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# An Overview of The Anxiolytic Potential of Cinnamon (*Cinnamomum spp.*)

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## Abstract

Anxiety disorders are common mental health conditions, and *Cinnamomum* spp. has emerged as a potential natural source of anxiolytic agents. The aim of this systematic review was to examine the anxiolytic potential of cinnamon (*Cinnamomum spp*.). depending on experimental animal studies available. We performed a PubMed, Cochrane, Wiley and Springer search and found 79 articles of which five met the inclusion criteria. Of the chosen studies, various plant parts (stems/branches/leaves), preparations of extracts, and essential oils from cinnamon species were evaluated. Overall, the findings showed that response were anxiety-reducing for cinnamon in several experimental measures such as elevated plus maze, open field test, forced swim test and social interaction test. One of the main bioactive constituent, cinnamaldehyde, was proposed to have contributed to these effects through antioxidant activity and/or regulation of neuronal function. Inhaled cinnamon essential oil was also shown to have a rapid restorative effect, thus supporting fast nasal pathways from nose to brain. In conclusion, there are promising potentials of cinnamon as an anxiolytic but more consistent studies and clinical trials should be carried out to confirm its effectiveness and safety for widespread use.

***Keywords*:** *Anxiolytic agents, Cinnamon, Essential oils, Mental health, Phytotherapy*

## Abstrak

**Tinjauan Potensi Ansiolitik Kayu Manis (*Cinnamomum* spp.).** Gangguan kecemasan merupakan masalah kesehatan mental yang umum, dan *Cinnamomum* spp. berpotensi menjadi sumber alami agen ansiolitik. Tinjauan sistematis ini bertujuan mengevaluasi potensi ansiolitik kayu manis (*Cinnamomum* spp.) berdasarkan bukti penelitian eksperimental pada hewan. Penelusuran literatur dilakukan melalui basis data PubMed, Cochrane, Wiley, dan Springer, yang menghasilkan 79 artikel, dengan lima artikel memenuhi kriteria inklusi. Studi yang terpilih mengevaluasi berbagai bagian tanaman (batang, cabang, dan daun), sediaan ekstrak, serta minyak atsiri dari berbagai spesies kayu manis. Secara keseluruhan, hasil penelitian menunjukkan bahwa kayu manis memberikan efek penurun kecemasan pada berbagai model pengujian, seperti *elevated plus maze*, *open field test*, *forced swim test*, dan *social interaction test*. Salah satu senyawa bioaktif utama, yaitu sinamaldehida (*cinnamaldehyde*), diduga berkontribusi terhadap efek tersebut melalui aktivitas antioksidan dan/atau regulasi fungsi neuron. Selain itu, pemberian minyak atsiri kayu manis secara inhalasi menunjukkan efek ansiolitik yang cepat, yang mendukung adanya jalur penghantaran langsung dari hidung ke otak (*nose-to-brain pathway*). Disimpulkan bahwa kayu manis memiliki potensi yang menjanjikan sebagai agen ansiolitik. Namun, penelitian yang lebih konsisten serta uji klinis masih diperlukan untuk mengonfirmasi efektivitas dan keamanannya sebelum dapat diterapkan secara luas.

**Kata Kunci:** Agen ansiolitik, Kayu manis, Minyak atsiri, Kesehatan mental, Fitoterapi

## Introduction

Mental disorders can be described as clinical conditions characterized by substantial alterations in an individual's thinking patterns, regulation of feelings, as well as observable actions, which collectively reflect disturbances occurring within psychological mechanisms, biological systems, or stages of human development that fundamentally support mental activity.[1] According to recent study, "more than 13% of teenagers globally suffer from mental disorders, with anxiety and depressive disorders accounting for almost 40% of the total".[2] Anxiolytic medications are generally classified into three principal categories, namely triskylic compounds such as amitriptyline, selective serotonin reuptake inhibitors which include fluoxetine and sertraline, as well as monoamine oxide inhibitors exemplified by moclobemide and tranylcypromine.[3,4] Despite their medicinal advantages, these medications have more adverse effects than pharmaceuticals produced from natural substances, which have essentially minimum side effects and are also less expensive.[5]

