

**Review Article**

**CINNAMOMUM GENUS: A REVIEW ON ITS BIOLOGICAL ACTIVITIES**

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**ABSTRACT**

The objective of this review is to systematically appraise the literature available to date on biological activities (*in vitro* and *in vivo*) of extracts and constituents from *Cinnamomum*. An extensive review of the literature available in various recognised databases including PubMed, Google Scholar and Scopus on the biological activities of various species of the *Cinnamomum* were undertaken. The literature provided information on biological activities of the species of the genus *Cinnamomum*. Crude extracts and constituents from about 30 species of *Cinnamomum* displayed significant antibacterial, antifungal, antiseptic, antiviral, anti-inflammatory, antipyretic, antioxidant, chemopreventive, cytotoxic, antidiabetic, hypolipidemic, antispasmodic, antiulcer, antiplatelet, anodyne, choleric, immunostimulant, anaesthetic and sedative activities. Essential oil, aqueous/alcoholic extracts, cinnamaldehyde and proanthocyanidins were reported to be mainly responsible for biological activities displayed by most of the plants. Plants of *Cinnamomum* genus possess a wide spread of biological activities validating their use in traditional medicine. However, most of the available references lack information on active constituents, doses, duration of the treatment, storage conditions and positive controls for examining biological activities. The molecular mechanisms involved in eliciting biological activities were not comprehensively elucidated. Investigations to prove the safe use of these plants in traditional medicine are very limited. Thus, more studies on identification of bioactive constituents and their molecular mechanisms are needed. In addition, given that various species of *Cinnamomum* are being widely used in traditional medicine and culinary purposes, their main therapeutic aspects, toxicity, and adverse effects warrant further investigation in the future.

**Keywords:** *Cinnamomum*, Biological activities, Ethnomedicinal uses, Bioactive constituents

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**INTRODUCTION**

In rural areas of the developing countries all over the world, plants have been used in the treatment of numerous human diseases for thousands of years and are the primary source of medicine [1]. The secondary metabolites produced by plants has been proven to possess various biological activities and was templates for the development of novel drugs.

There are a number of scientific reports on the use of medicinal plants and their secondary metabolites for the treatment of a wide array of diseases. Few natural products from plants have been recorded in pharmacopoeias. *Cinnamomum* is one such genus which has been extensively used for the treatment of wide-array of disorders in various traditional systems of medicine including western herbal medicine.

Apart from the wide array of medicinal uses of the genus *Cinnamomum*, the inner barks of the many species, commonly known as cinnamon, is used as a spice for cooking purposes across the world. In Ayurvedic medicine [2], cinnamon is being used for the common cold, cough, diabetes, fever, flatulence, indigestion, sinusitis and sore throat. Also it is a component of, herbal toothpaste to reduce the incidence of dental caries; chair a spiced black tea beverage consumed widely in India and in Yogi Bhajan's "Yogi Tea", used as a general tonic tea for a varied range of symptoms including digestive disorders, blood purification, and immunostimulation and as an antiparasitic. Ayurvedic physicians prescribe cinnamon for people with a "kapha dosha," an Ayurvedic term used to define a body type described by cold, heavy, slow functioning and wet.

Cinnamon is being prescribed in traditional Chinese medicine (TCM) for cold, diarrhoea, asthma, as an appetiser; to strengthen the uterus and increase fertility in women [2].

In Europe [2], cinnamon is used as a warming herb for the treatment of ailments associated with "cold". Cinnamon bark is approved by German health authorities (Commission E) for its use as an antispasmodic for mild gastrointestinal spasms, an appetiser, and for digestive disorders such as indigestion, bloating and gas.

In western herbal medicine [2], herbalists prescribe cinnamon for diabetes, diarrhoea, indigestion, nausea, toothache, and vomiting. Cinnamon oil is added in a few kinds of toothpaste for its antimicrobial properties and its capacity to reduce halitosis. The major constituent of cinnamon oil is eugenol which is still being widely used as a local anaesthetic and antibacterial agent in dental practice.

To the best of our knowledge, only two review articles focusing on a particular species of genus *cinnamomum* were published in the literature. One article [3] reviewed the ethnobotanical uses of *cinnamomum* species available in Tamilnadu, India. Another article [4] reviewed the phytoconstituents, ethnobotanical and pharmacological uses of *Cinnamomum zeylanicum*. With the objective of providing an eagle's eye view on scientific literature available on biological activities of genus *Cinnamomum* and for the benefit of those who are interested in Natural Products research we herewith made an attempt to review the entire available literature on biological activities of *Cinnamomum* genus.

