REVIEW PAPER

An overview of the therapeutic applications of cinnamon-loaded in nanosystems

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ABSTRACT

Cinnamon, a spice derived from the Cinnamomum genus, has a rich history of traditional medicinal applications. Its therapeutic potential arises from a diverse array of bioactive compounds exhibiting antioxidant, anti-inflammatory, and antimicrobial properties. However, the inherent properties of cinnamon, such as poor solubility and instability, have limited its clinical applications. Nanotechnology has emerged as a promising approach to overcome these challenges. By encapsulating cinnamon extract/essential oil within nanoscale carriers, researchers have achieved enhanced bioavailability, solubility, controlled release of its bioactive constituents and therapeutic outcomes. This review comprehensively explores various nano-formulations, to improve the cinnamon's bioactive compounds delivery for biomedical applications. Preclinical studies have demonstrated the efficacy of cinnamon-based nanomaterials in addressing a range of human diseases, including cancer, diabetes, infections, and neurodegenerative disorders. Despite these promising advancements, further research is imperative to elucidate the precise mechanisms of action, optimize formulations, and conduct accurate clinical trials to translate these findings into effective human therapies.

Keywords: *Cinnamon, Nanoparticles, Phytochemicals, Drug delivery systems, Biological availability*

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INTRODUCTION

Cinnamon is a genus within the *Lauraceae* family comprising over 250-300 aromatic, evergreen shrubs and trees. The economic prominence globally as a spice is *Cinnamomum zeylanicum* (true Ceylon cinnamon), *C. burmanni* (Indonesian cinnamon), *C. cassia* (Chinese cinnamon), and *C. loureirii* (Vietnamese cinnamon). [1]. Cinnamon contains a variety of phytochemical constituents and compound classes that contribute to its diverse pharmacological activities. These include essential oils, diterpenes, catechins, proanthocyanidins, tannins, pigments, phenolic carboxylic acids, lignans, and mucins. Cinnamon exhibit antifungal, antibacterial, antioxidant, anti-inflammatory, antidiabetic, antitumor, antimutagenic, cognitive and neuroprotective activities [2, 3]. This supports investigating cinnamon's potential applications for both prevention and treatment of illnesses influenced by multiple pathogenic mechanisms [4].

In recent years, there has been significant research focused on harnessing nanotechnology to enhance the properties of herbal medicines and drugs. Nanoparticles (NPs) exhibit important characteristics as drug carriers, mainly their small size and use of biodegradable materials [5, 6]. Medication delivery significantly relies on particle

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size, as drug NPs display enhanced solubility and bioavailability due to their dimensions and surface area [7, 8]. They can also cross biological barriers like the blood-brain barrier, penetrate the lungs, accumulate selectively in tumors, and permeate tight skin cell junctions. Their nano-scale permits uptake by various cell types and accumulation at target sites [9, 10]. Nanotechnological methods have significantly enhanced the delivery abilities of cinnamon by overcoming limitations such as poor solubility and instability through particle size reduction and formulation engineering [11, 12]. The objective of this review is to provide a comprehensive overview of the current research progress in utilizing nanotechnology approaches to optimize the bioactivity, delivery, and therapeutic efficacy of cinnamon. A detailed analysis of cinnamon's major bioactive phytochemicals and their current applications in human health will be presented. Subsequently, the preclinical investigations involving cinnamon NPs as drug delivery systems for the treatment of various inflammatory and proliferative diseases, both *in vitro* and *in vivo*, will be critically discussed. Special emphasis will be placed on key diseases, including cancer, diabetes, arthritis, and neurological disorders. By integrating findings from these areas, this review aims to shed light on how nanotechnological advancements are enhancing the bioavailability of cinnamon and unlocking its full medicinal potential.

Cinnamon

Photochemistry of Cinnamon

Cinnamon is rich in bioactive constituents such as essential oils, flavonoids, curcuminoids, coumarins, tannins, alkaloids, xanthones, and terpenoids [13, 14]. The essential oil composition from cinnamon bark depends on extraction source such as leaves, bark, roots or stems. Over forty volatile compounds have been isolated from Cinnamomum cassia bark oil [15].

GC-MS analysis has identified seventeen bioactive compounds in cinnamon bark oil. Key constituents involved in various biological effects include cinnamaldehyde, cinnamate, and cinnamic acid [16, 17]. Additional compounds of note include eugenol, linalool, cinnamyl acetate, benzyl benzoate, α-pinene, and β-caryophyllene. The synergistic interaction of these compounds is believed to underlie the therapeutic properties attributed to cinnamon essential oil (CEO) [16].

LC-MS data shows concentrations of condensed tannins, proanthocyanidins and epicatechin in cinnamon at 26.8%, 23.2%, and 3.6% respectively, indicating high polyphenol content. Anthocyanidins A and B procyanidins have also been identified [18]. Thus cinnamon possesses a medley of bioactive compounds that may underlie diverse pharmacological properties and health benefits through multiple targets upon further investigation [19].

The main volatile compounds in cinnamon oil depend on extraction source. For bark-derived oil, cinnamaldehyde comprises 55-78% and is the primary flavorant. Meanwhile, eugenol makes up 59-78% in leaf-derived oil [20]. Cinnamon bark contains approximately 0.6-1% essential oil and 1-2% phlobatannins, calcium oxalate, starch, mucilage, and mannitol [21].

Cinnamon in medicinal application

Cinnamon bark has widespread applications. It is commonly used as a cooking condiment and flavoring agent. Its multi-targeted pharmacological activities support continued inquiry into preventive and therapeutic applications [2].

Cinnamomum accessions contain various bioactive compounds of interest for human health applications. Key phytochemicals reported include vanillic acid, caffeic acid, gallic acid, p-coumaric acid, ferulic acid, proanthocyanidins A and B, and kaempferol, along with cinnamic acid and cinnamaldehyde. Researches have demonstrated these cinnamon constituents provide neuroprotective, hepatoprotective, cardioprotective and gastroprotective effects. Many are tied to antioxidant properties through enhancing activities of antioxidant enzymes such as catalase, superoxide dismutase and glutathione peroxidase [22, 23]. Research has unveiled cinnamon's potential as a potent antioxidant, rich in polyphenols that combat oxidative stress. Its anti-inflammatory effects have also garnered attention, suggesting a role in mitigating chronic inflammatory conditions [23, 24]. Moreover, cinnamon's antimicrobial properties, attributed to cinnamaldehyde, have demonstrated efficacy against various microorganisms [25]. In metabolic health, cinnamon has shown promise in modulating blood sugar levels and improving insulin sensitivity, potentially benefiting individuals with type 2 diabetes. Additionally, its lipid-lowering effects, including reductions in total cholesterol and LDL

Fig. 1. Schematic representation of cinnamon's encapsulation within various nanocarriers for enhanced biomedical applications.

cholesterol while preserving HDL cholesterol, support its potential role in cardiovascular health [2, 26]. Emerging evidence suggests cinnamon's neuroprotective potential, with studies indicating its ability to inhibit the aggregation of tau proteins associated with neurodegenerative diseases such as Alzheimer's and Parkinson's. Furthermore, the spice has shown promise in cancer prevention through its potential to suppress tumor growth and angiogenesis [27]. Overall, the diverse bioactive compounds in cinnamon accessions support investigating their applications as natural compounds with multi-targeted mechanisms for improving human health.

