

## CINNAMON AS A NATURAL ANTI-ACNE AGENT: A REVIEW OF ITS BIOLOGICAL, PHYTOCHEMICAL ACTIVITIES, MECHANISMS OF ACTION AND DERMATOLOGICAL POTENTIAL.

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### ABSTRACT

Cinnamon is a popular spice that comes from the bark and leaves of *Cinnamomum* trees. People have valued it for centuries due to its wonderful scent and flavor, as well as its many health benefits. The main active compounds in cinnamon, especially cinnamaldehyde, eugenol, and various polyphenols, give it strong antibacterial, anti-inflammatory, and antioxidant properties. Recent studies show that these natural substances can fight *Propionibacterium acnes*, the bacterium mainly linked to acne. They do this by disrupting bacterial cell membranes, preventing biofilm development, and reducing inflammation in skin follicles. Moreover, cinnamon extracts help lower oxidative stress and may speed up skin healing. Traditional acne treatments often cause irritation, can be costly, or may lead to antibiotic resistance. This makes cinnamon an attractive natural choice. This review highlights the biological and phytochemical features of cinnamon, elaborates the effects of its individual components on acne through their antimicrobial and anti-inflammatory actions, and examines its potential as a safe, plant-based treatment for acne in dermatology. In conclusion, current evidence suggests that cinnamon could be effectively used topically, but further clinical research is necessary to confirm its benefits for human skin.

**Keywords:** Cinnamon, Anti-acni activity, Cinnamaldehyde, Antimicrobial properties, Inflammation control

### INTRODUCTION

*Cinnamomum* comes from the Greek word 'kinnamomon,' which means 'spice' and 'sweet wood' (Kumar et al., 2019). The bark from different cinnamon species is one of the most important and widely used spices worldwide, not only in cooking but also in traditional and modern medicine. In total, around 250 species of the *Cinnamomum* genus have been identified, with trees found in many different regions. Cinnamon is mainly used in the fragrance and aroma industries because of its scent. This scent can be

added to many food items, perfumes, and medicinal products. The key compounds in cinnamon are cinnamaldehyde and trans-cinnamaldehyde (Cin), which are present in its essential oil. These compounds contribute to its scent and to the many health benefits linked to cinnamon (Rao & Gan, 2014). Cinnamon has strong aromatic qualities and is used in both food and pharmaceutical industries. Its leaves and bark help with digestion, clean the blood, act as astringents, provide warmth, and work as

antiseptics. They also have antibacterial, antifungal, and antiviral properties, as well as the ability to lower cholesterol and blood sugar levels. Camphor is an important chemical taken from *C. camphora*, used in medicines, especially in liniments and insecticides (Lee et al., 2015). Its bark contains procyanidins and catechins, which are not only popular as spices but are also useful in managing type 2 diabetes and insulin resistance (Nonaka et al., 1983; Killday et al., 2011). This genus includes four main economically important cinnamon species: *Cinnamomum verum* (known as 'true cinnamon,' Sri Lankan, or Ceylon cinnamon), *Cinnamomum cassia* (called Chinese cinnamon), *Cinnamomum burmannii* (known as Java or Indonesian cinnamon), and *Cinnamomum loureiroi* (often referred to as Vietnamese or Saigon cinnamon) (Killday et al., 2011).

Cinnamon is the fragrant bark and essential oils from trees in the genus *Cinnamomum*, mainly *C. verum* (commonly known as true or Ceylon cinnamon) and *C. cassia* (*Cassia*). People use these varieties worldwide as a spice in cooking and as traditional medicine in Asia and beyond. The differences in their trade and cultivars, such as bark thickness and coumarin levels, are significant for both flavor and safety. Current research in botany and phytochemistry keeps redefining species classifications, harvesting methods, and compositional differences. These factors affect both culinary value and biological activity (Singh et al., 2021). The plant's bioactivity results from a complex mix of volatile oils, particularly trans-cinnamaldehyde, tannins, polyphenols, and other phenylpropanoids. These components contribute to many of cinnamon's sensory qualities and its noted biological effects. Recent reviews in phytochemistry show that extraction method, plant part (bark versus leaf), and species significantly affect the amounts of cinnamaldehyde, eugenol, and coumarin. These variations influence antimicrobial effectiveness, antioxidant abilities, and safety profiles (Almatroodi et al., 2020). In the last five years, targeted studies have reinforced evidence for various pharmacological actions. These include antimicrobial and antibiofilm properties, which are important for food safety and topical uses, as well as anti-inflammatory and antioxidant functions. Some clinical trials have shown slight improvements in glycemic and lipid markers. Research is exploring nano and delivery systems to address issues of volatility and solubility,

which will help better formulate cinnamon components for medical or preservative uses. Recent studies have described mechanisms such as membrane disruption, enzyme modulation, and effects on the NF- $\kappa$ B/inflammatory pathway. They suggest promising applications while emphasizing the need for higher-quality clinical trials (Guo et al., 2024). Safety and regulatory concerns are vital. While normal dietary amounts of cinnamon are generally safe, high-dose supplements, particularly from *Cassia* cinnamon, raise concerns due to coumarin. This compound poses a risk of liver toxicity and may interact with drugs by modifying metabolic enzymes (Gu et al., 2022).

### Botanical distribution of cinnamon

*Cinnamomum* is a tropical-subtropical genus with over 250 species that are mostly found in Asia and Australasia. Due to imports, a few species are also found in tropical Africa and the Neotropics, and additional species are found on Pacific islands. The genus's biogeographic spread is demonstrated by the best researched commercial taxa, *C. verum* (Ceylon/"true" cinnamon), *C. cassia* (Chinese/*Cassia* cinnamon), and *C. camphora* (camphor tree): *C. camphora* is native to eastern Asia (China, Japan, Korea, Taiwan) and grows naturally in subtropical forests there; *C. verum* is native to Sri Lanka and southern India but is now grown more widely; and *C. cassia* is native to southern and eastern China, Vietnam, and parts of Southeast Asia and is widely produced in plantations in China and Indonesia (Sharifi-Rad et al., 2021). Many *Cinnamomum* taxa occupy different ecological niches at the species level, ranging from montane subtropical forests to lowland wet rainforests, and each species has different altitudinal and edaphic constraints. Numerous recent field, chemotype, and genomic studies have found species-specific habitat preferences and geographically connected chemical/phenotypic divergence (e.g., leaf- vs. bark-chemotypes, or high-elevation endemics in the Western Ghats and Taiwan). Owing to the genus's taxonomic complexity (polyphyly and cryptic lineages have been identified), modern *ka* phylogenomic and chemotaxonomic studies are elucidating which species are actually native to specific regions and which are cultivated (Xavier et al., 2022).

*Cinnamomum* has rapidly expanded beyond its natural limits due to human-mediated cultivation

and historical trade. During colonial and post-colonial commerce, *C. verum* and numerous other species were tamed and grown in Sri Lanka, Madagascar, the Caribbean, portions of Africa, and Latin America; *C. cassia* and related taxa are extensively planted in Southeast Asia and in plantation systems. Even though introduced populations may hybridize with local congeners or become naturalized, datasheets and compendia summarize both natural (native) distributions and introduced ranges used for commercial production. Due to ecological and safety (coumarin) differences, recent country-level and product-supply studies further highlight the necessity of recording species identity in commerce (Ceylon vs. Cassia) (Pathak & Sharma, 2021).

