

Phytochemical, pharmacological and ethnomedical properties of Citrus limetta Risso: A scoping review

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ABSTRACT

Citrus limetta Risso belongs to the rutaceae family is a perennial shrub and its various parts like fruit, peels and leaves used as traditional medicine in various parts of the world. It is a cultivated fruit in all parts of India and greater supplement of vitamin C. It is used as a traditional remedy for biliousness, fever, brain troubles, anthelmintic, antiemetic, scurvy, jaundice, diabetes, ulcers, urinary tract infections, skin problems, immune booster etc. The review provides a greater insight for pharmacological properties of Citrus limetta Risso for treatment of diseases like antidiabetic, antioxidant, antihypertensive, diuretic, anticancer, larvicidal, antibacterial, anti-inflammatory, analgesic, anti-pyretic, skin inflammation, antirheumatic, hepatoprotective, anti-anxiety, antidepressant and thrombolytic activity. The present review highlighted therapeutic potentials and provide evidence for future medicinal applications of Citrus limetta Risso.

KEYWORDS: Citrus limetta Risso; Rutaceae; Vitamin C; Traditional uses; Pharmacological activity;

I. INTRODUCTION

Plants have been used as an alternative source of medicine for centuries in various cultures around the world. Plants contain valuable bioactive compounds that have potential therapeutic effects and many modern pharmaceutical drugs are derived from plant compounds^[1,2]. Plants contain a wide variety of bioactive compounds, such as alkaloids, flavonoids, terpenes, and phenolics, which aids therapeutic effects on the human diseases^[3]. These compounds are derived from roots, barks, leaves, fruits, flowers, seeds, rhizome, bark, fruit peels and resins. Numerous drugs used in modern medicine are derived from plants are synthesized based on plant compounds^[4]. These natural products can be isolated from plants and used as drugs or serve as the basis for the development of synthetic analogues^[5]. Plant derivatives like curcumin, huperizine A, lycopene,

piperine etc. has been reported to produce various pharmacological properties^[6].

The citrus genus is the most cultivated and traded variety in the world and one of the most pivotal commercial fruit crops grown on all parts of the world^[7]. There are about 520 citrus species totally and 33 species have been cultivated in various parts of India^[8]. The essential oils of citrus species have been used in soaps, cosmetics, home care products and used in various other industries^[9].

The plant Citrus limetta Risso which belongs to the rutaceae family possess various traditional medicinal properties. It is well cultivated in mostly in Asian countries. The fruits are used as a major supplement of vitamin C. The fruits, peels and leaves are parts used as a folk medicine for various diseases^[10]. Various researchers had conducted many pharmacological studies using various parts of the plants and reported many aspects of its medicinal values which is discussed in this article.

TAXONOMICAL HIERARCHY OF Citrus limetta Risso

Kingdom: Plantae
Division: Magnoliophyta
Class: Dicotyledons
Sub class: Sapindales
Order: Rosidae
Family: Rutaceae
Sub family: Aurantoideae
Genera: Citrus
Sub genera: Papeda
Species: limetta

SYNONYMS OF Citrus limetta Risso

Hindi: Mosambi
Tamil: Sathukudi
Malayalam: Erimichanarakam
Gujarati: Mithalimbu
Urdu: Limunshirin
Sanskrit: Mathukukutika
English: Sweet lime

Persian: Limunshirin
French: Bergamotier
Portugese: Limeira
Spanish: Bergamota
Arabic: Limunalhava ^[11]

CHEMICAL CONSTITUENTS

The Citrus limetta Risso fruit peels are mostly used part analyzed by various researchers for its pharmacological activity. The d-limonene is the major component of the peels constitutes about 90 percent of its total composition. The various other components present in the peels are bergamol, β -pinene, linalool, α -pinene, 1,8 cineole, α -terpineol, neral, geranial, β -bisabolol, β -bisabolene, β -myrcene, sabinene, citronellal, α -terpineol acetate, camphene, α -bisabolol, bicyclogermacrene, farnesol, terpinen-4-ol, trans-nerodilol, β farnesene, nonanal, phytol, hinesol, α -phellandrene, borneol, myrcenil acetate, β -santalene etc. ^[12-17].

