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Pomelo: A brief review on ethano-medicinal and therapeutic applications

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Abstract
Pomelo (*Citrus maxima or Citrus grandis Osbeck*), a member of the Rutaceae family, is recognized as the largest citrus fruit and is available in a range of flesh colors, including red, pink, light pink, and white. It is a rich source of bioactive compounds such as phenolic acids, flavonoids, anthocyanins, and tannins, along with essential vitamins A and C, which collectively contribute to its high nutritional and therapeutic value. The predominant phytochemicals—hesperidin, narirutin, naringin, and their aglycone form, naringenin—are largely responsible for the fruit's functional properties. Despite being abundant in proteins, carbohydrates, minerals, essential oils, polysaccharides, and aroma-active volatiles, significant portions of the fruit, including the peel, pomace, and seeds, are typically discarded as agricultural waste. Numerous in *vitro* and in *vitro* studies have demonstrated the bioactive potential of these byproducts, revealing a wide array of biological activities such as antioxidant, antimicrobial, hypolipidemic, hypoglycemic, anti-inflammatory, and anticancer effects. In traditional medicine systems, particularly across Southeast Asia, pomelo has been used for its ethnomedicinal benefits in the treatment of ailments including cough, fever, asthma, ulcers, wounds, and gastrointestinal issues. Moreover, its extracts have been applied as natural sedatives, detoxifying agents, and remedies for metabolic disorders such as diabetes and hypertension. This review underscores the nutritional, therapeutic, and ethnomedicinal significance of pomelo and its derivatives, highlighting their promise in the development of functional foods and their potential role in promoting sustainable agricultural utilization.

Keywords: *Citrus grandis*, phytochemicals, hepatoprotective, anti-alzheimer's disease, anxiolytic

Introduction

Pomelo is a member of the family Rutaceae and is characterized by its large, spherical to pear-shaped fruits, thick rind, and sweet to slightly tangy pulp. The fruit can weigh up to 2 kilograms and measures between 15 to 25 centimeters in diameter. The plant *Citrus grandis or* pomelo, popularly known as Chakota in India, and grown in tropical, sub tropical and temperate regions. The fruit has two variations are pink – fleshed and pale - fleshed. The pink-fleshed variant is more prevalent in India. The pomelo tree is evergreen, with fragrant white blossoms and glossy, dark green foliage and a robust structure that allows it to thrive in tropical and subtropical climates. (Deb *et al*., 2024) [11].

Pomelo is predominantly cultivated in Southeast Asian nations such as Thailand, Malaysia, Indonesia, Vietnam, and the Philippines. It has also been successfully introduced to regions like India, China, and parts of the Caribbean and Central America. The adaptability of pomelo to various climates and soil types has facilitated its widespread cultivation.

Pomelo fruit is one of the largest citrus fruit; it is round, green in color, and range in width from 10 to 30 cm and depending on the cultivar up to 1 to 2 kg in weight. The history of pomelo usage and cultivation dates back 4,000 years. (Puglisi *et al*., 2017) [30]. The fruit known as various names, including chakotra, papanus, pummelo, shaddock and etc. in various parts of India.It is simple to separate the pulp from the skin. Usually the pulp has a coarse texture, pink or white color, and huge, spindly juice sacks. Because of its enormous shape and vibrant peel when fully mature, it is frequently grown as an attractive fruit. (Singh 2017 and Ani,2018) [3, 41].

The flavonoid naringin, which is present in citrus fruit tissues, is the compound that gives them their bitter taste. However, limonin, which is present in many fruit juices, is the cause of delayed-type bitterness. Naringin is the cause of immediate bitterness. (Sanjay,2021) [33].

The usage of pomelo in traditional medicine is incredibly historical, especially in the regions where it is native. Various parts of the pomelo tree, including the fruit, peel, leaves, and flowers, have been utilized for their medicinal properties. Traditional healers have employed pomelo in treating a wide range of ailments, from digestive disorders and respiratory conditions to skin problems and infections. Pomelo is a nutritional powerhouse, rich in essential vitamins, minerals, and bioactive compounds. It is especially well- known for having a high vitamin C content, which is essential for strengthening the immune system, supporting healthy skin, and improving the body's ability to absorb iron from plant-based diets. Pomelo also has high levels of potassium, dietary fibre and antioxidants such as carotenoids and flavonoids. These nutrients contribute to its potential health benefits, including improved digestive health, cardiovascular support, and anti-inflammatory effects. Pomelo is not only a delicious and nutritious fruit but also a valuable source of medicinal and therapeutic compounds. Its rich ethnomedicinal history and the growing body of scientific evidence supporting its health benefits make it a feasible choice for additional study and advancement in the discipline of alternative treatments. This comprehensive review aims to delve into the ethno-

medicinal and therapeutic applications of pomelo, providing a holistic understanding of its potential benefits.

