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PHARMACOLOGICAL IMPORTANCE OF *CITRUS MEDICA* PEEL

Santoshi Bisht*

India.

Corresponding Author: Santoshi Bisht
India.

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ABSTRACT

Citrus medica Linn. commonly known as citron in English and Bijapura in ayurvedic literature, is a fragrant fruit. It is a prominent member in the genus citrus, belonging to the Rutaceae or Rue family, sub-family Aurantioideae, which is widely used in traditional system of medicine. The objective of this paper is to review the literature regarding the pharmacological activity of *Citrus medica* Linn. peel. The citrus fruits and juices are a good source of antioxidants such as flavonoids, phenolic content, and ascorbic acid etc. Citrus fruit peel contains highest concentration of flavonoids, which represents almost one half of the fruit mass. *Citrus medica* byproducts also represent a rich source of naturally occurring flavonoids. Traditionally Citrus medica was used to combat sea sickness, pulmonary troubles, intestinal ailments and other disorders. Fruit of citron is ovate or oblong which bears numerous seeds. Owing to the presence of large quantity of albedo, citron's fruit shape is highly variable. The inner portion is thick, white and fleshly and the outer portion is uniformly thin. The pulps are usually acidic. Result shows that Citrus medica peel possess antioxidant & free radical scavenging activity, analgesic, anti-inflammatory, hypoglycaemic and anticholinesterase, cardiotonic, anti-implantation, antimicrobial, antidiabetic and antilipideamic properties.

KEYWORDS: *Citrus medica*, Chemical constituents, Distribution, Morphological characteristics and Pharmacological activities.

INTRODUCTION

For the promotion of good health and for the prevention or treatment of diseases, medicinal plants and herbs have been used for many centuries. (Munwar S,2015) (Sood S, 2009)[00] Medicinal plants can be used as raw materials for the extraction of active constituents which can be further synthesize into active compounds, and then which may be used as traditional preparation. The use of medicinal and aromatic plants is increasing by worldwide interest. India usage many herbal drugs which are officially recognized in alternative systems of health like Ayurveda, Unani, siddha, and Homeopathy. (Anggard E,1994, Babior BM,1984) [0] Human being itself uses herbal medicine since many centuries. When there was no development of synthetic drugs, all human being were totally depend on the naturally occurring medicinal plants for relieving or curing from diseases. In present time many compounds which are related to pharmacology derived from the plants. The primary and secondary metabolites of plants or their extract served as antioxidants which protect from diseases, caused by the oxidative stress. (Halliwell, 1996, 2006) Free radicals play an important role in the production of oxidative stress which are root cause of progression and pathogenesis of disease. Owing to the antioxidant action phenolic compounds obtained from natural products may reduce oxidative stress. (Vinson et al, 1998)[0].

According to many epidemiological studies it is shown that consumption of fruits of citrus genus is protective in a numerous human's diseases like cardiovascular disease, cancer and metabolic syndrome. (Minichini F, 2015)[0] Citrus fruits and juices are important source of antioxidants like ascorbic acid, flavonoids, phenolic compounds and pectins that are important to human nutrition. Owing to their lipid peroxidation activity these plants act as anti-carcinogenic and anti-inflammatory agents. *Citrus medica* byproducts contains a rich source of naturally occurring flavonoids. In citrus fruits the peel part has almost one half of fruit mass which contains the highest amount of flavonoids. Peels have a good total antioxidative potential (TAP). (Nandan MP, 2015)[0]

The citrus fruits peel is a good source of flavonones and many polymethoxylated flavonones. The occurance of these constituents are rare in other plants. Owing to the numerous applications of these compounds in food and pharmaceutical industries, they play an important physiological and ecological as well as commercial role. Presently, the most important commercial and industrial agricultural activities of the world is citrus cultivation.

