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THERAPEUTIC POTENTIAL OF THE PHYTOCHEMICAL COMPOSITION OF WILD POMEGRANATE JUICE (*Punica granatum* L.)

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review paper

Summary

Wild pomegranate (*Punica granatum* L.) is a fruit tree that grows in a wide range of subtropical and tropical geographic locations around the world. Wild pomegranate fruits are rich in nutritional and phytochemical components, and the most appreciated form of consumption is freshly squeezed juice. The chemical composition of wild pomegranate juice varies depending on the genotype, climatic conditions, degree of fruit ripeness and processing method. The juice is rich in organic acids and sugars that determine its organoleptic properties, while phenolic compounds, such as flavonoids, anthocyanins and ellagitannins, contribute to its bioactive properties. These phytochemical compounds are known for their antioxidant, anti-inflammatory, antimicrobial and potentially cardioprotective effects.

The therapeutic potential of wild pomegranate juice includes the prevention of oxidative stress, modulation of inflammatory processes, antibacterial activity and inhibition of cancer cell proliferation. The results of various studies indicate a significant possibility of using wild pomegranate in the prevention and treatment of various chronic diseases, including cardiovascular diseases and cancer.

This paper emphasizes the importance of further research aimed at optimizing the conditions for the production of wild pomegranate juice and the application of its bioactive properties in the medical and food industries.

Keywords: wild pomegranate juice, phytochemical composition, phenolic compounds, antioxidant effect, anticancer potential

Introduction

Wild pomegranate (*Punica granatum* L.) is geographically related to the Mediterranean and Iran, and is characterized by good adaptation to adverse environmental conditions (Eghbali et al., 2021). Wild pomegranate fruits are consumed fresh and processed, and freshly squeezed juice is the most preferred by consumers, due to its rich nutritional and phytochemical composition (Fahmy et al., 2020). The chemical composition of the juice is significantly influenced by the genotype, climatic conditions, and the degree of ripeness of the fruit at the time of harvest, as well as the method of juice preparation itself (Hegazi et al., 2021). The most common methods of juice preparation are cold pressing of whole fruits or only the edible part of the fruit (Mphahlele et al., 2016). The results of research on juice samples with regard to genotype, growing conditions, degree of ripeness, and method of preparation show significant differences in polyphenol concentrations, with special emphasis on differences in samples obtained from the whole fruit and the edible part (Topalović et al., 2021). The investigated wild pomegranate juice samples, regardless of the processing method, are characterized by high acidity, elevated electrical conductivity (EC) values, and a high proportion of soluble dry matter (Topalović et al., 2020). The composition of organic acids and sugars largely defines the organoleptic properties of wild pomegranate juice, including parameters such as pH, total titratable acidity, and sweetness levels (Ikegaya et al., 2019).

Wild pomegranate fruit is rich in bioactive compounds, which include flavonoids, phenolic acids, and vitamin C, contained in all parts of the fruit. It has been found to contain higher concentrations of total phenols and tannins compared to cultivated pomegranate varieties (Guo et al., 2022). Primary metabolites in pomegranate juice include sugars, organic acids, and vitamin C.

Numerous studies indicate that the consumption of foods rich in phenolic phytochemicals is significantly correlated with numerous beneficial effects on human health (Angelino et al., 2017). Phenolic phytochemicals are particularly well known for their antioxidant and antimicrobial activities, and are additionally attributed with anti-inflammatory, anti-allergic and anti-proliferative properties. The health effects of polyphenols largely depend on their concentration and antioxidant potential, which is subject to variation depending on genetic origin and agro-ecological conditions during ripening (Hulya et al., 2012).