Production and distribution of worldwide

Citrus grandis (L.)*Osbeck*, often known as the pomelo, is the largest kind of citrus fruit .A native citrus fruit belonging to the Rutaceae family is the pomelo. The Pomelo is a native citrus fruit that is a member of the Rutaceae family. Its origins are in the regions of Indo-China and Southeast Asia, both of which are tropical and subtropical. Table 1 summarizes the world's highest production of pomelo fruits based on planted area. It demonstrates that China (10 million tons/year), Vietnam (approximately 657 660 tons/year), and the United States (about 558 830 tons/year) are the three countries that produce the most grapefruits, including pomelo.China is the world's largest producer of pomelos, consistent with having the largest planted area (179, 823 13 ha). This indicates that annual production is 55.73 tons per hectare. Other nations including Malaysia, China, and Thailand have also grown pomelo. The pomelo types found in Malaysia, Thailand and China.

Table 1: Lists the top ten pomelo- producing regions in the globe based on planted area and volumes produced

Worldwide ranking	Nation	Area planted (ha)	Producing (tonnes)
1	China	179,823	10,022,099
2	Vietnam	86,370	657,660
3	United States of America	20,113	558,830
4	Mexico	18,823	459,610
5	South Africa	14,472	445,385
6	India	10,572	257,750
7	Turkey	5,182	250,000
8	Sudan	19,382	234,388
9	Thailand	24,664	219,838
10	Israel	2,259	148,896

Source: FAO (2018)

Ethano-medicinal

Traditionally, medicine has been a vital component of human health management, illness prevention, and treatment since the dawn of civilization. It's become a worldwide issue of curiosity even in this day of science and technology. Because of its many therapeutic benefits, *Citrus grandis* has proven promoted in traditional herbal medicine. The fruits of *Citrus grandis* are not the only portions of this plant that are utilized in traditional medicine in several Asian nations. For example, the leaves of the plant are used as an oil to cure headaches, stomachaches, and skin conditions (Tsai *et al.,* 2017) [46].It has been reported that a wide range of folk populations constitute extensive use of the plant's several portions. In traditional medicine, fruit peels are frequently used to treat epilepsy, cough, edema, and other conditions. They are also used cosmetically(Thavanapong N *et al.,* 2010) [44].*Citrus grandis*blooms are used to treat anxiety and sleep difficulties, while fruits are used to cure mental disorders, asthma, leprosy, coughing, hiccups, and epilepsy(Duan L *et al.,* 2014) [15]. Because *Citrus grandis* fruits are widely employed as flavoring or fragrance-enhancing agents in the food, perfume, cosmetics and pharmaceutical industries due to their sweet scent. (Van Hung P *et al.,* 2013) [48].*Citrus grandis* is also used to decrease cholesterol and encourage weight loss. (Sidana J *et al.,* 2013) [40]. Figure 1 illustrates a photographic representation of *Citrus grandis*(L.) *Osbeck* fruit (Anmol *et al.,* 2021) .

Fig 1: A photographic representation of a *Citrus grandis* (L.) *Osbeck* fruit (Anmol *et al.,* 2021).

Fruits are used as a digestive aid, heart stimulant, appetizer, and diarrhea cure (Borah M.*et al.,* 2012) [7], antipyretics ,cough,obesity, leprosy, mental health issues, asthma, and epilepsy. Traditionally, pulp has been utilized for cosmetic purposes(Sapkota *et al.,* 2022) [34].The seeds are applied topically for lumbago, dyspepsia, and coughing. The foliage is used to cure convulsive cough, cholera, and epilepsy; the decoction can be applied topically to soresand swellings(S. Das *et al.,* 2013) [10]. Table 2 provides details on the plant's traditional uses.

