

Effect of Concentrate from Bacillus natto Fermentation on Blood Lipoprotein of Patients with Hyperlipidemin

江明哲、張耀南

E-mail: 9417930@mail.dyu.edu.tw

ABSTRACT

In this study, the 39 patients of over 35-year-old with hyperlipidemin were diagnosed clinically by physicians in certain local hospital, Taichung city, Taiwan, from January to March in 2005. The total cholesterol (TC) or triglycerides (TG) of the patients was out of normal level (200mg/dl), as described one HTC group with 22 patients, one HTG with 17 ones, one HTCTG with 12 one in clinical trials. The acute toxic test of animal security experiment of the concentrate from Bacillus natto fermentation was carried out and had been passed the safety test for the oral administration of SD mouse in DCB (Development Center for Biotechnology), Taipei, Taiwan. The effect of the B. natto concentrate (BnC) diet on blood lipoprotein properties of the patients, such as lowering serum TC、TG、LDL or increasing serum HDL, was investigated. It was found that the serum TC of the 49 patients after 2 months of BnC diet treatments significantly decreased and was below 200mg/dl. For the patients only in HTG and HTCTG groups the serum TG of the patients statistically meaningfully decreased down to 200mg/dl after 3 months of BnC diet treatments. There was no significant difference for the LDL and HDL levels of the patients between before and after the BnC diet treatments. Therefore, the BnC may be good as health-care food for the diet treatment of the patients with hyperlipidemin for decreasing the TC and TG down to below normal level (200mg/dl).

Keywords : Bacillus natto ; Concentrate ; Hyperlipidemin ; Cholesterol ; Triglyceride

Table of Contents

封面內頁 簽名頁 授權書 iii 中文摘要 iv 英文摘要 v 誌謝 vii 目錄 viii 圖目錄 x 表目錄 xi 第一章 前言 1 第二章 文獻回顧 6 2.1 納豆的由來 6 2.2 納豆的主要成份及功效研究 7 2.3 血栓與栓塞的定義及形成機制與影響 9 2.3.1 血栓與栓塞的定義 9 2.3.2 血栓形成的過程及血栓的形態 12 2.3.3 血栓對機體的影響 13 2.4 高血脂症 15 2.4.1 疾病概述 15 2.4.2 診斷要點 15 2.4.3 高血脂症的危害 16 2.5 納豆和血栓 19 2.5.1 納豆和血液的關係 20 2.5.2 納豆激酶(Nattokinase)和尿激酶(puroUK) 21 2.5.3 納豆激酶的物理化學性質 22 2.5.4 納豆激酶的臨床實例 24 2.5.5 粘蛋白和血液 24 2.5.6 以納豆菌與納豆激酶預防血栓所引起的相關疾病(血栓症) 24 2.6 血栓與生活保健 26 第三章 材料與方法 29 3.1 實驗材料 29 3.2 研究方法 29 3.2.1 實驗對象處理 29 3.2.2 檢測指標與服用方法 32 3.2.3 實驗儀器設備 32 第四章 結果與討論 34 4.1 納豆醱酵萃取物對人體一般健康指標項目之變化 34 4.2 納豆醱酵萃取物對人體血液生化檢測指標項目之變化 41 第五章 結論 54 參考文獻 56 圖目錄 圖2.1 血栓形成機制 10 圖2.2 血栓(纖維蛋白)的分解與納豆激酶的作用機轉方式 23 圖2.3 The dosage of Nattokinase lyses an artificial fibrin and stimulates the flow of blood 25 圖4.1 食用納豆菌醱酵濃縮物依各分類組別受測者於試驗期間BMI平均值隨檢測月份之變化 36 圖4.2 食用納豆菌醱酵濃縮物依各分類組別受測者於試驗期間腹圍平均值隨檢測月份之變化 37 圖4.3 高膽固醇組食用納豆菌醱酵濃縮物於試驗期間受測者總膽固醇平均值隨檢測月份血液中濃度之變化 42 圖4.4 高三酸甘油脂組食用納豆菌醱酵濃縮物於試驗期間受測者三酸甘油脂平均值隨檢測月份血液中濃度之變化 45 圖4.5 混合型組食用納豆菌醱酵濃縮物於試驗期間受測者總膽固醇及三酸甘油脂平均值隨檢測月份血液中濃度之變化 47 圖4.6 食用納豆菌醱酵濃縮物依各分組受測者於試驗期間LDL-C (低密度膽固醇脂蛋白)平均值隨檢測月份之變化 50 圖4.7 食用納豆菌醱酵濃縮物依各分組受測者於試驗期間HDL-C (高密度膽固醇脂蛋白)平均值隨檢測月份之變化 51 表目錄 表1.1 2003年台灣地區國人主要死亡原因 2 表3.1 產品規格書及檢驗結果 30 表4.1 食用納豆菌醱酵濃縮物前受測者個人基本資料彙整 38 表4.2 食用納豆菌醱酵濃縮物後各組受測者BMI變化情形 39 表4.3 食用納豆菌醱酵濃縮物後各組受測者腹圍變化情形 40 表4.4 高膽固醇組食用納豆菌醱酵濃縮物血液生化檢測及生理量測均值變化情形 43 表4.5 高三酸甘油脂組食用納豆菌醱酵濃縮物血液生化檢測及生理量測均值變化情形 46 表4.6 混合型組食用納豆菌醱酵濃縮物血液生化檢測及生理量測均值變化情形 48 表4.7 食用納豆菌醱酵濃縮物後各組受測者LDL-C變化情形 52 表4.8 食用納豆菌醱酵濃縮物後各組受測者HDL-C變化情形 53

