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Review Paper

From Agricultural Waste to Dental Therapeutic Agent: A Comprehensive Review of Pomegranate Peel (*Punica granatum*) in Oral Health Care

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ABSTRACT

Pomegranate (*Punica granatum* L.) peel is a rich source of bioactive phytochemicals, including polyphenols, flavonoids, tannins, and phenolic acids such as punicalagin, ellagic acid, and gallic acid. These constituents impart potent antioxidant, antimicrobial, anti-inflammatory, wound healing, and anticancer activities. This review summarizes the botanical features, traditional and Ayurvedic uses, phytochemical profile, extraction methods, and pharmacological properties of pomegranate peel, with particular emphasis on its role in oral and dental health. Both conventional and advanced extraction techniques are discussed in relation to bioactive compound recovery. Experimental evidence supports the potential of pomegranate peel as a safe and effective natural alternative to synthetic agents in preventive and therapeutic dentistry. However, further clinical studies are required to establish its efficacy and clinical applicability.

INTRODUCTION

Pomegranate (*Punica granatum* L), a member of the family *Punicaceae*, is a widely cultivated medicinal fruit grown in regions such as India, Iran, Mediterranean countries, and Southeast Asia.^[1] The fruit is anatomically composed of peel, juice, and seeds, all of which are rich in bioactive constituents. Pomegranate contains essential vitamins and minerals along with high concentrations of polyphenols, flavonoids,

tannins, and anthocyanins, which are responsible for its potent antioxidant and antimicrobial properties. Several studies have demonstrated the strong antibacterial activity of pomegranate against cariogenic microorganisms, including *Streptococcus mutans*, *Streptococcus sanguinis*, and *Streptococcus mitis*.^[2] In addition to its antimicrobial effects, pomegranate exhibits significant antioxidant activity by scavenging reactive oxygen species, which play a crucial role

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in inflammation-mediated periodontal tissue destruction. Oral and dental health are integral components of general health and quality of life, influencing nutrition, communication, and overall well-being.^[3] Oral diseases such as dental caries, gingivitis, periodontitis, and pulpitis are among the most prevalent chronic conditions worldwide and are primarily caused by microbial infections, especially bacteria and fungi.^[4] The accumulation of dental plaque and microbial biofilm on tooth surfaces is widely recognized as the principal etiological factor in the initiation and progression of both caries and periodontal diseases.^[5]

Mechanical plaque control methods, including tooth brushing and interdental cleaning, form the foundation of oral hygiene practices. To enhance plaque control and prevent microbial growth, chemical agents such as chlorhexidine and fluorides are commonly used due to their proven antimicrobial and anticaries properties.^[6] However, long-term or repeated use of these chemical agents is associated with several adverse effects, including tooth staining, alteration of taste sensation, increased calculus formation due to mineral uptake within biofilms, irritation of oral mucosa, and xerostomia.^[7] These limitations have increased the demand for safer and more biocompatible alternatives suitable for prolonged oral care.

In recent years, herbal and plant-based products have gained increasing attention in dentistry as alternatives to synthetic oral care agents.^[8] Herbal medicines are widely preferred due to their natural origin, lower cost, reduced side effects, and broader safety margin. Numerous plant-derived products possess antibacterial, antifungal, antiviral, anti-inflammatory, anticaries, and anticancer activities, making them promising candidates for use in preventive and therapeutic dentistry.^[9] Due to these combined biological properties, pomegranate holds considerable potential as a natural agent for oral health

promotion. However, comprehensive systematic evaluations focusing on its application in oral and dental health remain limited, highlighting the need for further critical review.

