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## List of references supporting the assessment of *Cynara cardunculus* L. (syn. *Cynara scolymus* L.), folium

**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.**

Adzet T, Camarasa J, Laguna JC. Hepatoprotective activity of polyphenolic compounds from *Cynara scolymus* against CCl<sub>4</sub> toxicity in isolated rat hepatocytes. *J Nat Prod* 1987i, 50(4):612-617

Adzet T, Camarasa J, Hernandez JS, Laguna JC. Hepatoprotective activity of polyphenolic compounds from *Cynara scolymus* against CCl<sub>4</sub>-induced hepatotoxicity in rats. *Acta Pharm Jugosl* 1987ii, 37: 183-187 (abstract only)

Aktay G, Deliorman D, Ergun E, Ergun F, Yeşilada E, Cevik C. . Hepatoprotective effects of Turkish folk remedies on experimental liver injury. *J Ethnopharmacol* 2000, 73(1-2): 121-129

Anonymous. Caffeic acid. *IARC Monogr Eval Carcinog Risks Hum* 1993, 56: 115-134

Azzini E, Bugianesi R, Romano F, Di Venere D, Miccadei S, Durazzo A, Foddai MS, Catasta G, Linsalata V, Maiani G. Absorption and metabolism of bioactive molecules after oral consumption of cooked edible heads of *Cynara scolymus* L (cultivar Violetto di Provenza) in human subjects: a pilot study. *Br J Nutr* 2007, 97(5):963-969

Bianchini F, Corbetta F. Health Plants of the World Atlas of Medicinal Plants. Newsweek Books, New York 1977

Blaschek W, Ebel S, Hackenthal E, Holzgrabe U, Keller K, Reichling J, editors. *Cynarae folium*. HagerROM 2002: Hagers Handbuch der Drogen und Arzneistoffe, update. Springer Verlag, Berlin Heidelberg 2002

Blumenthal M, Goldberg A, Brinckmann J, editors. Herbal Medicine. Expanded Commission E Monographs. Commission E Monograph "Artichoke leaf". The American Botanical Council, Austin Texas 2000

Bombardelli E, Gabetta B, Martinelli EM. Gas Liquid Chromatography and Mass spectrometric Investigation on *Cynara scolymus* extracts. *Fitoterapia* 1977, 48:143-152



- British Herbal Pharmacopoeia (BHP). 4<sup>th</sup> ed. BHMA Monograph: Artichoke leaf. British Herbal Medicine Association, Exeter 1996
- Brown JE, Rice-Evans CA. Luteolin-rich artichoke extract protects low density lipoprotein from oxidation *in vitro*. *Free Radic Res* 1990, 29(3):247-255
- Bruneton J. Pharmacognosy, Phytochemistry, Medicinal Plants. Lavoisier Publishing, Paris 1999
- Budavari S, (ed.). The Merck Index: An Encyclopedia of Chemicals, Drugs, and Biologicals, 12<sup>th</sup> ed. Merck & Co, Inc. Whitehouse Station, New Jersey 1996, 467-468
- Bundy R, Walker AF, Middleton RW, Marakis G, Booth JC. Artichoke leaf extract reduces symptoms of irritable bowel syndrome and improves quality of life in otherwise healthy volunteers suffering from concomitant dyspepsia: a subset analysis. *J Altern Complement Med* 2004; 10(4):667-669
- Bundy R, Walker AF, Middleton RW, Wallis C, Simpson HC. Artichoke leaf extract (*Cynara scolymus*) reduces plasma cholesterol in otherwise healthy hypercholesterolemic adults : a randomized, double blind placebo controlled trial. *Phytomedicine* 2008, 15(9):668-675
- Cervellati R, Renzulli C, Guerra MC, Speroni E. Evaluation of antioxidant activity of some natural polyphenolic compounds using the Briggs-Rauscher reaction method. *J Agric Food Chem* 2002, 50(26):7504-7509
- Ciganda C, Laborde A. Herbal infusions used for induced abortion. *J Toxicol-Clin Toxicol* 2003, 235-239
- Commission E Monographs (Monographien der Kommission E: Zulassungs- und Aufbereitungskommission am BGA für den humanmed. Bereich, phytotherapeutische Therapierichtung und Stoffgruppe). Bundesanzeiger. Köln 1998
- Czeczot H, Kusztelak J. A study of the genotoxic potential of flavonoids using short-term bacterial assays. *Acta Biochimica Polonica* 1993, 40:549-554 (Polish)
- Dorne M. Improvement in raised lipid levels with artichoke juice (*Cynara scolymus*). *Br J Phytother* 1995, 96(4):21-26
- Edenharder R, Krieg H, Kottgen V, Platt KL. Inhibition of clastogenicity of benzo(a)pyrene and of its trans-7,8-dihydrodiol in mice *in vivo* by fruits, vegetables, and flavonoids. *Mut Res* 2003, 537(2):169-181
- Emendörfer F, Bellato F, Noldin VF, Niero R, Cechinel-Filho V, Cardozo AM. Evaluation of the relaxant action of some Brazilian medicinal plants in isolated guinea-pig ileum and rat duodenum. *J Pharm Pharm Sci* 2005ii, 8(1):63-68
- Emendörfer F, Emendörfer F, Bellato F, Noldin VF, Cechinel-Filho V, Yunes RA, Delle Monache F, Cardozo AM. Antispasmodic activity of fractions and cynaropicrin from *Cynara scolymus* on guinea-pig ileum. *Biol & Pharm Bull* 2005i, 28(5):902-904
- Englisch W, Beckers C, Unkauf M, Ruepp M, Zinserling V. Efficacy of Artichoke dry extract in patients with hyperlipoproteinemia. *Arzneimittelforschung* 2000, 50(3):260-265
- ESCOP Monographs 2<sup>nd</sup> ed. *Cynarae folium*. European Scientific Cooperative on Phytotherapy, editor. Georg Thieme Verlag, Stuttgart 2003
- ESCOP Monographs supplementary 2<sup>nd</sup> ed. *Cynarae folium*. European Scientific Cooperative on Phytotherapy, editor. Georg Thieme Verlag, Stuttgart 2009
- European Pharmacopoeia monograph number 1866, *Cynara cardunculus* Ed. 9