REFERENCES

1.木全一心、潘世綿 編著。2001。心絞痛與心肌梗塞。第38-96頁。文字復興有限公司。台北，台灣。 2.江晃榮 編著。2001。納豆的強力療效。第23頁。世茂出版社。台北，台灣。 3.行政院衛生署。2003。中華民國公共衛生概況。行政院衛生署編印。 4.林正盛。2003。納豆激酶在高血脂病患之降血脂效果分析:6-8。中山醫學大學醫學研究所碩士論文。台中。 5.林麗菁。2004。納豆菌之液態培養及其產

生納豆激?之探討:47-62。屏東科技大學食品科學系碩士論文。屏東。6.范敏慧。1994。枯草菌IMR-NK-1血纖維蛋白?之純化及性質研究:88-94。靜宜大學食品營養研究所碩士論文。台中。7.許元勳。2003。現代生物科技的新寵兒 - 神奇納豆菌。生物產業14(1):53-59。8.許元勳。2004。納豆菌的生理功能及其產業應用。生物產業15(4):73-78。9.黃弘博。2000。初診心血管疾病患者飲食介入之研究:12-19。中國文化大學生活應用科學研究所碩士論文。台北。10.黃宗慶。1999。攝食枯草菌發酵大豆、黑豆及薏仁對老鼠血液血纖維蛋白水解活性及凝血作用之影響:77-79。靜宜大學食品營養學系碩士論文。台中。11.須見洋行 編著。1993。納豆治百病。第112-115頁。培琳出版社。台北,台灣。12.張智慧。2005。調節血脂保健食品簡介。食品工業37(1):11-16。13.潘子明。2004。降膽固醇保健食品之開發。生物產業15(4):3-24。14.穆瑞蓮、張文翰、林秀芳。1988。台灣地區正常人血中脂肪、脂蛋白及脂蛋白原含量。中華醫誌41:255-262。15.廖曉玲 編著。2002。新世紀醫學-納豆天然的藥用食品。第156頁。安立出版社。台北,台灣。16.蘇遠志。2003。納豆菌代謝產物的開發與應用。生物產業14(2):45-58。17.Anderson, J. W., Smith, B. M., Washnock, C. S. 1999. Cardiovascular and renal benefits of dry bean and soybean intake. *American Journal of Clinical Nutrition* 70:464-474. 18.Anthony, M. S. 2000. Soy and cardiovascular disease: cholesterol lowering and beyond. *Journal of Nutrition* 130:662 – 663. 19.Astrup, T., Mullertz, S. 1952. The fibrin plate method for estimating fibrinolytic activity. *Archs Biochemical and Biophysical* 40:346-351. 20.Bergsdorf, N., Nilsson, T. and Wallen, P. 1983. An enzyme linked immunosorbent assay for determination of tissue plasminogen activator applied to patients with thromboembolic disease. *Thrombosis and Haemostasis* 50:740-744. 21.Fujita, M., Nomura, K., Hong, K., Ito, Y., Asada, A. and Nishimuro, S. 1993. Purification and characterization of a strong fibrinolytic enzyme (nattokinase) in the vegetable cheese natto, a popular soybean fermented food in Japan. *Biochemical and Biophysical Research Communications* 197:1340 – 1347. 22.Fujita, M., Ito, Y., Hong, K. and Nishimuro, S. 1995. Characterization of Nattokinase-degraded products from human fibrinogen or cross-linked fibrin. *Fibrinolysis* 9:157 – 164. 23.Hanagata, Y., Okamoto, A., Koizumi, Y. and Yanagida, T. 1994. Basic and Clinical Aspects of Japanese Traditional. *Food Natto* 1:89-99. 24.Kaida, T., Matsuno, H., Niwa, M., Kozawa, O., Miyata, H. and Uematsu, T. 1997. Antiplatelet effect of FK633, a platelet glycoprotein IIb/IIIa antagonist, on thrombus formation and vascular patency after thrombolysis in the injured hamster carotid artery. *Thrombosis and Haemostasis* 77: 562 – 567. 25.Kikuchi, S., Umemura, K., Kondo, K., Saniabadi, A. R. and Nakashima, M. 1998. Photochemically induced endothelial injury in the mouse as a screening model for inhibitors of vascular intimal thickening. *Arteriosclerosis, Thrombosis, and Vascular Biology* 18: 1069 – 1078. 