

REVIEW ON PHARMACOGNOSTIC AND PHARMACOLOGICAL STUDY OF PUNICA GRANATUM

Vaishnavi .B. Hingmire*¹, Priya .D. Jadhav*², Priyanka .K. Shinde*³

*^{1,2}Department Of Pharmacognosy, JBVP Vidya Niketan College Of Pharmacy, Lakhewadi, India.

*³Assistant Professor, Department Of Pharmacognosy JBVP Vidya Niketan College Of Pharmacy,
Lakhewadi, India.

ABSTRACT

Punica granatum L. (Pomegranate), from the Punicaceae family, is known for its medicinal uses across various medical systems. Different parts of the plant, including seeds, peels, flowers, juice, and leaves, contain powerful bioactive compounds that are beneficial in treating numerous diseases, such as gastrointestinal, cardiovascular, and endocrine disorders. The juice and seeds also play a protective role against liver damage.

Pomegranate is recognized for its strong antioxidant, anti-inflammatory, antifungal, anticancer, antiviral, antimicrobial, antidiabetic, and biopharmaceutical properties.

This study aims to evaluate the phytochemical and pharmacological properties of different extracts from *Punica granatum*.

Keywords: Pomegranate, Shrub, Flavonoids, Antioxidants, Anti-Inflammatory, Juice, Seed.

I. INTRODUCTION

Pomegranate, scientifically known as *Punica granatum*, is a fruit-bearing deciduous shrub or small tree from the Lythraceae family. It typically grows between 5 to 8 metres (16 to 26 feet) in height. Pomegranates are usually harvested between September to February in the Northern Hemisphere, and from March to May in the Southern Hemisphere. The genus name "Punica" comes from the Roman word for "Carthage," where the best pomegranates were known to thrive. Pomegranates, whether as whole juice or arils, are widely used in baking, juice blends, meal garnishes, cooking, and in alcoholic drinks like cocktails and wines.[1] Every part of *Punica granatum* is used in traditional medicine because it contains powerful phytochemicals that offer significant biological benefits. It is commonly consumed as a fruit or juice due to its richness in various active substances like acids, sugars, vitamins, and minerals.[2] Pomegranate *Punica granatum* L. is an ancient fruit tree that has been enjoyed in many countries for thousands of years. It symbolises life, longevity, health, beauty, fertility, wisdom, morality, and spirituality.[3] *Punica granatum* L., commonly known as pomegranate, is a deciduous shrub native to Iran. It has long been widely used in traditional medicine.[4,5] Today, pomegranate-based products are also used in the treatment of acquired immune deficiency syndrome (AIDS).[6] The peel and fruit extracts of *Punica granatum* have been shown to have various powerful pharmacological effects, including antioxidant, anti-inflammatory, and anticancer activities.[7]

1.1) Plant Profile :

The pomegranate belongs to the Lythraceae family (formerly known as Punicaceae) and includes only two species: *Punica granatum* and *Punica protopunica*. These plants are grown either for their edible fruit or as ornamental trees. *Punica granatum* var. *nana* is a dwarf variety of *P. granatum* commonly used as an ornamental plant in gardens. It is distinguished by its pink flowers (instead of red) and smaller, less sweet fruit.[8]



1.2) Geographical Source :

P. granatum is the most common species and is grown worldwide, while P. protopunica is limited to the island of Socotra in Yemen. The genus Punica originally comes from Persia (modern-day Iran). Pomegranates also thrive in the dry climates of California and Arizona and have been cultivated for thousands of years in countries like Iran, Iraq, Azerbaijan, Armenia, Afghanistan, Pakistan, India, Russia, Bangladesh, and throughout the Mediterranean region.[9,10]

A. PHYTOCHEMISTRY OF P. GRANATUM FRUIT Pomegranate fruit is rich in polyphenolic compounds. The peels contain various phytochemicals, including gallic acid, gallotannins, ellagic acid, punicalagins, and punicalin.[11]

The phytoconstituents found in various parts of the pomegranate are detailed in **Table 1**.

