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Pine bark

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Pines (*Pinus* spp.; Pinaceae) are native to most of the Northern Hemisphere and are grown in most temperate and subtropical regions of the world. These evergreen, coniferous, resinous trees can grow to heights of 3–80 m. Pine, particularly its bark, has a long history of use in traditional medicine systems. For example, pine tree bark was used for medicinal purposes by Native Americans for treating coughs and, using poultice made from the inner bark, to treat wounds. European explorers used pine bark for treating scurvy: maritime pine (*P. pinaster* Aiton), discovered by a French explorer in the 18th century, has a high concentration of vitamin C in its bark.

Today, pine bark extracts are sourced from different species of pine grown in different countries. Manufactured products containing pine bark extracts are marketed under different proprietary names, such as Pycnogenol®, Flavangenol®, Oligopin® (from *P. pinaster*; France), PineXol® (from *P. densiflora* Siebold & Zucc.; Korea) and Enzogenol® (from *P. radiata*; New Zealand).[1,2] Different proprietary products may contain different quantities of procyanidins, the primary active components of pine bark extract.

Pycnogenol® is a proprietary product derived from French maritime pine (*P. pinaster* Aiton) and is the most extensively studied pine bark extract in terms of clinical and pharmacological effects. Pycnogenol® was one of the first pine bark products launched globally, and sales data indicated that it was one of the top 100 top-selling herbal dietary supplements in the USA from 2013 to 2015.[3]

Common names

Cluster pine, maritime pine, turpentine [*English*], among others.

Preparations

Traditional preparations of pine bark typically comprised water decoctions, consumed as teas. Contemporary preparations in the global market usually consist of preparations of solid-dose forms (typically capsules, tablets, powders), formulated as single- and multi-ingredient products (with other herbal and non-herbal ingredients).

Summary message

Preclinical studies provide support for several pharmacological effects of pine bark extracts, which may be relevant for conditions such as cardiovascular disease, diabetes, Parkinson's disease, cancer, and skin ageing. Clinical studies with pine bark extracts have investigated its effects in several conditions, particularly cardiovascular health. However, clinical research on pine bark extracts has methodological limitations and, currently, there is no conclusive evidence of their efficacy in treating any specific health condition. Large, robust, long-term studies using pine bark extracts that meet accepted standards for pharmaceutical quality are required.

To date, pine bark extracts have not been associated with serious adverse effects when used at usual doses for limited periods of time. However, in general, pharmacovigilance for herbal medicines is limited. Reported adverse reactions associated with pine bark extracts mainly describe non-serious gastrointestinal symptoms. Comprehensive examination of the clinical safety profile of pine bark extracts, and their constituents, when used in a pharmaceutical/medicinal context is required.

Manufacturers' claims

Pine bark products are marketed to support cardiovascular health, brain function, eye health, gut health, and 'healthy' blood glucose concentrations. Pine bark extracts are also promoted for their anti-ageing properties, and for maintaining skin and hair health, among other claims.[3]

Active constituents

The main active constituents in pine bark extract are procyanidins (polymers consisting of (+)-catechin and/or (−)-epicatechin units), which belong to the proanthocyanidin class of flavonoids, a subgroup of polyphenols. Pine bark extract may also contain other flavonoid compounds and phenolic acids.

Pycnogenol® is derived from French maritime pine bark extract and is standardised to contain 70(±5)% procyanidins.[3] Enzogenol® is a water-based extract from the bark of *P. radiata* trees grown in New Zealand; the dry powder is standardised to contain more than 80% proanthocyanidins.[4]

Evidence for efficacy

Preclinical studies[1,3,5] have reported potential antioxidant, anti-inflammatory, anti-cancer, immunostimulant, cardioprotective, and renal protective effects for pine bark extracts. *In-vitro* and/or animal studies have also described improvements in blood glucose concentrations/diabetes, cognition, male fertility, wound healing, skin hydration, and elasticity. Furthermore, pine bark extracts have been found to reduce neuroinflammation, neurodegeneration, and behavioural impairments linked with Parkinson's disease, and to reduce presynaptic and postsynaptic protein loss in traumatic brain injury as well as bone loss postmenopause. Pine bark extract's antioxidant properties are well-described in preclinical studies, and are believed to explain many of its clinical effects.

Numerous clinical studies exploring pine bark extracts for various health conditions have been reported, with the most extensive research focused on pine bark extract's effects on cardiovascular health. Other potential applications of pine bark extracts have been identified from clinical research, including thrombosis, diabetes and its complications, asthma, attention deficit hyperactivity disorder (ADHD), endometriosis, dysmenorrhea, osteoarthritis, acute and post-partum haemorrhoids, and cognition.[3] However, there is presently no conclusive evidence supporting efficacy of pine bark extracts in treating or preventing these conditions.

A Cochrane systematic review on the effects of pine bark (*Pinus* spp.) extracts for treating chronic disorders included 27 randomised controlled trials (involving a total of 1641 participants) across 10 chronic disorders (asthma, ADHD, cardiovascular disease and risk factors, chronic venous insufficiency, diabetes mellitus, erectile dysfunction, female sexual function, osteoarthritis, osteopenia and traumatic brain injury).[1] The included studies tested different treatment durations (4 weeks–6 months), doses and dosages, as well as single-ingredient (Pygnogenol®, Flavangenol®, Oligopin®, Enzogenol®) and multi-ingredient products (eg pine bark extracts combined with L-arginine) with different chemical profiles. Currently, available evidence is insufficient to support the efficacy of pine bark extracts and the certainty of evidence across all outcomes is very low, partly due to the small sample sizes (11–156 participants), inconsistent outcome measures, and poor-quality reporting across the included studies.[1]

Larger trials are required involving patients sampled from other population groups and using robust outcome measures for the health conditions being studied. Also, trial reports should provide comprehensive descriptions of pine bark extracts tested, including whether the product meets accepted standards for pharmaceutical quality.

Several other clinical trials investigating the effects of pine bark extracts on different health conditions, including diabetes/pre-diabetes, cardiovascular disease, cancer, polycystic ovary syndrome, endometriosis, peri-menopause, metabolic syndrome, cognitive performance, and skin ageing, have been conducted or are underway.[1] However, apart from the Cochrane review discussed earlier, no rigorous systematic reviews or meta-analyses are available that evaluate the effectiveness and safety of pine bark extracts for these conditions.

Adverse effects

Between 2002 and 2013, spontaneous reports of suspected adverse reactions associated with pine bark extracts included urticaria, headache, nausea, diarrhoea, gastric pain, gas, eczema, non-traumatic nosebleed, joint pain, dizziness, bruising, mouth ulcers, coloured urine, and rash, with gastrointestinal symptoms being reported most often.[1,3] At present, there are no known safety concerns with pine bark extracts when consumed in usual quantities. However, comprehensive investigation of the clinical safety profile of pine bark extracts, including contemporary products, and their constituents, where used in a pharmaceutical/medicinal context, is required.

Due to insufficient safety data, the use of pine bark extracts by children, and by pregnant or breastfeeding women should be avoided.

Interactions

Although there have been no reported instances of drug or food interactions with pine bark extracts, caution should be

exercised because of the potential effects of these extracts in stimulating the immune system, reducing platelet aggregation, and lowering blood glucose concentrations. This is especially important for individuals taking immunosuppressants, antidiabetic, antiplatelet, and anticoagulant medications. *In vitro*, pycnogenol inhibits platelet aggregation and may enhance the inhibitory effects of aspirin on platelet aggregation; however, whether this is clinically relevant is not yet clear.[6]

Key references

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