Pycnogenol (Pinus pinaster ssp. atlantica)

While some complementary and alternative techniques have been studied scientifically, high-quality data regarding safety, effectiveness, and mechanism of action are limited or controversial for most therapies. Whenever possible, it is recommended that practitioners be licensed by a recognized professional organization that adheres to clearly published standards. In addition, before starting a new technique or engaging a practitioner, it is recommended that patients speak with their primary healthcare provider(s). Potential benefits, risks (including financial costs), and alternatives should be carefully considered. The below monograph is designed to provide historical background and an overview of clinically-oriented research, and neither advocates for or against the use of a particular therapy.

Related Terms:
- Cocklebut, condensed tannins, Evelle® (vitamins C and E, carotenoids, selenium, zinc, amino acids, glycosaminoglycans, blueberry extract, Pycnogenol), French maritime pine bark extract, French Pinus maritime bark, grape marc extract, leucoanthocyanidins, Pinus pinaster, Pinus maritima, oligomeric proanthocyanidin complexes (OPCs), Pinaceae (family), proanthocyanidins, PYC, pygenol, stickwort, Zinopin (Pycnogenol and Standardized Ginger Root Extract (SGRE).

Background

- Pycnogenol® is the patented trade name for a water extract of the bark of the French maritime pine (Pinus pinaster ssp. atlantica), which is grown in coastal south-west France. Pycnogenol® contains oligomeric proanthocyanidins (OPCs) as well as several other bioflavonoids: catechin, epicatechin, phenolic fruit acids (such as ferulic acid and caffeic acid), and taxifolin. Procyanidins are oligometric catechins found at high concentrations in red wine, grapes, cocoa, cranberries, apples, and some supplements such as Pycnogenol®.
- There has been some confusion in the U.S. market regarding OPC products containing Pycnogenol® or grape seed extract (GSE), because one of the generic terms for chemical constituents ("pycnogens") is the same as the patented trade name (Pycnogenol®). Some GSE products were formerly erroneously labeled and marketed in the U.S. as containing "pycnogens." Although GSE and Pycnogenol® do contain similar chemical constituents (primarily in the OPC fraction), the chemical, pharmacological, and clinical literature on the two products is distinct. The term Pycnogenol® should therefore only be used to refer to this specific proprietary pine bark extract. Scientific literature regarding this product should not be referenced as a basis for the safety or effectiveness of GSE.

Scientific Evidence

Uses
These uses have been tested in humans or animals. Safety and effectiveness have not always been proven. Some of these conditions are potentially serious, and should be evaluated by a qualified healthcare provider.

<table>
<thead>
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<th>Grade</th>
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<tr>
<th>Asthma</th>
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<tr>
<td>Condition</td>
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<td>-----------------------------------------------</td>
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<tr>
<td>Chronic venous insufficiency</td>
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<tr>
<td>ADHD (Attention Deficient Hyperactivity Disorder)</td>
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<tr>
<td>Antioxidant</td>
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<tr>
<td>Cramps (muscular pain)</td>
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<tr>
<td>Diabetes</td>
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<tr>
<td>Diabetic microangiopathy</td>
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<tr>
<td>Dysmenorrhea (painful menstruation)</td>
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Pycnogenol® may offer clinical benefit to both children and adults with asthma. Additional study is needed before a strong recommendation can be made.

**Chronic venous insufficiency**

Chronic venous insufficiency (CVI) is a syndrome that includes leg swelling, varicose veins, pain, itching, skin changes, and skin ulcers. The term is more commonly used in Europe than in the United States. Pycnogenol® used in people with chronic venous insufficiency is reported to reduce edema and pain. Pycnogenol® may also be used in the management of other CVI symptoms. Additional study is needed before a strong recommendation can be made.

**ADHD (Attention Deficient Hyperactivity Disorder)**

Pycnogenol® has been used in adult patients with ADHD to improve concentration, but does not appear to be more effective than placebo. Further research is necessary in this area before a firm conclusion can be reached.

