Pericarpium Granati

Definition

Pericarpium Granati consists of the dried pericarp of *Punica granatum* L. (Lythraceae) (*1–3*).

Synonyms

Punica nana L. (Punicaceae) (*4*).

Note: According to current botanical authorities, *Punica granatum* belongs to the Lythraceae family (*5*).

Selected vernacular names

Anar, anara, anar-ke-per, Carthaginian apple, dadam, dadima-phalam, dalima, dalimb, dalimbay, dalimbuhannu, dalimo, darakte-naiar, darimba, darinko bokra, daru, delima, delum, delun, dhalima, dila dae lok, dlima, ende limau, gangsalan, glima glineu mekah, granada, granade, granado, Granatbaum, granatum, grenadier, grenadillo, gul armini, gulnar, jaman, jeliman, kupchaphala, lelo kase, madalai, madalam, madalangkai, matalam, mathalanarkom, melograno, mkoma manga, nar, pomegranate, posnar, qsur roman, qsur rommam, quishr-al-romman, quishr-romman, ranato, romã, roman, romeira, rommam, roman amruj, romanzeira, roumammam-goulnar, ruman, rumau, sekiryuu-karpi, seog-ryu, seokryupi, sham-al-rumman, shajratur-rummam, shih liu pi, shiliupi, shukadana, talima, thab thim, thap thim, zakuro-hi (*2–4*, *6–12*).

Geographical distribution

Native to the Middle East (eastern Mediterranean to northern India), and now widely cultivated in warm regions throughout the world (*6*, *8*, *9*).

Description

A deciduous shrub or small tree, erect, up to 7 m high, much branched from the base; branches slender; branchlets often ending in spines, the young ones quadrangular or almost tetrapterous. Leaves: simple, oppo-

site, verticillate, oblong-lanceolate, glabrous, 1–9 cm long and 0.5–2.5 cm wide; apex acute, obtuse or emarginate; base cuneate. Flowers: 1–5 at the highest leaf axil of branchlets, 1 terminal, sessile or subsessile. Calyx 2–3 cm long, red or pale yellow; lobes erectopatent to recurved; petals round or obtuse, red or white. Fruit, a berry, globose, 5–13 cm in diameter, with a leathery rind enclosing numerous seeds, variously coloured, yellowish green, white, reddish brown or rarely blackish purple. Seeds: numerous, red, pink or yellowish white (*6*, *7*, *9*).

Plant material of interest: pericarp

General appearance

Irregular slices or gourd-shaped, brittle, varying in size, 1.5–3.0 mm thick. The outer surface reddish brown, brownish yellow or dark brown; somewhat lustrous, rough, with numerous warty protuberances. Some with a raised tubular persistent calyx and a stout and short peduncle or its scar. Inner surface yellow or reddish brown, with raised reticulated remains of the peduncle. Texture hard and fragile, fracture yellow, somewhat granular (*1*, *6*).

Organoleptic properties

Odourless; taste: bitter and astringent (*1*, *6*).

Microscopic characteristics

Transverse section of the pericarp shows the following: exocarp consists of irregular polygonal cells with slightly thickened but not lignified outer wall and a thick smooth cuticle. Mesocarp generally consists of thin-walled parenchyma cells containing starch granules, clusters or prisms of calcium oxalate. Scattered among the parenchyma cells are sclereids occurring singly or in small groups with strongly thickened lignified walls and rather small lumen or with slightly thickened somewhat lignified walls and wider lumen. Small bicollateral vascular bundles course through the parenchyma; rather thick-walled, non-lignified fibres occasionally accompanying the bundles. Larger bicollateral vascular bundles course through the central part of the mesocarp: phloem fibres are few and possess clear non-lignified walls and a narrow lumen; some phloem parenchyma contains prisms of calcium oxalate. Endocarp cells relatively small, containing starch granules and crystals of calcium oxalate, and stone cells also relatively small (*1*, *6*).

Powdered plant material

Reddish brown. Stone cells sub-rounded, rectangular or irregular, rarely branched, 27–102 μm in diameter, with relatively thick walls and a large lumen, some containing brown matter. Epidermal cells sub-square or sub-

rectangular, with slightly thickened walls. Clusters of calcium oxalate 10–25 µm in diameter, prisms infrequent. Spiral and reticulate vessels 12–18 µm in diameter. Starch granules sub-rounded, 2–10 µm in diameter (*1*).

General identity tests

Macroscopic and microscopic examinations (*1*, *2*, *6*), microchemical tests (*1*, *6*), and thin-layer chromatography (*2*, *6*).

