IJPSR (2013), Vol. 4, Issue 1 (Review Article)

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 21 September, 2012; received in revised form, 16 October, 2012; accepted, 15 December, 2012

PHARMACOLOGICAL IMPORTANCE OF CITRUS FRUITS

Amita Tomar*[1], Mridula Mall [2] and Pragya Rai [1]

Pharmacy College Itaura Chandeshwar [1], Azamgarh- 276128, Uttar Pradesh, India
Chandra Shaker Singh College of Pharmacy [2], Allahbad-211001, Uttar Pradesh, India

Keywords:
Citrus fruits, Antimicrobial, Anticancer, Antioxidant

Correspondence to Author:

Amita Tomar

Assistant Professor, Pharmacy College Itaura Chandeshwar, Azamgarh- 276128, Uttar Pradesh, India

E-mail: amitatomarmpharm@gmail.com

ABSTRACT

This paper reviews the pharmacological importance of citrus fruits. Citrus fruits are used for various pharmacological importance. According to literature the citrus fruit possess anti-cancer, antimicrobial, antioxidant, antiulcer, anti-inflammatory, and hypolipidemic and hepatoprotective properties.

INTRODUCTION: Citrus fruits have been collected and used by man for centuries for medicinal, herbal and agricultural purposes [1, 2]. Citrus fruits, belong to the family of Rutaceae, are one of the main fruit tree crops grown throughout the world [3]. All citrus fruits share in common their sweet and sour flavor. They possess refreshing juice and are available almost all round the year [4]. Citrus species are small to medium-size shrubs or trees that are cultivated throughout the tropics and subtropics (**Table 1**). They are native to parts of India, China, and northern Australia.

According to UN 2007 data, Brazil, China, the United States, Mexico, India, and Spain are the world's largest citrus-producing countries. Of these, Brazil is the world's largest producers of oranges, China produces most of the world's mandarins, and India is the world's largest producer of lemons and limes, and the United States produce the most grapefruit [5].

QUICK RESPONSE CODE

IJPSR: ICV- 5.07

Website: www.ijpsr.com

TABLE 1 : SIZE OF DIFFERENT CITRUS SPECIES

Species	Common name	Size and spines
C. Aurantifolia	Lime	Shrub/small tree to 4 m(13 ft), spiny
C. Aurantium	Sour orange	Tree to 10 m (33 ft), short spines
C. Grandis	Pummelo	Tree to 12 m (40 ft), spiny
C. Hystrix	Kaffir lime	Tree to 5 m (16 ft), short spines
C. Limon	Lemon	Tree to 6 m (20 ft), stout spines
C. Macroptera	Wild orange	Tree to 5 m (16 ft), spiny
C. Medica	Citron	Shrub to 3 m (10 ft)
C. Mitis	Calamondin	Tree to 12 m (40 ft), spiny
C. Paradise	Grapefruit	Tree to 15 m (50 ft)
C. Reticulate	Mandarin	Tree to 9 m (30 ft), usually spiny
C. Sinensis	Sweet orange	Tree to 12 m (40 ft)

PHARMACOLOGICAL IMPORTANCE:

Anticancer Properties"

1. Robert Jacob *et al*., reported the potential of citrus limonoids as anticancer agent in mice, it was found that five limonoids aglycones (limonin, nomilin, obacunone, isoobacunoic acid, ichangin) induced significant amounts of glutathione-S-transferase (GST) in the liver and intestinal mucosa.

GST is a major detoxifying enzyme system which catalyzes the conjugation of glutathione with many potentially carcinogenic compounds which are highly electrophilic in nature. A study of the inhibitory effects of two limonoid aglycones (limonin and nomilin) on the formation of benzo[a]pyrene induced neoplasia in the fore stomach of ICR/Ha mice showed that incidence of tumors could be reduced by more than 50% at 10mg/dose [6].

2. Maliheh Entezari *et al*., reported Antimutagenicity and Anticancer Effects of *Citrus Medica* Fruit Juice **.** They perform vital capacity test and Ames test to consider its anticancer effect with special emphasizes on application of *salmonella typhimurium* to identify antimutagenesis and anticancer level of chemicals. In this research, half-ripe and ripe fruit juice displayed anticancer and antimutagenesis effect which half-ripe fruit juice was more effective than ripe fruit juice. *In vitro* study on fruit juice effect on cancerous cell culture revealed that the fruit juice severely repressed division of cancerous cells which in this study the effect of half-ripe *Citrus medica* fruit juice was more than ripe one [7].

