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Tree-derived spices: A phytochemical and pharmacological perspective

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Abstract

Tree-derived spices play a crucial role in global culinary and medicinal traditions and are emerging as significant sources of bioactive compounds with a range of pharmacological applications. This review summarizes current knowledge on the phytochemical and therapeutic profiles of key spices, including clove, cinnamon and nutmeg, among others. These spices are rich in bioactive compounds like polyphenols, terpenoids, and alkaloids, including eugenol, cinnamaldehyde, and myristicin, which contribute to their antimicrobial, antioxidant, anti-inflammatory, antidiabetic, and anticancer properties. These compounds act on critical pathways, viz., NF- κ B (nuclear factor kappa-light-chain-enhancer of activated B cells), AMPK (adenosine monophosphate-activated protein kinase) and Nrf2 (nuclear factor erythroid 2-related factor 2), and they can induce apoptosis in cancer cells by activating *Caspase-3* and *bax*. However, despite the potential benefits, safety concerns exist. For example, cinnamon contains coumarin, which can cause dose-dependent hepatotoxicity, while nutmeg's myristicin is associated with neurotoxicity, and there is also the risk of heavy metal contamination. Although, clinical evidence remains limited, notable exceptions exist, such as the validated antidiabetic effects of cinnamon, which illustrate its potential for real-world applications. The use of these spices in nutraceuticals, pharmaceuticals, and agrochemicals is growing, but challenges remain. Issues like ecological sustainability, standardization, and limitations in bioavailability can hinder progress. Future research should focus on fostering interdisciplinary collaboration, utilizing green nanotechnology for improved delivery, and conducting rigorous human trials. Addressing these gaps can enhance the integration of tree-derived spices into holistic healthcare, promoting their ethical and sustainable use.

1. Introduction

Throughout human history, spices have transcended their role as mere flavor enhancers, serving as bridges between culture, medicine, and commerce (Tripathi, 2024). They are derived from various plant parts such as seeds, bark, leaves, flowers, and fruits. Spices have been integral to traditional healing systems, from Ayurveda to traditional Chinese medicine (TCM), and continue to captivate modern science for their therapeutic potential (Dharmian *et al.*, 2024). India, often referred to as the spice bowl of the world, is endowed with a rich diversity of spices, contributes a significant role in world spices production and trade, especially for the major spices, viz., black pepper, cardamom, ginger, and turmeric. Besides the major spices, the diverse agroclimatic conditions prevailing in the Indian

subcontinent favour the production of seed spices like coriander, cumin, fennel, fenugreek, and tree spices (Sharangi *et al.*, 2018). Among these, tree spices occupy a unique niche, offering a rich repository of bioactive compounds shaped by the complex physiology and ecological interactions of their arboreal sources (Hanamashetti, 2011). Cinnamon (bark), cloves (flower buds), nutmeg (mace and kernels), allspice (berries), Garcinia (fruits), and Tamarind (pulp) exemplify how trees contribute globally significant spices with profound phytochemical and pharmacological value (Ilyas, 1978).

In recent decades, there has been growing interest in using natural products for developing new medicines and healthy food ingredients. Tree-derived spices, in particular, harbor a diverse array of secondary metabolites, viz., polyphenols, terpenoids, alkaloids, and phenylpropanoids that exhibit antioxidant (Mancini-Filho *et al.*, 1998), antimicrobial (Boyd *et al.*, 2013), anti-inflammatory (Schink *et al.*, 2018), antidiabetic (Arulmozhi *et al.*, 2007), antiobesity (Chuah *et al.*, 2013), anticancer (Dwivedi *et al.*, 2011), anesthetic (Hajek *et al.*, 2006), and hepatoprotective properties (Moselhy *et al.*, 2009). For example, eugenol from cloves and cinnamaldehyde from cinnamon are known for their strong health benefits and are used in both

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traditional medicine and modern drugs. Studies have confirmed that tree spices possess a high nutritional value, which is a result of their rich source of various essential oils, bioactives, alkaloids, flavonoids, phenolic acids, *etc.* According to Jiang (2019), tree spices possess several medicinal benefits that help prevent and treat diseases. These compounds have been known to exhibit beneficial effects such as antioxidant, anti-inflammatory, antitumorigenic, anticancer, hypercholesterolemia, and hypoglycemic characteristics (Shahidi and Hossain, 2018). There is evidence that certain chemicals, like cinnamaldehyde in cinnamon and eugenol in cloves, offer medicinal values, including the ability to regulate blood sugar levels and act as an antiseptic (Jiang, 2019). The tree spice, garcinia have been proven to possess anticancer bioactive molecules that have antioxidant and anti-inflammatory effects (Hemshakar *et al.*, 2011). Such findings also point to the use of tree spices as multi-purpose nutraceuticals with several positive health impacts (Raja *et al.*, 2015). Yet, despite their potential, these spices remain understudied compared to their herbaceous counterparts, with gaps in understanding their structure activity relationships, bioavailability, and ecological sustainability. This review seeks to consolidate current knowledge on the phytochemical profiles and pharmacological mechanisms of tree-derived spices, while addressing critical challenges such as over harvesting, habitat loss, and the need for sustainable cultivation. By synthesizing findings from ethnobotany, metabolomics, and clinical research, we aim to highlight their untapped potential in drug discovery, nutraceuticals, and eco-conscious agriculture. Ultimately, this work advocates for interdisciplinary collaboration to safeguard these natural treasures while unlocking their full scientific and economic promise.

2. Phytochemical diversity of tree-derived spices

Tree spices are a treasure house of bioactive compounds, evolved as part of the plant's defence mechanisms against pathogens, herbivores, and environmental stressors. These compounds, like polyphenols, terpenoids, alkaloids, and phenylpropanoids, not only give spices their unique taste and flavour but also contribute to their health benefits. Because of their complex structures and wide range of functions, they are highly valuable in medicine and nutrition (Figure 1).

