International Journal of Pharmaceutical Research and Applications
Volume 8, Issue 6 Nov-Dec 2023, pp: 2623-2641 www.ijprajournal.com ISSN: 2249-7781

A comprehensive review in aspects of therapeutic properties of pomegranate recently conducted clinical researches.

YuvrajArjun[1], Sanjay k Bias[2], Jyoti Bugad[3]
Fabtech College of pharmacy Sangola 413307 India

Submitted: 20-12-2023 Accepted: 30-12-2023

ABSTRACT:
Background: Pomegranate is a highly valued functional food due to its numerous health benefits. Different fruit parts, like seeds, juice, root, leaves and bark are used for medicinal purposes. People consume the edible parts fresh or as juices, canned drinks, or in jams and jellies. Its versatility extends to medicine, cosmetics, and food seasoning. Studies show it offers various health advantages, acting as an antioxidant, promoting nitric oxide, and exhibiting properties like antihypertensive, antiviral, antibacterial, anticandidal, and anticancer effects and much more. Researchers are focusing on refining extraction methods to yield extracts rich in specific polyphenols with sustained biological activity from different fruit parts. Clinical research basically targets pg extracts and juice use in human health. Overall, ongoing research highlights the diverse medical benefits of this plant.
Materials and methods: In this various new advanced with traditional methods for extraction of pomegranate plant are discussed such asSupercritical fluid extraction (SFE), Microwave assisted extraction (MAE), Ultrasonic assisted extraction (UAE), Pulsed electric field extraction (PEF), Enzyme assisted extraction (EAE)and the traditionally used Manual method, blending method, bowl method, dehydration method, cold pressing rolling method.
Discussion: In this review found that the both clinical as well as preclinical studies shows the effectiveness of plant whereas, Pomegranate is rich in various compounds like polyphenols, alkaloids, and vitamins, which possess strong abilities to counteract free radicals. These radicals causes oxidative stress and which can lead to many chronic diseases such as sugar diseases, diseases of cancer, atherosclerosis, Alzheimer's, kidney and liver issues, pain, and other degenerative conditions. By further study we can explore more properties and leading to new formulation development for multiple disease treatment using advanced dosage formulation techniques.
Conclusion: The concentrated pomegranate juice or standardized extract capsules make it convenient for people to harness the numerous health benefits this fruit offers. But before plant ingredients can be transformed into pharmaceuticals, conducting clinical trials is imperative to establish their safety and efficacy.
Keywords: pg. - punica granatum, pomegranate, and pp.-pomegranate peels.

I. INTRODUCTION:

Pomegranates, scientifically known as Punica granatum (Pomegranate), are native to Iran, thriving in arid and semi-arid regions due to their adaptability to harsh ecological conditions. In regions like Sawi and Yazd in Iran, over 764 distinct varieties of pomegranates have been gathered, each showcasing unique fruit traits like taste, color, size, time required for ripening, and avoidance for diseases. This plant can be divided into different parts, such as seeds, juice, bark, leaves, flowers, and roots. Each of these parts has unique characteristics, both in terms of their chemical makeup and their effects on living organisms. The edible fruit is typically round, roughly 5-12 cm wide, with a thick, hexagonal, red skin housing around 600 seeds, each surrounded by juicy pulp called aryl, which can range from white to dark red or purple. The Quran refers to pomegranates twice, considering them a symbol of divine creation, while ancient Greek mythology associates them with the fruit of death.
The Punica granatum plant is widely grown in many regions, including the Middle East, Caucasus, North and tropical Africa, the Indian subcontinent, Central Asia, parts of Southeast Asia, and the Mediterranean area.

International Journal of Pharmaceutical Research and Applications
Volume 8, Issue 6 Nov-Dec 2023, pp: 2623-2641 www.ijprajournal.com ISSN: 2249-7781

Fig. 01

"A goblet of juice and clusters of seeds with sarcotesta inside the Punica granatum fruit have been discovered as the fruit split open."

History:

Pomegranates have a rich history of cultivation spanning millennia in regions like the Middle East, India, the Mediterranean, California's Central Valley, and Arizona. Evidence suggests their cultivation as early as 5000 BC, marking them among the earliest fruit trees grown in the eastern Mediterranean. Archaeological discoveries of carbonized pomegranate remains in sites like Hala Sultan Tekka in Cyprus, Tiryns, Tell es-Sultan (Jericho), and in Egyptian tombs indicate their ancient significance=.

The fruit's status as a luxury item is highlighted by its presence in the Uluburun shipwreck alongside perfume, ivory, and gold jewelry, dating back to the 14th century BC. Elite residences of the Late Bronze Age also yielded archaeological evidence supporting the pomegranate's esteemed status. Its introduction to Southeast Asia, southern China, and its popularity in Afghanistan's Kandahar region reflects its widespread cultivation along trade routes like the Silk Road and by sea traders.

Despite not being native to Korea or Japan, pomegranates have flourished there, leading to the development of numerous varieties. Their ornamental value, including distinctive flowers and twisted bark on mature trees, has made them popular choices for bonsai. While they were introduced to the Caribbean and the Americas by Spanish settlers, they were less common in British colonies.

The pomegranate's significance is underscored by its inclusion in cultural symbols, such as the pomegranate featured on the Spanish coat of arms representing the Kingdom of Granada. Historical references emphasize its value, with quotes highlighting its careful planting and its utility described as most beneficial among trees, as noted by Dr. Fothergill.

Fig.02

Etymology –

In Medieval Latin, the term "pomegranate" finds its roots in "pomum," meaning "apple," and "granatum," signifying "seeded." This name likely originated from the Old French term "pomme-grenade," reflecting the fruit. Early English referred to pomegranates as "Grenada apples," a term now only retained in heraldic coats of arms.

Description –

The pomegranate, small trees reaching heights of 5-10 meters (16-13 feet), boasts numerous thorny branches and remarkable longevity, with specific examples in France living up to 200 years. Its leaves, positioned opposite or nearly so, are shiny, slender, oblong, measuring 3 to 7 centimeters long and 2 centimeters wide. Featuring vibrant red flowers about 3 centimeters

International Journal of Pharmaceutical Research and Applications
Volume 8, Issue 6 Nov-Dec 2023, pp: 2623-2641 www.ijprajournal.com ISSN: 2249-7781

(1 1/4 inches) wide, these blooms typicallycontain three to seven petals. Some sterile variations of this plant are exclusively cultivated for their ornamental flowers.

Scientific classification:

Kingdom	**Plantae**
Clade	Tracheophytes
Clade	Angiosperm
Clade	Eudicots
Clade	Rosids
Order	Myrtales
Family	Lyrthraceae
Genus	Punica
Species	punica granatum

Biological name of the pomegranate is – Punica granatum

Synonym -

- Granatum punicum St.-Lag.
- Punica grand flora hort. ex Steud.
- Punica nana L.
- Punica Florida Salisb.
- Rhoea punica St.-Lag.
- Punica spinosa Lam.

These names represent various classifications or nomenclatures for the pomegranate plant, denoting different species or variations within the Punica genus

Benefits –

1. High in iron
2. Anticancer
3. Improve skin quality - for acne, dry skin, oily skin,
4. Protect against osteoarthritis
5. vitamin C and potassium are high
6. Helps fight Nausea and Morning Sickness
7. Dental protection
8. Potent Anti- inflammatory
9. Anti- aging
10. Destroys intestinal worms
11. Soothes stomachache
12. Useful for curing fever
13. It helps in lowering of the cholesterol
14. It helps in lowering of blood pressure
15. Improve Erectile Dysfunction
16. Helps improve memory
17. Immune system booster
18. Grate for pregnant women helps in neonatal care
19. Aphrodisiac
20. Potential to reduce PSA(prostate- specific antigen) levels
21. Keeps Alzheimer's at bay
22. Blood thinner
23. Artery protection
24. Anemia relief
25. Fight diabetes
26. Diarrhea & dysentery
27. Poor appetite
28. Loss of voice
29. Intestinal worms
30. Antioxidant powerhouse
31. Improves sexual health
32. Enhances physical performance and post exercise recovery
33. Strengthens bones & boost muscle power,Stress & depression

Different parts :

- **Fruit:**

Fig.03

The pomegranate fruit comprises numerous seeds enclosed in a white shell, encompassed by a thick pericarp skin that constitutes nearly half of the fruit's weight. The remaining 50% consists of the embryo (40%) and seeds (10%). Despite their small size, and the seeds having 20% oil, contributing just 10% of weight of

International Journal of Pharmaceutical Research and Applications
Volume 8, Issue 6 Nov-Dec 2023, pp: 2623-2641 www.ijprajournal.com ISSN: 2249-7781

fruit. Pomegranates are notably rich in polyphenols, with pomegranate juice showcasing significantly higher polyphenol concentrations compared to juices from fruits like apples, oranges, cherries, or grapes.