3. Jansen Silalahi reported the Anticancer and health protective properties of citrus fruit Components. Bioactive components present in citrus fruits that are implicated in degenerative disease prevention include vitamin C, β-carotene, flavonoids, limonoids, folic acid and dietary fibres. Vitamin C, flavonoids and β-carotene are potential antioxidants protecting against oxidation of biomolecules such as DNA, protein and lipid membranes, thereby reducing the risk of cancers, cataract and cardiovascular diseases Limonoids may protect against a variety of cancers by inducing GST activity to neutralise carcinogenic free radicals. Folic acid plays an important role in amino acid metabolism and hence, it is a critical factor for growth [8] .

Antimicrobial Activity:

1. Ashok Kumar *et al*., reported Antimicrobial Activity and Phytochemical Analysis of Citrus Fruit Peels Utilization of Fruit Waste. He reported antibacterial activity of five different solvent extracts(ethyl acetate, acetone, ethanol, petroleum ether and water) prepared by soxhlet extractor from two citrus fruit peel (*Citrus sinensis* and *Citrus limon)* were screened against five pathogenic bacteria *Staphylococcus aureus, Bacillus subtilis, Escherichia coli, Klebsiella pneumonia and Salmonella typhi*. The highest antibacterial potentiality was exhibited by the acetone peel extract of *Citrus sinensis* followed by the ethyl acetate peel extract of *Citrus limon.* The peel extract of *Citrus sinensis* and *Citrus limon* can be considered to be as equally potent as the antibiotics, such as metacillin and penicillin [9].

2. Ramakrishna Nannapanen *et al*., reported Antimicrobial Activity of Commercial Citrus-Based Natural Extracts against *Escherichia coli 0157:1-17* Isolates and Mutant Strains, Seven citrus essential oils used in this study. All these seven essential oils were evaluated for antimicrobial activities against 13*E. coli* strains. The most susceptible to limonene (C7 fraction) of the *E. coli* strains were ATCC 43888 and 0157:H7 932, which were not significantly different from *E. co/i* strains ATCC 43890, ATCC 43895 and ATCC 11775. With inhibition zones of 14.5±0.7 mm and 13.5+0.7mm, the *E. coli* 0157: H7ATCC 43890 and 0157: H7 301C were the most sensitive strains to C4 fraction. All other E. coli 0157: H7 strains yielded significantly smaller inhibition zones [10].

3. Nengguo Tao *et al*., reported carotenoids from the peel of Shatian Pummelo (Citrus grandis osbeck) and its antimicrobial activity. The antimicrobial activity of the carotenoids extract against *Bacillus subtili, Staphylococcus aureus, Escherichia coli, Aspergillus niger, Aspergillus flavu, Penicillium chrysogenum, Rhizopus oryzae* and *Saccharomyces cerevisiae* was also elucidated.

Results showed that the optimum extraction conditions was at a temperature of 50°C, a solvents-oil ratio of 10:1 and duration 40 min. The disc diffusion method and minimum inhibitory concentration determination showed that the extract has a wide spectrum of antimicrobial activities against *Escherichia coli, Staphylococcus aureus, Bacillus subtili, Saccharomyces cerevisiae*

and *Rhizopus oryzae* with their inhibition zones ranging from 8.97 mm to 19.47 mm and the MIC ranging from 18.75 µg/ml to 140 µg/ml. However, it showed no inhibition effect on A. niger, A. Flavus an P. chrysogenum [11] .

Antifungal Activity:

1. M. Chutia reported Antifungal activity and chemical composition of Citrus reticulata Blanco essential oil against phytopathogens from North East India. The essential oil (EO) isolated by hydro-distillation from the peel of fully matured ripen fruits of Citrus reticulata Blanco were analyzed by GC and GC–MS. Thirty seven different components were identified constituting approximately 99% of the oil. The major components were limonene (46.7%), geranial (19.0%), neral (14.5%), geranyl acetate (3.9%), geraniol (3.5%), b-caryophyllene (2.6%), nerol (2.3%), neryl acetate (1.1%) etc.

