



“*Citrus maxima* (Brum.) Merr. (Rutaceae): A Review On Its Chemical Constituents And Pharmacological Activities”

Maneswari Boro¹, Dr. Deeparani Urolagin², Vijaya Kumar J³, Harish N⁴.

Research Scholar, Department of Pharmacology, R R College of Pharmacy, Bangalore-560090

Abstract

Pomelo (*Citrus grandis* (L.) Osbeck or (*Citrus maxima*), popularly recognized through diverse neighborhood names together with pummelo, shaddock, or Chinese grapefruit. *Citrus maxima* (Burm.) Merr. (family Rutaceae), is an ethnomedicinally, pharmacologically, and phytochemically valued species. Various ethnomedicinal reports have revealed the use of *Citrus maxima* for cough, fever, asthma, diarrhea, ulcers, and diabetes and as a sedative. Numerous phytochemicals have been reported from *C. maxima* such as polyphenols, terpenoids, sterols, carotenoids, vitamins, and amino acids, flavonoids, alkaloids, coumarins. The plant was found to possess significant antidepressant, antimicrobial, antifungal, antibacterial, antidiabetic, anticancer antitumor, anti-inflammatory, and antioxidant properties. In the conversion of those pharmacological sports into contemporary-day drugs, the right clinical evaluation consists of the isolation of answerable phytochemicals, their mechanism of moves, and suitable standardization to be explored.

Keywords : *Citrus maxima* , ethnomedicinal , phytochemical , pharmacological, pomelo.

1. Introduction

Citrus maxima (Burm.) Merr. belongs to the family Rutaceae. It is a perennial tree usually referred to as Pomelo, Bhogate, Shaddock, Papanus, Pummelo, etc. It is scientifically also known as *C. grandis* (L.) Osbeck and the largest among the citrus fruits. The leaves, flowers, fruits, roots rind, and barks of *Citrus maxima* reveal the nutritional significance and pharmacological properties which highlight its use in traditional medicine to treat various diseases (1). *Citrus maxima* have revealed various pharmacological activities including antioxidant activity, anti-inflammatory activity, antidiabetic, anti-cancer and anti-tumor activity, anti-bacterial activity, antidepressant activity, antimicrobial activity, and anti-fungal activity. Pomelo contains abundant vitamin C like other citrus plants and is generally eaten as fruit. Different elements of this plant comprise numerous natural

compounds. Phytochemicals belonging to different chemical classes such as alkaloids, carbohydrates, flavonoids, amino acids, carotenoids, coumarins, steroids, and essential oils constituents are present in different parts of *Citrus maxima*. This evaluation article aims to offer a complete definition of the phytochemistry and pharmacological elements of the plant and to draw medical groups for in addition research on the possible utilization of *Citrus maxima* in the field of pharmaceutical, nutraceutical, and cosmeceutical industry (2).

2. Distribution and Habitat :

The plant *Citrus maxima* (Burm.) Merr. is an extensively dispensed indigenous flora observed in the Indian subcontinent. The plant is indigenous to Asia and is commercially grown in China, Nepal, Thailand, Malaysia, India, Indonesia, Vietnam, Philippines, Japan, and many other Asian countries. *Citrus maxima* are with a top of 5-15 m, and have thickness 10-30 cm (3). The tree has huge evergreen leaves that are dotted, glandular, alternate, ovate, and elliptic, 10.5 to 20 cm long, with winged petioles. The flowers and fruits are borne singly. The fruits are pear-shaped with a width of 10-30 cm and pale-yellow or greenish-yellow in color (4). It grows widely in temperatures 25–32°C and rainfall 1,500–2,500 mm within a 3-4 months dry season. In India, these fruits are known to grow from November through December and sometimes in the middle of the year (5). In figure shows various plant parts of *C. maxima*, which include the leaves, flower, whole plant, bark, and fruits.

3. Methodology

Methodology Scientific information about ethnomedicinal uses, phyto-constituents, and in vivo and in vitro biological activities of different parts of *C. Maxima* become amassed from posted articles retrieved through numerous applicable databases inclusive of Google Scholar, PubMed, Chemical Abstract, Scifinder, Web of Science, and Scopus. The database changed into a search with the key phrases consisting of *Citrus maxima*, pummelo, and *Citrus grandis* together with pharmacological activity, phytochemicals, ethnomedicinal uses, toxicity, etc.

Plant Profile : ⁽⁶⁾

Botanical name: *Citrus maxima*

Toxonomical classification:

- Kingdom- Plantae
- Division- Magnoliophyta
- Class- Magnoliopsida
- Order- Rosidae

- Family- Rutaceae
- Common name- Pamelo

Table 1: Some common names of Citrus maxima

Language	Common name
Nepali	Bhogate
Hindi	Sadaphal, Batawi nimbu, Cakotra
English	Pummelo, shaddock, pumelo
Sanskrit	Madhukarkati
Italian	Pompelmo
French	Pamplemousse
Portuguese	Jamboa
Spanish	Pamelmusa
Polish	Pompela
Indonesian	Jeruk Besar, Jerukbali

4. Traditional Uses

Leaves: Epilepsy, chorea, Convulsive cough, and additionally within side the remedy of hemorrhage disease. Oil from fresh leaves possesses anti dermatophytic activity, and fungicidal activity (7).

