Ilkogretim Online - Elementary Education Online, 2021; Vol 20 (Issue 2): pp. 2666-2678
http://ilkogretim-online.org
doi: 10.17051/ilkonline.2021.02.283

# Phytochemical, Pharmacological Properties And Bitterness Causing Compounds Of Pomelo (Citrus Maxima): A Mini Review

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**ABSTRACT**

Pomelo (Citrus grandis (L.) Osbeck or (Citrus maxima), popularly known by various local names including pummelo, shaddock or Chinese grapefruit. Among citrus fruits, pomelo fruits are recognized as largest fruit morphologically green in color, round in shape. The taste of pomelo is sweet and is slightly acidic with little bitterness. Citrus maxima is reported to possess phytocompounds. Beside common primary metabolites (common to all plant species) such as cellulose, hemicellulose, lipids, and sugars many secondary metabolites are also present. Different limonoids from seeds of C. grandis specifically limonin and nomilin have been identified to possess chemo-preventive biological activities, free radical-scavenging activity. The plant juice when consumed is believed to improve antioxidant ability reducing the risk of possible oxidative stress. This review focused on phytochemical and of citrus maxima juice and focused on pharmacological properties like anti-diabetic, anti-tumor, antioxidant properties of Citrus maxima.

**Key words:** Pharmacological properties, Bitterness, Citrus maxima, Pomelo

## 1. INTRODUCTION

Citrus maxima (Citrus grandis) or pomelo, is popularly called Chakotra in India. Two common varieties of pomelo are known, one which has white pulp and the other, pigmented has pink pulp. Specific characteristics features which also contribute to convenient identification of the species include huge leaves which are borne on broadly winged petioles, large sized flowers with fragrance. Among citrus fruits, pomelo fruits are recognized as largest fruit morphologically green in color, round in shape, around 20 cm diameter with an average weight of 1-2 Kg [1-2]. Owing to its flavor as well as aroma the endocarp (fleshy part of fruit) of pomelo fruits constitutes the edible part whereas the peel of fruit (comprising about 20% of total fruit) is economically characterized as agro waste [1, 3]. The taste of pomelo is sweet and is slightly acidic with little bitterness. Citrus fruit tissues contain flavonoid naringin which is responsible for causing bitterness. Immediate bitterness is caused by naringin and on the other hand, delayed-type bitterness is due to limonin in many fruits juices. This review focused on phytochemical and of citrus maxima juice and focused on pharmacological properties like anti-diabetic, anti-tumor, antioxidant properties of Citrus maxima.

**Phytochemicals of Citrus maxima Juice**

Every plant species is known to possess specific metabolites characterized as primary or secondary depending upon their synthesis, production and function. Golden yellow or red to pink coloured appearance of pulp as well as peel of Pomelo is attributed to presence of secondary metabolites carotenoids [4]. The peel as well as pulp of citrus fruit has been reported to contain more than 115 different carotenoids. On a comparative account juice of pulp of red-fleshed pomelo possesses about 7 times high β-carotene, lycopene compared to peels of the fruits [5]. Beside common primary metabolites (common to all plant species) such as cellulose, hemicellulose, lipids, and sugars many secondary metabolites are also present. Flavonoids are an important class of secondary metabolites found to be present in pomelo [6]. Flavonoids reported to be present in species include hesperidin, neohesperidin, naringenin, naringin, and rutin [7]. Several studies conducted have studied qualitative as well as quantitative properties of different metabolites and phytocompounds synthesized in Citrus maxima. Shao et al [8] analyzed Vitamin C through the technique of 2, 6-dichlorophenolindophenol and reported the plant to be rich in synthesis and production of vitamin C. Besides a prominent source of ascorbic acid, Citrus grandis also contains other economically valued metabolites with nutritive value, health-benefiting effects, etc. such as carotenoids, limonoids, acridone alkaloids, flavonoids, minerals, oils, Vitamin B complex [9-12].

