

**Review Article****COMPREHENSIVE REVIEW OF THE PHARMACOLOGICAL POTENTIAL OF *CITRUS RETICULATA* LEAVES: EVALUATING EFFICACY, SAFETY, AND THERAPEUTIC POTENTIAL****POOJA SHARMA\*, AJEET PAL SINGH, AMAR PAL SINGH**

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**ABSTRACT**

*Citrus reticulata*, known as the mandarin orange or tangerine, has gained acclaim for its fruit. Yet, the leaves of *Citrus reticulata* also possess remarkable pharmacological properties. Even though the leaves have been used in several cultures for centuries, the pharmacological potential of the leaves has yet to be formally reviewed and explored. Therefore, the aim of this paper is to critically evaluate the effectiveness, safety, and therapeutic potential of *Citrus reticulata* leaves using recent scientific evidence. *Citrus reticulata* leaves contain flavonoids (hesperidin and naringin) and essential oils, in addition to other bioactive compounds. Some of the pharmacological activities include potent antioxidant, anti-inflammatory, antimicrobial, and antidiabetic properties. The review discusses how these compounds interact with various biological targets, indicating there is some potential for the use of *Citrus reticulata* leaves, for example, in the management of oxidative stress, inflammation, and metabolic disorders. Given the pharmacological activities cited previously, *Citrus reticulata* leaves are a promising avenue for investigating therapeutic agents. The bioactive compounds derived from *Citrus reticulata* leaves demonstrate some potent pharmacological activities, which indicates potential for use in pharmaceutical formulations and functional foods. Still, more clinical studies and standardization of extracts from *Citrus reticulata* leaves need to be performed to ensure efficacy and safety for use in therapeutic settings.

**Keywords:** *Citrus reticulata* leaves, Bioactive compounds, Antioxidant, Anti-inflammatory, Therapeutic potential

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**INTRODUCTION**

*Citrus reticulata*, or Mandarin oranges, are little citrus fruits that are easily peeled and have a pleasant flavor. Beyond its fruit, *Citrus reticulata* leaves have drawn a lot of interest due to their many uses and advantages. For decades, the medicinal benefits of these leaves have been utilized in traditional medicine, particularly in Asian nations. They have a record for having the ability to treat a wide range of illnesses, such as respiratory and digestive disorders. The leaves' therapeutic potential is derived from the presence of flavonoids, essential oils, and other bioactive substances [1-3]. Additionally, recent research has emphasized the possible health advantages of *Citrus reticulata* leaves. Their antioxidant properties are of particular interest, as they may help combat oxidative stress and inflammation. Additionally, these leaves' anti-microbial and anti-viral properties make them valuable in natural health remedies. Their application extends to the realm of skincare, where extracts are utilized in products aimed at enhancing skin health and vitality [3]. The term "mandarin fruit" refers to *Citrus reticulata* Blanco,

which is one of the most useful commercial species [4]. East Asian, Southeast Asian, and Chinese regions are its native lands [5]. After renaming it Guānhuà in Chinese, the Portuguese gave *C. reticulata* the name "Mandarin" to indicate that it was originally from that nation [6]. Historically, folk medicine has employed several cultivars of *C. reticulata* to treat a range of conditions, including fever, bronchitis, asthma, snakebite, stomachaches, edema, and heart disorders [7]. Because of its wide range antibacterial and antifungal properties, mandarin oil is widely recognized [8-12]. Other effects were antidiabetic [13], schistosomicidal [14], antioxidant [15], and anti-proliferative.

**Plant profile**

Worldwide, citrus plants are widely recognized as crops with the ability to impact society and economy. Among the rue family (Rutaceae), the genus *Citrus* includes flowering trees and shrubs. Citrus fruits such as oranges, lemons, grapefruits, pomelos, and limes are produced by plants of this genus.



Fig. 1: Shows *Citrus reticulata* leaves

Table 1: Taxonomical classification of *Citrus Reticulata*

Kingdom	Plantae
Phylum	Tracheophyta
Class	Magnoliopsida
Order	Sapindales
Family	Rutaceae
Genus	Citrus
Species	<i>Citrus reticulata</i>

#### Citrus species

*Citrus reticulata*, commonly known as mandarin orange, is a small, evergreen tree native to Southeast Asia. It is characterized by the following features.

Table 2: Citrus species

Vernacular name	English: Mandarin orange, mandarin or mandarine Hindi: Narangi or Santra
Leaves	Shiny, deep green, and rather small, slightly winged.
Flowers	White and pleasantly perfumed that bloom in the leaf axils in spring
Fruits	Size: small 40–80 ml rounded/flattened globose shape Color: It's orange, yellow-orange, or red-orange. Taste: sweet, aromatic pulp, and thin yellow skin
Branches and tree trunk	Major thorns
Root	fibrous root system
Size	The tree can grow to 15-25 feet tall
Shape	It has a rounded, usually thorny crown with slender branches

#### General characteristics of *Citrus reticulata* leaves [16]

##### Leaf shape

Type: The leaves of *Citrus reticulata* are typically simple and alternate.