- **Pomegranate seeds :**

Fig.04

Pomegranate seed oil :

Fig.05

- **Pomegranate bark :**

Fig.06

- **Rind of pomegranate:**

Fig.07

- **Root of pg plant :**

Fig.08

- **Stem of the pg plant :**

Fig.09

International Journal of Pharmaceutical Research and Applications
Volume 8, Issue 6 Nov-Dec 2023, pp: 2623-2641 www.ijprajournal.com ISSN: 2249-7781

- **Leaf of the pg plant :**

Fig.10

- **Flower of the pomegranate plant :**

Fig.11

- **Pomegranate juice :**

Fig.12

Plant components along with the Constituents– [10]

1. Pomegranate juice :

Pomegranate juice is made from the fruit of the pomegranate tree, known for its sweet, tangy flavor and deep red color. The juice contains various constituents, including:

- Antioxidants: Pomegranate juice is rich in antioxidants, particularly polyphenols like flavonoids and tannins. These compounds help protect the body from damage caused by free radicals.
- Vitamins: It's a good source of vitamins, especially vitamin C, which boosts the immune system and promotes skin health.
- Minerals: Pomegranate juice contains minerals like potassium, which is crucial for maintaining proper heart and muscle function, as well as small amounts of other minerals like calcium and iron.
- Punicic acid: This is a type of conjugated linoleic acid (CLA) found in pomegranate seeds. It's believed to have potential health benefits, including anti-inflammatory properties.
- Sugar: Pomegranate juice contains natural sugars like fructose and glucose, which contribute to its sweetness.
- Fiber: While the juice lacks the fiber content found in the seeds and membranes of the fruit, there might be some dietary fiber present in the juice, albeit in smaller amounts.
- Anthocyanins, glucose, organic acid, ascorbic acid, EA, ETs, Gallic acid, catechin, Caffeic acid,quecertin, rutin, minerals

2. Pomegranate seed oil:

Pomegranate seed oil, derived from the seeds of the pomegranate fruit, is known for its various constituents that contribute to its health and beauty benefits. Some of the key constituents found in pomegranate seed oil include:

- Fatty Acids: Pomegranate seed oil is rich in fatty acids, particularly punicic acid (omega-5 fatty acid), which is unique to pomegranates. Punicic acid is believed to have potent anti-inflammatory properties and contributes significantly to the oil's overall benefits.
- Phytosterols: These compounds are similar to cholesterol in structure and can help support healthy skin by promoting collagen production and reducing inflammation.
- Tocopherols (Vitamin E): Pomegranate seed oil contains tocopherols, including alpha-

International Journal of Pharmaceutical Research and Applications
Volume 8, Issue 6 Nov-Dec 2023, pp: 2623-2641 www.ijprajournal.com ISSN: 2249-7781

tocopherol, a form of vitamin E. Vitamin E is an antioxidant that helps protect skin cells from damage caused by free radicals and UV radiation.

- Phenolic Compounds: Pomegranate seed oil contains phenolic compounds like flavonoids and tannins, which possess antioxidant and anti-inflammatory properties.
- Conjugated Linolenic Acid (CLA): Alongside punicic acid, pomegranate seed oil may contain other conjugated linolenic acids, which are beneficial for skin health and inflammation reduction.
- linoleic acid ,oleic acid, stearic acid, punicic acid,,eleostearic acid, catalpic acid.

3. Pomegranate peel:

The pomegranate peel, often discarded, is a rich source of various constituents that possess several potential health benefits. Some of the key constituents found in pomegranate peel include:

- Luteolin, quercetin, kaempferol, gallagic, EA glycosides, EA, punicalagin, punicalin,pedunculagin
- Polyphenols: Pomegranate peel is abundant in polyphenols, including ellagitannins such as punicalagins and punicalins. These compounds are potent antioxidants that contribute significantly to the peel's health-promoting properties.
- Flavonoids: Quercetin, kaempferol, and other flavonoids are present in pomegranate peel. These compounds have antioxidant and anti-inflammatory properties.
- Triterpenoids: Compounds like ursolic acid and oleanolic acid are found in the peel, which exhibit potential anti-cancer, anti-inflammatory, and hepatoprotective (liver-protecting) properties.
- Pectin and Fiber: Pomegranate peel contains pectin and dietary fiber, which can aid in digestion and promote gut health.
- Vitamins and Minerals: While in smaller amounts compared to the flesh of the fruit, the peel contains some vitamins (like vitamin C) and minerals (such as potassium) that contribute to its nutritional value.
- Essential Oils: Pomegranate peel also contains trace amounts of essential oils that contribute to its aroma and might have certain health benefits.

4. Pomegranate leaves:

The pomegranate peel, often discarded, is a rich source of various constituents that possess several potential health benefits. Some of the key constituents found in pomegranate peel include:

- Ea;fatty acid
- Polyphenols: Pomegranate peel is abundant in polyphenols, including ellagitannins such as punicalagins and punicalins. These compounds are potent antioxidants that contribute significantly to the peel's health-promoting properties.
- Flavonoids: Quercetin, kaempferol, and other flavonoids are present in pomegranate peel. These compounds have antioxidant and anti-inflammatory properties.
- Triterpenoids: Compounds like ursolic acid and oleanolic acid are found in the peel, which exhibit potential anti-cancer, anti-inflammatory, and hepatoprotective (liver-protecting) properties.
- Pectin and Fiber: Pomegranate peel contains pectin and dietary fiber, which can aid in digestion and promote gut health.
- Vitamins and Minerals: While in smaller amounts compared to the flesh of the fruit, the peel contains some vitamins (like vitamin C) and minerals (such as potassium) that contribute to its nutritional value.
- Essential Oils: Pomegranate peel also contains trace amounts of essential oils that contribute to its aroma and might have certain health benefits.

5. Pomegranate flower :

Pomegranate flowers, though less commonly utilized compared to other parts of the pomegranate tree, contain constituents that contribute to their potential medicinal properties. However, comprehensive scientific studies specifically focusing on the constituents of pomegranate flowers are somewhat limited. Here are some of the constituents found in pomegranate flowers:

- Polyphenols, punicalagin punicalin,EA
- Flavonoids: Like other parts of the pomegranate tree, pomegranate flowers contain flavonoids such as quercetin and kaempferol. Flavonoids are known for their antioxidant and anti-inflammatory properties.
- Tannins: Pomegranate flowers contain tannins, including ellagitannins. These compounds contribute to the astringent properties of the

International Journal of Pharmaceutical Research and Applications
Volume 8, Issue 6 Nov-Dec 2023, pp: 2623-2641 www.ijprajournal.com ISSN: 2249-7781

flowers and might have potential health benefits.

- Anthocyanins: These pigments are responsible for the red to purple coloration in certain pomegranate flower varieties. Anthocyanins are known antioxidants and might contribute to the flower's potential health effects.
- Phenolic Compounds: Various phenolic compounds, such as phenolic acids, are present in pomegranate flowers. These compounds have antioxidant properties and might contribute to the overall health benefits.