Plants have been regarded as a rich source of safe and effective remedies since antiquity.[5] Cinnamon known scientifically as Cinnamomum spp. is categorized within the Lauraceae botanical family, a group consisting of perennial woody plants such as trees and shrubs that typically possess pinnately structured foliage.[4-6] Cinnamon is one of the natural plant species widely discovered across Indonesia and is traditionally believed to possess therapeutic properties capable of addressing multiple kinds of medical problems affecting human health.[7] From early healing traditions, cinnamon has been widely employed by medical practitioners as a conventional treatment to reduce multiple health disorders including headaches, nerve related pain, stomach inflammation, respiratory issues, voice disorders, throat irritation, and even degenerative neurological conditions including Parkinson's and Alzheimer's disease.[4]

This paper focuses on assessing the effectiveness of cinnamon as a compound possessing anxiolytic characteristics, with the objective of discovering novel strategies applicable for the therapy and control of anxiety.

## Materials and Methods

This research seeks to examine the capability of Cinnamomum spp. plants as innovative anxiolytic medications. This article is a literature review study that was prepared using secondary data references from original studies that discussed the themes listed above. The search for reference articles was carried out using electronic databases such as Pubmed, Cochrane, Wiley, and Springer, with the keywords being ("Cinnamomum" OR "Cinnamon") AND ("Essential Oil OR Extract") AND ("Phytochemical" OR "Pharmacology") AND ("Anxiety" OR "Anxiolytic" OR "Anti-Anxiety").

The search results showed 79 articles matching the selected keywords. Next, the articles were sorted based on the inclusion and exclusion criteria. This research's inclusion criteria are: (1) publications published within the previous ten years, (2) in Indonesian or English, (3) open access, and (4) an experimental study. Review articles will be eliminated from the criterion. The selection procedure revealed that there were five papers that met the research requirements. The selected publications are anticipated to address the pharmacological responses of anxiolytics derived from *Cinnamomum* spp.

The collected data will be organized into a table with information (author, location, year, species, plant parts utilized, test methods, and results) to support the premise of this literature study. Further searching yields an overview of the active chemicals, as well as information regarding the class, activity, and mechanism of anxiolytics.

## Results

Cinnamaldehyde serves as the dominant bioactive compound present in cinnamon and is frequently integrated into various material systems such as polymer films, microspheres, liposomes, and nanoparticles where it functions to enhance the overall efficiency and performance of polymer-based structures.[8]

Cinnamaldehyde is an aromatic molecule recognized for its anti-anxiety, antioxidant, and sleep-promoting qualities.[9]

Essential oils derived from Cinnamomum cassia and Cinnamomum verum contain approximately 82.74% and 87.32% cinnamaldehyde, respectively.[4,10] The composition of volatile substances contained in cinnamon essential oil differs significantly based on the specific part of the plant that is utilized for extraction. The dominant compound obtained from the essential oil of cinnamon bark is cinnamaldehyde, typically present in concentrations ranging from 90% to approximately 62% hingga 73% depending on extraction conditions.[11] In addition, other compounds also contained in cinnamon extracts are summarized in Table 1 and an overview of their respective chemical structures in Figure 1.

**Table 1.** Active compounds in C. cassia[10]

| Active compound | Relative Percentage |
|---|---|
| **(E)-Cinnamaldehyde** | 82,74 |
| **Cinnamyl acetate** | 4,57 |
| **o-Methoxycinnamaldehyde** | 2,52 |
| **(Z)- Cinnamaldehyde** | 2,16 |
| **Coumarin** | 1,81 |
| **Benzenepropanol** | 1,63 |
| **$\alpha$-Copaene** | 1,36 |
| **Benzaldehyde** | 0,75 |