Optimizing of physichochemical characterization of Cinnamon through Nanotechnological Approaches

Cinnamon has demonstrated health-promoting effects. However, poor aqueous solubility and instability limit cinnamon's bioavailability and applications. Nanotechnology offers a promising strategy to overcome these challenges by encapsulating cinnamon extracts within particulate carriers. Several studies have developed innovative cinnamon nanosystems characterized by improved phytochemical protection, solubilization, and controlled release [28, 29] (Figure 1). The development of effective cinnamon-based nanoparticle formulations necessitates a comprehensive approach encompassing both synthesis and characterization. Nanoencapsulation techniques such as nanoprecipitation, emulsion-based encapsulation, and pulse laser ablation offer distinct advantages in producing NPs with desired properties. The selection of appropriate carrier materials, such as chitosan, whey protein, or soybean oil, significantly influences the physicochemical characteristics of the resulting NPs [30].

To achieve optimal particle size, distribution, and stability, meticulous optimization of process parameters is essential. Factors including temperature, pressure, pH, and sonication time must be carefully controlled. Furthermore, rigorous stability studies under various storage conditions are crucial to ensure the longevity and efficacy of the developed NPs. Advanced characterization techniques are indispensable for elucidating the physicochemical properties of cinnamon NPs. Dynamic light scattering (DLS) provides insights into particle size and polydispersity, while transmission electron microscopy (TEM) offers detailed information on particle morphology. Zeta potential measurements determine surface charge, a critical parameter for nanoparticle

Table 1. Advantages and disadvantages of different encapsulation methods of cinnamon.

Encapsulation method	Advantages	Disadvantages	References
Spray Drying	Simple, efficient, scalable, versatile	Requires optimization of parameters; can lead to loss of bioactive compounds	[34, 35]
Nanoemulsion	Improves solubility; enhances bioavailability	Complexity in maintaining stability of emulsions	[36, 37]
Liposome	Effective for encapsulating both hydrophilic and hydrophobic compounds	Production costs can be high; issues with scale-up	[38, 39]
Pulse Laser Ablation in Liquid (PLAL)	Allows precise control of nanoparticle size and morphology	Complexity in operation; potential safety concerns	[40, 41]
Ionic Gelation	Biocompatible; biodegradable; nontoxic solvents use	Limited to certain types of compounds	[42, 43]
Nanoprecipitation	Rapid and straightforward method with high encapsulation efficiency	Need for further optimization to meet requirements	[44, 45]

stability. Additionally, UPLC-MS/MS and FTIR spectroscopy enable comprehensive analysis of bioactive compounds and their interactions within the nanoparticle matrix [31, 32].

Different methods for encapsulation of cinnamon into NPs

Different nanoencapsulation techniques have been used to improve physichochemical characterization of Cinnamon including spray drying, emulsion-based encapsulation, liposome entrapment, pulse laser ablation in liquid (PLAL), ionic gelation, and nanoprecipitation. Each has distinct principles, parameters, and advantages/ disadvantages. Among these, spray drying is particularly emphasized due to its widespread use. The choice of synthesis or encapsulation method depends on factors such as the desired nanoparticle properties, the specific application, and the availability of resources. Each technique offers unique advantages and can be optimized to achieve the desired characteristics of cinnamon NPs [31, 33]. In the following, the studies related to the preparation of cinnamon NPs by different methods to improve their physico-chemical properties are mentioned and summarized in Table 1.

Spray drying

The spray drying method is a widely used for nanoencapsulation of CEO and other bioactive compounds. This process involves the atomization of a liquid feed containing the desired bioactives and a carrier material into a fine mist. Subsequent exposure to hot air leads to rapid solvent evaporation, resulting in the formation of dry powder particles encapsulating the cinnamon components. This method offers several advantages, including improved stability, controlled release, and enhanced solubility of the encapsulated compounds. The choice of carrier material is crucial for encapsulation efficiency and release properties. Polysaccharides, proteins, and synthetic polymers are commonly used as carriers. However, careful selection is essential to optimize the performance of the final product. While spray drying presents numerous advantages, challenges such as potential thermal degradation of heat-sensitive compounds and the need for precise process control must be addressed. Ongoing research aims to optimize process parameters and develop novel carrier materials to further enhance the encapsulation efficiency and stability of cinnamon bioactive [46, 47]. Study conducted by Santiago-Adame et al. have demonstrated the successful application of spray drying for encapsulating cinnamon essential oil and infusions, respectively. These studies provide valuable insights into optimizing spray drying conditions for achieving desired particle characteristics and encapsulation efficiency [35]. These findings demonstrate the potential of spray drying as a valuable approach for the microencapsulation of cinnamon compounds, enabling enhanced stability and preservation of their bioactive components.

Nanoemulsions

Emulsion-based encapsulation has emerged as a promising strategy for delivering CEO. This technique involves the dispersion of CEO as discrete droplets within a continuous aqueous phase, stabilized by emulsifiers. High-energy emulsification processes, such as ultrasonication and high-pressure homogenization, are employed to refine droplet size and enhance emulsion stability [48].

The resulting nanoemulsions offer several advantages, including improved bioavailability, enhanced stability, and controlled release of encapsulated compounds [49]. Numerous studies have validated the efficacy of this approach for delivering CEO across diverse applications. For instance, Chunhavacharatorn et al. demonstrated the antimicrobial potential of a cinnamon bark oil nanoemulsion [50], while Ben Jemaa et al. explored its application in meat product quality enhancement [51].

Formulation parameters, including surfactant type, concentration, and emulsification conditions, significantly affect the physicochemical properties of the nanoemulsion. Research has indicated that increasing CEO concentration correlates with larger droplet sizes, emphasizing the need for careful optimization. Additionally, nanoemulsions have exhibited superior physical stability compared to microemulsions [37, 52].

Encapsulation through emulsion techniques offers a robust approach to safeguarding the therapeutic properties of cinnamon essential oil. By shielding bioactive compounds from environmental factors, nanoemulsions extend the shelf life and efficacy of CEO-based products. However, challenges such as emulsion stability, droplet size control, and encapsulation efficiency necessitate ongoing research and development [53, 54].

