REVIEW ARTICLE

Utilization of Citrus Peel Waste: A Comprehensive Review on Pharmaceutical Approach

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Abstract

Citrus is one of the widely cultivated and economically significant fruit crops worldwide, extensively consumed in fresh and processed forms. It contains a rich source of essential nutrients, including vitamins, minerals, dietary fibers, and a diverse range of bioactive phytochemicals such as flavonoids, alkaloids, carotenoids, nitrogen-containing compounds, and various polyphenolic constituents. Large quantities of citrus processing wastes, mainly comprising peels, seeds, and pulp residues, are generated annually, which are often discarded despite their high potential value. In recent years, these citrus by-products have gained increasing attention as a promising, economical, and renewable source of biologically active compounds with wide-ranging applications. The present review highlights recent advances in the valorization of citrus peel waste, emphasizing its potential use in pharmaceutical, nutraceutical, food, and cosmetic industries. Citrus-derived nutraceuticals exhibit a broad spectrum of biological activities, including anti-carcinogenic, anti-mutagenic, anti-allergenic, anti-inflammatory, and anti-ageing properties. In addition, these compounds play an important role as natural antioxidants and serve as valuable alternatives or supplements to synthetic antioxidant agents. Beyond human health applications, citrus waste-derived products are also utilized in the development of functional foods, beverages, and value-added products contributing to sustainable waste management and circular bioeconomy approaches. Overall, citrus by-products represent a significant and underexploited resource with strong potential for industrial applications and health-promoting benefits.

Key words: Antioxidants flavonoids, citrus peel, food additives, nutraceuticals, phenolics, phytochemicals

INTRODUCTION

The global fruit processing industry generates substantial quantities of agro-industrial by-products, including peels, seeds, pulp residues, and pomace, which are often discarded despite their significant biochemical and economic potential. Among these, citrus fruits represent one of the most extensively cultivated and industrially processed horticultural commodities worldwide. According to recent Food and Agriculture Organization Corporate Statistical Database and United States Department of Agriculture Foreign Agricultural Service Foreign Agricultural Service estimates,[1] global citrus production remains remarkably high with oranges contributing approximately 45–50 million metric tons annually, followed by tangerines/mandarins (37–39 million metric tons), lemons/limes (23–24 million metric tons), and grapefruit (6.8–7.0 million metric tons). This large-scale production inevitably results in the generation of vast quantities of citrus processing waste, posing both environmental challenges and opportunities

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for resource recovery. India is among the leading citrus-producing nations, with an annual production estimated at approximately 12–14 million metric tons. Major citrus-growing regions include Maharashtra, Madhya Pradesh, Punjab, Rajasthan, Assam, and Karnataka. The rapid expansion of citrus cultivation and processing industries in India has consequently led to a significant increase in citrus-derived waste biomass. Inadequate utilization of these residues contributes to environmental burdens, including disposal issues and potential pollution, thereby necessitating sustainable valorization strategies. Citrus peel wastes are now widely recognized as a rich and renewable source of bioactive compounds, including dietary fibers, pectins, flavonoids, phenolic acids, essential oils, and natural pigments. These compounds exhibit diverse functional properties and have attracted considerable attention for applications in food, pharmaceutical, nutraceutical, and cosmetic industries. For instance, citrus-derived fibers have been extensively investigated for their role in improving gastrointestinal health and as functional food ingredients.[2] Similarly, flavonoids and other polyphenolic constituents have demonstrated strong antioxidant, anti-inflammatory, and therapeutic potential, supporting their use in health-promoting formulations.[3,4] At an industrial scale, citrus pomace generation is also significant in India generate 7.8 million tons of waste annually from citrus processing operations,[5] highlighting the global magnitude of this biomass stream. In parallel, increasing consumer demand for natural, clean-label, and sustainable ingredients has intensified research efforts toward the recovery and valorization of citrus waste. Consequently, the development of efficient extraction and biorefinery approaches for citrus by-products aligns strongly with circular bioeconomy principles, offering both environmental and economic benefits. This review highlights the diverse applications of citrus fruits and their by-products, including their use in food and beverages, traditional medicinal systems, and recent advancements in pharmaceutical and nutraceutical development.

