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REVIEW ARTICLE

Phytochemical Composition, Therapeutic Potential, and Applications Valorization of Pomegranate Peel

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Abstract: Pomegranate (*Punica granatum* L.) processing generates substantial quantities of peel by-products, representing approximately 26–30% of the total fruit weight. This agricultural residue is a concentrated reservoir of secondary metabolites, specifically hydrolyzable tannins such as punicalagins, punicalins, and ellagic acid, which contribute significantly to its biological potency. These bioactive constituents facilitate a range of health-promoting effects, including robust antioxidant, cardioprotective, anti-inflammatory, and antimicrobial activities. Global pomegranate cultivation produces millions of metric tons of waste annually, with pomegranate peels alone contributing nearly 1.6 billion tons to the global food waste stream. Recovery of these compounds through optimized drying and extraction processes enables their utilization in food fortification, pharmaceutical formulations, and sustainable packaging. Freeze-drying and microwave-assisted technologies have emerged as superior methods for preserving the structural and chemical integrity of the phenolic profile compared to traditional sun drying. The shift from conventional solvent extraction to green technologies like ultrasound-assisted and pressurized liquid extraction enhances yield efficiency while reducing environmental impact. The usage of these extracts into various industrial sectors serves as a strategy for waste reduction and the development of natural, high-value functional products. Sustainable management of this bio-resource supports the transition toward a circular economy in the fruit processing industry.

Keywords: *Punica granatum*; Punicalagin; Bioactive Extraction; Waste Valorization; Phytochemical Composition.

1. Introduction

The pomegranate (*Punica granatum* L.), a member of the Lythraceae family, is a deciduous shrub or small tree native to a region spanning from Iran to the Himalayas in northern India [1]. Historical cultivation patterns indicate its spread from the Mediterranean basin to the Americas, where it has been utilized for millennia in both dietary and medicinal contexts. The fruit is anatomically divided into the edible sarcotesta (arils) and the inedible pericarp, commonly referred to as the peel. This peel constitutes nearly one-third of the fruit mass and possesses a complex matrix rich in flavonoids, anthocyanins, and hydrolyzable tannins [2].

Figure 1. Flowers and Fruits of *Punica granatum* L.

Global food waste statistics indicate that approximately one-third of all food produced is lost or discarded. Within the horticultural sector, pomegranate peels represent a significant environmental challenge, with an estimated annual contribution of 1.6 billion tons to global waste [3]. In regions like India, which led production with 2.84 million metric tons in 2018, the accumulation of this by-

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product requires innovative valorization strategies [4]. The nutritional density of the peel, characterized by high concentrations of dietary fiber, organic acids, and minerals, positions it as a viable raw material for the nutraceutical and cosmetic industries. Current research emphasizes the transformation of this waste into functional ingredients, natural colorants, and active packaging films [5, 6].

2. Biological and Therapeutic Properties of Pomegranate Peel Extracts

The efficacy of pomegranate peel extracts (PPE) is primarily attributed to the presence of ellagitannins, with punicalagin being the most abundant and biologically active component. These compounds interact with various molecular pathways to modulate oxidative stress, inflammation, and cellular signaling.

Table 1. Major Phenolic Constituents and Associated Therapeutic Targets

Bioactive Compound	Class	Biological Activity	Molecular Mechanism
Punicalagin (α, β)	Ellagitannin	Antioxidant, Cardioprotective	Upregulation of PON1; LDL oxidation inhibition [8, 10]
Ellagic Acid	Phenolic Acid	Anticancer, Anti-inflammatory	Induction of apoptosis; suppression of PGE2 [12, 17]
Gallic Acid	Phenolic Acid	Antimicrobial, Antioxidant	Metal chelation; inhibition of bacterial enzymes [16, 21]
Catechin/Epicatechin	Flavonoid	Cardioprotective	Improvement of endothelial function; ROS scavenging [2, 19]
Anthocyanins	Flavonoid	Anti-inflammatory	Inhibition of COX-2 and NO production [13, 14]
Granatin B	Ellagitannin	Anti-allergic, Anti-inflammatory	Suppression of paw edema and neutrophil activity [12, 15]