Liposomes

Liposomes are spherical vesicles composed of lipid bilayers that can encapsulate hydrophilic and hydrophobic compounds, making them suitable carriers for essential oils like cinnamon. Liposomes are formed by phospholipids that self-assemble into bilayer structures in an aqueous environment. These structures can encapsulate cinnamon essential oil, protecting it from environmental degradation and enhancing its therapeutic properties. The typical liposome formulation involves incorporating CEO into a lipid mixture, often comprising phospholipids such as lecithin and cholesterol. Subsequent hydration leads to the spontaneous formation of liposomes. Characterization techniques, including dynamic light scattering (DLS) and transmission electron microscopy (TEM), provide valuable insights into liposome size, polydispersity, and morphology. Liposomes offer several advantages, including enhanced stability, controlled release, and improved bioavailability of encapsulated compounds. However, lipid composition, preparation method, and storage conditions can influence liposome characteristics and encapsulation efficiency [55]. Numerous studies have demonstrated the efficacy of liposomal encapsulation for CEO delivery. Antibacterial activity of liposomal cinnamon oil against methicillin-resistant Staphylococcus aureus (MRSA) has been shown in studies [56]. Ellboudy et al. reported the successful development of cinnamon oil-loaded nanoliposomes with potent antibacterial and antibiofilm properties [38]. Comparative studies have highlighted the distinct advantages of liposome and emulsion systems for encapsulating cinnamon essential oil (CEO). Liposomes, composed of phospholipids and often cholesterol, have demonstrated superior stability and controlled release properties compared to emulsion systems. This enhanced performance is attributed to the liposomal bilayer structure, which effectively protects the encapsulated CEO from degradation. In contrast, emulsions typically utilize a combination of CEO, surfactant, and an aqueous phase. While emulsions offer certain advantages, such as ease of preparation, they often exhibit lower stability than liposomes [57] . In the other study by Chen et al., prepared cinnamaldehyde-loaded liposomes with three different core-wall ratios (10%, 20%, and 30% cinnamaldehyde) to investigate the effect of this parameter on the stability and antibacterial activity of the liposomes during storage. Result exhibited cinnamaldehyde-loaded liposomes with higher lipid-to-drug ratios had better retention of the active compound during storage [39].

Pulse laser ablation in liquid (PLAL)

The PLAL is an emerging and innovative method for synthesizing cinnamon NPs. This technique offers unique advantages in producing high-purity NPs with controlled size and morphology. A key

advantage of PLAL is its eco-friendly nature, as it avoids using harmful chemicals often associated with other synthesis methods. Moreover, the technique offers precise control over nanoparticle size and morphology, facilitating the production of NPs with tailored properties. The choice of liquid medium can significantly influence the resulting nanoparticle characteristics [58]. Several studies have explored the potential of PLAL for cinnamon nanoparticle synthesis. Salim et al. synthesized crystalline cinnamon NPs (CNPs) via pulse laser ablation of cinnamon immersed in methanol. By varying the laser fluency, they could control the CNP structure, morphology, and optical properties. Characterization using UV-Vis spectroscopy, FTIR, XRD, TEM, and DLS revealed that the NPs formed were around 20-50 nm in size with a crystalline, face-centered cubic structure. Compared to bulk cinnamon extract, the laser-generated CNPs exhibited enhanced antibacterial activity in assays against *E. coli*, *S. aureus*, *B. subtilis*, and *P. aeruginosa*, likely due to their larger specific surface area, enabling stronger interaction with bacterial membranes. This green synthesis approach for producing low-cost CNPs with potent antibacterial action represented an innovative application of traditional spice compounds at the nanoscale [59]. Al-Azawi et al. focused on the optical and structural characterization of cinnamon NPs produced via PLAL, providing insights into their properties [40]. Gondal et al. investigated the impact of different liquid media on the resulting nanoparticle morphology, emphasizing the importance of medium selection in PLAL [60]. Hamad et al. successfully synthesized spherical cinnamon nanoclusters with antibacterial properties using PLAL, highlighting the technique's potential for biomedical applications [41].

Lonic gelation

Ionic gelation is a versatile technique for encapsulating bioactive compounds, including CEO. This method leverages the electrostatic interactions between oppositely charged polymers to form polymeric matrices encapsulating the desired substance. Chitosan, a positively charged biopolymer, is commonly employed as the primary material due to its biocompatibility, biodegradability, and mucoadhesive properties. A negatively charged cross-linking agent, such as sodium tripolyphosphate (TPP), is typically used to induce gelation. The process involves mixing a chitosan solution containing CEO with a TPP solution, leading to the formation of NPs through electrostatic interactions. This method offers several advantages, including simplicity, cost-effectiveness, and the ability to control particle size and release kinetics. Moreover, using biocompatible polymers enhances the safety and potential applications of the encapsulated product, particularly in the food and pharmaceutical industries. While ionic gelation is a promising technique, optimizing parameters such as polymer concentration, pH, and temperature is crucial for achieving desired nanoparticle characteristics and encapsulation efficiency [61, 62].

Studies have demonstrated the successful encapsulation of CEO within chitosan NPs, resulting in particles with an average size of 100-190 nm and high encapsulation efficiency. These encapsulated CEO formulations have shown extended shelf life for food products, such as cucumbers [63], while also exhibiting antimicrobial activity against various microorganisms, including Candida and Leishmania species [64]. The encapsulation process protects CEO from degradation, allowing for controlled release of its bioactive compounds.

Nanoprecipitation

The precipitation method constitutes a versatile approach for encapsulating CEO and its bioactive constituents within a nanoparticulate matrix. This technique involves the dissolution of CEO and a suitable carrier material in a solvent, followed by the rapid induction of precipitation by adding an antisolvent. The resulting NPs exhibit controlled size and morphology, facilitating their incorporation into various applications. Key advantages of the precipitation method include its simplicity, scalability, and potential for achieving high encapsulation efficiency. This technique is particularly suitable for thermolabile compounds, as it minimizes exposure to elevated temperatures [65]. Studies have explored the application of nanoprecipitation for cinnamon encapsulation. Muhammad et al. synthesized stable shellac NPs loading cinnamon bark extract through anti-solvent precipitation. SEM revealed uniform, smooth spherical particles in the 150-200 nm range. The NPs exhibited similar antioxidant activity to reference standards and released over 90% cinnamon polyphenols at intestinal pH. Significantly, nanoencapsulation enhanced thermal stability, retaining over 90% of

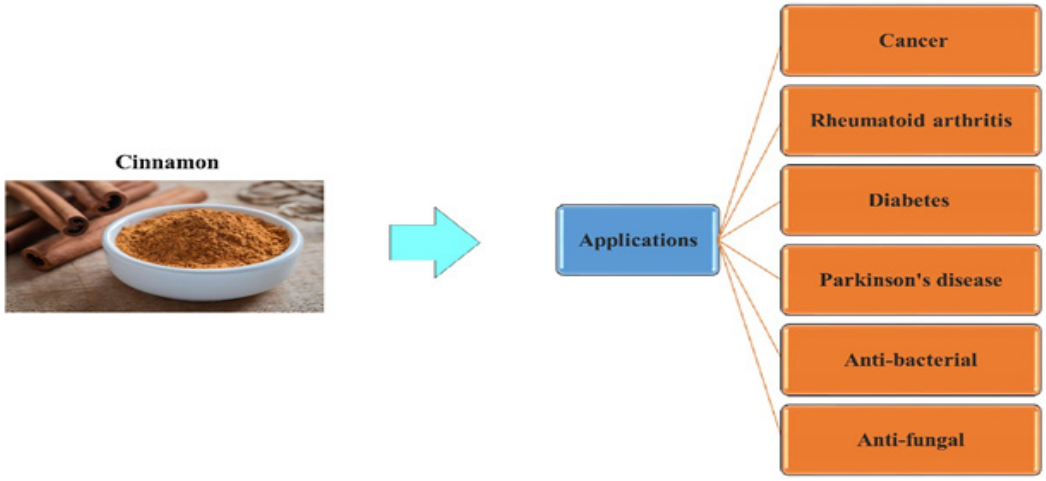

Fig. 2. Overview of the potential biomedical applications of cinnamon.

polyphenols after heating to 90°C [44]. Liu et al. (2021) successfully employed chitosan and whey protein as carrier materials to encapsulate CEO, resulting in nanocapsules with enhanced stability and retention of volatile compounds [33].

