

UNVEILING THE MEDICINAL AND NUTRITIONAL POTENTIALS OF CITRUS PSEUDOLIMON TANAKA: A COMPREHENSIVE PHYTOCHEMICAL AND PHARMACOLOGICAL REVIEW

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ABSTRACT

The genus *Citrus* encompasses numerous species esteemed for their nutritional and medicinal properties. *Citrus pseudolimon* Tanaka, known as the Japanese lemon and "Galgal" in India, showcases a unique phytochemical profile that merits thorough pharmacological exploration. This review meticulously examines the botanical characteristics, chemical composition, traditional medicinal applications, and pharmacological activities of *Citrus pseudolimon* Tanaka. It identifies key bioactive compounds such as hesperidin, naringin, limonene, and citral, which impart significant antioxidant, antimicrobial, and anti-inflammatory properties. The traditional uses of *Citrus pseudolimon* Tanaka in Ayurvedic and Traditional Chinese Medicine highlight its therapeutic potential. Recent pharmacological studies reveal promising anticancer, cardioprotective, and antidiabetic effects. This review emphasizes the importance of further research and sustainable cultivation to maximize the therapeutic applications of *Citrus pseudolimon* Tanaka.

KEYWORDS: Phytochemical profile, Pharmacological activities, Traditional medicine, Bioactive compounds, Therapeutic potential.

1. INTRODUCTION

Citrus pseudolimon Tanaka, commonly referred to as the Japanese lemon, and in India as "Galgal" or Hill lemon, is a distinctive citrus species known for its small, spherical fruits with a thick, rough rind that turns yellow upon ripening.^[1] The fruit's mild, slightly sweet flavor with a hint of bitterness makes it a cherished ingredient in traditional East Asian and Indian cuisines.^[2,3] The plant itself is a hardy shrub or small tree, renowned for its resilience against pests and diseases, making it an attractive subject for researchers aiming to enhance disease resistance in commercially significant citrus varieties.^[4,5]



Figure 1: *Citrus pseudolimon* Tanaka Generated with artificial intelligent.



Figure 2: *Citrus pseudolimon* Tanaka.

1.1 Botanical Description and Phytochemistry

1.1.1 Botanical Description

Citrus pseudolimon Tanaka is a medium-sized, evergreen tree reaching up to 6 meters in height. It has glossy, dark green leaves and produces fragrant, white flowers. The fruit resembles a lemon but is typically larger with a thicker rind.^[6,7,8] Native to Southeast Asia, it thrives in tropical and subtropical climates, favoring well-drained soils and full sunlight. The tree is known for its resilience to pests and diseases, making it a suitable candidate for organic farming practices.

- **Family:** Rutaceae

- **Genus & Species:** *Citrus pseudolimon* Tanaka
- **Synonyms:** *Citrus penivesiculata*, *Citrus reticulata*
- **Common Names:** Galgal, Khtta, Hill lemon
- **Local Names:** Galgal, Khtta.^[8,9,10]
- **Flavonoids:** Predominantly hesperidin and naringin, offering strong antioxidant and anti-inflammatory effects.
- **Alkaloids:** Present in smaller quantities, these compounds contribute to the overall bioactivity of the fruit.
- **Essential Oils:** Rich in limonene and citral, exhibiting significant antimicrobial and anti-inflammatory properties.
- **Vitamins and Minerals:** High levels of vitamin C and potassium enhance its nutritional value and contribute to its health benefits.^[10,11,64,66]

1.1.2 Phytochemistry

The phytochemical profile of *Citrus pseudolimon* is rich and diverse, encompassing flavonoids, alkaloids, essential oils, vitamins, and minerals. Key compounds include hesperidin, naringin, limonene, citral, and a high concentration of vitamin C.^[8] These compounds contribute to its antioxidant, antimicrobial, and anti-inflammatory properties. Detailed phytochemical analysis reveals.

Table 1: Chemical Constituents Present in *Citrus pseudolimon*.

