WORLD JOURNAL OF PHARMACY AND PHARMACEUTICAL RESEARCH

Research Article

Coden USA: WJPPCL

2026
Volume: 03
Issue: 11
Page: 01 - 10

THERAPEUTIC EFFECT AND ADR MONITORING OF LEMON SEED AND LEMON JUICE: A NARRATIVE REVIEW

Varsha Aniket Patole*[1], Suvarna Santosh Naikwade[2], Pradnya Kailas Murade[3], Nilesh Bhagwan Khedkar[4]

[1]Assistant Professor of Pharmacology Department, Pravara Rural College of Pharmacy, Pravaranagar. India 413714.

[2,3,4]B. Pharmacy Pravara Rural College of Pharmacy, Pravaranagar. India 413714.

Received: 24 September 2026 **Revised: 04 October 2026** **Accepted: 24 October 2026**

Corresponding Author: Varsha Aniket Patole
Address: Assistant Professor of Pharmacology Department, Pravara Rural College of Pharmacy, Pravaranagar. India 413714. **ORCID:** https://orcid.org/0009-0004-4364-7725,
DOI: http://doi.org/10.5281/zenodo.23984914,

ABSTRACT

Lemon (Citrus limon (L.) Burm. f.), a widely consumed fruit of the family Rutaceae, is valued for its nutritional and medicinal properties.[1,6] Lemon juice is rich in vitamin C, citric acid, flavonoids and phenolic compounds, while lemon seeds contain limonoids, fixed oils, fatty acids and other phytochemicals.[6,9–11] These constituents may contribute to antioxidant, anti-inflammatory, antimicrobial, antidiabetic, cardioprotective and neuroprotective activities, largely demonstrated in laboratory and animal studies.[3–5,8,23] Lemon juice may also reduce the risk of calcium stone formation by raising urinary citrate.[2,12,22] However, excessive consumption may cause dental enamel erosion, gastrointestinal discomfort and acid reflux, and contact with the skin followed by sunlight may cause phytophotodermatitis.[13–15, 24] The safety of concentrated lemon seed extracts is insufficiently investigated and long-term human effects are not established. Adverse drug reaction (ADR) monitoring is therefore important and should document the preparation, dose, frequency, duration, symptoms, comorbidities and concomitant medicines, with renal and hepatic parameters assessed where clinically indicated.[16–20] This review summarises the therapeutic potential, safety considerations and pharmacovigilance approach for lemon juice and lemon seed preparations, and highlights the need for toxicological and clinical studies to establish efficacy, dose and long-term safety.

KEYWORDS: *Citrus limon; lemon juice; lemon seed; limonoids; flavonoids; antioxidant activity; adverse drug reaction; pharmacovigilance.*

1. INTRODUCTION

Lemon (Citrus limon), a member of the family Rutaceae, is widely used in food, beverages and traditional systems of medicine because of its nutritional value and potential medicinal properties.[1,6,9] Lemon juice is a source of vitamin C, flavonoids, citric acid and phenolic compounds[7,9,23], whereas lemon seeds contain limonoids, fatty acids, fixed oils and phenolic compounds that are being investigated for biological activity.[10,11,21]

Research suggests that lemon juice and certain lemon-derived extracts may possess antioxidant, antimicrobial, anti-inflammatory, antidiabetic, cardioprotective and neuroprotective properties.[3,4,6,8] However, the strength of the evidence varies with preparation, concentration and type of study; many reported effects arise from in vitro or animal experiments, and clinical research is needed to confirm effectiveness in humans. Lemon juice and lemon seed extracts should therefore not be considered replacements for approved medical treatments.

2. Review Methodology

This article is a narrative review. It is based on the published literature listed in the reference list, comprising peer-reviewed research and review articles on Citrus limon, citrus flavonoids and limonoids, citrate and kidney stone disease, and citrus-related adverse reactions, together with clinical guidelines and World Health Organization and national pharmacovigilance documents. Sources were selected for relevance to the therapeutic potential, safety and ADR monitoring of lemon juice and lemon seed. No formal systematic search protocol, quality scoring or meta-analysis was applied, and findings are therefore presented descriptively.

3. Phytochemical Constituents

Lemon juice contains citric acid (the principal organic acid), ascorbic acid, and flavanones and flavones such as eriocitrin, hesperidin and diosmin, together with other phenolic compounds.[7,8,9,22] Lemon seeds contain limonoids (for example limonin and nomilin), fixed oils rich in unsaturated fatty acids, phenolics and flavonoids.[10,11,21] The composition varies with cultivar, maturity, extraction method and solvent, which complicates comparison between studies.