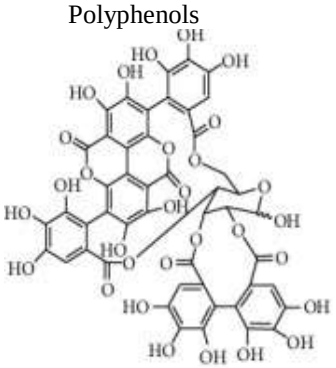
6. Pomegranate roots and bark :

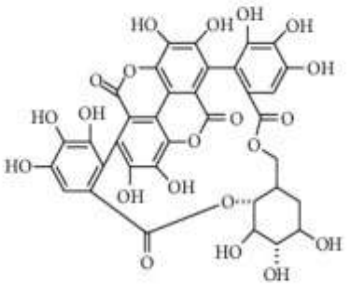
Pomegranate roots and bark, although less commonly used compared to other parts of the tree, contain constituents that contribute to their potential medicinal properties. However, scientific studies specifically focusing on the constituents of pomegranate roots and bark are limited compared to other parts of the plant. Here are some constituents found in pomegranate roots and bark:

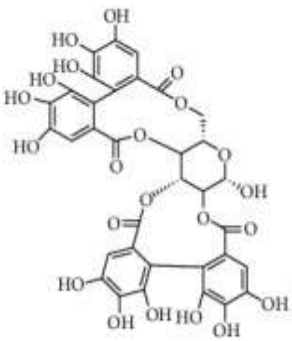
- Tannins: Pomegranate roots and bark contain tannins, including ellagitannins. These compounds are known for their astringent properties and might have potential health benefits.
- Alkaloids: Some studies suggest the presence of alkaloids in pomegranate roots and bark. Alkaloids are a diverse group of compounds found in many plants, some of which may have pharmacological effects.
- Polyphenols: Similar to other parts of the pomegranate tree, roots and bark may contain polyphenolic compounds, including flavonoids and phenolic acids, which have antioxidant and potentially other health-promoting properties.
- Terpenoids: While there's limited information, terpenoids could potentially be present in pomegranate roots and bark. Terpenoids are diverse compounds found in plants and have various biological activities.

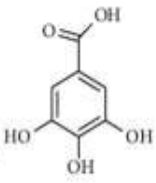
Constituent chemistry –

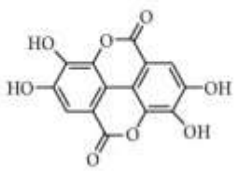
1. Polyphenols

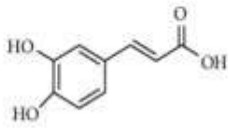

punicalagin

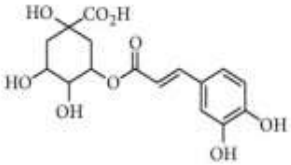

punicalin

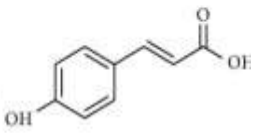

pedunculagin


gallic acid

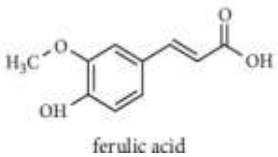

ellagic acid


caffeic acid


chlorogenic acid

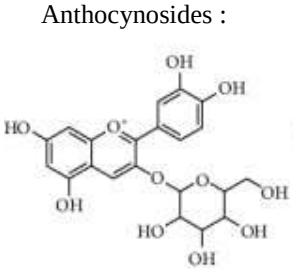

p-coumaric acid

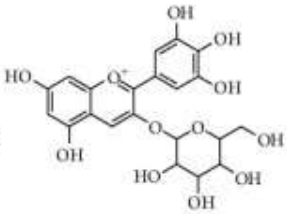
:

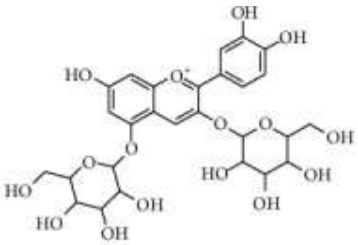

ferulic acid

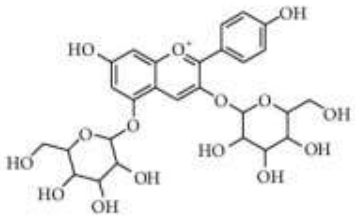
International Journal of Pharmaceutical Research and Applications
Volume 8, Issue 6 Nov-Dec 2023, pp: 2623-2641 www.ijprajournal.com ISSN: 2249-7781

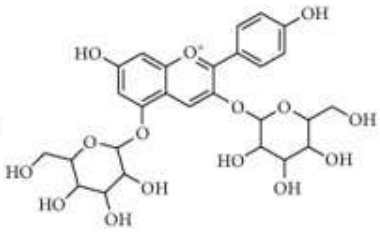
2. Anthocynosides :

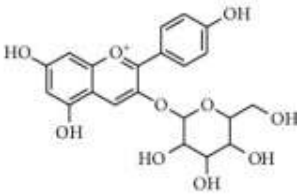

cyanidin-3-glucoside

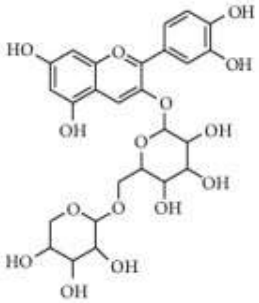

cyanidin-3,5-diglucoside


delfinidin-3-glucoside

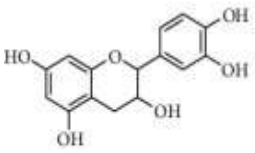

delfinidin-3,5-diglucoside

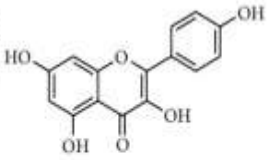

pelargonidin-3-glucoside

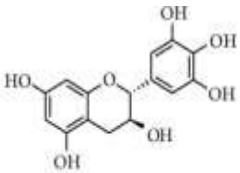

pelargonidin-3,5-diglucoside

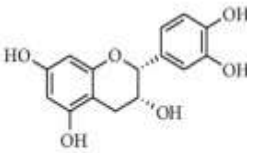

cyanidin 3-rutinoside

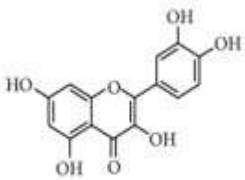
3. Flavonoid and alkaloids :

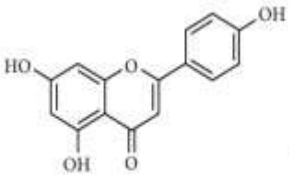

catechin

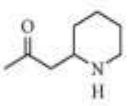

epi-catechin

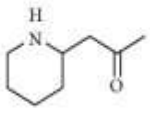

gallocatechin


kaempferol


quercetin


apigenin


pelletierine


isopelletierine

International Journal of Pharmaceutical Research and Applications
Volume 8, Issue 6 Nov-Dec 2023, pp: 2623-2641 www.ijprajournal.com ISSN: 2249-7781

II. TECHNIQUES AND METHODS FOR EXTRACTION:

Extraction involves the separation and retrieval of specific substances from plant material through solvents, adsorption membranes, and instrumental techniques. It's a process that shifts meaning from solid to liquid phases. Utilizing various extraction methods, the target substance is isolated from the mixture by dissolving in interaction of the solvent. Initially it can be solid or liquid. Different extraction techniques are applied based on the nature of the raw material used.

- **Pomegranate Juice Extraction:**

1. Manual Juicing: Cut the pomegranate in half and manually squeeze or press the halves to extract juice. This method is suitable for small quantities.
2. Citrus Juicer: Use a citrus juicer or reamer to extract juice from the pomegranate. This is more efficient for larger quantities.
3. Blender Method: Blend the arils (seed sacs) and then strain the mixture to separate the juice from the pulp. This method retains more of the fruit's nutrients.