Table 1: Phytoconstituents

Sr.no	Parts of Punica granatum	Reported Phytoconstituents
1.	Root	Piperidine alkaloids, ellagitannins including punicalin and punicalagin.[12]
2.	Bark	Ellagitannins including punicalin, punicalagin, punicalcortin, pelletierine alkaloids [13]
3.	Leaves	Flavonols: quercetin, flavones, apigenin, flavonoids glycosides: luteolin, ellagitannins: punicalin, punicalagin corilagin, puniceifolia, piperidine alkaloids [14]
4.	Flowers	Flavonoids, gallic acid, ellagic acids linoleic acid, palmitic acid, sterols, triterpenoids[15]
5.	Peels	Flavonoids: Anthocyanins such as pelargonidin, delphinidin, cyanidin and anthoxanthins such as catechin, epicatechin and quercetin. Tannins: ellagitannins and ellagic acid derivatives such as punicalagin, punicalin. Phenolic acids: chlorogenic acid, caffeic acid, ellagic acid, gallic acid [16]
6.	Juice	Anthocyanins, glucose, fructose, ascorbic acid, ellagic acid, Gallic acid, caffeic acid, catechin, quercetin, rutin, various minerals like iron and amino acids [17]

B. PHARMACOGNOSTIC STUDY :

1.3) Punica granatum bark

The bark of P. granatum is tough, woody, and brown, often appearing twisted, and can grow up to 5 metres tall. Traditionally, this bark has been used to treat diarrhea. [18] The bark is also traditionally used to treat inflammation, nosebleeds, sore throat, ulcers, and hoarseness. Additionally, it's used to fight parasitic diseases like malaria.[19] Another use of P. granatum bark is that its extracts help prevent iron corrosion, thanks to their high thermal properties and acidity.[20] Additionally, the bark is rich in tannins, proanthocyanidins, anthocyanins, and terpenoids.[21, 22,23]

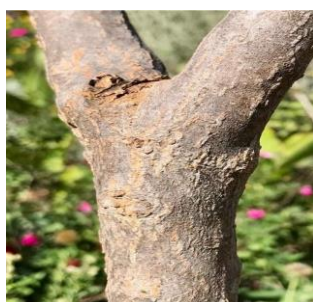


Fig 1: Punica granatum bark

1.4) Punica granatum flowers

Pomegranate flowers bloom in the summertime, attracting various birds to the trees. [24 Pomegranate flowers are known for their layered oval petals, which are light pink in color.[25 Traditionally, pomegranate flowers have been used to treat cardiovascular disorders, diabetes, and manage obesity.[26 Pomegranate flowers, known for their antimicrobial properties, have been found effective in treating common bacteria like Salmonella Enteritidis and Kentucky, which cause intestinal infections.[27] The flowers are also rich in bioactive compounds, including tannins, terpenes, terpenoids, flavonoids, and essential oils [28,29,30]



Fig 2: Punica granatum flower

1.4.1) Pomegranate Seeds

Pomegranate seeds are rich in sugars, vitamins, polysaccharides, minerals, and polyphenols. Due to the presence of polyphenol compounds like anthocyanins, condensed tannins such as proanthocyanidins, and hydrolysable tannins like ellagitannins and gallotannins, they have strong antioxidant properties. These compounds help reduce the formation of free radicals, which are linked to oxidation reactions that can lead to ageing, cardiovascular disease, and cancer.



Fig 3: Pomegranate Seeds

1.4.2) Pomegranate peels

Pomegranate peel extract has shown higher antioxidant activity compared to seeds and juice. The peel contains significantly more total phenolics, flavonoids, and flavonols than the seeds and juice. With increasing interest in using natural preservatives in the food industry, the waste products of pomegranate, such as the peel and seeds, with their high antioxidant activity, could be beneficial.[31 Pomegranate peels also offer great benefits for the skin, helping to keep it soft and supple by restoring balance. They can be used as a facial scrub, act as a natural sunscreen, combat hair loss, and prevent dandruff. Additionally, they support overall health, provide an excellent remedy for sore throats, protect against heart disease, improve dental hygiene, and boost bone health.[32]



Fig 4: Pomegranate Peels

1.4.3) Pomegranate juice

Pomegranate juice has a higher antioxidant content than most other fruit juices, containing three times more antioxidants than red wine and green tea. These antioxidants help remove free radicals, protect cells from damage, and reduce inflammation. The juice offers numerous health benefits, including cancer prevention, boosting skin and immune health, and aiding in wound healing. It also helps lower blood pressure—150 ml of juice twice a week can help prevent heart diseases. Additionally, pomegranate juice can relieve arthritis symptoms and improve memory, including in conditions like Alzheimer's disease.[33]

