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Review article

Advancements in the nanodelivery of azole-based fungicides to control oil palm pathogenic fungi

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ABSTRACT

The cultivation of oil palms is of great importance in the global agricultural industry due to its role as a primary source of vegetable oil with a wide range of applications. However, the sustainability of this industry is threatened by the presence of pathogenic fungi, particularly *Ganoderma* spp., which cause detrimental oil palm disease known as basal stem rot (BSR). This unfavorable condition eventually leads to significant productivity losses in the harvest, with reported yield reductions of 50–80 % in severely affected plantations. Azole-based fungicides offer potential solutions to control BSR, but their efficacy is hampered by limited solubility, penetration, distribution, and bioavailability. Recent advances in nanotechnology have paved the way for the development of nanosized delivery systems. These systems enable effective fungicide delivery to target pathogens and enhance the bioavailability of azole fungicides while minimising environmental and human health risks. In field trials, the application of azole-based nanofungicides resulted in up to 75 % reduction in disease incidence compared to conventional fungicide treatments. These innovations offer opportunities for the development of sustainable agricultural practices. This review highlights the importance of oil palm cultivation concerning the ongoing challenges posed by pathogenic fungi and examines the potential of azole-based fungicides for disease control. It also reviews recent advances in nanotechnology for fungicide delivery, explores the mechanisms behind these nanodelivery systems, and emphasises the opportunities and challenges associated with azole-based nanofungicides. Hence, this review provides valuable insights for future nanofungicide development in effective oil palm disease control.

1. Introduction

The oil palm is a tropical plant that contributes significantly to the global economic and agricultural sector by providing edible oils, fats, and a variety of essential byproducts. Palm oil currently leads the global vegetable oil market, accounting for around 35.7 % of

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total consumption, surpassing soybean, rapeseed, and sunflower oils [1]. Global palm oil consumption is projected to intensify, driven by increasing global demand for vegetable oils, particularly in the biofuel and food industries [2,3]. The largest share of palm oil production, around 83 %, comes from Malaysia and Indonesia, collectively earning approximately USD 29.17 billion and USD 29.66 billion in export revenue from palm oil and its related products [1,4]. However, the sustainability and productivity of this crop are under constant threat from a range of pathogenic fungi. Basal stem rot (BSR), attributed to *Ganoderma boninense*, represents a profoundly detrimental fungal disease in major oil palm-producing countries [5–7]. BSR has substantially reduced oil palm density per hectare and fresh fruit bunch productivity, resulting in significant yield losses of up to 80 % [6,8,9]. Consequently, BSR poses considerable economic challenges to oil palm cultivation, and the high persistent and widespread presence of *G. boninense* in the soil poses difficulties in effectively managing the disease.

Conventional control measures for pathogenic fungi rely heavily on the application of chemical fungicides. Among the fungicide classes, azole-based fungicides have been widely used for fungal infections in humans and plants since the 1970s [6,10]. They are prevalent in agriculture due to their broad-spectrum systemic mode of action, inexpensive and able to remain chemically stable, allowing them to endure in the environment for extended durations [10–12]. Azoles, specifically 14-demethylase inhibitors, have been shown to be effective against fungal diseases by inhibiting the ergosterol production pathway, which is a critical component of their cell membrane [13,14]. However, azole use in agriculture is highly debated due to concerns about endocrine disruption, environmental persistence, fungicide resistance, and potential health effects [15–17]. Furthermore, strict regulatory control has decreased the number of novel fungicides being discovered and registered, owing to the high cost and complexity of the procedure. As a result, these challenges have received increased worldwide attention, necessitating the development of alternative, efficient and sustainable control measures. In the wake of these challenges, the utilisation of nanotechnology has emerged as a viable and promising strategy for the effective delivery of agrochemicals, particularly azole-based fungicides.

Nanocarrier systems with unique properties and controllable size, offer a novel platform to enhance the efficacy and delivery of these fungicides. Through targeted delivery, increased penetration, and sustained release, nanodelivery not only addresses the shortcomings of conventional applications but also potentiates to mitigate fungal resistance development [17,18]. While significant progress has been made in exploring the potential uses of nanotechnology in agriculture over the past few decades, research on the role of nanocarriers in fungicide delivery remains limited. Besides, numerous challenges must be resolved in the near future before this technology can make meaningful contributions, notably in oil palm cultivation. Hence, it is crucial to continue research and development in this field in order to overcome the problems and turn nanotechnology into a sustainable and effective strategy. This aligns with the United Nations Sustainable Development Goals (UNSDGs), particularly Goal 2 (Zero Hunger) and Goal 12 (Responsible Consumption and Production). Additionally, nanotechnology in fungicide delivery supports Goal 3 (Good Health and Well-being) by reducing health risks associated with conventional fungicides and Goal 13 (Climate Action) by minimising environmental impact and promoting resilient agricultural systems. Herein, this review highlights advancements in the nanodelivery of azole-based fungicides and their sustainable application.

2. Oil Palm's Significance Amidst pathogenic fungal challenges

2.1. The importance of the oil palm industry

Elaeis guineensis is an oil palm variety indigenous to the West African tropical rainforests. It is distinguished by its monoecious nature, in which female and male reproductive organs coexist on the same tree. This leads to an allogamy or cross-pollination, where both genetic and external variables affect the "sex ratio" of the oil palm population [19,20]. The height of these palm trees can exceed 30 m, and they start bearing fruit bunches within three years after being planted. Their average lifespan is from 25 to 30 years, and each tree has the capacity to yield around 8 to 12 fruit bunches annually [21]. Palm oil is widely recognised as the oldest and most functional vegetable oilseed globally, primarily due to its remarkable potential for oil production. In comparison to other primary oilseed sources like sunflower, soybeans, and canola, a single hectare of oil palm plantation can yield oil quantities that are ten times higher [22,23]. This efficiency reduces the amount of land required to meet the oil demand. Besides, oil palm stands out in its dual oil production, which benefits various industries. Palm kernel oil is extracted from the seed or kernel, whilst palm oil is derived from the fruit's mesocarp or flesh, accounting for around 11 % and 89 % of the overall fruit oil production. Over three billion people consume palm oil daily, and it is a key ingredient in food preparation, particularly in Asia and Africa [23].

Projections from diverse industry reports indicate that the demand for palm oil could increase up to 156 million tonnes by the year 2050 [23,24]. The consistent rise in global demand has prompted numerous tropical countries to opt for oil palm cultivation as a means to bolster their economies [9,25]. Palm oil is currently grown predominantly in Asia, Africa and Latin America, with Malaysia and Indonesia having the highest certified area of planted oil palms by the Roundtable on Sustainable Palm Oil (RSPO) [26]. Notably, there was a significant increase in oil palm plantation expansion in this region from 2001 to 2016, with Malaysia and Indonesia experiencing 2.5-fold and 4.2-fold increases, respectively [27]. Furthermore, the oil palm industry is expanding in tropical Africa, with Côte d'Ivoire, Nigeria, Ghana, Cameroon, Angola, the Democratic Republic of Congo, Sierra Leone and Benin among the most prominent producers. Nonetheless, African oil palm crops are primarily used for domestic consumption, with only the Ivory Coast and Cameroon serving as major palm oil exporters [23]. In the Americas, oil palm plantations were initially introduced in Costa Rica and Honduras, followed by the subsequent emergence of the primary oil palm producers in Ecuador, Colombia and Guatemala [23,28]. However, this expansion has posed risks to deforestation, loss of biodiversity, and greenhouse gas emissions. In order to meet the projected demand for palm oil without significantly expanding land usage, it is crucial to achieve a significant improvement in crop productivity.

