

# The Application of Chitin and Chitosan on Dietary Nutrition

李美葉、王三郎

E-mail: 9115138@mail.dyu.edu.tw

## ABSTRACT

In the biochemistry of human nutrition, chitin-chitosan has been reported as capable of reducing the level of cholesterol, or decreasing the digestion and absorption of the fats of food in the intestinal canal. It is also reported that this function is linked to the positive charge it carries. The scholar points out that chitin processed with deacetylation can be used as a material of health foods capable of reducing the level of cholesterol. There's no enzyme in the human intestinal canal, which decompose chitin-chitosan due to its structure is similar to dietary fiber. And it has the same physiological functions as do dietary fibers. Moreover, the chitin-chitosan in the stomach or intestinal canal may chelate other mineral elements and fat-soluble vitamins to decrease the absorption of chitin-chitosan by human body and excrete it. Besides, more studies should be conducted to verify the proliferation of beneficial bacteria in the intestinal canal by chitosan, the influence of chitosan on mucous cells on intestine wall, the optimal amount of chitosan contained in diet (refer to the smallest side effect), the effect of the degree of deacetylation / or effect of molecular weight, and the action of chitosan on other organic molecules with positive/negative charge or polarity in the stomach and intestine, and to confirm the advantages and disadvantages of chitosan. The Cabinet Department of Health has been unwilling to certify and endorse chitin-chitosan as health food, which may be attributable to the fact that some possible negative effects of this substance are still unknown and should be clarified. Therefore, when the special efficacy and functions of chitin-chitosan are being emphasized, we should investigate, with objective thinking, into other possible characteristics of this substance. This study will, from the viewpoint of animal experimentations and cellular research, discuss the physiological impacts of chitin-chitosan and its application to dietary nutrition.

Keywords : chitosan ; chitin ; cholesterol ; health foods ; dietary fiber

## Table of Contents

目錄頁次	封面內頁	簽名頁	授權書	iii	中文摘要	-----	v
英文摘要	-----	vi	誌謝	-----	xiii	目錄	-----
錄	-----	ix	圖目錄	-----	xi	表目	-----
錄	-----	xii	前言	-----	1	文獻整理	-----
介	-----	2	1.1甲殼質之構造	-----	2	1.2甲殼質之性	-----
質	-----	6	1.3甲殼質及其相關產物之製備	-----	11	1.3.1幾丁質的製	-----
備	-----	11	1.3.2幾丁聚醣之製備	-----	14	1.3.3N-乙醯幾丁寡醣的製備與分	-----
離	-----	17	1.4甲殼質及其相關產物之應用	-----	27	第二章甲殼質在膳食營養之應	-----
用	-----	30	2.1 甲殼質在食品應用之相關報告	-----	30	2.2 甲殼質之安全性試	-----
驗	-----	35	第三章 膳食甲殼質對醣類代謝之影響	-----	37	3.1 膳食纖	-----
維	-----	39	3.2 甲殼質似膳食纖維之生理功能	-----	50	3.3 幾丁寡醣之生理功	-----
能	-----	62	第四章 膳食甲殼質對脂質代謝之影響	-----	72	4.1 膳食脂質之消化吸	-----
收	-----	79	4.2 膳食膽固醇對脂質代謝之影響	-----	84	4.3 膳食甲殼質對血脂質代謝之	-----
影響	-----	93	4.4 膳食甲殼質、脂質與健康問題	-----	110	第五章 膳食甲殼質對體內維生素與礦	-----
物質吸收之影響	-----	113	5.1 膳食甲殼質對體內維生素吸收之影響	-----	113	5.2 膳食甲殼質對體內礦物質吸	-----
收之影響	-----	117	第六章 膳食甲殼質在膳食營養應用之未來展望	-----	121	6.1 膳食甲殼質對免疫功能之	-----
影響	-----	121	6.2 膳食甲殼質對建造修補組織之影響	-----	133	6.3 膳食甲殼質對抗菌活性之影	-----
響	-----	139	第七章 討論與結語	-----	150	7.1 討	-----
論	-----	150	7.2 結語	-----	155	參考文	-----
獻	-----	156	圖目錄	-----	156	圖1-1 幾丁質、幾丁聚醣、纖維素的構造	-----
圖目錄	-----	16	圖1-2 幾丁質與幾丁聚醣製備流程	-----	16	圖2-1 幾丁質、幾丁聚醣之製備及其在食品之應用型式	-----
圖1-2 幾丁質與幾丁聚醣製備流程	-----	16	圖2-2 攝食低纖維質或無纖維質飲食對人體之不良影響	-----	49	圖3-1 膳食纖維對降低腸道疾患及對代謝的影響	-----
圖2-2 攝食低纖維質或無纖維質飲食對人體之不良影響	-----	49	圖3-3 幾丁質類物質對降低腸道疾患及對代謝的影響	-----	51	圖3-4 醣類、脂肪、蛋白質代謝共同進入檸檬酸循	-----
圖3-3 幾丁質類物質對降低腸道疾患及對代謝的影響	-----	51	圖4-1 脂質消化、吸收、代謝過程	-----	82	圖4-2 脂質之消化、吸收及運	-----
圖4-1 脂質消化、吸收、代謝過程	-----	82					