CITRUS FRUIT: ANATOMY AND BIOCHEMICAL COMPOSITION

Citrus fruits belong to the genus *Citrus* within the family Rutaceae and are widely recognized for their characteristic aroma, refreshing taste, and thirst-quenching properties. In addition to their nutritional value, citrus fruits have been valued for their medicinal importance since ancient times. The genus includes several major cultivated groups such as sweet orange (*Citrus sinensis*), mandarin (*Citrus reticulata*), lime (Citrus aurantiifolia), lemon (*Citrus limon*), pomelo (*Citrus maxima*), and grapefruit (*Citrus paradisi*), which are extensively grown across tropical and subtropical regions worldwide. The anatomical structure of citrus fruits varies depending on the species, cultivar, maturity stage, and fruit quality. A typical citrus fruit consists of distinct non-edible components illustrated in Figure 1. The edible portion mainly includes the juice vesicles, while the non-edible fractions comprise the peel, which is further differentiated into flavedo and albedo along with seeds and segment membranes. The quantitative physical composition and internal structure of a representative citrus fruit are presented in Figure 2.

From a compositional perspective, citrus by-products or waste fractions exhibit a complex chemical profile. The non-edible parts, particularly peel flavedo, albedo, and seeds, are rich in dietary fiber, soluble sugars, starch, proteins, lipids, ash, and structural polysaccharides such as cellulose, hemicellulose, lignin, and pectin, along with a wide range of bioactive phytochemicals [Figure 3].

In addition, the macro and micronutrient composition of citrus residues further highlights their nutritional and functional potential [Figure 4]. Citrus processing waste typically accounts for nearly 55–60% of the total fresh fruit weight, making it one of the largest agro-industrial by-products generated by fruit processing industries. Globally, citrus waste generation exceeds 15×10^6 tons annually.[6,7] Despite its rich biochemical composition, improper disposal of citrus waste poses significant environmental challenges, particularly in developing countries where infrastructure for biomass management is limited. Accumulation of such waste without adequate treatment can lead to environmental pollution due to microbial degradation and bioactive compound release. Therefore, understanding the anatomical structure and chemical composition of citrus fruits is essential for efficient utilization and valorization of their by-products, particularly in the context of sustainable waste management and industrial bioprocessing applications.

BIOACTIVE COMPOUNDS RECOVERY FROM CITRUS WASTES

The valorization of citrus peel waste has attracted considerable interest because it is a rich source of bioactive compounds with applications in the food, nutraceutical, pharmaceutical, and cosmetic industries. Recovery of these compounds involves sequential steps, including extraction, purification, identification, and structural characterization, with the choice of extraction method depending on the physicochemical properties of the target compounds. Common extraction solvents range from polar to non-polar systems, followed by purification using chromatographic or membrane-based techniques. Advanced analytical methods are then employed to characterize the recovered compounds, while bioaccessibility and bioavailability studies are conducted to evaluate their physiological effectiveness before their incorporation into functional foods, nutraceuticals, or pharmaceutical products [Figure 5].

The composition of citrus by-products varies according to the processing method and industry. Food processing residues