Despite the imperative to carefully assess the environmental effects of expanding oil palm cultivation, numerous initiatives are underway to promote sustainable palm oil production on a global scale. The RSPO is the preeminent non-profit organisation responsible for regulating sustainable palm oil [9,23]. Palm oil produced to RSPO standards is required to be deforestation-free. For instance, efforts are being made to convert only land currently utilised for pasture or unauthorised cultivation, and strategies are being implemented to enhance crop yields, thus minimising the need for additional land [29]. This will be crucial due to the limited availability of land in Malaysia and Indonesia. Malaysia's government has taken measures to curb further expansion of cultivated areas by preserving some of their forest regions [30]. Furthermore, crop growth has been declining since 2009, partly due to the oil palm's susceptibility to several diseases. The most severe incidences of these diseases are linked to pathogenic fungi and are especially common in replanted regions [9,23]. Implementing disease management measures can effectively curtail the undesired expansion of plantings by enhancing through mitigating disease infection in existing plantings. However, until now, most control strategies have only been able to extend the productive lifespan of infected palm trees without eradicating the diseases. As a result, discovering more efficient disease control strategies remains a crucial part of sustainable palm oil production.

2.2. *Critical pathogenic fungi affecting oil palm*

Critical pathogenic fungi have emerged as a significant cause of concern in the global palm oil industry, posing a threat to the health and productivity of oil palm plantations [5,31]. There is a range of diseases affecting oil palm plantations attributed to these harmful fungi, including basal stem rot (BSR), upper stem rot (USR) vascular wilt, brunch rot, sooty mold, and grey leaf blight. The impact of these diseases on oil palm cultivation varies according to the symptoms observed and the geographic regions where the crops are cultivated (Table 1). *Ganoderma* spp. stands out as the most destructive pathogen for oil palms, responsible for both BSR and USR infections. These infections are prevalent across Southeast Asia and particularly pronounced in replanted regions [6,21,32]. Additionally, *Fusarium* spp., particularly *F. oxysporum*, poses a significant threat by causing vascular wilt, which stands as the most devastating disease for oil palm cultivation in Africa and South America, resulting in severe losses in affected regions [33,34]. Various fungal infections, such as *Ustulina deusta*, *Marasmius palmivorus*, *Meliola elaeidis*, *Pestalotiopsis palmarum* and *Curvularia eragrostidis,* have been isolated from oil palm roots and leaves [35–39]. Lesions caused by these pathogenic fungi are frequently observed in oil palm cultivations, contributing to the complexity of disease control.

Controlling the disease poses a significant challenge due to the persistent and soil-bound nature of the pathogen, particularly in the case of *Ganoderma* spp. This parasitic organism thrives by obtaining nutrients from tree stumps and roots. One significant challenge in dealing with *Ganoderma* infections is the difficulty in detecting early symptoms. Symptoms often manifest when the infection has progressed to an advanced stage, typically ranging from 60 % to 70 % [4]. Immature oil palms, once infected, usually succumb to the infection within a relatively short span of 1–24 months. In contrast, mature palms may persist for one to two years after the initial symptoms manifest [6,46]. The research findings indicate that out of all the *Ganoderma* spp. only *G. boninense*, *G. miniatocinctum* and *G. zonatum* were identified as pathogenic to oil palm. In contrast, *G. tornatum*, *G. applanatum*, *G. pfeifferi, G. lucidum* and *G. philippi* were shown to be non-pathogenic [47,48]. *G. boninense* is known to be the causal pathogen of BSR and USR, which are the most destructive diseases of oil palm in Southeast Asia [7,15,49]. More than 40 %–80 % of potential yield was lost as these diseases reduced fresh fruit bunch (FFB) and killed 80 % of palms in the middle of their economic life [21,23,50]. This resulted in an estimated potential yield loss of over 400,000 ha of matured oil palm [6,40,51]. *G. boninense* employs multiple pathways for host plant transmission, including

Table 1
Overview of global palm oil diseases caused by pathogenic fungi.

Oil Palm Disease	Pathogen	Typical Damage/Symptoms	Current Distribution	Ref.
Basal stem rot (BSR)	*Ganoderma* spp.	Damage to internal basal stem, yellowing and wilting of leaves and frond collapse, crown loss, reduced fruit production, root decay and palm death or collapse	Indonesia, Malaysia, Thailand, Papua New Guinea, Nigeria, Colombia Cameroon, Solomon Island	[4,6,7,40]
Upper stem rot (USR)	*Ganoderma* spp.	Infect and damage the upper region of the stem, yellowing and wilting of leaves and frond collapse, and palm death or collapse	Malaysia, Indonesia, Thailand, Papua New Guinea, Nigeria	[7,40,41]
Vascular wilt	*Fusarium oxysporum*	Leaf yellowing, leaf drooping and wilting, vascular browning, reduced yield, and stunted growth	Nigeria, Ghana, Cameroon, Ivory coast,	[7,23,33]
Charcoal rot	*Ustulina deusta*	Black rot at the base, leaves chlorotic, frond drooping and wilt, reduced fruit production and premature death of palms	Indonesia, Malaysia, Thailand	[36,42]
Brunch rot	*Marasmius palmivorus*	Soft and mushy brunch tissue, foul odour, formation of fungal spores and mycelium on the surface of the fruits, premature fruit drop and reduced yield	Malaysia, Indonesia, Taiwan	[35,43]
Sooty mold	*Meliola elaeidis,* *Brooksia tropicalis, Ceramothyrium* spp.*, Capnodium* spp.	The presence of a black, powdery coating on the surface of leaves and fronds and cause stunted growth if the coverage is extensive	Africa, Malaysia, Thailand, India	[36,44]
Leaf blight/ Leaf spot	*Pestalotiopsis palmarum,* *Curvularia* spp.*, Helminthosporium* spp.*, Cylindrocladium macrospores*	Circular or irregular spots, yellowing of surrounding tissue, leaf wilting or drooping and premature leaf drop	Colombia, Honduras, Venezuela, Peru, China, Ghana, Malaysia, Indonesia, Thailand	[36,40,45]

basidiospore dispersion, the presence of secondary inoculum in the soil and root-to-root contact [4,6,8].

Ganoderma spp. have five stages in their life cycle: spores, spore germination, mycelium, primordia, and basidiocarp or fruiting body. As illustrated in Fig. 1, the fungus reproduces via spores and mycelia, with environmental variables such as wind and insects assisting in spore dissemination to other healthy oil palms [52,53]. Under favourable conditions, *Ganoderma* spores can successfully germinate, giving rise to primary hyphae, which eventually develop into primordia with more prolonged and denser mycelial structures. The pathogen's mycelium then infiltrates the tree's vascular system, producing enzymes that break down lignin, cellulose, and polysaccharides within the plant cell walls. This disruption significantly impairs the flow of nutrients and water, leading to a progressive deterioration in the tree's overall health [54,55]. Over time, these debilitating effects manifest in various symptoms, including the presence of basidiocarps resembling a fan or hoof on the surface of tree trunks on the stem, mottling of the lower fronds, growth retardation, water stress, a pale leaf canopy, and unopened spear leaves [6]. By this point, cultural measures frequently failed because more than half of the internal tissues were rotten after the disease symptoms appeared [56]. If left unaddressed, this relentless assault by *Ganoderma* ultimately ends in the collapse of the oil palm [6,40].