   The antifungal activity of the oil was tested by poisoned food (PF) technique and the volatile activity (VA) assay against five plant pathogenic fungi viz *Alternaria alternata* (Aa), *Rhizoctonia solani* (Rs), *Curvularia lunata* (Cl), *Fusarium oxysporum* (Fo) and *Helminthosporium oryzae* (Ho). The oil showed better activity in VA assay. The Minimum inhibitory concentration (MIC) for Aa, Rs and Cl was 0.2 ml/100 ml whereas >0.2 ml/100 ml for Fo and Ho in PF technique. Fungal sporulation was also completely inhibited at 2 ml/100 ml of the oil except for Cl and Ho, which was only 0.5% (0.5) and 0.25% (0.25) respectively as compared to control [12].

Antityphoid Activity:

1. Vivek Kumar R. *et al.,* reported Anti typhoid activity of aqueous extract of fruit peel citrus sinensis. Phytochemical constituents present in the fruit peel extract included flavonoids, saponins, alkaloids Results of the antimicrobial activity of the fruit extracts. The highest activity (diameter of zone of inhibition 180 mm) was demonstrated by aqueous extracts of fruit peel *Citrus sinensis* (L.) OSBECK against *Salmonella typhi* A while the lowest activity (diameter of zone of inhibition 10 mm) was demonstrated against *Salmonella Typhi* [13].

Antioxidant Activity:

1. Aleksandra Duda Chodak *et al*., reported Antioxidant properties of different fruits seeds and peels. Seeds and peels of commercially available domestic (gooseberry, apples, plums) and imported (watermelon, lemon, grapefruit, kiwi fruit, melon, orange, grapes) fruits were used in the investigation. Among the fruits' parts examined, the highest antioxidant activity was found in the peels of the Sampion cultivar and white grapes , and the seeds of the Idared cultivar and orange [14].

Anti-Inflammatory Activity:

1. Mehmet Karaca *et al*., reported the Investigation of anti-inflammatory activity of Bergamot oil.Essential oil of Bergamot (BO) was investigated for anti-inflammatory activity using carrageenan-induced rat paw oedema test. For the anti-inflammatory activity measurement six different groups were established and BO was administered in three different doses: 0.025, 0.05 and 0.10 mL/kg. Indomethacin was used as a reference agent.

   It was found that reduction in the inflammation was 95.70% with indomethacin, 27.56% with 0.025 mL/kg BO, 30.77% with 0.05 mL/kg BO and 63.39% with 0.10 mL/kg BO. Indomethacin showed the strongest anti-inflammatory activity among the drugs used. The strongest anti-inflammatory activity of BO was seen with 0.10 mL/kg dosage. Median effective dose (ED50) value of BO was found to be 0.079 mL/kg. The results showed that BO posseses promising anti-inflammatory effect [15].

Antiulcer Activity:

1. B. Nagaraju, *et al*., reported Antiulcer Activity of Aqueous Extract of *Citrus medica* Linn. Fruit against Ethanol-Induced Ulcer in Rats. The extract was subjected to phytochemical screening and found to contain carbohydrates, proteins, amino acids and flavonoids. The rats were pretreated

with the extract at two doses (250 and 500 mg kgG1 p.o.) and the antiulcer effect was compared with that of ranitidine (20 mg kgG1 p.o.). The extract of both doses showed a significant reduction in ulcer formation. Histopathological sections showed significant decrease in mucosal ulceration, inflammatory mucosal changes and submucosal edema compared to ethanol treated group and the ranitidine group. It is concluded that, the fruits of *C. medica* possesses significant antiulcer activity against ethanol-induced ulcers in rats and the antiulcer activity could be due to the presence of flavonoids as these compounds have well documented antiulcer activity [16].

2. Nagaraju B *et al*., reported Anti ulcer effect of aqueous extract of *Citrus medica Linn*. on water immersion restraint stress induced gastric ulcer in rats The extract was subjected to phytochemical screening and found to contain carbohydrates, proteins, amino acids and flavonoids. The rats were pretreated with the extract (250 mg kg^{-1} p.o.) and the antiulcer effect was compared with that of omeprazole (10 mg kg^{-1} p.o.). The extract pretreatment showed a significant reduction in ulcer formation and gastric lesions.

