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Review Article

A PHYTOPHARMACOLOGICAL REVIEW OF *DADIM-PUNICA GRANATUM* LINN.

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ABSTRACT

Punica granatum Linn. is a well-known nature power fruit rich in natural bioactive constituents, edible phytoestrogen like substances and other nutritional elements, grown all over the world from Iran to Mediterranean region and Central Asia. It is also described in Ayurveda as *Dadim* for treating *Amlapitta, Raktapitta* and used as *Hridya* and *Atisaraghna*. It is used for its good nutritive values generally used in the form of *Avaleha, Swaras* or Juices and Jellies. Several studies conducted previously showed that pomegranate exhibits antibacterial and antifungal activity.

Description of pomegranate is being found since Vedic period. Pomegranate is mentioned in Rigveda also. Aacharya sushrut described pomegranate or *Dadim* (Sanskrit name) as a best fruit i.e. *Shrestha* under *Phalavarga*.

According to *Acharya Vagbhata*, *Dadim* is also included in *Shramghna* and *Hrudya Gana*. In various studies in human and rodent models, pomegranate juice has been found to wield antiatherogenic, antioxidant, anti-carcinogenic, and anti-inflammatory, antidiabetic, gastroprotective, hepatoprotective and nephroprotective activities. Several studies on the antioxidant, anti-carcinogenic, and anti-inflammatory and many more potential properties of various parts of pomegranate and its constituents have been already published. Many studies had proved the latent efficacy of pomegranate and its applications including male infertility, Alzheimer's disease, and obesity. So, the present study aims to discuss the collective information on pomegranate which can provide a summary to study the diverse array of biological actions of pomegranate and thus provide easy accessibility for treating various common diseases.

KEYWORDS: Nutritive Values, Antibacterial, antiatherogenic, antioxidant, anti-carcinogenic, and anti-inflammatory, antidiabetic.

INTRODUCTION

Pomegranate is an ancient individual nutritional fruit which encompasses innumerable biological activities due its rich source of natural bioactive constituents.

Description of pomegranate is being found since Vedic period. Pomegranate is mentioned in Rigveda also.

Aacharya sushruth[1] described pomegranate or *Dadim* (Sanskrit name) as a best fruit i.e., *Shrestha* under *Phalavarga*. According to *Acharya Vagbhata*[2], *Dadim* is also included in *Shramghna* and *Hrudya Gana*.

In Ayurved Pomegranate known as *Dadim*, is an important fruit known for its *Rochana, Deepana*, and *Hrudya* effect.[3]

It is described in *Brihattrayi* as *Hrudya*, and also described to be used in the treatment of *Grahani, Atisara*[4] because of its *Rochana*, *Deepan* and *Grahi* properties.

In European World also, the pomegranate fruit have also been praised since ancient times for its medicinal properties and is being considered sacred by many of the world's major religions.

Historical description and references of Pomegranate

There are several references of pomegranate seed as best-known contraceptives in Greek mythology, also various uses described in Bible and Babylonian Talmud.[5]

In Greek mythology, pomegranate has been stated to represent life, rejuvenation, marriages and various references are being found to elucidate the invincible use of pomegranate in ancient Zoroastrian ceremonies and domestic devotions.[6,7,8]

Pomegranate seeds are considered to be 613 in number which represent each of the Bible's 613 directives along with sanctity, fertility, and abundance.[9]

In Buddhism, pomegranate is considered as one of the three sacred fruits, along with citrus and peach, which symbolizes the occurrence of favorable influences.[10]

Pomegranate has been represented in Chinese ceramic art and considered to denote fertility, abundance, posterity, and numerous and righteous off springs, with a prosperous future in China.[11]

Pomegranate is considered as assign of revival and life eternal in Christian art, and is often found in devotional statues and paintings of the Virgin and Child.[12]

Islamic mythologies states that each pomegranate contains one seed that has come down from paradise and the fruit plays a distinct role in the ritual of marriages as a fertility symbol in the Bedouins of the Middle East.[13]

In India since ancient times, the pomegranate called as *Beejpur* in Sanskrit, meaning replete with seeds, is considered to indicates prosperity and fertility and is related with the earth goddess and Lord Ganesha, who is also called *Bijapuraphalasakta*, the one who is fond of the many-seeded fruit.[14]

Even in the present epoch, archaeologists have found carbonized pomegranate exocarps originated from the early Bronze Age (3000 BC), e.g., in Jericho and from the Late Bronze Age in Cyprus.[15]

Pomegranate and its various usages are being known since ancient times in different cultures throughout the world. Various scientific articles emphasizing the health benefits of pomegranate are published in numerous scientific journals describing its varied medicinal uses so, the aim of the present article is to study the vivid and varied aspects of medicinal uses and knowledge about the nature's power fruit – Pomegranate.