Fruits: Leprosy, Asthma, Cough, hiccough, intellectual aberration, Epilepsy, cardi tonic. Fruits of *C. maxima* are also used in food, cosmetic, perfume, and pharmaceutical industries as flavoring or fragrance-enhancing agents (8).

The fruits and peels: are Appetizers, stomach-tonic, inflammation, cardiac stimulants, and coughs (9).

Fruit juice: Fruit juice has the potential to influence weight loss and promote cholesterol reduction. The fruit juice is utilized in belly tubules. The fruit is nutritive, cardi tonic and refrigent (10).

Flower: Used as a sedative in nervous affection.

Rind: Antiasthmatic, sedative in fearful affection, Brain tonic, Useful in vomiting, griping of the abdomen, diarrhea, Headache, and eye troubles.

Root and Bark: Antimicrobial activity (11).



Figure 1: Leaves



Figure 2 : Flower



Figure 3 : Whole plant



Figure 4: Bark



Figure 5: Fruits

5. Chemical Constituents:

Phytochemicals belonging to different chemical classes such as alkaloids, flavonoids, carbohydrates, carotenoids, steroids, coumarins, amino acids, and essential oils constituents are present. The information of phytoconstituents present, their classes, and plant components used for isolation.

Flavonoids: Flavonoids isolated are naringin, pondering, rhoifolin, marmesin, hesperidin, tangeretin, nobiletin, glychalcone, glyflavanone, lemairone, acacetin 3,6-di-C-glucoside, vicenin-2, lucenin-2 4'-methyl ether, narirutin 4'-O-glucoside, apigenin 8-C-neohesperidoside, phloretin 3', 5'-di-C-glucoside, rutin, rhamnetin, dihydrokaempferol, dihydrokaempferol 3-O-rhamnoside (engeletin) and kaempferol, excavaside A and B, myricetin 3-O- β -D-rutinoside, myricetin 3,3'-di- α -L-rhamnopyranoside, myricetin 3'- α -L-rhamnopyranoside, and others (12).

Carotenoids: The pulp and peel of *Citrus maxima* (Pomelo) appear golden yellow to red or pink color due to the presence of carotenoids. The peel and pulp of citrus result incorporates more than a hundred and fifteen distinctive carotenoids. Singh et al (2016) stated the presence of Aurapte, Auraptene, carotene, 5-Geranyloxy-7-methoxy-coumarin, roseoside, and bergamottin within the side of the peel, and also, 5-methyltodannol, 6-hydroxymethylherniarin, 5-methoxy seselinin the stem bark and roots (13).

Alkaloids: Alkaloids were remoted from a maximum of the components along with the stem, flower, fruit, peel, root, and bark of the plant. The structures of the isolated alkaloids. Some of the isolated acridone alkaloids are citpressine-I and II, 5-hydroxynoracronycine, buntanine, citracridone-I, II, and III, citrusinine-I, grandisine-I and II, glycocitrine-I, natsucitrine-II, and prenylcitpressine. Alkaloids like buntanbismine, buntanmine A, afole, baiyumine-A and -B, caffeine, citbismine-A, -B, and -C, citropone-A and -B, geibalansine, honyumine, pumiline, p-synephrine, theobromine, theophylline, and paraxanthine also are suggested from the plant (14).

Steroids: The steroid compounds determined withinside the peel of pomelo are β -sitosterol and β -sitosterol-3-O- β -D-glucopyranoside (15).

Coumarins: Coumarins compound has additionally been diagnosed from numerous different research in pomelo peel. The technique used to obtain the compound is using solvent extraction. Most of the coumarin compounds will be received withinside the ethyl acetate fraction. The isolation of natural compounds is achieved the usage of column chromatography (conventional, LC or HPLC). Some of the coumarin compounds obtained from the peel extract of pomelo include umbelliferone, hopeyhopin, toddanone, 7-geranyloxy coumarin, marmin, epoxyaurapten, 7-(6-hydroxy-7-methoxy-3,7-dimethyl-(2E)-2-octenyloxy) coumarin, 7-(6-hydroxy 3,7dimethyl-2E,7-octadienyloxy) coumarin, osthenol, isomeranzin, meranzin hydrate, 7-hydroxy-8-(2'-hydroxy-3'-methylbut-3'-enyl) coumarin, auraptenol, 7-methoxy-8-(2-formyl-2-methylpropyl) coumarin, yuehgesin B, yuehgesin C, 5-methyltodannol, 6-hydroxy methylherniarin are present in the roots and stem bark (16).

