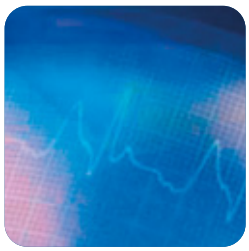
PYCNOGENOL®

Bibliography

V.05.03



HORPHAG

Index

1. Review Articles

Ref. 346

A review on the broad applicability of Pycnogenol® for personalized health care, for prevention as well as treatment.
Strong J
French maritime pine bark extract (Pycnogenol®) and the use of health supplements in the age of personalized medicine.
Panminerva Med 53: 1-2, 2011

Ref. 326

A comprehensive review of the composition and pharmacology of Pycnogenol® as well as the published medical research.
Maimoona A, Naeem I, Saddiqe Z, Jameel K
A review on biological, nutraceutical and clinical aspects of French maritime pine bark extract.
J Ethnopharmacol 133: 261-277, 2011

Ref. 269

A clinical overview based on the full monograph covering published scientific and clinical research on Pycnogenol®.
Oliff H
Scientific and clinical monograph on Pycnogenol®.
The American Botanical Council 2009

Ref. 266

A comprehensive review of research on Pycnogenol® in the field of venous insufficiency.
Gulati OP
Pycnogenol®: a nutraceutical for venous health.
Biomedical Reviews 19: 33-43, 2008

Ref. 261

This review article covers the wide range of contributions of Pycnogenol® for diabetic people, such as lowering of blood glucose and helping with a majority of diabetic complications.
Rohdewald P
Regulation of diabetes by Pycnogenol®.
Botanical medicine in clinical practice. (ed.) Watson, R.R., Preedy, V.R.; Wallingford, England, CABI Publishing, Ch. 62: 587-594, 2008

Ref. 259

A comprehensive review of Pycnogenol®'s anti-inflammatory activity and its role for controlling diverse inflammatory disorders.
Farid R
Pycnogenol® in the treatment of inflammatory diseases: osteoarthritis, asthma and heart disease.
Botanical medicine in clinical practice. (ed.) Watson RR, Preedy VR; Wallingford, England, CABI Publishing, chapter 68: 633-640, 2008

Ref. 258

A review of the extensive number of studies related to treatment of edema with Pycnogenol® including findings on leg swellings occuring during long haul travelling.
Belcaro G, Cesarone MR, Cornelli U, Rohdewald P, Ledda A, Di Renzo A, Stuard, S, Cacchio M, Vinciguerra G, Gizzi G, Pellegrini L, Dugall M, Ricci A, Ruffini I, Fano F
Treatment of chronic venous insufficiency and prevention of economy class syndrome.
Botanical medicine in clinical practice. (ed.) Watson, R.R., Preedy, V.R.; Wallingford, England, CABI Publishing, Ch. 64: 603-609, 2008

Ref. 257
Review of Pycnogenol®'s manifold benefits for cardiovascular health.
Watson RR, Argüelles MC
Pycnogenol® and cardiovascular health.
Botanical medicine in clinical practice. (ed.) Watson, R.R., Preedy, V.R.; Wallingford, England, CABI Publishing, Ch. 56: 538-544, 2008

Ref. 228
Introduction to the pathology of myocarditis and a discussion on mechanisms by which Pycnogenol® may help the heart to recover.
Matsumori A
Treatment Options in Myocarditis.
Herz 32: 452-456, 2007

Ref. 210
Clinical Pharmacology of Pycnogenol® - A review.
Rohdewald P
Clinical Pharmacology of Pycnogenol®.
Pharma Bio World 5: 79-81, 2006

Ref. 180
Pycnogenol®'s beneficial effects in blood micro-circulation, dysmenorrheal, stiff shoulder, and pregnancy associated pain.
Kohama T
Nutritional supplements in clinical practice.
Progr Med 24: 1503-1510, 2004

Ref. 169
Monograph on Safety and efficacy aspects of Pycnogenol®.
Blumenthal M
Pycnogenol® (French Maritime Pine Bark Extract) *Pinus Pinaster* Aiton subsp. *atlantica*.
The American Botanical Council guide to Herbs, 369-373, 2003

Ref. 168
Pycnogenol® as a nutraceutical in cardiovascular health and diabetes.
Gulati OP
The Nutraceutical Pycnogenol®: Its role in cardiovascular health and blood glucose control.
Biomed Rev 16: 49-57, 2005

Ref. 160
Monograph on Pycnogenol® covering pharmacological activities and clinical benefits.
Rohdewald P
Pycnogenol®, French Maritime Pine Bark Extract.
Encyclopedia of Dietary Supplements; Ed. Marcel Dekker, digital publisher, 545-553, 2005

Ref. 114
Review of the cardiovascular health benefits of Pycnogenol®.
Watson RR
Pycnogenol® and cardiovascular health.
Evid Based Integr Med 1: 27-32, 2003

Ref. 094
Summary of beneficial effects of Pycnogenol® for skin care.
Schönlau F
The cosmeceutical Pycnogenol®.
J Appl Cosmetol 20: 241-246, 2002

Ref. 092
Summary of five clinical studies describing the effects of Pycnogenol® in patients with diabetic retinopathy.
Schönlau F, Rohdewald P
Pycnogenol® for diabetic retinopathy: A review.
Int Ophthalmol 24: 161-171, 2002

Review Articles

Ref. 085

Review article on the pharmacologic activities of Pycnogenol®.
Rohdewald P
A review of the French maritime pine bark extract (Pycnogenol®), a herbal medication with a diverse clinical pharmacology.
Int J Clin Pharmacol Ther 40: 158-168, 2002

Ref. 041

A review of the efficacy and safety of Pycnogenol® for treatment of venous disorders.
Gulati OP
Pycnogenol® in venous disorders: A review.
Eur Bull Drug Res 7: 8-13, 1999

Ref. 039

The cardiovascular pharmacological profile of Pycnogenol®, with focus on platelet aggregation prevention is reviewed.
Watson R
Reduction of cardiovascular disease risk factors by French Maritime Pine Bark Extract.
Cardiovasc Rev Rep XX: 326-329, 1999

Ref. 038

This article reviews the antioxidant activity of Pycnogenol® and its effects on the immune system and modulation of inducible nitric oxide synthase.
Virgili F, Kobuchi H, Noda Y, Cossins E, Packer L
Procyanidins from Pinus maritima bark: Antioxidant activity, effects on the immune system and Modulation of Nitrogen Monoxide Metabolism.
In "Antioxidant Food Supplements in human health", ed. L. Packer, M. Hiramatsu and T. Yoshikawa, published by Academic Press, Chapter 21, pages 323-342, 1999

Ref. 034

An introduction to the chemistry, antioxidant activity and biologic properties of Pycnogenol®.
Packer L, Rimbach G, Virgili F
Antioxidant activity and biologic properties of a procyanidin-rich extract from pine (*Pinus maritima*) bark, Pycnogenol®.
J Free Radic Biol Med 27: 704-724, 1999

Ref. 031

The history of ancient pine bark uses to the present day development of Pycnogenol®.
Drehsen G
From ancient pine bark uses to Pycnogenol®
In "Antioxidant Food Supplements in human health", ed. L. Packer, M. Hiramatsu and T. Yoshikawa, published by Academic Press, Chapter 20, pages 311-322, 1999

2. Cardiovascular System

Ref. 349

CLINICAL STUDY: Pycnogenol® taken in addition to heart medications significantly enhances endothelial function in individuals who previously suffered a heart attack.
Enseleit F, Sudano I, Périat D, Winnik S, Wolfrum M, Flammer AJ, Fröhlich GM, Kaiser P, Hirt A, Haile SR, Krasniqi N, Matter CM, Uhlenhut K, Högger P, Neidhart M, Lüscher TF, Ruschitzka F, Noll G
Effects of Pycnogenol® on endothelial function in patients with stable coronary artery disease: a double-blind, randomized, placebo-controlled, cross-over study.
Eur Heart J 33(13): 1589-97, 2012

Ref. 295

CLINICAL STUDY: Pycnogenol® reduces the disturbing "ringing" or "hissing" noise sensation in tinnitus patients which is suggested to result from an improved blood flow to the cochlea of the ears.
Grossi MG, Belcaro G, Cesarone MR, Duggall M, Hosoi M, Cacchio M, Ippolito E, Bavera P
Improvement in cochlear flow with Pycnogenol® in patients with tinnitus: a pilot evaluation.
Panminerva Med 52 (suppl. 1 to No. 2): 63-67, 2010

Ref. 294

CLINICAL STUDY: Pycnogenol® in synergy with CoQ10 strengthens the heart for higher ejection fraction, lower heart rate and a significant increase of physical capacity.
Belcaro G, Cesarone MR, Dugall M, Hosoi M, Ippolito E, Bavera P, Grossi MG
Investigation of Pycnogenol® in combination with coenzymeQ10 in heart failure patients (NYHA II/III).
Panminerva Med 52 (suppl. 1 to No. 2): 21-25, 2010

Ref. 293

CLINICAL STUDY: Pycnogenol® restores compromised kidney function of metabolic syndrome patients as judged by decreased urinary protein and improved blood flow to kidneys.
Stuard S, Belcaro G, Cesarone MR, Ricci A, Cornelli U, Gizzi G
Kidney function in metabolic syndrome may be improved with Pycnogenol®.
Panminerva Med 52 (suppl. 1 to No. 2): 27-32, 2010

Ref. 291

Pycnogenol® protects cardiac muscle from damage resulting from diabetes in an animal model.
Klimas J, Kmecova J, Jankyova S, Yaghi D, Priesolova E, Kyselova Z, Musil P, Ochodnicky P, Krenek P, Kyselovic J, Matyas S
Pycnogenol® improves left ventricular function in streptozotocin-induced diabetic cardiomyopathy in rats.
Phytother Res 24: 969-974, 2010

Ref. 283

CLINICAL STUDY: Pycnogenol® taken as an adjunct to hypertensive medication improves kidney flow and function and further improves blood pressure.
Cesarone MR, Belcaro G, Stuard S, Schönlau F, Di Renzo A, Grossi MG, Dugall M, Cornelli U, Cacchio M, Gizzi G, Pellegrini L
Kidney Flow and Function in Hypertension: Protective Effects of Pycnogenol® in Hypertensive Participants A Controlled Study.
J Cardiovasc Pharmacol Ther 15: 41-46, 2010

Ref. 281

Pycnogenol® protects the kidneys from damage caused by oxidative stress and ischemia in an animal model.
Ozer Sehirli A, Sener G, Ercan F
Protective effects of Pycnogenol® against ischemia reperfusion-induced oxidative renal injury in rats.
Ren Fail 31: 690-697, 2009

Ref. 257

Review of Pycnogenol®'s manifold benefits for cardiovascular health.
Watson RR, Argüelles MC
Pycnogenol® and cardiovascular health.
Botanical medicine in clinical practice. (ed.) Watson, R.R., Preedy, V.R.; Wallingford, England, CABI Publishing, Ch. 56: 538-544, 2008

Ref. 237

CLINICAL STUDY: Pycnogenol® given in addition to diabetic and hypertensive medication significantly further improves blood sugar and cardio-vascular risk factors and allows a majority of patients to lower anti-hypertensive medication.
Zibadi S, Rohdewald P, Park D, Watson RR
Reduction of cardiovascular risk factors in subjects with Type 2 Diabetes by Pycnogenol® supplementation.
Nutr Res 28: 315-320, 2008

Ref. 233

Pycnogenol® lowers platelet hyperactivity more effectively than aspirin in a type I diabetes pharmacologic model suggesting a protective effect from thrombosis in diabetes.
Nocun M, Ulicna O, Muchova J, Durackova Z, Watala C
French maritime pine bark extract (Pycnogenol®) reduces thromboxane generation in blood from diabetic male rats.
Biomed Pharmacother 62: 168-172, 2007

Ref. 230

CLINICAL STUDY: Pycnogenol® increases endothelium-dependent vasodilation by 42%, by enhancing the synthesis of nitric oxide in young healthy men.
Nishioka K, Hidaka T, Nakamura S, Umemura T, Jitsuiki D, Soga J, Goto C, Chayama K, Yoshizumi M, Higashi Y
Pycnogenol®, French Maritime Pine Bark Extract, augments endothelium-dependent vasodilation in humans.
Hypertens Res 30: 775-780, 2007

Ref. 229

Pycnogenol® counteracts viral infection and prevents development of virus-induced heart muscle inflammation.
Matsumori A, Higuchi H, Shimada M
French maritime pine bark extract inhibits viral replication and prevents development of viral myocarditis.
J Card Fail 13: 785-791, 2007

Ref. 216

Pycnogenol® prevents heart failure damage in mice.
Zibadi S, Yu Q, Rohdewald PJ, Larson DF, Watson RR
Impact of Pycnogenol® on cardiac extracellular matrix remodeling induced by L-NAME administration to old mice.
Cardiovasc Toxicol 7: 10-18, 2007

Ref. 207

Pycnogenol® shows strengthening of heart muscle cells *in vitro*.
Hasegawa N, Kinoshita H, Mochizuki M
Pycnogenol® increases the probability of the contraction state in chick embryonic cardiomyocytes, indicating inotropic effects.
Phytother Res 21: 181-182, 2007

