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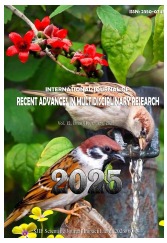

RESEARCH ARTICLE

POMEGRANATEIN BREAST CANCER: A COMPERHENSIVE REVIEW OF ITS THERAPEUTIC POTENTIAL

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ABSTRACT

Punica granatum L., commonly known as the pomegranate, is a fruit-bearing plant native to Iran and belonging to the Punicaceae family. Characterized by its large, globular berries containing numerous seeds enveloped in a juicy, edible pulp, pomegranate has been employed for centuries in various cultures to prevent and treat a multitude of health disorders, including inflammation, diabetes, diarrhea, dysentery, and dental plaque. Aim of the Review: This review aims to provide an up-to-date, comprehensive overview of the chemical constituents, traditional uses, phytochemistry, pharmacology, and toxicology of Punica granatum L. Specifically, this review focuses on the potential exploitation of this species to treat diverse diseases and suggests future investigations. The increasing demand for complementary medicine has driven the search for effective alternative therapies that minimize adverse effects associated with conventional drugs. Pomegranate has garnered significant attention due to its remarkable nutritional and medicinal properties. In Mexico, the harvest and consumption of pomegranate have surged, driven by recent discoveries of phytochemical compounds exhibiting antioxidant, anti-inflammatory, and antiviral activities, with promising applications in the food industry.

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INTRODUCTION

Pomegranate (Punica granatum) is a tree belonging to the Punicaceae family with a height around 3 to 6 m. Pomegranates are one of the oldest edible fruits, originating in Central Asia.It has rounded fruit with a dry outer covering (husk) made up of two layers: (1) a hard-outer layer called an epicarp, (2) a soft inner layer called a mesocarp[1]. The inner mesocarp has distinct chambers that contain fleshy seeds[2]. This plant's leaves are bright green, elongated, smooth, shiny, and slightly wavy. The flowers are notable for their flared shape and bright orange petals, usually numbering 5 to 8[3]. Approximately 26-30% of the pomegranate's total weight is comprised of peels, which are rich in phenolic compounds[4]. This includes flavonoids, such as anthocyanins, catechins, and complex flavonoids, as well as hydrolyzable tannins like punicalin, and ellagic acid, all of which are highly concentrated in pomegranate peel and juice[5]. The principal constituents of pomegranate arils include 85% water, 10% total sugars (mainly fructose and glucose), and 1.5% pectin. Furthermore, arils contain organic acids like ascorbic acid, citric acid, and malic acid, as well as bioactive phenolics and flavonoids, with anthocyanins being the primary flavonoid[6].

Pomegranates are a nutrient-rich fruit, boasting an array of bioactive compounds, including anthocyanins, flavonoids, tannins, phenolics, proanthocyanidins, sterols, terpenes, and terpenoids. Additionally, they contain organic acids (ascorbic, citric, and malic), sugars (fructose and glucose), pectin, and fatty acids in their seeds. Pomegranates are also a good source of minerals like iron, copper, sodium, magnesium, and zinc[7].

Traditional medicinal uses:-Pomegranate peel has been traditionally used to address various health concerns[8]. Its aqueous extract, obtained by boiling for 10-40 minutes, treats diarrhea, dysentery, dental plaque, and is used as a douche and enema agent[9]. Topical application of PoP powder heals bleeding gums and plaque in periodontitis patients. Additionally, PoP is gargled to relieve sore throats and hoarseness[10]. In the Indian Subcontinent, dried PoP, bark, and flower infusions treat diarrhea, intestinal worms, nosebleeds, and ulcers. Hyperacidity is treated with 5-10g of peel powder taken orally two to three times daily[11].

- Relieves symptoms of anemia[12].
- Lower risk of heart attacks and strokes[13].
- Reduces risk of developing cancer.

- Lowers dental plaque.
- Helps overcome depression.
- Rich in antioxidants.
- Packed with anti-ageing properties[14,15,16].

Phytochemistry of Pomegranate

Major Phytoconstituents

- Ellagic Acid
- Flavonoids
- Phenolic Acid (gallic, ferulic)
- Tannins
- Terpenes

Other Bioactive Compounds

- Alkaloids (Pomegranatin)
- Glycosides
- Saponins
- Sterols (beta-sitosterol)
- Fatty acid (oleic)
- Vitamins (C,E,K)
- Minerals (potassium ,Mg)[20,21]

Pharmacological Mechanisms

- **Anticancer activity:** Inducing apoptosis, inhibiting cell proliferation.
- **Cardiovascular protection:** Improving lipid profiles, reducing blood pressure.
- **Anti-inflammatory activity:** Inhibiting pro-inflammatory cytokines, enzymes.
- **Antioxidant activity:** Scavenging free radicals, reducing oxidative stress[22].

