

# Pharmacological and Therapeutic Potential of Neem (*Azadirachta indica*) and Clove (*Syzygium aromaticum*): A Comprehensive Review

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## Abstract

Medicinal plants have played a crucial role in traditional and modern healthcare systems. Among them, neem (*Azadirachta indica*) and clove (*Syzygium aromaticum*) are widely recognized for their diverse pharmacological properties including antimicrobial, antioxidant, anti-inflammatory, analgesic, and therapeutic activities. Neem contains bioactive compounds such as azadirachtin, nimbin, nimbolide, and quercetin, which contribute to its medicinal potential. Clove contains eugenol as its primary active component and is widely used in dentistry and pharmaceutical formulations. The present review summarizes botanical characteristics, phytochemical composition, pharmacological activities, and pharmaceutical applications of neem and clove with special emphasis on their role in oral healthcare and herbal medicine. The increasing interest in natural medicines highlights the importance of these plants in developing safe and effective therapeutic formulations.

## Introduction

Natural products have been used for centuries in traditional medicine systems such as Ayurveda, Unani, and Traditional Chinese Medicine. Plants remain one of the most important sources of biologically active compounds used in modern pharmaceutical development. Herbal medicines are gaining global attention due to their safety, availability, affordability, and fewer side effects compared with synthetic drugs.

Neem (*Azadirachta indica*) is commonly referred to as the "village pharmacy" in India because almost every part of the tree possesses medicinal value. Leaves, bark, seeds, flowers, and stems have been used for centuries in treating infections, inflammation, skin diseases, and dental disorders. The neem tree is mostly grown in southern Asia and

Africa, where it has long been utilized in traditional medicine. It should be noted that the leaves, bark, fruit, flowers, oil, gum, and other parts of the neem tree are linked to the previously described medicinal folklore in the treatment of a number of illnesses, including diabetes, cancer, heart disease, and hypertension. Cellular and molecular mechanisms, such as free radical scavenging, detoxification, DNA repair, cell cycle modification, programmed cell death mitigation and autophagy, immune surveillance, anti-inflammatory, anti-angiogenic, and anti-metastatic activities, and the capacity to modulate different signaling pathways, are undoubtedly responsible for the possible effects observed when using these extracts.

*Azadirachta indica* is rich in a variety of chemicals, some of which have therapeutic potential, according to research conducted over time. Triterpenes are the most therapeutically useful of all these substances. It has been demonstrated that nimbin (a triterpene) has antipyretic, fungicidal, antihistamine, and antiseptic qualities. Additionally, nimbin has antioxidant and anti-inflammatory properties that lessen damage by lowering the generation of reactive oxygen species. (Schumacher et al., 2011; Naik et al., 2014). Flavonoids, which inhibit prostaglandin production, endoperoxides, and inflammatory enzymes like phosphodiesterases and protein kinases are also present in neem (Batista et al., 2018, Hernández-Aquino and Muriel, 2018, Naik et al., 2014). As previously indicated, oil extracts are the most commonly used form of neem, and a thorough phytochemical analysis has confirmed that triterpenes, flavonoids, and saponins are present in high concentrations, while catechins and nimbins appear to be present in lower amounts (Naik et al., 2014, Schumacher et al., 2011). Limonoids, tannins, alkaloids, terpenoids, reducing sugar, catechins, sterols, and gallic acid are other metabolites present in neem extracts (Naik et al., 2014, Roma et al., 2015, Saleem et al., 2018, Schumacher et al., 2011). Extracts from neem have demonstrated antibacterial and insecticidal properties. Azadirachtin, a complex tetranortriterpenoid limonoid found in neem seeds, is a major component of the plant and is responsible for its poisonous effects on insects

Clove (*Syzygium aromaticum*) is another important medicinal plant widely used as a spice and herbal remedy. Clove flower buds are rich in essential oils, particularly eugenol, which has strong antimicrobial, antioxidant, and analgesic properties. Clove oil is widely used in dentistry for toothache relief and oral infections.

Because of their strong antimicrobial activity, neem and clove are frequently incorporated into herbal formulations such as mouthwash, toothpaste, dental gels, and medicated chewing gums. In coastal regions, clove trees are commonly grown up to 200 meters above sea level. After four years of plantation, the commercialized portion of this tree—flower buds—begins to be produced. Prior to flowering, flower buds are gathered during the maturation stage. A natural phytohormone that releases ethylene in the vegetal tissue and causes premature maturation can be used to collect the material manually or chemically. These days, Indonesia, India, Malaysia, Sri Lanka, Madagascar, and Tanzania, particularly the island of Zanzibar, are the top producers of cloves [2]. In the northeastern part of Brazil, cloves are grown in the areas of Valaãna, Ituberá, and Taperoá in the state of Bahia. Camamu and NiloPeçanha, where over 8,000 hectares are farmed, yielding about 2,500 tons annually

## Biological Activity

Because of its many pharmacological effects, which have been documented in literature and cemented from centuries of traditional use, clove is a significant medicinal plant. The next paragraphs provide an overview of multiple scientific findings on the most significant biological activity of clove and eugenol.

