

Therapeutic Effects of Pomegranate (*Punica Granatum*)

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Abstract - *Punica Granatum L.* is in the family *Punicaceae*, which has a lot of different species. Pomegranate contains a high concentration of potentially bioactive compounds throughout the fruit, including the kernel, peel, juice and leaves. In traditional medical practise, these plants have been utilised to treat a variety of conditions, including those related to the digestive tract, cardiovascular health, and the endocrine system. The goal of this study was to give an overview of what scientists and traditional healers know about *P. Granatum* in terms of its phytochemical composition and medicinal uses. This information could be used to make new medicines in the near future. There have been reports that the plant has a wide variety of phytochemical components: these components include polyphenolics, flavonoids, anthocyanosides, alkaloids, and terpenes. In randomised clinical trials, the pharmacological effects of pomegranate have been found to be beneficial for a variety of diseases and conditions. These conditions and diseases include diabetes, cardiovascular disease, problems with the oral mucosa, endocrine disorders, and cancer. Some of the traditional applications of the plants have been backed by scientific research, specifically their use in the diagnosis of cardiovascular and endocrine disorders.

Index Terms—*Punica Granatum L.*, Phytochemical, Pomegranate, Haemorrhoids.

1. Introduction

A deciduous tree is the pomegranate (*Punica granatum L.*). Pomegranate juice is considered to have medicinal properties in a wide variety of various societies and civilizations. Pomegranate fruit, which comes from the fruit of the pomegranate tree, has a number of health benefits, including properties that reduce inflammation and fight infection. It has been demonstrated that the oil that is extracted from pomegranate seeds can inhibit the progression of breast and skin cancer. The pomegranate seed oil contains compounds that are phytoestrogenic, while the pomegranate fruit itself is filled with phenolic chemicals that have high antioxidant action. Pomegranate, both fruit and the bark of plant, can be used to cure a wide range of gastrointestinal diseases, such as dysentery, diarrhoea and intestinal parasites [1]. Pomegranate can be taken as either a fruit or as the bark of the plant. In traditional medicine, both juice and seeds are used as a tonic for throat and heart, respectively. In addition to its use in the therapy of haemorrhoids, it is also effective in preventing bleeding from gums and nostrils [2].

A. Application of Pomegranate

The use of pomegranates in traditional medicine:

Pomegranates have been known to inhabitants of many various cultures since the ancient ages, which span from 4000 to 3000 BCE. Pomegranate blossoms have been seen as symbols of life, immortality, knowledge, femaleness, fertility, and holiness.

The pomegranate's roots, bark, flowers, fruits, and leaves are all utilised in the Ayurvedic school of medicine, which results in a wide variety of therapeutic concoctions being created from these parts of the plant. Ayurvedic medicine considers both the bark and the root of the having plant to possess anthelmintic, vermifugic, and anti-parasitic characteristics [3]. These features make the having plant an effective treatment for diarrhoea, dysentery, and ulcers. Pomegranate is considered to be its own "pharmacy" in Ayurvedic medicine. As well as having anti-parasitic properties, it also acts as a blood tonic. In traditional Indian medicine, dry pomegranate peel extract, bark, and flower infusions were used to treat, among other things, ulcers, nose

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bleeding, diarrhea and intestinal worms. Gargling the liquid form of it was another method used to soothe a sore throat. In the field of dentistry, pomegranate was utilised as a treatment for periodontitis patients suffering from bleeding gums and plaque [4].