- Fintelmann V and HG Menssen. Artischockenblätterextrakt-Aktuelle Erkenntnis zur Wirkung als Lipidsenker und Antidyspeptium. *Dtsch Apoth Ztg* 1996, 136(17):1405-1414
- Fintelmann V, Petrowicz O. Long term administration of artichoke extracts for dyspepsia symptoms. Results of an observation study. *Natura Med* 1998, 13: 17-26
- Franck P, Moneret-Vautrin DA, Morisset M, Kanny G, Megret-Gabeaux ML, Olivier JL. Anaphylactic reaction to inulin: first identification of specific IgEs to an inulin protein compound. *Int Archiv allergy immunol* 2005, 136(2): 155-158
- Fritsche J, Beindorff CM, Dachtler M, Uhang H, Lammers JG. Isolation, characterization and determination of minor artichoke (*Cynara scolymus* L.) leaf extract compounds. *Eur Food Res Technol* 2002, 215(2):149-157
- Gadban H, Gilbey P, Talmon Y, Samet A. Acute oedema of the tongue: a life-threatening condition. *Ann Otol Rhinol Laryngol* 2003, 112(7):651-3
- Gebhardt R. Artischockenextrakt. In vitro Nachweis einer Hemmwirkung auf die Cholesterin Biosynthese. *Med Welt* 1995i, 46:348-350
- Gebhardt R. Protektive antioxidative Wirkungen von Artischocken extrakt an der Leberzelle. *Med Welt* 1995ii, 46:393-395
- Gebhardt R. Antioxidative and protective properties of extracts from leaves of the artichoke (*Cynara scolymus*), against hydroperoxide induced oxidative stress in cultured rat hepatocytes. *Toxicol Appl Pharmacol* 1997i, 144:279-286
- Gebhardt R, Fausel M. Antioxidant hepatoprotective effects of artichoke extracts and constituents in cultured rat hepatocytes. *Toxicol in Vitro* 1997ii, 11:669-672
- Gebhardt R. Inhibition of cholesterol biosynthesis in primary cultured rat hepatocytes by artichoke (*Cynara scolymus* L.) extracts. *J Pharmacol Exp Ther* 1998, 286(3):1122-8
- Gebhardt R. Anticholestatic activity of flavonoids from artichoke (*Cynara scolymus* L.) and of their metabolites. *Med Sci Monit* 2001, 7(1):316-320
- Gebhardt R. Inhibition of cholesterol biosynthesis in HepG2 cells by artichoke extracts is reinforced by glucosidase pretreatment. *Phytother Res* 2002i, 16(4):368-372
- Gebhardt R. Prevention of taurolythate-induced hepatic bile canalicular distortions by HPLC-characterized extracts of artichoke (*Cynara scolymus*) leaves. *Planta Med* 2002ii, 68(9):776-779
- Grieve M. A Modern Herbal. Dover Publications Inc, New York 1971, 60
- Hänsel RK, Keller H, Rimpler G, Schneider (eds.). Hagers Handbuch der Pharmazeutischen Praxis, 5<sup>th</sup> ed. Vol 46. Springer Verlag, Berlin-Heidelberg 1992/1994
- Hilgendorf C, Döppenschmidt S. Popular herbal drugs: screening of potential CYP inhibition/activation based metabolic interactions. *Int J Clin Pharmacol Therap* 2003, 41(11):537
- Holtmann G, Adam B, Haag S, Collet W, Grunewald E, Windeck T. Efficacy of artichoke leaf extract in the treatment of patients with functional dyspepsia: a six-week placebo-controlled, double-blind, multicenter trial. *Aliment Pharmacol Ther* 2003i, 18:1099-1105
- Holtmann G, Liebrechts T, Collet W, Windeck T. Functional dyspepsia and irritable bowel syndrome: treatment effects of artichoke-leaf-extract; a placebo-controlled, randomised, multicenter trial. *Gastroenterol* 2003ii, 124(4)-A182