輸-----83 圖4-3 正常營養狀況下脂質之代謝-----91 圖4-4 動物中脂質的利用，各部份所擔任的角色-----92 圖4-5 肝臟及脂肪組織是脂肪新陳代謝之首要器官-----96 圖4-6 膽固醇之合成-----109 圖4-7 膽酸與致癌之相關性-----111 圖5-1 維生素 D 之代謝與功能-----115 圖6-1 N-乙醯幾丁寡糖六單元體之抗腫瘤活性與抗微生物活性 之作用機制-----131 圖6-2 兔子胛骨手術後 12 週骨骼癒後情形-----137 圖6-3 成骨細胞經幾丁聚醣處理後培養五天，細胞形成鈣沉積 的立體結構情形-----137 表目錄 頁次 表1-1 幾丁質之分類-----5 表1-2 日本國內甲殼類健康食品之商品規格-----10 表1-3 幾丁質/幾丁聚醣及其衍生物在食品工業之應用-----29 表2-1 甲殼質及其衍生物在膳食營養應用之相關報告-----31 表3-1 餵食不同飼料四週對倉鼠盲腸內菌相組成之影響-----68 表4-1 幾丁質或幾丁聚醣對脂質代謝的影響-----73 表4-2 脂蛋白的大約組成-----89 表4-3 脂蛋白的種類、組成以及代謝角色-----90 表4-4 幾丁聚醣與人體血清膽固醇量之關係-----94 表4-5 攝食幾丁聚醣(四週)對大白鼠脂質代謝的影響-----97 表4-6 攝食幾丁聚醣(十週)對大白鼠脂質代謝的影響-----100 表5-1 維生素 D、維生素 E 之生理功能與缺乏症-----115 表5-2 礦物質的性質-----120 表6-1 大白鼠餵食不同飼料實驗五週血液中白血球、紅血球、 血紅素、血比容積濃度、平均血球血紅素的變化-----123 表6-2 大白鼠餵食不同飼料實驗十週血液中白血球、紅血球、 血紅素、血比容積濃度、平均血球血紅素和血小板含量 的變化-----124 表6-3 餵食不同飼料老鼠血漿中免疫球蛋白 IgA、IgG、游離 脂肪酸、 -羥丁酸、鹼性磷酸?及 -醛醣酸?的含量 -----127
---