1.5 PHYTOCHEMICALS SCREENING :

1.5.1) Tannins: Dark blue and greenish-black colour was obtained by adding 1 mL bark extract to 1 mL 5% of ferric chloride.[34]

1.5.2) Saponins: The frothing layer on the upper surface of solution was obtained by shaking 1 mL bark extract with 1 mL distilled water. [35]

1.5.3) Quinones: Red colour of the solution was confirmed by using 1 mL bark extract with 1 mL conc. H₂SO₄. [35]

1.5.4) Alkaloids: The yellow cream-coloured formation for alkaloids was obtained by adding 1 mL bark extract in 2 mL conc. HCl and few drops of Mayer's reagent. [35]

1.5.5) Flavonoids: Yellow shading of solution appeared by analysing 1 mL bark extract with 1 mL of sodium hydroxide. [35]

1.5.6) Glycosides: The formation of pink colour for glycosides was obtained by using 1 mL peel extract to 3 mL chloroform and 10% ammonium solution. [34]

II. MATERIALS AND METHODS

- **Study area:** The research was conducted between June 2023 and December 2023, with samples collected from various locations in the Hazara Division of Khyber Pakhtunkhwa, Pakistan.
- **Drying and powder process:** Three kilograms of fruit bark were air-dried at room temperature for 12 days. Then, the bark was ground into a powder using an electric grinder for further analysis.
- **Preservation:** When the bark was finely powdered, it was packed into beakers with methanol at a ratio of 140 g of powder to 550 mL of methanol and left to soak for several days.[36] The powder was evenly distributed throughout the solvent by shaking it daily.

A. MICROSCOPICAL CHARACTERS :

The powdered bark was examined under a microscope using an established protocol to analyse the cells and tissues present.[37] The mixture was heated for at least 30 minutes, then a pinch of powder and approximately 70% chloral hydrate solution were added to the test tube.[38]

Afterward, a spirit lamp was used to melt safranin gel on a slide. To prepare the slides for observation, the solution from the test tube was poured onto the safranin gel, and a cover slip was placed on top.

Secondary metabolites analysis: A standard protocol was followed to analyse secondary metabolites after performing phytochemical tests on the powdered bark sample. [39, 40]

B. PHARMACOLOGICAL STUDY OF POMEGRANATE :

Anti-inflammatory Activity:

Inflammation is the body's localised response of living tissues to injury. [41]

The inflammatory process involves white blood cells becoming active, the immune system releasing chemicals, the production of substances that cause inflammation, and the release of prostaglandins.[42]

Punicic acid, the main component of pomegranate fatty acids, is a well-known anti-inflammatory substance. It reduces inflammation by stopping the production of prostaglandins.[43]

Anti cancer Activity:

Cancer is a genetic disease marked by uncontrolled cell growth. Phytochemicals are plant-based substances that can help prevent and fight cancer. [44]

Pomegranate juice, peel, and seed oil have been shown to have anti-cancer effects by stopping cell growth, slowing the cell cycle, and preventing the formation of new bloodvessels (angiogenesis). [45]

Anti-diabetic Activity:

Cardiovascular diseases develop when risk factors like diabetes and insulin resistance arise. These diseases can damage organ function and may cause problems with the immune system. [46,47] The development of cardiovascular risk factors like diabetes and insulin resistance can lead to heart diseases, which damage organ function and may result in immune system dysfunction. [48, 49] Diabetes is an endocrine disorder caused by insufficient insulin, leading to long-term high blood sugar levels. [50]

Antimicrobial Properties :

Phytochemical studies show that pomegranate peel contains powerful inhibitors like flavonoids and phenolic compounds. [51]

Antifungal Activity :

P. granatum is linked to several pharmacological activities, such as antifungal and antibacterial effects.

Antioxidant properties :

Research has explored the antioxidant benefits of pomegranates both in living organisms (in-vivo) and in lab settings (in-vitro). These studies show that drinking pomegranate juice can reduce the activation of cancer-causing compounds by affecting the activity and expression of enzymes like CYP1A2 and CYP3A. [52]