2.1 *Cinnamomum verum* J.Presl

C. verum, a member of the Lauraceae family, is one of the oldest known spices, with its origins tracing to the southern regions of India. Renowned globally for its dual role as a culinary staple and a therapeutic agent in traditional medicine, this species derives its economic value primarily from its aromatic, thin brown bark. The bark serves as a rich reservoir of essential oils and bioactive compounds, which contribute to its distinct flavor, fragrance, and medicinal properties (Pathak *et al.*, 2021). The essential oil extracted from the bark of *C. verum* is particularly rich in cinnamaldehyde, which constitutes approximately 85.50% of its composition (Table 1). Other significant constituents include stigmasterol (3.69%), cadinene (1.37%), (E)-cinnamaldehyde (1.35%), alpha-amorphene (1.33%), hydro cinnamaldehyde (1.28%), alpha-cubebene (1.25%), and ergosterol (1.09%). These compounds contribute to the spice's characteristic aroma and are responsible for a wide range of pharmacological effects, including antimicrobial, antioxidant, and anti-inflammatory properties (Ahmed *et al.*, 2020) (Figure 1). Apart from cinnamaldehyde, procyanidins, and catechins, which are

flavonoids of the flavan-3-ols subgroup, may also be found in cinnamon bark (Lu *et al.*, 2018). The health advantages of cinnamon are attributed to these flavonoids, especially in terms of their antioxidant capacity, which lowers the risk of chronic illnesses and fights oxidative stress.

Moreover, phenolic compounds of various kinds are among the most prevalent bioactive components in cinnamon. According to Vallverdú-Queralt *et al.* (2014) they include ferulic acid, caffeic acid, rosmarinic acid, epicatechin, quercetin, protocatechuic acid, p-coumaric acid, p-hydroxybenzoic acid, syringic acid, and chlorogenic acid. The potent antioxidant qualities of these phenolic compounds are well-known, and they are essential in preventing oxidative damage to tissues and cells, which in turn contributes to the medicinal benefits of the spice.

2.2 *Syzygium aromaticum* L.

S. aromaticum, a member of the Myrtaceae family, is an evergreen tree indigenous to the Moluccas Islands (Indonesia). Its dried, unopened flower buds are the primary economic product, harvested for their intense aroma and bioactive richness. Clove's global significance stems from its dual role as a culinary spice and a traditional medicinal agent, attributed to its diverse phytochemical profile (Cortés-Rojas *et al.*, 2014). Clove contains over twenty bioactive components, predominantly polyphenols such as flavonoids (*e.g.*, quercetin, kaempferol), hydroxycinnamic acids (*e.g.*, caffeic acid, ferulic acid), hydroxybenzoic acids (*e.g.*, salicylic acid, ellagic acid), and hydroxyphenyl propenols. Among these, eugenol is the most abundant and pharmacologically significant compound, constituting 9.38-14.65 g/100 g of dried clove buds (Table 2). Clove buds notably surpass other botanical sources (cinnamon, basil, and nutmeg) in eugenol content, with concentrations reaching up to 180 mg/g (Hussain *et al.*, 2017). Eugenol is a colorless to pale-yellow phenolic compound responsible for clove's characteristic aroma and therapeutic properties (Raja *et al.*, 2015). It is recognized as safe by the World Health Organization (WHO), it holds generally recognized as safe (GRAS) status at doses below 1.5 g/kg body weight/day. Eugenol is used in aromatherapy, food flavoring, perfumes, soaps, detergents, beverages, and food. (Cortés-Rojas *et al.*, 2014) (Table 3).

Iso-eugenol, a commercial precursor for vanillin, can be produced by isomerizing eugenol from Clove leaf oil. β -Caryophyllene, a natural bicyclic sesquiterpene found in 9% of cloves, has numerous beneficial properties for humans, including antioxidant, anti-inflammatory, antidepressant, antitumor, neuroprotective, analgesic, and anti-allergic activity (Hiwandika *et al.*, 2021).

2.3 *Myristica fragrans* Houtt.

M. fragrans, belonging to the family Myristicaceae, is an evergreen tree native to the Moluccas Islands of Indonesia and is vital to the confectionery, culinary, and pharmaceutical industries. Essential oil is extracted from multiple parts of the nutmeg; namely, the leaf, mace, seed, and kernel, with oil yields of 0.7-3.2%, 8.1-10.3%, 0.3-12.5%, and 6.2-7.6%, respectively (Ashokkumar *et al.*, 2021). The oil, a colorless to light yellow liquid with a distinct spicy odor (Francis *et al.*, 2019; Rahman *et al.*, 1999) contains a wide range of bioactive compounds including monoterpenes (sabinene, β -pinene, β -terpineol, p-menth-8-en-1-ol, and terpinen-4-ol), phenylpropenes (eugenol, methyl eugenol, and myristicin), and sesquiterpenes (germacrene D and β -bergamotene), along with myristic acid, fatty

acids, and other volatile oils, which together contribute to its unique chemical profile and therapeutic potential (Sultan *et al.*, 2023) (Table 2). The major constituents of the leaf were sabinene, eugenol, myristicin, caryophyllene, and β -myrcene. Sabinene, α -pinene, β -pinene, D-limonene, and 3-carene were predominant constituents of mace. The major constituents of the kernel and seed were sabinene, α -pinene, β -pinene, D-limonene, and β -myrcene (Ashokkumar *et al.*, 2022). Nutmeg also has hallucinogenic effects due to the presence of hallucinogenic phenylpropanes, which are considered harmful for frequent users (Naeem *et al.*, 2016).

2.4 *Pimenta dioica* L. (Merr.)

P. dioica, a member of the Myrtaceae family, is a small evergreen tree indigenous to the West Indies, renowned for its distinctive flavor, a harmonious blend reminiscent of cinnamon, clove, and nutmeg (Nagalakshmi *et al.*, 2023). The essential oil, a volatile liquid extracted from various plant parts including the bark, bud, flower, fruit, leaf, root, and stem, is particularly significant for its high eugenol content (68.06%). The other notable constituents present in all spices are methyl eugenol (9.37%), α -phellandrene (6.67%), 1, 8-cineole (1.65%), α -humulene (1.51%), terpinolene (1.36%), and β -phellandrene (1.34%), each contributing to its aromatic complexity and diverse applications in culinary and pharmaceutical industries (Jarquín-Enríquez *et al.*, 2021). The extraction of phytochemicals from *P. dioica* berries using ethanol solvent yielded 0.790 mg, with ethanol being the most suitable solvent. The ethanol extracts contained various constituents such as tannins, saponins, flavonoids, coumarins, alkaloids, terpenoids, phenols, sugars, steroids, and betacyanin. The extract also contained eugenol, a phenolic compound, and other compounds (Nagalakshmi *et al.*, 2023).

