Technical Report

Significance of Clove Extract in CanXida Remove (Formula RMV)

In CanXida Remove (Formula RMV), clove extract's natural antimicrobial compounds, along with anti-inflammatory and analgesic properties, synergize for effective pathogen clearance.

Contents

Executive Summary

Clove extract, derived from the dried flower buds of *Syzygium aromaticum*, is a versatile natural remedy known for its rich health benefits and therapeutic properties. With historical significance and global cultivation, clove extract is extracted from buds, stems, and flowers using a straightforward process primarily involving water-based solvents. This results in a non-toxic and relatively pure substance enriched with a diverse array of bioactive compounds.

Key compounds in clove extract, including eugenol, contribute to its distinct aroma and therapeutic effects. Beyond eugenol, flavonoids like kaempferol and quercetin, polyphenolic tannins, terpenoids, and other bioactive compounds enhance its medicinal profile. Considered safe by the FDA, clove extract finds applications in dental remedies and as a food additive. Its wide-ranging health benefits include antiparasitic effects, effectiveness against bacterial and fungal strains, and the capability to combat viral infections and also Candida infections. Incorporating a 4:1 clove extract in CanXida Remove not only boosts its ability to eliminate parasites and pathogens but also provides pain-relieving benefits, contributing to overall gut health. *****

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1. Introduction

Clove, also known as *Syzygium aromaticum*, is derived from the dried flower bud of the *Myrtaceae* family. It is native to the Maluku islands in Indonesia. Although originating from the Maluku islands, this plant is now cultivated worldwide. Clove extract, derived from buds, stems, and flowers, has obtained interest for its potent antioxidant, anti-inflammatory and antimicrobial properties, setting it apart from other spices. This is mainly attributed to the high concentration of eugenol, a primary phenolic compound. (Abdul Aziz et al., 2023)

Clove extract is a rich source of bioactive compounds, with eugenol as the predominant phenolic compound, boasting antioxidant, anti-inflammatory, and antimicrobial properties. In addition to flavonoids like kaempferol and quercetin, cloves also contain polyphenolic tannins, terpenoids, and other compounds that have a variety of health effects. (Rodríguez et al., 2018)

Cloves' nutritional value is further enhanced by minor components including vitamins and sterols, which makes them an excellent choice for nutraceutical and medicinal applications.* (Gengatharan & Rahim, 2023)

Clove has various uses, including in cooking and as an ingredient in pain-relieving ailments due to its analgesic properties. Recent studies have investigated its potential in treating neuropathic pain and vaginal candidiasis, showing encouraging outcomes. (Kumar Pandey et al., 2022)

Clove oil is considered safe by the FDA and is approved for use in dental remedies and as a food additive.

2. Bioactive Compounds of Clove Extract

Clove is a spice known for its abundance of bioactive compounds. *Table 1* presents the constituents that are found in clove extracts. Emerging pharmaceuticals and nutraceuticals have been facilitated by the bioactive compounds discovered in cloves. Some of the key bioactive compounds found in clove extract include:

2.1. Phenolic Compounds:

The composition of clove extract is abundant in a variety of phenolic compounds, with eugenol being the predominant one. The

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main phenolic substances in clove extract include the following:

- ***Eugenol:*** This compound is the main bioactive component found in clove, giving it its distinct aroma and numerous medicinal benefits. Eugenol possesses properties that contribute to its antioxidant, anti-inflammatory, and analgesic effects. Additionally, it possesses antimicrobial properties, rendering it highly effective in combating bacteria and fungi.* (Ulanowska & Olas, 2021).

Eugenol, *the primary bioactive compound in clove, is known for anti-inflammatory, antioxidant, analgesic, and antimicrobial effects, contributing to its role in traditional medicine and health applications.*

- ***Acetyl-eugenol:*** This compound is structurally related to eugenol It also possesses antioxidant and anti-inflammatory properties. (Abdul Aziz et al., 2023).
- ***Gallic acid:*** This is a phenolic acid with antioxidant and anti-inflammatory properties.

Gallic acid is known to contribute to the overall antioxidant capacity of clove extract.

2.2. Terpenoids:

Clove (Syzygium aromaticum) contains a variety of terpenoids, which are natural compounds with diverse biological effects. Terpenoids are derived from isoprene units. Clove possesses aromatic and medicinal properties due to the presence of terpenoids.

- ***Caryophyllene***: A sesquiterpene found in clove, and can be extracted from flower and stem of clove. The caryophyllene has anti-inflammatory and analgesic effects.
- ***Beta-caryophyllene oxide:*** This compound is a derivative of caryophyllene and contributes to the overall biological activity of clove extract. It contains both the anti-inflammatory and antimicrobial effects. (Fidyt et al., 2016).