Botanical Description

It is a shrub or a small tree growing upto 12–16 feet, deciduous, globose, often with spines cent bracelets, leaves– opposite or sub opposite, often fascicled on short petioles, oblong or obviate, Flowers–terminal or axillary, red, white, large, solitary. Fruits are large globose having many seeds separated by membranous pericarp. Seed– angular, brown, wedge shaped having sweetish-sour taste. The leaves are glossy and lance shaped. The bark of the tree turns gray as the tree ages.[16] Powder is reddish brown and consisting few starch grains, oil globules, stone cells.

Botanical Classification [17]

Kingdom– Plantae

Subkingdom- Viridiplantae

Infrakingdom- Streptophyta

Super division- Embryophyta

Division-Tracheophyta

Subdivision Spermatophyta

Class- Magnoliopsida

Super order – Rosanae

Order - Myrtales

Family – Lytheraceae

Genus - Punica L.

Species - *Punica granatum L*.

Flowering period: April - June

Fruiting period: June - August

Distribution: Cultivated throughout India, mostly North West region.

Vernacular Names

Hindi: Anar, Sanskrit: *Dadimah*, English: Pomegranate, Marath: Dalimba, Gujarati: Dalimba, Bengali: Dadim, Tamil: Madalai, Telgu: Danimma, Malayalam: Talimatatalum, Pharsi: Anar tursa, Arabi: Roman: Hamiz, German: Granatapfels, Latin name- *Punica granatum*

Synonyms [18,19]

Dadimisar, Kuttim, Phalashadav, Madhuramla, Raktabeeja, Dantabeeja, Shukapriya, Karak, Raktakusum, Balmarka, Swadamla, Rasalak, Lohitpushpa, Lohitpushpak, Vruttaphala, Shukeshta, Pathyakari, Manibeeja, Madhubeeja, Kuchaphala, Shukavallabha, Valkphala.

Gunadharma[20]

Aacharya Bhavprakash mentioned *Dadim* in *Aamradiphala Varga* (102-104) has *Madhur Snigdha rasa, Kashaya anurasa, Sheeta veerya, Madhur vipaka, Laghu guna* having effect of *Trushajwara nashak, Tarpana, Shukrala, Grahi, Medhavardhan, Balavardhan.*

Species

Socotran pomegranate or *Punica protopunica*.

Varieties of *Punica granatum* Linn.

According to *Dhanvantari Nighantu* there are two varieties of *Dadim* [21]

1. *Madhur* and 2. *Amla*

And *Kaiyyadeva and Bhavaparakash Nighantu*[22] had described one more variety –*Svadvamla.* Nowadays different breeds and seedless varieties are available.

Flowering period: April - June

Fruiting period: June - August

Distribution: Pomegranate plants are cultivated throughout the world including India, Iran, European countries, etc.

Cultivation: Grown as a fruit crop plant and as ornamental trees. Mature specimens develop sculptural twisted bark multi trunks and distinctive

overall form. Pomegranate is drought resistant and can be grown in dry areas.

Harvesting: When fruits are ripe they have change in a colour and make a metallic sound when tapped. The fruits must be picked before over maturity when they tend to crack open particularly when rained on.

Habitat

Pomegranate is an excellent tree cultivated in widely across the world especially in Central Asia region, Iran, Afghanistan, Baluchistan, Mediterranean, in tropical and subtropical areas. It is found in Himalayan and all over India.

Parts used: Fruit, fruit rind, root bark, floral bud, seeds, seed oil.

Properties[22]

Guna– Laghu, Snigdha, Rasa– Kashya, Madhura, Amla, Virya– Sheeta, Vipak– Madhur (*Madhur* variety), *Amla* (*Amla* variety). *Karma– Tridoshahara, Hrudya, Skrala, Grahi*

Dosha karma–Tridoshahar, Dhatu– Rakta, Mala– Sangrahi, Mutra– Daha shamak

Mainly acts as– *Hridya, Kanthya* etc.