Ref. 200

CLINICAL STUDY: Pycnogenol® reduces oedema as side effect from hypotensive medication in hypertensive subjects.
Belcaro G, Cesarone MR, Ricci A, Cornelli U, Rohdewald P, Ledda A, Di Renzo A, Stuard S, Cacchio M, Vinciguerra G, Gizzi G, Pellegrini L, Dugall M, Fano F
Control of edema in hypertensive subjects treated with calcium antagonist (Nifedipine) or angiotensin-converting enzyme inhibitors with Pycnogenol®.
Clin Appl Thromb Hemost 12: 440-444, 2006

Ref. 187 CLINICAL STUDY: Pycnogenol® significantly lowered LDL and increased HDL in 155 menopausal women during a treatment period of 6 months.
Yang HM, Liao MF. Zhu SY, Liao MN, Rohdewald P
A randomized, double-blind, placebo-controlled trial on the effect of Pycnogenol® on the climacteric syndrome in peri-menopausal women.
Acta Obstet Gynecol Scand 86: 978-985, 2007

Ref. 177 Pycnogenol® and Coenzyme Q10 enhance cardiovascular health synergistically.
Watson RR
Nutraceutical Synergism: Pycnogenol® and Coenzyme Q10 Enhance Cardiovascular Health.
Evid Based Integrative Med 2: 67-70, 2005

Ref. 168 Pycnogenol® as a nutraceutical in cardiovascular health and diabetes (Review).
Gulati OP
The Nutraceutical Pycnogenol®: its role in cardiovascular health and blood glucose control.
Biomed Rev 16: 49-57, 2005

Ref. 140 Pycnogenol® increases red blood cell membrane fluidity and protects erythrocytes against oxidative stress.
Sivonova M, Waczulikova I, Kilanczyk E, Hrnciarova M, Bryszewska M, Klajnert B, Durackova Z
The effect of Pycnogenol® on the erythrocyte membrane fluidity.
Gen Physiol Biophys 23: 39-51, 2004

Ref. 117 CLINICAL STUDY: Pycnogenol® as an adjunct to hypotensive medication with Nifedipine improves endothelial function and allows for lowering the drug dosage.
Liu X, Wei J, Tan F, Zhou S, Würthwein G, Rohdewald P
Pycnogenol® French maritime pine bark extract, improves endothelial function of hypertensive patients.
Life Sci 74: 855-862, 2004

Ref. 114 A review of published beneficial effects of Pycnogenol® for cardiovascular health.
Watson RR
Pycnogenol® and cardiovascular health.
Evid Based Integrative Med 1: 27-32, 2003

Ref. 093 CLINICAL STUDY: Pycnogenol® supplementation lowered total cholesterol and LDL and increased HDL, resulting in a better atherosclerotic index.
Durackova Z, Trebaticka B, Novotny V, Zitnanova I, Breza J
Lipid metabolism and erectile function improvement by Pycnogenol®, extract from the bark of *Pinus pinaster* in patients suffering from erectile Dysfunction - a pilot study
Nutr Res 23: 1189-1198, 2003

Ref. 090 CLINICAL STUDY: Pycnogenol® supplementation improves blood antioxidant capacity, lowers LDL and increases HDL cholesterol in human volunteers.
Devaraj S, Vega-López S, Kaul N, Schönlau F, Rohdewald P, Jialal I
Supplementation with a pine bark extract rich in polyphenols increases plasma antioxidant capacity and alters plasma lipoprotein profile.
Lipids 37: 931-934, 2002

Ref. 079 CLINICAL STUDY: Pycnogenol® lowered LDL significantly in patients with chronic venous insufficiency while horse chestnut seed extract had no effect.
Koch R
Comparative study of Venostasin® and Pycnogenol® in chronic venous insufficiency.
Phytother Res 16: 1-5, 2002

Ref. 080

CLINICAL STUDY: Pycnogenol® reduces blood pressure in hypertensive patients not taking medication.
Hosseini S, Lee J, Sepulveda RT, Rohdewald P, Watson RR
A randomized, double-blind, placebo-controlled, prospective, 16 week crossover study to determine the role of Pycnogenol® in modifying blood pressure in mildly hypertensive patients.
Nutr Res 21: 1251-1260, 2001

Ref. 053

CLINICAL STUDY: Pycnogenol® inhibits smoking-induced increase of thromboxane B_2 levels, which explains the decreased platelet aggregation observed with Pycnogenol® in smokers.
Araghi-Niknam M, Hosseini S, Larson D, Rohdewald P, Watson RR
Pine bark extract reduces platelet aggregation.
Int Med 2: 73-77, 1999

Ref. 043

CLINICAL STUDY: Pycnogenol® inhibits platelet aggregation and adhesion and improves blood micro-circulation in heart disease patients.
Wang S, Tan D, Zhao Y, Gao G, Gao X, Hu L
The effect of Pycnogenol® on the microcirculation, platelet function and ischemic myocardium in patients with coronary artery diseases.
Eur Bull Drug Res 7: 19-25, 1999

Ref. 042

Pycnogenol® helps to maintain a healthy circulation through vasodilatation, anti platelet aggregation, free radical scavenging and capillary sealing effects. The role of endothelial nitric oxide (NO) is also discussed.
Rohdewald P
Reducing the risk for stroke and heart infarction with Pycnogenol®.
Eur Bull Drug Res 7: 14-18, 1999

Ref. 036

CLINICAL STUDY: Pycnogenol® inhibits smoking induced platelet aggregation in dose-dependent manner in humans. The effect lasts for more than 6 days and unlike aspirin does not increase bleeding.
Pütter M, Grotemeyer KHM, Würthwein G, Araghi-Niknam M, Watson RR, Hosseini S, Rohdewald P
Inhibition of smoking-induced platelet aggregation by aspirin and Pycnogenol®.
Thromb Res 95: 155-161, 1999

Ref. 027

Pycnogenol® counteracts the constriction of blood vessels. The vaso-relaxant activity of Pycnogenol® is mediated through nitric oxide.
Fitzpatrick DF, Bing B, Rohdewald P
Endothelium-dependent vascular effects of Pycnogenol®.
J Cardiovasc Pharmacol 32: 509-515, 1998

Ref. 017

Pycnogenol® inhibits the angiotensin II converting enzyme (ACE) and produces a moderate hypotensive effect in rats.
Blazso G, Gaspar R, Gabor M, Rüve H-J, Rohdewald P
ACE inhibition and hypotensive effect of procyanidinis containing extract from the bark of *Pinus pinaster* Sol.
Pharm Pharmacol Lett 6: 8-11, 1996

3. Venous Disorders

Ref. 370

A concise, yet comprehensive, up to date review on preclinical and clinical research on Pycnogenol® related to venous insufficiency and thrombosis management.
Gulati OP
Pycnogenol® in Chronic Venous Insufficiency and Related Venous Disorders.
Phytother Res – ahead of print, 2013

Ref. 337

CLINICAL STUDY: Pycnogenol® protects people who suffered deep vein thrombosis from subsequently developing edema and recurring thrombosis over a 12 month investigation period.
Errichi BM, Belcaro G, Hosoi M, Cesarone MR, Dugall M, Feragalli B, Bavera P, Hosoi M, Zulli C, Corsi M, Ledda A, Luzzi R, Ricci A
Prevention of post thrombotic syndrome with Pycnogenol® in a twelve month study.
Panminerva Med 53: 21-27, 2011

Ref. 292

CLINICAL STUDY: Pycnogenol® is as effective as compression stockings for relieving signs and symptoms of chronic venous insufficiency.
Cesarone MR, Belcaro G, Rohdewald P, Pellegrini L, Ledda A, Vinciguerra G, Ricci A, Ippolito E, Fano F, Dugall M, Cacchio M, Di Renzo A, Hosoi M, Stuard S, Corsi M
Improvement of signs and symptoms of chronic venous insufficiency and microangiopathy with Pycnogenol®: A prospective, controlled study.
Phytomedicine 17: 835-839, 2010

Ref. 280

CLINICAL STUDY: Pycnogenol® treatment lowers pain and bleeding in acute haemorroids and improves recovery.
Belcaro G, Cesarone MR, Errichi B, Di Renzo A, Grossi MG, Ricci A, Dugall M, Cornelli U, Cacchio M, Rohdewald P
Pycnogenol® Treatment of Acute Hemorrhoidal Episodes.
Phytother Res 24: 438-444, 2010

Ref. 258

A review of the extensive number of studies related to treatment of edema with Pycnogenol® including findings on leg swellings occuring during long haul travelling.
Belcaro G, Cesarone MR, Cornelli U, Rohdewald P, Ledda A, Di Renzo A, Stuard S, Cacchio M, Vinciguerra G, Gizzi G, Pellegrini L, Dugall M, Ricci A, Ruffini I, Fano F
Treatment of chronic venous insufficiency and prevention of economy class syndrome.
Botanical medicine in clinical practice. (ed.) Watson, R.R., Preedy, V.R.; Wallingford, England, CABI Publishing, Ch. 64: 603-609, 2008

Ref. 206

CLINICAL STUDY: Pycnogenol® provides relief in venous microangiopathy.
Cesarone MR, Belcaro G, Rohdewald P, Pellegrini L, Ledda A, Vinciguerra G, Ricci A, Gizzi G, Ippolito E, Fano F, Dugall M, Acerbi G, Cacchio M, Di Renzo A, Hosoi M, Stuard S, Corsi M
Rapid Relief of Signs/Symptoms in Chronic Venous Microangiopathy With Pycnogenol®: A Prospective, Controlled Study.
Angiology 57: 569-576, 2006

Ref. 200

CLINICAL STUDY: Pycnogenol® reduces oedema, a common side effect of chronic treatment with anti-hypertensive medication.
Belcaro G, Cesarone MR, Ricci A, Cornelli U, Rohdewald P, Ledda A, Di Renzo A, Stuard S, Cacchio M, Vinciguerra G, Gizzi G, Pellegrini L, Dugall M, Fano F
Control of Edema in Hypertensive Subjects Treated With Calcium Antagonist (Nifedipine) or Angiotensin-Converting Enzyme Inhibitors with Pycnogenol®.
Clin Appl Thromb Hemost 12: 440-444, 2006

Ref. 195

CLINICAL STUDY: Pycnogenol® accelerates healing of diabetic ulcers.
Belcaro G, Cesarone MR, Errichi BM, Ledda A, Di Renzo A, Stuard S, Dugall M, Pellegrini L, Gizzi G, Rohdewald P, Ippolito E, Ricci A, Cacchio M, Cipollone G, Ruffini I, Fano F, Hosoi M
Diabetic Ulcers: Microcirculatory Improvement and Faster Healing with Pycnogenol®.
Clin Appl Thromb Hemost 12: 318-323, 2006

Ref. 182

CLINICAL STUDY: Pycnogenol® demonstrates superior activity versus Daflon® in treatment of chronic venous insufficiency in a comparative clinical study.
Cesarone MR, Belcaro G, Rohdewald P, Pellegrini L, Ledda A, Vinciguerra G, Ricci A, Gizzi G, Ippolito E, Fano F, Dugall M, Acerbi G, Cacchio M, Di Renzo A, Hosoi M, Stuard S, Corsi M
Comparison of Pycnogenol® and Daflon® in Treating Chronic Venous Insufficiency: A Prospective, Controlled Study.
Clin Appl Thromb Hemost 12: 205-212, 2006

Ref. 172

CLINICAL STUDY: Ulcers of the lower legs heal faster after oral plus topical application of Pycnogenol®.
Belcaro G, Cesarone MR, Errichi BM, Ledda A, Di Renzo A, Stuard S, Dugall M, Pellegrini L, Rohdewald P, Ippolito E, Ricci A, Cacchio M, Ruffini I, Fano F, Hosoi M
Venous Ulcers: Microcirculatory Improvement and Faster Healing with Local Use of Pycnogenol®.
Angiology 56: 699-705, 2005

Ref. 151

CLINICAL STUDY: Pycnogenol® effectively counteracts ankle swellings occurring during long-haul travelling in a double-blind, placebo-controlled study.
Cesarone MR, Belcaro G, Rohdewald P, Pellegrini L, Ippolito E, Scoccianti M, Ricci A, Dugall M, Cacchio M, Ruffini I, Fano F, Acerbi G, Vinciguerra MG, Bavera P, Di Renzo A, Errichi BM, Mucci F
Prevention of edema in long flights with Pycnogenol®.
Clin Appl Thromb Hemost 11: 289-294, 2004

Ref. 134

CLINICAL STUDY: Pycnogenol® prevents thrombosis and thrombophlebitis on long-haul flights.
Belcaro G, Cesarone MR, Rohdewald P, Ricci A, Ippolito E, Dugall M, Griffin M, Ruffini I, Acerbi G, Vinciguerra MG, Bavera P, Di Renzo A, Errichi BM, Cerritelli F
Prevention of venous thrombosis and thrombophlebitis in long-haul flights with Pycnogenol®.
Clin Appl Thromb Hemost 10: 373-377, 2004

