

ETHNO MEDICINAL VALUES OF CITRUS GENUS —A REVIEW OF THE CHEMISTRY, PHARMACOLOGICAL PROPERTIES, APPLICATIONS IN THE MODERN PHARMACEUTICAL, FOOD, AND COSMETICS INDUSTRIES**Dr. Vishal Garg^{1*}, Naveen Garg¹, Dinesh Jindal¹ and Kriti Gupta¹**¹Jaipur School of Pharmacy, Maharaj Vinayak Global University Jaipur.***Corresponding Author: Dr. Vishal Garg**

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ABSTRACT

Citrus plants belonging to the family Rutaceae which include fruits such as orange, mandarin, lime, lemon, sour orange and grape fruit appear as a well-known promising source of multiple beneficial nutrients for human beings.^[1] Fruits of Citrus genus play an important role as a dietary supplement and therapeutic agent as well since ages. The present review summarizes some such attributes of Citrus genus. The peel of citrus fruits is a rich source of flavanones and many polymethoxylated flavones, which are very rare in other plants. The citrus peel oils show strong antimicrobial activity. These compounds, not only play an important physiological and ecological role, but are also of commercial interest because of their multitude of applications in the food and pharmaceutical industries.^[2] Numerous studies have focused on *Citrus* secondary metabolites as well as bioactivities and have been intended to develop new chemotherapeutic or complementary medicine in recent decades. *Citrus*-derived secondary metabolites, including flavonoids, alkaloids, limonoids, coumarins, carotenoids, phenolic acids and essential oils, are of vital importance to human health due to their active properties. These characteristics include anti-oxidative, anti-inflammatory, anti-cancer, as well as cardiovascular protective effects, neuro-protective effects, etc.^[3]

KEYWORDS: *Citrus* fruits, Secondary metabolites, Flavonoids, anti-oxidative, anti-inflammatory Antibacterial, antifungal etc.

INTRODUCTION

The World Health Organization (WHO) reported that 4 billion people (80% of the world's population) use herbal medicines for some aspect of primary healthcare (Fabricant DS and Farnsworth NR, 2001). In developing countries, 80% of people use traditional medicines which are based on plant products. Currently 80% of the world population depends on plant derived medicine for the first line of primary health care for human alleviation because it has no side effects.^[7] Citrus (*Citrus L.* from *Rutaceae*) is one of the most popular world fruit crops, contains active phytochemicals that can protect health. In addition to this, it provides an ample supply of vitamin C, folic acid, potassium and pectin and citrus flavonoids exhibit a wide range of promising biological properties due to their phenolic profile and antioxidant properties.^[4] Citrus fruits having lots of therapeutic remedies like oranges to cure scurvy, orange juice to prevent and modulate inflammatory processes, lime, and lemon juices to prevent kidney stones formation, grapefruits to lower blood pressure and to interfere with calcium channel blockers, grapefruit juice having anti-genotoxic effects citrus flavonoids as effective in vivo agents able to modulate hepatic lipid

metabolism, and several others.^[1] *Citrus* fruits are good sources of nutrition with an ample amount of vitamin C. Besides, the fruits are abundant in other macronutrients, including sugars, dietary fiber, potassium, folate, calcium, thiamin, niacin, vitamin B6, phosphorus, magnesium, copper, riboflavin and pantothenic acid. *Citrus* fruits contain a number of secondary metabolites, such as flavonoids (especially flavanone, flavanonol and methoxylated flavones), flavonoids are more active compared to other secondary metabolites in *Citrus* for their remarkable various bioactivities. Studies on plentiful bioactivities from hesperetin/hesperidin (flavanone) naringenin/ naringin (flavanone), tangeretin (polymethoxylatedflavone) and nobiletin (polymethoxylatedflavone) have been widely reported and other ingredient like alkaloids, coumarins, limonoids, carotenoids, phenol acids and essential oils are also present. These active secondary metabolites show several bioactivities of vital importance to human health, including anti-oxidative, anti-inflammatory, anti-cancer, anti-allergy activities, neuroprotective effect, hepatoprotective effect, obesity control, etc as well as cardiovascular protective effects, neuroprotective effects, etc.^[3]

