

**A PHYTO-PHARMACOLOGICAL REVIEW ON CITRUS MAXIMA**

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**ABSTRACT**

Citrus fruits have been used worldwide due to their vibrant colors, pleasant flavor as well as aroma, citrus fruits as well as whole plants have many nutrient values. There are different species of Citrus as Sweet Orange (*C.sinensis*) Pamela (*C. maxima*), Citron (*C. medica*), and Lemon (*C. limon*). *Citrus maxima* is having good antioxidant properties which help in promoting good health as well as preventing disease. *Citrus maxima* is having hesperidin, naringenin, naringin, quercetin, scopoletin, honyodisin, xanthyletin, caffeic acid, 4 hydroxy connamic acid, vanillic acid as major phytoconstituents. *C. maxima* also reported for different pharmacological activities such as anticancer, antimicrobial, aflatoxigenic, cytoprotective, anti-glycation, hepatoprotective, nephroprotective and antibacterial activities.

**KEYWORDS:** *Citrus maxima*, Pharmacological activities, Phyto-Pharmacology.

**INTRODUCTION**

The plant *Citrus grandis* or *Citrus maxima*, which is known as pomelo belongs to the family Rutaceae. It is said to be the ancestor of grapefruit.<sup>[1-3]</sup> Some common names for *C. maxima* are *Pomelo, Bhogate, Shaddock, Papanus, Pummelo, etc.* These plants and fruits are found commonly in Asian regions such as India, Nepal, China, and Vietnam, and are commonly indigenous to China.<sup>[4]</sup> *C. maxima* is a popular species in which every part has pharmacological activity. Most of the pharmacological properties of the various parts of this plant are undiscovered.<sup>[5]</sup>

The bark and the root of *C. maxima* contain many bioactive chemical constituents which are used to treat many diseases. The bark and root contain alkaloids and coumarins. The leaves contain some amount of essential oils, little amount of tannins, polyphenols, flavonoids, etc and the fruit (unripped) contains some amount of limonin, geraniol, etc.<sup>[6]</sup> The ripped fruit can be eaten directly and also contains a good amount of vitamin C. Pomelo has a bit sweet and bitter tangy taste. *C. maxima* flowers can be used to treat diseases like sleep disorders and anxiety.<sup>[3]</sup>

*C. maxima* also shows different pharmacological activities such as anticancer potential, antimicrobial activity, aflatoxigenic activity, cytoprotective effect, anti-glycation, hepatoprotective and nephroprotective activity, antibacterial activities.<sup>[3]</sup>

**Plant Description**

**Taxonomical Classification**<sup>[6]</sup>

Botanical Name: *Citrus maxima*

Kingdom: Plantae  
Phylum: Tracheophyta  
Division: Magnoliophyta  
Family: Rutaceae  
Genus: Citrus

**Common Name:** pomelo, pomelo, bhogate, jabog, shaddock.<sup>[6]</sup>

**Vernacular name**<sup>[6]</sup>

Dialect	General name
Hindi	Chakotara
Manipuri	Nobab
Nepali	Bhogate
Bengali	Chakotra
English	Pomelo
Telegu	Pampara
Sanskrit	Madhukarkati
Japanese	Zabon

**Botanical Description**

**Tree:** 5-15 meters tall with trunk thickness of 12-30 cm. They have low branches with spines up to 1 cm long.<sup>[7]</sup>

**Leaves:** The leaves are oval, obligate, elliptical, 5-20 cm long, and 2-6 cm wide. The texture of the leaf is leathery.<sup>[7]</sup>

**Fruits:** The fruits are round or sometimes pear in shape with thick peel which can be removed easily. The taste of the fruit is sweet and sour, and the pulp of the fruits can be seen in pink or white color. The pulp is divided into segments.

