

What Are K Vitamins – Absorption & Half-Life Time

[1] Unpublished clinical studies, NattoPharma. On file.

What Are K Vitamins – Accumulation in the Serum

[2] Unpublished clinical studies, NattoPharma. On file.

What Are K Vitamins – Efficacy

[3] Knapen, M.H.J., Schurgers, L.J., Vermeer, C. Vitamin K2 supplementation improves bone geometry and bone strength indices in postmenopausal women. *Osteoporosis Int.* 18 (2007) 963-972.

What Are K Vitamins – History

[4] Dam H, The antihemorrhagic vitamin of the chick. *Biochem J* 1935; 29(6):1273-85.

What Are K Vitamins – Deficiency

[5] Plantalech L, Guillaumont M, Vergnaud P, Leclercq M, Delmas PD. Impairment of gamma carboxylation of circulating osteocalcin (bone gla protein) in elderly women. *J Bone Miner Res.* 1991;6(11):1211-6.

[6] van Summeren M, Braam L, Noirt F, Kuis W, Vermeer C. Pronounced elevation of undercarboxylated osteocalcin in healthy children. *Pediatr Res.* 2007;61(3):366-70.

[7] Prynne CJ, Thane CW, Prentice A, Wadsworth ME. Intake and sources of phylo-quinone (vitamin K(1)) in 4-year-old British children: comparison between 1950 and the 1990s. *Public Health Nutr.* 2005 Apr;8(2):171-80.

[8] Suttie JW. The importance of menaquinones in human nutrition. *Annu Rev Nutr.* 1995;15:399-417.

[9] Booth SL, Suttie JW. Dietary intake and adequacy of K vitamins. *J Nutr.* 1998;128(5):785-8.

What Are K Vitamins – Sources

[10] Suttie JW. The importance of menaquinones in human nutrition. *Annu Rev Nutr.* 1995;15:399-417.

[11] Kaneki M, Hodges SJ, Hosoi T, Fujiwara S, Lyons A, Crean SJ, Ishida N, Nakagawa M, Takechi M, Sano Y, Mizuno Y, Hoshino S, Miyao M, Inoue S, Horiki K, Shiraki M, Ouchi Y, Orimo H. Japanese fermented soybean food as the major determinant of the large geographic difference in circulating levels of K vitamins: possible implications for hip-fracture risk. *Nutrition.* 2001;17(4):315-21.

Why MenaQ7 – Superiority

[12] J. T. 1970 Occurrence and biopotency of various forms of vitamin K. In: *The Fat-soluble Vitamins*, ed., H. F. DeLuca and J. W. Suttie, University of Wisconsin, Press, Madison, Wis., p. 377.

[13] Lowenthal L and Vergel Rival, GM: Comparison of the Activity of the cis- and trans-isomer of Vitamin K1 in Vitamin K-Deficient and Coumarin Anticoagulant-Pre-treated Rats. *J Pharma Exp Thera*, vol 209 1979.

[14] Knauer TE, Siegfried C, Willingham AK, Matschiner JT. Metabolism and biological activity of cis- and trans-Phylloquinone in the rat. *J Nutr.* 1975 Dec;105(12):1519-24.

[15] Theuwissen E et al. Dose-finding and safety study for vitamin K2 in human volunteers. *Br J Nutr.* 2012; 28;108(6):1017-24.

Health Benefits – Bone Health

[16] Vergnaud P, Garnero P, Meunier PJ, Bréart G, Kamihagi K, Delmas PD. Undercarboxylated osteocalcin measured with a specific immunoassay predicts hip fracture in elderly women: the EPIDOS Study. *J Clin Endocrinol Metab.* 1997;82(3):719-24.

[17] Booth SL, Broe KE, Peterson JW, Cheng DM, Dawson-Hughes B, Gundberg CM, Cupples LA, Wilson PW, Kiel DP. Associations between K vitamins biochemical measures and bone mineral density in men and women. *J Clin Endocrinol Metab.* 2004;89(10):4904-9.

[18] Knapen MH, Nieuwenhuijzen Kruseman AC, Wouters RS, Vermeer C. Correlation of serum osteocalcin fractions with bone mineral density in women during the first 10 years after menopause. *Calcif Tissue Int.* 1998;63(5):375-9.

[19] Schurgers LJ, Knapen MH, Vermeer C. K vitamins2 supplementation improves hip bone geometry and bone strength indices in postmenopausal women. *Int. Congr. Series* 2007; 179-187.

[20] Knapen MH, Schurgers LJ, Vermeer C. Vitamin K2 supplementation improves hip bone geometry and bone strength indices in postmenopausal women. *Osteoporosis Int.* 2007;18(7):963-72.

