INTERNATIONAL RESEARCH JOURNAL OF PHARMACY **ISSN 2230 – 8407**
Available online http://www.irjponline.com
Review Article

A REVIEW ON CITRON-PHARMACOGNOSY, PHYTOCHEMISTRY AND MEDICINAL USES

Meena A K[1*], Kandale Ajit[1], Rao M M[1], Panda P.[1] and Reddy Govind[2]
[1]National Institute of Ayurvedic Pharmaceutical Research, Patiala, Punjab, India
[2]Central Research Institute (Ayurveda), Mumbai, India

*Ajay Kumar Meena, Research Officer (Chemistry), National Institute of Ayurvedic Pharmaceutical Research, Patiala, Punjab, India Email: ajaysheera@gmail.com
Article Received on: 18/12/10 Revised on: 19/12/10 Approved for publication: 07/01/11

ABSTRACT
The citron is a fragrant fruit with the botanical name *Citrus medica*, which applies to both the Swingle and Tanaka systems. It is a prominent member in the genus Citrus, belonging to the Rutaceae or Rue family, sub-family Aurantioideae. The citron is unlike the more common citrus species like the lemon or orange. While the most popular fruits are peeled to consume their pulpy and juicy segments, the citron's pulp is very dry, containing only little insipid juice. Moreover, the main content of a citron is the thick white rind, which is very adherent to the segments, and cannot be separated from them easily. Thus, from ancient through medieval times, the citron was used mainly for medical purposes: to combat sea sickness, pulmonary troubles, intestinal ailments, and other disorders. The essential oil of the flavedo (the outermost, pigmented layer of rind) was also regarded as an antibiotic. Citron juice with honey was considered an effective antidote to poison. In India, the peel is a remedy for dysentery and is eaten to overcome halitosis. The distilled juice is given as a sedative. The candied peel is sold in China as a stomachic, stimulant, expectorant and tonic. In West Tropical Africa, the citron is used only as a medicine, particularly against rheumatism. The flowers are used medicinally by the Chinese. In Malaya, a decoction of the fruit is taken to drive off evil spirits. A decoction of the shoots of wild plants is administered to improve appetite, relieve stomachache and expel intestinal worms. The leaf juice, combined with that of Polygonum and Indigofera is taken after childbirth. A leaf infusion is given as an antispasmodic. In Southeast Asia, citron seeds are given as a vennifuge. In Panama, they are ground up and combined with other ingredients and given as an antidote for poison. The essential oil of the peel is regarded as an antibiotic.

The citron fruit is usually ovate or oblong, narrowing towards the stylar end. However, the citron's fruit shape is highly variable, due to the large quantity of albedo, which forms independently according to the fruits' position on the tree, twig orientation, and many other factors. This could also be the reason for its being protuberant, forming a "v" shape after the end of the segments towards the stylar end. The rind is leathery, furrowed, and adherent. The inner portion thick, white and fleshy – the outer uniformly thin, and very fragrant. The pulp is usually acidic, but also sweet and even pulps less variety are found.Most citron varieties contain a large number of seeds. The monoembryonic seeds are white colored; with dark inner coat and red-purplish chalazal spot for the acidic varieties, and colorless for the sweet ones. Some citron varieties are also distinct with their persistent style.

KEYWORDS: *Citrus medica*, antioxidant, anti-inflammatory, Rutaceae, Pharmacology,

INTRODUCTION
The citron is a fragrant fruit with the botanical name *Citrus medica*, which applies to both the Swingle and Tanaka systems. It is a prominent member in the genus Citrus, belonging to the Rutaceae or Rue family, sub-family Aurantioideae. The designation medica is apparently derived from the similar ancient names media, Median apple etc., which were influenced by Theophrastus, who

believed the citron was native to Medes, Persia or Assyria. The citron has many similar names in diverse languages, e.g. cederat, cedro, etc. Most confusing are
the Polish, Czech, Slovak, French,Dutch, German, Yiddish and Scandinavian languages in which the false friend "citron" refers to the fruit called lemon in English.