Historical Perspective And Traditional uses of Pomegranate peel (*Punica grantum L.*)

Pomegranate (*Punica granatum L.*) is an ancient fruit crop with a cultivation history extending over four millennia. Originating from the region between Iran and northern India, the plant gradually disseminated to the Mediterranean basin, Middle East, and Asia through early trade networks. Although the edible arils gained prominence as a food source, traditional medical systems consistently emphasized the therapeutic value of the fruit peel, particularly due to its astringent and preservative characteristics.^[1] Historical records indicate that pomegranate peel played an important role in ancient Egyptian medicine, where it was used for the management of intestinal parasitic infections, diarrhea, and infected wounds. Medical papyri document its use as an anthelmintic and topical healing agent, reflecting early empirical recognition of its antimicrobial properties.^[10]

In the Indian subcontinent, pomegranate peel has been extensively described in classical Ayurvedic literature. Known as Dadima twak, the peel was traditionally prescribed for gastrointestinal disturbances, oral ulcers, bleeding gums, and inflammatory conditions. These applications, recorded in texts such as Charaka Samhita and Sushruta Samhita, demonstrate the long-standing use of pomegranate peel in managing both systemic and oral diseases.^[11]

The medicinal significance of pomegranate peel was also well recognized in Greco-Roman medicine. Classical physicians, including Hippocrates and Dioscorides, described its use in the treatment of dysentery, ulcers, and infectious



conditions. Dioscorides, in *De Materia Medica*, emphasized the strong astringent nature of the peel, attributing its therapeutic effects to its ability to contract tissues and control excessive secretions.^[1]

In Traditional Chinese Medicine, dried pomegranate peel (Shi Liu Pi) has been used for centuries to treat chronic diarrhea, bleeding disorders, and parasitic infestations. Similarly, Unani medicine incorporated pomegranate peel as a cooling and drying agent, particularly in the management of throat infections, oral inflammatory conditions, and hemorrhagic disorders. These systems collectively highlight the broad therapeutic relevance of pomegranate peel across diverse cultures.^[12]

The transition from traditional usage to scientific validation occurred primarily in the twentieth century with advances in phytochemical research. Investigations revealed that pomegranate peel contains a rich spectrum of bioactive compounds, including hydrolysable tannins such as punicalagin and punicalin, phenolic acids including ellagic and gallic acids, flavonoids, and alkaloids. Notably, the concentration of these compounds in the peel is significantly higher than in the edible pulp, supporting its superior biological activity.^[13]

In recent decades, pomegranate peel has gained increasing attention as a valuable natural resource for pharmaceutical, dental, nutraceutical, and food preservation applications. Its documented antioxidant, antibacterial, antifungal, and anti-inflammatory properties have renewed interest in its use as an alternative to synthetic agents, particularly in the context of antimicrobial resistance and demand for plant-based therapeutics. Thus, pomegranate peel represents a compelling example of traditional medicinal knowledge substantiated by modern scientific evidence.^[14]

AYURVEDIC SIGNIFICANCE

In Ayurveda, pomegranate (*Punica granatum* L.), known as Dadima, is regarded as a medicinal plant with multifaceted therapeutic value. Classical Ayurvedic texts describe different parts of the plant, including the fruit peel (Dadima twak), as therapeutically active. The peel is characterized by Kashaya rasa (astringent taste), Laghu and Ruksha guna (light and dry qualities), and Sheeta virya (cooling potency), making it particularly useful in conditions associated with excessive secretions, inflammation, and microbial imbalance.^[15]

The application of pomegranate peel in oral health is well recognized in Ayurveda. It was traditionally used in the form of Kavala and Gandusha (mouth rinses) for treating Mukha roga, including bleeding gums, oral ulcers, halitosis, and throat infections. These practices align with modern observations regarding the peel's antibacterial and anti-inflammatory activities against oral pathogens.^[16]

Vernacular Names

Kannada: Dalimbeya togalu
English: Pomegranate peel or rind
Hindi: Anar Ka chhilka
Tamil: Madhulai thol
Malayalam : Urumamapazha tholi
Marathi : Dalimbache saal.^[17]

Synonyms

Dadima-twak
Pericarpium punicae
Pomegranate pericarp
Post-e-Anar
Qishar al-Rumman.^[17]

