

Specific Application of *Punicagranatum Linn*

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ABSTRACT

Throughout the world, pomegranates are a popular therapeutic and nutritive fruit. *Punicagranatum.L* (Punicaceae) plays a significant role in medicine. It has an intriguing pharmacological activity on each compartment of the pomegranate. Certain segments, such as the juice, leaf, flower, and peels, possess strong antioxidant properties, while the juice, peel, and oil have weak estrogenic activity. The following major properties include anti-inflammatory, antioxidant, nephroprotective, hepatoprotective, anti-oxidant, anti-cancer, Overview of the *punicagranatum L.*'s chemical composition, traditional use, phytochemistry, pharmacology, and toxicology current information about the punicaceae is provided.

INTRODUCTION

Iranian native *Punicagranatum L.*, also known as the pomegranate, is a deciduous shrub. Traditional medicine has frequently employed pomegranates as a source. Pomegranate fruit offers therapeutic qualities like anti-inflammatory and antibacterial effects^[1,2]. Breast and skin cancers are inhibited by pomegranate seed oil. Pomegranate fruit is abundant in phenolic compounds with great antioxidant action, while the seed oil contains phytoestrogenic chemicals. Pomegranate fruit and bark are used to treat diarrhoea, dysentery, and intestinal parasites.^[1] The juice and seeds are regarded as a heart and throat tonic. It is used to treat haemorrhoids and halt nose and gum bleeding.^[3]

Punicagranatum L. is a fruit that is currently very popular with consumers and the subject of extensive research into its culinary and medical uses.^[3] As a result, numerous research projects in this area have already been started. On the other hand, not enough research has been done on the therapeutic benefits of pomegranates. This review article offers the most recent research on many elements of this plant, with an emphasis on its

therapeutic benefits.

The researchers are interested in natural goods as an alternative source of therapeutic ingredients. Due to their popularity, lack of side effects, ease of production, and safety, medicinal plants are increasingly being used and researched as treatments and preventatives for ailments.

Some significant medications, like digoxine, quinine, and vinca alkaloids, are made from herbal remedies^[4-6]. Plants produce a variety of chemical substances as part of their regular metabolic processes. Currently, about 120 active substances are isolated from therapeutic plants.

Pomegranates, or *Punicagranatum L.*, have a distinguished medical history and impressive medicinal qualities.^[7]

Pomegranates are an Asian fruit that are grown from Northern India to Iran. It has been grown and permitted to spontaneously occur throughout the entire Mediterranean region since antiquity.^[8] Pomegranates have recently grown in popularity as a natural remedy with numerous therapeutic uses. Because of its ability to heal a number of disorders, studies have indicated that

pomegranates may be utilised as a natural alternative to conventional medical care.

The antibacterial properties of nearly every component of the pomegranate, including the fruit juice, peel, arils, blossoms, and bark, have been studied. Pomegranate has a variety of phytochemical characteristics that are shown to have antibacterial effects. The most active tannins are those that can be hydrolyzed, including punicalagin and elagic acid.^[9]

Pomegranate juice, peel, and oil have been shown to have anticancer properties, which include inhibiting the proliferation, cell cycle, invasion, and angiogenesis of tumour cells.

These might be connected to the pomegranate's anti-inflammatory properties. Pomegranate phytochemistry and pharmacological effects suggest a wide range of clinical applications for the prevention and treatment of cancer as well as other diseases where chronic inflammation is likely to play a major etiologic role.^[10] Over the past ten years, a tone of studies on the components of pomegranates have been published. According to the findings, pomegranate constituents contain antioxidant, anti-carcinogenic, and anti-inflammatory properties that make them useful in the treatment and prevention of cancer as well as other chronic and infectious disorders.^[11-13]

The objective of this systematic review was to provide an overview of the current knowledge regarding the therapeutic potential of pomegranate products in prevention and treatment of breast, lung, prostate, colon, skin, and hepatic cell malignancies from both animal and human clinical studies.

