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An In-Depth Examination of Pomegranate's (Punica Granatum) Production, Culture, Characteristics, And Pharmacological Applications

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Abstract-

Pomegranates have a number of therapeutic applications due to the bioactive compounds they contain, which are produced in tropical climes. Rich in antioxidants, this fruit has been used since ancient times to treat a variety of ailments, such as infertility, diabetes, cancer, inflammation, and high blood pressure. It is currently utilized in the medical and nutrition fields because to its enormous potential. The polyphenols in pomegranates have strong anti-proliferative properties. Numerous in vitro and in vivo studies have shown how abundant the organic acids, anthocyanins, sterols, and catechins present in pomegranates are. One of the world's top growers and exporters of this fruit is India. Some of its variations are used for commercial and decorative purposes. However, in order to increase its production and cultivation on a national level, a number of stress factors must be addressed in the future. Improved fertility and weather conditions should also be provided to the pomegranate-producing region in order to increase demand.

Keywords: *Pomegranate; Cultivation; Medicinal properties; Nutritional properties.*

INTRODUCTION

The Punicacae family includes the pomegranate, a fruit that grows on trees or shrubs that can grow to a height of around 16 to 26 feet. Punica granatum is its scientific name. It is also known as the Chinese apple and nameseed apple. In the north, this fruit grows from September to February, whereas in the south, it grows from March to May. The pomegranate fruit's leaves are 2 cm wide and 3–7 cm long, and it contains multiple long-lived branches [1]. Red flowers feature three to seven petals, and there can be anywhere from 200 to 1400 seeds in each flower. Still, you can use seeds in salads, appetisers, soups, and desserts. In parks and gardens, this fruit can be grown as a decorative tree. They can live in arid environments and are resistant to drought. They are considered healthier fruits and are high in fiber, making them ideal winter eats. Pomegranates are well recognized for their ability to lower blood pressure, prevent diabetes, improve heart health, and shield the prostate from cancer. They are also a great source of antioxidants, which help prevent cancer and the production of free radicals. Seeram [2]. Three times as much vitamins, potassium, and antioxidants are found in pomegranate juice and seeds as in green tea. In Pakistani cuisine, seeds are usually used as a spice called Anar dana. Dried seeds are utilized to make curries. Although supplements are sold in dry form, one can prevent high blood pressure and high cholesterol by consuming concentrated juice that contains polyphenolic antioxidants Heftmann.

Edible fruit contains 20% seed and 80% juice. The levels of fructose and glucose in juice are equal. The polyphenol component is composed of anthocyanins, ellagic acid, tannins, and catechins. Its seeds include a lot of pectin, fiber, and carbs, all of which can help avoid heart disease. Pomegranate protects against atherosclerosis and reduces LDL cholesterol levels in the body [3-6].

Synonyms
Hindi: Anar,
Sanskrit: Dadimah,
English: Pomegranate,
Marathi: Dalimba,
Gujarati: Dalimba,
Bengali: Dadim,
Tamil: Madalai,

Telegu: Danimma,
Malayalam: Talimatatalum,
Pharsi: Anar tursa,
Arabi: Roman Hamiz,
German: Granatapfels.
Botanical Classification
Botanical name*: Punica granatum*
Kingdom: Plantae (Angiosperms)
Order: Myrtales
Family*: Lythraceae*
Genus: Punica Species: P. granatum

Cultivation
The main fruit produced in Pakistan is the pomegranate. Punjab and KPK contribute to its production in isolated locations, although Balochistan is the main producer. On nine thousand hectares, forty thousand tons are produced. This fruit thrives on tropical and subtropical climates and its propagation can be done sexually as well as asexually. Pakistan boasts excellent pomegranate growing circumstances, however the effective production of AR Awan was hindered by farmers' ignorance, poor management of trees, and a lack of fundamental contemporary practices.