Size may vary from 10cm to 30 cm wide.<sup>[7]</sup>

**Seeds:** The fruit contains less amount of seeds which are bitter and the color may be yellowish white and white inside.<sup>[7]</sup>

**Flowers:** Flowers are white and have some fragrance.

**Ecology:** Pommelo is a topical or sub-tropical fruit found in the low altitude area of 0-400 m and at temperatures of 25-30°C.<sup>[7]</sup>

#### Traditional Uses

Since human civilization, traditional medicine has been playing a major role in the treatment of ailments. Since the medieval period, traditional healers have been using *C.maxima* for its healing purposes like the treatment of gastrointestinal disorders, coughs, and fevers. In the present era of science and technology, it has become a topic of global interest. In Asian countries, *C.maxima* fruits are just not used for consumption as a food but the

various other parts are also recorded to be used widely by diverse folk populations as leaves oil of *C.maxima* are applied to treat skin disorders and abdominal pain.<sup>[10]</sup>

*C.maxima* has been used in traditional herbal medicine as a diabetic medication for diabetes.<sup>[8][9]</sup> The fruits and peels have been used as an appetizer, stomach -tonic, inflammation, cardiac stimulant, and cough. According to reports leaves can be used in epilepsy and cough. Decoction was used to treat swellings as well as ulcers.<sup>[11][12]</sup> Traditionally the fruit pulp is used in cosmetics. The study has also proven that it is used for ethnomedical values around the globe. The seeds are active against dyspepsia and coughs. Fruit juice is effective against weight gain and reduces cholesterol.

The roots and barks are said to have antimicrobial activity.<sup>[13][5][14]</sup> Due to the sweet aroma of *C.maxima* fruits, these are also used as a perfume, flavoring agent, fragrant enhancing agent, and cosmetics in the pharmaceutical industries.<sup>[15][16][17]</sup>

**Table 1: Traditional application of distinct parts of *C. maxima* in different regions.**

Segment	Application in various ailments	Region	Citation
Fruits pulp	Its juice is an appetizer, stomach tonic, antitoxic, and cardiac stimulant	Mediterranean region	[18]
Fruits	It is used to treat asthma, hiccough, epilepsy and leprosy	India	[19]
Fruits rind	Headache, abdominal griping, tonic and antiasthmatics	India	[19]
Fruits	The liquid is used to treat bumps and flakes	Kathmandu	[20]
Fruits	Diabetes mellitus	Nigeria	[21]
Leaves	Leaves can be chewed to eject the intestinal worms	Nepal	[20]
Fruit	Headache, flu, fever, sore throats, breathing disorders, and dyspepsia	Thailand	[22]
Fruits peel	The infusion of peel can be used to help with epilepsy, swelling, ulcers, and cough	Kenya	[23]
Fruits peel	High blood pressure and stoutness	Republic of China	[24]
Flowers and leaves	Lotion of leaves can be used to relieve painful inflammations. Flowers are used as a sedative in epilepsy, convulsive cough, cholera, nervous affections	India	[25]
Flowers, fruits, seeds and leaves	Their decoctions are used to treat gastric disorders, cough, and fever	The Philippines Islands and Southeastern Asia	[26]
Ethereal oil	Used as a sedative in cough, hemorrhagic shock, epilepsy, and nervous affection	India	[27]



Fig. 1.1: Citrus maxima tree Location: Majhitar East Sikkim.



Fig. 1.2: C.maxima bark Stem bark



Fig. 1.3: C.maxima leaf.



Fig. 1.4: C.maxima fruit

Fig. 1: Different Parts of Citrus maxima.

### Bioactive Chemical Constituents

*C. grandis* or *C. maxima* contains various chemical constituents that can be found in different parts of the plants. 2 varieties of citrus maxima are widely cultivated i.e. Malaysian *C.maxuma* with white and pink pulp respectively. The fruit contains many micronutrients such as Potassium, Phosphorus, vitamin B1, Vitamin B2, folic acid, vitamins, sugar, pectin, water, etc.<sup>[28][29]</sup> Besides *C.maxima* pulp, peel, and fruit, *C.maxima* seed also contains active compounds that show biological action. Although the seed is contemplated as a derivative of the fruit. Limolin and nomilin can be obtained from its seed.<sup>[4]</sup>

### Chemical constituents

#### Phenylpropanoids

Phenylpropanoid compounds discovered in the peel of *C.maxima* include eleuthero side B, chlorogenic acid, and caffeic acid.<sup>[30]</sup>