Major chemical constituents

1. **Each fruit grain (*Anardana*)–** Moisture 78%, Carbohydrates 18.79 %, Minerals 0.7%, Calcium 10mg, Magnesium 12mg, Oxalic acid 14mg, Phosphorus 70mg, Sodium 0.9mg, Potassium - 259mg, Copper 0.2 mg, Sulphur 12mg, Chlorine 2mg, Iron – o.3-1.2 mg, Zn -0.3 mg,

   Nicotinic acid 0.30mg

   Nutritive values [23]

   Energy -346KJ(83 KCal), Proteins 1.6 %, Fats – 1.2 gm, Dietary fibres 5.1%, Thiamine Vit B1 - 0.06 mg, Riboflavin Vit B2 - 0.10mg, Pantothanic acid Vit B5 – 0.38%, Niacin Vit.B3 – 0.29mg Vit B6 – 6%, Vitamin C - 14 mg/100mgs.

   Folate B9 - 38µg
2. **Seed**- estrone, punicic acid
3. ***Swaras***- reducing sugars- 7.8-13.7 gms/ 100mgs, tannins, sucrose, galactose, citric acid 90 %
4. **Fruit peels**- resin 4.5, manitol 1.8, sugars 27, inulin 1, mucilage 0.6, tannin 10.4, galic acid 4, calcium oxalate 4, pectin 2-4%

   Tannins like– punicalin, punicalogin
5. ***Kanda twak, Mula twak***– alkaloids, Pelletierine, isopelletierine, etc alkaloids which are mainly effective in tape worms.[24]

Formulations

Dadim chatusam, Dadimashatak, Dadimadi churna, Dadimadya taila.

Doses

Phala swaras-20-50ml, *Twak kwath*-40-80 ml

Food uses/edible uses:

Juice, *Avaleha*, paste, Jellies, etc.

Table 1: Chemical constituents and biological activities of parts of *Punica granatum*

Parts	Constituents	Biological activities
Stem	N-methylisopelletierine, Anthocyanidins Pelargonidin, ellagotannins,[25] Gallic acid alkaloids, Pelletierine, isopelletierine[26]	Anthelmintic
Seeds oil	steroidal estrogen, estrone, Non-steroidal comesten, coumestrol, and the isoflavones, genistein and daidzein Punic acid, sterols[27]	Suppressive effect on breast cancer Antioxidant property
	Masclinic acid, Gallic acids, Ursolic acid, Triterpinoids, Fatty acids[28]	Diabetes
Rind	Alkaloids, Glycosides, Saponin, Tannins, Vitamin C Free Amino Acids, Protein[29]	bactericidal, antiviral, antitumor

Pharmacological activities of Pomegranate

Pomegranate is a commonly available fruit cultivated all over the world and comprising various promising therapeutic activities such as Antibacterial, Anti-inflammatory, Immuno-modulatory, Antitumor, Wound healing, Antifungal that have been attributed to the different constituents of its seeds, bark, juice, pericarp[30] etc, discussed as follows.

Anticarcinogenic activity

A study was conducted on mice, the mice model was prepared by inducing the prostate cancer lines - DU-145, LNCAP, PC-3 cells, the cells were then separated and study was conducted by treating these cells with various forms of pomegranate like - seed oil obtained by cold pressing, polyphenols obtained after fermentation of pomegranate juice, and also polyphenols obtained from pericarp of pomegranate.

The study determined their inhibitory action on the growth of prostate cancer cells. It was found to cause cell cycle disruption, and induced apoptosis by modulation of the proteins regulating apoptosis.[31, 32] thereby reducing and hindering the tumor growth.[33,34]

Various newer researches also suggest inhibitory cyclooxygenase (COX) and lipoxygenase enzymes[35] and also inhibitory angiogenesis action of pomegranate seed oil and fermented juice polyphenols through the down regulation of growth factor in MCF-7, of the vascular endothelium of breast cancer cells and also in the human umbilical vein endothelium cells.[36]

In another study, pomegranate plant was divided into anatomical structures such as seed, bark, leaf, flower, roots, juice, peels and study was conducted in which results showed that the juice, peel and oil showed anticancer activity.[37]

