



NATURAL HEALTH PRODUCT

BETA-GLUCAN

This monograph is intended to serve as a guide to industry for the preparation of Product Licence Applications (PLAs) and labels for natural health product market authorization. It is not intended to be a comprehensive review of the medicinal ingredient.

Notes

- ▶ Text in parentheses is additional optional information which can be included on the PLA and product label at the applicant's discretion.
- ▶ The solidus (/) indicates that the terms and/or the statements are synonymous. Either term or statement may be selected by the applicant.

Date

September 27, 2013

Proper name(s)

Beta-glucan (Charlton et al. 2012; EFSA 2011a,b,2010; Queenan et al. 2007; Braaten et al. 1994; Uusitupa et al. 1992)

Common name(s)

Beta-glucan (Charlton et al. 2012; EFSA 2011a,b,2010; Queenan et al. 2007; Braaten et al. 1994; Uusitupa et al. 1992)

Source material(s)

- ▶ *Avena sativa* L. (oat) (USDA 2008) seed and/or seed bran (Charlton et al. 2012; Queenan et al. 2007)
- ▶ *Hordeum vulgare* L. (barley) (USDA 2010) seed and/or seed bran (Queenan et al. 2007)

Route(s) of administration

Oral

Dosage form(s)

- ▶ The acceptable pharmaceutical dosage forms include, but are not limited to capsules, chewables (e.g. gummies, tablets), liquids, powders, strips or tablets.



- ▶ This monograph is not intended to include foods or food-like dosage forms such as bars, chewing gums or beverages.

Use(s) or Purpose(s) Statement(s) to the effect of

- ▶ Helps reduce/lower (LDL) cholesterol (which is one risk factor for the development of coronary heart disease) (Charlton et al. 2012; EFSA 2011a,b,2010; AbuMweiss et al. 2010; HC 2010; Wolever et al. 2010; Delahoy et al. 2009; Queenan et al. 2007; Wood 2007; Biorklund et al. 2005; NECP 2002; Brown et al. 1999; Ripsin et al. 1992).
- ▶ Provides support for healthy (postprandial) glucose metabolism (within two hours after a meal) (EFSA 2011a,b; Ulmius et al. 2011; Granfeldt et al. 2008; Panahi et al. 2007; Biorklund et al. 2005; Kabir et al. 2002).
- ▶ Helps improve (postprandial) glucose metabolism (within two hours after a meal) (EFSA 2011a,b; Ulmius et al 2011; Granfeldt et al. 2008; Panahi et al. 2007; Biorklund et al. 2005; Kabir et al. 2002).
- ▶ Source of fiber for the maintenance of good health (CFIA 2012; IOM 2005).
- ▶ Helps support and maintain a healthy digestive system (CFIA 2012; IOM 2005).

Dose(s)

Subpopulation(s)

Adults (\geq 18 years)

Quantity(ies)

2-10 g beta-glucan, per day (Charlton et al. 2011; EFSA 2011a,b,2010; AbuMweiss et al. 2010; Queenan et al. 2007; IOM 2005; Johnston et al. 1998; Braaten et al. 1994; Torronen et al. 1992; Uusitupa et al. 1992).

Directions for use

No statement required.

Duration of use

No statement required.

Risk information

Caution(s) and warning(s)



No statement required.

Contraindication(s)

No statement required.

Known adverse reaction(s)

No statement required.

Non-medicinal ingredients

Must be chosen from the current NHPD *Natural Health Products Ingredients Database* (NHPID) and must meet the limitations outlined in the database.

Storage conditions

Statement(s) to the effect of

Preserve in well-closed containers (USP 35).

Specifications

- ▶ The finished product specifications must be established in accordance with the requirements described in the NHPD *Quality of Natural Health Products Guide*.
- ▶ The medicinal ingredient must comply with the requirements outlined in the *Natural Health Products Ingredients Database* (NHPID). In addition, the medicinal ingredient may comply with the specifications outlined in the United States Pharmacopeia monograph Colloidal Oatmeal (USP 35).

References cited

AbuMweis SS, Jew S, Ames NP. Beta-glucan from barley and its lipid lowering capacity: a meta-analysis of randomized, controlled trials. *European Journal of Clinical Nutrition* 2010;64:1472-1480.

Bjorklund M, van Rees A, Mensink RP, Onning G. Changes in serum lipids and postprandial glucose and insulin concentrations after consumption of beverages with beta-glucans from oats or barley: a randomised dose-controlled trial. *European Journal of Clinical Nutrition* 2005;59(11):1272-1281.

