



DOSSIER · SUBSTANCE

Pine Bark Extract

Pine bark extract, in particular from the French maritime pine (*Pinus pinaster*), counts among the most frequently investigated plant extracts. A substantial portion of the work focuses on studies conducted in humans. The most interesting finding: The majority of controlled studies examine **antioxidative** and **cardiovascular** effects, while other areas of application are often supported only by observational studies or laboratory findings.

510

STUDIES IN
TOTAL

119

IN HUMANS

54

OF WHICH
CONTROLLED

81

IN ANIMALS

66

IN THE LAB

Figures from the IHR study database · Last updated 2026-10-15

How to Read This Dossier

ESTABLISHED

measured in humans, with a comparison group

PLAUSIBLE

supported by mechanism, animal studies or observation

HYPOTHESIS

a likely connection that still needs to be tested

Pine Bark Extract at a Glance

ORIGIN:

Pine bark extract is obtained from the bark of the French maritime pine (*Pinus pinaster* Aiton), which grows on the south-western French Atlantic coast. The extract contains a standardised complex of oligomeric proanthocyanidins (OPCs), monomeric flavonoids such as catechin and taxifolin, as well as phenolic acids. The bioavailability of the OPCs is limited, but their monomeric metabolites are detectable systemically.

EVIDENCE BASE:

510 evaluated studies · 54 controlled human studies · 65 observational studies · 17 review articles · 81 animal studies · 50 cell culture studies

STRONGEST INDICATIONS:

- **Oxidative stress** Controlled studies show a significant increase in the antioxidant capacity of plasma (ORAC) and an improvement in endothelial function (e.g. flow-mediated dilatation, FMD). Preclinical data provide an indication of an NO-mediated mechanism.
- **Cardiovascular markers** Controlled studies showed an improvement in endothelial dysfunction and a reduction in systolic blood pressure. A modulation of the lipid profile (e.g. increase in HDL cholesterol, reduction in oxidised LDL) was observed.
- **Inflammatory processes:** Controlled studies show a reduction in pro-inflammatory cytokines (IL-6, IL-1 β) and an inhibition of matrix metalloproteinases (MMPs) in osteoarthritis. The preclinical findings on endothelial function require further investigation in humans.
- **Metabolism:** Clinical studies report a reduction in the HbA_{1c} value and an improvement in the lipid profile. Preclinical in-vitro data suggest a possible inhibition of α -glucosidase; the effect in humans has not been investigated.
- **Safety and tolerability:** Studies show good tolerability without serious adverse effects. Gastrointestinal complaints occur as frequently as in placebo groups.

LIMITATIONS:

- Long-term studies with clinically relevant endpoints (e.g. cardiovascular events, progression of osteoarthritis) are still outstanding.
- The findings on gut health, bone density and cognitive functions stem predominantly from observational studies or preclinical laboratory findings.
- Many controlled studies originate from the environment of a manufacturer, which may limit the independence of the results. Dose-response relationships are rarely investigated systematically.

CLASSIFICATION:

Pine bark extract, rich in oligomeric proanthocyanidins, shows in controlled studies an increased antioxidant capacity, lower inflammation markers and an improved endothelial function. The clinical relevance of these findings for long-term courses and hard endpoints is still outstanding.

1. What Pine Bark Extract Is

Pine bark extract is obtained from the bark of the French maritime pine (*Pinus pinaster* Aiton), which grows on the south-western French Atlantic coast. The OPCs consist predominantly of dimers and trimers of catechin and epicatechin, linked via C4-C8 or C4-C6 bonds. The chemical composition varies according to the extraction method, with aqueous-ethanolic methods yielding the highest amounts of bioactive polyphenols.

For the evidence base, the **bioavailability** of the constituents is decisive. OPCs are only limitedly absorbed in the intestine, whereas their monomeric metabolites – for example through microbial cleavage – are detectable systemically. Most controlled studies use standardised extracts such as *Pycnogenol*®, which is standardised to a minimum content of 70 % OPCs. However, direct comparisons between different extract qualities or manufacturing processes are often lacking. The measurement of effects is usually carried out via **surrogate markers** (e.g. antioxidant capacity in plasma), less frequently via clinical endpoints.

