



## Review

## A review on biological, nutraceutical and clinical aspects of French maritime pine bark extract

Alya Maimoona<sup>a,\*</sup>, Ismat Naeem<sup>a</sup>, Zeb Saddiqe<sup>a</sup>, Khalid Jameel<sup>b</sup>

<sup>a</sup> Department of Chemistry, Lahore College for Women University Lahore, Lahore, Pakistan

<sup>b</sup> Combined military hospital, Kharian Cantt., Pakistan

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## ABSTRACT

Bark extract of *Pinus pinaster* has a long history of ethnomedicinal use and is available commercially as herbal dietary supplement with proprietary name pycnogenol. It is used as a food supplement to overcome many degenerative disorders. Rohdewald (2002) wrote the first comprehensive review of extract highlighting its antioxidative nature and its role in different diseases. Later, Watson (2003) and Gulati (2005) in their reviews about cardiovascular health, described the extract as a best nutraceutical agent in this regard. The objective of this paper is to review the current research on this extract in terms of extraction methods, its pharmacological, toxicological and nutraceutical effects and clinical studies. Web sites of Google Scholar, Pubmed and Medline were searched for articles written in English and published in peer-reviewed journals from 2006 to 2009 and sixty-nine research articles were extracted. Of these, two are about extraction advancement and analysis while the rest relate to its clinical, biological and nutraceutical aspects.

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**Abbreviations:** A, adrenaline; ACE, angiotensin converting enzyme; AD, Alzheimer's disease; ADHD, attention deficit hyperactivity disorder; ADRP, adipose differentiation-related protein; AIDS, acquired immunodeficiency syndrome; ALP, alkaline phosphatase; ALT, alanine aminotransferase; AP, activator protein; ASA, acetylsalicylic acid; AST, aspartate aminotransferase; BHT, butylated hydroxytoluene; BUN, blood urea nitrogen; CAP, child attention problem; COX-1, cyclooxygenase-1; COX-2, cyclooxygenase-2; CPRS, Conner's Parents Rating Scale; CTARS, Conner's Teacher Rating Scale; CVD, cardiovascular disease risk; CVI, chronic venous insufficiency; DFO, desferrioxamine; DHEA, dehydroepiandrosteroid; DNP, dinitrophenyl; E, estrogen; EMC, encephalomyocarditis; EMCV, encephalomyocarditis virus; eNOS, endothelial nitric oxide synthase; ESR, electron spin resonance; FBF, forearm blood flow; FLAP, five-lipoxygenase activating protein; fMLP, formyl-methionyl-leucyl-phenylalanine; FRAP, ferric reducing antioxidant power; GE, grape extract; Gn-RHa, gonadotropin-releasing hormone agonist; GSH, glutathione; GSSG, oxidized glutathione; GST, glutathione-S-transferase; HPLC, high performance liquid chromatography; ICSVSTZ, intracerebro ventricular streptozotocin; IgE, immunoglobulin E; IOP, intraocular pressure; IR, ischemia-reperfusion; LDH, lactate dehydrogenase; LOX, lipoxygenase; LPS, lipopolysaccharide; MDA, malonaldehyde; MIC, minimum inhibitory concentration; MIDAS, migraine disability assessment; MMP, matrix metalloproteinases; MNCV, motor nerve conduction velocity; Mn-SOD, manganese superoxide dismutase; MPO, myeloperoxidase; NADPH, nicotinamide adenine diphosphate hydrogenase; NAGA-N, acetyl beta-D-glucosaminidase; NA, noradrenaline; NS, not significant; NSAIDs, non-steroidal anti-inflammatory drugs; OA, osteoarthritis; OPC, oligomeric proanthocyanidins; PBE, pine bark extract; PC, protein carbonyl; PLA2, phospholipid A2; PMNL, polymorpho nuclear leukocyte; PMN, polymorpho nuclear neutrophils; PBE, pine bark extract; ROS, reactive oxygen species; RPMC, rat peritoneal mast cells; SNP, sodium nitroprusside; STZ, streptozotocin; TAS, total antioxidant status; TBARS, thiobarbituric acid reactive substances; TLR4, toll like receptors 4-mediated signal; TXB2, thromboxane B2; VE, vitamin E; WBEA, whole blood electrical aggregate; WHO, women's health questionnaire; WOMAC, western Ontario McMaster; TXA2, thromboxane A2.

\* Corresponding author. Tel.: +92 42 99203801-9x245.

E-mail address: [alya.maimoona@yahoo.com](mailto:alya.maimoona@yahoo.com) (A. Maimoona).

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## 1. Introduction

For thousands of years, natural products have played a promising role throughout the globe in the treatment and prevention of human diseases. To date, many natural products have been extracted from barks of plants. A wide variety of products of diverse chemical nature have their origin from bark, e.g. salicylic acid, the acetylated form of which is aspirin, is obtained from *Salix alba* bark (Tulp and Bohlin, 2004); flavoring agent cinnamon from *Cinnamomum zeylanicum* (Jaradat, 2005) and alkaloids like Quinine from *Cinchona calisaya* and *Cinchona pubescens* bark (Farnsworth and Soejarto, 1985) and yohimbine from the bark of *Corynanthe yohimbe* (Giampreti et al., 2008). The bark extracts which are a rich source of phytochemicals with biological and physiological properties and potential to be used as a medicine are of interest to humans.

Use of pine bark to reduce inflammation can be traced back to Hippocrates, the “Father of Medicine” (400 BC) (Packer et al., 1999). Pine bark extract (PBE) from European coastal pine (*Pinus pinaster*) was used by native Indians of Quebec. They introduced French explorer Jacques Cartier and his crew, the pine-bark tea during the winter of 1534 which proved wonderful in preventing scurvy, a disease caused by deficiency of vitamin C. Fascinated by this information, Professor Jack Masquelier who was working on bioflavonoids suspected that bioflavonoids might be used in the treatment of scurvy. Later he determined that pine bark extract was rich in bioflavonoids including organic acids. These phytonutrients exhibit best free-radical scavenging activities. Such remedies

are the human need because with better health cure facilities and improved living conditions, the average life span of human beings has increased adding a vast number of patients with degenerative disorders caused by free radicals.

The present article encompasses all the research reports on PBE for the period mentioned above. However, only controlled human and animal trials, with better design and dose indication are tabulated in Appendix A. Pilot studies with no control group or untreated control group or methodological limitations are only discussed.

### 1.1. Taxonomy and description

*Pinus* is the largest extant genus of the conifers in the family Pinaceae (Farjon, 1984) with more than 100 species (Price et al., 1998; Farjon, 2001). Some of them are cultivated world-wide (Le Maitre, 1998). Kramer and Green (1990) placed the genus *Pinus* in family Pinaceae under the class Pinatae in the subdivision Conifero-phytina of Gymnosperms.

*Pinus pinaster* is a medium-sized pine up to 30 m tall with bright reddish brown bark. Needles in the leaf spur are paired. Its cones are oval, brown in colour and up to 2 cm long (Pullaiah, 2006).

## 2. Extraction and finger print analysis

Braga et al. (2008) revolutionized the extraction of antioxidants from *Pinus pinaster* bark. Fractionated supercritical fluid extraction

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