Braaten JT, Wood PJ, Scott FW, Wolynetz MS, Lowe MK, Bradley-White P, Collins MW. Oat beta-glucan reduces blood cholesterol concentration in hypercholesterolemic subjects. *European Journal of Clinical Nutrition* 1994;48(7):465-474.

Brown L, Rosner B, Willett WW, Sacks FM. Cholesterol-lowering effects of dietary fiber: a meta-analysis. *American Journal of Clinical Nutrition* 1999;69(1):30-42.

CFIA 2012: Canadian Food Inspection Agency, Guide to Food Labelling and Advertising, Chapter 6: The Elements Within the Nutrition Facts Table Section 6.8.1 Dietary Fibre. [Date modified 2012 September 24; Accessed 2013 April 16]. Available from: <http://www.inspection.gc.ca/english/fssa/labeti/guide/ch6ae.shtml>

Charlton KE, Tapsell LC, Batterham MJ, O'Shea J, Thorne R, Beck E, Tosh SM. Effect of 6 weeks' consumption of β -glucan-rich oat products on cholesterol levels in mildly hypercholesterolaemic overweight adults. *British Journal of Nutrition* 2012;107:1037-1047.

Delahoy PJ, Magliano DJ, Webb K, Grobler M, Liew D. The relationship between reduction in low-density lipoprotein cholesterol by statins and reduction in risk of cardiovascular outcomes: an updated meta-analysis. *Clinical Therapeutics* 2009;31(2):236-244.

EFSA 2010: Scientific Opinion: Scientific Opinion on the substantiation of a health claim related to oat beta-glucans and lowering blood cholesterol and reduced risk of (coronary) heart disease pursuant to Article 14 of Regulation (EC) No 1924/2006. [Internet]. EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA), European Food Safety Authority (EFSA), Parma, Italy. [Accessed 2012 April 10]. Available from: <http://www.efsa.europa.eu/en/efsajournal/doc/1885.pdf>

EFSA 2011a: Scientific Opinion: Scientific Opinion on the substantiation of health claims related to beta-glucans from oats and barley and maintenance of normal blood LDL-cholesterol concentrations (ID 1236, 1299), increase in satiety leading to a reduction in energy intake (ID 851, 852), reduction of post-prandial glycaemic responses (ID 821, 824), and 'digestive function' (ID 850) pursuant to Article 13(1) of Regulation (EC) No 1924/2006. [Internet]. EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA), European Food Safety Authority (EFSA), Parma, Italy. [Accessed 2013 August 21]. Available from: <http://www.efsa.europa.eu/en/efsajournal/doc/2207.pdf>

EFSA 2011b: Scientific Opinion: Scientific Opinion on the substantiation of a health claim related to barley beta-glucans and lowering of blood cholesterol and reduced risk of (coronary) heart disease pursuant to Article 14 of Regulation (EC) No 1924/2006. [Internet]. EFSA Panel on Dietetic Products, Nutrition and Allergies (DNA), European Food Safety Authority (EFSA), Parma, Italy. [Accessed 2013 August 21]. Available from: <http://www.efsa.europa.eu/en/efsajournal/doc/2471.pdf>

Granfeldt Y, Nyberg L, Bjorck I. Muesli with 4 g oat beta-glucans lowers glucose and insulin responses after a bread meal in healthy subjects. *European Journal of Clinical Nutrition* 2008;62(5):600-607.



HC 2010. Oat Products and Blood Cholesterol Lowering; Summary of Assessment of a Health Claim about Oat Products and Blood Cholesterol Lowering. [Accessed 2012 April 10]. Available from: <http://www.hc-sc.gc.ca/fn-an/label-etiquet/claims-reclam/assess-evalu/oat-avoine-eng.php>

IOM 2005: Institute of Medicine of the National Academies. Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids. Food and Nutrition Board. [Access 2013 April 16]. Available from: http://www.nap.edu/openbook.php?record_id=10490&page=680

Johnston LRH, Hunninghake DB, Schultz K, Westereng B. Cholesterol-lowering benefits of a whole grain oat ready to eat cereal. *Nutrition in Clinical Care* 1998;1(1):6-12.

Kabir M, Oppert JM, Vidal H, Bruzzo F, Fiquet C, Wursch P, Slama G, Rizkalla SW. Four-week low-glycemic index breakfast with a modest amount of soluble fibers in type 2 diabetic men. *Metabolism* 2002;51(7):819-826.