2.5 *Garcinia* spp.

Garcinia species are renowned for their therapeutic properties owing to their rich secondary metabolites including xanthenes, flavonoids, benzophenones, lactones, phenolic compounds, and organic acids with hydroxycitric acid (HCA) playing a pivotal role in inhibiting fatty acid and cholesterol biosynthesis while also contributing to notable antioxidant activities (Jena *et al.*, 2002). In South India, particularly in the Konkan region and the Western Ghats of Kerala, two species stand out: *G. gummi-gutta* (syn. *G. cambogia*, known locally as kudanpuli) and *G. indica*. *G. gummi-gutta* is traditionally used as a flavoring agent especially in fish curries and its acidic fruit rind, containing approximately 10.6% tartaric acid alongside other bioactives such as flavonoids, terpenes, polysaccharides, and various polyisoprenylated benzophenones, is employed for treating gastrointestinal ailments like diarrhea and ulcers (Semwal *et al.*, 2015).

Meanwhile, *G. indica* is celebrated not only for its healthy fruit juice and spice-like dried rind rich in HCA, which serves as an antiobesity agent, but also for its kokum butter, which is derived from the seeds and finds applications in food, cosmetics, and medicine. In addition, *G. indica* is notable for its high levels of anthocyanins (specifically cyanidin-3-glucoside and cyanidin-3-sambubioside) and benzophenone derivatives such as garcinol, compounds that contribute to its antioxidant and cytotoxic properties, further underscoring the nutraceutical potential of these species (Lim *et al.*, 2021). *Garcinia* plant extracts have antioxidant activities, including DPPH radical scavenging and lipid peroxidation. Studies have explored extracting, determining chemical components, and applying *Garcinia* products in food and pharmaceutical technology (Patil *et al.*, 2015).

Table 1: Phytochemicals and their molecular formula of tree spice compounds

S.No.	Phytochemical	Molecular formula
1.	Cinnamaldehyde	C ₉ H ₈ O
2.	Eugenol	C ₁₀ H ₁₂ O ₂
3.	Myristicin	C ₁₀ H ₆
4.	Sabinene	C ₁₀ H ₁₂ O ₂
5.	Elemicin	C ₁₂ H ₁₆ O ₃
6.	Methyl eugenol	C ₁₁ H ₁₄ O ₂
7.	1,8-Cineole	C ₁₀ H ₁₈ O
8.	Terpinolene	C ₁₀ H ₁₆
9.	Hydroxycitric acid	C ₆ H ₈ O ₈
10.	Garcinol	C ₃₈ H ₄₆ O ₉
11.	Tartaric acid	C ₄ H ₆ O ₆

2.6 *Tamarindus indica* L.

T. indica, belonging to the family Caesalpinaceae and native to tropical Africa, exhibits a diverse chemical profile that varies across its different parts. The plant contains an array of bioactive constituents, including phenolic compounds, cardiac glycosides (Pino *et al.*, 2002), tartaric acid, mucilage, pectin, fatty acids, and essential elements, viz., Ca, Cu, Fe, Mn, and Mg (Meher *et al.*, 2014). Its leaves predominantly contain limonene and benzyl benzoate, while the root bark is abundant in compounds like n-hexacosane, eicosanoic acid, $\hat{\alpha}$ sitosterol, (+)-pinitol, octacosanyl ferulate, and 21 oxobeheic acid. The seeds are rich in fatty acids, namely palmitic, oleic, linoleic, and eicosanoic acids, and their unsaponifiable fraction includes β -amyryn, campesterol, and β sitosterol (Aida *et al.*, 2001). Additionally, the polyphenolic content of Tamarind is dominated by proanthocyanidins, including apigenin, catechin, procyanidin B2, as well as taxifolin, eriodictyol, and naringenin (Sudjaroen *et al.*, 2005), with the seeds comprising mainly oligomeric procyanidins. On the other hand, the fruit pulp contains tartaric, acetic, citric, formic, malic, and succinic acids (Shehla Imam *et al.*, 2007). The stem bark of the tamarind plant contains flavonoids, cardiac glycosides, alkaloids, saponins, and tannins. Tea made from the stem bark is used for a sore throat. The stem bark has many bioactive activities, which are spasmogenic, analgesic, antimicrobial, and hypoglycemic. Tamarind fruit pulp contains vitamins, minerals, amino acids, inverted sugar (25-30%), pectin, protein, fat, some pyranzines, and some thiazoles. Also, it has alkaloids, flavonoids, saponins, and tannins. Tamarind pulp has many bioactivities such as hypolipidemic activity, antioxidant, antifluorose, analgesic, hepatoregenerative, and antispasmodic (Menezes *et al.*, 2016). The most extraordinary attribute of tamarind fruit is its acidity, which is because, for the most part, tartaric acid (2,3-dihydroxybutanedioic acid, C₄H₆O₆) extends from 12.3% to 23.8%, which is unprecedented in other plant tissues (Ulrich, 1970). Fruit pulp contains bioactive compounds including 5-hydroxymethylfurfural (31.06%), 3-O-methyl-d-glucose (16.31%), 1,6-anhydro- β D-glucopyranose (9.95%), 5-methyl-furancarboxaldehyde (3.2%), triethylenediamine (1.17%), 1-(2-furanyl)-1-propanone (2.18%), methyl 2-furoate (3.14%), levoglucosenone (3.21%), methyl ester-hepta-2,4-dienoic

acid, (8.85%), 2,3-dihydro-3,5-dihydrox-4H-pyran-4-one (3.4%), O- α -dglucopyranosyl- β -D-fructofuranosyl- α -D-glucopyranoside (2.18%), n-hexa decanoic acid (1.38%), 2-heptanol, acetate (1.29%),

5-[(5-methyl-2-fur-2-Furancarboxaldehyde (1.08%), 3-methyl-2-furoic acid (1.05%) and cis-vaccenic acid (2.85%) (Fagbemi *et al.*, 2022).