Antioxidant activity: The antioxidant activity of Citrus fruits and their roles in the prevention and treatment of various human chronic and degenerative diseases such as cancer, diabetes and cardiovascular disease and denotes the ability of a bioactive compound to maintain cell structure and function by effectively clearing free radicals, inhibiting lipid peroxidation reactions, preventing other oxidative damage and other biological functions, such as anti-cancers, anti-inflammation and anti-aging.^[5] Vitamins are organic substances vital for body function and indispensable to our life. About 06 vitamins reported in Citrus fruits, including vitamin A, vitamin B1, vitamin B2, vitamin C, vitamin E and vitamin B3. Of these vitamins, vitamin A, vitamin C and vitamin E were evaluated for their antioxidant activities.^[6] Citrus extracts such as *Citrus karna* peel extracts, *Citrus limetta* peel extracts and *Citrus bergamia* juice extracts were found to have potential antioxidant bioactivity.^[19]

Antimicrobial activity: Antibacterial effects of extract from citrus peels have been reported against *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Shigella flexneri*, *Bacillus subtilis* and *Escherichia coli*.^[8] Phenolic compounds in citrus peels are responsible for antimicrobial activity.^[9] Methanolic extract of fruit peel of *Citrus aurantium* (sour orange) and *Citrus medica* (lemon), Kagji Lemon peel, South African Malta, and Dargiling Orange have very high antibacterial activity on *B. cereus*.^[10] Fruit juice and ethanolic extracts of root, leaf, bark, peel and pulp of citron (*Citrus medica* Linn., Rutaceae) was examined against seven bacteria (*Bacillus subtilis*, *Staphylococcus aureus*, *Enterococcus faecalis*, *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa* and *Proteus vulgaris*), two fungi (*Aspergillus flavus* and *A. niger*) and a yeast *Candida albicans* of clinical origin.^[11] Orange Essential oil and lime Essential Oils exhibited significant inhibition of *Staphylococcus aureus*, *Bacillus subtilis*.^[25]

CITRUS ESSENTIAL OILS USES IN FOODS

Klebsiella pneumoniae in a study performed by Prabuseenivasan et al.^[37] to evaluate plant essential oil activities again

Anticancer activity

studies showed that citrus intake is associated with a reduced risk of multiple cancer types, including cancer of the digestive tract, respiratory tract, pancreatic cancer, prostate cancer, breast cancer, nasopharyngeal cancer and cutaneous melanoma (Jian et al., 2005; Foschi et al., 2010). Recent findings suggest that citrus consumption is associated with reduced all-cancer incidence, especially for subjects having simultaneously high green tea consumption. Accumulated evidence from experimental and epidemiological studies also indicates that dietary consumption of citrus fruit or juice appears to be inversely associated with lower risk of many infectious diseases including cancers. Studies showed that citrus intake is associated with a reduced risk of multiple cancer types, including cancer of the digestive tract, respiratory tract, pancreatic cancer, prostate cancer, breast cancer, nasopharyngeal cancer and cutaneous melanoma (Jian et al., 2005; Foschi et al., 2010). The anti-cancer benefits of citrus fruits are mainly found in the significant quantities of monoterpenes and flavanones, two classes of compounds that are believed to cut the risks of cancers of the digestive track in half. These compounds reduce cancer risks in two significant ways. First, they interfere with some of the processes necessary for cancer cell growth, making it difficult for tumours to develop, and second, they inhibit inflammation, an important stimulus for cancer cell growth.^[12] *C. aurantifolia* was studied for its effect against carcinogenesis by mechanisms such as stopping cancer cell mobility in circulatory system; so, inhibiting the metastasis, blocking the angiogenesis, and inducing tumor suppressor gene and apoptosis.^[13] Flavonoids in citrus peel exhibit a remarkable spectrum of efficacious biological activities, particularly in antitumorigenesis. Excellent permeability through membrane allows citrus flavonoids to possess great bioavailability which consequently attracts researchers to perform scientific studies for effective disease prevention and treatment.^[14]

