ABSTRACT
The pomegranate, Punica granatum L., is an ancient, mystical, unique fruit borne on a small, long-living tree cultivated throughout the Mediterranean region, as far north as the Himalayas, in Southeast Asia, and in and Arizona in the United States. In addition to its ancient historical uses, pomegranate is used in several systems of medicine for a variety of ailments. The synergistic action of the pomegranate constituents appears to be superior to that of single constituents. In the past decade, numerous studies on the antioxidant, anticarcinogenic, and anti-inflammatory properties of pomegranate constituents have been published, focusing on treatment and prevention of cancer, cardiovascular disease, diabetes, dental conditions, wound healing, bacterial infections and antibiotic resistance, and ultraviolet radiation-induced skin damage. Other potential applications include Alzheimer’s disease, arthritis, myocardial infarction and obesity. The health benefits of pomegranate have been attributed to its wide range of phytochemicals, which are predominantly polyphenols, including primarily hydrolyzable ellagitannins, anthocyanins, and other polyphenols. The aim of this review was to present an overview of the phytochemical and pharmacological properties of P. granatum.

Keywords: Punica granatum L.; Phytochemicals; Pharmacological properties.

INTRODUCTION
History: The genus punica consists at the present time of two species, the one under consideration and P. protopunica, described in 1882 by Balfour, from the island of Socotra. The pomegranate, Punica granatum L., is one of the oldest known edible fruits. This fruit is mentioned in the Bible and Koran and is often associated with fertility. In the ancient Egyptian culture the pomegranate fruit was regarded as a symbol of prosperity and ambition, making it common practice to decorate sarcophagi with depictions of the plant.

Distribution: The pomegranate tree is native from Iran to the Himalayas in northern India and has been cultivated since ancient times throughout the Mediterranean region of Asia, Africa and Europe.

Local Names: Despite its ancient background, the pomegranate has acquired only a relatively few commonly recognized vernacular names apart from its many regional
epithets in India, most of which are variations on the Sanskrit dadima or dalim, and the Persian dulim or dulima. By the French it is called grenade; by the Spanish, granada (the fruit), granado (the plant); by the Dutch, granaatappel, and Germans, granatapfel; by the Italians, melogranato, melograno granato, pomo granato, or pomo punico. In Indonesia, it is gangsalan; in Thailand, tab tim; and in Malaya, delima. Brazilians know it as roma, romeira or romazeira. The Quechua Indian name in Guatemala is granad. The Samoan name is limoni. The generic term, Punica, was the Roman name for Carthage from whence the best pomegranates came to Italy.

Family: Punicaceae

Botanical Description: An attractive shrub or small tree, to 20 or 30 ft (6 or 10 m) high, the pomegranate is much-branched, more or less spiny, and extremely long-lived, some specimens at Versailles known to have survived two centuries. It has a strong tendency to sucker from the base. The leaves are evergreen or deciduous, opposite or in whorls of 5 or 6, short-stemmed, oblong-lanceolate, 3/8 to 4 in (1-10 cm) long, leathery. Showy flowers are borne on the branch tips singly or as many as 5 in a cluster. They are 1 1/4 in (3 cm) wide and characterized by the thick, tubular, red calyx having 5 to 8 fleshy, pointed sepals forming a vase from which emerge the 3 to 7 crinkled, red, white or variegated petals enclosing the numerous stamens. Nearly round, but crowned at the base by the prominent calyx, the fruit, 2 1/2 to 5 in (6.25-12.5 cm) wide, has a tough, leathery skin or rind, basically yellow more or less overlaid with light or deep pink or rich red. The interior is separated by membranous walls and white spongy tissue (rag) into compartments packed with transparent sacs filled with tart, flavorful, fleshy, juicy, red, pink or whitish pulp (technically the aril). In each sac, there is one white or red, angular, soft or hard seed. The seeds represent about 52% of the weight of the whole fruit.
CHEMICAL CONSTITUENTS

Pomegranate is an amazing source of cyaniding, delphinidin (both are anthocyanidins), caffeic acid, chlorogenic acid (both are phenolic acids), luteolin, quercetin (flavones), kaempferol (a flavonol), naringenin (a flavanone) as well as 17-alphaestradiol, estrone, estriol, testosterone, betasistosterol, coumesterol, gamma-tocopherol, punicie acid. [1]