Table 2: Traditional uses of various *Citrus grandis* parts in different countries

Parts	illness and mode of application	Areas	References
Fruits	The juice is used for dandruff and zits.	Nepal	Dhami (2008) [12].
	Diabetes	Nigeria	Oyedepot and Babarinde (2012)
	Headache, fever, illness, sore throats, dyspepsia, and breathing problems	Thailand	Hutadilok *et al.*,(2006) [21, 28].
	Asthma, epilepsy, mental abnormalities, coughing, and hiccoughing	India	Kharjul *et al.*,(2012) [23].
Fruits rind	Antiemetics, gripping in the abdomen, diarrhoea, headache, and brain tonic	India	Kharjul *et al.*,(2012) [23],
Essential oil	Sedative for epilepsy, convulsive cough, hemorrhagic illnesses, and nervous disorders	India	Potdar and Kibile (2011) [29],
Fruits peel	Coughs, swellings, ulcers, and epilepsy have all been treated with a peel decoction.	Kenya	Njoroge *et al.*,(2005) [26],
Leaves, flowers,	As infusions to cure fevers, coughing, and	The Philippines and southeast	Sawant and Panhekar(2017) [35].

fruits, and seed	stomach issues	Asia	
Leaves and flowers	As a sedative for nervous illnesses, cholera, epilepsy, convulsive cough, hemorrhagic ailments, and as a lotion made from boiling leaves for sore swellings	India	Khare(2007) [22].
Fruits peel	Hypertension and obesity	China	Hong *et al.,*(2010) [20],
Leaves	Chewing leaves helps remove intestinal worms	Nepal	Dhami(2008) [12].
Fruits pulp	Pulp juice as a heart stimulant, appetiser, stomach tonic, and antitoxin	Mediterranean region	Arias and Ramon (2005) [4].

Therapeutic Applications

Citrus grandis's pharmacological characteristics are illustrated in the Figure 2.

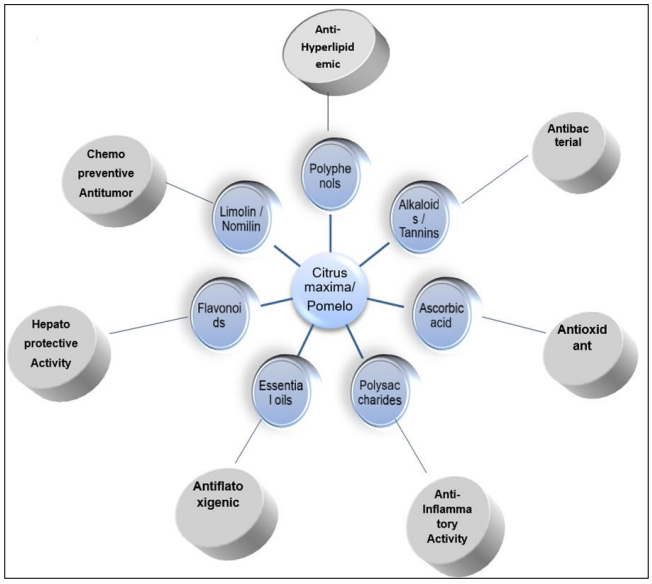

Fig 2: *Citrus grandis* Pharmacological Characteristic

1. Antioxidant Potential

The human body constantly produces unstable atoms called free radicals through a variety of metabolic processes. One mechanism by which free radicals might damage cells is oxidation, a process linked to the onset of cancer, atherosclerosis, Parkinson's disease, Alzheimer's disease, and other ailments. Foods containing functional units hydroxylated (OH) are believed to possess antioxidant potential since they give free radicals their electrons, preventing oxidative damage (Koleva II *et al.,* 2002) [24]. Flavonoids, polyphenols, and ascorbic acid are antioxidants found in abundance in *Citrus grandis*. These compounds effectively counteract the effects of free radicals, with polyphenols being the key component preventing oxidative damage(Tsai HL *et al.,* 2007) [47]. Oxidation stress is a outcome of free radicals, and *C. grandis* contains flavonoids, ascorbic acid and polyphenolic substances that primarily prevent this damage by scavenging free radicals. In the study by Dulay et al. (2016) [16], the antioxidant activity of leaf extracts from C. maxima and two other plants, C. microcarpa and C. aurantium, was examined using the 2,2-diphenyl-1-picrylhydrazyl (DPPH) scavenging assay. The results showed that Citrus microcarpa had the highest antioxidant capacity (48.67%), followed by *Citrus grandis* (43.51%), and Citrus aurantium (lowest antioxidant capacity). Fidrianny et al. (2016) [18]. verified the antioxidant capacity of the peel, leaves, and cortex extracts using the phosphomolybdenum and DPPH tests. According to the data, the ethyl acetate leaf extracts had an IC50 value of 101.36 µg/ml for the phosphomolybdenum assay, while the ethyl acetate extract of cortex had the lowest IC50 value of 0.68 µg/ml for its DPPH scavenging activity.