Kestin M, Moss R, Clifton PM, Nestel PJ. Comparative effects of three cereal brans on plasma lipids, blood pressure, and glucose metabolism in mildly hypercholesterolemic men. *American Journal of Clinical Nutrition* 1990;52:661-666.

NECP 2002: Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Third report of the National Cholesterol Education Program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (Adult Treatment Panel III): final report. *Circulation* 2002;106:3143-3421. [Accessed 2012 April 10]. Available from: <http://circ.ahajournals.org/content/106/25/3143.full.pdf>

Panahi S, Ezatagha A, Temelli F, Vasanthan T, Vuksan V. Beta-glucan from two sources of oat concentrates affect postprandial glycemia in relation to the level of viscosity. *Journal of the American College of Nutrition* 2007;26(6):639-644.

Queenan KM, Stewart ML, Smith KN, Thomas W, Fulcher RG, Slavin JL. Concentrated oat β -glucan, a fermentable fiber, lowers serum cholesterol in hypercholesterolemic adults in a randomized controlled trial. *Nutrition Journal* 2007;6:1-8.

Ripsin CM, Keenan JM, Jacobs DR Jr, Elmer PJ, Welch RR, Van Horn L, Liu K, Turnbull WH, Thye FW, Kestin M, Hegsted M, Davidson DM, Davidson MH, Dugan LD, Wahnefried WD, Beling S. Oat products and lipid lowering. A meta-analysis. *Journal of the American Medical Association* 1992;267(24):3317-3325.

Torronen R, Kansanen L, Uusitupa M, Hanninen O, Myllymaki O, Harkonen H, Malkki Y. Effects of an oat bran concentrate on serum lipids in free-living men with mild to moderate hypercholesterolaemia. *European Journal of Clinical Nutrition* 1992;46(9):621-627.

Ulmius M, Persson AJ, Krogh M, Olsson P, Onning G. An oat bran meal influences blood insulin levels and related gene sets in peripheral blood mononuclear cells of healthy subjects. *Genes & Nutrition* 2011;6(4):429-439.



USDA 2008: United States Department of Agriculture, Agricultural Research Service, National Genetic Resources Program. Germplasm Resources Information Network (GRIN). [Internet]. National Germplasm Resources Laboratory, Beltsville (MD). [*Avena sativa* L. Last updated 2008 September 25; Accessed 2013 April 8]. Available from: http://www.ars-grin.gov/cgi-bin/npgs/html/tax_search.pl

USP 35: The United States Pharmacopeia and the National Formulary (USP 35/NF 30). Rockville (MD): United States Pharmacopeial Convention, Inc.; 2012.

Uusitupa MI, Ruuskanen E, Mäkinen E, Laitinen J, Toskala E, Kervinen K, Kesäniemi YA. A controlled study on the effect of beta-glucan-rich oat bran on serum lipids in hypercholesterolemic subjects: relation to apolipoprotein E phenotype. *Journal of American College of Nutrition* 1992;11(6):651-659.

Wolever TMS, Tosh SM, Gibbs AL, Brand-Miller J, Duncan AM, Hart V, Lamarche B, Thomson BA, Duss R, Wood PJ. Physicochemical properties of oat β -glucan influence its ability to reduce serum LDL cholesterol in humans: a randomized clinical trial. *American Journal of Clinical Nutrition* 2010;92(4):723-732.

Wood P. Cereal β -glucans in diet and health. *Journal of Cereal Science* 2007;46(3):230-238.

References reviewed

Amundsen AL, Haugum B, Anderson H. Changes in serum cholesterol and sterol metabolites after intake of products enriched with an oat bran concentrate within a controlled diet. *Scandinavian Journal of Nutrition* 2003;47(2):68-74.

Anceau CC, Nazare JA, Björklund M, Le Coquil E, Sassolas A, Sothier M, Holm J, Landin-Olsson M, Onning G, Laville M, Moulin P. A controlled study of consumption of beta-glucan-enriched soups for 2 months by type 2 diabetic free-living subjects. *British Journal of Nutrition* 2010;103(3):422-428.

Babineau TJ, Hackford A, Kenler A, Bistrain B, Forse RA, Fairchild PG, Heard S, Keroack M, Caushaj P, Benotti P. A phase II multicenter, double-blind, randomized, placebo-controlled study of three dosages of an immunomodulator (PGG-glucan) in high-risk surgical patients. *Archives of Surgery* 1994;129(11):1204-1210.