Table 2. Proximate Nutritional and Mineral Composition of Pomegranate Peel

Parameter	Composition (Range per 100g dry weight)	Mineral Components	concentration (mg/100g)
Moisture Content	70% – 75% (Fresh)	Potassium (K)	1,200 – 1,600
Total Carbohydrates	78.0 – 82.0 g	Calcium (Ca)	300 – 500
Crude Protein	3.0 – 5.5 g	Magnesium (Mg)	150 – 250
Total Dietary Fiber	35.0 – 50.0 g	Phosphorus (P)	70 – 110
Crude Fat	0.8 – 2.0 g	Iron (Fe)	5.0 – 12.0
Ash Content	3.5 – 6.0 g	Sodium (Na)	30 – 60

2.1. Cardioprotective Mechanisms

Atherosclerosis involves the accumulation and subsequent oxidation of low-density lipoproteins (LDL) within the arterial wall, a process that initiates foam cell formation and plaque development. Pomegranate polyphenols show potent inhibitory effects against LDL oxidation, thereby mitigating the progression of atherosclerotic lesions [7]. Specific compounds like punicalagin and gallic acid facilitate the up-regulation of paraoxonase 1 (PON1) expression in hepatic cells, an enzyme that protects lipoproteins from oxidative damage [8].

In vivo evidence suggests that PPE administration at dosages of 100 mg/kg provides significant protection against myocardial injury by reducing markers such as creatine kinase-MB and lactate dehydrogenase [9]. These effects are further supported by the modulation of nitric oxide synthase and the suppression of redox-sensitive transcription factors, which maintain vascular endothelial function under physiological stress [10]. Additionally, the dietary inclusion of pomegranate peel powder has been shown to lower serum cholesterol and triglycerides in hypercholesterolemic models, indicating its potential as a fiber-rich supplement for lipid management [11].

2.2. Anti-inflammatory and Anti-allergic Activity

Systemic inflammation is a precursor to various chronic pathologies, including rheumatoid arthritis and respiratory distress syndromes. Methanolic extracts of the pomegranate rind contain phytochemicals like granatin B and strictinin A, which suppress pro-inflammatory mediators including nitric oxide (NO) and prostaglandin E2 (PGE2) [12]. These compounds inhibit the expression of inducible enzymes like cyclooxygenase-2 (COX-2) within macrophages and neutrophils.

Experimental data show that aqueous PPE suppresses neutrophil myeloperoxidase activity, effectively limiting the production of hypochlorous acid and preventing collateral tissue damage [13]. In animal models, the intraperitoneal administration of pomegranate polyphenols at doses between 25 and 100 mg/kg significantly reduced paw edema and pain indices, showing efficacy comparable to standard non-steroidal anti-inflammatory drugs like indomethacin [14, 15].

2.3. Anticancer Potential

The role of reactive oxygen species (ROS) in DNA damage and malignant transformation is well-documented. Plant-derived antioxidants, particularly the flavonoids found in pomegranate peel, act as metal chelators to prevent radical-induced mutations [16]. Punicalagin and ellagic acid have been shown to induce apoptosis in various cancer cell lines by activating programmed cell death pathways and inhibiting tumor cell proliferation [17]. Unlike synthetic antioxidants, these natural compounds offer a safer profile for long-term dietary inclusion, making them prime candidates for cancer chemoprevention strategies.