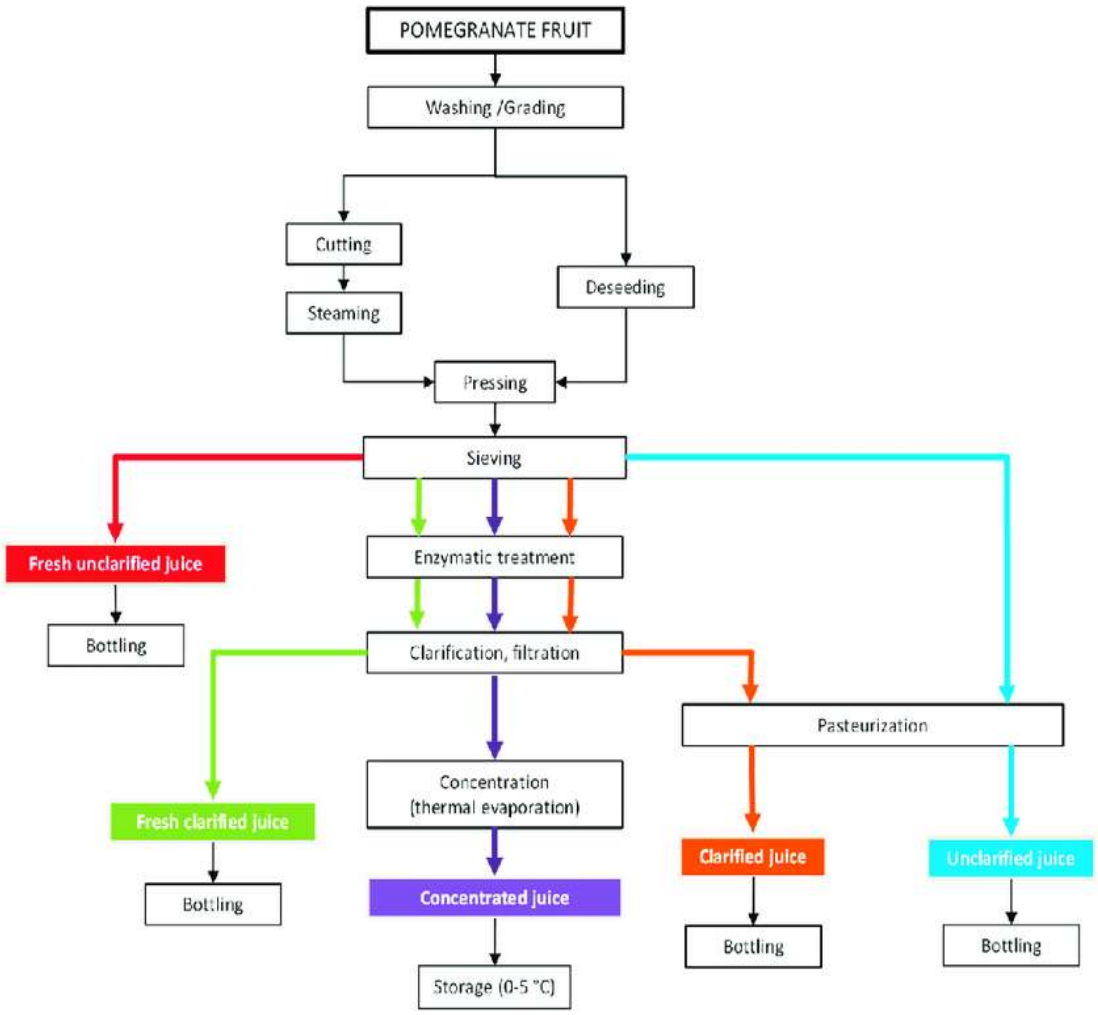


Fig.13

- **Pomegranate Aril (Seed) Extraction:**

1. Method: Submerge a halved pomegranate in a bowl of water and gently tap the back with a spoon to release the seeds. The seeds will sink, and the pith Underwaterwill float, making separation easier.
2. Rolling Method: Roll the whole pomegranate on a countertop before cutting it open. This helps loosen the seeds, making extraction easier.
3. Bowl Method: Hold a pomegranate half over a bowl, seed side down, and tap the back with a

International Journal of Pharmaceutical Research and Applications
Volume 8, Issue 6 Nov-Dec 2023, pp: 2623-2641 www.ijprajournal.com ISSN: 2249-7781

wooden spoon to release the seeds into the bowl.

- **Pomegranate Peel Extraction** (for Zest or Extract)**:**

Grater: Use a fine grater to zest the outer peel of the pomegranate. This is useful for adding citrusy flavor to dishes.

Infusion: Infuse the peel in liquids like vinegar or alcohol to create pomegranate extracts for culinary use.

- **Pomegranate Molasses Extraction:**

Reducing Juice: Simmer pomegranate juice on low heat until it thickens into a syrupy consistency. This concentrated liquid is known as pomegranate molasses.

- **Pomegranate Seed Oil Extraction:**

Cold Pressing: Extract oil from pomegranate seeds using a cold-press method. This is often done commercially and yields pomegranate seed oil, which is used in cosmetics and culinary applications.

- **Pomegranate Concentrate Extraction:**

Reducing Juice: Similar to making molasses, you can reduce pomegranate juice to create a concentrated form suitable for use in sauces, dressings, or beverages.

- **Pomegranate Powder Extraction:**

Dehydration: Dry pomegranate arils or juice to create pomegranate powder. This can be done using a food dehydrator or low-temperature oven.

Advanced techniques:

1. SUPERFICIAL FLUID EXTRACTION (SFE): This method involves using supercritical carbon dioxide as a solvent to extract bioactive compounds from pomegranate seeds, such as antioxidants or polyphenols. The supercritical CO2 acts as a solvent under specific pressure and temperature conditions, effectively extracting desired compounds without leaving residual solvents.[32]

Fig.14

2. MICROWAVE ASSISTED EXTRACTION (MAE): it employs microwave energy to heat the pomegranate material and enhance the extraction process. By applying microwaves, it facilitates the breakdown of cell structures, aiding in the extraction of compounds like polyphenols, anthocyanin's, or enzymes in a shorter time compared to conventional methods.[33]

Fig.15

International Journal of Pharmaceutical Research and Applications
Volume 8, Issue 6 Nov-Dec 2023, pp: 2623-2641 www.ijprajournal.com ISSN: 2249-7781

3. ULTRASOUND ASSISTED EXTRACTION (UAE): This method utilizes high-frequency ultrasound waves to disrupt cell walls, allowing the release of bioactive compounds. The cavitation effect created by ultrasound helps break down the plant material, thereby improving extraction efficiency and reducing extraction time.

Fig.16

4. PULSED ELECTRIC FIELD EXTRACTION (PEF): involves applying short pulses of high-voltage electricity to the pomegranate material. This disrupts cell membranes, enhancing the extraction of compounds. It's known for maintaining the quality of extracted compounds due to its minimal thermal effect.

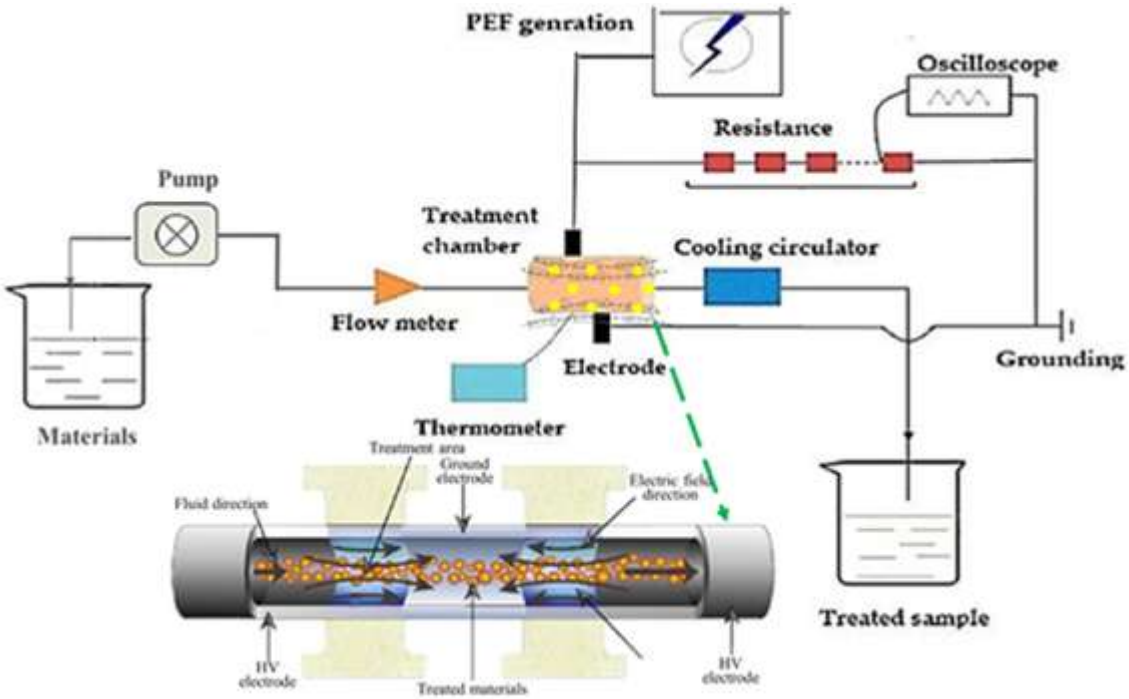


Fig.17

5. ENZYME ASSISTED EXTRACTION (EAE): Enzymes, such as pectinase or cellulose, can be used to degrade the cell walls of pomegranate seeds, facilitating the release of bioactive compounds. This method is particularly effective in extracting high molecular weight compounds like polysaccharides or proteins.

