Pomegranate

Health Care Professional Information

**Scientific Name**
Punica granatum L.

**Common Name**
Chinese apple

**Clinical Summary**
Pomegranate is a small fruit-bearing tree native to Asia but is cultivated in many parts of the world including the United States. The fruit juice extracted from the arils of the seeds is used in drinks and as a dietary supplement. Several studies have shown that pomegranate has antioxidant and antiatherosclerotic properties attributed to the presence of multiple polyphenols such as tannins, flavonols, anthocyanins and ellagic acid (1) (2).

Consumption of pomegranate juice was found to benefit patients with carotid artery stenosis (6), in those with hypertension (7), hyperlipidemia (21), mild to moderate erectile dysfunction (19), and in patients with coronary heart disease (CHD) (8), but had no effect in patients with chronic obstructive pulmonary disease (COPD) (9).

In a study of postmenopausal women, intake of pomegranate seed oil did not reduce hot flashes (22).

Pomegranate juice has been shown to suppress inflammatory cell signaling (1), inhibit prostate tumor growth and lower serum PSA levels (3) (4), and also inhibit aromatase activity, endogenous estrogen biosynthesis and breast cancer cell proliferation (5) in vitro.

A pomegranate seed extract alleviated cisplatin-induced hepatotoxicity in animal studies (23).

Pomegranate juice was reported to slow the rate of increase of PSA in men with high PSA levels, but data are conflicting (2) (24).

**Food Sources**
Whole fruit, juice

**Purported Uses**
- Cancer treatment and prevention
- Atherosclerosis
- Coronary heart Disease
- Hypercholesterolemia
- Hyperlipidemia
- Hypertension
- HIV

**Constituents**
- Tannins
- Flavonols
- Anthocyanins
- Ellagic acid (14) (15) (16)
Mechanism of Action
Several studies have indicated that pomegranate juice has antioxidant and antiatherosclerotic properties due to the presence of multiple polyphenols such as tannins, flavonols, anthocyanins and ellagic acid. Punicalagin, an ellagitannin, is the most abundant polyphenol that accounts for >50% of the antioxidant activity (1) (2). Some commercial pomegranate juices are marketed with claims of higher antioxidant activity than green tea and red wine (13). However such effects could be due to colonic microflora metabolites and not the polyphenols present in the juice (14). Pomegranate extract can inhibit aromatase activity and decrease the endogenous synthesis of estrogen (5).

Pharmacokinetics
Studies in rats suggest that most punicalagin is absorbed but only 3-6% is excreted in the feces and urine suggesting that the majority is converted to CO$_2$ or other undetectable metabolites (15). The metabolites that are present in urine in both rats and humans, 6H-dibenzo[b,d]pyran-6-one derivatives, are the products of intestinal microflora metabolizing the pomegranate tannins. A recent human study has shown that ellagic acid is absorbed from pomegranate juice and detected in plasma samples. It is unclear whether free ellagic acid is due to hydrolysis of the pomegranate ellagitannins, physiological pH, or gut microflora activity (16).

Warnings
Pomegranate juice may increase the risk of rhabdomyolysis for patients on statin therapy possibly due to the inhibition of CYP 450 enzymes (17). Diabetic patients should be careful because of the sugar content of pomegranate.

Adverse Reactions
No significant adverse effects were seen with daily consumption of 8 ounces of pomegranate juice in men for over two years (2).

Herb-Drug Interactions
- **Cytochrome P4503A substrates**: Studies in rats indicate that pomegranate juice may inhibit cytochrome P450 3A (CYP3A) activity similar to grapefruit juice (10) (11). But a study in humans demonstrated that pomegranate juice did not alter clearance of intravenous or oral midazolam, whereas grapefruit juice is known to have this effect (12).
- **CYP 2C9 substrates**: A study done in rats showed that pomegranate juice inhibited CYP2C9 activity and increased tolbutamide bioavailability (18).
- **Warfarin**: According to a case report, pomegranate juice may interact with warfarin (20).

Literature Summary and Critique
**Pantuck AJ, Leppert JT, Zomorodian N, et al.** Phase II study of pomegranate juice for men with rising prostate-specific antigen following surgery or radiation for prostate cancer. Clin Cancer Res. 2006;12(13):4018-4026. A phase II clinical trial was conducted with 46 men with rising PSA following surgery or radiotherapy. Subjects were given 240ml (8 ounces) of pomegranate juice daily until progression of disease. Researchers found a significant increase in the mean PSA doubling time following the study period. These results warrant further testing via a placebo-controlled study.

**Sumner MD, Elliott-Eller M, Weidner G, et al.** Effects of pomegranate juice consumption on myocardial perfusion in patients with coronary heart disease. Am J Cardiol 2005;96(6):810-814. Forty-five patients with stable coronary heart disease (CHD) received 240mL/day of pomegranate juice or placebo for three months. After three months, stress-induced ischemia decreased in the pomegranate group (SDS -0.8 +/- 2.7), but an increase was observed in the placebo group. The authors conclude that pomegranate juice may be of benefit in improving stress-induced myocardial ischemia in CHD patients.

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References


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### Consumer Information

#### How It Works

**Bottom Line:** Pomegranate was shown effective in lowering blood pressure and high cholesterol. More research is needed to know its benefits for cancer.

Pomegranate is a small fruit-bearing tree native to Asia. Juice from the seed pulp contains compounds known as polyphenols that may contribute to its activity. A few studies suggest pomegranate juice can benefit patients with heart disease and can lower cholesterol and blood pressure. It was shown in laboratory studies to prevent growth of cancer cells. In a human study, intake of pomegranate juice was found to have some benefit in patients with prostate cancer. But more clinical trials are needed to confirm such effects.

#### Purported Uses

- **Cancer prevention**
  
  Data from laboratory studies showed that pomegranate is effective against tumor cells. A single study in humans showed some indirect benefit of pomegranate juice for patients with prostate cancer. More studies are needed.

- **Hypercholesterolemia**
  
  There is evidence from a few studies that pomegranate lowers cholesterol level.

- **Hypertension**
  
  A few small scale studies suggest that drinking pomegranate juice may reduce hypertension. More studies are needed to verify this effect.

#### Research Evidence

**Prostate Cancer**

In this study, 46 men with rising levels of Prostate Specific Antigen (PSA), a protein found in prostate cancer patients, were given 240ml (8 ounces) of pomegranate juice daily after surgery or radiation therapy. The rise of PSA was slowed after 54 months which suggests slower disease progression. More studies are needed to confirm such effects.

**Cardiovascular Disease**

Forty-five patients with coronary heart disease (CHD) were assigned to receive 240mL/day of pomegranate juice or placebo for three months. Researchers reported a decrease in stress-induced ischemia (reduction in blood supply to heart muscle) following the study period. Pomegranate juice may benefit patients with CHD.

#### Patient Warnings

- Pomegranate juice may increase the risk of rhabdomyolysis (breakdown of muscle fibers and release of muscle fiber contents into circulation) for patients on statin therapy.

- Diabetic patients should be careful because of the sugar content of pomegranate.
Do Not Take If

- You are taking medications that interact with grapefruit juice (pomegranate may have effects similar to grapefruit juice.)
- You are taking warfarin (pomegranate juice may interact with warfarin).

Side Effects

No significant side effects were reported with use of pomegranate juice.

Special Point

Patients should be aware that pomegranate is not an approved cancer treatment.

E-mail your questions and comments to aboutherbs@mskcc.org.