Antioxidants are key components of the human diet, and there is growing interest in natural sources of antioxidants, especially from plants. Among the most important natural antioxidants are vitamins, such as vitamin E, vitamin C and β-carotene, and plant

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polyphenols. Their advantage is reflected in the ability to neutralize free radicals and reactive oxygen species, thereby contributing to the preservation of the nutritional value of food and reducing the risk of developing chronic diseases (Aloqbi et al., 2016). Antioxidants have diverse chemical structures and mechanisms of action, and the ability to inhibit or slow down the oxidation of free radicals and reactive oxygen species represents a key defense mechanism against oxidative stress. This process can cause damage to cellular lipids, DNA and proteins, which is considered one of the main causes of the development of chronic diseases, including cancer (Escarcega et al., 2020).

The aim of this work is to investigate and analyze the phytochemical composition of wild pomegranate juice (*Punica granatum* L.) and, through a comprehensive review of the scientific literature, evaluate its therapeutic potential by examining the biological activities of its constituents, with particular emphasis on antioxidant, anti-inflammatory, antimicrobial, and cardioprotective effects.

Chemical composition of wild pomegranate juice

Considering the growing interest in the functional components of wild pomegranate (*Punica granatum* L.), numerous studies have focused on understanding how various factors – from processing technology to geographical origin – influence its chemical composition and biological properties. The results of various studies indicate a high variability in the content and stability of primary and secondary metabolites of wild pomegranate, depending on the processing method, growing location, variety and part of the fruit analyzed (Bar-Ya'akov et al., 2019).

Primary metabolites

Water is the most abundant component of wild pomegranate juice, followed by soluble sugars, including sucrose, fructose and glucose. The content of total sugars and organic acids in wild pomegranate juice is subject to the influence of genotype, climatic conditions and the degree of fruit maturity. According to Li et al. (2015), pomegranate fruits grown in colder climates contain more glucose and fructose compared to those from warmer areas. As the fruit develops, a significant increase in the level of total soluble solids is recorded, which correlates with an increase in glucose and fructose concentrations, indicating a connection between the developmental stage of the pomegranate fruit and the process of sugar accumulation (Bar-Ya'akov et al., 2019).

Analysis of the content of organic acids in the edible part of the pomegranate fruit confirmed the presence of citric, malic, oxalic, succinic, tartaric and ascorbic acids. Among the identified acids, malic acid was the most abundant, while citric acid followed in concentration. Similar patterns of concentration distribution were recorded in all analyzed samples (Topalović et al., 2020).

Organic acid and sugar profiles represent key determinants of pomegranate fruit flavor (Nafeesa et al., 2020). Among organic acids, citric and malic acids are the most abundant, with the concentration of citric acid standing out as a reliable chemical indicator for differentiating varieties according to the sensory flavor profile (sweet, sour-sweet and sour). The conclusion of Peng's et al. (2025) research is the definition of fructose and citric acid as the main flavor components, and the variability of phenolic and volatile compounds of different varieties defines the potential for the selection of specific genotype intended for industrial processing.

Secondary metabolites

Phytochemicals, often referred to as bioactive substances, are a group of secondary plant metabolites that, although not essential nutrients, can have a significant biological effect on human health (Singh et al., 2023).

Results of research by Topalović et al. (2020) in wild pomegranate juice samples from Montenegro, a total of 97 phenolic compounds were determined. The presence of 23 anthocyanins and their derivatives, 33 ellagitannins and ellagic acid derivatives, 12 flavanols, 4 flavonol glycosides, 1 flavone, 17 hydroxybenzoic and 7 hydroxycinnamic acids and their derivatives was recorded. The highest concentrations were recorded for flavanols and ellagitannins and ellagic acid derivatives. Recent studies conducted on samples of commercial pomegranate juices indicate exceptionally high concentrations of bioactive phytochemicals, including flavan-3-ols, ellagitannins, hydroxybenzoic acids, and vitamin C (Topalović et al., 2021; Topalović et al., 2024). Comparative analysis of juice obtained from the whole fruit and only the edible part showed that juice from the whole fruit contains a higher concentration of total phenolic compounds and a lower pH value, which indicates a higher degree of bioactivity and greater functional value of such a preparation. The high content of antioxidant components, especially ellagitannins and punicalagins, further confirms the potential of wild pomegranate as a valuable functional food product. The presence of high-molecular condensed tannins further expands the understanding of phenolic

variability, indicating polymerization processes that contribute to the stability of antioxidant capacity (El Moujahed et al., 2022). The results of the study by Escarceg et al. (2020) indicate the influence of geographical factors on the chemical composition of the pomegranate fruit, with different contents of phenols, flavonoids and antioxidants in different regions. This further emphasizes the importance of environmental and agronomic factors in the bioactive profile of pomegranate.