Pharmacokinetics

- **Distribution:** Wide distribution, including brain, heart, liver.
- **Metabolism:** Hepatic metabolism, primarily through CYP3A4.
- **Excretion:** Renal excretion, fecal elimination.
- **Absorption:** Bioactive compounds absorbed through gut, skin[23].

Therapeutic Applications:

- Neurodegenerative disease management.
- Anti-inflammatory and antimicrobial applications.
- Cardiovascular disease prevention.
- Cancer prevention and treatment[24].

Pomegranate is a rich source of bioactive compounds, including ellagic acid, punicalagins, and anthocyanins. These compounds have been shown to possess anti-proliferative, anti-inflammatory, and pro-apoptotic effects[25].

Anti-Cancer Mechanisms

- Inhibition of cell proliferation and induction of apoptosis
- Anti-angiogenic effects
- Inhibition of cancer cell invasion and metastasis
- Modulation of signaling pathways (e.g., NF-κB, PI3K/Akt)[26]

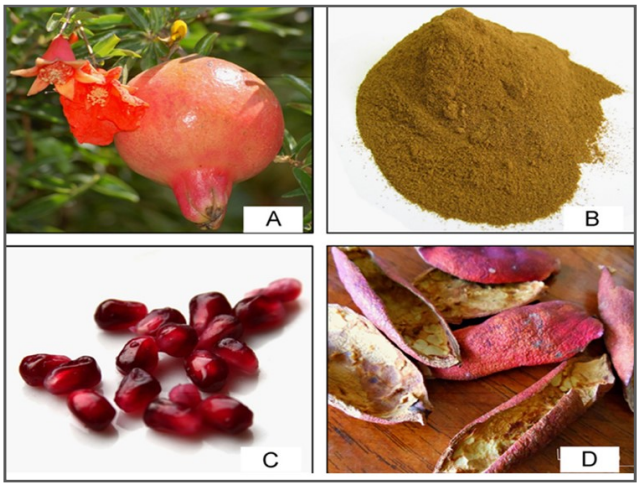


Fig. 1. A) Pomegranate Fruit, B) Pomegranate Peel Powder, C) Pomegranate Seeds D) Sundried Pomegranate Peel

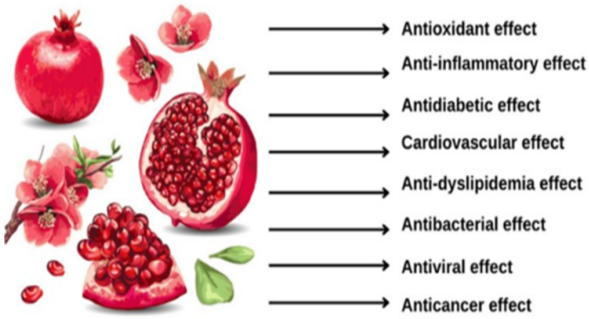
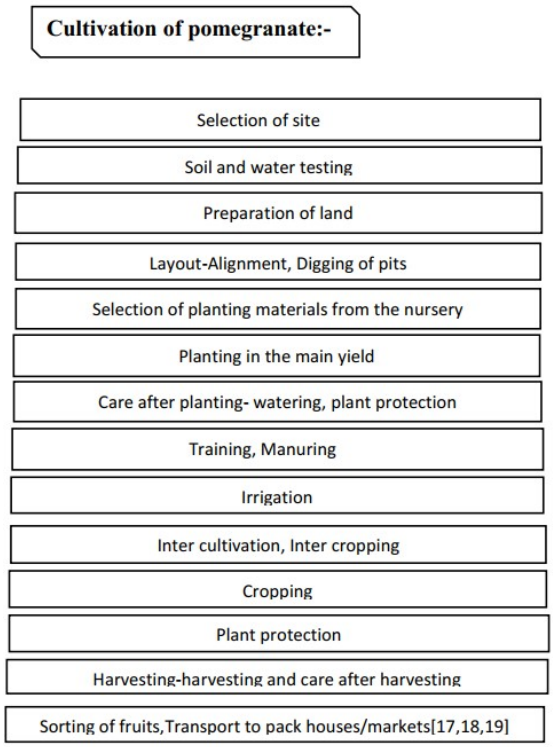