ETYMOLOGY

The words "apple" and "seeded" in mediaeval Latin are combined to form the word "pomegranate."^[14] The term "apple of Grenada" for the pomegranate, which today only exists in heraldic blazons, may have originated from the previous French title for the fruit, pomme-grenade. This is a folk etymology that conflates the Arabic-derived name of the Spanish city of Granada with the Latin granatus.^[15]

By metathesis, the word garnet is derived from Medieval Latin granatum, which originally meant "of a dark red tint." This term may have been derived from either granum, which meant "red dye, cochineal," or from pomumgranatum, which described the hue of pomegranate pulp.^[16] The military grenade was given its name from the contemporary French word for pomegranate, grenade.^[17]

DESCRIPTION

The pomegranate is a long-living shrub or small tree that can reach heights of 5 to 10 m (16 to 33 ft) and has several thorny branches. Some examples in France have lived for 200 years.^[18] The leaves of *P. granatum* are opposite or subopposite, shiny, narrowly oblong, whole, and measure 3-7 cm (1+1/4-2+3/4 in) long by 2 cm (3/4 in). The flowers have three to seven petals, are brilliant red, and are 3 cm (1+1/4 in) in diameter.^[18] Some kinds that bear no fruit are planted only for their flowers.^[20]

FRUIT, SARCOTESTA AND SEEDS

The pomegranate fruit husk, which is reddish-purple in colour, is made up of two layers: an outer, hard pericarp and an interior, spongy mesocarp (white "albedo"), which makes up the inner wall of the fruit to which the seeds are attached. Mesocarp membranes are arranged as nonsymmetric chambers that house



An opened pomegranate



Pomegranate flower



Fruit setting

seeds inside sarcotestas that are embedded but not attached to the mesocarp^[20]. The sarcotesta, a thin membrane that contains juice, is created from the seeds' epidermal cells.^{[21] [22]} A pomegranate can contain anywhere from 200 to 1,400 seeds.^[23]

According to botany, the edible fruit is a berry containing seeds and pulp that develops from a single flower's ovary.^[21] The fruit has a diameter of 5.12 cm (2-4+12 in), is spherical in shape, and has a thick, reddish husk. It is in between the size of a lemon and a grapefruit.^[18] Due to its low pH (4.4) and high polyphenol content, the juice extracted from mature fruits' seeds has a sour flavour and may leave a permanent crimson stain on fabrics.^[25] Anthocyanins and ellagitannins are primarily responsible for the pomegranate juice's colouring.^{[24] [26]}

CULTIVATION

In addition to being planted for its fruit, *P. granatum* is also used as decorative trees and shrubs in parks and gardens. When mature, specimens can have many trunks, sculpture-like twisted bark, and a unique overall shape. Pomegranates can be grown in dry places with either a Mediterranean winter rainfall environment or a summer rainfall climate since they are drought-tolerant. They may be more susceptible to fungal diseases that cause root degradation in wetter locations. They are able to withstand light frost down to about 12 °C (10 °F).^[27] The butterflies *Viracholaisocrates*, *Iraotatimoleon*, *Deudorixepijarbas*, and the leaf-footed bug *Leptoglossuszonatus* are among the pomegranate's insect enemies^[28]. Fruit flies and ants are also drawn to the unharvested, ripe fruit.^[18]

VARIETIES

The dwarf variation of *P. granatum*, known as *P. granatum* var. *nana*, is frequently grown as a decorative plant in gardens and bigger containers and as a bonsai specimen tree. It's possible that it's a wild variety with a unique ancestry. It has received the Award of Garden Merit from the Royal Horticultural Society.^{[29] [30]} The sole other member of the genus *Punica* is the Socotran pomegranate (*P. protopunica*), which is unique to the four islands that make up the Socotran archipelago in the Arabian Sea, the largest of which is also referred to as Socotra. The area is a part of Yemen. It is different in that it has smaller, less delicious fruit and pink (not red) blossoms.^[31]