(Kabra AO, 2012)[0] The production of citrus in whole world is 116 million tons and it is most produced fruit in all over the world. It is grown wherever climate is suitable like tropical, subtropical and borderline subtropical/ temperate.[0](uzun A, 2012)

Citrus fruits have distinct characteristics

The citron (*Citrus medica* L) was the first citrus fruit in Europe and it was only one known fruit for many years. It is a fruit which better known to most consumers in its preserved form rather than in its natural form. Citron was first describe by the latin writer *Virgil (7019 B.C). Pliny*, was other writer who gave several names to the citron (Malus medica, Malus Assyria and Citrus) which was published in his *Natural History*, about 77 A.D and he described its use as a medicine, poison, antidote, perfume and protection from moths.[0] (conforti F, 2007)

Citrus medica is commonly known as citron is a fragrant fruit. It is the prominent member in the genus citrus, which belongs to the Rutaceae or Rue family and sub family is Aurantioideae. The *medica* word is derived from ancient name media, median apple etc which is coined by Theophrastus. (Meena AK, 2011)[0]

CLASSIFICATION

Citrus medica Linn

Kingdom: Plantae- plants
Class: Magnoliopsida –Dicotyledons
Sub class: Rosidae
Oder: Sapindales
Family: Rutaceae- Rue family
Genus: Citrus
Species: Citrus medica L. - Citron

GEOGRAPHICAL DISTRIBUTION

Citrus medica Linn, commonly known as Citron and in ayurvedic literature it is known as *bijapura*. Citron is widely distributed in base region of Himalaya from Garhwal to Sikkim, kumaon, Pachamarhi, Khasia Hills, Garo hills, Chittagong, Upper Yunzalin valley, the Western Ghats and Satpura range in Central India and Mediterranean Region and central and southern parts of America.[0] (Meena AK, 2011) (panara K)

MORPHOLOGICAL CHARACTERISTIC

It is a slow-growing shrub or small tree with a height of 2.4-4.5 m with stiff branches, stiff twigs and short or long spines in the leaf axils:- The leaflets are evergreen which is 6-18 cm long with wingless or nearly wingless petioles. Flowers are about 4 cm wide, in short clusters 4-5 petalled, often pinkish or purplish on the outside. The fruit is fragrant, mostly oblong, obovoid or oval in shape but sometimes there are many smooth or rough fruits with various shapes are occur on the same branch. Peels are yellow in colour when fully ripe, usually rough and bumpy, mostly very thick, fleshy. Pulps are pale-yellow or greenish divided into 14-15 segments, which are acid or sweet with numerous seeds.[0] (Nicolosi E, 2005)

PHYTOCHEMICAL CONSTITUENT

The peels of *Citrus medica* contains citroflavonoids which is a mixture of Hesperidoside (rhamnoglucoside of hesperetol), naringoside and ecryodietyoside (flvonones). The peel also contains flavonoids and phenols, alkaloids, steroids, and carbohydrates, rutin, Vitamin C, Glucoside hisperidin (vitamin P). (Kacharoo M, 2011).

VARITIES OF *CITRUS MEDICA*

There are two cultivars of citron:

1. Citron which has pinkish new growth, purple flower buds and petals are purple –tined, acid pulp, inner seed is dark.
2. Citron without pink or purple tint in the new growth nor in the flowers, pulps are non acid, inner seed coat is colourless.

There are following varities of citron:

Corsican

Origin of Corsican is unknown but it is the most important citron of Corsica. It was introduced into the united states around 1891 and this cultivar grown in California. Its base is ellipsoid or faintly obovate, and furrowed. It has yellow, rough, lumpy, very thick, flushy peel. Pulp of Corsican is crisp, non-juicy, non- acid, and seedy. These are small tree , spreading, moderately thorny with some large spines.

Diamante
Origin of this cultivar is unknown but it is the most important cultivar of Italy. It is a small tree, spreading, thorny as corsican. Base of this plant is long-oval or ellipsoid and furrowed and nippled at apex. Peels are yellow in colour, smooth or faintly ribbed and very thick and fleshy. Pulps are crisp, non-juicy, acid and seedy. It is called as **Easle** in **Cuba**.

Etrog
It is most important cultivar of Israel. Base of its ellipsoid, spindle-shaped or lemon like with moderate neck. Appex is prominent nippled. Fruit should be 142 gm in weight, not oblong in shape for ritual use. Peels are yellow in colour, semi-rough and bumpy, faintly ribbed, thick and fleshy. Pulp is crisp, frif, with little juice, acid and seedy.