   Histopathological sections showed significant decrease in neutrophil infiltration in gastric mucosal tissues, mucosal ulceration, inflammatory mucosal changes and submucosal edema with regenerated epithelial cells compared to untreated and omeprazole-treated rats. The results emphasize that, the fruits of *C. medica* possesses significant antiulcer activity against stress-induced ulcers in rats and the antiulcer activity could be due to the presence of flavonoids as these compounds have well documented antiulcer activity [17].

Hypolipidemic Activity:

1. Rafeeq Alam Khan *et al*., reported Evaluation of Hypolipidemic effect of citrus lemon the comparative effects of citrus lemon on cholesterol, triglycerides, LDL and HDL at the dose of 1ml/kg citrus lemon for 30 and 45 days respectively in animals received high cholesterol diet for 30 days. After 30 days animals showed highly significant decrease in cholesterol 150.8 ± 19.1mg/dl in comparison to control animals i.e. 345.3± 28 mg/dl. While after 45 days decrease in cholesterol continued and a highly significant decrease was observed i.e.16.9 ± 2.8 mg/dl in comparison to the value of control animals i.e. 232.6±9.0 mg/dl. Similarly a highly significant decrease in LDL concentration was observed after 30 days i.e. 122.6± 13 mg/dl in comparison to control animals i.e. 273 ± 38 mg/dl. The decrease in the levels of cholesterol and LDL persisted even after 45 days.

   Whereas HDL concentration was increased significantly after 30 days i.e. 7.27 ± 1.7 mg/dl than as compared to control i.e. 3.07 ± 0.26 mg/dl. However increase in HDL level became insignificant after 45 days i.e. 2.15 ± 0.31 mg/dl as compared to control i.e. 2.1±0.32 mg/dl. Decrease in triglycerides was insignificant after 30 days as compared to control animals. However a highly significant decrease was observed in triglyceride levels after 45 days i.e. 26.69 ± 1.4 mg/dl in comparison to control 40.3±3.5 mg/dl [18].

Hepatoprotective Activity:

1. Mehmet Karaca *et al*., reported Evaluation of hepatoprotective activity of Bergamot orange in rats Essential oil extract of Bergamot orange (BO) was investigated for its hepatoprotective effect on carbon tetrachloride-induced hepatotoxicity in rats. Six different groups were established. Silibinin was used as the reference agent. BO significantly reduced the serum ALT level when compared to CCl_4 group while it did not affect the serum AST level. The histopathological findings did not show any significant difference between the BO and CCl_4 groups. The results suggest that BO has a weak hepatoprotective effect in carbon tetrachloride induced acute liver toxicity [19].

2. V. A. Kangralkar *et al*., reported protective effect of essential oils of citrus reticulata on isoniazid induced hepatotoxicity in wistar rats. Liver damage was produced by isoniazid (50gm/kg, p.o. for 30days). The essential oil (200mg/kg, p.o.) was administered every 24hrs for thirty days, while standard group received Liv52. At the end of the study the marker enzymes in serum were

estimated. The group treated with isoniazid alone (positive control) showed significantly elevated level of ALT, AST, bilirubin and significantly decreased total protein content as compared to negative control (not challenged with isoniazid) animals. The animals treated with essential oil of Citrus reticulata and Liv52 showed significant reduction in all the biochemical parameters [20].

CONCLUSION:

Citrus is part of a group of evergreen shrubs and small trees, native to tropical and subtropical regions. The fruits are relatively large, fleshy and juicy and contain significant amounts of citric acid and vitamin C. It is well established that citrus products are a rich source of vitamins , minerals and dietary fibre that are essential for normal growth and development . It is reveals from the literature that the citrus fruit possess anti-cancer, antimicrobial, antioxidant, antiulcer, anti-inflammatory, and hypolipidemic antityphoid and hepatoprotective properties.

ACKNOWLEDGEMENTS

The authors wish to thanks to all the staff of Pharmacy college azamgarh for their unresrved support and cooperation in collecting different articles for the preparation of this review article.