Abirami et al [13] comprised a comparative study of fresh juices of C. hystrix and C. grandis (red and white fruit). The study reported 333.33 - 523.21 mg of tannin, and 769.05 - 909.52 mg GAE phenols to be the maximum in white fruit juice of grandis variety. The concentration was found to be low for C. hystrix and even lower for red fruit juice of C. grandis. Besides tannin and phenolic content, the study also reported C. grandis (white pulp) fruit juice to possess high flavonoid compared to the other two juices studied. From the biochemical perspective presence of high flavonoids is linked /related to the high phenolic content of the fruit juice [13]. Sodium and potassium are the two most important ions which are key players in maintaining electrolyte balance between cellular and extracellular environment and among other fluids present in a living system. Citrus fruits have been reported to contain more potassium than sodium. C. grandis peel was found to be 7-5 times high in sodium compared to that pulp. Also, the concentration of K was 20% more in peel compared to the value of K in pulp [14].

**Pharmacological Properties of Citrus maxima**

**Anitumor / Anticancerous property**

Citrus maxima is reported to possess phytocompounds with the potential to suppress proliferation of cancer. Leaves of C. maxima have been identified to harbor anticancer potential which is attributed to the presence of different flavonoids. Further studies on these flavonoids, their biochemistry, and pharmacology can be a vital approach toward finding novel anticancer agents [15]. Pomelo rind is highly rich in flavonoid content. Studies conducted a report that bioflavonoid in the fruit facilitates the elimination of extra estrogen from the body along with restricting the migration of breast cancer cells. Besides the medicinal application, the rind of Pomelo is a common ingredient in Chinese cooking to provide flavor to different food preparations. Hela cell lines are among the most commonly utilized to analyze the effect of different plant extracts, and oil on the proliferation of cancer cells. Extract of the peel of fruit and leaf of C. maxima were analyzed to assess their anti-cancer property through cell lines and it was reported that the plant species can be utilized for the prevention of cancer [16].

Different limonoids from seeds of C. grandis specifically limonin and nomilin have been identified to possess chemopreventive biological activities, free radical-scavenging activity, and glutathione S-transferase inducing activity being among specific activities [17-18]. Intraperitoneal administration of methanolic extract of C. grandis was reported to enhance the longevity and count of non-viable tumor cells with a decrease in the volume of tumor [11]. Sen and Samanta [19] used Swiss albino mice to test the anti-tumor potential of a methanolic extract prepared from C. grandis leaves (MECM) against the Ehrlich Ascites Carcinoma (EAC) cell line. MECM was given to mice for 9 days and was found to reduce tumor parameters like hematological parameters, tumor volume, increased body weight, viable cell count of the tumor, and life span when compared to control mice. MECM administered intraperitoneally at dosages of 200 and 400 mg/kg was shown to have anticancer action. The presence of flavonoids and limonoids in C. grandis facilitated anticancer/anti-inflammatory activities, according to the research. Another study conducted by Wang et al [20] reported C. grandis juice contains 1,1- diphenyl-2-picrylhydrazyl (DPPH), b-carotene, and lycopene which have been reported to be related to antioxidant activity. Lycopene and b-carotene have been specifically reported to be abundant in the red variety of Citrus grandis and can be a potential candidate for anticancer activity [21]. The extract of C. grandis binds with secondary bile acids which are reported to be associated with the development of colorectal cancer. Evidence-Based Integrative Medicine results from conducted study provide vital insight into Citrus grandis extract’s potential to reduce the risk of colorectal cancer [22].

## Antioxidant effect

C. maxima is among the well-known plant to possess antioxidant properties. The plant juice when consumed is believed to improve antioxidant ability reducing the risk of possible oxidative stress. C. grandis being identified as a potential antioxidant source is due to the presence of metabolites including polyphenols, vitamin C, flavonoids, etc. Such metabolites have been reported to act as neutralizers of free radicals and hence provide protection against oxidative stress. Besides antioxidant activity, C. maxima also depict an inhibitory role against α-glucosidase, tyrosinase, α-amylase, and acetylcholinesterase [9, 13].