Amino Acids: Alanine, Asparagine, Aspartic acid, Coline, Glutamic acid, Glycine And proline are present in the leaves(17).

Carbohydrates: Phytol, Synephrine, Methyl antralinate, Fructose, Glucose, and Pectin are present in the Leaf, peel, and flowers (18).

Essential Oil Constituents: Essential oils are also recorded from its leaves, flower, and peel which includes (Z)-ocimene, 4-methyl-1-hexene, 3,3-dimethyl-1-hexene, geraniol, geranyl acetate, limonene, geranyl formate, linalool, nerol, nerolidol, sabinene, α , β -pinene, β -farnesene, and β -myrcene (19).

6. Pharmacological Activities:

Various studies have been performed regarding the pharmacological effects of *C. maxima* extracts and their isolated compounds. Modern pharmacological studies confirm the traditional efficacy of this plant as an antidepressant and anti-inflammatory agent. The plant is highly potent for treating anxiety, depression, diabetes, and other neurological diseases. The plant also exhibits additional antioxidant, anti-inflammatory, antidiabetic, antimicrobial, antifungal, and anticancer activities. In this review, we collected the available information and described major pharmacological properties like antidepressant, antioxidant, antimicrobial, antidiabetic, anticancer and antitumor activity, anti-inflammatory, and antifungal.

Antidepressant Activity:

The aqueous leaf extracts (100, 200, and 300 mg/kg) of *Citrus maxima* have been evaluated in mice for their antidepressant capacity and the usage of one-of-a-kind models. Fluoxetine (20 mg/kg, *i.p.*) and imipramine (30 mg/kg, *i.p.*) have been used as widespread drugs. The aqueous leaf extracts decreased the immobility time in each of the tail suspension tests (TST) and the forced swimming test (FST). The actual mechanism for displaying antidepressants turned into now no longer reported, however it is probably because of the enhancement of norepinephrine neurotransmission in mice (20). Similarly, the per-oral management of ethanolic extracts (two hundred and four hundred mg/kg) of *C. Maxima* in mice extended the range of rearing in each of the TST and FST fashions even as imipramine (1 mg/kg) quite decreased the immobility time (21). Hesperidin and naringin were evaluated towards antidepressant interest with the use of the FST and TST models. Both compounds exhibited significant antidepressant activity (22). The antidepressant results of plant extracts is probably because of the interplay with the serotonergic 5-HT_{1A} and κ -opioid receptors (23, 24). It was concluded that *C. Maxima* extract becomes beneficial in its motor-stimulating effects.

Antimicrobial Activity:

Antifungal activity:

Research turned into performed with the aid of Singh and Navneet (2016) to stumble interest in *Citrus grandis* and *C. Sinensis* critical oils, in conjunction with their critical oil mixture towards fungus and aflatoxins. The foremost additives of the vital oils have been DL-limonene, a cyclic monoterpene, carveol and E-citral, and Z-

citral (monoterpene aldehydes) (25). In the study carried out by Singh and Navneet (2016), it was found that according to ANOVA and Tukey's comparison tests ($p < 0.05$), different concentrations (250,500,750 and 1000 ppm) of EOs had been located extensively powerful in opposition to fungal increase in vitro. Different species of *Aspergillus* like *A. alternate*, *A. niger*, *A. fumigatus*, *A. terreus*, and other filamentous fungi like *F. oxysporum*, *H. oryzae*, *C. herbarium*, *C. lunata*, and *T. Viride* have been taken in which entire inhibition of *A. Flavus* was discovered at 750 ppm via way of means of vital oil of each the culmination and their vital oil combination. The vital oil of *Citrus grandis* confirmed greater efficacy than that of each *C. sinensis* and their essential oil combination. A vast spectrum of fungi poisonous interest became visible via way means of whole inhibition of the mycelium increase of *A. alternata*, *A. terreus*, *F. oxysporum*, *A. fumigatus*, *H. oryzae*, and *T. Viride* via way means of the crucial oil and their aggregate at 750 ppm. At 500 ppm the crucial oil of *Citrus grandis* inhibited *A. flavus* up to 48.1% and the combination of EOs inhibited the species up to 44.0% respectively. This leads to the conclusion that the essential oil of *C. grandis* can be a good candidate to perform as an antifungal agent. In a take a look done by Bijun (2004) the ethanolic extract of *Citrus grandis* peel changed into visible to be powerful towards a few collections of mold. The extract was found to inhibit the growth of *Aspergillus niger* V, *Tiegh*, *Penicillium*, and *Aspergillus otyzae* with an inhibition rate of 60.5%, 59.5%, and 34.3% respectively. Antifungal activity of the seed extracts of *Citrus grandis* was observed by Singh and Navneet (2016) against *Aspergillus niger* (MTCC 921) and *Candida albicans* (MTCC 227). The minimal inhibition sector towards *Candida albicans* became 7.66 ± 0.32 mm and MICs became between 3.12 to 25mg/mL for MeOH (1:3, 100g seed powder into 300 ml methanol) extract of the fruit's seed (26).