Therapeutic role of nano-cinnamon in various conditions

Cinnamon has been traditionally used for its antimicrobial properties and contains diverse bioactive compounds imparting health benefits.

Key disease areas like colon cancer, ovarian cancer, breast cancer, lung cancer, rheumatoid arthritis, diabetes and Parkinson's disease where cinnamon NPs were investigated as drug carriers are discussed in this section. The different applications of cinnamon NPs are summarized in figure 2 and table 2.

Cancer

Cinnamon and its bioactive compounds have shown promising anticancer properties, particularly when formulated as NPs. Considering the severe side effects of chemotherapy and radiation that diminish quality of life, natural agents hold worthy promise as complementary approaches [85]. Cinnamon extracts contain bioactive polyphenols like cinnamaldehyde exerting apoptotic, anti-oxidant and anti-inflammatory activities against various cancer types [86]. These nanostructures exhibit a multifaceted mechanism of action, encompassing apoptosis induction, angiogenesis inhibition, anti-proliferative effects, and antioxidant properties. By modulating apoptotic pathways, inhibiting tumor neovascularization, and interfering with cell cycle progression, cinnamon NPs demonstrate potential as effective anticancer agents. Furthermore, their antioxidant capacity contributes to their overall therapeutic efficacy by mitigating oxidative stress, a critical hallmark of cancer progression [87, 88].

Kamel et al. prepared chitosan-coated solid lipid NPs (SLNs) loaded with cinnamon and oregano extracts. The combination of cinnamon/oregano-loaded SLNs with 5-fluorouracil (5-FU) demonstrated enhanced therapeutic efficacy compared to 5-FU alone. This combination regimen exhibited reduced side effects while maintaining therapeutic efficacy, suggesting a potential advantage over conventional chemotherapy. Notably, the nanoencapsulated cinnamon/oregano extracts displayed superior cytotoxic activity compared to their unencapsulated counterparts, highlighting the benefits of the SLN delivery system [66].

Alkhatib et al. developed a cinnamon oil nanoemulsion loaded with bleomycin against cervical cancer HeLa cells. In vitro testing demonstrated over 50% inhibition of cell viability, exceeding free bleomycin. Apoptosis was markedly elevated as well, seen in higher apoptosis levels, morphological alterations and DNA fragmentation induction [89].

Cinnamon-lactobionic acid (CLC) hybrid NPs represent a promising strategy for cancer treatment by combining targeted delivery with oxidative stress-induced cytotoxicity. The incorporation of lactobionic acid confers tumor-targeting capabilities, while cinnamaldehyde acts as a potent generator of ROS. This

Table 2. Summary of Therapeutic Roles of Nano-Cinnamon.

Nanoparticles	Size (nm)	Applications	Experimental model/Route of administration	Results	References
Chitosan-Coated Cinnamon/Oregano-Loaded Solid Lipid NPs	254.77	Colorectal cancer	HCT-116 cell line	Achieving treatment for human colon carcinoma with reduced side effects	[66]
Cinnamon Silver NPs	201	Liver cancer	Bj-1 normal cells and HepG-2 cancer cell line	Higher antioxidant activity higher anti-proliferative effects	[67]
Cinnamaldehyde-modified chitosan hybrid /doxorubicin NPs	296.1	Liver cancer	H22 cell line HepG2 cell line Mice tumor model/ Intravenous (I.V.) injection	Anticancer activity with ROS-induced apoptosis	[68]
Chitosan NPs loaded with cinnamon essential oil	215.4	Breast cancer	4T1 breast cancer cell line and transplanted into mice/ Intraperitoneal (IP) injection	Enhanced stability and potent antitumor activity	[69]
Chitosan NPs Containing Cinnamomum	161 ± 6	Melanoma and Breast Cancer	A-375 and MDA-MB-468 cells	Significant inhibitory effects against melanoma and breast cancer cells	[70]
Vitamin D encapsulated cinnamon oil nanoemulsion	40.52 - 48.96	Lung cancer Bacterial infection	A549 cells E. coli	Exhibit cytotoxic, genotoxic, and antibacterial potential	[71]
Cinnamon nanocomplex loaded with MTX	8.317	Arthritis	Complete Freunds (CFA Adjuvant) in male albino rats/ Oral	Reduced arthritis effects, lowered IL-8 levels, and improved histological parameters.	[72]
Cinnamon nanocomplex loaded with MTX	8.317	Rheumatoid arthritis	Complete Freunds (CFA Adjuvant) in male albino rats/ Oral	Anti-arthritic effects, reduced IL-1β and IL-6 levels, and inhibited inflammatory cytokines in RA-induced rats	[73]
Nano-Cinnamomum Capsule	10	Type 2 Diabetic	High fat diet and STZ induced diabetic rat/ Oral	Reduced HbA1C, fasting blood sugar, triglycerides, and BMI in diabetic rats	[74]
Cinnamon NPs + HAMLET	10 to100	Infection and Diabetes	Infected with MRSA in Diabetic Rats/ Topical application on the wounds	Accelerated healing of MRSA-infected diabetic wounds	[75]
Silver/gold nano-cinnamon	45.34	Diabetes	STZ induced diabetic rat/ Oral	Exhibited antihyperglycemic effects, improved insulin sensitivity, and decreased body weight in diabetic rats	[76]
Cinnamon leaf nanoemulsion	30.1	Parkinson's disease	Rotenone induced rat Parkinson disorder model/ Tube Feeding	Demonstrated stability and improved Parkinson's disease symptoms in rats, including increased dopamine levels, reduced α-synuclein levels, and enhanced antioxidant enzyme activities	[32]