4. Pharmacological and Therapeutic Effects

4.1 Nootropic and Neuroprotective Effects

Nootropics are substances, including foods, supplements and medicines, used to improve

cognitive functions such as memory, learning, attention and concentration. The vitamin C, flavonoids and phenolics of lemon juice may protect neurons from oxidative stress, which is associated with neuronal damage and age-related cognitive decline.[3,23] Some experimental studies have examined the effect of lemon juice on memory-related behaviour in animals, but evidence for lemon seeds is limited, and cognitive benefit in humans has not been established. Standardised preparations, appropriate doses and validated memory and learning tests are required.

4.2 Anti-Ageing Effects

Oxidative stress, ultraviolet radiation and free radicals contribute to skin ageing. Vitamin C is essential for collagen synthesis, which supports skin firmness and tissue repair, and lemon flavonoids may protect cells against oxidative damage.[6,9] Lemon seed constituents show antioxidant activity under experimental conditions, but laboratory antioxidant activity is not equivalent to proven anti-ageing benefit in humans.[10] Direct application of concentrated lemon juice to skin may cause irritation and photosensitivity.[13,24]

4.3 Anticancer Activity

Citrus flavonoids and limonoids have been examined for effects on cell proliferation, apoptosis and oxidative stress in cell-culture and animal models.[4,5,21] Results vary with extract concentration, cancer-cell type and extraction method. Laboratory findings do not establish that lemon juice or seed extracts prevent or treat cancer in people, direct human evidence for lemon seeds is scarce, and lemon products must not be regarded as cancer treatments.

4.4 Antioxidant Activity

Lemon juice and seeds contain vitamin C, flavonoids, phenolics and limonoids that scavenge free radicals.[7–10,23] In vitro assays such as DPPH, ABTS and FRAP are commonly used, and measured activity depends on extraction technique, concentration and chemical composition.[10,23] The clinical relevance of lemon seed antioxidant capacity in humans remains to be established.

4.5 Anti-inflammatory Activity

Certain citrus flavonoids may modulate inflammatory pathways and mediators such as cytokines and prostaglandins.[4,5,8] Lemon seed constituents (flavonoids, phenolics, limonoids and fatty acids) are being studied for similar effects.[10,21] Findings from other parts of the plant cannot automatically be applied to seeds, and lemon products should not replace prescribed anti-inflammatory medicines.

4.6 Antimicrobial Activity

The acidity of lemon juice and its citric acid, flavonoids and other components can create an unfavourable environment for some bacteria and fungi, depending on organism, concentration and conditions of use.[6,9] Seed phenolics, flavonoids and limonoids show antimicrobial effects in controlled laboratory settings that vary with extraction method and solvent.[10,11] These preliminary findings are insufficient to establish clinical effectiveness.

4.7 Cardioprotective Activity

Citrus flavonoids and vitamin C may support vascular function by reducing oxidative stress.[4,8] Consuming lemon juice as part of a balanced diet may provide beneficial plant compounds. Effects of lemon-derived compounds on blood pressure and coagulation depend on dose, preparation and individual health condition, and specific cardioprotective effects of seed extracts have not been sufficiently established.[6,9]

4.8 Anti-Allergic Effect

Some citrus flavonoids show anti-inflammatory or anti-allergic effects in experimental studies, including possible effects on mediators such as histamine.[4,5,8] Anti-allergic activity of lemon seeds remains insufficiently established. Lemon products are not proven substitutes for established allergy medicines, and lemon juice may cause irritation in sensitive individuals.[14]

4.9 Antiurolithiatic Effect

Lemon juice contains a high concentration of citrate.[22] Citrate binds urinary calcium and inhibits calcium crystal formation, and increased urinary citrate is associated with a lower risk of calcium kidney stones; lemon juice and lemonade have therefore been considered as dietary adjuncts in stone prevention.[2,12,22] The effect depends on the urinary citrate response and the wider clinical context.

Table 1: Summary of reported activities of lemon juice and lemon seed and the nature of the evidence.