Hydrolysable tannin including ellagittannin and gallotannin constitute most prevalent compound present in various part of pomegranate. The most abundant of these polyphenols is punicalagin an implicated as being the bioactive constituent responsible for the juice’s potent antioxidant activity. Alkaloids are mainly present in bark, stem and fruit. There are mainly two types of alkaloid including piperidines and pyrrolidines reported in the plant such as pelleteirine, psuedopelleteirine, N-methylpsuedopelleteirine and norpsuedopelleteirine are major alkaloid of root and bark. [2]

Two new compounds, coniferyl 9-O-[beta-D-apiofuranosyl(1-->6)]-O-beta-D-glucopyranoside and sinapyl 9-O-[beta-d-apiofuranosyl(1-->6)]-O-beta-D-glucopyranoside , were isolated from the seeds of Punica granatum (pomegranate), together with five known compounds, 3,3'-di-O-methylellagic acid, 3,3',4'-tri-O-methylellagic acid, phenethyl rutinoside, icariside D1, and daucosterol. [3]

PHARMACOLOGICAL PROPERTIES

Wound healing activity

In the study wound healing activity of Punica granatum ethanolic flower extract was evaluated. The percentage of wound closure was calculated. The wound area measurement showed the wound size of the test groups were reduced early as compared
to control group. The best results of histopathological evaluation were obtained with Punica granatum, when compared to the other groups as well as to the control and the standard drug. These results offer pharmacological evidence on the folkloric use of Punica granatum flowers for healing wounds.\textsuperscript{[4]} Punica granatum leaves and fruit rinds have also been shown to be effective in wound healing.\textsuperscript{[5]} Tannins, polyphenol and flavanoids are the major phytoconstituents present in P. granatum plant which may be responsible for wound healing action tannins promote the wound healing through the several cellular mechanisms; chelating of the free radicals and reactive species of oxygen promoting contraction of the wound and increasing the formation of capillary vessels and fibroblasts.\textsuperscript{[6, 7]} Moreover, flavonoids and their derivatives are known to decrease lipid peroxidation by improving vascularity and preventing or slowing down the progress of cell necrosis.\textsuperscript{[8]} Flavonoids are also known to endorse wound healing processes primarily owing to their antimicrobial and astringent properties, which appear to be responsible for wound contraction and elevated rate of epithelisation.\textsuperscript{[9]}

Antidiarrhoeal activity

The Methanol extract of Punica granatum seed has inhibitory effect on castor oil induce diarrhea and PGE\textsubscript{2} induce entero pooling in rat.\textsuperscript{[10]} The aqueous extract of Punica granatum peels was evaluated for anti diarrheal activity using diphenoxylate as positive control. The results revealed that, in a dose-dependent manner, the aqueous extract of Punica granatum peels appears to contain substance(s) that reduced diarrhea by inhibiting intestinal motility and intestinal fluid accumulation. The antidiarrheal activity of Punica granatum peels extract could be due to several mechanisms: (1) The extract may increase the reabsorption of water and NaCl by decreasing intestinal motility. (2) Reduced mucosal secretion, and (3) inhibition of prostaglandin release from intestinal mucosa.\textsuperscript{[11]} Tannates are known to reduce mucosal secretion and make the intestinal mucosa more resistant\textsuperscript{[12, 13]} Flavonoids and alkaloids are known for inhibiting release of autocoids and prostaglandins, thereby mucosal inhibiting secretion\textsuperscript{[14, 15]}. The anti diarrheal activity of Punica granatum may be due to anti bacterial effect of hydrolysable tannin\textsuperscript{[16]}.

