



Effects of citrus fruit and their bioactive components on immunity

Rakhi Sahu, Anurag Pandey, Mamta Tiwari, Nripendra Mishra, Atul Varshney

¹PG Scholar, ²Assistant Professor, Department of Vikriti Vigyan, Faculty of Ayurveda, Institute of Medical Sciences, Banaras Hindu University, Varanasi, U.P., India.

³Assistant Professor, Department of Swasthavritta and Yoga, Faculty of Ayurveda, Institute of Medical Sciences, Banaras Hindu University, Varanasi, U.P., India.

⁴Professor, Department of Panchakarma, Govt. Dhanwantari Ayurvedic College, Ujjiain, MP, India

⁵Professor, Department of Vikriti Vigyan, Government of Uttar Pradesh, India.

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ABSTRACT

The genus *Citrus* contains a vast range of antioxidant metabolites, dietary metabolites and antioxidant polyphenols that protect plants from unfavourable environmental conditions, enhance their tolerance to abiotic and biotic stresses and possess multiple health-promoting effects in humans along with specifically Immunity boosting. Immunity is described as a condition of being able to resist a particular disease especially through preventing the development of a pathogenic microorganism or by counteracting the effects of its products. The immune system is a bodily system that produces the immune response to defend your body from foreign substances, cells and tissues. The immune system includes various parts of the body including the thymus, spleen, lymph nodes, special deposits of lymphoid tissue (such as those in the gastrointestinal tract and bone marrow), macrophages, lymphocytes including the B cells and T cells and antibodies. This review summarizes various citrus fruit and their bioactive components having a positive effect to promote immunity responses in humans body. Additionally, we highlight the health-promoting properties along with Pharmacodynamic and Phytochemical properties of Citrus fruit described in Ayurveda and their potential usage.

Key words: Ayurveda, Citrus fruit, Flavonoids, Immunity, nutrients; orange juice

Address for Correspondence: Rakhi Sahu, PG Scholar, Department of Vikriti Vigyan, Faculty of Ayurveda, Institute of Medical Sciences, Banaras Hindu University, Varanasi-221005, Uttar Pradesh, India.
E-mail: rakhibhudr@gmail.com

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INTRODUCTION

The immune system provides the defence to the host against pathogenic organisms. A weak immune system increases susceptibility to infections and allows infections to become more severe. The role of the immune system is to protect the individual against pathogenic organisms including bacteria, viruses, fungi, and parasites. There is a wide array of potentially threatening organisms in the environment. Thus, to provide effective protection, the human immune system has evolved to include many different cell types and communicating molecules and multiple functional responses. Citrus fruits include many types of fruits, such as lemons, limes, grapefruit and several types of oranges. Fruits in the citrus family grow on evergreen trees or shrubs. They have fairly thick skins and pulpy flesh that's divided into segments. Citrus fruits come in a variety of sizes, vibrant colours and incredible scents. They provide many health benefits from boosting your immune system to reducing your risk of heart disease.

Citrus fruit juices contain a wide range of micronutrients (vitamins and minerals) and bioactive compounds, a comprehensive nutrient composition of orange juice has been provided elsewhere. Several of these micronutrients are important in immune function support and citrus fruit juice is a particularly good source of two of these, vitamin C and folate. Citrus fruits grow on flowering trees and shrubs. They are characterized by a leathery rind and white pith that encases juicy segments. We can find all kinds of citrus fruits year-round.

Here are some popular varieties of citrus fruits:

- Sweet oranges: Valencia, navel, blood orange, caracara
- Mandarins: Satsuma, clementine, tangor, tangelo
- Limes: Persian, key lime, kaffir
- Grapefruit: White, ruby red, oroblanco
- Lemons: Eureka, Meyer
- Other kinds: Citron, sudachi, yuzu, pomelos

Ayurveda pharmacodynamic properties of Citrus fruit

PLANT	BOTANICAL NAME	RASA	GUNA	VIRYA	VIPAKA	PRABHAVA	BIOACTIVITY
Lemon	<i>C. limon</i>	Amla	Teekshna and Guru	Usha	Amla	Vata Kapha Shamaka and increase pitta	Anticancer and antioxidant
Sweet orange	<i>C. sinensis</i>	Amla, Madhur and Tikta	Guru and Ushna	Ushna	Madhur	Vata Shamaka	Antimicrobial and Antioxidant
Lime	<i>C. aurantiifolia</i>	Amla	Laghu	Anushna	Madhur	Tridosha Shamaka	Anticancer activity
Sour orange	<i>C. aurantium</i>	Amla	Guru and Teekshna	Ushna	Amla	Kapha vata Shamaka	Antioxidant and Antiplatelet
Tangerine	<i>C. reticulata</i>	Madhurslightly Amla	Laghu	Sheeta	Madhur	Vata Shamaka, Increasing pitta and Nourishing Kapha	Antioxidant
Citron	<i>C. medica</i>	Amla	Teekshna	Ushns	Amla	Vata and Kapha Shamaka	Analgesic, Insulin secretagogue, anticancer and antiulcer