GEOGRAPHICAL DISTRIBUTION

The plant Citrus limetta Risso which is also known as sweet lime is a native plant of Asia and it is best cultivated in India, China, South Japan, Vietnam, Malaysia, Indonesia and Thailand.

PLANT DESCRIPTION

It is a large straggling shrub with leaves light green in colour and with more prominent oil glands. Petiole is winged. Flowers large and white in colour. Fruit is globoid or ovoid (7.5- 12.5 cm in diameter) smooth pale yellow or light green. Rind is thin. Pulp is adhered close to rind. Juice is abundant, sweet and not aromatic.

TRADITIONAL USES

The plant is traditionally used in biliousness, fever, brain troubles, haemorrhage. It is also used as anthelmintic, astringent, antiemetic, scurvy, jaundice, diabetes, ulcers, urinary tract infections, skin problems, immune booster and weight reduction ^[18].

PHARMACOLOGICAL ACTIVITIES

Hepatoprotective

The methanol extract of Citrus limetta Risso peels showed hepatoprotective activity in Wistar albino rats induced by carbon tetrachloride and paracetamol. The rats exhibited a decrease in the levels of SGPT, SGOT, ALP, ACP, LDH, total bilirubin and increased the level of total protein ^[19].

Anti-cancer

The essential oils of Citrus limetta Risso peels was obtained using Clevenger's apparatus by hydro distillation method. The essential oils possess anti-cancer properties in MCF-7 and MDAMB231 cell lines and their IC₅₀ values was found to be 47.31 ± 3.11 μ g/ml and 55.11 ± 4.62 μ g/ml ^[20].

Anti-diabetic

The methanol extract of Citrus limetta Risso peels 200mg/kg and 400mg/kg dose dependently normalized blood glucose levels in different periods of study in streptozotocin induced diabetes in Wistar rats. Serum biochemical parameters like SGPT, SGOT and ALP was also normalized. It also decreased lipid peroxidation and glutathione levels in pancreas, kidney and liver tissue homogenates compared to that of streptozotocin control group.

The extracts also inhibited α -amylase and α -glucosidase enzymes at a concentration of 20 mg/ml by 49.6% and 28.2% respectively to contribute to its diabetes treatment for type 2 diabetes mellitus.

Citrus limetta peel flour showed a glucose adsorption capacity of 16.58 mM and glucose dialysis retardation index of 33.79% in BALB/c mice. Postprandial serum glucose levels in the animal group treated with Citrus limetta peel flour showed a glucose level of 41.4 mg/dl which is less than streptozotocin control groups ^[21-23].

Anti-hypertensive

The aqueous extract of Citrus limetta Risso leaves prevented the raise of systolic, diastolic and mean blood pressure in male ICR mice with a dose dependent decrease in diastolic pressures at 125, 250, 500 and 1000 mg/kg doses. The 500 and 1000 mg/kg doses inhibited the action of angiotensin-II in a similar extent to 3 mg/kg telmisartan ^[24].

Diuretic

The aqueous extract of Citrus limetta Risso peels produced diuretic activity. It increases the urine excretion volume and sodium, potassium excretion levels which contribute to diuretic activity. It also considered to lower the blood pressure because of diuresis ^[25].

Anti-anxiety

The methanol extract of Citrus limetta Risso fruit 100mg/kg showed anti-anxiety activity.

This was depicted in Swiss albino mice model of elevated plus maze. The time spent is increased in open arm of elevated plus maze of Citrus limetta fruit extracts 100mg/kg is higher than that of standard diazepam 2mg/kg. This demonstrated the anti-anxiety activity in mice ^[26].

Anti-depressant

The methanol extract of leaves of Citrus limetta Risso 200mg/kg was claimed to have antidepressant properties. The orally administered extract in rats demonstrated antidepressant activity in behavioral models like forced swim test, tail suspension test and locomotion test using actophotometer. The improvement in neurotransmitters like serotonin, norepinephrine and dopamine showed antidepressant activity ^[27].

Anti-bacterial

Citrus limetta Risso peels essential oils produce inhibitory effects in bacterial colonies such as of *Pseudomonas aeruginosa*, *Escherichia coli*, *Staphylococcus aureus*, *Salmonella enteric* and their percentage inhibition was found to be 92.19 ± 1.2 , 90.6 ± 1.6 , 95.6 ± 2.1 , 93.8 ± 1.5 respectively ^[28].

