Journal of Ethnopharmacology 143 (2012) 397–405

Contents lists available at SciVerse ScienceDirect

Journal of Ethnopharmacology

journal homepage: www.elsevier.com/locate/jep

Review

Pomegranate peel and fruit extracts: A review of potential anti-inflammatory and anti-infective effects

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ARTICLE INFO

Article history:
Received 2 March 2012
Received in revised form
6 July 2012
Accepted 9 July 2012
Available online 20 July 2012

Keywords:
Pomegranate
Ellagitannins
Punicalagin
Antioxidant
Atherosclerosis

ABSTRACT

Ethnopharmacological relevance: *Punica granatum* L. (Punicaceae) has been used for centuries in many cultures for the prevention and treatment of a wide number of health disorders such as inflammation, diabetes, diarrhea, dysentery, dental plaque and to combat intestinal infections and malarial parasites.
Aim of the review: This review aims at providing an up-to-date overview of the chemical constituents, traditional uses, phytochemistry, pharmacology and toxicology of *Punica granatum* L. Moreover, the focus of this review is the possible exploitation of this species to treat different diseases and to suggest future investigations.
Materials and methods: An extensive and systematic review of the extant literature was carried out, and the data under various sections were identified by using a computerized bibliographic search via PubMed, Web of Science and Google Scholar. All abstracts and full-text articles were examined. The most relevant articles were selected for screening and inclusion in this review.
Key findings: A variety of pomegranate ethnomedical uses have been recorded. Additionally, over the last decade, there has been a dramatic increase of interest in pomegranate as a medicinal and nutritional product due to its n1ewly identified potential health effects, which include treatment and prevention of cancer and cardiovascular diseases. From the toxicological perspective, pomegranate fruit juice, extracts and preparations have been proven to be safe.
Conclusions: The ethnopharmacological relevance of pomegranate is fully justified by the most recent findings indicating the fruit is a medicinal and nutritional agent useful for treating a wide range of human disorders and maladies. Further investigations are needed to fully understand the mode of action of the active constituents and to fully exploit pomegranate's preventive and therapeutic potential.

Contents

Abbreviations: PoP, Pomegranate peel; PoPx, Pomegranate peel extract; PoMx, Pomegranate extracts; DPPH, Diphenyl-1-picrylhydrazyl; ROS, Reactive oxygen species; LDL, Low density lipoproteins; Ox LDL, Oxidized low density lipoproteins; SPRE, Standardized pomegranate rind extract; IC, Inhibitory concentration; iNOS, Inducible nitric oxide synthase; COX-2, Cyclohexogenase-2; PGE_2, Prostaglandin-2; NF-kB, Nuclear factor *kappa* B; MIC, Minimum inhibitory concentration; OMARIA, Orissa malaria research indigenous attempt; NOAEL, No observed adverse effects level; LD, Lethal doses; LPS, Lipopolysaccharide.; FRAP, Ferric reducing antioxidant power; PPAR-γ, Peroxisome proliferator-activated receptor gamma; PON 1, Paraoxonase 1; MMP-9, Metalloprotease-9; TNF, Tumor Necrosis Factor

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http://dx.doi.org/10.1016/j.jep.2012.07.004

1. Introduction

Pomegranate (*Punica granatum L. Punicaceae*; the common name is derived from Latin words ponus and granatus), a seeded or granular apple, is a delicious fruit consumed worldwide. The fruit is native to Afghanistan, Iran, China and the Indian subcontinent. The ancient sources of pomegranate linked Iran to Pakistan, China and eastern India, where pomegranates had been under cultivation for thousands of years. From the west of Persia (modern day Iran), pomegranate cultivation stretched through the Mediterranean region to the Turkish European borders and American southwest, California and Mexico (Celik et al., 2009; Lansky and Newman, 2007).