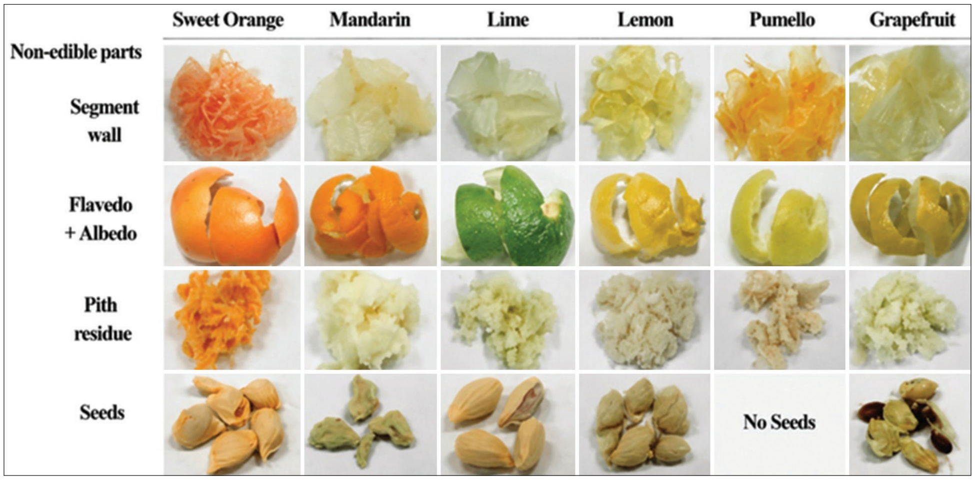


Figure 1: Distribution of non-edible parts of different Citrus species

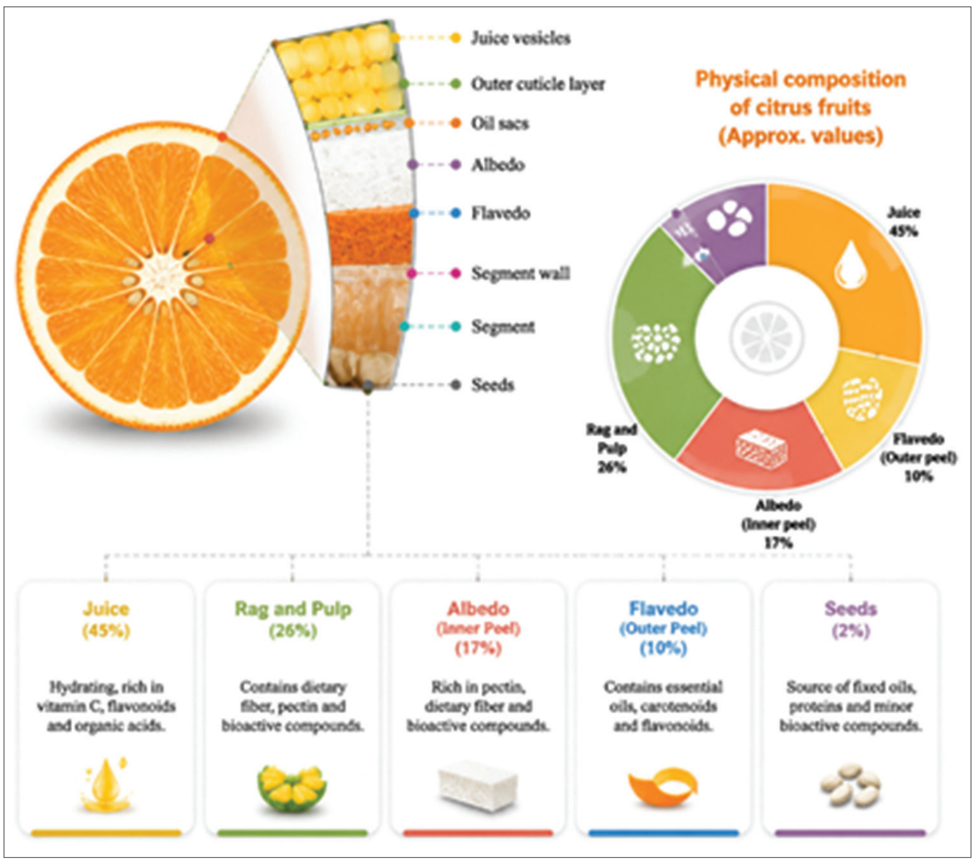


Figure 2: Structural anatomy and overall physical composition of a typical citrus fruit

generally retain higher levels of valuable compounds such as pectin and flavonoids, whereas chemical processing and harsh alkaline treatments may reduce their concentration while increasing lignin and ash content. Among the recovered bioactive compounds, polyphenols, carotenoids, flavonoids, and essential oils are the most valuable due to their potent antioxidant, anti-inflammatory, anticancer, and cardioprotective properties. Consequently, citrus by-products have emerged as sustainable, renewable resources for developing functional foods, pharmaceuticals, cosmetics, and other value-added products, with ongoing research exploring diverse citrus species to identify novel bioactive compounds with enhanced therapeutic potential.[4,8,9]

HEALTH BENEFITS OF BIOACTIVE COMPOUNDS FROM CITRUS WASTE

Citrus processing wastes are a rich and sustainable source of bioactive compounds, including polyphenols,

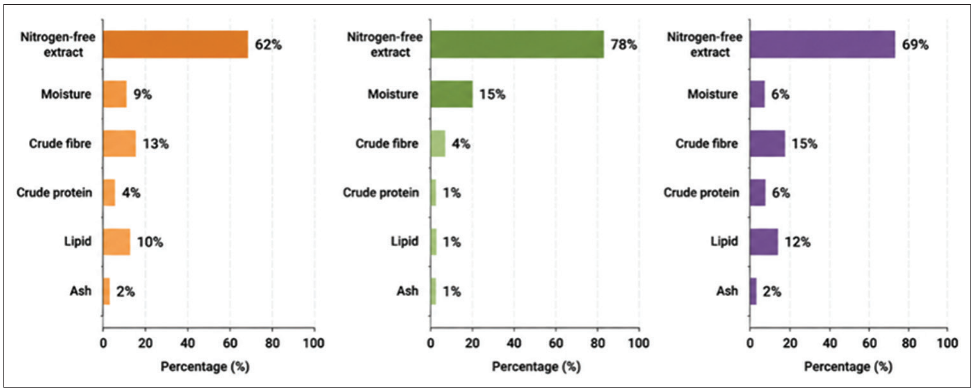


Figure 3: Chemical compositional profile of peel layers including flavedo, albedo, and seeds