CULTIVARS



Black pomegranate

P. granatum has more than 500 identified cultivars, although there is clearly significant synonymy, where the same genotype is given many names in different parts of the world.^[20] The most significant differences between pomegranate genotypes are in fruit size, exocarpcolour (which can range from yellow to purple, with pink and red being the most common), seed coat colour (which can range from white to red), seed hardness, maturity, juice content and its acidity, sweetness, and astringency.^[20]

NUTRITION

Pomegranates contain 78% water, 19% carbs, 2% protein, and 1% fat in their edible section when they are uncooked (table). Pomegranate sarcotesta has 12% of the Daily Value (DV) for vitamin C, 16% DV for vitamin K, and 10% DV for folate in a 100 g (3.5 oz) serving (table). Dietary fibre from pomegranate seeds is abundant (20% DV), and it is totally present in the edible seeds.^[32]

Punicagranatum L. compound

Pomegranates are a significant source of bioactive elements and have demonstrated anticancer effects. Pomegranate has a high content of ellagitannins, anthocyanins, and hydrolysable tannins and has considerable antioxidant activity.^[33] Tannin and polyphenols make up the majority of pomegranates' chemical makeup. According to phytochemical investigations, pomegranate peels contain active inhibitors such as phenolics and flavonoids. Ellagitannins, ellagic acid, gallic acid, and hydroxybenzoic acids such as ellagic acid, gallagic acid, and ellagic acid glycosides are present in pomegranate peel. Punicalagin is the primary bioactive component of pomegranate peel. Cyanidin, pelargonidin, and delphinidin are the principal anthocyanidins, along with flavonoids including kaempferol, luteolin, and quercetin.

(16) found that delphinidin exhibits growth inhibitory efficacy in breast cancer cells of many molecular subtypes, but that when combined with other targeted therapies, it may increase the risk of drug antagonism. measured the gallic acid (34.03%) and catechin (3.31%) present in the methanolic extract of pomegranate peel using a chromatographic method (i.e. HPLC). demonstrated that the methanol and aqueous extracts of *P. granatum* peel extract have antioxidant activity, polyphenolic, nutritional content, and phenolic characteristics. The use of botanical antioxidants as photochemopreventive agents has drawn a lot of attention.

(19) (HPLC analysis of the phenolic content of the methanolic extracts revealed the presence of roughly five different flavonoids, phenolic acids, and their derivatives, including quercetin, rutin, gallic acid, ellagic acid, and punicalagin as a significant ellagitannin. In a study by Akbarpour et al., the physical and chemical characteristics of twelve cultivars of pomegranate (*P. granatum* L.) from various Iranian locations were examined. The ellagic acid concentration of the juice and peel were between 1-2.38 mg/100 mL and 10-50.00 mg/100 g, according to the HPLC results. Total antioxidant activity in peel and juice was determined using the FRAP test, with respective ranges of 157.33-419.33 (mmol/100 mL) and 225.17-705.50 (mmol/100 g).^[33]

PHYTOCHEMICALS

The polyphenols, or punicalagins, which are created when ellagic acid and gallic acid combine with a carbohydrate to form pomegranate ellagitannins, are the most prevalent phytochemicals in pomegranate juice. These ellagitannins can be

hydrolyzed.^[34]Anthocyanins such delphinidin, cyanidin, and pelargonidin glycosides are thought to be responsible for the juice's red hue. Generally speaking, juice pigmentation rises as fruit ripens. Processing and pasteurisation methods degrade the phenolic content of pomegranate juice. Pomegranate peel is rich in catechins, prodelphinidins, condensed tannins, and polyphenols. The peel's greater phenolic content produces extracts that can be used as food preservatives and dietary supplements. Punicic acid makes up 65% of the punicic acid content of pomegranate seed oil, along with palmitic acid, stearic acid, oleic acid, and linoleic acid.^[34]