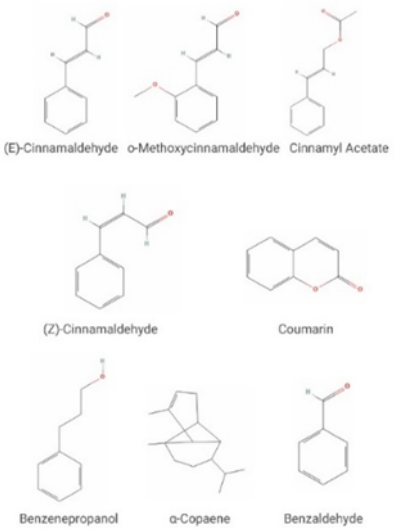


**Figure 1.** Chemical structure of cinnamon secondary metabolites[12-19]

The selected publications differ in the methodologies employed in the trials to establish cinnamon's potential as an anxiolytic drug. Table 1 summarizes all of these variances. In the five studies that were selected for analysis, four distinct cinnamon species were designated as research samples, namely C. tamala, C. verum, C. zeylanicum, and C. cassia.[4,5,20,21] The variation among these species is highly likely to produce a wide range of differing experimental results due to inherent biological distinctions. In addition, differences in agricultural regions will also result in differences in the percentage of active compounds in a plant.[22]

## Discussion

In vivo studies in mice revealed that cinnamon essential oil extract had an anxiolytic effect.[4,5,10,20,21] Animal behavior originates from the functional activity of the central nervous system. A particular study monitored behavior both in enclosed cages and open field environments to evaluate the anxiogenic effects of deltamethrin, characterized by diminished locomotion, and to assess whether cinnamon oil could counteract this condition in albino mice. The administration of cinnamon essential oil led to heightened locomotor activity, increased rearing behavior, greater feeding and drinking activity, along with a reduction in both the frequency and duration of sleep, indicating its anxiolytic effect.[20]