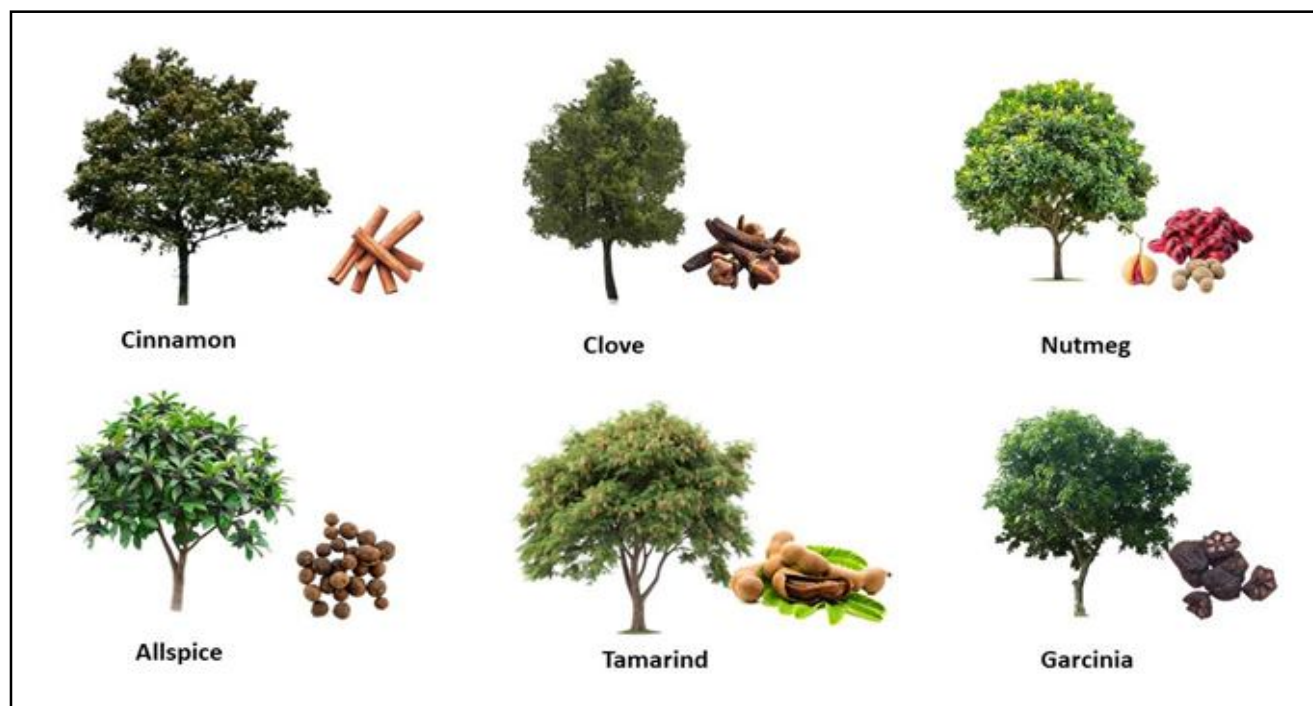


Figure 1: Important tree spices and their economic parts.

Table 2: Bioactive compounds and its therapeutic uses in various tree spices

Spices	Key phytochemicals	Pharmacological activity	Mechanism	References
Cinnamon	Cinnamaldehyde, Epicatechin-equivalent polyphenols, Proanthocyanidins	Antidiabetic, Antioxidant, Hepatoprotective	Activates AMPK; suppresses NF- κ B; upregulates SOD, CAT, GPx enzymes.	Lin <i>et al.</i> , 2003 Eidi <i>et al.</i> , 2012 Gunawardena <i>et al.</i> , 2015 Hayward <i>et al.</i> , 2019 Mohapatra <i>et al.</i> , 2023 El-Baz <i>et al.</i> , 2023
Clove	Eugenol, β -caryophyllene	Antimicrobial, Anti-inflammatory, Anesthetic	Disrupts microbial cell membranes; inhibits COX-2, NF- κ B; modulates GABA receptors.	Keene <i>et al.</i> , 1998 Gülçin <i>et al.</i> , 2012 Bachiega <i>et al.</i> , 2012 Mohapatra <i>et al.</i> , 2023
Nutmeg	Myristicin, Elemicin	Antioxidant, Neuroprotective	Scavenges free radicals; modulates mitochondrial apoptosis pathways.	Adiani <i>et al.</i> , 2015 Perumalsamy <i>et al.</i> , 2022 Mohapatra <i>et al.</i> , 2023
Allspice	Eugenol, Flavonoids	Antimicrobial, Antioxidant	Damages bacterial membranes; inhibits microbial enzymes; chelates metal ions.	Nagalakshmi <i>et al.</i> , 2023
Garcinia	Hydroxycitric acid (HCA), Garcinol	Hepatoprotective, Antiobesity	Restores glutathione; inhibits lipid peroxidation; suppresses mTOR signaling.	Ramachandran <i>et al.</i> , 2021
Tamarind	silver nanoparticles (AgNPs)	Anticancer (MCF-7 cells)	Induces ROS generation; disrupts mitochondrial membrane potential (Rho123 assay).	Gomathi <i>et al.</i> , 2020

3. Pharmacological properties of tree-derived spices

Tree-derived spices are not only culinary staples but also treasure troves of bioactive compounds with diverse therapeutic potentials.

Their pharmacological activities, rooted in their unique phytochemical profiles, have been validated through *in vitro*, *in vivo*, and clinical studies. Below, we explore the most prominent pharmacological properties of these spices (Table 2).