Larvicidal

The larvicidal potential of hexane and petroleum ether extract of Citrus limetta Risso peels was assessed against dengue fever vector *Aedes aegypti* and malarial vector *Anopheles stephensi*. Hexane extract resulted in LC_{50} values of 132.45 and 96.15 ppm against *Anopheles stephensi* and *Anopheles aegypti* respectively. The petroleum ether extract resulted in LC_{50} values of 244.59 and 145.50 ppm against *Anopheles stephensi* and *Anopheles aegypti* respectively ^[29].

Skin inflammation treatment

Citrus limetta Risso peels essential oils inhibits macrophages was able to inhibit the production of pro-inflammatory cytokines like tumor necrosis factor- α , interleukin-6, interleukin- 1β and reduce the production of reactive oxygen species pretreated with macrophages by in vitro method.

The topical application of the essential oil in the ear of female New Zealand rabbits and female BALB/c mice reduced the skin inflammation induced by 12-O-tetradecanoylphorbol-13-acetate (TPA). It also reduced the ear thickness, ear weight, lipid peroxidation, pro-inflammatory cytokines

production and improves the histopathological damage in ear tissue ^[30].

Anti-rheumatic

Oral administration of ethanol extract of Citrus limetta Risso peels 30, 100 and 300 mg/kg doses reduced the arthritis score and arthritis index in elbow and knee joints against collagen-induced arthritis in Charles foster rats.

Serum biochemical parameters like TNF- α , IL-6, IL-17A, and C-reactive protein levels were decreased in rats treated with 30, 100 and 300 mg/kg doses. The histological changes were also improved compared to collagen induced arthritic groups.

Anti-pyretic

Ethanol extract of Citrus limetta Risso peels possess antipyretic activity in Brewer's yeast-induced pyrexia in Charles foster rats. The rectal temperature was decreased in 30, 100 and 300 mg/kg doses in a dose dependent manner.

Anti-inflammatory

The acute anti-inflammatory effects of ethanol extract of Citrus limetta Risso peels was obtained using carrageenan-induced paw acute inflammation in Charles foster rats. The doses 30, 100 and 300 mg/kg doses decreased the paw volume measured in plethysmometer in dose dependently which contribute to acute inflammatory activity.

The same doses 30, 100 and 300 mg/kg decreased the serum proinflammatory cytokine levels like TNF- α and IL-6 in the lipopolysaccharide (LPS)- induced systemic inflammation in Swiss albino mice.

Analgesic

Ethanol extract of Citrus limetta Risso peels 30, 100 and 300 mg/kg possess analgesic activity in chemical-induced pain model in Swiss albino mice. The writhing in mice were reduced in acetic acid-induced writhing and licking time was reduced in formalin-induced paw licking in mice.

It also produced analgesic activity in thermal-induced pain model in Swiss albino mice. Latency period was increased in hot plate and tail immersion method which leads to analgesic activity in increasing doses ^[31].

Anti-oxidant

The Citrus limetta Risso peel essential oil possess antioxidant property and the IC_{50} values of

antioxidant activities were DPPH free radical scavenging ($11.35 \pm 0.51 \mu\text{g/ml}$), ABTS scavenging ($10.36 \pm 0.55 \mu\text{g/ml}$), H_2O_2 radical scavenging ($8.28 \pm 0.35 \mu\text{g/ml}$), Ferric reducing antioxidant power ($8.67 \pm 0.21 \mu\text{g/ml}$), Lipid peroxidation inhibition ($30.19 \pm 0.27 \mu\text{g/ml}$)^[32,33].

Thrombolytic

Citrus limetta Risso peels essential oil produced thrombolytic activity by in vitro clot lysis method, showed a maximum effect of $72 \pm 1.17\%$ at $100 \mu\text{g/ml}$ concentration^[34].

II. CONCLUSION

In this article, the relevant literatures were used to summarize the chemical constituents and pharmacological activities of the Citrus limetta Risso peels both in vitro and in vivo animal studies. Plant parts of Citrus limetta Risso provides evidence for its therapeutic potential at a preclinical level, furthermore these studies can be carried out in the future to examine the toxicity studies and can be proceeded to clinical studies.

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