Antidiabetic activity:
The Punica granatum has hypoglycemic activity noted from its flowers, seeds, and juice in canons of the traditional folk medicines of India. Punica granatum seed, rind and flower have shown anti diabetic effect in alloxan-induced diabetic albino rats. The extracts of seeds and rind significantly reduced the rise in blood glucose induced by alloxan, with the rind extract exhibiting significantly better activity than seed extract. Both the extracts also produced significant increase in liver glycogen and significantly reduced adrenaline-induced hyperglycemia. The antidiabetic effect of these extracts may be partly, due to their positive effect on glycogen synthesis in liver, skeletal muscle and heart muscle, and partly, due to their stimulatory action on insulin release. These results support strong antidiabetic action in favor of P. granatum seed and rind extracts \[17\] The antidiabetic activity of the seed and rind of P. granatum might be attributed to the presence of tannins, flavonoids and phenolic glycosides, known to be natural antioxidants \[18\] Punica granatum flower extract have also shown significant antidiabetic activity and the results suggest that the anti-diabetic activity of PGF extract may result from improved sensitivity of the insulin receptor. Phytochemical investigation demonstrated that gallic acid in PGF extract is mostly responsible for this activity \[19\]. The antidiabetic effect of flower may be due to increase peripheral glucose utilization and retardation of intestinal glucose absorption may be partly responsible \[20\] Recent research suggests pomegranate flowers and juice may prevent diabetic sequelae via peroxisome proliferator-activated receptor-gamma binding and nitric oxide production. Pomegranate compounds associated with antidiabetic effects include oleanolic, ursolic, and gallic acids \[21\].

Antimicrobial Activity:
Punica granatum has been used for many years in folk medicine for its antimicrobial effect. Punica granatum has been used extensively as a traditional medicine in many countries for the treatment of dysentery, diarrhea, helminthiasis, acidosis, hemorrhage and respiratory pathologies. In the study, the Punica granatum peel extract (PGPE) exhibited antibacterial activity against all 16 strains of eight different Salmonella serotypes S. typhi ATCC 19943, S. paratyphi A, S. enteritidis, S. typhimurium, S. typhimurium, S. typhimurium, S. enteritidis, S. typhimurium, S. dublin ATCC 39184, S. derby ATCC 6960, S. choleraesuis ATCC 7001, S. gallinarum, S. gallinarum, S.
gallinarum, S. gallinarum and S. gallinarum ATCC 9184. The PGPE also exhibited antibacterial activities against Salmonella strains JOL 389, JOL 411, JOL 419, JOL 420, JOL 421 and JOL 423, all of which have been shown to be resistant to two to five antibiotics. The in vivo antibacterial assay also revealed that the extract effectively inhibited the growth of S. typhimurium and significantly reduced mouse mortality. Furthermore, clinical signs of infection and histological damage were rarely observed in test mice. In another study author proved that methanolic extracts of peels were more active than water extracts against E. coli, S. aureus and B. subtilis. The antibacterial activity of pomegranate peels may be indicative of the presence of some metabolic toxins or broadspectrum antibiotic compounds. The mechanism responsible for phenolic toxicity to microorganisms was related to reaction with sulfhydryl groups of proteins and unavailability of substrates to microorganism. Pomegranate extracts interfered with bacterial protein secretions. Punica granatum peel methanolic extract was also effective against some common oral pathogens such as S. epidermidis, S. aureus, L. acidophilus, S. mutans, S. sanguinis and S. salivarius, but not effective against A. viscosus and C. albicans. Another study reported that alcohol extracts of pomegranate fruits showed antibacterial activity when tested against S. aureus, E. coli, and Shigella dysenteriae. Another study antimicrobial activities of Punica granatum from six different cultivars were evaluated. The extracts obtained from fruits of six popular pomegranate cultivars were found to be effective against the bacteria B. megaterium, P. aeruginosa, S. aureus, C. xerosis, E. coli, E. faecalis and M. luteus. There were significant differences between the inhibition effects on different microorganisms. For example, the highest inhibition was obtained for E. coli, while the lowest was observed for E. faecalis. The inhibition responses also varied among pomegranate cultivars. In another study author showed that methanol, ethanol, acetone, and water extracts obtained from pomegranate were active and effective against the tested microorganisms (S. aureus, E. coli, Salmonella typhi, Vibrio cholera, S. dysenteriae, S. sonnei, S. flexneri, S. boydii) The amphipathicity of these compounds can explain their interactions with bio-membranes and thus the antimicrobial activity. In fact, the hydrophilic part of the molecule interacts with the polar part of the membrane, while the hydrophobic benzene ring and
the aliphatic side chains are buried in the hydrophobic inner part of the bacterial membrane\textsuperscript{[28]}

