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## Ethnomedical Importance of *Citrus Aurantifolia* (Christm) Swingle

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### Abstract

*Citrus aurantifolia* is an important medicinal and food plant widely cultivated in many parts of the world. It is valued for its nutritional qualities and numerous health benefits. The plant is used in traditional medicine as an antiseptic, antiviral, antifungal, anthelmintic, astringent, diuretic, mosquito bite repellent, for the treatment of stomach ailments, constipation, headache, arthritis, colds, coughs, sore throats and used as appetite stimulant. These health benefits of *Citrus aurantifolia* are associated with its high amounts of photochemical and bioactive compounds such as flavonoids, limonoids, phenols, carotenoids, minerals and vitamins. This review examined the domestic, ethnomedical and pharmacological importance of the plant.

**Keywords:** Citrus aurantifolia, Health benefits, Phytochemicals, Minerals, Vitamins, Plants.

### 1. Introduction

*Citrus aurantifolia* (Christm) Swingle (*C. aurantifolia*) is a polyembryonic plant cultivated in many countries all over the world and grows in hot subtropical or tropical regions such as Southern Florida, India, Mexico, Egypt, and the West Indies [1]. The plant belongs to the kingdom: Plantae; Phylum: Magnoliophyta; Class: Magnoliopsida; Order: Sapindales; Family: Rutaceae; Genus: Citrus and Species: *Citrus aurantifolia* [2].

*C. aurantifolia* is commonly called Lime (Nigeria), Key lime, Mexican lime, Sour lime, Dayap, bilolo, Indian lime, Egyptian lime [3].

### Plant Description

*C. aurantifolia* is a small shrubby tree, about 5 m tall. It is an evergreen and ever bearing tree that is densely and irregularly branched and possesses short and stiff spines (thorns). The leaves are alternate; elliptical to oblong-ovate (4-8cm×2-5cm) shaped and has a crenulate margin. The flowers are 1 inch in diameter and are yellowish white with a light purple tinge on the margin. The fruits are globose to ovoid berry of about 3 - 6 cm in diameter and sometimes have apical papilla. It is yellow when ripe but usually picked green commercially. The fruits and flowers appear throughout the year but are most abundant from May to September in the Northern hemisphere. The fruit peels are very thin with densely glandular segments with yellow-green pulp vesicles. The fruit juice is acidic and fragrant, sour as lemon juice but more aromatic. It is usually valued for its unique flavor compared to other limes. The seeds are small, plump, ovoid, pale, and smooth with white embryo [2, 4, 5].

### Brief history and geographical distribution of *C. aurantifolia*

*C. aurantifolia* is believed to have originated from the south East Asia around 4000 BC and it is native to the Indo-Malayan region. It was assumed to have been carried to North Africa and the near east by the Arabs; and was taken by crusaders from Palestine to Mediterranean Europe. It was introduced to the Caribbean Island and Mexico by the Spaniards and readily became naturalized in the West Indies and Mexico [6]. The current major citrus producing countries in the world are Spain, USA, Israel, Morocco, South Africa, Japan, India, Brazil, Turkey and Cuba [1].

In Nigeria, about 930,000 tons of citrus fruits are produced annually from an estimated 3 million hectares of land [7]. The major citrus producing States in Nigeria are: Benue, Nassarawa, Kogi, Ogun, Oyo, Ebonyi, Kaduna, Taraba, Ekiti, Imo, Kwara, Edo and Delta [8].

### Domestic Uses of *Citrus aurantifolia*

Citrus fruits are consumed worldwide in form of fresh fruit or are processed into citrus products and citrus-by-products. Approximately, one third of total citrus production is utilized for processing [5]. *C. aurantifolia* juice is used as flavorings in beverages [9]; and it is also used by juice producing companies to produce fruit juice which are presented in form of freshly squeezed orange juice or frozen concentrated orange juice. The juice is squeezed from fresh fruit and packaged in paper cartons, glass or plastic containers, without being pasteurized [10]. In addition, *C. aurantifolia* fruits can be processed to obtain other food products such as dehydrated citrus products or marmalades, jams, sorbet, pickles, jellies, candies and sugar boiled [5].