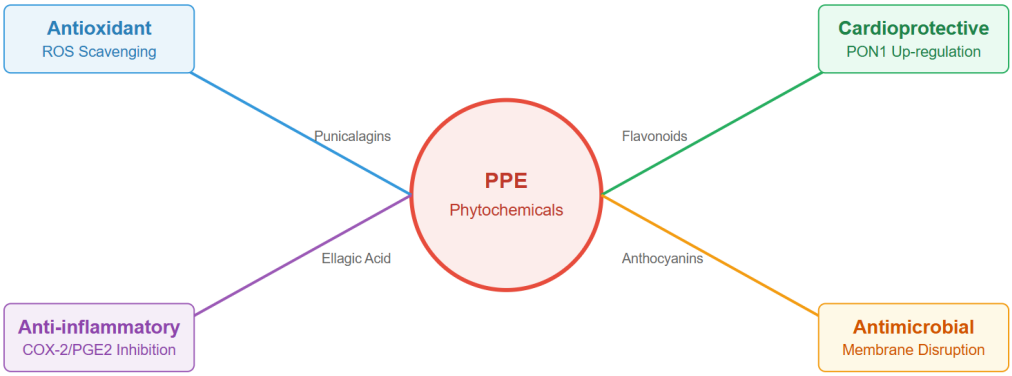

Figure 2. Mechanisms of Bioactivity of Pomegranate Peel

2.4. Antioxidant Capacity

The antioxidant potency of pomegranate peel is significantly higher than that of the edible arils or other fruit by-products like grape pomace. Quantitative analysis reveals a total phenolic content reaching 134.79 mg gallic acid equivalents (GAE) per gram of extract [18]. This high capacity is largely due to the synergistic interaction between various ellagitannins [19]. Clinical and laboratory observations confirm that PPE consumption reduces lipid peroxidation and thiobarbituric acid reactive substances (TBARS), thereby enhancing the overall antioxidant status in humans [20].

2.5. Antibacterial and Antimicrobial Action

The antimicrobial properties of the peel are linked to the ability of polyphenols to precipitate membrane proteins and inhibit essential bacterial enzymes. PPE has showed effectiveness against a broad spectrum of pathogens, including *Staphylococcus aureus*, *Escherichia coli*, and *Listeria monocytogenes* [21]. Extracts standardized to 13% ellagic acid exhibit specific inhibitory effects against *Propionibacterium acnes*, supporting their use in dermatological applications [22]. The integration of these extracts into gelatin-based films has also proven effective in creating active packaging that inhibits foodborne pathogens during storage [23].

2.6. Wound Healing and Gastroprotective Effects

Topical applications of PPE facilitate accelerated wound closure by enhancing epithelialization and increasing collagen deposition. In excisional wound models, treatment with pomegranate-derived gels improved hydroxyproline levels and granulation tissue strength [24]. In addition to external repair, methanolic extracts provide substantial protection against gastric mucosal injury. Oral administration has been shown to reduce aspirin- and ethanol-induced gastric ulcers by up to 74%, likely through the reinforcement of the gastric mucosal barrier and the reduction of oxidative stress within the stomach lining [25].

3. Preservation and Processing

Pomegranate peel possesses a high initial moisture content, rendering it highly susceptible to microbial degradation and enzymatic oxidation. Effective preservation is required to maintain the stability of the polyphenolic profile prior to extraction. Drying reduces

water activity, thereby extending shelf life and concentrating bioactive compounds, although the choice of technique significantly influences the final quality of the product [26, 27].

Table 3. Comparison of Dehydration Techniques on Peel Quality

Drying Method	Temperature/Conditions	Processing Time	Impact on Bioactivity	Quality Retention
Sun Drying	Ambient (25–35°C)	3 – 5 Days	High Vitamin C retention; risk of contamination	Moderate [28, 29]
Oven Drying	40°C – 60°C	16 – 29 Hours	Moderate degradation of heat-sensitive tannins	Moderate/Good [30, 31]
Microwave	240W – 600W	5 – 9 Minutes	High punicalagin isomers; uniform heating	Very Good [32, 33]
Freeze-Drying	Sub-zero (Vacuum)	24 – 48 Hours	Maximum retention of TPC and TTC; minimal shrinkage	Excellent [30, 35, 36]
Vacuum Drying	40°C – 50°C (100 mbar)	4 – 8 Hours	Protected from oxidation; efficient for heat-sensitive	Good [29]

3.1. Sun Drying

As a traditional low-cost preservation technique, sun drying relies on solar radiation to remove moisture. While economical for small-scale operations, its slow kinetics and exposure to environmental variables often lead to inconsistencies in phytochemical retention. However, studies have indicated that the gradual moisture reduction at low temperatures associated with sun drying can preserve vitamin C levels more effectively than rapid high-heat treatments [28]. In comparative assessments, sun-dried samples yielded phenolic contents (approximately 3670 mg GAE/100 g) that were competitive with commercial drying methods, although the risk of environmental contamination remains a primary drawback for industrial scaling [29].