2. What the Studies Show in Detail

The key human studies and the most important reviews — by application area, with population, duration, preparation, measured variable and result, as the original studies report them. Numbers appear only where the study states them.

Distribution of the **controlled human studies** by application area — the numbers are not additive, as one study may be assigned to several areas:

APPLICATION AREA	CONTROLLED STUDIES
Oxidative stress	21
Heart and circulation	19
Inflammatory processes	18
Metabolism	16
Fatigue and stress	15
Safety and tolerability	14
Musculoskeletal system	9

APPLICATION AREA	CONTROLLED STUDIES
Bones and joints	8

Metabolism

Fasting plasma glucose, HbA_{1c}, endothelin-1, 6-keto-prostaglandin F_{1α} and nitric oxide (NO) were measured as laboratory parameters. The HbA_{1c} value decreased significantly in the verum group in the first month ($p < 0.05$ vs. placebo), but showed no significant difference in the following months. NO increased in both groups, without significant difference. Tolerability was good; adverse effects (e.g. gastrointestinal complaints) occurred equally frequently in both groups. The study provides an indication of a short-term change in the HbA_{1c} laboratory value, but without evidence of a clinical effect on the course of diabetes. Limiting factors are the short observation period and the lack of dose-response analysis ¹.

Primary endpoints were HDL cholesterol, apolipoprotein A-1, the apolipoprotein B-100/A-1 ratio, systolic blood pressure and oxidised LDL (ox-LDL) as laboratory parameters. After 5 weeks, HDL cholesterol rose by 14.06 % ($p = 0.012$) and apolipoprotein A-1 by 8.12 % ($p = 0.038$), while the apolipoprotein B-100/A-1 ratio fell by 10.26 % ($p = 0.046$). Systolic blood pressure decreased by 6.36 mmHg ($p = 0.014$ vs. baseline), and ox-LDL fell significantly ($p < 0.05$). The study shows an improvement in the laboratory parameters of the lipid profile and a reduction in systolic blood pressure, but without placebo comparison for blood pressure and without evidence of a clinical effect on cardiovascular events. The small sample size and short duration limit the strength of the findings ⁹.

In a preclinical in vitro study the inhibitory effect of pine bark extract (Pycnogenol) on α -glucosidase, a key enzyme in carbohydrate digestion, was investigated. The extract showed an IC₅₀ of approximately 5 μ g/ml, markedly more potent than green tea extract (IC₅₀ ~20 μ g/ml) or acarbose (IC₅₀ ~1 mg/ml). Fractionated analyses revealed that higher-molecular-weight procyanidin oligomers produced the strongest inhibitory effect. The results suggest preclinically a possible enzyme inhibition in the intestine; such inhibition was observed in vitro. Evidence of enzyme inhibition in vivo or an effect in humans remains outstanding ²⁵.

HYPOTHESIS Some controlled studies showed indications that pine bark extract, via inhibition of α -glucosidase and improvement of endothelial function, could favourably influence metabolic parameters. The data on lipid modulation and blood pressure reduction provide initial indications; however, long-term studies with clinically relevant endpoints (e.g. cardiovascular events) remain outstanding.

Intestine and Microbiome

The primary endpoints were endothelial function (measured by endothelin-1, 6-keto-prostaglandin F_{1α} and NO) as well as the dose of the calcium antagonist nifedipine. NO rose in both groups without significant difference. Angiotensin II decreased more strongly in the placebo group. The study provided indications, based on laboratory values, regarding parameters of endothelial function, however no clinical effect on the cardiovascular system or other clinical endpoints ².

Targeted studies on the effect of pine bark extract on the gut microbiome, intestinal permeability or inflammatory bowel diseases are lacking. The available data are limited to indirect indications from metabolic and inflammation studies.

Inflammatory Processes

The primary endpoint was endothelial function, measured as flow-mediated dilatation (FMD) of the brachial artery. Secondary endpoints included oxidative stress markers (e.g. malondialdehyde), inflammatory parameters (e.g. CRP) and platelet adhesion. FMD improved in the Pycnogenol group from 5.3 ± 2.6 % to 7.0 ± 3.1 % ($p < 0.0001$), whereas it declined in the placebo group from 5.4 ± 2.4 % to 4.7 ± 2.0 % ($p = 0.051$). The difference between groups was significant (estimated treatment effect 2.75 %; $p < 0.001$). Oxidative stress and inflammatory markers showed no significant changes. The study demonstrated an improvement in endothelial function in patients with coronary heart disease, however no significant change in the measured systemic inflammatory parameters and no assessment of clinical endpoints ⁴.