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Antidiabetic activity

Administration of *C. medica* L. fruit juice (1 ml/100 gm) led to a significant fall in the level of triglycerides, total cholesterol, LDL and VLDL while HDL level was not increased significantly when streptozotocin induced diabetic rats showed significant decrease in the level of blood glucose, total cholesterol, triglycerides, LDL and VLDL and decrease in the level of good cholesterol HDL. The protective action of *C. medica* L. juice in diabetic animals may be because of its antioxidant potential and presence of flavonoids, vitamin C and higher total phenolic content.^[15] The methanol extract of fruit peel of *C. limetta* has potent antihyperglycemic activity against STZ induced diabetes as well as having hypoglycemic activity in normoglycemic rat and glucose overloaded rats. The citrus plants are rich in flavonoids which are polyphenolic compounds having potent antioxidant property. The fruits peel of *C. limetta* contain flavonoids hesperidin and naringin both are proven to be potent hypoglycaemic agents.^[16] Flavonoids are the most abundant phenolic compounds present in Citrus fruits. The content of flavonoids in peels is 10-time greater than the content of the juice. Among them, flavanone glycosides predominate, together with other low amount flavonoids such as methoxylated flavones, flavones glycosides and anthocyanins.^[17] that the methanol extract of the fruit peels of *C. limetta* has potent antihyperglycemic activity against STZ-induced diabetes as well as having hypoglycemic activity in normoglycemic rats and in glucose overloaded rats. The Citrus plants are rich in flavonoids which are polyphenolic compounds having potent antioxidant property that the methanol extract of the fruit peels of *C. limetta* has potent antihyperglycemic activity against STZ-induced diabetes as well as having hypoglycemic activity in normoglycemic rats and in glucose overloaded rats. The Citrus plants are rich in flavonoids which are polyphenolic compounds having potent antioxidant property that the methanol extract of the fruit peels of *C. limetta* has potent antihyperglycemic activity against STZ-induced diabetes as well as having hypoglycemic activity in normoglycemic rats and in glucose overloaded rats. The Citrus plants are rich in flavonoids which are polyphenolic compounds having potent antioxidant property

Anti-inflammatory and analgesic activity:

The anti-inflammatory and analgesic potentials in peels of some commercially grown Citrus fruits like Lime, Orange, Sour Orange, Pomello and Citron, The anti-inflammatory activity of extracts at 250 and 500 mg/Kg body weight concentrations were assessed by in vivo Carrageenan induced rat paw edema model and in vitro HRBC membrane stabilization assay whereas Tail immersion and Hot plate methods have been used to evaluate their analgesic property, in a dose dependent manner and are more effective in the later phase so Citrus peels are good sources of anti-inflammatory and anti-nociceptive agents.^[18] Flavonoids, coumarin and volatile oil from *Citrus* fruit are showing anti-

inflammatory activity, which can be used as supplement to protect against or ameliorate this chronic inflammatory diseases. Naringin reduced lipopolysaccharide- or infection-induced endotoxin shock in mice, attenuated chronic pulmonary neutrophilic inflammation in cigarette smoke-exposed rats.^[20] And its aglycone, naringenin, exerted anti-inflammatory activities in macrophages and in human blood.^[21] Hesperidin exerted noticeable in vivo anti-inflammatory systemic effects in mouse models of LPS-induced lung inflammation and of endotoxin-induced infection.^[22]

Neuroprotective activity

C. aurantium L. aqueous extract and its major constituents (naringin, hesperidin, neohesperidin, and nobiletin) had neuroprotective effect on corticosterone-induced neurotoxicity in PC12 cells. The in vivo and in vitro results suggest that *C. aurantium* L. aqueous extract had an antidepressant effect.^[23]

Anti-Obesity Activity

Lemon juice was used in a low-calorie diet ('lemon detox diet'). The diet consisted of 2 L of lemon detox juice containing 140 g 'Neera' syrup, 140 g lemon juice, and 2 L water per day. *C. limon* juice caused a reduction in serum high-sensitive C-reactive protein (hs-CRP) in comparison with the placebo and normal diet group. Haemoglobin and haematocrit levels remained stable in the group on the lemon detox diet, while they decreased in the placebo and normal diet groups.^[29] Studies have shown that D-limonene is beneficial to people with dyslipidaemia and hyperglycaemia. D-limonene at a dose of 400 mg/kg per day for 30 days promotes in male rats a decrease in LDL-cholesterol, prevents the accumulation of lipids, and affects the blood sugar level. Its antioxidant action enhances these effects. Dietary supplementation with D-limonene would restore pathological alteration of the liver and pancreas. It could help in the prevention of obesity.^[30]