Activity	Main constituents implicated	Nature of evidence	Refs.
Antioxidant	Vitamin C, flavonoids, phenolics, limonoids	In vitro assays (DPPH, ABTS, FRAP); limited human data	7-10, 23
Anti-inflammatory	Flavonoids, limonoids, fatty acids	Mainly experimental	4, 5, 8, 10, 21
Anticancer	Flavonoids, limonoids	Cell-culture and animal models; no	4, 5, 21

		human evidence of treatment effect	
Antimicrobial	Citric acid, phenolics, limonoids	In vitro	6, 9-11
Cardioprotective	Flavonoids, vitamin C	Experimental; limited evidence for seed extracts	4, 6, 8, 9
Neuroprotective / nootropic	Vitamin C, flavonoids, phenolics	Animal studies; human benefit not established	3, 23
Anti-allergic	Flavonoids	Experimental	4, 5, 8
Antiurolithiatic	Citrate (lemon juice)	Dietary adjunct discussed in guidelines and reviews	2, 12, 22

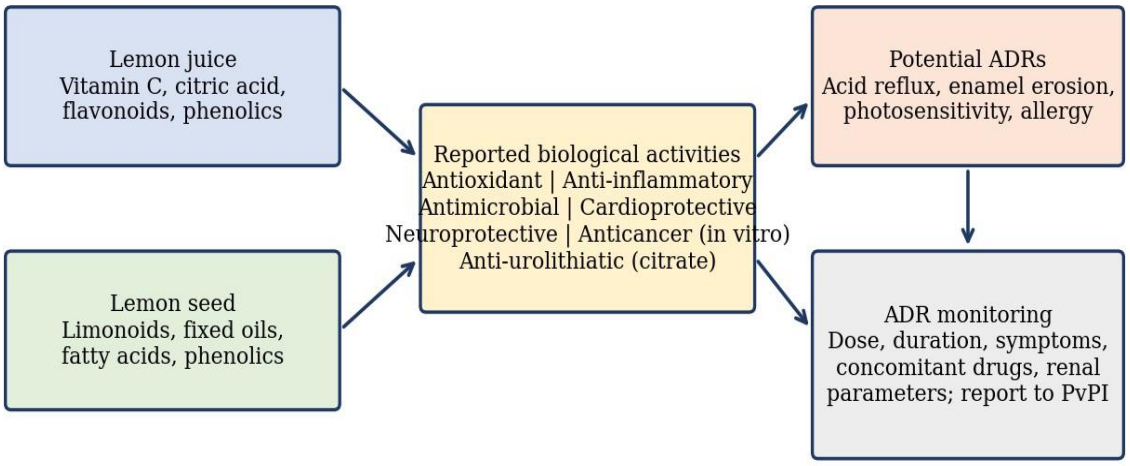


Figure 1. Schematic overview: constituents, reported activities, potential ADRs and monitoring approach

5. Adverse Drug Reaction Monitoring of Lemon Juice and Lemon Seed

An adverse drug reaction is a response to a medicinal product that is noxious and unintended.[16,18] Pharmacovigilance covers the detection, assessment, understanding and prevention of adverse effects of medicines, including herbal and traditional products.[17] National programmes such as the Pharmacovigilance Programme of India (PvPI) feed reports into the WHO Programme for International Drug Monitoring coordinated by the Uppsala Monitoring Centre.[19,20]

5.1 Lemon Juice

Although lemon juice is a common dietary ingredient, its acidity may irritate the stomach in sensitive individuals and worsen acid reflux, heartburn or gastric discomfort. Frequent exposure may cause dental enamel erosion.[15] Skin contact followed by sunlight exposure may cause phytophotodermatitis, because citrus fruits contain photosensitising furocoumarins.[13,14,24]

5.2 Lemon Seed

Information on the safety, toxicity and adverse effects of lemon seed consumption is limited compared with lemon juice. Concentrated seed extracts should be used cautiously; digestive discomfort or allergic reactions are possible, but their frequency and severity are not well characterised. Safety during pregnancy, lactation and long-term use has not been adequately established.

5.3 Interactions

Interactions of lemon products with conventional medicines are not well characterised. Some other citrus products (notably grapefruit) alter drug metabolism and transport and show how a fruit product can cause clinically significant interactions[25], so concomitant use with narrow-therapeutic-index medicines should be recorded and assessed.

5.4 Suggested ADR Monitoring Framework

Table 2: Suggested framework for ADR documentation and monitoring.