Babineau TJ, Marcello P, Swails W, Kenler A, Bistrain B, Forse RA. Randomized phase I/II trial of a macrophage-specific immunomodulator (PGG-glucan) in high-risk surgical patients. *Annals of Surgery* 1994;220: 601-609.

Bays H, Frestedt JL, Bell M, Williams C, Kolberg L, Schmelzer W, Anderson JW. Reduced viscosity Barley β -Glucan versus placebo: a randomized controlled trial of the effects on insulin

sensitivity for individuals at risk for diabetes mellitus. *Nutrition Metabolism* (London) 2011;16:8:58.

Beck EJ, Tapsell LC, Batterham MJ, Tosh SM, Huang XF. Oat beta-glucan supplementation does not enhance the effectiveness of an energy-restricted diet in overweight women. *British Journal of Nutrition* 2010;103(8):1212-1222.

Beer MU, Arrigoni E, Amado R. Effects of oat gum on blood cholesterol levels in healthy young men. *European Journal of Clinical Nutrition* 1995;49(7):517-522.

Bremer JM, Scott RS, Lintott CJ. Oat bran and cholesterol reduction: evidence against specific effect. *Australian and New Zealand journal of medicine* 1991;21(4):422-426.

Brinker 2010: Brinker F. Final updates and additions for Herb Contraindications and Drug Interactions, 3rd edition, including extensive Appendices addressing common problematic conditions, medications and nutritional supplements, and influences on Phase I, II & III metabolism with new appendix on botanicals as complementary adjuncts with drugs. [Internet]. Sandy (OR): Eclectic Medical Publications. [Updated July 13, 2010; Accessed 2012 April 19]. Available from: <http://www.eclecticherb.com/emp/updatesHCIDI.html>

Brinker F. *Herbal Contraindications and Drug Interactions: Plus Herbal Adjuncts With Medicines*, expanded 4th Edition. Sandy (OR): Eclectic Medical Publications; 2010.

Brown GD, Herre J, Williams DL, Willment JA, Marshall AS, Gordon S. Dectin-1 mediates the biological effects of beta-glucans. *The Journal of experimental medicine* 2003;197(9):1119-1124.

Brown GD. Dectin-1: a signalling non-TLR pattern-recognition receptor. *Nature Reviews Immunology* 2006;6(1):33-43.

Chen J, He J, Wildman RP, Reynolds K, Streiffer RH, Whelton PK. A randomized controlled trial of dietary fiber intake on serum lipids. *European Journal of Clinical Nutrition* 2006;60(1):62-68.

Chen J, Seviour R. Medicinal importance of fungal beta-(1->3), (1->6)-glucans. *Mycology Research* 2007;111(6):635-652.

Dais P, Perlin AS. High field, ¹³C-NMR spectroscopy of β-D-glucans, amylopectin and glycogen. *Carbohydrate Research* 1982;100(1):103-116.

Davy BM, Melby CL, Beske SD, Ho RC, Davrath LR, Davy KP. Oat consumption does not affect resting casual and ambulatory 24-h arterial blood pressure in men with high-normal blood pressure to stage I hypertension. *The Journal of Nutrition* 2002;132(3):394-398.

Demir G, Klein HO, Molinas MN, Tuzuner N. Beta glucan induces proliferation and activation of monocytes in peripheral blood of patients with advanced breast cancer. *International Immunopharmacology* 2007;7(1):113-116.

Estrada A, Yun CH, Van Kessel A, Li B, Hauta S, Laarveld B. Immunomodulatory activities of oat beta-glucan in vitro and in vivo. *Microbiology and Immunology* 1997;41(12):991-998.

FAOSTAT: food and agricultural commodities production. Countries by commodity. [Accessed 2013 March 23]. Available from: <http://faostat3.fao.org/faostat-gateway/go/to/home/E>

Felippe DJ, Rocha DESM, Maciel FM, Ade SM, Mendes NF. Infection prevention in patients with severe multiple trauma with the immunomodulator beta 1-3 polyglucose (glucan). *Surgery, gynecology & obstetrics* 1993;177(4):383-388.

Frank J, Sundberg B, Eldin KA, Vessby B, Aman P. Yeast leavened oat breads with high or low molecular weight betaglucan do not differ in their effects on blood concentrations of lipids, insulin, or glucose in humans. *Journal of Nutrition* 2004;134(6):1384-1388.

