Clinical Studies on Pycnogenol®, French Maritime Pine Bark extract (*Pinus pinaster* Aiton subsp *atlantica*)

Chronic venous insufficiency

Author/Year	Subject	Design	Duration	Dosage	Preparation	Results/Conclusion
Arcangeli, 2000	Chronic venous insufficiency	R,DB,PC n=40	3 months	300 mg (1 capsule 3x/day)	100 mg capsules	Reduction of heaviness, swelling, and pain were 54%, 64%, and 64% respectively. The elimination of these symptoms was in the order of 33%, 63%, and 58%, respectively.
Petrassi *et al.*, 2000	Chronic venous insufficiency	R,DB,PC n=40	3 months	300 mg (1 capsule 3x/day)	100 mg capsules	Reduction of heaviness and swelling were 60% and 74%, respectively. Elimination of these symptoms was in the order of 33% and 88%, respectively.
Schmidtke and Schoop, 1995	Hydrostatic edema of the lower limbs	DB,PC,R n=40 22 men, 18 women	6 days	360 mg/day vs. placebo (no compression therapy during the course of treatment)	20 mg tablets	After 6 day treatment, leg volume increased from maintaining sitting position for 1 and 2 hours respectively, was significantly reduced ($p<0.001$) in active group and not in the placebo group. Authors concluded, based on objective and subjective effects, that Pycnogenol® is an effective and well-tolerated remedy that can be recommended in the treatment of venous disorders.
Sirnelli-Walter and Weil-Masson, 1988	Chronic venous insufficiency, PMS	O n=80	3 months	80 mg (2 tablets 2x/day)	20 mg tablets	Elimination of symptoms: 89% edema, 85% swelling, 83% heaviness of legs, 77% night cramps, 75% hemorrhoids, 73% pruritis, 69% pain, 44% ecchymoses, and 39% varicose vein. Mammary tension and abdominal pain eliminated in 61.58% and 44% cases, respectively. In menopausal disorders, nocturnal sweating and hot flashes eliminated in 77% and 62% cases, respectively.
Doucet *et al.*, 1987	Chronic venous insufficiency	O n=65	2 months	80 mg (4 tablets daily), for 20 days each month after end of menstruation	20 mg tablets	Improvement of 100% pruritus, 89% night cramps, 79% sensation of swelling, 59% edema, and 62.5% heaviness of legs.
Schmidtke and Schoop, 1984	Chronic venous insufficiency	PC n=29	4 days	120 mg (2 tablets 3x/day)	20 mg tablets	Significantly less increase in leg volume ($p<0.01$).
Feine-Haake, 1975	Chronic venous insufficiency	O n=110	4–12 weeks	2 tablets 3x daily for 1st week (90 mg/day); 1 tablet 3x/day (45 mg/day) thereafter for 3–12 weeks)	15 mg tablets	Efficacy rate was 70% to 83% for reduction of cramps, pain, and swelling of legs.

Retinal Vascular Disorders

Author/Year	Subject	Design	Duration	Dosage	Preparation	Results/Conclusion
Spadea and Balestrazzi, 2001	Retinal vascular disorders	R,DB,PC n=40	2 months	150 mg	50 mg capsules	The deterioration of vision was not only prevented, but even improved significantly. Retinal vascularization improved. Electroretinogram confirmed beneficial effects of Pycnogenol®.
Magnard *et al.*,1970	Diabetic retinopathy	O n=40	1–6 months	Initial dose: 80–120 mg (2–3 tablets 2x/day 1st week); Maintenance dose: 40–80 mg (1–2 tablets/day)	20 mg tablets	Improvement Score was good to excellent in 36 subjects, moderate in 3, and no effect in 1.

KEY: C – controlled, **CC** – case-control, **CH** – cohort, **CI** – confidence interval, **Cm** – comparison, **CO** – crossover, **CS** – cross-sectional, **DB** – double-blind, **E** – epidemiological, **LC** – longitudinal cohort, **MA** – meta-analysis, **MC** – multi-center, **n** – number of patients, **O** – open, **OB** – observational, **OL** – open label, **OR** – odds ratio, **P** – prospective, **PB** – patient-blind, **PC** – placebo-controlled, **PG** – parallel group, **PS** – pilot study, **R** – randomized, **RC** – reference-controlled, **RCS** – retrospective cross-sectional, **RS** - retrospective, **S** – surveillance, **SB** – single-blind, **SC** – single-center, **U** – uncontrolled, **UP** – unpublished, **VC** – vehicle-controlled.

Clinical Studies on Pycnogenol®, French Maritime Pine Bark extract (*Pinus pinaster* Aiton subsp *atlantica*) (cont.)

Platelet Aggregation

Author/Year	Subject	Design	Duration	Dosage	Preparation	Results/Conclusion
Pütter *et al*., 1999	Smoking-induced platelet aggregation	PC n=38	Single dose	25–200 mg (single doses)	25 mg tablets	Complete prevention of smoking-induced platelet aggregation.
Wang *et al*., 1999	Platelet aggregation in cardiovascular patients	R,DB,PC n=40	4 weeks	450 mg (3 tablets 3x/day)	50 mg tablets	Significant reduction of platelet aggregation ($p<0.05$), increased microcirculation.

Other

Author/Year	Subject	Design	Duration	Dosage	Preparation	Results/Conclusion
Hosseini *et al*., 2001a	Mild hypertension (140–159 mmHG)	R,DB,PC, CO n=11	16 weeks	200 mg (2 capsules 2x/day)	50 mg capsules	Significant decrease of systolic blood pressure ($p<0.05$) compared to placebo. Decrease of diastolic blood pressure did not reach significance. Thromboxane levels decreased significantly ($p<0.05$).
Hosseini *et al*., 2001b	Asthma	R,DB,PC,CO n=22	8 weeks	1 mg/lb/day, max 200 mg/day	20 mg capsules	Lung function (FEV1/FVC) was significantly improved ($p< 0.003$) compared to placebo. Asthma Symptom Scores improved. Leukotriene levels decreased significantly ($p< 0.003$) compared to placebo.
Stefanescu *et al*., 2001	Systemic lupus erythematosus (SLE), second line therapy beside standard medication	DB,PC,PS n=11 10 women, 1 man	2 months	120 mg/day for 30 days, thereafter 60 mg for 30 days	20 mg tablets	Index for SLE was significantly decreased compared to placebo ($p< 0.018$). Non-significant improvement shown by reduction of reactive oxygen species production. Spontaneous apoptosis, $p56^{lck}$ specific activity in peripheral blood lymphocytes, and erythrocyte sedimentation rate.
Kohama and Suzuki, 1999	Endometriosis, menstrual pain, chronic abdominal pain	O n=39	14–30 days	30–60 mg (2 capsules/day for 2–4 wks; 4 capsules on demand)	15 mg capsules	Improvement of cramps 70%, abdominal pain 80–90%.

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