Varieties
Various varieties are present and are famous for their taste. Some famous are:
Bedana: Its pale or brown seeds have a delicate texture. Fruit that ranges in size from medium to large makes up the pink, sweet pulp.
Kandhar: It has pulp that is blood red in hue and firm seeds. This fruit tastes sour and is enormous in size.
Alandi: It has extremely hard seeds. It is a medium-sized fruit with a pink fleshy color and a subacid pulp.
Dholki: This fruit has significant commercial value. Its pulp is white and delicious, with firm seeds. Its base is colored with dark purple patterns. It is known as evergreen plant.
Kabul: This huge pomegranate type has a dark yellow peel and a pulp with a bitter flavor.
Muscat Red:contain firm seeds and a luscious pulp. Typically, this fruit has a thick covering and is tiny in size.
Paper shell: Its seeds are frequently soft, and its pulp is extremely sweet and luscious with a meaty covering. It has a primarily spherical shape.
Poona: This has a grey to green colored rind that is frequently speckled. This fruit is huge and has a color combination of orange and red.
Spanish Ruby: It consists of a blend of fragrant, rosy pulp and frequently delicate, vibrantly colored seeds. The fruit ranges in size from medium to giant.
Vellodu: It is of average quality with sweet pulp and large size seeds Holland.

Global production
The United States, Iran, India, Pakistan, and China are the world's leading producers of this fruit, based on current global conditions. Global production is estimated to reach 1.5 million tons per year. India has being placed #1 in the output of 1.140 million tones on 0.125 million hectares. The largest exporter, at 60,000 tons, is Iran. India is a major supplier of pomegranates to Bangladesh, Saudi Arabia, and the United Arab Emirates. In past centuries, this fruit was imported to India from West Pakistan. This fruit is used as an ornamental tree in several nations, including Mexico, France, Italy, Egypt, and Greece. Every component of the pomegranate—its peel, seeds, roots, and leaves—has economic value to the global community [7–10].

Fig.1; Pomegranate.

Characteristics of Punica granatum
A. Punica granatum bark

P. granatum bark can grow up to 5 meters tall and is distinguished by its strong, woody brown appearance that appears twisted. The bark of P. granatum has long been used to cure a variety of conditions, including ulcers, sore throats, inflammation, bleeding from the nose, diarrhea, and hoarseness [11]. Additionally, the bark portion is applied to treat parasitic illnesses like malaria [12]. Among P. granatum's other relevant applications, the bark extracts' strong thermal and acidic characteristics prevent iron corrosion [13]. In addition, the bark has high concentrations of terpenoids, proanthocyanidins, and anthocyanins [14–16]. The bark component acts as a natural green corrosion inhibitor due to the presence of these compounds [13].

Punica granatum flowers

Pomegranate trees attract a variety of birds to their blooms throughout the summer [17]. The bright pink, piled oval petals of pomegranate blooms are one of their distinguishing features [18]. Pomegranate flowers have long been used to treat diabetes, obesity, and cardiovascular conditions [15]. The antibacterial characteristics of pomegranate blossoms were discovered, and it was discovered that these flowers could effectively treat common bacteria that cause intestinal illnesses, such Kentucky and Salmonella entteriditis [19]. Furthermore, a variety of bioactive substances, including flavonoids, terpenoids, terpenes, and organic oils, are abundant in flowers [12, 15, 19]. Garlic acid, punicatannin C, and ellagic acids are the major tannins found in flowers [16].

B. Punica granatum leaves

The ovate, green, glossy leaves of *P. granatum* can reach a maximum length of 3 cm. [18] states that the plant's leaves are perennial. Many traditional use of pomegranate leaves has been documented and researched over time. The leaves are used, among other things, to treat and manage diabetic nephropathy [20], cholesterol, and weight loss [15, 16]. The plant's leaves have cytotoxic, anti-cholinesterase, and anti-inflammatory qualities [21]. The study also reported antimicrobial and antibacterial properties [22]. Additionally, [20,23] determined the anti-diabetic and [16] found the anti-cancerous characteristics. A different study found that the leaf extract has anti-lice and anti-dandruff characteristics, leading to the conclusion that it might be utilized to promote hair growth [24]. Because of the diversity

C. *Punica granatum* seeds

The seeds of the P. granatum plant are the portion that has been studied and recorded the most. Pomegranate seeds are found in hundreds and are encased within the fruit, which is covered in red-appearing arils [18]. Pomegranate seeds are frequently used for treating urinary tract issues [16] and preventing miscarriages [25]. Pomegranate seeds have been shown to have additional medicinal qualities, such as antibacterial [19, 26], anti-cancerous, and antioxidant [27]. Numerous phytochemical components, such as anthocyanins, tannins, fatty acids, flavonoids, ligands, and sterols like certain organic volatile oils, are abundant in pomegranate seeds [12,28,29,25, 30].