Ref. 116

CLINICAL STUDY: Pycnogenol® in combination with nattokinase prevents deep vein thrombosis during long–haul flights.
Cesarone MR, Belcaro G, Nicolaides AN, Ricci A, Geroulakos G, Ippolito E, Brandolini R, Vinciguerra G, Dugall M, Griffin M, Ruffini I, Acerbi G, Corsi M, Riordan N, Stuard S, Bavera P, Di Renzo A, Kenyon J, Errichi BM
Prevention of venous thrombosis in long-haul flights with Flite Tabs: The Lonflit- Flite randomized controlled trial.
Angiology 54: 531-539, 2003

Ref. 112

CLINICAL STUDY: Addition of Pycnogenol® to troxerutin significantly enhances the efficacy of chronic venous insufficiency treatment and prolongs symptom relief.
Riccioni C, Sarcinella R, Izzo A, Palermo G, Liguori L
Efficacia della troxerutina associata al Pycnogenol® nel trattamento farmacologico dell'insufficienza venosa.
Minerva Cardioangiol 52: 43-48, 2004

Ref. 079

CLINICAL STUDY: Pycnogenol® demonstrated higher efficacy for treatment of venous insufficiency than horse chestnut seed extract in a clinical trial.
Koch R
Comparative study of Venostasin® and Pycnogenol® in chronic venous insufficiency.
Phytother Res 16: 1-5, 2002

Ref. 067

CLINICAL STUDY: Pycnogenol® provides significant symptoms relief from chronic venous insufficiency symptoms.
Petrassi C, Mastromarino A, Spartera C
Pycnogenol® in chronic venous insufficiency.
Phytomed 7: 383-388, 2000

Ref. 066

CLINICAL STUDY: Pycnogenol® significantly improves chronic venous insufficiency and relieves disappearance of symptoms of chronic venous insufficiency.
Arcangeli P
Pycnogenol® in chronic venous insufficiency.
Fitoterapia 71: 236-244, 2000

Ref. 041

Review article: Describes efficacy and safety profile of Pycnogenol® in treating venous disorders in humans. Mechanisms of reducing oedema are also discussed.
Gulati OP
Pycnogenol® in venous disorders: A review.
Eur Bull Drug Res 7: 8-13, 1999

Ref. 009

Pycnogenol® increases the pathologically low capillary wall resistance. Pycnogenol® is shown to be the most potent among other bioflavonoids tested for strengthening capillary walls to decrease capillary filtration.
Gabor M, Engi E, Sonkodi S
Die Kapillarwandresistenz und ihre Beeinflussung durch wasserlösliche Flavonderivate bei spontan hypertonischen Ratten.
Phlebologie 22: 178-182, 1993

4. Diabetic Syndrome

Ref. 360

CLINICAL STUDY: Pycnogenol® improves all signs and symptoms of metabolic syndrome to healthy values within three months.
Belcaro G, Cornelli U, Luzzi R, Cesarone MR, Dugall M, Feragalli B, Errichi S, Ippolito E, Grossi MG, Hosoi M, Cornelli M, Gizzi G.
Pycnogenol® supplementation improves health risk factors in subjects with metabolic syndrome
Phytother Res 27: 1572-1578, 2013

Ref. 334

In pharmacological experiments Pycnogenol® is demonstrated to protect renal cells from glucose damage in a diabetic nephropathy model.
Kim YJ, Kim YA, Yokozawa T
Pycnogenol® modulates apoptosis by suppressing oxidative stress and inflammation in high glucose-treated renal tubular cells.
Food Chem Toxicol 49: 2196-2201, 2011

Ref. 308

Pycnogenol® provides antioxidant protective effects to the liver in an animal diabetes model.
Parveen K, Khan MR, Mujeeb M, Siddiqui WA
Protective effects of Pycnogenol® on hyperglycemia-induced oxidative damage in the liver of type 2 diabetic rats.
Chem Biol Interact 186: 219 -227, 2010

Ref. 300

Pycnogenol® is shown in an in vitro model to facilitate better glucose uptake by fat cells which suggests anti-diabetic benefits.
Lee HH, Kim K-J, Lee OH, KJ, Lee BY
Effect of Pycnogenol® on glucose transport in mature 3T3-L1 adipocytes.
Phytother Res 24: 1242-1249, 2010

Ref. 293

CLINICAL STUDY: Pycnogenol® improves kidney function of metabolic syndrome patients as judged by lowered urinary albumins and improved kidney perfusion.
Stuard S, Belcaro G, Cesarone MR, Ricci A, Cornelli U, Gizzi G
Kidney function in metabolic syndrome may be improved with Pycnogenol®.
Panminerva Med 52 (suppl. 1 to No. 2): 27-32, 2010

Ref. 288

Pycnogenol® improves endothelial function and blood vessel morphology in an animal model.
Rezzani R, Porteri E, De Ciuceis C, Bonomini F, Rodella LF, Paiardi S, Boari GEM, Platto C, Pilu A, Avanzi D, Rizzoni D, Rosei EA
Effects of melatonin and Pycnogenol® on small artery structure and function in spontaneously hypertensive rats.
Hypertension 55: 1373-1380, 2010

Ref. 271

CLINICAL STUDY: Pycnogenol® taken at early stages of diabetic retinopathy may partially restore vision further to strengthening retinal capillaries.
Steigerwalt R, Belcaro G, Cesarone MR, Di Renzo A, Grossi MG, Ricci A, Dugall M, Cacchio M, Schönlau F
Pycnogenol® improves microcirculation, retinal edema, and visual acuity in early diabetic retinopathy.
J Ocul Pharmacol Ther 25: 537-540, 2009

Ref. 261

This review article comprises the manifold contributions of Pycnogenol® to people who have diabetes.
Rohdewald P
Regulation of diabetes by Pycnogenol®.
Botanical medicine in clinical practice. (ed.) Watson, R.R., Preedy, V.R.; Wallingford, England, CABI Publishing, Ch. 62: 587-594, 2008

Ref. 237

CLINICAL STUDY: Pycnogenol® given in addition to diabetic and hypertensive medication significantly further improves blood sugar and cardio-vascular risk factors and allows a majority of patients to lower anti-hypertensive medication.
Zibadi S, Rohdewald P, Park D, Watson RR
Reduction of cardiovascular risk factors in subjects with Type 2 Diabetes by Pycnogenol® supplementation.
Nutr Res 28: 315-320, 2008

Ref. 233

Pycnogenol® lowers platelet hyperactivity more effectively than aspirin in a type I diabetes pharmacologic model suggesting a protective effect from thrombosis in diabetes.
Nocun M, Ulicna O, Muchova J, Durackova Z, Watala C
French maritime pine bark extract (Pycnogenol®) reduces thromboxane generation in blood from diabetic male rats.
Biomed Pharmacother 62: 168-172, 2007

Ref. 209

Pycnogenol® inhibits dietary carbohydrate absorption by inhibition of alpha-glucosidase.
Schäfer A, Högger P
Oligomeric procyanidins of French maritime pine bark extract (Pycnogenol®) effectively inhibit alpha-glucosidase.
Diabetes Res Clin Pract 77: 41-46, 2007

Ref. 199

CLINICAL STUDY: Pycnogenol® reduces diabetic microangiopathy.
Cesarone MR, Belcaro G, Rohdewald P, Pellegrini L, Ledda A, Vinciguerra G, Ricci A, Gizzi G, Ippolito E, Fano F, Dugall M, Cipollone G, Acerbi G, Cacchio M, Del Boccio G, Di Renzo A, Stuard S, Corsi M
Improvement of diabetic microangiopathy with Pycnogenol®: A prospective, controlled study.
Angiology 57: 431-436, 2006

Ref. 195

CLINICAL STUDY: Pycnogenol® accelerates healing of diabetic ulcers.
Belcaro G, Cesarone MR, Errichi BM, Ledda A, Di Renzo A, Stuard S, Dugall M, Pellegrini L, Gizzi G, Rohdewald P, Ippolito E, Ricci A, Cacchio M, Cipollone G, Ruffini I, Fano F, Hosoi M
Diabetic ulcers: microcirculatory improvement and faster healing with Pycnogenol®.
Clin Appl Thromb Hemost 12: 318-323, 2006

Ref. 184

Pycnogenol® increases anti-oxidative enzyme concentrations in the retina of rats, suggesting a lower risk for retinopathy and cataract formation.
Kamuren ZT, McPeek CG, Sanders RA, Watkins JB
Effects of low-carbohydrate diet and Pycnogenol® treatment on retinal antioxidant enzymes in normal and diabetic rats.
J Ocul Pharmacol Ther 22: 10-18, 2006

Ref. 156

Pycnogenol® either alone or in combination with other antioxidants stimulates antioxidant enzyme activities in the retina of diabetic rats.
Dene BA, Maritime AC, Sanders RA, Watkins JB
Effects of Antioxidant Treatment on Normal and Diabetic rat retinal enzyme activities.
J Ocul Pharmacol Ther 21: 28-35, 2005

Ref. 153

Pycnogenol® either alone or in combination with other antioxidants reduces parameters of oxidative stress in diabetic rats.
Berryman AM, Maritim AC, Sanders RA, Watkins JB
Influence of treatment of Diabetic rats with combinations of Pycnogenol®, beta-carotene, and alpha-lipoic acid on parameters of oxidative stress.
J Biochem Mol Toxicol 18: 345-352, 2004

Ref. 142

CLINICAL STUDY: Pycnogenol® supplementation to diabetic patients lowers glucose levels.
Liu X, Wei J, Tan F, Zhou S, Würthwein G, Rohdewald P
Antidiabetic effect of Pycnogenol® French maritime pine bark extract in patients with diabetes type II.
Life Sci, 75: 2505-2513, 2004

Ref. 109

CLINICAL STUDY: In a dose-finding study Pycnogenol® lowers glucose levels of type II diabetic patients and improves endothelial function.
Liu X, Zhou H-J, Rohdewald P
French maritime pine bark extract Pycnogenol® dose-dependently lowers glucose in type II diabetic patients.
Diabetes Care 27: 839, 2004

Ref. 110

Pycnogenol® inhibits *in vitro* the Maillard reaction which results in advanced glycation end products (AGE) in diabetes.
Zhang TM, Han CH, Han YW, Gong H, Zhang EY, Zhang Y
Inhibitory effect of Pycnogenol® on generation of advanced glycation end products *in vitro*.
Chin Pharmacol Bull 19: 437-440, 2003

Ref. 105

Pycnogenol® lowers blood glucose and increases intracellular antioxidant defense mechanism in diabetic rats.
Maritim A, Dene BA, Sanders RA, Watkins JB
Effect of Pycnogenol® treatment on oxidative stress in streptozotocin-induced diabetic rats.
J Biochem Mol Toxicol 17: 193-199, 2003

Ref. 092

CLINICAL STUDY: The review presents results of five clinical studies with Pycnogenol® showing the efficacy of Pycnogenol® for patients with diabetic retinopathy.
Schönlau F, Rohdewald P
Pycnogenol® for diabetic retinopathy: A review.
Int Ophthalmol 24: 161-171, 2002

Ref. 090

CLINICAL STUDY: Pycnogenol® supplementation reduced blood levels of the "bad" cholesterol LDL in human volunteers.
Devaraj S, Vega-López S, Kaul N, Schönlau F, Rohdewald P, Jialal, I
Supplementation with a pine bark extract rich in polyphenols increases plasma antioxidant capacity and alters plasma lipoprotein profile.
Lipids 37: 931-934, 2002

Ref. 080

CLINICAL STUDY: Pycnogenol® reduces blood pressure, as shown in a randomized, double-blind, placebo-controlled study performed in mildly hypertensive patients. Furthermore, Pycnogenol® significantly decreases the level of the vasoconstrictor factor (thromboxane) in blood of these patients.
Hosseini S, Lee J, Sepulveda RT, Rohdewald P, Watson RR
A randomized, double-blind, placebo-controlled, prospective, 16 week crossover study to determine the role of Pycnogenol® in modifying blood pressure in mildly hypertensive patients.
Nutr Res 21: 1251-1260, 2001

5. Eye Health

Ref. 271

CLINICAL STUDY: Pycnogenol® taken at early stages of diabetic retinopathy may partially restore vision further to strengthening retinal capillaries.
Steigerwalt R, Belcaro G, Cesarone MR, Di Renzo A, Grossi MG, Ricci A, Dugall M, Cacchio M, Schönlau F
Pycnogenol® improves microcirculation, retinal edema, and visual acuity in early diabetic retinopathy.
J Ocul Pharmacol Ther 25: 537-540, 2009

Ref. 227

Pycnogenol® in combination with Lutein provides synergistic antioxidant activity for protecting retinal lipids from oxidation.
Nakanishi-Ueda T, Kamegawa M, Ishigaki S, Tsukahara M, Yano S, Wada K, Yasuhara H
Inhibitory Effect of Lutein and Pycnogenol® on Lipid Peroxidation in Porcine Retinal Homogenate.
J Clin Biochem Nutr 38: 204-210, 2006

Ref. 184

Pycnogenol® increases anti-oxidative enzyme concentrations in the retina of rats, suggesting a lower risk for retinopathy and cataract formation.
Kamuren ZT, McPeek CG, Sanders RA, Watkins JB
Effects of low-carbohydrate diet and Pycnogenol® treatment on retinal antioxidant enzymes in normal and diabetic rats.
J Ocul Pharmacol Ther 22: 10-18, 2006

Ref. 156

Pycnogenol® either alone or in combination with other antioxidants stimulates antioxidant enzyme activities in the retina of diabetic rats.
Dene BA, Maritime AC, Sanders RA, Watkins JB
Effects of Antioxidant Treatment on Normal and Diabetic rat retinal enzyme activities.
J Ocul Pharmacol Ther 21: 28-35, 2005

Ref. 092

CLINICAL STUDY: The review contains results of 5 clinical studies with Pycnogenol® showing the efficacy of Pycnogenol® supplementation for patients with diabetic retinopathy.
Schönlau F, Rohdewald P
Pycnogenol® for diabetic retinopathy: A review.
Int Ophthalmol 24: 161-171, 2002

Ref. 075

CLINICAL STUDY: Pycnogenol® shows beneficial effects in retinopathy.
Spadea L, Balestrazzi E
Treatment of vascular retinopathies with Pycnogenol®.
Phytother Res 15: 219-223, 2001

Ref. 051

Pycnogenol® protects the retina against oxidative damage more effectively than any other antioxidant tested. Pycnogenol® shows synergistic antioxidant effectiveness when combined with other antioxidants such as Coenzyme Q_{10}.
Chida M, Suzuki K, Nakanishi-Ueda T, Ueda T, Yasuhara H, Koide R, Armstrong D
In vitro testing of antioxidants and biochemical end-points in bovine retinal tissue.
Ophthalmic Res 31: 407-415, 1999.