- Iwu MM. Handbook of African Medicinal Plants. CRC Press, Boca Raton 1993, 167-168
- Jacociunas LV, Rodrigues d'Andrade HH, Lehmann M, Pedersini LW Protective activity of *Cynara scolymus* L. leaf extract against chemically induced complex genomic alteration in CHO cells. *Phytomedicine* 2013a, 20: 1131–1134
- Jacociunas LV., Rodrigues de Andrade HH, Lehmann M., Ribas de Abreu B.R., de Barros Falcão Ferraz A., da Silva J., Grivicich I., Rodrigues Dihl R. Artichoke induces genetic toxicity in the cytokinesis-block micronucleus (CBMN) cytome assay Food Chemical Toxicol 2013b, 55: 56–59
- Jacociunas L V, Rodrigues Dihl R, Lehmann M, de Barros Falcão Ferraz A, François Richter M, da Silva J Rodrigues de Andrade, H H. Effects of artichoke (*Cynara scolymus*) leaf and bloom head extracts on chemically induced DNA lesions in *Drosophila melanogaster* *Genet Mol Biol.* 2014, 37(1): 90–104.
- Jimenez-Escrig A, Ove Dragsted L, Daneshvar B, Pulido R, Saura-Calixto F. *In vitro* antioxidant activities of edible artichoke (*Cynara scolymus* L.) and effect on biomarkers of antioxidants in rats. *J Agric Food Chem* 2003, 51(18):5540-5545
- Kirchhoff R, Beckers C, Kirschhoff GM, Trinczek-Gartner H, Petrowicz O, Reimann HJ. Increase in choleresis by means of artichoke extract. *Phytomedicine* 1994, 1:107-115
- Kraft K. Artichoke leaf extract recent findings reflecting effects on lipid metabolism, liver, and gastrointestinal tracts. *Phytomedicine* 1997, 4(4):369-378
- Krizkova L, P Mucaji, M Nagy and J Krajcovic. Triterpenoid cynara saponins from *Cynara cardunculus* L. reduce chemically induced mutagenesis *in vitro*. *Phytomedicine.* 11, 2004, 673 – 678
- Li H, Xia N, Brausch I, Yao Y, Forstermann U. Flavonoids from artichoke (*Cynara scolymus* L.) up-regulate endothelial-type nitric-oxide synthase gene expression in human endothelial cells. *J Pharmacol Exp Ther* 2004, 310(3): 926-932
- Lietti A. Choleric and cholesterol lowering properties of two artichoke extracts. *Fitoterapia* 1977, (48): 153-158
- Llorach R, Espín JC, Tomás-Barberán FA, Ferreres F. Artichoke (*Cynara scolymus* L.) byproducts as a potential source of health-promoting antioxidant phenolics. *J Agric Food Chem* 2002, 50(12): 3458-3464
- Lupattelli G, Marchesi S, Lombardini R, Roscini AR, Trinca F, Gemelli F, Vaudo G, Mannarino E. Artichoke juice improves endothelial function in hyperlipemia. *Life Sci* 2004, 76(7):775-782
- Mahmoodabadi NA, Madani H, Mahzooni P, Vahdati A. Preventive effect of hydroalcoholic *Cynara scolymus* extract on appearance of type 1 diabetes mellitus in male rats. *Iran J Diabet Lipid Disord* 2007, 6: 37-44
- Marakis G, Walker AF, Middleton RW, Booth JCL, Wright J, Pike DJ. Artichoke leaf extract reduces mild dyspepsia in an open study. *Phytomedicine* 2002, 9:694-699
- Marakis G, Walker AF, Booth JCL, Wright J. Improvement of dyspeptic symptoms and quality of life in healthy individuals after administration of artichoke leaf extract (ALE). *Gut* 2003, 52(1):A81
- Maros T, Racz G, Katonai B, Kovacs VV. Wirkungen der *Cynara scolymus*-Extrakte auf die Regeneration der Rattenleber (Effects of *Cynara scolymus* extracts on the regeneration of rat liver). *Arzneimforsch* 1966, 16(2):127-129
- Maros T, Racz G, Katonai B, Kovacs VV. Wirkungen der *Cynara scolymus*-Extrakte auf die Regeneration der Rattenleber (Effects of *Cynara scolymus* extracts on the regeneration of rat liver). *Arzneimforsch* 1968, 18:884-886