**Antioxidant**

Due to conflicting study results, it is unclear if Pycnogenol® has significant antioxidant effects in humans. Further research is necessary.

**Cramps (muscular pain)**

Pycnogenol® may effectively prevent cramps, muscular pain at rest, and pain after/during exercise in normals, in athletes prone to cramps, in patients with venous disease, in claudicants, and in diabetics with microangiopathy. Further high quality trials are needed to make a firm recommendation.

**Diabetes**

Supplementation of Pycnogenol® with conventional diabetes treatment may lower glucose levels and improve endothelial function. Further research is needed to confirm these results.

**Diabetic microangiopathy**

Supplementation with Pycnogenol® may improve symptoms associated with diabetic microangiopathy. Further research is needed to confirm these results.
Preliminary human data shows that Pycnogenol® may have a potential analgesic (pain relieving) effect on menstrual pain. Further research is needed to confirm these results.

<table>
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<tr>
<th><strong>Erectile dysfunction</strong></th>
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<tr>
<td>Pycnogenol®, in combination with L-arginine, may cause an improvement in sexual function in men with erectile dysfunction. It is not known what effect each of the individual compounds may have directly on this condition. Further research is needed.</td>
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<tr>
<th><strong>Gingival bleeding / plaque</strong></th>
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<tr>
<td>Chewing gum containing Pycnogenol® is reported to minimize gingival bleeding and plaque formation. Pyconogenol® has also been added to toothpaste for antioxidant effect. Further research is needed to confirm these results.</td>
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<table>
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<tr>
<th><strong>High blood pressure</strong></th>
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<tr>
<td>Use of Pycnogenol® may reduce the need for nifedipine and decrease systolic blood pressure in patients with high blood pressure. Further research is needed to confirm these results.</td>
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<th><strong>Platelet aggregation</strong></th>
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<td>One human study reports reduced platelet aggregation in smokers. Further research is needed before a clear conclusion can be reached.</td>
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<th><strong>Prevention of blood clots/edema during long airplane fights</strong></th>
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<tr>
<td>Pycnogenol® treatment may be effective in decreasing the number of thrombotic events (DVT and SVT) in moderate-to-high risk subjects, during long-haul flights. Edema (swelling) may also be reduced. Further research is needed to confirm these results.</td>
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<th><strong>Retinopathy</strong></th>
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<tr>
<td>Several studies report benefits of Pycnogenol® in the treatment and prevention of retinopathy, including slowing the progression of retinopathy in diabetics. Better-quality research is needed before a firm conclusion can be reached.</td>
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<th><strong>High cholesterol</strong></th>
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<tr>
<td>Pycnogenol® may reduce low-density lipoprotein (LDL/&quot;bad cholesterol&quot;) levels and increased high-density lipoprotein (HDL/&quot;good cholesterol&quot;) levels. Due to conflicting</td>
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increased high-density lipoprotein (HDL/"good cholesterol") levels. Due to conflicting data, further studies are necessary before a clear conclusion can be drawn.

**Male infertility**

Human studies report that Pycnogenol® may improve sperm quality and function in sub-fertile men. Further research is needed to confirm these results.

**Melasma (chloasma)**

Melasma (or chloasma) is a common disorder of hyperpigmentation of the skin predominately affecting sun-exposed areas in women. Formations of tan or brown patches/spots may occur. Pycnogenol® has been reported to decrease the darkened area and the pigment intensity of melasma and improve symptoms of fatigue, constipation, body pains, and anxiety. Additional research is needed before a clear recommendation can be made.

**Sunburn**

Pycnogenol®, taken by mouth, may reduce erythema (redness of the skin) caused by solar ultraviolet light. Further study is needed before a recommendation can be made.