Shape: The shape of the leaves is generally ovate to lanceolate. They can vary slightly but are commonly elongated with a tapered tip.

Size: The leaves are medium-sized, usually ranging from 6 to 10 centimeters (2.4 to 4 inches) in length and 3 to 5 centimeters (1.2 to 2 inches) in width.

##### Leaf color

Surface: The upper surface of the leaves is dark green and glossy.

Underside: The underside of the leaves is paler, often with a slightly lighter green or yellowish hue.

##### Leaf texture

Texture: The texture of the leaf surface is smooth and leathery. The leaf has a waxy coating that contributes to its glossy appearance.

Edge: The margin of the leaf is smooth, with no serrations or indentations.

##### Leaf petiole

Petiole: The leaf is attached to the stem by a petiole, which is typically short and winged. The winged petiole has a broad, flattened base that connects the leaf blade to the stem.

##### Leaf aroma

Fragrance: *Citrus reticulata* leaves have a distinct citrus aroma, which is due to the presence of essential oils. The scent can be described as fresh and slightly spicy.

##### Leaf arrangement

The leaves are arranged alternately along the stem, meaning that each leaf grows in a staggered fashion on either side of the stem and usually its do not have prominent stipules, but the petiole may be slightly winged.

##### Leaf vein structure

The leaves exhibit a pinnate venation pattern. There is a central primary vein with several secondary veins branching out in a regular pattern and they are generally prominent and visible on the lower side of the leaf.

#### Nutrient profile [17]

##### Flavonoids

Quercetin and hesperidin are prominent flavonoids found in *Citrus reticulata* leaves. These compounds are known for their antioxidant properties, which help neutralize free radicals and reduce oxidative stress in the body.

##### Essential oils

Limonene and linalool are essential oils present in the leaves. These oils have been shown to possess anti-inflammatory, antimicrobial, and antioxidant properties.

##### Vitamins

**Vitamin C:** *Citrus reticulata* leaves contain vitamin C, though in smaller amounts compared to the fruit. Vitamin C is crucial for immune system function, skin health, and wound healing.

#### Minerals

Calcium and potassium are present in *Citrus reticulata* leaves. These minerals are essential for maintaining bone health, regulating blood pressure, and ensuring proper muscle function.

#### Health benefits

##### Antioxidant activity

The flavonoids and essential oils in *Citrus reticulata* leaves exhibit strong antioxidant effects. These antioxidants help protect cells from oxidative damage, which is linked to chronic diseases such as cancer and heart disease.

##### Anti-inflammatory effects

The anti-inflammatory properties of essential oils and flavonoids can help reduce inflammation in the body. This can be beneficial for conditions such as arthritis and other inflammatory disorders.

##### Digestive health

Traditionally, *Citrus reticulata* leaves have been used to aid digestion. The compounds in the leaves may help in soothing digestive tract inflammation and improving overall digestive function.

#### Immune support

The vitamin C content, though relatively modest, contributes to immune system support by enhancing the body's ability to fend off infections and illnesses.

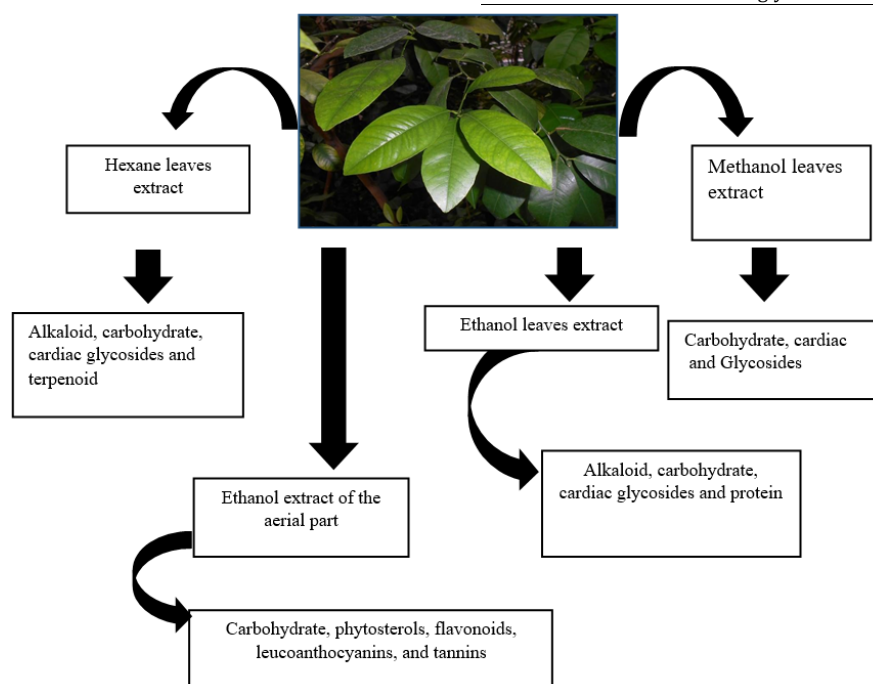
#### Skin health

The antioxidant and anti-inflammatory properties of *Citrus reticulata* leaves make them valuable in skincare. Extracts from the leaves can help in reducing signs of aging and improving skin texture.