International Journal of Pharmaceutical Research and Applications
Volume 8, Issue 6 Nov-Dec 2023, pp: 2623-2641 www.ijprajournal.com ISSN: 2249-7781

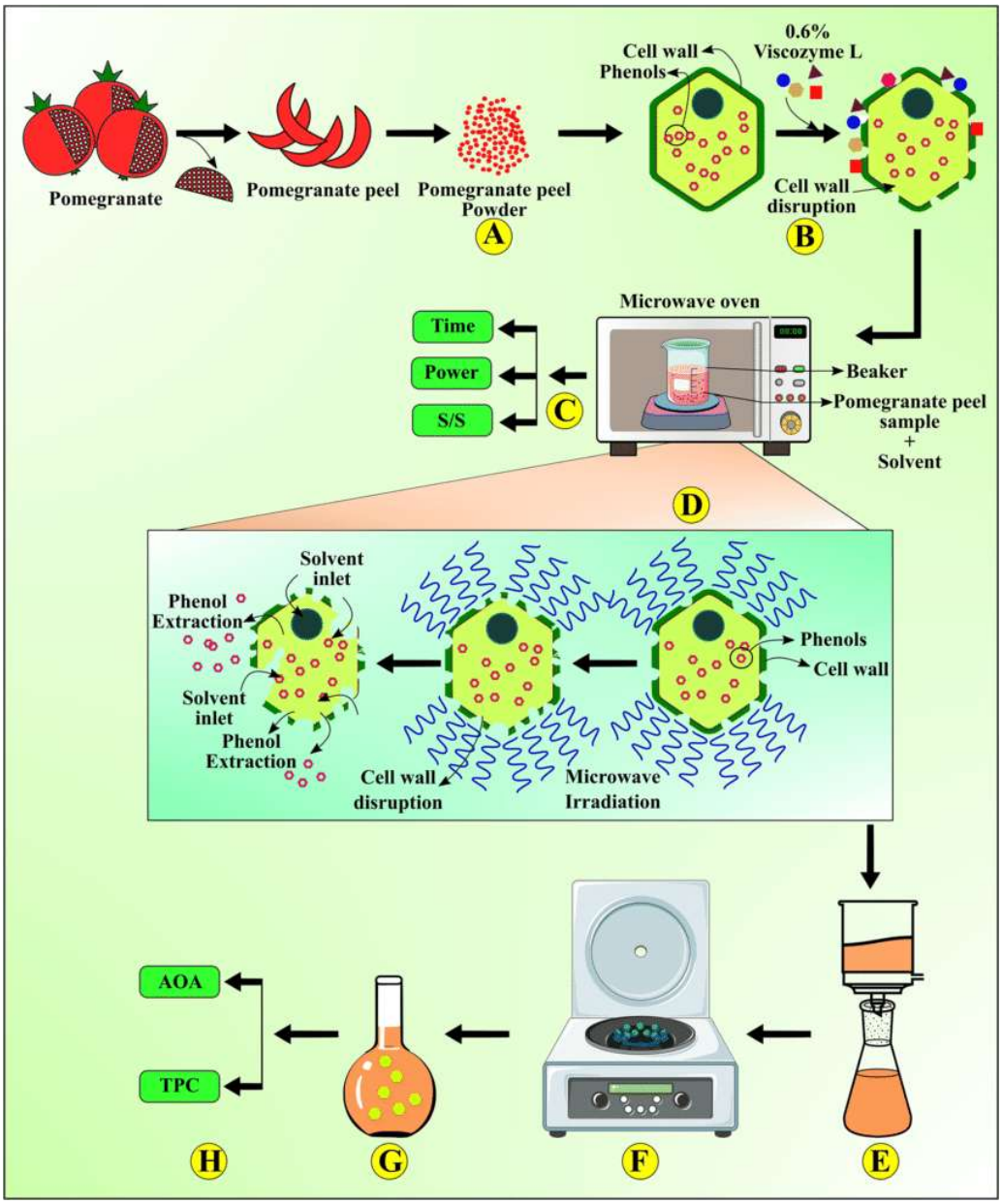


Fig.18

schematic diagram for enzyme-assisted microwave extraction (EMAE): A) dried PP powder; B) pre-treatment of Viscozyme L; C) optimization of microwave-assisted extraction at optimized conditions; D) The mechanism of action for the extraction of phenolics from PP using cellulolytic enzyme-assisted microwave extraction (EMAE); E) filtration; F) centrifugation; G) purified PP phenolic extract; H) analysis of total phenolic content (TPC) and antioxidant activity (AOA)

International Journal of Pharmaceutical Research and Applications
Volume 8, Issue 6 Nov-Dec 2023, pp: 2623-2641 www.ijprajournal.com ISSN: 2249-7781

Different Therapeutic activities by punica granatum

Fermented pomegranate juice showcases antioxidant properties, while extracted pomegranate flower juice might contribute to lowering blood sugar and lipid levels. The flavonoids and tannins present in pomegranate juice are thought to impede cancer cell growth. Flavonoids from pomegranate extract exhibit estrogenic activity. Compounds like luteolin and naringenin display hormone-like actions similar to those secreted in women before pregnancy.

Polyphenols in fermented pomegranate extracts exhibit potent antioxidant effects, because of breakdown during the fermentation process, resulting in highly active free polyphenols. These compounds, notably in their glycoside form, interfere with estrogen activity by binding to estrogen receptors. The aqueous part of pg may inhibit cancer cells, with heightened effects in estrogen-dependent cases.

pg peels having the ingredients like ellagic acid, demonstrate antimutagenic, antiviral, and antioxidant properties. The antioxidant property of the pg peels extract is from Gallic and ellagic acid as well as tannin likes compounds. Studies using the Ames test suggest pg peel juice extract can inhibit mutations. As well as it can inhibit the cancer (caused by sodium azide in Salmonella species).

Pg seeds with the thin layered peels, constituting 13% by fruit, are crucial in diagnosing diseases, maintaining fruit health, and preventing discoloration. They serve as a resource for active biological substances, including punicalazine, a robust antioxidant abundant in these parts.

Punicalagin, predominantly extracted using methanol, is a key component known for modulating peroxide and DPPH radicals. It's effective in inhibiting lipid peroxidation due to its structure containing hydroxyl groups that terminate peroxidation chain reactions. Antioxidant capacity testing reveals varying FRAP values in different fruit parts, with peel exhibiting the highest value.

Studies examining human plasma after consuming pomegranate juice rich in ellagic acid and ellagitannins demonstrated their bioavailability, indicating peaks of ellagic acid in post-consumer plasma at different time intervals. Pomegranate seed oil, rich in punicic acid, shows potential in inhibiting eicosanoid enzymes and cyclooxygenase, similar to conjugated linoleic acids with anticancer effects.

Pomegranate seed oil, composed mainly of punicic acid, displays promise in preventing skin cancer by inhibiting prostaglandin biosynthesis and potentially protecting against cancer-causing agents like DMBA and TPA.Its role in impeding skin cancer progression by modulating ornithine decarboxylase, a critical enzyme in polyamine synthesis, is under study.

Extracts from pomegranate seed oil and its fermented versions are recognized for their antioxidant properties and their ability to inhibit prostaglandins, contributing to breast cancer prevention in humans. Both the aqueous and oily components of the fruit show inhibitory effects on breast cancer cells, potentially targeting estrogen biosynthesis enzymes and functioning via distinct mechanisms in cancer prevention. Pomegranate seed oil, catalyzed by E2 (17-β) and 17-β-estradiol, is considered to inhibit β-hydroxysteroid enzymes responsible for biosynthesis, potentially preventing cancer cell invasion and promoting apoptosis. Extracted pomegranate seed oil polyphenols may hinder cyclooxygenase activity.