2.3. Flavonoids:

Cloves are not as rich in flavonoids as some other plant sources, they do contain certain flavonoids. (Cortés-Rojas et al., 2014).Here

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are some flavonoids that can be found in clove:

- ***Quercetin:*** A flavonoid present in clove, quercetin has antioxidant and anti-inflammatory effects. It is known for its potential in supporting cardiovascular health.
- ***Kaempferol:*** Another flavonoid found in clove, kaempferol has antioxidant and anti-inflammatory properties.

2.4. Tannins:

Clove extract contains tannins, which are polyphenolic compounds with antioxidant properties. (Batiha et al., 2020) Tannins may also have anti-inflammatory and antiviral effects.

2.5. Other Bioactive Compounds:

Clove is rich in sterols and vitamins, including A, K, C, B1, B6, and β-carotene, The minor constituents found in cloves, which make up about 5-10% of their composition, play a significant role in enhancing their nutritional value and providing various benefits. (M. El-Maati et al., 2016).

Table 1: *List of Bioactive Compounds present in Clove. Source:* (Abdul Aziz et al., 2023; M. F. A. El-Maati et al., 2016; Rodríguez et al., 2018)

Bioactive Compound	Category	Properties
Phenolic Compounds		
Eugenol	Phenolic compound	• Antioxidant • Anti-inflammatory • Analgesic • Antimicrobial
Acetyl-eugenol	Phenolic compound	• Antioxidant • Anti-inflammatory

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Gallic Acid	Phenolic acid	• Antioxidant, • Anti-inflammatory
Terpenoids		
Caryophyllene	Sesquiterpene	• Anti-inflammatory • Analgesic
Beta-Caryophyllene Oxide	Sesquiterpene derivative	• Anti-inflammatory • Antimicrobial
Flavonoids		
Quercetin	Flavonoid	• Antioxidant • Anti-inflammatory
Kaempferol	Flavonoid	• Antioxidant • Anti-inflammatory
Other Bioactive Compounds		
Tannins	Polyphenolic compounds	• Antioxidant • Anti-inflammatory • Antiviral effects
Stigmasterol	Phytosterol	• Potential • Anti-inflammatory effects.
Campesterol	Phytosterol	• Potential health benefits.
Beta-Sitosterol	Phytosterol	• Anti-inflammatory
Vitamins (A, K, C, B1, B6)	Vitamins	• Support overall health
β-Carotene	Vitamins	• Antioxidant

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3. Health Benefits of Clove Extract

The health benefits of clove extract are linked to its bioactive compounds, such as eugenol, caryophyllene, and flavonoids.

Here are some of the potential health benefits of clove extract:

3.1. Antioxidant Properties:

Clove extract has exceptional antioxidant effects due to its high concentration of phenolic components and flavonoids. Antioxidants play a vital role in neutralizing free radicals, highly reactive molecules that can damage cells and contribute to oxidative stress. *Eugenol*, with other phenolic components, is the main antioxidant found in clove extract. (Gengatharan & Rahim, 2023) Together, these antioxidants scavenge free radicals and avert inflammation and cellular damage.

Furthermore, a research study examined the antioxidant properties of various spices, including onion, garlic, pepper, cinnamon, mint, ginger, and clove. An analysis was conducted on phenolic and flavonoid compounds, which are well-known for their antioxidant properties. All spices, to different extents, inhibited lipid oxidation. Clove had the highest inhibition, while onion had the least. This study emphasizes the strong antioxidant capabilities of clove compared to other spices. (Hussain et al., 2017)

Clove extract's antioxidant qualities are linked to potential health advantages by reducing oxidative stress, which may lower the risk of chronic diseases and promote overall health.*

3.2. Antibacterial Properties:

Studies have shown that clove possesses potent antibacterial properties, which can be attributed to its key constituents including eugenol, eugenyl acetate, β-caryophyllene, acetyl-eugenol, and more. These compounds can cause protein denaturation and change the permeability of cell membranes.

Clove oil has demonstrated efficacy against non-toxigenic strains of E. coli O157:H7 and a range of foodborne gram-positive and gram-negative bacteria. (Cui et al., 2020)

Clove extracts have shown significant efficacy in inhibiting the growth of bacteria that are resistant to a wide range of antibiotics, such as tetracyclines, beta-

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lactams, fluoroquinolones, aminoglycosides, and macrolides. (Mittal et al., 2014)

In addition, clove contains eugenol, which has demonstrated significant inhibitory effects against 31 strains of Helicobacter pylori. (Elbestawy et al., 2023) The findings highlight the potential of clove and its constituents as effective alternatives for fighting antibiotic-resistant bacteria and specific pathogens such as H. pylori.