### Geographical Distribution and Ecological Significance of Cinnamon

The genus *Cinnamomum* is mostly Asian-Australasian, with its center of diversity located in eastern Asia and Southeast Asia (Malesia). The most popular commercial variety, *C. verum* (Ceylon/"true" cinnamon), is grown on plantations throughout the Caribbean,

Madagascar, Sri Lanka, and areas of southern India. Chinese cinnamon, or *C. cassia*, and similar taxa, on the other hand, are endemic to mainland Southeast Asia, Vietnam, and southern/eastern China. They are widely planted for their wood and spice. Genomic and population studies confirm these regional trends and identify a number of farmed and introduced populations outside of natural areas (Kumar et al., 2019). *Cinnamomum* species can be found in a wide range of ecological situations, from subtropical and montane forests to lowland humid tropical rainforests. They vary in their preference for altitude and edaphic conditions (some are lowland specialists, while others are montane endemics). Climate variables (temperature, precipitation, seasonality, and elevation) significantly shape suitable ranges for species like *C. camphora*, *C. cassia*, and *C. parthenoxylon*, as well as contractions under warming scenarios, according to recent ecological-niche modeling, population genetics, and genome-resources work. This information is being used for conservation, crop planning, and germplasm management (Li et al., 2023).

Table 1. Taxonomic and Botanical Classification of Cinnamon

Category	Distribution
Family	Lauraceae
Genus	<i>Cinnamomum</i> Schaeffer
Scientific name	<i>Cinnamomum verum</i> J. Presl (syn. <i>C. zeylanicum</i> Blume)
Common names	Cinnamon, True cinnamon, Cassia, Dalchini (Hindi/Urdu)
Etymology	The name <i>Cinnamomum</i> comes from the Greek word "kinneomon", which is derived from the Hebrew word "qinnamon", which means "spice" or "sweet wood."
Important Species	<i>Cinnamomum burmannii</i> (Java or Indonesian cinnamon), <i>Cinnamomum loureiroi</i> (Vietnamese or Saigon cinnamon), <i>C. verum</i> (Ceylon cinnamon), and <i>C. cassia</i> (Chinese cinnamon)
Habit & Growth Form	Large shrub or evergreen, fragrant tree, 6-15 m tall, with a straight trunk and roll-peeling grayish-brown bark
Stem/Bark	Young bark is smooth, but as it ages, it becomes rough. The inner bark is reddish-brown and fragrant, and it contains volatile oils, most notably trans-cinnamaldehyde.
Leaves	Simple, opposite/sub-opposite, ovate to elliptic, 7-18 cm long, leathery, with three noticeable parallel veins extending from the base; crushed, aromatic
Inflorescence	Axillary or terminal panicles; tiny greenish-white or yellowish blooms
Flowers	Bisexual, with a tubular, 6-lobed perianth, 3 whorls of 9 fertile stamens, a superior ovary, and 2- or 4-celled anthers.
Fruit	Ripe, a drupe is ovoid or ellipsoid (1-2 cm), dark purple or black, and contains a single seed.

<b>Chromosome Number</b>	Reports in <i>C. verum</i> and <i>C. cassia</i> state that $2n = 24$
<b>Phytochemical Constituents</b>	Catechins, polyphenols, proanthocyanidins, coumarin, linalool, eugenol, cinnamaldehyde, and cinnamic acid

### Phytochemical Constituents of Cinnamon

Numerous resinous substances, including cinnamaldehyde, cinnamate, cinnamic acid, and other essential oils, are found in cinnamon. Cinnamon has a strong scent and a spicy taste because to the cinnamaldehyde component. Cinnamon contains several essential oils, including trans cinnamaldehyde, cinnamyl acetate, eugenol, L-borneol, caryophyllene oxide,  $\beta$ -caryophyllene, L-borneol acetate, Eneolidol, alpha-cubebene, alpha-terpineol, terpinolene, and alpha thujene (Pathak & Sharma, 2021). Trans cinnamaldehyde, eugenol, linalool, cinnamyl acetate, cinnamic acid, and sesquiterpenes like  $\beta$ -caryophyllene are the main volatile (essential oil) components of cinnamon bark and leaves. Their proportions differ by plant part (leaf vs. bark) and species (*C. zeylanicum* vs. *C. cassia* vs. others) (Aggarwal et al., 2022). Simple phenolic acids, proanthocyanidins (procyanidins), coumarins (particularly high in *C. cassia*), tannins, and derivatives of cinnamic acid are examples of non-volatile phenolics that are abundant and have antioxidant and metabolic effects (Sharifi-Rad et al., 2021). Terpenoids, flavonoids (such as catechin, epicatechin, and quercetin glycosides), and trace levels of sterols or other minor ingredients have also been observed in various species (Sharifi-Rad et al., 2021). According to numerous GC-MS investigations, trans-cinnamaldehyde, the primary bioactive responsible for scent and numerous pharmacological effects, is usually the predominant component of bark oil (Singh et al., 2021). Eugenol adds to antibacterial and analgesic qualities, particularly in leaf oils and in certain species (Sharifi-Rad et al., 2021).

A common component of the floral/lavender-like fraction, linalool is found to make up a significant portion of certain oils (~80% combined in some assessments) together with cinnamon aldehyde and eugenol (Aggarwal et al., 2022). Bark and leaf oils frequently contain repeating volatiles such as cinnamic acid,  $\beta$ -caryophyllene,  $\alpha$ -pinene, limonene, copaene, muurolen, and others (amounts vary by species and provenance) (Amran et al., 2023). Cinnamic acid and its byproducts, such as cinnamaldehyde oxidation products and cinnamyl alcohol, are widely available (Singh et al., 2021). Particularly in *C. cassia* (*Cassia cinnamon*), coumarin is found in significant quantities and is of toxicological relevance due to its potential for hepatotoxicity at high concentrations. Condensed tannins, proanthocyanidins (procyanidins A/B), and simple phenolics (catechins, epicatechins) are found in cinnamon. These play a significant role in the extracts' antioxidant properties (Sharifi-Rad et al., 2021). Catechin, epicatechin, quercetin and glycosides, kaempferol derivatives, and other flavonoids are typically found in the non-volatile fraction (methanol/ethanol extracts). According to Sharifi-Rad et al. (2021), flavonoid profiles differ according on the species and extraction technique (Sharifi-Rad et al., 2021). The essential oil fraction frequently contains  $\beta$ -caryophyllene, muurolene, copaene, and other mono-/sesquiterpenes that have antibacterial and anti-inflammatory properties (Singh et al., 2021). Depending on the species and extraction, trace levels of alkaloids, sterols, fatty acids, and polysaccharides are present; these are frequently identified in thorough phytochemical screens (Nawaz et al., 2023).