In a randomised, placebo-controlled study with 100 patients with knee osteoarthritis (stage I-II), 150 mg pine bark extract (Pycnogenol) was supplemented daily for 3 months. Primary endpoints were the WOMAC score (Western Ontario and McMaster Universities Osteoarthritis Index) and pain intensity (visual analogue scale, VAS). Analgesic consumption decreased in the verum group and increased in the placebo group. The study provides an indication of symptomatic improvement in osteoarthritis, however without structural or biochemical inflammatory markers (e.g. IL-6, CRP) ⁷.

In a randomised, placebo-controlled pilot study with 33 patients with severe knee osteoarthritis (scheduled for total knee arthroplasty), 200 mg Pycnogenol was supplemented daily for 3 weeks. Primary endpoints were gene expression of cartilage-degradation and inflammatory markers in chondrocytes as well as protein concentrations in serum and synovial fluid. Gene expression of MMP3, MMP13 and IL1B decreased significantly ($p \leq 0.05$), while ADAMTS-5 concentration in serum fell by 30 % ($p \leq 0.05$). The study showed changes in gene and protein markers for inflammatory and cartilage-degradation processes, however without clinical endpoints or long-term data ¹⁶.

The primary endpoints were inflammatory markers (IL-6, IL-1 β , CRP) and clinical scores (APACHE II, SOFA). The 28-day survival rate was higher in the verum group ($p = 0.04$). The study provides an indication of a possible effect in severe head trauma, however without data on long-term sequelae or functional outcomes ¹³.

HYPOTHESIS Individual studies suggest inflammation-modulating effects of pine bark extract in various models (osteoarthritis, severe head trauma). The mechanisms may include inhibition of NF- κ B and MMPs as well as reduction of pro-inflammatory cytokines. However, comparative studies with uniform inflammatory markers and clinical endpoints remain outstanding.

Oxidative Stress

In a randomised, placebo-controlled double-blind study with 16 healthy young men, 180 mg pine bark extract (Pycnogenol) was supplemented daily for 2 weeks. The primary endpoint was endothelium-dependent vasodilatation, measured as forearm blood flow (FBF) after acetylcholine stimulation. After 2 weeks FBF rose in the Pycnogenol group from 13.1 ± 7.0 to 18.5 ± 4.0 ml/min/100 ml tissue ($p < 0.05$), whereas the placebo group showed no change.

Endothelium-independent vasodilatation (after sodium nitroprusside) remained unchanged. Administration of the NO-synthase inhibitor L-NMMA abolished the effect of Pycnogenol, indicating an NO-mediated action. The study demonstrated an improvement in endothelial function, however without direct measurement of oxidative stress ⁵.

In an observational study with 25 healthy volunteers, 150 mg pine bark extract (Pycnogenol) was supplemented daily for 6 weeks. Primary endpoints were the antioxidant capacity of plasma (ORAC) and the lipid profile. After 6 weeks the ORAC value rose significantly ($p < 0.05$) and returned to baseline after a 4-week washout phase. LDL oxidisability and lipid peroxides showed no significant changes. The study demonstrated an increase in antioxidant capacity, however without direct correlation to clinical endpoints ²³.

In an ex-vivo study with 7 healthy volunteers, after 5-day intake of 200 mg Pycnogenol daily the effect of plasma on MMP-9 secretion in monocytes and NF- κ B activation was examined. The volunteers' plasma inhibited MMP-9 secretion significantly ($p < 0.05$) and reduced NF- κ B activation. The study provides preclinical indications that bioavailable constituents of the extract may exert anti-inflammatory effects, however without direct measurement of oxidative stress in vivo or clinical endpoints ²⁴.

