

22 November 2016  
EMA/HMPC/464683/2016  
Committee on Herbal Medicinal Products (HMPC)

## List of references supporting the assessment of *Vitis vinifera L., folium*

Draft

**The European Medicines Agency acknowledges that copies of the underlying works used to produce this monograph were provided for research only with exclusion of any commercial purpose.**

- Abascal K, Yarnell E. Botanicals for chronic venous insufficiency. *Altern Complem Therap* 2007; 3(6): 304-311.
- Agence du médicament (AFSSAPS): Médicaments à base de plantes. Les cahiers de l'Agence n°3: Vigne rouge. Sant Denis, Paris 1998.
- Alguire PC, Mathes BM. Chronic venous insufficiency and venous ulceration. *J Gen Intern Med* 1997; 12: 374-383.
- Andrian M, Jeandet R, Bessis R, Joubert JM. Induction of phytoalexin (Resveratrol) synthesis in grapevine leaves treated with Aluminum Chloride (AlCl). *J Agric Food Chem* 1996; 44(8): 1979-81.
- Anonymous. A review of evidence on red vine leaf extract in the prevention and management of venous disease. *J Wound Care* 2006; 15(9): 393-396.
- Anonymous. Chronisch-venöse Insuffizienz: bessere Mikrovaskuläre Durchblutung durch roten Weinlaubextrakt AS 195. *Phlebologie* 2004; 33(4): 52-53.
- Anonymous. Roter Weinlaubextrakt. *Deutsche Apotheker Zeitung* 2005; 145(46): 113. Antistax® SPC, 2005.
- Aziz AA, Edwards CA, Lean ME, Crozier A. Absorption and excretion of conjugated flavonols, including quercetin-4'-O-beta-glucoside and isorhamnetin-4'-O-beta-glucoside by human volunteers after the consumption of onions. *Free Radic Res* 1998; 29(3): 257-269.
- Bilgrami KS, Jeswal P. Control of citrinin caused nephrotoxicosis through aqueous leaf extract of *Vitis vinifera* L., mercurious corrosivus and cortisone. *Indian J Exp Biol* 1993; 31: 482-484.



Bombardelli E, Morazzoni P, Carini M, et al. Biological activity of procyanidins from *Vitis vinifera* L. *BioFactors* **1997**; 6: 429-431.

Bombardelli E. & Morazzoni P. *Vitis vinifera*, L. *Fitoterapia* **1995**; 66: 291-317.

Bonnet D, Mejdoubi S, Sommet A, Alric L. Acute hepatitis probably induced by *fumaria* and *vitis vinifera* var *tinctoria* plant therapy products. *Gastroenterol Clin Biol*, **2007**; 31(11): 1041-1042.

Boucheny A, Brum-Bousquet M. Contribution à l'étude de la feuille de vigne rouge (*Vitis vinifera* L.). *Plantes Méd Phytothér* **1990**; 24: 179-92.

Brito FF, Gimeno PM, Bartolome B, Alonso AM, Lara P, Fernández LA, Martínez A. Vine pollen allergy in areas with a high density of vineyards. *Annal Allerg Asthma Immunol* **2008**; 100(6): 596-600.

Bruneton J. *Phytothérapie – Les données de l'évaluation* Ed. TEC & DOC- EM Inter **2002**; 167-172.

Bruneton J. *Pharmacognosie. Phytochimie. Plantes médicinales* (3ème éd.) Ed. TEC & DOC- EM Inter **1999**; 365-366.

Butcher M. A review of evidence on red wine leaf extract in the prevention and management of venous disease. *J Wound Care* **2006**; 15: 393-396.

Capitao LM, Menezes JD, Gouveia-Oliveira A. A multivariate analysis of the factors associated with the severity of chronic venous insufficiency. *Acta Med Port* **1993**; 6: 501-506.

Cahier de l'Agence n° 3: Médicaments à base de plantes *Vigne rouge* Ed. Agence du Médicament, Paris **1998**.

Chevallier L. *Médicaments à base de plantes* (2ème éd.) Ed. MASSON **2004**, 230.

