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## List of references supporting the assessment of *Allium cepa* L., bulbos

Draft

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

Agarwal RK, Dewar HA, Newell DJ, Das B. Controlled trial of the effect of cycloalliin on the fibrinolytic activity of venous blood. *Atherosclerosis* 1977, 27:347-351

Amaral DR, Da Rocha Oliveira FE, Oliveira DF, Campos VP. Purification of two substances from bulbs of onion (*Allium cepa* L.) with nematicidal activity against *Meloidogyne exigua* Goeldi. *Nematology* 2003, 5:859-864

Arnault I, Auger J. Seleno-compounds in garlic and onion. *J Chromatogr A* 2006, 1112:23-30

Arung ET, Furuta S, Ishikawa H, Kusuma IW, Shimizu K, Kondo R. Anti-melanogenesis properties of quercetin- and its derivative-rich extract from *Allium cepa*. *Food Chem* 2011, 124:1024-1028

Bang MA, Kim HA. Dietary supplementation of onion inhibits diethylnitrosamine-induced rat hepatocellular carcinogenesis. *Food Sci Biotechnol* 2010, 19:77-82

Benkeblia N. Antimicrobial activity of essential oil extracts of various onions (*Allium cepa*) and garlic (*Allium sativum*). *Lebensm.-Wiss. u.-Technol* 2004, 37:263-268

Bibak A, Behrens A, Stürup S, Knudsen L, Gundersen V. Concentrations of 63 Major and Trace Elements in Danish Agricultural Crops Measured by Inductively Coupled Plasma Mass Spectrometry. 1. Onion (*Allium cepa* Hysam). *J Agri Food Chem* 1998, 46:3139-3145

Blaschek W, Ebel S, Hackenthal E, Holzgrabe U, Keller K *et al.* (editors) *Hagers Handbuch der Drogen und Arzneistoffe*. 2006. HagerROM 2006; Springer electronic media

Bordia A, Bansal HC, Arora SK, Singh SV. Effect of the essential oils of garlic and onion on alimentary hyperlipemia. *Atherosclerosis* 1975, 21:15-9

Bordia T, Mohammed N, Thomson M, Ali M. An evaluation of garlic and onion as antithrombotic agents. *Prostaglandins Leukot Essent Fatty Acids* 1996, 54:183-186



- Breu W, Dorsch W. *Allium cepa* L. (onion). Chemistry, analysis and pharmacology. In: *Economic Medicinal Plant Research*, Vol 6, Wagner H, Farnsworth NR (eds), Academic Press, London 1994, 115-147
- Briggs WH, Folts JD, Osman HE, Goldman IL. Administration of Raw Onion Inhibits Platelet-Mediated Thrombosis in Dogs. *J Nutr* 2001, 131:2619–2622
- Campos KE, Diniz YS, Cataneo AC, Faine LA, Alves MJQF, Novelli ELB. Hypoglycaemic and antioxidant effects of onion, *Allium cepa*: dietary onion addition, antioxidant activity and hypoglycaemic effects on diabetic rats. *Int J Food Sci Nutr* 2003, 54:241-246
- Claeys M, Üstünes L, Laekeman GM, Herman AG, Vlietinck AJ, Özer A. Mass spectral characterization of two onion constituents with prostaglandin E-like activity as lipoxygenase metabolites of linoleic acid. *Prostaglandins* 1984, 28:663-663
- Corea G, Fattorusso E, Lanzotti V, Caparasso R, Izzo AA. Antispasmodic Saponins from Bulbs of Red Onion, *Allium cepa* L. var. Tropea. *J Agric Food Chem* 2005, 53:935-940
- El-Demerdash FM, Yousef MI, Abou El-Naga NI. Biochemical study on the hypoglycemic effects of onion and garlic in alloxan-induced diabetic rats. *Food Chem Toxicol* 2005, 43:57-63
- Donner H, Gao L, Mazza G. Separation and characterization of simple and malonylated anthocyanins in red onions, *Allium cepa* L. *Food Res Int* 1997, 30:637-643
- Dorant E, van den Brandt PA, Goldbohm RA, Sturmans F. Consumption of onions and a reduced risk of stomach carcinoma. *Gastroenterology* 1996, 110:12-20
- Dorsch W, Scharff J, Bayer T, Wagner H. Antiasthmatic effects of onions. Prevention of platelet-activating factor induced hyperactivity to histamine guinea pigs by diphenylthiosulfinate. *Int Arch Appl Immunol* 1989, 88:228-230
- Dorsch W. *Allium cepa* L. (onion). Part 2. Chemistry, analysis and pharmacology. *Phytomed.* 1996, 3:391-397
- Fischer G, Krug E. Heilkräuter und Arzneipflanzen. 6. Aufl. Haug, Heidelberg 1980
- Flamm S, Kroeber L, Seel H. Pharmakodynamik Deutscher Heilpflanzen. Hippokrates, Stuttgart 1940
- Fossen T, Andersen ØM, Øvstedal DO, Pedersen AT, Raknes, Å. Characteristic anthocyanin pattern from onions and other *Allium* spp. *J Food Sc.* 1996, 64:703-706
- Fu HY. Free Radical Scavenging and Leukemia Cell Growth Inhibitory Properties of Onion Powders Treated by Different Heating Processes. *J Food Sci* 2004, 69:50-54
- Galdón BR, González RO, Rodríguez ER, Romero CD. Comparison of mineral and trace element contents in onion cultivars (*Allium cepa* L.). *J Sci Food Agric* 2008, 88:1554-1561
- Galdón BR, Rodríguez CT, Rodríguez EMR, Romero CD. Fructans and major compounds in onion cultivars (*Allium cepa*). *J Food Comp Anal* 2009, 22:25-32
- Goldman IL, Kopelberg M, Debaene JEP, Schwartz BS. Antiplatelet activity of onion (*Allium cepa*) is sulfur dependent. *Thromb Haemost* 1996, 76:450-453
- Gorinstein S, Park YS, Heo BG, Namiesnik J, Leontowicz H, Leontowicz M *et al.* A comparative study of phenolic compounds and antioxidant and antiproliferative activities in frequently consumed raw vegetables. *Eur Food Res Technol* 2009, 228:903-911