**Antihelmentic Activity:**

Methanolic extracts from the leaves of Pergularia daemia Linn. and leaves of \textit{Punica granatum} are investigated for their anthelmintic activity against the earthworm \textit{Pheretima posthuma}. Dose dependent activity was observed in both plant extracts. Both the extracts exhibit significant anthelmintic activity at highest concentration of 150 mg/ml.\textsuperscript{[29]}

**Antioxidant activity**

Biological and chemical research in Life Science evidenced that free radical and reactive oxygen species can be involved in a high number of diseases. An \textit{in vitro} assay using four separate testing methods demonstrated pomegranate juice and seed extracts have 2-3 times the antioxidant capacity of either red wine or green tea\textsuperscript{[30]} The antioxidant substance mainly exist in fruit and leaves including seed, juice and pericarp. Aqueous & alcoholic extracts of \textit{Punica granatum} fruit rind has been studied for its antioxidant properties. \textit{Punica granatum} fruit rind extracts showed good antioxidant effect in various in vitro model. On the basis of the results author concluded that the extracts contain higher quantities of phenolic compounds, which exhibit antioxidant and free radical scavenging activity. It also chelates iron and possesses reducing power.\textsuperscript{[31]} Juice and aqueous extract of leaves can effectively scavenge free radicals such as reactive oxygen species (ROS), reactive nitrogen species (RNS), super oxide, hydrogen peroxide H\textsubscript{2}O\textsubscript{2} and the effect was significantly superior than the extract of other fruits.\textsuperscript{[32, 33, 34, 35], Another study demonstrated correlation coefficients of total phenols and total flavonoids to the antioxidant activity measured through the ABTS and DPPH methods either in peel or juice.\textsuperscript{[36]} In the comparative study of \textit{Punica granatum} peel extract and pulp extract, the results showed that pomegranate peel extract had markedly higher antioxidant capacity than the pulp extract in scavenging or preventive capacity against superoxide anion, hydroxyl and peroxyl radicals as well as inhibiting CuSO\textsubscript{4}-induced LDL oxidation.\textsuperscript{[37]} The antioxidant constituent of pomegranate mainly comprise of the compound with phenolic hydroxyl groups and double bonds including tannin, flavanoid and unsaturated fatty acid. Tannin posses ability to donate proton as well as to form a stable free radicals.\textsuperscript{[38]} Pomegranate fruits constituent inhibited nuclear factor k B (NFkB) a transcription
factor activated by ROS and hence implicated in pathophysiology of numerous disease. \[39\] Two namely ellagic acid and punicagalin are considered to play important role in antioxidant activity of tannin in pomegranate.\[40\] Ellagic acid can react with free radical due to its ability to chelate with metal ions, is a potent antioxidant against lipid peroxidation in mitochondrion and microsomes.\[41\] Punicagalin contribute to antioxidant action due to its inhibition of lipid peroxidation. This kind of inhibition is due to its ability to provide electrons so as to eliminate free radicals resulted from lipid peroxidation.\[42, 43\]