2.3. Current strategies in Ganoderma basal stem rot (BSR) disease control

The current approaches to managing *Ganoderma* spp. in oil palm plantations encompass cultural practices, chemical and biological techniques. Cultural practices employed in the *Ganoderma* BSR disease management involve a range of physical techniques aimed at creating an environment that is less conducive to the growth and spread of the pathogen. These approaches include surgery, soil mounding, trenching, clean clearing, and windrowing [6,57]. Soil mounding treatment can be effective in prolonging the productivity of infected palms, but it may not be effective in mitigating the BSR disease [4,6,58]. It involves removing any infected tissue through surgery and constructing elevated soil beds or mounds, typically with a diameter of around 1 m and a height of up to 0.75 m, around the tree base [59]. This method enhances soil drainage and aeration, making it less favourable to *Ganoderma* growth and preventing the weakened bole from being collapsed [21]. Besides, this approach can effectively extend the infected palm's lifespan, with a mortality rate of up to 4.45 % [57]. Moreover, excavating trenches with dimensions of 4 x 4 × 0.75 m around the infected palms had been recommended to mitigate the risk of infection through infected soil and root contact with nearby healthy palm trees by creating a barrier around the tree's roots [41,60]. However, the efficacy of trenches has been compromised due to either inadequate maintenance or insufficient depths, resulting in roots being able to cross underneath [60].

In addition, clean clearing and windrowing are two sanitation practices employed to reduce the dissemination of *Ganoderma* inoculum in oil palm cultivations. The process of clean clearing entails the elimination of infected palms, whereas windrowing involves chipping, pulverising, and stacking infected palms in windrows between planting, but at a considerable cost [4,7]. Open burning, traditionally employed for land-clearing activities in oil palm plantations by burning agricultural residue, infected palms, and

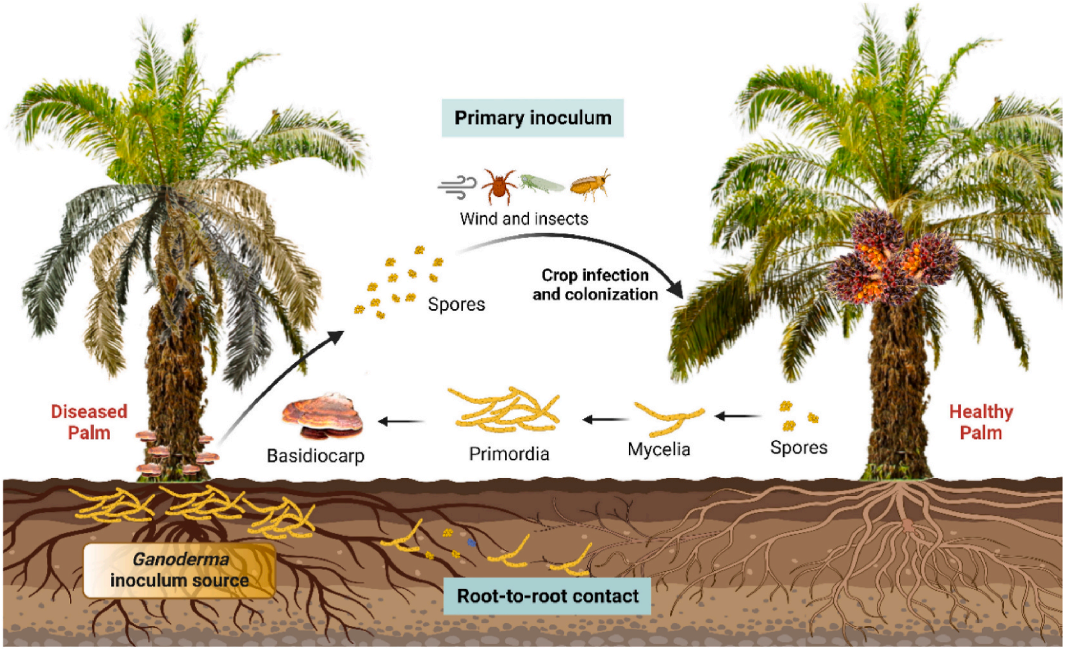

Fig. 1. ***Ganoderma* spp. life cycle.** The fruiting bodies of *Ganoderma* spp. produce millions of basidiospores, which can be dispersed by wind, insects, or through root-to-root contact. The germinating basidiospores form mycelia and mate with compatible partners to form pathogenic dikaryotic mycelia. Subsequently, these mycelia progress to form primordia and colonise the oil palm's root and basal stem, eventually leading to the growth of basidiocarps on the affected tree's lower trunk. Figure created with BioRender.com.

undergrowth was a quick method for pest and disease control and soil enrichment. However, its detrimental effects on the environment, biodiversity, public health, and air quality led to significant regulatory changes over the past two decades. Countries began implementing laws to restrict or ban the practice, supported by the Association of Southeast Asian Nations (ASEAN) Agreement on Transboundary Haze Pollution in 2002, ratified by all ASEAN countries. Similarly, European Union regulation 1306/2013 banned the practice across all EU countries, with many other regions following suit, opting instead for natural decomposition techniques [49,57,61]. Nevertheless, these practices may be less effective due to the persistence of residual spores or mycelia, hence continue to pose a risk to any nearby healthy palm trees. According to a study conducted by Virdiana et al. [62], it has been demonstrated that in the absence of chemical treatment and fallowing prior to windrowing, a significant proportion of oil palms, up to 41 %, remain susceptible to pathogen infection within the first seven years after planting. Therefore, using these measures does not successfully impede the proliferation of *Ganoderma* spp., thus necessitating exploring other disease management options.

Biocontrol measures, specifically the use of *Trichoderma* spp., have garnered significant interest as potential alternatives for managing *Ganoderma* BSR disease. Works done by Angel et al. [63], Muniroh et al. [64], Nurzannah et al. [65], and Wang et al. [66], have emphasised the potential of *Trichoderma* spp. as biocontrol agents (BCAs) against *G. boninense*. For instance, *T. asperellum* exhibited notable suppression of *G. boninense* growth, resulting in a radial growth inhibition percentage (PIRG) of over 50 % [64]. In another study, *T. harzianum* was combined with other BCAs, including *Lecanicillium* spp., *Streptomyces sundarbansensis,* and *Pseudomonas aeruginosa* as biocontrol formulation [67]. Treatment with this method significantly decreased ergosterol concentration in the samples compared to the control, showing its potential efficacy in combating *G. boninense*. Nevertheless, in the nursery trial by Alexander et al. [68], the bioformulation contained a combination of *Trichoderma* spp. and *Bacillus* spp. did not demonstrate any inhibitory effects on *G. boninense*. This highlights the need for careful selection and thorough evaluation of BCAs to determine their efficacy. Although biocontrol therapies are commonly perceived as new and environmentally friendly options, there is a shortage of substantial evidence regarding their effectiveness in field testing. Their efficiency can be influenced by several factors, including the genetic diversity of the target pathogen, the ability to colonise different types of soil, susceptibility to climatic conditions, and interactions with non-target organisms [69–71]. Furthermore, the development of mutant strains of BCAs with reduced efficacy must be carefully considered.

Chemical treatments, such as the application of fungicides, are essential for efficient *Ganoderma* BSR disease control in agricultural fields. These treatments employ several modes of action to target the pathogenic fungi [72,73] specifically. These include copper-based compounds, dithiocarbamates, and azoles, each possessing distinct advantages and potential drawbacks [4]. Copper-based fungicides liberate copper ions that exhibit toxicity toward a broad spectrum of fungi [72,73]. They are available in many forms, such as copper hydroxide, copper oxychloride, and Bordeaux combination [74]. Nevertheless, the effectiveness of copper-based compounds against *Ganoderma* spp. can differ, and their application may pose risks to beneficial soil microbes and trigger phytotoxicity in certain plant species [75]. Dithiocarbamates are another type of fungicide that is known for its ability to control a wide range of fungal species effectively. They function by impeding crucial fungal enzymes and suppressing their development [76]. A well-known dithiocarbamate fungicide is Mancozeb, but it carries the risk of developing fungal resistance and causing adverse effects on aquatic ecosystems [77]. Furthermore, the azole fungicide group has proven effective against *Ganoderma* BSR disease, and its ongoing success in disease management is due to advancements in more potent formulations with a reduced risk of resistance [10,13,78]. This emphasises the importance of azoles in *Ganoderma* BSR disease management. However, appropriate and sustainable use of these fungicides in the field requires thoughtful consideration of their selection and application.