26.Kluft, C., Brakman, P. and Veldhuyzen-Stolk, E. C. 1976. Screening of fibrinolytic activity in plasma euglobulin fractions on the fibrinplate; in Davidson, Samama, Desnoyers, *Progress in chemical fibrinolysis and thrombolysis*. p.57-65. Raven Press, New York. 27.Liu, M. W., Roubin, G. S. and King, S. B. 1989. Restenosis after coronary angioplasty. Potential biologic determinants and role of intimal hyperplasia. *Circulation* 79: 1374 – 1387. 28.Miyazawa, N., Umemura, K., Kondo, K. and Nakashima, M. 1997. Effects of pemirolast and tranilast on intimal thickening after arterial injury in the rat. *Journal of Cardiovascular Pharmacology* 30:157 – 162. 29.Milstone, H. 1941. A factor in normal human blood which participates in streptococcal fibrinolysis. *Journal of Immunology* 42:109-116. 30.Natto Research Center. 1977. National Federation of Cooperatives on Natto:A historical record of natto. p.1-367. Food Pionia, Tokyo. 31.Sherry, S. 1987. Thrombolytic agents for acute evolving myocardial infarction:Comparative effects. *Rational Drug Ther* 21:1-7. 32.Sumii, H. 1977. Oral streptokinase. *Japan Tokyo Koho JP 54-28804*. 33.Sumii, H. and Sasaki, K. 1978. Oral administration of urokinase. 17th Int. p.327. Congr. Hematology, Paris. 34.Sumii, H., Toki, N., Sasaki, K. and Robbins, K. C. 1980. Oral administration of urokinase. *Thrombosis Research* 20:711-714. 35.Sumii, H., Hamada, H., Tsushima, H. and Mihara, H. 1987. A novel fibrinolytic enzyme (Nattokinase) in the vegetable cheese natto: A typical and popular soybean food in the Japanese diet. *Experientia* 43:1110-1111. 36.Sumii, H., Hamada, H., Mihara, H., Nakanishi, K. and Hiratani, H. 1989. Fibrinolytic effect of The Japanese traditional food "NATTO" (Nattokinase). *Thrombosis Haemostas* 62:549. 37.H. Sumii, H. Hamada, K. Nakanishi and H. Hiratani 1990. Enhancement of the fibrinolytic activity in plasma by oral administration of nattokinase, *Acta Haematol.*, 84: 139. 38.Sumii, H., Hamada, H., Tsushima, H. and Mihara, H. 1998. A novel strong fibrinolytic enzyme (nattokinase) in the vegetable cheese "NATTO". *Fibrinolysis* 2(1):67- 185. 39.Saiura, A., Sata, M., Hirata, Y., Nagai, R. and Makuuchi, M. 2001. Circulating smooth muscle progenitor cells contribute to atherosclerosis. *Nature Medicine* 7: 382 – 383. 40.Toki, N., Sumii, H., Sasaki, K., Boreisha, I. and Robbins, K. C. 1985. Transport of urokinase across the intestinal tract of normal human subjects with stimulation of synthesis and/or release of urokinase-type proteins. *Journal clin. Invest* 75: 1212-1222. 41.Third report of the National Cholesterol Education Program (ECEP). 2002. Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III): final report. *Circulation* 106:3143-3421.