PHARMACOLOGICAL PROPERTIES OF POMEGRANATE

Pomegranate juice that has been fermented has been discovered to have antioxidant properties. Pomegranate blossom juice can lower cholesterol and blood sugar levels.^[35] Pomegranate juice's flavonoids and tannins can inhibit the development of cancer cells. Flavonoids found in the fruit peel and watery extract have estrogenic action. In addition, luteolin and naringenin have shown activities like the hormone typically secreted by women prior to conception. The pomegranate fruit's fermented extract contains polyphenols that may have antioxidant activity, while pericarp tannins may boost the fruit extract's antioxidant capacity.^[35]

Due to the breakdown of flavonoids sugar complexes during fermentation, the final products will contain greater concentrations of free polyphenols and have stronger polyphenol activities than nonfermented extract (with high biological activity). It has been established that the flavonoids in peels exist as glycosides. In their glycoside forms, they exhibit no estrogenic activity, but when they are released and hydrolyzed, they exhibit the opposite behaviour. In order to prevent the estrogenic action of 17- β -estradiol, estrogenic flavonoids such kaempferol, quercetin, naringenin, luteolin, and weak 17- α -estradiol oestrogen bind to the oestrogen receptors in the pericarp polyphenols and the fermented juice of pomegranates.

Breast cancer cells that are both estrogen-dependent and estrogen-independent can be inhibited by pomegranate juice. However, it has been noted that in estrogen-dependent cases, this inhibitory effect is doubled. Ellagic acid, a dimeric derivative of gallic acid that is mostly present in higher plants like fruits and

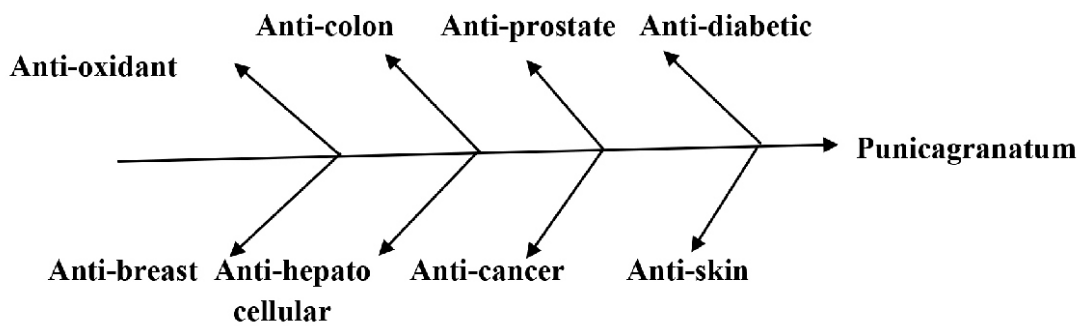
nuts, is one of the substances discovered in pomegranate peels along with gallic acid.^[35] Ellagic acid has already been added to food in Japan as an antioxidant and exhibits antimutagenic, antiviral, antioxidant, and skin-bleaching effects. Pomegranate peel extracts have been tested for their ability to produce phospholipid complex while also possessing antioxidant properties.

Pomegranate seeds with a thin, yellowish membrane make up 13% of the fruit. These two components are essential for illness diagnosis, maintaining the health of the fruit's edible sections, and particularly for preventing browning and discoloration of the fruit. Such tissues ought to be a rich source of biologically active compounds.

The ratios that were found to be highest and lowest were found at one hour and 4, 5, and six hours after intake, respectively. Its breakdown at the biological pH of the stomach causes the presence of free ellagic acid in the plasma. In bioavailability studies proving the ingestion of ellagic acid from food sources, it can therefore be employed as a biologic marker.^[73] Oil polyphenols stop cyclooxygenase and eicosanoid enzymes from working. Conjugated linoleic acid, an 18C trans fatty acid with a structural affinity for punicic acid, has the ability to stop the growth of cancer. Pomegranate seed oil's chemical protective effects were examined for potential skin cancer development. One of the most common forms of cancer in the US is skin cancer.