3. The role of azole-based fungicides in managing fungal pathogens

3.1. Efficacy of azole-based fungicides and their mode of actions

Azoles are a class of chemical compounds that are characterised by their distinctive five-membered ring structure. This ring structure contains one or more nitrogen atoms with or without heteroatoms in the ring and can be classified into several subsets, including triazoles, imidazoles, tetrazoles, pyrimidines and dioxolanes [79]. The agricultural industry experienced a significant transformation in the 1970s with the advent of azole compounds, particularly imazalil (IMZ), which falls within the category of imidazole fungicides [10]. This compound was widely utilised as a seed treatment for potatoes and cereals and a post-harvest treatment for pome fruits, citrus, pineapple, and banana. IMZ effectively inhibited the growth of *Penicillium italicum* and *Penicillium digitatum*, which are known to cause storage diseases like blue and green moulds in citrus fruit [80]. Several significant azoles were further discovered to combat various diseases in crops and boost fruit production, namely triadimenol (1973), fenarimol (1975), prochloraz (1977), propiconazole (1979) and bitertanol (1979) [10]. Later, in the early 1980s, the discovery of new azoles, such as prochloraz in Europe, represented a notable advancement in the management of eyespot disease in wheat crops caused by *Oculimacula yallundae* [81]. The efficacy of these compounds has also been demonstrated in the management of other diseases, including citrus green mold (*P. digitatum*), rice bakanae disease (*F. fujikuroi*), and fusarium wilt (*F. oxysporum*) [10,82–84].

Over time, an increasing number of azole compounds have been synthesised to manage plant diseases in various crops efficiently, demonstrating the continual progress and improvement in fungicide formulations. Flusilazole and Triticonazole, introduced in 1983 and 1995, have shown efficacy in treating powdery mildews and diseases affecting the leaves and ears of cereal crops, respectively. Imibenconazole, which became available in 2011, has been utilised to combat fungal infections in many crops, such as rice and vegetables [10]. Finally, mefentrifluconazole represents a recent addition that specifically targets *Septoria tritici* blotch (STB), a plant disease caused by the fungal pathogen *Zymoseptoria tritici* [85,86]. STB is a significant foliar disease in wheat that can lead to substantial yield losses if left uncontrolled. In addition, azole-based fungicides, particularly triazole have consistently proven their effectiveness in providing extended control over various *Ganoderma* spp. in oil palm, making them valuable tools in disease management strategies. For instance, hexaconazole applications have significantly reduced the severity of BSR induced by *G. boninense* [87,88]. These findings highlight the importance of different azole fungicides in addressing the challenges posed by *Ganoderma* spp., ultimately contributing to the resilience and sustainability of the oil palm industry.

Treatment with azole-based fungicides is highly effective in disrupting fungal cell membranes by altering sterol composition. Azoles exert their action by inhibiting the enzyme sterol 14α-demethylase, CYP51, which is a member of the cytochrome P450 family [89,90]. This enzyme is crucial in the ergosterol biosynthetic pathway and essential for the maintenance of fungal membrane fluidity and permeability [13]. Fig. 2 elucidates the process through which azoles disrupt the fungal cell membrane. Azoles initially caused the reduction of ergosterol levels in the fungal cell membrane. Ergosterol is a critical component of fungal membranes, and its decrease significantly affects the membrane properties. Ergosterol contributes to membrane fluidity and stability, and its absence weakens the membrane's structural integrity [91]. Furthermore, the action of azoles in inhibiting CYP51 leads to the buildup of 14α-methylated sterols in the fungal cell membrane. These sterols, devoid of the methyl group at the 14α position, exhibit distinct structural dissimilarities compared to ergosterol. The accumulation of these abnormal sterols disrupts the normal composition of the membrane [90,92]. Consequently, the function of membrane transport mechanisms is impeded, resulting in fungistasis [13]. This is a crucial outcome in disease management, as it prevents the pathogen from causing further damage to the host.

3.2. *Challenges in azole-based fungicide applications*

The application of azole-based fungicide is considered crucial and widely used in agricultural commodities. However, due to the inherent low stability and poor water solubility of azole compounds, many fungicide formulations heavily rely on organic solvents for dissolution and dispersion [93,94]. Unfortunately, these formulations face problems, including burst release and suboptimal delivery, necessitating higher dosages and more frequent applications [95]. These challenges not only compromise their disease control efficacy but also raise concerns about environmental contamination through runoff into water bodies and posing health risks to non-target organisms. A comprehensive investigation has been conducted to evaluate the extent of azole contamination and its associated risks. For instance, studies in China found that azole fungicides, such as tebuconazole and tricyclazole, were found in agriculturally intensive regions, indicating their widespread presence in aquatic ecosystems [27,66,96,97]. Similarly, European assessments by the European Topic Centre on Inland, Coastal and Marine water confirmed the presence of azole fungicides, particularly tebuconazole, propiconazole and epoxiconazole, in various European lakes, rivers and coastal seas [98]. The widespread detection of azole fungicides in water bodies raises concerns about their potential ecological consequences. These fungicides can adversely affect non-target aquatic organisms and disrupt aquatic ecosystems. Implementing buffer zones, reducing fungicide use, and adopting integrated pest management approaches that include fungicide rotation and alternative disease control methods can help mitigate fungicide contamination in water bodies while safeguarding the environment [99,100].

Moreover, the widespread and excessive use of azole compounds has resulted in decreased sensitivity in the field, fostering the development of mutations and the emergence of resistance within plant fungal pathogens. For instance, cereal powdery mildews

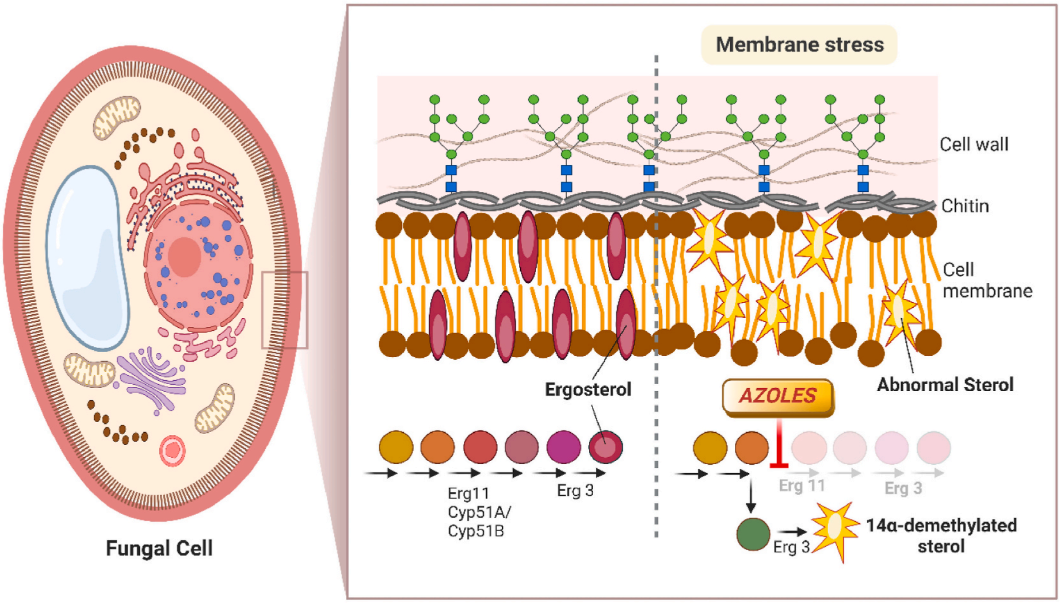

Fig. 2. The mode of action of azoles on the fungal membrane. The azole compounds act by inhibiting the synthesis of the sterol components and leading to the accumulation of abnormal sterol (14α-methylated sterol) that destabilises the cell membrane, ultimately resulting in cell lysis and death. Figure created with BioRender.com.