Action in Leukemia

In an invitro study, pomegranate juice extract was tested with leukemia cells, it was observed that pomegranate juice extract showed potential effect on the process of induction of apoptosis in the leukemia cells and also caused inhibition of cellular proliferation in lymphoid and myeloid leukemia and also in non-tumor hematopoietic stem cells which were used as control. Pomegranate juice extracts induced apoptosis considerably in all cell lines, including non-tumor control cells, but lymphoid cells and myeloid cells showed better response. The DAPI analysis and the count for viability of leukemia cells carried out with the help of trypan blue exclusion assay indicated that the pomegranate juice extract proved to be efficient to inhibit the cell cycle. This proved that pomegranate juice extract contains potent constituents or bioactive contents which prove efficient to treat leukemia.[38]

Antidiabetic activity

The pomegranate flower and peel aqueous extract has been observed causing improvement in insulin sensitivity, thus reducing glucose levels in a study conducted in alloxan induced diabetic rats. It inhibited alpha-glucosidase activity and caused regeneration of pancreatic beta cells.[39, 40]

Antinociceptive

A study was conducted to assess the anti-inflammatory and antinociceptive effect of pomegranate invitro, it was observed that pomegranate shows potent antinociceptive and anti-inflammatory activity[41] due to its various active constituents.

Hepatoprotective activity

In a study conducted on animal model of type II diabetes and obesity, it was observed that pomegranate flower significantly reduced the associated fatty liver by activating the hepatic expression of genes responsible for the fatty acid oxidation.[42]

In an animal experiment in mice, hepatotoxicity and resultant oxidative stress was induced by ferric nitrilotriacetate (Fe-NTA) and pomegranate flower extract was induced at a dose of at a dose of 50-150 mg / kg body weight, for a week, it weight, for a week, it was observed that the flower extract reduced the hepatic lipid peroxidation rate up to 60%, it increased glutathione (GSH) levels and also increased the activities of the antioxidant enzymes such as catalase (CAT) up to 36%, glutathione – up to 28.5%, peroxidase (GPX)–up to 28.7%, glutathione reductase (GR)- 40.2%, and glutathione-S-transferase (GST) up to 42.5%. It also caused protection of liver which was observed from the inhibition of liver markers like aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), bilirubin, and albumin, in the serum. It reduced the histopathological changes like ballooning degeneration, fatty changes, and Necrosis which were induced by Fe-NTA. This study proved that the pomegranate flower is an effective antioxidant and hepato protective drug.[43]

Cardioprotective action of pomegranate

A randomized, placebo-controlled, double-blind study was conducted to assess the effect of daily intake of Pomegranate juice in 45 patients of myocardial ischemia and Coronary Heart Disease (CHD). Daily intake of juice was advised for three months. After three months it was observed that the level of stress-induced ischemia was reduced in the trial group and increased in placebo control group. From this observation, the researchers concluded that pomegranate juice is effective in reducing the stress-induced myocardial ischemia in the patients of CHD with daily consumption and this effect may be due to the antioxidants (polyphenols), tannins or anthocyanins which shows anti-atherosclerotic activity.[44]

In another study, it was observed that Pomegranate juice inhibits serum angiotensin converting enzyme activity, thus reducing blood pressure and cardiovascular diseases.[45]

Pomegranate juice concentrate decreased cholesterol absorption, increased fecal cholesterol excretion, and improved cholesterol metabolizing enzymes, PPAR-gamma, etc. thus improving total / HDL and LDL / HDL cholesterol ratio.[46]

Skin diseases

Polyphenol containing food commodities like fruits, vegetables, dry legumes, and beverages have been proved to be a protective and efficient factor for the treatment of skin damage occurring due to UV radiation.

Pomegranate is a fruit which is a rich source of polyphenols exploring various pharmacological activities like anti-inflammatory, antioxidant, and anti-carcinogenic revealed in several in vivo and invitro studies.

An invitro study was conducted to assess the effect of pomegranate fruit juice extract which was standardized to punicalaginsin UV-A and UV-B rays induced skin damage in the model of SKU-1064 human skin fibroblast cells.

Pomegranate juice extract was used in a range of 5 to 60 mg/L, it was observed that PJE efficiently protected the human skin fibroblasts and reduced cell death, may be due to the factor that PJE reduced the induction of the pro-inflammatory transcription factor NF-kappa B, and pro-apoptotic caspase-3 associated with an increase in G 0 / G 1 phase and enhanced the process of DNA repair of the damaged skin cells. From these results the researchers concluded that the pomegranate fruit extract shows protective effects against UVA and UVB-induced cell damage and can be used effectively as source of polyphenols in topical applications.[47]

In another experimental study on UV B irradiated human skin damage and pigmentation, oral administration of pomegranate fruit extract was observed to be effective photoprotective agent by reducing the area of pigmentation due to presence of Ellagic acid as it caused the collagen breakdown and inflammatory processes. This was proved in the above study as it was observed that ellagic acid reduced the induced skin photo toxicity of HaCaT keratinocytes and human dermal fibroblasts. It was observed that ellagic acid also prevented the degradation of collagen by blocking matrix metalloproteinase enzyme production from the fibroblast due to UV-B-exposure.