Anti cardiovascular activity :

Compounds such as flavonoids, tannins, ellagitannins, ellagic acid, anthocyanins, punicalagin, punicalin, gallic acid, urolithins, punicalic acid, and naringin, extracted from *P. granatum*, have demonstrated potential to protect blood vessels. [53]

III. CONCLUSION

Pomegranate peel, once regarded as waste in the food industry, has recently been found to contain bioactive compounds with various health benefits. The WHO states that this medicinal plant is one of the best sources for various drugs. Around 80% of people in developed countries use it in traditional medicine. Research has revealed that pomegranate peel has several beneficial properties, such as antioxidant, anti-inflammatory, anticancer, and antimicrobial effects. This makes it a promising ingredient for use in the pharmaceutical and cosmetic industries.

IV. REFERENCES

- [1] R. Adsule, P. Kotecha, S. Kadam. (1992). Preparation of wine from pomegranate. Beverage and food world. 19(4): 13-14.
- [2] Eghbali S, Askari SF, Avan R, Sahebkar A. Therapeutic Effects of Punica granatum (Pomegranate): An Updated Review of Clinical Trials. J NutrMetab. 2021;2021:5297162. Published 2021 Nov 16. doi 10.1155/2021/5297162
- [3] S.M. Outline of the beginnings of alchemy and its antecedents. Am J Chin Med.1984;12:21-32.
- [4] Al-Said FA, Opara LU, Al-Yahyai RA. Physical, chemical and textural quality attributes of pomegranate cultivars (*Punica granatum* L.) cultivars in the EasternMediterranean region of Turkey. Afr J Biotechnol. 2009;7:1294-1301.
- [5] 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.]
- [6] Lee J.,Watson R.R., Pomegranate: a role in health promotion and AIDS? In: Watson, R.R. (Ed.), Nutrients and Foods in AIDS. CRC Press, Boca Raton, FL, 179 (1998).
- [7] Magangana TP, Makunga NP, Fawole OA, Opara UL. Processing Factors Affecting the Phytochemical and Nutritional Properties of Pomegranate (*Punica granatum* L.) Peel Waste: A Review. Molecules. 2020;25(20):4690. Published 2020 Oct 14.
- [8] Stover E. The pomegranate: A new look at the fruit of paradise. Hort Science. 2007; 42(5):1088-92.
- [9] Jurenka JS. Therapeutic applications of pomegranate (*Punica Granatum* L.): Areview. Altern Med Rev. 2008; 13(2):128-44.