Chun HS, Kim JM, Choi EH, Chang N. Neuroprotective effects of several korean medicinal plants traditionally used for stroke remedy. **2008**.

Chung EY, Byung H, Lee MK, Yun YP, Lee SH, Min KR, Kim Y. Anti-inflammatory effect of the oligomeric stilbene a-viniferin and its mode of the action through inhibition of cyclooxygenase-2 and inducible nitric oxide synthase. *Planta Med* **2003**; 69(8): 710-714.

Costantini A, De Bernardi T, Gotti A. [Clinical and capillaroscopic evaluation of chronic uncomplicated venous insufficiency with procyandins extracted from *Vitis vinifera*][Article in Italian]. *Minerva Cardioangiologica* **1999**; 47(1-2): 39-46.

Cowell JA, Korytko PJ, Morrissey RL, Booth TD, Levine BS. Resveratrol-associated renal toxicity. *Toxicol Sci* **2004**; 82(2): 614-619.

Darné G, Glories Y. Les anthocyanes des feuilles de différentes variétés de *Vitis vinifera* L. entre la véraison des raisins et la chute des feuilles. *Vitis* **1988**; 27: 71-78.

De Mey C. The oedema-protective effectiveness of Antistax® in chronic venous insufficiency: comments from the point of view of evidence-based medicine. *Fortschr Med* **2000**; 118(3): 125-133.

De Smet PAGM. Health risks of herbal remedies: an update. *Clin Pharm Therap* **2004**; 76(1): 1-17.

Diaz Lanza AM, Elias R, Maillard C, Faure R, de Sotto M, Balansard G. Mise au point sur les dérivés flavoniques des feuilles de trois cultivars de Vigne *Vitis vinifera* L. var. *tinctoria* (Alicante, Carignan, Grand noir). Intérêt dans le contrôle chimique. *Ann Pharm Franç* **1995**; 47: 229-234.

Duke JA. Handbook of Medicinal Herbs. 2<sup>nd</sup> ed. CRC Press, Boca Raton, Florida **2002**; 349.

Ebadi M, Pharmacodynamic Basis of Herbal Medicine . CRC Press, **2002**.

ESCOP. Vitis Viniferae Folium (Red vine Leaf). In: ESCOP Monographs. 2nd edition, supplement **2009**; 284-288.

Fagrell B. Vital microscopy and the pathophysiology of deep venous insufficiency. *Int Angiol* **1995**; 14: 18-22.

Fine A.M. Oligomeric Proanthocyanidin Complexes: History, structure, and phytopharmaceutical applications. *Altern Med Rev* **2000**; 5(2): 144-151.

Fricke U. Vein products. Arzneiverordnungsreport 1998. Schwabe U, Paffrath D (eds.). Springer Verlag, Berlin **1998**; 538-550.

Gharib Naseri MK, Zarei M, Amiri O. Spasmolytic effect of *Vitis vinifera* leaf extract on rat colon. *Daru* **2007**; 14(4): 203-207, (<http://diglib.tums.ac.ir/pub/magmng/pdf/3017.pdf>)

Gharib Naseri MK, Heidari A. Spasmolytic effect of *Vitis vinifera* leaf extract on rat trachea. *J Med Plants* **2006**; 5(17): 39-49.

Gharib Naseri MK, Heidari A. Bronchodilatory activity of *Vitis vinifera* leaf hydroalcoholic extract in rat. *Iran Biomed J* **2006**; 10(2): 79-83.

Gharib Naseri MK, Navid Hamidi M, Heidari A. Vasorelaxant effects of *Vitis vinifera* L. leaf extract on isolated rat aorta. *J Med Plants* **2004**; 3(9): 43-54.

German "Rote List" entries for Antistax® since 1974

Girre L, Amoros M, Kaij-Kamb M, Baril F, Simões CMO. Le pouvoir antiherpétique *in vitro* des feuilles de vigne rouge (*Vitis vinifera*). *Fitoterapia* **1990**; 61: 201-205.

Graefe EU, Wittig J, Mueller S, Riethling AK, Uehleke B, Drewelow B, Pforte H, Jacobasch G, Derendorf H, Veit M. Pharmacokinetics and bioavailability of quercetin glycosides in humans. *J Clin Pharmacol* **2001**; 41(5): 492-499.