Antibacterial activity:

Borah et al. (2012) studied the antibacterial pastime of EtOH extracts of *Citrus maxima* in opposition to *S. aureus*, *E. coli*, and *P.aeruginosa*. Antibacterial sports of the phytochemical ingredients of the pericarp, mesocarp, and section membrane crude EtOH extracts of *C. Maxima* fruit had been examined in opposition to *E. coli* and *Salmonella typhimurium* (27). The antibacterial interest of the EtOH extract of *C. maxima* leaves against *E. coli* and *P. aeruginosa* was investigated through Das et al.,(2013) (28). Similar antibacterial activity of *C. maxima* oil was reported against *Bacillus subtilis*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Staphylococcus aureus*, and *Salmonella typhi* at 1000 ppm concentration with 52.0, 62.2, 57.4, 52.5 and 53.3%, respectively (29). Abirami et., (2013) stated the in vitro antibacterial interest of MeOH extracts of *C. Maxima* (pink and white fruit) extract in opposition to *S. aureus*, *K. pneumonia*, *P. aeruginosa*, *S. typhi*, and *E. coli*. MeOH extract of leaves and pulp were found to have maximum activity as compared to peel extracts against all tested microorganisms (30). In another similar study, the antibacterial activity of the volatile constituents of *C. maxima* (fruit epicarp) against *Bacillus pumilus*, *B.subtilis*, *S.aureus*, *Escherichia coli*, *Klebsiella pneumonia*, *Pseudomonas aeruginosa*, and *Salmonella typhi* was reported by Pandey et al., (2010) (31). Kichaoi et al., (2015) reported in-vitro antimicrobial activity of EtOH, MeOH, and H₂O extracts of *C. maxima* pulp against *Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa*, and *Candida albicans* and MIC (Micro-dilution method) at different concentrations

(100-0.195mg/mL) for *S. aureus*, *E. coli*, and *P. aeruginosa*, and (200- 0.39 mg/mL) for *Candida albicans* (32). The antibacterial activity of the phytochemical constituents of the pericarp, mesocarp, and segment membrane crude EtOH extracts of *C. maxima* fruit were tested against *E. coli* and *S. Typhimurium*. In terms of antimicrobial activity, the pericarp, mesocarp, and segment membrane extracts generated zones of inhibitions measuring 17.10, 18.00, and 17.03 mm for *Salmonella typhimurium*, respectively at 100% concentration. *E. coli* was noted to be inactive in all three sample extracts at 100% concentration (33). The antibacterial activity of pomeloethyl alcohol (EtOH) and ethyl acetate extracts. All Citrus peels showed antibacterial activities against pathogenic bacteria with MIC (minimum inhibitory concentration) and MBC (minimum bactericidal concentration) ranging between 0.4 to 50.0 mg/ml (34). Hindi et al., (2014) stated the antimicrobial hobby of various kinds and a part of Citrus species in opposition to one-of-a-kind microbial isolates. The antimicrobial results of H₂O extracts of peel, juice, and leaves from sparkling *C. grandis* in opposition to *S. aureus*, *S. pyogenes*, *E. feacalis*, *P. aeruginosa*, *K. pneumoniae*, *E. coli*, *S. typhi*, *Proteus spp.*, *M. catarrhalis*, all of them were studied. Citrus juices confirmed the best antibacterial hobby in opposition to the maximum of the have a look at bacterial isolates. Moderate hobby is produced with the aid of using the Citrus peels and the bottom impact is produced with the aid of using the extract of the Citrus leaves (35). In an observation, it became additionally assayed that the distilled *C. Grandis* oil exhibited higher antimicrobial sports than distilled *C. Paradisi* oil, especially towards *E. coli* and *Salmonella enteric subs* (36).

The antimicrobial sports of 5 unique extracts of peel and pulp of *C. maxima* fruits have also been investigated against isolated *E. faecalis* and *P. putida*. Kinnow peel and pulp showed maximum antimicrobial activity in methanolic (MeOH) extracts form, against *P.putida*, which was ~73% and ~64% respectively compared to gentamicin. The orange peel and pulp showed maximum antimicrobial activity in MeOH and EtOH(ethanolic or ethyl alcohol) extracts form respectively, against *P.putida*. The most antimicrobial pastime many of the chakotra peel and pulp became confirmed in EtOH extracts in opposition to *E. faecalis* (37).

Anti Diabetic Activity :

Antidiabetic property is among the prominent reported activity of *C. maxima*. Utilizing ethanol as solvent extract prepared from the bark and stem of *C. maxima* through a 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 increased 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 50% shaddock fruit juice (acquired with the aid of using centrifuging fruit juice) resulting in decreased water and meal consumption with the aid of using 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 (38,39).