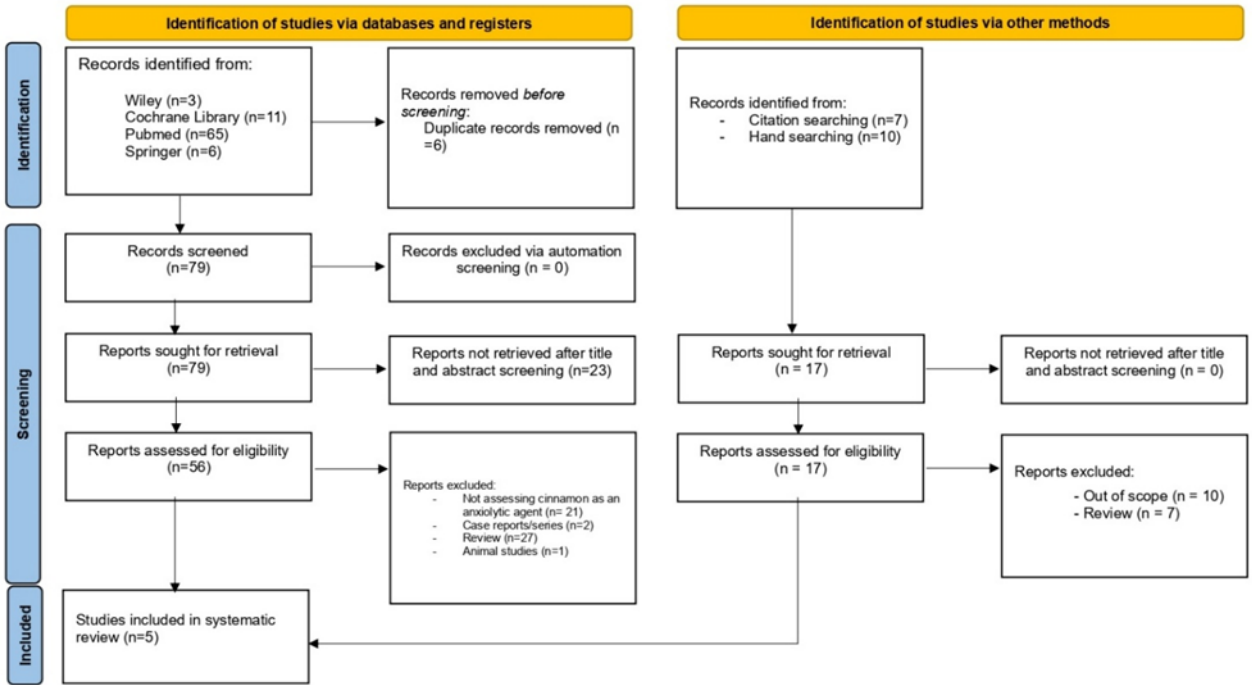


**Figure 2.** PRISMA flowchart for selection of included studies

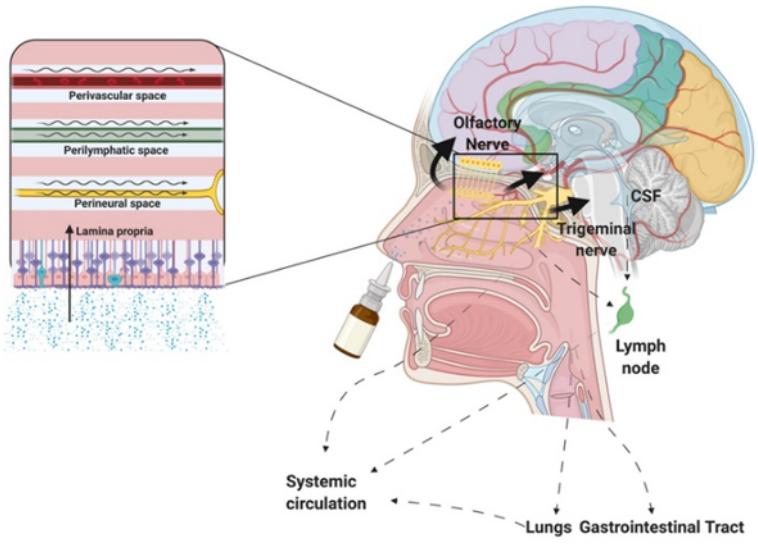


**Figure 3.** Drug delivery pathway via nose-to-brain route (inhalation**).**[28]

**Table 2.** Summary of species, methods, and findings from selected articles[4,5,10,20,21]

| Author, Year, Location | Species | Part of Plant | Methods | Findings |
|---|---|---|---|---|
| **Upadhyay *et al.*, 2016, India** | *Cinnamomum tamala* | Leaves extract | • *Oral administration of C. tamala (100, 200, and 400 mg/kg) was conducted daily for 7 days, and the observed efficacy was similar to lorazepam (1 mg/kg, p.o.) and imipramine (10 mg/kg, p.o.)*.<br>• Conventional drugs were administered a single time, 30 minutes prior to behavioral evaluation. | • Delivery of C. tamala at 400 mg/kg exhibited anxiolytic effects comparable to lorazepam based on elevated plus maze, open field assessment, and social interaction experiments.<br>• Administration of C. tamala at 400 mg/kg generated antidepressant like responses equivalent to imipramine as indicated by behavioral despair assessment, learned helplessness evaluation, and tail suspension testing within the examined dosage range.<br>• Under integrated stress management conditions, delivery of C. tamala at 400 mg/kg produced significant anti stress outcomes similar to W. somnifera in water immersion restraint stress experiments by lowering ulcer index, decreasing adrenal gland mass, and maintaining plasma levels of corticosterone, glucose, cholesterol, and triglycerides. |
| **Sohrabi *et al.*, 2017, Iran** | *Cinnamomum verum* | Essential oil | • In an acute experiment, the forced swim test (FST) was applied to evaluate antidepressant like behavior in mice receiving intraperitoneal (IP) cinnamon essential oil at three dosage levels (0.5, 1, and 2 mg/kg).<br>• In a sub-acute study (14 days with 24-hour intervals), antidepressant-like properties of essential oil (0.5, 1, and 2 mg/kg) delivered through the same route were examined using the FST and tail suspension test (TST). Elevated plus maze (EPM) and open field tests were utilized to measure anxiolytic effects and motor performance.<br>• The composition of compounds contained in the oil sample was identified through gas chromatography mass spectrometry GC MS examination. | • In forced swim and tail suspension trials, repeated delivery of cinnamon essential oil at 0.5, 1, and 2 mg/kg for 14 days resulted in markedly shorter immobility time compared with the control group.<br>• Mice treated with oil at 2 mg/kg showed extended time spent in the open arms of the elevated plus maze relative to animals receiving only vehicle as control.<br>• GC MS analysis revealed 46 different chemical components in the examined cinnamon essential oil, where trans cinnamaldehyde was the major compound at 87.32%. |
| **Jain et al., 2019, India** | *Cinnamomum zeylanicum* | Bark extract | Bark extract was administered orally at 100, 200, and 400 mg/kg, while diazepam 1 mg/kg intraperitoneally served as positive control in the anxiety model. The elevated plus maze assay assessed anxiety related responses. | Administration of Cinnamomum zeylanicum extract at 200 and 400 mg/kg significantly increased time spent in open arms compared to control group. |
| **Ahmed *et al.*, 2021, Eigypt** | *Cinnamomum cassia* | Essential oil | Four groups were employed, each consisting of 10 male Wistar albino mice.<br>• Group I as control received saline only.<br>• Group II received intraperitoneal injection of cinnamon oil at 0.5 mg/kg BW.<br>• Group III received oral administration of deltamethrin at 6 mg/kg BW.<br>• Group IV was treated with both cinnamon oil and deltamethrin for 21 days to induce neurotoxicity.<br>Behavioral patterns, brain acetylcholine esterase AChE activity, serotonin concentration, and oxidative stress markers were assessed in mice. Serum samples determined corticosterone concentration. Expression of CYP1A1 and iNOS genes along with brain histology were also analyzed. | • Combined cinnamon oil treatment improved behavior and brain antioxidant status, indicated by increased AChE activity with decreased serotonin, corticosterone, and MDA levels.<br>• Cinnamon oil treatment decreased CYP1A1 and iNOS enzyme activity and promoted better histological structure in the examined tissues.<br>• Overall, cinnamon oil successfully reduces DLM induced neurotoxicity in rats through lowering DNA damage caused by oxidative stress and restraining cell death mechanisms in brain tissue. |
| **Nguyen *et al.*, 2022, South Korea** | *Cinnamomum cassia* | Essential oil | The mice were allocated into four distinct groups with 8 individuals in each group.<br>• The control group identified as CON<br>• One set was administered 5% CIEO known as CIEO5 whereas a different set obtained 10% CIEO.<br>• A group was exposed to 5% lavender essential oil identified as LAEO.<br>The inhalation method used filter paper infused with essential oil or vehicle placed inside a plastic cage containing rats for one hour prior to behavioral assessment. | • The breathing of cinnamon essential oil termed CIEO exhibited anxiety reducing effects in the elevated plus maze indicated by increased time in open arms and reduced time in closed arms. Administration of CIEO improved social interaction by raising contact frequency, prolonging time in the rehabilitation zone, enlarging movement range in that area, and increasing total distance during social testing. |