Grossmann K. Comparative efficacy of a combined treatment with compression stockings and oxerutin (Venoruton ®) versus compression stockings and placebo inpatients with CVI. *Phlebol* (Stuttgart) **1997**; 26: 105-110.

Güthenke, K. "Wesen und Behandlung der Bindegewebsschwäche, insbesondere der Veneninsuffizienz mit Weinblattextrakt". *Deutsch. Medizin. J.* **1960**; 11: 370-373.

Hebash KAH, Fadel HM, Soliman MMA. Volatile components of grape leaves. *J Islam Acad Sci* 1991; 4(1): 26-28.

Hertog MG, Hollman PC. Potential health effects of the dietary flavonol quercetin. *European J Clin Nutr* **1996**; 50(2): 63-71.

Hmamouchi M, Es-Safi N, Essassi EM. Oligomeric and polymeric proanthocyanidins from Moroccan grapewine (*Vitis vinifera*) leaves. *Fitoterapia* **1997**; 68: 332-337.

Hollman PC, Katan MB. Health effects and bioavailability of dietary flavonols. *Free Radic Res* **1999**; 31: 75-80.

Janssen K, Mensink RP, Cox FJ, Harryvan JL, Hovenier R, Hollman PC, Katan MB. Effects of the flavonoids quercetin and apigenin on hemostasis in healthy volunteers: results from an *in vitro* and a dietary supplement study. *Am J Clin Nutr* **1998**; 67(2): 255-262.

Jonadet M., Meunier MT, Bastide J. et P. Anthocyanosides extraits de *Vitis vinifera*, de *Vaccinium myrtillus* et de *Pinus maritima* *J Pharm Belg* **1983**; 38: 41-46.

Jünger M, Hahn U, Bort S, Klyszcz T, Hahn M, Rassner G. Importance of cutaneous microangiopathy for the development of skin diseases due to chronic venous insufficiency (CVI). *Wien Med Wochenschr* **1994**; 144(10/11): 206-210.

Jünger M, Klyszcz T, Hahn M, Rassner G. Disturbed blood flow regulation in venous leg ulcers. *Int J Microcirc* **1996**; 16: 259-265.

Kalogeromitros DC, Makris MP, Gregoriou SG, Mousatou VG, Lyris NG, Tarassi KE, Papasteriades CA. Grape anaphylaxis : a study of 11 adult onset cases. *Allergy Asthma Proc* **2005**; 26(1): 53-58.

Kalus U, Koscielny J, Grigorov A, Schaefer E, Peil H, Kiesewetter H. Improvement of cutaneous microcirculation and oxygen supply in patients with chronic venous insufficiency by orally administered extract of red vine leaves AS195. A randomised, double-blind, placebo-controlled, cross-over study. *Drugs R&D* **2004**; 5(2): 63-71.

Kiesewetter H., Koscielny J., Kalus U., Vix JM, Peil H, Petrini O, van Toor BS, de Mey C. Efficacy of orally administrated extract of red wine leaf AS 195 (folia *Vitis viniferae*) in chronic venous insufficiency (stages I-II). A randomized double-blind, placebo-controlled trials. *Arzneim Forsch* **2000**; 50: 109-117.

Kiesewetter H. [Good clinical practice in accordance with clinical studies on the efficacy and tolerability of red wine leaf extract AS 195 in chronic venous insufficiency.] *Vasomed* **2002**; 14(1): 18-20.

Klopp R, Schippel W, Niemer W. Compression therapy and microcirculation: vital microscope investigations in patients suffering from chronic venous insufficiency before and after compression therapy. *Phlebol* 1996; 1: 19-25.

Kosar M, Kupeli E, Malyer H, Uylaser V, Turkben C, Baser KH. Effect of brining on biological activity of leaves of *Vitis vinifera* L. (Cv. Sultani Cekirdeksiz) from Turkey. *J Agric Food Chem* **2007**; 55 (11): 4596-4603.

