

Summary of studies on Polyphenols (June 2016)

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Vascular protection by dietary polyphenols

Jean-Claude Stocklet | Thierry Cataigneau | Madamdou Ndiaye | Min-Ho Oak | Jasser El Bedoui | Marta Chataigneau | Valerie B. Schini-Kerth
Pharmacologie et Physico-Chimie des Interactions Cellulaires et Moleculaires, UMR CNRS 7034, Faculte de Pharmacie, Universite Louis Pasteur de Strassbourg, B.P. 60024, 74 route du Rhin, F67401 Illkirch, France

Bonum vinum laetificat cor hominum (ben sirach, the sage, abstract): Beneficial effects of wine consumption on health have been suspected since the antiquity. Recent epidemiological studies show that coronary heart disease mortality markedly decreases from northern to southern Europe and is lower in Mediterranean than in other developed countries. Because wine is a component of the Mediterranean diet, it has been suggested that moderate wine especially red wine consumption may produce additional beneficial effects on cardiovascular morbidity and mortality compared to consuming the same quantity of alcohol in other beverages. Polyphenols are good candidates to explain the putative cardiovascular protective effect of wine

Clinical Nutrition (2012), doi: 10.1016/j.clnu.2012.08.022

Effects of red wine polyphenols and alcohol on glucose metabolism and the lipid profile: A randomized clinical trial

Gemma Chiva-Blanch | Mireia Urpi-Sarda | Emilio Ros | Palmira Valderas-Martinez | Rosa Casas | Sara Arranz | Marisa Guillén | Rosa M. Lamuela-Raventós | Rafael Llorach | Cristina Andres-Lacueva | Ramon Estruch

Conclusions: *“The results support a beneficial effect of the non-alcoholic fraction of red wine (mainly polyphenols) on insulin resistance, conferring greater protective effects on cardiovascular disease to red wine than other alcoholic beverages”*

Pharmacol Res. 2012 Jun;65(6):609-14. Epub 2012 Mar 30.

Intake of alcohol-free red wine modulates antioxidant enzyme activities in a human intervention study.

Noguer MA, Cerezo AB, Donoso Navarro E, Garcia-Parrilla MC.

conclusion: *“The alcohol-free wine could be an excellent source of antioxidants to protect people suffering from oxidative stress (cancer, diabetes, alzheimer, etc.) who should not consume alcohol.”*

Curr Top Med Chem. 2011;11(14):1780-96.

Potential application of dietary polyphenols from red wine to attaining healthy ageing.

Magrone T, Jirillo E.

University of Bari, Faculty of Medicine, Immunology, Bari, Italy. thea.magrone@libero.it

“In conclusion, polyphenols in virtue of the plethora of protective effects manifested in various experimental models and clinical trials seem to be appropriate as dietary supplements for preventing the functional decline of organs with age. “

Curr Top Med Chem. 2011;11(14):1767-79.

Effects of antioxidant polyphenols on TNF-alpha-related diseases.

Kawaguchi K, Matsumoto T, Kumazawa Y.

Laboratory of Pharmacognosy, Faculty of Pharmacy, Iwaki Meisei University, 5-5-1 Chuodai-Iino, Iwaki, Fukushima 970-8551, Japan. kiichi-k@iwakimu.ac.jp

Conclusion: *“The present review, supplemented by hitherto unpublished data of the authors and their coworkers, shows that the intake of polyphenols contained in natural sources, such as hydroxytyrosol, tyrosol, oleuropein (olives), naringin and hesperidin (Citrus fruits), resveratrol, procyanidins or oligomeric procyanidin (grapes or grape seed extracts), (-)-epigallocatechin gallate (green tea) and quercetin (grapes, green tea) etc., are able to modulate chronic inflammatory diseases, such as type 2 diabetes, rheumatoid arthritis, inflammatory bowel disease”*

Proc Jpn Acad Ser B Phys Biol Sci. 2011;87(3):104-13.

Procyanidins are potent inhibitors of LOX-1: a new player in the French Paradox.

Nishizuka T, Fujita Y, Sato Y, Nakano A, Kakino A, Ohshima S, Kanda T, Yoshimoto R, Sawamura T. Department of Vascular Physiology, National Cerebral and Cardiovascular Center, Osaka, Japan.