- Martindale W, Reynolds JEF, editor. The Extra Pharmacopoeia, 28<sup>th</sup> ed. The Pharmaceutical Press, London 1993
- Matuschowski P, Nahrstedt A, Winterhoff H. Pharmakologische Untersuchungen eines Frischpflanzenpresssaftes aus *Cynara scolymus* auf choleretische Wirkung. *Z Phytother* 2005, 26:216-221
- Meyer-Buchtela E. Tee-Rezepturen. Ein Handbuch für Apotheker und Ärzte. Deutscher Apotheker Verlag, Stuttgart 1999
- Miadakova E, Nadova S, Trebaticka M, Grolmus J, Kopaskova M, Rauko P, Mucaji P, Grancai D. Research on biomodulatory effect of natural compounds. *Neuro Endocrinol Letts* 2006, 27(2):53-56
- Miadokova E, Nadova S, Vlckova V, Duhova V, Kopaskova M, Cipak L, Rauko P, Mucaji P, Grancai D. Antigenotoxic effect of extract from *Cynara cardunculus* L. *Phytotherapy Res* 2008, 22(1):77-81
- Miralles JC, Garcia-Sells J, Bartolome B, Negro JM. Occupational rhinitis and bronchial asthma due to artichoke (*Cynara scolymus*). *Ann Allergy Asthma Immunol* 2003, 91:92-5
- Montini M, Levoni P, Ongaro A, Pagani G. Controlled application of cynarin in the treatment of hyperlipemic syndrome. Observations in 60 cases. *Arzneimittelforsch* 1975, 25(8):1311-4
- Mortier F, Bogaert J-P, Jouany J-M, Dixneuf P, Delaveau P. Action d'un extrait purifié de *Cynara scolymus* L. (Composées) sur l'intoxication aiguë par l'éthanol. *Plantes Méd Phytothér* 1976, 10:36-43
- Newall CA, Anderson LA, Phillipson JD. Herbal Medicines: A Guide for Health-Care Professionals. The Pharmaceutical Press, London 1996, 37-38
- Nkondjock A. Coffee consumption and the risk of cancer: an overview. *Cancer Lett* 2009, 277:121-125
- Palacz O, Czepita D, Wójcicki J. Electroretinographic investigations in subjects in chronic exposure to carbon disulphide. III. Cynarex effect on ERG related to blood lipid pattern. *Klin Oczna* 1981, 83:223-5 (Polish/English summary).
- Pérez-García F, Adzet T, Cañigueral S. Activity of artichoke leaf extract on reactive oxygen in human leukocytes. *Free Rad Res* 2000, 33(5):661-65
- Petrowicz O, Gebhardt R, Donner M, Schwandt P, Kraft K. Effects of artichoke leaf extract (ALE) on lipoprotein metabolism *in vitro* and *in vivo*. *Atherosclerosis* 1997, 129:147 (abstract)
- Pharmacopée française (French pharmacopoeia). Adrapharm, Paris 1987
- Pittler MH, Ernst E. Artichoke leaf extract for serum cholesterol reduction. *Perfusion* 1998, 11:338-340
- Preziosi P, Loscalzo B. Pharmacological properties of 1, 4-dicaffeoylquinic acid, the active principle of *Cynara scolymus*. *Arch Int Pharmacodyn* 1958, 117:63-80
- Preziosi P, Loscalzo B, Marmo E. Comparison of choleretic effects of CYN and Na-dehydrocholate. *Experientia* 1959, 15:135-138
- Preziosi P, Loscalzo B. L'azione sulla coleresi, sul colesterolo ematico e sulla lipidosi colesterolica del principio attivo del carciofo e di sostanze ad esso correlate. *Fitoterapia* 1956, 27:666-672
- Preziosi P, Loscalzo B, Marmo E, Miele E. Effects of single or repeated treatment with several anticholesterolemic compounds on biliary excretion of cholesterol. *Biochem Pharmacol* 1960, 5:251-262
- Proctor DM, Gatto NM, Hong SJ, Allamneni KP. Mode-of-action framework for evaluating the relevance of rodent forestomach tumors in cancer risk assessment. *Toxicol Sci* 2007, 98:313-326