Purity tests

Microbiological

Tests for specific microorganisms and microbial contamination limits are as described in the WHO guidelines on assessing quality of herbal medicines with reference to contaminants and residues (*13*).

Foreign organic matter

Not more than 6% (*1*).

Total ash

Not more than 4% (*2*, *6*).

Acid-insoluble ash

Not more than 1% (*6*).

Water-soluble extractive

Pericarp: not less than 30% (*6*).

Alcohol-soluble extractive

Pericarp: not less than 15% (*6*).

Loss on drying

Not more than 10% (*6*).

Pesticide residues

The recommended maximum limit of aldrin and dieldrin is not more than 0.05 mg/kg (*14*). For other pesticides see the *European pharmacopoeia* (*14*) and the WHO guidelines on assessing quality of herbal medicines with reference to contaminants and residues (*13*) and pesticide residues (*15*).

Heavy metals

For maximum limits and analysis of heavy metals, consult the WHO guidelines on assessing quality of herbal medicines with reference to contaminants and residues (*13*).

Radioactive residues

Where applicable, consult the WHO guidelines on assessing quality of herbal medicines with reference to contaminants and residues (*13*).

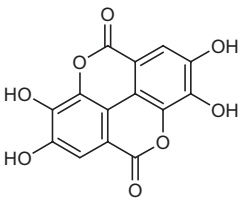
Chemical assays

Total tannins not less than 10% (*1*).

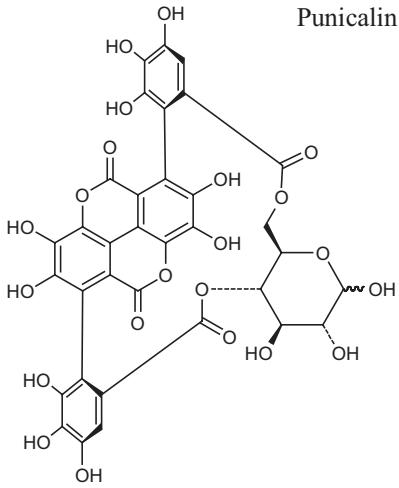
Major chemical constituents

The major constituents are hydrolysable ellagitannins (up to 28%) and other polyphenols (*3*, *12*, *16*, *17*). Structures of ellagic acid and punicalin are presented below.

Ellagic acid



Punicalin



Medicinal uses

Uses supported by clinical data

None.

Uses described in pharmacopoeias and well established documents

Orally for the treatment of chronic diarrhoea, dysentery, gingivitis and intestinal parasites (*1*, *7*, *18*).

Uses described in traditional medicine

Treatment of bronchitis, fever, gastrointestinal ailments, menorrhagia, respiratory tract infections, skin rashes, vaginal infections and worms (*12*, *19*).

Pharmacology

Experimental pharmacology

Antidiarrhoeal activity

Intragastric administration of a decoction or a 95% ethanol extract of the crude drug at a dose of 200.0 mg/kg or 50.0 mg/kg body weight (bw), respectively, reduced faecal output in rats with castor-oil induced diarrhoea (*21*). The same extracts, at a dose of 500.0 mg/kg bw, exhibited intestinal antisecretory activity in rats with magnesium sulfate-induced enteropooling (*20*).

Antimicrobial, antiparasitic and antiviral activity

An aqueous, butanol, or 95% ethanol extract of the crude drug had in vitro activity against *Proteus mirabilis*, *Haemophilus influenzae*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Streptococcus aureus*, *Staphylococcus aureus* and *Candida albicans* at a concentration of 60.0 µg/ml (*21*, *22*). An aqueous extract and a 95% ethanol extract of the fruit rind had weak in vitro activity against *Bacillus cereus*, *Enterococcus faecalis*, *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa* and *Staphylococcus aureus* at a concentration of 25 mg/well (*23*, *24*).

A decoction of the crude drug weakly inhibited the growth of *Trichophyton tonsurans, T. rubrum*, *T. simii, Trichosporon beigelii*, *Microsporum fulvum*, *M. gypseum* and *Candida albicans* when added to the nutrient medium at a concentration of 5% (*25*).

Tannins separated from the crude drug were effective against genital herpes virus (herpes simplex virus type 2). The tannin not only inhibited replication of the virus, but also blocked herpes type 2 viral adsorption in cultured cells (*26*).

An aqueous extract of the crude drug had antiviral activity against hepatitis B virus in PLC/PRF/5 cells in vitro (*27*). An aqueous extract inhibited hepatitis C virus in vitro at a concentration of 100 µg/ml. An acetone extract of the crude drug had larvicidal activity against *Chrysomya albiceps* at a concentration of 25 µg/ml (*28*). At a concentration of 10.0 ml/plate, an aqueous extract of the crude drug weakly inhibited the growth of *Ascaris galli, Pheritima posthuma* and *Taenia solium* (*29*), as well as *Ascaris lumbricoides* (*30*).