Citrus essential oils are another by-product of citrus fruits. Essential oils are volatile oils obtained from the citrus fruit peels' sacks. They are used by the food industry to give flavor to drinks and foods. They are also a component for the pharmaceutical industry for the preparation of drugs, soaps, perfumes, hair cream, body oil and other cosmetics as well as for home cleaning products [11]. *C. aurantifolia* juice and sometimes fruit peels are combined with vinegar to produce disinfectant; it is combined with salt to clean copper pot. It is used to polish brass, aluminum and copper. It is combined with peroxide or used alone to bleach cloth, remove ink, rusty and mineral stains from cloths; whitening tannin shoe and soften fabrics [11]. *C. aurantifolia* fruit juice has been used to preserve the quality of "zobo" drink in Nigeria. It was reported to decrease the total coliform and other bacterial counts in "zobo" drink. Thus, the plant can be used to prolong the shelf life of "zobo" drink [12].

*C. aurantifolia* fruit peels have been found very useful domestically. In the kitchen, it is used for cooking, to add flavour to food, cakes and roasted chicken. It is used to garnish salad and to add flavor to drinking water. It is used for bathing and washing of hair, and also, used as a deodorizer to freshen up smelly garbage and composite pile. It also serves as natural room freshener [13]. It has been found useful as a repellent; used to repel mosquitoes from the body [14], moth from cloth and cats from gardens [13]. Citrus fruit peels have been transformed into volatile gases through a high-powered microwave. The gasses are then distilled into liquid that is used for making plastics [15]. The pulp of citrus fruit peels is used as cereal substitute in ruminant feeds due to its high energy content and good digestibility in ruminant species [16].

### Ethnomedical Uses of *Citrus aurantifolia*

*C. aurantifolia* in its natural state is widely used in West Africa, particularly in Nigeria where it is employed in herbal medicine to treat several illnesses. It forms an essential ingredient in the preparation of most herbal concoctions [17]. Different parts of the tree have been used traditionally to cure some illnesses:

#### Leaves

The decoction of pounded leaves is drunk for stomach ache, used as eye wash and to bath feverish patient. Poultice of leaves are applied to ulcer wounds, used for skin disease and also applied to abdomen after child birth. Crushed leaves are applied to forehead to treat headache and it is squeezed near the nostril for irritant inhalation to treat nausea and resuscitate fainting individuals [18]. Infusion of *C. aurantifolia* leaves have been given to treat fever with jaundice, sore throat and oral thrush [19]. A decoction of the flower is believed to help induce sleep for those with insomnia [18]. In southwest Nigeria, the

roots, bark, stem twigs, leaves and fruits are used in the treatment of malaria [20].

#### Juice

In Nigeria, *C. aurantifolia* fruit juice is added to sugar and palm oil or honey to relief cough. In Malayan medicine, the juice is considered as tonic for libido and as antidote for poison. It is also used to increase stamina, treat dysfunctional uterine bleeding, used as facial wash to rejuvenate the skin and remove stain, drunk to control epistaxis and given in pure form as remedy for auralgia, diabetes and atherosclerosis. The diluted form of the *C. aurantifolia* fruit juice is used for mouth wash to treat sore mouth and sore throat [17, 20]. The juice has been found useful to treat irritation, diarrhoea and swelling due to mosquito bites. It is sometimes mixed with oil and used as vermifuge and also incorporated into weight management diet [21].

#### Other parts of the plant

Decoction of roots is used to treat dysentery, diarrhea, colic, gonorrhoea and fever [19]. The rind is burnt in some homes to act as insecticide against mosquitoes. The mesocarp is used for facial scrubbing to prevent pimples [17]. The *C. aurantifolia* oil extracted by steam distillation of the fruit rinds is used for cold, sore throat, bronchitis, asthma, arthritis and obesity. It is used as an astringent and toning action to clear oily skin acne and treat cuts. Decoction of the bark can help relieve flatulence [19].

#### Pharmacological Activities of *C. aurantifolia*

Pharmacological activities of the extract of different parts of *C. aurantifolia* have been studied and it has been shown that the plant possesses the following pharmacological activities:

#### Antibacterial activity

Studies revealed that the extracts of root of *C. aurantifolia* have been found effective in inhibiting the growth of *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Proteus mirabilis*, *Pseudomonas aeruginosa*, *Beta-haemolytic streptococci*, *Escherichia coli* and *Neisseria gonorrhoeae* [17]. The fruit on the other hand was found to inhibit anaerobic facultative bacteria as well [22]. *C. aurantifolia* has been proved to have significant antimycobacterial activity especially against the isoniazid-resistant strain of Mycobacteria [23]. The antimycobacterial activity have been attributed to the presence of some phytochemicals in *C. aurantifolia* which include: 5, 8-dimethoxypsoralen, 5-geranyloxypsoralen, palmitic acid, linoleic acid, oleic acid, 4-hexan-3-one and citral [24].