HYPOTHESIS Preclinical and surrogate-endpoint studies suggest antioxidant effects of pine bark extract that manifest as improved endothelial function and increased systemic antioxidant capacity. Whether these effects are clinically relevant (e.g. for cardiovascular events) remains outstanding, as long-term studies with hard endpoints are lacking.

Bone and Joints

The primary endpoints were the distribution of extract constituents and their metabolites in serum, blood cells and synovial fluid as well as gene expression of cartilage-degradation and inflammatory markers. Catechin and taxifolin were detected primarily in blood cells, whereas the microbial metabolite δ -(3,4-dihydroxy-phenyl)- γ -valerolactone, ferulic acid and caffeic acid were present mainly in synovial fluid. Taxifolin was detectable exclusively in the Pycnogenol group. The study demonstrated distribution of the polyphenols into relevant compartments, however without direct clinical endpoints or structural changes ¹⁰.

Studies on the effect of pine bark extract on bone density, fracture risk or structural joint changes (e.g. on MRI) remain outstanding. The available controlled studies examined symptomatic improvements in osteoarthritis and showed effects on pain and function scores.

Safety and Tolerability

In a randomised, placebo-controlled double-blind study with 40 patients with chronic venous insufficiency (CVI), 300 mg pine bark extract (Pycnogenol) was supplemented daily for 2 months. Primary endpoints were symptom scores (oedema, heaviness, pain) and venous blood flow (Doppler sonography). Adverse effects were recorded; laboratory parameters (haematology, blood chemistry) showed no abnormalities. The study provided indications of good tolerability, however without long-term data or dose-finding studies ¹².

In a review of herbal interventions in asthma, two studies on pine bark extract (Pycnogenol) were identified that formed part of a larger analysis of various agents. One of the included studies examined 200 peri- and postmenopausal women (200 mg/day for 8 weeks) and reported no adverse effects. The data suggest good tolerability; however, systematic surveys on long-term adverse effects or drug interactions remain outstanding.

Overall Picture

The available studies consistently show antioxidant, anti-inflammatory and endothelium-protective effects of pine bark extract in preclinical and clinical models. Particularly well investigated are preclinical indications as well as initial clinical data on surrogate parameters of endothelial function (e.g. FMD, NO bioavailability), a reduction of pro-inflammatory cytokines (IL-6, IL-1 β) as well as findings on antioxidant capacity (ORAC) and MMP-9 inhibition. Preclinical studies—for example from animal and cell models—provide indications of influences on metabolic parameters (glucose, lipids), blood pressure, osteoarthritis symptoms and chronic venous insufficiency, although the effect in humans has not yet been investigated. The mechanisms probably include inhibition of NF- κ B, modulation of NO synthase and a direct radical-scavenging function of the procyanidins.

The controlled studies are nevertheless incomplete: many are small ($n < 100$), of short duration (< 3 months) and employ different extract preparations and dosages (50–300 mg/day). Direct comparisons with established therapies (e.g. statins, NSAIDs) are lacking, as are long-term studies with hard endpoints (e.g. cardiovascular events, progression of osteoarthritis). In addition, the mechanisms of action at the cellular level (e.g. signalling pathways, gene expression) are only incompletely elucidated.

Methodology of the Evidence Base

The controlled studies on pine bark extract comprise randomised, placebo-controlled double-blind studies (RCTs) with small sample sizes ($n = 20$ –100) and short duration (2–12 weeks). Typical endpoints are surrogate parameters such as glucose, lipids, blood pressure, inflammatory markers (CRP, IL-6) or functional tests (FMD, WOMAC-Score). Observational studies and ex-vivo experiments supplement the data on mechanisms (e.g. enzyme inhibition, gene expression). However, the following are systematically lacking: (1) dose-response studies, (2) long-term data (> 6 months), (3) direct comparisons with standard therapies, (4) studies on structural endpoints (e.g. joint space width, plaque volume) and (5) data on interactions with medications (e.g. anticoagulants, antidiabetics).

Antioxidative Effects $\neq$ Clinical Benefit

The great majority of controlled studies on pine bark extract examine

ANTIOXIDATIVE MARKERS

such as **plasma total antioxidant capacity** or **LDL oxidation**. These parameters are, however, **not valid predictors of clinical endpoints**. Even when the extract increases antioxidant capacity in vitro or ex vivo, it remains unclear whether this leads to a measurable improvement in disease courses. The **transferability** of such laboratory findings to the human organism is limited, because oxidative processes in the body are complexly regulated and do not correlate linearly with disease risks.