Artherosclerosis

A recently reported study on the supplementation of pomegranate juice (PJ), pomegranate fruit liquid extract (POMxl), pomegranate polyphenol powder extract (POMxp), or pomegranate ground flowers extract (POMf) in an atherosclerotic mouse model for 3 months revealed a significant reduction in the atherosclerotic lesion area compared to the water-treated group.\[44\] Interestingly, the largest decrease in lesion area (70%) was observed in mice supplemented with POMf, which had the highest content of total dietary fiber (30.2%) among all fruit parts, and also led to a concomitant decrease in serum glucose and cholesterol levels, compared to the placebo group. PJ led to a significant reduction in the atherosclerotic lesion area (44%), had no effects on serum glucose and lipid levels, caused a significant decrease in native LDL uptake by the peritoneal macrophages in mice, and stimulated HDL-mediated cholesterol efflux from mice peritoneal macrophages, compared to the placebo animals. While PJ had no fiber and a higher polyphenol content (3600 mg/mL) compared to POMf (166 mg/gm), the latter led to a larger decrease in lesion area, which the authors attribute to the synergistic action of polyphenols, dietary fiber, and other carbohydrates in POMf. The anti-atherogenic and vasculoprotective activities of pomegranate fruit or extracts have also been shown previously in mouse models.\[45, 46\] The principal mechanisms of action of pomegranate juice may include the following: increased serum antioxidant capacity, decreased plasma lipids and lipid peroxidation, decreased oxidized-LDL uptake by macrophages, decreased intima media thickness, decreased atherosclerotic lesion areas, enhanced biological actions of nitric oxide, decreased inflammation, decreased angiotensin converting enzyme activity, and decreased systolic blood pressure, thereby causing an overall
favorable effect on the progression of atherosclerosis and the subsequent potential development of coronary heart disease. Another study reported that pomegranate juice exerts a direct effect on macrophage cholesterol metabolism by reducing cellular uptake of oxidized LDL and inhibiting cellular cholesterol biosynthesis. Both of these processes eventually lead to a reduction in macrophage cholesterol accumulation and foam cell formation and attenuation of atherosclerosis development. Another study suggest that pomegranate juice can exert beneficial effects on the evolution of clinical vascular complications, coronary heart disease, and atherogenesis in humans by enhancing the endothelial nitric-oxide synthase (NOSIII) bioactivity because the pomegranate juice reverts the potent down-regulation of the expression of NOSIII induced by oxidized low-density lipoprotein (oxLDL) in human coronary endothelial cells. Pomegranate juice inhibited atherogenic modifications of LDL, including its retention, oxidation, and aggregation. The antiatherogenicity capability of pomegranate juice is related to 3 components of atherosclerosis: plasma lipoproteins, arterial macrophages, and blood platelets. The potent antioxidative capacity of pomegranate juice against lipid peroxidation may be the central link for the antiatherogenic effects of pomegranate juice on lipoproteins, macrophages, and platelets.

Myocardial Infarction

The study was designed to investigate the effect of aqueous extract of Punica granatum flower (PG) against isoproterenol (ISO) induced myocardial infarction (MI) in rats by studying cardiac markers and electrocardiographic changes. In the study, author observed an elevation of ST-segment, increased heart rate and QT interval in ISO treated rats, and pretreatment with PG markedly inhibited ISO induced ECG alterations. Extent of cardioprotection offered by the drug is associated with significant attenuation of serum LDH, CKMB, ALT, AST levels. The flower was found to be most effective in restoration of biochemical and ECG alterations in ISO induced MI. Another study determines the protective role of Punica granatum L. (Punicaceae) seed juice extract and its butanolic fraction in isoproterenol-induced myocardial infarction in male Wistar rats. Rats treated with isoproterenol showed a significant increase in heart rate, ST elevation in ECG, pressure rate index and a significant increase in the levels of cardiac marker enzymes-lactate dehydrogenase, and creatine kinase in serum. Isoproterenol significantly reduced
superoxide dismutase and catalase activity and increased vascular reactivity to various catecholamines. Pretreatment with PJ (100 mg/kg, p.o. and 300 mg/kg, p.o.) and B-PJ (100 mg/kg., p.o.) for a period of 21 days significantly inhibited the effects of ISO on heart rate, PRI, ECG patterns, levels of LDH, CK, SOD, CAT, and vascular reactivity changes. *Punica granatum* ameliorates cardiotoxic effects of isoproterenol and may be of value in the treatment of MI.[51]