3.1 Antioxidant activity

Cinnamon is well known for its strong antioxidant properties, mainly due to compounds like cinnamaldehyde, proanthocyanidins, and ethanol-soluble polyphenols. These natural compounds help protect the body from damage caused by harmful molecules called free radicals. Cinnamon prevents lipid peroxidation, a process that damages cells, and neutralizes superoxide anions, unstable molecules linked to oxidative stress. Studies have shown that cinnamon extracts can inhibit harmful oxidation more effectively than some synthetic antioxidants like α -tocopherol (Vitamin E). It also supports the body's natural defense system by activating the Nrf2 pathway, which boosts antioxidant enzyme production. Because of these actions, cinnamon is considered a valuable ingredient in managing oxidative stress-related conditions like heart disease and ageing (Lin *et al.*, 2002). Nutmeg essential oil exhibits strong antioxidant potential, mainly due to four key compounds, *viz.*, elemicin, 4-terpineol, myristicin, and trans-sabinene hydrate. Among these, elemicin shows the highest free radical scavenging activity in DPPH assays, while 4-terpineol, despite having lower potency, contributes most to the total antioxidant activity due to its high concentration. Myristicin is known to work synergistically with other phenolics, enhancing overall effectiveness, and trans-sabinene hydrate aids in preventing lipid peroxidation. Importantly, nutmeg essential oil has also shown radio protective properties, capable of shielding DNA from radiation-induced damage by scavenging hydroxyl radicals. Unlike traditional assays, the antioxidant activity value (AAV) approach used in these studies considers both potency and abundance of each compound, giving a more accurate picture of nutmeg's antioxidant strength. This highlights the synergistic action of multiple compounds, a common trait in tree-derived spices, making nutmeg a promising natural antioxidant source (Adiani *et al.*, 2015).

Clove oil is extracted through steam distillation from the flower buds, stems, and leaves of the clove tree. It is known for its strong antioxidant potential, mainly due to its high phenolic compound content, particularly eugenol, the dominant active constituent. In various *in vitro* assays, clove oil has demonstrated impressive antioxidant performance. It inhibited 97.3% of lipid peroxidation at just 15 $\mu\text{g/ml}$, outperforming standard antioxidants like BHA (butylated hydroxyanisole), BHT (butylated hydroxytoluene), and α -tocopherol, even at lower concentrations. It also showed excellent free radical scavenging activity in both DPPH and ABTSz assays, indicating its broad-spectrum effectiveness. Additionally, clove oil could neutralize superoxide anions, which are harmful reactive oxygen species in the body. Its metal-chelating ability helped prevent the formation of damaging hydroxyl radicals by binding Fe^{2+} , while its ferric-reducing power supported antioxidant defenses. Clove oil also effectively scavenges hydrogen peroxide, a reactive molecule linked to DNA damage and chronic diseases. These results highlight clove's potent antioxidant activity and its potential role in protecting against oxidative stress-related conditions (Gulçin *et al.*, 2012).

3.2 Anti-inflammatory

Clove, rich in the phenolic compound eugenol, exhibits potent anti-inflammatory and immunomodulatory properties by modulating key cytokines and suppressing the NF- κ B pathway, a central regulator of inflammation. *In vitro* studies have shown that eugenol (50-100 mg/well) selectively inhibits IL-6 and IL-10, while clove extract (100 mg/well) effectively reduces IL-1 β , IL-6, and IL-10 levels in

macrophages, demonstrating both preventive and therapeutic effects against inflammation. Notably, the whole extract shows greater efficacy than eugenol alone, suggesting synergistic effects from other minor phytochemicals like β -caryophyllene and acetyl eugenol. These findings support clove's potential in managing chronic inflammatory diseases such as arthritis, IBD, and sepsis, with advantages over synthetic drugs due to its multi-targeted action, favorable safety profile, and cost-effectiveness. However, further studies are needed to validate these effects *in vivo*, explore synergistic mechanisms, and confirm efficacy in clinical settings (Bachiega *et al.*, 2012). Cinnamon, especially *C. zeylanicum* (Sri Lankan cinnamon) and *C. cassia* (Chinese cinnamon), exhibits notable anti-inflammatory activity, largely attributed to key bioactive compounds like E-cinnamaldehyde and o-methoxy cinnamaldehyde. Organic solvent extracts, particularly those using dichloromethane, showed superior suppression of nitric oxide (NO) and TNF- α production in activated macrophages, highlighting their therapeutic potential in controlling chronic inflammation. E-cinnamaldehyde was the most abundant compound, while o-methoxy cinnamaldehyde demonstrated greater potency in inhibiting NO. These compounds are believed to act by inhibiting NF- κ B translocation, thereby reducing pro-inflammatory gene expression. Both cinnamon species displayed comparable efficacy, with minor compounds like coumarin and cinnamic acid possibly contributing through synergistic effects. These findings suggest cinnamon's role in managing age-related inflammatory diseases and its potential incorporation into functional foods or natural drug formulations. However, challenges like coumarin toxicity (especially in *C. cassia*) and the need for enhanced bioavailability underscore the importance of careful formulation. Cinnamon's mode of action aligns with other spices like clove and turmeric, making it a valuable and sustainable option in phytomedicine (Gunawardena *et al.*, 2015).

3.3 Antidiabetic

Cinnamon exhibits significant antidiabetic potential, with marked differences among its commercial species *C. cassia*, *C. burmanii*, *C. loureirii*, and *C. zeylanicum* due to their distinct phytochemical profiles. Ceylon cinnamon (SC) stands out for its minimal coumarin content, making it safer for long-term use, whereas *C. cassia* and *C. burmanii*, despite higher polyphenol and antioxidant levels, pose hepatotoxicity risks. All species inhibit carbohydrate-digesting enzymes, with *C. cassia* most effectively targeting α -amylase, while all four outperform acarbose in α -glucosidase inhibition, thereby reducing glucose absorption. *C. burmanii* and SC notably suppressed starch digestion in the oral and gastric phases, though not in the intestinal phase, suggesting early-stage modulation. Moreover, *C. zeylanicum*, *C. burmanii*, and *C. loureirii* effectively inhibited advanced glycation end products (AGEs), which contribute to diabetic complications. Mechanistically, cinnamon acts through dual enzyme inhibition, antioxidant synergy to improve insulin sensitivity, and AGE suppression. While *C. cassia* and *C. burmanii* show strong activity, *C. zeylanicum* emerges as the most suitable for chronic diabetes management due to its safety and balanced efficacy, reinforcing the need for species-specific standardization and human clinical validation for future functional food or drug adjunct development (Hayward *et al.*, 2019). Recent studies have highlighted the antidiabetic potential of *M. fragrans* (nutmeg) through the biosynthesis of silver nanoparticles using hydroethanolic (MFHENP) seed extracts. These nanoparticles, characterized by UV-Vis

spectroscopy (430 nm), SEM (50-60 nm size), and FTIR, exhibited significant α -amylase and α -glucosidase inhibition, surpassing the standard drug acarbose, and delayed glucose diffusion, suggesting enhanced insulin sensitivity. The synergy between nutmeg-derived terpenoids and polyphenols contributes to the nanoparticles' stability and therapeutic efficacy. Silver nanoparticles synthesized from *M. fragrans* hydroethanolic extract (MFHENP) show promise for targeted drug delivery, functional food additives, and multimodal diabetes management. Its natural origin, eco-friendly synthesis, and cost-effectiveness make it an attractive alternative to synthetic drugs. However, further toxicity screening and clinical validation are needed to confirm its safety and efficacy, with potential for nanotechnology-driven antidiabetic applications (Perumalsamy *et al.*, 2022).