A further problem is the

MIXING OF CORRELATION AND CAUSALITY

. Many studies show **associations** between intake of pine bark extract and improved markers – for example a reduction in **blood pressure** or a decrease in **inflammatory parameters**. Whether these effects are, however, **causally** attributable to the extract or mediated by other factors (e.g. lifestyle changes) often remains unresolved. In addition, **comparisons with established therapies** are frequently absent, so that the **clinical relevance** of the observed effects is difficult to assess.

3. How Robust the Research Is

Research on pine bark extract is distributed across **basic investigations**, **animal studies** and **human studies**, with the latter conducted in controlled fashion in roughly half of cases. The controlled human studies focus on **antioxidative effects**, **cardiovascular diseases** and **inflammatory processes**, followed by metabolic disorders and exhaustion syndromes. Individual works also examine **cognitive functions**, **gut health** and **bone diseases**, albeit with markedly lower study numbers. The most frequently cited controlled studies date from the 2000s and deal with **diabetes**, **endothelial dysfunction** and **ADHD**.

The methodological quality of the controlled studies is **heterogeneous**. While some randomised, placebo-controlled double-blind studies exist, **long-term data** or **replications** by independent research groups are often lacking. Many works were conducted with small sample sizes, and **dose-response relationships** are rarely investigated systematically. In addition, numerous controlled studies originate from the environment of the manufacturer *Pycnogenol®*, which can limit the **independence** of the results. Observational studies and laboratory findings dominate the evidence base for application areas such as **bone metabolism** or **gut health**, whereas controlled studies are scarcely available here.

4. What Is Frequently Claimed — and What the Data Provide

CLAIM	EVIDENCE BASE
Chronic Venous Insufficiency	Older controlled studies show improvements in subjective symptoms. More recent replications or long-term data are lacking. The research base is still building.
ADHD	A controlled study reports effects in children. Independent confirmations or studies in adults are still pending. Further research is still pending.
Osteoarthritis	A controlled study shows symptomatic improvements. Mechanistic studies or long-term data are lacking. The evidence is preliminary.
Cognitive Performance	Individual controlled studies investigate healthy subjects or mild cognitive impairments. No data on neurodegenerative diseases exist.

5. The Most Robust Works

Ordered by strength of evidence, not by prominence. The complete evaluation comprises considerably more works; the most robust are shown here.

Controlled Studies in Humans

- ¹ Antidiabetic effect of Pycnogenol French maritime pine bark extract in patients with diabetes type II (2004)
- ² Pycnogenol, French maritime pine bark extract, improves endothelial function of hypertensive patients (2004)
- ³ Treatment of ADHD with French maritime pine bark extract, Pycnogenol (2006)
- ⁴ Effects of Pycnogenol on endothelial function in patients with stable coronary artery disease: a double-blind, randomized, placebo-controlled, cross-o (2012)
- ⁵ Pycnogenol, French maritime pine bark extract, augments endothelium-dependent vasodilation in humans (2007)
- ⁶ PYCNOGENOL in chronic venous insufficiency (2000)
- ⁷ Effect of pine bark extract (Pycnogenol) on symptoms of knee osteoarthritis (2008)
- ⁸ A randomised, double-blind, placebo-controlled trial on the effect of Pycnogenol on the climacteric syndrome in peri-menopausal women (2007)
- The role of food supplements in the treatment of the infertile man (2003)
- ⁹ Effects of low molecular weight procyanidin rich extract from french maritime pine bark on cardiovascular disease risk factors in stage-1 hypertensive (2016)
- ¹⁰ Distribution of Constituents and Metabolites of Maritime Pine Bark Extract (Pycnogenol[®]) into Serum, Blood Cells, and Synovial Fluid of Pat (2017)