#### Essential oils

These are volatile substances that have the characteristic aroma of the source from which these are

obtained. The essential oil present in the peel of *C.maxima* belongs to the terpenoid group (sesquiterpenoids and monoterpenoids). The most dominant component is limolene.<sup>[30]</sup>

#### Phenolics

These are essential phytochemicals that are active to counter stress in plants. These consist of benzene rings with hydroxyl groups. Peel of *C.maxima* include 4-hydroxy-benzaldehyde, ellagic acid, methyl 4-hydroxybenzoate, and gallic acid.<sup>[31][32][33]</sup>

#### Terpenoids

*C.maxima* is enriched with terpenoids like deoxylimolin, nomilinic acid, nomilin glucoside, and limolin and are the prime terpenoids.<sup>[4]</sup>

#### Coumarins

It has also been identified to be present in *C.maxima* and the technique used to procure the compound was by solvent extraction. The separation of pure compounds can be carried out by using column chromatography. Few of the compounds acquired from *C.maxima* (peel) include

marmin, osthenol, umbelliferone, 7-hydroxy-8-(2'-hydroxy-3'-methylbut-3'-enyl)coumarin.<sup>[31][34][35]</sup>

### Flavonoids

Parts such as leaves and peel of the plants when studied showed that there are flavanoids present in good quantity. Flavonoids can be extracted by the process of ethanol extraction, methanol extraction, as well as use of

aqueous solvents. the separation of the pure compounds is done by using various chromatographic techniques. These studies concluded that there are various flavonoid components present like catechin(1.1) and epicatechin(1.2). The study also exhibited the existence of glycoside derivatives and they form the plant metabolites that produce sugar which gives the possibility that it contains sugar.<sup>[31][36][32]</sup>