Conclusion: *“These results suggest that procyanidins are LOX-1 inhibitors and LOX-1 inhibition might be a possible underlying mechanism of the well-known vascular protective effects of red wine, the French Paradox.”*

J Agric Food Chem. 2011 May 11;59(9):4489-95. Epub 2011 Apr 7.

Protective effect of structurally diverse grape procyanidin fractions against UV-induced cell damage and death.

Matito C, Agell N, Sanchez-Tena S, Torres JL, Cascante M. Department of Biochemistry and Molecular Biology, Faculty of Biology, University of Barcelona and IBUB, Unit Associated with CSIC, Barcelona, Spain.

Conclusion: *“These encouraging in vitro results support further research and should be taken into consideration into the clinical pharmacology of plant-derived polyphenolic extracts as novel agents for skin photoprotection”*

Mol Nutr Food Res. 2009 Jul;53(7):805-14.

Dietary procyanidins enhance transcriptional activity of bile acid-activated FXR in vitro and reduce triglyceridemia in vivo in a FXR-dependent manner.

Del Bas JM, Ricketts ML, Vaqué M, Sala E, Quesada H, Ardevol A, Salvadó MJ, Blay M, Arola L, Moore DD, Pujadas G, Fernandez-Larrea J, Bladé C. Departament de Bioquímica i Biotecnologia, Universitat Rovira i Virgili, Campus Sescelades, Tarragona, Spain.

Summary: *“Consumption of dietary flavonoids has been associated with reduced mortality and risk of cardiovascular disease, partially by reducing triglyceridemia. We have previously reported that a grape seed procyanidin extract (GSPE) reduces postprandial triglyceridemia ... This study adds dietary procyanidins to the arsenal of FXR ligands with potential therapeutic use to combat hypertriglyceridemia, type 2 diabetes and metabolic syndrome.”*

Mol Nutr Food Res. 2008 Oct;52(10):1172-81.

Dietary procyanidins lower triglyceride levels signaling through the nuclear receptor small heterodimer partner.

Del Bas JM, Ricketts ML, Vaqué M, Sala E, Quesada H, Ardevol A, Salvadó MJ, Blay M, Arola L, Moore DD, Pujadas G, Fernandez-Larrea J, Bladé C.
Departament de Bioquímica i Biotecnologia, Universitat Rovira i Virgili, Campus Sescelades, Tarragona, Spain.

Summary: "Hypertriglyceridemia is an independent risk factor in the development of cardiovascular diseases, and we have previously reported that oral administration of a grape seed procyanidin extract (GSPE) drastically decreases plasma levels of triglycerides (TG) ... This novel signaling pathway of procyanidins through SHP may be relevant to explain the health effects ascribed to the regular consumption of dietary flavonoids"

Nitric Oxide. 2012 Feb 15;26(2):102-10. Epub 2012 Jan 4.

Cardiovascular effects and molecular targets of resveratrol.

Li H, Xia N, Förstermann U.
Department of Pharmacology, University Medical Center, Johannes Gutenberg University, Mainz, Germany. huigeli@uni-mainz.de

Summary: "Resveratrol is a polyphenol phytoalexin present in a variety of plant species and has been implicated to explain the health benefits of red wine. A wide range of health beneficial effects have been demonstrated for resveratrol ...In this regard, resveratrol stimulates endothelial production of nitric oxide, reduces oxidative stress, inhibits vascular inflammation and prevents platelet aggregation. In animal models of cardiovascular disease, resveratrol protects the heart from ischemia-reperfusion injury, reduces blood pressure and cardiac hypertrophy in hypertensive animals, and slows the progression of atherosclerosis... "

Biochimie. 2012 Feb;94(2):269-76. Epub 2011 Nov 22.

Antioxidant effects of resveratrol and other stilbene derivatives on oxidative stress and *NO bioavailability: Potential benefits to cardiovascular diseases.