## REFERENCES

- 1.光岡知足。1990。腸內-健康。New Food Industry. 32(10): 1-8。2.?本廣司、次田隆志(1994)????生理機能? 利用。食品? 開發29(3):22-22。
- 3.河合忠、水島裕。1991。今日?臨床檢查。pp.235-238。南江堂。東京。4.橋本俊郎。1998。淺漬??變敗乳酸菌?對??、抗菌作用。日本食品科學工學會。45(6):368。
- 5.王三郎、李旭弘。1994。水產廢棄物脫臭加工研究。中華生質能源學會誌。13:229-235。
- 6.王三郎編著。1996。水產資源利用學。高立圖書公司。
- 7.王三郎編著。1997。應用微生物學。高立圖書公司。
- 8.王三郎。1999。海洋未利用生物資源之回收再利用 幾丁質、幾丁聚醣。生物資源生物技術。1:1-8。
- 9.王三郎編著。2000。生物技術。高立圖書公司。
- 10.王三郎。2000。有機廢棄物資源回收再利用 生物資源的開發是無限的寶庫(1)。生物資源、生物技術。2:38-47。
- 11.王綺芬。1989。蟹殼幾丁質產品理化性質測定製 備方法之研究。國立台灣大學食品科技研究所士 論文。
- 12.王貴譽、詹前朕編著。1994。簡明微生物學。129-142。
- 13.江晃榮。1993。農業生物技術。國立編輯館。華香園出版社。
- 14.江晃榮。1995。新時代的生質資源 - 甲殼質的管理與應用。中日 chitosan 第二次學術交流研討會論文集。
- 15.江晃榮。1996。新生技產品:幾丁質、幾丁聚醣(甲殼質)產業現況與展望。經濟部 IT IS 叢書。
- 16.江孟燦、陳敏俐。1999。膳食幾丁聚醣對大白鼠脂質代謝的影響。中國農業化學會誌。
- 17.江孟燦。2000。幾丁質類物質對脂質代謝及腸道生理之影響。2000年台灣幾丁質生物科技研討會論文集。
- 18.呂明洲。1994。Pseudomonas aeruginosa K-181 所生產幾丁質之探討。
- 19.阮進蕙、林翰良、羅淑珍。1997。幾丁聚糖水解物之連續式生產及其抑菌作用。中國農業化學會誌。35:596-611。
- 20.李勳宜。1988。草蝦幾丁聚醣之製備及其應用研究。國立台灣大學食品科技研究所碩士論文。
- 21.李遠豐。1998。蟹殼膠特性應用及其生產技術。9:27-30。
- 22.吳仁永。1999。以酵素生產抑菌性幾丁寡糖及其在牛乳保鮮上的應用。國立台灣海洋大學水產食品科學研究所碩士論文。
- 23.余嘉萱。1999。幾丁聚醣對STZ所誘發之糖尿病大白鼠脂質及碳水化合物代謝之影響。國立海洋大學水產食品科學研究所碩士論文。
- 24.林俊煌。1992。不同去乙醯程度之幾丁聚醣的流便性質與鏈柔軟度、膜之物理特性的關係。國立台灣海洋大學食品科學研究所碩士論文。
- 25.林文源。1995。幾丁聚醣抗菌作用的研究。國立台灣大學食品科技研究所博士論文。
- 26.林宗美。1996。飲食膽固醇與脂肪含量對禁食大白鼠之脂質代謝的影響。私立輔仁大學食品營養 究所碩士論文。
- 27.林欣榜。1999。幾丁類物類在食品加工上之應用。食品工業月刊。31(10)。
- 28.林泓廷。2000。利用纖維素?製備幾丁寡糖及其免疫功能評估。國立海洋大學水產食品科學研究所碩士論文。
- 29.金蘭馨、黃秀珠、洪淑麗、陳文麗、陳秀華、鄭惠珍合著。1995。實用營養學。永大書局。
- 30.邱少華。1997。利用綠膿桿菌 K-187 發酵蝦蟹殼 廢棄物生產幾丁質之應用及量產條件之研究。31.姚賢宗。1998。短期或長期攝食幾丁聚醣對大白鼠 之脂質代謝的影響。國立海洋大學水產食品科學研究 所碩士論文。
- 32.胡淑文、徐善慧、蔡清霖、謝國煌。2001。以三種細胞來評估 gelatin 和 chitosan 之細胞相2001 年幾丁質幾丁聚醣研討會論文集。33.袁國芳。2000。食品工業。食品工業發展研究所。32:1-8。Chitin, chitosan, Proceedings of 1st Inter- national Symposium, 1997。
- 34.袁國芳。2000。幾丁質/幾丁聚醣在膳食與醫療之助益及潛在問題。食品工業月刊。32:1-7。
- 35.梁舜欣。1990。N-乙醯幾丁寡糖之製備。國立台灣 大學農業化學研究所碩士論文。
- 36.郭建良。1995。低分子量幾丁聚醣對雙叉桿菌及其他細菌之影響。國立台灣大學食品科技研究所碩士 論文。
- 37.陳維昭、趙玫君編著。1991。食用營養學。華杏出版公司。
- 38.陳河吉、趙世彬、鄧煦林、蔡東璣、李文齡、周大中編譯。1996。生物化學。藝軒出版社。
- 39.陳坤上、黃佩芬、陳聰松及陳幸臣。1996。幾丁 寡糖製備條件之探討。食品科學。23:874-883。
- 40.陳美惠、莊淑惠及吳志律。1999。幾丁聚醣的物化特性。食品工業月刊。31(10)。
- 41.陳美惠。2000。幾丁聚醣之抑菌作用。食品工業月刊。32(4)。
- 42.游宜屏。1997。幾丁質與幾丁聚醣對吳郭魚及草蝦成長及營養素消化率之影響。 國立台灣海洋大學水產食品科學研究所碩士論文。
- 43.張文智。1996。蝦蟹殼加工之廢棄物回收與再 利用。大葉大學食品工程研究所碩士論文。
- 44.張詔欽。2000。N-乙醯幾丁寡糖的製備與純化及其對腸內細菌生長的影響。國立海洋大學食品科學研究所碩士論文。
- 45.黃昭仁。1998。微生物生產幾丁質塗之研究。大葉大學食品工程研究所碩士論文。
- 46.黃怡雯、蔡國珍。2001。藉動物模式探討具抗菌性幾丁寡糖對腸內細菌之影響。2001年幾丁質幾丁聚醣研討會論文集。
- 47.蔡政芳、林文源、李錦楓