In this review article, the scientifically proven biological activities of all the species from the genus *Cinnamomum* were reported. Literature searches were performed using a keyword '*cinnamomum*' in the databases; PubMed, Scopus, and Google Scholar (all from inception to August 2016). All the biological studies including *ex vivo*, *in vitro* and *in vivo* studies related to the species of the genus *Cinnamomum* published in the English language were included.

Biological activities of *Cinnamomum* species

Species	Parts	Extracts/Chemical constituents	Biological activities	References				
1.	<i>C. Osmo phloem</i>	Leaf	Essential oil	Antifungal	[5, 6]			
				Antidiabetic	[7]			
				Insecticidal	[8-10]			
				Antitermitic	[11]			
				Larvicidal	[12, 13]			
				xanthine oxidase (XOD) inhibitory and anti-hyperuricemic	[14]			
				Treatment of renal interstitial fibroblasts.	[15]			
				Anti-inflammatory	[16-19]			
				Antibacterial	[20-22]			
				Apoptosis in cancer cells.	[23]			
Affects insulin signalling pathway	[24]							
Anxiolytic	[25]							
Antioxidant	[26]							
2.	<i>C. camphora</i>	Twig	Ethanol extract	Tyrosinase inhibitory activity	[27]			
				Water extract	Antioxidant wound healing	[27]		
				Essential oil	Antioxidant	[28]		
				Water Extract	Antihyperglycemic and antioxidant	[29]		
				leaf	Water extract	Antimicrobial	[30, 31]	
					Essential oil	Acaricidal	[32]	
				Twig	Essential oil	Anti-inflammatory	[33, 34]	
					Methanol extract	Antioxidant	[35]	
				Bark	Essential oil	Anti-inflammatory	[36]	
						Anticancer	[36]	
3.	<i>C. burmannii</i>	Leaf	Water extract	Cytotoxic	[37]			
				Bark	Molluscicidal	[38]		
					Antigenotoxic	[39]		
				Seed	Essential oil	Antimicrobial	[40-42]	
						Repellant and insecticidal	[43]	
				Bark	Methanol extract	Medium chain acyl-ACP hydrolysis activity	[44]	
						Insecticidal	[45]	
				Leaf	Water extract	Antioxidant, Anti-inflammatory	[46]	
						Antioxidant	[47]	
				4.	<i>C. zeylanicum</i>	Leaf	Essential oil	Antidiabetic
Cytotoxic	[51]							
Inhibition of cytochrome P450 3A4 (CYP3A4) and CYP2D6	[52]							
Antibacterial	[53]							
Acaricidal	[54]							
Ameliorative	[55]							
Antifungal	[56-59]							
Antioxidant and Antimicrobial	[60-64]							
Antioxidant	[65, 66]							
Bark	Unknown	Spermatogenesis	[67]					
		Ovicidal and adulticidal	[68]					
5.	<i>C. parthenoxylon</i>	Bark	Essential oil	Antimicrobial	[69, 70]			
				Insecticidal	[71-73]			
				Cognitive impairment and oxidative stress	[74, 75]			
				Increase sexuality	[76]			
				Antiasthmatic	[77, 78]			
				Analgesic	[79]			
				Gastroprotective	[80]			
				Insect repellent	[81]			
				Antibacterial and antifungal	[82, 83]			
				Antioxidant	[84-86]			
6.	<i>C. kanehira</i>	Leaf	Methanol extract	Anti-nociceptive and Anti-inflammatory	[87, 88]			
				Antidiabetic	[89-93]			
7.	<i>C. cassia</i>	Unknown	Water extract	Mutagenic	[94, 95]			
				Osteoclastogenesis	[96]			
				Antioxidant and antimutagenic	[97]			
				Hypoglycemic	[98]			
				Antileukaemic	[99]			
				Bark	Wood	Hinokenin, Cubebin	Antioxidant	[100]
							Anticancer	[101]
				Leaf	Essential oil	Volatile oil, Cinnamaldehyde	Antibacterial	[102]
							Anticancer	[103]
				Twig	Essential oil	Coumarins	Antioxidant	[47, 104-106]
Antimutagenic	[107, 108]							