In 2002, there were estimated to be 10,00,000 instances of skin cancer and 9000 related fatalities. The constant exposure of skin to environmental cancer-causing substances, particularly chemicals and UV radiation, is the main cause of the increased prevalence of this type of cancer. Previous studies on the prevention of skin cancer have demonstrated the usefulness and practicality of natural compounds made from onion and garlic oil. UV rays and chemicals can cause skin cancer in three different ways: (1) initiation, (2) escalation, and (3) promotion. Application of the skin carcinogen 7,12-dimethyl benzanthracene (DMBA) in vivo, which is irreversible, can stimulate the initiation stage;

Punic acid and octadecatrienoic acid are two of the conjugated fatty acids that make up the majority of the pomegranate seed oil.^[35] Punic acid functions as a cytotoxin for cancer w2a cells as well as a prostaglandin biosynthesis inhibitor; this activity may be caused by the inhibitory effect against fat peroxidation.



Illegal health claims.

ILLEGAL HEALTH CLAIMS

Pomegranate juice producers and marketers have freely leveraged preliminary research findings to advertise products despite the paucity of research data. One such producer, POM Wonderful, received a warning notice from the FDA in February 2010 for making improper claims about the anti-disease properties of published literature.^[36] The US Federal Trade Commission ruled in May 2016 that POM Wonderful could not make health claims in its advertising, and the FTC's judgement was upheld by the US Supreme Court, which denied POM Wonderful's request for a review of the decision^[37]

ANTIDIABETIC PROPERTIES

The prevalence of diabetes, the most prevalent metabolic disease worldwide, is still rising. According to the International Diabetes Federation, 333 million people will have diabetes by 2025, up from 194 million in 2003. After cardiovascular and oncological problems, it is the third most common disease, according to the World Health Organization. Pomegranate fruits and derivatives can help with diabetes mellitus management through nutrition, which is one method. In fact, its antidiabetic action has been described in multiple research. For instance, Katz and colleagues reported on the hypoglycemic action of pomegranate juice, seeds, and blossoms.^[38]

The exact processes causing these effects are uncertain, but recent study indicates that pomegranate juice and flowers may reduce diabetes sequelae by binding to peroxisome proliferator-activated receptors and producing nitric oxide. Oleanolic, ursolic, and gallic acids are pomegranate constituents with antidiabetic properties. Li and others contend that intestine -glucosidase activity is at least partially responsible for how pomegranate flower extract reduces postprandial hyperglycemia in people with type 2 diabetes and obesity. The activation of PPAR-, however, was one of the putative mechanisms Huang and colleagues showed for the antidiabetic effect of pomegranate flower extract.

The substance largely responsible for this effect in vitro has been identified as gallic acid, which is present in many herbal medications that are anti-diabetic and anti-inflammatory. Caffeic acid, another component, also stimulates glucose uptake by rat adipocytes and mouse myoblasts. In normal, glucose-fed hyperglycemic, and alloxan-induced diabetic rats, oral administration of an aqueous-ethanolic (50%, v/v) pomegranate flower extract significantly lowered blood sugar levels. At 400 mg/kg, the extract had its greatest effect.^[39]

Underscoring the antidiabetic and antiperoxidative potential of pomegranate, Parmar and Kar reported that the administration of 200 mg/kg of pomegranate peel extract normalised all the adverse changes induced by alloxan, a commonly used substance for causing diabetes mellitus because it increases the serum levels of glucose and -amylase activity and the rate of water consumption and lipid peroxidation in hepatic, cardiac, and renal tissues while decreasing serum insulin. In rats induced diabetic by streptozotocin, Das and colleagues examined the hypoglycemic effect of pomegranate seed extract. In induced diabetic rats, the seed extract (300 and 600 mg/kg, orally) resulted in a significant drop in blood glucose levels of 47% and 52%, respectively, after 12 hours.