D. *Punica granatum* peels

When pomegranate fruit peels are ripe, their pericarp, a hard shield, retains its orange and greenish hue. The peel envelops the arils, which are separated within the peel by a thin membrane. Forty-three percent of the fruit is made up of pomegranate peels [29]. The peel extracts are traditionally used to cure ulcers, and diarrhea [25], suppress ribonucleic acid (RNA) replication [14], and are utilized as ruminant feeds [31]. Pomegranate peels have been found to have a variety of medicinal qualities, such as anti-inflammatory, anti-proliferative, and anti-cancer actions [27, 32, 16]. It was shown that apple peels had anti-breast cancer antioxidant properties [25]. Pomegranate peels have also been shown to contain over 48 chemical components, including xanthonoids, alkaloids, tannins, flavonoids, phenolics, proanthocyanidins, sterols, and terpenes [12,18,15,16,33,34].

E. *Punica granatum* juice extracts

Pomegranate juice is one of the highly recommended beverages with vitamin C, the juice is produced from the fruit’s sweet red arils pulps and peels. Pomegranate juice is thought to contain phenolic compounds [12]. Pomegranate juice preparations were used to separate polyphenolic substances as punicalagin and punicalin [18, 35]. Furthermore, the juice has been found as a source of potassium, phosphorus, calcium, manganese, zinc, and copper [14].

Phytochemicals in pomegranate

Pomegranates are a significant source of advantageous substances that are essential for preserving homeostasis and overall health, as has been extensively shown in the literature [36,37,38, 39]. Figure 2 provides a description of the pomegranate's natural components. Squeezing the arils yields a juice that contains lignans, fatty acids, alkaloids, triterpenoids, phytosterols, hydrolysable tannins, flavonoids, and various organic acids like gallic and ellagic acid (40, 41). Hydrolyzable tannins, flavonoids, ellagitan-nins, and punicalagins are present in the pericarp. The pericarp has been shown to contain a number of minerals, including potassium and phosphorus, sodium, calcium, magnesium, and nitrogen [42, 43].

In addition,the seeds comprise polyphenols, isoflavones and a range of organic acids, including ascorbic, citric and malic acid. Additionally, they have significant levels of polyunsaturated fatty acids (linolenic and linoleic acid) and lipids (punicic, oleic, stearic, and palmitic acid) [44, 45]. In conclusion, pomegranate leaves are abundant in flavone glycosides such luteolin and apigenin, as well as tannins like punicalin and punicafolin.Minerals have also been found in the leaves, just like in the pericarp [46, 47]. It is challenging to determine the precise phytochemical profile of the various pomegranate sections, though, as this can depend on a number of factors, including the cultivar, climate, cultivation techniques, transformation, and preservation of the processed products [48–51].

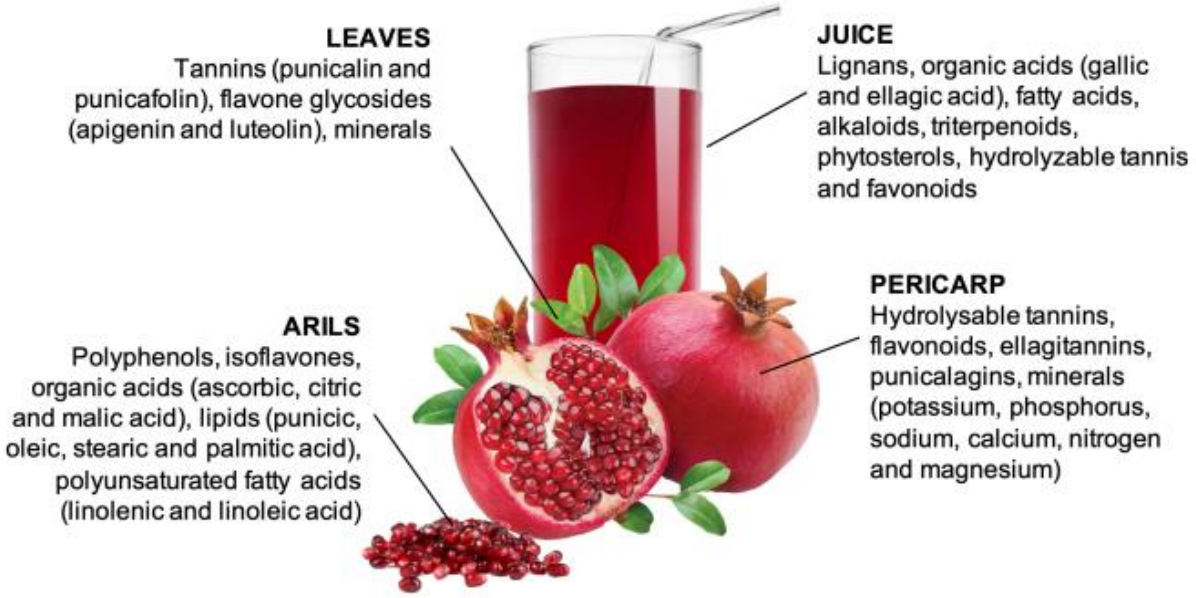

Fig.2. The Natural Compounds of Pomegranate.