Cinnamon essential oil contains cinnamaldehyde referred to as cinnamic aldehyde or trans cinnamaldehyde which functions as a key metabolic substance with antioxidant, anti-inflammatory, and anti-angiogenic activities.[23] The therapeutic properties of cinnamaldehyde have been well documented in earlier research, indicating that cinnamon essential oil has the potential to prevent neurotoxic effects while simultaneously enhancing memory retention and cognitive performance. Furthermore, aromatic compounds such as $\alpha$-terpinene and 1,8-cineole have demonstrated a strong capacity to act as antioxidants in various experimental findings.[10]

The anxiolytic effect may be due to the activation of cinnamon's anti-inflammatory and antioxidant capabilities.[21] *Cinnamomum cassia* extract was found in one research to have anxiolytic effects by regulating the serotonin and Gamma-Aminobutyric Acid (GABA) pathways.[24] Many experimental animal investigations have shown the vital role of GABAergic neurotransmission in the amygdala for regulating behaviors linked to anxiety. In multiple animal models studied in neuroscience, delivering GABA or agents stimulating GABA receptors into the amygdala markedly lowers behavioral and physiological signs of fear and anxiety whereas substances that block GABA function result in heightened anxiety responses.[25] GABAA receptors have been identified as possessing multiple specific binding locations that interact with a diverse group of pharmacological substances such as anti-anxiety medications, seizure controlling drugs, anesthetic agents, barbiturates, ethanol, and neurosteroids, each of which contributes to distinct biological and therapeutic effects.[26] Therefore, it can be assumed that cinnamon bark extract may produce anxiolytic effects through modulation of this pathway.[21]