Gantner BN, Simmons RM, Canavera SJ, Akira S, Underhill DM. Collaborative induction of inflammatory responses by dectin-1 and Toll-like receptor 2. *The Journal of experimental medicine* 2003;197(9):1107-1117.

Gao Y, Zhou SH, Chen G, Dai X, Ye J. A phase I/II study of a Ganoderma lucidum (Curt.: Fr.) P. Karst. Extract (ganopoly) in patients with advanced cancer. *International Journal of Medicinal Mushrooms* 2002;4(3):207-214.

Gerhardt AL, Gallo NB. Full-fat rice bran and oat bran similarly reduce hypercholesterolemia in humans. *Journal of Nutrition* 1998;128(5):865-869.

Goodridge HS, Simmons RM, Underhill DM. Dectin-1 stimulation by Candida albicans yeast or zymosan triggers NFAT activation in macrophages and dendritic cells. *Journal of Immunology* 2007;178(5):3107-3115.

Gordon M, Guralnik M, Kaneko Y, Mimura T, Goodgame J, DeMarzo C, Pierce D, Baker M, Lang W. A phase II controlled study of a combination of the immune modulator, lentinan, with didanosine (ddI) in HIV patients with CD4 cells of 200-500/mm³. *Journal of Medicine* 1995;26(5-6):193-207.

Gross O, Gewies A, Finger K, Schafer M, Sparwasser T, Peschel C, Forster I, Ruland J. Card9 controls a non-TLR signalling pathway for innate anti-fungal immunity. *Nature* 2006, 442(7103):651-656.

Hamano K, Gohra H, Katoh T, Fujimura Y, Zempo N, Esato K. The preoperative administration of lentinan ameliorated the impairment of natural killer activity after cardiopulmonary bypass. *International Journal of Immunopharmacology* 1999;21(8):531-540.



Hayakawa K, Mitsuhashi N, Saito Y, Takahashi M, Katano S, Shiojima K, Furuta M, Niibe H. Effect of Krestin (PSK) as adjuvant treatment on the prognosis after radical radiotherapy in patients with non-small cell lung cancer. *Anticancer Research* 1993;13:1815-1820.

Herre J, Gordon S, Brown GD. Dectin-1 and its role in the recognition of beta-glucans by macrophages. *Molecular immunology* 2004;40(12):869-876.

Herre J, Marshall AS, Caron E, Edwards AD, Williams DL, Schweighoffer E, Tybulewicz V, Reis e Sousa C, Gordon S, Brown GD. Dectin-1 uses novel mechanisms for yeast phagocytosis in macrophages. *Blood* 2004;104(13):4038-4045.

Jenkins AL, Jenkins DJA, Zdravkovic U, Würsch P, Vuksan V. Depression of the glycemic index by high levels of β -glucan fiber in two functional foods tested in type 2 diabetes. *European Journal of Clinical Nutrition* 2002;56(7):622-628.

Juntunen KS, Niskanen LK, Liukkonen KH, Poutanen KS, Holst JJ, Mykkanen HM. Postprandial glucose, insulin, and incretin responses to grain products in healthy subjects. *American Journal of Clinical Nutrition* 2002;75(2):254-262.

Karmally W, Montez MG, Palmas W, Martinez W, Branstetter A, Ramakrishnan R, Holleran SF, Haffner SM, Ginsberg HN. Cholesterol-lowering benefits of oat-containing cereal in Hispanic Americans. *Journal of American Dietetic Association* 2005;105(6):967-970.

Keenan JM, Goulson M, Shamliyan T, Knutson N, Kolberg L, Curry L. The effects of concentrated barley beta-glucan on blood lipids in a population of hypercholesterolaemic men and women. *British Journal of Nutrition* 2007;97(6):1162-1168.

Keenan JM, Pins JJ, Frazel C, Moran A, Turnquist L. Oat ingestion reduces systolic and diastolic blood pressure in patients with mild or borderline hypertension: a pilot trial. *The Journal of Family Practice* 2002;51(4):369.

Kempen HJ, Glatz JF, Gevers Leuven JA, van der Voort HA, Katan MB. Serum lathosterol concentration is an indicator of whole-body cholesterol synthesis in humans. *Journal of Lipid Research* 1988;29(9):1149-1155.