Domain	Details to document / monitor
Product	Juice, seed powder or concentrated extract; source, batch, preparation method
Exposure	Dose, frequency, duration and route (oral or topical)
Symptoms	Gastrointestinal, dental, dermatological (photosensitivity), allergic reactions; onset and course
Patient factors	Age, pregnancy or lactation, kidney disease, reflux disease, allergy history
Concomitant therapy	Prescription medicines, supplements and other herbal products
Laboratory (if clinically indicated)	Hydration status, urine output, serum creatinine, blood urea nitrogen, estimated GFR
Assessment and reporting	Causality assessment by a healthcare professional; report via PvPI / national pharmacovigilance channels

Suspected reactions should be assessed by a healthcare professional and reported through appropriate pharmacovigilance channels.[16,17,20] Preclinical toxicity studies and well-designed clinical trials are needed to evaluate dose-dependent effects, interactions and long-term safety. Lemon juice is generally consumed safely as food, but the safety of concentrated seed extracts should not be assumed without adequate evidence.

6. DISCUSSION

Lemon juice and seeds provide a range of bioactive compounds, including vitamin C, citric acid, flavonoids, phenolics, limonoids and fixed oils.[6, 9–11] Studies have explored antioxidant, anti-inflammatory, antimicrobial, antidiabetic, cardioprotective and

neuroprotective properties; these effects are mostly experimental, and translation to patient benefit has not been demonstrated.[3–5,8] The best-supported clinical application is the dietary use of lemon juice to increase urinary citrate in stone-prone patients.[2,12,22]

Excessive lemon juice intake may contribute to acidity, heartburn and dental erosion[15], while the safety profile of concentrated lemon seed extracts remains uncertain. A systematic approach to ADR monitoring that records dose, symptoms, concurrent medicines and, where indicated, laboratory parameters will help close this evidence gap.[16–20] The current evidence supports further investigation rather than the assumption that all proposed therapeutic effects are established in humans.

7. Limitations and Future Perspectives

As a narrative review, this article is subject to selection bias and did not apply formal quality assessment of the included studies. The available studies differ widely in extraction methods, doses and models, which limits comparison. Human data on lemon seed preparations are particularly scarce. Future work should include standardised, chemically characterised seed extracts; acute and sub-chronic toxicity studies; studies of herb-drug interactions; well-designed randomised controlled trials of lemon juice and seed preparations; and structured collection of case reports through pharmacovigilance systems.

8. CONCLUSION

Citrus limon contains bioactive substances that may contribute to antioxidant, anti-inflammatory, antimicrobial, antidiabetic and other biological activities, and has a long history in traditional medicine. These findings suggest areas for future research, but they do not establish lemon juice or lemon seed extracts as treatments for any condition. ADR monitoring is important for detecting side effects, allergic responses and interactions, particularly when lemon juice or concentrated seed extracts are used in large amounts or for therapeutic purposes. Further pharmacological, toxicological and clinical studies are needed to clarify benefits and risks and to support evidence-based use.

DECLARATIONS

Conflict of interest: [to be declared by the author]. Funding: [to be declared by the author].

Ethical approval: Not applicable; this review is based on published literature and involved no human participants or animals.

Author contribution: [to be declared by the author]. Acknowledgements: [to be added by the author].

Use of AI tools: [declare in line with the target journal policy].

ABBREVIATIONS

ABTS: 2,2'-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid); ADR: adverse drug reaction; BUN: blood urea nitrogen; DPPH: 2,2-diphenyl-1-picrylhydrazyl; eGFR: estimated glomerular filtration rate; FRAP: ferric reducing antioxidant power; PvPI: Pharmacovigilance Programme of India; UMC: Uppsala Monitoring Centre; WHO: World Health Organization.

REFERENCES

1. Singh N, Yarla NS, Siddiqi NJ, Pereira M de L, Sharma B. Features, pharmacological chemistry, molecular mechanism and health benefits of lemon. Med Chem. 2021. PMID: 32901586.
2. Barghouthy Y, Somani BK. Role of citrus fruit juices in prevention of kidney stone disease (KSD): a narrative review. Nutrients., 2021; 13(11): 4117. DOI: 10.3390/nu13114117.
3. Barreca D, Gattuso G, Bellocco E, et al. Flavanones: citrus phytochemical with health-promoting properties. BioFactors., 2017; 43(4): 495-506. DOI:10.1002/biof.1363.
4. Benavente-García O, Castillo J. Update on uses and properties of citrus flavonoids: new findings in anticancer, cardiovascular, and anti-inflammatory activity. J Agric Food Chem., 2008; 56(15): 6185-6205. DOI:10.1021/jf8006568.
5. Manthey JA, Grohmann K, Guthrie N. Biological properties of citrus flavonoids pertaining to cancer and inflammation. Curr Med Chem., 2001; 8(2): 135-153. DOI:10.2174/0929867013373723.
6. Klimek-Szczykutowicz M, Szopa A, Ekiert H. Citrus limon (lemon) phenomenon—a review of the chemistry, pharmacological properties, applications in the modern pharmaceutical, food, and cosmetics industries, and biotechnological studies. Plants., 2020; 9(1): 119. doi:10.3390/plants9010119.
7. Gattuso G, Barreca D, Gargiulli C, Leuzzi U, Caristi C. Flavonoid composition of citrus juices. Molecules., 2007; 12(8): 1641-1673. doi:10.3390/12081641.
8. Tripoli E, La Guardia M, Giammanco S, Di Majo D, Giammanco M. Citrus flavonoids: molecular structure, biological activity and nutritional properties: a review. Food Chem., 2007; 104(2): 466-479. doi:10.1016/j.foodchem.2006.11.054.