。1993。不同去乙酰度幾丁聚醣的抑菌作用及其澀味。中華生質能源學會會誌。12 (1,2):74。48.蔡國珍、蘇文慧、吳仁永、林泓廷及陳齊聖。2000。幾丁聚醣與幾丁寡醣之抗菌與免疫活性。2000年台灣幾丁質生物科技研討會論文集。49.歐宜書。1998。Pseudomonas aeruginosa K-187生產蛋白質塗之研究。私立大葉大學食品工程研究所碩士論文。50.賴淑琪。1979。水產廢棄物蝦、蟹外殼之高度利用。食品工業。11:23-28。51.簡淑倩、劉一慧。1994。水產食品。22:13。52.蘇遠志。2001。幾丁質與幾丁聚醣之機能及其有效利用。2001年幾丁質幾丁聚醣研討會論文集專輯。53.Abraham, Z. D. and Mehta, T. 1988. Three-week psyllium-husk supplementation:effect on plasma cholesterol concentrations, fecal steroid excretion, and carbohydrate absorption in men. *Am. J. Clin. Nutr.* 47:67-74. 54.Abrams, G. D. 1977. Microbial effects on mucosal structure and function. *Am. J. Clin. Nutr.* 30:1880- 1886. 55.Aiba, S. 1994. Preparation of N-acetylchitooligosaccharides from lysozmic hydrolysates of partially of N-acetylated chitosans. *Carbohydr. Res.* 261:297-306. 56.Aiba, S., and Muraki. E. 1998. Preparation of higher N-acetylchitooligosaccharides in high yields. In *Advances in chitin science*, R. H. Chen, and H. C. Chen. (Ed)., Vol. 3, pp.89-96. Rita Advertising Co., ROC. 57.Allan, C. R. and Hadwiger. L. A. 1979. The fungicidal effect of chitosan on fungi of varying cell wall composition. *Exp. Mycol.* 3:285-287. 58.Allan, G. G, and Peyron. M. 1995a. Molecular weight manipulation of chitosan I: kinetic of depolymerization by nitrous acid. *Carbohydr. Res.* 277:257-272. 59.Allan, G. G., and Peyron. M. 1995b. Molecular weight manipulation of chitosan II: prediction and control of extent of depolymerization by nitrous acid. *Carbohydr. Res.* 277:273-282. 60.Anderson, J. W. and Bridges, S. R. 1984. Short-chain fatty acid fermentation products of plant fiber affect glucose metabolism of isolated rat hepatocytes. *Proc. Soc. Exp. Biol. Med.* 177:372-376. 61.Anderson, J. W. and Akanji, A. O. 1991. Dietary fiber-an overview. *Diabetes Care* 14:1126-1131. 62.Anderson. J. W., Jones, A. E and Mason, S. R. 1994. Ten different dietary fiber have significantly different effect on serum and liver lipids of cholesterol-fed rats. *J. Nutr.* 124:78-83. 63.Austin, P. R., Brine, C. J., Castle, J. E., and Zikakis, J. P. 1981. Chitin new facets of research. *Science* 212:749-753. 64.Bengtsson, G. and Olivercrona, T. 1979. Apolipoprotein CII enhances hydrolysis of monoglycerides by lipoprotein lipase, but the effect is abolished by fatty acids.*FEBS Lett* 106:345-348. 65.Bengtsson, G. and Olivercrona, T. 1980. Lipoprotein lipase. Mechanism of-product inhibition. *Eur. J. Biochem.*106:557-562. 66.Barker, S. A., Foster, A. B., and Webber, J. M. 1958. Amino-sugars and related compounds. Part IV. Isolation and properties of oligosaccharides obtained by controlled fragmentation of chitin. *J. Chem. Soc.* 2218-2227. 67.Berggren, A. M., Nyman, E. M. G. L., Lundquist, I., and Bjorck, I. M. E. 1996. Influence of orally and rectally administered propionate on cholesterol and glucose metabolism in obese rats. *Br. J. Nutr.* 76:287-294. 68.Bingham, S., Williams, D. D. R., and Cummings, J. H. 1985. Dietary fiber consumption in Britain; new estimates and their relation to large bowel cancer mortality *Br. J. Cancer* 52:399-402. 69.Bingham, S. 1987. Definitions and intakes of dietary fiber. *Am. J. Clin. Nutr.* 45:1226-1231. 70.Biagini, G., Muzzarelli, R. A. A., Giardino, R., and Castaldini, C. 1992. Biological materials for wound healing. In "Advance in chitin and chitosan" Brine, C. J., Sandford. P. A., and Zikakis. J. P. (eds.). pp.16-24. Elsevier Applied Science. London and New York. 71.Borah. G., Scott, G., and Wortham. K. 1992. Bone induction by chitosan in endochondral bones of the extremities. In "Advance in chitin and chitosan". Brine. C. J., Sandford. P. A. and Zikakis, J.P. (eds.), pp.47-53. Elsevier Applied Science, London and New York. 72.Bornet, F. R. J., Alamowitch, C., and Slama, G. 1995. Methods to assess glucose metabolism in humans in relation to carbohydrate and fibre in the diet. *Eur. J. Clin. Nutr.* 49 (3) : S97-S104. 73.Bouhnik, Y., Fourie, B., Riottot, M., Bisetti, N., Gailing, M. F., Guibert, A., Bornet, F., and Rambaut, J. C. 1996. Effects of fructo-oligosaccharides ingestion on fecal bifidobacteria and selected metabolic indexes of colon carcinogenesis in healthy humans. *Nutr. Cancer.* 26:21-29. 74.Bouhnik, Y., Vahedi, K., Achour, L., Attar, A., Salfati, J., Pochart, P., Marteau, P., Flourie, B., Bornet, F., and Rambaut, J. C. 1999. Short-chain fructooligosaccharide administration dosedependently increases fecal bifidobacteria in healthy humans. *J. Nutr.* 129:113-116. 75.Bridges, S. R., Anderson, J. W., Deakins, D. A., Dillon, D. W., and Wood, C. L. 1992. Oat bran increases serum acetate of hypercholesterolemic men. *Am. J. Clin. Nutr.* 56:455-459. 76.Brown, M. S. and Goldstein, J. L. 1975. Regulation of activity of the low density lipoprotein receptor in human fibroblast. *Cell.*6:307-316. 77.Brown M. S. and Goldstein, J. L. 1986. A receptor-mediated pathway for cholesterol homeostasis. *Science.*232:34-47. 78.Brown, N. J., Worldling, J., Rumsey, R. D. E., and Read, N. W. 1988. The effect of guar gum on the distribution of a radiolabelled meal in the gastrointestinal tract of the rat. *Br. J. Nutr.* 59:223-231. 79.Bueno, L., Praddaude, J., Fioramonti, J., and Ruckebusch, Y. 1981. Effect of dietary fiber on gastrointestinal motility and jejunal transit time in dogs. *Gastroenterology* 80:701-707. 80.Bugaut, M. and Bentejac, M. 1993. *Annu. Rev. nutr.* 13:217-241. 81.Crociani, F., Alessandrini, A., Mucci, M. M., and Biavati, B. 1994. Degradation of complex carbohydrates by Bifidobacterium spp. *Int. J. Food Microbiol.* 24:199-210. 81.Burkitt, W. P. 1971. Epidemiology of cancer of the colon and rectum. *Cancer* 28:3-13. 82.Caderni, G., Luceri, C., Lancioni, L., Tessitore, L., and Dolara, P. 1998. Slow release pellets of sodium butyrate increase apoptosis in the colon of rats treated with azoxymethane, without affecting aberrant crypt foci and colonic proliferation. *Nutr. Cancer* 30:175-181. 83.Campbell, P. J., Mandarino, L. J., and Gerich, J. E. 1988. Quantification of the relative impairment in actions of insulin on hepatic glucose production and peripheral glucose uptake in non-insulin-dependent diabetes mellitus. *Metabolism* 37:15-21. 84.Carolan, C. A., Blair, H. S., Allen, S. J., and McKay, G. N. 1991. O-carboxymethyl chitosan a water soluble derivative and potential green food preservative. *Trans IChemE* 69:195. 85.Cassidy, M. M., Lightfoot, F. G., and Vahouny, G. V. 1982. Morphological aspects of dietary fiber in the intestine. *Adv. Lipid Res.* 19:203-229. 86.Chang, J. J. and Hash, J. H. 1979. The use of an amino acid analyzer for the rapid identification and quantitative determination of chitosan oligo- saccharides. *Anal. Biochem.* 95:563-567. 87.Chatelet, C., Damour, O., and Domard, A. 2001. "Influence of the degree of acetylation on some biological properties of chitosan film", *biomaterials*, 22:261-268. 88.Cheetham, N. W. H. and Sirimanne, P. 1981. High-performance liquid chromatographic separation of carbohydrate oligomers. *J. chromatogr.* 207:439-444. 89.Chen, W. L., Anderson, J. W., and Jennings, D. 1984. Propionate may mediate the hypocholesterolemic effects of certain soluble plant fibers in cholesterol feed rats. *Pro. Soc. Exp. Bio. Med.* 174:2158-2158. 90.Chen, S. W., and Chen, H. C. 1999. Effect of oral administration of Cellulomonasflavigena NTOU 1- degraded