Fingered citron
It is called as fu shou in China, bushukon in Japan, liman jari, jeruk tangan in Malaya. The fruit is wrinkled, wholly or partly split into about 5 finger- like segments, often seedless or with loose seeds. The fruit is offering in temples because it is very fragrant. It is commonly grown in China and Japan.[0] (morton JF 1987)

USES
Various parts of Citrus medica are widely used in Indian traditional system of medicine. Parts like ripe fruits are used as antiscorbutic, stomachic, cardiac tonic, stimulant, sedative, analgesic and also used in dyspepsia, bilious vomiting, cold, fever, palpitation, sore throat, cough, asthma, thirst, hiccough and earache. Roots of Citrus medica are analgesic, antispasmodic and it is also used in diarrhoea, piles and constipation. Seeds are anthelmintic, stomachic, sedative, cardiac tonic and useful in palpitation; flowers and buds have astringent property and used in blood disorders and peels are anthelmintic. (hooker JB, 1883) Fruit extracts have also shown good antioxidant activity. (jayaprakash GK, 2007) In ancient literature citron was used as an antidote for various kind of poison.(Beatriz AA, 2005)

Traditional uses
Citrus medica was traditionally used as a remedy for sea sickness, pulmonary troubles. Peel was used for dysentery and it was eaten to overcome halitosis. Candied peel was used as stomachic, stimulant, expectorant and tonic. Essential oil of the peel is used as an antibiotic.

Citron juice with wine was used as an effective purgative, distilled juice is given as sedative. The decoction of fruits is taken to drive off evil spirits. The decoction of shoots is administered to improve appetite, relieve stomachache and for expel intestinal worms. (Meena AK, 2011)

Food uses
Candied peel is used in food industry, especially as an ingredient in fruit cake, plum pudding, buns, sweet rolls and candy. (Shamerez B et al, 2013).

PHARMACOLOGICAL ACTIVITIES OF CITRUS MEDICA PEEL

- **Antioxidant and free radical scavenging activity**

Free radicals are chemical species, which are highly unstable due the presence of one or more unpaired electrons which then try to steal electron from other stable molecules to gain stability. This process causes the cascade of free radicals which damage body's cells and tissues. Antioxidants are endogenous and exogenous chemicals which neutralizes the action of free radicals, thus it prevents cell and tissues from damage. Citrus fruits and juices are the good source of antioxidants such as ascorbic acid, phenolic compounds and flavonoids. According to this study methanolic extract of citrus medica peel contains highest amount of phenolic and flavonoid compounds. This study showed that methanolic extract of citrus medica peel reduces ABTS or 2, 2'-azino-bis (3-ethylbenzothiazoline-6-sulphonic acid). Thus the amount that the ABTS has decoloured can be used to measure the antioxidant activity. Therefore, Citrus medica peel extract can be used for the treatment of diseases which are caused by free radical production. (Nandan MP, 2015).

- **Cardiotonic activity**

The methanolic extract of *Citrus medica* peel on isolated rat by using Langendorff's assembly at a dose of 100 mg/ml significantly increase force of contraction and % force of contraction 42.16± 1.07 mm, 129.5± 3..62 mm of isolate rat as compared to normal which may potentiate activity on heart muscles and also gave potential diuretic effect, hence it may help to treat congestive heart failure (CHF). (Joshi AI, 2013).

- **Analgesic and anti-inflammatory**

Citrus medica peel showed potentiate 1,1-diphenyl-2-picrylhydrazyl (DPPH) and hydrogen peroxide radical scavenging activity when extracted with Ethyl acetate in a dose dependent manner. In paw oedema test all three doses (200, 300, and 400mg/kg) of ethyl acetate extract of *Citrus medica* peel were found to be potant anti-inflammatory and analgesic on carrageenan induced inflammatory pain in rats. Hot plate, plantar, pin prick and mechanical allodynia test was used for the evaluation of the analgesic activity. The ethyl acetate extract of *Citrus medica* linn, in a dose of 400mg/kg inhibited paw volume and pain produced by paw oedema and hot plate with potency comparable to diclofenac. Hence this study concluded that *Citrus medica* peel extract may be used as antioxidant for the treatment of inflammation and pain. The analgesic and anti-inflammatory activity of *Citrus medica* could be due to flavonoids and phenolic compounds. (Sood S, 2009).