#### Antifungal and antiaflatoxic activity

Studies on the essential oil of *C. aurantifolia* shows that the plant has inhibitory action against *Phaeoramularia angolensis* [25], *Aspergillus niger*, *Aspergillus parasiticus* and its aflatoxins, and *Candida albicans* [17]. The antifungal activity of the plant have been attributed to the presence of monoterpenes and the plant is currently used as a fungicide for citrus fruit crop, and it has also been suggested that the plant may be a potential candidate used for the protection of food and feeds from toxigenic fungal growth as well as their aflatoxin contamination [25].

#### Anticancer/ cytotoxic activity

*C. aurantifolia* has been shown to inhibit colon cancer [26], breast cancer, neuroblastoma [27], pancreas cancer [1] and prostate cancer cells [28]. D-limonene, D-dihydrocarvone,

limonoids and flavonoids are among the major phytoconstituent in *C. aurantifolia* responsible for the anticancer activity [26, 29]. The essential oil of *C. aurantifolia* has 78% inhibition of human colon cancer cells, DNA fragmentation and apoptosis induction as revealed from a study and it is suggestive of the potential use of the plant for prevention of cancer especially colon cancer [27].

#### Antioxidant activity

Studies of the juice and fruit peels [30] as well as leaves [31] of *C. aurantifolia* revealed that the plant has a concentration-dependent effect on low density lipoprotein (LDL) oxidation. The antioxidant activity of *C. aurantifolia* was ascribed to their hydrogen donating ability which may be due to the presence of flavonoids, carotenoids and Vitamin C [30]. Flavonoids present in *C. aurantifolia* fruit juice and peels demonstrate their antioxidant activity by inhibiting the enzymes responsible for superoxide anion production such as xanthine oxidase and protein kinase C [32]. Flavonoids also inhibit cyclooxygenase, lipoxygenase, microsomal monooxygenase, glutathione S-transferase (St), mitochondrial succinoxidase and NADH oxidase; all involved in generating reactive oxygen species [33]. Vitamin C is predominant in *C. aurantifolia* and it acts as antioxidant both *in vitro* and *in vivo*. Vitamin C protects the plasma lipids and LDL against peroxidative damage induced by various types of oxidation [34].

#### Immuno-modulatory activity

*C. aurantifolia* juice has been shown to possess immune modulatory activity when it was tested in mitogen activated culture mononuclear cells. The result revealed that the juice could significantly inhibit the proliferation of phytohaemagglutinin activated mononuclear cells at 250 and 500 microgram per litre of the juice extract [35]. Studies by Pourhossein *et al.*, [36] on the effects of different levels of sweet orange (*Citrus sinensis*) peel extract (SOPE) on humoral immune system responses in broiler chickens showed that dietary supplementation of Citrus peels extract caused the improvement of immune response and disease resistance of the broiler. In addition, Vitamin C, one of the components of Citrus juice and peels have been shown to play an important role in enhancing immune system, fighting against the formation of free radicals that cause muscle damage. Several cells of the immune system, especially phagocytes and t-cells accumulate vitamin C and need the vitamin to perform their task. Thus, Vitamin C deficiency results in a reduced resistance against certain pathogens whilst a higher supply enhances several immune system parameters [37].

#### Antiobesity activity

Studies by [38] on the effect of essential oil of *C. aurantifolia* on weight gain in mice showed that mice treated with the extract displayed a reduction in both the amount of food intake and body weight compared with the control group. Another interesting finding was that co-administration of *C. aurantifolia* essential oil and ketotifen caused a significant suppression of weight gain and also decreased weight gain in mice. The weight loss was ascribed to the fact that *C. aurantifolia* may possibly promote anorexia which may play significant role on weight loss.

#### Antifertility activity

*C. aurantifolia* juice have been shown to reduce the number of ova shed in Sprague-Dawley rats and also caused irregularities of the estrous cycle, partially blocked ovulation and also

caused irregularities in the histology of the ovaries and uterus and thus may possibly compromise fertility. More so, *C. aurantifolia* juice showed abortifacient effect, although it does not possess teratogenic effect on foetus [39]. In Nigeria, a survey conducted by Imade *et al.* [40] in Jos and Mairiga *et al.* [41] in Borno revealed that it is a common practice for women to use *C. aurantifolia* juice solutions as a post coital douche with the believe that it prevents pregnancy or sexually transmitted diseases such as HIV, and that it enhances sexual pleasure. Though recent research by Bakare *et al.* [39] has proved the contraceptive effect of *C. aurantifolia* juice but there are no reports on its ability to prevent sexual transmission of HIV infections.