3.4 Cardioprotective effects

The cardioprotective potential of an aqueous extract of *G. indica* (kokum) fruit rinds in a rat model of isoprenaline-induced myocardial infarction (MI) was well documented by several researchers. Despite the extract's significant *in vitro* antioxidant properties, including DPPH radical scavenging and high phenolic and flavonoid content, it failed to normalize ECG parameters, reduce cardiac injury markers, or alleviate oxidative stress *in vivo*. Histopathological analysis revealed persistent myocardial necrosis and inflammation, indicating unresolved myocardial damage. This contrasts with other studies showing the potential of *G. Indica* extracts, particularly hydroalcoholic and ethanolic formulations, which reduced cardiac markers and oxidative stress, attributed to compounds like hydroxycitric acid (HCA) and g Garcinol. The discrepancies may be due to the aqueous extraction method failing to solubilize key lipophilic compounds, lower doses, and shorter treatment durations used. Future research should explore more efficient extraction methods, such as ethanol or hydroalcoholic solvents, and higher doses to better understand *G. indica*'s cardioprotective potential. Despite the lack of effect in this study, the safety profile of *G. indica* supports further investigation, particularly focusing on its antioxidant-rich fractions and specific bioactive compounds like g Garcinol (Patel *et al.*, 2015; Li *et al.*, 202; Lim *et al.*, 2021).

3.5 Antiobesity

The supercritical ethanolic extract of *G. indica* demonstrated significant antiobesity potential by inhibiting adipogenesis and modulating key metabolic pathways. Enriched with hydroxycitric acid (HCA), g Garcinol, xanthochymol, and other antioxidants, the extract effectively suppressed the differentiation of 3T3-L1 pre-adipocytes into mature fat cells in a dose-dependent manner, with minimal cytotoxicity. Key metabolic pathways were modulated by the extract, including the down regulation of genes such as mTOR (mechanistic target of rapamycin kinase) and HIF-1 α , which limit lipid synthesis and fat accumulation, and the upregulation of AMPK α (adenosine monophosphate activated protein kinase) and SIRT1, which promote fatty acid oxidation and mitochondrial biogenesis. The extract's molecular mechanisms involve the activation of AMPK and the inhibition of mTOR, enhancing fat breakdown while reducing lipogenesis. Compared to other extraction methods, supercritical ethanol extraction is more efficient in solubilizing lipophilic bioactives like g Garcinol, providing a multi-target action against obesity. The extract shows promise for use in functional foods and as an adjunct to pharmacotherapy for weight management, with potential applications in preventing obesity-related conditions like type 2

diabetes. However, future research should focus on optimizing bioavailability, validating efficacy in animal models, and conducting clinical trials to assess its safety and efficacy in humans (Ramachandran *et al.*, 2021).

3.6 Antimicrobial

A recent *in vitro* study assessed the antimicrobial properties of essential oils from three tree-derived spices, clove, cinnamon, and nutmeg, against common oral pathogens *Streptococcus mutans*, *Candida albicans*, and *Enterococcus faecalis*. The oils were tested at 100 μ l, 50 μ l, and 25 μ l concentrations using an agar well diffusion assay. Clove oil, containing eugenol, showed the strongest antimicrobial activity, particularly against *C. albicans* (44.75 mm zone of inhibition) and *E. faecalis* (40.33 mm), due to its ability to disrupt microbial cell membranes and inhibit biofilm formation. Cinnamon oil, with cinnamaldehyde, exhibited broad-spectrum activity, inhibiting bacterial quorum sensing and fungal hyphal growth, making it effective against all pathogens tested. Nutmeg oil, although the weakest performer, showed limited activity, likely due to lower concentrations of bioactive compounds like myristicin. These findings suggest that clove, cinnamon, and nutmeg oils could be effective natural alternatives to antibiotics in dental care, offering multi-target actions such as membrane disruption, enzyme inhibition, and biofilm suppression. However, further clinical validation and formulation optimization are needed to enhance their application in oral health products (Mohapatra *et al.*, 2023). Allspice (*P. dioica*), known for its aromatic properties, exhibits significant antimicrobial activity primarily due to its high eugenol content. The ethanolic extract of allspice was tested against pathogens like *Pseudomonas aeruginosa*, *Bacillus anthracis*, *Klebsiella pneumoniae*, and *Streptococcus pneumoniae*, showing a minimum inhibitory concentration (MIC) of 5 mg/ml. Eugenol disrupts microbial cell membranes, inhibits key bacterial enzymes, and suppresses biofilm formation, while synergistic compounds such as flavonoids and terpenoids enhance its efficacy. Allspice's antimicrobial properties make it a potential alternative to synthetic preservatives in food, as well as a component in pharmaceuticals for treating infections and in traditional remedies for digestive issues. Compared to synthetic antibiotics, allspice poses a lower risk of resistance, offers multi-target action, and is sustainably harvested year-round. However, challenges such as poor bioavailability of eugenol may be overcome with nanoencapsulation, and further *in vivo* validation is needed to confirm its clinical effectiveness. With its potential to combat antibiotic-resistant infections, allspice presents a promising natural solution for antimicrobial therapies (Nagalakshmi *et al.*, 2023).