Nanoparticles	Size (nm)	Applications	Experimental model/Route of administration	Results	References
Cinnamon oil nanoemulsion	65	Anti-bacterial	*Bacillus cereus*	Bactericidal efficacy against *Bacillus cereus*, altering membrane permeability	[77]
Cinnamon oil and silver NPs	15 to 50	Anti-bacterial	*Streptococcus agalactiae*	Antimicrobial and antibiofilm activity against multidrug-resistant *S. agalactiae*, with synergistic effects observed in their combination	[78]
Cinnamon oil emulsion-zein-pectin composite NPs	660.8 ± 8.1	Anti-bacterial	*Alternaria alternata* and *Botrytis cinerea*	Improved antimicrobial activity against food-related microorganism	[36]
Cinnamon oil loaded solid lipid NPs	337.6	Anti-bacterial	*E. coli*	Enhanced antibacterial activity against drug-resistant *E. coli*, with reduced MIC values and inhibition of biofilm formation	[79].
Fusidic Acid-Cinnamon Oil Nano-Lipid Carrier	209 ± 2.6 - 308 ± 4.8	Anti-bacterial	*S. aureus, E. coli*	Exhibited stability, extended release, and enhanced antibacterial activity against multidrug-resistant bacteria	[80]
Chitosan or SLN nano-delivery for cinnamon oil	40.65 116.1	Anti-bacterial	*Klebsiella pneumonia, E. coli*	Increase in antibacterial effect	[81]
AgNPs/ cinnamon	20-50	Anti-bacterial	*Salmonella, Pseudomonas, Staphylococcus, and E. coli*	Exhibited antibacterial properties	[82]
Nano-emulsion cinnamon oil	242–362	Anti-fungal	*A. niger and M. racemous*	Exhibited lower water vapor permeability (WVP) and increased strain at break (SAB). Improved antifungal activity against *Aspergillus niger* and *Mucor racemosus*	[83]
Cinnamon essential oil formulated in polycaprolactone (PCL) NPs	-	Anti-fungal	*Candida auris.*	Exhibited comparable antifungal efficacy against *Candida auris*	[84]

synergistic approach enhances the efficacy of chemotherapeutic agents, such as doxorubicin (DOX). Preclinical studies have demonstrated the superior antitumor activity of DOX-loaded CLC NPs compared to free DOX or single-component nanoparticle formulations. These hybrid NPs effectively induce apoptosis, inhibit tumor growth, and overcome drug resistance challenges. The enhanced therapeutic efficacy is attributed to the combined effects of targeted delivery, ROS generation, and the synergistic interaction with chemotherapeutic agents. [68]. Similarly, Alkhatib et al. investigated a bleomycin-loaded cinnamon oil nanoemulsion against ovarian cancer SKOV-3 cells.

Compared to free bleomycin, the nanoemulsion showed significantly higher cytotoxicity in vitro as evidenced by greater morphological changes and apoptotic indices including Annexin V-FITC binding (28.9% vs 11.5%) and caspase-3 activation [90].

Kamyar et al. prepared chitosan NPs encasing either cinnamon essential oil or its main constituent, cinnamaldehyde. Characterization demonstrated the NPs could entrap the cargo efficiently. In vitro cytotoxicity screening found cinnamon oil-loaded NPs more potently inhibited melanoma and breast cancer cell lines versus free cinnamon oil or cinnamaldehyde, as evidenced by lower IC_{50} values [70]. Moreover, a recent study encapsulated cinnamon extract in PLGA NPs and evaluated particle size, antioxidant activity, and cytotoxicity against C6 brain cancer cells. NPs maintained cinnamon's antioxidant capacity while inhibiting cancer cell growth, suggesting potential as a glioblastoma treatment when optimized [91].

Accumulating research suggests cinnamon holds therapeutic potential against breast cancer. Bioactive phenolics like cinnamaldehyde in cinnamon essential oil induce apoptosis through caspase activation and suppressing tumor growth in breast cancer models. Towards this, Xu et al. developed chitosan NPs loaded with cinnamon essential oil (CS-CEO) for enhanced stability and intracellular transport. CS-CEO were uniformly spherical with a size of 215.4 nm, retained anticancer properties after storage, and exhibited improved inhibition of breast cancer cell proliferation and tumor growth compared to free cinnamon oil in vitro and in vivo. Mechanistically, CS-CEO upregulated caspase-3 and AIF apoptotic proteins to a greater extent [69].

Rheumatoid arthritis

Rheumatoid arthritis (RA) is a chronic, systemic inflammatory condition characterized predominantly by joint involvement. The worldwide distribution of RA varies, with typically higher reported rates in more developed nations potentially attributable to environmental exposures, diverse population demographics, and underdiagnosis in other regions. It causes painful swelling and stiffness of the joints, disability, reduced quality of life, and increased mortality risk from comorbidities like cardiovascular disease. Current treatments aim to control symptoms, slow disease progression, and minimize joint damage through nonsteroidal anti-inflammatory drugs, disease-modifying antirheumatic drugs, glucocorticoids, and biologics that target specific inflammatory pathways. However, these therapies carry adverse effects that diminish adherence and expose patients to comorbidity risks. Thus, safer adjuvant therapies derived from natural products hold appeal [92].

Cinnamon contains bioactive compounds with potent anti-inflammatory and antioxidant properties, making it a promising candidate for managing RA pathological processes. Recent studies have evaluated cinnamon supplementation for RA symptoms and investigated cinnamon-based nanodelivery systems [93-95]. Intisar Mohammed and Kiaser Abdulsajjad encapsulated cinnamon compounds into NPs and administered them to arthritic rat models. X-ray and inflammatory marker analyses demonstrated the cinnamon nanocomposite mitigated joint deformities, tissue damage, and elevated IL-1β and IL-6 levels approximately 50% versus controls, showcasing potent anti-arthritic properties partially mediated by cytokine inhibition [72]. In other work, the researchers evaluated methotrexate-loaded cinnamon nanocomplexes in rats. The nanocomplex treatment normalized histological changes, reduced IL-8 concentrations and white blood cell counts significantly more than plain cinnamon or arthritic controls, indicating additive anti-inflammatory impacts beyond methotrexate alone through cinnamon's antioxidant actions [73]. Collectively, these investigations underscore cinnamon's therapeutic potential for RA via modulating inflammatory and oxidative stress pathways central to disease pathogenesis. Developing standardized cinnamon formulations and further exploring nanotechnology-based delivery may optimize cinnamon's bioavailability and efficacy as an adjunct or natural alternative to conventional RA therapies.

Diabetes

Diabetes mellitus is a widespread metabolic disorder typified by hyperglycemia that has numerous serious long-term complications if left uncontrolled. Research explores herbal medicines like cinnamon, ginger, garlic and aloe vera as safer alternatives to standard therapies, seeking to modulate insulin signaling, oxidation and inflammation underlying the condition [96]. Cinnamon NPs have emerged as a promising therapeutic strategy for addressing

the complexities of diabetes mellitus. These nanoformulations exhibit several mechanisms of action contributing to their potential anti-diabetic effects. Firstly, cinnamon NPs have demonstrated insulin-mimetic properties, enhancing glucose uptake and cell utilization. This is particularly beneficial for individuals with type 2 diabetes who often experience insulin resistance. Secondly, these NPs can improve glucose metabolism by upregulating glucose transporter 4 (GLUT4) translocation, thereby facilitating glucose uptake into cells. Concurrently, they downregulate phosphoenolpyruvate carboxykinase (PEPCK) in the liver, reducing glucose production. Beyond glucose metabolism, cinnamon NPs exhibit antioxidant properties, which are crucial for mitigating oxidative stress associated with diabetic complications. Additionally, these NPs have shown potential in improving lipid profiles, thereby reducing the risk of cardiovascular diseases often comorbid with diabetes.