Frombaum M, Le Clanche S, Bonnefont-Rousselot D, Borderie D.
EA 4466 Stress Cellulaire, Physiopathologie, Stratégies nutritionnelles et thérapeutiques innovantes, Université Paris Descartes, Sorbonne Paris Cité, UFR des Sciences Pharmaceutiques et Biologiques, 4, Avenue de l'Observatoire, 75006 Paris, France.
mathieu@newmed.fr

*Summary: "The "French paradox" is a phenomenon that associates a diet rich in saturated fatty acids and a moderate consumption of wine to a low prevalence of cardiovascular diseases. During the past 10 years, the beneficial effects of wine on cardiovascular diseases have been attributed to the actions of resveratrol and other polyphenols. One of the mechanisms involved in these beneficial effects is the capacity of resveratrol and some other stilbene derivatives to maintain sufficient *NO bioavailability in vascular endothelium. This review presents the latest findings on the molecular effects of resveratrol and other stilbene derivatives on the various actors that modulate *NO bioavailability during oxidative stress "*

Pol Merkur Lekarski. 2012 Feb;32(188):143-6.

Resveratrol--phytophenol with wide activity.

Fraczek M, Szumiło J, Podlodowska J, Burdan F.
Department of Ophthalmology, Medical University of Lublin, Poland.

Summary: "Resveratrol is a natural phytophenol. It is found in many plants, but the highest concentration was detected in different grape-derived products, especially in red wine. Numbers of epidemiological and experimental studies have proved a complex chemiopreventive activity of resveratrol against various cardio-vascular disorders and cancer. Furthermore, the compound possesses anti-inflammatory activity and positively regulates glucose level and metabolism of adipose tissue. Diet rich in resveratrol promotes longevity and attenuates neurodegenerative diseases.

Ann N Y Acad Sci. 2011 Jan;1215:16-21. doi: 10.1111/j.1749-6632.2010.05854.x.

Resveratrol: a cardioprotective substance.

Wu JM, Hsieh TC.

Department of Biochemistry and Molecular Biology, New York Medical College, Valhalla, 10595, USA. Joseph.Wu@nymc.edu

Summary: "Coronary heart disease (CHD) is a major and preventable cause of morbidity and death in the United States. Recently, significant research efforts have been directed at an epidemiological phenomenon known as the "French paradox." This observation refers to the coexistence of high risk factors with unanticipated low incidence of CHD, and is postulated to be associated with low-to-moderate consumption of red wine. In vivo studies have shown that red wine intake is more CHD-preventative in comparison to other alcoholic drinks; enhanced cardioprotection may be attributed to grape-derived polyphenols, e.g., resveratrol, in red wine. This review summarizes results of in vitro and animal studies showing that resveratrol exerts multifaceted cardioprotective activities, as well as evidence demonstrating the presence of proteins specifically targeted by resveratrol, as exemplified by N-ribosyldihydronicotinamide:quinone oxidoreductase, NQO2. A mechanism encompassing nongenomic and genomic effects and a research roadmap is proposed as a framework for uncovering further insights on cardioprotection by resveratrol "

Semin Thromb Hemost. 2010 Feb;36(1):59-70. Epub 2010 Apr 13.

Moderate red wine consumption and cardiovascular disease risk: beyond the "French paradox".

Lippi G, Franchini M, Favaloro EJ, Targher G.

U.O. Diagnostica Ematochimica, Azienda Ospedaliero-Universitaria di Parma, Parma, Italy. giuseppe.lippi@univr.it

Summary: "The term FRENCH PARADOX was coined in 1992 to describe the relatively low incidence of cardiovascular disease in the French population, despite a relatively high dietary intake of saturated fats, and potentially attributable to the consumption of red wine. After nearly 20 years, several studies have investigated the fascinating, overwhelmingly positive biological and clinical associations of red wine consumption with cardiovascular disease and mortality. Light to moderate intake of red wine produces a kaleidoscope of potentially beneficial effects that target all phases of the atherosclerotic process, from atherogenesis (early plaque development and growth) to vessel occlusion (flow-mediated dilatation, thrombosis)... Red wine components, especially alcohol, resveratrol, and other polyphenolic compounds, may decrease oxidative stress, enhance cholesterol efflux from vessel walls (mainly by increasing levels of high-density lipoprotein cholesterol), and inhibit lipoproteins oxidation, macrophage cholesterol accumulation, and foam-cell formation... In conclusion, although mounting evidence strongly supports beneficial cardiovascular effects of moderate red wine consumption (one to two drinks per day; 10-30 g alcohol) in most populations, clinical advice to abstainers to initiate daily alcohol consumption has not yet been substantiated in the literature and must be considered with caution on an individual basis."