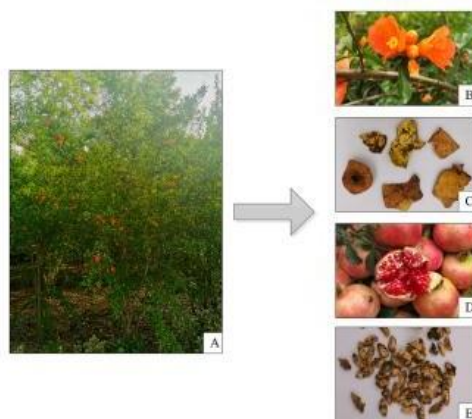


Fig. 1: Different parts of pomegranate (*Punica Granatum* L.) (A) tree (B) flower (C) Peel (D) fruit and (E) seeds

B. Common Name

- Hindi: Anar
- English: Pomegranate
- Latin: *Punica Granatum*
- Sanskrit: Dadimah

C. Chemical Constituent

A recent study found that the parts of pomegranate that are most useful for therapeutic uses are ellagic acid, ellagitannins, flavonoid, anthocyanins and estrogenic flavonols and flavones. Other components of pomegranate include anthocyanins, flavonoids, and estrogenic flavonol Ellagic acid is a natural acid that is present in a wide range of plant species from all over the world. Due to the fact that it exhibits powerful anticancerogenic and antioxidant properties, recent research on *Punica granatum* has placed it at the forefront of the field. Standardization work is currently being done on a significant number of pomegranate extract that are already for sale on the market. In order to meet the requirements, these extracts must contain forty percent ellagic acid or more [5]. Lansky, a well-known researcher on the therapeutic qualities of *Punica granatum*, says that we shouldn't just focus on normalizing ellagic acid and leave out other parts of *Punica granatum* that are especially important from a therapeutic point of view. Lansky believes that this is a mistake because there are many other constituents of *Punica granatum* that seem to be particularly significant. This is because doing so would mean ignoring other components of *Punica granatum* that contain medicinal properties. He is worried that this might result in an inaccurate diagnosis of the illness [6].

D. Pomegranate Phytochemicals

Pomegranate contains numerous different types of bioactive compounds, including flavonoids (including flavonols, flavanols, flavones, flavanones, anthocyanins, and anthocyanidins), tannins (both hydrolyzable and non-hydrolyzable), lipids, simple organic acids, and alkaloids.

Flavonoids are primarily found in the plant in glycosylated forms, and they have powerful antioxidant and anti-inflammatory activities. Pomegranate juice contains a number of different flavonoids, the most significant of which being the group known as anthocyanins. The most bioactive chemicals are those that can be hydrolyzed, such as these and tannins. Anthocyanins discovered in the pomegranate include delphinidin 3-glucoside, delphinidin 3, 5-diglucoside, cyanidin 3 rutinoside, cyanidin 3, 5-diglucoside, cyanidin 3-hexoside. Anthocyanidins are also called aglycones, and cyaniding, delphinidin, peonidin, pelargonidin, and petunidin are all examples of anthocyanidins. Pomegranates also have rutin, kaempferol, kaempferol 3-O- glucoside, kaempferol 3-Orhamnoglycoside, quercetin, dihydrokaempferol- hexoside, catechin, epigallocatechin 3-gallate, epicatechin, apigenin, luteolin 7-0-glucoside and epicatechin [7].

E. Pharmacology Activity

Anticancer Activity

Cancer is a medical disorder in which excess and inappropriate cell growth leads to significant infiltration all through the body to disrupt various organ functions. This illness is characterized by the presence of tumors, which are masses of malignant cells. Cancerous tumors are a telltale sign of this illness, which is characterized by their presence. It is common knowledge that chemotherapeutic drugs, due to their capacity to kill normal cells, are themselves a candidate for the development of cancer.

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This is because of the potential of these medicines to induce cell death. Therefore, therapeutic techniques for the treatment of cancer and preventative measures against cancer are evaluated depending on the benefit-to-risk ratio. The potential beneficial impacts that consuming pomegranate (*Punica granatum*) fruit can have on an individual's health, in addition to the underlying mechanism that causes it to slow the progression of cancer [8]. Pomegranate extract has been shown to have anti-proliferative, pro, and anti-invasive effects on a variety of tumor cell lines, in both *in vitro* and in clinical investigations involving humans. The nutritional and medicinal benefits of pomegranate fruit are causing it to grow in popularity. Polyphenols, which are found in high concentrations in the fruit, are one of the reasons for its popularity. Treatments for inflammation of tissues, cancer, diabetes, skin illnesses, blood disorders, cardiovascular diseases have all been implemented in the standard medicine system. In today's society, it is essential to carry out research that is supported by evidence, to document the results of said study, and to pinpoint any potential mode of action that may be related to the outcomes of the research. Before pomegranate can be seriously evaluated for inclusion in the category of functional foods, it will need to be subjected to additional clinical research and testing [9].