- Rechner AR, Pannala AS, Rice-Evans CA. Caffeic acid derivatives in artichoke extract are metabolised to phenolic acids *in vivo*. *Free Radic Res* 2001, 35:195-202
- Saenz Rodriguez T, Garcia Gimenez D, de la Puerta Vazquez R. Choloretic activity and biliary elimination of lipids and bile acids induced by an artichoke leaf extract in rats. *Phytomedicine* 2002, 9(8):687-693
- Salem BM, Affes H, Ksouda K., Dhoubi R, Sahnoun Zr, Hammami S, Mounir Zeghal K. Pharmacological studies of artichoke leaf extract and their health benefits. *Plant Foods Hum Nutr* 2015, 70:441–453
- Samochowiec L. Investigations on experimental atherosclerosis. Part XV. The effect of *Cynara scolymus* L. and *Cynara cardunculus* L. on the development of experimental atherosclerosis in white rats. *Diss Pharm* 1959, 11:99-113 (Polish/English summary)
- Samochowiec L. The action of herbs and roots of artichokes (*Cynara scolymus* L.) and cardoons (*Cynara cardunculus* L.) on the development of experimental atherosclerosis in white rats. *Diss Pharm* 1962i, 14:115-22 (Polish/English summary)
- Samochowiec L, Habczynska D, Wazna-Bogunska C. The influence of atherogenic diet and artichokes (*Cynara scolymus* L) and cardoons (*Cynara cardunculus* L.) on the histopathology of coronary arteries and myocardium in white rats. *Patologia Polska* 1962ii, 13:337-48 (Polish/English summary)
- Samochowiec L. The effect of artichokes (*Cynara scolymus* L.) and cardoons (*Cynara cardunculus* L.) on developed atherosclerotic changes in white rats. *Folia Biol* 1962iii, 10:75-83
- Samochowiec L, Wojcicki J, Kadykow M. The influence of 1,5-dicaffeoylquinic acid on serum lipids in the experimentally alcoholised rat. *Panminerva Med* 1971, 13:87-8
- Sarawek S, Feistel B, Pichel I, Butterweck V. Flavonoids of *Cynara scolymus* possess potent xanthinoxidase inhibitory activity *in vitro* but are devoid of hypouricemic effects in rats after oral application. *Planta medica* 2008, 74(3):221-227
- Schilcher H. Phytotherapy in Paediatrics: Handbook for Physicians and Pharmacists. Medpharm Scientific Publishers, Stuttgart 1997, 45-46
- Schmiedel V. Senkung des Cholesterinspiegels durch Artischocke und Ballaststoffe. *Erfahrungsheilkunde* 2002, 51:405-414
- Sinayoko L, Menecier D, El Jahir Y, Corberand D, Harnois F, Tiolet C, Farret O. Acute hepatic injury secondary to ingestion of artichoke extracts (Hepanephrol). *Gastroenterol Clin Biol* 2007, 31(11):1039-1040
- Speroni E, Cervellati R, Govoni P, Guizzardi S, Renzulli C, Guerra MC. Efficacy of different *Cynara scolymus* preparations on liver complaints. *J Ethnopharmacol* 2003, 86(2-3):203-211
- Stoev SD, Stefanov M, Denev S, Radic B, Domijan AM, Peraica M. Experimental mycotoxicosis in chickens induced by ochratoxin A and penicillic acid and intervention with natural plant extracts. *Vet Res Commun* 2004, 28(8):727-46
- Thompson Coon JS, Ernst E. Systematic review: herbal medicinal products for non-ulcer dyspepsia. *Aliment Pharmacol & Therap* 2002, 16(10):1689-1699
- Thompson Coon JS, Ernst E. Herbs for serum cholesterol reduction: a systematic view. *J Fam Pract* 2003, 52(6):468-478