➢ **Hypoglycaemic and anticholinesterase activity**

Free radicals cause oxidative damage which may act as the root cause of progression and pathogenesis of various chronic diseases including diabetes and Alzheimer's disease. The n-hexane extract of diamante citron (Citrus medica L. cv Diamante) peel contains monoterpenes (limonene and gamma-terpinene) and sesquiterpenes which showed antioxidant activity by using different assays (DPPH test, beta-carotene bleaching test and bovine brain peroxidation test). Thus in vitro diamante peel extract showed hypoglycaemic and anticholinesterase activity. Hence according to this study Diamante citron can be used in the treatment of diabetes and Alzheimer's disease. (Conforti F, 2007)

➢ **Anti –implantation activity**

Oral administration of oil, ethanolic and chloroform extract of *Citrus medica* peel at the dose of 100mg/kg, 2.5mg/kg and 1.0gm/kg respectively were used for the anti-implantation activity. The oil, ethanolic and chloroform extract of *Citrus medica* peel showed mean anti-implantation activity 48.84%, 71.96% and 77.19% respectively on female wistar rats on 1-7 *post-coital* days. Thus *Citrus medica* peel could be used as anti-implantation. (Kacharoo M, 2011)

➢ **Antimicrobial activity**

Agar cup method was employed for the evaluation of in vitro antimicrobial effect of ethanolic extract of *Citrus medica* peel. According to this study it was found that the ethanolic extract of *Citrus medica* peels was effective against bacterial strains like *Staphylococcus aureus, Escherichia coli, Proteus vulgaris, Bacillus subtilis, Klebsiella pneumonia,* and *pseudomonas aeruginosa* as compared to standard antibiotic Streptomycin. Thus this study concluded that peels of *Citrus medica* L can be used in the treatment of diseases which are caused by the test organisms. (Kabra AO, 2012)

➢ **Antioxidant, antidiabetic and antilipidaemic activity**

Oxidative stress is the root cause of the progression and pathogenesis of chronic diseases like diabetes, hiperlipidaemia etc,. The hydroalcoholic extract of Citrus medica cv Diamante peel showed antidiabetic, antilipidaemic and antioxidant activities in Zucker diabetic fatty (ZDF) rats. Reactive oxygen metabolites-derived compounds (d- ROMs) test and the biological antioxidant potential test (BAP) were used to assess antidiabetic, antilipidaemic and antioxidant activities of Citrus medica cv Diamante peel extract against oxidative stress. Due the presence of flavonoids like naringine, apigenin, hesperitin, and quercetin CD peel extract at a dose 600 mg/kg significantly reduces blood glucose levels, triglyceride levels and cholesterol levels in type -2 diabetic animals. The cholesterol lowering activity was related to the reduction of hepatic 3-hydroxy-3-methyl Co A (HMG-Co A) reductase activity. Hence according to this study CD supplement improves lipid metabolism in ZDF rats. This study suggested that CD supplement could be used in the treatment of diabetes, and hyperlipidaemia. (Minichini F, 2015)

➢ **As nutraceuticals**

A α- amylase and α- glucosidase inhibition assays were used to evaluate the *in vitro* hypoglycaemic potential of *C. medica* cv Diamante peel extract. This activity was showed by CD extract due the presence of hesperetin, quercetin and apigenin. According to this study *Citrus medica* L. cv Diamante peel extract showed *in vitro* inhibition of carbohydrate- hydrolysing enzymes, and stimulation of insulin secretion. Plasma glucose concentration, plasma cholesterol levels, and triglycerides levels were reduced by the administration of C. medic acv Diamante peel extract. This study concluded that Citrus medic acv Diamante could be used as new potential source with functional properties for food or neutraceutical products. (Menichini F, 2011).

CONCLUSION

The present study demonstrate that *Citrus medica* is the most common fruit of genus citrus. It is a fragrant fruit which is grown in all over the world. It is a slow growing shrub. Peel of this plant is the major source of flavonoid content which shows maximum antioxidant activity. According to this study *Citrus medica* peel could be used in diseases which are caused by the production of free radicals.