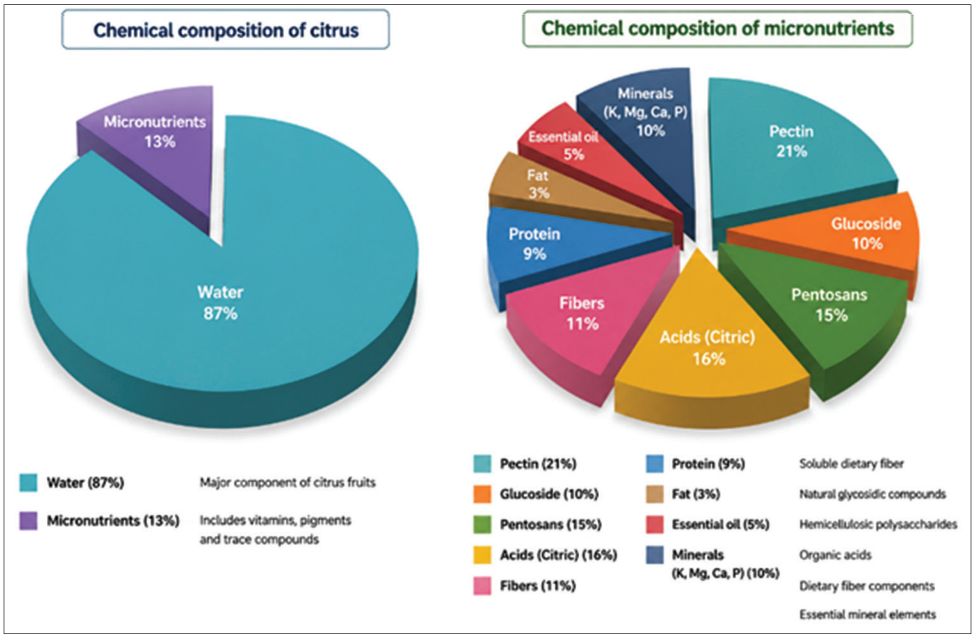


Figure 4: Chemical composition of nutrient constituents of citrus fruit

Figure 5: Schematic representation of the recovery process

flavonoids, carotenoids, vitamins, minerals, and dietary fiber, with extensive applications in the food, nutraceutical, pharmaceutical, and cosmetic industries. These phytochemicals are incorporated into functional foods, dietary supplements, natural preservatives, health beverages, and personal care products due to their antioxidant, antimicrobial, and antifungal properties, while also enhancing the sensory and nutritional quality of food products.

Increasing scientific interest has focused on the potential of citrus-derived bioactive compounds to prevent and manage chronic diseases associated with oxidative stress, including obesity, type 2 diabetes, cardiovascular diseases, and certain cancers. Natural antioxidants from citrus by-products help combat oxidative damage and may provide safer alternatives to conventional pharmacological therapies, which are often associated with adverse side effects.[10-13]

Among the most promising compounds, polymethoxyflavones, flavonoids, and citrus peel polyphenols have demonstrated potent antioxidant, anti-inflammatory, anticancer, and antidiabetic activities. Citrus peel extracts have also been shown to inhibit carbohydrate-digesting enzymes such as α-amylase and α-glucosidase, thereby improving postprandial glucose regulation and supporting metabolic health. These findings highlight the potential of citrus waste as a sustainable source of multifunctional bioactive compounds for developing safer nutraceutical and pharmaceutical products targeting metabolic and degenerative disorders.[14-16]

Citric acid derived from citrus fruits plays an important role in kidney stone prevention by promoting the conversion of insoluble oxalates into more soluble citrate complexes. These citrate complexes are readily excreted through urine, thereby reducing calcium oxalate crystallization and lowering the risk of renal stone formation. Several studies supporting this mechanism have been reported in the literature.[42] Table 1 summarizes recent scientific investigations highlighting the effects of citrus-derived phytochemicals on various diseases and human health outcomes.