Phytochemicals effect of Citrus fruits

Ingredient	Phytochemicals Containing
Citrus limon	Flavonoids, phenolic acids (e.g., ferulic, synapic, p-hydroxybenzoic acids) and essential oil is rich in bioactive monoterpenoids such as D-limonene, β -pinene, γ -terpinene.
Citrus sinensis	Gama limonene, Hesperidin, Iso Hesperidin, Aurantiamarin, Auranetin, Tannin, Terpene and Geraniol

Citrus aurantifolia	Citric acid, Malic acid, Phosphoric acid, Volatile oil
Citrus aurantium	Volatile oil, Gum- resin, Aurantin, Ascorbic acid, 1- strachydrine
Citrus reticulata	Sabinene, Linalool, Methyl N-methylantranilate
Citrus paradise	flavanones narirutin and naringin and their aglycone (naringenin)
Citrus medica	Citrene, Citrol, Cymene, Citronellal

THE HEALTH BENEFITS OF CITRUS FRUITS

Citrus fruits provide us extra sunshine and warmth to your diet. Bright, colourful, fragrant, refreshing and juicy citrus fruits are not only delicious for their balanced tart and sweet taste, they are also an essential part of everyday nutrition. Citrus fruits are rich in multiple nutrients such as vitamin C, flavonoids and fibre which confer vascular protection, reduce inflammation, improve gastrointestinal function and health and play an important role in preventing conditions like diabetes, cancer, neurological disease. Like Lemons, limes, grapefruits and oranges are high in phytonutrients, such as carotenoids, flavonoids, and polyphenols. These nutrients are types of antioxidants and give the fruits their bright colours and strong scents. They can also help protect your body and prevent many health issues. The other beneficial effect of citrus fruits as per their active compound are as follows:

Vitamin C: Vitamin C (ascorbic acid) is one of the most popular vitamins in the world. Citrus fruits are notably rich in vitamin C. This vitamin is needed to form and maintain healthy skin, bones, blood vessels and connective tissues. Vitamin C plays an important role in supporting the immune system and also acts as an antioxidant that might help protect your cells against the effects of free radicals and fight inflammation. By reducing inflammation, vitamin C may prevent or delay heart disease conditions like arthritis and some types of cancer. Vitamin C helps the body to absorb iron from plant foods (non-heme iron). Therefore, eating citrus fruit alongside plant foods like leafy green vegetables, nuts, seeds and legumes will help the body better absorb iron. Citrus fruits are rich in vitamin C that is essential for building healthy body tissues.

Furthermore, Vitamin C contributes to immune defence by supporting various cellular functions of both the innate and adaptive immune systems. Vitamin C supports epithelial barrier function against pathogens and promotes the oxidant scavenging activity of the skin, thereby potentially protecting against environmental oxidative stress. Vitamin C accumulates in phagocytic cells, such as neutrophils, and can enhance chemotaxis, phagocytosis, generation of reactive oxygen species, and ultimately microbial killing. It is also needed for apoptosis and clearance of the spent

neutrophils from sites of infection by macrophages, thereby decreasing necrosis and potential tissue damage

Flavonoids: Flavonoids, a group of natural substances with variable phenolic structures, are found in fruits, vegetables, grains, bark, roots, stems, flowers, tea and wine. These natural products are well known for their beneficial effects on health. Flavonoids are now considered an indispensable component in a variety of nutraceutical, pharmaceutical, medicinal and cosmetic applications. This is attributed to their anti-oxidative, anti-inflammatory, anti-mutagenic and anti-carcinogenic properties coupled with their capacity to modulate key cellular enzyme function. Research on flavonoids received an added impulse with the discovery of the low cardiovascular mortality rate and also prevention of CHD.