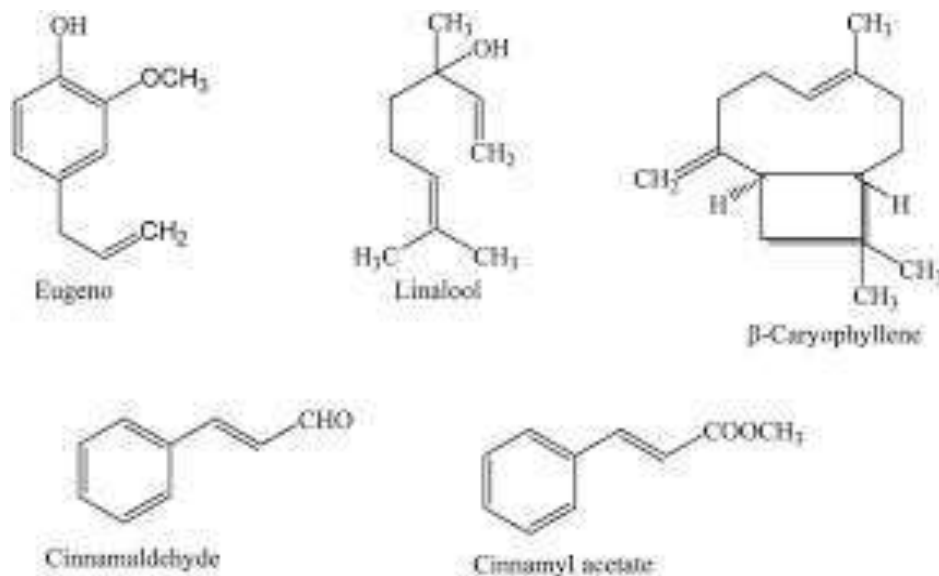


Figure 1. Major Phytochemicals of Cinnamon

### Cinnamon in treatment of various diseases

In preclinical and some clinical studies, cinnamon has been shown to be beneficial as an adjunct for metabolic disorders (type 2 diabetes, metabolic syndrome, dyslipidemia, PCOS), and it has anti-inflammatory, antimicrobial, neuro-protective, and anticancer effects. However, clinical results vary by formulation, dose, and study quality and safety (coumarin in *Cassia cinnamon*) must be taken into account (Zarezadeh et al., 2023). Supplementing with cinnamon lowers fasting blood glucose, HOMA-IR (insulin resistance), and in certain studies, HbA1c and postprandial glucose. The impact sizes vary depending on the type, dosage, and duration of the cinnamon. The majority of RCTs employed 1-3 g/day, although typical trial doses range from 1-6 g/day (Moridpour et al., 2024). Cinnamaldehyde contains antioxidant or anti-inflammatory properties that improve insulin sensitivity, inhibits enzymes that break down carbohydrates, and seems to improve insulin signaling and glucose uptake (GLUT4 translocation) (Guo et al., 2024). According to Guo et al. (2024), cinnamon has antioxidant properties, modulates genes related to lipid metabolism, inhibits pancreatic lipase, and increases insulin sensitivity (Guo et al., 2024). In women with PCOS, cinnamon can improve insulin resistance and some metabolic or reproductive parameters; its effects on ovulation or menstrual cyclicity are encouraging but require further research (Dastgheib et al., 2022).

In preclinical animals, cinnamon exhibits cardioprotective properties and reduces some CV risk variables (lipids, blood pressure) (Das et al., 2022). In animal or cell models, cinnamaldehyde decreases pro-inflammatory signaling (e.g., NF-κB, COX, MMPs), joint inflammation, and cartilage degradation (Sankaranarayanan et al., 2024). In vitro and in vivo, cinnamon essential oil and cinnamaldehyde exhibit wide antibacterial, anti-biofilm, and antifungal activity; multiple studies show activity against oral biofilms and resistant organisms (Iseppi et al., 2024). In animal models, cinnamon and substances (such as cinnamaldehyde, eugenol, and metabolites of sodium benzoate) may lessen Aβ aggregation, prevent tau hyperphosphorylation, reduce neuroinflammation, and enhance memory (Nakhaee et al., 2024). In several cancer cell lines (breast, colon, hepatic, and hematologic), cinnamon extracts and cinnamaldehyde cause apoptosis, suppress proliferation, lessen metastasis, and alter angiogenesis (Caserta et al., 2023).

### Cinnamon in Treatment of Acne Vulgaris

A number of problems, such as patient noncompliance, ignorance of drug usage, fear of possible side effects, and the high cost of treatment, continue to impede the effectiveness of pharmacological therapy of AV despite much study on the subject (Moradi Tuchayi et al., 2016). Comedolytic agents, antibiotics, and various anti-inflammatory drugs are frequently used in topical therapy for acne, whilst hormones zinc, and

antibiotics are used in systemic therapy. However, long-term overuse of antibiotics may make acne bacteria more resilient. Antibiotic resistance can be replaced by safer, more effective, and versatile essential oils and extracts from medicinal plants. When applied topically to treat acne, medicinal plant extracts are less likely to have negative side effects than synthetic medications (Daud et al., 2013). Cinnamon may have antimicrobial qualities, according to some research. Cinnamonaldehyde, one of the primary components of cinnamon, has anti-inflammatory qualities. It stops the body from producing nitric oxide, which leads to inflammatory illnesses. Furthermore, it has been shown that cinnamon prevents the production of COX-2, a molecule that promotes inflammation. Cinnamon possesses antibacterial and anti-inflammatory properties as a result. In contrast to root-bark oil (camphor) and cinnamon leaf oil (eugenol), Wijesekera (1978) claims that the chemistry of cinnamon bark oil mostly consists of a cinnamaldehyde (Wijesekera & Chichester, 1978).

Many chemicals, including cinnamyl acetate, eugenol, L-boronyl, caryophyllene oxide, terpenylene, pinene, and cymene, are found in cinnamon, whereas thyme contains apigenin, eugenol, linalool, thymol, carvacrol, and rosmarinic acid. These components have a variety of qualities, including antiseptic, antibacterial, antifungal, antioxidant, and antimicrobial qualities. Cinnamon is believed to contain chemical compounds that have antibacterial properties, including flavonoids, 0.5–2% essential oils (like eugenol, saffrol, cinnamon aldehyde, and linalool), 10% polysaccharides (like coumarin and diterpenes), and 4–10% phenolic components (like tannins) (Parisa et al., 2019). Cinnamon has potential anti-inflammatory and antioxidant properties in addition to its consistent in vitro antibacterial action against bacteria linked to acne (Bhati et al., 2020). In lab tests, ethanolic extracts and cinnamon essential oil exhibit low minimum inhibitory concentrations (MICs) and strong inhibition zones against *C. acnes* and other Gram-positive skin germs. Cinnamaldehyde and other phenylpropanoids are mostly responsible for this (Bhati et al., 2020). In cell and molecular investigations, cinnamaldehyde and related derivatives of cinnamic acid diminish the production of inflammatory mediators (e.g., NF- $\kappa$ B pathway modulation, cytokine suppression), which

is a potential strategy to reduce inflammatory acne lesions (Guo et al., 2024). Cinnamon extracts have been shown to have antioxidant qualities and may help lower oxidative stress in follicles afflicted by acne; several formulations claim sebostatic effects, although there are few direct clinical assessments of sebum reduction (Błaszczuk et al., 2021).

### **Acni Vulgaris**

Acne vulgaris is a chronic dermatological condition that involves inflammation of the pilosebaceous unit (Zouboulis, C.C. 2004). According to epidemiology, this illness affects 9.4% of people worldwide, making it the eighth most prevalent disease globally (Tan & Bhate, 2015). The term acne is derived from Greek word "acme," which means "prime of life". Even while acne is usually thought of as a harmless, self-limiting disorder, it can result in lifelong disfiguring scars or serious psychological issues. Acne is pleomorphic condition, affects 85% of the population which can appear at any stage of life but most frequently presents between the ages of 12 and 24. However, a lot of adult women do experience acne in the days leading up to their periods. Although it can occur at any age, including infancy, acne is most frequent in teenagers. Acne affects three out of four teenagers to some degree, most likely due to hormonal changes that increase oil production. But acne can also strike people in their 30s and 40s. At some point in their lives, most people encounter this circumstance, particularly during adolescence (Tahir, CM. 2016). Non-inflammatory (comedones) and inflammatory (papules, pustules, nodules, and cysts) skin lesions are the hallmarks of this condition, which primarily affects sebum-rich regions including the face, back, and chest (Ghowati 2019). High sebum secretion, hyper keratinization, hormonal fluctuations, and bacterial infection are some of the multifactorial underlying pathophysiology of these lesions (Hazarika & Archana., 2016).