caused by *Blumeria graminis* developed resistance to the azoles triadimefon and triadimenol within four years of their introduction in the late 1970s [10,101]. However, certain azoles like prothiconazole, registered under the Federal Insecticide, Fungicide, and Rodenticide Act in 2022, still offer a satisfactory level of control for powdery mildew, indicating the absence of cross-resistance [102–104]. Subsequently, other concerns regarding the resistance or shifting sensitivity emerged in many plant diseases. For instance, the rapid evolution of azole resistance is observed in the wheat disease *Z. tritici*, which causes septoria leaf blotch. This resistance is caused by the mutations in the CYP51 enzyme, the target of these fungicides [95,105,106]. Similarly, *Botrytis cinerea*, a fungal pathogen affecting various crops, has developed resistance to azoles. This resistance has been attributed to the target site of G143A mutation in the CYP51 enzyme, which has raised concerns in fruit and vegetable production [107]. Furthermore, azole resistance has also been identified in the wheat and rice blast fungus (*Pyricularia oryzae Triticum*), specifically against triazole fungicides like tebuconazole [108]. Resistance mechanisms in this pathogen involve alterations in both CYP51A and CYP51B genes. These mutations can result in alterations in the fungicide's affinity to the enzyme, leading to the development of azole tolerance. Nevertheless, it was discovered that the strategy of fungicide application and the level of intensity in the management program greatly influence the level of resistance [10,109]. Despite the prevalence of azole resistance, the use of azoles has still contributed to approximately a 10 % increase in crop yields [95].

Additionally, azole fungicides can exert detrimental impacts on human health. They have the ability to interfere with the functioning of many enzymes that are part of the CYP superfamily, found in numerous organisms, including humans. This interaction occurs due to the structural resemblances between azoles and naturally occurring substrates that are typically metabolised by human CYPs, namely CYP3A4, CYP2D6, and CYP2C9 [89]. Consequently, this interaction can potentially result in adverse drug reactions, increased drug toxicity, or altered therapeutic effects. For instance, medications metabolised by CYP3A4, such as certain statins, immunosuppressants, and antiretroviral drugs, can be affected by azole-induced inhibition [110]. This requires careful dosage adjustments or alternative treatment options. Notably, CYP19, also known as aromatase, serves as a primary target for many azole fungicides, both in agriculture and medicine. This enzyme plays a vital role in regulating sex hormones, particularly in converting androgens to estrogens during pubertal development [111–114]. Furthermore, cross-resistance is found in *Aspergillus fumigatus*, a fungal pathogen capable of infecting humans and crops. Mutations in the CYP51A gene of *A. fumigatus* have been shown to confer resistance not only to therapeutic azoles like posaconazole, itraconazole, voriconazole, and isavuconazole, but also to agricultural azoles such as propiconazole, tebuconazole and cyproconazole [115–117]. This limits the range of antifungal agents that can be used to treat infections. Consequently, this can result in reduced crop yields and economic losses. Therefore, it is imperative to consistently enhance the formulation and delivery strategy to address the shortcomings associated with utilising these fungicides.

4. Recent advances in nanotechnology for fungicide delivery

4.1. Nanoparticle-based fungicides

In recent years, nanotechnology has brought about a profound transformation in the delivery of fungicides within agriculture and across diverse sectors. Although nanotechnology has made significant advancements in the pharmacology and medicine domain [118–121], its exploration in agricultural applications has been comparatively limited. Nanotechnology offers precise and effective methods for delivering fungicides through nanocarrier systems, effectively tackling many persistent issues related to conventional fungicide applications. The nanocarriers, constructed from a variety of materials, such as lipids, polymers, and inorganic materials, possess different attributes, such as pore size, surface properties, and shape, and serve as protective carriers for fungicides [21,122]. Table 2 provides a comprehensive overview of the nanocarriers used for plant pathogen management. These nanocarrier systems offer potential solutions to improve the effectiveness and sustainability of fungicide applications in agriculture. The fungicides' active ingredient is protected from environmental degradation, their solubility is increased, and they can be released in a sustained manner over extended periods. Consequently, the encapsulation maintains the fungicides' efficacy for extended periods, reducing the necessity for frequent applications and mitigating their environmental and health impacts. Besides, their small size in the nanometer range allows for excellent penetration and interaction with pathogens, enhancing their overall efficacy.

Lipid-based nanocarriers, such as nanoemulsions, liposomes, nanostructured lipid carriers (NLCs), and solid lipid nanoparticles (SLNs), are known for their ability to encapsulate hydrophobic fungicides within their lipid structures, effectively addressing the challenge of distributing these compounds in agriculture. Surfactants are used to stabilise the nanocarriers when dispersed into water. They mitigate the reliance on organic solvents commonly used to dissolve the compounds, promoting environmentally friendly and safer fungicide applications. These nanocarriers enhance the mobility of fungicide active compounds through lipid interactions, facilitating controlled release. For example, Zhang et al. [123] developed a liposomal system incorporating cholesterol and stearylamine to encapsulate cymoxanil, resulting in significantly improved fungicide stability and controlled release. Additionally, SLNs made from glyceryl tripalmitate have demonstrated utility in enhancing the delivery of fungicides like carbendazim and tebuconazole, effectively mitigating burst release and toxicity concerns [125]. Their strong adhesion to plant surfaces reduces runoff, ensuring better disease control. Furthermore, nanoemulsion formulations, consisting of a mixture of nonionic (Tween 80) and anionic (Agnique BL1754) surfactants with fungicide tebuconazole, are prominent for their enhanced solubility and user-friendly application. Mosa et al. demonstrated the efficacy of an eco-friendly nanoemulsion composed of water, *Nigella sativa* (black seed) oil, and nonionic surfactants, namely Tween 20 and Tween 80, in outperforming the control in inhibiting the growth of *Penicillium verrucosum* infection in maize seeds [126].

Polymeric nanoparticles have emerged as promising fungicide carriers, with notable studies focusing on materials like chitosan and polylactic-co-glycolic acid (PLGA). The utilisation of these nanoparticles has demonstrated considerable promise in augmenting the

Table 2

Types of fungicide nanocarriers for plant Pathogen management.