- [10] Adhami VM, Khan N, Mukhtar H. Cancer chemoprevention by Pomegranate: Laboratory and clinical evidence. *Nutr Cancer*. 2009;61(6):8115.
- [11] A.J. Ullmann, J.H. Lipton, D.H. Vesole, P. Chandrasekar, A. Langston, S.R. Tarantolo, H. Greinix, W. Morais de Azevedo, V.Reddy, N. Boparai. (2007). Posaconazole or fluconazole for prophylaxis in severe graft-versus-host disease. *New England Journal of Medicine*. 356(4): 335-347.
- [12] Lavaee F, Motaghi D, Jassbi AR, Jafarian H, Ghasemi F, Badiie P. Antifungal effect of the bark and root extracts of *Punica granatum* on oral *Candida* isolates. *Curr Med Mycol*. 2018;4(4):20-24.
doi:10.18502/cmm.4.4.382
- [13] Saeed M, Naveed M, BiBi J, et al. The Promising Pharmacological Effects and Therapeutic/Medicinal Applications of *Punica granatum* L. (Pomegranate) as a Functional Food in Humans and Animals. *Recent Pat Inflamm Allergy Drug Discov*.2018;12(1):24-38. doi:10.2174/1872213X12666180221154713
- [14] Deng YL, Li YL, Zheng TT, et al. *Sichuan Da Xue Xue Bao Yi Xue Ban*.2018;49(1):8-12.
- [15] Xu J, Zhao Y, Aisa HA. Anti-inflammatory effect of pomegranate flower in lipopolysaccharide (LPS)-stimulated RAW264.7 macrophages. *Pharm Biol*.2017;55(1):2095-2101.
doi:10.1080/13880209.2017.1357737
- [16] Mubarak MA, Hafiz TA, Dkhil MA, Al-Quraishy S. Beneficial effect of *Punica granatum* peel extract on murine malaria-induced spleen injury. *BMC Complement Altern Med*. 2016;16:221.Published 2016 Jul 16.doi:10.1186/s12906-016-1207-9
- [17] Fahmy H, Hegazi N, El-Shamy S, Farag MA. Pomegranate juice as a functional food: a comprehensive review of its polyphenols, therapeutic merits, and recent patents. *Food Funct*. 2020;11(7):5768-5781. doi:10.1039/d0fo01251c
- [18] K.L. Mashavhathakha, Yield and Quality of Pomegranate on Selected Geographical Areas in Western Cape Province, South Africa, University of South Africa, 2014.
- [19] S. Ge, L. Duo, J. Wang, Yang GegenZhula, J, Z. Li, Y. Tu, A unique understanding of traditional medicine of pomegranate, *Punica granatum* L. and its current research status, *J.Ethnopharmacol*.271 (27) (2021), 113877,https://doi.org/10.1016/j.jep.2021.113877.
- [20] A. Marsoul, M. Ijjaali, F. Elhajjaji, M. Taleb, R. Salim, A. Boukir, Phytochemical screening, total phenolic and flavonoid methanolic extract of pomegranate bark (*Punica granatum* L): Evaluation of the inhibitory effect in acidic medium 1 M HCl, *Mater. Today.: Proc.* 27 (2020) 3193–3198, https://doi.org/10.1016/j.matpr.2020.04.202.
- [21] M. Karimi, R. Sadeghi, J. Kokini, Pomegranate as a promising opportunity in medicine and nanotechnology, *Trends Food Sci. Technol.* 69 (2017) 59–73, https://doi.org/10.1016/j.tifs.2017.08.019.
- [22] D. Wang, C. Ozen, I.M. Abu-Reidah, S. Chigurupati, J.K. Patra, J.O. Horbanczuk, A. Jozwik, N.T. Tzvetkov, P. Uhrin, A.G. Atanasov, Vasculoprotective effects of pomegranate (*Punica granatum* L.), in: *Frontiers in Pharmacology*, Vol. 9, FrontiersMedia S.A., 2018, https://doi.org/10.3389/fphar.2018.00544.
- [23] T.L. Wong, K.R. Strandberg, C.R. Croley, S.E. Fraser, K.C. Nagulapalli Venkata, C. Fimognari, G. Sethi, A. Bishayee, Pomegranate bioactive constituents target multiple oncogenic and oncosuppressive signalling for cancer prevention and intervention, *Semin. Cancer Biol.* 73 (2021) 265–293, https://doi.org/10.1016/j.semcancer.2021.01.006.
- [24] L. Pienaar, The economic contribution of south africa's pomegranate industry, *Div.Macro Resour. Econ.* (Issue March) (2021)
- [25] J.A. Guerrero-Solano, O.A. Jaramillo-Morales, T. Jimenez-Cabrera, T.A. Urrutia-Hernandez, A. Chehue-Romero, E.G. Olvera-Hernandez, M. Bautista, *Punica protopunica* balf., the forgotten sister of the common pomegranate (*Punica granatum* L.): Features and medicinal properties—a review, *Plants* 9 (9) (2020) 1–15, https://doi.org/10.3390/plants9091214.
- [26] D. Wang, C. Ozen, I.M. Abu-Reidah, S. Chigurupati, J.K. Patra, J.O. Horbanczuk, A. Jozwik, N.T. Tzvetkov, P. Uhrin, A.G. Atanasov, Vasculoprotective effects of pomegranate (*Punica granatum* L.), in: *Frontiers in Pharmacology*, Vol. 9, FrontiersMedia S.A., 2018, https://doi.org/10.3389/fphar.2018.00544.