Anti inflammatory activity

*Punica granatum* has been used for centuries as a therapeutic agent for the treatment of inflammatory diseases. The aqueous-ethanolic (50%) extracts of fruit rind (PGR), flower (PGF), and leaves (PGL) of *Punica granatum* have shown oral anti-inflammatory activity.[52] In the study, NO inhibition assay combined with column chromatography was used to determine which components in pomegranate would have effective anti-inflammatory activity. Four hydrolysable tannins, punicalagin, punicalin, strictinin A, and granatin B, were isolated from pomegranate by bioassay-guided fractionation. Each of them displayed a dose-dependently and significantly inhibitory effect on NO production in LPS-induced RAW 264.7 macrophage cells. The author found that granatin B could significantly decrease NO and PGE2 production through inhibiting NOS and COX-2 expression. Little NO production was found in LPS-induced RAW 264.7 for 8 h. [53] In another study the authors suggest that polyphenol-rich pomegranate fruit extract exerts its inhibitory effect on IL-6 and IL-8 expression via modulation of the activation and DNA binding activity of NF-kB. [54] The anti inflammatory compounds in pomegranate were mainly investigated in the seeds and result exhibited polyphenol and fatty acid were the major anti inflammatory constituents. Cold pressed pomegranate seed oil has been shown to inhibit both cyclooxygenase and lipoxygenase enzymes in *vitro*. Cyclooxygenase, a key enzyme in the conversion of arachidonic acid to prostaglandins (important inflammatory mediators), was inhibited by 37 percent by a CPSO extract. Lipoxygenase, which catalyzes the conversion of arachidonic acid to leukotrienes, also key mediators of inflammation, was inhibited by 75 percent by a CPSO extract. By comparison, an FPJ extract resulted in a 23.8-percent inhibition of lipoxygenase in *vitro*. [55] The polyphenol in cold press seeds oil were also reported to suppress inflammatory cell signalling in colon cancer cell [56]. There is a finding that acetone extracts of whole
pomegranate fruits (WPFE) inhibited phosphorylation of several cytokines in UV-B irradiated keratinocytes, including mitogen activated protein kinases (MAPK). The extracts also diminished activation of NF-κB \[^{[57]}\]. Another study reported that pomegranate extract could be particularly promising for dietary prevention of inflammation as it inhibited cytokine IL-8, prostaglandin PGE2, and nitric oxide secretion.\[^{[58]}\]

**Hepato toxicity**

The study evaluates ability of pomegranate flower extract to inhibit oxidative stress and the allied damage in vivo in Fe-NTA induced hepatotoxicity model. The amounts of endogenous hepatic antioxidants such as GSH and antioxidant enzymes including CAT, GPX and GR as well as the MDA levels showed a clear correlation with Fe-NTA induced hepatotoxicity. A weeklong pretreatment with pomegranate flower extract significantly prevented Fe-NTA induced oxidative stress and also inhibited hepatic injury the liver retained almost normal hepatic architecture, with much less pathological changes. Similar hepatoprotective effects have been reported with pomegranate peel extract, which inhibited CCl\(^4\) induced oxidative stress and hepatic injury.\[^{[59]}\]

**Anticarcinogenic activity**

A study reported that pomegranate fruit, pomegranate juice, pomegranate seed and seed oil act in prostate, breast, skin, colon, lung, oral and leukaemia cancers, through antioxidant, antiproliferation (growth inhibition, cell cycle disruption and apoptosis), antiangiogenisis and anti-inflammatory mechanisms of action. In mouse mammary organ culture (MMOC), an \textit{ex vivo} model for pre-cancerous tumor initiation via exposure to chemical carcinogen 7,12-dimethyl-benz[a]anthracene (DMBA), cold-pressed PSO resulted in up to an 87% reduction in tumor occurrence. Notably, 1g/ml PSO resulted in higher suppression than a 10g/ml dose suggesting that an optimal biological dose is more important and relevant than a maximally tolerated one.\[^{[60, 61]}\] Another study result reported that polyphenol in pericarp and seeds oil supressed proliferation xenograft and supression of human prostate cancer cells by 60% in vivo.\[^{[62]}\] \textit{Punica granatum} juice and extracts, which are rich sources of ellagitannins, have been shown to have chemopreventive potential against prostate cancer. POM inhibited the proliferation of Human prostate cancer cells (LNCaP) and human umbilical vein endothelial cells (HUVEC) cells
significantly under both normoxic and hypoxic conditions. POM decreased prostate cancer xenograft size, tumor vessel density, VEGF peptide levels and HIF-1alpha expression after 4 weeks of treatment in SCID mice. These results demonstrate that an ellagitannin-rich pomegranate extract can inhibit tumor-associated angiogenesis as one of several potential mechanisms for slowing the growth of prostate cancer in chemopreventive applications. The roseate fruit is exceptional in that various parts of the fruit, eg. seed oil, juice, fermented juice and peel extract have been shown to exert suppressive effects on human breast cancer cells in vitro. Both pomegranate extracts and genistein inhibit the growth of MCF-7 breast cancer cells through induction of apoptosis, with combination treatment being more efficacious than single treatments. Another study reported that pomegranate juice showed greatest antiproliferative activity against all cell lines by inhibiting proliferation from 30% to 100%. González-Sarrías and others (2009) suggest that EA and its colonic metabolites, urolithin-A and -B, at concentrations achievable in the lumen from the diet, might contribute to colon cancer prevention by modulating the expression of multiple genes in epithelial cells lining the colon. Some of these genes are involved in key cellular processes associated with cancer development and are currently being investigated as potential chemopreventive targets. Schubert and others (2002) have shown that pomegranate wine may serve as a potent inhibitor of NF-κB in vascular endothelial cells. It has been shown that pomegranate seed oil and polyphenols in the fermented juice retard oxidation and prostaglandin synthesis, inhibit breast cancer cell proliferation and invasion, and promote breast cancer cell apoptosis.