Klyszcz T, Juenger M, Schanz S, Janz M, Rassner G, Kohnen R. Quality of life with chronic venous insufficiency (CVI): Result of a study using the newly developed Tuebingen questionnaire for measuring the quality of life in patients with CVI (TLQ-CVI). *Hautarzt* **1998**; 49(5): 372-381.

Lala G, Malik M, Zhao C, He J, Kwon Y, Giusti MM, Magnuson BA. Anthocyanin-rich extracts inhibit multiple biomarkers of colon cancer in rats. *Nutr Cancer* **2006**; 54(1): 84-93.

Langcake P, Cornford CA, Pryce RJ. [Identification of pterostilbene as a phytoalexin from \*Vitis vinifera\* leaves](#). *Phytochemistry* **1979**; 18(6): 1025-1027.

Laparra J, Darné G. La feuille de vigne rouge en phytothérapie: étude des composés anthocyaniques de quelques présentations pharmaceutiques. *Plantes Méd Phytothér* **1989**; 23: 129-35.

Lapidot T, Harel S, Granit R, Kanner J. Bioavailability of Red Wine Anthocyanins As Detected in Human Urine. *J Agric Food Chem* **1998**; 46: 4297-4302.

Lardos, A. and M. H. Kreuter. **2000**. Red vine leaf. Ed. by Dr. M. H. Kreuter, R & D Department, Phytopharm. and Phytochem. Products, Flachsmann AG, Butzenstrasse 60, 8038 Zurich, Switzerland. Publ. Ask Intercity Pharmaceut.: <http://www.askic.co.jp/vitis-vinifera/vitis-vinifera-Full-article.htm>

Leuschner F, Mitterer KE. Examination of the influence of *Extractum Vitis viniferae* L. on the pregnant rabbit and the foetus by oral administration. LPT Report No. 7441/92. **1993** (U93-1144)

Liviero L, Puglisi P, Morazzoni P, Bombardelli E. Antimutagenic activity of procyanidins from *Vitis vinifera*. *Fitoterapia* **1993**; 65: 203-209.

- Lizarraga D, Lozano C, Briedé JJ, Van Delft JH, Touriño S, Centelles JJ, Torres JL, Cascante M. The importance of polymerization and galloylation for the antiproliferative properties of procyanidin-rich natural extracts. *FEBS Journal* **2007**; 274(18): 4802–4811.
- Maffei Facino et al. Free radicals scavenging action and antienzyme activity of proantocyanidines from *Vitis vinifera*. A mechanism for their capillary protective action. *Arzneim Forsch* **1994**; 44: 592-601.
- Manach C, Donovan JL. Pharmacokinetics and metabolism of dietary flavonoids in humans. *Free Radical Res* **2004**; 38(8): 771-785.
- Manach C, Williamson G, Morand C, Scalbert A, Rémésy C. Bioavailability and bioefficacy of polyphenols in humans. I. Review of 97 bioavailability studies. *Am J Clin Nutr* **2005**; 81: 230-242.
- Middleton E Jr. Biological properties of plant flavonoids: An overview. *Int J Pharmacogn* **1996**; 34(5): 344-348.
- Middleton E Jr, Kandaswami C. Effects of flavonoids on immune and inflammatory cell functions. *Biochem Pharmacol* **1992**; 43(6): 1167-1179.
- Mills S and Bone K. Principles and Practice of Phytotherapy (Modern Herbal Medicine). Churchill Livingstone **2000**.
- Monagas M, Hernandez-Ledesma B, Gómez-Cordovés C, Bartolomé B. Commercial dietary ingredients from *Vitis vinifera* L. leaves and grape skins: antioxidant and chemical characterization. *J Agric Food Chem* **2006**; 54(2): 319-327.
- Monsieur R, Van Snick G. Action de l'extrait de feuilles de vigne rouge AS 195 dans l'insuffisance veineuse chronique. *Praxis* **2006**; 95: 187-90.
- Muellerschoen H. Gene mutation assay in Chinese hamster V79 cells *in vitro* with Weinlaub-Extrakt (Extract of vine leaves). CCR Project No 329207. **1993**.
- Mukherjee, PK. Plant products with hypercholesterolemic potentials. *Advances in Food Nut Res* **2003**; 47: 277-338.
- Mur P, Feo Brito F, Bartolomé B, Galindo PA, Gómez E, Borja J, Alonso A. Simultaneous allergy to vine pollen and grape. *J Investig Allergol Clin Immunol* **2006**, 16(4): 271-273.
- Nassiri-Asl M, Hosseinzadeh H. Review of the Pharmacological Effects of *Vitis vinifera* (Grape) and its Bioactive Compounds. *Phytother Res* **2009**; 23: 1197-1204
- Nees S, Weiss DR, Reichenbach-Klinke E, Rampp F, Heilmeier B, Kanbach J, Esperester A. Protective effects of flavonoids contained in the red vine leaf on venular endothelium against the attack of activated blood components *in vitro*. *Arzneim-Forsch/Drug Res* **2003i**; 53(5): 330-341.
- Nees S, Reichenbach-Klinke E, Rampp F, Weiss DR. Human venular endothelial cells as preferred targets in inflammatory edema: influence of thrombin, platelets, polymorphonuclear leukocytes and flavonoid extracts of red vine leafs. *Exper. Biol.* **2003** – [Translating the Genome, San Diego, Apr 11-15, 2003. FASEB J **2003ii**; 17(4/5): Abstr]
- Neumann HAM, Broek MJTB van den. A comparative clinical trial of graduated compression stockings and O-(beta-hydroxyethyl)-rutosides (HR), in the treatment of patients, with chronic venous insufficiency. *Lymphol* **1995**; 19: 8-11.
- Nocker W, Diebschlag W. Dose-effect study with O-(beta-hydroxyethyl)-rutoside solutions for oral administration. *Vasa* **1987**; 16(4): 365-369.