Cinnamon derivatives may downregulate toll-like receptor pathways and cytokines linked to inflammation, supporting cinnamon's potential to manage diabetes complications through modulating toll-like receptor signaling implicated in disease pathogenesis [96].

Some investigations synthesized cinnamon NPs for improved bioavailability in this condition. A study by Sengsuk et al. (2016) found that cinnamon supplementation significantly reduced fasting blood glucose, HbA1c, and improved lipid profiles in type 2 diabetes patients [97].

Elobeid synthesized silver/gold composite NPs loaded with cinnamon using a green method, then evaluated antidiabetic efficacy in streptozotocin-induced diabetic rats. The nano-cinnamon formulation demonstrated the most potent antihyperglycemic activity, decreasing glucose levels compared to metformin and plain cinnamon extracts. This enhancement resulted from improved insulin sensitivity when cinnamon was delivered via the nanocarrier [76]

Research by Talaei et al. (2017) demonstrated that cinnamon consumption reduced glycemic indicators and advanced glycation end products in type 2 diabetic patients [98].

A meta-analysis by Deyno et al. (2019) concluded that cinnamon supplementation improved glycemic control in diabetes and pre-diabetes patients [99].

In a recent study by Ali et al., investigate the effects of the cinnamon NPs and HAMLET (human alpha-lactalbumin made lethal to tumor cells) on wound healing in diabetic rats infected with methicillin-resistant *S. aureus*. HAMLET is a protein-lipid complex derived from human milk. HAMLET's function is characterized by its ability to disrupt cell membranes, leading to cell death in tumor cells and bacteria. This mechanism, combined with its potential to modulate wound healing processes, makes HAMLET a promising therapeutic agent for various conditions, including cancer, bacterial infections, and wound healing. The dual treatment group exhibited significantly accelerated healing based on reduced wound area and bacterial load and enhanced tissue regeneration versus cinnamon NPs alone [75]. Another study developed nano micelle cinnamomum and evaluated its effects on blood glucose and lipids in streptozotocin-induced diabetic rats. Parameters measured before and after 4 weeks of treatment revealed nano-cinnamon significantly reduced HbA1c, fasting glucose, triglycerides, BMI levels compared to pretreatment. This suggests nano-cinnamon helped blood sugar controlling and beneficially impacted metabolic markers in diabetes [74].

Collectively, these studies underline cinnamon's therapeutic functionality for diabetes and demonstrate nanotechnology augments its bioactivity, offering a perspective for developing standardized cinnamon nanoformulations and delivery strategies to combat diabetes and its prevalent complications.

Parkinson's disease (PD)

Parkinson's disease (PD) is the second most common neurodegenerative disorder characterized by progressive loss of dopaminergic neurons in the substantia nigra pars compacta and the presence of intracellular Lewy bodies. The precise cause remains elusive, and current treatments only manage motor symptoms, with no disease-modifying options available [100-102]. This presents an urgent need to explore novel therapeutic strategies, including herbal medicines, as more efficient and safer alternatives. Cinnamon and its derived compounds have garnered significant attention for their potential neuroprotective effects in PD. The spice's capacity to mitigate oxidative stress, reduce neuroinflammation, and inhibit α-synuclein aggregation presents promising avenues for

therapeutic intervention. By safeguarding dopaminergic neurons from oxidative damage and autophagy dysfunction, cinnamon compounds contribute to neuroprotection. Additionally, the spice's ability to modulate the TLR/NF-κB pathway, a key inflammatory signaling pathway, offers potential benefits in reducing neuroinflammation associated with PD. Furthermore, cinnamon's influence on α-synuclein aggregation, a pathological hallmark of PD, underscores its potential to slow disease progression [30]. Preclinical studies have demonstrated the neuroprotective potential of cinnamon in PD models. Oral administration of cinnamon powder and its metabolite, sodium benzoate, has shown promising results in ameliorating PD-associated symptoms. These studies have reported improvements in motor function, normalization of neurotransmitter levels, and protection of dopaminergic neurons. Moreover, upregulation of neuroprotective proteins, such as Parkin and DJ-1(two essential proteins involved in maintaining neuronal health, particularly in the context of PD), has been observed, suggesting a potential mechanism for cinnamon's beneficial effects [103]. Additionally, the formulation of cinnamon into nanostructures, such as gold-cinnamon leaf nanoemulsions, has been explored to enhance its bioavailability and therapeutic efficacy. These nanoformulations have demonstrated increased antioxidant capacity and reduced oxidative damage in PD models [104].

Anti-bacterial

Bacterial pathogens pose a significant threat to human health, as they are capable of causing severe infectious diseases. While conventional antibiotics have historically been utilized for treating such infections, widespread antibiotic overuse and misuse have led to a worrisome rise in multidrug-resistant bacterial strains in recent decades [105]. This underscores an urgent need to explore novel antibacterial agents with activity against antibiotic-resistant bacteria. Cinnamon is a spice with a long history of traditional medicinal uses and contains an array of bioactive phytochemicals conferring antimicrobial properties [106].

One primary mechanism of action involves the disruption of bacterial cell membrane integrity, leading to leakage of intracellular components and subsequent cell death. Moreover, cinnamon NPs induce oxidative stress by generating reactive oxygen species (ROS), which damage essential cellular components such as proteins, lipids, and DNA. Another critical aspect of their antimicrobial activity is the inhibition of biofilm formation. Biofilms, extracellular polymeric substances produced by bacteria, confer increased resistance to antimicrobial agents. Cinnamon NPs have demonstrated the ability to disrupt this process, thereby enhancing the efficacy of antimicrobial treatments. Additionally, these NPs can interfere with bacterial quorum sensing, a cell-cell communication system that regulates biofilm formation and virulence factor production [107, 108].

Studies have consistently reported the antibacterial efficacy of cinnamon essential oil and extracts against a broad spectrum of Gram-positive and Gram-negative bacteria. Ghosh et al. developed a cinnamon oil nanoemulsion using ultrasonic emulsification and surfactants. Optimization of variables such as surfactant concentration and emulsification time yielded a stable formulation with 65 nm droplets. Interestingly, this nanoemulsion exhibited time- and concentration-dependent anti-bactericidal effects against *Bacillus cereus* through membrane disruption mechanisms. Microscopy, spectroscopy, and staining techniques revealed it altered permeability and caused deformation of phospholipids, membrane distortion, and cell lysis. These results demonstrated promise for using such nanoemulsions as a natural preservative against foodborne pathogens by leveraging cinnamon oil's membrane activity [77].