Propionibacterium acnes play an important part in the pathophysiology of acne. This bacterium has the ability to convert sebaceous triglycerides into fatty acids and activate certain inflammatory mediators, which draw white blood cells to the clogged follicle and cause inflammation of the skin. Sebum, dead cells, and bacteria are released when the hair follicle membrane breaks down, resulting in a range of acne severity (Shweta Kapoor & Swarnlata Saraf, 2011). Anaerobic obligatory

diphtheroid, *P. acnes*, live beneath the epidermis and are found in androgen-stimulated sebaceous follicles. This Gram-positive bacterium thrives in anaerobic environments, which are created when oxidative stress occurs within the pilosebaceous unit. Inflammatory acne is the result of it. *Staphylococcus epidermidis*, an aerobic bacterium linked to superficial infections in the sebaceous units is also a resident of the human skin flora. The first line of treatment for mild to moderate acne vulgaris is topical antibacterial medicines. *P. acnes* are the main pathogens linked to the emergence of inflammatory acne. Concern over the slow global rise in antibiotic-resistant *P. acnes* strains has grown over the last 20 years (Leyden, J. J. 2004).

### Epidemiology

Acne is a fairly common skin illness that affects at least 80% of adolescents (Romańska-Gocka et al., 2016, Elsaie, ML. 2016, Minh et al., 2019, Goodman, G. 2009). 80% of them are teenagers (Sparavigna et al., 2015, Williams, H et al., 2012, Purdy et al., 2003- Villani et al., 2022). About 80% to 90% of teenagers in the Western world suffer from behavioral, emotional, and physical/psychological problems brought on by acne, despite the fact that this inquisitive nature is regarded as a typical part of the development process (Ettel et al., 2017). Approximately 60% of impacted teenagers use over-the-counter products to treat their minor acne without seeing a doctor. According to Gollnick (2015), the remaining 40% of individuals with acne represent the population seen in medical practice (Gollnick, H. P. M. 2015). The prevalence is lower among Asians and African-Americans than among Caucasians (Kucharska et al., 2016). Approximately 20% of those impacted experience severe acne, which leaves scars behind (Zaenglein, A. L. 2018). Obesity and overweight have a dose-dependent negative correlation with acne in young people (Snast et al., 2019). Girls between the ages of 18 and 19 who are overweight or obese have acne, whereas boys do not have this

correlation (Halvorsen et al., 2012). Pregnancy is often associated with acne. It is indeed possible for more than one in two pregnant women to experience acne (Gupta et al., 2024). Certain forms of post-inflammatory hyperpigmentation, such "pomade acne," are more common in Black people. In first-degree relatives, acne is over 80% heritable (Bhate & Williams, 2013). Adolescents who regularly consume soft drinks are much more likely to develop moderate-to-severe acne, particularly if their daily sugar intake from all soft drinks exceeds 100 g (Huang et al., 2019).

### LESION TYPES

Acne lesions can be classified as either inflammatory or non-inflammatory. Some medications have been created that solely target one of these two distinct subsets of acne vulgaris lesions, despite the fact that the majority of acne medications are designed to treat the entire spectrum of acne vulgaris (Hentsch & Schwarz, 2007). The open (blackheads) or closed (whiteheads) comedones are non-inflammatory acne lesions. Stretching the skin may be necessary to help visualize closed comedones, which can be more challenging to spot visually.

These lesions are of clinical significance because they may be precursors to the larger inflammatory lesions, particularly closed comedones. Based on the degree and location of inflammation within the dermis, inflammatory lesions are classified as papules, pustules, or nodules/nodulocystic lesions. It is possible to classify the papules and pustules as inflammatory due to the erythema halos that surround them. Usually erythematous, nodules are frequently unpleasant and/or uncomfortable. They are also deeply seated in the skin, with the dermis or subcutis at their center. Nodules are characterized as having a diameter of more than 5 mm. Because of the accompanying erythema and inflammation, it may be challenging to identify the boundaries of these lesions.



Figure 2. Papules acne



Figure 3. Pustules acne



Figure 4. Nodular acne



Figure 5. Cystic acne

### Salient causes for the development of acne

Acne develops when the skin's pores are clogged by bacteria, dead skin, oil, or all. Every skin pore is the entrance to a follicle, which is composed of a sebaceous oily gland and a hair. Sebum, a naturally occurring material released by the oil gland, lubricates and protects the skin as it travels through the pores and up to the hair root. Acne has now spread because of one or more issues with the lubrication process, which resulted in increased oil production and a follicular pore clog. If the plug is exposed to the air, the darker exposed part of the plug is called a blackhead; if it is covered by a thin layer of skin, it looks to be a whitehead. The clogged hair follicle slowly became visible as a lump. As the follicle grows, the wall bursts, allowing normal skin bacteria to enter the deeper layers of the skin. This causes inflammation, which in turn causes a pustule to form on the skin's surface, a pimple to form, and a cyst to form if the inflammation spreads further, potentially leaving the skin with permanent, incurable scars. The occurrence of pimples is brought on by an overabundance of oil, germs, and plugged pores from dead skin cells. When bacteria proliferate in the plugged pore and the oil cannot leave, a zit forms.

### Pathogenesis

The primary causes of acne include Propionibacterium acne-induced inflammation, sebocyte differentiation, and excessive sebum

production. Normally found on healthy skin flora, anaerobic gram-positive bacteria proliferate quickly on skin that is preferably blocked and has a lot of sebum. Triglycerides are changed into fatty acids, which are found in the glands, and these result in inflammation. The bacteria also encourage the production of cytokines and proinflammatory mediators (Radha et al., 2013). Increased sebum production, follicular hyperkeratinization, and blockage are all part of the complex pathophysiology of acne vulgaris. P. acnes cause inflammation by binding to immune receptors. Follicle hyperkeratinization and keratinocyte deposition restrict the follicular orifice, resulting in microcomedones. Comedones can be categorized into two types: open and closed. Closed comedones are invisible, whereas open comedones are readily removed and visible. Additionally, some factors may be contributory factors as they increase the expression of IL1alpha, K16, and filaggrin in conjunction with follicular hyperkeratinization (Fang et al., 2001).

Furthermore, health-related quality of life (HRQoL) has been linked to acne, sometimes with detrimental effects comparable to those of serious and even fatal illnesses (Tanghetti et al., 2014). Psychiatric comorbidity and undesirable stressful life events were more prevalent in acne sufferers than in controls. According to Zari and Alrahmani (2017) and Uhlenhake (2010), there is a positive correlation between the severity of acne and stress and depression (Zari & Alrahmani, 2017;

Uhlenhake et al., 2010). Four elements combine to cause acne (Oberemok & Shalita, 2002).

**Comedogenesis-** Comedogenesis, or sebum follicle blockage, can result from either hyperproliferation of ductal keratinocytes or enhanced cohesiveness of follicular epithelial cells.

**Excessive sebum production-** Sebaceous glands stimulated androgenically at or near the site of excessive sebum production.

**Proliferation of Propionibacterium acnes-** Propionibacterium acnes, an anaerobic diphtheroid that normally constitutes cutaneous

flora and populates sebaceous follicles, is proliferating. Proinflammatory mediators and chemotactic factors are produced by P acnes, which may cause inflammation.

**Inflammation-** The growth of P. acnes can either directly or indirectly cause inflammation. Inflammatory lesions of acne vulgaris, such as papules, pustules, and nodules, are caused by follicular rupture and inflammation spreading into the dermis.