Singh et al [23] worked on essential oil of two species namely C. grandis and C. sinensis, to figure out the potential of microbial strains against the oxidation by the free radical scavenging by using spectrophotometric analysis and DPPH assay. The IC50 value of essential oil was 8.84 mg/ml which reflects its powerful antioxidant potential. He et al [24] evaluated superoxide anion radical scavenging rate and antioxidant activity, DPPH of essential oil from peels of C. grandis were studied with varying concentrations, where the IC50 of oil was reported to be 70.12 mg/ml. The study concluded higher antioxidant activity at a high concentration of oil.

Mäkynen et al [25] analyzed the antioxidant potential of six different cultivars of C. grandis and reported flavonoids hesperidin and neohesperidine dihydrochalcone present in fruit to exhibit activity against the formation of superoxide along with scavenging reactive oxygen species. Spectrophotometric analysis was used by Zarina and Tan [26] to study flavonoid activity of C. grandis peel w.r.t lipid peroxidation among fish tissue which was treated with C. grandis peel, reduced peroxide value (PV) reflected its activity. In a study by Chang and Azrina [27] antioxidant potential of C. grandis (different parts and by-products of the plant) reported albedo to possess maximum total phenolic as well as total flavonoid content. On the contrary flavedo depicted maximum antioxidant activity in DPPH as well as FRAP assays.

## Analgesic and Anti-Inflammatory Activities

Studies conducted by Shivananda et al [28] have depicted phytocompounds of C. maxima to exhibit analgesic activity against noxious stimuli (both chemical as well as thermal) during early as well as late phases of pain. Anti-inflammatory activity among formalin-induced paw edema models as compared to that of control, C. maxima has also been reported.

Different parts of C. maxima (to mention fruit peel, leaves, bark, stem) were soaked for a period of 72 h in ethanol, aqueous medium, and acetone. All the extracts were subjected to analyze their analgesic property through mice model among which writhing was introduced by action of acetic acid, method of the flick, method of the hot plate along with acute/chronic anti-inflammatory activity. The anti-inflammatory potential was assessed through Paw edema of rats induced by formalin. Among different extracts studied ethanolic extract prepared from mentioned plant parts of C. maxima potentially exhibited decreased writhes in animals compared to that obtained in control along with an increase in time of tail flicking. Also, the results of ethanolic extract were comparable to that of diclofenac (standard) [29,28].

**Antimicrobial Activity**

In a study conducted by Singh and Navneet [30] antimicrobial potential of essential oil extracted from C. grandis, C. sinensis, and the combination of oil of both species against fungi and aflatoxins was studied. Major phytocompounds to be present in the essential oils were identified to be D L-limonene, acyclic monoterpenes, carveoland E-citral [31]. Species of the genus Aspergillus include A. niger, A. alternate, A. terreus, A. fumigatus along with fungi (filamentous) namely F. oxysporum, C. herbarum, H. oryzae, C. lunata, T. viride were studied. Complete growth inhibition of A. flavus was observed around approx. concentration of oil 750 ppm (individual oil extracted from the two species as well as their combination reported same inhibition). The essential oil obtained from C. grandis species depicted a greater inhibitory effect when compared to oil of C. sinensis and also combined oil of both species. Toxic property of fungi species was exhibited by inhibition of mycelia growth of F. oxysporum, H. oryzae, A. fumigatus, A. alternata, and T. viride by their respective oil, also by the oil obtained by mixing the oil of both the species. A concentration of 500 ppm oil of C. grandis was reported to inhibit the growth of A. flavus to 48.1% whereas the combination of oil of the two species resulted in 44.0% growth inhibition of fungi species. From the findings it can be concluded, that the essential oil of C. grandis is a potential source to be utilized as an effective antifungal agent.

