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Review Article

Brief review study on citrus fruits: Blessing of nature

Sudeshna Sengupta#, Sayantani Biswas#, Aheli Pradhan# and Malavika Bhattacharya*

* Department of Biotechnology, Techno India University west Bengal 700091

ABSTRACT

The term "citrus" originated from the Latin form of the Greek word 'Kedros', referring to trees such as pine, cedar, and cypress. Citrus is a widely recognized as one of the world's important fruit crops. This genus encompasses flowering trees and shrubs within the Rutaceae family. Citrus fruits are abundant in ascorbic acid and citric acid, contributing to the reinforcement of the immune system by stimulating the production of white blood cells. Additionally, these fruits contain significant levels of macronutrients which include dietary fiber, potassium, folate, thiamine, phosphorus, magnesium, riboflavin, and Vitamin B6. Citrus fruits are also denoted as acid fruits owing to their soluble solids comprised of organic acids and sugar. They are noteworthy for their antioxidants and anti-inflammatory properties. While the seeds of these fruits can generate new trees, they are inedible and considered waste products. The findings indicate that citrus seeds contain various macronutrients, including protein, carbohydrates, vitamins, flavonoids, carotenoids, alkaloids, limonoids, and essential oils. They also demonstrate potential antimicrobial activities, with reports suggesting components such as anticancer (e.g., Taxol), antiviral, chemotherapeutic, and other bioactive constituents, further highlighting citrus fruits' pivotal role as essential components in functional food. This study concludes that the nutraceutical values of citrus fruits also bear implications for agro-industrial waste management, given their distinctive attributes.

KEY WORDS: Valorization, nutraceuticals, antimicrobial, vitamin C, citrus seeds, anticancer effects, antioxidant.

Introduction

The most traded agricultural crop worldwide is citrus, which is the biggest genus in the Rutaceae family. Australia and Southeast Asia are the origins of citrus.(Thakur & Kumari, 2022). With over 160 genera, the Rutaceae family comprises flowering plants. Family members who hold the greatest financial significance include Citrus aurantifolia (lime), Citrus maxima (pomelo), Citrus limeta (sweet lemon), Citrus sinensis (sweet orange), Citrus reticulate (mandarin orange).

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***Address for Correspondence:** Department of Biotechnology, Techno India University, EM-4, EM, Sector V Salt Lake, Kolkata, West Bengal, India

E-mail: malavikab@gmail.com

(Ben Hsouna et al., 2023) Citrus trees were first cultivated in the tropical and subtropical regions of Asia and the Malay Archipelago; some types are also found in Mediterranean nations. Because of the improved soil and climate here, orange, mandarin, and lemon trees can grow to a higher degree of fruit quality than they could in their original areas..(Ollitrault et al., 2020) The ancestral species of citrus consists of Citrus maxima – Pomelo Citrus 34eticulate – Mandarin orange amongwhichthe important hybrids areCitrus × aurantiifolia – Key limeCitrus × sinensis – Sweet orange.

The main benefit of citrus species is their abundance in vitamin C. Vitamin C has antioxidant qualities and is an antiscorbutic agent. (Yu et al., 2005) Vitamin C and folate, which are essential for maintaining the integrity of immune barriers and supporting the activity of various immune cell types such as phagocytes, natural killer cells, T-cells, and B-cells, may be found in citrus fruit juices. As an antioxidant, vitamin C lowers several components of the inflammatory response(Miles & Calder, 2021). For optimal health throughout the life cycle, vitamin C, one of the main antioxidants in circulation, has anti-inflammatory and immune-supporting properties.(Sengupta et al., 2023). During the COVID-19 pandemic, there has been an increase in the proportion of individuals consuming recommended amounts of fruits, including citrus fruits. (Kołota & Głabska, 2021).

Citrus fruits have become more significant since the COVID-19 pandemic because of their possible antiviral and anti-inflammatory properties, link to a lower chance of developing some malignancies, and positive benefits on cardiovascular and mental health.Citrus fruit juices are high in vitamin C and folate, which help to maintain immunological barriers and promote the activity of numerous immune cells. Vitamin C serves as an antioxidant, reducing certain components of the inflammatory response. Citrus fruit juice polyphenols, such as hesperidin, narirutin, and naringin, exhibit anti-inflammatory properties in model systems and have been demonstrated to lower inflammatory markers in human studies.(Miles & Calder, 2021).The contribution of citrus species in deterrence of life threatening diseases have been assessed (Rafiq et al., 2018) and it has been reported that citrus fruits, citrus fruit extracts and citrus flavonoids exhibit a wide range of promising biological properties due to their phenolic profile and antioxidant properties ((Ramful et al., 2010)Citrus (Citrus L. From Rutaceae), contains active phytochemicals that can protect health. In addition to this, it provides an ample supply of vitamin C, folic acid, potassium and pectin). Studies conducted in vivo and in vitro have demonstrated the potential antidiabetic benefits of citrus flavonoids. It has been discovered that they influence lipid profiles, renal function, and indicators of glycemic management. They also alter 35eticulate pathways linked to insulin sensitivity and glucose absorption.(Gandhi et al., 2020)