9. González-Molina E, Domínguez-Perles R, Moreno DA, García-Viguera C. Natural bioactive compounds of Citrus limon for food and health. J Pharm Biomed Anal., 2010; 51(2): 327-345. DOI: 10.1016/j.jpba.2009.07.027.
10. Liu W, Mao X, Zhou Z. Analysis of physicochemical properties, fatty acid composition and antioxidant activity of seed oil extracted from 12 citrus materials. Int J Food Sci Technol., 2022; 57(10): 6480-6491. DOI:10.1111/ijfs.15973.
11. Al Juhaimi F, Matthäus B, Özcan MM, Ghafoor K. The physico-chemical properties of some citrus seeds and seed oils. Z Naturforsch C., 2016; 71(3-4): 79-85. DOI: 10.1515/znc-2016-0004.
12. Türk C, Neisius A, Petrik A, et al. EAU Guidelines on Urolithiasis. European Association of Urology. https://uroweb.org/guidelines/urolithiasis.
13. Rossi AM, De Silva D, Meyer P, et al. New insights concerning phytophotodermatitis induced by phototoxic plants. Life., 2024; 14(8): 1019. DOI: 10.3390/life14081019.
14. Martínez-Escribano JA, et al. A spotlight on lime: a review about adverse reactions and clinical manifestations due to Citrus aurantiifolia. Int J Dermatol., 2021. https://pmc.ncbi.nlm.nih.gov/articles/PMC8310597/.
15. Grando LJ, Tames DR, Cardoso AC, Gabilan NH. In vitro study of enamel erosion caused by soft drinks and lemon juice in deciduous teeth analysed by stereomicroscopy and scanning electron microscopy. Caries Res., 1996; 30(5): 373-378. DOI: 10.1159/000262345.
16. World Health Organization. Safety of Medicines: A Guide to Detecting and Reporting Adverse Drug Reactions—Why Health Professionals Need to Take Action. Geneva: WHO; 2002. WHO/EDM/QSM/2002.2.
17. World Health Organization. The Importance of Pharmacovigilance: Safety Monitoring of Medicinal Products. Geneva: WHO; 2002. ISBN: 9241590157.
18. Edwards IR, Aronson JK. Adverse drug reactions: definitions, diagnosis, and management. Lancet., 2000; 356(9237): 1255-1259. DOI:10.1016/S0140-6736(00)02799-9.
19. Uppsala Monitoring Centre. WHO Programme for International Drug Monitoring. https://who-umc.org/ (accessed October 2026).
20. Pharmacovigilance Programme of India (PvPI), Indian Pharmacopoeia Commission. https://ipc.gov.in/ (accessed October 2026).
21. Limón-Rocha S, et al. Limonoids from Citrus: chemistry, anti-tumor potential, and other bioactivities. J Funct Foods., 2020; 75: 104213. DOI: 10.1016/j.jff.2020.104213.

22. Penniston KL, Nakada SY, Holmes RP, Assimos DG. Quantitative assessment of citric acid in lemon juice, lime juice, and commercially-available fruit juice products. J Endourol., 2008; 22(3): 567-570. DOI:10.1089/end.2007.0304.
23. Zou Z, Xi W, Hu Y, Nie C, Zhou Z. Antioxidant activity of Citrus fruits. Food Chem., 2016; 196: 885-896. DOI:10.1016/j.foodchem.2015.09.072.
24. Moore DE. Drug-induced cutaneous photosensitivity: incidence, mechanism, prevention and management. Drug Saf., 2002; 25(5): 345-372. DOI:10.2165/00002018-200225050-00004.
25. Bailey DG, Dresser G, Arnold JMO. Grapefruit–medication interactions: forbidden fruit or avoidable consequences? CMAJ., 2013; 185(4): 309-316. DOI:10.1503/cmaj.120951.