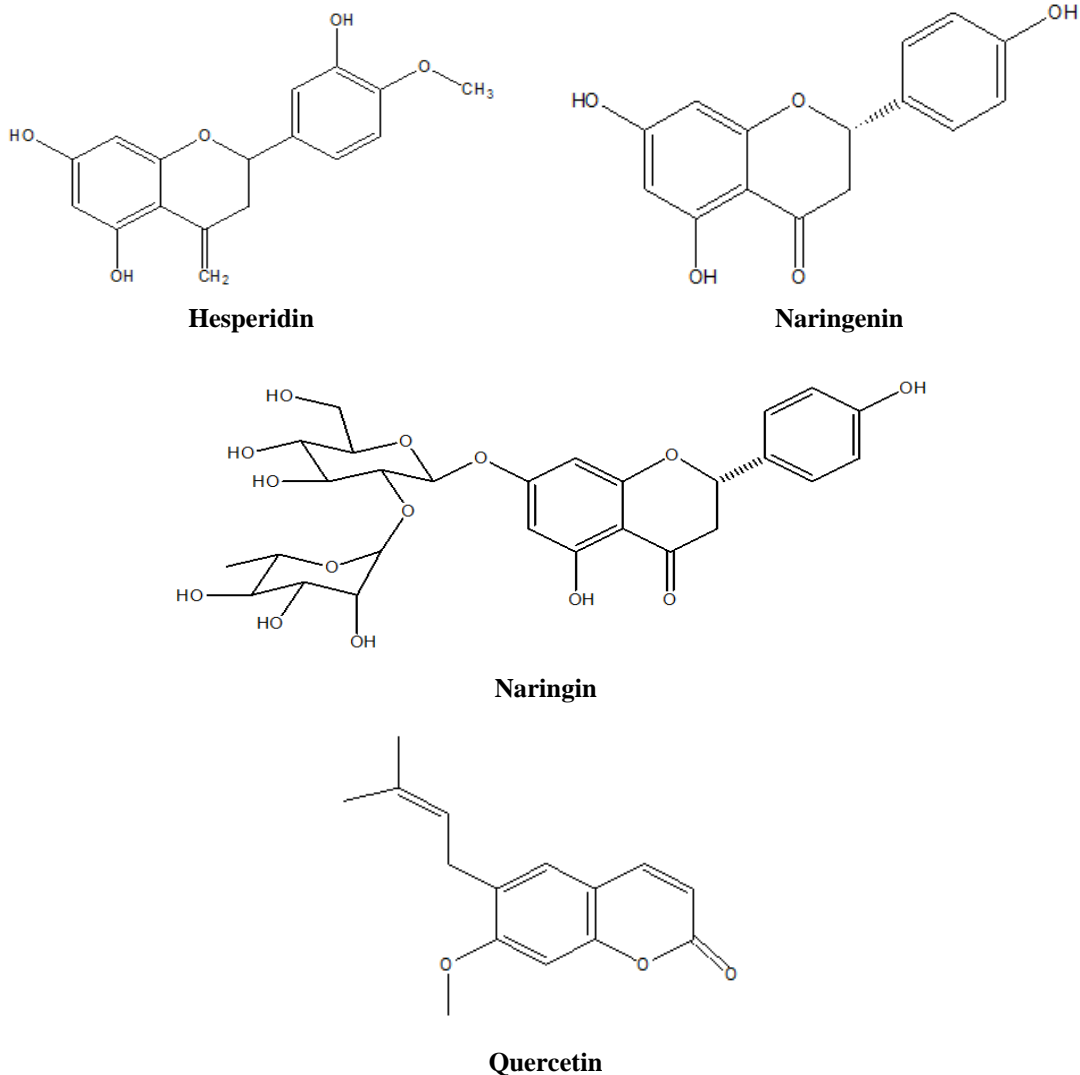
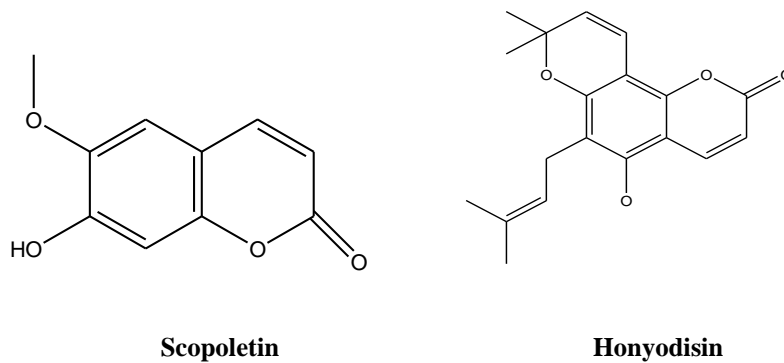
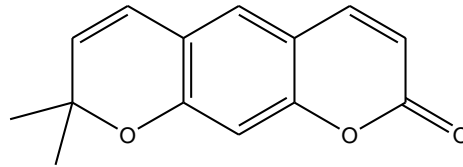
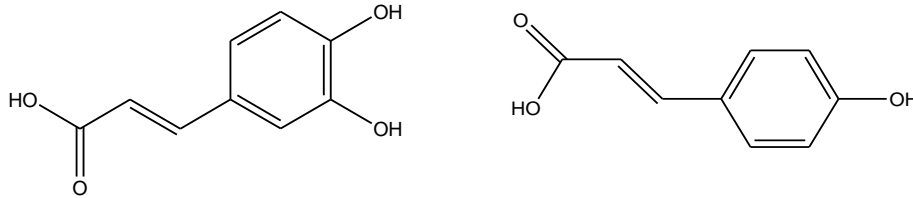


Fig. 2: Chemical structures of few flavonoids from *Citrus maxima*.



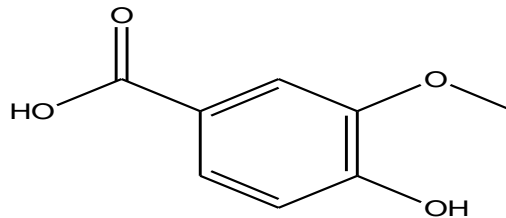


Xanthyletin

Fig. 3: Chemical structures of few coumarins from *Citrus maxima*.

Caffeic acid

4-Hydroxycinnamic acid



Vanillic acid

Fig. 4: Chemical structures of phenolic acids from *Citrus maxima*.