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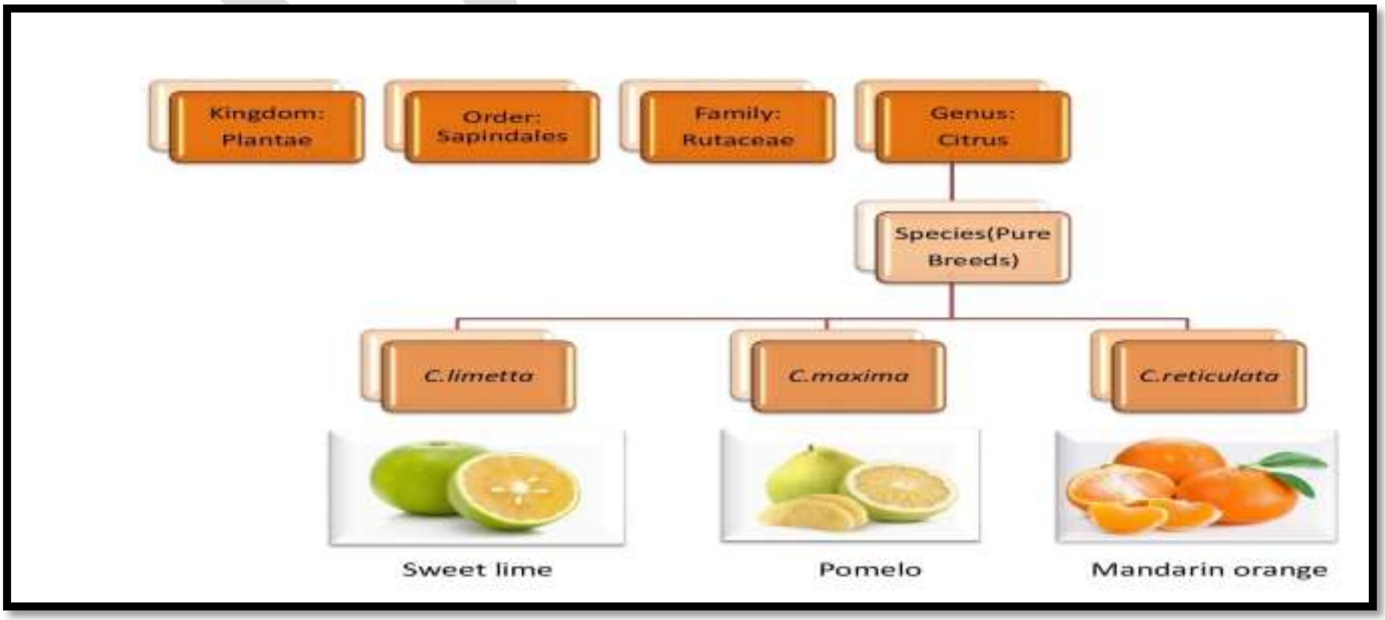
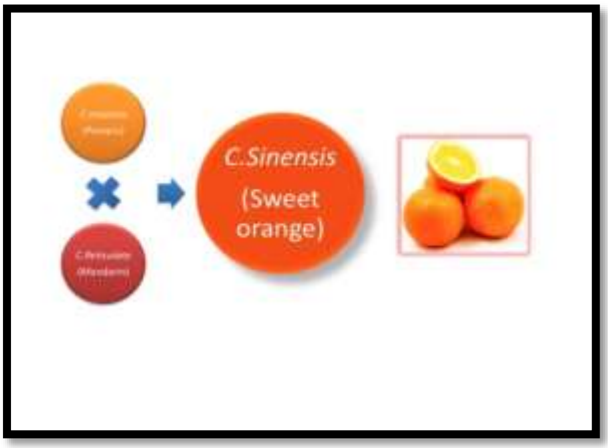
Over 50 nations in tropical and subtropical climates cultivate citrus for commercial purposes; the total production is 115.52 million tons. With an average productivity of 9.69 tonnes/ha, India ranks as the fourth-largest citrus producer worldwide.(Kumar & Chahal, 2018) After processing, approximately 50% of the fruit is wasted since it cannot be consumed. Fruit pith remains, peels, and seeds fall under the latter category. These wastes include bioactive compounds, thus dumping them directly into the environment can cause serious problems. Disposal in water bodies or seepage into the subsurface water table degrades water quality and endangers aquatic life. The release of these bioactive compounds into open landfills spreads illnesses and emits disagreeable odors (Sharma et al., 2019)