- Truillas P, Calliste CA, Allais DP, Simon A, Marfak A, Delage C, Duroux J. Antioxidant, anti-inflammatory and antiproliferative properties of sixteen water plant extracts used in Limousin countryside as herbal teas. *Food Chem* 2003, 80(3):399-407
- Wang M, Simon JE, Aviles IF, He K, Zengh QY, Tadmor Y. Analysis of antioxidative phenolic compounds in artichoke (*Cynara scolymus* L.). *J Agric Food Chem* 2003, 51(3):601-608
- Walker AF, Middleton RW, Petrowicz O. Artichoke leaf extract reduces symptoms of irritable bowel syndrome in a post-marketing surveillance study. *Phytother Res* 2001, 15(1):58-61
- WHO monographs on selected medicinal plants. Vol 4. Folium Cynarae World Health Organisation Geneva 2009, 92-107
- Wittemer SM, Veit M. Validated method for the determination of six metabolites derived from artichoke leaf extract in human plasma by high performance liquid chromatography- colorimetric array detection. *J Chromatogr B* 2003, 793:367-375
- Wittemer SM, Ploch M, Muller SC, Drewelow B, Derendorf H, Veit M. Bioavailability of caffeoylquinic acids and flavonoids in humans after application of two different artichoke leaves extracts. *Archiv Pharmacol* 2002, 1:143
- Wittemer SM, Ploch M, Windeck T, Muller SC, Drewelow B, Derendorf H, Veit M. Bioavailability and pharmacokinetics of caffeoylquinic acids and flavonoids after oral administration of Artichoke leaf extracts in humans. *Phytomedicine* 2005, 12(1-2):28-38
- Wójcicki J, Winter S. Effect of preparation Cynarex on the blood serum lipids level of the workers exposed to the chronic action of carbon disulphide. *Medycyna Pracy* 1975, 6:213-217 (Polish/English summary)
- Wójcicki J, Olejak B, Pieczul-Mróż J, Torbus-Lisiecka B, Bukowska H, Gregorczyk J. The use of Cynarex in the treatment of primary hyperlipidemia. Study Report. Szczecin, Poland 1980 (previously unpublished)
- Wojcicki J, Samochovec L, Kosmider K. Influence of an extract from artichoke (*Cynara scolymus* L.) on the level of lipids in serum of aged men. *Herba Polonica* 1981, 27:265-268
- Wójcicki J, Olejak B, Pieczul-Mróż J, Torbus-Lisiecka B, Bukowska H, Gregorczyk J. The use of 1,5-dicaffeoylquinic acid in the treatment of hypertriglyceridemia. *Przegląd Lek* 1982, 9:601-606 (Polish/English summary)
- Wone E, Barondra-Haaby E, de Lauture H. Intérêt de l'intégration systématique du chophytol dans le traitement ambulatoire du paludisme. *Afrique Médicale* 1986, 25:233-240
- Yang B, Meng Z, Dong J, Yan L, Zou L, Tang Z, Dou G. Metabolic profile of 1,5-dicaffeoylquinic acid in rats, an in vivo and in vitro study. *Drug Metab Dispos* 2005, 33(7):930-936
- Zapolska-Downar D, Zapolski-Downar A, Naruszewicz M, Siennicka A, Kranodebska B, Koldziej B. Protective properties of artichoke (*Cynara scolymus*) against oxidative stress induced in cultured endothelial cells and monocytes. *Life Sci* 2002, 71(24):2897
- Zhu XF, Zhang HX, Lo R. Antifungal activity of *Cynara scolymus* L. extracts. *Fitoterapia* 2005, 76(1):108-111
- Zhu X, Zhang HX, Lo R. Phenolic compounds from the leaf extract of artichoke (*Cynara scolymus* L.) and their antimicrobial activities. *J Agric Food Chem* 2004, 52(24):7272-7278

### References investigated but not cited in assessment report:

- Abels S, Eschmann K. Antidyspeptische und cholesterinsenkende Wirkung von Artischockenextrakt. *Der Kassenarzt* 2000, (20):44-50
- Abascal K, Yarnell E. Combining herbs in a formula for irritable bowel syndrome. *Altern Complement Therap* 2005, 11(1):17-23
- Barbetti P et al. Grosulfeimin and new related guaianolides from *Cynara scolymus*. *Ars Pharmac* 1992, 33:433-439
- Barbetti P, et al. Grosulfeimin and new related guaianolides from *Cynara scolymus*. *Nat Prod Lett* 1993, 3:21-30
- Barnes J, Anderson L, Phillipson JD. Artichoke. In: *Herbal Medicines*. Pharmaceutical Press, London Chicago 2002, 61-66
- Barnes J. Herbal therapeutics: Gastrointestinal system and liver disorders. *Pharm J* 2002, 228:848-850
- Barret M. Artichoke. In: *The handbook of clinically tested herbal remedies*. Haworth series in Evidence Based Phytotherapy. The Haworth Herbal Press, New York 2004
- Benedek B, et al. Choleric effects of yarrow (*Achillea millefolium* S.L.) in the isolated perfused rat liver. *Phytomedicine* 2006, 13(9-10):702-706
- Betancor-Fernandez A, Perez-Galvez A, Sies H, Stahl W. Screening pharmaceutical preparations containing extracts of turmeric rhizome, artichoke leaf, devil's claw root and garlic or salmon oil for antioxidant capacity. *J Pharm Pharmacol* 2003, 55(7):981-986
- Bilia AR, Bergonzi MC, Mazzi G, Vincieri FF. Analysis and stability of the constituents of artichoke and St. John's wort tinctures by HPLC-DAD and HPLC-MS. *Drug Dev Industr Pharm* 2002, 28:609-619
- Bobnis W, et al. Case of primary hyperlipemia treated with cynarin. *Wiad Lek* 1973, 26(13):1267-1270
- Bogaert JP, Mortier F, Jouany JM, Pelt JM, Delaveau P. Caracterisation et dosage de l'acide acrylique dans les feuilles de *Cynara scolymus* L. (Compositae). *Plantes Med Phytother* 1974, 8:199-203
- Bogaert JP, Mortier F, Jouany JM, Delaveau P, Pelt JM. Organic Acids, particularly acids -alcohols, in *Cynara scolymus* L. *Ann Pharm Fr* 1972, 30:401-408
- Brand N. *Cynara scolymus*, Die Artichoke. *Z Phytother* 1990, 11:169-175
- Brand N, Weschta H. Die analytische Bewertung der Artichocke und ihrer Präparate. *Z Phytother* 1991, 12:15-21
- Brand N. Die Artichoke – eine Dekade interdisziplinärer Forschung. *Z Phytother* 1999, 20:292-302
- Bradley PR editor. *British Herbal Compendium*. Vol 2. British Herbal Medicine Association, Bournemouth 2006
- Bradley PR editor. *British Herbal Compendium*. Vol 2. British Herbal Medicine Association, Bournemouth 1996, 35-39
- Bühning U. Naturheilkundliche Therapie bei Lebererkrankungen. *Zeitsch Phytother* 2005, 26:84-86
- Chrubasik S, Roufogalis B. Effectiveness of herbal medicines: where is the evidence? *New Zealand pharmacy* 2002, 22(12):31-33
- Dickel ML, Rates SM, Ritter MR. Plants popularly used for losing weight purposes in Porto Alegre, South Brazil. *J Ethnopharmacol* 2007, 109(1):60-71