In an animal study, antiwrinkle activity of ellagic acid was observed using the above extract for topical application of 10 µmol/l, on UV B skin damage (exposed for 8 weeks) induced SKH-1 hairless mice, as it reduced the epidermal thickening and even further wrinkle formation. It was observed to reduce production of pro-inflammatory cytokines, IL-1beta and IL-6, and caused the blockage of infiltration of inflammatory macrophages in the integuments. Thus, the study proved that the fruits rich in ellagic acid may be a promising source of skin wrinkle, aging, damage caused due to UV exposure or photoaging.[48]

Gastroprotective

In another study, gastric ulcers were induced in rats by alcohol, indomethacin and aspirin, and these rats were treated by aqueous methanolic extract of pomegranate fruit. It was observed that the gastric ulcer lesion index was significantly reduced, along with reduction in total acidity by increasing the gastric pH and mucus secretion.[49]

Obesity

Various plant-based medicines have been proved effective in treating obesity and can be helpful to reduce the adverse effects of the present chemically synthesized anti-obesity drugs.

In a study on pomegranate fruit extract in obesity, it was observed that pomegranate fruit extract exhibits significant results in reduction of fat in the obese patients. It was observed that the beneficial effect was due to the presence of anthocyanins, tannins, very high levels of antioxidants, polyphenols and flavonoids.[50]

Activity against Trichomonial Vaginalis

Trichomoniasis vaginalis is an important worldwide gynecological ailment treated with antifungal drugs like Metronidazole. Various metronidazole resistant cases have been observed which leads to unpleasant adverse effects and cause repeated vaginal trichomoniasis which is found to be challenging to treat with the present drug regimens. In an invitro and in vivo study conducted on T. vaginalis infected female patients, pomegranate juice extract caused effective and complete cure of the trichomonial infection. This proved the anti-*trichomoniasis vaginalis* activity of pomegranate extract and a promising treatment for such infections.[51]

Erectile dysfunction

A randomised, placebo-controlled, double-blind crossover study was conducted in 53 male patients with mild to moderate erectile dysfunction, trial group was treated with pomegranate juice orally for four weeks and control was given placebo. The treatment was discontinued after four weeks and after a latent phase of two weeks the treatment was interchanged in the two groups again for four weeks. The study showed improved scores during the treatment of pomegranate juice as compared to placebo in both groups.[52]

Antiviral properties

In an invitro study, four major polyphenols of the pomegranate extract namely EA, caffeic acid, luteolin, and punicalagin were separated and were studied against influenza virus.

It was observed that out of these polyphenols punicalagin efficiently blocked the replication of RNA

of the influenza virus, it also caused inhibition of agglutination of RBCs of chicken caused by the influenza viruses, and replication of human influenza A/ Hong Kong (H3N2) in the above experiment.[53]

In an another invitro study of evaluation of the natural viricidal activity, for use in the phage amplification assay, pomegranate was observed to bea potent viricidal drug.[54]

Pomegranate juice extract also proved its HIV-1 entry inhibitory and topical microbicidal action on HIV-1 virus in the study.[55]

Anti- osteoporotic action of pomegranate

Anti-osteoporotic action of various drugs is being studied using tissue selective estrogen agonist and antagonists, in postmenopausal osteoporosis.[56-58] Bone resorption rate is increased as compared to bone formation after ovariectomy.[59]

In an invitro study, well-characterized osteoblastic cells (osteoblastic MC3T3-E1 cells) were treated with Pomegranate Methanolic Extract with Alkaline Phosphatase (ALP), used as a bone remodeling marker. It was observed that PME significantly increased the APL activity, thus proving its efficient role in osteoblastic cell formation.[60]

In another comparative study, ovariectomized young adult mice[61,62] of 6-8 weeks of age, were studied in one group and in another sham surgery (SS) control in another group, the osteoporosis was assessed by bone turnover using serum ALP as a parameter in both groups. The ovariectomized group was treated with pomegranate methanol soluble extract PME, and the another with tamoxifen, it was observed that the ovariectomized group was having an increased bone turnover rate indicated by increased serum ALP levels as compared to the SS group, thus indicating the increased bone resorption before treatment, after treating these groups with respective drugs, it was observed that the PME in higher concentration was found equally effective in decreasing bone turnover and also in controlling the accelerated bone turnover.