**Systemic lupus erythematosus (SLE)**

Pycnogenol® may be useful as a second line therapy to reduce inflammatory features of SLE. Further research is needed before a recommendation can be made.

**Venous leg ulcers**

Pycnogenol® may be useful for reduction of leg ulcers. Further research is needed before a recommendation can be made.

*Key to grades: A: Strong scientific evidence for this use; B: Good scientific evidence for this use; C: Unclear scientific evidence for this use; D: Fair scientific evidence against this use (it may not work); F: Strong scientific evidence against this use (it likely does not work).*

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**TRADITION/THEORY**

The below uses are based on tradition, scientific theories, or limited research. They often have not been thoroughly tested in humans, and safety and effectiveness have not always been proven. Some of these conditions are potentially serious, and should be evaluated by a qualified healthcare provider. There may be other proposed uses that are not listed below.

- ACE-inhibitor activity, Alzheimer's disease, antihistamine, antimicrobial, anti-parasitic, arthritis,
atherosclerosis, autoimmune disorders, bleeding, bone marrow production, cancer prevention, cancer treatment, cardiac mitral valve prolapse, cardiovascular disease, cerebral ischemia, chemotherapy side effects, easy bruising, Ehlers-Danlos syndrome, exercise capacity, fat burning, G6PD deficiency, gout prevention (xanthine oxidase and dehydrogenase inhibitor), hemorrhoids, immune enhancement, immune suppression, improving skin smoothness and elasticity, inflammation, inflammatory bowel disease, inhibition of TNF-alpha, increased human growth hormone, joint hypermobility, leukemia, lung cancer, musculoskeletal problems, osteoporosis, periodontitis, poor tissue healing, premenstrual syndrome, macular degeneration, motion sickness, myocardial ischemia/reperfusion injury, myalgia, myopathy, night vision, pelvic pain, neurodegenerative diseases, prevention of fat formation, psoriasis, reducing scar formation, retinal protection, rheumatoid arthritis, sickle cell anemia, skin disorders, skin aging, spinal scoliosis, varicose veins, vascular problems, vasorelaxant, venous thromboembolism (VTE), wound healing.

DOsing

The below doses are based on scientific research, publications, traditional use, or expert opinion. Many herbs and supplements have not been thoroughly tested, and safety and effectiveness may not be proven. Brands may be made differently, with variable ingredients, even within the same brand. The below doses may not apply to all products. You should read product labels, and discuss doses with a qualified healthcare provider before starting therapy.

Adults (18 years and older)
- In general, 25-360 milligrams has been taken by in divided dosed by mouth per day. For gum health, 5 milligrams Pycnogenol® in chewing gum for 14 days has been used.
- Pycnogenol® appears to be absorbed into the bloodstream in about 20 minutes. Once absorbed, therapeutic effects are purported to last for approximately 72 hours, followed by excretion in the urine. Because of its astringent taste and occasional minor stomach discomfort, it may be best to take Pycnogenol® with or after meals.

Children (younger than 18 years)
- Due to insufficient data, Pycnogenol® is not recommended for use by children.

Safety

The U.S. Food and Drug Administration does not strictly regulate herbs and supplements. There is no guarantee of strength, purity or safety of products, and effects may vary. You should always read product labels. If you have a medical condition, or are taking other drugs, herbs, or supplements, you should speak with a qualified healthcare provider before starting a new therapy. Consult a healthcare provider immediately if you experience side effects.

Allergies
- Individuals should not take Pycnogenol® if allergic to it or any of its components.

Side Effects and Warnings
- Pycnogenol® is generally reported as being well tolerated. Low acute and chronic toxicity with mild unwanted effects may occur in a small percentage of patients following oral administration. Because of its astringent taste and occasional minor stomach discomfort, it may be best to take Pycnogenol® with or after meals. To date, no serious adverse effects
have been reported in the available scientific literature, although systematic study of safety is not available.