				Angiogenesis	[109]
			Ethanol,	Antimicrobial	[110-117]
			Water extract	Antifungal	[118, 119]
			Essential oil	Hypouricemic	[120]
		Stem bark	Hexane extract	Anticancer	[121]
			Essential oil	Immunomodulatory	[122, 123]
			Hot water extract	Anticancer	[124]
			Ethanol extract	Antiviral	[125]
			Methanol extract	Antiproliferative	[126, 127]
				Antioxidant	[128-130]
				Antiulcerogenic	[131]
				Antidiabetic	[90, 132-138]
				Antihyperglycemic and Antihyperlipidemic	[139]
				Antitumor	[140-142]
				Antiallergic	[143-146]
				Anti-inflammatory	[147-152]
				Antipyretic	[153]
				Inhibitory activity on nitric oxide production and metalloproteinases-2 and-9 (MMP-2/9)	[154, 155]
				Stimulation of steroid hormones	[156]
				Diabetic nephropathy	[157]
				Insecticidal and larvicidal	[68, 158, 159]
			Diterpenoids	Immunosuppressant activity	[160]
			Lignans, tetrahydrofuran derivatives, gamma-butyrolactone	Anti-inflammatory	[161]
			Proanthocyanidin oligomers	Antihyperglycaemic	[162]
				Immunosuppressive effect	[163]
		Shoot	Essential oil	Antibacterial	[164, 165]
				Antiestrogenic	[166, 167]
		Plant	Water extract	Anxiolytic	[168, 169]
			Methanol extract	Stimulates angiogenesis	[170, 171]
			Essential oil	Xanthine oxidase inhibitor	[172-174]
				Antiprotozoal	[175]
		Twig	Methanol extract	Xanthine oxidase inhibitor	[176]
8.	<i>C. pauciflorum</i>	Leaf	Water extract	Antioxidant	[65]
9.	<i>C. tamala</i>	Leaf	Water extract	Antioxidant	[65]
			Essential oil	Gastroprotective	[177]
			Ethanol extract	Antidiarrhoeal	[178]
				Hypoglycaemic	[179]
10.	<i>C. carolinense</i>	Bark	Hot water extract	Medicinal tea and hot beverage	[180]
11.	<i>C. philippinense</i>	Root	Water extract	Antioxidant, Antiplatelet aggregation and Vasorelaxant	[181]
			Essential oil	Thromboxane A2 receptor antagonist	[182]
12.	<i>C. insularimontanum</i>	Fruit	Essential oil	Anti-inflammatory	[183]
		Leaf	Methanol extract	Cytotoxic	[184]
13.	<i>C. verum</i>	Unknown	Essential oil	Antiparasitic	[185]
		Unknown	Unknown extract	Inhibition of amyloid fibril formation	[186]
		Leaf	Methanol extract	Antioxidant	[187-189]
			Water extract	Antimicrobial	[61, 110, 190-193]
			Essential oil		
			Ethanol and aqueous extracts	Antioxidant, Analgesic	[194]
		Cortex	Essential oil	Insecticidal	[195-197]
			Water extract	Bening prostatic hyperplasia	[198]
			2-Methoxycinnamaldehyde	Anticancer	[199-203]
		Bark	Essential oil	Antioxidant	[188, 204-206]
			Cuminaldedhyde	Anticancer	[207-209]
			Water extract	Anthelmintic	[210]
14.	<i>C. loureirii</i>	Unknown	Extract	Acetylcholinesterase activity	[211]
15.	<i>C. micranthum</i>	Fruit	Water extract	Anti-inflammatory	[34]
16.	<i>C. ketoense</i>	Leaf	Methanol extract	Antiproliferative	[212]
				Induces caspase-dependent and-independent apoptosis in Hep G2 cells	[213]
				Anticancer	[212, 214, 215]
		Stem wood	Hot water extract	Antitubercular	[216]
17.	<i>C. longepaniculatum</i>	Leaf	Volatile oil	Anti-inflammatory	[217]
				Antibacterial	[218]
				Antihepatoma	[219]
18.	<i>C. japonicum</i>	Bark	Procyanidin oligomer-rich extract	Hypoglycaemic	[136]