Nanocarrier	Active Ingredient	Treatment	Composition	Particle size	Ref.
Lipid-based Nanocarriers					
Liposome	Cymoxanil	Antifungal treatment on *Saccharomyces cerevisiae* as model target fungal	Cholesterol and stearylamine	128 nm	[123]
Liposome	Carboxin	Antifungal treatment in potato tubers	Phosphatidylcholines and Tween 20	–	[124]
SLNs	Carbendazim and tebuconazole	*Phaseolus vulgaris* seeds	Glyceryl tripalmitate	542 nm	[125]
Nanoemulsion	Tebuconazole	*Penicillium verrucosum* infection in maise seeds	Tween 80 and Agnique BL1754 surfactants	168.6–345.3 nm	[126]
Nanoemulsion	Mancozeb	Inhibition against early blight disease on *Stemphylium lycopersici* and *Sclerotinia sclerotiorum*	Guar gam, glycerol, glutaraldehyde	246.6 ± 0.9 nm	[127]
Nanoemulsion	Clove oil	Inhibition against *Neoscytalidium* Blight Disease of *Carum carvi* L.	Tween 80	36.4–57.1 nm	[128]
Nanoemulsion	Clove, black seed, lemon, and orange oils	Inhibition against grey mold disease on *Botrytis cinerea*	Tween 80	82.6–131.9 nm	[129]
Nanoemulsion	Eugenol oil	Antifungal activity against *Fusarium oxysporum* in cottonseeds	Tween 20	50–120 nm	[130]
Nanoemulsion	Peppermint oil	Treatment of Early blight disease against *Solanum lycopersicum*	Tween 80	20–40 nm	[131]
Polymeric Nanoparticles					
PLGA	Cyazofamid	Inhibition against *Phytophthora infestans* infections in tomato leaves	Poly lactic-co-glycolic acid (PLGA) and polyvinyl alcohol	126 ± 8 nm	[132]
PLGA	Coumarin	Inhibition against grapevine-pathogenic fungi and *Vitis vinifera*	Poly lactic-co-glycolic acid	30–600 nm	[133]
Lignin	azoxystrobin, pyraclostrobin, tebuconazole, and boscalid	Antifungal activity against *Phaeomoniella chlamydospora* and *Phaeoacremonium minimum*	Lignin methacrylate, spermine and spermidine	170–230 nm	[134]
Chitosan	Hexaconazole and dazomet	Treatment against *Ganoderma boninense* on basal stem rot disease	Chitosan, sodium tripolyphosphate and Tween 80	6.5–220.2 nm	[15, 88]
Chitosan	Thymol	Antifungal activity against *Botrytis cinerea*	Chitosan and sodium tripolyphosphate	<200 nm	[135]
Polymeric micelles	Geranylorcinol compounds	Antifungal activity against *Botrytis cinerea*	Pluronic F-127 and poly (ethylene oxide)-b-poly (caprolactone)	–	[136]
Inorganic Nanoparticles					
Mesoporous silica	Thifluzamide	Prevent negative effects of antifungal activity in rice seedlings	Cetyltrimethylammonium bromide, tetraethyl orthosilicate and n-[3-(Trimethoxysilyl)propyl] ethylenediamine	80–120 nm	[137]
Mesoporous silica	Prochloraz	Smart management of wilt disease against *Rhizoctonia solani*	Cellulose, 3-aminopropyltriethoxy silane, tetraethyl orthosilicate, cetyl trimethyl ammonium bromide	255.0 ± 5.3 nm, 531.2 ± 4.9 nm	[138]
Silica nanoparticle	Silica	Antifungal activity against *Fusarium oxysporum* and *Aspergillus niger*	Silica powder from sugarcane bagasse and corn cob	17.23 nm	[139]
Silver nanoparticle	Silver	Antifungal activity on phytopathogenic citrus fruit fungi against *Alternaria alternata*, *Alternaria citri* and *Penicillium digitatum*	Silver nitrate and polyvinyl pyrrolidone (PVP40)	10 ± 5 nm	[140]
Silver nanoparticle	Silver	Antifungal activity against *Fusarium avenaceum* and *Fusarium equiseti*	Silver nitrate, trisodium citrate dihydrate, sodium borohydride, and cysteamine hydrochloride	12 ± 4 nm, 15 ± 4 nm	[141]
Magnetite nanoparticle	Iron oxide	Treatment on *Fusarium* wilt against *Fusarium oxysporum* f. sp. *lycopersici*	Burned spinach powder	~20 nm	[142]
Iron oxide nanoparticle	Iron oxide	Antifungal activity against *Aspergillus niger* and *Mucor piriformis*	Iron oxide and leaf extract *Platanus orientalis*	38 nm	[143]
Copper nanoparticles	Copper	Antifungal activity against *Fusarium solani*, *Neofusicoccum* sp., and *Fusarium* oxysporum	Copper (II) sulfate pentahydrate and ascorbic acid	200–500 nm	[144]

efficacy of fungicides across several applications. Chitosan, a biopolymer made from chitin, possesses several desirable characteristics such as biodegradable, biocompatible, non-toxic, and effectively combatting a wide range of plant diseases [145–148]. These exceptional properties have positioned chitosan as a prominent material for nanoparticle development, rendering it a highly favourable option for a wide range of cutting-edge applications. According to a study conducted by Maluin et al. [88], it was shown that the chitosan-loaded hexaconazole nanoparticles with a diameter of 68.1 nm exhibited the highest efficacy in combating *G. boninense*. These nanoparticles achieved an EC_{50} value of 8 ppb, significantly outperforming pure hexaconazole with an EC_{50} value of 21.4 ppb. Their subsequent field trials, in combination with dazomet, demonstrated a noteworthy decrease in the occurrence of basal stem rot disease caused by *G. boninense*, with a reduction of up to 74.5 % [15]. This demonstrates the prospective application of combined nanofungicides for efficient disease control. Moreover, chitosan nanoparticles synthesised through the ionic gelation technique have effectively controlled rice blast diseases caused by *Phyricularia grisea* and *Phyricularia oryzae* [149,150]. Chitosan nanoparticles containing low-water soluble fungicides have also been reported for their effectiveness in combating Fusarium wilt of chickpea [151], and Fusarium crown and root rot in tomatoes [152,153] caused by *F. oxysporum*.

In a study conducted by Fukamachi et al. [132], they developed PLGA nanoparticles loaded with the cyazofamid fungicide. These nanoparticles demonstrated remarkable fungicidal efficacy when used against *Phytophthora infestans* infections in tomato leaves. They found that the PLGA nanoparticles exhibited thermodynamically favourable characteristics that promoted their stable attachment to tomato leaves even after simulated rainfall and were highly effective against *P. infestans*. In another study, Valletta et al. [133] demonstrated that PLGA nanoparticles can penetrate the cell wall and membrane of grapevine-pathogenic fungi (*Vitis vinifera*) through TEM analysis. They found that the cell wall selectively allows nanoparticles with an average diameter of 30–50 nm to enter the interior cytoplasm while bigger nanoparticles remain attached to the cell wall. In addition to chitosan and PLGA, MacHado et al. [154] have developed a bio-based polymeric nanocarrier made from lignin to encapsulate various fungicides, including azoxystrobin, pyraclostrobin, tebuconazole, and boscalid. These nanocarriers with a 200–300 nm diameter showed high encapsulation efficiencies, reaching up to 99 % depending on the solubility of the active ingredients. These carriers demonstrated strong inhibitory effects against the growth of *Phaeoacremonium minimum* and *Phaeomoniella chlamydospora*, both of which are lignin-producing fungi linked to the prevalent fungal grapevine trunk disease known as Esca.

In recent years, the utilisation of inorganic or metallic nanoparticles, particularly silver nanoparticles (AgNPs), has garnered considerable interest within the area of fungicides and their delivery. One key advantage of AgNPs in agriculture is their green synthesis, which aligns with sustainable practices. AgNPs can be synthesised using eco-friendly methods that employ various biological sources, including plant extracts, bacteria, fungi, or yeast, to efficiently convert silver ions into AgNPs [155–157]. This process significantly reduces the reliance on toxic chemicals in nanoparticle production. They can encapsulate or adsorb fungicidal compounds, enhancing their stability and targeted delivery to plant surfaces or fungal pathogens. AgNPs at a concentration of 75 ppm successfully inhibit the growth of mycelium and the germination of spores in four kiwifruit rot-causing pathogens, including *Pestalotiopsis microspore, Botryosphaeria dothidea, Alternaria alternata* and *Diaporthe actinidiae*. The AgNPs were found to increase the permeability of the mycelium's cellular membrane, resulting in intracellular substance leakage [157]. Similarly, AgNPs at a concentration of 150 ppm were found to have strong antifungal activity against fungal pathogens isolated from fruit spots and citrus leaf, specifically *P. digitatum*, *A. citri,* and *A. alternata*, when compared to the fungicides iprodione and difenoconazole solution [140].