Table 2. Cinnamon activities in treatment of Acne vulgaris

S. No	Species, part used/ active constituents	Biological activities	Phytochemical activities	Anti-acni activity	Dose/Method	References
1.	Cinnamomum validinerve Stem	Anti-inflammatory and Antibacterial activity	Validinol and Validinolide, emphasizing their high butanolide content associated with potential anti-acne properties.	In vitro, Cinnamtannin B1 from cinnamon exhibits potent anti-acne action by suppressing P. acnes and lowering inflammation in vivo.	Disk diffusion method, MIC assays and P. acnes ear infection model.	Yang et al., 2020
2.	Cinnamomum zeylanicum Bark	Antibacterial Activity	Cinnamon Oil demonstrated significant antimicrobial activity against S. aureus and S. epidermidis.	At low MIC values (1.6%, 6.3%, and 12.5%), cinnamon oil exhibits potent anti-acne activity against S. pyogenes, S. aureus, and S. epidermidis.	25% - 100% concentrations; disk diffusion; MIC determination	Shabani et al., 2016
3.	Cinnamomum verum Bark	Antibacterial activity	Cinnamaldehyde is responsible for its antibacterial properties.	In vitro, 5% cinnamon bark oil, which had a zone of inhibition of 2.03 ± 0.06 cm.	..... Nanoemulsion, Carbopol nanoemulgel, or ganoleptic tests, pH, viscosity, stability testing and Agar well diffusion method.	Ameliana & Rosyidi, 2024

4.	Cinnamomum verum  Bark	Antibacterial activity	Cinnamaldehyde and other phenolic compounds, have known antimicrobial effects.	In vitro, Cinnamon-containing proniosomal gel had antibacterial efficacy against P. acnes.	10, 20, 30, 40, 50 µg/mL; hydroalcoholic extraction; proniosomal gel via coacervation phase separation.	Bhati et al., 2020
5.	Cinnamomum verum  Bark	Sebostatic Anti-bacterial and Anti-inflammatory activity	Cinnamaldehyde (CA) contains antioxidant, antimicrobial, and anti-inflammatory properties.	In vivo, after two months of treatment, cinnamon gels decreased overall (47%, p=0.000), inflammatory (42%, p=0.026), and non-inflammatory (48%, p=0.002) acne lesions.	Applied twice a day for eight weeks; open-label, assessor-blind, uncontrolled clinical trial.	Ghowvati et al., 2019
6.	Commercially available  Bark	Antimicrobial activity	Cinnamaldehyde shows antimicrobial activity against P. acnes, supporting its potential as an anti-acne cosmetic ingredient.	In vitro, Cinnamon oil determines strong anti-acne activity against P. acnes, with a 36.75 mm inhibition zone and an MIC of 5 mg/mL.	Cinnamon oil 0.5% w/w; agar disc diffusion and broth dilution methods.	Veerasophon, J., et al., 2020
7.	Cinnamomum cassia  Bark spice	Antioxidant and antibacterial activity	Cinnamon contains polyphenols and flavonoids, which contribute to its antioxidant properties.	In vitro, Cinnamon inhibits acne-associated microorganisms demonstrating substantial antibacterial activities at 50 mg/mL with inhibition zones up to 29 mm against E. coli, 23 mm against P. aeruginosa, 22 mm against S. aureus, and 33 mm against C. albicans.	50 µL and 2.5 mL DPPH assay, FRAP assay and agar disc diffusion method.	Annou & El Hadj-Khelil, 2021

8.	Cinnamomum verum  Bark and leaf	Anti-inflammatory, antioxidant and antimicrobial activity	Cinnamon treats acne through phytochemicals like CA, eugenol, and coumarin, have potent antibacterial and anti-inflammatory properties against microorganisms that cause acne.	Cinnamon oil is effective for anti-P. acnes activity.	.....	Wijayadi, L. J. 2022
9.	Cinnamomum cassia  Bark	Anti-microbial, Anti-inflammatory and Antioxidant activity	The phenyl ring either increases or decreases biological effectiveness.	Antimicrobial and anti-inflammatory properties could strongly contribute to anti acni effects.	The drugs were only assessed in vitro; no precise in vivo dose or methodology was disclosed.	Ruwizhi & Aderibigbe, 2020
10.	Cinnamomum zeylanicum  Bark	Antibacterial activity	Aqueous, ethanolic, and hydroalcoholic extracts from cinnamon exposed varying antibacterial effects.	In vitro, cinnamon extracts demonstrated potent anti-acne efficacy with zones of inhibition of about 18 mm against P. acnes and up to 22 mm against S. epidermidis.	250 µL- 500 µL; The well diffusion method.	Chaudhary et al., 2013
11.	Cinnamomum zeylanicum  Bark	Antibacterial, Anti-inflammatory, Antioxidant and Antifungal activity	cinnamaldehyde, eugenol, coumarins, and polyphenols demonstrate anti-acne efficacy by lowering inflammation, offering antioxidant benefits, and creating inhibitory zones against bacteria that cause acne.	In vitro, Cinnamon has anti-acne action with zones of inhibition of about 18 mm against P. acnes and up to 22 mm against S. epidermidis, lowering pore blockage, inflammation, and bacterial growth.	For topical use, cover the afflicted area with a paste made of 1 teaspoon of cinnamon powder and 2 tablespoons of honey for the entire night.	Sharma et al., 2012

12.	Cinnamomum verum  Bark	Antibacterial Activity	Cinnamaldehyde, eugenol, and coumarin provide anti-acne benefits through their antimicrobial and anti-inflammatory properties.	In vitro, Cinnamon bark extract have antibacterial properties against P. acnes and S. epidermidis, the combination exhibits an additive effect with a FICI value of 0.625.	256 µg/mL and 1024 µg/mL; Disc diffusion, and CLSI methods.	Julianti et al., 2017
13.	Cinnamomum burmannii  Bark	Antibacterial Activity	α-Limonene, α-terpineol, eucalyptol, cinnamaldehyde, and cinnamon acetate contribute to the antibacterial qualities.	In vitro, Cinnamomum burmannii oil exhibits anti-acne action by blocking S. aureus and S. epidermidis, two bacteria linked to acne.	0.03–4 mg/mL; GC-MS, MIC, and checkerboard methods, with FICI calculated for concentration effects	Mulyaningsih et al., 2023
14.	Cinnamomum verum Bark  Cinnamomum zeylanicum Leaf	Antifungal activity	.....	In vitro, Cinnamon essential oils may have antibacterial and anti-inflammatory qualities in vitro, which may help prevent acne.	50 µL; Broth microdilution to determine MIC, with synergy assessed via ΣFIC index and isobolograms.	Orchard et al., 2019
15.	Cinnamomum zeylanicum Blume  Bark	Antioxidant, Anti-inflammatory, Antimicrobial, and Anti-fungal properties.	Eugenol, coumarin, and cinnamonaldehyde all have antibacterial and anti-inflammatory properties that help prevent acne.	In vitro, Cinnamon reduces inflammation, redness, and edema in acne-affected skin by inhibiting Cutibacterium acnes.	.....	Abozeid et al., 2023
16.	Cinnamomum burmanii  Bark	Antibacterial activity	Alkaloids, flavonoids, tannins, and saponins illustrate anti-acne activity through their	In vitro, cinnamon extract shows anti-acne activity by deterring Staphylococcus aureus.	12%; The disc diffusion method.	Lianingsih et al., 2024