Taxonomical position of the citrus species





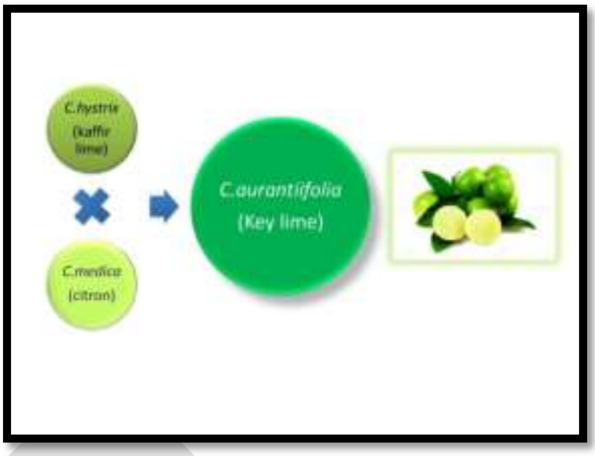


Figure 2: ***C.sinensis*** and ***C. aurantifolia***

Review Literature

The literature review is structured onAntimicrobial, anticancer, and antioxidant activities of the citrus species.

C.aurantifolia

Promising findings have been obtained from studies on Citrus aurantifolia seeds' antibacterial properties. Mohammed (2016), (Mohammed & Ayoub, 2016) discovered that the seed extracts in ethanol, methanol, and chloroform all had strong antibacterial activity, with the methanol extract working especially well.

Salih (2015) provided additional support for these results, demonstrating that extracts from Citrus aurantifolia impeded the development of harmful bacteria isolated from individuals suffering from sinusitis and asthma. (Salih, 2015) (Mohammed, A. H. Et al., 2016) A zone of inhibition of 19 mm is produced by the aqueous extract against S. Paratyphi A, while a zone of inhibition of 13 mm is produced by the chloroform extract against the same bacteria. S. Typhi was sensitive to the ethanolic extract of C. Aurantifolia, even at the lowest concentration, but resistant to both the aqueous and chloroform extracts of the plant. S. Paratyphi A and S. Paratyphi B both shown resistance to C. Aurantifolia ethanolic extracts.

(Valarmathy et al., 2010) shows that plant extracts from Citrus aurantifolia and Mangifera indica significantly limit the growth of Penicillium oxalicum, Aspergillus niger, Aspergillus terreus, and Staphylococcus albus(Mohammed & Ayoub, 2016)The minimum inhibitory concentration (MIC) ranges for C. Aurantifolia water extracts were 12.5µg/ml to 25µg/ml, ethanolic extracts were 12.5µg/ml to 50µg/ml, and chloroform extracts were 25µg/ml to 100µg/ml.The MBC range for both extracts was 25µg/m to 100µg/m.On the other hand, the MIC and MBC ranges for amoxicillin, the typical antibiotic, were 6.25µg/m-12.5µg/m and 12.5µg/m25µg/m, respectively.

C.limetta

(Shakya et al., 2019) With a maximal zone of inhibition of 15.33±0.577 against Bacillus spp., the peel extract of Citrus limetta was shown to be more efficient against Gram-positive bacteria than its juice extract. Exceptfor Klebsiella on which the peel extract was more effective with a zone of inhibition (10.33±1.527), 10% DMSO showed no zone of inhibition. Among the Gram-negative bacteria, the juice extract of C2 was found to be more effective than its peel extract against the four other bacteria chosen with a maximum zone of inhibition (8.33±2.081) against E. Coli ATCC 25922.

C.maxima

(Br Karo et al., 2020) used the disc diffusion method to assess the antibacterial activity of the ethyl acetate fraction of C. Maxima peel extract against various microorganisms. These bacterial strains were gram-positive S. Aureus and gram-negative E. Coli, two species commonly associated with infectious illnesses. The presence or absence of an inhibition zone was used to determine the antibacterial activity of the C. Maxima ethyl acetate fraction. The diameter of the inhibition zones surrounding each disk was then measured in 36eticulate36. The ethyl acetate portion of C. Maxima peel extract exhibited mild antibacterial activity in all concentration treatments (25 ppm, 50 ppm, 75 ppm, and 100 ppm) according to the inhibition zone that was obtained. Despite the fact that S. Aureus showed the largest zone of inhibition at a dose of 100 ppm,E. Coli was at a concentration of 75 ppm.