REFERENCES:

1. Dawood El-Antaki, Tazkret Oli El-Halaby & Co., Cairo, Vol. 1, 1952.
2. Waterman PG and Grundon MF: Chemistry and Chemical Taxonomy of the Rutales. Academic Press Inc., New York, 1983.
3. Okwu DE, Emenike IN:Evaluation of the phytonutrientsand vitamins content of citrus fruits. International Journal of Molecular Medicine and Advance Sciences 2006; 2: 1; 1-6.
4. Roger GDP: Encyclopedia of medicinal plants, Education and Health. Library editorial safeliz S. L. Spain: 153-154, 265-267.
5. Harley I, Manner S, Richard, Buker, Virginia Easton Smith, Deborah Ward and Craig R. Elevitch: Species Profiles for Pacific Island Agro forestry.
6. Jacob R, Hasegawa S, and Gary Manners : The potential of *Citrus limonoids* as anticancer agents.Perishables Handling Quarterly; 2000: 102.
7. Maliheh E, Ahmad M, Fathollah F, Sedigheh M, Mehrdad H and Abdolreza AL: Antimutagenicity and anticancer effects of *Citrus medica* fruit juice. Acta Medica Iranica 2009; 47: 5; 373-377.
8. Jansen S: Anticancer and health protective properties of citrus fruits components. Asia Pacific Journal of Clinical Nutrition 2002; 11: 1; 79–84.
9. Kumar A, Narayani M, Subanthini A and Jayakumar M: Antimicrobial activity and phytochemical analysis of citrus fruits peel utilization of fruit waste. International Journal of Engineering Science and Technology 2011; 3:6; 5414-5421.
10. Ramakrishna N, Arunachalam M, Philip G, Michael G, Johnson A, Vesela I, Chalova TR, Jeff AC, John D, Arthington DJ and Steven CR: Antimicrobial activity of commercial citrus based natural extract against *Escherichia coli* O157: H7 Isolates and mutant strains. Food borne Pathogens and disease 2008; 5: 5.
11. Nengguo T, Yumei G, Yuejin L and Fei G: Carotenoids from the peel of Shatian Pummelo (*Citrus grandis* Osbeck) and its antimicrobial activity. American Eurasian Journal of agricultural and environmental science 2010; 7: 1; 110-115.
12. Chutia M., Deka BP, Pathak MG, Sarma TC and Boruah P: Antifungal activity and chemical composition of *Citrus reticulata* blanco essential oil against phytopathogens from North East India. Food Science and Technology 2009; 42: 777–780.
13. Kumar RV, Nandini S, and Anitha S: Antityphoid activity of aqueous extract of fruit peel *Citrus sinensis*. International Journal of Pharma. Research and Development 2010; 2: 1; 217-212.
14. Aleksandra DC and Tomasz T: Antioxidant properties of different fruit seeds and peels, ACTA Scientiarum Polonorum Technologia Alimentaria 2007; 6: 3; 29-36.
15. Mehmet K, Hanefi O, Aydın H, Mehmet T, Hasan AA, and Veysel K: Investigation of antiinflammatory activity of Bergamot oil. European Journal of General Medicines 2007; 4: 4; 176-179.
16. Nagaraju B, Anand SC, Nazeer A, Narendra SC, Faiyaz A and Padmavathi GV; Antiulcer activity of aqueous extract of *Citrus medica* Linn. fruit against ethanol induced ulcer in rats. Advances in Biological Research 2012; 6:1; 24-29.
17. Nagaraju B, Puranik DS, Patan F, Padmavathi GV, Faiyaz A, Dattathreya G and Sharma YK: Antiulcer effect of aqueous extract of *Citrus medica* Linn. on water immersion restraint stress induced gastric ulcer in rats. Journal of Pharmacy Research 2011; 4: 11; 3994-3996.
18. Khan Y, Khan RA , Syeda A, and Afshan S: Evaluation of hypolipidemic effect of *Citrus lemon*. Journal of Basic and Applied Sciences 2010; 6: 1; 39-43.
19. Mehmet K, Fatma İ, Hasan A, Aydın H, Mehmet T and Hanefi O: Evaluation of hepatoprotective activity of *Bergamot orange* in rats. Eastern Journal of Medicine 2005; 10: 1- 4.
20. Kangralkar VA, Gavimath CV, Venkatesh V, Gowri B, Vinay RH and Priya M: P rotective effect of essential oils of *citrus reticulata* on isoniazid induced hepatotoxicity in wistar rats. International Journal of Pharmaceutical Applications 2010; 1: 2; 59-61.

How to cite this article:
Tomar A, Mall M and Rai P: Pharmacological Importance of Citrus Fruits. *Int J Pharm Sci Res*. 2013; 4(1); 156-160.