			antibacterial effects.			
17.	Cinnamomum zeylanicum  Bark	antibacterial, anti-inflammatory and antioxidant activity	Cinnamon bark water extract assesses the biological effects.	In vitro, Cinnamomum zeylanicum bark shows anti-acne efficacy by suppressing bacteria such as Streptococcus mutans, S. sanguis, Staphylococcus aureus, and Porphyromonas gingivalis.	..... Agar disc diffusion method, Minimum Inhibitory Concentration (MIC), Lipoxygenase inhibition assay, Hyaluronidase inhibition assay, ABTS assay and DPPH assay.	Tanwar, E. 2019
18.	Cinnamomum zeylanicum  Bark oil	Antioxidant activity and Inhibitory activity	Chief constituents of cinnamon essential oil: Cinnamaldehyde (68.80%) Eugenyl acetate (4.60%) Caryophyllene (4.18%)	In vitro, cinnamon essential oil exhibits anti-acne potential by blocking tyrosinase and supporting skin health, which may help control pigmentation and acne scars.	125 µg/mL-1000 µg/mL; DPPH assay, ABTS assay, Tyrosinase inhibition assay, Collagenase inhibition assay, Elastase inhibition assay.	Wanakhachornkrai et al., 2020
19.	Cinnamomum verum and Cinnamomum cassia  Bark and essential oil of cinnamon	Antibacterial and Antimicrobial activity	Cinnamaldehyde and eugenol show antibacterial effects.	Cinnamon's antibacterial activities help moderate acne lesions by inhibiting Propionibacterium acnes growth.		Nabavi et al., 2015
20.	Cinnamomum verum  Essential oil of cinnamon	Antimicrobial Activity		In vitro: Cinnamon essential oil presented effective inhibition of 18.00±0.0, mm against P. acnes.	2%; Kirby-Bauer disc diffusion, Minimum Inhibitory Concentration (MIC) by broth dilution method.	Thombare & Mukundan, 2012
21.	Cinnamomum verum and Cinnamomum cassia	Antioxidant, anti-inflammatory and	Cinnamaldehyde, cinnamic alcohol, cinnamic acid and cinnamate	Cinnamon may help treat bacterial acne because of its	.....	Błaszczuk et al., 2021

	Bark and leaves	Antibacterial activity	cause numerous therapeutic benefits.	antimicrobial properties.		
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### Biological activities of cinnamon in treatment of acne

#### Anti-inflammatory activity

According to Ghovvati, M., et al., using cinnamon gel twice a day for eight weeks dramatically decreased the number of total lesions (~47%), inflammatory lesions (~42%), erythema, and sebum content in individuals with mild to moderate facial acne. These are clinical correlates of reduced inflammation (Ghovvati et al., 2019). Human monocytes (THP-1) treated with LPS, cinnamon extract, or isolated chemicals (trans-cinnamaldehyde, p-cymene) decreased IL-8 secretion, Akt phosphorylation, and  $\text{I}\kappa\text{B}\alpha$ , these pathways are comparable to those that *C. acnes* activates in acne (Schink et al., 2018). Pagliari, S., et al. stated that cinnamon bark extract continued to have anti-inflammatory properties in vitro after simulating digestion, lowering oxidative stress indicators or inflammatory markers. This implies possible topical or systemic advantages (Pagliari et al., 2023). According to research by Ameliana and Rosyidi (2024), cinnamon bark oil in the form of a nanoemulgel shows good anti-acne activity (antibacterial against *P. acnes*) (Ameliana & Rosyidi, 2024). Cinnamon essential oil nanogels dramatically decreased inflammation in animal models of inflammation (paw edema) (Esmaeili et al., 2022). Davoudi, F. proposed that cinnamon species improve antioxidant enzyme activities, inhibit NF- $\kappa$ B and MAPKs, and decrease TNF- $\alpha$ , IL-1 $\beta$ , and IL-6 (Davoudi & Ramazani, 2024).

Vallion et al., found that when cells are challenged with a TLR2/TLR-agonist (zymosan), cinnamaldehyde causes the transcription factor Nrf2 to accumulate at a lower concentration (100  $\mu$ M). This is linked to the suppression of pro-inflammatory cytokine mRNAs (such as IL-1 $\beta$  and TNF- $\alpha$ ) and a decrease in the pro-inflammatory response. However, at a greater dose (250  $\mu$ M), CinA had a pro-inflammatory effect via increasing the levels of those cytokines rather than inducing Nrf2 (Vallion et al., 2022). The study also demonstrated that the lower dose's anti-inflammatory effects (i.e., increased cytokine release) were lost in keratinocytes with Nrf2 knockdown. Thus, Nrf2 appears to be crucial in changing the equilibrium. This is significant

because acne lesions are associated with keratinocyte inflammation, which results in the production of IL-1 $\beta$ , IL-8, and other chemicals. This suggests that cinnamaldehyde has a dose-dependent potential; at the right dosage, it may help reduce cytokines related to acne via Nrf2, but a high dose may make the condition worse (Vallion et al., 2022). The study discovered that via blocking NF- $\kappa$ B and JNK signaling, cinnamon aldehyde inhibited keratinocyte growth and decreased the expression of important pro-inflammatory mediators (Ding et al., 2021). Additionally, it improved psoriasis-like lesions in mice, proving it's in vivo applicability. These findings support the idea that cinnamon aldehyde has anti-inflammatory effects in skin via signaling suppression, which may be applied to acne, even if psoriasis and acne differ (e.g., participation of *P. acnes*, sebum, etc.) (Ding et al., 2021).

#### Anti-bacterial activity

The oil had a strong anti-*C. acnes* action (Peng et al., 2024). For *P. acnes*, Ameliana, L. & Rosyidi, V.A. discovered a formula (F3) with excellent antibacterial activity and good physical qualities. The nanoemulgel enhances transport, possibly by boosting interaction with bacterial cells and improving stability (Ameliana & Rosyidi, 2024). Different doses of cinnamon oil demonstrated inhibitory zones against MRSA and *S. aureus*; membrane damage is one of the causes (Guo et al., 2024). Cinnamon oil had a broad inhibition zone (~36.75 mm) against *P. acnes*; MIC was ~5 mg/mL. The concealer formulation with 0.5% cinnamon oil retained antibacterial action (Veerasophon et al., 2020). According to Wijayadi (2022), cinnamon essential oil has antibacterial properties that can combat acne germs (Wijayadi, L.J. 2022). According to the study, the main bioactive component is trans-cinnamaldehyde. It disrupts amino acid transport and energy balance in bacteria by covalently altering their proteins (such as the ATP-binding protein, ABC transporter, and NADH-quinone oxidoreductase). In addition to membrane damage, this provides a more profound understanding of the mechanisms influencing bacterial metabolism (Peng et al., 2024).

Using disc diffusion, the extract's inhibition zone against *P. acnes* was approximately 17.2 mm, whereas it was approximately 16.8 mm for *S. epidermidis*. The action of honey was comparable (inhibitory zones ~ 16 mm). According to Julianti et al. (2017), the combination of cinnamon extract and honey had an additive effect (FICI = 0.625), which suggests that a combined treatment may permit lower doses of both (Julianti et al., 2017). Cinnamaldehyde, eucalyptol, cinnamonyl acetate, and  $\alpha$ -limonene were the primary constituents in *C. burmannii* oil, according to the GC-MS study, whereas geraniol, citronellal, and citral were detected in *C. nardus* oil. The results of the Checkerboard assay indicated that there was no significant synergy or antagonism between the two oils and those microorganisms. Therefore, depending on the species and dosage, combination may not always increase effect (Mulyaningsih et al., 2023).