- Gorinstein S, Leontowicz H, Leontowicz M, Jastrzebski Z, Najman K, Tashma Z *et al.* The Influence of Raw and Processed Garlic and Onions on Plasma Classical and Non-classical Atherosclerosis Indices: Investigations In Vitro and In Vivo. *Phytother Res* 2010, 24:706-714
- Guyonnet D, Siess MH, Le Bon AM, Suschetet M. Modulation of Phase II Enzymes by Organosulfur Compounds from Allium Vegetables in Rat Tissues. *Toxicol Appl Pharmacol* 1999, 154:50-58
- Hu J, La Vecchia C, Negri E, Chatenoud L, Bosetti C, Jia CX *et al.* Diet and brain cancer in adults: A case-control study in Northeast China. *Int. J. Cancer* 1999, 81:20-23
- Hwang IK, Lee CH, Yoo KY, Choi JH, Park OK, Lim SS *et al.* Neuroprotective Effects of Onion Extract and Quercetin Against Ischemic Neuronal Damage in the Gerbil Hippocampus. *J Med Food* 2009, 12:990-995
- Jaime L, Martín-Cabrejas MA, Mollá E, López-Andréu FJ, Esteban RM. Effect of storage on fructan and fructooligosaccharide of onion (*Allium cepa* L.). *J Agric Food Chem* 2001, 49:982-988
- Jain RC. Onion and garlic in experimental cholesterol induced atherosclerosis. *Ind J Med Res* 1976, 64:1509-1515
- Jelodar GA, Maleki M, Motadayen MH, SIRUS S. Effect of foenukgree, onion and garlic on blood glucose and histopathology of pankreas of alloxan-induced diabetic rats. *Indian J Med Sci* 2005, 59:64-69
- Jung YS, Kim MH, Lee SH, Baik EJ, Park SW, Moon CH. Antithrombotic effect of onion in streptozotocin-induced diabetic rat. *Prostaglandins Leukot Essent Fatty Acids* 2002, 66:453-458
- Jung JY, Lim Y, Moon MS, Kim JY, Kwon O. Onion peel extracts ameliorate hyperglycemia and insulin resistance. *Nutrition & Metabolism* 2011, 8:18-46
- Kaiser P, Youssef MS, Tasduq SA, Singh S, Sharma SC, Singh GD *et al.* Anti-Allergic Effects of Herbal Product from *Allium cepa* (Bulb). *J Med Food* 2009, 12:374-382
- Kalus U, Pindur G, Jung F, Mayer B, Radtke H, Bachmann K *et al.* Influence of the onion as an essential ingredient of the Mediterranean diet on arterial blood pressure and blood fluidity. *Arzneimittel-Forschung* 2000, 50:795-801
- Kawane H. Bronchial asthma caused by onion. *J Allergy Clin Immunol* 1995, 95:568-568
- Kim MH, Jo SH, Jang HD, Lee MS, Kwon Yi. Antioxidant Activity and  $\alpha$ -Glucosidase Inhibitory Potential of Onion (*Allium cepa* L.) Extracts. *Food Sci Biotechnol* 2010, 19:59-164
- Kivirantat J, Huovinen K, Seppanen-Laakso T, Hiltunen R, Karppanen H, Kilpelainen MP. Effects of onion and garlic extracts on spontaneously hypertensive rats. *Phytother Res* 1989, 3:132-135
- Kook S, Kim GH, Choi K. The Antidiabetic Effect of Onion and Garlic in Experimental Diabetic Rats: Meta-Analysis. *J Med Food* 2009, 12:552-560
- Kubo I., Nitoda T, Nihei K. Effects of quercetin on mushroom tyrosinase and B16-F10 melanoma cells. *Molecules* 2007, 12:1045-1056
- Kumari K, Augusti KT. Lipid lowering effect of S-methyl cysteine sulfoxide from *Allium cepa* Linn in high cholesterol diet fed rats. *J Ethnopharmacol* 2007, 109:367-371
- Lanzotti V. The analysis of onion and garlic. *J Chromatogr A*, 2006, 1112:3-22
- Madaus G. Lehrbuch der biologischen Heilmittel. Band. I, Thieme Verlag, Leipzig 1938
- Makheja AN, Bailey JM. Antiplatelet constituents of garlic and onion. *Agents Action* 1990, 29:360-364