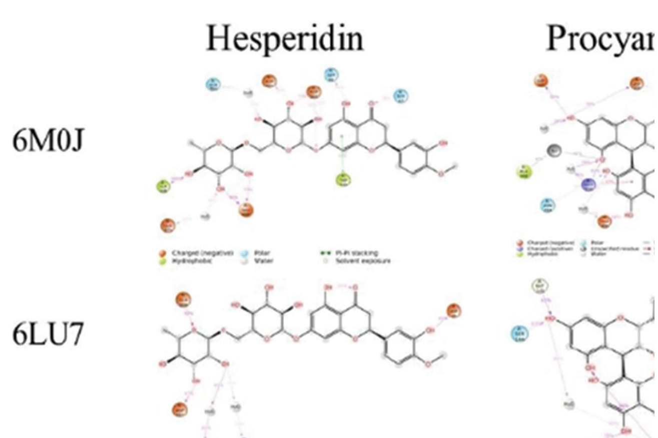
FOOD AND BEVERAGE APPLICATIONS OF DERIVED CITRUS WASTE

Citrus processing by-products have gained considerable attention as sustainable sources of functional ingredients due to their high concentrations of dietary fiber, pectin, flavonoids, phenolic compounds, essential oils, and natural antioxidants. Citrus peels, particularly the albedo, are rich in cellulose, hemicellulose, and pectin, making them suitable for the development of fiber-enriched functional foods. The incorporation of citrus fiber into bakery, dairy, and meat products improves water- and fat-binding capacity, cooking yield, texture, shelf stability, and nutritional quality while reducing the need for synthetic additives.[7,43,44] Moreover, citrus fiber has been reported to lower residual nitrite levels in processed meat products, thereby minimizing the formation of potentially carcinogenic nitrosamines and improving food safety.[45]

In the beverage industry, citrus waste provides a valuable source of natural pigments, pectin, essential oils, and clouding agents that enhance the sensory quality, stability, and nutritional value of fruit-based beverages. Citrus peel extracts are increasingly incorporated into functional beverages, herbal teas, jams, marmalades, and fermented products because of their pleasant aroma and rich phytochemical composition.[46,47] Traditional preparations such as honey citron tea, prepared using citrus fruits and peels with honey or medicinal herbs, further demonstrate the nutritional and therapeutic potential of citrus by-products. In addition, powdered citrus peel has been successfully incorporated into yogurt, ice cream, and bakery products to enhance antioxidant activity, dietary fiber content, and overall functional value.[4,8]

Beyond human nutrition, citrus processing residues such as dried citrus pulp and citrus molasses are valuable feed ingredients for livestock because of their high digestibility, soluble carbohydrates, and fermentable fiber. Dried citrus pulp can partially replace cereal grains in ruminant diets without adversely affecting feed intake, milk yield, or nutrient digestibility while improving rumen fermentation and animal health.[48,49] Although its application in monogastric animals is limited by high fiber content and bitter compounds such as limonin, processing methods, including drying, pelleting, and ensiling, improve palatability and feed value.[50] Overall, the utilization of citrus waste in food, beverage, and animal feed industries represents an effective strategy for producing sustainable value-added products, reducing agro-industrial waste, and supporting circular bioeconomy initiatives.[8]

LIGAND-PROTEIN INTERACTION



In Table 2, Jayaprakash *et al*.[62] revealed that the molecular docking interaction analysis that both hesperidin and procyanidin B_2 exhibited favorable binding interactions

Table 1: Citrus fruits waste reuse for various pharmaceutical/nutraceutical formulations