The pomegranate's biological characteristics

Egyptians have long used pomegranate peel extract to cure common conditions like inflammation, diarrhea, and infertility [52] more recent studies have shown additional biological activities of this kind, including the following:

Activity of Antioxidants

1. During cellular metabolic processes, there are reactive oxygen species, such as superoxide anion (hydrogen peroxide (H2O2) and hydroxyl radical (HO−) [53], which cause diseases such as cancer and cardiovascular diseases, induced by factors such as exposure to ionizing factors and xenobiotics; the toxic effects of reactive oxygen species depend on their ability to damage important and sensitive biological substrates such as RNA, DNA, lipids, and plasma membrane proteins [52]. According to [54], pomegranate peel possesses antiproliferative properties against breast cancer cell lines. [55] demonstrated that the pomegranate peel extracts suppressed the proliferation of prostate cancer cells, as these extracts may cause apoptosis of this type of cancer.

Similarly, colon cancer cell lines have demonstrated anti-carcinogenic potential [56-58]. The phenolic content of the peel extract was found to be 2.8 times higher than that of the pomegranate leaf extract. [59] compared the antioxidant capacity of pomegranate seed, peel, and leaf extracts and found that, among mango, kinnow, banana, and loquat fruits, the highest pomegranate peel extract removal activity of (DPPH) 2,2-diphenyl-1-picrylhydrazyl and 2,2′-azinobis [3-ethylbenzothiazoline-6-sulfonic acid] (ABTS) was found. These results were attributed to the peel extract's phenolic content.

antimicrobial efficacy

Extracts from pomegranate peels have been investigated as potential therapeutics or preventative measures for a variety of diseases brought on by various pathogens. [52] Oral gavage of 100 mL (300 mg/kg) of pomegranate peel extract demonstrated that Giardia lamblia cyst counts in male Swiss albino mice (Mus musculus) could be reduced by up to 75% 20 days post-infection; similarly, experimental groups supplemented with pomegranate peel showed protection against infection 10 days post-start [60]. Pomegranate peel extract has been utilized in similar experiments to reduce cyst formation, inflammation, and jejunal damage in coccidiosis caused by the pathogen *Eimeria papillata* [61]. Similar to this, in vitro research has demonstrated inhibitory effects on pathogenic bacteria, particularly against gram-positive bacteria including Bacillus subtilis [63], Staphylococcus aureus [62], and Propionibacterium acnes [62]. Similarly, [64] demonstrated that punicalagin from *P. granatum L*. crude peel extract inhibited the growth of cariogenic Streptococcus

mutans. After 6 hours of exposure to 1.56, 3.125, and 6.25 mg/mL crude peel extract, S. mutans biofilms were reduced by 94.7, 96.6, and 90.97%, respectively. This suggests that pomegranate peel extract may be useful in preventing dental caries; punicalagin from pomegranate by-products has been reported to inhibit the growth of pathogenic clostridia and *Staphyloccocus aureus* [65]. Additionally, studies have shown that pomegranate peel methanolic extracts are highly effective against strains of bacteria like Shigella dysenteriae serotype 2, Salmonella typhimurium [66], and Escherichia coli [67]. Taken together, these findings, along with findings from another study conducted on mice, indicate that infections caused by Citrobacter rodentium—a type of bacteria that infects mice—have been shown to have decreased pathogenicity. This model is useful for studying the health benefits of food additives and their effects on the microbiota because it replicates aspects of human enteropathogenic bacterial infections, such as gastrointestinal pathogens. This discovery suggests that pomegranate polyphenols could be a source of advantageous substances for the management of digestive disorders [68]. Furthermore, methanolic extracts of pomegranate peel have been tested for their antifungal properties against *Penicillium expansum*, *Penicillium digitatum*, and *Botrytis cinerea*. In comparison to the control, the vitality of *B. cinerea* conidia was significantly decreased by 94 and 80% at 1.2 g/L and blocked by 12 g/L after 20 hours of incubation [69]. With MIC (Minimum Inhibitory Concentration) values of 125 mg/mL and 250 mg/mL, respectively, for each species, [70] showed that pomegranate peel extracts could suppress the growth of *Trichophyton mentagrophytes, T. rubrum, Microsporum canis, and M. gypseum* fungi at the conidial and hyphal stages.