Ref. 018

Pycnogenol® protects the retina of the eye against free radicals damage.
Ueda T, Ueda T, Armstrong D
Preventive effect of natural and synthetic antioxidants on lipid peroxidation in the mammalian eye.
Ophthalmic Res 28: 184-192, 1996.

6. Inflammation

Ref. 283

CLINICAL STUDY: Pycnogenol® significantly lowers the inflammatory marker CRP in hypertensive patients with chronic kidney disease.
Cesarone MR, Belcaro G, Stuard S, Schönlau F, Di Renzo A, Grossi MG, Dugall M, Cornelli U, Cacchio M, Gizzi G, Pellegrini L.
Kidney Flow and Function in Hypertension: Protective Effects of Pycnogenol® in Hypertensive Participants--A Controlled Study.
J Cardiovasc Pharmacol Ther 15: 41-46, 2010

Ref. 272

CLINICAL STUDY: Pycnogenol® inhibits the generation of COX-2 and 5-LOX enyzmes in pharmacological investigations of inflammatory processes in humans.
Canali R, Comitato R, Schönlau F, Virgili F
The anti-inflammatory pharmacology of Pycnogenol® in humans involves COX-2 and 5-LOX mRNA expression in leukocytes.
Int Immunopharmacol 9: 1145-1149, 2009

Ref. 250

CLINICAL STUDY: Pycnogenol® significantly lowers the inflammatory marker CRP in patients with osteoarthritis, thus demonstrating its anti-inflammatory potency.
Belcaro G, Cesarone MR, Errichi S, Zulli C, Errichi BM, Vinciguerra G, Ledda A, Di Renzo A, Stuard S, Dugall M, Pellegrini L, Gizzi G, Ippolito E, Ricci A, Cacchio M, Cipollone G, Ruffini I, Fano F, Hosoi M, Rohdewald P
Variations in C-reactive protein, plasma free radicals and fibrinogen values in patients with osteoarthritis treated with Pycnogenol®.
Redox Rep 13: 271-276, 2008

Ref. 208

Pycnogenol® *in vitro* study provides evidence of chemoprevention.
Buz'Zard AR, Lau BHS
Pycnogenol® reduces Talc-induced Neoplastic Transformation in Human Ovarian Cell Cultures.
Phytother Res 21: 579-586, 2007

Ref. 185

CLINICAL STUDY: Pycnogenol® inhibits key triggers involved in the initiation of an inflammation in a pharmacological investigation in humans.
Grimm T, Chovanova Z, Muchova J, Sumegova K, Liptakova A, Durackova Z, Högger P
Inhibition of NF-kappaB activation and MMP-9 secretion by plasma of human volunteers after ingestion of maritime pine bark extract (Pycnogenol®).
J Inflamm 3: 1-6, 2006

Ref. 183

Pycnogenol® protects intestinal mucosa against radiotherapy induced damage: histo-morphological evidence in rats.
Ramos FM, Schönlau F, Novaes PD, Manzi FR, Bóscolo FN, Almeida SM
Pycnogenol® protects against ionizing radiation as shown in the intestinal mucosa of rats exposed to X-rays.
Phytother Res 20: 676-679, 2006

Ref. 176

Pycnogenol® non-selectively inhibits the activity of enzymes involved in pain sensation during inflammation.
Schäfer A, Chovanová Z, Muchová J, Sumegová K, Liptáková A, Duracková Z, Högger P
Inhibition of COX-1 and COX-2 activity by plasma of human volunteers after ingestion of French maritime pine bark extract (Pycnogenol®).
Biomed Pharmacother 60: 5-9, 2005

Ref. 154

Pycnogenol® significantly counteracts inflammatory damage of the colon in an experimental animal model.
Mochizuki M, Hasegawa N
Therapeutic efficacy of Pycnogenol® in experimental inflammatory bowel diseases.
Phytother Res 18: 1027-1028, 2004

Ref. 107

Matrix metalloproteinases, enzymes involved in connective tissue destruction, are potently inhibited by Pycnogenol® as well as its metabolites found in blood of humans.
Grimm T, Schäfer A, Högger P
Antioxidant activity and inhibition of matrix metalloproteinases by metabolites of maritime pine bark extract (Pycnogenol®).
J Free Radic Biol Med 36: 811-822, 2004

Ref. 074

CLINICAL STUDY: Pycnogenol® dose-dependently inhibits UV-induced erythema in humans. This effect was found to be associated to the anti-inflammatory potency of Pycnogenol®.
Saliou C, Rimbach G, Moini H, McLaughlin L, Hosseini S, Lee J, Watson RR, Packer L
Solar ultraviolet-induced erythema in human skin and nuclear factor-kappa-B-dependent gene expression in keratinocytes are modulated by French maritime pine bark extract.
J Free Radic Biol Med 30: 154-160, 2001

Ref. 068

Pycnogenol® inhibits several mechanisms related to recruitment of leukocytes to tissue which results in anti-inflammatory activity.
Peng Q, Wei Z, Lau BHS
Pycnogenol® inhibits tumor necrosis factor-α-induced nuclear factor kappa B activation and adhesion molecule expression in human vascular endothelial cells.
Cell Mol Life Sci 57: 834-841, 2000

Ref. 019

Pycnogenol® produces anti-inflammatory and anti-oedema effects in two different models. Topical application of Pycnogenol® gel protects the skin against UV radiation.
Blazso G, Gabor M, Rohdewald P
Antiinflammatory activities of procyanidin containing extracts from *Pinus pinaster* Ait. after oral and cutaneous application.
Pharmazie 52: 380-382, 1997

Ref. 010

Pycnogenol® scavenges superoxide radicals *in vitro* and inhibits oedema *in vivo*. The anti-inflammatory and free radical scavenging activities are closely correlated.
Blazso G, Gabor M, Sibbel R, Rohdewald P
Anti-inflammatory and superoxide radical scavenging activities of a procyanidins containing extract from the bark of *Pinus pinaster* sol. and its fractions.
Pharm Parmacol Lett 3: 217-220, 1994

7. Joint Health

Ref. 330

Pycnogenol® helps prevent bone demineralization in an osteoporosis animal model.
Takano T, Kozai Y, Kawamata R, Wakao H, Sakurai T, Kashima I
Inhibitory effect of maritime pine bark extract (Pycnogenol®) on deterioration of bone structure in the distal femoral epiphysis of ovariectomized mice.
Oral Radiol 27: 8-16, 2011

Ref. 272

CLINICAL STUDY: Pycnogenol® inhibits the generation of COX-2 and 5-LOX enyzmes in pharmacological investigations of inflammatory processes in humans.
Canali R, Comitato R, Schonlau F, Virgili F
The anti-inflammatory pharmacology of Pycnogenol® in humans involves COX-2 and 5-LOX mRNA expression in leukocytes.
Int Immunopharmacol 9: 1145-1149, 2009

Ref. 250

CLINICAL STUDY: Pycnogenol® significantly lowers the inflammatory marker CRP in patients with osteoarthritis, thus demonstrating its anti-inflammatory potency.
Belcaro G, Cesarone MR, Errichi S, Zulli C, Errichi BM, Vinciguerra G, Ledda A, Di Renzo A, Stuard S, Dugall M, Pellegrini L, Gizzi G, Ippolito E, Ricci A, Cacchio M, Cipollone G, Ruffini I, Fano F, Hosoi M, Rohdewald P
Variations in C-reactive protein, plasma free radicals and fibrinogen values in patients with osteoarthritis treated with Pycnogenol®.
Redox Rep 13: 271-276, 2008

Ref. 249

CLINICAL STUDY: Pycnogenol® improves flexibility of osteoarthritic joints, lowers pain and allows patients to decrease their pain medication.
Cisar P, Jany R, Waczulikova I, Sumegova K, Muchova J, Vojtassak J, Durackova Z, Lisy M, Rohdewald P
Effect of pine bark extract (Pycnogenol®) on symptoms of knee osteoarthritis.
Phytother Res 22: 1087-1092, 2008

Ref. 223

CLINICAL STUDY: Pycnogenol® improves pain and mobility in osteoarthritis in 156 patients.
Belcaro G, Cesarone MR, Errichi S, Zulli C, Errichi BM, Vinciguerra G, Ledda A, Di Renzo A, Stuard S, Dugall M, Pellegrini L, Errichi S, Gizzi G, Ippolito E, Ricci A, Cacchio M, Cipollone G, Ruffini I, Fano F, Hosoi M, Rohdewald P
Treatment of osteoarthritis with Pycnogenol®. The SVOS (San Valentino Osteo-Arthrosis Study). Evaluation of Signs, Symptoms, Physical Performance and Vascular Aspects.
Phytother Res 22: 518-523, 2008

Ref. 188

CLINICAL STUDY: In osteoarthritis Pycnogenol® reduces pain and joint stiffness and decreases the required NSAID medication.
Farid R, Mirfeizi Z, Mirheidari M, Rezaieyazdi Z, Mansouri H, Esmaelli H, Zibadi S, Rohdewald P, Watson RR
Pycnogenol® supplementation reduces pain and stiffness and improves physical function in adults with knee osteoarthritis.
Nutr Res 27: 692-697, 2007

Ref. 185

CLINICAL STUDY: Pycnogenol® inhibits key triggers involved in the initiation of an inflammation in a pharmacological investigation in humans.
Grimm T, Chovanova Z, Muchova J, Sumegova K, Liptakova A, Durackova Z, Högger P
Inhibition of NF-kappaB activation and MMP-9 secretion by plasma of human volunteers after ingestion of maritime pine bark extract (Pycnogenol®).
J Inflamm 3: 1-6, 2006

Ref. 176

Pycnogenol® non-selectively inhibits the activity of enzymes involved in pain sensation during inflammation in humans.
Schäfer A, Chovanová Z, Muchová J, Sumegová K, Liptáková A, Duracková Z, Högger P
Inhibition of COX-1 and COX-2 activity by plasma of human volunteers after ingestion of French maritime pine bark extract (Pycnogenol®).
Biomed Pharmacother 60: 5-9, 2005

Ref. 107

Pycnogenol® as well as its metabolites found in blood of humans potently inhibit matrix metalloproteinases, enzymes involved in cartilage destruction.
Grimm T, Schäfer A, Högger P
Antioxidant activity and inhibition of matrix metalloproteinases by metabolites of maritime pine bark extract (Pycnogenol®).
J Free Radic Biol Med 36: 811-822, 2004

8. Allergy & Asthma

Ref. 344

CLINICAL STUDY: Pycnogenol® helps to deal with allergic asthma symptoms and allows for lowering medication dosage.
Belcaro G, Luzzi R, Cesinaro Di Rocco P, Cesarone MR, Dugall M, Feragalli B, Errichi BM, Ippolito E, Grossi MG, Hosoi M, Errichi S, Cornelli U, Ledda A, Gizzi G
Pycnogenol® improvements in asthma management.
Panminerva Med 53: 57-64, 2011

Ref. 287

CLINICAL STUDY: Pycnogenol® taken prior to the onset of allergen season lowers hay-fever symptoms and pollen-specific antibodies in allergic people.
Wilson D, Evans M, Guthrie N, Sharma, P, Baisley J, Schönlau F, Burki C
A randomized, double blind, placebo controlled exploratory study to evaluate the potential of Pycnogenol® for improving allergic rhinitis symptoms.
Phytother Res 24: 1115-1119, 2010

Ref. 270

In animal experiments Pycnogenol® suppressed an immediate immunoglobulin type E mediated allergic response. This suggests that Pycnogenol® would have general anti-allergic effectiveness.
Choi YH, Yan GH
Pycnogenol® inhibits immunoglobulin E-mediated allergic response in mast cells.
Phytother Res 23: 1691-1695, 2009

Ref. 149

CLINICAL STUDY: Pycnogenol® improves pulmonary functions and reduces symptoms of asthma in children.
Lau BHS, Riesen SK, Truong KP, Lau EW, Rohdewald P, Barreta RA
Pycnogenol® as an adjunct in the management of childhood Asthma.
J Asthma 41: 825-832, 2004