Citrus fruit	Fruit part extract/compound	Effect on health	Experiment model	Analytical/biochemical methods	References
C. grandis (Pummelo)	Peel extract and essential oil rich in naringin, limonene, and polymethoxyflavones; supercritical CO_2 extracted fractions	Antioxidant, antimicrobial, anti-inflammatory, cardioprotective potential	*In vitro* antimicrobial assays and molecular docking studies	GC-MS, supercritical CO_2 extraction, DPPH assay, MIC determination, molecular docking	[17]
C. sinensis (Sweet orange)	Peel extract (ethanol/hexane), rich in flavonoids (hesperidin, narirutin), phenolics, limonene, fatty acids	Antioxidant, anti-inflammatory, antimicrobial, antidiabetic potential	*In vitro* assays (DPPH, FRAP, CUPRAC, H_2O_2 scavenging), HepG2 cell-based antioxidant evaluation	Soxhlet extraction, GC–MS, HPLC, phytochemical screening	[18]
C. sinensis (Sweet orange)	Peel waste extracted using green solvents (carotenoids, flavonoids, phenolics)	Antioxidant, nutraceutical, anti-aging potential	*In vitro* antioxidant assays	Green solvent extraction, spectrophotometric assays	[19]
C. sinensis (Sweet orange)	Peel flavonoids (naringin, hesperidin-rich fraction)	Antioxidant, anti-diabetic, anti-obesity potential	*In vitro* enzyme inhibition assays	DPPH assay, α-amylase and α-glucosidase inhibition	[20]
C. sinensis (Sweet orange)	Hydrodistilled peel residue (polyphenols)	Antioxidant, antidiabetic potential	*In vitro* antioxidant and enzyme inhibition assays	ABTS, DPPH, α-amylase, α-glucosidase assays	[21]
C. sinensis (Sweet orange)	Peel phenolics (flavonoids, organic acids, catechins)	Antioxidant, antimicrobial, anticancer potential	*In vitro* biochemical assays	HPLC, UPLC, ORAC, FRAP assays	[22]
C. reticulata (Mandarin)	Peel extract (phenolics, flavonoids, hesperidin, narirutin, polymethoxyflavones)	Antioxidant, anti-inflammatory, anti-obesity, antidiabetic potential	*In vitro* antioxidant assays; enzyme inhibition studies; cell-based lipid metabolism models	GC-MS, UPLC-MS/MS, DPPH, FRAP, ABTS, α-amylase and α-glucosidase inhibition assays	[23]
C. reticulata (Mandarin)	Peel phenolic extract using green solvents (ethanol–water systems, ultrasound-assisted extraction)	Antioxidant, nutraceutical, anti-aging potential	*In vitro* assays; response surface optimization	Ultrasound-assisted extraction, green solvent extraction, HPLC-DAD	[24]
C. reticulata (Mandarin)	Peel metabolites (flavonoids, carotenoids, organic acids)	Anti-obesity, antidiabetic, antioxidant	Metabolomics-based *in vitro* bioactivity assays	UPLC-MS/MS, GC-MS, PCA/OPLS-DA, enzyme inhibition assays	[25]
C. reticulata (Mandarin)	Peel powder and extract fractions	Antioxidant, antimicrobial, functional food potential	*In vitro* antimicrobial and antioxidant assays	GC-MS profiling, MIC assay, DPPH radical scavenging	[26]
C. reticulata (Mandarin)	Peel flavonoid fraction (polymethoxyflavones, hesperidin derivatives)	Anti-inflammatory, antioxidant, metabolic regulation	*In vitro* cell culture (A549 inflammation model)	UPLC-Q-TOF-MS/MS, cytokine analysis (IL-6, TNF-α, IL-8)	[21]
C. aurantiifolia	Peel essential oil (limonene, citral, α-pinene, β-pinene)	Antioxidant, antimicrobial	*In vitro* bacterial inhibition assays	GC–MS, DPPH assay, MIC determination	[27]

(Contd...)

Table 1: *(Continued)*

Citrus fruit	Fruit part extract/compound	Effect on health	Experiment model	Analytical/biochemical methods	References
C. aurantiifolia	Peel extract (limonin, luteolin, flavonoids)	Antiplasmodial, antioxidant	*In vitro Plasmodium falciparum* assay	LC-MS, molecular docking, IC_{50} assay	[28]
C. aurantiifolia	Ethanolic peel extract (hesperidin-rich fraction)	Anticancer, anti-proliferative	Human hepatocellular carcinoma (PLC/PRF/5) cells	LC-qTOF/MS, MTT assay, apoptosis assay	[29]
C. aurantiifolia	Peel powder extract (flavonoids, tannins, limonoids)	Antimicrobial, insecticidal	*Bemisiatabaci* (whitefly) bioassay	GC-MS, LC-MS, mortality assay	[30]
C. aurantiifolia	Peel essential oil and phenolic extract	Antioxidant, antimicrobial, cytotoxic	*In vitro* antioxidant+microbial contamination model	GC-MS, LC-MS, DPPH, ABTS assays	[27]
C. limon (Lemon)	Peel extract rich in polyphenols (eriocitrin, hesperidin, naringin, limonoids)	Antioxidant, anti-diabetic, and antihypertensive potential	*In vitro* enzyme inhibition (α-amylase, α-glucosidase, ACE)	Enzyme assays, LC-MS, DPPH, ABTS assays	[31]
C. limon (Lemon)	Non-extractable phenolic fraction from peel	Antioxidant, anti-diabetic, antihypertensive	*In vitro* enzymatic+antioxidant assays	Ultrasound-assisted extraction, enzyme-assisted extraction, LC-MS	[32]
C. limon (Lemon)	Methanolic peel extract (flavonoids, tannins, alkaloids, terpenoids)	Antioxidant, antimicrobial, anticancer potential	*In vitro* GC-MS based phytochemical screening	GC-MS, phytochemical screening, qualitative assays	[33]
C. limon (Lemon)	Peel extract (phenolics, ascorbic acid, flavonoids)	Antioxidant, nutraceutical potential	*In vitro* antioxidant assays	Cloud point extraction, UV-Vis, phenolic quantification	[34]
C. limon (Lemon)	Limonoids isolated from peel	Anti-diabetic, antioxidant, metabolic regulation	*In vitro* enzyme inhibition+molecular docking studies	Molecular docking, enzymatic assays, computational modeling	[35]
C. paradisi	Peel extract (flavonoids: naringin, narirutin, hesperidin; limonoids; essential oils)	Antioxidant, anti-inflammatory, anticancer potential	*In vitro* HepG2 cancer cell line	GC-MS, LC–MS, MTT assay, molecular docking	[36]
C. paradisi	Peel phytochemicals (phenolics, flavonoids, saponins)	Antioxidant, anti-lipid peroxidation	*In vitro* antioxidant model	DPPH assay, lipid peroxidation assay, blending extraction	[18]
C. paradisi	Peel fractions (naringin-rich fraction)	Antibacterial, food preservative potential	*In vitro* bacterial strains (Gram±-)	Soxhlet extraction, TLC, NMR, column chromatography	[37]