J Agric Food Chem. 2008 Oct 22;56(20):9362-73. Epub 2008 Sep 27.

Does white wine qualify for French paradox? Comparison of the cardioprotective effects of red and white wines and their constituents: resveratrol, tyrosol, and hydroxytyrosol.

Dudley JI, Lekli I, Mukherjee S, Das M, Bertelli AA, Das DK.
Cardiovascular Research Center, University of Connecticut School of Medicine,
Farmington, Connecticut 06030-1110, USA.

Conclusion: "It is generally believed that the French paradox is related to the consumption of red wine and not other varieties of wine, including white wine or champagne. Some recent studies have indicated that white wine could also be as cardioprotective as red wine. The present investigation compares the cardioprotective abilities of red wine, white wine, and their principal cardioprotective constituents... The results of this study suggest that white wine can provide cardioprotection similar to red wine if it is rich in tyrosol and hydroxytyrosol."

Cancer Biol Ther. 2007 Dec;6(12):1833-6. Epub 2007 Oct 13.

New enlightenment of French Paradox: resveratrol's potential for cancer chemoprevention and anti-cancer therapy.

Liu BL, Zhang X, Zhang W, Zhen HN.
Department of Neurosurgery, Xijing Institute of Clinical Neuroscience, Xijing Hospital,
Fourth Military Medical University, Xi'an, Shaanxi Province, PR China.

Summary: "Resveratrol is a phytoalexin produced by many plants, and the skin of red grapes is particularly rich in resveratrol which accounts for the "French Paradox". Besides its protection of the cardiovascular system, it can affect the processes underlying all three stages of carcinogenesis, involving tumor initiation, promotion and progression. It has also been shown to suppress angiogenesis and metastasis. The anti-carcinogenic effects of resveratrol appear to be closely associated with its capacity to interact with multiple molecular targets involved in cancer development, while minimizing toxicity in normal tissues as tested. By reviewing many in vitro and in vivo studies, also considering both the supporting and challenging evidences, we are provided with a theory in support of the use of resveratrol in human cancer chemoprevention, in combination with either chemotherapeutic drugs or cytotoxic factors for the highly efficient treatment of drug refractory tumor cells. Anti-carcinogenic potential for cancer chemoprevention and anticancer therapy, which is one of the pleiotropic effects of resveratrol, is so called a new enlightenment of French Paradox."

Br J Nutr. 2011 Oct;106(7):1090-9. Epub 2011 Apr 12.

Estimation of the intake of anthocyanidins and their food sources in the European Prospective Investigation into Cancer and Nutrition (EPIC) study.

Zamora-Ros R, Knaze V, Luján-Barroso L, Slimani N, Romieu I, Touillaud M, Kaaks R, Teucher B, Mattiello A, Grioni S, Crowe F, Boeing H, Förster J, Quirós JR, Molina E, Huerta JM, Engeset D, Skeie G, Trichopoulou A, Dilis V, Tsiotas K, Peeters PH, Khaw KT, Wareham N, Bueno-de-Mesquita B, Ocké MC, Olsen A, Tjønneland A, Tumino R, Johansson G, Johansson I, Ardanaz E, Sacerdote C, Sonestedt E, Ericson U, Clavel-Chapelon F, Boutron-Ruault MC, Fagherazzi G, Salvini S, Amiano P, Riboli E, González CA.

Unit of Nutrition, Environment and Cancer, Cancer Epidemiology Research Programme, Catalan Institute of Oncology, IDIBELL, Barcelona, Spain. rzamora@iconcologia.net

Summary: "Anthocyanidins are bioactive flavonoids with potential health-promoting effects. These may vary among single anthocyanidins considering differences in their bioavailability and some of the mechanisms involved. The aim of the present study was to estimate the dietary intake of anthocyanidins, their food sources and the lifestyle factors (sex, age, BMI, smoking status, educational level and physical activity) involved among twenty-seven centres in ten European countries participating in the European Prospective Investigation into Cancer and Nutrition (EPIC) study. Anthocyanidin intake and their food sources for 36 037 subjects, aged between 35 and 74 years, in twenty-seven redefined centres were obtained using standardised 24 h dietary recall software (EPIC-SOFT)... A clear south to north gradient intake was observed. Cyanidins and malvidins were the main anthocyanidin contributors depending on the region and sex. Anthocyanidin intake was higher in non-obese older females, non-smokers, and increased with educational level and physical activity. The major food sources were fruits, wine, non-alcoholic beverages and some vegetables. The present study shows... differences in both total and individual anthocyanidin intakes and various lifestyle factors throughout Europe, with some geographical variability in their food sources."