Moreover, AgNPs and other metallic nanoparticles, such as copper nanoparticles (CuNPs) embedded with natural fungicide chitosan, in inhibiting the growth of pathogenic fungi has been extensively demonstrated. These nanoparticles have shown remarkable efficacy against fungi, including *F. oxysporum* and *Neoscytalidium dimidiatum*, which are known to cause significant damage to various crops [158–160]. In another study, CuNPs have also been widely tested for the antifungal activities on different pathogenic fungal species, including *F. oxysporum, F. solani* and *Neofusicoccum* sp [72,144,161,162]. These studies highlight the versatility of CuNPs as effective antifungal agents with potential applications across different fungal pathogens, further highlighting their promise in agriculture. These findings suggest that nanoparticles could significantly advance fungicide delivery in agriculture, particularly azoles, similar to their successful applications in the biomedical fields.

4.2. *Mechanism of nanodelivery of Azole in fungicide management*

The mechanism of nanodelivery of azole fungicides begins with encapsulating these hydrophobic compounds within nanocarriers. The compounds are entrapped or loaded into the structure of nanoparticles during the encapsulation process. The choice of nanocarrier depends on factors like the azole's properties and the desired delivery system. Many azoles suffer from limited solubility in water, which can hinder their efficacy in disease management [94,163–165]. Nanocarriers are pivotal in addressing this challenge by providing a hydrophilic shell or matrix surrounding the hydrophobic fungicide molecules. This encapsulation increases the fungicide's solubility for better distribution, ensuring thorough coverage during fungicide application and reaching all plant parts [166,167]. Crop injury may occur when some areas receive excess fungicide, resulting in phytotoxicity and potential yield loss [168]. Conversely, insufficient coverage or suboptimal delivery can lead to poor protection and the development of fungal resistance [172,173], thus jeopardising crop health and productivity. Hence, this encapsulation ensures that the fungicide remains stable and effective over extended periods. In work conducted by Gao et al. [169], they utilised this approach with difenoconazole, a commonly used triazole fungicide known for its poor water solubility. Through the formation of a β-cyclodextrin inclusion complex, they successfully improved both its solubility and fungicidal efficacy. Similarly, a recent study by Ahmad et al. [170] developed a nanoemulsion formulation with increased solubility of ketoconazole and demonstrated superior effectiveness compared to ketoconazole alone.

The rate of fungicides release from nanocarriers can be affected by variables like the type of nanocarrier, the size of the nanoparticles, and the environment in which they are applied. For instance, Wanyika [171] demonstrated that metalaxyl encapsulated in mesoporous silica nanoparticles showed an increased release rate in water (47 %) compared to soil (11.5 %). In another study, the release rate of tebuconazole from cross-linked lignin nanocarriers was found to be dependent on the ratio of fungicide to lignin sulfonate [134]. Overall, nanocarriers can improve the release rate of fungicides in plants by providing a controlled and sustained release, which can enhance the fungicide's overall efficacy while reducing the amount of fungicide required. The controlled release mechanism allows for the gradual and consistent delivery of the active ingredient over an extended period, maintaining effective concentrations of the fungicide within the plant system for longer durations. Furthermore, these nanocarriers can be engineered to break down into non-toxic components or beneficial by-products after delivering their payload, minimising their environmental footprint. Ahmad Aljafree et al. [172] demonstrated this with nano metal-organic frameworks (MOFs) for the delivery of hexaconazole. Their study showed prolonged fungicidal activity against *G.boninense*, reducing the need for repeated applications. Remarkably, the progression of *Ganoderma* BSR disease was completely halted after 26 weeks of *in vivo* nursery trial and seedling growth was accelerated due to additional nutrients from the disassembly of the MOF carrier system in the soil [172]. This dual function of effective disease management and improved plant health offers a promising solution for sustainable agriculture.

Moreover, nanoformulation can improve the adhesion of azole to plant surfaces, decreasing the likelihood of these chemicals being

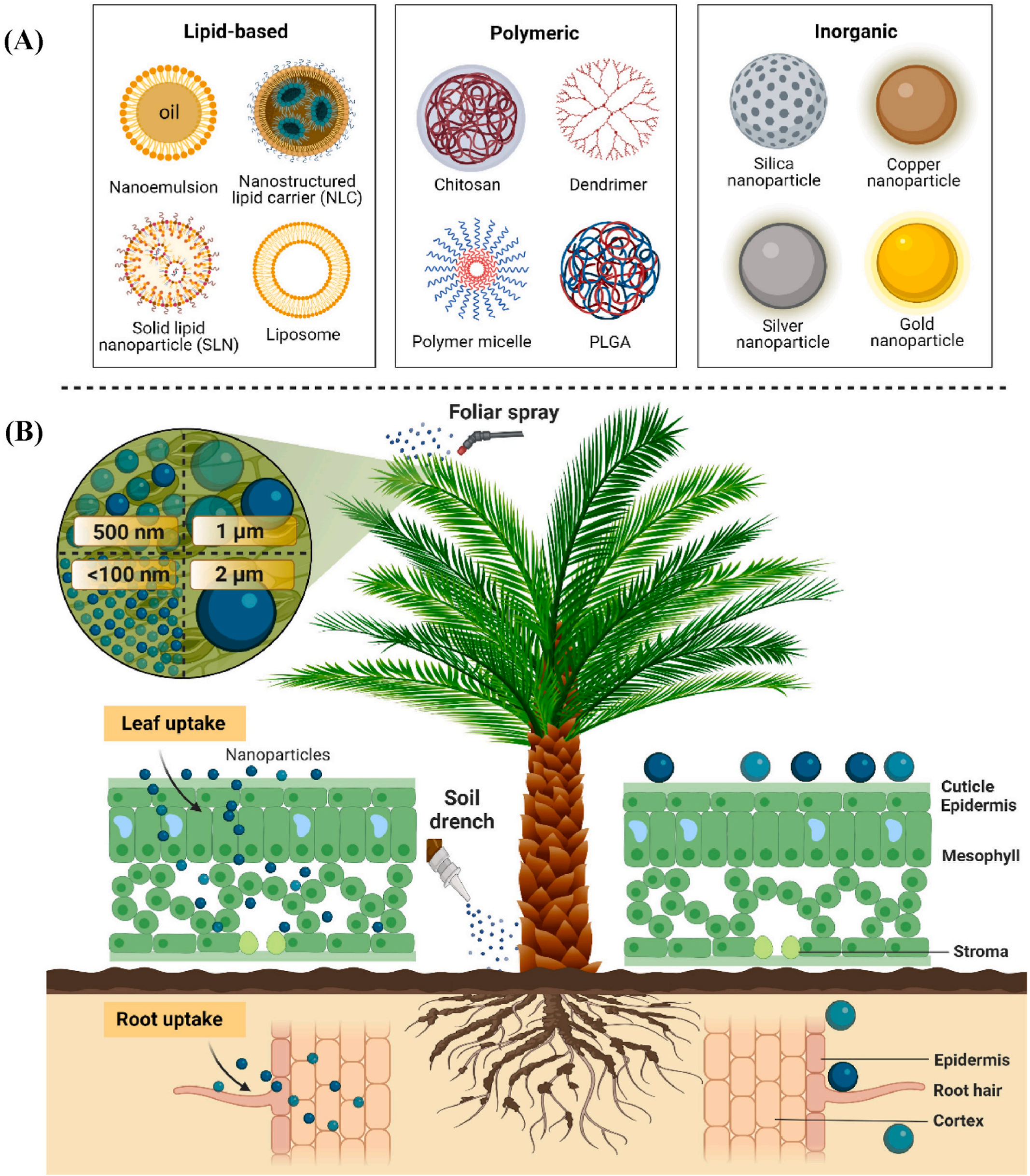

Fig. 3. The application of nanocarrier in fungicide delivery. (A) The types of nanoparticles employed for fungicides encapsulation and delivery, (B) intricate the transportation pathways of nanoparticles in plants through foliar and root uptakes. Figure created with BioRender.com.