Anti-Inflammatory Activity

The primary pomegranate constituents with anti-inflammatory effects are urolithins. Ellagitannins and ellagic acid combine to become urolithins as the gut flora processes them. The pomegranate extract contains extremely high amounts of ellagic acid and ellagitannins. According to pharmacokinetic studies, the flavonoids procyanidin, which is present in the juice, kaempferol, luteolin, and apigenin, which are present in the peel and leaves, all have potent anti-inflammatory activities. Gallic acid, which may be found in flower, juice, leaves, and peel, as well as granatin B and gallagyl dilacton all of which are found in the peel, are tannins that have been proven to have anti-inflammatory qualities. Pomegranate juice contains the alkaloid melatonin, which has anti-inflammatory benefits [10].

Nephroprotective Activity

Rats were pre-treated with pomegranate flower hydroalcoholic extracts, which significantly decreased the amount of tumors. The dosages used to achieve this result were 125 and 250 mg/kg *p.o.* twice day for 3 days. In individuals who had myoglobinuria, there was a considerable improvement in renal dysfunction brought on by hypertonic glycerol, and this improvement was dose-dependent. It was shown that the renoprotective impacts of *Punica granatum* were mediated through the activation of PPAR- γ and a signalling pathway that was dependent on nitric oxide [11].

Neuroprotective Activity

Multiple factors contribute to the neurodegeneration seen in Parkinson's, Alzheimer's disease, and other neurodegenerative diseases. This is referred to as multifactorial. Adverse reactions include inflammation, glutamatergic neurotoxicity, an increase in iron and nitric oxide, a decrease in the expression of nutrients, and the formation proapoptotic proteins [12-18]. Every aspect of the situation has been considered. In addition to phenolic acids and ellagic tannins, pomegranate contains flavonoids (anthocyanin, catechins, rutin, & epigallocatechin-3-gallate) and anthocyanins (punicalin, punicalagin, gallagic, and ellagic acid). It also contains punicalin and punicalin, which are both types of phenolic acids and ellagic tannins (delphinidin, cyaniding, and pelargonidin). Antioxidant properties of polyphenols have long been recognized [19]. A pomegranate juice extract was discovered to have significant antioxidant activity in a mouse model, contributing to a extract's neuroprotective properties. Pomegranate juice added to the mother's diet during pregnancy protected the developing brain of a newborn against a hypoxic-ischemic insult. Even seven days after the baby was born, this neuroprotection was found to be effective [20]. Neuroprotection can be handed down from moms to their newborn offspring via pomegranate polyphenols, which are abundant throughout the fruit. Methanolic It is also known that in addition to reducing aluminium buildup and raising anti-apoptotic protein like Bcl-2, pomegranate peel extracts can improve antioxidant activity in the brain [21].

F. Anticancer Activity

It has been demonstrated that pomegranate extracts are superior to several other cancer-fighting drugs in their ability to inhibit the development of cancer cells in the breast, prostate, colon, and lungs. Participants in a first clinical study utilising pomegranate juice as a therapy for prostate cancer showed a significant prolongation of the time it takes for the prostate specific antigen to double [22].

It has been demonstrated that several components of the pomegranate fruit, including the seed oil, juices, fermented juice and peel extract, can stop the development of human breast cancer cells when they are cultured in a petri dish under controlled laboratory conditions. In this context, it was discovered that the extract from the fruit peel includes three different estrogenic chemicals. These components are luteolin, quercetin and kaempferol [23].