antiviral action

Pomegranate's well-established antiviral properties have contributed to its rising popularity in recent years [71]. Gallic acid is one of the substances in pomegranate peels that has been linked to their antiviral effects. Known by the name 3,4,5-trihydroxy benzoic acid, gallic acid (GA) is a phenolic chemical that is present in fruits and vegetables, particularly pomegranates [72]. studied the impact of GA on the expression of the hepatitis C virus (HCV) utilizing a cell culture system that expressed HCV non-structural (NS) proteins through HCV sub genomic replicon**.**GA, in comparison to levels in untreated cells, down-regulated the protein expression levels of HCV-RNA (∼50%) and NS5A-HCV (∼55%) in a time-dependent manner. Therefore, GA therapy has been shown to lessen oxidative stress in cells by decreasing the generation of reactive oxygen species (ROS), which is detrimental to HCV. GA is a potential adjuvant in HCV therapy as a result. Moreover, at 600 and 100 mg/mL doses, GA does not cause cytotoxicity. Pomegranate peel has been found to have antiviral properties against influenza viruses, which are thought to be responsible for the prevention of influenza virus RNA replication. Punicalagin compounds are the most effective at preventing viral RNA replication and exhibit inhibitory efficacy up to 40 mg/mL [74].With a case fatality rate of 3%, SARS-CoV2 has emerged as a highly contagious infection that is responsible for the COVID-19 pandemic [75]. Antiviral medications are not yet available to treat COVID-19 patients. Since secondary metabolites from fruits and vegetables have antiviral qualities against COVID-19, one expectation for the current scenario is to turn to them [76,77]. The ability of S-glycoprotein, which is important in virus attachment to particular receptors on host cells, has been shown to be attenuated by punicalin and punicalagin, as well as by angiotensin converting enzyme 2 (ACE2). additionally shown that urolithin A, a naturally occurring substance from the human gut microbiome that is created in the colon following the microbiome-mediated transformation of naturally occurring polyphenols found in foods like pomegranates, is responsible for the bioactivity of pomegranate peel extracts. Pomegranate peel extracts and urolithin A are responsible for a notable blockage of the S-glycoprotein-ACE2 interaction. [78–80]. The affinities and interactions between punicalagin, punicalin, gallic acid, and ellagic acid from pomegranate peel extract on four protein targets chosen based on the process of virus entry into a host cell were described in another work by [81]. Angiotensin converting enzyme type II, furin, SARS-CoV-2 transmembrane serine protease, and SARS-CoV-2 spike glycoprotein were the targets. Punicalagin and punicalin have been suggested as alternatives for in vivo evaluations because the results demonstrated their major influence on interactions with target proteins.

Additional health advantages

Pomegranate peel, on the other hand, contains additional advantageous health properties, such anti-inflammatory and anti-allergic properties. White blood cell activation, immune system chemical release, and the synthesis and release of prostaglandins and inflammatory mediators are all components of the inflammatory response [82]. The two most significant enzymes for the metabolism of arachidonic acid are called Lox and Cox. These enzymes produce prostaglandins as well as the inflammatory mediators cyclooxygenases (COX) and lipoxygenases (LOX)[83]. The flavonoid identified as (2E)-3- (4-hydroxy-3-pentylphenyl)-1- (2-hydroxy4,5-di (E)-prop-1-enyl) phenyl) prop-2-en-1-one inhibits both cyclooxygenase (COX) and lipoxygenase (LOX). [83]. This is a result of the compound's polyphenolic composition, which inhibits inflammation by acting as a primary oxidant or as a free radical scavenger or inhibitor [83]. Pomegranate peel extracts standardized to contain 13% w/w ellagic acid were shown to have a marked inhibitory activity against the release of β-hexosaminidase from antigen-stimulated rat basophilic leukemia (RBL-2H3) cells, as reported by research [84]. The results showed that the standardized pomegranate peel extract had IC50 values of 20. 9 and 4.3 g/mL, respectively, indicating that pomegranate extracts standardized to obtain 13% w/w can function therapeutically with anti-allergic effects.