Researchers also worked to stabilize and deliver cinnamon compounds using nanoparticle carriers. Kumari and Sangal formulated cinnamon NPs approximately 10 nm in size using a solvent evaporation method and surfactants like PVA. These NPs achieved high encapsulation efficiency of cinnamon compounds and showed inhibition zones of 9-10 mm against pathogens like *S. aureus* and *B. pumilus* [109].

The antibacterial and antibiofilm activities of cinnamon essential oil nanoemulsion (CEON) against oral biofilms demonstrated that CEON inhibited the maturation of multi-species oral biofilms and the growth of oral microorganisms, including aciduric bacteria that cause dental caries [110].

Cinnamon oil and silver NPs (AgNPs) have demonstrated potent antimicrobial and antibiofilm activities against *Streptococcus agalactiae*, a

significant pathogen in bovine mastitis. Cinnamon oil exhibited superior antimicrobial efficacy compared to AgNPs, with significantly lower minimum inhibitory concentrations (MICs) against planktonic cells. Time-kill kinetic studies revealed the rapid bactericidal effect of cinnamon oil, achieving complete inhibition within four hours. Both cinnamon oil and AgNPs demonstrated antibiofilm properties, with cinnamon oil exhibiting greater efficacy in disrupting biofilm formation. Scanning electron microscopy (SEM) confirmed the destructive impact of cinnamon oil on biofilm architecture. Mechanistically, cinnamon oil was found to downregulate key genes involved in biofilm formation, suggesting its ability to interfere with biofilm development at the molecular level. The combination of cinnamon oil and AgNPs displayed synergistic effects in certain aspects of antimicrobial and antibiofilm activities. While the combination enhanced antimicrobial efficacy, its antibiofilm activity was less pronounced than cinnamon oil alone. These findings highlight the potential of cinnamon oil and its combination with AgNPs as promising alternatives to conventional antibiotics in managing bovine mastitis [78].

Shahabi, M. et al. evaluated the antibacterial activity of glass ionomer cement (GIC) containing cinnamon NPs against Streptococcus mutans. The results showed that GIC with cinnamon NPs exhibited significant antibacterial activity and lower cytotoxicity than other NPs [111].

In another work, Nemattalab et al. prepared cinnamon oil-loaded solid lipid NPs (CO-SLN) that exhibited enhanced antibacterial activity against 10 drug-resistant *E. coli* strains compared to free cinnamon oil, and antibiofilm assays found CO-SLN significantly reduced biofilm formation more effectively. The SLN stabilized and facilitated cinnamon oil transport through bacterial membranes [79]. Rohani et al. compared chitosan NPs loaded with cinnamon oil to SLN and found the former had higher encapsulation efficiency, released cinnamon oil more gradually, and were 6-10 times stronger antibacterially against *E. coli* and *K. pneumoniae* clinical isolates [81]. Different researchers have also combined cinnamon with other antimicrobial agents. Nagarajan et al. synthesized selenium NPs containing cinnamon extract which has comparable activity to commercial drugs when evaluated against oral bacteria [112]. Similarly, Elsewedy et al. optimized a fusidic acid-cinnamon oil nanoemulsion hydrogel, which maintained pH and viscosity stability for topical delivery while synergistically inhibiting multi-drug resistant pathogens more potently than individual components alone [80]. Also, the synergistic antibacterial properties of AgNPs combined with cinnamon were evaluated. The combination showed enhanced antibacterial activity, suggesting a promising potential for use as antimicrobial agents [113].

Anti-fungal

Invasive fungal diseases have emerged as an increasingly serious public health issue, suspiciously impacting patients with underlying conditions weakened by medical treatment [114]. Cinnamon has a history of traditional antifungal use [115].

Cinnamon NPs exhibit potent antifungal properties through multiple mechanisms of action. Primarily, they disrupt the integrity of fungal cell membranes, leading to leakage of cellular constituents and subsequent cell death. Additionally, these NPs induce oxidative stress within fungal cells by generating ROS, which damage critical cellular components. Cinnamon NPs also demonstrate efficacy in inhibiting fungal spore germination and mycelial growth, thereby preventing fungal infections. Furthermore, they can disrupt fungal biofilms, complex microbial communities that confer increased resistance to antifungal agents. This multifaceted approach to fungal cell disruption underscores the potential of cinnamon NPs as a promising antifungal agent [2, 116].

Recent investigations have explored harnessing cinnamon's antifungal powers through nanotechnology. Kumari and Sangal developed cinnamon-loaded PLGA NPs using a solvent evaporation method. These NPs inhibited growth with MIC of 4000 ppm and zones of inhibition around 7-8 mm against common fungal pathogens *Saccharomyces cerevisiae* and *Candida albicans*. Compared to raw cinnamon, drug release studies confirmed the NPs improved cinnamon's controlled release characteristics [109]. In other work, cinnamon oil nanoemulsions and macroemulsions were incorporated into carboxymethyl cellulose films. Scanning and atomic force microscopy revealed the nanoemulsion films exhibited a denser, more uniform microstructure versus macroemulsion films. Capitalizing on the nanoemulsion's improved stability, and the films

were thicker with lower water vapor permeability but greater flexibility. Both emulsified films demonstrated enhanced antifungal actions compared to controls, with the nanoemulsion films inhibiting fungal growth superior to the macroemulsion films [83]. The CEO loaded into mesoporous silica NPs (MSNPs) demonstrated significant antifungal activity, particularly against molds such as Mucor sp. and Mucor circinelloides. Incorporating CEO into MSNPs enhances its stability and slow-release properties, allowing for prolonged antifungal effects. The CEO-MSNPs can be utilized in biodegradable packaging films, providing an effective barrier against fungal contamination in food products, particularly post-harvest mushrooms [117]. More recently, Rosato et al. evaluated cinnamon essential oil (CC-EO) and its main component, cinnamaldehyde, in polycaprolactone NPs (nano-CC-EO), against *Candida auris strains*. Minimum inhibitory concentration (MIC) tests found equivalent antifungal activity for CC-EO (MIC 0.01 mg/mL) and nano-CC-EO (MIC 0.02 mg/mL) against planktonic and biofilm forms of *C. auris* [84]. Collectively, these studies highlight cinnamon's underutilized antifungal potential and how nanotechnological approaches amplify cinnamon's inherent activity by enhancing stability, targeting, and controlled delivery against medically-relevant fungi.

Antioxidant effects

Much research has explored harnessing cinnamon NPs to boost immunity and antioxidant defenses against oxidative stress and disease. Abdel-Tawwab et al. evaluated cinnamon nanoparticle (CNP) effects on Nile tilapia performance, finding improved growth, crude protein content, and digestive enzyme activities with increasing CNP levels versus controls. Notably, immune markers like nitric oxide, lysozyme, and nitroblue tetrazolium experienced significant elevations, and CNP-fed fish faced zero mortality against bacterial infection compared to 66.7% in controls. This demonstrated CNP's protective immunostimulatory impacts at the optimal 3.0 g/kg dietary level (Abdel-Tawwab et al., 2018).