- Dingermann T, Loew D. Artischockenblätter (14.1). In: Phytopharmakologie, Experimentelle und klinische Pharmakologie pflanzlicher Arzneimittel. WVG, Stuttgart 2003
- Eich J, Paper DH, Grun M. Luteolin-7-O- $\beta$ -glucuronide from artichoke leaves. *Pharmacol Lett* 2001, 1:9-10
- El-Negoumi SI, Al-Sayed NH, Saleh NAM. Flavonoid glycosides of *Cynara scolymus*. *Fitoterapia* 1987, 58:178-180
- Emendorfer F, Emendorfer F, Bellato F, Noldin VF, Cechinel-Filho V, Yunes RA, Delle Monache F, Cardozo AM. Antispasmodic activity of fractions and cynaropicrin from *Cynara scolymus* on guinea-pig ileum. *Biol Pharm Bull* 2005, 28(5):902-904
- Gebhardt R. Choleric and anticholestatic activities of flavonoids of artichoke (*Cynara cardunculus* L. subsp. *scolymus* (L.) Hayek). *Acta Horticulturae* 2005, 681:429-435
- Glasl S, Tsendayush D, Batchimeg U, Holec N, Wurm E, Kletter C, Gunbilig D, Daariimaa K, Narantuya S, Thalhammer T. Choleric effects of the Mongolian medicinal plant *Saussurea amara* in the isolated perfused rat liver. *Planta Med* 2007, 73(1):59-66
- Grogan J L, et al. Potential hypocholesterolemic agents: dicinnamoyl esters as analogs of cynarin. *J Pharm Sci* 1972, 61(5):802-803
- Gruenwald J, et al. PDR for Herbal Medicines. 2<sup>nd</sup> ed. Thomson PDR, Montvale 2000
- Hammouda FM, et al. Quantitative determination of the active constituents of Egyptian cultivated *Cynara scolymus*. *Int Pharmacogn* 1993, 31:299-304
- Heckers H, et al. Inefficiency of cynarin as therapeutic regimen in familial type II hyperlipoproteinaemia. *Atherosclerosis* 1977, 26:249-253
- Hiner AN, et al. Kinetic study of the effects of calcium ions on cationic artichoke (*Cynara scolymus* L.) peroxidase: calcium binding, steady-state kinetics and reactions with hydrogen peroxide. *Biochimie* 2004, 86(9-10):667-676
- Hinou J, Harvala C, Philianos S. Polyphenolic substances of *Cynara scolymus* leaves. *Ann Pharm Fr* 1987, 58:95-98
- Jänicke, Grünwald, Brendler. Artischoke – *Cynara scolymus*. Handbuch Phytotherapie. WVG, Stuttgart 2003
- Jouany JM et al. Dosage indirect de la cynaropicrine dans la *Cynara scolymus* (Compositae) par liberation de la chaine laterale hydroxymethylacrylique. *Planta Med Phytotherapie* 1975, 9:72-78
- Joy JF, Haber SL. Clinical uses of artichoke leaf extract. *Am J Health-Syst Pharm* 2007, 64(18):1904-1909
- Kamel MY, Ghazy AM. Peroxidase of *Cynara scolymus* (global artichoke) leaves, purification and properties. *Acta Biol Med Germ* 1973, 31:39-49
- Kupke D, et al. Prufung der choloretischen Aktivitat eines pflanzlichen Cholagogums. *Z Allg Med* 1991, 67:1046-1058
- Macchia L, Passaro SB, Di Gioia R, Kourtis G, Caiaffa MF, Tursi A. Allergy to artichoke: A case report. *Rev. Franc. Allergol Immunol Clin* 2004, 44:646-648
- Martinet A, Hostettmann K, Schutz Y. Thermogenic effects of commercially available plant preparations aimed at treating human obesity. *Phytomedicine* 1999, 6:231-238