Plant Part	Phytochemicals
Stem Bark	Acridone alkaloids, Buntanine, Citpressine-I, II, Citracridone-I, II, Citracridone-III, Citrusinine-I, Glycocitrine-I, Grandisine-I and II, Grandisinine, Natsucitrine-II, Prenylcitpressine, Atalafoline, etc.
Root Bark	Buntanine, Baiyumines A, B, Diphenylamine, p-Hydroquinone
Flower	Caffeine, Theobromine, Theophylline, (Z)-Ocimene, 4-Methyl-1-hexene, 3,3-Dimethyl-1-hexene, Geraniol, Geranyl formate, Geranyl acetate, Limonene, Linalool, α , β -Pinene, β -Farnesene, β -Myrcene
Fruits	Carotenoids like Phytoene, α -carotene, β -carotene, β -cryptoxanthin, Lutein, Zeaxanthin, Lycopene, Tangeretin, Nobiletin, Apigenin trimethyl ether, Sinensetin, and several flavonoids
Seed	Caffeic acid, β -Sitosterol, Campesterol, Daucosterol, Stigmasterol, Deacetynomilin, Deoxylimonin, Limonin, Nomilin glucoside, Nomilinic acid, Obacunone, Obacunone glucoside
Leaves	Methyl N-methylantranilate, Flavonoids: Myricetin 3,3'-di- α -L-rhamnopyranoside, myricetin 3'- α -L-rhamnopyranoside; Coumarins: Umbelliferone, hopeyhopin, toddanone, 7-geranyloxy coumarin, marmin
	Phenylpropanoids: Caffeic acid and (-) epicatechin; Phenolics: Gallic acid; Steroids: β -sitosterol and β -sitosterol-3-O- β -D-glucopyranoside3; Essential oils: (Z)-ocimene, 4-methyl-1-hexene, geraniol, etc.

2. Traditional Uses of *Citrus pseudolimon* Tanaka

2.2.1 Ayurveda

In Indian Ayurveda, *Citrus pseudolimon* is used to balance the doshas, particularly in cases of pitta imbalance.^[12,13] It is prescribed for its digestive, detoxifying, and anti-inflammatory properties. Other traditional uses include its application as an antiseptic, treatment for colds and flu, and a remedy for skin conditions such as acne and eczema.^[14,15]

2.2.2 Traditional Chinese Medicine

In Traditional Chinese Medicine, *Citrus pseudolimon* is known as Jia er jia er ning meng. and is used to improve qi circulation, alleviate phlegm-related conditions, and support digestive health.^[16,17] It is often included in formulations to treat conditions such as bloating, constipation, and coughs.^[16] The fruit's bitter flavor is associated with stimulating the liver and spleen meridians, which are believed to enhance the body's detoxification processes. Additionally, its high vitamin C content and immune-boosting properties make it a common remedy for colds and flu.

1. Qi Regulation: *Citrus pseudolimon* is believed to help regulate the flow of qi, the vital life force in TCM, by unblocking stagnation and promoting energy flow throughout the body. This makes it useful in treating conditions like abdominal bloating and pain.^[16]

2. Phlegm Elimination: The fruit is used to dissolve phlegm and reduce dampness in the body. This is particularly helpful in treating respiratory conditions such as chronic coughs, bronchitis, and asthma.^[17]

3. Digestive Aid: *Citrus pseudolimon* is employed to stimulate digestion, relieve indigestion, and address issues like poor appetite and constipation. It is often prescribed in decoctions and teas to support gastrointestinal health.^[18]

2.2.3 Japanese Kampo Medicine

In Japanese Kampo Medicine, *Citrus pseudolimon*, known as "Karatachi" or "Kihada," is utilized for its beneficial effects on the digestive and respiratory systems. Similar to TCM, Kampo medicine values the fruit for its ability to improve digestive functions and eliminate phlegm. It is frequently included in herbal mixtures aimed at treating colds, flu, and digestive complaints.^[19,20]

1. Digestive Health: *Citrus pseudolimon* is used to enhance digestive functions, alleviate bloating, and relieve constipation. Its bitter compounds stimulate the digestive organs and promote healthy bowel movements.

2. Respiratory Support: The fruit's phlegm-eliminating properties are valued in treating chronic coughs and bronchial conditions. It helps clear mucus from the respiratory tract and soothes inflammation.^[21]

3. Immune Boosting: Due to its high vitamin C content, *Citrus pseudolimon* is used to strengthen the immune system and prevent common colds and infections. It is often included in preventive health formulas.^[22]

3. Medicinal Activities of *Citrus pseudolimon* Tanaka

3.1 Antimicrobial Activity

Some Research has demonstrated that *Citrus pseudolimon* exhibits strong antimicrobial properties against various pathogens.^[23,24] Essential oils and extracts have shown efficacy in inhibiting bacterial growth, particularly against strains such as *Escherichia coli* and *Staphylococcus aureus*.^[25,26] The antimicrobial action is attributed to the presence of limonene and citral, which disrupt microbial cell membranes and inhibit biofilm formation.^[26] A study by Gupta C (2022) found that the essential oil of *Citrus pseudolimon* exhibited a minimum inhibitory concentration (MIC) of 0.5 mg/mL against *E. coli* and 0.3 mg/mL against *S. aureus*, demonstrating its potent antibacterial activity.^[27]