The primary substances with antidiabetic characteristics are polyphenols, which can influence glycemia in a variety of ways,

such as by inhibiting stomach absorption of glucose or uptake by peripheral organs. When maltose was the source of the glucose, the hypoglycemic effects of diacetylatedanthocyanins in a 10 mg/kg meal dosage were seen, but not when sucrose or glucose itself was used. This shows that the inhibition of glucosidase in the gastrointestinal mucosa is the cause of these effects. Numerous in vitro studies in cultured cells have demonstrated that polyphenols may enhance peripheral tissues' absorption of glucose, which would reduce glycemia. The processes include gluconeogenesis inhibition, adrenergic stimulation of glucose uptake, and stimulation of pancreatic -cell release of insulin^[38,39].

ANTIOXIDANT ACTIVITY

Because ellagic acid, the primary polyphenol in pomegranates, has significant antioxidant activity, pomegranate peel extracts are rich in phytochemicals explained the first study on the antioxidant properties of pomegranate peel extract. The antioxidant activity of the pomegranate peel extract is ten times greater than that of the pulp extract. Peel extract had a very high capacity for removing hydroxyl and superoxide anion radicals^[40]. Pomegranate extracts are thus shown as two functional agents that combine antioxidant and aldose reductase regulatory activity. Pomegranate peel and juice include anti-oxidant properties and block pro-inflammatory enzymes like cyclooxygenases and lipoxygenases. Pomegranate seed oil is the source of polyphenolic chemicals.

Studies in rats with CCl₄-induced liver damage demonstrated that pomegranate peel pretreatment evaluated the free radical inhibitory effect of superoxide dismutase, the hepatic enzymes catalase, and peroxidase resulted in 54% lowering of lipid peroxidation values in comparison to control group, confirming the antioxidant content of the pomegranate peel. Another study showed that rats fed with pomegranate peel enabled protective activity.

ANTI-CANCER ACTIVITY

There is currently a shift toward finding natural compounds that may be helpful in preventing and treating cancers due to issues with current chemotherapeutic regimens. With regard to prostate, colon, oral, and breast cancer cell lines, pomegranates have anti-proliferative and anti-cancer properties. Pomegranate has been linked to anti-inflammatory and anti-cancer properties, and it effectively protects diabetic rats from oxidative damage.^[41] In several organs, pomegranate extract has shown promising anti-tumor properties. Pomegranate contains polyphenols that have been shown in in vitro and in vivo studies to have anticarcinogenic properties.

Pomegranate juice and extract both significantly increased apoptosis and decreased proliferation in lymphoid and myeloid leukaemia cell lines, which was accompanied by cell cycle arrest. Pomegranate extracts were found to inhibit the growth of breast, prostate, colon, and lung cancer cells in an in vitro experiment, according to research by Adhmi et al. In preclinical animal experiments, pomegranate extract had the capacity to suppress the growth of prostate, lung, skin, and colon malignancies. In a preliminary phase II clinical trial, pomegranate juice significantly prolonged the prostate-specific antigen doubling time in patients with prostate cancer. Pomegranate peel extracts have been shown to slow cell proliferation in a variety of cancer cell lines^[41]

Adams et al. investigated the anti-carcinogenic capabilities of several pomegranate phytochemical combinations. Punicalagin has been shown through research by Tang et al. to have

chemopreventive and chemotherapeutic effects against cervical cancer in humans by inhibiting the β -catenin signalling pathway. Punicalagin, a forerunner of purified ellagic acid, and the total tannin content in pomegranate juice were compared. All of them decreased the number of human oral and colon tumour cells that were alive, but pomegranate juice had the strongest effect and was the most potent antioxidant sample examined.

Ellagic acid may be the key ingredient in pomegranate juice that performs these anti-cancer actions, according to a review by Naiki et al.^[41] who reported that pomegranate juice and ellagic acid are prospective chemo preventive medicines for prostate cancer. Pomegranate juice also induced apoptosis when isolated tannin concentrations that were matched to pomegranate juice levels had no impact. The juice also has phytochemicals including anthocyanins and flavonoids, which have anti-proliferative and antioxidant properties. The combined effects of the pomegranate's elements appear to be more effective than their individual effects.