Citrus medica is found in the base region of Himalaya from Gadwall to Sikkim at the height of 4000 feet. It is also seen in Assam, central India and Western Ghats of India. It is more commonly present in the Mediterranean region and central and southern parts of America[1]

The citron is borne by a slow-growing shrub or small tree reaching 8 to 15 ft (2.4-4.5 m) high with stiff branches and stiff twigs and short or long spines in the leaf axils. The leaflets are evergreen, lemon-scented, ovate-lanceolate or ovate elliptic, 6-18 cm long; leathery, with short, wingless or nearly wingless petioles; the flower buds are large and white or purplish; the fragrant flowers about 4 cm wide, in short clusters, are mostly perfect but some male because of pistil abortion; 4 to 5 petalled, often pinkish or purplish on the outside, with 30 to 60 stamens. The fruit is fragrant, mostly oblong, obovoid or oval, occasionally pyriform, but highly variable; various shapes and smooth or rough fruits sometimes occurring on the same branch; one form is deeply divided from the apex into slender sections; frequently there is a protruding style; size also varies greatly from 9- 22 or 30 cm long; peel is yellow when fully ripe; usually rough and bumpy but sometimes smooth; mostly very thick, fleshy, tightly clinging; pulp pale-yellow or greenish divided into as many as 14 or 15 segments, firm, not very juicy, acid or sweet; contains numerous monoembryonic seeds. [2]

The citron fruit is usually ovate or oblong, narrowing towards the stylar end. However, the citron's fruit shape is highly variable, due to the large quantity of albedo, which forms independently according to the fruits' position on the tree, twig orientation, and many other factors. This could also be the reason for its being protuberant, forming a "v" shape after the end of the segments towards the stylar end. The rind is leathery, furrowed, and adherent. The inner portion is thick, white and fleshy – the outer is uniform thin, and very fragrant. The pulp is usually acidic, but also sweet and even pulp less varieties are found.

Most citron varieties contain a large number of seeds. The monoembryonic seeds are white colored; with dark inner coat and red-purplish chalazal spot for the acidic varieties, and colorless for the sweet ones. Some citron varieties are also distinct with their persistent style, which is highly appreciated by the Jewish community.

Some citrons have medium sized oil bubbles at the outer surface, medially distant to each other. Some fruits are ribbed and faintly warted on the outer surface, adding life and attraction to its beauty. There is also a fingered citron variety called Buddha's Hand. The color varies from green, when unripe, to a yellow-orange when overripe. The citron does not fall from the tree and can reach 4–5 kg if not picked when ripe or even early. However, they should be picked before the winter as the branches might break, or bend to the ground and may cause numerous fungal diseases for the tree.

The acidic varieties include the Florentine and Diamante citron from Italy, the Greek citron and the Balady citron from Palestine. The sweet varieties include the Corsican and Moroccan citrons. Between the pulp less are also some fingered varieties and the Yemenite citron.

Despite the variation among the cultivars, authorities agree that the citron species is a very old one. There is molecular evidence that all other cultivated citrus species only arose by hybridization among the ancestral types, which are the citron, pummelo, mandarin and papeda. The citron is believed to be the purest of them all, since it is usually fertilized by self-pollination, it hardly accepts foreign pollen, and is therefore generally considered to be a male parent of a hybrid rather than a female one.

Varieties

Citron cultivars are mainly of two types

1) Those with pinkish new growth, purple flower buds and purple-tinted petals, acid pulp and dark inner seed coat and chalazal spot

2) Those with no pink or purple tint in the new growth nor the flowers, with non-acid pulp, colorless inner seed coat, and pale-yellow chalazal spot.

Among the better-known cultivars are 'Corsican', the leading citron of Corsica; introduced into the United States around 1891 and apparently the cultivar grown in California; ellipsoid or faintly obovate, furrowed at base; large; peel yellow, rough, lumpy, very thick, fleshy; pulp crisp, non-juicy, non-acid, seedy. Tree small, spreading, moderately thorny with some large spines.