(Contd...)

Table 1: *(Continued)*

Citrus fruit	Fruit part extract/compound	Effect on health	Experiment model	Analytical/biochemical methods	References
C. paradisi	Peel pulp bioactive compounds (flavonoids, carotenoids, limonoids)	Antioxidant, anticancer, metabolic regulation	Post-harvest processing study (irradiation, storage, freeze-drying)	LC–MS, GC–MS, HPLC	[38]
C. paradisi	Peel essential oil (limonene, myrcene, pinene)	Antimicrobial, antioxidant, functional food use	*In vitro* microbial inhibition studies	GC-MS, MIC assay, phytochemical screening	[39]
C. grandis	Peel extract rich in flavanones (naringin, narirutin), phenolics, limonoids	Antioxidant, anti-inflammatory, cardioprotective potential	*In vitro* antioxidant assays	DPPH, FRAP, ABTS assays; GC-MS profiling	[18]
C. grandis	Physiologically dropped fruit peel (flavanones, phenolic acids)	Antioxidant, nutraceutical, metabolic regulation	*In vitro* enzyme and antioxidant assays	LC-MS, HPLC, drying treatment analysis	[40]
C. grandis	Peel essential oil (limonene, β-pinene, myrcene)	Antimicrobial, anti-inflammatory, anticancer potential	*In vitro* antimicrobial and cytotoxic assays	GC-MS, MIC assay, MTT assay	[41]
C. grandis	Peel phenolic fraction (naringin-dominant extract)	Anti-obesity, antidiabetic potential	*In vitro* enzyme inhibition studies	α-amylase, α-glucosidase inhibition assays; molecular docking	[40]
C. grandis	Peel bioactive fraction (flavonoids, limonoids)	Antioxidant, anticancer, anti-inflammatory	*In vitro* cell line studies	LC-MS/MS, HPLC, MTT assay, ROS assays	[40]

C. paradisi: *Citrus paradisi*, *C. grandis: Citrus grandis, C. sinensis*: *Citrus sinensis*, *C. limon: Citrus limon, C. reticulata*: *Citrus reticulata*, *C. aurantiifolia*: *Citrus aurantiifolia*, TNF: Tumor necrosis factor-alpha, IL-8: Interleukin-8, IL-6: Interleukin-6, GC-MS: Gas chromatography–mass spectrometry, UPLC-MS/MS: Ultra-performance liquid chromatography-tandem mass spectrometry, MIC: Minimum inhibitory concentration, LC-MS/MS: Liquid chromatography-tandem mass spectrometry, HPLC: High-performance liquid chromatography, ABTS: 2,2'-azino-bis (3-ethylbenzothiazoline-6-sulfonic acid), ROS: Reactive oxygen species, DPPH: 2,2-diphenyl-1-picrylhydrazyl, FRAP: Ferric reducing antioxidant power, ACE: Angiotensin-converting enzyme, TLC: Thin-layer chromatography, NMR: Nuclear magnetic resonance, ORAC: Oxygen radical absorbance capacity, MTT: 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide, LC-qTOF/MS: Liquid chromatography coupled with quadrupole time-of-flight mass spectrometry, PCA: Principal component analysis, OPLS-DA: Orthogonal partial least squares discriminant analysis, HPLC-DAD: High-Performance liquid chromatography with diode-array detection, H_2O_2: Hydrogen peroxide, CUPRAC: Cupric reducing antioxidant capacity, HepG2: Hepatocellular carcinoma G2