Antihypertensive

The renin-angiotensin system (RAS) with its effector hormone angiotensin II is a key regulator of blood pressure (BP). The pressor responses to Adr, NA, PE, Ang II and 5-HT were significantly (p<0.05) reduced in case of Ang II treated rats that received PJ extract (100 and 300 mg/kg/day, p.o.) for 4 weeks as compared to only Ang II treated rats. The study concluded that there was a significant correlation between the reduction in serum ACE activity and vascular reactivity to various drugs and thus reduction in ACE activity may contribute to lowering of blood pressure. It is known that reactive oxygen species (ROS) contribute to the pathogenesis of numerous cardiovascular diseases including hypertension. The study reveals pretreatment with pomegranate juice (PJ)
restored the antioxidant enzyme level and decreased TBARS level, which in turn indicate the protective effect of PJ against oxidative stress. The antioxidant activity, serum ACE inhibition activity and blockade of angiotensin receptor may be partly responsible for its antihypertensive action \[66\]. An earlier clinical trial also found reduced systolic blood pressure and serum angiotensin converting enzyme activity following 2 weeks of pomegranate juice consumption (50 mL/day) in 10 hypertensive subjects, adding further support to the anti-hypertensive effect of pomegranate juice. \[67\]. Many polyphenol such as punicaglais can increase production of endothelial nitric oxide (NO) which is a relaxing factor produced in the endothelium via activation of endothelial NO synthatase and act as a vasodilator indicating its antihypertensive effect. \[68,69\]

Alzheimer Disease

The neuroprotective properties of pomegranate polyphenols were evaluated in an animal model of Alzheimer’s disease. *Punica granatum* juice had shown had 50-percent less accumulation of soluble amyloid-beta and less hippocampal amyloid deposition suggesting *Punica granatum* juice may be neuroprotective. Animals also exhibited improved learning of water maze tasks and swam faster than control animals \[70\]. In another study, the antioxidative and neuronal protective effects of *Punica granatum* extract were investigated against oxidative stress induced cytotoxicity in PC12 cells. The ethanol extracts of *P. granatum* protected PC12 cells from hydrogen peroxide (H\(_2\)O\(_2\))-induced oxidative stress. To examine the effects of *P. granatum* on Amyloid β-induced learning and memory impairment in mice, *in vivo* behavioral tests were performed. Treatment with the extract of *P. granatum* increased step-through latency in mice injected with Amyloid id β. The results of this study suggest that the ethanol extract of *P. granatum* mitigated H\(_2\)O\(_2\)-induced oxidative stress in PC12 cells. In addition, the extract inhibited neuronal cell death caused by Amyβ-induced oxidative stress and Aβ-induced learning and memory deficiency \[71\]

Obesity

Cerdá and others (2003) investigated the effects of pomegranate extract (6% punicalagin) in female rats following exposure to a diet containing 20% of the extract for 37 d. A significant decrease in feed consumption and body weight of the animals during the early part of the study was noted \[72\]. *Punica granatum* flower extract given to obese
hyperlipidemic mice for five weeks caused significant decrease in body weight, percentage of adipose pad weights, energy intake, and serum cholesterol, triglyceride, glucose, and total cholesterol/HDL ratios. Decreased appetite and intestinal fat absorption were also observed. \[^{73}\] Its inhibition may correlate with inhibition of HMG-CoA reductase, pancreatic lipase and ACAT, as well as suppression of energy intake \[^{74, 75}\].