Furthermore, they are plant-based nutrients (phytonutrients) responsible for the plant qualities such as its bright colour and the familiar aroma. Citrus fruits represent an important source of dietary flavonoids including hesperidin, hesperetin, naringin, naringenin, diosmin, quercetin, rutin, nobiletin, tangeretin and others. Flavonoids also have multiple therapeutic benefits. Studies indicate that citrus flavonoids protect the cells against the damage of free radicals. Through direct scavenging of free radicals, citrus flavonoids can reduce inflammation. Consequently, those anti-inflammatory pathways provide therapeutic benefits against cancer, neurodegenerative disorders, atherosclerosis, cardiovascular disease (CVD) and diabetes. For instance, Flavonoids may have a preventive action against atherosclerosis and CVD by scavenging free radicals, Flavonoids inhibit low-density lipoprotein (LDL) oxidation, reduce oxidative stress and inflammation, improve endothelial function and arterial blood pressure. Citrus flavonoids can protect against diabetes by improving glucose tolerance, increasing insulin secretion and sensitivity and decreasing insulin resistance and also may play a significant role in the development of antiobesity agents, reducing obesity and adipose tissue inflammation. Last but not least, citrus flavonoids can modulate gut bacteria (microbiome) composition and activity and exert beneficial effects on intestinal barrier function and gastrointestinal (GI) inflammation. This effect on the GI microbiome suggests that intake of citrus flavonoids can contribute to improved GI functioning and health.

Dietary Fiber: Dietary Fiber is a type of complex carbohydrate found in plant foods. It is made of many sugar molecules linked together in a way that cannot be entirely digested in the small intestine. Dietary fiber can be divided into two types: soluble and insoluble fiber and citrus fruits contain some of each kind.

Soluble fiber can help lower LDL cholesterol, consequently reducing cardiovascular disease. This type of fiber can also help improve glucose control by slowing the absorption of sugar resulting in better blood sugar levels. Insoluble fiber can help relieve constipation by helping food move more efficiently through the digestive system and increasing stool bulk.

Citrus fruits are also abundant in multiple other nutrients, including potassium, folate, calcium, thiamin, niacin, vitamin B6, phosphorus, magnesium, copper, riboflavin and pantothenic acid, making consumption of citrus fruits as part of a balanced diet is essential to our health.

Folate: Folate is essential for the synthesis of RNA and DNA and consequently for cell division, protein synthesis and tissue growth. It is not a surprise therefore that folate is required for the immune system to function. In common with other B vitamins, folate (vitamin B9) is involved in intestinal immune regulation, thus contributing to gut barrier function. Folate is essential for the survival of regulatory T cells in the small intestine wall, suggesting it plays a role in preventing adverse immune responses at that site. Regulatory T cells express high levels of folate receptor 4 (FR4) and administration of anti-FR4 antibody to mice results in a specific reduction in the regulatory T cell population, indicating that the folate-FR4 axis is required for regulatory T cell maintenance

FRUIT INTAKE RECOMMENDATIONS

The consumption of fruits and vegetables is associated with a reduced risk of many chronic diseases, including cardiovascular disease (Dauchet et al., 2006). Fruits and vegetables are nutrient-dense and relatively low in calories, which may help adults and children achieve and maintain a healthy weight. For individuals who get less than 30 minutes per day of moderate physical activity, daily recommendations for fruit intake range from 1 to 2 cups for children and adolescents and 1½ to 2 cups for adults depending on age (USDA, 2011). Based on NHANES 2001–2004 data, over 60% of children four to eight years of age over 78% of older children, and at least 80% of adults have usual intakes of fruit that fall below recommended intake amounts (Krebs-Smith et al., 2010) Excess body weight and associated comorbidities are a

paramount health issue in the world as well as in many developed countries. Consumption of 100% fruit juice has been marked as a potential contributor to overweight/obesity, particularly in children and adolescents (AAP, 2001; Faith et al., 2006). The intake of 100% fruit juice is recommended for children and adolescents, especially for those who are overweight or obese. In 2001, the American Academy of Pediatrics (AAP) published recommendations for fruit juice intake, stating that fruit juice consumption should be limited to 4 to 6 ounces per day for children 1–6 years of age, and 8 to 12 ounces/day for children 7–18 years of age (AAP, 2001). The AAP recognized that while 100% fruit juice can be a healthy part of the diet when consumed as part of a well-balanced diet, it has the potential to be over-consumed by children because of its taste and the willingness of parents to provide juice because of its healthfulness.

THE MAIN HEALTH BENEFITS OF CITRUS

Anti-carcinogenic properties: Citrus flavonoids possess anticarcinogenic and anti-tumor activities.