3.3. Anti-fungal Properties:

Both clove oil and eugenol have been shown to have potent antifungal action against a wide range of yeasts and filamentous fungi, including several that are known to cause illness in humans. Clove contains phenolic components, such as carvacrol and eugenol, which have fungicidal properties. (Marchese et al., 2017)

Eugenol, identified as the main compound responsible for antifungal activity, acts by causing lysis of spores and micelles. Similar mechanisms involving membrane disruption and deformation of macromolecules have been reported by other studies.

Clove oil and eugenol have a broad range of fungicidal activity that includes Aspergillus, Candida, and dermatophytes. Their mechanism of action is linked to damage in the cytoplasmic membrane. (Biernasiuk et al., 2023)

3.4. Antiviral Properties:

Some studies have explored the antiviral properties of eugenol against certain viruses, such as herpes simplex virus and human immunodeficiency virus, in laboratory. However, these findings are preliminary, and further research is needed to establish the efficacy and safety of clove extract or its components as antiviral agents in clinical settings.(Kiki, 2023)

3.5. Analgesic Activity:

Clove extract, particularly its main component eugenol, has been studied for its potential analgesic (pain-relieving) properties. Eugenol is known for its anti-inflammatory and analgesic effects, and it has been traditionally used in various cultures for managing pain.

The analgesic effects of clove extract are believed to be associated with its ability to

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interact with various signaling pathways involved in pain perception. Eugenol may affect neurotransmitters and receptors involved in pain sensation. (Asl et al., 2013)

3.6. Improving Digestive Health:

Clove extract has been traditionally used for various medicinal purposes, and some studies suggest that it may have potential benefits for certain gut-related issues. However, it's important to note that research in this area is still evolving.

Clove oil is effective in relieving gas and bloating by reducing stomach pressure. Additionally, it can help alleviate the discomfort caused by peptic ulcers. The oil has been found to be beneficial for various stomach-related conditions such as nausea, motion sickness, hiccups, and vomiting. (M. F. A. El-Maati et al., 2016)

3.7. Anti-inflammatory Property:

Clove extract, has demonstrated anti-inflammatory properties. Inflammation plays a role in various gut-related issues, and substances with anti-inflammatory effects may help alleviate symptoms associated with inflammation.

Research indicates that eugenol has the potential to reduce the production and activity of inflammatory mediators, including cytokines. Eugenol's modulation of signaling molecules may help suppress inflammatory responses. (Barboza et al., 2018)

3.8. Other Health Benefits:

Clove extract, especially clove oil, is thought to provide additional benefits. It is thought to stimulate the circulatory system, which may help to reduce mental tiredness and lethargy. Furthermore, clove oil has traditionally been used to treat illnesses such as insomnia, sadness, anxiety, and memory loss, according to a study by (Bhowmik et al., 2012)

4. Biosafety Profile

The biosafety profile of clove extract, obtained from the Syzygium aromaticum plant, has generally been shown to be favorable. The safety of clove extract is influenced by various factors, including the method of extraction, concentration, and the specific bioactive compounds it contains. (Vijayasteltar et al., 2016)

Clove extract is commonly derived from different components of the clove tree,

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including leaves, seeds, and bark. Commonly used extraction methods include solvent extraction or cold pressing. When it comes to solvent extraction, organic solvents such as ethanol or hexane are commonly employed to separate bioactive compounds. On the other hand, cold pressing entails the mechanical pressing of cloves to extract essential oils. (Haro-González et al., 2021)

The US Food and Drug Administration (FDA) has granted approval for the incorporation of clove buds, clove oil, oleoresins, and its phenolic component eugenol as generally recognized as safe (GRAS) food additives.

Eugenol, a significant compound found in clove oil, is widely acknowledged as safe (GRAS) for use in food and nutraceutical items. Skin contact may cause irritation, dermatitis, and inflammation, attributed to the irritant nature of eugenol present in clove oil, so it is important to exercise caution. (emc, 2014)

Furthermore, the clove essential oil is considered safe for consumption in concentrations below 1,500 mg/kg. However, the World Health Organisation (WHO) has determined that the recommended daily amount of clove for humans is 2.5 mg/kg of body weight.(Gülçin et al., 2012)

Although clove extract has long been utilised in medicine for its antibacterial, anti-inflammatory, and antioxidant properties, there is a lack of extensive data regarding its biosafety. Several studies have highlighted potential toxicity concerns, particularly when higher doses or specific formulations are used. When taken properly, it is regarded safe with limited side effect.