#### Anticholinesterase and antiplatelet activity

The extracts of the fruit peels, leaves and the essential oil of the leaves of *C. aurantifolia* showed anticholinesterase and butyrylcholinesterase activity [31, 42]. Similarly, the hydroalcohol extract of *C. aurantifolia* in the form of tincture has been found to have anti-platelet aggregation activity. It was found to have significantly inhibited ADP and epinephrine-induced platelet aggregation in a concentration-dependent manner [43].

#### Cardiovascular activity

Akhtar [21] evaluated the cardiovascular effects of *C. aurantifolia* fruit on three hypertensive models and found that the methanol extract of the fruit produces hypotensive and antihypertensive effects. Mechanisms responsible for these had been proposed by Souza *et al.* [44] to be related to cardiodepression and vaso-relaxation.

#### Effects on the bone

The efficacy of *C. aurantifolia* and *C. sinensis* against osteoporosis was evaluated in an ovariectomized rat model, and the result revealed that the administration of citrus extracts increased the trabecular bone mineral content, and bone mineral density of tibia, improved the levels of phosphorus and calcium. The result demonstrates that *C. aurantifolia* possesses the ability to reduce bone loss [45].

#### Anthelmintic activity

*In vitro* and *in vivo* anthelmintic evaluation of ethanol extract of three species of citrus fruit peels against *Ascaridia galli* by Abdelqader *et al.* [46] showed that the extracts caused a significant reduction in worm burden and fecal egg count in chicken compared with the control treated with fenbendazole. More so, *C. aurantifolia* fruit juice and peels have been shown to possess a remarkable anthelmintic activities against *Heligmosomoides bakeri*. The *in vitro* and *in vivo* anthelmintic study revealed that *C. aurantifolia* fruit juice and peels significantly inhibited the hatching of *H. bakeri* eggs and killed the larvae of the helminth as well as reduced the worm burdens in mice in a concentration and dose-dependent manner [47, 48].

#### Other effects

Citrus fruits are highly recommended for persons suffering from kidney stones, gout and arthritis. *C. aurantifolia* juice contains potassium citrate which prevents the formation of kidney stones and eases their dissolution [49]. Due to the high content of vitamin C, citrus fruits are used in the treatment of scurvy. The anti-scurvy effect of citrus fruits is very strong because of the balanced composition of organic acids and minerals [5].

### Toxicity studies

Acute and subchronic toxicity studies of water extract from root of *C. aurantifolia* in rats showed no signs of toxicity and no significant histopathological changes in the internal organs; but the expressed *C. aurantifolia* oil contained certain coumarins which are known to cause phototoxicity in humans and has been found to promote tumor formation on the skin and fore stomach epithelium of mice [18]. Chunlaratthanaphorn *et al.* [50] reported a non-toxic effect of water extract of the root of the plant in rats in both acute and subchronic toxicity studies. Acute toxicity of the fruit by Akhtar [21] showed that doses above 3.5 g/kg were toxic to rats. Similarly, acute toxicity of the methanol extract of the fruit peels in mice showed that the plant has no toxic effect even at the dose of 5 g/kg [51].

### Phytochemical Constituent of Citrus aurantifolia

Until recently, health-promoting properties of citrus had always been associated with their content of Vitamin C. However, studies within the last decade have focused on identifying the bioactive compounds [1]. Some of the major classes of compounds in citrus include: flavonoids, limonoids, coumarins and phytosterols [52]. Preliminary screening of *C. aurantifolia* fruit and other parts showed the presence of alkaloids, flavanoids, tannins, saponins, steroids, cardiac glycosides, carbohydrates, phenols and reducing sugars [21, 25, 48, 52, 54].

Detailed analysis of *C. aurantifolia* using High-performance Lipid Chromatography (HPLC) and Gas chromatography Mass spectrometry have led to the identification of phytochemicals from the plant, which include: 2,4,6-trichloroanisole; 5-geranoxo-7-methoxy-coumarin; 6,7-dimethoxycoumarin; 8-geranoxypsoralen; 9,10-dimethyl-1,2-benzanthracene; a-bergamotene; a-phellandrene; a-pinene; a-terpineol; b-bisabolene; b-caryophyllene; b-pinene, d-limonene; camphene; g-terpene; p-cymene; apigenin; bergapten; bergamottin; ciral; citronellol; fenchol; germacrene B; imperatorin; isoimperatorin; isopimpinellin; isovitexin; kaempferol; kaempferol *C. aurantifoliattin*; limonene; nobiletin; o-cymene; oxypeucedanin hydrate; phellopterin; quercetin; rutin; sabinene; terpinolene [18, 31, 42, 55].