### Activity of antioxidant

A database containing the polyphenol content and antioxidant activity of various food types was recently created by the US Department of Agriculture in partnership with universities and private businesses. •-Jiménez et al. categorized the top 100 dietary sources of polyphenols using this database [8]. The results show that foods having a greater polyphenol concentration are spice plants, followed by fruits, seeds, and vegetables. Clove was the spice with the highest concentration of antioxidants and polyphenols. Using a variety of in vitro models, including b-carotene-linoleate, ferric thiocyanate, 1,1-diphenyl-2-picryl hydroxyl (DPPH) radical, hydroxyl radical, and reducing power model systems, the antioxidant activity of clove and caraway was found to be similar to butylatedhydroxytoluene (BHT), a synthetic compound frequently used as a food preservative Bamdad et al. [9]. Gülçin et al. [10] reported that the antioxidant activity of clove oil decreased in the following order when compared to synthetic antioxidants as evaluated by the scavenging of the DPPH radical :clove oil>BHT>alfa-tocopherol>butylatedhydroxyanisole>Trolox.

### Antimicrobial action

Clove's antibacterial properties have been demonstrated against a number of bacterial and fungal species. Mint, cinnamon, mustard, ginger, garlic, clove, and other Indian spices were examined by Sofia et al. for their antibacterial properties [18]. The aqueous extract of clove at 3% was the only sample that shown full bactericidal activity against all food-borne pathogens tested, including *Bacillus cereus*, *Staphylococcus aureus*, and *Escherichia coli*. Clove extract also shown strong inhibitory action at 1% concentration.

Black pepper, geranium, nutmeg, oregano, thyme, and clove were investigated for their antibacterial properties against 25 types of Gram positive and Gram negative bacteria in a different study by Dorman and Deans [19]. The oils that exhibited the broadest range of activity were clove, oregano, and thyme.

## Botanical Description of Neem

Neem is a fast-growing evergreen tree belonging to the family Meliaceae. It is native to the Indian subcontinent and grows in tropical and subtropical regions. The tree can reach a height of 15–20 meters and produces small white fragrant flowers.

Taxonomy:

Kingdom: Plantae

Family: Meliaceae

Genus: *Azadirachta*

Species: *Azadirachta indica*

Various parts of the neem plant including leaves, bark, seeds, roots, and stems contain medicinally active compounds and are widely used in herbal medicine.

## Botanical Description of Clove

Clove is an evergreen tree belonging to the family Myrtaceae. The dried flower buds of the clove tree are commonly used as spice and medicine. The plant is native to Indonesia but is cultivated in several tropical countries.

Taxonomy:

Kingdom: Plantae

Family: Myrtaceae

Genus: Syzygium

Species: Syzygium aromaticum

Clove buds are harvested before flowering and dried to produce the aromatic spice widely used in culinary and medicinal preparations.

## Phytochemical Constituents for neem

Test for alkaloids

The neem plant was tested for alkaloids using the procedure described in [6]. Dragendroff's reagent (a potassium bismuth iodide solution) was added to 2 milliliters of filtered material after 0.5 grams of the sample were dissolved in hydrochloric acid and filtered through filter paper. The test is known as Dragendroff's test because the presence of alkaloid was confirmed by the formation of a red precipitate. When Hager's reagent was added to two milliliters of filtrates, the production of a yellow color indicated the presence of alkaloid.

Test for saponins

The neem plant was tested for saponins using the method described in [5]. 50 milliliters of distilled water were used to boil 0.5 grams of the sample, which was then filtered. Three milliliters of distilled water were added to five milliliters of each filtrate.

Test for glycosides

The neem plant was tested for glycosides using the [7] technique. For appropriate extraction, 0.5 g of the sample was dissolved in ethanol for roughly ten minutes before being filtered. 0.3 ml of Fehlings solution A to 5 ml of each filtrate and B was added until it became alkaline, signifying the presence of glycoside.