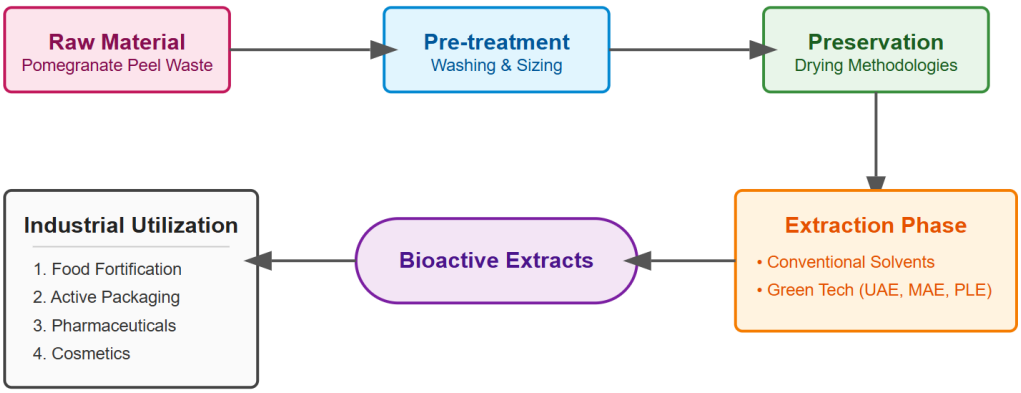

Figure 3. Valorization Process for Pomegranate Peel Waste

3.2. Oven and Thermal Drying

Oven drying utilizes forced air or thermal energy to accelerate dehydration. This method is characterized by its simplicity and speed compared to ambient techniques. Research indicates that pomegranate peels dried at 50°C exhibit the strongest antibacterial properties, whereas higher temperatures (60°C) may enhance the recovery of specific molecules like p-coumaric acid but lead to a decline in heat-sensitive vitamin C [30, 31]. While oven drying is accessible and cost-effective, prolonged exposure to elevated temperatures can induce thermal degradation of sensitive ellagitannins.

3.3. Microwave Drying

Microwave-assisted dehydration has emerged as a rapid and energy-efficient alternative, typically achieving complete drying within 5 to 9 minutes compared to hours or days required by other methods [32]. The volumetric heating provided by microwaves ensures uniform moisture removal. Vacuum microwave drying at 240 W has been shown to produce high concentrations of punicalagin isomers (α- and β-PC) in specific cultivars [33]. Advanced variations, such as microwave hydrodiffusion and gravity (MHG), further optimize the recovery of total phenolics and antioxidant activity while drastically shortening the processing time [34].

3.4. Freeze-Drying (Lyophilization)

Freeze-drying is widely regarded as the gold standard for preserving the chemical integrity of botanical materials. By operating via sublimation under vacuum at sub-zero temperatures, it minimizes structural shrinkage and prevents the thermal degradation of phytochemicals [35]. Freeze-dried pomegranate peels consistently exhibit the highest levels of total phenolics, tannins, and flavonoids, often 3 to 5 times greater than oven-dried counterparts [30]. Specifically, retention of punicalagins and ellagic acid is maximized through this method, with values reaching 113 mg/g and 3.2 mg/g, respectively [33, 36]. Despite its superior quality, high operational costs and energy requirements limit its application to high-value pharmaceutical and cosmetic products.

3.5. Vacuum Drying

Vacuum drying operates at reduced pressure, allowing for moisture evaporation at lower temperatures. This environment protects heat-sensitive compounds and prevents oxidative changes. While effective for various fruit peels, research on its specific application to pomegranate is relatively sparse. Some data suggest that while it is energy-efficient and eco-friendly, it may occasionally yield lower phenolic retention compared to freeze-drying, depending on the extraction solvent used [29].

4. Extraction Methods for Bioactive Recovery

The separation of bioactive compounds from the peel matrix is a critical step in valorization. The evolution of extraction science has shifted focus from traditional solvent-based methods to green, sustainable technologies.