chitin hydrolysate on physiological changes in rates. *Food Sci. Agric. Chem.* 1:186-189. 91. Cherbut, C., Albina, E., Champ, M., Doublier, J. L., and Lecannu, G. 1990. Action of guar gum on the viscosity of digestive contents and on the gastrointestinal motor function in pigs. *Digestion* 46:205-213. 92. Cherbut, C. 1995. Role of gastrointestinal motility in the delay of absorption by dietary fibre. *Eur. J. Clin Nutr.* 49 (3) : S74-S80. 93. Chitin, chitosan, Proceedings of 3rd International Symposium, 1985. 94. Chitin, chitosan, Proceedings of 5th International Symposium, 1991. 95. Chitin, chitosan, Proceedings of 1st Asia-Pacific chitin and chitosan Symposium, 1994. 96. Chung, L. Y., Schmidt, R. J., Hamlyn, P. F., Sagar, B. F., Andrew, A. M., and Turner, T. D. 1994. Biocompatibility of potential wound management products: fungal mycelia as a source of chitin/chitosan and their effect on the proliferation of human F1000 fibroblasts in culture. *J. Biomed. Mater. Res.* 28:463-469. 97. Costa, M. A., Meththa, T., Males, J. R. 1989. Effects of dietary cellulose, psyllium husk and cholesterol level on fecal and colonic microbial metabolism in monkeys. *J. Nutr.* 119:986-992. 98. Cummings, J. H., Hill, M. J., Bone, E. S., Branch, W. J., and Jenkins, D. J. A. 1979. The effect of meat protein and dietary fiber on colonic function and metabolism. 2. Bacterial metabolites in feces and urine. *Am. J. Clin Nutr.* 32:2094-2101. 99. Cumming, J. H., Gibson, G. R., and MacFarlane, G. T. 1989. *Vet. Scand.* 86:76-82. 100. Cummings, J. H. and Englyst, H. N. 1991. Trends in food science and technology. April, pp.99-103. 101. Dambekodi, P. C. and Gilliland, S. E. 1998. Incorporation of cholesterol into the cellular membrane of *Bifidobacterium longum*. *J. Dairy Sci.* 81:1818-1824. 102. Darmadji, P. and Izumimoto, M. 1994. Effect of chitosan in meat preservation. *Meat Sci.* 38:243-254. 103. Davis, R. A., McNeal, M. M., and Moses, R. L. 1982. Intrahepatic assembly of very low density lipoprotein. *J. Biol. Chem.* 257:2634-2640. 104. Defaye, J., Gabelle, A., and Pedersen, C. 1989. Chitin and chitosan oligosaccharides. In *Chitin and Chitosan*, G. Sajak-Brek, T. Anthonsen, and P. Sandford (Ed.), pp.415-429. Elsevier Science Publishers Ltd, England. 105. Deguchi, Y., Makino, A., Iwabuchi, A., Watanuki, M., and Yamashita, T. 1993. Microbial Ecology in health and disease. 6:85-94. 106. Delben, F., Stefanichi, S., and Muzzaralli, R. A. A. 1992. Chelating ability and enzymatic hydrolysis of water-soluble chitosan. *Carbohydr. Polym.* 19:17-23. 107. De Man, F. H. A. F., Castro Cabezas, M., Van Barlingen, H. H. J. J., Erkelens, D. W., and De Bruin, T. W. A. 1996. Triglyceride-rich lipoprotein in non-insulin-dependent diabetes mellitus: post-prandial metabolism and relation to premature atherosclerosis. *Eur. J. Clin. Invest.* 26:89-108. 108. Deshpande, M. V. 1986. Enzymatic degradation of chitin & its biological application. *J. Sci & Ind. Res.* 45:273-277. 109. Deuchi, K., Kanauchi, O., Imasato, Y., and Kobayashi, E. 1994. Decreasing effect of chitosan on the apparent fat digestibility by rats fed on a high-fat diet. *Biosci. Biotech. Biochem.* 58 : 1613-1616. 110. Deuchi, K., Kanauchi, O., Imasato, Y., and Kobayashi, E. 1995. Effect of the viscosity or deacetylation degree of chitosan on fecal fat excreted from rats fed on a high-fat diet. *Biosci. Biotech. Biochem.* 59 : 781-785. 111. Dietrich K. 1984. " Use of chitinous polymers in food " *Food Technol.* 86-97. Jan. 112. Dietrich K. 1991. " Recovery and utilization of chitin and chitosan in food processing waste management " . *Food Technol.* pp.114-122. Jan. 113. Ding, Y. A., Chang, W. K., and Chen, M. L. 1992. Changes in nutritional supply and atherosclerotic disease from 1945 to 1989 in Taiwan. *J. Clin. Biochem. Nutr.* 13:137-146. 