Kerckhoffs DA, Hornstra G, Mensink RP. Cholesterol-lowering effect of beta-glucan from oat bran in mildly hypercholesterolemic subjects may decrease when beta-glucan is incorporated into bread and cookies. *American Journal of Clinical Nutrition* 2003;78(2):221-227.

Knudsen KE, Jensen BB, Hansen I. Digestion of polysaccharides and other major components in the small and large intestine of pigs fed on diets consisting of oat fractions rich in beta-Dglucan. *British Journal of Nutrition* 1993;70(2):537-556.

Leadbetter J, Ball MJ, Mann JI. Effects of increasing quantities of oat bran in hypercholesterolemic people. *American Journal of Clinical Nutrition* 1991;54(5):841-845.



Lei LS, Lin ZB. Effects of ganoderma polysaccharides on T cell subpopulations and production of interleukin-2 in mixed lymphocytes response. *Yao Hsueh Hsueh Pao* 1992;27(5):331-335.

Li B, Cai Y, Qi C, Hansen R, Ding C, Mitchell TC, Yan J. Orally Administered Particular β -Glucan Modulates Tumor-capturing Dendritic Cells and Improves Anti-tumor T Cell Responses in Cancer. *Clinical Cancer Research* 2010;16(21):5153-5164.

Liao ML, Zhao JM. The II stage clinical tests of PSP in the treatment of lung cancer, in: Yang QY, Kwok CY(eds.), *Proceedings of PSP International Symposium*. Shanghai, China: Fudan University Press, 1993;243-256.

Liatis S, Tsapogas P, Chala E, Dimosthenopoulos C, Kyriakopoulos K, Kapantais E, Katsilambros N. The consumption of bread enriched with betaglucan reduces LDL-cholesterol and improves insulin resistance in patients with type 2 diabetes. *Diabetes & Metabolism* 2009;35(2):115-120.

Lin YL, Liang YC, Lee SS, Chiang BL. Polysaccharide purified from *Ganoderma lucidum* induced activation and maturation of human monocyte-derived dendritic cells by the NF-kappaB and p38 mitogen-activated protein kinase pathways. *Journal of Leukocyte Biology* 2005;78(2):533-543.

Lovegrove JA, Clohessy A, Milon H, Williams CM. Modest doses of beta-glucan do not reduce concentrations of potentially atherogenic lipoproteins. *American Journal of Clinical Nutrition* 2000;72(1):49-55.

Maki KC, Galant R, Samuel P, Tesser J, Witchger MS, Ribaya-Mercado JD, Blumberg JB, Geohas J. Effects of consuming foods containing oat beta-glucan on blood pressure, carbohydrate metabolism and biomarkers of oxidative stress in men and women with elevated blood pressure. *European Journal of Clinical Nutrition* 2007;61(6):786-795.

Maki KC, Shinnick F, Seeley MA, Veith PE, Quinn LC, Hallissey PJ, Temer A, Davidson MH. Food products containing free tall oil-based phytosterols and oat beta-glucan lower serum total and LDL cholesterol in hypercholesterolemic adults. *Journal of Nutrition* 2003;133(3):808-813.

Morimoto T, Ogawa M, Orita K, Sugimachi K, Toge T, Dohi K, Nomura Y, Monden Y, Ogawa N. Postoperative adjuvant randomized trial comparing chemoendocrine therapy, chemotherapy and immunotherapy for patients with stage II breast cancer: 5-year results from the Nishinohon Cooperative Study Group of Adjuvant Chemoendocrine Therapy for Breast Cancer (ACETBC) of Japan. *European Journal of Cancer* 1996;32A(2):235-242.

Nakazato H, Koike A, Saji S, Ogawa N, Sakamoto J. Efficacy of immunochemotherapy as adjuvant treatment after curative resection of gastric cancer. Study Group of Immunochemotherapy with PSK for Gastric Cancer. *Lancet* 1994;343(8906):1122-1126.



Naumann E, van Rees AB, Onning G, Oste R, Wydra M, Mensink RP. Beta-glucan incorporated into a fruit drink effectively lowers serum LDL-cholesterol concentrations. *American Journal of Clinical Nutrition* 2006;83(3):601-605.

Ohno N, Terui T, Chiba N, Kurachi K, Adachi Y, Yadomae T. Resistance of highly branched (1->3)-beta-D-glucans to formolysis. *Chemical & Pharmaceutical Bulletin (Tokyo)* 1995;43(6):1057-1060.