Ref. 089

Pycnogenol® blocks release of histamine from mast cells *in vitro* to the same extent as the antiasthmatic drug DNCG.
Sharma SC, Sharma S, Gulati OP
Pycnogenol® inhibits the release of histamine from mast cells.
Phytother Res 17: 66-69, 2003

Ref. 077

CLINICAL STUDY: Pycnogenol® reduces asthma symptoms and improves lung function of asthmatic patients in a placebo-controlled, cross-over study.
Hosseini S, Pishnamazi S, Sadrzadeh MH, Farid F, Farid R, Watson RR
Pycnogenol® in the management of asthma.
J Med Food 4: 201-209, 2001

9. Women's Health, Fertility & the Reproductive System

Ref. 378
Pycnogenol® taken with oral contraceptives alleviates endometriosis related pain.
Maia H, Haddad C, Casoy J
Combining oral contraceptives with a natural nuclear factor-kappa B inhibitor for the treatment of endometriosis-related pain.
Int J Womens Health 6: 35-39, 2014

Ref. 376
CLINICAL STUDY: Pycnogenol® significantly improved peri-menopausal symptoms at relatively low daily dosage of 60 mg and was demonstrated to not interfere with sexual hormone levels.
Kohama T, Negami M
Effect of low-dose French maritime pine bark extract on climacteric syndrome in 170 perimenopausal women.
J Reprod Med 58(1-2): 39-46, 2013

Ref. 336
CLINICAL STUDY: Pycnogenol® significantly contributes to reduce signs and symptoms related to the menopausal transition period.
Errichi S, Bottari A, Belcaro G, Cesarone MR, Hosoi M, Cornelli U, Dugall M, Ledda A, Feragalli B
Supplementation with Pycnogenol® improves signs and symptoms of menopausal transition.
Panminerva Med 53: 65-70, 2011

Ref. 220
CLINICAL STUDY: Pycnogenol® significantly lowers menstrual pain and the quantity of required analgesic medication in a multi-center study with four hospitals in Japan.
Suzuki N, Uebaba K, Kohama T, Moniwa N, Kanayama N, Koike K
French Maritime Pine Bark Extract Significantly Lowers the Requirement for Analgesic Medication in Dysmenorrhea. A multicenter, randomized, double-blind, placebo-controlled study.
J Reprod Med 53: 338-346, 2008

Ref. 219
CLINICAL STUDY: Pycnogenol® reduces pain from endometriosis, shows less side effects than hormonal treatment and enabled some women to conceive.
Kohama T, Herai K, Inoue M
Effect of French Martime Pine Bark Extract on endometriosis as compared with Leuprorelin acetate.
J Reprod Med 52: 703-708, 2007

Ref. 187
CLINICAL STUDY: Pycnogenol® improves a broad range of climacteric symptoms in a study with 200 menopausal women.
Yang H-M, Liao M-F, Zhu SY, Liao M-N, Rohdewald P
A randomized, double-blind, placebo-controlled trial on the effect of Pycnogenol® on the climacteric syndrome in peri-menopausal women.
Acta Obstet Gynecol Scand 86: 978-985, 2007

Ref. 174
CLINICAL STUDY: Pycnogenol® reduces low-back pain in late period of pregnancy.
Kohama T, Inoue M
Pycnogenol® Alleviates Pain Associated with Pregnancy.
Phytother Res 20: 232-234, 2006

Ref. 145
CLINICAL STUDY: Pycnogenol® produces analgesic effect in gynaecological disorders such as endometriosis and dysmenorrhea. It reduces menstrual cramps, abdominal pain and tenderness.
Kohama T, Suzuki N, Ohno S, Inoue M
Analgesic efficacy of French maritime pine bark extract in dysmenorrhea. An open clinical trial.
J Reprod Med 49: 828-832, 2004

Ref. 091

CLINICAL STUDY: After treatment with Pycnogenol® increase in functionally normal sperm may allow infertile couples to forgo *in vitro* fertilization.
Roseff SJ
Improvement in sperm quality and function with French maritime pine tree bark extract.
J Reprod Med 47: 821-824, 2002

Ref. 046

CLINICAL STUDY: Pycnogenol® improves the morphology of spermatozoa. The percentage of non-deformed sperms in sub-fertile men was increased by 99% after supplementation with Pycnogenol®.
Roseff S, Gulati R
Improvement of sperm quality by Pycnogenol®.
Eur Bull Drug Res 7: 33-36, 1999

Ref. 045

CLINICAL STUDY: Pycnogenol® helps in gynaecological disorders such as endometriosis and dysmenorrhea. It reduces menstrual cramps, abdominal pain and tenderness.
Kohama T, Suzuki N
The treatment of gynaecological disorders with Pycnogenol®.
Eur Bull Drug Res 7: 30-32, 1999

10. Sport & Endurance

Ref. 368

CLINICAL STUDY: Pycnogenol® reduces oxidative stress and improves physical performance in athletes.
Vinciguerra G, Belcaro G, Bonanni E, Cesarone MR, Ledda A, Hosoi M, Dugall M, Cacchio M, Cornelli U
Evaluation of the effects of supplementation with Pycnogenol® on fitness in normal subjects with the Army Physical Fitness Test and in performances of athletes in the 100-minute triathlon.
J sports Med Phys Fitness 53(6): 644-654

Ref. 230

CLINICAL STUDY: Pycnogenol® consumption increases vasodilatation by 42% in young healthy men, which warrants sufficient blood and oxygen supply to performing muscle.
Nishioka K, Hidaka T, Nakamura S, Umemura T, Jitsuiki D, Soga J, Goto C, Chayama K, Yoshizumi M, Higashi Y
Pycnogenol®, French Maritime Pine Bark Extract, augments endothelium-dependent vasodilation in humans.
Hypertens Res 30: 775-780, 2007

Ref. 189

CLINICAL STUDY: Pycnogenol® reduces muscular pain and cramps in athletes and in patients with vascular problems or poor blood circulation of the legs.
Vinciguerra G, Belcaro G, Cesarone MR, Rohdewald P, Stuard S, Ricci A, Di Renzo A, Hosoi M, Dugall M, Ledda A, Cacchio M, Acerbi G, Fano F
Cramps and muscular pain: prevention with Pycnogenol® in normal subjects, venous patients, athletes, claudicants and in diabetic microangiopathy.
Angiology 57: 331-339, 2006

Ref. 044

CLINICAL STUDY: Pycnogenol® increases exercise endurance in recreational athletes by 21% on a treadmill.
Pavlovic P
Improved endurance by use of antioxidants.
Eur Bull Drug Res 7: 26-29, 1999

11. Cognitive Function

Ref. 345

CLINICAL STUDY: Pycnogenol® significantly improves memory, cognition, attention and mood in healthy students.
Luzzi R, Belcaro G, Zulli C, Cesarone MR, Cornelli U, Dugall M, Hosoi M, Feragalli B
Pycnogenol® supplementation improves cognitive function, attention and mental performance in students.
Panminerva Med 53: 75-82, 2011

Ref. 241

CLINICAL STUDY: Pycnogenol® significantly improves memory in 101 senior citizens with memory deficits and saves their poly-unsaturated fatty acids, such as from neuronal membranes, from oxidative destruction.
Ryan J, Croft K, Wesnes K, Stough C
An examination of the effects of the antioxidant Pycnogenol® on cognitive performance, serum lipid profile, endocrinological and oxidative stress biomarkers in an elderly population.
J Psycopharmacol 22: 553-562, 2008

Ref. 231

CLINICAL STUDY: Pycnogenol® lowers stress-hormones in children with ADHD.
Dvorakova M, Jezova D, Blazicek P, Trebaticka J, Skodacek I, Suba J, Waczulikova I, Rohdewald P, Durackova Z
Urinary catecholamines in children with attention deficit hyperactivity disorder (ADHD): modulation by a polyphenolic extract from pine bark (Pycnogenol®).
Nutr Neurosci 10: 151-157, 2007

Ref. 205

CLINICAL STUDY: Pycnogenol® improves antioxidant status in children with Attention Deficit Hyperactivity Disorder (ADHD).
Dvorakova M, Sivonova M, Trebaticka J, Skodacek I, Waczulikova I, Muchova J, Durackova Z
Research Article: The effect of polyphenolic extract from pine bark, Pycnogenol®, on the level of glutathione in children suffering from attention deficit hyperactivity disorder (ADHD).
Redox Rep 11: 163-172, 2006

Ref. 204

CLINICAL STUDY: Pycnogenol® protects DNA against oxidation in children with Attention Deficit Hyperactivity Disorder (ADHD).
Chovanova Z, Muchova J, Sivonova M, Dvorakova M, Zitnanova I, Waczulikova I, Trebaticka J, Skodacek I, Durackova Z
Effect of polyphenolic extract, Pycnogenol®, on the level of 8-oxoguanine in children suffering from attention deficit/hyperactivity disorder.
Free Radic Res 40: 1003-1010, 2006

Ref. 190

CLINICAL STUDY: Pycnogenol® relieves hyperactivity and improves attention in children with ADHD in a double-blind placebo controlled study.
Trebaticka J, Kopasova S, Hradecna Z, Cinovsky K, Skodacek I, Suba J, Muchova J, Zitnanova I, Waczulikova I, Rohdewald P, Durackova Z
Treatment of ADHD with French maritime pine bark extract, Pycnogenol®.
Eur Child Adolesc Psychiatry 15: 329-335, 2006

Ref. 083

Neuronal apoptosis (early cell death) is induced by the amyloid-β-peptide in the brain of Alzheimer patients. *In vitro* experiments demonstrated an inhibition of cell death of neurons by Pycnogenol®.
Peng QL, Buz'Zard AR, Lau BHS
Pycnogenol® protects neurones from amyloid β peptide-induced apoptosis.
Brain Res Mol Brain Res 104: 55-65, 2002

Ref. 069

Pycnogenol® produces significant reduction in vascular damage caused by β-amyloid protein. β-amyloidosis is one of the neuropathological hallmarks of Alzheimer's disease (AD). This explains the role of Pycnogenol® in reducing the risk of AD.
Liu F, Lau BHS, Peng Q, Shah V
Pycnogenol® protects vascular endothelial cells from β-amyloid-induced injury.
Biol Pharm Bull 23: 735-737, 2000

Ref. 052

Pycnogenol® improves learning impairment and loss of memory, common symptoms of the ageing process.
Liu F, Zhang Y, Lau BHS
Pycnogenol® improves learning impairment and memory deficit in senescence-accelerated mice.
J Anti Aging Med 2: 349-355, 1999

Ref. 048

CLINICAL STUDY: Pycnogenol® is recommended for treatment of Attention Deficit Disorder.
Hanley JL
Attention Deficit Disorder.
Impact Communications Inc., Green Bay, WI, USA, 17-19, 1999

Ref. 047

CLINICAL STUDY: Positive experience with Pycnogenol® in treating ADHD is mentioned in this letter to the Editor.
Heimann SW
Pycnogenol® for ADHD?
J Am Acad Child Adolesc Psychiatry 38: 357-358, 1999

12. Skin Care

Ref. 348

CLINICAL STUDY: Pycnogenol® increases women's skin elasticity and hydration which coincides with significantly new collagen and hyaluronic acid synthesis in their skin.
Marini A, Grether-Beck S, Jaenicke T, Weber M, Burki C, Formann P, Brenden H, Schönlau F, Krutmann J
Pycnogenol® Effects on Skin Elasticity and Hydration Coincide with Increased Gene Expressions of Collagen Type I and Hyaluronic Acid Synthase in Women.
Skin Pharmacol Physiol 25: 86-92, 2012

Ref. 243

Pycnogenol® inhibits pigment formation in skin cells four times more potently than kojic acid, a compound commonly used in skin-whitening products.
Kim YJ, Kang KS, Yokozawa T
The anti-melanogenic effect of Pycnogenol® by its anti-oxidative actions.
Food and Chemical Toxicol 46: 2466-2471, 2008

Ref. 211

Beneficial effects of Pycnogenol® in wrinkles- A review article.
Rona C, Vailati F, Berardesca E
The cosmetic treatment of wrinkles.
J Cosmet Dermatol 3: 26-34, 2004

Ref. 195

CLINICAL STUDY: Pycnogenol® accelerates healing of diabetic ulcers in humans.
Belcaro G, Cesarone MR, Errichi BM, Ledda A, Di Renzo A, Stuard S, Dugall M, Pellegrini L, Gizzi G, Rohdewald P, Ippolito E, Ricci A, Cacchio M, Cipollone G, Ruffini I, Fano F, Hosoi M
Diabetic Ulcers: Microcirculatory Improvement and Faster Healing with Pycnogenol®.
Clin Appl Thromb Hemost 12: 318-323, 2006

Ref. 193

Oral administration of Pycnogenol® is able to delay and to reduce skin cancer following UV radiation.
Kyriazi M, Yova D, Rallis M, Lima A
Cancer chemopreventive effects of Pinus maritima bark extract on ultraviolet radiation and ultraviolet radiation -7,12 dimethylbenz(a) anthracene induced skin carcinogenesis of hairless mice.
Cancer Lett 237: 234-241, 2006