Pomegranate is a rich source of anthocyanins, which are responsible for the red color of the fruit. The dominant anthocyanins include cyanidin-3-O-glucoside, cyanidin-3,5-di-O-glucoside, delphinidin-3-O-glucoside, delphinidin-3,5-di-O-glucoside, pelargonidin-3-O-glucoside, and pelargonidin-3,5-di-O-glucoside. In addition to anthocyanins, the edible part of pomegranate also contains phenolic acids, among which *p*-coumaric acid, chlorogenic acid, ellagic acid and gallic acid stand out (Redha et al., 2018).

Research by Wu and Tian (2017) investigated the phytochemical diversity of pomegranate in detail, with special emphasis on anthocyanins and hydrolyzable tannins, such as punicalagin and ellagic acid, which are converted in the body into urolithins – secondary metabolites with pronounced biological effects. Legua et al. (2012) found a high anthocyanin content in Spanish pomegranate varieties, with cyanidin-3-glucoside playing a dominant role.

The results of research by Catania et al. (2020) showed that variations in applied pressure levels during the pressing process led to significant quantitative and qualitative changes in the concentrations of bioactive compounds. Increasing the pressure leads to an increase in the total content of polyphenols, while the anthocyanin concentration has the highest value at the beginning of the process, only to decrease significantly later. This change indicates a high sensitivity of anthocyanins to mechanical and oxidative processes, while volatile compounds show selective stability, whereby some compounds extract better, while others undergo degradation. This research highlights the importance of optimizing pressing conditions to preserve the functional and sensory properties of the juice.

A comparison of different methods of extracting juices from pomegranate fruit, including crushing and grinding of the edible part, whole fruit and halved fruit, resulted in higher concentrations of phenolic compounds and tannins in juices obtained from halved fruits, compared to other extraction methods (Mphahlele et al., 2016).

Industrial processing and type of packaging have a significant impact on the preservation of phenolic compounds in commercial juices. Research by Nilova et al. (2023) showed that directly squeezed juices have the highest antioxidant index, with tannins and total phenols playing a key role in the formation of bioactivity of juices.

Therapeutic potential of wild pomegranate juice

Wild pomegranate juice (*Punica granatum* L.) shows significant pharmacological properties, including antioxidant, anticancer, antiviral and antidiabetic activities, as well as a potential role in the prevention of cardiovascular diseases. The therapeutic effects of the extracts are primarily attributed to the presence and concentration of bioactive secondary metabolites, i.e. the high content of phenolic compounds, including anthocyanins, tannins, flavonoids and copigments (Guo et al., 2022).

A study by Aloqbi et al. (2016) was conducted to compare the antioxidant properties of standard punicalagin, the main polyphenolic compound present in pomegranate, and pomegranate juice, covering different mechanisms of antioxidant activity. In free radical scavenging tests, pomegranate juice was found to be more effective than standard punicalagin at higher concentrations. In contrast, in the reduction power test, an increase in activity was recorded with increasing concentration, with punicalagin being more effective than juice. The obtained results indicate the existence of different, but mutually complementary antioxidant mechanisms of action of punicalagin and pomegranate juice, which further supports their potential in the prevention of oxidative stress.

A solution of total pomegranate tannins significantly reduces the expression of a key mediator of the inflammatory response by 40.5% in an *ex vivo* model of human skin. Despite their high molecular weight, the extracts successfully penetrated the skin. The obtained results indicate the important role of tannin compounds, especially punicalagin, in the modulation of inflammatory processes, and support the potential of pomegranate peel extracts for topical application in the treatment of inflammatory skin conditions (Houston et al., 2017).