In this study the osteoporosis was developed only by inducing estrogen deficiency artificially and not by bone loss due to increased age. It was observed that PME played an efficient and protective role in hormone deficiency related osteoporosis and thus showed its bone preserving effect.[63]

Lipid lowering effect

A study was commenced to determine the effect of pomegranate juice extract on the lipid profiles of type II diabetic patients with hyperlipidemia (total cholesterol or triglycerides >or = 200 mg / dL).

The pomegranate extract was given for oral administration for a period of over 2 months it was observed that, there was a significant decrease in total cholesterol ($P < 0.006$), low-density lipoprotein-cholesterol (LDL-c) ($P < 0.006$), LDL-c /high-density lipoprotein-cholesterol (HDL-c) ($P < 0.001$), and total cholesterol / HDL-c ($P < 0.001$). Thus, it was proved that pomegranate juice extract consumption can be used to modify heart disease risk factors in type II diabetic hyperlipidemic patients, so regular consumption in diet must be prescribed.[46][64]

Chemotherapy-induced toxicity

Anticancer drugs are frequently associated with various side effects on major body systems and are observed to cause nephrotoxicity and hepatotoxicity. Cisplatin (CDDP) is one of these cytotoxic against cancer drugs. In a study, the potential protective effect of pomegranate seed extract against oxidative stress caused by the Cisplatin (CDDP) injury of the kidneys and liver, was studied. The parameters used to check the damage were biochemical and antioxidant variables and immunohisto chemically testing caspase-3-positive cells.[65]

The pomegranate seed extract proved a significant protective effect on liver and kidney cells by reducing the lipid peroxidation level.

Also, the glutathione S-transferase concentrations were increased, activities of glutathione peroxidase, glutathione S-transferase, and superoxide dismutase were improved.The immunohistochemical findings were also significantly improved which was suggestive of diminished nephrotoxicity and hepatotoxicity of pomegranate seed extract due to its antioxidant, radical-scavenging, and anti-apoptotic activities. From this study it was concluded that pomegranate seed extract should be a part of dietary supplement in the patients taking chemotherapy medications.[66]

Antibacterial Activity

A study for assessing the antibacterial activity of pomegranate fruit was carried out using fine fruit powder of *Punica granatum* (24 mesh). It was extracted with 250 ml of 80% methanol in water at room temperature and kept in shaking water bath. After 24 hours, the extract was filtered with Millipore filter and was stored at 4^0c.

The bacterial strains used for antibacterial activity were *bacillus coagulancs* MTCC 3184, *Bacillus cereus* MTCC 1307, *Bacillus subtilis*, *Escherichia coli* MTCC 732, *Klebsiella pneumonia* MTCC 7028, and *Pseudomonas aeruginosa* MTCC 4302 and *staphylococcus aureus* MTCC 7405, all were cultured on Nutrient agar medium at 37^0c. Nutrient agar medium at 37^0 c. The stored extract was dissolved in

the phosphate buffered saline. Bacteria's were suspended in sterile water diluted approximately 10^6 CFU/mL. The suspension spread over surface of nutrient agar medium, wells cut from agar with sterile borer and 60µ extract solution was applied.

Antibacterial activity measured by diameter of inhibition (zone of inhibition). Out of seven bacterial cultures tested, the highest antibacterial activity by methanolic extract of pomegranate on *S.aureus.* DIZ value 10-25mm in which rind extract shown 25mm, Juice 23mm, red seed 19mm and whole fruit with 16mm.[67]

Antifungal activity

The study of antifungal activity conducted by using fungal strains *Aspergillus niger* MTCC 2196, *Mucor indicus* MTCC 3318*, citrinum* MTCC 7124, *Rhizopus oryzae* MTCC 1987, *Trichoderma reesei* MTCC 3929. For antifungal activity conidial suspension was prepared by *S. Guleria et al.* the conidial suspension was filtered by double muslin cloth. Agar well diffusion was followed by inoculated spore suspension prepared by molten potato dextrose medium. DIZ was measured, it showed highest inhibitory activity A.niger DIZ ranges 8.0-23 rind extract 23mm juice, 20mm least white seed 8.0 zone recorded. Result shown as A. niger > P. citrinum >R.oryzae > T. reesei > M. indicus.[68]