(Das et al., n.d.) discovered that Pseudomonas aeruginosa and Escherichia coli were both responsive to Citrus maxima (Burm.) Merr.'s ethanolic extract at both concentrations (10 mg/ml & 5 mg/ml). Pseudomonas aeruginosa demonstrated the maximum zone of inhibition. Pseudomonas aeruginosa had a lower MIC value (0.312 mg/ml) of the extract than Escherichia coli (0.625 mg/ml), although both bacteria had the same MBC value (1.25 mg/ml). Pseudomonas aeruginosa was the chosen bacteria that responded more strongly to the plant extract than Escherichia coli. Given that Pseudomonas aeruginosa is the most prevalent gram-negative bacterium that causes both nosocomial and community-acquired illnesses, this indicates the extract's strong antibacterial action. One of the biggest obstacles to the efficient treatment of infections at the moment is the emergence of multidrug-resistant Pseudomonas aeruginosa.(Anjum & Mir, 2010).

C.sinensis

(Egbuonu& Osuji, 2016) found when compared to the peels (90.21%), the percentage yield of the C. Sinensis seeds sample (54.49%) was lower ($p<0.05$)The orange peels and seeds water extracts demonstrated activity (measured as inhibition zone diameter, IZD in mm) against Staphylococcus aureus (14.00±1.00, 8.67±1.15) and Escherichia coli (11.33±1.52, 9.67±1.15), respectively, with the peels extract eliciting significantly ($P<0.05$) higher activity.The ethanol extract of orange peels exhibited greater activity (mm) against both Escherichia coli (20.00±1.73) and Staphylococcus aureus (19.00±1.73), with p-values less than 0.05, in comparison to the seeds (12.33±0.38, 13.33±1.16).

C.reticulata

Different fractions from C.reticulata peel inhibited the growth of gram-positive bacteria at quantities that were less than necessary for gram-negative bacteria. Of all the bacterial strains, the EtO H soluble fraction was the most effective. Out of all the fractions examined, the acetone extract was shown to be the least effective. For Staphylococcus aureus and Bacillus cereus, the minimum inhibitory concentration (MIC) in the EtOH-soluble fraction was found to be 300 µg/ml, whereas B. Coagulans and B. Subtilis required 500 µg/ml to completely block growth. For gram-negative bacteria, Pseudomonas aeruginosa and Escherichia coli It was discovered that the MIC of the EtO H soluble fraction was 1 2 0 0 and 600 jig/ml, respectively. EtO H soluble fraction's MIC levels were lower than those of the other fractions, most likely as a result of its increased polymethoxylated37eticula concentration. (Jayaprakasha et al., 2000).

Anticancer Effects

C.aurantifolia

PLC/PRF/5 liver cancer cells with a p53 mutation may be susceptible to inhibition of cell division and induction of apoptosis by lime peel extract. Limonin, hesperidin, and lime peel extract can all be used at non-toxic doses to prevent PLC/PRF/5 cells from invading. This study also found that the isolated components of limonin and hesperidin had less of an effect in inducing apoptosis than did the lime peel extract. Furthermore, the extract's greater efficacy can be explained by the synergistic action of limonin and hesperidin on apoptosis induction. The anti-cancer effect of the extract is probably due to the combinatorial effects of multiple other compounds found in the metabolome, rather than just the synergistic effect of hesperidin and limonin, as the extract's effect is still greater than that of the combination of the two. (Phucharoenrak et al., 2023).