### Miscellaneous

Apart from the compounds stated above, other compounds such as L-ascorbic acid, pentadecanoic acid, succinic acid, decyl acetate,  $\alpha$ -tocopherol, tetradecanoic acid, citric acid, hexanal were isolated from peel, leaves, and fruit juice of *C. maxima*.<sup>[26][37]</sup>

### Pharmacological Activities

It is found that several studies have been performed on the pharmacological effects of *C. maxima* extracts and their isolated compounds. Pharmacological studies have provided accurate results regarding their use as traditional medicine. In this review we have accumulated available information and described the pharmacological properties, like Anti-oxidant potential, Anti-inflammatory activity, Anti-hyperlipidemia, Anticancer and Antitumor Activity, Anti-microbial Activity, Anti-fungal activity, anti-aflatoxicogenic activity, Cytoprotective Effect, Anti-Glycation, Analgesic activity, CNS Depressant activity, Anti-Alzheimer's Disease Activity, Anti-Obesity Activity.

### Antioxidant Activity

Free radicals are unstable atoms that are formed within the human body through various biochemical reactions and are likely to cause damage to the cells through oxidation.

When the generation of the oxidative stress exceeds the antioxidant capacity of the system it leads to oxidative stress in the cellular system.

Oxidative stress is one of the major causes that leads to aging and also leads to the development of numerous diseases like diabetes, cancer, neurodegenerative diseases, and respiratory tract disorders.<sup>[38]</sup>

To curb oxidative stress, the body produces a depot of anti-oxidants to defend itself. The antioxidant acts by neutralizing or disposing of the free radicals that harm the cells improved in the antioxidation status helps to minimize the redox imbalance and thus prevent or decrease the cause of developing many chronic age-related free radical-induced diseases. The body's internal production of antioxidants is not enough to neutralize all the free radicals so the intake of dietary antioxidants can help defend.

Methanolic leaf extract (200 and 400 mg/kg b w) was evaluated for its anti-oxidant property against paracetamol-induced hepatotoxicity in Wistar albino rats.

The leaf extract at 400mg/kg b.w showed a reduction in lipid peroxidation in paracetamol-treated rat liver as compared to the saline control. it also restores the

depleted catalase and reduces the glutathione levels in the paracetamol-intoxicated rat liver to its normal value. The existence of a few major phytochemicals might be the main reason for its antioxidant activity in *C. maxima*.<sup>[3]</sup>

**Antidepressant Activity:** Antidepressant activity may be defined as the mechanism involving neurotransmitters, transcription pathways, neurogenesis, anti-inflammatory, and immune pathways.

Antidepressants are mostly exploited for the remedy of tension and melancholy which affect the population. Evident studies on consternation and gloom can be performed on animals using an elevated plus maze and the enforced swim test. These studies help in the elucidation of antidepressant activity.<sup>[39]</sup>

The leaf extracts of *C. maxima* were evaluated in mice to determine antidepressant activity with the help of various models. The use of Fluoxetine (20mg/kg, i.p.) and imipramine (30mg/kg) as standard drugs. The leaf extracts will reduce the immobility time in both the Tail Suspension Test (TST) and the Forced Swimming Test (FST). The process of showing antidepressant activity was not shown, it could have been due to enhancement of norepinephrine neurotransmission in mice.<sup>[3]</sup>

Naringin is a depressant activity. But Naringin reduces brain acetylcholinesterase activity in mice brains. When taken together, the treatment with Naringin can be handy to construct functional behavioral effects through the process which are coupled to the intensification of cholinergic conveyance, free radical scavengers fortification mechanism, and inhibition of lipid oxidation.<sup>[40]</sup>

#### **Anticancer and Antitumor Activity**

The other name of cancer is Malignant carcinoma and it is a grade of disease in which the abnormal growth of cells in the body occurs which destroys the body cells.

*Citrus maxima* possess a strong anticancer activity which can be assigned to the flavonoids present in it. Flavonoids have a chemo-preventive role in cancer due to their effect on signal transduction on cell proliferation and angiogenesis. The flavonoids present in *C. maxima* are assumed to be the cause of anticancer and antitumor effects.<sup>[41]</sup>

The leaf extract of *C. maxima* was examined against Ehrlich Ascites Carcinoma (EAC) models in Swiss albino rats where the white blood cell (WBC) count was decreased and the lifespan was increased. Naringin showed strong antineoplastic properties in several practices. Naringin was administered on rats carrying walker 256 carcinosarcoma and showed a reduction in the growth of the tumor by 75% The antitumor activity of naringin which was loaded with lyotropic nanocrystals was evaluated on man lung epithelial carcinoma and

arteries epithelial obtain stratum germinativum. Especially the study of anti-colony formation, anti-migratory, and antiproliferative activity was done in which naringin LCNs showed anticancer properties by the inhibition of relocating and increasing properties of cells.<sup>[3]</sup>

#### **Anti-diabetic Activity**

Diabetes is a chronic disease resulting in increased blood glucose levels. The types of diabetes are Type 2, Type 1, Prediabetes, and Gestational diabetes.