5. Effective Targets

Clove extract is also known for its antimicrobial properties and has been studied for its effectiveness against various microbial targets.* Here are some common microbial targets of clove extract:

5.1. Bacterial species:

The primary bioactive compound in clove extract, eugenol, is responsible for its potent antibacterial activity:

- ***Staphylococcus aureus:*** Both eugenol and Clove oil has shown antibacterial

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activity against Staphylococcus aureus, including antibiotic-resistant strains.

- ***Escherichia coli (E. coli):*** Studies suggest that clove extract may hinder the growth of Escherichia coli, a bacterium commonly associated with gastrointestinal infections. (Bai et al., 2023)
- ***Bacillus subtilis:*** Clove extract has been investigated for its antibacterial effects against Bacillus subtilis, a Gram-positive bacterium.
- ***Salmonella:*** Clove extract has been investigated for its potential to inhibit the growth of Salmonella; a bacterium often associated with foodborne illnesses.
- ***Helicobacter pylori:*** Clove extract has been explored for its potential inhibitory effects against Helicobacter pylori, a bacterium associated with gastric ulcers and other gastrointestinal issues.
- ***Klebsiella pneumoniae:***
  Clove's inhibitory effects, due to eugenol, indicate its potential in controlling Klebsiella pneumoniae infections. This bacterium is notorious for causing pneumonia, urinary tract infections (UTIs), and bloodstream infections.
- ***Enterobacter species:***
  They demonstrate a strong sensitivity to clove extract. Enterobacter species are opportunistic pathogens that can cause infections in different body systems.
- ***Citrobacter species:***
  Highly effective against Citrobacter species, which can cause urinary and respiratory tract infections.
- ***Pseudomonas aeruginosa:*** This bacterium, known for its resistance to many antibiotics, has been studied in relation to the antibacterial activity of clove extract. (Faujdar et al., 2020)

5.2. Fungal Species:

Clove oil and eugenol have been found to have antifungal properties that can combat a wide range of yeasts and filamentous fungi. This includes both fungi found in food and those that can cause harm to humans. (Mittal et al., 2014) Various studies have identified specific fungal targets of clove extract:

- Mucor sp.
- Microsporum gypseum
- Fusarium species
- Trichophyton rubrum
- Aspergillus sp.
- Candida species
- Aspergillus species

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- Dermatophytes

5.3. Viral Species:

Research on clove extract, specifically its active compound eugenol, suggests potential antiviral properties. However, it is important to note that further studies are needed to fully understand the extent of its antiviral effects.

- ***Herpes Simplex Virus (HSV):*** Clove extract has been studied for its potential antiviral effects against Herpes Simplex Virus.(Kiki, 2023)

6. Significance of Clove Extract in CanXida Remove

The incorporation of Clove extract (4:1) to CanXida Remove (Formula CXR) greatly improves the product's effectiveness as a powerful supplement for treating Candida infections, with strong antifungal and anti-inflammatory properties. The concentrated bioactive compounds in clove extract work in harmony with other active ingredients in the formulation, offering comprehensive support in fighting Candida overgrowth and promoting optimal gut health. *

CanXida CXR features a 4:1 clove extract, indicating its notable potency and high concentration of active compounds.

The clove extract possesses a wide range of antimicrobial properties, effectively combating various bacterial strains, including both Gram-positive and Gram-negative. This enhances the product's capacity to combat bacterial infections, a vital element in managing Candida overgrowth. The effectiveness of clove extract also includes its ability to combat various fungal infections, such as Candida, which further strengthens the antifungal properties of CanXida CXR. In addition, the antiviral properties of clove extract align perfectly with the product's objectives, offering thorough protection against viral threats. *

The clove extract in the CanXida CXR formulation has important properties that support digestive health, including immune modulation, anti-inflammatory effects, and antioxidant properties. These attributes help improve the health of the digestive system and reduce symptoms related to Candida infections. The clove extract's analgesic activity, primarily due to its main component

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eugenol, provides an additional benefit to the product by potentially alleviating pain related to digestive problems.*

In conclusion, CanXida Remove's antifungal, antibacterial, anti-inflammatory, and analgesic properties are significantly augmented by the inclusion of Clove extract. This formulation offers a comprehensive approach to addressing Candida-related issues, providing support against fungal and bacterial infections, as well as contributing to overall gut health.*

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