114. Djouzi, B. Z., and Andrieux, C. 1997. Compared effects of three oligosaccharides on metabolism of intestinal microflora in rats inoculated with a human faecal flora. *Brit. J. Nutr.* 78:313-324. 115. Domard, A. and Cartier, N. 1989. Glucosamine oligomers: 1. Preparation and characterization. *Int. Biol. Macromol.* 11:297-302. 116. Duechi, K., Kanauchi, O., Shizukuishi, M., and Kobayashi, E. 1995. Continuous and massive intake of chitosan effects mineral and fat-soluble vitamin status in rats fed on a high-fat diet. *Biosci. Biochem.* 59:1211-1216. 117. Eckel, R. E. 1989. Lipoprotein Lipase. A multi-functional enzyme relevant to common metabolic diseases. *N. Engl. J. Med.* 320:1060-8. 118. Eveson, G. T., Daggy, B. P., McKinley, C., and Story, J. A. 1992. Effects of psyllium hydrophilic mucilloid on LDL-cholesterol and bile acid synthesis in hypercholesterolemic men. *J. Lipid Res.* 33:1183-1192. 119. Fang, S. W., Li, C. F., and Shih, D. Y. C. 1994. Antifungal activity of chitosan and its preservative effect on low-sugar candied kumquat. *J. Food Prot.* 56 :136-140. 120. Fernandez, M. L., Conde, A., Ruiz, L. R., Montano, C., Ebner, J., and McNamara, D. J. 1995. Carbohydrate type and amount alter intravascular processing and catabolism of plasma lipoprotein in guinea pigs. *Lipids* 30:619-626. 121. Forstner, J. F. 1978. Intestinal mucins in health and disease. *Digestion.* 17:234-263. 122. Francis Suh, J. K. and Matthew, H. W. T. 2000. Application of chitosan-based polysaccharide biomaterials in cartilage tissue engineering: a review, *Biomaterials.* 21:2589-2598. 123. Fukada, Y., Kimura, K., and Ayaki, Y. 1991. Effect of chitosan feeding on intestinal bile acid metabolism in rats. *Lipids* 26:395-399. 124. Fukugawa, N. K., Anderson, J. W., Hageman, G., Young, V. R., and Minaker, K. L. 1990. High carbohydrate, high-fiber diets increase peripheral insulin sensitivity in healthy young and old adults. *Am. J. Clin. Nutr.* 52:524-528. 125. Fungwe, T. V., Cagen, L. M., Wilcox, H. G., and Heimberg, M. 1992. Regulation of hepatic secretion of very low density lipoprotein by dietary cholesterol. *J. Lipid Res.* 33:179-191. 126. Gallathar, D. D., Hassel, C. A., Lee, K., and Gallaher, C. M. 1993. Viscosity and fermentability as attributes of dietary fiber responsible for the hypocholesterolemic effect in hamsters. *J. Nutr.* 123:244-252. 127. Gambera, P. J., Schnessman, B. O., and Davis, P. A. 1995. Use of the food guide pyramid and US dietary guidelines to improve dietary intake and reduce cardiovascular risk in active-duty air force members. *J. Am. Diet. Assoc.* 95:1268-1273. 128. Gee, J. M., Lee-Finglas, W., Wortley, G. W., and Johnson, I. T. 1991. Fermentable carbohydrates elevate plasma enteroglucagon but high viscosity is also necessary to stimulate small bowel mucosal cell proliferation in rats. *J. Nutr.* 126:373-379. 129. Gestel, G., Besacon, P., and Rouanet, J. M. 1994. Comparative evaluation of the effects of two different forms of dietary fibre (rice bran vs. wheat bran) on rat colonic mucosa and fecal microflora. *Ann. Nutr. Metab.* 38:249-256. 130. Gibson, G. R. and MacFarlane, G. T. 1994. In: *Human Health: The Contribution of Microorganism.* pp.53-62. Springer-Verlag, London, U.K. Gibson, G. R., Beatty, E. R., Wang, X., and Cummings, J. H. 1995. *Gastroenterology.* 108:975-982. 131. Gilliland, S. E., Nelson, C. R., and Maxwell, C. 1985. Assimilation of cholesterol by *Lactobacillus acidophilus*. *Appl. Environ. Microbiol.* 49:377-381. 132. Gleen, R. G. and George, T. M. 1995. Human colonic bacteria: role in nutrition, physiology and pathology. Cummings, J. H. (Ed.), pp.61-72. CRC Press. Inc. 133. Glore, S. R., Treeck, D. V., Knehans, N. W., and Guild, M. 1994. Soluble fiber and serum lipids: a literature review, *J. Am. Diet. Assoc.* 94:425-436. 134. Goldin, B. R., Swenson, L., Dwyer, J.,