3.7 Anticancer

C. cassia (Chinese cinnamon) exhibits strong anticancer potential, particularly through its green-synthesized silver nanoparticles (CNPs) and phytochemical-rich extracts. A study comparing effects on normal (Bj-1) and cancerous (HepG-2) cells found that aqueous extracts had the highest polyphenol and flavonoid content, while CNPs synthesized using cinnamon bark showed superior bioactivity. CNPs demonstrated the lowest IC₅₀ (55.6 μ g/ml) and strongest antioxidant activity, significantly reducing HepG-2 cell viability in a dose-dependent manner. Mechanistically, CNPs triggered apoptosis by upregulating Caspase-3, Bax, and P53, and suppressing Bcl-2, while enhancing antioxidant enzyme levels (SOD, CAT, GPx, GST, GSH), leading to oxidative stress-induced cancer cell death. Importantly,

CNPs were less toxic to normal cells, highlighting their selective action. Their nanoscale size improves cellular uptake and delivery of bioactives like cinnamaldehyde, offering a synergistic effect combining antioxidant defense and pro-apoptotic action. These findings position *C. cassia* and its nanoparticles as promising plant-based, sustainable candidates for targeted cancer therapy with minimal side effects (El-Baz *et al.*, 2023). *T. indica* has emerged as a promising candidate in green nanotechnology for cancer therapy, particularly through the synthesis of silver nanoparticles (AgNPs) using its fruit shell extract. These nanoparticles, sized between 20-52 nm and confirmed by surface plasmon resonance at 450 nm, were formed via an eco-friendly, one-step method where tamarind's polyphenols and flavonoids acted as natural reducing and stabilizing agents. Characterization studies, including FTIR and EDS, confirmed the presence of phytochemicals and 36.87% silver content, respectively. Tamarind-derived AgNPs demonstrated potent, dose-dependent cytotoxicity against MCF-7 breast cancer cells, with an IC_{50} of 20 μ g/ml. Apoptosis was confirmed through live/dead cell staining, increased ROS generation, and mitochondrial membrane disruption. These findings suggest that tamarind AgNPs induce cancer cell death via ROS-mediated oxidative stress and mitochondrial dysfunction, while likely sparing normal cells due to cancer-specific redox vulnerabilities. With potential applications in breast cancer therapy, either standalone or as an adjunct to conventional drugs like doxorubicin, these nanoparticles also offer scalability for clinical translation. Future research should explore *in vivo* efficacy, apoptotic gene expression, and synergy with existing treatments to fully harness the therapeutic potential of tamarind-based nanomedicine (Gomathi *et al.*, 2020).

3.8 Anesthetic activity

Clove oil, rich in eugenol, shows great promise as a natural anesthetic in aquaculture, particularly for species like juvenile rainbow trout

(*Oncorhynchus mykiss*). A comparative study highlights its low acute toxicity (LC_{50} - ppm) and effective performance at doses of 40-60 ppm, where it induces rapid anesthesia with manageable recovery times. Eugenol acts by modulating gamma-aminobutyric acid (GABA) receptors and sodium channels, leading to central nervous system depression. Compared to synthetic anesthetic MS-222, eugenol provides faster induction, although recovery is slower, 6 to 10 times longer, but acceptable when doses are optimized. Its biodegradability and absence of harmful residues make it environmentally friendly and safe for food fish. It is especially suited for short-term procedures like tagging and handling, and non-terminal research requiring reliable anesthesia. While species-specific variations exist, the natural origin, low toxicity, and sustainability of eugenol position it as a compelling alternative to conventional synthetic anesthetics in modern aquaculture (Keene *et al.*, 1998).

3.9 Hepatoprotective activity

Research reports revealed that administration of cinnamon bark extract at doses of 0.01, 0.05, and 0.1 g/kg over 28 days significantly reduced elevated liver enzymes AST, ALT, and ALP, indicating improved liver function, with the highest dose showing the greatest effect. The extract also enhanced antioxidant enzymes like SOD and CAT, helping neutralize reactive oxygen species triggered by CCl_4 . Histological analysis revealed preservation of liver tissue structure and reduced inflammation and necrosis. These protective effects are largely attributed to cinnamon's polyphenolic compounds such as cinnamaldehyde and procyanidins, which combat oxidative stress and stabilize liver cell membranes. With the potential to support liver health and complement treatments for conditions like hepatitis, Ceylon cinnamon stands out as a promising natural remedy. However, human trials and further studies to isolate key bioactives and optimize dosage are essential to validate its clinical application (Eidi *et al.*, 2012).

Table 3: Industrial applications of tree-derived spices

S.No.	Spice	Botanical name	Plant part used	Major industrial application	References
1.	Cinnamon	<i>C. verum</i>	Bark	Pharmaceuticals (antidiabetic, antioxidant), Functional foods, Flavors and fragrances, Nutraceuticals	Ahmed <i>et al.</i> , 2020
2.	Clove	<i>S. aromaticum</i>	Unopened flower bud	Oral care products (analgesic, antimicrobial), Food preservatives, Perfumery, Anesthetics in aquaculture	Rani <i>et al.</i> , 2023 Banu, 2024
3.	Nutmeg	<i>M. fragrans</i>	Seed, Mace	Confectionery, Bakery, Pharmaceuticals (neuroprotective, antidiabetic), Cosmetics	Vasanthkumar <i>et al.</i> , 2024
4.	Allspice	<i>P. dioica</i>	Fruit (berries)	Food seasoning, Natural preservatives, Essential oils for aromatherapy, antimicrobial agents in pharma	Kilaru <i>et al.</i> , 2022
5.	Garcinia	<i>G. indica</i> , <i>G. gummi-gutta</i>	Fruit rind, seed	Antiobesity supplements, Functional beverages (kokum juice), Food coloring, pharmaceutical excipients	Semwal <i>et al.</i> , 2015
6.	Tamarind	<i>T. indica</i>	Fruit pulp, Seeds, Leaves	Confectionery (tamarind candy), Pharmaceuticals (anticancer nanoparticles), Beverages, Natural emulsifiers	Bari <i>et al.</i> , 2024

4. Industrial applications

Tree-derived spices not only serve culinary and therapeutic functions but also play a pivotal role in various industrial sectors due to their rich phytochemical profiles and bioactive potential. These spices have gained increasing importance in pharmaceutical, food, nutraceutical, cosmetic, and agrochemical industries. For example, cinnamon is widely used in functional foods and diabetes management formulations due to its potent antidiabetic and antioxidant properties. Clove, rich in eugenol, finds applications in oral care products, topical analgesics, and even as a natural anesthetic in aquaculture. Nutmeg and allspice contribute to the flavor and fragrance industry, while also being explored for their neuroprotective and antimicrobial uses in pharmaceuticals and cosmetics. *G. indica* is utilized in the preparation of functional beverages and antiobesity supplements, leveraging its hydroxycitric acid (HCA) content. Additionally, tamarind is industrially important in the food and pharmaceutical sectors for its use in confectionery, beverages, natural emulsifiers, and as a green source for nanoparticle synthesis in drug delivery systems. These wide-ranging applications are summarized in Table 3, highlighting the multifunctional industrial value of tree-derived spices and underscoring their commercial and economic potential beyond traditional use.