Antioxidant activity

Aqueous, alcohol and ethyl acetate extracts of the crude drug have shown significant antioxidant activity in various in vitro and in vivo models. A methanol extract of the crude drug had antioxidant activity in vitro, in the β-carotene-linoleate and 1,1-diphenyl-2-picrylhydrazyl radical model

systems. The methanol extract exhibited 83% and 81% antioxidant activity at a concentration of 50.0 µg/ml using the β-carotene-linoleate and 1,1-diphenyl-2-picrylhydrazyl radical model systems, respectively (*31*). A dried methanol extract fed to rats (50.0 mg/kg bw) following treatment with carbon tetrachloride (CCl_4) (2.0 g/kg bw) decreased the levels of catalase, superoxide dismutase and peroxidase by 81, 49 and 89%, respectively. Pretreatment of the rats with the methanol extract maintained the levels of catalase, peroxidase and superoxide dismutase at values comparable with control values, whereas lipid peroxidation was reduced by 54% compared to the control group (*32*).

Antiulcer activity

Intragastric administration of an aqueous extract (5 ml/kg bw) or an unspecified protein-containing fraction (50 mg/kg bw) of the crude drug to rats prevented hydrochloric acid and ethanol-induced gastric ulceration (*33*). The gastroprotective effects of tannic acid and the aqueous extract of the crude drug against ethanol-induced damage were investigated in rats. Oral administration of the extract or tannic acid induced a significant decrease in gastric lesions (48–76%). The protection observed was more pronounced when the test solution was given at the same time as the ethanol. The acid content of the stomach was increased by 368% after administration of the ethanol extract (*34*).

Immune effects

Oral administration of a powder made from the fruit rind, at a dose of 100.0 mg/kg bw, as an aqueous suspension, stimulated cell-mediated and humoral components of the immune system in rabbits. The suspension elicited an increase in antibody titre to typhoid-H antigen. It also enhanced the inhibition of leukocyte migration in the leukocyte migration inhibition test and induration of skin in the delayed hypersensitivity test with purified protein derivative, confirming its stimulatory effect on the cell-mediated immune response (*35*).

Toxicology

An aqueous extract of the crude drug was reported to stimulate uterine contractions in non-pregnant rats but the dose and the route of administration were not stated (*36*).

Clinical pharmacology

A water-soluble component derived from an ethanol extract of the crude drug possessing antimicrobial activity was used in an antibacterial mouthwash at a concentration of 0.8% w/w (*18*). The mouthwash was composed of a combination of the water-soluble component (0.8 g/100 ml),

menthol (0.03 g/100 ml), and absolute alcohol (5 g/100 ml). Eighty volunteers (30 healthy and 50 with dental caries) were required to rinse their mouths with 20 ml of the mouthwash for 30 seconds, they then closed their mouths for 90 seconds and then spat out their saliva for analysis. The salivary microbes were cultured and identified. Oral pathogens such as *Staphylococcus aureus*, *S. mutans* and *Lactobacillus* spp. were killed whereas *Candida albicans* was not (*18*).

Adverse reactions

No information was found.

Contraindications

Hypersensitivity or allergy to the plant material.

Warnings

In cases of diarrhoea lasting for longer than 3 days, or associated with fever, nausea and vomiting, or bloody stools, contact a health care provider. Do not exceed recommended dose.

Precautions

Carcinogenesis, mutagenesis, impairment of fertility

The genotoxic effects of the crude drug were examined in established human cell lines, Raji and P3HR-1. Cells were treated with a decoction of the crude drug at various concentrations for 24 and 48 hours in vitro. Cell growth and viability were dose-dependently reduced. No apparent chromosomal aberrations were induced by the treatment. Administration of the extract induced apoptotic DNA fragmentation (*37*).

Pregnancy: teratogenic effects

No information was found.

Pregnancy: non-teratogenic effects

Due to the lack of safety data, the use of the crude drug during pregnancy is not recommended.

Nursing mothers

Due to the lack of safety and efficacy studies, the use of the crude drug by breastfeeding mothers is not recommended.

Paediatric use

Due to the lack of safety data, the use of the crude drug for the treatment of children under the age of 12 years is not recommended.

Other precautions
No information was found.

Dosage forms
Crude drug, extracts and tablets. Store in a cool dry place (*1*).

Posology
(Unless otherwise indicated)
Oral daily dose: 2.5–4.5 g (*1*, *7*).

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