#### Anti-oxidant activity

In cell models, the digested extract decreased indicators of oxidative stress and retained significant antioxidant ability (such as radical scavenging and reducing power). This implies that the antioxidants in cinnamon may have systemic effects and survive digestion (Pagliari et al., 2023). They observe a significant drop in red fluorescence spots in addition to a decrease in lesion counts, which is associated with oxidative activity and porphyrin synthesis by *C. acnes*. Decreased erythema and improved skin biophysical parameters also suggested less oxidative/inflammatory stress (Ghovvati et al., 2019). Cinnamon dramatically reduced malondialdehyde (MDA), an indication of oxidative stress, and raised serum total antioxidant capacity. Acne is widespread in PCOS and is linked to increased systemic oxidative stress, even though PCOS is not the same as acne (Borzoei et al., 2018). Cinnamaldehyde decreased the production of reactive oxygen species (ROS), stimulated the antioxidative enzyme Hmox1, decreased the buildup of malondialdehyde, and stopped the breakdown of collagen. While photoaging is not acne, oxidative stress and inflammation are similar mechanisms (Tanaka et al., 2019). These tests revealed that cinnamon essential oil had extremely high antioxidant activity. For instance, cinnamon EO was one of the best in the DPPH assay, the FOE (fish oil emulsion), and the RBC systems. This

implies that lipid peroxidation and oxidative stress in skin and lipids may be lessened by cinnamon essential oil (Chen et al., 2023). Although the main goals were antibacterial/delivery rather than direct ROS or antioxidant assays, they do note that cinnamon oil contains cinnamaldehyde, which is known to have antioxidant action. This suggests that it may be an antioxidant (Ameliana & Rosyidi, 2024).

#### Other potential therapeutic activities (e.g., Sebostatic, Anti-fungal)

Twenty patients with mild-to-moderate facial acne utilized a topical cinnamon gel twice a day for eight weeks, according to Ghovvati, M., et al. This study used a Sebumeter to evaluate sebum content, among other things. By week 8, the sebum content had significantly decreased to  $31.05 \pm 36.15$  units (baseline vs. week 8;  $p = 0.001$ ) (Ghovvati et al., 2019). Alongside this decline, there were improvements in other skin biophysical parameters (such as pH and erythema) and decreases in the numbers of total, inflammatory, and non-inflammatory acne lesions (~47–48%) (Ghovvati et al., 2019). Although the study claimed that excessive sebum production is frequently the cause of acne, it did not provide direct measures of sebum content or excretion after using the cinnamon formulation (Ameliana & Rosyidi, 2024).

The study investigated a number of bioactive substances that were isolated from *Cinnamomum cassia*, including coumarin, *o*-methoxycinnamaldehyde, *cis*-2-methoxycinnamic acid, and *trans*-cinnamaldehyde. 0.30 to 8.55 mmol/L were the lowest inhibitory concentrations (MICs). The components were found to decrease the amount of ergosterol, a crucial component of fungal cell membranes, raise levels of malondialdehyde, a sign of lipid peroxidation, and disrupt fungal cell membranes (increased electrical conductivity, cytoplasmic leakage) (Liu et al., 2024). An additional 2023 study published in the Middle East Journal of Applied Sciences assessed the antifungal properties of cinnamon essential oil, fennel oil, and their combination against food-and environmental-related fungus like *Aspergillus flavus*, *Alternaria alternata*, and *Penicillium expansum*. Fungal growth was strongly suppressed by the oils at concentrations of 0.125%, 0.25%, and 0.50%; at all tested concentrations, *Alternaria alternata*, or *P. expansum*, was entirely inhibited by

cinnamon oil alone (Younos & Abdel-Galil, 2023). Martinko, K. & Mioč, E. showed that aqueous cinnamon bark extracts at 3% -5% significantly suppressed the growth of *Fusarium sporotrichioides* in vitro, deforming hyphae and lowering sporulation (Martinko & Mioč, 2024).

Ameliana, L., & Rosyidi, V. A. assessed cinnamon bark oil in the form of a nanoemulgel. The antibacterial inhibitory efficacy against *P. acnes* was evaluated. In that investigation, the best formula (Formula 3) had the strongest antibacterial efficacy against *P. acnes* and good physical quality. This implies that cinnamon oil has a far stronger inhibitory impact when administered correctly (nanoemulsion + gel) as opposed to in simpler formulations (Ameliana & Rosyidi, 2024). According to another pertinent investigation, in agar disc diffusion, cinnamon oil had the highest

inhibitory action against *P. acnes* (zone of inhibition  $36.75 \pm 1.06$  mm) when compared to galangal and eucalyptus oils. Cinnamon oil's minimum inhibitory concentration (MIC) was found to be 5 mg/mL. In that same investigation, it showed substantial inhibitory potency that was superior to several conventional drugs (Veerasophon, J., et al., 2020). Last but not least, there is convincing evidence that cinnamon, particularly its constituents like cinnamaldehyde from bark oil, has inhibitory effects on mild-to-moderate acne in vivo (e.g., a decrease in lesion counts and bacterial flora), which can be attributed to both growth suppression and bacterial killing (Ghovvati et al., 2019).

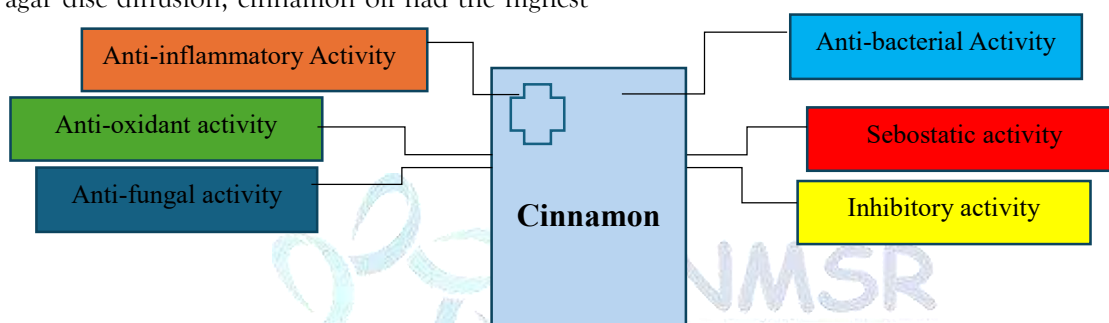


Figure 2. Biological activities of Cinnamon in treatment of Acni

Table 3. A comprehensive over view of phytochemical activities of Cinnamon relevant to acne treatment