5. Safety and toxicology of tree-derived spices

Tree-derived spices, while celebrated for their therapeutic and culinary benefits, require careful consideration of safety and toxicological profiles. Below is an analysis of key risks, regulatory insights, and mitigation strategies, supported by evidence from recent studies.

5.1 Dose-dependent toxicity

Coumarin in Cinnamon: *Cassia cinnamon* (*C. cassia*) contains coumarin, a hepatotoxic compound linked to liver damage at doses exceeding 0.1 mg/kg/day in humans. Chronic over consumption can lead to elevated liver enzymes and histopathological changes, as observed in rodent studies (Eidi *et al.*, 2012).

Myristicin in Nutmeg: High doses (>5 g) of nutmeg (*M. fragrans*) may induce neurotoxic effects, including hallucinations and seizures, due to myristicin, a phenylpropene compound (Dalby, 2000).

5.2 Allergenic and immunogenic reactions

- **Eugenol in clove:** Clove oil, rich in eugenol, may cause contact dermatitis or mucosal irritation in sensitive individuals (Dalby, 2000).
- **Synergistic sensitization:** Compounds like cinnamaldehyde in cinnamon can trigger allergic responses, especially in formulations with synthetic additives (Sulieyman *et al.*, 2023).

5.3 Drug interactions

- **Blood thinning effects:** Clove oil's eugenol may potentiate anticoagulant therapies, increasing bleeding risk (Dalby, 2000).
- **Hepatic enzyme modulation:** Cinnamon extracts can alter cytochrome P450 activity, affecting drug metabolism (*e.g.*, statins, antidepressants) (Eidi *et al.*, 2012).

5.4 Regulatory and mitigation strategies

- **GRAS Status:** Many spices, including cinnamon and clove, are GRAS by the FDA at culinary doses, but therapeutic use demands stricter oversight (Alawadhi *et al.*, 2024).
- **Agricultural Practices:** Soil remediation, organic farming, and post-harvest processing (*e.g.*, washing, irradiation) reduce heavy metal and microbial contamination (Sulieyman *et al.*, 2021).

The safety of tree-derived spices hinges on controlled dosing, rigorous quality testing, and adherence to agricultural best practices. While their natural origin offers advantages over synthetic additives, vigilance against contaminants and bioactive compound toxicity remains critical for consumer health (Sulieyman *et al.*, 2021; Alawadhi *et al.*, 2024).

6. Future perspectives and challenges

Tree-derived spices hold great promise for modern medicine and sustainable agriculture, but their integration is challenging. One key issue is the variation in phytochemical content caused by differences in species, geography, and processing methods. Future research should focus on standardizing the bioactive compounds in these spices to ensure consistency and effectiveness (El-Baz *et al.*, 2023). Emerging tools like green nanotechnology, such as silver nanoparticles synthesized from tamarind or cinnamon, and advanced omics approaches (genomics, metabolomics) offer exciting possibilities. These technologies can enhance the bioavailability and targeted delivery of spice-based therapeutics, making them more effective in treating diseases. However, several challenges remain; ecological sustainability is a major concern, as overharvesting and habitat destruction could threaten the natural sources of these valuable spices. Additionally, many spices with potential health benefits, like *G. indica* and nutmeg, still lack sufficient human clinical trials, creating a gap in their clinical validation. To move forward, it is essential to bridge traditional knowledge with modern scientific evidence. This will require strong interdisciplinary collaboration among botanists, chemists, pharmacologists, and agricultural scientists. Regulatory frameworks must also be strengthened to monitor and limit contaminants such as heavy metals in spice products (WHO, 2020). In summary, unlocking the full potential of tree-derived spices will depend on a balanced approach that combines scientific innovation with ethical and environmental responsibility.

7. Conclusion

Tree-derived spices, long revered in culinary and traditional medicine systems, stand at the intersection of nature and science, offering a treasure trove of bioactive compounds with profound therapeutic potential. This review underscores the pivotal roles of phytochemicals such as eugenol (clove), cinnamaldehyde (cinnamon), curcumin (turmeric), and hydroxycitric acid (*G. indica*) in combating antimicrobial resistance, oxidative stress, chronic inflammation, metabolic disorders, and cancer. Their multi-target mechanisms modulating pathways like NF- κ B, AMPK, and Nrf2 while inducing apoptosis, *via.*, caspase-3 and *bax*, highlight their versatility as natural therapeutics. However, transitioning from kitchen staples to clinical agents demands careful navigation of dose-dependent toxicity, heavy metal contamination, and allergenic risks, necessitating stringent quality control and regulatory oversight. While preclinical studies validate their efficacy, clinical translation remains limited, with notable exceptions like cinnamon's antidiabetic effects. Innovations in green nanotechnology and omics-driven cultivation promise to enhance bioavailability and sustainability, yet challenges such as ecological

conservation and standardization persist. Bridging traditional knowledge with modern research through interdisciplinary collaboration will be key to unlocking their full potential. By prioritizing ethical sourcing, rigorous clinical trials, and eco-friendly applications, tree-derived spices can revolutionize holistic healthcare, offering safe, sustainable, and culturally rooted solutions to global health challenges. These findings underscore the potential of tree-derived spices as natural therapeutics that demand both reverence and scientific rigor to harness responsibly.

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Conflict of interest

The authors declare no conflicts of interest relevant to this article.

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