Pomegranate peels are characterized by an interior network of membranes comprising almost 26–30% of total fruit weight and are characterized by substantial amounts of phenolic compounds, including flavonoids (anthocyanins, catechins and other complex flavonoids) and hydrolyzable tannins (punicalin, pedunculagin, punicalagin, gallic and ellagic acid). These compounds are concentrated in pomegranate peel (PoP) and juice, which account for 92% of the antioxidant activity associated with the fruit (Afaq et al., 2005; Negi et al., 2003; Zahin et al., 2010). Fig. 1.

Gallic acid, ellagic acid and punicalagin, in addition to their free radical-scavenging properties, also possess antibacterial activities against intestinal flora, particularly enteric pathogens, i.e., *Escherichia coli*, *Salmonella spp. Shigella spp.*, as well as *Vibrio cholerae* (Aviram et al., 2008; Lu et al., 2007; Pai et al., 2011; Taguri et al., 2004).

The therapeutic potential of PoP has been widely recognized by different cultures. In Egyptian culture, several common ailments such as inflammation, diarrhea, intestinal worms, cough and infertility have been treated by exploiting pomegranate peel extract (PoPx). The exceptional antioxidant potential and strong medicinal properties of PoP led the international scientific community to initiate intensive research in the last decade to further investigate its role in human health (Lansky and Newman, 2007).

Several studies have demonstrated the antimicrobial, antihelminthic, and antioxidant potential of the active ingredients of pomegranate extracts (PoMx), suggesting their preventive and curative role in gastro-mucosal injuries, cancer chemoprevention, ethanol- and acetone-induced ulceration and diabetic oxidative damage (Al-zoreky and Nakahara, 2003; Arun and Singh, 2012; Negi et al., 2003). The mechanism of antimicrobial activity of

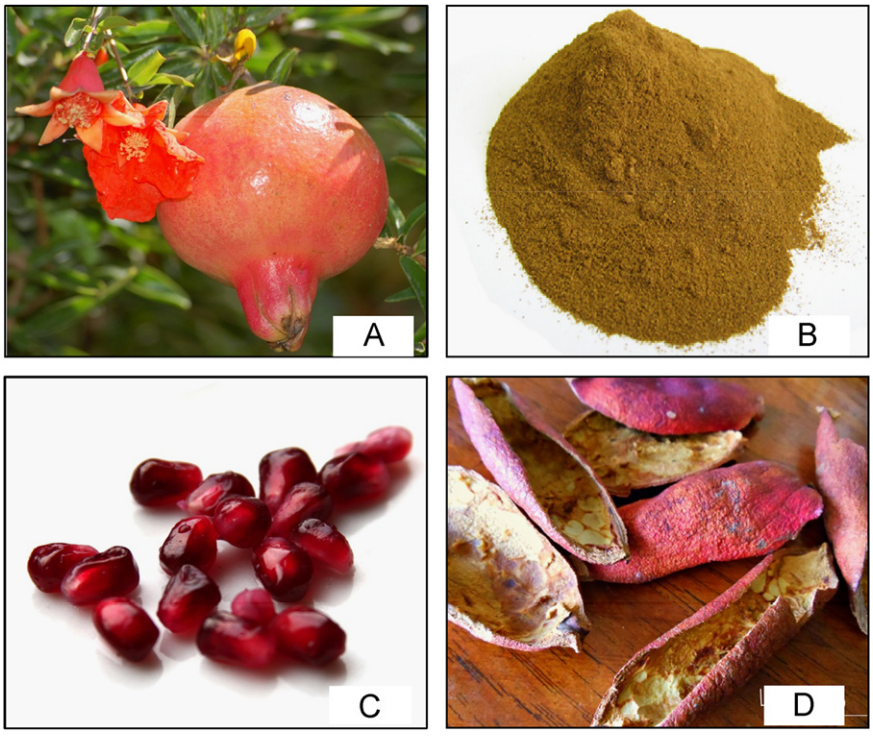

Fig. 1. Pomegranate fruit (A) and its anatomical components, pomegranate peel powder (B) pomegranate seeds (C) and sundried pomegranate peel (D).