2. Antihyperlipidemic Activity

Hyperlipidaemia, a type of metabolic disorder brought on by high blood triglyceride and cholesterol levels, can be avoided by blocking pancreatic lipase, which postpones the breakdown of triglycerides into absorbable free fatty acids. (Birari *et al.,* 2007) [6].

Phenolic chemicals from the pulp of six different *Citrus grandis* cultivars demonstrated potent antioxidant and antihyperlipidemic properties, according to a study by Makynen *et al.,* (2013) [14, 25], This investigation showed that the pancreatic lipase and cholesterol esterase enzymes were blocked by the aqueous methanolic extract of C *Citrus grandis* pulp, preventing hyperlipidaemia. It also had a connection to primary bile acids, which made cholesterol less soluble in micelles. Fruit pulp extract is a helpful anti-hyperlipdemic drug due to its solubility and interaction with the enzymes that break down cholesterol.

3. Anticancer Potentials

Research on *Citrus grandis's* natural components is ongoing in an effort to slow the growth of cancer. Through the use of DPPH radical-scavenging activity and FRAP assays, *Citrus grandis* has been found to have antioxidant potential. Through a variety of intricate biochemical processes, antioxidants function as bioactive reducing agents, neutralizing free radicals created by the body. These radicals can cause a number of severe and possibly life-threatening illnesses, including cancer(Tsai *et al.,* 2017) [46]. Particularly limonin and nomilin, the limonoids derived from *Citrus grandis* seeds, have been shown to have chemopreventive bioactivities, including the ability to scavenge free radicals (Yu *et al.,* 2015)and induce glutathione S-transferase. It has been shown that when *Citrus grandis* methanolic extract is administrated intraperitoneal, the tumour volume decreases and the survival and number of non-viable tumour cells rise.

In 2015, Sen and Samanta investigated on the studied on the *Citrus grandis* (MECM) leaf methanol extract's anticancer effectiveness using Swiss albino mice and the Ehrlich Ascites Carcinoma (EAC) cell line. The EAC control mice were given MECM for nine consecutive days. As a result, body weight, haematological parameters, and life span all increased dose-dependently, but tumour characteristics like viable tumour cell count and tumour volume decreased. The antitumor effect of intraperitoneally injections of MECM at 200 and 400 mg/kg was proven. *Citrus grandis* contains flavonoids and limonoids, which have been shown in studies to mediate anticancer and anti-inflammatory effects. (Sen T and Samanta SK, 2015) [37].

4. Anti-Alzheimer's Disease Activity

Alzheimer's disease is a gradual degenerative neurological condition that mainly affects the elderly. Using Ellman's

colorimetric and scopolamine-induced Alzheimer's procedures, fruit peel extracts from Citrus grandis shown significant anti-Alzheimer's activity in ethanolic, hexane, ethyl acetate, and aqueous solutions respectively. In a similar vein, leaf extract was discovered to have anti-Alzheimer's properties and to lower brain acetylcholinesterase levels. (A. Roohbakhsh *et al*., 2014) [32]. Naringin (40 and 80 mg/kg, p.o.) showed anti-Alzheimer's effect in colchicine-tempted cognitively impaired rats, as evidenced by the Morris water maze and elevated plus maze procedures in the study by Sohi S. *et al.,* (2018) [43].Following the intracerebroventricular administration of colchicine (15 µg/5 mL), memory retention is impaired and acetylcholinesterase activity is decreased in both mice. The anti-Alzheimer's effect may be explained by decreased oxidative stress brought on by lowering nitrite and malondialdehyde levels as well as potential improvements in cognitive function. It might also be because superoxide dismutase, catalase, and glutathione S-transferase had returned to normal in the mice under examination, while acetylcholinesterase and glutathione levels were decreased.