ANTI-BREAST CANCER

Pomegranate extract demonstrated anti-inflammatory and cytotoxic properties in breast cancer cells both in vitro and in vivo. Pomegranate extract's ability to inhibit breast cancer growth in part results from targeting microRNAs 155 and 27a. These cell lines' proliferative and inflammatory phenotypes are significantly influenced by pathways. Pomegranate seed oil has been shown in experimental investigations to inhibit mammary carcinogenesis in the mouse mammary organ and to suppress proliferation of various tumour cell types^[42]. Pomegranate extracts induce apoptosis, which slows the growth of MCF-7 breast cancer cells.

Mehta found that the refined component and pomegranate seed oil had greater ability to prevent breast cancer than the polyphenols found in the fermented juice of pomegranates. Pomegranates are able to prevent the growth of new blood vessels^[133]. To provide oxygen and nutrients for the growth and metastasis of the tumour, angiogenesis must develop. The study by Kim et al found that pomegranate components had a preventative effect against various breast cancers and raises the possibility that pomegranates may have a function in the treatment and suppression of cancer. According to a study by Shirode et al., encapsulating pomegranate polyphenols increases their bioactivity and inhibits the growth of MCF-7 and Hs578T breast cancer cells.^[43]

ANTI-PROSTATE CANCER

Animal and cell culture models have been used to evaluate the effects of pomegranates on prostate cancer. Pomegranate juice has significantly extended the prostate specific antigen's doubling time in patients with prostate cancer who were participating in an initial phase II clinical research. Preclinical studies on animals demonstrated that taking pomegranate extract orally prevented prostate tumour growth. The prostate-specific antigen (PSA) doubling time was statistically significantly prolonged in the first pomegranate juice clinical trial in patients with prostate cancer, as reported by Pantuck et al.^[44]. Changes in the distribution of the cell cycle and the triggering of apoptosis were shown to be the mediators of these actions against lung cancer. Authors have looked at the impact of pomegranate extract on the development of lung tumours both in vitro and in vivo. These researchers proposed that by preventing proliferation, inducing apoptosis, cell cycle arrest, and hindering cell migration and invasion, pomegranate leaves extract might be a useful and secure chemotherapeutic drug in the treatment of non-small cell lung

cancer.

Pomegranate extract has the ability to prevent tumour growth in nude mice and pro survival pathways in human A549 lung cancer cells. According to research by Khan et al., pomegranate extract significantly slows down the development of lung cancer in mice, and it may also be effective against human lung cancer. Therefore, pomegranate extract has the potential to be an effective chemotherapeutic and chemopreventive agent against human lung cancer.^[45]

ANTI-COLON CANCER

Different anti-inflammatory drugs have shown promise for colon cancer prevention. Inflammation plays a major part in the development of colon cancer. Pomegranate seed oil has chemopreventive properties against colon cancer in lab animals. Pomegranate juice's anti-inflammatory effects on the signalling proteins in the HT-29 human colon cancer cell line have been documented by Adams et al.^[46]. Pomegranate seed oil administration increased the expression of the PPAR gamma protein in the non-tumor mucosa and dramatically reduced the risk of developing colonic adeno-carcinomas.

The anti-inflammatory properties of pomegranate extract and its metabolite urolithin-A may be the most potent anti-inflammatory compound derived from pomegranate consumption in healthy individuals, whereas colon inflammation may be caused by the non-metabolized ellagitannin-related fraction, according to research by Larrosa et al. (1982) in the colitis in the rat model and the effect of colon inflammation on phenolic metabolism. According to findings by Kohno et al.^[46] pomegranate seed oil can inhibit azoxymethane-induced colon carcinogenesis, and this inhibition is associated in part with higher levels of conjugated linoleic acid in the colon and liver as well as higher levels of PPAR gamma protein expression in the colon mucosa.