- Menon IS, Kendal RY, Dewar HA, Newell DJ. Effect of onions on blood fibrinolytic activity. *Br Med J* 1968, 3:351-352
- Monographie BGA/BfArM (Kommission E). In: Bundesanzeiger Nr. 50 vom 13.3. 1986, *Allii cepae bulbus* (Zwiebel)
- Moon CH, Jung YS, Kim MH, Lee SH, Baik EJ, Park SW. Mechanism for antiplatelet effect of onion: AA release inhibition, thromboxane A2 synthase inhibition and TXA2/ PGH2 receptor blockade, *Prostaglandins Leukot Essent Fatty Acids* 2000, 62:277-283
- Naseri MKG, Yahyavi H, Arabian M. Antispasmodic Activity of Onion (*Allium cepa* L.) Peel Extract on Rat Ileum. *Iran J Pharm Res* 2008, 7:155-159
- Nishimura H, Higuchi O, Tateshita K, Tomobe K, Okuma Y, Nomura Y. Antioxidative activity and ameliorative effects of memory impairment of sulfur-containing compounds in *Allium* species. *Biofactors* 2006, 26:135-46
- Park S, Kim MY, Lee DH, Lee SH, Baik EJ, Moon CH et al. Methanolic extract of onion (*Allium cepa*) attenuates ischemia/hypoxia-induced apoptosis in cardiomyocytes via antioxidant effect. *Eur J Nutr* 2009, 48:235-242
- Perchellet JP, Perchellet EM, Bellman S. Inhibition of DMBA-induced mouse skin tumorigenesis by garlic oil and inhibition of two tumor-promotion stages by garlic and onion oil. *Nutr Cancer* 1990, 14:183-193
- Poletti A, Schilcher H, Müller A. Heilkräftige Pflanzen. Hädecke Verlag, Weil der Stadt 1990
- Ramos FA, Takaishi Y, Shirotori M, Kawaguchi Y, Tsuchiya K, Shibata H et al. Antibacterial and Antioxidant Activities of Quercetin Oxidation Products from Yellow Onion (*Allium cepa*) Skin. *J Agric Food Chem* 2006, 54:3551-3557
- Saleheen D, Ali SA, Yasinzai MM. Antileishmanial activity of aqueous onion extract in vitro. *Fitoterapia* 2004, 75:9-13
- Santas J, Pilar Almajano M, Carbo R. Antimicrobial and antioxidant activity of crude onion (*Allium cepa*, L.) extracts. *Int J Food Sci Technol* 2010, 45:403-409
- Shahidul I, Du Toit L, Haymie C. Higher dietary fat impairs anti-diabetic effects of onion (*Allium cepa* L.) in rats. *Diabetes Res Clin Practice* 2008, 79:108
- Shams-Ghahfarokhi M, Shokoohamiri MR, Amirrajab N, Moghadasi B, Ghajari A, Zeini F et al. *In vitro* antifungal activities of *Allium cepa*, *Allium sativum* and ketoconazole against some pathogenic yeasts and dermatophytes. *Fitoterapia* 2006, 77:321-323
- Sharquie KE, Al-Obaidi HK. Onion juice (*Allium cepa* L.), a new topical treatment for alopecia areata. *J Dermatol* 2002, 29:343-346
- Shri R, Bora KS. Neuroprotective effect of methanolic extracts of *Allium cepa* on ischemia and reperfusion-induced cerebral injury. *Fitoterapia* 2008, 79:86-96
- Slimestadt R, Fossen T, Vågen I M. Onions: A Source of Unique Dietary Flavonoids. *J Agric Food Chem* 2007, 55:10067-10080
- Srivastava KC. Effect of onion and ginger consumption on platelet thromboxane production in humans. *Prostaglandins, leukotrienes, and essential fatty acids* 1989, 35:183-185
- Srivastava SK, Hu X, Xia H, Zaren HA, Chatterjee ML, Agarwal R, Singh SV. Mechanism of differential efficacy of garlic organosulfides in preventing benzo(a)pyrene-induced cancer in mice *Cancer Lett* 1997, 118:61-67