G. Antiatherogenic Effect

Pomegranate fruit, pomegranate juice and the polyphenols found in pomegranate fruit have all shown promise in reducing risk factor for cardiovascular disease. LDL oxidation, blood pressure, serum adrenalin converting enzyme (ACE) activity, cholesterol esterification, macrophage oxidative state, and the production of macrophage foam cells are all components of

atherosclerosis and cardiovascular disease [24]. Other things that contribute significantly to atherosclerosis and cardiovascular problems are cholesterol esterification and the oxidative state of macrophages. Healthy people who drank pomegranate juice had less LDL that clumped together and got stuck, and their serum paraoxonase activities went up [25].

H. Oral Cavity

Pomegranate extract can lower the level of oxidative stress experienced by macrophages as well as lipid peroxidation. In addition to these functions, it also acts as a molecule that reduces inflammation and scavenges free radicals. Gingivitis is warded off not only by the direct antioxidant activities of the flavonoid content but also by the indirect impacts of an increase in the number of free radical scavengers [26].

The actual advantages of pomegranates as a treatment and preventative measure against the oral plaque-causing bacteria, the specific active ingredients in pomegranates that may have an impact as anti-caries and anti-plaque agents and the safest dosage of pomegranate juice that people can consume at once [27].

2. Literature Review

Chenyan-hui (2022) [18] studied on pomegranate products has greatly expanded and been successful in bringing consumers' attention to the fruit's health benefits. This has helped the global pomegranate industry grow. However, there is scant information available on pomegranates grown in China. 20 pomegranate cultivars from six different locations of China were examined for their fruits and arils' morphological and chemical characteristics. It was unexpected that 'Mollar' produced in China had larger fruits and more moisture in the arils than in Spain.

Jing-Hui Ruan (2022) [21] Ten distinct phenolic compounds with a hexahydroxy diphenol monomer were found in *Punica granatum* L. peel phytochemical activity. The three compounds that were first found there have been given the designations pomegranatins A through C. For the first time, pomegranate peels were used to identify two of the leftover seven pomegranatins. A detailed spectroscopic analysis was used to establish their structures. In order to gain a basic grasp of the biological activities being carried out by these compounds, *in vitro* antibacterial, antioxidant and anticancer experiments were also conducted. In the DPPH antioxidant assay, six different substances showed substantial ability to scavenge free radicals. Two of the compounds showed some antibacterial activity against *Candida albicans* and one of the compounds had the ability to inhibit the growth of both *C. albicans* and *Escherichia coli* to some amount. Four distinct compounds each displayed a low amount of anticancer activity when tested on the Hela cell line. This held true whether or not ellagitannins' bioavailability was taken into consideration. In conclusion, these discoveries have increased our knowledge of the structural variety of bioactive compounds found in pomegranate peels as well as the biological functions of the bioactive components themselves.

Isha Kumari (2021) [19] studied *Punica granatum* L.'s medicinal properties as well as its phytochemistry, traditional uses in Ayurveda, and folk medical systems. The plant has been used for a very long time in a wide range of cultures all across the world. The plant was used as a symbol for many ideas, including fertility, prosperity, life, and happiness. Traditional medical practises like Ayurveda and folk medicine use it to treat a variety of illnesses. It is a well-respected plant-based therapy. This is in addition to the ethnic beliefs that are associated with the plant. According to ayurvedic doctrine, it is considered to be a Rasayana. It is used in a wide variety of ayurvedic polyherbal formulations that are employed in the treatment of a variety of ailments. Polysaccharides, metals, polyphenols, tannin, saponins, quinones, alkaloids, flavonoids, tannins, terpenoids, and steroids are some of the plant's phytochemical components. Phytochemicals are useful in medicine because of the variety of health benefits they each provide. This supper dish is well across the world for its high anti-oxidant content. It also has anti-microbial, hepato- and cardioprotective, anti-diabetic, and cancer prevention capabilities, as well as immune- and inflammation-suppressing, anti-hypertensive and anemic-lowering effects. characteristics, among others.