Cardiovascular properties: Citrus flavonoids show an antiadhesive and antiaggregation action against red cell clumping.

Hyperglycemia: Citrus flavonoids play important roles in preventing the progression of hyperglycemia, partly through binding with starch, increasing hepatic glycolysis and the glycogen concentration, and lowering hepatic gluconeogenesis.

Anti-inflammatory, Antiallergic and Analgesic activity: Citrus flavonoids like hesperidin, diosmin, quercetin, and other flavonoids have shown dose-dependent anti-inflammatory activity by influencing metabolism of arachidonic acid and histamine release.

Anti-microbial activity: One of the properties of flavonoids with their physiological action in the plants are their antifungal and antiviral activity.

Anti-anxiety, antidepressant, and antiallergic activity: Apigenin shows antidepressant activity, some flavonoids show antiallergic.

Citrus and lipids control: Many clinical studies reported that the citrus juice is helpful for control higher cholesterol and major lipid problem of the human body, due to the higher content of soluble and insoluble fiber in citrus juice.

CONCLUSION

The immune system provides the defence to the host against pathogenic organisms. It includes barrier functions and capabilities for the recognition and elimination of pathogens and for immunologic memory. A weak immune system increases susceptibility to infections and allows infections to become more severe. Nutrition is one

of many determinants of the immune response including the inflammatory component. Micronutrients (vitamins and minerals) are especially important for supporting normal immune response and plant polyphenols have also emerged as having important roles, not only in helping to control oxidative and inflammatory stress but also in supporting the activities of the cellular aspects of innate and acquired immunity. Citrus fruit juices contain a wide range of vitamins, minerals and polyphenols, with 100% orange juices being a particularly good source of vitamin C and folate. vitamin C is an antioxidant. As described earlier, both vitamin C and folate support the function of many types of the immune cell including phagocytes, natural killer cells, T-cells, and B-cells. Values for vitamin C and folate are 80 mg

and 200 µg respectively. it is well known that a balanced diet that satisfies the daily intake of vitamin C positively affects the immune system and reduces susceptibility to infections. Researchers are studying the effects of high dose intravenous (IV) vitamin C on the new coronavirus, can prevent or treat COVID-19 also. In summary, micronutrients and another bioactive present in citrus fruit juices have established plausible pathways for controlling oxidative stress and for supporting innate and acquired immune responses. Trials in humans demonstrate that orange juice effects on innate and acquired immunity require further exploration in well-designed trials inappropriate population sub-groups, such as older people.

REFERENCES

1. Miles EA, Calder PC. Effects of Citrus Fruit Juices and Their Bioactive Components on Inflammation and Immunity: A Narrative Review. *Front Immunol.* 2021;12:712608. Published 2021 Jun 24. doi:10.3389/fimmu.2021.712608
2. Department of Health. Nutrient Analysis of Fruit and Vegetables: Summary Report. London: Department of Health (2013). Available at: <https://www.gov.uk/government/publications/nutrient-analysis-of-fruit-and-vegetables>.
3. Calder PC. Feeding the Immune System. *Proc Nutr Soc* (2013) 72:299–309. doi: 10.1017/S0029665113001286
4. Maggini S, Pierre A, Calder PC. Immune Function and Micronutrient Requirements Change Over the Life Course. *Nutrients* (2018) 10:1531. doi: 10.3390/nu10101531
5. Gombart AF, Pierre A, Maggini S. A Review of Micronutrients and the Immune System-Working in Harmony to Reduce the Risk of Infection. *Nutrients* (2020) 12:236. doi: 10.3390/nu12010236
6. Calder PC. Nutrition, Immunity and COVID-19. *BMJ Nutr Prev Health* (2020) 3:74–92. doi: 10.1136/bmjnp-2020-000085
7. Calder PC, Carr AC, Gombart AF, Eggersdorfer M. Optimal Nutritional Status for a Well-Functioning Immune System is an Important Factor to Protect Against Viral Infections. *Nutrients* (2020) 12:1181. doi: 10.3390/nu12041181
8. Panche AN, Diwan AD, Chandra SR. Flavonoids: an overview. *J Nutr Sci.* 2016;5:e47. Published 2016 Dec 29. doi:10.1017/jns.2016.41
9. Carr, A. C., & Maggini, S. (2017). Vitamin C and Immune Function. *Nutrients*, 9(11), 1211. <https://doi.org/10.3390/nu9111211>
10. Bergsten P, Yu R, Kehrl J, Levine M. Ascorbic Acid Transport and Distribution in Human B Lymphocytes. *Arch Biochem Biophys* (1995) 317:208–14. doi: 10.1006/abbi.1995.1155
11. Jacob RA, Kelley DS, Pianalto FS, Swendseid ME, Henning SM, Zhang JZ, et al. Immunocompetence and Oxidant Defense During Ascorbate Depletion of Healthy Men. *Am J Clin Nutr* (1991) 54(6 Suppl):1302S–9S. doi: 10.1093/ajcn/54.6.1302s
12. Huijskens MJ, Walczak M, Koller N, Briede JJ, Senden-Gijsbers BL, Schnijderberg MC, et al. Technical Advance: Ascorbic Acid Induces Development of Double-Positive T Cells From Human Hematopoietic Stem Cells in the Absence of Stromal Cells. *J Leukoc Biol* (2014) 96:1165–75. doi: 10.1189/jlb.1TA0214-121RR
13. Manning J, Mitchell B, Appadurai DA, Shakya A, Pierce LJ, Wang H, et al. Vitamin C Promotes Maturation of T-Cells. *Antioxid Redox Signal* (2013) 19:2054–67. doi: 10.1089/ars.2012.4988
14. Sasidharan Nair V, Song MH, Oh KI. Vitamin C Facilitates Demethylation of the Foxp3 Enhancer in a Tet-dependent Manner. *J Immunol* (2016) 196:2119–31. doi: 10.4049/jimmunol.1502352
15. Nikolouli E, Hardtke-Wolenski M, Hapke M, Beckstette M, Geffers R, Floess S, et al. Alloantigen-Induced Regulatory T Cells Generated in Presence of Vitamin C Display Enhanced Stability of Foxp3 Expression and Promote Skin Allograft Acceptance. *Front Immunol* (2017) 8:748. doi: 10.3389/fimmu.2017.00748