Regarding anticancer properties, various pomegranate extracts exhibit therapeutic effects against different cancer types, particularly breast cancer, a significant cause of female mortality worldwide. These extracts interfere with mutation processes, malignant cell proliferation, invasion, inflammation, angiogenesis, and metastasis, acting through diverse pathways depending on breast cancer subtypes. Key therapeutically active polyphenols found in pomegranates include ellagitannins, flavonoids, punicic acid, anthocyanin, ellagic acid, and estrogenic flavonols. The development of commercial drugs against breast cancer might involve isolating phytochemicals from pomegranate peel or rind, which have exhibited similar anticancer effects to current chemotherapy drugs, potentially overcoming the limitations of existing treatments, like multidrug resistance. Some extracts might even boost the efficacy of chemo preventive drugs like tamoxifen.

Dermatological activity:

In the dermatology activity is shown by the pg seed oil with addition of resin extract of croton lechery, aims to enhance skin quality by addressing stretch marks, skin hydration, skin elasticity and thickness of the skin layers i.e. dermal. Immobilized leucotomiesor pg combinations show enhanced biophysical

International Journal of Pharmaceutical Research and Applications
Volume 8, Issue 6 Nov-Dec 2023, pp: 2623-2641 www.ijprajournal.com ISSN: 2249-7781

parameters of skin compared to leucotomies in Caucasian adults. (polypodiumleucotomos)

Skin damage, particularly from natural aging and chronic sun exposure (photo aging), has been extensively studied. While a high exposure to ultraviolet (UV) radiation is found to be a major cause for ADE on skin of humans, in that it also found other effects such as sun burning/ tan, cancer of skin, and maybe the suppression of immunity.

Studies have shown that pomegranate seed oil stimulates keratinocyte proliferation, benefiting epidermal regeneration, while pomegranate water-soluble extracts, particularly from the peel, promote dermal regeneration. Additionally, standardized pomegranate extracts possess chemo preventive and protective properties in case of human dermal fibroblast which occurred by the UVA and UVB radiation damaging. These extracts reduce intracellular ROS production and increases the intracellular antioxidant capacity and decreases intracellular toxic metabolite production in mitochondrial resp. chain , potentially preventing skin damage induced by UVA and UVB rays.

Further research suggests that oral administration of pomegranate extract inhibits UV-irradiated pigmentation in guinea pigs, possibly due to its ability to inhibit melanocyte proliferation and melanin synthesis by melanocyte tyrosinase. Pomegranate extract may also prevent ultraviolet A-mediated cell damage by modulating cellular pathways, offering potential as a preventive agent against photochemical damage.

Cardiovascular disease:

Pomegranate juice has demonstrated significant effects on cholesterol levels, reducing LDL cholesterol by 39% and elevating HDL cholesterol by 27%. These changes can potentially reduce cardiovascular disease risk by 12–18%. Moreover, the juice showcased a remarkable 24% decrease in blood pressure and exhibited anti-atherosclerotic effects by lowering sE-selectin levels by 42%.

In addition to these effects, pomegranate juice increased adiponectin levels in adipose tissue while decreasing inflammatory markers like TNF-α, PAI-1, and interleukin-17A. It also inhibited various other inflammatory markers such as IL-17A, IL-6, IL-1β, and MCP-1. However, further clinical research is necessary to confirm and understand the immune modulatory and therapeutic advantages of pomegranate juice in reducing atherosclerosis and cardiovascular risk.

Cancer of the lungs

Pomegranate fruit extract exhibits potential in hindering multiple signaling pathways associated with human lung cancer, like the mitogen-activated protein kinase pathway and NF-B pathways. In experimental studies involving mice transplanted with A549 cells, the extract notably delayed tumor development by approximately four days, highlighting its possible chemo preventive qualities. [34]

Dental effects:-

Maintaining a healthy oral micro biota involves antibacterial interactions and aggregation. Dried pomegranate peel powder has demonstrated notable inhibition against C. albicans. Another study has confirmed the anti-plaque effects of pomegranate mouthwash. Furthermore, the hydro alcoholic extract derived from pomegranate significantly reduced plaque bacteria by 84% (CFU/ml).

Reproductive system effects:-

Pomegranate seed extract containing beta-sitosterol has been observed to boost uterine phase activity in rats and shield against adrianisin-triggered oxidative stress. Additionally, it enhances epididymal sperm characteristics, including concentration, motility, density, seminiferous tubule diameter, and germ cell layer thickness.

Clinical Applications of Pomegranate

Pomegranate stands out as a potent source of various physiological elements that hold significant implications for human health. Its fruit is recommended as a pharmaceutical and nutritional component for addressing HIV/AIDS due to its rich bioflavonoids that combat free radicals and inhibit lipoxygenase—an enzyme linked to leukotriene's production.

Traditionally, pomegranate peel has been employed to treat dysentery and common diarrhea. Future research aims to develop a natural anti-diarrheal agent derived from pg peel, potentially for OTC prescription or the medications. Considered anti-parasitic for both animals and humans, pomegranates owe their benefits to flavonoids that possess potent antioxidant properties.

Juices and oils from pomegranates exhibit enzyme-inhibiting effects, positioning them as potential dietary supplements that could aid in extending longevity and preventing cardiovascular diseases and cancer. Pomegranate oil extracts effectively hinder the production of prostaglandins

International Journal of Pharmaceutical Research and Applications
Volume 8, Issue 6 Nov-Dec 2023, pp: 2623-2641 www.ijprajournal.com ISSN: 2249-7781

and leukotriene's by targeting eicosanoid enzymes like cyclooxygenase and lipoxygenase, potentially serving as an internal or external anti-inflammatory agent.

With the growing interest in phytoestrogen compounds for medical purposes—addressing cardiovascular issues related to menopause, osteoporosis, estrogen decline, and cancer—there's potential to consider pg seed oil and pg juices as used for women's after menopause. They could serve as alternatives to hormone replacement therapy by providing exogenous phytoestrogens.

III. DISCUSSION:

Pomegranate is rich in various compounds like polyphenols, alkaloids, and vitamins, which possess strong abilities to counteract free radicals. These radicals causes oxidative stress and which can lead to many chronic diseases such as sugar diseases, diseases of cancer, atherosclerosis, Alzheimer's, kidney and liver issues, pain, and other degenerative conditions. The antioxidant effects found in pomegranate are attributed to compounds like ascorbic acid, punicalagin, punicalin, Gallic acid, ellagic acid, anthocyanin, and ellagitannins, particularly potent polyphenols that scavenge free radicals effectively.

Notably, punicalagins and ellagitannins convert into urolithins through intestinal bacteria, contributing further to their antioxidant capabilities. The vibrant red hue of pomegranate juice is due to anthocyanin's like cyanidins-glycosides, and delphinidin, which leads to antioxidant properties.

Both clinical as well as preclinical studies shows the effectiveness of plant antioxidants in combating complications arising from free radicals, including conditions like LDL oxidation, heart disease, diabetes, cancer, cognitive issues, diseases of infection. Consequently, the therapeutic qualities of pg can be attributed, partially to these antioxidant-rich components. Similar properties might be found in other medicinal plants boasting antioxidant activity.

The antioxidant content in pomegranate varies during fruit development,it can be shown with peak antioxidant activity given by the newly formed fruits (around 20 days). From maturation of fruit, there's a decline in antioxidant activity due to reduced levels of ascorbic and phenolic acids. Additionally, different varieties of pomegranate exhibit varying antioxidant potential, suggesting that not all varieties possess the same medicinal properties. Fresh consumption during the early developmental stages might offer better benefits. Further exploration and evaluation of other components within pomegranate are necessary to understand their roles in disease treatment.

IV. CONCLUSION:

The popularity of consuming pomegranate has surged owing to its widely acknowledged health benefits. Pomegranate, along with its derivative's such as juice, peels, and seeds, contains a rich array of valuable compounds that offer potential advantages fir the body. Its diverse bioactive profile positions it as a highly nutritious and desirable fruit crop. Increasingly, research indicates that regular consumption of pg juice or extract may provide protection against various diseases, including diabetes and cvs issues. Additionally, it may play role a role in preventing and impending the progression of sp. Cancers, while also contributing to oral and skin health. Notably, side effects are exceedingly rare.