Pflugers Arch. 2010 May;459(6):853-62. doi: 10.1007/s00424-010-0806-4. Epub 2010 Mar 12.

Nutritional improvement of the endothelial control of vascular tone by polyphenols: role of NO and EDHF.

Schini-Kerth VB, Auger C, Kim JH, Etienne-Selloum N, Chataigneau T.
UMR CNRS 7213, Laboratoire de Biophotonique et Pharmacologie, Faculté de Pharmacie, Université de Strasbourg, 74, route du Rhin, 67401, Illkirch, France.
valerie.schini-kerth@unistra.fr

Abstract: Numerous studies indicate that regular intake of polyphenol-rich beverages (red wine and tea) and foods (chocolate, fruit, and vegetables) is associated with a protective effect on the cardiovascular system in humans and animals. Beyond the well-known antioxidant properties of polyphenols, several other mechanisms have been shown to contribute to their beneficial cardiovascular effects. Indeed, both experimental

and clinical studies indicate that polyphenols improve the ability of endothelial cells to control vascular tone

Planta Med. 2011 Jul;77(11):1161-7. doi: 10.1055/s-0030-1250737. Epub 2011 Jan 25.

Vascular protection by natural product-derived polyphenols: in vitro and in vivo evidence.

Schini-Kerth VB, Etienne-Selloum N, Chataigneau T, Auger C.
Laboratoire de Biophotonique et Pharmacologie, Université de Strasbourg, Faculté de Pharmacie, Illkirch, France. valerie.schini-kerth@unistra.fr

Abstract: Epidemiological studies have indicated that regular intake of fruit and vegetables and beverages such as red wine and tea, which contain high levels of polyphenols, is associated with a reduced risk of cardiovascular diseases. The beneficial effect of polyphenol-rich natural products has been attributable, at least in part, to their direct effect on blood vessels, and in particular on endothelial cells.

J Nutr Biochem. 2005 Jan;16(1):1-8.

Antiangiogenic properties of natural polyphenols from red wine and green tea.

Oak MH, El Bedoui J, Schini-Kerth VB.
Pharmacologie et Physico-Chimie des Interactions Cellulaires et Moléculaires, UMR CNRS 7034, Faculté de Pharmacie, Université Louis Pasteur de Strasbourg, F-67401 Illkirch, France.

Abstract

Epidemiological studies have indicated that regular consumption of red wine and green tea is associated with a reduced risk of coronary heart disease and tumor progression. The development of tumors and of atherosclerosis lesions to advanced plaques, which are prone to rupture, is accelerated by the formation of new blood vessels. These new blood vessels provide oxygen and nutrients to neighboring cells. Therefore, recent studies have examined whether red wine polyphenolic compounds (RWPCs) and green tea polyphenols (GTPs) have antiangiogenic properties. In vitro investigations have indicated that RWPCs and GTPs are able to inhibit several key events of the angiogenic process such as proliferation and migration of endothelial cells and vascular smooth muscle cells and the expression of two major proangiogenic factors, vascular endothelial growth factor (VEGF) and matrix metalloproteinase-2, by both redox-sensitive and redox-insensitive mechanisms. Antiangiogenic properties of polyphenols have also been observed in the chick embryo chorioallantoic membrane since the local application of RWPCs and GTPs strongly inhibited the formation of new blood vessels. Moreover, intake of resveratrol or green tea has been shown to reduce corneal neovascularization induced by proangiogenic factors such as VEGF and fibroblast growth factor in mice. The ability of RWPCs and GTPs to prevent the formation of new blood vessels contributes, at least in part, to explain their beneficial effect on coronary heart disease

and cancer. This review focuses on the antiangiogenic properties of natural polyphenols and examines underlying mechanisms