Nocker W, Diebschlag W, Lehmacher W. Three-month, randomized, double-blind dose-effect study of O-( $\beta$ -hydroxethyl) rutoside solutions for oral administration. *Vasa* **1989**; 18(3): 235-238.

NTP: Toxicology and carcinogenesis studies of quercetin (CAS No. 117-39-5) in F344 rats (feed studies). **1992**

NTP: Quercetin CAS No. 117-39-5. **2001**.

Orhan DD, Orhan N, Ergun E, Ergun F. Hepatoprotective effect of *Vitis vinifera* L. leaves on carbon tetrachloride-induced acute liver damage in rats. *J Ethnopharmacol* **2007**; 112(1): 145-151.

Orhan N, Aslan M, Deliorman Orhan D, Ergun F and Yesilada E. *In-vivo* assessment of antidiabetic and antioxidant activities of grapevine leaves (*Vitis vinifera*) in diabetic rats. *J Ethnopharmacol* **2006**; 108: 280-286.

Oskay M, Sari D. Antimicrobial screening of some Turkish medicinal plants. *Pharm Biol* **2007**; 45(3): 176-181.

Pari L, Suresh A. Effect of grape (*Vitis vinifera* L.) leaf extract on alcohol induced oxidative stress in rats. *Food Chem Toxicol* **2008**; 46(5): 1627-1634.

Partsch H. Classification and grading of chronic venous disease in the lower limbs – A consensus statement. 6<sup>th</sup> Ann Congr, Maui, Feb 22-25, **1994**. *Phlebol* (Stuttgart) 1995; 24: 125-129.

Pedopur Tropfen (Austria), Information extracted from the online search of Austrian Agency for Medicines. [http://pharmaweb.ages.at/pharma\\_web/index.jsf](http://pharmaweb.ages.at/pharma_web/index.jsf)

Pharmacopée Française. Vigne rouge - *Vitis vinifera*. Xe édition, La Commission Nationale de Pharmacopée **1996**; Paris.

PDR for Herbal Medicines. 3rd edition. Thomson PDR **2004**; 400-404, 988.

Petrini O, Schäfer E, Ambrosetti L, Schröder-Rumsfeld H, Bubeck J. Roter Weinlaubextrakt bei chronisch-venöser Insuffizienz. *Dtsch Apoth Ztg* **2003**; 143: 4847-4850.

Pietta PG. Flavonoids as antioxidants. *J Nat Prod* **2000**; 63(7): 1035-1042.