Another method for testing the anxiolytic effect of *Cinnamomum spp*. is nose-to-brain (inhalation). The inhalation approach is thought to have fewer negative effects and work faster than other ways of medication delivery.[10] The olfactory sensory area is positioned at the top part of the nasal cavity approximately 7 cm from the nostril entrance and this region is covered by pseudostratified columnar epithelium called the olfactory epithelium and includes the olfactory nerve CN I which connects directly to the central nervous system across the blood brain barrier.[27] Within a rigorously regulated laboratory experiment, inhaling essential oil extracted from Cinnamomum spp. for 1 hour generated outcomes comparable to decreased anxiety in the elevated plus maze test, demonstrated through extended time in open arms and reduced time in closed arms. Evidence from an earlier investigation, intraperitoneal injection of *Cinnamomum spp.* essential oil was repeated for 14 days and demonstrated favorable benefits by lowering anxiety in rats. These findings indicate that the inhalation mode of delivery of *Cinnamomum spp.* essential oil may have a faster anxiolytic impact than systemic administration.[10]

The process of drug uptake through inhalation starts when the administered substance passes into the nasal vestibule as illustrated in Figure 3, where air turbulence along with interaction with the mucosal surface acts to remove particles that exceed a size of 12 μm.[28] The medication ingredient will pass through the nasal valve, which is made up of the nasal turbinate and cartilage, and enter the respiratory system. This method will minimize the amount of material that enters the olfactory area. The olfactory epithelium has long been considered a principal site where drug absorption predominantly occurs when substances are administered through inhalation due to its structural and functional characteristics. Once the medication has passed through the olfactory epithelium, it is transported intracellularly and extracellularly along the olfactory nerve. Lipophilic medications are transported via paracellular passive diffusion, while hydrophilic pharmaceuticals are transported via carrier-mediated transport, with endocytosis and axonal transport playing minor roles. The olfactory nerve cells traverse the cribriform plate of the ethmoid bone and project to the olfactory bulbs in the central nervous system as components of this sensory signaling pathway.[29] The olfactory bulb is a relay station transmitting sensory information to the amygdala, orbitofrontal cortex and hippocampus, with substances within it reaching the brain by axonal transport, passive diffusion or carrier-enhanced diffusion dependent on chemical properties. After reaching the olfactory region, pharmaceutical substances that do not bind immediately undergo enzymatic degradation and are eliminated via the mucociliary clearance system but a small fraction of residual drug can still be reabsorbed into systemic circulation through the respiratory mucosa.[30]

***Strength and limitations***

This systematic review has several strengths including the use of a clearly defined and comprehensive search strategy across multiple databases, with an explicit selection process that enhances the validity and reliability of the findings. The inclusion of different plant parts as well as the addition of multiple species represents a more complete picture of how Cinnamomum may affect anxiety and the role/s that cinnamaldehyde and other bioactive compounds play. However, this review has several limitations including a small number of included studies, discrepancies alluding to experimental methodologies and dosage levels in the context of meta-analysis as a consequence of animal model only input that hinder the generalization of results in human populations. Future research should be directed toward standardized approaches, detailed phytochemical analysis in determining a clearer picture of the potential associated with Cinnamomum spp.,Clinical studies well-designed to capitalize on favorable pharmacokinetic properties must also be performed. as an anxiolytic agent.

## Conclusions

This robust structured assessment finds that Cinnamomum spp. demonstrates anxiolytic activity in numerous animal-based studies and therefore suggests that cinnamon and its bioactive compounds especially cinnamaldehyde is a considerable modulator of anxiety related behaviours. In accordance with scientific evidence demonstrating active compounds found in cinnamon improve antioxidant processes yet modulating neurotransmitter homeostasis which are both fundamentally associated with the biological pathways of anxiety. Additionally, research suggests that essential oils can cut down on the timeframe within which they are able to elicit responses when administered via inhalation, as they have a more direct pathway into the central nervous system. To strengthen the scientific basis of these Cinnamomum species, future studies should focus on (1) well-defined experimental protocols; (2) detailed phytochemical profiling of all Cinnamomum plants studied and account for the different chemical forms in delivery modes and dosage as observed among medicines; and (3) further elevations towards final phase preclinical and clinical research stages. Such initiatives are needed in order to obtain accurate and high-quality data on the clinical properties and safety profile of Cinnamomum spp. as a second-line alternative for treating anxiety.

### Conflict of Interest

The researchers clearly declare the absence of any competing interests related to this study and its dissemination.

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