Anticancer and Antitumor Activity:

The leaf extract of *C. Maxima* examined Ehrlich ascites carcinoma (EAC) fashions in Swiss albino rats reduced the white blood cell (WBC) counted number and expanded the lifespan. The biochemical parameters were also at the normal level as compared to the control group (40). The methanolic extract of the leaves and its fractions in n-hexane, n-butanol, chloroform, ethyl acetate, and water were tested in normal cells and different cancerous cells through 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl-tetrazolium (MTT) assay. Importantly, the chloroform fraction of leaf extract reduced the survival of HeLa cells (41). Naringin exhibited amazing anticancer hobbies in numerous experiments. Naringin (10, 25, and 35 mg/kg *i.p.*), when treated on rats bearing Walker 256 carcinosarcoma (W256) reduced tumor growth by 75%, and TNF- α and IL-6 levels decreased in comparison with the control (42,43). Naringenin additionally exhibited molecular proliferation and molecular migration in B16F10 murine and SK-MEL-28 human cancer cells. Hesperidin exhibited chemopreventive results in opposition to azoxymethane (AOM) brought on carcinogenesis inside the mouse colon. It was discovered to have full-size decreasing electricity for the multiplicities of AOM-brought-on aberrant crypt foci (ACF) and tumor incidence. It also decreased the proliferative marker proliferating cell nuclear antigen (PCNA) against AOM-induced colon carcinogenesis (44,45). The presence of flavonoids, limonoids, alkaloids, tannins, saponins, and bioflavonoids plays a prominent role in cancer prevention (46). The anticancer activity of naringenin-loaded liquid crystalline nanoparticles (LCNs) was evaluated towards human lung epithelial carcinoma (A549) and airway epithelium-derived basal cells (BCi-NS1.1). Mainly antiproliferative, anti-migratory, and ant colony formation activity were studied in which naringenin LCNs showed significant anticancer properties by inhibiting the migratory and proliferation properties of cells (47).

Anti-inflammatory activities :

Acute and Chronic inflammatory activity had been studied in rats via way of means of formalin-prompted paw edema fashions respectively. In each model, the same old drug used turned into diclofenac sodium 10 mg/kg, 100mg/kg. A dose of 300 mg/kg ethanolic extract of leaves and bark exhibited significant anti-inflammatory activity in formalin-induced paw edema models in comparison to control (48).

Antioxidant activities:

Antioxidant ability changed into examined for the juice of *C. maxima* in rats. The enhanced antioxidant status observed in *C. Maxima* dealt with rats and its shielding position in opposition to H₂O₂, STZ, and nitric oxide producing gadget brought about DNA damages is probably because of the impact of various kinds of active standards performing in my opinion or synergistically, every with an unmarried or a numerous variety of organic

sports in opposition to oxidative stress (49). Antioxidants including total phenolic content, total flavonoid content, and ascorbic acid content were determined using the Folin-Ciocalteu reagent assay, aluminum chloride colorimetric assay, and AOAC method, respectively. The peels of each Citrus culmination had better antioxidant content material and ability than their pulps. It was also reported that the white variety of Citrus had higher antioxidant content and capacity compared to the pink counterpart. Citrus peel from the white range possessed better antioxidant homes and its miles doubtlessly wealthy assets of herbal antioxidants (50). The peel of Citrus fruit contains a better quantity of antioxidants in comparison to its pulp because the peel defends the antioxidants inside the fruit from oxidation. In another study, it was assayed that EO exhibited DPPH radical scavenging activity in dose dose-dependent manner (51). Aimee et al., (2014) reported the antioxidant activity of the phytochemical constituents of the pericarp, mesocarp, and segment membrane crude EtOH extracts of *C. maxima* fruit. The strongest antioxidant activity was obtained by the pericarp extract (29.64 expressed as % lipid peroxidation). The antioxidant effects of different tropical Citrus peel extracts (kaffir lime, lime, and pomelo) obtained from EtOH and ethyl acetate extraction in raw chicken drumettes during storage at 4°C were studied. The overall possible counts, 2-thiobarbituric acid-reactive materials values of KEa-handled hen wing samples have been decreasing than the ones of manage samples whilst the sensory properties maintained significantly significantly ($p < 0.05$) higher values during 14 days of storage (52).

Conclusion:

Citrus maxima is used as a cure for different types of diseases. After the conventional and folks' claims, little or no efforts were made with the aid of using the researchers to find out the healing capability of *Citrus maxima*. It is attractive to word that natural compounds and crude natural extracts of leaves, seeds, peels, pulp, results, and roots of *C. maxima* have been screened for some pharmacological activities and found to possess antidepressant activity, anti-inflammatory activity, anti-diabetic activity, antioxidant activity, antimicrobial activity, antibacterial activity, antifungal activity, anti-cancer and antitumor activity. The particular statistics supplied on this evaluate may upload fee to the medical assessment of the medicinal software of *C. maxima*. A phytochemical profile confirmed the presence of many bioactive chemical ingredients beneathneath numerous chemical training such as alkaloids, benzenoids, coumarins, carotenoids, phenols, flavonoids, tannin, terpenoids, saponins, amino acids, and carbohydrates. Isolated compounds like hesperidin, limonene, naringenin, naringin, and neohesperidin have been reported to possess bioactivities like antioxidant, antidepressant, antitumor, anticancer, antimicrobial, hepatoprotective, anti-obesity, insecticidal, analgesic activity, anxiolytic, anti-Alzheimer, antiulcer, and antidiabetic activities. The essential oils from fruits and leaves have enhanced their use in the perfumery and cosmeceutical industry.