El-Baz et al. highlighted that cinnamon silver NPs (CNPs) exhibit remarkable antioxidant properties. The assessment of these properties primarily involved measuring the DPPH (2,2-Diphenyl-1-picrylhydrazyl) radical scavenging activity, a common method to evaluate antioxidant potential. Results indicated higher DPPH radical scavenging percentages in both Bj 1 normal cells and HepG 2 cancer cells when treated with CNPs, in comparison to other cinnamon extracts and fractions. In terms of enzyme activity, the research verified several antioxidant enzymes, such as superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx), glutathione S-transferase (GST), and reduced glutathione (GSH). The CNPs positively influenced the levels of these biomarkers, enhancing their activity which, in turn, promotes cellular antioxidant defenses. The overall antioxidant effectiveness of the CNPs was higher than that of the other samples, exhibiting a lower IC50 value (55.6 µg/mL) compared to others—with the IC50 value of vitamin C noted as 5.4 µg/mL for context. Furthermore, the research found that CNPs showcased a higher antioxidant activity both inside and outside the cells compared to other cinnamon samples. [118].

Challenges, limitations, and future perspectives

While significant advances have been made in optimizing cinnamon delivery through nanotechnology, several challenges warrant further investigation. Firstly, more work is needed to standardize nanoparticle production methods to reproducibly synthesize cinnamon formulations with consistent physiochemical properties. Parameters like particle size, surface charge, composition, and encapsulation efficiency can impact biological performance. Developing scalable, green fabrication processes will be crucial for translational potential. Elucidating the composition of cinnamon NPs post-production and during degradation within biological systems poses a challenge. Advanced analytical tools will be needed to track changes over time and correlate bioactivity with specific constituents. Better insight into structure-activity relationships could guide more targeted formulation designs [119].

Toxicity profiling represents another important aspect requiring deeper exploration. While cinnamon is generally recognized as safe, nanoscale effects on biodistribution, metabolism, and clearance require comprehensive evaluation. Both acute and long-term toxicity of optimized cinnamon nanoparticle systems needs to be evaluated using multiple *in vitro* and *in vivo* models before clinical use [118].

Delivery route optimization is another

limitation, as most investigations to date have utilized oral or topical administration. Exploring alternative routes like inhalation, ocular, or injection could expand applications. Targeted delivery to specific organs or intracellular compartments also needs more focus [120].

Combinatorial approaches pairing cinnamon NPs with other therapeutic agents hold promise but synergistic mechanisms require deeper investigative. Multi-modal combinations may achieve additive or synergistic effects by attacking disease from complementary angles.

Regulatory affairs for cinnamon and its nanoparticles are essential to ensure their safety and efficacy in various applications, particularly in food and health products. The regulatory landscape is complex, as it must address the unique characteristics of nanomaterials, which can exhibit different properties compared to their bulk counterparts. Regulatory agencies, such as the Food and Drug Administration (FDA) and the European Medicines Agency (EMA), emphasize the need for rigorous safety assessments that include toxicological evaluations, biodistribution studies, and long-term exposure assessments to establish a risk-benefit balance before granting marketing authorization [121]. Moreover, quality assessments for NPs are conducted on a case-by-case basis, necessitating the development of standardized characterization methods to evaluate their pharmaceutical quality effectively [122].

On March 6, 2024, the FDA issued a safety alert about certain ground cinnamon products due to containing elevated levels of lead. Therefore, it is necessary to reduce chemical hazards through changes to agricultural or manufacturing practices.

Additionally, Clinical trials involving cinnamon have demonstrated its potential benefits in managing various health conditions. In recent years, several clinical trials have investigated the therapeutic potential of cinnamon, including its nanoparticles, particularly in the context of glycemic control and wound healing.

A double-blind, placebo-controlled trial investigated the influence of cinnamon on glycemic control in individuals with prediabetes. In this study involving 54 adults, participants received either 500 mg of cinnamon or a placebo thrice daily for 12 weeks. The results demonstrated that fasting plasma glucose levels remained stable in the cinnamon group while increasing in the placebo group. Additionally, there was a significant decrease in area under the curve (AUC) for plasma glucose during oral glucose tolerance tests (OGTT) among those receiving cinnamon [123].

In another randomized, placebo-controlled, triple-blind clinical trial involving 160 individuals with type 2 diabetes, researchers assessed the efficacy of cinnamon supplementation at a dosage of 3 grams per day over 90 days. The findings revealed statistically significant reductions in HbA1c levels (0.2%) and fasting blood glucose levels (0.55 mmol/L) in the cinnamon group compared to placebo, highlighting its potential as an effective adjunct treatment for glycemic control [124].

One notable study focused on the accelerative effect of cinnamon nanoparticles (CNPs) on wound healing in diabetic rats. This randomized controlled trial involved 50 diabetic male rats, where CNPs were applied topically to infected wounds. The results indicated a significant improvement in the wound healing rate in the CNP-treated group compared to control groups, suggesting the potential of cinnamon nanoparticles as a therapeutic agent for enhancing wound healing in diabetic conditions [125].

While promising preclinical evidence exists, clinical validation of cinnamon nanoparticle formulations is still lacking. Well-designed human feasibility and efficacy trials are necessary to translate this research toward approved therapeutic options [126].

CONCLUSION

In conclusion, the therapeutic application of cinnamon NPs holds great promise in nanomedicine. Cinnamon, with its rich phytochemical composition and diverse pharmacological activities, has long been recognized for its potential health benefits. However, harnessing nanotechnology to enhance the properties of cinnamon and enable targeted drug delivery has opened up new avenues for its therapeutic utilization. NPs offer numerous advantages as drug carriers, including their small size, biodegradability, and ability to cross biological barriers. By reducing particle size and employing formulation engineering, nanotechnological methods have overcome limitations such as poor solubility and instability associated with cinnamon. This has improved the bioavailability and efficacy of cinnamon-based treatments for various inflammatory and proliferative diseases. The synthesis and characterization methods of NPs are

crucial in optimizing the bioactivity and delivery of cinnamon. Various types of NPs, such as liposomes, polymeric NPs, and solid lipid NPs, have been explored for encapsulating cinnamon's bioactive compounds. These formulations enhance drug retention time, solubilize hydrophobic drugs, and improve targeting and penetration at specific sites. The applications of cinnamon NPs have shown promising results in preclinical investigations, both in vitro and in vivo. They have demonstrated potential in treating cancer, diabetes, arthritis, and neurological disorders. The ability of NPs to deliver therapeutic agents directly to the affected sites and their sustained-release properties contribute to improved treatment outcomes and reduced side effects.

AUTHOR CONTRIBUTION

M.H. had the idea for the article. A.A. and M.H. performed the literature search and drafted the work. F.K., S.M., and Z.S. review and edit the manuscript. All authors have read and revised it.

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No datasets were generated or analyzed during the current study.

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Not applicable.

CONFLICT OF INTEREST

The authors declare no competing interests.

RESEARCH INVOLVING HUMANS AND ANIMALS STATEMENT

None.

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