'Diamante' ('Cedro Liscio'; possibly the same as 'Italian' and 'Sicilian')–of unknown origin but the leading cultivar in Italy and preferred by processor's elsewhere; long-oval or ellipsoid, furrowed at base, broadly nippled at apex; peel yellow, smooth or faintly ribbed; very thick, fleshy; pulp crisp, non-juicy, acid; seedy. Tree small, spreading, thorny as 'Corsican'. Very similar is a cultivar called "Earle" in Cuba.

'Etrog' ('Ethrog', 'Atrog'; C. medica var. Ethrog Engl.)–the leading cultivar in Israel; ellipsoid, spindle-shaped or lemon-like with moderate neck and often with persistent style at base; usually with prominent nipple at apex; medium-small as harvested; if not picked early, it will remain on the tree, continuing to enlarge for years until the branch cannot support it. For ritual use, the fruit should be about 5 oz (142 g) and not oblong in form. Peel is yellow, semi-rough and bumpy, faintly ribbed, thick, fleshy; flesh is crisp, firm, with little juice; acid; seedy. Tree is small, not vigorous; leaves rounded at apex and cupped. This cultivar has been the official citron for use in the Feast of the Tabernacles ritual but if unavailable, any yellow, unblemished, lemon-sized citron with adhering style can be substituted.

'Fingered Citron', Plate XXI, ('Buddha's Hand', or 'Buddha's Fingers'; C. medica var. sarcodactylus Swing.); called fushou in China, bushukon in Japan, limau jari, jeruk tangan, limau kerat lingtang,in Malaya; djerook tangan in Indonesia; som-mu in Thailand; phât thu in Vietnam. The fruit is corrugated, wholly or partly split into about 5 finger-like segments, with little or no flesh; seedless or with loose seeds. The fruit is highly fragrant and is placed as an offering on temple altars. It is commonly grown in China and Japan; is candied in China. In India, there are several named types, in addition to the 'Fingered', in the northwest: 'Bajoura'–small, with thin peel, much acid juice. 'Chhangura'–believed to be the wild form and commonly found in a natural state; fruit rough, small, without pulp. 'Madhankri' or 'Madhkunkur'–fruit large with sweetish pulp. 'Turunj'–fruit large, with thick peel, the white inner part sweet and edible; pulp scant, dry, acid. Leaves are oblong and distinctly notched at the apex.[3]

Chemical constituents

It contains good amount of citric acid, glucose and sulphuric acid. Its peel contains volatile oil containing citrine (76 %), citrol (7-8 %), cymene and citronellal. The constituents of *Citrus medica* var. sarcodactylis have been isolated and purified. Nine compounds were isolated and identified as 5-methoxyfurfural (I); 5-hydroxy-2-hydroxymethyl-4H-pyran-4-one (II); diosmetin (III); diosmin (IV); obacunone (V); aviprin (VI); 3-(3-methoxy-4-hydroxyphenyl)-acrylic acid (VII); vanillic acid (VIII); and 3,4-dihydroxy-benzoic acid (IX). Compound I was a new natural compound. Compounds II and IV-IX were isolated for the first time from the genus Citrus, and compound III from *Citrus medica*[4].

Tables 1 and 2 report the constituents of the leaves and peels essential oils of *Citrus medica*. Results showed that the leaves and peels oils were a complex mixture of numerous compounds; many of which were present in trace amounts. It is worth mentioning here that there is a great variation in the chemical composition of the leaf and peel essential oil of C. medica. Erucylamide and isolimonene are the most important and main components in leaf and peel oil of Bangladesh but it is totally absent in all other reported oils. So, we can conclude that erucylamide and isolimonene are the first reported component in *Citrus medica* leaf and peel oils. Linalool, γ-terpinene, (Z)-citral ,(E)-citral, citronellal, citronellol, citronellyl acetate, isopulegol, r-cymene, geranial, citronellic acid, α-terineol, which have been reported as major constituents in the leaves and peels oil of others countries. This confirms that the variations in the cultivar reported is not due to geographic divergence and ecological conditions, it may be due to different chemotype. On the basis of above fact it may be concluded that *Citrus medica*, growing widely in Bangladesh, may be utilized as a source for the isolation of natural erucylamide and isolimonene respectively. The high concentration of erucylamide and isolimonene in leaf and peel oil make it potentially useful in the medicines because they exhibit fungitoxicity. It is worth mentioning that the oil of *Citrus medica* has been reported to be used in folk medicine in the treatment of dysentery, rheumatism, diabetes and alzheimer's disease.