16. Tanaka M, Muto N, Gohda E, Yamamoto I. Enhancement by Ascorbic Acid 2-Glucoside or Repeated Additions of Ascorbate of Mitogen-Induced IgM and IgG Productions by Human Peripheral Blood Lymphocytes. *Jpn J Pharmacol* (1994) 66:451–6. doi: 10.1254/jjp.66.451
17. Fraser RC, Pavlovic S, Kurahara CG, Murata A, Peterson NS, Taylor KB, et al. The Effect of Variations in Vitamin C Intake on the Cellular Immune Response of Guinea Pigs. *Am J Clin Nutr* (1980) 33:839–47. doi: 10.1093/ajcn/33.4.839
18. AAP (American Academy of Pediatrics), Committee on Nutrition. (2001). The use and misuse of fruit juice in pediatrics. *Pediatrics*. **107**:1210–1213.
19. Akhtar-Danesh, N. and Dehghan, M. (2010). Association between fruit juice consumption and self-reported body mass index among adult Canadians. *J. Hum. Nutr. Diet.* **23**:162–168
20. Kuo SM. Antiproliferative potency of structurally distinct dietary flavonoids on human colon cancer cells. *Cancer Lett.* 1996 Dec 20;110(1-2):41-8. doi: 10.1016/s0304-3835(96)04458-8. PMID: 9018079.
21. Kurowska EM, Spence JD, Jordan J, Wetmore S, Freeman DJ, Piché LA, Serratore P. HDL-cholesterol-raising effect of orange juice in subjects with hypercholesterolemia. *Am J Clin Nutr.* 2000 Nov;72(5):1095-100. doi: 10.1093/ajcn/72.5.1095. PMID: 11063434.
22. Sasidharan Nair V, Song MH, Oh KI. Vitamin C Facilitates Demethylation of the Foxp3 Enhancer in a Tet-dependent Manner. *J Immunol* (2016) 196:2119–31. doi: 10.4049/jimmunol.1502352
23. Shen W, Xu Y, Lu YH. Inhibitory effects of Citrus flavonoids on starch digestion and antihyperglycemic effects in HepG2 cells. *J Agric Food Chem.* 2012 Sep 26;60(38):9609-19. doi: 10.1021/jf3032556. Epub 2012 Sep 17. PMID: 22958058.
24. Shen W, Xu Y, Lu YH. Inhibitory effects of Citrus flavonoids on starch digestion and antihyperglycemic effects in HepG2 cells. *J Agric Food Chem.* 2012 Sep 26;60(38):9609-19. doi: 10.1021/jf3032556. Epub 2012 Sep 17. PMID: 22958058.