Onning G, Wallmark A, Persson M, Akesson B, Elmstahl S, Oste R. Consumption of oat milk for 5 weeks lowers serum cholesterol and LDL cholesterol in free-living men with moderate hypercholesterolemia. *Annals of Nutrition & Metabolism* 1999;43(5):301-309.

Othman RA, Moghadasian MH, Jones PJH. Cholesterol-lowering effects of oat b-glucan. *Nutrition Reviews* 2011;69(6):299-309.

Parrish FW, Perlin AS, Reese ET. Selective enzymolysis of polyb-D-glucan and structure of the polymers. *Canadian Journal of Chemistry* 1960;38(11):2094-2104.

Pick ME, Hawrysh ZJ, Gee MI, Toth E, Garg ML, Hardin RT. Oat bran concentrate bread products improve long-term control of diabetes: a pilot study. *Journal of the American Dietetic Association* 1996;96(12):1254-1261.

Ramakers JD, Volman JJ, Biorlund M, Onning G, Mensink RP, Plat J. Fecal water from ileostomic patients consuming oat beta-glucan enhances immune responses in enterocytes. *Molecular Nutrition and Food Research* 2007;51(2):211-220.

Reyna NY, Cano C, Bermudez VJ, Medina MT, Souki AJ, Ambard M, Nunez M, Ferrer MA, Inglett GE. Sweeteners and beta-glucans improve metabolic and anthropometrics variables in well controlled type 2 diabetic patients. *American Journal of Therapeutics* 2003;10(6):438-443.

Rogers NC, Slack EC, Edwards AD, Nolte MA, Schulz O, Schweighoffer E, Williams DL, Gordon S, Tybulewicz VL, Brown GD, Reis e Sousa C. Syk-dependent cytokine induction by Dectin-1 reveals a novel pattern recognition pathway for C type lectins. *Immunity* 2005;22(4):507-517.

Ruxton CHS and Derbyshire E. A systematic review of the association between cardiovascular risk factors and regular consumption of oats. *British Food Journal* 2008;110(11):1119-1132.

Schorey JS, Lawrence C. The pattern recognition receptor Dectin-1: from fungi to mycobacteria. *Current Drug Targets* 2008;9(2):123-129.

Shi JH, Chen T, Lian ZR. The clinical research of the effect of PSP on the immunological function of stomach cancer patients during operation and chemotherapy, in: Yang QY, Kwok CY (eds.), *Proceedings of PSP International Symposium*. Shanghai, China: Fudan University Press, 1993;232-240.



Smith KN, Queenan KM, Thomas W, Fulcher RG, Slavin JL. Physiological effects of concentrated barley beta-glucan in mildly hypercholesterolemic adults. *Journal of American College of Nutrition* 2008;27(3):434-40.

Sun L, Zhao Y. The biological role of dectin-1 in immune response. *International reviews of immunology* 2007;26(5-6):349-364.

Suto M, Fukuda S, Moriya N, Watanabe W, Sasaki D, Yoshida Y. Clinical study of biological response modifiers as maintenance therapy for hepatocellular carcinoma. *Cancer Chemotherapy Pharmacology* 1994;33(Suppl.),S145-S148.

Taylor PR, Brown GD, Herre J, Williams DL, Willment JA, Gordon S. The role of SIGNR1 and the beta-glucan receptor (dectin-1) in the nonopsonic recognition of yeast by specific macrophages. *Journal of Immunology* 2004;172(2):1157-1162.

Taylor PR, Brown GD, Reid DM, Willment JA, Martinez-Pomares L, Gordon S, Wong SY. The beta-glucan receptor, dectin-1, is predominantly expressed on the surface of cells of the monocyte/macrophage and neutrophil lineages. *Journal of Immunology* 2002;169(7):3876-3882.

Theuwissen E, Mensink RP. Simultaneous intake of beta-glucan and plant stanol esters affects lipid metabolism in slightly hypercholesterolemic subjects. *Journal of Nutrition* 2007;137(3):583-588.

Toi M, Hattori T, Akagi M, Inokuchi K, Orita K, Sugimachi K, Dohi K, Nomura Y, Monden Y, Hamada Y, Morimoto T, Ogawa N. Randomized adjuvant trial to evaluate the addition of tamoxifen and PSK to chemotherapy in patients with primary breast cancer. *Cancer* 1992;70(10):2475-2483.

Van Horn L, Liu K, Gerber J, et al. Oats and soy in lipid lowering diets for women with hypercholesterolemia: is there synergy? *Journal of the American Dietetic Association* 2001;101(11):1319-1325.