Other bioactive compounds present in *citrus* include: pectin, furocoumarins, coumarins, lycopene (in grape fruit), pyranocoumarins, sitosterol, monoterpenes and sesquiterpenes [1, 31].

### Nutritional content of C. aurantifolia fruit juice

The nutritional content of raw *C. aurantifolia* fruit juice per 242 g (1 cup) of the juice include: water (220 g), total calories (60.5 KJ), protein and amino acids (1.0 g), total carbohydrate (20 g), dietary fibre (1.0 g), sugar (4.1 g), total fat (0.2 g), vitamin A (121 IU), vitamin C (172 mg), vitamin E (0.5 mg), vitamin K (1.5 mcg), thiamine (0.1 mg), niacin (0.3 mg), vitamin B6 (0.1 mg), folate (24.2 mcg), pantothenic acid (0.3 mg), choline (12.3 mg), betaine (0.5 mg), calcium (33.9 mg), iron (0.2 mg), magnesium (19.4 mg), phosphorus (33.9 mg), sodium (4.8 mg), zinc (0.2 mg), copper (0.1 mg), selenium (0.2 mg) and ash (0.8 mg) [3].

### Health Benefits of Phytochemicals Obtained From Citrus

There is an increasing interest in citrus fruits consumption across the world because of their rich sources of vitamin C, folate, dietary fibre, and minerals as well as many phytochemicals, including flavonoids, amino acids, triterpenes, phenolic acids and carotenoids. There are about 37 limonoid aglycones and 19 glycosides in *C. aurantifolia* and their

hybrids [1]. Limonoids are principally found in citrus fruit peels where they produce the bitter taste and the zest aroma. They are also found in large amount in the citrus fruit juice, tissue and seeds [26]. Limonoids possess the ability to inhibit tumor formation by stimulating the enzyme glutathione S-transferase (GST) which is a detoxifying enzyme that catalyzes the reaction of glutathione to form less toxic and more importantly water soluble compounds that can be easily excreted from the body [56]. Citrus is rich in flavonoids and the most abundant flavonoids in *C. aurantifolia* extracts include: apigenin, rutin, quercetin, kaempferol, nobiletin, hesperidin, hesperitin, and neohesperidin [26, 31]. The flavonoids have strong inherent ability to modify the body's reaction to allergens, viruses and carcinogens. They show anti-allergic, anti-inflammatory, antimicrobial and anti-cancer activity [57]. It has been demonstrated that quercetin, one of the most active flavonoids possess significant anti-inflammatory activity because of direct inhibition of several initial processes of inflammation. Quercetin also showed remarkable anti-tumor properties and may have positive effects in combating or helping to prevent cancer, prostatitis, heart diseases, cataracts, allergies/inflammations and respiratory diseases such as bronchitis and asthma [9]. Carotenoids are also found in citrus and are believed to reduce the incidence of age-related macular degeneration, the leading cause of blindness in human after the age of sixty five [58]. They play essential roles as sources of Vitamin A. The most active role is protection against serious disorders such as cancer, heart diseases and degenerative eye diseases. It is an antioxidant and acts as regulators of the immune system. Carotenoids commonly found in citrus are  $\beta$ -carotene, lutein, zeaxanthin and cryptoxanthin [59].

Citrus is one of the main sources of Vitamin C [60]. Ascorbic acid in the body aids in iron absorption from the intestines. It is required for connective tissue metabolism especially the scar tissue, bones and teeth. It is necessary as an anti-stress and protector against cold, chills and damp. It prevents muscle fatigue and scurvy. It is needed for normal wound healing [61]. The production of collagens is also dependent on Vitamin C. It helps in the promotion and restoration of skin [49].

### 2. Conclusion

The importance of *C. aurantifolia* in both domestic and ethnomedical use cannot be overemphasized. It has been traditionally used in the management of several diseases and has the prospects of being developed into useful drugs. The consumption rates can thus be increased either for nourishment, disease prevention or treatment/management of ailments. The plant is of economic value. Therefore, its cultivation should be increased. Though *C. aurantifolia* juice have been incorporated into many fruit juice drinks commercially sold in the market, the consumption of the freshly harvested, raw fruit juice is better with respect to nutritional values. Finally, there should be a translation from pre-clinical screening of the plant's fruit juice, fruit peels, leaves, seed, stem barks and roots to the isolation of active compounds and the actual development of useful drugs from the plant.

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