- ¹¹ A randomized controlled trial investigating the effect of Pycnogenol and Bacopa CDRI08 herbal medicines on cognitive, cardiovascular, and biochemical (2012)
- ¹² Pycnogenol in chronic venous insufficiency (2000)
- ¹³ The effect of French maritime pine bark extract supplementation on inflammation, nutritional and clinical status in critically ill patients with trauma (2021)
- ¹⁴ Pycnogenol® (extract of French maritime pine bark) for the treatment of chronic disorders (2012)
- ¹⁵ Evaluation of the effects of pycnogenol (French maritime pine bark extract) supplementation on inflammatory biomarkers and nutritional and clinical status (2020)
- ¹⁶ Cellular pharmacodynamic effects of Pycnogenol® in patients with severe osteoarthritis: a randomized controlled pilot study (2017)
- ¹⁷ Effect of Pycnogenol® on attention-deficit hyperactivity disorder (ADHD): study protocol for a randomised controlled trial (2017)
- ¹⁸ French maritime pine bark extract (pycnogenol) in association with triple combination cream for the treatment of facial melasma in women: a double-blind study (2021)
- ¹⁹ No beneficial effects of pine bark extract on cardiovascular disease risk factors (2010)
- ²⁰ Pycnogenol® French maritime pine bark extract in randomized, double-blind, placebo-controlled human clinical studies (2024)
- ²¹ Effects of French maritime pine bark extract (Oligopin®) supplementation on bone remodeling markers in postmenopausal osteopenic women: A randomized controlled trial (2019)
- Investigation of a complex plant extract for mild to moderate erectile dysfunction in a randomized, double-blind, placebo-controlled, parallel-arm study (2010)
- ²² Pilot study on the clinical effects of dietary supplementation with Enzogenol, a flavonoid extract of pine bark and vitamin C (2003)

6. Summary

B.

The inflammation-modulating effect could influence structural processes in osteoarthritis or acute inflammations (e.g. traumatic brain injury). However, studies with uniform inflammatory markers and clinical endpoints are lacking to conclusively evaluate these effects. The antioxidant effect is plausible, but its clinical relevance remains unclear, as long-term data with hard endpoints are missing.

To clarify the clinical relevance of pine bark extract, long-term studies with large samples and hard endpoints (e.g. cardiovascular events, progression of osteoarthritis) would be necessary. Systematic dose-response analyses and direct comparisons with established therapies (e.g. statins, NSAIDs) are also lacking, as are studies on mechanisms of action at the cellular level (e.g. signalling pathways, gene expression). In addition, independent replications of the existing findings should be carried out to rule out possible biases due to manufacturer interests.

7. What Remains Open

- **Dose-response relationship:** Systematic investigations into optimal dosages are lacking. Most studies use fixed doses without titration.
- **Long-term safety:** Data on intake over more than 6 months are rare. It is unclear whether effects diminish or side effects accumulate.
- **Interactions:** Possible interactions with medications (e.g. anticoagulants) have hardly been investigated. Laboratory findings suggest CYP enzyme modulation.

Frequently Asked Questions

Can pine bark extract be used in diabetes?

A frequently cited controlled study reports investigations into the prevention of diabetic effects in type 2 diabetes; the results are inconsistent. However, **replications** by independent groups or **long-term data** are lacking. The study examined **surrogate parameters** such as **fasting blood glucose**, but not hard endpoints such as diabetic sequelae. The **clinical relevance** of the observed effects is therefore unclear. Other controlled studies on metabolic disorders show **inconsistent results**.

How strong is the evidence base for cardiovascular diseases?

Most controlled studies on cardiovascular diseases examine **endothelial function** or **blood pressure**. Some works show **improvements** in these parameters, though often in small samples and without **long-term follow-up**. One study in patients with **coronary heart disease** found no significant effects on clinical endpoints. The **evidence** is therefore **preliminary** and insufficient for a therapeutic recommendation.

Are there indications of anti-inflammatory effects?

Several controlled studies report **reductions in inflammatory markers** such as **CRP** or **IL-6**. However, many of these data come from **small studies** with short duration. In addition, **comparisons with established anti-inflammatory agents** are lacking. The **clinical relevance** of the observed effects is unclear, as no studies on **chronic inflammatory diseases** (e.g. rheumatoid arthritis) are available. The evidence base is **exploratory**, not confirmatory.

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International Health Research

Research, put in context. Every statement leads to the original paper; the decision in the individual case rests with the treating professional.
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