- Thomson M, Alnaqeeb MA, Bordia T, Al-Hassan JM, Afzal M, Ali M. Effects of aqueous extract of onion on the liver and lung of rats. *J Ethnopharmacol* 1998, 61:91-99
- Tjokroprawiro A, Pikir BS, Budhiarta AAG, Pranawa, Soewondo H, Donosepoetro M *et al.* Metabolic effects of onion and green beans on diabetic patients. *Tohoku J Exp Med* 1983, 141 Suppl, 671-676
- Üstünes L, Claeys M, Laekeman G, Herman AG, Vlietinck AJ, Özer A. Isolation and identification of two isomeric trihydroxy octadecenoic acids with prostaglandin E-like activity from onion bulbs (*Allium cepa*). *Prostaglandins* 1985, 29: 847-865
- Valdivieso R, Subiza J, Varela-Losada S, Subiza JL, Narganes MJ, Martinez-Cocera C *et al.* Bronchial asthma, rhinoconjunctivitis, and contact dermatitis caused by onion. *J Allergy Clin Immunol* 1994, 94:928-330
- Wang HX, Ng TB. Isolation of allicepin, a novel antifungal peptide from onion (*Allium cepa*) bulbs. *J Peptide Sci* 2004, 10:173-177
- Weiss RF. Lehrbuch der Phytotherapie. 5. Aufl. Hippokrates, Stuttgart 1982
- WHO monographs on selected medicinal plants, Vol. 1, Bulbus Allii Cepae, World Health Organization, Geneva 1999, 5-15
- Xiao H, Parkin K. Isolation and identification of phase II enzyme-inducing agents from nonpolar extracts of green onion (*Allium spp.*). *J Agric Food Chem* 2006, 54:8417-8424
- Xiao H, Parkin K. Isolation and identification of potential cancer chemopreventive agents from methanolic extracts of green onion (*Allium cepa*). *Phytochemistry* 2007, 68:1059-1067
- Yanagita T, Han SY, Wang YM, Tsuruta Y, Anno T. Cycloalliin, a Cyclic Sulfur Imino Acid, Reduces Serum Triacylglycerol in Rats. *Nutrition* 2003,19:140-143
- Zohri AN, Abdel-Gawad K, Saber S. Antibacterial, antidermatophytic and antioxidigenic activities of onion (*Allium cepa* L.) oil. *Microbiol Res* 1995, 150:167-172
- Zouhir AM, Kheadr E, Tahiri I, Ben Hamida J, Fliss I. Combination with plant extracts improves the inhibitory action of Divergicin M35 against *Listeria monocytogenes*. *J Food Qual* 2008, 31:13-33