Mohamed Taha Yassin (2021) [20] investigated the prospect of employing extracts from pomegranate peel as a raw material for the creation of non-hazardous food preservatives, cancer-preventing chemicals, and antioxidants through the application of biotechnology. Given the high rates of illness and mortality that it causes all around the world, antimicrobial resistance is a concern for public health. A growing number of people are falling ill from food-borne illnesses, and the use of artificial food additives can have consequences that could be damaging to human health. As a result, there is an increased need for natural food preservatives that are completely risk-free. Research has revealed that the negative impacts of free radicals on public health are linked to significant diseases such as cancer, diabetes, and heart issues. As a result, it is crucial to discover secure sources of antioxidants because of this research. So, the current study was done to see how well various solvents extracts of pomegranate peels prevent cancer, bacterial growth, and damage from free radicals.

Shasha Ge (2021) [14] studied the current state of pomegranate traditional medicine beliefs, as well as their spread along the Silk Road, ethnopharmacological uses, chemical composition, pharmacological actions, toxicity, and involved pathways. Tannins, organic acids, flavonoid, alkaloids, and volatile oils are just a few examples of the phytochemicals that can be found in the many different portions of the pomegranate. These molecules exhibit a variety of functions, including the capacity to confer resistance to cerebrovascular sickness, antioxidant features, antibacterial properties and anti-oncogenic qualities, amongst other things. There is also a summary of the 4 promising pharmacological pathways mentioned in this research.

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Adhami et al., [28] examined Pomegranate has extremely potent anti-oxidant, anti-inflammatory, and antibacterial qualities because it contains large concentrations of anthocyanins, anthocyanidins, flavones, flavanones, flavanols, flavonols, hydrolysable and non-hydrolysable tannins, and alkaloids. Free radicals are responsible for several types of inflammation, and the antioxidant pomegranate is particularly effective in reducing oxidative stress, which results in chronic inflammation and a number of disorders. Pomegranate phytochemicals have been proven to have antibacterial effects, making them useful in inflammations caused by germs. Pomegranate includes phytochemicals with multiple biological activities, which allows it to have an impact on a variety of inflammatory incident and method components and speed up the healing process. It is noteworthy to note that pomegranate demonstrated helpful activity where commercially drugs were dangerous, produced equivalent outcomes to commercial drugs in employed doses, and did so without side effects, suggesting that pomegranate may offer an alternative to commercial anti-inflammatory medications.

Fabio Mastrogiovanni (2019) [15] examined pomegranate peel extracts (PPE), which were formed from pulp that was left over after processing pomegranate juice, were tested for their ability to minimize inflammation in two different ways: in vitro, with Caco-2 cells; and ex vivo, with pig colonic tissue explants. Both methods were successful. The PPE were made from leftovers from pomegranate juice production. Lipopolysaccharide was employed to activate colonic tissue explants ex vivo, whereas tumour necrosis factor alpha (TNF) was used to activate caco-2 cells in vitro (LPS). PPE was added to both tissues in mixtures at doses of 0, 1, 2, 5, 10, and 25 ng/mL. In both test supernatants, the release of CXCL8 was assessed using an enzyme-linked immunosorbent assay (ELISA), and quantitative polymerase chain reaction was used to assess relative expression of inflammatory cytokines in the colonic tissue (QPCR). Although this impact was only noticeable at concentrations of 5 and 25 g/mL in colonic explants, PPE reduced the generation of CXCL8 in Caco-2 cells at levels ranging from 2.5 to 25 g/mL ($p < 0.001$). ($p < 0.01$). In contrast to the controls, the treatment with 5 g/mL of PPE inhibited the expression of IL1A, IL6 and CXCL8 in the colonic tissue that had been subjected to LPS. This was the case when compared to the other group.