Taxonomical Classification

Kingdom: Plantae
Division: Magnoliophyta(Angiosperm)
Class: Mangoliopsida(Dicotyledonds)
Order: Myrtales



Family: Lythraceae

Genus: *punica*

Species: *punica granatum L.*

Medicinal part: Fruit peel (Pericarp).^[18]

Botanical Description

Pomegranate (*Punica granatum L.*) is a perennial deciduous shrub or small tree belonging to the family *Lythraceae*. The plant typically grows to a height of 2–5 m and has a dense, bushy growth habit with multiple branched stems. The bark is smooth and greyish-brown, while young branches are slender and often bear sharp spines. Leaves are arranged oppositely or sub-oppositely, narrow to elliptic in shape, with a glossy surface and entire margins.

The plant produces large, solitary, showy flowers that are bright red to orange-red in color. Flowers are bisexual, with a tubular calyx that later persists and forms the crown-like structure at the apex of the fruit. Pomegranate fruits are spherical to slightly flattened berries with a thick, leathery pericarp. Internally, the fruit is divided into chambers by membranous septa, containing numerous seeds surrounded by juicy, translucent arils. Each aril encloses a hard seed and serves as the edible portion of the fruit. The plant is well adapted to tropical and subtropical climates and is widely cultivated for its nutritional, medicinal, and therapeutic value.^[19]

Distribution

Pomegranate (*Punica granatum L.*) is widely distributed across tropical and subtropical regions of the world. The plant is believed to have originated in the region extending from Iran to northern India and has been cultivated for several centuries in the Mediterranean basin, the Middle East, and South Asia. At present, pomegranate is extensively grown in countries such as India, Iran, Afghanistan, China, Turkey, Spain, and parts of North Africa. In India, cultivation is prominent in

states including Maharashtra, Karnataka, Andhra Pradesh, Telangana, Gujarat, and Tamil Nadu.

The fruit peel, which constitutes a substantial proportion of the total fruit weight, is readily available as an agricultural by-product during fruit processing and juice extraction. Due to the widespread cultivation of pomegranate, the peel is abundantly obtainable in both rural and commercial farming regions, making it an easily accessible raw material for medicinal and pharmaceutical applications.^[19]

Cultivation of pomegranate plant

Pomegranate (*Punica granatum L.*) is cultivated extensively in tropical and subtropical regions due to its adaptability to a wide range of climatic and soil conditions. The plant grows well in areas with hot, dry summers and mild winters, and it can tolerate drought conditions better than many other fruit crops. Optimal growth and fruit development are achieved in regions receiving low to moderate rainfall, as excessive moisture may predispose the plant to fungal diseases.

The crop prefers deep, well-drained loamy or sandy loam soils with good aeration, although it can also be cultivated successfully in moderately alkaline soils. Propagation is commonly carried out through hardwood cuttings, which ensure uniform growth and early fruit bearing. Pomegranate plants are usually spaced adequately to allow proper sunlight penetration and air circulation, which are essential for healthy growth and fruit quality.

Regular irrigation is required during the early stages of plant establishment and fruit development; however, controlled water stress during flowering can enhance fruit set. Pruning practices are adopted to remove diseased, weak, or overcrowded branches, thereby improving yield and facilitating better plant management. With appropriate agronomic practices, pomegranate



plants begin fruiting within two to three years of planting and remain productive for several decades.^[20]

Methods of Extraction for pomegranate peel

Solvent Extraction.