Vasanthan T, Temelli F. Beta-glucan isolation/concentration technologies and their impact on molecular structure and functionality. Department of Agricultural, Food and Nutritional Science, University of Alberta, Edmonton, AB, Canada. In: *The Future of Barley. Cereal Foods World* 2005;50(5):271-277.

Volman JJ, Mensink RP, Buurman WA, Plat J. In vivo effects of dietary (1→3), (1→4)-β-D-glucans from oat on mucosal immune responses in man and mice. *Scandinavian Journal of Gastroenterology* 2011;46(5):603-610.

Volman JJ, Mensink RP, Ramakers JD, de Winther MP, Carlsen H, Blomhoff R, Buurman WA, Plat J. Dietary (1→3), (1→4)-beta-D-glucans from oat activate nuclear factor-kappaB in intestinal leukocytes and enterocytes from mice. *Nutrition Research* 2010;30(1):40-48.



Vos A, M'Rabet L, Stahl B, Boehm G, Garssen J. Immune-modulatory effects and potential working mechanisms of orally applied nondigestible carbohydrates. *Critical Reviews in Immunology* 2007;27(2):97-140.

Wang H, Weening D, Jonkers E, Boer T, Stellaard F, Small AC, Preston T, Vonk RJ, Priebe MG. A curve fitting approach to estimate the extent of fermentation of indigestible carbohydrates. *European Journal of Clinical Investigation* 2008;38(11):863-868.

Wang SY, Hsu ML, Hsu HC, Tzeng CH, Lee SS, Shiao MS, Ho CK. The anti-tumor effect of *Ganoderma lucidum* is mediated by cytokines released from activated macrophages and T lymphocytes. *International Journal of Cancer* 1997;70(6):699-705.

Wolever TMS, Gibbs AL, Miller JB, Duncan AM, Hart V, Lamarche B, Tosh SM, Duss R. Bioactive oat β -glucan reduces LDL cholesterol in Caucasians and non-Caucasians. *Nutrition Journal* 2011;10:130.

Wood PJ. Oat β -glucan physicochemical properties and physiological effects. *Trends in Food Science & Technology* 1991;2:311-314.

Wood PJ. Evaluation of oat bran as a soluble fibre source. Characterization of oat β -glucan and its effects on glycaemic response. *Carbohydrate Polymers* 1994;25(4):331-336.

Wu Z, Ming J, Gao R, Wang Y, Liang Q, Yu H, Zhao G. Characterization and antioxidant activity of the complex of tea polyphenols and oat β -glucan. *Journal of Agricultural and Food Chemistry* 2011;59(19):10737-10746.

Xie SQ. The effect of PSP on red cell immunity: a clinical study on gastric cancer patients, in: Yang QY, Kwok CY (eds.), *Proceedings of PSP International Symposium*. Shanghai, China: Fudan University Press, 1993;241-242.

Yatawara L, Wickramasinghe S, Nagataki M, Takamoto M, Nomura H, Ikeue Y, Watanabe Y, Agatsuma T. Aureobasidium-Derived Soluble Branched (1,3-1,6) β -Glucan (Sophy β -glucan) Enhances Natural Killer Activity in *Leishmania amazonensis*-Infected Mice. *Korean Journal of Parasitology* 2009;47(4):345-351.

Yun CH, Estrada A, Van Kessel A, Gajadhar A, Redmond M, Laarveld B. Immunomodulatory effects of oat beta-glucan administered intragastrically or parenterally on mice infected with *Eimeria vermiformis*. *Microbiology and Immunology* 1998;42(6):457-465.

Yun CH, Estrada A, Van Kessel A, Gajadhar AA, Redmond MJ, Laarveld B. beta-(1-->3, 1-->4) oat glucan enhances resistance to *Eimeria vermiformis* infection in immunosuppressed mice. *International Journal for Parasitology* 1997;27(3):329-337.

Yun CH, Estrada A, Van Kessel A, Park BC, Laarveld B. Beta-glucan, extracted from oat, enhances disease resistance against bacterial and parasitic infections. *FEMS Immunology and Medical Microbiology* 2003;35(1):67-75.



Zhang LX, Mong H, Zhou HB. Effect of Japanese Ganoderma lucidum on production of interleukin-2 from murine splenocytes. Chinese journal of integrated traditional and Western medicine 1993;13(10):613-615.