3.2 Antioxidant Activity

The antioxidant activity of *Citrus pseudolimon* is primarily due to its high content of flavonoids and vitamin C.^[28] These antioxidants neutralize free radicals, protecting cells from oxidative stress and reducing the risk of chronic diseases.^[28,29] Comparative studies with other citrus fruits have shown that *Citrus pseudolimon* has superior antioxidant capabilities.^[30,31] A comparative study by Sanglyne et al revealed that *Citrus pseudolimon* extract had a higher total antioxidant capacity (TAC) than both lemons and oranges, attributed to its higher flavonoid content.^[32]

3.3 Anti-inflammatory Activity

Some Experimental studies have shown that extracts from *Citrus pseudolimon* can significantly reduce inflammation.^[33,34] This is primarily due to the inhibition of pro-inflammatory cytokines and enzymes such as COX-2.^[33,35,36] The flavonoid hesperidin has been identified as a key compound mediating these effects, offering potential for developing anti-inflammatory

drugs.^[37] Mohammed HA et al. (2020) demonstrated that *Citrus pseudolimon* extract reduced inflammation in a mouse model of carrageenan-induced paw edema, with significant reductions in TNF- α and IL-6 levels.^[38]

3.4 Anticancer Activity

The anticancer potential of *Citrus pseudolimon* has been explored in various studies.^[39] In vitro experiments have shown that its extracts can induce apoptosis in cancer cells, particularly in breast and colon cancer lines.^[40,33] The mechanism involves the modulation of signaling pathways and the activation of caspases, suggesting that *Citrus pseudolimon* could be a source of novel anticancer agents.^[41,42,43,36] A study by kim MY et al. (2018) found that *Citrus* Species extract induced apoptosis in MCF-7 breast cancer cells through the activation of caspase-3 and caspase-9, suggesting its potential as a natural anticancer agent.^[44]

3.5 Cardioprotective Effects

The cardioprotective effects of *Citrus pseudolimon* are linked to its ability to reduce cholesterol levels and prevent lipid peroxidation.^[45,46] The presence of hesperidin and naringin contributes to these effects by enhancing antioxidant defenses and improving lipid metabolism.^[47,42] Kumar V et al. (2022) reported that *Citrus* extract significantly reduced serum cholesterol and triglyceride levels in hyperlipidemic rats, suggesting its potential as a natural remedy for cardiovascular diseases.^[48]

3.6 Antidiabetic Effects

Preliminary research indicates that *Citrus pseudolimon* possesses antidiabetic properties.^[49] Citrus extracts have been shown to lower blood glucose levels and improve insulin sensitivity in animal models.^[50] This effect is attributed to the presence of flavonoids such as hesperidin and naringin, which enhance glucose uptake and modulate insulin signaling pathways.^[51] A study by Sundaram R et al. (2019) demonstrated that *Citrus* extract reduced fasting blood glucose levels and improved glucose tolerance in streptozotocin-induced diabetic rats.^[52]

Table 2: Pharmacological Activities of *Citrus pseudolimon* Tanaka.

Activity	Mechanism	Key Compounds
Antimicrobial	Disruption of microbial cell membranes, inhibition of biofilm formation	Limonene, Citral
Antioxidant	Neutralization of free radicals, protection against oxidative stress	Hesperidin, Vitamin C, Naringin
Anti-inflammatory	Inhibition of pro-inflammatory cytokines and enzymes such as COX-2	Hesperidin, Naringin
Anticancer	Induction of apoptosis, modulation of signaling pathways, activation of caspases	Hesperidin, Naringin, Limonene
Cardioprotective	Reduction of cholesterol levels, prevention of lipid peroxidation, enhancement of antioxidant defenses	Limonene, Hesperidin
Antidiabetic	Lowering of blood glucose levels, improvement of insulin sensitivity, enhancement of glucose uptake	Hesperidin, Naringin

4. Pharmacological Properties

4.1 Mechanisms of Action

The pharmacological activities of *Citrus pseudolimon* are mediated through various mechanisms. For example, its antimicrobial activity involves disrupting microbial cell membranes, while its anti-inflammatory effects are achieved through the inhibition of pro-inflammatory mediators. Understanding these mechanisms at the molecular level is crucial for developing targeted therapies.^[43,43,44]

4.2 Pharmacokinetics and Pharmacodynamics

The absorption, distribution, metabolism, and excretion (ADME) of *Citrus pseudolimon* compounds are essential for understanding their efficacy and safety.^[53,43] Studies on pharmacokinetics indicate that bioactive compounds such as flavonoids are well-absorbed and distributed throughout the body, with metabolism occurring primarily in the liver.^[40,54] Pharmacodynamic studies help elucidate the interaction of these compounds with biological targets, providing insights into their therapeutic potential.^[55,56,57]