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Alcohol-Attributable Cancer Deaths and Years of Potential Life Lost in the United States

David E. Nelson, MD, MPH, Dwayne W. Jarman, DVM, MPH, Jürgen Rehm, PhD, Thomas K. Greenfield, PhD, Grégoire Rey, PhD, William C. Kerr, PhD, Paige Miller, PhD, MPH, Kevin D. Shield, MHSc, Yu Ye, MA, and Timothy S. Naimi, MD, MPH
David E. Nelson and Paige Miller are with National Cancer Institute, Bethesda, MD. Dwayne W. Jarman is with Food and Drug Administration, Detroit, MI, and US Public Health Service, Rockville, MD. Jürgen Rehm and Kevin D. Shield are with Centre for Addiction and Mental Health, Toronto, Ontario. Thomas K. Greenfield, William C. Kerr, and Yu Ye are with Alcohol Research Group, Public Health Institute, Emeryville, CA. Grégoire Rey is with INSERM, CépiDc, Le Kremlin-Bicêtre, France. Timothy S. Naimi is with Boston University Medical Center, Boston, MA.

Objectives. Our goal was to provide current estimates of alcohol-attributable cancer mortality and years of potential life lost (YPLL) in the United States.

Conclusions. Alcohol remains a major contributor to cancer mortality and YPLL. Higher consumption increases risk but there is no safe threshold for alcohol and cancer risk. Reducing alcohol consumption is an important and underemphasized cancer prevention strategy. (Am J Public Health. Published)

Ciência Téc. Vitiv. 26 (1) 33-44. 2011

Wine and health relationships. A question of moderation?

C. Santos-Buelga, S. González-Manzano

Grupo de Investigación en Polifenoles, Universidad de Salamanca, Unidad de Nutrición y Bromatología, Facultad de Farmacia, Miguel de Unamuno, E-37007. Salamanca, Spain

ABSTRACT: Evidences accumulated over the last thirty years suggest that light to moderate alcohol consumption, especially in the form of red wine, can have beneficial effects for health. Those benefits mostly refer to improvement in cardiovascular health, although relationships with a lower risk of other pathologies such as type 2 diabetes, dementia or cognitive decline in old age have also been established. Most evidences derive from observational studies or from in vitro or animal assays, whereas direct scientific data in human are scarce and incomplete. On the other hand, alcohol is a toxic product whose irresponsible and excessive consumption has well-established consequences for health and serious social implications. Furthermore, some adverse

effects have been related with the moderate consumption of alcoholic beverages, including an increase in the incidence of different types of cancer.

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Vascular protection by dietary polyphenols

Jean-Claude Stocklet | Thierry Cataigneau | Madamdou Ndiaye | Min-Ho Oak | Jasser El Bedoui | Marta Chataigneau | Valerie B. Schini-Kerth
Pharmacologie et Physico-Chimie des Interactions Cellulaires et Moleculaires, UMR CNRS 7034, Faculte de Pharmacie, Universite Louis Pasteur de Strassbourg, B.P. 60024, 74 route du Rhin, F67401 Illkirch, France

Abstract (cont. page1)