In the majority of reported studies, pomegranate peel extracts (PPEs) are prepared using conventional solvent-based extraction techniques.^[21] Pomegranate peel is commonly processed using solvents such as methanol, chloroform, acetone, water, ethanol, and ethyl acetate to obtain antioxidant compounds. Among these, traditional extraction methods predominantly employ methanol alone or in combination with other organic solvents.^[22]

The efficiency of different solvents, including water, methanol, and ethanol, in extracting phenolic compounds from pomegranate peel (Helow variety) was evaluated. The findings

indicated that the aqueous extract showed superior extraction efficiency and a higher total phenolic content compared to methanolic and ethanolic extracts.^[23] Another investigation examined the effectiveness of different extraction solvents—water, 70% ethanol, and absolute ethanol—in obtaining antioxidant constituents such as phenolics and total flavonoids from pomegranate peel. Based on antioxidant activity assessed using DPPH and CUPRAC assays, the 70% ethanol extract demonstrated superior antioxidant potential compared to both aqueous and absolute ethanol extracts.^[24] Extraction efficiency generally improves with increasing temperature, as heat disrupts cell wall structures, enhances solubility and diffusion of target compounds, and lowers solvent viscosity, allowing easier penetration into the solid matrix. However, temperatures exceeding 40 °C may lead to a reduction in total polyphenol and flavonoid content, possibly due to thermal degradation.^[25]

Soxhlet Extraction

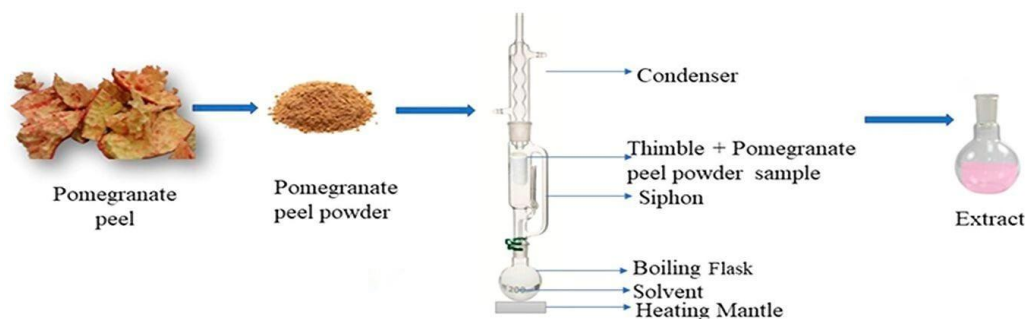


Figure 01.

This technique continues to be widely applied for isolating a range of natural bioactive compounds, particularly phenolic substances, from diverse sources. In this process, pretreated plant materials are exposed to different solvents such as water, ether, hexane, chloroform, benzene, methanol, acetonitrile, and ethanol to facilitate the extraction of polyphenolic compounds.^[26]

The sample was loaded into a thimble, which was then positioned within the Soxhlet extractor connected to a round-bottom flask containing the

solvent and fitted with a condenser.^[27] The reflux process was carried out repeatedly until the extraction was fully completed.^[28] During the extraction process, compounds were separated according to their polarity and the solvent used. Non-polar constituents of the dried material were initially extracted using low-polarity solvents such as petroleum ether, while progressively more polar solvents, up to water, enabled the extraction of highly polar compounds.^[29]

Pressurized Liquid Extraction(PLE)

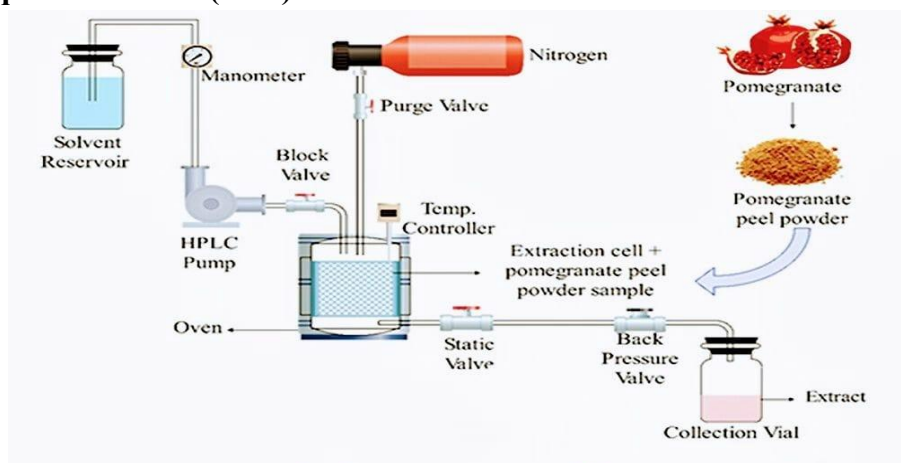


Figure 02.