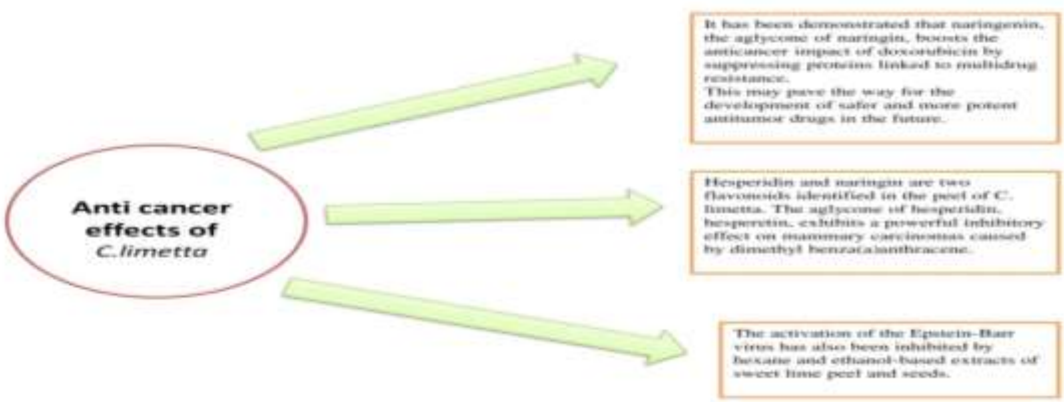


Figure3: Anticancer effects of *C. limetta*

C.maxima

By raising intracellular ROS levels, CM has demonstrated strong anticancer effects in metastatic breast cancer cells in this study. These results suggested that more research should be done on CM as a potent natural anticancer therapy for breast cancer. Growing research suggests that raising oxidative stress may be a useful tactic for eliminating cancer cells [4]. In breast cancer cells, agents that may raise ROS levels have anticancer properties. (Mursiti et al., 2021).

C.reticulata

This experiment provided a concise summary of peel extract's cytotoxic activity as well as the relationship between total phenolic content. Each cell line's toxicity was then assessed using its IC50 value. When it comes to colon cancer (HCT) and human breast cancer (MCF7) cell lines, the cytotoxicity of 70% peel extract was typically ineffective since the IC50 was higher than 15. However, the same extract revealed minimal toxicity to normal cells but a significant cytotoxic impact against human hepatocellular liver cancer (HepG2, IC50 9.9 µg/mL). Finally, flavonoids with a high total phenolic content exhibit more potent cytotoxic properties.

Citrus peel extract has been demonstrated to be effective against liver cancer due to its high phenolic content, which includes flavonoids and coumarone compounds.(Ya et al., 2019)

Antioxidant Properties

CITRUS SPECIES	ANTIOXIDANT POTENTIAL
C.maxima	Studies have shown that the fruit juice of Citrus maxima can improve antioxidant status and reduce the risk of oxidative stress (Oyedepo, 2012). This potential is further supported by the presence of phytochemicals, minerals, and vitamins C and E in the fruit juice (Ezeanyikaa, 2022). The leaves of Citrus maxima have also been found to exhibit in vivo antioxidant and hepatoprotective activity (KunduSen, 2011), as well as in vitro antioxidant capacity and in vivo antidiabetic properties (Islam, 2021). These findings collectively suggest that Citrus maxima, particularly its fruit juice and leaves, can be a valuable source of antioxidants.
C.aurantiifolia	Research on the antioxidant potential of Citrus aurantifolia, or lime, has consistently shown promising results. Kumari (2013) found that both unripen and ripen lime juices possess strong antioxidant activity, with unripen juices showing higher scavenging activity. This was attributed to the higher levels of ascorbic acid and total phenolic content in unripen juices. Similarly, Namani (2018) reported that lime leaves from Oman contain significant levels of flavonoids and phenolic compounds, which contribute to their moderate antioxidant activity.
	Research has consistently shown the high antioxidant potential of Citrus reticulata. Bocco (1998) and Kamal (2013) both found that the peel and essential oils of this citrus species have significant antioxidant activity. Parhiz (2015) further highlighted the antioxidant and anti-inflammatory properties of the citrus flavonoids hesperidin and hesperetin, which are present in Citrus reticulata. Mishra (2023) specifically identified rutin, a flavonoid found in Citrus

C.reticulata	reticulata, as an effective antioxidant and anti-cancer agent.
C.limetta	Research on the antioxidant potential of Citrus limetta, particularly its juice, leaves, fruits, and peel extracts, has shown promising results. Kumari (2017) found that the juice extract exhibited high antioxidant activity, while Pl (2012) and KunduSen (2011) reported effective free radical scavenging and antioxidant activities in the leaves, fruits, and peel extracts. Javed (2013) further supported these findings, demonstrating the antioxidant activity of the essential oil of Citrus limetta var. Mitha. These studies collectively suggest that Citrus limetta possesses significant antioxidant potential.

Conclusion

Citrus species are an easily available treasure trove of mother nature, they contain vitamin C, flavonols, flavonoids, bioactive compounds, limonoids, folic acids, and dietary fibers; thus they can be vividly used ethnopharmacologically. They are used for different types of treatments not only by the medical practitioners also used as home remedies. So, it is highly essential to conduct research study on the different parts of citrus fruits. Valorization of the waste parts of the samples also needs to be enlightened. Overall, this review study sheds light on the protective effects of citrus species. Thinking about the efficacy of the genus, this review paper will draw research attention towards it. It can be categorized as a functional foods because of its high antioxidant activities, also from the different parts of the fruits nutraceuticals can be produced.

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