Test for terpenoids

The neem plant was tested for terpenoids using the method described in [7]. For appropriate extraction, 0.5 g of the material was dissolved in ethanol for approximately ten minutes before being filtered. One milliliter of acetic

anhydride was added to five milliliters of each filtrate, and then concentrated H<sub>2</sub>SO<sub>4</sub> was added. The presence of terpenoid was shown by a color shift from pink to violet.

#### Test for flavonoids

The neem plant was tested for flavonoids using the method described in [6]. After dissolving 0.5 g of the material in distilled water and filtering it into 5 ml of filtration, 3 ml of lead ethanoate solution was added. The existence of flavonoids was established by their pale yellow-brown (buff-colored) appearance.

#### Test for steroids

The neem plant was tested for steroids using the method described in [6]. After dissolving 0.5 g of the sample in distilled water and filtering it into 4 ml of filtrate, 2 ml of acetic acid was added, and the mixture was carefully allowed to cool in the refrigerator before concentrated H<sub>2</sub>SO<sub>4</sub> was added. The presence of a steroidal ring was revealed by a color shift from violet to bluish green.

#### Test for phenol

The [6] technique was used to test the neem plant for phenol. After boiling 0.5 g of the sample with 15 ml of distilled water, it was filtered. A few drops of a 10% ferric chloride solution were then added to two milliliters of the filtrate. The existence of phenolic hydroxyl groups was confirmed by the formation of a violet color.

## Phytochemical Constituents of Neem

Neem contains a large number of biologically active compounds including limonoids, flavonoids, tannins, and polyphenols. More than 300 compounds have been identified from different parts of the neem plant.

Major compounds include:

- Azadirachtin
- Nimbin
- Nimbidin
- Nimbolide
- Gedunin
- Salannin
- Quercetin
- Tannins
- Flavonoids

These compounds contribute to antimicrobial, anti-inflammatory, antioxidant, and therapeutic properties of neem.

## Extraction of neem stem

In order to extract bioactive chemicals like nimbin, nimbinin, and nimbidin from neem stem (bark), fresh bark must be collected, dried for about 48 hours, ground into a powder, and then extracted using solvent extraction techniques like methanol or ethanol. These substances have important therapeutic qualities, such as antibacterial and anti-inflammatory effects.

To maximize the extraction yield, the stem bark is gathered, dried, and processed into a powder.

**Methodology:** Methanol is frequently used in solvent extraction to extract phytochemicals and evaluate antibacterial effectiveness against microorganisms.

**Active Components:** The bark's therapeutic qualities are attributed to a variety of limonoids and triterpenoids, including nimbidin.

**Characterization:** Samples that have been extracted are analyzed through methods such as Fourier-transform infrared spectroscopy (FTIR) and UV-visible spectroscopy for identification purposes. **Potential Applications:** The extracts are explored for possible applications in medicinal balms and various pharmaceutical uses owing to their high stability.

## Phytochemical Constituents for Clove

Test for carbohydrates

**Molisch's test:** 0.4 ml of Molisch's reagent was mixed with 1 ml of plant extract. One milliliter of concentrated sulfuric acid was then added down the test tube's side. The presence of carbohydrates (starch) is indicated by a purple color.

**Benedict's test:** One milliliter of Benedict's reagent and one milliliter of plant extract were cooked for five minutes. The production of an orange precipitate indicated the presence of carbohydrates (disaccharides).

**Fehling's Test:** Boil and filter two milliliters of pure water with one milliliter of plant extract. After that, two milliliters of Fehling's reagent were added to two milliliters of filtrate, and the mixture was heated. The presence of carbohydrates (glucose) is indicated by a reddish-brown precipitate

Test for Proteins:

**Xanthoprotic test:** 1 milliliter of plant extract was mixed with 0.25 milliliters of nitric acid. Proteins were present because of the white precipitate's appearance.

**Biuret test:** 4% NaOH and 1% CuSO<sub>4</sub> were added to a test tube containing 1 milliliter of plant extract. The emergence of a violet pink color showed the presence of proteins.

#### Test for lipids:

One milliliter of plant extract was evaporated to a dried powder for the solubility test. The test tube was filled with a few drops of petroleum ether and thoroughly shaken. The presence of lipids was determined by the extract's complete disintegration.

Glycerol test: Five drops of the plant extract were added to one milliliter of a 1%  $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$  solution, and the mixture was thoroughly mixed. Five drops of a 10% sodium hydroxide solution were then added to it. Glycerol was present because a clear blue solution was produced.

Sudan III test: A few drops of Sudan III solution were added to one milliliter of plant extract. The presence of lipids was indicated by the appearance of red.

#### Test for alkaloids:

(a) Mayer's Test: Two drops of chloroform, two drops of Mayer's reagent, and one milliliter of clove flower bud extract were added. White deposits were produced as a result of a positive alkaloid response.