19.	<i>C. pubescens</i>	Leaf	Methanol extract	Platelet-activating factor (PAF) receptor-binding antagonist activity	[220]
20.	<i>C. altissimum</i>	Leaf	Methanol extract	PAF receptor-binding antagonist activity	[220]
21.	<i>C. bejolghota</i>	Leaf	Essential oil	Antimicrobial	[221]
22.	<i>C. griffithii</i>	Leaf/twig/ro ot	Methanol extract	Antiplasmodial	[222]
23.	<i>C. loureirii</i>	Leaf/Bark bark	Essential oil Methanol extract	Antioxidant, Anticholinesterase Anti-inflammatory	[223] [173]
24.	<i>C. massoiae</i>	Plant	Alcohol extract	Antihistaminic	[224]
25.	<i>C. mairei</i>	Plant	Boiling water extract	Mutagenic	[225]
26.	<i>C. aromaticum</i>	Herbs	Methylene chloride extract Water extract	Insecticidal Immunotherapy for respiratory allergy	[226] [227]
27.	<i>C. migao</i>	Leaf	Essential oil	the relaxation effect on smooth muscles	[228]
28.	<i>C. longa</i>	Plant	Acetone extract	Antioxidant	[229]
29.	<i>C. rhizome</i>	Plant	Acetone extract	Antioxidant	[229]
30.	<i>C. laubatii</i>	Fruit	Spiroacetals	Anticancer	[230]
31.	<i>C. bodineiri</i>	Leaf	Subamolide A	Antioxidant	[231]
32.	<i>C. impressinervium</i>		Water extract	Antidiabetic	[232]
33.	<i>C. glaucescens</i>		Essential oil	Insecticidal, antifungal, anti aflatoxin and antioxidant	[233]
34.	<i>C. subavenium</i>	Stem	Subamolide A	Cytotoxic	[231]
35.	<i>C. jensenianum</i>	Bark	Essential oil	Antifungal	[234]
36.	<i>C. iners</i>	Stembark	Volatile oil	Antibacterial	[235]
37.	<i>C. impressicostatum</i>	Stembark	Volatile oil	Antibacterial	[235]
38.	<i>C. porrectum</i>	Stembark	Volatile oil	Antibacterial	[235]
39.	<i>C. altissimum</i>	Stembark	Water extract	Antibacterial	[235]
40.	<i>C. mollissimum</i>	Stembark	Aporphine alkaloids	Antioxidant, Antibacterial	[236]

## DISCUSSION

The genus *Cinnamomum* has been used in various traditional systems of medicine including Indian and traditional Chinese systems of medicine to treat a multitude of disorders, like indigestion, cold, cough, microbial infections. Only 40 out of the approximate 300 *Cinnamomum* species have been studied in some detail. The leaves and stem barks have been reported to be the main source for biological activities displayed by *Cinnamomum* species. One of the most widely investigated constituents of *Cinnamomum* species is essential oil and reported to exhibit a wide array biological activities including antibacterial, antifungal, antioxidant, antidiabetic, antitermitic, anticancer, anticholinesterase, larvicidal, hypouricemic, immunomodulatory and xanthine oxidase inhibitory activities. Very recently, few attempts are being made to isolate the bioactive constituents and to identify the molecular mechanisms. Adfa, M. et al. [99] reported lignans and phenylpropanoids isolated from *C. parthenoxylon* possess antileukemic activity mediated through apoptosis in human leukaemia HL-60 and U-937 cells. Chang, W. L. et al. [102] reported cinnamaldehyde, a major constituent of *Cinnamomum* essential oils, exhibit anticancer activity in human oral squamous cell carcinoma HSC-3 cells mediated through apoptosis, induced mitochondrial dysfunction, increased reactive oxygen species (ROS) production and antioxidant actions. Chen, L. et al. [163] reported procyanidin oligomer compounds, cinnamtannin B1, cinnamtannin D1, para meri tannin A1, procyanidin B2 and procyanidin C1 from *C. tamla* or *C. cassia* display immune-suppressive effects mediated through significant reduction of IFN- $\gamma$  and IL-2 in LPS induced splenocytes proliferation model. Chen, T. W. et al. [207] and Yang, S. M. et al. [209] reported cuminaldehyde, a novel anticancer agent, isolated from *C. verum* exhibited significant anticancer activity in human lung adenocarcinoma A549 cells and human lung squamous cell carcinoma NCI-H520 cells accompanied by down regulations of proliferative control involving apoptosis, both topoisomerase I and II as well as telomerase activities, together with an upregulation of lysosomal vacuolation with increased volumes of acidic compartments. Tsai K. D. et al. [208] reported cuminaldehyde possess anticancer activity in human colorectal adenocarcinoma COLO 205 cells through downregulation of topoisomerases 1 and II. Cheng, B. H. et al. [25] reported linalool from *C. osmophloeum* essential oil has significant anxiolytic activity in mice model whose action is mediated through a decrease in the