This extraction method employs solvents under high pressure and elevated temperatures, which enhances extraction efficiency.^[30] This technique employs liquid solvents under elevated pressure, typically above 4 MPa, and operates across a range of mild to high temperatures. The applied pressure facilitates deeper penetration of the solvent into the sample matrix, thereby enhancing the dissolution of target compounds.^[31] The sample was mixed with sea sand and then packed into a stainless-steel extraction cell. A circular cellulose filter was positioned at the bottom of the cell to prevent fine particles from passing into the collection vials.^[32] After heating the extraction cell, the system was pressurized using an HPLC pump. Once the desired pressure was achieved by

closing the solvent outlet with a blocking valve, static extraction was carried out until equilibrium was reached. Subsequently, the static and back-pressure valves were carefully adjusted to maintain the required pressure. The solvent was then pumped through the matrix to initiate the dynamic extraction phase, during which soluble bioactive compounds were extracted at a constant flow rate. Following nitrogen purging, the collected extract was transferred into collection vials.^[33-35] Since water and ethanol are classified as generally recognized as safe (GRAS) solvents, their use in pressurized liquid extraction (PLE) makes this approach particularly attractive.^[36]

Ultrasound Assisted Extraction (UAE)

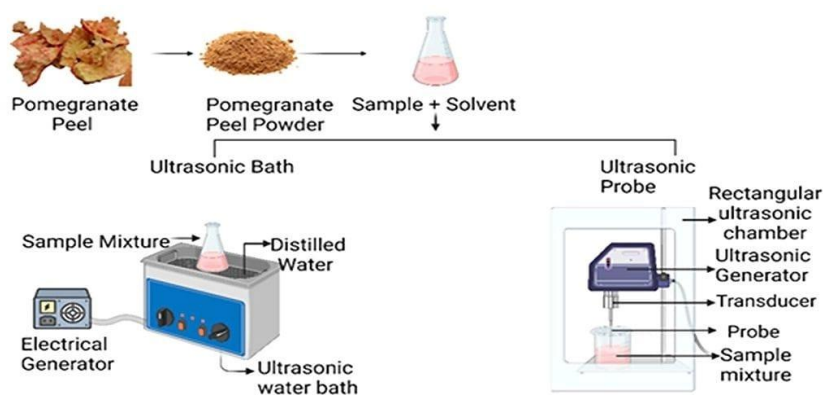


Figure 03.

This technique operates on the principle of acoustic cavitation, where the formation and

collapse of bubbles lead to the release of bioactive compounds. The extent of this rupture is

influenced by the extraction conditions.^[37] In ultrasound-assisted extraction, sound waves with frequencies over 20 kHz and intensities between 5 and 1000 W/cm² are applied. Extraction can be performed using ultrasonic water baths or direct probes, with the latter transmitting continuous waves directly into the suspension.^[38] Within a duration of 5 minutes or less, ultrasonic power from a probe is at least 100 times more intense than that of an ultrasonic bath.^[39] In contrast, with

ultrasonic bath systems, the sample receives ultrasonic energy indirectly through the vessel walls.^[40] Earlier research reported the use of various solvents—including methanol, acetone, ethanol, ethyl acetate, aqueous methanol, and water—for the extraction of phenolics and antioxidant compounds from pomegranate peel.^[39,41]

Microwave- Assisted Extraction (MAE)