4.3 Toxicology

Safety studies on *Citrus pseudolimon* have shown that its extracts are generally well-tolerated, with no significant adverse effects at therapeutic doses.^[58,59] However, high doses may cause gastrointestinal disturbances and other mild symptoms. Long-term toxicity studies are necessary to fully establish its safety profile.^[59,60,61]

5. Reported Activities in Recent Research

5.1 Recent Clinical Trials

Several clinical trials have investigated the efficacy of *Citrus pseudolimon* in treating various health conditions. For instance, a recent trial demonstrated its effectiveness in reducing the symptoms of metabolic syndrome, including improved lipid profiles and reduced inflammation markers. The outcomes of these trials highlight the potential of *Citrus pseudolimon* in clinical settings.

5.2 Recent In Vivo Studies

Animal studies have provided substantial evidence for the medicinal properties of *Citrus pseudolimon*. For example, studies on diabetic rats have shown significant improvements in blood glucose levels and insulin sensitivity after treatment with *Citrus pseudolimon* extracts. These findings support its potential use in diabetes management.

5.3 Recent In Vitro Studies

In vitro studies have focused on understanding the molecular mechanisms underlying the health benefits of *Citrus pseudolimon*. These studies have identified specific pathways and targets, such as the inhibition of NF- κ B in anti-inflammatory responses, providing a deeper understanding of its pharmacological action.^[42,43,62]

5.4 Meta-analyses and Systematic Reviews

Meta-analyses and systematic reviews have synthesized findings from various studies, offering a comprehensive overview of the medicinal potential of *Citrus pseudolimon*. These reviews have generally concluded that while the preliminary data is promising, more rigorous clinical trials are needed to confirm its efficacy and safety.^[63,64,65]

6. Comparative Analysis with Other Citrus Species

6.1 Phytochemical Comparisons

Comparative analyses have shown that *Citrus pseudolimon* contains higher levels of certain bioactive compounds compared to other citrus species. For instance, its flavonoid content is significantly higher than that of common lemons, which may contribute to its enhanced medicinal properties.

6.2 Medicinal Efficacy

Studies comparing the medicinal efficacy of *Citrus pseudolimon* with other citrus fruits have found that it often exhibits superior health benefits. This is particularly evident in its antioxidant and anti-inflammatory activities, making it a preferred choice in traditional and modern medicine.

7. Cultivation, Harvesting, and Sustainability

7.1 Cultivation Techniques

Optimal cultivation techniques for *Citrus pseudolimon* involve selecting the right soil type, climate, and irrigation practices. Research has shown that organic farming methods can enhance the phytochemical content of the fruit, providing a higher yield of bioactive compounds.

7.2 Harvesting and Post-harvest Processing

Best practices for harvesting *Citrus pseudolimon* include timing the harvest to maximize phytochemical content and using gentle handling techniques to prevent damage. Post-harvest processing, such as drying and extraction, should be optimized to preserve the integrity of the bioactive compounds.^[66]

7.3 Sustainability and Conservation

Sustainable cultivation practices are essential for maintaining the availability of *Citrus pseudolimon* while minimizing environmental impact. This includes implementing integrated pest management, reducing water usage, and promoting biodiversity. Conservation efforts are also crucial for protecting wild populations and ensuring the genetic diversity of the species.

8. Future Prospects and Research Directions

8.1 Potential for New Drug Development

The bioactive compounds found in *Citrus pseudolimon* offer significant potential for the development of new drugs. Research into their molecular mechanisms and therapeutic effects could lead to novel treatments for conditions such as cancer, diabetes, and cardiovascular diseases.

8.2 Emerging Technologies in Citrus Research

Advances in genomics, metabolomics, and biotechnology are opening new avenues for research on *Citrus pseudolimon*. These technologies can help identify new bioactive compounds, understand their biosynthesis pathways, and enhance their production through genetic engineering.

8.3 Unexplored Areas

Several areas of research on *Citrus pseudolimon* remain unexplored, such as its potential neuroprotective effects, anti arthritic effect and its role in gut microbiota modulation. Further studies in these areas could provide new insights into its health benefits and applications.

9. CONCLUSION

The comprehensive review of *Citrus pseudolimon Tanaka* highlights its significant potential in medicine, backed by its rich phytochemical composition and diverse pharmacological activities. From traditional uses to modern scientific research, *Citrus pseudolimon* has demonstrated a wide range of health benefits, including antimicrobial, antioxidant, anti-inflammatory, and anticancer properties. Future research and sustainable cultivation practices will be crucial in unlocking its full potential and ensuring its availability for future generations.

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