Accessible concentrated pomegranate juice or standardized extract capsules make it convenient for people to harness the numerous health benefits this fruit offers. Therefore, it can be inferred that pomegranate (Punica granatum) serves as a significant source of polyphenol compounds possessing anti-inflammatory, antioxidant, anti-angiogenic, and anti-aging properties. The flavonoids and tannins present in the plant have stimulated patent and industrial applications. However, before these plant ingredients can be transformed into pharmaceuticals, conducting clinical trials is imperative to establish their safety and efficacy.

REFERENCES:

1. Vini, R.; Sreeja, S. Punica granatumand its therapeutic implications on breast carcinogenesis: A review. BioFactors **2015**, 41, 78–89. [**Google Scholar**] [**CrossRef**] [**PubMed**]
2. Sreekumar, S.; Sithul, H.; Muraleedharan, P.; Azeez, J.M.; Sreeharshan, S. Pomegranate Fruit as a Rich Source of Biologically Active Compounds. BioMed Res. Int. **2014**, 2014, 1–12. [**Google Scholar**] [**CrossRef**]
3. Higgins, M.J.; Baselga, J. Targeted therapies for breast cancer. J. Clin. Investig. **2011**, 121, 3797–3803. [**Google Scholar**] [**CrossRef**]

International Journal of Pharmaceutical Research and Applications
Volume 8, Issue 6 Nov-Dec 2023, pp: 2623-2641 www.ijprajournal.com ISSN: 2249-7781

4. Poyrazoglu and others (2002); Ignarro and others (2006); Lansky and Newman (2007); Heber and others (2007); Mousavinejad and others (2009); Jaiswal and others (2010)
5. Ozgul-Yucel (2005);Fadavi and others (2006); El-Nemr and others (2006);Sassano and others (2009)
6. Van Elswijk and others (2004); Amakura and others (2000); Seeram and others (2005b)
7. Ercisli and others (2007) Lan and others (2009)
8. Kaur and others (2006) Aviram and others (2008)
9. Neuhofer and others (1993) Gil and others (2000)
10. PomegranateanditsMany-FunctionalComponentsasRelatedtoHuman-Health.pdf
11. Sturgeon, S.R.; Ronnenberg, A.G. Pomegranate and breast cancer: Possible mechanisms of prevention. Nutr. Rev. **2010**, 68, 122–128. [**Google Scholar**] [**CrossRef**]
12. Banerjee, S.; Kambhampati, S.; Haque, I.; Banerjee, S.K. Pomegranate sensitizes Tamoxifen action in ER-α positive breast cancer cells. J. Cell Commun. Signal. **2011**, 5, 317–324. [**Google Scholar**] [**CrossRef**][**Green Version**]
13. https://www.mdpi.com/1420-3049/26/4/1054
14. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3832175/
15. https://europepmc.org/article/med/34796029
16. Hasnaoui, N.; Wathelet, B.; Jiménez-Araujo, A. Valorization of pomegranate peel from 12 cultivars: Dietary fibre composition,antioxidant capacity and functional properties. Food Chem. 2014,160, 196–203. [CrossRef] [PubMed]
17. Pan, Z.; Qu, W.; Ma, H.; Atungulu, G.G.; McHugh, T.H. Continuous and pulsed ultrasound-assisted extractions of antioxidantsfrom pomegranate peel. Ultrason. Sonochem. 2011,18, 1249–1257. [CrossRef] [PubMed]
18. Wang, Z.; Pan, Z.; Ma, H.; Atungulu, G.G. Extract of phenolics from pomegranate peels. Open Food Sci. J.2011,5, 17–25. [CrossRef]
19. Alonso-Salces, R.; Korta, E.; Barranco, A.; Berrueta, L.; Gallo, B.; Vicente, F. Pressurized liquid extraction for the determination ofpolyphenols in apple. J. Chromatogr. A 2001,933, 37–43. [CrossRef]
20. Li, B.; Smith, B.; Hossain, M.M. Extraction of phenolics from citrus peels: II. Enzyme-assisted extraction method.Sep. Purif. Technol. 2006,48, 189–196. [CrossRef]
21. Sharayei, P.; Azarpazhooh, E.; Zomorodi, S.; Ramaswamy, H.S. Ultrasound assisted extraction of bioactive compounds frompomegranate (Punica granatum L.) peel. LWT 2019,101, 342–350. [CrossRef]
22. Hernández-Corroto, E.; Plaza, M.; Marina, M.L.; García, M.C. Sustainable extraction of proteins and bioactive substances frompomegranate peel (Punica granatum L.) using pressurized liquids and deep eutectic solvents. Innov. Food Sci. Emerg. Technol.2020,60, 102314. [CrossRef]
23. Xu, K.; Wang, Y.; Huang, Y.; Li, N.; Wen, Q. A green deep eutectic solvent-based aqueous two-phase system for protein ex-tracting.Anal. Chim. Acta 2015,864, 9–20. [CrossRef]
24. More, P.R.; Arya, S.S. A novel, green cloud point extraction and separation of phenols and flavonoids from pomegranate peel: Anoptimization study using RCCD. J. Environ. Chem. Eng. 2019,7, 103306. [CrossRef]
25. Skenderidis, P.; Leontopoulos, S.; Petrotos, K.; Giavasis, I. Optimization of vacuum microwave-assisted extraction of pomegranatefruits peels by the evaluation of extracts' phenolic content and antioxidant activity. Foods 2020,9, 1655. [CrossRef] [PubMed]
26. Magangana, T.P.; Makunga, N.P.; Fawole, O.A.; Opara, U.L. Processing factors affecting the phytochemical and nutritionalproperties of pomegranate (Punica granatum L.) peel waste: A review. Molecules 2020,25, 4690. [CrossRef] [PubMed]
27. Gorgani, L.; Mohammadi, M.; Najafpour, G.D.; Nikzad, M. Piperine, the bioactive compound of black pepper: From isolation tomedicinal formulations. Compr. Rev. Food Sci. Food Saf. 2017,16, 124–140. [CrossRef] [PubMed]
28. Anjaly, P.; Mahendran, R. Pomegranate seed oil in food industry: Extraction, characterization, and applications.Trends Food Sci. Technol. 2020,105, 273–283