Food Uses

The most important part of the citron is the peel which is a fairly important article in international trade. The fruits are halved, depulped, immersed in sea water or ordinary salt water to ferment for about 40 days, the brine being changed every 2 weeks; rinsed, put in denser brine in wooden barrels for storage and for export. After partial de-salting and boiling to soften the peel, it is candied in a strong sucrose/glucose solution. The candied peel is sun-dried or put up in jars for future use. Candying is done mainly in England, France and the United States. The candied peel is widely employed in the food industry, especially as an ingredient in fruit cake, plum pudding, buns, sweet rolls and candy.

The fruit of the wild 'Chhangura' is pickled in India. In Indonesia, citron peel is eaten raw with rice. The entire fruit of the 'Fingered citron' is eaten. If there is sufficient juice in the better cultivars, it is utilized for beverages and to make desserts. In Guatemala, it is used as flavoring for carbonated soft-drinks. In Malaya, citron juice is used as a substitute for the juice of imported, expensive lemons. A product called "citron water" is made in Barbados and shipped to France for flavoring wine and vermouth.

Other Uses

Fruit

Chinese and Japanese people prize the citron for its fragrance and it is a common practice in central and northern China to carry a ripe fruit in the hand or place the fruit in a dish on a table to perfume the air of a room. The dried fruits are put with stored clothing to repel moths. In southern China, the juice is used to wash fine linen. Formerly, the essential oil was distilled from the peel for use in perfumery.

Leaves and twigs

In some of the South Pacific islands, "Cedrat Petitgrain Oil" is distilled from the leaves and twigs of citron trees for the French perfume industry.

Flowers

The flowers have been distilled for essential oil which has limited use in scent manufacturing.

Wood

Branches of the citron tree are used as walking-sticks in India. The wood is white, rather hard and heavy, and of fine grain. In India, it is used for agricultural implements.

Medicinal Uses

In ancient times and in the Middle Ages, the 'Etrog' was employed as a remedy for sea sickness, pulmonary troubles, intestinal ailments and other disorders. Citron juice with wine was considered an effective purgative to rid the system of poison. In India, the peel is a remedy for dysentery and is eaten to overcome halitosis. The distilled juice is given as a sedative. The candied peel is sold in China as a stomachic, stimulant, expectorant and tonic. In West Tropical Africa, the citron is used only as a medicine, particularly against rheumatism. The flowers are used medicinally by the Chinese. In Malaya, a decoction of the fruit is taken to drive off evil spirits. A decoction of the shoots of wild plants is administered to improve appetite, relieve stomachache and expel intestinal worms. The leaf juice, combined with that of Polygonum and Indigofera is taken after childbirth. A leaf infusion is given as an antispasmodic. In Southeast Asia, citron seeds are given as a vennifuge. In Panama, they are ground up and combined with other ingredients and given as an antidote for poison. The essential oil of the peel is regarded as an antibiotic.

The petroleum ether extract of *Citrus medica* seeds has been tested for its estrogenic activity. The results have been consistent with the trend for uterine weight gain in the test rats. Other studies have shown that the post coital effectiveness of plant agents is roughly parallel to their estrogenecity.

Administration of extract to ovariectomised rats tended to increase uterine weight, indicating that both the doses contain oestrogen-like compounds. Petroleum ether extract affected the uterus and its parameters. Estrogenic stimuli are highly complex and a variety of promoter regions upstream from oestrogen responsive genes confer specificity of tissue activation. In vitro studies have confirmed that isoflavones tend to have a higher affinity for oestrogen receptor-β not for oestrogen receptor-α, thus a simple interpretation of oestrogen receptor specificity as the key determinate of tissue-specific estrogenic proportion of *Citrus medica* seeds extract is sufficient studying mixture of phytoestrogens like

isoflavones, coumestans, lignans, resveratrol and 8-prehylnarinagenin such as found in *Citrus medica* extract might help uncover potential mechanisms whole by exogenous estrogens confirm tissue selectivity. Flavonoids have been reported to possess antifertility activity, the estrogenic activity of the petroleum ether of *Citrus medica* seeds might be due to the presence of flavonoids or other constituents.[5]