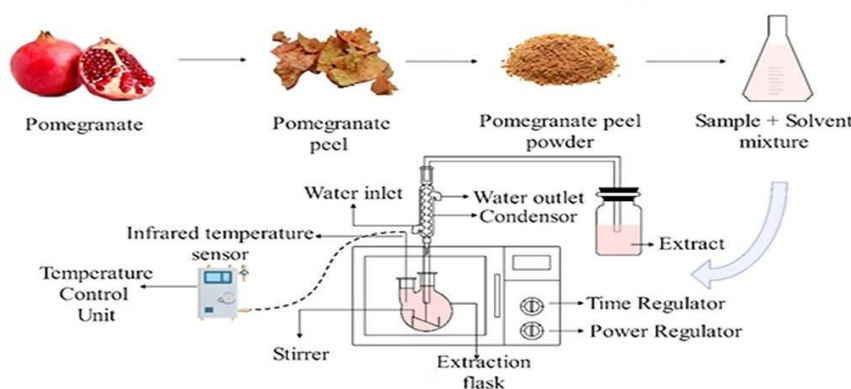


Figure 04.

Microwaves are a form of high-frequency electromagnetic radiation located in the portion of the electromagnetic spectrum between radio waves and far-infrared radiation. They are characterized by wavelengths ranging approximately from 1 mm to 1 cm and corresponding frequencies between 0.3 and 300 GHz.^[42] After placing the dried samples into the extraction vessels, the solvent was added and the containers were securely sealed. The extraction system was then activated, while temperature was continuously monitored using a built-in sensor. Once the preset temperature was reached, the heating unit automatically shut down and resumed operation only after the temperature decreased.^[43] Microwave-assisted extraction is considered efficient because it enables uniform heating of the sample both internally and externally, thereby minimizing the formation of thermal gradients. Microwave radiation is readily absorbed by polar

molecules and ionic species, such as phenolic constituents and solvent systems. Furthermore, the rapid superheating of water present within the sample matrix promotes structural disruption, which enhances the release and recovery of target compounds.^[28] In microwave-assisted extraction, electromagnetic radiation is generated by a cavity magnetron and directed toward the sample. These waves interact with plant tissues, including cell walls and intracellular components, within the matrix. Absorption of microwave energy leads to rapid moisture loss and localized heating, creating internal pressure at both cellular and subcellular levels. This pressure causes plant cells to swell and undergo structural alterations. As a result, disruption of the plant matrix occurs, which enhances solute diffusion and mass transfer, thereby facilitating the release of phytochemicals from plant cells into the surrounding extraction solvent.^[44] In a reported investigation, powdered

pomegranate peel was extracted using a range of solvent-to-solid ratios over a fixed extraction duration. The influence of varying microwave power levels and solvent-to-peel ratios on extraction efficiency was systematically evaluated. A total of thirteen experimental runs were conducted using five different solvents, namely water, 50% and 70% aqueous ethanol, and 50% and 70% aqueous methanol. The results demonstrated that microwave-assisted extraction achieved approximately 1.7-fold higher extraction yields compared with ultrasound-assisted extraction, while requiring a substantially shorter processing time.^[45]