The results of the application of adsorptive membrane chromatography, as an advanced technique for the isolation of anthocyanin and copigment fractions from pomegranate juice extracts, indicate the synergistic effect of polyphenolic compounds, which is manifested in a significantly increased ability to neutralize free radicals and in a pronounced cytoprotective effect on cells exposed to oxidative stress (Kostka et al., 2020).

Pomegranate peel extracts, rich in polyphenolic compounds, further confirm their therapeutic potential, especially in the context of cardiovascular diseases. The use of a standardized hydroethanolic extract of pomegranate peel results in a reduction in plasma glucose and lipid levels, modulation of inflammatory processes, and stabilization of atherosclerotic plaques through an increase in collagen content and a reduction in the area of necrosis. In addition, the observed improvement in efferocytosis within atherosclerotic lesions suggests an additional mechanism by which pomegranate peel extract may reduce the progression and complications of atherosclerotic plaques, which has direct implications for the prevention of cardiovascular events. These findings are based on the study by Manickam et al. (2022). In addition to the pronounced cardioprotective and anti-inflammatory effects, the study by Daoutidou et al. (2021) further expands the spectrum of biological activity of pomegranate peel extracts by confirming their antibacterial potential. Efficacy was found against a wide range of pathogenic bacteria, including *Pseudomonas aeruginosa*, *Escherichia coli*, *Listeria monocytogenes*, *Salmonella spp.* and *Staphylococcus aureus*. These antimicrobial properties further highlight the potential for multiple applications of pomegranate peel extracts, especially within integrated therapeutic approaches aimed at the treatment and prevention of chronic non-communicable diseases with simultaneous antimicrobial protection. The results of the study indicate that wild pomegranate is a rich source of phytochemicals with potential medicinal applications, including quercetin, pyrogallol, malic acid and chlorogenic acid. These compounds may be responsible for the reported antibacterial activity and pronounced antioxidant potential against the bacterium *Xanthomonas oryzae* (Ullah et al., 2025).

In the work of Topalović et al. (2024), the *in vitro* cytotoxicity of wild pomegranate juices and their relationship with phytochemical composition were investigated. The analysis included different juice samples, identifying key bioactive compounds, including anthocyanins and ellagitannins, which act synergistically to inhibit the proliferation of cancer cells. The most pronounced cytotoxic effects were observed on lung and cervical cancer cells. The effects on breast cancer cells were less pronounced, and the lack of a significant effect of anthocyanin-rich juices on these cells suggests the importance of additional compounds, such as vitamin C and ellagic acid, for achieving the antitumor effect. Wild pomegranate juices did not show cytotoxicity towards normal cells, which highlights their potential as selective antitumor agents. The obtained results indicate that the combination and mutual ratios of phenolic compounds may be crucial for the targeted biological activity, rather than their total amount.

The research of Minutolo et al. (2023) is also significant, proving high antiproliferative effectiveness against breast cancer cells, without harmful effects on healthy cells, using hydrodynamic cavitation to extract phytocomplexes from whole pomegranate fruits.

Conclusion

Wild pomegranate juice (*Punica granatum* L.) shows significant therapeutic potential due to its rich phytochemical composition, which includes high concentrations of phenolic compounds such as anthocyanins, ellagitannins, flavonoids and vitamin C. These compounds possess pronounced biological properties, including antioxidant, anti-inflammatory, antimicrobial and cardioprotective effects, making wild pomegranate juice a valuable functional food product with potential for the prevention and therapy of various diseases, including cardiovascular diseases, cancer and infections. Also, research shows that different processing methods and growing conditions can significantly affect the concentration of bioactive compounds, highlighting the importance of optimizing production processes to preserve the functional properties of the juice. Wild pomegranate juice not only has the potential for use in the prevention and treatment of diseases, but also as a useful dietary supplement, due to its multiple health benefits. Due to its biological activity, wild pomegranate represents a source of valuable phytonutrients and can be considered important components of future therapeutic approaches.

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