By kinetic analysis on the hypoglycemic patterns of the intraperitoneal glucose tolerance (IPGTT) and the insulin–glucose tolerance tests (IGTT), its insulin secretagogue effect has been confirmed. In conclusion, fruits that concomitantly possess insulin secretagogue and slimming effects would be very beneficial to type 2 diabetes mellitus patients.[6]

Ethyl acetate extract of *Citrus medica* peels (EtCM) reduced carrageenan induced paw edema and showed analgesic action in rats. Its free radical scavenging action may be responsible for the observed ameliorative effects. Therefore, this herbal candidate may act as a potent anti-inflammatory and analgesic agent in human subjects[7].

REFERENCES

1. Country report to the FAO international technical conference on plant genetic resources (Leipzig, 1996); Nepal Agricultural Research Council; Kathmandu, June 1995.
2. The search for the authentic citron: Historic and Genetic Analysis; Horticultural Science, 2005; 40(7):1963–1968.
3. Morton, Julia F, Miami F J. Fruits of warm climates. Citron 1987; 179–182.
4. M. N. I. Bhuiyan1, J. Begum, "Constituents of peel and leaf essential oils of Citrus Medica L", Journal of Scientific Research 2009; 1(2): 387-392
5. Sharangouda, Saraswati B Patil. Estrogenic activity of petroleum ether extract of seeds of *Citrus medica* on immature albino rats, International Journal of Green Pharmacy 2008; 2 (2): 91-94.
6. Chiung-Huei Peng, Yaw-Bee Ker. Insulin secretagogue bioactivity of finger citron fruit (*Citrus medica* L. var. Sarcodactylis Hort, Rutaceae) J. Agriculture and Food Chemistry 2009; 57(19): 8812–8819.
7. Sood S, Bansal S, Muthuraman A. 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.

Table 1: Constituents of leaf essential oil from *Citrus medica* Linn

S. No	Name of constituent	Percentage
1	Limonene	18.36
2	1-Monolinoleoylglycerol trimethylsilyl ether	0.86
3	n-pentyl(1-propenyl)dimethylsilane	0.82
4	citral	12.95
5	2-Oxocycloheptyl acetate	0.87
6	Methoprene	3.51
7	Geranyl methyl ether	1.42
8	13-Heptadecyn-1-ol	1.05
9	Erucylamide	28.43

Table 2: Constituents of peel essential oil from *Citrus medica* Linn

Sr.No.	Name of constituent	Percentage
1	(1R)-2,6,6-Trimethylbicyclo[3.1.1]hept-2-ene	0.14
2	α-Pinene	0.41
3	3-Octyn-2-ol	0.10
4	β-Myrcene	2.70
5	2-Acetyl-5-methylfuran	0.05

6	Cyclooctyl alcohol	0.17
7	Limonene	21.78
8	Isolimonene	39.37
9	Linalool	0.94
10	Nonanal	0.25
11	trans-p-Mentha-2,8-dienol	0.04
12	citral	23.12
13	cis-Verbenol	0.09
14	4-Terpineol	0.08
15	Terpinyl acetate	0.16
16	β-Terpinyl acetate	0.52
17	Decanal	0.33
18	Neryl acetate	2.51
19	Neryl Alcohol	2.25
20	Undecanal	0.10
21	Neryl acetate	0.60
22	Dodecanal	0.08
23	(Z,E)-α-Farnesene	0.05
24	Caryophyllene	0.59
25	α-Bergamotene	0.48
26	Tetrakis(trimethylsiloxy)silane	0.04
27	α-Caryophyllene	0.08
28	Germacrene D	0.05
29	cis-.α-Bisabolene	0.07
30	γ-Elemene	0.05
31	β-Bisabolene	0.71
32	δ-Cadinene	0.05
33	Tetradecanal	0.10
34	β-Bisabolol	0.12
35	n-Hexadecanoic acid	0.12