, Software, Methodology,  
700 Investigation, Formal analysis, Data curation, Conceptualization. **BI and A. A. K:** Writing-review  
701 & editing, Supervision, Resources, Project administration, Methodology, Funding acquisition,  
702 Formal analysis, Conceptualization, Data curation. **S A and LL:** Writing review & editing, funding  
703 acquisition, Formal analysis, Conceptualization, Data curation. **S.M.K and IH** Writing-review &  
704 editing, Software, Methodology, Data curation, Formal analysis, Validation.

705 **Declaration of competing interest:**

706 The authors declare that they have no known competing financial interests or personal  
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708

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715 **Conflict of Interest**

716 The authors declare no conflicts of interest.

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720 **References**

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