The detailed information provided in this review might add value to the scientific evaluation of the medicinal application of *C. maxima*. In a future study, the conversion of these pharmacological activities into modern drugs,

proper scientific evaluation includes isolation of answerable phytochemicals, their mechanism of actions, toxicity, and appropriate standardization need to be explored.

References:

- (1) Ayesha Nazeer, Ashoka Shenoy M. *et al.* *Citrus maxima*: A Brief Review on the World's Largest Citrus Fruit. *Int. J. Pharm. Sci. Rev. Res.*, 74(1), May - June 2022; Article No. 16, Pages: 91-95.
- (2) Shaheena Sohi , Richa Shri *et al.* Neuropharmacological potential of the *genus Citrus*: A review. *Journal of Pharmacognosy and Phytochemistry* 2018; 7(2): 1538-1548.
- (3) Ajeet Singh, Navneet *et al.* *Citrus maxima* (Burm.)Merr. A Traditional Medicine: Its Antimicrobial Potential And Pharmacological Update For Commercial Exploitation in Herbal Drugs – A Review. *International Journal of ChemTech Research*, 2017,10(5): 642-651.
- (4) Kirtikar RR and Basu BD. 2008. Indian Medicinal Plants, vol-1. *International Book Distributors*, 495- 496.
- (5) Ratna Susandarini, Siti Subandiyah *et al.* Assessment of Taxonomic Affinity of Indonesian Pummelo (*Citrus maxima* (Burm.) Merr.) Based on Morphological Characters. *American Journal of Agricultural and Biological Sciences*, 2013, 8 (3): 182-190.
- (6) Aswini Kharjul , Mangesh Kharjul *et al.* PHARMACOGNOSTIC INVESTIGATION ON LEAVES OF *CITRUS MAXIMA* (BURM.) MERR. (RUTACEAE). *IJPSR*, 2012; Vol. 3(12): 1000-1005.
- (7) P. Vijaylakshmi, R. Radh *et al.* An overview: *Citrus maxima*. *The Journal of Phytopharmacology*, 2015; 4(5): 263-267.
- (8) Thavanapong N, Wetwitayalung P *et al.* Comparison of essential oils compositions of *Citrus maxima* Merr. Peel obtained by cold press and vacuum steam distillation methods and of its peel and flower extract obtained by supercritical carbon dioxide extraction method and their antimicrobial activity. *J. Ess. Oil Res.*, 2010; 22: 71-77.
- (9) Sidana J., Saini V. *et al.* A Review on Citrus – “The Boon of Nature”. *Int J Pharma Sci Rev Res*, 2013; 18(2). 20-27.
- (10) Chopra R.N, Nayar, S.L, and Chopra I.C., *Glossary of Indian Medicinal Plants*, New Delhi: Nati Inst Sci Co Inform Resou. 1956, 68.
- (11) Dubey N.K., Kumar R. and Tripathi P. Global Promotion of Herbal Medicines: India's Opportunity, *Curr. Sci.*, 2004; 86(1): 37-41.
- (12) Moh. Ajirul Abiq, Sutrisno *et al.* Chemical Content and Pharmacology of Pomelo Orange (*Citrus maxima*) Fruit Peel: A Review *ICS Chem* 2023.
- (13) Rusat Jahin Anmol, Shabnam Marium *et al.* Phytochemical and Therapeutic Potential of *Citrus grandis* (L.) Osbeck: A Review. *Journal of Evidence-Based Integrative Medicine*, 2021; Volume 26: 1-20.