Sexton, M., and Gorbach, S. L. 1980. Effect of diet and *Lactobacillus acidophilus* supplements on human fecal bacterial enzyme. *JNCI* 64:255-261.

135. Goodlad, R. A., Ratcliffe, B., Fordham, J. P., and Wright, N. A. 1989. Dose dietary fiber stimulate intestinal epithelial cell proliferation in germ free rats? *Gut*. 30:820-825.

136. Goodlad, R. A., Ratcliffe, B., Lee, C. Y., and Wright, N. A. 1995. Dietary fibre and the gastrointestinal tract: differing trophic effects on muscle and mucosa of the stomach, small intestine and colon. *Eur. J. Clin. Nutr.* 49 (3) : S178-S181.

137. Gorbach, V. I., Krasikova, I. N., Lukyanov, P. A., Loenko, Y. N., Soloveva, T. F., Ovodov, Y. S., Deev, V. V., and Pimenov, A. A. 1994. New glycolipids (chitooligosaccharide derivatives) possessing immunostimulating and antitumor activities. *Carbohydrate Res.* 260:73-78.

138. Groop, L. C., Bonadonna, R. C., Delprato, S. et al. 1989. Glucose and free fatty acid metabolism in non-insulin-dependent diabetes mellitus. Evidence for multiple sites of insulin resistance. *J. Chem. Invest.* 84:205-13.

139. Grundy, S. M. 1983. Absorption and metabolism of dietary cholesterol. *Ann. Rev. Nutr.* 3:71-96.

140. Grundy, S. M. 1986. Cholesterol and coronary heart disease.: A new era. *JAMA* 256:2849-2858.

141. Han, L. K., Kimura, Han, L. K., and Okuba, H. 1999. Reduction in fat storage during chitin-chitosan treatment in mice fed a high-fat diet. *International J. Obesity.* 23 (2) : 174-179.

142. Hara, H., Haga, S., Kasai, T., and Kiriya, S. 1998. Fermentation products of sugar-beet fiber by cecal bacteria lower plasma cholesterol concentration in rats. *J. Nutr.* 138:688-693.

143. Hasegawa, M., Isogi, A., and Onabe, F. 1993. Preparation of low-molecular-weight chitosan using phosphoric acid. *Carbohydr. Polym.* 20:279-283.

144. Heller, S., Hackler, L., Rivers, J., Van Soest, P., Roe, D., Lewis, B., and Robertson, J. 1980. Dietary fiber: the effect of particle size of wheat bran on colonic function in young adult men. *Am. J. Clin. Nutr.* 33:1734-1744.

145. Hicks, K. B. 1988. Isolation of oligomeric fragments of chitin by preparative high- performance liquid chromatography. *Meth. Enzymol.* 161:410-416.

146. Hill, M. J., Crowther, J. S., Drasar, B. S., Hawksworth, G., Aries, V., and Williams, R. E. O. 1971. Bacteria and the aetiology of cancer of the large bowel. *Lancet* i. pp.95-100.