- [27] B.A. Wafa, M. Makni, S. Ammar, L. Khannous, A. Hassana, Ben, M. Bouaziz, N. E. Es-Safi, R. Gdoura, Antimicrobial effect of the Tunisian Nana variety *Punica granatum* L. extracts against *Salmonella enterica* (serovars Kentucky and Enteritidis) isolated from chicken meat and phenolic composition of its peel extract, *Int. J. Food Microbiol.* 241 (2017) 123–131, <https://doi.org/10.1016/j.ijfoodmicro.2016.10.007>.
- [28] S. Ge, L. Duo, J. Wang, Yang GegenZhula, J, Z. Li, Y. Tu, A unique understanding of traditional medicine of pomegranate, *Punica granatum* L. and its current research status, *J. Ethnopharmacol.* 271 (27) (2021), 113877, <https://doi.org/10.1016/j.jep.2021.113877>.
- [29] B.A. Wafa, M. Makni, S. Ammar, L. Khannous, A. Hassana, Ben, M. Bouaziz, N. E. Es-Safi, R. Gdoura, Antimicrobial effect of the Tunisian Nana variety *Punica granatum* L. extracts against *Salmonella enterica* (serovars Kentucky and Enteritidis) isolated from chicken meat and phenolic composition of its peel extract, *Int. J. Food Microbiol.* 241 (2017) 123–131, <https://doi.org/10.1016/j.ijfoodmicro.2016.10.007>
- [30] D. Wang, C. Ozen, I.M. Abu-Reidah, S. Chhatrapati, J.K. Patra, J.O. Horbanczuk, A. Jozwik, N.T. Tzvetkov, P. Uhrin, A.G. Atanasov, Vasculoprotective effects of pomegranate (*Punica granatum* L.), in: *Frontiers in Pharmacology*, Vol. 9, FrontiersMedia S.A., 2018, <https://doi.org/10.3389/fphar.2018.00544>.
- [31] <http://apeda.in/agriexchange/Market20Profile/MOA/Product/Pomegranate.pdf>
- [32] <https://www.ndtv.com/health/pomegranate-juice-know-impressive-health-benefits-of-drinking-this-juice-2323973>
- [33] <https://www.ndtv.com/health/pomegranate-juice-know-impressive-health-benefits-of-drinking-this-juice-2323973>
- [34] Ajayi, I.A., O. Ajibade and R.A. Oderinde, 2011. Preliminary phytochemical analysis of some plant seeds. *Res. J. Chem. Sci.*, 1: 58-62.
- [35] Omar, G.A. and L.Y. Mohammed 2023. Physicochemical standardization and phytochemical screening of *Urtica dioica* L. leaves growing in Zakho, Kurdistan Region, Iraq. *Sci. J. Univ. Zakho*, 11: 306-316.
- [36] Soural, I., N. Vrchotova, J. Triska, J. Balik, S. Hornik, P. Curinova and J. Sykora, 2015. Various extraction methods for obtaining stilbenes from grape cane of *Vitis vinifera* L. *Molecules*, 20: 6093-6112.
- [37] Ahmed, D., V. Kumar, A. Verma, P.S. Gupta and H. Kumar et al., 2014. Antidiabetic, renal/hepatic/pancreas/cardiac protective and antioxidant potential of methanol/dichloromethane extract of *Albizia Lebbeck* Benth. stem bark (ALEX) on streptozotocin induced diabetic rats. *BMC Complementary Med. Ther.*, 14.
- [38] Namadina, M.M., B.S. Aliyu, H. Haruna, U. Sunusi and R.M. Kamal et al., 2020. Pharmacognostic and acute toxicity study of *Burkea africana* root. *J. Appl. Sci. Environ. Manage.*, 24: 565-573.
- [39] Savithamma, N., M.L. Rao and D. Suhrulatha, 2011. Screening of medicinal plants for secondary metabolites. *Middle-East J. Sci. Res.*, 8: 579-584.
- [40] Omar, G.A. and L.Y. Mohammed, 2023. Physicochemical standardisation and phytochemical screening of *Urtica dioica* L. leaves growing in Zakho, Kurdistan Region, Iraq. *Sci. J. Univ. Zakho*, 11: 306-316.
- [41] Malleshappa, P.; Kumaran, R. C.; Venkatarangiah, K.; Parveen, S. Peels of citrus fruits: A potential source of anti-inflammatory and anti-nociceptive agents. *Pharmacogn. J.* 2018, 10, s172–s178.
- [42] Sudheesh, S.; Soumya, K.; James, J. A novel chalcone derivative *Punica granatum* peel inhibits LOX/COX enzyme activity. *Beni-Suef Univ. J. Basic Appl. Sci.* 2018, 7, 593–597.
- [43] Nugteren DH, Christ-Hazelhoff E: Naturally occurring conjugated octadecatrienoic acids are strong inhibitors of prostaglandin biosynthesis. *Prostaglandins* 1987; 33, 403-417.
- [44] Nasr, M.; Naeem, S. A.; El-Shenbaby, I.; Mohamed, F. M. A.; Mahmoud, S. M.; Abuamara, T. M.; Abd-Elhay, W. M.; Elbayoumy, F. M.; Elkot, A.; Shikhon, T.; Abo-Akrab, M.; Doma, M. A.; Hasan, A. Pomegranate Seeds and Peel Ethanolic Extracts Anticancer Potentials and Related Genetic, Histological, Immunohistochemical, Apoptotic and Oxidative Stress Profiles: In-vitro Study. *J. Exp. Pharmacol.* 2023, Volume 15, 191–205.
- [45] Lansky EP and Newman RA: *Punica granatum* (pomegranate) and its potential for prevention and