- (14) Biswash Sapkota , Hari Prasad Devkota *et al.* *Citrus maxima* (Brum.) Merr. (Rutaceae): Bioactive Chemical Constituents and Pharmacological Activities. *Hindawi Evidence-Based Complementary and Alternative Medicine*, Volume 2022; Article ID 8741669, 16 pages <https://doi.org/10.1155/2022/8741669>
- (15) B. A. Arias , L. Ram´on-Laca *et al.* “Pharmacological properties of *Citrus* and their ancient and medieval uses in the mediterranean region.” *Journal of Ethnopharmacology*, 2005; vol. 97, no. 1, pp. 89–95.
- (16) L. Zhang, Y. Geng, H. Zhu *et al.* “Preparative separation of six coumarins from the pummelo (*Citrus maxima* (burm.) merr. Cv. shatian yu) peel by high-speed countercurrent chromatography.” *Journal of Liquid Chromatography & Related Technologies*, 2017; vol. 40, no.19, pp. 991–996.
- (17) Behrooz Nateghpour, Gholamreza Kavooosi *et al.* Amino acid profile of the peel of three citrus species and its effect on the combination of amino acids and fatty acids *Chlorella vulgaris*. *Journal of Food Composition and Analysis*, May 2021; Volume 98,103808.
- (18) Athira U *et al.* Evaluation of carbohydrate and phenol content of citrus fruits species. *International Journal of Applied Research* 2017; 3(9): 160-164.
- (19) MARIE-LAURE LOTA, DOMINIQUE DE ROCCA SERRA *et al.* Volatile Components of Peel and Leaf Oils of Lemon and Lime Species. *J. Agric. Food Chem.* 2002; 50, 796–805.
- (20) V. H. Potdar and S. J. Kibile *et al.* “Evaluation of antidepressantlike effect of *Citrus maxima* leaves in animal models of depression,” *Iranian Journal of Basic Medical Sciences*, 2011; vol. 14, no. 5, pp. 478–483.
- (21) Sheik, N. Vedhaiyan *et at.* Evaluation of central nervous system activities of *Citrus maxima* leaf extract on rodents. *Journal of Applied Pharmaceutical Science*, 2014; vol. 4, no. 9, pp. 77–82.
- (22) Benneth Ben-Azua , Eken H. S. e EneKabokom Nwokeb *et al.* Possible neuroprotective mechanisms of action involved in the neurobehavioral property of naringin in mice. *Biomedicine & Pharmacotherapy* 109 (2019) 536–54.
- (23) Jegan Sakthivel Nadar, Pravin Popatrao Kale *et al.* Potentiation of Antidepressant Effects of Agomelatine and Bupropion by Hesperidin in Mice. *Hindawi Neurology Research International*, Volume 2018; Article ID 9828639, 7 pages .
- (24) A. Roohbakhsh, H. Parhiz *et al.* Neuropharmacological properties and pharmacokinetics of the citrus flavonoids hesperidin and hesperetin—a mini-review. *Life Sciences*, 2014; vol. 113, no. 1–2, pp. 1–6.
- (25) Ruberto G, Baratta MT *et al.* Antioxidant activity of selected essential oil components in two lipid model systems. *Food Chem.* 2000; 69 (2):167-174.
- (26) Bijun LCDJX *et al.* Antimicrobial activity of shaddock peels extract [J]. *Food Ferment Ind.* 2004;1.
- (27) Baroh M., Ahmed S. *et al.* A comparative study of the antibacterial activity of the ethanolic extracts of *Vitex negunda* L., *Fragaria vesca* L., *Terminalia arjuna* and *Citrus maxima*. *Asi J Pharma Biol Res*, 2012; 2(3): 183-187.

- (28) Das S., Baroh M. *et al.* Antibacterial Activity of the Ethanolic extract of Leaves of *Citrus Maxima* (Burm.) Merr. On Escherichiacoli and Pseudomonas aeruginosa. *Asi. J. Pharma. Clin. Res.*, 2013; 6(4): 136-139.
- (29) Kumar S, Saini S. *et al.* Antimicrobial activity of von-volatile essential oils of certain medicinal plants against some enteric bacterial pathogens. *J. Scient Transac in Enviro. Technovation*, 2015; 9(1): 1-4.
- (30) Abirami A., Nagarani G., and Siddhuraju P. *et al.* Antibacterial activity of crude extract of *Citrushystrix* and *Citrusmaxima*. *Int J Pharma Sci Res*, 2013; 4(1): 296-300.
- (31) Pandey R.R, Dubey R.C *et al.* Phytochemical and Antimicrobial Studies on Essential Oils of Some Aromatic Plants. *Afri. J. Biotech*, 2010; 9(28), 4364-4368.
- (32) Kichaoi A. E, El-Hindi M, Mosleh F. *et al.* The antimicrobial effects of the fruit extract of *Punica granatum*, *Actinidia deliciosa* and *Citrus maxima* on Some Human Pathogenic Microorganisms. *Am Int J Bio*, 2015; 3(2): 63-75
- (33) Aimee S.A.B., Wilma A.H, Irene A.P *et al.* Phytochemical Composition, Antioxidant and Antibacterial Properties of Pummelo(*Citrus maxima* (Burm.)) Merr. Against Escherichia coli and Salmonella typhimurium. *Food and Nutrition Sciences*, 2014; 5, 749-758.
- (34) Klangpetch W., Phromsurin K *et al.* Antibacterial and antioxidant effects of tropical Citrus peel extracts to improve the shelf life of raw chicken drumettes. *Int. Food Res. J.*, 2016; 23(2): 700-707.
- (35) Hindi N.K.K., Chabuck Z.A.G. and Hindi S.K.K. *et al.* Antibacterial evaluation of aqueous extracts of four Citrus species in Hilla, Iraq. *Int J Pharmacol Scree Methd*, 2014; 4(1): 43-48.
- (36) Ou MC, Liu Y.H, Sun Y.W and Chang C.F. *et al.* The composition, antioxidant and antibacterial activities of cold-pressed and distilled essential oils of *Citrus paradisi* and *Citrus grandis* (L.) Osbeck, *Evid-Based Comp. Alte Med.*, 2015; 1-9.
- (37) Mehra S., Srivastava R, Shukla S. *et al.* comparative study on antimicrobial activity of five extract of few Citrus fruit: peel and pulp vs gentamicin. *Aus J. Basi. Appl. Sci*, 2015; 9(1): 165-173.
- (38) Oyedepot, A., & Babarinde, S. O. *et al.* Effects of shaddock (*Citrus maxima*) fruit juice on glucose tolerance and lipid profile in type-II diabetic rats. *Chemical Science Transactions*, 2013; 2(1), 19-24.
- (39) Abdul, M., Shenoy, A., Hegde, K. *et al.* Evaluation of the anti-diabetic activity of ethanolic extract of *Citrus maxima* Stem Bark. *International journal of pharmaceutical and chemical sciences*, 2014; 3(1), 642-650.
- (40) S. Kundu Sen, M. Gupta, U. K. Mazumder *et al.* "Antitumor activity of *citrus maxima* (burm.) merr. Leaves in ehrlich's ascites carcinoma celltreated mice." *ISRN Pharmacology*, vol. 2011.
- (41) H. Kim, J. Y. Moon, A. Mosaddik *et al.* "Induction of apoptosis in human cervical carcinoma hela cells by polymethoxylated flavone-rich *Citrus grandis* osbeck (dangyuja) leaf extract." *Food and Chemical Toxicology*, 2010; vol. 48, no. 8-9, pp. 2435-2442.