Consumption of polyphenol-rich foods, such as fruits and vegetables, and beverages derived from plants, such as cocoa, red wine and tea, may represent a beneficial diet in terms of cardiovascular protection. Indeed, epidemiological studies demonstrate a significant inverse correlation between polyphenols consumption and cardiovascular risk. Among the numerous plausible mechanisms by which polyphenols may confer cardiovascular protection, improvement of the endothelial function and inhibition of angiogenesis and cell migration and proliferation in blood vessels have been the focus of recent studies. These studies have indicated that, in addition to and independently from their antioxidant effects, plant polyphenols (1) enhance the production of vasodilating factors [nitric oxide (NO), endothelium-derived hyperpolarizing factor (EDHF) and prostacyclin] and inhibit the synthesis of vasoconstrictor endothelin-1 in endothelial cells; and (2) inhibit the expression of two major pro-angiogenic factors, vascular endothelial growth factor (VEGF) and matrix metalloproteinase-2 (MMP-2) in smooth muscle cells. The mechanisms of these effects involve: (1) in endothelial cells, increased Ca²⁺ level and redox-sensitive activation of the phosphoinositide 3 (PI3)-kinase/Akt pathway (leading to rapid and sustained activation of nitric oxide synthase and formation of EDHF) and enhanced expression of nitric oxide synthase; and (2) in smooth muscle cells, both redox-sensitive inhibition of the p38 mitogen-activated protein kinase (p38 MAPK) pathway activation (leading to inhibition of platelet-derived growth factor (PDGF)-induced VEGF gene expression) and redox-insensitive mechanisms (leading to inhibition of thrombin-induced MMP-2 formation). The current evidence suggests that all these mechanisms are triggered by polyphenols with specific structures, although the structural requirements may be different from one effect to the other, and that they all contribute to the vasoprotective, anti-angiogenic, anti-atherogenic, vasorelaxant and anti-hypertensive effects of acute or chronic administration of plant polyphenols found in vivo in animals and in patients.

Cardiovascular Research 54 (2002) 503–515

Mediterranean diet and the French paradox: Two distinct biogeographic concepts for one consolidated scientific theory on the role of nutrition in coronary heart disease

Michel de Lorgeril, Patricia Salena, Francois Paillardab, Franocis Laporte, Francois Boucher , Joel de Leiris

a Laboratoire du Stress Cardiovasculaire et Pathologies Associe´es, Laboratoire de Biologie du Stress Oxydant, UFR de Medecine et Pharmacie, Grenoble, France, Departement de Cardiologie, CHU de Rennes,

Scientists and physicians have long been debating the Mediterranean-style diet and the French paradox for coronary heart disease (CHD). However, folksy they sound, these two biogeographic concepts can still be very useful to explain unexpected or controversial medical and scientific data, such as the low mortality rate from CHD in Mediterranean Southern Europe and in France as with other European countries. Understanding these concepts may help improve our ability to treat and prevent CHD. Most of the present confusion probably comes from the consistent underestimation by physicians and scientists of the role of nutrition in CHD.

Circulation Research is published by the American Heart Association, September 6, 2012

De-alcoholized Red Wine Decreases Systolic and Diastolic Blood Pressure and Increases Plasma Nitric Oxide

Rosa Casas, Emilio Sacanella, Rafael Llorach, Rosa M. Lamuela-Raventos, Cristina Andres-Lacueva Gemma Chiva-Blanch, Mireia Urpi-Sarda, Emilio Ros, Sara Arranz, Palmira Valderas-Martinez,

Conclusions: De-alcoholized red wine decreases systolic and diastolic BP. Our results point out through a NO-mediated mechanism. The daily consumption of de-alcoholized red wine could be useful for the prevention of low to moderate hypertension. Trial registered at controlledtrials.com: ISRCTN88720134 (A study from Spain concludes that the blood-pressure-lowering effects of red wine come from the beneficial chemicals called polyphenols that it contains, though alcohol may limit their effects)

Advanced Knowledge of Three Important Classes of Grape Phenolics: Anthocyanins, Stilbenes and Flavonols

Riccardo Flamini, Fulvio Mattivi, Mirko De Rosso, Panagiotis Arapitsas and Luigi Bavaresco

Abstract: Grape is qualitatively and quantitatively very rich in polyphenols. In particular, anthocyanins, flavonols and stilbene derivatives play very important roles in plant metabolism, thanks to their peculiar characteristics.

They are natural colorants, have antioxidant, antimicrobial and anticarcinogenic activity, exert protective effects on the human cardiovascular system, and are used in the food and pharmaceutical industries. Stilbenes are vine phytoalexins present in grape berries and associated with the beneficial effects of drinking wine. The principal stilbene, resveratrol, is characterized by anticancer, antioxidant, anti-inflammatory and cardioprotective activity. Resveratrol dimers and oligomers also occur in grape, and are synthesized by the vine as active defenses against exogenous attack, or produced by extracellular enzymes released from pathogens in an attempt to eliminate undesirable toxic compounds. Flavonols are a ubiquitous class of flavonoids with photo-protection and copigmentation (together with anthocyanins) functions. Anthocyanins are responsible for the color of red grapes and wines.