Shahindokht Bassiri-Jahromi (2018) [16] investigated the pomegranate's therapeutic benefits against different cancers and its functioning qualities. In addition, the potential applications of pomegranate characteristics in future human and animal therapeutic trials are investigated. According to the information available, pomegranates (*Punica granatum*) may be used to treat certain illness conditions, control other disorders, and improve human health. In many nations, cancer has risen to the top of the list of deadly diseases. Cancer continues to be a major issue despite advances in medical care. Most malignancies are resistant to most treatments. Therefore, research into new, more effective, and side-effect-free therapy options continues. Strong antioxidant activity in pomegranates has the potential to be beneficial to health. Pomegranates' ability to fight cancer thanks to their high polyphenol content has researchers more interested in them than before. We highlight the possible health benefits of pomegranates, particularly their ability to slow the progression of cancer. Several different cancer cell lines have been used for in vitro, in vivo, and clinical research, and the results have indicated that pomegranate has anti-invasive, anti-metastasizing, and anti-proliferative capabilities.

Janani Jacob (2019) [17] in Ayurvedic medicine, the studied pomegranate, also known as *Punica granatum*, is referred to as "A pharmacy unto itself." This fruit is also utilized in a broad number of other healthcare systems. The plant is a member of the Lythraceae family, which is best known for its many pomegranate species. Due to the plant's extensive spectrum of potentially bioactive chemicals, certain plant sections have notable pharmacological properties. Anti-inflammatory, anti-cancer, anti-bacterial, anti-atherosclerotic and anti-diabetic properties were found in it after being subjected to several biological studies.

3. Conclusion

A conclusion section is not required. Although a conclusion may review the main points of the paper, do not replicate the abstract as the conclusion.

Punica granatum's numerous medicinal properties have gained a lot of attention in the last decade. Antioxidants and anti-inflammatory actions are among these qualities. One of these characteristics is the ability to treat inflammation. As a result, various in vitro, animal and clinical investigations have been carried out as a direct result of this interest. Pomegranate juice has an antioxidant capacity that is on par with that of green tea and even surpasses that of red wine. Pomegranate juice is packed with polyphenols. Because it inhibits the development of cancerous cells and lowers inflammation, there is a higher probability that it can be used as a diagnosis or as an adjuvant therapy for the diagnosis and prevention of a wide variety of cancers and cardiovascular illnesses. This is due to the fact that it reduces the risk of these conditions occurring in the first place. Pomegranate's antibacterial qualities may aid in preventing illnesses brought on by germs that are resistant to medications and dental diseases. Because the effect of pomegranate on bacterial infections has only been investigated in vitro, clinical investigations on humans are required before any clinical advantage can be demonstrated or refuted. The significance of undertaking additional clinical research is underscored by the possibility that pomegranate extracts may also affect a variety of other disease processes, including obesity, osteoarthritis, neonatal brain injury, Alzheimer's disease, and other inflammatory diseases.

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Polyphenolics, flavonoids, anthocyanosides, alkaloids, lignans, and triterpenes are just some of the phytochemical components that have been found as being present in the plant. Other components include polyphenolics and terpenes. Randomized clinical trials have shown that the most important pharmacological advantages of pomegranate are related to a number of diseases, such as diabetes, heart disease, oral problems, endocrine disorders, and cancer. The current research has shed some light on how the plants have been used in the past, and it has also shown that some of these uses are supported by scientific evidence. In particular, the use of the plants as treatments for cardiovascular and endocrine diseases has been supported by scientific evidence. There is a wide variety of pharmacological effects and clinical applications that may be attributed to *Punica granatum* and its constituent parts. Inflammation, cardiovascular disorders (such as hyperlipidemia and hypertension), endocrinopathies (such as diabetes), and cancer are only some of the conditions that have been investigated in large-scale clinical trials looking at its potential therapeutic effects. On the other hand, the underlying molecular mechanism of pomegranate has not yet been established, and further RCTs are required for this.

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