4.1. Conventional Extraction Techniques

4.1.1. Solvent Extraction

Maceration and stirring using organic solvents such as methanol, ethanol, and acetone remain common laboratory practices. Methanol is frequently cited for its high efficiency in recovering a broad spectrum of polyphenols [37]. However, ethanol-water mixtures (typically 70% ethanol) are preferred for food-grade applications due to their lower toxicity and higher safety profile. Research indicates that while higher temperatures can improve solubility and diffusion by disrupting cell walls, exceeding 40 °C often leads to the thermal degradation of flavonoids and anthocyanins [38, 39].

4.1.2. Soxhlet Extraction

Soxhlet extraction involves continuous reflux of the solvent through the plant material. This method ensures exhaustive extraction of solutes based on their polarity. While effective for isolating specific fractions, the prolonged exposure to boiling temperatures and the high volume of solvent required make it less desirable for heat-sensitive compounds and modern environmental standards [40].

4.2. Green Technologies

4.2.1. Ultrasound-Assisted Extraction (UAE)

UAE utilizes acoustic cavitation—the formation and collapse of microscopic bubbles—to mechanically disrupt plant tissues and release intracellular compounds into the solvent [41].

Table 4. Technical Parameters of Advanced Extraction Technologies

Technology	Typical Parameters	Advantages	Limitations
Conventional (Solvent)	25°C–40°C; 24h	Low equipment cost; simple operation	High solvent use; slow [37, 38]
Ultrasound (UAE)	20–40 kHz; 15–30 min	Acoustic cavitation; cell wall disruption	Scalability issues [41, 42]
Microwave (MAE)	400W–800W; 2–5 min	Rapid heating; high throughput	Risk of thermal degradation [43-45]
Pressurized (PLE)	4–10 MPa; 100°C–150°C	High purity; reduced solvent volume	High equipment cost [46, 47]

This technology typically operates at frequencies above 20 kHz and can be implemented via ultrasonic baths or high-intensity probes. UAE offers significant advantages over conventional methods, including reduced solvent consumption, shorter extraction times, and higher yields of phenolic and antioxidant compounds [42, 43].