REFERENCES

1. Munwar S, Roy H, Rahaman SA. Analgesic and antidiabetic activity of *Citrus medica* extracts. International Journal of Life and Biosciences, 2015; 1(3): 46-50.
2. Sood S, Bansal S, Mathuraman A, Gill NS, Bali M. therapeutic potential of *Citrus medica* L. peel extract in carrageenan induced inflammatory pain in rat. Research Journal of Medicinal Plant, 2009; 3(4): 123-133.
3. Anggard E. Nitric oxide mediator, murderer and medicine. Lancet, 1994; 343: 1199-1206.
4. Babior BM. Oxidants from phagocytes: agents of defense and destruction. Blood, 1984; 64: 959-966.
5. Halliwell B. Antioxidants in human health and disease. Annual Review of Nutrition, 1996; 16: 33-50.
6. Halliwell B. Polyphenols: Antioxidant treats for healthy living or covert toxins? Journal of Science of food and Agriculture, 2006; 86: 1992-1995.
7. Vinson JA, Hao Y, Zubik L. Phenol antioxidant quantity and quality in foods: vegetables. Journal of Agricultural and Food Chemistry, 1998; 46: 3630-3634.
8. Menichini F, Tundis R, Loizzo MR, Bonesi M. *Citrus medica* L. cv Diamante (Rutaceae) peel extract improves glycaemic status of Zucker diabetic fatty (ZDf) rats and protects against oxidative stress. Journal of Enzyme Inhibition and Medicinal Chemistry, 2015; 1-7.

9. Nandan MP, Vangalapati M. Antioxidant assay of *Citrus medica* L peel methanolic extract by using ABTS decolourisation method. World Journal of Pharmacy and Pharmaceutical Sciences, 2015; 4(10): 2143-2150.
10. Kabra AO, Bairagi GB, Mahamuni AS, Wanare RS. In vitro Antimicrobial Activity and phytochemical Analysis of the Peels of *Citrus medica* L. International Journal of Research in Pharmaceutical and Biomedical Sciences, 2012; 3(1): 34-37.
11. Uzun A, Yesiloglu T. Genetic Diversity in citrus, 2012; 213-230.
12. Conforti F, Statti GA, Tundis R, Loizzo MR. *In vitro* activities of *Citrus medica* L. cv Diamante (Diamante citron) relevant to treatment of Diabetes and Alzheimer's disease. Phytotherapy Research, 2007; 21: 427-433.
13. Meena AK, Kandale Ajit, Rao MM, Panda P, Reddy Govind. A Review on citron- Pharmacognosy, Phytochemistry and Medicinal uses. International Research Journal of Pharmacy, 2011; 2(1): 14-19.
14. Panara K, Joshi K, Nishteswar K. A review on phytochemical and pharmacological properties of *Citrus medica* inn. International Journal of pharmaceutical and biological archives, 2012; 3 (6): 1292-1297.
15. Nicolosi E, Malfa SL. The search for the Authentic citron (*Citrus medica* L.): Historic and Genetic Analysis. Hortscience, 2005; 40(7): 1963-1968.
16. Kachroo M, Agarwal SS. Anti –implantation activity of different extract of the peelsof *Citrus medica*, linn. International Journal of PharmTech Research, 2011; 3(1): 535-539.
17. Morton JF, Miami FL. Fruits of warm climates, citron, 1987: 179-182.
18. Hooker JB. The Flora of British India. International book distributors, 1885: 514.
19. The Ayurvedic Pharmacopoeia of India, Part I, Vol III, Govt of India, New Delhi, 2001; 27-28.
20. Kirtikar KR, Basu BD, Singh BP, Singh MP. Indian Medicinal Plants, ed. Dehradun, 1993; 1: 485-490.
21. Jayaprakash GK, Patil BS. Invitro evaluation of the antioxidant activities in fruit extracts from citron and blood orange. Food Chemistry, 2007; 101: 410-418.
22. Beatriz AA, Luis RL. Pharmacological properties of Citrus and their ancient and medieval uses in the Mediterranean region. Journal of Ethanopharmacology, 2005; 97: 89-95.
23. Joshi AI, Tirgar PR. Evaluation of cardiotonic effect of peels of *Citrus medica* in congestive heart failure. An international journal of pharmaceutical sciences, 2013; 4(4): 1-10.
24. Kabra AO, Bairagi GB, Mahamuni AS, Wanare RS. *In vitro* antimicrobial activity and phytochemical analysis of the peels of Citrus medica L. International Journal of Research in Pharmaceutical and Biomedical Sciences, 2012; 3(1): 34-37.
25. Menichini F, Tundis R, Loizzo MR, Bonesi M, Jones P. *C. medica* cv Diamante peel chemical composition and influence on glucose homeostasis and metabolic parameters. Food Chemistry, 2011; 124: 1083-1089.