29. https://www.researchgate.net/figure/Flow-diagram-of-processing-operations-for-pomegranate-juice-production-adapted-from-9_fig1_342771113
30. https://www.researchgate.net/figure/Schema-1-Schematic-representation-for-preparation-of-pomegranate-peel-extracts_fig3_352737251
31. Gil M, Tomas B. Antioxidant activity of pomegranate juice and its relationship with phenolic composition and processing. J Agric Food Chem. 2000;48:4581–4589.
32. Lavande SK Bais Pawar ND Advanced Herbal Technology International Journal of Creative Research Thoughts Volume 11 Issue 1 January 2023 ISSN (online) 2320-2882 P Noc497
33. SD sonawane s k bais mh pawar recent herbal technology international journal of advanced research in science communication and technology volume 3 issue 1 january 2023 issn (online)2581-9429 p no 510
34. Aviram M, Dornfeld L, Kaplan M. Pomegranate juice flavonoids inhibit low-density lipoprotein oxidation and cardiovascular diseases: studies in atherosclerotic mice and in humans. Drugs Exp Clin Res. 2000; 28:49–62.
35. Michicotl-Meneses M. M., Thompson-Bonilla M. d. R., Reyes-López C. A., et al. Inflammation markers in adipose tissue and cardiovascular risk reduction by pomegranate juice in obesity induced by a hypercaloric diet in Wistar rats. Nutrients . 2021;13(8):p. 2577. 10.3390/nu13082577
36. Al-Azhar Dental Journal for Girls. 2019 Oct; 6(4): 467-73. doi: 10.21608/adjg.2019.7614.1084.Al-Habib OA and Adam LN. Pomegranate (Punica granatum) juice attenuates Rat Uterine Contractions. 2023. doi: 10.21203/rs.3.rs-2818749/v1
37. El-Sharkawy MS. Evaluation of the antimicrobial effect of pomegranate extract on Streptococcus mutans.
38. Farooqi AA. Regulation of deregulated cell signaling pathways by pomegranate in different cancers: Re-interpretation of knowledge gaps. InSeminars in Cancer Biology. Academic Press. 2021 Aug; 73: 294-301. doi: 10.1016/j.semcancer.2021.01.008
39. Schubert S, Lansky E, Neeman I. Antioxidant and eiocsanoid enzyme inhibition properties of pomegranate seed oil and fermented juice flavonoids. J Ethnopharmacol. 1999;66:11–17.
40. Kulkarni AP, Mahal HS, Kapoor S, Aradhya SM. In vitro studies on the binding, antioxidant, and cytotoxic actions of punicalagin. Agric Food Chem. 2007;55:1491–1500.
41. Shirzad H, Shahrani M, Rafieian-Kopaei M. Comparison of morphine and tramadol effects on phagocytic activity of mice peritoneal phagocytes in vivo. Int Immunopharmacol. 2009;9:968–970.
42. Shirzad H, Taji F, Rafieian-Kopaei M. Correlation between antioxidant activity of garlic extracts and WEHI-164 fibrosarcoma tumor growth in BALB/c mice. Med Food. 2011;14:969–974.
43. Bahmani M, Zargaran A, Rafieian-Kopaei M, Saki M. Ethnobotanical study of medicinal plants used in the management of diabetes mellitus in the Urmia, Northwest Iran. Asian Pac J Trop Med. 2014;7:348–354.
44. Nasri H, Rafieian-Kopaei M. Protective effects of herbal antioxidants on diabetic kidney disease. Res Med Sci. 2014;19:82–83.
45. Nasri H, Sahinfard N, Rafieian M, Rafieian S, Shirzad M, Rafieian-Kopaei M. Effects of Allium sativum on liver enzymes and atherosclerotic risk factors. J HerbMed Pharmacol. 2013;2(2):23–28.
46. Rafieian-Kopaei M, Setorki M, Doudi M, Baradaran A, Nasri H. Atherosclerosis: process, indicators, risk factors and new hopes. Int J Prev Med. 2014;5:927–946.
47. Rahnama S, Rabiei Z, Alibabaei Z, Mokhtari S, Rafieian-Kopaei M, Deris F. Anti-amnesic activity of Citrus aurantium flowers extract against scopolamine-induced memory impairments in rats. Neurol Sci. 2015;36:553–560.
48. Rabiei Z, Rafieian-Kopaei M, Heidarian E, Saghaei E, Mokhtari S. Effects of zizyphus jujube extract on memory and learning impairment induced by bilateral electric lesions of the nucleus basalis of Meynert in rat. Neurochem Res. 2014;39:353–360.
49. Baradaran A, Nasri H, Nematbakhsh M, Rafieian-Kopaei M. Antioxidant activity and preventive effect of aqueous leaf extract of

Aloe Vera on gentamicin-induced nephrotoxicity in male Wistar rats. Clin Ter. 2014;165:7–11
50. Rafieian-Kopaei M, Nasri H. The ameliorative effect of Zingiber officinale in diabetic nephropathy. Iran Red Crescent Med J. 2014;16(5):e11324.
51. Bahmani M, Rafieian M, Baradaran A, Rafieian S, Rafieian-Kopaei M. Nephrotoxicity and hepatotoxicity evaluation of Crocus sativus stigmas in neonates of nursing mice. J Nephropathol. 2014;3:81–85.
52. Taghikhani A, Afrough H, Ansari-Samani R, Shahinfard N, Rafieian-Kopaei M. Assessing the toxic effects of hydroalcoholic extract of Stachys lavandulifolia Vahl on rat's liver. Bratisl Lek Listy. 2014;115:121–124.
53. Delfan B, Bahmani M, Hassanzadazar H, Saki K, Rafieian-Kopaei M. Identification of medicinal plants affecting on headaches and migraines in Lorestan Province, West of Iran. Asian Pac J Trop Med. 2014;7(suppl 1):376–379.
54. Rafieian-Kopaei M, Sewell RDE. Opioid tolerance and K_{ATP} channel mediated antinociception. Analgesia. 1995;1(4-6):667–670.
55. Akbarpour V, Hemmati K, Sharifani M. Physical and chemical properties of pomegranate, fruit in maturation stage. Am Eurasian J Agric Environ Sci. 2009;6:411–416
56. Rafieian-Kopaei M, Shahinfard N, Rouhi-Boroujeni H, Gharipour M, Darvishzadeh-Boroujeni P. Effects of Ferulago angulata extract on serum lipids and lipid peroxidation. Evid Based Complement Alternat Med. 2014;2014:680856.
57. Asgary S, Sahebkar A, Afshani M, Keshvari M., Haghjooyjavanmard SH, Rafieian-Kopaei M. Clinical evaluation of blood pressure lowering, endothelial function improving, hypolipidemic and anti-inflammatory effects of pomegranate juice in hypertensive subjects. Phytother Res. 2014;28:193–199.
58. Khosravi-Boroujeni H, Sarrafzadegan N, Mohammadifard N, et al. White rice consumption and CVD risk factors among Iranian population. J Health Popul Nutr. 2013;31:252–261.
59. Sadeghi M, Khosravi-Boroujeni H, Sarrafzadegan N, et al. Cheese consumption in relation to cardiovascular risk factors among Iranian adults—IHHP Study. Nutr Res Pract. 2014;8:336–341.
60. Asgary S, Rafieian-Kopaei M, Shamsi F, Najafi S, Sahebkar A. Biochemical and histopathological study of the anti-hyperglycemic and anti-hyperlipidemic effects of cornelian cherry (Cornus mas L.) in alloxan-induced diabetic rats. J Complement Integr Med. 2014;11:63–69.
61. Nasri H, Rafieian-Kopaei M. Protective effects of herbal antioxidants on diabetic kidney disease. J Res Med Sci. 2014;19:82–83.
62. Shirzad H, Kiani M, Shirzad M. Impacts of tomato extract on the mice fibrosarcoma cells. J HerbMed Pharmacol. 2013;2:13–16.
63. Asadi-Samani M, Bahmani M, Rafieian-Kopaei M. The chemical composition, botanical characteristic and biological activities of Borago officinalis: a review. Asian Pac J Trop Med. 2014;7(suppl 1):22–28.
64. Rabiei Z, Hojjati M, Rafieian-Kopaeia M, Alibabaei Z. Effect of Cyperus rotundus tubers ethanolic extract on learning and memory in animal model of Alzheimer. Biomed Aging Pathol. 2013;3:185–191.
65. Bahmani M, Rafieian-Kopaei M, Jeloudari M, et al. A review of the health effects and uses of drugs of plant licorice (Glycyrrhiza glabra L.) in Iran. Asian Pac J Trop Dis. 2014;4(suppl 2):847–849.
66. Bahmani M, Saki K, Rafieian-Kopaei M, Karamati SA, Eftekhari Z, Jelodari M. The most common herbal medicines affecting Sarcomastigophora branches: a review study. Asian Pac J Trop Med. 2014;7(suppl 1):14–21.
67. Bagheri N, Rahimian GH, Salimzadeh L, et al. Association of the virulence factors of Helicobacter pylori and gastric mucosal interleukin-17/23 mRNA expression in dyspeptic patients. EXCLI J. 2013;12:5–14.
68. Bahmani M, Rafieian-Kopaei M, Hassanzadazar H, Saki K, Karamati SA, Delfan B. A review on most important herbal and synthetic antihelmintic drugs. Asian Pac J Trop Med. 2014;7(suppl 1):29–33.

69. Bahmani M, Eftekhari Z. An ethnoveterinary study of medicinal plants in treatment of diseases and syndromes of herd dog in southern regions of Ilam province, Iran. Comp Clin Path. 2012;22:403–407.
70. Noda Y, Kaneyuki T, Mori A, Packer A. Antioxidant activities of pomegranate fruit extract and its anthocyanidin: delphinidin, cyanidin and pelargonidin. J Agric Food Chem. 2002;50:166–171.
71. https://www.researchgate.net/publication/374537046_Phytochemicals_and_Therapeutic_Potential_of_Pomegranate_Therapeutic_potential_of_Pomegranate.
72. https://europepmc.org/article/med/34796029
73. https://journals.sagepub.com/doi/full/10.1177/2156587215598039#bibr19-2156587215598039