washed away into waterways or leaching into the soil. This adherence reduces environmental contamination and ensures that the azoles are effectively utilised where they are needed. Research by Yao et al. [173] highlighted that nanosuspension azoxystrobin formulation improved the retention of fungicides and reduced contact angle, indicating enhanced wettability and adhesion capability on plant surfaces, thereby reducing potential run-off and environmental contamination. This, in turn, minimises the toxicity and environmental impact associated with fungicide run-off and contamination of soil and water. In addition, functionalizing nanocarriers with ligands or surface modifications allows for site-specific targeting, increasing the fungicide's effectiveness while minimising off-target effects [163,174]. Fig. 3 illustrates the varieties of nanoparticles and their potential uptake pathways within plant systems. These nanoparticles can be administered directly to seeds, applied through soil drenching for root absorption, or delivered via foliar sprays for leaf absorption. The small size of nanocarriers enables them to distribute evenly and penetrate plant tissues effectively. This enhanced bioavailability allows the fungicide to reach target sites within the plant, such as fungal pathogens or vulnerable plant tissues, with greater precision. The improved bioavailability enhances the fungicide's overall efficacy. Reduced fungicide usage aligns with sustainable agricultural practices.

5. Opportunities and challenges in azole-based nanofungicides

Despite the prospects of nanotechnology to revolutionise azole-based fungicide delivery, there remain several key challenges that need to be addressed. Ensuring the stability of azole-based nanofungicide formulations over time can be a challenge, particularly for lipid-based nanocarriers. The susceptibility of the nanocarriers to variations in environmental conditions, such as pH and temperature, can greatly undermine their stability and efficacy [175–177]. One approach to enhancing stability involves the careful selection of lipid excipients based on their Hydrophilic-Lipophilic Balance (HLB). Lipid excipients with appropriate HLB values can form more stable emulsions, improving the consistency and longevity of nanofungicide formulations [178]. Additionally, using mixed surfactants can further increase stability by providing higher molecular interactions between them that enhance the integrity of the nanocarrier structure under varying environmental conditions [178,179]. This was proved by Chang and McClements when using medium chain triglyceride (MCT) and orange oil, the smallest droplets nanocarrier were formed in the system containing Tween 80 and 60, belonging to HLB values of 15.0 and 14.9, respectively [180]. This is in agreement with other studies showing that the most stable and smallest lipid-based carrier system was produced with an HLB value of 13.4, achieved by changing ratios between Tween 80 and Span 20 to 3:1 [181]. This emphasises the need for meticulous excipient selection, quality control, and stability studies to prevent any premature release and suboptimal delivery of azoles.

Efforts to develop sustainable, low-cost methods for synthesising nanoparticles and more research on the interaction mechanism of nanoparticles with crops at the molecular level are needed to make this technology accessible and feasible for agriculture applications. In addition, the long-term environmental impact of nanotechnology remains a subject of concern. The nanocarrier systems and azole residues may persist in soil for extended periods primarily due to their small size and resistance to microbial degradation. This persistence can cause the accumulation of these materials in agricultural fields over time, potentially affecting soil health and the land's long-term productivity. The residues may leach into groundwater, introducing the potential for contamination of water bodies. Besides, the degradation rate of the nanocarrier may vary depending on the choice of their composition and conditions, including the type of surfactant, polymer, temperature, and pH level, all of which have the potential to affect their structural integrity and performance in the field [88,182]. Surfactants such as lecithin degrade more rapidly compared to synthetic counterparts like polysorbate 80, while polymers such as PLA exhibit a slower degradation rate than PLGA due to differences in their hydrolysis rates [183]. On top of that, elevated temperatures can accelerate the degradation of nanomaterial, as seen in hyperthermia treatments [184] and pH levels further influence degradation, with alkaline environments accelerating the breakdown of polymers than neutral conditions [185]. Collectively, these factors are pivotal in determining the structural integrity and efficacy of nanocarriers in agricultural settings. Hence, it is crucial to take into account concerns related to the composition and development of nanocarrier systems that can specifically target plant pathogens while minimising unintended consequences.

The emergence of resistance is a crucial issue that needs immediate attention. An over-reliance on azole-based nanofungicides may lead to the development of resistance in fungal populations, thereby posing a significant challenge to long-term disease management. To address this, it is imperative to encourage an integrated approach by combining various disease management strategies. This approach includes cultural practices, the rotation and mixing of fungicides, the use of biological controls through biopesticides, and the development of disease-resistant crop varieties. Furthermore, the use of nanocarrier systems can significantly enhance the delivery and effectiveness of fungicides, thereby mitigating the risk of resistance and ensuring the sustainable application of nanotechnology in agriculture. Additionally, fostering interdisciplinary collaborations between scientists, agronomists, environmental researchers, and policymakers is crucial to advancing this field. This collaborative approach can lead to the design of novel azole compounds and nanocarrier systems with enhanced efficiency and safety profiles. Besides, it is also essential to establish guidelines and regulations governing the use of nanoparticles in the delivery of fungicides, particularly azoles, to ensure their responsible and sustainable deployment in oil palm plantations. Concurrently, it is imperative to establish acceptable limits for nanocarriers and azole residues by implementing more accurate screening and detection methods. Researchers and industry experts must meticulously evaluate their choice of azole compounds and nanocarrier systems, considering the intricate dynamics of crop-pathogen interactions, ecological aspects, and adherence to regulatory standards. In doing so, we can harness the full potential of azole-based nanofungicides while mitigating any associated risks to agriculture and the environment.

6. Conclusions

Pathogenic fungi present an ongoing threat to oil palm production and exhibit exceptional persistence. Azole-based fungicides were used for nearly half a century to effectively manage oil palm infections and reduce agricultural losses caused by plant diseases. However, this threat is progressively escalating because of growing issues with suboptimal delivery, resistance and the emergence of diseases that threaten arable output. The utilisation of nanotechnology provides an excellent opportunity to improve the effectiveness and long-term viability of disease control. Encapsulating azole-based fungicides within nanocarriers has enhanced fungicidal action, minimised environmental impact, and improved bioavailability. As research in this field continues to evolve, it is clear that nano-delivery systems have the potential to revolutionise the approach to combat diseases, ultimately leading to improved crop yields, economic sustainability, and environmental conservation. Hence, further exploration and development in the nanodelivery of azole-based fungicides are needed for future innovations in oil palm disease management.

Data availability statement

Data will be made available on request.

CRediT authorship contribution statement

Azren Aida Asmawi: Writing – original draft, Visualization, Investigation, Data curation, Conceptualization. **Fatmawati Adam:** Writing – review & editing, Supervision, Investigation, Conceptualization. **Nurul Aini Mohd Azman:** Writing – review & editing, Supervision, Investigation, Conceptualization. **Mohd Basyaruddin Abdul Rahman:** Writing – review & editing, Supervision.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Fatmawati Adam reports financial support was provided by Universiti Malaysia Pahang Al-Sultan Abdullah, Malaysia. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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