In Food industries

Citrus and citrus products are extremely important for their fruit that is eaten fresh or processed in numerous ways. Fruit juices of all species can be used in beverages. Leaves of lemon and sweet orange are boiled to make tea. In Egypt and elsewhere, sour orange juice has been fermented to make wine, Most of the citrus species has flavoring agents. For example, lime and lemon are commonly used to marinate raw fish and to flavor food. Whole limes are also pickled as a relish (Achar). Essential oils are volatile oils obtained from the citrus fruits peel's sacks. They are used by the food industry to give flavor to drinks and foods. They are also a component for the pharmaceutical industry for the preparation of medicines and soaps, perfumes and other cosmetics, as well as for home cleaning products. D-limonene is a major component of the oil extracted from lemon and orange rinds or solids. It is considered as one of the purest sources of monocyclic terpene. It is used for

industrial solvents and as an element for the synthesis of other chemical materials. It is also used as a flavor and aromatic component. Citrus pulp pellets are the result of the conversion of peels and pulps that have been left behind once the juice has been extracted. They are used for animal feeding.^[24] Citrus essential oils are used as flavouring agents in beverages, candy, and gelatines. Based on their long history of consumption, citrus oils are considered “Generally recognised as Safe” by many food regulatory bodies. The most promising use is as natural preservative agents. Citrus essential oils contain more than 85% volatile compounds, which can be lost at room temperature or above.^[26] The antimicrobial properties are attributed more to these volatile compounds; hence, combine their use in food preservation with improved packaging materials and techniques. Vacuum-packed foods, canned foods, and bottled juices could be the first food commodities in which essential oils are used commercially. Combining the use of essential oils with other methods of food preservation can be of great economic and sensory value.^[27]

6.1. CEOs as Preservatives

Extraordinary medicinal uses of citrus plant

A leaf infusion made from sweet orange is used against mouth sores in infants. Citrus leaves are used together with other plant parts to make infusion for treating stomach and for internal ailments and fractures; the scraped root of pummelo is used to treat hemorrhoids. In the United States, citrus is suggested as part of a healthy diet because of its high vitamin C, content and its flavonoids, which are known to reduce breast cancer risk, reduce viral effects. Citrus flavonoids have potential antioxidant (prevents aging), anti-cancer, antiviral, anti-inflammatory activities, effects on capillarity, and cholesterol-lowering ability. The principal carotenoids in pink grapefruit are lycopene and beta-carotene. Lycopene-containing fruits and vegetables have been shown to contribute to a significant, reduction in prostate and mammary cancer risk.^[24]

In cosmetic industry

Citrus fruits can be used in cosmetics in the form of oils obtained from various organs, in the form of extracts, hydrolates, powdered parts of the plant, wax and juice and raw material of citrus plants is to keep the skin in good condition, to improve the odour of cosmetic products, and to mask the smell of other ingredients of cosmetic preparations.^[31] Geranium oil is a cleansing, toning and sharpening oil and is so helping with those problems that come with greasy, over-oily skin, acne, congested skin and eczema. It is very important component of high grade perfumes due to its strong rose – like odour.^[28] Citrus fruits used in cosmetics in various way like skin conditioning masking, perfuming, emollient, skin protecting, tonic and absorbent.^[31]

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CONCLUSION

From this review, we can see that Citrus fruits are a rich source of very pharmacological activities with lots of use in natural cosmetics and play excellent role in betterment of human health. Due to the low cost and easy availability of fruit. Rich in bioactive compounds,. The extracts from fruit peel hold promise in food industry as sources of bioactive compounds.¹ The Citrus fruit is a raw material that can be used in different forms, e.g.,

extracts, juice and essential oil. The rich chemical composition of this species determines a wide range of its biological activity and its being recommended for use in phyto-pharmacology. Extracts from Citrus fruits are rich in flavonoids such as naringenin and hesperetin. Current pharmacological studies have confirmed the health-promoting activities of Citrus fruits, especially its anti-cancer and antioxidant properties and many more. A C. fruit also finds increasing application in cosmetology and food production.

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