Pittler MH, Ernst E. Horse-chestnut seed extract for chronic venous insufficiency. A criteria-based systematic review. *Arch Dermatol* **1998**; 134: 1356-1360.

Porter JM, Moneta GL, International Consensus Committee on Chronic Venous Disease. Reporting standards in venous disease: an update. *J Vasc Surg* **1995**; 21(4): 635-645.

Prior RL, Absorption and metabolism of anthocyanins: potential health effects. In: Meskin MS, Bidlack WR, Davies AJ, Lewis DS, Randolph RK, editors. *Phytochemicals: mechanisms of action*. Boca Raton: CRC Press **2004**; 1-19.

Rabe E, Pannier F, Larenz B. [Red vine leaf extract (AX 195) for chronic venous insufficiency] [Article in German] *Med Monatsschr Pharm* **2005**; 28(2): 55-59.

Rabe E, Stücker M, Esperester A, Schäfer E, Ottillinger B. Efficacy and tolerability of red-vine-leaf extract in patients suffering from chronic venous insufficiency--results of a double-blind placebo-controlled study. *Eur J Vasc Endovasc Surg* **2011**; 41(4): 540-7.

Rabe E, Guex JJ, Morrison N, Ramelet AA, Schuller-Petrovic S, Scuderi A, et al. Treatment of chronic venous disease with flavonoids: recommendations for treatment and further studies. *Phlebology* **2013**; 28(6): 308-19.

Raynaud J. *Prescription et conseil en phytothérapie*. Lavoisier **2005**; 206-208.

Rehn D, Brunnauer H, Diebschlag W, Lehmacher W. Investigation of the therapeutic equivalence of different galenical preparations of O-(beta-hydroxyethyl)-rutosides following multiple dose peroral administration. *Arzneim Forsch/Drug Res* **1996**; 46(5): 488-492.

Rehn D, Unkauf M, Vix JM. O-( β-hydroxyethyl)-rutosides for vein diseases. *Pharm Ztg* **1994**; 139(27): 36-44.

Royer RJ, Schmidt CL. Evaluation of venotropic drugs by venous gas plethysmography. A study of procyanidolic oligomers. *Sem Hop* **1981**; 57: 2009-2013.

Schaefer E, Peil H, Ambrosetti L, Petrini O. Oedema protective properties of the red vine leaf extract AS 195 (*Folia Vitis viniferae*) in the treatment of chronic venous insufficiency. A 6-week observational clinical trial. *Arzneimittelforschung* **2003**; 53(4): 243-246.

Schimmer O. Pflanzliche Antimutagene. *Dtsch Apoth Ztg* **1999**; 19: 51-62.

Schneider E. Rotes Weinlaub - Geschichte der verwendung- Red wine leaves: The history of their applications. *Zeitsch Phytother* **2007**; 28(5): 250-258.

Schneider E. Rotes Weinlaub - Eine venenwirksame Arzneidroge- Red wine leaf - An effective herbal drug for the treatment of chronic venous insufficiency. *Deutsch Apoth Zeit* **2007**; 147: 3380-3386.

Schneider E, Von der Heydt H, Espereter A. Evaluation of polyphenol composition in red leaves from different varieties of *Vitis vinifera* Species. *Planta Med* **2008**; 74: 1-8.

Sendogdu N, Aslan M, Deliorman Orhan D, Ergun F, Yesilada E. Antidiabetic and antioxidant effects of *Vitis vinifera* L. leaves in streptozotocin-diabetic rats. *Turkish J Pharm Sci* **2006**; 3(1): 7-17. // [http://www.eczakademi.org/journal/\\_pdf/7syf-Vol3No12006.pdf](http://www.eczakademi.org/journal/_pdf/7syf-Vol3No12006.pdf)

Shastry CS, Ashok K, Aravind MB, Joshi SD. Diuretic activity of the extracts of *Vitis vinifera* leaves. *Indian Drugs* **2002**; 39(9): 497-499.

Smith PD. Neutrophil activation and mediators of inflammation in chronic venous insufficiency. *J Vasc Res* **1999**; 36(1): 24-36.