Applications of pomegranates

Due to the large amounts of peel that must be disposed of, the increasing demand for pomegranate-based products could be harmful to the environment [85]. In order to expand the uses that can be obtained from waste like pomegranate peel, several researchers have been working on the search for useful products, in addition to making their uses more attractive to each specific audience and obtaining economic benefits. This means that it is necessary to investigate the opportunity area that this waste has in the industrial sector. This is because pomegranate peel is a source of bioactive compounds that have a wide range of biological properties that are being valued and studied by different research groups, examples of which were detailed earlier in the paper.

Utilizations in food items

Fruit peels are currently used as animal feed according to animal health and nutrition guidelines [86]. Such peels are rich in carbohydrates, crude fiber, crude protein, and ash, and they also include a large amount of minerals and nutrients required for a healthy animal's development [87]. Pomegranate peel extract components are currently found in a wide range of feasible applications as feed preservatives, stabilizers, and quality enhancers [86]. The investigation that investigated the effectiveness of pomegranate peel extracts in feed matrix application is described below. Since biopolymer films are thought to operate as a barrier to shield food from environmental elements such oxygen, UV light, water vapor, pressure, and heat, they have been created in recent decades for usage in food [88]. Pomegranate peel extracts have been shown in studies to enhance the functional properties of zein, chitosan, and gelatin-based materials for the creation of films as food coatings [89, 90]. worked with a fish gelatin film, adding pomegranate peel extract and used a control group that did not have extract. The results of the ABTS and DPPH radical scavenging activity tests demonstrated a considerable improvement in the antioxidant capabilities of the films containing pomegranate peel extracts. This is because punicalagin, ellagic acid, and other flavonoids with phenolic hydroxyl groups—such as quercetin, kaempferol, and luteolin glycosides—transfer hydroxyl groups to free radicals, quenching these dangerous species and triggering an antioxidant capacity response [92,93].

Prospects for the future

These data force us to consider the steps we've done to help create advances in this area. The entire fruit of the pomegranate has bioactivities that are ascribed to its functional qualities. Studies on the fruit have concentrated on its juice, seed, and peel; these three components have demonstrated remarkable potential for human health due to the high efficacy of each bioactivity that has been examined. Compared to the other residues discussed before, the peel offers a greater concentration of ellagitannins and, since it makes up half of the fruit's weight, can be used as a resource.The research does have several limitations, though, including the need for more advanced equipment for compound extraction and purification and the absence of precise knowledge regarding the enzymes involved in the biodegradation of ellagitannins. The peel of the red dragon fruit *(Hylocereus polyrhizus L.)*, on the other hand, is rich in bioactive compounds like betacyanin, natural pigments with desirable bioactive and antioxidant properties, and has demonstrated positive results as an effective additive and for oral administration [94]. Other works have also been used as examples for future applications, where other fruits and residues have been used. Resveratrol, a bioactive molecule derived from grapes that is utilized for health and cosmetic purposes because of its antioxidant action, has also been widely marketed [95]; the more common form is the capsule. This review emphasizes the use of peel, seed, and fruit residues because, like other fruits, pomegranate peel residues contain compounds of interest like punicalagin that can be used to formulate food supplements in various forms, such as gums or encapsulated forms that can target different markets like children or the general public. As was already noted, it is crucial that the equipment is costly and typically a limitation; yet, the cost-benefit analysis balances the difference.High-end extraction and purification technology has benefits that are significant for the environment and the customer since it allows substances to be recovered at higher concentrations and minimizes the need for excessive solvent consumption. Conversely, food supplements containing bioactive substances have long been significant, but as technology develops and the number of ailments rises, younger generations are growing more concerned about their health. The market for supplements has grown, so adding phenolic compounds to appealing formulations that enhance daily living gives us the chance to use a raw material that is often regarded as "waste" but has a ton of promise.

Conclusion

Pomegranate fruit *(Punica granatum L.)* is primarily grown in Mexico due to its climate adaptability. The pomegranate has been studied for applications of biological activities since numerous scientific studies have reported the presence of various bioactive compounds, such as ellagitannins like punicalagin, punicalin, punicic acid, and ellagic acid, which have been evaluated by in vitro and in vivo assays to counteract certain diseases like cancer, obesity, diabetes, some viruses like influenza, bacterial infections, and inflammation. Further investigation into the action mechanisms and metabolism in vivo trials in the food, pharmaceutical, and cosmetic industries is necessary to evaluate their potential and unfavorable effects as well as to establish concentrations for the use of the currently available bioactive chemicals.

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