Ref. 185

CLINICAL STUDY: Pycnogenol® inhibits release of enzymes involved in breaking-down collagen and elastin in inflamed skin in humans.
Grimm T, Chovanova Z, Muchova J, Sumegova K, Liptakova A, Durackova Z, Högger P
Inhibition of NF-kappaB activation and MMP-9 secretion by plasma of human volunteers after ingestion of maritime pine bark extract (Pycnogenol®).
J Inflamm 3: 1-6, 2006

Ref. 172

CLINICAL STUDY: Ulcers of the lower legs heal faster with orally and topically applied Pycnogenol®.
Belcaro G, Cesarone MR, Errichi BM, Ledda A, Di Renzo A, Stuard S, Dugall M, Pellegrini L, Rohdewald P, Ippolito E, Ricci A, Cacchio M, Ruffini I, Fano F, Hosoi M
Venous Ulcers: Microcirculatory Improvement and Faster Healing with Local Use of Pycnogenol®.
Angiology 56: 699-705, 2005

Ref. 150

Pycnogenol® shows antimicrobial activity at very low concentration.
Torras MAC, Faura CA, Schönlau F, Rohdewald P
Anti-microbial activity of Pycnogenol®.
Phytother Res 19: 647-648, 2005

Ref. 137

Evidence of percutaneous absorption of Pycnogenol® in human skin.
Sarikaki V, Rallis M, Tanojo H, Panteri I, Dotsikas Y, Loukas YL, Papaioannou G, Demetzos C, Weber S, Moini H, Maibach HI, Packer L
In vitro percutaneous absorption of pine bark extract (Pycnogenol®) in human skin.
J Toxicol Cutaneous Ocul Toxicol 23: 149-158, 2004

Ref. 133

Topically applied Pycnogenol® dose-dependently speeds-up the wound healing process and reduces scar formation.
Blazso G, Gabor M, Schönlau F, Rohdewald P
Pycnogenol® accelerates wound healing and reduces scar formation.
Phytother Res 18: 579-581, 2004

Ref. 132

CLINICAL STUDY: Supplementation with Pycnogenol® in combination with vitamins, minerals improves skin smoothness and elasticity in women.
Segger D, Schönlau F
Supplementation with Evelle® improves smoothness and elasticity in a double blind, placebo- controlled study with 62 women.
J Dermatolog Treat 15: 222-226, 2004

Ref. 111

Pycnogenol® applied topically after sunburn inhibits photocarcinogenesis.
Sime S, Reeve VE
Protection from inflammation, immunosuppression and carcinogenesis induced by UV radiation in mice by topical Pycnogenol®.
Photochem Photobiol 79: 193-198, 2004

Ref. 107

CLINICAL STUDY: The collagen and elastin destroying enzymes are potently inhibited by Pycnogenol® as well as its metabolites prevailing in humans after oral consumption.
Grimm T, Schäfer A, Högger P
Antioxidant activity and inhibition of matrix metalloproteinases by metabolites of maritime pine bark extract (Pycnogenol®).
J Free Radic Biol Med 36: 811-822, 2004

Ref. 094

Review summarizing the beneficial effects of Pycnogenol® for skin care.
Schönlau F
The cosmeceutical Pycnogenol®.
J Appl Cosmetol 20: 241-246, 2002

Ref. 081

CLINICAL STUDY: Pycnogenol® counteracts skin hyper-pigmentation in women.
Ni Z, Mu Y, Gulati O
Treatment of melasma with Pycnogenol®.
Phytother Res 16: 567-571, 2002

Ref. 074

CLINICAL STUDY: Pycnogenol® dose-dependently inhibits UV-induced erythema in humans, demonstrating a potent anti-photoageing effect.
Saliou C, Rimbach G, Moini H, McLaughlin L, Hosseini S, Lee J, Watson RR, Packer L
Solar ultraviolet-induced erythema in human skin and nuclear factor-kappa-B-dependent gene expression in keratinocytes are modulated by French maritime pine bark extract.
J Free Radic Biol Med 30: 154-160, 2001

Ref. 073

Pycnogenol® favourably affects the gene expression profile in human keratinocytes, indicating a promising potential for improving inflammatory skin disorders such as psoriasis and dermatoses.
Rihn B, Saliou C, Bottin MC, Keith G, Packer L
From ancient remedies to modern therapeutics: Pine bark uses in skin disorders revisited.
Phytother Res 15: 76-78, 2001

Ref. 057

Pycnogenol® inhibits the production of adhesion molecules in human skin cells during inflammation which would contribute to relieving inflammatory skin disorders.
Bito T, Roy S, Sen CK, Packer L
Pine bark extract Pycnogenol® down regulates IFN-γ - induced adhesion of T cells to human keratinocytes by inhibiting inducible ICAM-1 expression.
J Free Radic Biol Med 28: 219-227, 2000

Ref. 030

Pycnogenol® prolongs the lifetime of vitamin C which will contribute to higher vitamin C presence in the skin.
Cossins E, Lee R, Packer L
ESR studies of vitamin C regeneration, order of reactivity of natural source phytochemical preparations.
Biochem Mol Biol Int 45: 583-597, 1998

Ref. 026

Pycnogenol® protects α-tocopherol from oxidation and extends its life-time in endothelial cells.
Virgili F, Kim D, Packer L
Procyanidins extracted from pine bark protect α-tocopherol in ECV 304 endothelial cells challenged by activated RAW 264.7 macrophages: role of nitric oxide peroxynitrite.
FEBS Lett 431: 315-318, 1998

Ref. 019

Pycnogenol® produces an anti-oedema effect in two different models. Topical application of Pycnogenol® gel protects the skin against UV radiation.
Blazso G, Gabor M, Rohdewald P
Anti-inflammatory activities of procyanidin containing extracts from *Pinus pinaster* Ait. after oral and cutaneous application.
Pharmazie 52: 380-382, 1997

Ref. 009

Pycnogenol® increases pathologically low capillary wall resistance. Pycnogenol® is shown to be the most potent among other bioflavonoids tested. Pycnogenol® provides strength to capillary walls and makes them less permeable and thus contributes to anti-oedema, anti-inflammatory effects.
Gabor M, Engi E, Sonkodi S
Die Kapillarwandresistenz und ihre Beeinflussung durch wasserlösliche Flavonderivate bei spontan hypertonischen Ratten.
Phlebologie 22: 178-182, 1993

Ref. 008

Pycnogenol® dose-dependently protects the skin from ultraviolet-radiation-induced oxidative stress injury (lipid peroxidation and cytotoxicity).
Guochang Z
Ultraviolet radiation-induced oxidative stress in cultured human skin fibroblasts and antioxidant protection.
Bio Res Rep Univ Jyväskylä 33: 1-86, 1993

13. Oral Health Care

Ref. 356	CLINICAL STUDY: Pycnogenol® applied orally, dissolved in glycerol, significantly helps control mucositis in children undergoing chemotherapy. Khurana H, Pandey RK, Saksena AK, Kumar A An evaluation of vitamin E and Pycnogenol® in children suffering from oral mucositis during cancer chemotherapy. Oral Dis 19(5): 456-464, 2012
Ref. 150	Pycnogenol® inhibits growth of gram-positive and negative bacteria and *candida albicans* at concentrations of 0.025%. Torras MAC, Faura CA, Schönlau F, Rohdewald P Short Communication: Antimicrobial activity of Pycnogenol®. Phytother Res 19: 647-648, 2005
Ref. 133	Local application of Pycnogenol® dose-dependently speeds-up the wound healing process and reduces scar formation. Blazso G, Gabor M, Schönlau F, Rohdewald P Pycnogenol® accelerates wound healing and reduces scar formation. Phytother Res 18: 579-581, 2004
Ref. 084	CLINICAL STUDY: Pycnogenol® administered in chewing gum reduced bleeding of the gum and reduced plaque formation on the teeth in a controlled clinical trial. Kimbrough C, Chun M, de la Roca G, Lau BHS Pycnogenol® chewing gum minimizes gingival bleeding and plaque formation. Phytomed 9: 410-413, 2002
Ref. 030	Pycnogenol® prolongs the lifetime of vitamin C more than other flavonoids. Cossins E, Lee R, Packer L ESR studies of vitamin C regeneration, order of reactivity of natural source phytochemical preparations. Biochem Mol Biol Int 45: 583-597, 1998

14. Benefits for Travelers

Ref. 244

CLINICAL STUDY: Pycnogenol® significantly lowers the severity of a wide range of typical jet-lag symptoms of flight passengers travelling intercontinental routes.
Belcaro G, Cesarone MR, Steigerwalt RJ, Di Renzo A, Grossi MG, Ricci A, Stuard S, Ledda A, Dugall M, Cornelli U, Cacchio M
Jet-lag: Prevention with Pycnogenol®. Preliminary report: evaluation in healthy individuals and in hypertensive patients.
Minerva Cardioangiol 56(5 Suppl): 3-9, 2008

Ref. 151

CLINICAL STUDY: Pycnogenol® effectively counteracts swelling of the lower-legs and ankles of passengers during long flights in a double-blind, placebo-controlled study.
Cesarone MR, Belcaro G, Rohdewald P, Pellegrini L, Ippolito E, Scoccianti M, Ricci A, Dugall M, Cacchio M, Ruffini I, Fano F, Acerbi G, Vinciguerra MG, Bavera P, Di Renzo A, Errichi BM, Mucci F
Prevention of edema in long flights with Pycnogenol®.
Clin Appl Thromb Hemost 11: 289-294, 2004

Ref. 135

Zinopin® (a combination of Pycnogenol® and Standardized Ginger Root Extract) – Rationale of its use as Food Supplement in Traveller's thrombosis and motion sickness.
Scurr JH, Gulati OP
Review article: Zinopin®- the Rationale for its use as Food Supplement in Traveller's thrombosis and motion sickness.
Phytother Res 18: 687-695, 2004

Ref. 134

CLINICAL STUDY: Pycnogenol® prevents thrombosis in passengers on long haul flights in a double-blind, placebo-controlled trial with 200 participants.
Belcaro G, Cesarone MR, Rohdewald P, Ricci A, Ippolito E, Dugall M, Griffin M, Ruffini I, Acerbi G, Vinciguerra MG, Bavera P, Di Renzo A, Errichi BM, Cerritelli F
Prevention of Venous Thrombosis and Thrombophlebitis in Long-Haul Flights with Pycnogenol®.
Clin Appl Thromb Hemost 10: 373-377, 2004

Ref. 116

CLINICAL STUDY: Pycnogenol® in combination with nattokinase prevents deep vein thrombosis in long–haul flights.
Cesarone MR, Belcaro G, Nicolaides AN, Ricci A, Geroulakos G, Ippolito E, Brandolini R, Vinciguerra G, Dugall M, Griffin M, Ruffini I, Acerbi G, Corsi M, Riordan N, Stuard S, Bavera P, Di Renzo A, Kenyon J, Errichi BM
Prevention of venous thrombosis in long-haul flights with Flite Tabs: The Lonflit- Flite randomized controlled trial.
Angiology 54: 531-539, 2003

Ref. 036

CLINICAL STUDY: Pycnogenol® inhibits platelet aggregation in a dose-dependent manner in humans. The effect lasts for more than 6 days and unlike aspirin, it does not produce an increase in bleeding time.
Pütter M, Grotemeyer KHM, Würthwein G, Araghi-Niknam M, Watson RR, Hosseini S, Rohdewald P
Inhibition of smoking-induced platelet aggregation by Aspirin and Pycnogenol®.
Thromb Res 95: 155-161, 1999

15. Immunology, Anti-Microbial & Anti-Viral Activity

Ref. 375

CLINICAL STUDY: Pycnogenol® given to children with Crohn's Disease at remission stage decreases oxidative stress levels.
Kolacek M, Muchova J, Dvorakova M, Paduchova Z, Zitnanova I, Cierna I, Orszaghova Z, Szekyova D, Jajcaiova-Zednickova N, Kovacs L, Durackova Z
Effects of natural polyphenols (Pycnogenol®) on oxidative stress markers in children suffering from Crohn's disease – a pilot study.
Free Rad Res 47(8): 624-634, 2013

Ref. 369

CLINICAL STUDY: Pycnogenol® supplementation speeds-up recovery from a common cold, and even more efficiently in combination with vitamin C and zinc.
Belcaro G, Luzzi R, Umberto C, Hu S, Dugall M, Ippolito E, Cesarone MR, Corsi M, Pellegrini L, Ledda A, Appendino G
The common cold Winter Study: Effects of Pycnogenol® on Signs, Symptoms, Complications & Costs.
Otorinolaringol 63: 151-161, 2013

Ref. 361

Pycnogenol® shows protective effects for prevention of Parkinson's Disease in a model system.
Khan M, Kempuraj D, Thangavel R, Zaheer A
Protection of MPTP-induced neuroinflammation and neurodegeneration by Pycnogenol®.
Neurochem Int 62: 379-388, 2013

Ref. 356

CLINICAL STUDY: Pycnogenol® applied orally, dissolved in glycerol, significantly helps control mucositis in children undergoing chemotherapy.
Khurana H, Pandey RK, Saksena AK, Kumar A
An evaluation of vitamin E and Pycnogenol® in children suffering from oral mucositis during cancer chemotherapy.
Oral Diseaes 19: 456-464, 2012