- Meding B. Allergic contact dermatitis from Artichoke *Cynara scolymus*. *Contact Dermatitis* 1983, 9:314
- Meier R, Brignoli R. Artichoke leaf extract for functional dyspepsia. Result of an open, prospective, multicentre, phase IV trial. *Schweizer Zeitschr GanzheitsMed* 2005, 17:216-221
- Meletis CD. Cardiovascular disease: phytochemical and nutritional prevention and treatment. *Altern Complement Ther* 2003, 9(4):158-162
- Mills SY. The Dictionary of Modern Herbalism. Thorsons, Wellingborough 1985
- Miszputen SJ, Szejnfeld J, Ambrogini J, Shigueoka D, Thuler FPBM, De Oliveira. Avaliacao ultrasonografica da resposta motora da vesicula biliar em adultos assintomaticos apos medicacao fitoterapica - ultrasound evaluation of the gallbladder motor response in asymptomatic adults after phytotherapeutic medication. *Gastroenterolog Endoscope Digest* 2005, 24(4):181-185
- Mitchell JC. Recent Advances in Phytochemistry. Vol 9. Plenum, New York 1975
- Mukherjee PK. Plant products with hypocholesterolemic potentials. *Adv Food Nutr Res* 2003, 47:277-338
- Pittler MH, White AR, Stevinson C, Ernst E. Effectiveness of artichoke extract in preventing alcohol-induced hangovers: a randomized controlled trial. *CMAJ* 2003, 169(12):1269-73
- Pittler MH, Thompson-Coon J, Ernst E. Artichoke leaf extract for treating hypercholesterolaemia. *Cochrane Database System Reviews* 2002, 3:1-11
- Pristautz H, et al. Cynarin in the modern management of hyperlipemia. *Wien Med Wochenschr* 1975, 125(49):705-9
- Quirce S, et al. Occupational contact urticaria syndrome caused by globe artichoke (*Cynara scolymus*). *J Allergy Clin Immunol* 1996, 97:710-711
- Rensen van I, Wittemer SM. *Cynara cardunculus* subsp. *Flavescens* (bisher *Cynara scolymus*) – die Artischocke. *Z Phytother* 2003, 24:267-276
- Romano C, Ferrara A, Falagiani P. A case of allergy to globe artichoke and other clinical cases of rare food allergy. *J Allergol Clin Immunol* 2000, 10:102-104
- Schneider G, Thiele KI. Die Verteilung des Bitterstoffes Cynaropicrin in der Artischocke. *Planta Medica* 1974, 26:174-183
- Schultz V, Hänsel R, Tyler VE. Rational Phytotherapy: A Physicians' Guide to Herbal Medicine. Springer-Verlag, Berlin 1998, 173-175
- Shimoda H, Ninomiya K, Nishida N, Yoshino T, Morikawa T, Matsuda H, Yoshikawa M. Anti-hyperlipidemic sesquiterpenes and new sesquiterpene glycosides from the leaves of artichoke (*Cynara scolymus* L.): structure requirement and mode of action. *Bioorg Med Chem Lett* 2003, 13(2):223-228
- Verspohl EJ, Ploch M, Windeck, T, Klaes M, Schmidt T, Bauer K. Effect of two artichoke extracts (36\_U and 36\_EB) on rat ileum (with respect to bowel syndrome) and the peristaltic threshold. *Phytomedicine* 2008, 15(11):1002-1009
- Visioli F, Bogani P, Grande S, Detopoulou V, Manios Y, Galli C. Local food and cardioprotection: the role of phytochemicals. *Forum nutr* 2006, 59:116-129
- Visioli F, Bogani P, Grande S, Galli C. Mediterranean food and health: building human evidence. *J Physiol Pharmacol* 2005, 56(1):37-49

- Wegener T. Zum Stellenwert phytotherapeutischer Lipidsenker. *Wien Med Wschr* 2002, 152:412-417
- Wegener T, et al. Pharmacological properties and therapeutic profile of artichoke (*Cynara scolymus* L.). *Wien Med Wochenschr* 1999, 149(8-10):241-247
- Wegener T. The status of herbal antilipemic agents. *Wien Med Wochenschr* 2002, 152(15-16):412-417
- Wichtl M. Teedrogen und Phytopharmaka. 4<sup>th</sup> ed. WVG, Stuttgart 2002
- Wider B., Pittler MH., Thompson-Coon J, Ernst E. Artichoke leaf extract for treating hypercholesterolaemia. (Review) The Cochrane database of systematic reviews 3, 2013, CD003335  
DOI: 10.1002/14651858.
- Wojcicki J, Samochovec L, Kosmider K. Cynarin and hyperlipidemia. *Wiad Lek* 1977, 30(19):1539-1541 (abstract only)