Table 2: Molecular docking against targeted protein

Compound class	Molecular target/protein	Biological role	Evidence source
Flavonoids (hesperidin, diosmin)	NF-κB, COX-2, iNOS	Anti-inflammatory pathway inhibition	[51]
Hesperidin	ACE2	Viral entry inhibition (SARS-CoV-2)	[52]
Naringenin	TMPRSS2, ACE2, Mpro, PLpro	Antiviral (COVID-19 docking targets)	[53]
Quercetin	SARS-CoV-2 Mpro (3CLpro), RdRp	Viral replication inhibition	[54]
Limonoids	Caspase-3	Apoptosis induction (anti-cancer)	[55]
Limonoids	NF-κB	Anti-inflammatory regulation	[56]
Citrus triterpenoids	Bcl-2, Bax pathway	Cancer cell apoptosis	[57]
Phenolics	ACE	Anti-hypertensive effect	[58]
Chlorogenic acid	α-glucosidase, α-amylase	Glycemic control	[59]
D-limonene	EGFR, PI3K/Akt pathway	Anticancer signaling inhibition	[60]
Citrus terpenoids	COX-2, NF-κB	Anti-inflammatory activity	[51]
Essential oils	SARS-CoV-2 Mpro, ACE2	Antiviral docking potential	[61]

NF-κB: Nuclear factor kappa-light-chain-enhancer of activated B cells, COX-2: Cyclooxygenase-2, iNOS: Inducible nitric oxide synthase, SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2, PI3K: Phosphoinositide 3-kinase, EGFR: Epidermal growth factor receptor, Akt: Activates protein Kinase B, ACE: Angiotensin converting enzyme, TMPRSS2: Transmembrane protease, serine 2

with the Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) target proteins 6M0J (Spike protein–angiotensin converting enzyme 2 complex) and 6LU7 (Main protease, Mpro). Both phytocompounds formed multiple hydrogen bonds with key amino acid residues within the binding pockets, indicating strong and stable ligand–protein interactions. In addition to hydrogen bonding, hydrophobic interactions, π-π stacking, water-mediated contacts, and solvent exposure further contributed to the stabilization of the ligand–receptor complexes. Hesperidin displayed extensive interactions through its hydroxyl and glycosidic groups, while procyanidin B_2 formed an even denser hydrogen-bonding network due to its abundant phenolic hydroxyl groups. These interaction profiles suggest that both compounds possess a high affinity for the selected viral targets and may effectively interfere with viral entry by targeting the spike protein as well as inhibit viral replication by binding to the catalytic site of the main protease.

FUTURE PROSPECTS

Plant-derived nutraceuticals are gaining increasing attention as natural alternatives to synthetic supplements, with citrus by-products emerging as a sustainable and economical source of valuable bioactive compounds for food, pharmaceutical, and nutraceutical applications. Future research should focus on developing efficient waste collection systems, standardized and eco-friendly extraction technologies, comprehensive characterization of bioactive compounds, and scalable processing methods to enable commercial utilization. In addition, economic feasibility assessments, supportive regulatory frameworks, and interdisciplinary collaboration are essential to facilitate industrial adoption. Finally, rigorous stability studies, toxicological assessments, and well-designed *in vivo* and clinical trials are required to validate the safety, efficacy, and health benefits of citrus-derived products before their widespread commercialization.

CONCLUSION

Citrus waste valorization represents a sustainable and cost-effective strategy for converting agro-industrial residues into high-value bioactive products with applications in the food, nutraceutical, pharmaceutical, cosmetic, and health beverage industries. Rich in flavonoids, phenolics, essential oils, and dietary fiber, citrus by-products provide natural alternatives to synthetic ingredients while supporting environmental sustainability, waste reduction, and circular bioeconomy initiatives. Their broad therapeutic potential and economic value highlight citrus waste as a promising resource for promoting human health and sustainable industrial development.

AUTHORS' CONTRIBUTIONS

A. Thamizhvanan: Writing original draft, visualization, resources data curation, conceptualization. S. Muthulakshmi: Review and editing, visualization, validation, supervision. T. Anitha: Visualization, validation, supervision, formal analysis. D. Lenin Raja: Formal analysis, conceptualization. S. Muthuramalingam: Conceptualization.

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