Pomegranate peel phytochemistry

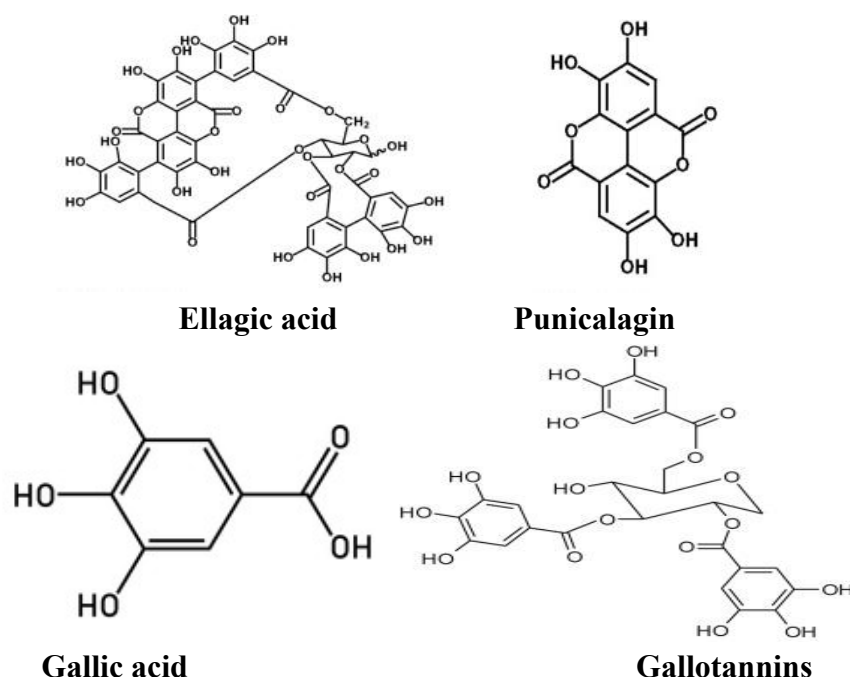


Figure 05.

The antimicrobial activity of pomegranate peel extract (PPE) is mainly due to its rich phytochemical profile, including gallic acid, punicalagin, rutin, resorcinol, quercetin, and syringic acid.^[49] The solvent type and extraction method significantly influence the phenolic content, antioxidant potential, antibacterial

Phytochemicals are plant-derived bioactive compounds that, although not essential for human nutrition, provide significant health benefits.^[46] Pomegranate peel, often regarded as agricultural waste, is a rich source of antioxidants and phytochemicals such as gallotannins, ellagic acid, punicalins, punicalagins, and gallic acid (Figure 1).^[47] Studies by El-Hamamsy and El-Khamissi^[48] reported that pomegranate peel extract contains diverse phytochemicals, including tannins, phenolics, flavonoids, alkaloids, terpenoids, steroids, and saponins. HPLC analysis further identified several polyphenolic acids, notably ellagic, caffeic, p-coumaric, syringic, and protocatechuic acids.

efficacy, and other biological activities of pomegranate peel.^[50] Table 2 summarizes the quantitative levels of selected phytochemicals present in pomegranate peel.

Table:01 Quantitative Analysis of Phytochemicals Present in Pomegranate Peel ^[51-55]

Sl.No	Compounds	Conc(mg/100g)
01	Total phenolic content (GAE)	4892.00-6138.20
02	Total Flavanoid content (QE)	529.50-862.50
03	Ellagic acid	44.19-52.03
04	Catechin	850.00-892.00
05	Gallic acid	125.80-128.10
06	<i>p</i> -Coumaric acid	14.00-17.64
07	Quercetin	5
08	Ferulic	5.00-6.11

Pharmacological Properties of Pomegranate Peel

Pomegranate peel is rich in bioactive phytochemicals such as catechins, flavonoids, tannins, gallic acid, ellagic acid, and anthocyanins, contributing to its medicinal properties.^[56] Studies report that the peel contains higher concentrations of biologically active compounds than other edible parts of the fruit.^[57-60] Key constituents, including punicalagin (α and β) and ellagic acid derivatives, induce S-phase cell cycle arrest and apoptosis.^[61] Administration of pomegranate peel extract also enhances antioxidant enzymes (SOD, GSH, CAT) while reducing malondialdehyde levels.^[62]

Cardio-protective Properties

Cardiovascular diseases are the leading cause of death worldwide.^[63] Many conditions such as obesity, fatty liver disease, insulin resistance, atherosclerosis, and hypertension are linked to abnormal lipid metabolism.^[64] Plant-derived bioactive compounds are known to offer strong cardio protective effects.^[65]

Anticancer Properties

Cancer is a genetic disease marked by uncontrolled cell growth. Plant-derived phytochemicals are known to have cancer-preventive and anticancer effects.^[66]