In another study employed by Bijun [32] on ethanolic extract prepared from the peel of C. grandis and findings reported extract to possess the potential to control the growth of mold. Extract of the species grandis exhibited enough potential to inhibit the growth of numerous fungi species including Aspergillus niger (60.5% inhibition), Penicillium (59.5% inhibition), Aspergillus otyzae (34.3% inhibition). Antifungal potential of extracts prepared from seeds of C. grandis seed extract when analyzed for their antifungal potential [30], the extract was found effective enough to restrict against fungi Aspergillus niger and Candida albicans. The minimum inhibitory zone against species Candida albicans was around 7.66 ± 0.32 mm with the value of MIC ranging from around 3.12 to 25 mg/mL for the MeOH fruit seed extract. Das et al [33] evaluated the antibacterial potential of prepared ethanolic (90%) extract of leaves of C. grandis against bacterial P. aeruginosa and E. coli. Their findings reported maximum zone of inhibition (ZOI) for species P. aeruginosa and E. coli depicted a high MIC for extract compared to P. aeruginosa (0.312 mg/ml). However, the value of the minimum bactericidal concentration (1.25 mg/ml) for both bacterial strains studied was found to be the same. Singh and Navneet [30], in their extensive study prepared extract from the seed of C. grandis to possess and analyzed to identify the antibacterial activity of the same against some common pathogens of the human respiratory tract such as including Pseudomonas aeruginosa, Staphylococcus aureus, Haemophillus influenzae, Streptococcus pneumonia, S. pyogens. Maximum growth inhibition was exhibited by methanolic extract which was followed by acetone and subsequently by aqueous extract and petroleum ether.

## Anti Diabetic Activity

Antidiabetic property is among the prominent reported activity of C. maxima. Utilizing ethanol as solvent extract prepared from bark and stem of C. maxima through hot percolation technique was reported to possess antidiabetic activity. An acute toxicity assessment was conducted as per OECD-425 guidelines. The activity was assessed using alloxan and streptozotocin-induced ADA and oral glucose tolerance assay. The extract depicted high values of LD 50 increasing the safety of extracts, and the fasting glucose level of blood in both alloxan, as well as streptozotocin-induced rats, was reported to be in the normal range. Extract of C. maxima also resulted in an increase in animal weight when compared to control animals. A decrease in blood glucose level was exhibited by the oral glucose tolerance test as well. Standard biomarkers of serum namely SGPT, and SGOT also decreased in animals treated with plant extract, and glibenclamide model rat animals with Type II diabetics were used to study glucose tolerance and lipid profile. Animals were administered with 50% shaddock fruit juice (obtained by centrifuging fruit juice) resulted in reduced water and food intake by rats. Improved glucose tolerance (oral) was achieved in streptozotocin-induced type II diabetic rats. Along with this increased VCDL, cholesterol, and triglyceride levels were also reported, compared to which level of HDL decreased [34,35].

## Hepatoprotective activity

C. maxima (Pomelo) leaves were analyzed for their inherent hepatotoxic activity in rats against paracetamol-induced hepatotoxicity. Methanolic extract from leaves was prepared which was subsequently evaporated to procure crude extract. The paracetamol was administered for the liver damage among rats. For assessment of the hepatoprotective potential of prepared extract, silymarin was utilized as a standard drug for comparative study. C. maxima methanolic extract exerted a sound effect on thiobarbituric acid reactive substances and reduced glutathione levels along with catalase activities were reportedly restored to normal levels after administration of C. maxima plant extract. Histopathological investigations show that paracetamol administration causes hepatocellular vacuolization and localized hepatic necrosis in control mice, resulting in a substantial decrease in MECM 400 mg/kg and silymarin treated animals. C. maxima peels were shown to have a protective effect against $CCl_4$-induced liver damage in a $CCl_4$-induced hepatotoxicity model. The benefit of C. maxima peel powder against the liver disorders was discovered to be due to anti-oxidant components like caffeic acid and epicatechin [29, 36]. Oboh et al [37] conducted a study to depict the reduction of the level of plasma triglyceride by C. grandis juice in a dose-dependent manner. The presence of flavonoids was reported to be the reason for the activity, which inhibits hepatic apolipoprotein (apo) B secretion thereby resulting in a hepatoprotective effect [38].