While *Citrus reticulata* leaves are not a major dietary component, their nutritional content and bioactive compounds contribute valuable health benefits. They offer antioxidant, anti-inflammatory, and immune-supportive properties, making them a valuable addition to traditional medicine and complementary health practices. Further research could provide deeper insights into their full nutritional potential and broader health applications.

**Table 3: Chemical constituents of *citrus reticulata* leave [18]**

Hexane leaves extract	Alkaloid, Carbohydrate, Cardiac glycosides and terpenoid
Methanol leaves extract	Carbohydrate and Cardiac Glycosides
Ethanol leaves extract	Alkaloid, Carbohydrate, Cardiac glycosides and protein



**Fig. 2: Extraction of *citrus reticulata* leaves**

#### Mechanism of action of *C. reticulata*

##### Antioxidant activity

**Compounds involved:** Flavonoids such as hesperidin and quercetin, and phenolic compounds.

**Mechanism:** These compounds neutralize free radicals through their antioxidant properties, reducing oxidative stress and preventing cellular damage. They scavenge reactive oxygen species (ROS) and inhibit lipid peroxidation [18].

##### Anti-cancer effects

**Compounds Involved:** Flavonoids and essential oils.

**Mechanism:** The compounds induce apoptosis (programmed cell death) in cancer cells by activating caspase pathways and inhibiting

tumor growth. They also exhibit anti-proliferative effects by disrupting cell cycle progression [19].

##### Anti-inflammatory effects

**Compounds involved:** Essential oils such as limonene and linalool, flavonoids.

**Mechanism:** These compounds inhibit pro-inflammatory cytokines and enzymes like cyclooxygenase-2 (COX-2) and lipoxygenase (LOX). They modulate inflammatory pathways, reducing the expression of inflammatory mediators [20].

##### Antimicrobial activity

**Compounds Involved:** Essential oils and flavonoids.

**Mechanism:** Essential oils exhibit antimicrobial properties by disrupting microbial cell membranes and inhibiting microbial growth. Flavonoids interfere with microbial enzyme systems and inhibit bacterial biofilm formation [3].

#### Digestive health benefits

**Compounds Involved:** Flavonoids, essential oils.

**Mechanism:** The leaves' compounds help in soothing gastrointestinal inflammation, enhancing digestive enzyme activity, and improving gut motility. They may also protect the gastric mucosa from damage [21].

#### Evaluating the efficacy and therapeutic potential of *Citrus reticulata* leaves

- Effective antibacterial activity against *B. subtilis*, *E. coli*, and *S. aureus* was demonstrated by *C. reticulata* [22].
- The *Citrus reticulata* leaf extract is a corrosion inhibitor that is cheap, environmentally friendly and has good solubility. In recent years, corrosion work has developed a large number of plant extracts as green and environmentally friendly corrosion inhibitors [23].
- The synthesized AgNPs play a vital role in developing resistance against *Alternaria* brown spot disease and the enhanced production of phytochemicals in *C. reticulata*. These phytochemicals act as reducing and stabilizing agent for the synthesis of AgNPs, thus escaping the utilization of hazardous substances [24].
- The essential oils of mandarin show antifungal activity against the fungi *A. niger*, *A. flavus*, *P. chrysogenum* and *P. verrucosum*. Mandarin is the best inhibitor of *A. flavus* [25].
- The ability of the essential oils to block the main aging-related enzymes, hyaluronidase, collagenase, and amylase, was measured to assess their antiaging potential [26].
- The antioxidant and radical scavenging properties of *Citrus reticulata* Blanco cv. Murcot (Honey) oils may be partially responsible for their *in vivo* effectiveness against degenerative disorders such as diabetes mellitus [27].
- *Citrus reticulata* dried peel powder is used as a skin conditioning, tightening agent [16].
- The *Citrus reticulata* leaves may offer protective benefits against liver damage caused by various toxins [28].
- *Citrus reticulata* extracts might positively influence lipid metabolism, potentially benefiting cardiovascular health [29].
- The extract from *Citrus reticulata* leaves has demonstrated notable anti-inflammatory and analgesic properties [30].

#### Evaluating the safety of *Citrus reticulata* leaves

##### General safety and toxicity

*Citrus reticulata* leaf extracts are generally considered safe at recommended doses, but high doses may lead to adverse effects [31].

##### Allergic reactions

Allergic reactions to *Citrus reticulata* are rare but possible, particularly in individuals with citrus allergies [32].

##### Interaction with medications

There is limited evidence on interactions between *Citrus reticulata* and pharmaceuticals, but caution is advised when used alongside certain medications [33].

#### CONCLUSION

The leaves of *Citrus reticulata* are highly valued for their anti-inflammatory, antioxidant, and possibly antidiabetic properties. Additionally, they appear to be promising for cardiovascular and liver health. Although large dosages and possible allergic responses should be watched out for, safety profiles indicate that they are generally safe for the majority of people.

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#### AUTHORS CONTRIBUTIONS

All the authors have contributed equally.

#### CONFLICTS OF INTERESTS

There are no conflicts of interest

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