Cinnamon Constituent Used	Acne-Relevant Activity	Key Evidence and findings	References
Oleum cinnamomi (volatile oil from <i>Cinnamomum cassia</i> )	Antibacterial against <i>C. acnes</i> , along with mechanistic insights (covalent inhibition)	Demonstrated a notable suppression of <i>C. acnes</i>	(Peng et al., 2024)
Cinnamon bark oil ( <i>Cinnamomum burmannii</i> ) in nanoemulgel formulation	Antibacterial against <i>Propionibacterium acnes</i> and enhanced delivery/formulation	In vitro the formula demonstrated strongest antibacterial activity and good physical stability via <i>P. acnes</i>	(Ameliana & Rosyidi, 2024)
Bark extract of <i>Cinnamomum verum</i> , after in vitro digestion	Antioxidant potential and anti-inflammatory impact (in cell-based models)	The extract retained anti-inflammatory and antioxidant activity after digestion and reduced inflammatory markers like TNF- $\alpha$ and IL-6 in cell models	(Pagliari et al., 2023)
A cinnamon-based topical gel having ~0.38%	Clinical trial results showed reduced erythema, sebum	Total lesion count ~47%; inflammatory ~42%; non-inflammatory ~48%;	(Ghovvati et al., 2019)

cinnamaldehyde was applied twice daily for eight weeks	production, acne lesion counts, and red fluorescence (porphyrins)	sebum and erythema reduced; mild irritation reduced at first	
Concealer product containing 0.5% w/w cinnamon oil	Anti-P. acnes activity of the concealer; a cosmetic compound that also hides flaws	Against P. acnes, cinnamon oil had a distinct zone of inhibition (~36.75 mm); the concealer formulation F4 had a suitable texture and stability	(Veerasophon, J., et al., 2020)
Ethanollic extract of cinnamon bark	Antibacterial (individually and in combination)	MIC values for P. acnes and S. epidermidis are 256 µg/mL and 1024 µg/mL, respectively, MBC > 2048 µg/mL	Julianti et al., 2017
Cinnamon Gel	In vitro, antibacterial against P. acnes	The gel with 0.5% cinnamon oil showed inhibitory zones > 18 mm in comparison to P. acnes	Gurjar et al., 2012

### Mechanism of action

C. acnes are inhibited in vitro by cinnamon essential oil and cinnamon extracts (rich in cinnamaldehyde, eugenol, and related phenolics). According to recent proteomics research, cinnamaldehyde covalently modifies bacterial proteins, interfering with bacterial transporters and metabolism (Julianti et al., 2017). Cinnamon acnes contribute to inflammation in the pilosebaceous unit; reducing bacterial load reduces a key inflammatory stimulus (Sutaria et al., 2023). Cinnamaldehyde and a number of treatments containing cinnamon have been shown to interfere with the production of biofilms or lower their viability. Disrupting biofilms reduces chronic inflammation and makes bacteria more susceptible to antibiotics (Peng et al., 2024). In mammalian cells, cinnamon's components inhibit pro-inflammatory signaling. Laboratory studies have demonstrated mechanisms such as decreased expression of adhesion molecules and chemokines, suppression of NF-κB signaling, and down regulation of inflammatory mediators (e.g., TNF-α, IL-1β, and IL-6). These measures lessen the follicle's local inflammation and the recruitment of neutrophils and macrophages (Liao et al., 2012). In vitro, cinnamon extracts increase antioxidant responses and scavenge reactive oxygen species (ROS). Cinnamon may lessen tissue damage and inflammatory amplification that exacerbate lesion

formation by reducing oxidative stress surrounding the pilosebaceous unit (Rao & Gan, 2014). In individuals with mild-to-moderate acne, topical cinnamon gel was found to lower erythema, sebum levels, and lesion counts in small clinical pilot investigations. Although the exact molecular mechanism for sebum reduction is not fully understood, this shows cinnamon preparations may also influence sebum. According to Ghovvati et al. these clinical findings are tentative and require larger trials (Ghovvati et al., 2019). When synthesized in liposomes cinnamon essential oil or cinnamaldehyde frequently exhibits synergy with other antimicrobials (increased transport to follicles). Because essential oils can be irritating at greater quantities, formulation is crucial for both efficacy and tolerability (He et al., 2025).

### Potential molecular mechanism underlying the pharmacological effects of cinnamon

Cinnamaldehyde and other phenylpropanoids in cinnamon interfere with vital bacterial enzymes, damage membrane integrity and intracellular homeostasis, and cross bacterial cell envelopes, which inhibit growth and causes cell death. Enzyme inactivation, membrane permeabilization, and cellular contents leaking are some of the mechanisms. As an electrophile (α, β-unsaturated aldehyde), cinnamaldehyde can react with

nucleophilic residues on bacterial proteins, particularly thiol, cysteine, or amino groups, changing the activity of enzymes and possibly causing proteostasis stress. It was directly shown that *Oleum cinnamomi* acted on *C. acnes* through covalent alteration of bacterial proteins (Nabavi et al., 2015). By (a) interfering with bacterial adhesion molecules or exopolysaccharide synthesis, (b) inhibiting quorum-sensing regulated gene expression, or (c) making biofilm bacteria more susceptible to death through membrane disruption and decreased extracellular matrix integrity, cinnamon compounds prevent the formation of biofilms or disturb established biofilms. Follicle persistence and chronic inflammation are decreased when biofilm production is reduced (Millezi et al., 2019). Cinnamaldehyde is an  $\alpha$ ,  $\beta$ -unsaturated aldehyde that can covalently modify nucleophilic residues (lysine, cysteine) in proteins by acting as a Michael acceptor and forming Schiff base adducts. This can cause proteotoxic stress, bacterial death or growth arrest, disrupt redox sensors and thiol-dependent stress responses, and inactivate vital enzymes in bacteria (metabolism, cell-wall biosynthesis) (Peng et al., 2024). In keratinocytes, macrophages, and other skin immune cells, cinnamonaldehyde and other cinnamon components alter intracellular signaling, which lowers pro-inflammatory transcriptional programs that are essential to acne lesions. Cinnamaldehyde decreases the transcription of TNF- $\alpha$ , IL-1 $\beta$ , IL-6, and other mediators via decreasing I $\kappa$ B $\alpha$  phosphorylation and p65 nuclear translocation. Modulation lowers the expression of MMP and the generation of inflammatory cytokines, both of which lead to tissue injury (Kim et al., 2007). Cinnamon polyphenols alter cellular antioxidant defenses (e.g., SOD, catalase, glutathione levels) and scavenge reactive oxygen species (ROS). Cinnamon contributes to lesion development and scarring by reducing ROS, which in turn inhibits oxidative amplification of inflammation and downstream damage (lipid peroxidation, MMP activation) (Nabavi et al., 2015). Cinnamaldehyde may lessen connective tissue degradation and inflammation-related remodeling that impairs scarring by down regulating the expression of matrix metalloproteinase (e.g., MMP-2/MMP-13 in certain models) and COX enzymes. Suppression of NF- $\kappa$ B/MAPK mediates this (Sankaranarayanan et al., 2024).

Cinnamaldehyde can inhibit JAK/STAT activation (e.g., IL-1 $\beta$ -induced signaling), according to several research (in non-skin inflammatory models). This is significant because these pathways can intensify skin inflammation (Cheng et al., 2020). However, there are currently few direct mechanistic data on sebocyte lipid metabolism and cinnamaldehyde, so this remains speculative. A small clinical pilot reported reductions in sebum and erythema with a topical cinnamon gel; the molecular basis could be indirect (reduced inflammation, reduced sebaceous gland stimulation) or direct (cinnamon components affecting lipogenesis signaling in sebocytes) (Ghovvati et al., 2019).

### Conclusion

Cinnamon generally has tremendous potential as a natural anti-acne agent due to its richness of bioactive compounds, such as cinnamonaldehyde, eugenol, coumarins, and other flavonoids. Together, these components reduce oxidative stress, inflammation, and excessive sebum production, three major factors in the development of acne; while also fighting acne-causing bacteria like *P. acnes*, *S. aureus*, *S. epidermidis*, and *S. pyogenes*. Cinnamon essential oil, gels, and other extracts have been shown in lab experiments to have antibacterial, antioxidant, and anti-inflammatory qualities. Although current research suggests that cinnamon may be a moderate and effective alternative to conventional acne medications, well-designed clinical trials are still needed to assess the safest dosages, the best formulations, and the long-term effects. In conclusion, cinnamon has a lot of potential in dermatology, particularly for managing acne, but more human-centered research is necessary before it can be widely advised in clinical practice.

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