**Ultraviolet Radiation**

A pomegranate extract (PE) from the rind containing 90% ellagic acid was tested for its skin-whitening effect. The results suggest that the skin-whitening effect of PE was probably due to inhibition of the proliferation of melanocytes and melanin synthesis by tyrosinase in melanocytes. The peel (pericarp) is well regarded for its astringent properties; the seeds for conferring invulnerability in combat and stimulating beauty and fertility. Pomegranate has heuristic potential for facilitating skin repair in a polar manner, namely aqueous extracts (especially of pomegranate peel) promoting regeneration of dermis, and pomegranate seed oil promoting regeneration of epidermis. \[^{76}\] Another study described the protective and chemopreventive properties of standardized Punica granatum polyphenolic extract in human skin fibroblasts against UVA- and UVB-induced damage. The protective effects of pomegranate polyphenolics against UVA- and UVB-induced cell death of human skin fibroblasts may be attributed to reduced generation of intracellular ROS and increased intracellular antioxidant capacity. \[^{77}\]

**Toxicological studies**

various investigation focuses on the toxicity evaluation of Punica granatum L. (Punicaceae), Vourela et al, in chick embryo model, found that doses of the extract of less than 0.1 mg per embryo are not toxic. The LD50 of Punica granatum extracts administered intraperitoneally to mice was 731.1 mg/kg. Confidence limits are 565–945 mg/kg. No differences in acute toxicity in relation to sex were recorded. At the doses of 0.4 and 1.2 mg/kg of extract, the repeated intranasal administration to Wistar rats produced no toxic effects in terms of food intake, weight gain, behavioural or biochemical parameters, or results of histopathological studies. The results reported, together with the large safety margin considered, indicate the lack of toxic effect of punicalagin in rats. \[^{78}\]
Miscellaneous
In addition to the biological activities of pomegranate reported so far in the present work, others were also found during our database research. The extracts of flowers of *Punica granatum* were investigated for analgesic activity in mice using hot plate method. The various extract of the flowers showed significant analgesic activity at a dose of 50 mg/kg body weight. Pomegranate juice consumption led to an increase in epididymal sperm concentration, sperm motility, spermatogenic cell density, it also decreased the abnormal sperm rate when compared to the control group. The polyphenol in pericarp can significantly protect from ethanol induce gastric mucosal damage In another investigation extract of the leaves rich in tannin exhibited good gastro protective property. It increases activity of pepsin, secretion of bile, decrease secretion of gastric acid *Punica granatum* fruit rind extract was reported to have immunomodulatory effect. It enhanced the inhibition of leucocye migration in Leucocyte Migration Inhibition test and induration of skin in delayed hypersensitivity test with Purified Protein Derivative (PPD) confirming its stimulatory effect on cell-mediated immune response

CONCLUSION
In recent years, medicinal plants have been significantly studied for their phytomedicinal properties which brings known and unknown medicinal virtues. Phytochemical and pharmacological screening of *Punica granatum* Linn. reveals it as a valuable medicinal plant with numerous medicinal properties. Many new drugs can be developed from *P. granatum* to control several diseases with no side effects as it is from natural source. A typical research and developmental work needs to be carried out for its better therapeutic and commercial utilization.

REFERENCES


22. Jang-Gi Choi, Ok-Hwa Kang, Young-Seob Lee, Hee-Sung Chae, You-Chang Oh, Obiang-Obounou Brice, Min-San Kim, Dong-Hwan Sohn, Hun-Soo Kim, Hyun Park, Dong-Won Shin, Jung-Rae Rho, and Dong-Yeul Kwon. “In Vitro and In Vivo Antibacterial Activity of Punica granatum Peel Ethanol Extract against


39. Afaq F, Saleem M, Krueger CG, Reed JD and Mukhtar H 2005 “Anthocyanin-and hydrolyzable tannin-rich pomegranate fruit extract modulates MAPK and


For Correspondence:
Sharmin Soni
Email: sharmin.soni@yahoo.com