**Bitterness causing compounds**

Citrus fruits have been reported to be enriched with diverse types and nature of phytonutrients / phytocompounds, each of them having one or more biological activities [39-41]. Among different metabolites belonging to different organic classes (flavonols, flavones, terpenes, glycosides, etc) some compounds contribute to the bitterness of the fruits whereas other compounds have no influence on bitterness. The type and nature of the glycoside chain critically influence the bitterness effect of a particular plant metabolite. Naringin, sinensetin, nobiletin, limonin, quercetin, and nomilin are among the most common phytocompounds identified to be responsible for the bitterness of fruits. The presence of such metabolites is responsible for the characteristic bitter flavor of citrus fruits. Type, as well as the concentration of bitterness, depends upon the type of fruit, physiology, cultivation conditions, etc.

**Naringin**

Naringin ($C_{27}H_{32}O_{14}$) is a disaccharide derivative. Chemically naringin is (S)-naringenin possessing 2-O-(α -L-rhamnopyranosyl)-β -D-glucopyranosyl moiety substituted at the 7$^{th}$ position through glycosidic linkage [42-43]. The number of hydrogen bond donor, acceptor, and rotatable bonds is 8, 14, and 6 respectively. Naringin, a flavanone-7-O-glycoside is reported to be present in citrus fruits and is considered to be the prime reason for the bitter taste of respective fruits. Naringin is also part of the inhibitory mechanism of specific drugs which generally deals with drug-metabolizing enzymes cytochrome P450, CYP3A4, and CYP1A2. Naringin powder (inhaled or ingested) is known to affect the absorption of drugs as well as their circulation. It is found in citrus fruits including grapes, lemon, lime, and oranges however the concentration varies from fruit to fruit [44]. Almost all processed citrus fruit juices possess naringin which confers bitterness to the respective juices [45]. Albedo, pitn, flavedo, juice, and seeds of grapefruit have been evaluated in several studies to determine these plant parts contain naringin [46-48].

**Limonin**

Limonin a well-known derived metabolite of limonoid glycones is considered to be an oxygenated metabolite. It has also been linked to the derivatives of triterpenes. Fruits of the family Meliaceae and Rutaceae are among the prominent source of limonin [49-51]. Limonoids have been categorized into two groups. Aglycones represent the first group whereas glycosides comprise the second group of limonoids. Common limonoids include changing, limonin, nomilinic acid, nomilin, and others [52-55]. In appearance, limonin is a white color, found to be present in citrus fruits. It is more commonly known by the names limonoic acid and belongs to the metabolite group furlactones. Limonin exhibits little solubility in water whereas it is highly soluble in an organic solvent to maintain glacial acetic acid, ethanol. Comprising different plant families Rutaceae is a common source of limonin, including the wild as well as hybrid varieties about 30 different limonoids have been identified so far [56-59]. In the study by Hasegawa and Miyake [60] citruses were reported to synthesize limonoids through terpenoids synthetic pathway, the process beginning with cyclization of squalene precursor via CAM pathway. Limonoids have been characterized as engendered compounds, possessing a furan ring in the structure that is linked to the D ring. Beside this limonoids are also classified according to their spatial arrangement and oxidation reaction [61]. Varying concentration of limonin has been reported in different parts of grapefruit [62].

## 4. CONCLUSIONS

From the above review it can be concluded that citrus maxima shows various health benefits such as antimicrobial, anti-tumor, anti-diabetic activity. Besides of the above health benefits citrus maxima juice gain less popularity due to presence of bitterness compounds like naringin content. By reducing its bitterness marketability can be enhance so that anyone can get its health benefits.

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