- treatment of inflammation and cancer. *Journal of Ethnopharmacology* 2007; 109(2): 177- 206.
- [46] C. Mayasankaravalli, K. Deepika, D. Esther Lydia, R. Agada, D. Thagriki, C. Govindasamy, V. Chinnadurai, O.M. Othman Gatar, A. Khusro, Y.O. Kim, H. J. Kim, Profiling the phyto-constituents of Punica granatum fruits peel extract and accessing its in-vitro antioxidant, anti-diabetic, anti-obesity, and angiotensin-converting enzyme inhibitory properties, *Saudi J. Biol. Sci.* 27 (12) (2020) 3228–3234, <https://doi.org/10.1016/j.sjbs.2020.09.046>.
- [47] M. Bastien, P. Poirier, I. Lemieux, J. Després, Overview of epidemiology and contribution of obesity to cardiovascular disease, *Prog. Cardiovasc. Dis.* 6 (56)(2014) 369–381, <https://doi.org/10.1016/j.pcad.2013.10.016>.
- [48] M. Bastien, P. Poirier, I. Lemieux, J. Després Overview of epidemiology and contribution of obesity to cardiovascular disease *Prog. Cardiovasc. Dis.*, 6 (56) (2014), pp. 369-381, 10.1016/j.pcad.2013.10.016 View PDF View article View in Scopus Google Scholar
- [49] C. Mayasankaravalli, K. Deepika, D. Esther Lydia, R. Agada, D. Thagriki, C. Govindasamy, V. Chinnadurai, O.M. Othman Gatar, A. Khusro, Y.O. Kim, H.J. Kim Profiling the phyto-constituents of Punica granatum fruits peel extract and accessing its in-vitro antioxidant, anti-diabetic, anti-obesity, and angiotensin-converting enzyme inhibitory properties *Saudi J. Biol. Sci.*, 27 (12) (2020), pp. 3228-3234, 10.1016/j.sjbs.2020.09.046 View PDF View article View in Scopus Google Scholar
- [50] S.N. Mestry, J.B. Dhodi, S.B. Kumbhar, A.R. Juvekar Attenuation of diabetic nephropathy in streptozotocin-induced diabetic rats by Punica granatum Linn. leaves extract *J. Tradit. Complement. Med.*, 7 (3) (2017), pp. 273-280, 10.1016/j.jtcme.2016.06.008 View PDF View article View in Scopus Google Scholar
- [51] Rosas-Burgos, E. C. Burgos-Hernández, A.; Noguera-Artiaga, L.; Kacániová, M.; Hernández-García, F.; Cárdenas-López, J. L. Carbonell-Barrachina, Á A. Antimicrobial activity of pomegranate peel extracts as affected by cultivar. *J. Sci. Food Agric.* 2017, 97, 802–810.
- [52] Faria A, Monteiro R, Azevedo I, Calhau C. Pomegranate juice effects on cytochrome P450S expression: in-vivo studies. *J. Med. Food.* 2007;10:643–639. [PubMed] [Google Scholar]
- [53] Wang D, Özen C, Abu-Reidah IM, Chigurupati S, Patra JK, Horbanczuk JO, et al. Vasculoprotective effects of pomegranate (*Punica granatum L.*). *Frontiers in Pharmacology.* 2018;:1-15. DOI:10.3389/fphar.2018.00544