Studied the effects of punicalagin and ellagic acid on liver cancer cells (HepG2) in vitro. Both compounds reduced cancer cell growth without affecting normal liver cells. Punicalagin showed stronger anticancer activity than ellagic acid by stopping the cell cycle, increasing oxidative stress, and triggering apoptosis through activation of caspases and apoptosis-related proteins.^[67]

Investigated the effects of punicalagin on breast cancer cells (MCF-7 and MDA-MB-231). Punicalagin reduced cell viability, migration, and invasion in a dose-dependent manner. It also lowered the expression of GOLPH3 and proteins involved in cancer spread, while increasing E-cadherin expression. These findings suggest that punicalagin can inhibit breast cancer progression by regulating cell growth and metastasis-related pathways.^[68]

Antimicrobial Properties

Pomegranate peel is rich in flavonoids and phenolic compounds that show strong antimicrobial activity.^[69] These polyphenols work together to inhibit microbial growth by damaging cell walls, disrupting membranes, and blocking key enzymes, ultimately leading to cell death.^[70,71] Pomegranate peel extract (PPE) is particularly effective against bacteria such as *Staphylococcus aureus* and *Salmonella*, mainly due to its high tannin content.^[72]

Demonstrated that pomegranate peel polyphenols inhibited the growth of *Ralstonia solanacearum* in vitro. Treated bacteria showed reduced growth, damaged cell walls and membranes, and decreased motility. Punicalagin played a key role by disrupting bacterial regulatory proteins, leading to impaired bacterial function.^[73]

Wound Healing Potential

Wound healing is a complex process involving four stages: homeostasis, inflammation, proliferation, and remodeling.^[74] Pomegranate



peel is rich in polyphenols such as gallic acid and ellagic acid, which contribute to its wound healing activity by supporting tissue repair and regeneration.^[75]

Anti-inflammatory Properties

Inflammation is the body's response to tissue injury and involves immune cell activation and release of inflammatory mediators.^[76,77] Pomegranate (*Punica granatum*) peels have traditionally been used to treat inflammatory conditions due to their anti-inflammatory properties.^[78] Studied the anti-inflammatory effects of pomegranate peel polyphenols in macrophages in vitro. The results showed that polyphenols, including punicalagin and ellagic acid, reduced inflammation in a dose-dependent manner by inhibiting NO and PGE₂ production and lowering iNOS and COX-2 expression. They also decreased proinflammatory cytokines such as TNF- α , IL-1 β , and IL-6 and suppressed MAPK signaling pathways. These findings confirm that pomegranate peel extract has strong anti-inflammatory potential.^[79]

CONCLUSION

Pomegranate peel, once considered an agricultural by-product, has gained considerable attention as a rich source of biologically active compounds with significant therapeutic potential. Phytochemical studies reveal that the peel contains higher concentrations of polyphenols, tannins, flavonoids, and phenolic acids than other parts of the fruit, which contribute to its potent antioxidant, antimicrobial, anti-inflammatory, wound healing, and anticancer properties. Traditional medical systems, including Ayurvedic and folk medicine, have long utilized pomegranate peel for treating oral and inflammatory conditions, and these uses are increasingly supported by modern scientific evidence. Recent studies demonstrate that pomegranate peel extract effectively inhibits oral

pathogens, modulates inflammatory mediators, enhances antioxidant defense systems, and promotes tissue regeneration, highlighting its promise in oral and dental healthcare applications. Advances in extraction technologies have further improved the recovery and bioavailability of its high-value phytochemicals, thereby enhancing therapeutic efficacy. Considering the adverse effects and limitations associated with long-term use of synthetic oral care products, pomegranate peel represents a safer, cost-effective, and biocompatible natural alternative. Nevertheless, despite encouraging in vitro and preclinical findings, further research is required to standardize extraction methods, optimize formulations, and conduct well-designed clinical trials to establish appropriate dosage, safety, and long-term effectiveness. Overall, pomegranate peel stands out as a sustainable natural resource with strong potential for oral health promotion and disease prevention.

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