The anti-diabetic activity on the foliole take-out of *C. maxima* was assessed in STZ-induced diabetic rats with the help of Glibenclamide utilized as the caliber. The blood glucose concentration was measured and was found to be normal in experimental animals than in the dominance class. The anti-diabetic undertaking of ethanolic take out of *C. maxima* leaf was evaluated in the case of alloxan persuades diabetes model in mice where the Glibenclamide was being used as the caliber.<sup>[3]</sup>

Polyphenols like Hesperidin and Hesperitin are found in citrus fruits and they possess pharmacological activities like anti-diabetic activity and neuroprotective activity, but they are decreased due to low solvability.<sup>[42]</sup>

#### **Anti-Alzheimer's Disease**

Alzheimer's is indicated by the presence of amyloid (A $\beta$ ) plaques and due to neurofibrillary tangles, which coincide with neurodegeneration. It is most common in older people. It is specified by the early salient loss of dopaminergic neurons in the substantia nigra pars compacta.<sup>[43]</sup> There is no currently available treatment for this particular disease, but citrus maxima have the properties to enhance cognitive effects and also refine motor and cognitive deficiency. The extract of citrus maxima is found to decrease the acetylcholinesterase levels in the brain. Anti-Alzheimer's activity is shown by the phytochemicals known as 'Naringin' which is found in the extract of citrus maxima.

In an experiment, Naringin (40 and 80 mg/kg, p.o.) exhibited anti-Alzheimer's properties in colchicine enticing cognitively impaired rats through the Morris water maze methods and elevated plus maze. About (15  $\mu$ g/5 mL) Colchicine was given intracerebroventricularly which resulted in weak memory hold and lessened acetylcholinesterase project. The anti-Alzheimer's activity might be due to the occurrence in the reasonable act and lessening oxidative stress by decreasing propane-dial and nitrite degree.<sup>[44][45]</sup>

#### **Anti-inflammatory and analgesic Activity**

The body's natural defense mechanism that protects the body from foreign particles is called inflammation and it engages in the main role in the healing process.

Due to the existence of Polysaccharides in *C. maxima*, they have anti-inflammatory activity. Auraptene,

Isoauraptene, and Meranzin hydrate present in *C. maxima* peel showed depletion in swelling after intraperitoneal injection for 3 repeated days in the mice.<sup>[43]</sup>

Anti-inflammatory activity was shown in rats by evaluating the use of Formalin, Carrageenan-induced severe rat paw edema replica. Various studies have shown that the process in charge of analgesic and anti-inflammatory are because of the inhibition of prostaglandin synthesis. And also the existence of flavonoids and their specific aglycones like Hesperitin and Naringenin can be the cause for influential anti-inflammations and analgesic activity.<sup>[3]</sup>

Several characteristics of *C. maxima* also show analgesic activities. The methanolic take out of the peel of *C. maxima* was inspected by the Formalin-induced defeat and biting model and also an acetic acid-persuade suffering model. In other procedures, the analgesic activity of leaves, stems, and fruits were differentiated with the help of the tail-flick process in rats, acetic acid-induced writhing, and hot plate process in mice. The outcome showed analgesic venture in all the models.<sup>[3]</sup>

#### Anti-microbial activity

The process by which the virus or bacteria can cause chemical and biological changes in cells or organisms is called microbial activity. Various studies on anti-microbial activity have been conducted and it showed that according to ANOVA and Tukey's comparison tests, different concentrations of essential oils were found effective in case of fungal growth in in-vitro. Several species of *Aspergillus* like *A. alternate*, *A. niger*, etc were taken and found that 750ppm of essential oils were present in it.<sup>[43]</sup>