(b) Wagner's test: one milliliter of extract was treated with Wagner's reagent; the presence of alkaloids is indicated by the production of a brown-red precipitate.

(c) Dragendorff's test: 1 ml of plant extract was combined with 2 ml of Dragendorff's reagent. Alkaloids were present when an orange-white precipitate formed.

#### Check for Tannins:

Gelatine test: 1% gelatine solution was added to 500  $\mu\text{l}$  of the filtrate. The presence of tannin was detected by the formation of a curdy white precipitate.

Lead acetate test: Five milliliters of a 10% lead acetate solution were added to the filtrate. Tannin is present when white precipitation forms.

Ferric chloride test: The filtrate was mixed with five drops of a 5% ferric chloride solution. Tannin was detected by the formation of a blue-green hue.

#### Test for saponin:

Foam test: One milliliter of plant extract and a tiny amount of water were added to a test tube. After adding sodium bicarbonate, it was forcefully shook for five minutes. The presence of saponins was shown by the formation of foam.

Test for Flavonoids: 5 ml of diluted ammonia and 1 ml of concentrated sulfuric acid were added to 0.5 ml of plant extract. The presence of flavonoids was indicated by a yellow coloring that vanished upon standing.

### Test for Resins:

Add two drops of conc and 0.5 ml of acetic acid to a dry test tube. They added sulfuric acid. The presence of resins was evident as the hue changed from purple to violet in roughly ten minutes.

## Phytochemical Constituents of Clove

Clove contains essential oils and phenolic compounds responsible for its pharmacological properties.

Major constituents include:

- Eugenol (70–85%)
- Eugenyl acetate
- $\beta$ -caryophyllene
- Tannins
- Flavonoids
- Gallic acid

Eugenol is the principal component responsible for clove's analgesic, antimicrobial, and antioxidant properties.

### Extraction of clove oil

Clove oil is obtained from dried *Syzygium aromaticum* buds mainly via steam distillation, producing a light, milky liquid abundant in eugenol. Typical techniques include distillation for 3 to 6 hours, succeeded by extraction using solvents such as

n-hexane. Alternatively, soaking or microwave-assisted extraction can be utilized for improved quality or quicker extraction

**Steam Distillation Process:** Clove powder is combined with water in a round-bottom flask. Steam is introduced, and the resulting distillate (which includes water and oil) is gathered.

**Separation and Drying:** The distillate is processed using a solvent such as cyclohexane or hexane in a separatory funnel to extract the oil. Anhydrous sodium sulfate removes leftover water, and then evaporation produces pure clove oil.

**Ideal Conditions:** Traditional distillation usually requires 4–6 hours, but techniques utilizing microwave energy or ultrasonic waves are quicker and more effective.

**Yield Enhancement:** Prior to distillation, fermenting clove leaves with *Rhizopus oligosporus* can boost the yield.

## Pharmacological Activities

Both neem and clove exhibit multiple pharmacological activities.

- Antimicrobial action
- Neem and clove extracts show strong antibacterial activity against several pathogenic microorganisms including *Staphylococcus aureus*, *Escherichia coli*, and oral pathogens.
- Antifungal action
- Both plants inhibit fungal species such as *Candida albicans* responsible for oral infections.
- Anti-inflammatory action
- Bioactive compounds in neem and clove reduce inflammation by inhibiting inflammatory mediators.
- Antioxidant action
- Polyphenols and flavonoids present in both plants act as free-radical scavengers protecting cells from oxidative stress.
- Analgesic action
- Clove oil, due to eugenol, acts as a natural anesthetic and relieves dental pain.

## Applications in Dentistry

Neem and clove have significant applications in oral healthcare.

Common uses include:

- Herbal toothpaste
- Mouthwash
- Dentalgels
- Medicated chewing gums
- Antiseptic oral formulations

Neem extracts inhibit *Streptococcus mutans*, which causes dental plaque and caries. Clove oil is widely used to relieve toothache and dental pain due to its analgesic properties.

## Pharmaceutical Applications

Neem and clove extracts are used in several pharmaceutical formulations including antimicrobial preparations, anti-inflammatory drugs, dental care products, and herbal medicines.

The combination of neem and clove has shown synergistic antimicrobial activity, making them useful in oral hygiene formulations.

## Conclusion

Neem and clove are highly valuable medicinal plants with significant pharmacological properties. Their antimicrobial, antioxidant, anti-inflammatory, and analgesic effects make them promising candidates for herbal formulations. Increasing research on these plants supports their therapeutic potential in pharmaceutical and dental applications.

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