ANTI-HEPATOCELLULAR CARCINOMA

Oxidative stress greatly stimulates hepatocellular carcinoma, a frequent and deadly malignancy. Hepatoprotective properties are present in the pomegranate peel. In vivo testing was done to see how pomegranate extract affected the development of hepatocellular carcinoma in DENA-induced liver cells. Due to reductions in hepatic nodule incidence, size, volume, and multiplicity, significant chemo-preventive potential was identified. Pomegranate extract also decreased the oxidation of proteins and lipids in the liver. pomegranate administration derived compounds in the treatment and prevention of hepatocellular in humans were suggested and supported by Bishayee et al.^[47]

Rats fed on pomegranate pulp had potential to be protected from the toxicity of carbon tetra chloride. The antioxidant property of the pomegranate pulp was demonstrated in studies in rats with carbon tetra chloride toxicity-induced liver damage. Pomegranate pretreatment increased or retained the free radical inhibiting activity of the hepatic enzymes catalase, superoxide, peroxidase, and dismutase, and resulted in a 54% decrease of lipid per-oxidation values compared to control groups. By reducing hepatic oxidation, Bishayee et al.^[49] showed that pomegranate bioactive components have a chemo protective effect against diethylnitrosamine-induced rat liver carcinogenesis. Pomegranate's chemo-preventive properties are strong against hepatic cancer, probably due to antioxidant signalling systems

that do not manifest as toxicity. Pomegranate bioactive substances cause apoptosis, control cell cycle progression, and limit cell proliferation in Sprague-Dawley rats.^[47]

APPLICATION OF POMEGRANATE IN TRADITIONAL MEDICINE

Traditional uses of *Punicagranatum L* fruit include the flowers, leaves, bark of young shoots and roots, fruit peel, and pomegranate sauce.^[48] All *Punicagranatum L* fruit parts with high tannins display relatively significant astringent effects. Traditional medicines have used a variety of infusions or decoctions of the plant's flowers to treat simple diarrhoea, vaginal discharge, and also this extract combined with pomegranate peel have typically been gurgled to relieve pancreas inflammation.^[52] Refreshing juice of *Punicagranatum L* fruit is advised to heal gallbladder diseases.

Strong tannin found in the fruit is thought to be a bitter food. Its decoction seems to be effective in treating conditions including common diarrhoea, dysentery, and stomach issues. 222 *Journal of Evidence-Based Complementary & Alternative Medicine* 21(3)^[49] Pomegranate seeds' tannin concentration, however, is not very noteworthy, and they are typically used to treat women's vaginal discharge and wound healing. Due to the presence of alkaloid compounds, fresh or dried root barks or pomegranate ethanol extracts are used to get rid of intestinal parasites. Due to its antibacterial and anti-inflammatory qualities, it is also utilised in conventional medicine.^[50]

CONCLUSION

According to the review's findings, in addition to safeguarding the health of the mouth and skin, it may even help prevent and stop the development of some cancers. Very rarely do side effects occur. Anticancer, anti-inflammatory, anti-atherogenic, anti-diabetic, hepato protective, antioxidant, and other therapeutic effects have been described for all fruit portions. The current study provides solid evidence that pomegranate-derived compounds have anticancer, anti-inflammatory, and anti-proliferative characteristics. This is especially true of their anticancer properties. For their pharmacological actions against major illnesses such stomach ulcers, cardiovascular diseases, digestive problems, liver, colon, and prostate cancers, they have attained widespread acclaim. This fruit and its peel have the ability to stop some human carcinomas from developing thanks to their cytoprotective and inhibitory properties. Numerous substances, such as polyphenols, alkaloids, and vitamins with strong free radical scavenging activities, can be found in pomegranates. Free radicals have the potential to generate oxidative stress, which can harm biomolecules and result in a variety of chronic diseases, including cancer, diabetes, atherosclerosis, Alzheimer's disease, nephrotoxicity, hepatotoxicity, pain, and other degenerative conditions. The presence of certain substances, such as ascorbic acid and phenolic compounds, such as punicalagin, punicalin, gallic acid, ellagic acid, and anthocyanins, has been linked to the pomegranate's antioxidant action.

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