The ethanolic extract of *C. maxima* leaf showed anti-microbial activity towards *Pseudomonasaeruginosa* and *Escherichiacoli*. The pulp and seed extract also showed anti-microbial venture as opposed to *Bacillussubtilis*, and *Staphylococcus aureus*. The appearance of Naringin and Hesperidin can be the cause for anti-microbial activity. The remarkable anti-microbial venture of ethanolic and saturated extract of *Citrus maxima* leaves against *Fusarium moniliforme*, and *Aspergillus niger* were reported.<sup>[3]</sup> *Citrus* crucial oils are as well known to possess or carry anti-microbial activity. They show antimicrobial activity against *Lactobacillus*, the main genus of bacteria that contaminates the fermentation process.<sup>[46]</sup>

#### Hepatoprotective Activity

The essence of *Citrusmaxima* contains compounds that can reduce the damage caused by hepatotoxic substances. In a research hepatoprotective consequence of *Citrus maxima* in methanolic leaf extract (200mg/kg,b.w) was scrutinized in acetaminophen-cause cirrhosis in mice, in the experiment the foliole takeout of *Citrusmaxima* was allotted for a maximum of 7 days, on

the 5<sup>th</sup> day paracetamol (2g/kg) was given, and the standard drug used was silymarin (100mg/kg, b.w), after that the liver was withdrawn and the liver function markers, total bilirubin, total protein in blood serums and hepatic antioxidants in liver homogenate were observed and found to be normal as collated to the control group. The presence of this activity is due to its antioxidant characteristics. it shows the extract can overall inhibit ROS that may lead to the depletion in the oxidative damage to the hepatocytes and enhance the activity of the liver antioxidant enzymes, which leads to protecting the liver from paracetamol-induced damage.<sup>[45][46]</sup>

#### Anti-obesity activity

Obesity is a disease specified by unneeded body weight which is related to chronic subclinical inflammation caused by an increase in adipokines in the body.

The ethanolic decoction of the leaf of *Citrus maxima* for anti-obesity activity was performed towards olanzapine-induced and cafeteria-induced obesity in rats. The body weight, temperature, and serum parameters were assessed and established to be remarkably decreased in their principles in contrast to the obese dominant group. Hesperidin also controls the glucose and lipid metabolism and accidentally eases NF- $\kappa$ B showing methods to dominate inflammation which in turn helps in dominating obesity.<sup>[3]</sup>

#### Cytoprotective effect

Cytoprotective is a procedure where the reagent mixture issues conservation to cells as opposed to dangerous agents. A study showed that the use of *C. maxima* in food protected the cells from Doxorubicin-induced cytotoxicity, enlarging the phase 2 enzyme activity and advancing the metabolism of cytotoxic agents in rats. The appearance of antioxidant compounds like phenolics, flavonoids, vitamins, etc reduces oxidative stress. Doxorubicin-treated mice decreased Glutathione S Transferase (GST) which is required to protect the cellular macromolecules from the electrophiles. However, the addition of *Citrus maxima* fruit fluid reversed the Doxorubicin effect by increasing the enzyme activity.<sup>[43]</sup>

#### CONCLUSION

*Citrus maxima* has various nutritional and medicinal uses. The different parts of the plant such as bark, leaves, fruits, fruit pulp, fruit juice, flowers, ethereal oil, and seeds have different medicinal properties such as treating intestinal worms, reducing inflammation, treating, gastric disorders, treating asthma, epilepsy, flakes, diabetes mellitus, cardiac stimulants, stomach tonic, cough, fever, and hemorrhagic shock respectively.

According to several studies, it has shown that *C. maxima* has different pharmacological activities like anti-oxidant, anti-hyperlipidemia, anti-cancer, anti-microbial activity, cytoprotective, anti-depressant, anti-alzheimer and anti-obesity activities.



*C. maxima* contains various chemical constituents under chemical classes such as phenylpropanoids, essential oils, phenolics, coumarins, terpenoids, flavonoids, and other miscellaneous compounds.

According to the studies the *C. maxima* has ethnomedicinal values. Due to their medicinal and nutritional properties, mass cultivation can benefit the local farmers in India and it is commonly found in Asian regions.

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