5. Antimicrobial Activity

a. Antibacterial Activity: The antibacterial qualities of *Citrus grandis* have been the subject of numerous investigations. The study conducted by Das S. *et al.*, (2013) [10]. proved the antibacterial effectiveness of ethanolic leaf extract against Pseudomonas aeruginosa and Escherichia coli. Using the disc diffusion method, the ethanolic pulp and seed extracts showed antibacterial activity against Escherichia coli, Bacillus subtilis, and Staphylococcus aureus. In a different study Sahlan M. *et al.,* (2018) [36]**,** methanolic extracts of leaves, seeds, and fruit, peels and barks against Staphylococcus aureus, Klebsiella pneumonia, and Escherichia coli. When it comes to Klebsiella pneumonia, pulp extract had the largest zone of inhibition (201) at 26 mm, while none of the other extracts displayed any appreciable ZOI. The pulp's aqueous extract showed the strongest antibacterial activity (ZOI of 27 mm) when tested for Staphylococcus aureus Yathiender S., (2017) [50]. Its antibacterial properties can be explained by the presence of naringenin and hesperidin.

b. Antiflatoxigenic Activity: Aspergillus flavus and Aspergillus parasiticus are two fungus that generate aflatoxin, a mutagen and poison that causes cancer. IAs per a study conducted by Singh *et al.,* (2010) [42]. In SMKY broth (200 g sucrose, 0.5 g MgSO47H20, 0.3 g KNO3, 7.0 g yeast extract, 1000 ml distilled water, pH 5.60.2), essential oils (EOs) of C. grandis and C. sinensis, as well as their combination at 500 ppm, totally suppressed allatoxin B1 (AFB1). As such, the essential oil of C. grandis combined with the essential oil of C. sinensis can prevent the growth of aflatoxin.

6. Antidiabetic Activity

Shibata *et al*., (1995) [39]. and Chen ***et al***., (2007) [8]. have provided illustrations of both the pancreatic alpha-cells' reduction of glucagon release and the inhibition of beta-cell glucotoxicity by steviosides, which could lead to an antioxidant effect. *Citrus grandis* fruit juice was tested in vitro for its capacity to inhibit o-amylase and a-glucosidase in a study by Abirami *et al*., (2014) [1], Fruit juice showed a-amylase inhibition of 75.55%–79.75% and a-glucosidase inhibition of 70.68%–72.83%. The hypoglycemic property of fruit juice was investigated utilising a streptozotocin (STZ)-induced model of diabetic mellitus. The reason for the difference in glucose levels between the experimental and control rats was either the peripheral utilisation of glucose or the inhibition of gluconeogenic enzymes.(A.Oyedepot and S. O. Babarinde., 2012) [28].

7. Hepatoprotective Activity

For the metabolism, separation, storage, and detoxification of both endogenous and exogenous chemicals, the liver is an essential component organ. Free radicals and oxidative stress increase the severity of liver damage, which can be lessened by the antioxidant system. Plant extracts are the best source of these antioxidants, which also have hepatoprotective properties. (PubMed)

According to Feksa D.L. *et al.,* (2017), the hepatoprotective effects of C. maxima leaf and peel extracts were found to lessen the hepatotoxicity caused by carbon tetrachloride in Wistar rats. This was demonstrated by the experimental rats' significantly lower levels of aspartate aminotransferase (AST), alanine transaminase (ALT), and alkaline phosphatase (ALP). The hepatoprotective effects of C. maxima methanolic leaf extract (200 mg/kg, b.w.) in rats exhibiting hepatotoxicity induced by paracetamol were examined in a different study. In this trial, the standard treatment was silymarin (100 mg/kg, b.w.), leaf extracts were given for seven days, and on the fifth day, paracetamol (2 g/kg) was given. total bilirubin, liver function indicator analysis, and liver removal. blood serum total protein, and when compared to the control group, the hepatic antioxidants in liver homogenate showed normal levels. By increasing the levels of hepatic antioxidant enzymes, liver extracts possessing antioxidant properties have the potential to reduce hepatocyte deformation.

8. Anti-obesity Activity

In a research by Dinesh S.S. *et al*., (2016) [13], the potential of ethanolic leat extract (200 and 400 mg/kg) to prevent obesity was compared to two different methods of causing obesity in rats: the cafeteria diet and glanzapine. It was discovered that measurements of serum purameters, body temperature, and body weight were substantially lower than those of the obese control group. For eight weeks, Ding *et al*., (2013) gave the mice a peel extract from C. maxima and a Chowmsal. Together with ethanolic lowering serum insulin and liver fat levels, the diet also significantly decreased taste blood glucose levels.Furthermore, hesperidin regulates the metabolism of fats and carbohydrates and indirectly stimulates NF-kB signalling, which lowers inflammation and helps manage obesity; these findings have been illustrated in both investigations.by Xiong H. *et al*., (2019) [49]. and Akiyama S.*et al*., (2010) [2].