Fig.2) Benefits of Pomegranates



Constituents	Concentraition
Water (g)	82.5
Food fiber (g)	3.1
Protein(g)	0.7
Lípids (g)	0.6
Carbohydrates(g)	16.7
Fructose	7.9
Sacarose	1.0
Minerals (mg)	
Sodium	7.0
Potassium	290.0
Calcium	8.0
Magnesium	3.0
Fosforus	17.0
Iron	0.5
Vitamins (mg)	
T hiamine	0.05
Riboflavin	0.02
Ascorbic acide	7.0
Organics acides (g)	0.77
Malic acide	0.1
Citric acide	0.5

Tab. 1) fraction composition of Punica granatum fruit

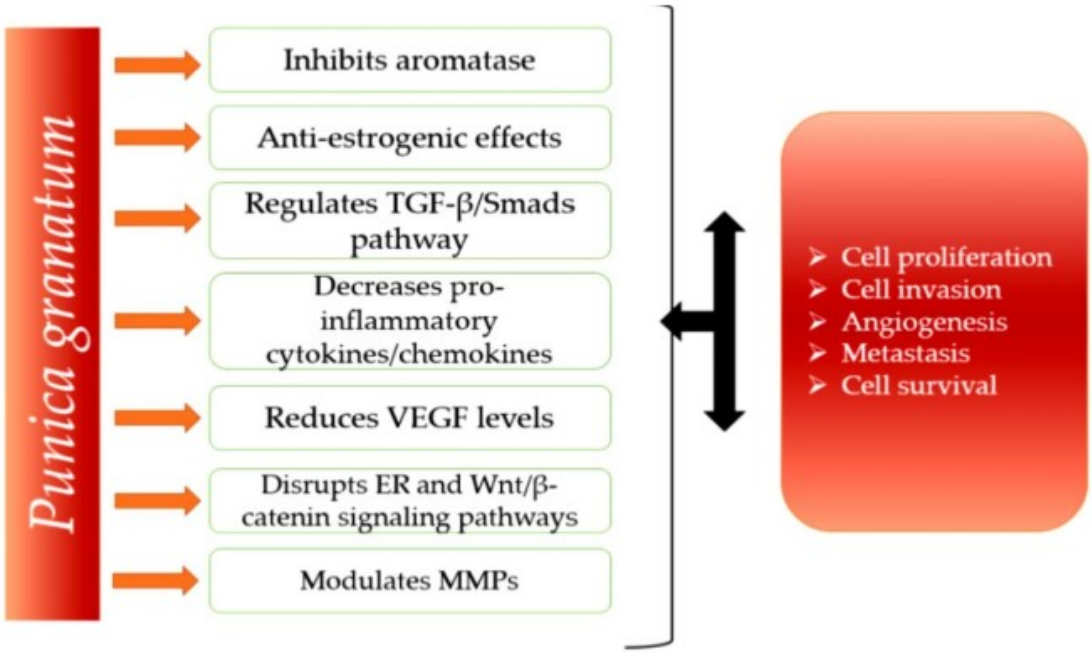


Fig.3) Anti-Cancer Mechanism of Punica granatum and molecular targets

Anti-Cancer Efficacy

- Prostate cancer: Inhibition of tumor growth and reduction of PSA levels
- Breast cancer: Inhibition of tumor growth and induction of apoptosis
- Colon cancer: Inhibition of tumor growth and reduction of inflammation
- Lung cancer: Inhibition of tumor growth and induction of apoptosis[27].

MATERIALS AND METHODS

Breast cancer's increasing global burden and the expanding evidence on natural compounds' benefits motivated this literature review on Punica granatum's (pomegranate) anti-cancer properties.

Chemoprevention

- Pomegranate extract supplements
- Ellagic acid (EA) and punicalagins (PC) extracts
- Pomegranate juice consumption[29].

Therapeutic approaches

- Combination therapy with conventional treatments (e.g., chemotherapy, hormone therapy)
- Targeting specific breast cancer subtypes (e.g., ER+, HER2+)
- Inhibition of cancer stem cells and metastasis[30].

Consistent with previous findings, treatment of human breast cancer cells with pomegranate extract led to dose-dependent growth inhibition and cytotoxicity. This outcome aligns with another study demonstrating that pomegranate seed extract decreased viability and hindered growth of human breast cancer cells[31].

CONCLUSION

Our study demonstrates significant antiproliferative and pro-apoptotic effects on breast cancer cells, highlighting the potential of [Substance/Method] as a therapeutic strategy against breast cancer. These findings warrant further investigation for clinical applications. This review highlights the potential of pomegranate as a novel adjunctive treatment for breast cancer, demonstrating anti-proliferative, anti-inflammatory, and pro-apoptotic effects.

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