[21] Knapen M. H. J., N. E. Drummen, E. Smit, C. Vermeer, E. Theuwissen. Three-year low-dose menaquinone-7 supplementation helps decrease bone loss in healthy postmenopausal women. *Osteoporosis Int.* 2013 Sep;24(9):2499-507.

Health Benefits – Cardiovascular Health

[22] Schurgers, LJ, Cranenburg, ECM and Vermeer, C. Matrix Gla-protein: The calcification inhibitor in need of vitamin K. Theme issue article. *Thromb Haemost* 2008; 100: 593-603.

[23] Schurgers, LJ: Unpublished data

[24] Iribarren C, Sidney S, Sternfeld B, Browner WS. Calcification of the aortic arch: risk factors and association with coronary heart disease, stroke, and peripheral vascular disease. *JAMA.* 2000;283(21):2810-5.

[25] Shaw LJ, Raggi P, Berman DS, Callister TQ. Coronary artery calcium as a measure of biologic age. *Atherosclerosis.* 2006;188(1):112-9.

[26] Geleijnse JM, Vermeer C, Grobbee DE, Schurgers LJ, Knapen MH, van der Meer IM, Hofman A, Witteman JC. Dietary intake of menaquinone is associated with a reduced risk of coronary heart disease: the Rotterdam Study. *J Nutr.* 2004;134(11):3100-5.

[27] Gast G.C.M., et al. A high menaquinone reduces the incidence of coronary heart disease in women. *Nutr Metab Cardiovasc Dis.* 2009; 19:504-10.

[28] Knapen MHJ, Braam LAJL, Drummen NE, Bekers O, Hoeks APG, Vermeer C. Menaquinone-7 supplementation improves arterial stiffness in healthy postmenopausal women: double-blind randomised clinical trial. *Thromb Haemost* 2015 May; 19:113(5)

Health Benefits – Children’s Health

- [29] O’Connor E, Mølgaard C, Michaelsen KF, Jakobsen J, Lamberg-Allardt CJ, Cashman KD. Serum percentage undercarboxylated osteocalcin, a sensitive measure of K vitamins status, and its relationship to bone health indices in Danish girls. *Br J Nutr.* 2007;97(4):661-6.
- [30] Kalkwarf HJ, Khoury JC, Bean J, Elliot JG. K vitamins, bone turnover, and bone mass in girls. *Am J Clin Nutr.* 2004;80(4):1075-80.
- [31] Theuwissen E, Magdeleyns EJ, Braam LAJLM, Teunissen KJ, Knapen MH, Binnekamp IAG, van Summeren MJH, Vermeer C. Vitamin K status in healthy volunteers. *Food & Function.* 2014;5(2):229-34.
- [32] Prynne CJ, Thane CW, Prentice A, Wadsworth ME. Intake and sources of phylloquinone (K vitamins(1)) in 4-year-old British children: comparison between 1950 and the 1990s. *Public Health Nutr.* 2005;8(2):171-80.
- [33] Khosla S, Melton LJ 3rd, Dekutoski MB, Achenbach SJ, Oberg AL, Riggs BL. Incidence of childhood distal forearm fractures over 30 years: a population-based study. *JAMA.* 2003 Sep 17;290(11):1479-85.
- [34] van Summeren MJ, van Coeverden SC, Schurgers LJ, Braam LA, Noirt F, Uiterwaal CS, Kuis W, Vermeer C. K vitamins status is associated with childhood bone mineral content. *Br J Nutr.* 2008;1-7.

Health Benefits – Health Concerns

- [35] Caraballo PJ, Gabriel SE, Castro MR, Atkinson EJ, Melton LJ 3rd. Changes in bone density after exposure to oral anticoagulants: a meta-analysis. *Osteoporosis Int.* 1999;9(5):441-8.
- [36] Schurgers LJ, Aabert H, Vermeer C, Bültmann B, Janzen J. Oral anticoagulant treatment: friend or foe in cardiovascular disease? *Blood.* 2004 15;104(10):3231-2.
- [37] Koos R, Mahnken AH, Mülenbruch V, Pflueger B, Wildberger JE, Kühl HP. Relation of oral anticoagulation to cardiac valvular and coronary calcium assessed by multislice spiral computed tomography. *Am J Cardiol.* 2005;96(6):747-9.

www.nattopharma.com
www.menaq7.com

NattoPharma[®]

NattoPharma ASA
(Head Office)
Kirkeveien 59B
1368 Hovik, Norway
info@nattopharma.com
Phone: (+47) 40 00 90 08

NattoPharma USA, Inc.
(North American Subsidiary)
328 Amboy Avenue, Suite D
Metuchen, NJ 08840
info.US@nattopharma.com
Phone: (+1) 609-454-2992