Stagos D, Kazantzoglou G, Theofanidou D, Kakalopoulou G, Magiatis P, Mitaku S, Kouretas D. Activity of grape extracts from Greek varieties of *Vitis vinifera* against mutagenicity induced by bleomycin and hydrogen peroxide in *Salmonella typhimurium* strain TA102. *Mutat Res* **2006**; 609(2): 165171.

Steins A, Hahn M, Juenger M. Venous leg ulcers and microcirculation. *Clin Hemorheol Microcirc* **2001**; 24: 147-53.

Tebib K, Bessanicon P, Rouanet J. Dietary grape seed tannins affect lipoproteins, lipoproteinlipases, and tissue lipids in rats fed hypercholesterolemic diets. *J Nutr* **1994**; 124: 2451-2457.

Tenant RW, Spalding JW, Stasiewicz S, Caspary WD, Mason JM, Resnick MA. Comparative evaluation of genetic toxicity patterns of carcinogens and noncarcinogens: strategies for predictive use of short-term assays. *Environ Health Perspect* **1987**; 75: 87-95.

Valnet J. Vigne rouge IN: Phytothérapie – Traitment des maladies par les plantes, 6th ed. Paris.Maloine, **1992** : 607-608

Van Helemont J. *Vitis vinifera* IN: Compendium de Phytothérapie, Bruxelles: Association Pharmaceutiques Belge, **1986**:430-431

Vanaclocha B, Cañigueral S, editors. Vid- *Vitis vinifera* L. In: Fitoterapia- Vademecum de Prescription, 4th Ed. Barcelona- Masson, 2003; 500-2

Volonté M, Petrini O. Extract of red vine leaves: effects on microcirculation. *Integr Nutr* 2004; 7(3): 15-21.

Volonté M, Schaefer E, Ambrosetti L, Petrini O. Extract of red vine leaves in chronic venous insufficiency: clinical aspects. *Integr Nutr* 2003; 6(2): 13-21.

Vix JM, Dieterich S, Peil H. A 12-week, double-blind, randomised, placebo-controlled, multicentre trial to evaluate efficacy and tolerability of Antistax® film-coated tablets, 360 mg/day orally, in male and female patients suffering from chronic venous insufficiency. Boehringer Ingelheim in-house files 2007. Confidential

Wadsworth AN, Faulds D. Hydroxyethylrutosides: a review of its pharmacology, and therapeutic efficacy in venous insufficiency and related disorders. *Drugs* 1992; 44(6): 1013-1032.

Weber C. Red vine leaf protects the veins. News Conf 'Current Knowledge in the Therapy of Venous Diseases', *Dtsch Apoth Ztg* 2000; 140(28): 50-52 (German).

Wegrowski J, Robert AM, Moczar M. The effect of procyanidolic oligomers on the composition of normal and hypercholesterolemic rabbit aortas. *Biochem Pharmacol* 1984; 33: 3491-3497.

Willa-Craps C, Wuethrich B. Contact allergy in chronic venous insufficiency. *Phlebol* (Stuttg) 1995; 24: 93-97.

Wollina U, Abdel-Naser MB, Mani R. A review of the microcirculation in skin in patients with chronic venous insufficiency: The problem and the evidence available for therapeutic options. *Int J Low Extr Wounds* 2006; 5(3): 169-180.

Widmer LK, Staehelin HB, Nissen C, Silva da A. Venous, arterial diseases, coronary heart disease in working people. Basler Studie I-III. Verlag Hans Huber, Bern 1981.

Wright DDI, Franks PJ, Blair SD, Backhouse CM, Moffatt C, McCollum CN. Oxerutins in the prevention of recurrence in chronic venous ulceration: randomized controlled trial. *Br J Surg* 1991; 78(10): 1269-1270.

#### Further Literature References

Schaefer E & Petrini O. 2004; unpublished study report provided by Boehringer Ingelheim. 5 – Clinical Study Reports March 2015

- Rabe E, Guex JJ, Morrison N, Ramelet AA, Schuller-Petrovic S, Scuderi A, et al. Treatment of chronic venous disease with flavonoids: recommendations for treatment and further studies. *Phlebology* 2013 Sep;28(6):308-19.