- In theory, Pycnogenol® may alter blood sugar levels. Caution is advised in patients with diabetes or hypoglycemia, and in those taking drugs, herbs, or supplements that affect blood sugar. Serum glucose levels may need to be monitored by a healthcare provider, and medication adjustments may be necessary.

- In theory, Pycnogenol® may increase the risk of bleeding. Caution is advised in patients with bleeding disorders or taking drugs that may increase the risk of bleeding. Dosing adjustments may be necessary.

**Pregnancy & Breastfeeding**

- Pycnogenol® is not recommended during pregnancy or breastfeeding due to lack of scientific evidence.

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## Interactions

Most herbs and supplements have not been thoroughly tested for interactions with other herbs, supplements, drugs, or foods. The interactions listed below are based on reports in scientific publications, laboratory experiments, or traditional use. You should always read product labels. If you have a medical condition, or are taking other drugs, herbs, or supplements, you should speak with a qualified healthcare provider before starting a new therapy.

### Interactions with Drugs

- Pycnogenol® may interact with other blood pressure lowering medications, specifically angiotensin converting enzyme inhibitors (ACE-I) such as benazepril (Lotensin®), captopril (Capoten®), enalapril (Vasotec®), fosinopril (Monopril®), lisinopril (Prinivil®), moexipril (Univasc®), perindopril (Aceon®), quinapril (Accupril®), ramipril (Altace®), trandolapril (Mavik®), or angiotensin converting enzyme receptor blockers such as losartan (Cozaar®), irbesartan (Avapro®), candesartan, cilexetil (Atacand®), or valsartan (Diovan®).

- Pycnogenol® may lower blood sugar levels. Caution is advised when using medications that may also lower blood sugar. Patients taking drugs for diabetes by mouth (such as metformin, glyburide, glipizide) or insulin should be monitored closely by a qualified healthcare provider. Medication adjustments may be necessary.

- Pycnogenol® may increase the risk of bleeding when taken with drugs that increase the risk of bleeding. Some examples include aspirin, anticoagulants ("blood thinners") such as warfarin (Coumadin®) or heparin, anti-platelet drugs such as clopidogrel (Plavix®), and non-steroidal anti-inflammatory drugs such as ibuprofen (Motrin®, Advil®) or naproxen (Naprosyn®, Aleve®).

- Pycnogenol® may interfere with immunosuppressant or immunostimulant drugs.

- In theory, Pycnogenol® and antioxidants may have additive effects.

- Pycnogenol® prevented fluoride induced kidney damage.

- Pycnogenol® may have protective effects against alcohol's effects on brain neurons, but further research is needed to confirm these results.

### Interactions with Herbs and Dietary Supplements

- Although data has yet to confirm this claim, it has been proposed that Pycnogenol® may increase vitamin C levels.
Pycnogenol® may lower blood sugar levels. Caution is advised when using herbs or supplements that may also lower blood sugar. Blood glucose levels may require monitoring, and doses may need adjustment.

Pycnogenol® may increase the risk of bleeding when taken with herbs and supplements that are believed to increase the risk of bleeding. Multiple cases of bleeding have been reported with the use of Ginkgo biloba, and fewer cases with garlic and saw palmetto. Numerous other agents may theoretically increase the risk of bleeding, although this has not been proven in most cases.

In theory, Pycnogenol® may interact with herbs and supplements that effect blood pressure. Caution is advised.

Pycnogenol® may interfere with immunosuppressant or immunostimulant herbs and supplements.

Pycnogenol® and other antioxidants may have additive effects.

**AUTHOR INFORMATION**

This information is based on a systematic review of scientific literature edited and peer-reviewed by contributors to the Natural Standard Research Collaboration (www.naturalstandard.com).

**REFERENCES**

Natural Standard developed the above evidence-based information based on a thorough systematic review of the available scientific articles. For comprehensive information about alternative and complementary therapies on the professional level, go to www.naturalstandard.com. Selected references are listed below.