Ref. 247

Pycnogenol® decreases HIV viral replication and T-cell interaction in cell culture experiments.
Feng WY, Tanaka R, Inagaki Y, Saitoh Y, Chang MO, Amet T, Yamamoto N, Yamaoka S, Yoshinaka Y
Pycnogenol®, a procyanidin-rich extract from French maritime pine, inhibits intracellular replication of HIV-1 as well as its binding to host cells.
Jpn J Infect Dis 61: 279-285, 2008

Ref. 245

CLINICAL STUDY: Pycnogenol® helps to lower a wide range of typical side-effects patients suffer from during cancer chemo- and radiotherapy.
Belcaro G, Cesarone MR, Genovesi D, Ledda A, Vinciguerra G, Ricci A, Pellegrini L, Gizzi G, Ippolito E, Dugall M, Cacchio M, Di Renzo A, Stuard S
Pycnogenol® may alleviate adverse effects in oncologic treatment.
Panminerva Med 50: 227-234, 2008

Ref. 236

Pycnogenol® increases phagocytosis of macrophages suggesting better defence against pathogenic infections.
Wu TF, Hsu CY, Huang HS, Chou SP, Wu H
Proteomic analysis of Pycnogenol® effects in RAW 264.7 macrophage reveals induction of cathepsin D expression and enhancement of phagocytosis.
J Agric Food Chem 55: 9784-9791, 2007

Ref. 229

Pycnogenol® inhibits viral replication in heart muscle (myocarditis).
Matsumori A, Higuchi H, Shimada M
French maritime pine bark extract inhibits viral replication and prevents development of viral myocarditis.
J Card Fail 13: 785-791, 2007

Ref. 228
Pycnogenol® inhibits viral replication in myocarditis.
Matsumori A
Treatment Options in Myocarditis.
Herz 32: 452-456, 2007

Ref. 225
Pycnogenol® inhibits growth of *Helicobacter pylori* and their adherence to mucosal cells of the stomach.
Rohdewald P, Beil W
In vitro inhibition of *Helicobacter pylori* growth and adherence to gastric mucosal cells by Pycnogenol®.
Phytother Res 22: 685-688, 2007

Ref. 221
Pycnogenol® inhibits the harmful effects of two mutagenic chemicals.
Krizkova L, Chovanova Z, Durackova Z, Krajcovic J
Antimutagenic *in vitro* Activity of Plant Polyphenols: Pycnogenol® and Ginkgo biloba Extract (EGb 761).
Phytother Res 22: 384-388, 2007

Ref. 208
Pycnogenol® reduces cancerogenesis in human ovarian cells.
Buzzard AR, Lau BHS
Pycnogenol® reduces Talc-induced Neoplastic Transformation in Human Ovarian Cell Cultures.
Phytother Res 21: 579-586, 2007

Ref. 150
Pycnogenol® shows broad anti-microbial activity *in vitro*.
Torras MAC, Faura CA, Schönlau F, Rohdewald P
Antimicrobial activity of Pycnogenol®.
Phytother Res 19: 647-648, 2005

Ref. 173
Pycnogenol® selectively kills cancerous ovarian germ cells.
Buzzard AR, Lau BHS
Research article: Selective toxicity of Pycnogenol® for malignant ovarian germ cells *in vitro*.
Int J Cancer Prev 1: 207-212, 2004

Ref. 111
Pycnogenol® applied after sunburn inhibits UV-induced suppression of immune system.
Sime S, Reeve VE
Protection from inflammation, immunosuppression and carcinogenesis induced by UV radiation in mice by topical Pycnogenol®.
Photochem Photobiol 79: 193-198, 2004

Ref. 102
Pycnogenol® consumption by mice infected with protozoan parasite provides several protective benefits.
Kim HC, Healey JM
Effects of Pine bark extract administered to immunosuppressed adult mice infected with Cryptosporidium parvum.
Am J Chin Med 29: 469-475, 2001

Ref. 095
Pycnogenol® activates *in vitro* macrophages to kill more effectively invading bacteria.
Shah V, Bayeta E, Lau BHS
Pycnogenol® augments macrophage phagocytosis and cytokine secretion.
Pak J Nutr 1: 196-201, 2002

Ref. 082
CLINICAL STUDY: Pycnogenol® shows beneficial effects in patients with lupus erythematosus.
Stefanescu M, Matache C, Onu A, Tanaseanu S, Dragomir C, Constantinescu I, Schönlau F, Rohdewald P, Szegli G
Pycnogenol® Efficacy in the Treatment of Systemic Lupus Erythematosus Patients.
Phytother Res 15: 698-704, 2001

Ref. 059

Pycnogenol® selectively kills cancerous human mammary cells (MCF-7), without affecting the normal mammary cells (MCF-10).
Huynh HT, Teel RW
Selective induction of apoptosis in human mammary cancer cells (MCF-7) by Pycnogenol®.
Anticancer Res 20: 2417-2420, 2000

Ref. 055

Pycnogenol® increases TNF-α secretion in the macrophage system in a concentration and time dependent manner indicating that it acts as modulator of the immune response in macrophages.
Park YC, Rimbach G, Saliou C, Valacchi G, Packer L
Activity of monomeric, dimeric, and trimeric flavonoids on NO production, TNF-alpha secretion, and NF-kappaB-dependent gene expression in RAW 264.7 macrophages.
FEBS Lett 465: 93-97, 2000

Ref. 029

Pycnogenol® slows down the aging related process of decline in the activities of immune- and blood cells generating systems and restores their functions to normal.
Liu FJ, Zhang YX, Lau BHS
Pycnogenol® enhances immune and haemopoietic functions in senescence-accelerated mice.
Cell Mol Life Sci 54: 1168-1172, 1998

Ref. 016

Pycnogenol® enhances the activity of the immune system in mice infected with a leukemia-causing retrovirus. Pycnogenol® increases the natural killer cell cytotoxicity.
Cheshier JE, Ardestani-Kaboudanian S, Liang B, Araghi Niknam M, Chung S, Lane L, Castro A, Watson RR
Immunomodulation by Pycnogenol® in retro-virus infected or ethanol-fed mice.
Life Sci 58: 87-96, 1996

16. Antioxidant-& Anti-Ageing Activity

Ref. 367

CLINICAL STUDY: Pycnogenol® given at 50 mg daily dosage to 155 volunteers significantly neutralises free radicals and quenches oxidative stress.
Belcaro G, Hu S, Cesarone MR, Dugall M
A controlled study shows daily intake of 50mg Pycnogenol® significantly lowers plasma reactive oxygen metabolites in 155 healthy smokers.
Minerva Med 104(4): 439-446, 2013

Ref. 349

CLINICAL STUDY: Pycnogenol® significantly lowers oxidative stress in heart attack patients as judged from lowered blood F2-isoprostane level.
Enseleit F, Sudano I, Périat D, Winnik S, Wolfrum M, Flammer AJ, Fröhlich GM, Kaiser P, Hirt A, Haile SR, Krasniqi N, Matter CM, Uhlenhut K, Högger P, Neidhart M, Lüscher TF, Ruschitzka F, Noll G
Effects of Pycnogenol® on endothelial function in patients with stable coronary artery disease: a double-blind, randomized, placebo-controlled, cross-over study.
Eur Heart J 33(13): 1589-97, 2012

Ref. 336

CLINICAL STUDY: Pycnogenol® significantly reduces oxidative stress in menopausal women.
Errichi S, Bottari A, Belcaro G, Cesarone MR, Hosoi M, Cornelli U, Dugall M, Ledda A, Feragalli B
Supplementation with Pycnogenol® improves signs and symptoms of menopausal transition.
Panminerva Med 53: 65-70, 2011

Ref. 241

CLINICAL STUDY: Pycnogenol® significantly decreases F2-isoprostane plasma levels in 101 senior citizens indicating that poly-unsaturated fatty acids, such as those from neuronal membranes, are saved from oxidative destruction.
Ryan J, Croft K, Wesnes K, Stough C
An examination of the effects of the antioxidant Pycnogenol® on cognitive performance, serum lipid profile, endocrinological and oxidative stress biomarkers in an elderly population.
J Psychopharmacol 22: 553-562, 2008

Ref. 227

Pycnogenol® and Lutein display synergistic antioxidant effects for prevention of lipid peroxidation.
Nakanishi-Ueda T, Kamegawa M, Ishigaki S, Tsukahara M, Yano S, Wada K, Yasuhara H
Inhibitory Effect of Lutein and Pycnogenol® on Lipid Peroxidation in Porcine Retinal Homogenate.
J Clin Biochem Nutr 38: 204-210, 2006

Ref. 226

Pycnogenol® demonstrates liver protective effects, shown in animal models with acute chemical intoxication.
Yang Y-S, Ahn T-H, Lee J-C, Moon C-J, Kim S-H, Jun W, Park S-C, Kim H-C, Kim J-C
Protective effects of Pycnogenol® on carbon tetrachloride-induced hepato-toxicity in Sprague Dawley rats.
Food Chem Toxicol 46: 380-387, 2008

Ref. 218

Pycnogenol® lowers oxidative stress in the liver of rats challenged with a chemical toxin.
Ahn T-H, Yang Y-S, Lee J-C, Moon C-J, Kim S-H, Jun W, Park S-C, Kim J-C
Ameliorative Effects of Pycnogenol® on Carbon Tetrachloride-Induced Hepatic Oxidative Damage in Rats.
Phytother Res 21: 1015-1019, 2007

Ref. 215

Pycnogenol® protects liposomes from lipid peroxidation and shows synergistic protective effects with vitamin C and vitamin E.
Sivonova M, Zitnanova I, Horakova L, Strosova M, Muchova J, Balgavy P, Dobrota D, Durackova Z
The Combined Effect of Pycnogenol® with Ascorbic Acid and Trolox on the Oxidation of Lipids and Proteins.
Gen Physiol Biophys 25: 379-396, 2006

Ref. 205

CLINICAL STUDY: Pycnogenol® improves antioxidant status in children with Attention Deficit Hyperactivity Disorder (ADHD).
Dvorakova M, Sivonova M, Trebaticka J, Skodacek I, Waczulikova I, Muchova J, Durackova Z
The effect of polyphenolic extract from pine bark, Pycnogenol® on the level of glutathione in children suffering from attention deficit hyperactivity disorder (ADHD).
Redox Rep 11: 163-172, 2006

Ref. 204

CLINICAL STUDY: Pycnogenol® significantly protects DNA against oxidation in children with ADHD in a double-blind, placebo-controlled study.
Chovanova Z, Muchova J, Sivonova M, Dvorakova M, Zitnanova I, Waczulikova I, Trebaticka J, Skodacek I, Durackova Z
Effect of polyphenolic extract, Pycnogenol®, on the level of 8-oxoguanine in children suffering from attention deficit/ hyperactivity disorder.
Free Radic Res 40: 1003-1010, 2006

Ref. 203

Pycnogenol® prevents accumulation of oxidative damaged proteins and may reduce the risk of Alzheimer's, Parkinson's and Huntington's diseases.
Voss P, Horakova L, Jakstadt M, Kiekebusch D, Grune T
Ferritin oxidation and proteasomal degradation: Protection by antioxidants.
Free Radic Res 40: 673-683, 2006

Ref. 187

CLINICAL STUDY: Pycnogenol® significantly increases total antioxidant status (TAS) in a double-blind, placebo-controlled study with 155 menopausal women.
Yang HM, Liao MF, Zhu SY, Liao MN, Rohdewald P
A randomised, double-blind, placebo-controlled trial on the effect of Pycnogenol® on the climacteric syndrome in peri-menopausal women.
Acta Obstet Gynecol Scand 86: 978-985, 2007

Ref. 183

Pycnogenol® protects intestinal mucosa against radiotherapy induced damage: Histo-morphological evidence in rats.
Ramos FM, Schönlau F, Novaes PD, Manzi FR, Bóscolo FN, Almeida SM
Pycnogenol® protects against ionizing radiation as shown in the intestinal mucosa of rats exposed to X-rays.
Phytother Res 20: 676-679, 2006

Ref. 140

Pycnogenol® protects the membrane of human red blood cells from oxidative damage.
Sivonová M, Waczulíková I, Kilanczyk E, Hrnciarová M, Bryszewska M, Klajnert B, Duracková Z
The effect of Pycnogenol® on the erythrocyte membrane fluidity.
Gen Physiol Biophys 23: 39-51, 2004

Ref. 105

Pycnogenol® lowers blood glucose and increases intracellular antioxidant defense mechanism in diabetic rats.
Maritim A, Dene BA, Sanders RA, Watkins JB
Effect of Pycnogenol® treatment on oxidative stress in streptozotocin-induced diabetic rats.
J Biochem Mol Toxicol 17: 193-199, 2003

Ref. 099

Pycnogenol® in combination with other antioxidants administered as dietary supplement increases the life-span of mice. The findings suggest also beneficial effects against neurogenerative diseases.
Veurink G, Liu D, Taddei K, Perry G, Smith MA, Robertson TA, Hone E, Groth DM, Atwood CS, Martins RN
Reduction of inclusion body pathology in ApoE-deficient mice fed a combination of antioxidants.
J Free Radic Biol Med 34: 1070-1077, 2003