mice brain levels of serotonin, dopamine and norepinephrine. He, S. et al. [161] reported six new compounds including one  $\gamma$ -butyrolactone, cinnassin A, two tetrahydrofuran derivatives, cinnassins B and C, two lignans, cinnassins D and E, and one phenyl propanol glucoside, cinnacassoside D possessing anti-inflammatory activity in LPS induced inflammation in BV-2 microglial cells. Kang, B. H. et al. [162] reported proanthocyanidins from *C. cassia* do exhibit anti-hyperglycemic activity via carbohydrate hydrolyzing enzyme inhibition. Kim, C. R. et al. [211] reported 2, 4-bis (1,1-dimethylethyl) phenol inhibited acetyl cholinesterase activity and ameliorates trimethyl tin-induced cognitive dysfunction in mice. Lee, S. C. et al. [19] reported essential oil from *C. osmophloeum* kanehira protected endotoxin-induced intestinal injury in mice associated with suppression of toll-like receptor 4 (TLR4) and Nod-like receptor family, pyrin domain containing 3 (NLRP3) signalling pathways. Li, L. et al. [218] reported  $\gamma$ -terpinene,  $\alpha$ -terpineol, 1,8-cineole isolated from *C. longepaniculatum* leaf essential oil displayed significant antibacterial activity against *Staphylococcus aureus*, *Escherichia coli* and *Salmonella enteritidis*. Liu, Y. H. et al. [199].

Perng, D. S. et al. [200, 201], Tsai K. D. et al. [202] and Wong Y. H. et al. [203] reported 2-methoxycinnamaldehyde exhibited anticancer activity in human lung squamous cell carcinoma NCI-H520 cells, hepatocellular carcinoma Hep 3B cells, human colorectal adenocarcinoma COLO 205 cells and human lung adenocarcinoma A549 cells through targeting topoisomerase I and II. Manson, F. F. et al. [236] reported five aporphine alkaloids; N-methyl-1,2,10-trimethoxyaporphine, N-methylhernagine, N-methylhernovine, hernagine and hernovine; showed significant antibacterial and antioxidant activities. Ngoc, T. M. et al. [103] reported a new coumarin derivative, coumacasia possessing significant growth inhibitory effects in two human cancer cell lines, HL-60 and A-549. Song, X. et al. [219] reported safole from *C. longepaniculatum* exhibited anti-hepatoma effect mediated through apoptosis. Williams A. R. et al. [210] reported trans-cinnamaldehyde and A- and B-type proanthocyanidins obtained from *C. verum* exhibited anthelmintic activity. Yan Y. M. et al. [157] reported sesquiterpenoids may be responsible for anti-diabetic nephropathy displayed by *C. cassia* bark. Yang, F. et al. [38] reported linalool obtained from *C. camphora* leaf extracts exhibited molluscicidal activity against *Oncomelania hupensis* and inhibits infection of

*schistosoma japonicum*. Zeng, J. et al. [160] reported diterpenoids isolated from *C. aromaticum* possess immunosuppressive effect.

## CONCLUSION

In this review, we summarised the existing studies on the biological activities of *Cinnamomum* genus. Only 40 out of available 300 *Cinnamomum* species were scientifically investigated for biological activities which implies that there is a huge potential for researchers to explore further the potential biological activities of *Cinnamomum* species because majority of the species have been used for various purposes in different traditional systems of medicine and as a food ingredient all over the world for a quite long time. *C. verum*, *C. cassia*, *C. zeylanicum*, *C. camphora* and *C. osmophloeum* are the only five species that have been somewhat thoroughly investigated in the identification of potential biological activities, bioactive constituents and molecular mechanisms. Also, the majority of the studies have been concentrated on essential oil and aqueous/alcohol extracts of leaves and stem barks with the main focus on validating the uses of *Cinnamomum* in various traditional systems of medicine. Detailed studies were performed only on two bioactive compounds namely 2-methoxycinnamaldehyde and cuminaldehyde for their anticancer activity in various human cancer cells. Based on the published results in the literature, these two compounds have exhibited promising effects and could be good leads in anticancer drug discovery. However, further studies have to be carried out to assess the bioavailability, toxicity, drug-like properties, *in vivo* efficacy and molecular targets. Also, there is an opportunity for the medicinal chemists to look at structure-activity relationship studies on these two compounds.

## CONFLICTS OF INTERESTS

Declared none

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