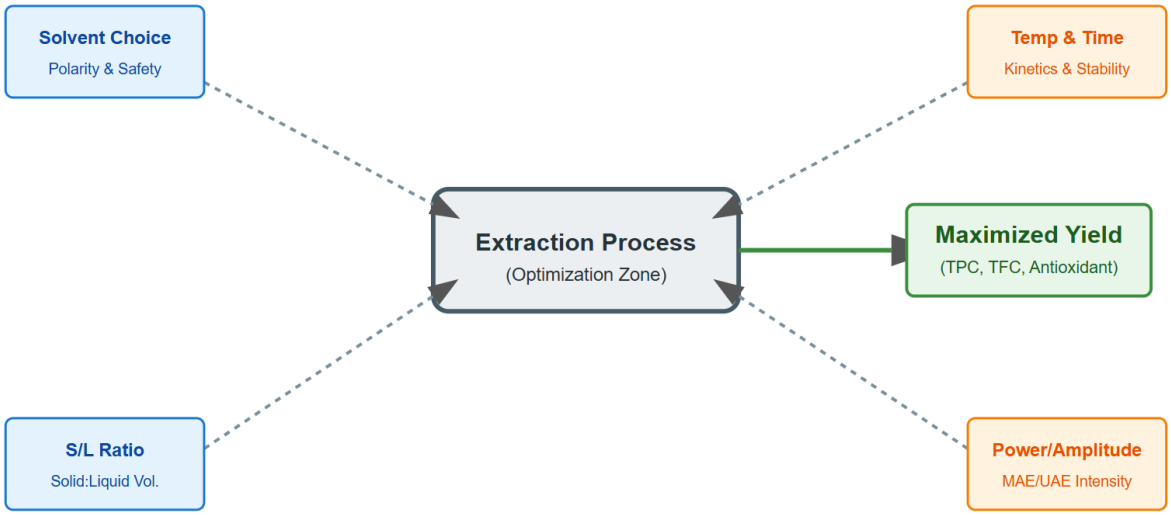

Figure 4. Critical Factors Influencing Bioactive Extraction Yield

4.2.2. Microwave-Assisted Extraction (MAE)

MAE leverages electromagnetic radiation to induce dipolar rotation and ionic conduction, resulting in rapid, uniform heating of the extraction mixture. The internal pressure generated by the evaporation of moisture within the plant cells causes structural disintegration, facilitating the rapid diffusion of phytochemicals [44]. Studies have shown that MAE can achieve up to 1.7 times higher extraction yields in a fraction of the time required by ultrasound-based methods, making it highly suitable for industrial throughput [45].

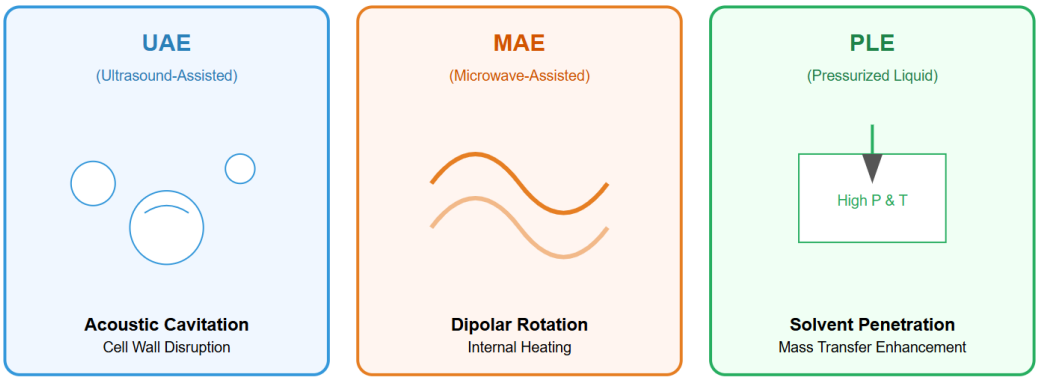

Figure 5. Principles of Modern Green Extraction Techniques

4.2.3. Pressurized Liquid Extraction (PLE)

PLE, also known as accelerated solvent extraction, employs solvents at elevated temperatures and pressures (above 4 MPa) to maintain the solvent in a liquid state while enhancing its penetration into the sample matrix [46]. This technique is particularly effective for recovering polar compounds like phenolics and anthocyanins. When combined with ultrasound (UAPLE), the efficiency is further enhanced. PLE provides high-purity extracts with minimal solvent waste, although the initial equipment cost is relatively high [47].

Table 5. Industrial Applications of Pomegranate Peel Extracts (PPE)

Industrial Sector	Application Type	Functional Role
Food Industry	Meat Preservation	Inhibition of lipid oxidation and microbial growth in chicken/pork [13, 15, 18]
Dairy Sector	Yogurt Fortification	Enhancement of antioxidant capacity and nutritional profile [9, 31]
Packaging	Active Bio-films	Antimicrobial barrier against *L. monocytogenes* and *E. coli* [23]
Cosmeceuticals	Skincare	Anti-tyrosinase activity; UV protection; wound healing [20, 24]
Pharmaceuticals	Dietary Supplements	Management of hypercholesterolemia and gastric ulcers [11, 25]
Bioenergy	Biofuel Feedstock	Renewable energy source from agricultural residue [1, 3]

5. Conclusion

Pomegranate peel represents a significant biological resource that transcends its status as agricultural waste. The abundance of hydrolyzable tannins and flavonoids within the peel matrix confers a diverse range of therapeutic benefits, notably in the management of oxidative stress, inflammation, and cardiovascular health. The industrial potential of these extracts is vast, spanning from natural food preservatives to therapeutic agents in the pharmaceutical sector. However, the retention of bioactive potency is strictly dependent on post-harvest processing. Freeze-drying remains the most effective method for preserving chemical integrity, while green extraction technologies like UAE and MAE provide sustainable pathways for large-scale compound recovery. Future development should focus on standardizing these extracts for clinical applications and exploring their bioavailability within human physiological systems to fully realize the commercial value of this multifunctional by-product.

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