Antioxidant activity

The Antioxidant activity of pomegranate peel and seed extract was carried out using ethyl acetate, methanol, chloroform and water. Antioxidant activity was determined by screening extracts 1, 1-diphenyl-2-picryl hydrazyl (DPPH), the methanol extract of peels showed 83% and 81% antioxidant activity at 50 ppm and methanol extract of seed showed 22.6 and 23.2% at 100ppm antioxidant activity using DPPH model system. Results showed that methanol, ethanol and water extract of pomegranate peel was having highest antioxidant activity.[69]

Immunomodulatory Activity

In-vivo study of *Dadim* was done in rabbits in which Fruit rind powder of *Dadim (Punica granatum* Linn*.)* was given at the dose of 100 mg/kg orally. The result showed that pomegranate fruit rind powder caused an increase in antibody titre to typhoid-H antigen and also there was an increase in inhibition of leucocyte migration.[70]

Anthelmintic activity

Anthelmintic activity studied by Pomegranate peel extract used as Anthelmintic in female Ascaris lumbricoid. The study was carried out in 900 female Ascaris lumbricoid in vitro. By dividing in 5 groups group I extract 25%, group II 50% group III 75%, group IV 0.9% Nacl negative control and group V mebendazole used as positive control. The study showed result as Mean % dead worms in Group I was 39%, Group II was 61%, Group III was 82% and significant difference was found between negative control NaCl and mebendazole which killed 100% worms.[71]

Wound Healing Activity-

Wound healing activity was studied using methanolic extract of *Punica granatum* peel and after removal of fatty acid. This study was employed on wistar rat skin model which showed the result of 56% wound healing after 15 applications and2.5% water soluble gel. Pomegranate showed good wound healing property.[72]

Antidiarrheal activity

Antidiarrheal activity of *Dadim (Punica granatum* Linn*.)* is mentioned in classical text to justify this, rind of *Punica granatum* fruit was used.[73] Methanolic extract of rind of Pomegranate was prepared in one group and in another group Loperamide was used. To induce diarrhoea castor oil and Magnesium sulphate were used in the dose as per 200-400mg/kg body weight.

Result showed that the pomegranate extract proved to be a potent antidiarrheal drug in these animal models as compared to the standard loperamide. Castor oil- induced diarrhoea dose inhibited 31.25% defecation of 200 mg/kg and 53.75% at the dose of 400 mg/kg. In magnesium sulphate induced diarrhoea 45.71% at 200mg/kg and 57.14 at 400mg/kg inhibition of Diarrhoea. While standard drug Loperamide inhibited 71.25%.[74, 75]

CONCLUSION

Dadim or Pomegranate is a magical fruit which shows remarkable therapeutic activities in several diseases and serves as nutritive dietary supplement in various ailments even to subside the adverse effects of chemotherapy treatments and hence can be used in various types of carcinomas as a preventive drug or for treatment of cancer. It is a highly distinctive fruit used since ancient times with rich source of natural bioactive constituents. Various invitro and in vivo studies had proved the protective effects of pomegranate on the cardiovascular system, including reduction in oxidative stress, lowering lipid peroxidation, reduction in blood glucose levels, vasodilatory effects as well as decreasing blood pressure via an inhibition of ACE activity. It also exhibits antiulcer activity, antidiarrheal activity, antimicrobial i.e. antibacterial and antifungal activity, wound healing property, anthelmintic activity, immunomodulatory and hepatoprotective activity, and much more. Besides these, in numerous preclinical and clinical studies, pomegranate has

been proved to be effective in male infertility cases such as in erectile dysfunction, as an antiviral drug, in chronic vaginal infections, as an Antinociceptive drug. Among the enormous therapeutic uses of pomegranate, it has been proved to an effective medication therapy for osteoporosis, diabetes, obesity and even in leukemia. It had also been proved that pomegranate is effective in various skin diseases like UV skin damage, skin wrinkle and even in photo aging used in the form of topical ointments and can serve as a promising drug in the rising skin illnesses.

Thus, it is the prerequisite to conduct further clinical trials with large number of samples to explore, establish, validate and substantiate the therapeutic benefits of pomegranate. Consequently, it can be stated that pomegranate is a natural remedy which has potential uses in various chronic diseases.

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