9. Anti-Inflammatory Activity

The natural defense system of the body, inflammation aids in the healing process and shields the body from foreign intruders.In the research conducted by Shah NN. *et al*., (2015) [38],*Citrus grandis*polysaccharides have the ability to reduce inflammation. *Citrus grandis* has anti-inflammatory properties, as demonstrated by a study on clinical patients and ammonia-stimulated rabbits, which found that the fruit's

polysaccharide content both reduced chronic inflammation and alleviated symptoms. After a 14-day course of treatment with PCG (Polysaccharides of *Citrus grandis*), inflammatory symptoms significantly decreased in 14 individuals with chronic pharyngitis ($p < 0.01$). In an animal model using a combination of ammonia spraw and subcutaneous turpentine oil injection, inflammatory symptoms significantly decreased after a 14-day course of treatment with PCG (Polysaccharides of *Citrus grandis*) ($p < 0.01$). This further explored the potential of PCG to reduce chronic inflammation. This model was designed to assess the consequences of oral PCG use. PCG treatment reduced the high levels of inflammatory mediators in rabbits with chronic pharyngitis, including IFN-a, IL-2, and IL-4. In an animal model of chronic pharyngitis, exogenous PCG treatment ($p < 0.01$) demonstrated dose-dependent suppression of chronic inflammation, which was consistent with clinical data findings. 120 It has been shown in several investigations that increased release of inflammatory mediators is a result of NF-kB activation. (Chen L *et al.*, 2007) [8].

10. Other Uses

The distinctive flavor of *C. maxima* fruits makes them effective preferences for breakfast. In food, medicine, cosmetics, and fragrance products, peel oil is utilized as a flavoring agent. (S.M. *et al*., 2005)Because of its invigorating and fragrant qualities, its essential oils are also included in products for toiletries and insecticides. (L. Biao, *et al*., 2012) [5]. Jellies and candies are made from the pectin found in rinds, and wood can be used to make useful tool handles. (C. Orwa *et al*., 2009) [27].

Table 3: Therapeutic Applications of *Citrus grandis*

S.No.	Activity	Extracts and compounds tested	Mechanism of Action	References
1.	Antioxidant	leaf extracts	DPPH assay show highest antioxidant capacity of *C. macrocarpa*	Dulay *et al.*, (2016) [16],
		extracts from the peel, leaves, and cortex	the phosphomolybdenum assay revealed that the IC_{50} value of ethyl acetate leaf extracts was 101.36 μg/mL. Conversely, the cortical ethyl acetate extract exhibited the lowest IC_{50} value in terms of DPPH scavenging action, at 0.68 μg/mL .	Fidrianny *et al.*, (2016) [18].
2.	Antihyperlipidemic	pulp	the aqueous methanolic extract decreased the amount of cholesterol that was soluble in micelles by inhibiting the enzymes pancreatic lipase and cholesterol esterase	Makynen *et al.*, (2013) [25].
3.	Anticancer	leaf extract	growth in life expectancy, haematological parameters, and body weight while decreasing tumour parameters	Sen T and Samanta SK., (2015)
4.	Anti-Alzheimer's Disease Activity	rats	reduction in oxidative stress by reducing malondialdehyde and nitrite levels as well as improvement in cognitive function	Kumar. *et al*., (2010)
5.	Antibacterial Activity	ethanolic leaf	demonstrated ability to combat Pseudomonas aeruginosa and Escherichia coli with antibacterial activity	Das S. *et al.*, (2013) [10].
6.	Antiflatoxigenic Activity:	essential oils	a total suppression of Aflatoxin B1(AFB1) in broth made with SMKY	Singh *et al*., (2010) [42].
7.	Antidiabetic Activity:	*C. maxima* fruit juice	The decreased glucose levels in the experimental rats compared to the control cats may be due to peripheral glucose utilisation or inhibition of gluconeogenic enzymes.	Abirami *et al.*, (2014) [1].
8.	Hepatoprotective Activity:	leaf and peel extracts	decreases in the enzyme levels aspartate aminotransferase (AST), alanine transaminase (ALT), and alkaline phosphatase (ALP)	Feksa D.L. *et al.*, (2017)
9.	Anti-obesity Activity	leaf extract	body weight, temperature and serum and body parameters all decreased in value	Dinesh S.S. *et al.*, (2016) [13].
10.	Anti-Inflammatory Activity	rabbit and patient	increased release of inflammatory mediators is the result of NF-kB activation	Shah NN. *et al*., (2015) [38].

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