Ref. 098

Pycnogenol® delays the aging process as shown by an increased life-span of fruit flies.
Shuguang L, Xinwen Z, Sihong X, Gulati OP
Role of Pycnogenol® in aging by increasing the Drosophila's life-span.
Eur Bull Drug Res 11: 39-45, 2003

Ref. 093

CLINICAL STUDY: Pycnogenol® significantly elevates plasma FRAP values of men with dyslipidemia in a double-blind, placebo-controlled study.
Durackova Z, Trebaticky B, Novotny V, Zitnanova I, Breza J
Lipid metabolism and erectile function improvement by Pycnogenol®, extract from the bark of *Pinus pinaster* in patients suffering from erectile dysfunction-a pilot study.
Nutr Res 23: 1189–1198, 2003

Ref. 090

CLINICAL STUDY: Pycnogenol® increases blood plasma oxygen radical absorbance capacity (ORAC) after oral consumption in human volunteers.
Devaraj S, Vega-López S, Kaul N, Schönlau F, Rohdewald P, Jialal I
Supplementation with a pine bark extract rich in polyphenols increases plasma antioxidant capacity and alters plasma lipoprotein profile.
Lipids 37: 931-934, 2002

Ref. 086

Pycnogenol® in combination with whey increases antioxidative capacity of plasma.
Janisch K, Hippeli S, Dornisch K, Kern S, Elstner EF
Determination of the antioxidative potential of human plasma after supplementation with Pycnogenol® and whey.
Food Res Intern 35: 257-266, 2002

Ref. 072

Pycnogenol® selectively enhances activity of intracellular antioxidative enzymes.
Bayeta E, Lau BHS
Pycnogenol® inhibits generation of inflammatory mediators in macrophages.
Nutr Res 20: 249-259, 2000

Ref. 070

Pycnogenol® by virtue of its high content of procyanidins has higher antioxidant potency than other plant-derived antioxidants containing relatively higher content of regular flavon(ol)s. This fact is explained on structural and functional basis.
Bors W, Michel C, Stettmaier K
Electron paramagnetic resonance studies of radical species of proanthocyanidins and gallate esters.
Arch Biochem Biophys 374: 347-355, 2000

Ref. 069

Pycnogenol® produces significant reduction in vascular damage caused by β-amyloid protein. β-amyloidosis is one of the neuropathological hallmarks of Alzheimer's disease (AD). This explains the role of Pycnogenol® in reducing the risk of AD.
Liu F, Lau BHS, Peng Q, Shah V
Pycnogenol® protects vascular endothelial cells from β-amyloid-induced injury.
Biol Pharm Bull 23: 735-737, 2000

Ref. 063

Pycnogenol® shows free radical scavenging activity against reactive oxygen species. It inhibits the generation of pro-inflammatory mediators confirming the anti-inflammatory and immuno-modulatory profile of Pycnogenol®.
Cho K-J, Yun C-H, Yoon D-Y, Cho Y-S, Rimbach G, Packer L, Chung A-S
Effect of bioflavonoids extracted from the bark of Pinus maritime on proinflammatory cytokine interleukin-1 production in lipopolysaccharide-stimulated raw 264.7.
Toxicol Appl Pharmacol 168: 64-71, 2000

Ref. 062

Pycnogenol® blocks oxidative modification of cellular proteins more effectively than other antioxidants.
Kim J, Chehade J, Pinnas JL, Mooradian AD
Effect of select antioxidants on malondialdehyde modification of proteins.
Nutrition 16: 1079-1081, 2000

Ref. 052

Pycnogenol® improves learning impairment and loss of memory, common symptoms of the ageing process.
Liu F, Zhang Y, Lau BHS
Pycnogenol® improves learning impairment and memory deficit in senescence-accelerated mice.
J Anti Aging Med 2: 349-355, 1999

Ref. 051

In a comparative study Pycnogenol® shows more potent antioxidant activity than vitamin C and E, α-lipoic acid, Co-Q_{10} and grape seed. In combination Pycnogenol® enhances the effects of other antioxidants like Coenzyme Q_{10}.
Chida M, Suzuki K, Nakanishi-Ueda T, Ueda T, Yasuhara H, Koide R, Armstrong D
In vitro testing of antioxidants and biochemical end-points in bovine retinal tissue.
Ophthalmic Res 31: 407-415, 1999

Ref. 033

Pycnogenol® is an efficient antioxidant due to the relative stability of its corresponding radical and its regeneration by vitamin C and vitamin E homologue Trolox.
Guo Q, Zhao B, Packer L
Electron spin resonance study of free radicals formed from a procyanidin-rich pine (Pinus maritime) bark extract, Pycnogenol®.
J Free Radic Biol Med 27: 1308-1312, 1999

Ref. 030

Pycnogenol® protects vitamin C from oxidation and recycles oxidized vitamin C more effectively than other flavonoids.
Cossins E, Lee R, Packer L
ESR studies of vitamin C regeneration, order of reactivity of natural source phytochemical preparations.
Biochem Mol Biol Int 45: 583-597, 1998

Ref. 029

Pycnogenol® slows down the aging related process of decline in activities of immune- and blood cells generating systems and restores their functions to normal.
Liu FJ, Zhang YX, Lau BHS
Pycnogenol® enhances immune and haemopoietic functions in senescence-accelerated mice.
Cell Mol Life Sci 54: 1168-1172, 1998

Ref. 026

Pycnogenol® protects α-tocopherol in endothelial cells.
Virgili F, Kim D, Packer L
Procyanidins extracted from pine bark protect α-tocopherol in ECV 304 endothelial cells challenged by activated RAW 264.7 macrophages: role of nitric oxide and peroxynitrite.
FEBS Lett 431: 315-318, 1998

Ref. 025

Pycnogenol® inhibits the effect of oxidative stress and minimises hydroxyl radical-induced DNA damage *in vitro*.
Nelson AB, Lau BHS, Ide N, Rong Y
Pycnogenol® inhibits macrophage oxidative burst, lipoprotein oxidation and hydroxyl radical-induced DNA damage.
Drug Dev Ind Pharm 24: 139-144, 1998

Ref. 022

Pycnogenol® in addition to its free radical scavenging property, modulates the production of nitric oxide radicals in activated inflammatory cells.
Virgili F, Kobuchi H, Packer L
Procyanidins extracted from Pinus maritima (Pycnogenol®): scavengers of free radical species and modulators of nitrogen monoxide metabolism in activated murine raw 264.7 macrophages.
J Free Radic Biol Med 24: 1120-1129, 1998

Ref. 021

Pycnogenol® is shown to be the strongest hydroxyl- and superoxide radical scavenger among other extracts tested. In addition, Pycnogenol® is shown to be resistant to heat.
Noda Y, Anzai K, Mori A, Kohno M, Shinmei M, Packer L
Hydroxyl and superoxide anion radical scavenging activities of natural source antioxidants using the computerized JES-FR30 ESR spectrometer system.
Biochem Mol Biol Int 42: 35-44, 1997

Ref. 020

Pycnogenol® stimulates synthesis of antioxidative enzymes in cell lining arteries thereby doubling their amount.
Wei ZH, Peng QL, Lau BHS
Pycnogenol® enhances endothelial cell antioxidant defenses.
Redox Rep 3: 219-224, 1997

Ref. 014

Pycnogenol® protects endothelial cells lining from free radical damage. Damage to endothelial cells is considered a primary cause for atherosclerosis.
Rong Y, Li L, Shah V, Lau BHS
Pycnogenol® protects vascular endothelial cells from t-butyl hydroperoxide induced oxidant injury.
Biotechnol Ther 5: 117-126, 1995

Ref. 010

Pycnogenol® scavenges superoxide radicals *in vitro* and inhibits oedema *in vivo*. The anti-inflammatory and free radical scavenging activities are closely correlated.
Blazso G, Gabor M, Sibbel R, Rohdewald P
Anti-inflammatory and superoxide radical scavenging activities of a procyanidins containing extract from the bark of *Pinus pinaster* sol. and its fractions.
Pharm Parmacol Lett 3: 217-220, 1994

Ref. 007

Pycnogenol® is proven an excellent radical scavenger of enzymatically produced hydroxyl and singlet oxygen free radicals, two of the most dangerous free radical species.
Elstner EF, Kleber E
Radical scavenger properties of leucocyanidine.
In: Das NP, ed. Flavonoids in Biology & Medicine III: Current issues in Flavonoid Research: National University of Singapore Press: 227-235, 1990

17. Analytics, Bio-Availability & Metabolism

Ref. 372

The metabolites developing in humans after consumption of Pycnogenol® are actively internalised by red blood cells, leukocytes, endothelial cells and neurons via the GLUT1 transporter. The tissue-specific accumulation represents the common denominator for Pycnogenol principal modes of action, as related to inflammation control, endothelial function, and cognition benefits.
Kurlbaum M, Mülek M, Högger P
Facilitated Uptake of a Bioactive Metabolite of Maritime Pine Bark Extract (Pycnogenol®) into Human Erythrocytes.
PLOS ONE 8(4): 1-10, 2013

Ref. 371

Pycnogenol® as a natural blend performs better in endothelial dysfunction than fractions of the extract.
Jankyova S, Hlavackova L, Kralova E, Slazneva J, Drobna V, Zuzik P, Drafi F, Mucaji P, Racanska E
The Evaluation of Efficacy of Pycnogenol® Fractions on Endothelial Dysfunction.
Acta Fac Pharm Univ Comen LX(1): 7-14, 2013

Ref. 353

Pycnogenol® metabolites developing after consumption by humans accumulate in immune cells (leukocytes) for modulation of inflammatory processes.
Uhlenhut K, Högger P
Facilitated cellular uptake and suppression of inducible nitric oxide synthase by a metabolite of maritime pine bark extract (Pycnogenol®).
Free Radic Biol Med, 53: 305-313, 2012

Ref. 301

Pycnogenol® constituents are transported in the blood stream bound to albumin, whereas the metabolites are not associated to blood proteins.
Kurlbaum M, Högger P
Plasma protein binding of polyphenols from maritime pine bark extract (USP).
J Pharm Biomed Anal 54: 127-132, 2011

Ref. 239

Pycnogenol® antagonises the neurotoxicity of alcohol, suggesting mitigation of hang-over symptoms.
Siler-Marsiglio KI, Paiva M, Madorsky I, Serrano Y, Neeley A, Heaton MB
Protective mechanisms of Pycnogenol® in ethanol-insulted cerebellar granule cells.
J Neurobiol 61: 267-276, 2004

Ref. 197

CLINICAL STUDY: This study presents the appearance of Pycnogenol® constituents and metabolites in blood after oral administration in humans.
Grimm T, Skrabala R, Chovanova Z, Muchova J, Sumegova K, Liptakova A, Durackova Z, Högger P
Single and multiple dose pharmacokinetics of maritime pine bark extract (Pycnogenol®) after oral administration to healthy volunteers.
BMC Clin Pharmacol 6:4, 2006

Ref. 171

USP Monograph.
Maritime Pine Extract – USP 34.1196-1197
The United States Pharmacopeia, United States Pharmacopeial Convention, Inc. official from May 1, 2011

Ref. 170

USP Monograph.
Maritime Pine – USP-30.964-965
The United States Pharmacopeia, United States Pharmacopeial Convention, Inc. official from May 1, 2007

Ref. 137

Evidence of percutaneous absorption of Pycnogenol® in human skin.
Sarikaki V, Rallis M, Tanojo H, Panteri I, Dotsikas Y, Loukas YL, Papaioannou G, Demetzos C, Weber S, Moini H, Maibach HI, Packer L
In vitro Percutaneous Absorption of Pine Bark Extract (Pycnogenol®) in Human Skin.
J Toxicol Cutaneous Ocul Toxicol 23: 149-158, 2004

Ref. 060

CLINICAL STUDY: Bio-kinetics (absorption, metabolism and excretion) of Pycnogenol® in healthy human subjects has been demonstrated by studying the excretion pattern of ferulic acid (one of the components of Pycnogenol®).
Virgili F, Pagana G, Bourne L, Rimbach G, Natella F, Rice-Evance C, Packer L
Ferulic acid excretion as a marker of consumption of a French maritime pine (Pinus maritima) bark extract.
J Free Radic Biol Med 28: 1249-1256, 2000

Ref. 058

CLINICAL STUDY: Pycnogenol®, its components and metabolites are bio-available in humans for more than 24 hours to exert their beneficial effects.
Grosse-Düweler K, Rohdewald P
Urinary metabolites of French maritime pine bark extract in humans.
Pharmazie 55: 364-368, 2000

Ref. 040

Pycnogenol® is shown to be bioavailable based on its therapeutic effects *in vivo*: The prevention of platelet aggregation and the capillary sealing effect. Valerolactones as sulphates or glucuronides appear in the urine and they represent the active metabolites of Pycnogenol®.
Rohdewald P
Bioavailabilty and metabolism of Pycnogenol®.
Eur Bull Drug Res 7: 5-7, 1999

Horphag Research
Administrative Office
P.O. Box 80
71 Av. Louis Casaï
CH-1216 Cointrin/Geneva
Switzerland
Phone +41 (0)22 710 26 26
Fax +41 (0)22 710 26 00
info@pycnogenol.com
www.pycnogenol.com