- (42) P. Sharma, V. Kumar *et al.* Naringin: biosynthesis and pharmaceutical applications. *Indian Journal of Pharmaceutical Sciences*, 2019; vol. 81, no. 6, pp. 988–999.
- (43) C. A. Camargo, M. C. C. Gomes-Marcondes *et al.* Naringin inhibits tumor growth and reduces interleukin-6 and tumor necrosis factor α levels in rats with Walker 256 carcinosarcoma. *Anticancer Research*, 2012; vol. 32, no. 1, pp. 129–133.
- (44) G. Saiprasad, P. Chitra, R. Manikandan *et al.* Hesperidin alleviates oxidative stress and down regulates the expressions of proliferative and inflammatory markers in azoxymethane-induced experimental colon carcinogenesis in mice. *Inflammation Research*, 2013; vol. 62, no. 4, pp. 425–440.
- (45) D. Stanisic, A. F. Costa, W. J. Favaro, L. Tasic *et al.* Anticancer activities of hesperidin and hesperetin in vivo and their potentiality against bladder cancer. *Journal of Nanomedicine & Nanotechnology*, 2018; vol. 9, no. 5.
- (46) S. A. Nair, R. K. Sr and A. S. Nair *et al.* *Citrus* peels prevent cancer. *Phytomedicine*, 2018; vol. 50, pp. 231–237.
- (47) R. Wadhwa, K. R. Paudel, L. H. Chin *et al.* Anti-inflammatory and anticancer activities of naringenin-loaded liquid crystalline nanoparticles in vitro. *Journal of Food Biochemistry*, 2021; vol. 45, no.1.
- (48) Shivananda A, Muralidhara R.D *et al.* Analgesic and Anti-Inflammatory Activities of *Citrus Maxima* (J. Burm) Merr. in Animal Models. *Res J. Pharma, Biol. Chem Sci.*, 2013; 4 (2): 1800.
- (49) Toh J.J, Khoo H.E, and Azrina A. *et al.* Comparison of antioxidant properties of pomelo [*Citrus grandis* (L) Osbeck] varieties. *Int. Food Res. J*, 2013; 20(4): 1661-1668.
- (50) Singh P., Shukla R, Prakash B. *et al.* Chemical Profile, Antifungal, Antiaflatoxic and Antioxidant Activity of *Citrus maxima* (Burm.) And *Citrus sinensis* (L.) Osbeck essential oils and their cyclic monoterpene, DL- limonene. *Food Chem. Toxicol.*, 2010; 48: 1734-1740.
- (51) Aimee S.A.B., Wilma A.H *et al.* Phytochemical Composition, Antioxidant and Antibacterial Properties of Pummelo(*Citrus maxima* (Burm.)) Merr. Against *Escherichia coli* and *Salmonella typhimurium*. *Food and Nutrition Sciences*, 2014, 5, 749-758.
- (52) Klangpetch W., Phromsurin K *et al.* Antibacterial and antioxidant effects of tropical *Citrus* peel extracts to improve the shelf life of raw chicken drumettes. *Int. Food Res. J.*, 2016; 23(2): 700-707.