147. Hirano, S. and Nagao, N. 1989. Effects of chitosan, pectic acid, lysozyme and chitinase on the growth of several phytopathogens. *Agric. Biol. Chem.* 53:3065-3066.

148. Hirano, S. 1989. Production and application of chitin and chitosan in Japan. I " Chitin and Chitosan. Skjak-Braek, G., Anthonsen. T.. Sand-ford, P. (Eds). Elsevier Applied Science. London, UK.

149. Hirano, S., Itakura, C., Seino, H., Akiyama, Y., Nonaka, I., Kanbara, N., and Kawakami, T. 1990. Chitosan as an ingredient for domestic animal feeds. *J. Agric. Food Chem.* 38:1214.

150. Hirano, S. and Akiyama, Y. 1995. Absence of hypocholesterolaemic action of chitosan in high serum cholesterol rabbits. *J. Sci. Food Agric* 69:91-94.

151. Hoskins, L. C. and Zamcheck, N. 1968. Bacterial degradation of gastrointestinal mucins. *Gastroenterology* 54:210-217.

152. Ikeda, I., Tomari, Y., and Sugano, M. 1989. Interrelated effect of dietary fiber and fat on lymphatic cholesterol and triglyceride absorption in rats. *J. Nutr.* 119:1383-1387.

153. Ikeda, I., Sugano, M., Yoshida, K., Sasaki, E., Iwamoto, Y., and Hatano, K. 1993. Effects of chitosan hydrolysates on lipid absorption and on serum and liver lipid concentration in rats. *J. Agric. Food Chem.* 41:431-435.

154. Ink, S. L. and Hurt, H. D. 1987. Nutritional implications of gums. *Food. Tech.* 41:77-82.

155. Ishibashi, N. and Shimamura, S. 1993. Bifidobacteria : research and development in Japan. *Food Technol.* 6:126-135.

156. Ishikawa, F., Takayama, H., Matsunoto, K., Ito, M., Deguchi, O., Kikuchi-Hayakawa, H., and Watanuki, M. 1995. Bifidus. 9:5-18 (in Japanese).

157. Ito, M., Deguchi, Y., Matsumoto, K., Kimura, M., Onodera, N., and Yajima, T. 1993. Influence of galactooligosaccharides on the human fecal microflora. *J. Nutr. Sci. Vitaminol.* 39:635-640.

158. Izume, M. and Ohtakara, A. 1987. Preparation of D-glucosamine oligosaccharides by the enzymatic hydrolysis of chitosan. *Agric. Biol. Chem.* 51:1189-1191.

159. Izume, M., Nagae, S., Kawagishi, H., Mitsutomi, M., and Ohtakara, A. 1992. Biosci. Biotech. Biochem. 56:448-453.

160. Izume, M., Nagae, S., Kawagishi, H., and Ohtakara, A. 1992. Preparation of N-acetylchitooligosaccharides from enzymatic hydrolysates of chitosan. *Biosci. Biotech. Biochem.* 56:1327-1328.

161. Jacobs, L. R. 1987. Effect of dietary fiber on colon cell proliferation and its relationship to colon carcinogenesis. *Prev. Med.* 16:566-571.

162. Jao, Y. C., Mikolajcik, E. M., and Hansen, R. M. T. 1978. Growth of *Bifidobacterium bifidum* var. *pennsylvanicus* in laboratory media supplemented with amino sugars and spent broth from *Escherichia coli* *J. Food Sci.* 43:1257-1263.

163. Jenkins, D. J. A., Leeds, A. R., Newton, C., and Cummings, J. H. 1975. Effect of pectin, guar gum and wheat fibre on serum-cholesterol. *Lancet* i. pp.116-117.

164. Jenkins, D. J. A., Wolever, T. M. S., Leens, A. R., Gassull, M. S., Haisman, P., Dilawari, J., Goff, D. V., Metz, G. L., and Alberti, K. G. M. M. 1978. Dietary fibers, fibre analogues and glucose tolerance importance of viscosity. *Br. Med. J.* 1:1392-1394.

165. Jenkins, D. J. A., Jenkins, A. L., Wolever, T. M. S., Vuksan, V., and Venken, A. 1995. Effect of reduced rate of carbohydrate absorption on carbohydrate and lipid metabolism. *Eur. J. Clin. Nutr.* 49 (3) : S68-S73.

166. Jennings, C. D., Boleyn, K., Bridges, S. R., Wood, P. L., and Anderson, J. W. 1988. A comparison of the lipid lowering and intestine morphological effect of cholestyramine, chitosan, and oat gum in rats. *Soc. Exp. Biol. Med.*, 189:13-20.

167. Jensen, C. D., Spiller, G. A., Gates, J. E., Miller, A. F., and Whittan, J. H. 1993. The effect of acacia gum and a water soluble dietary fibre mixture on blood lipids in humans. *J. Am. Coll. Nutr.* 12:147-154.

168. Jeon, Y. J., and Kim, S. K. 1998. Bioactivities of chitosan oligosaccharides and their derivatives. In *Advances in Chitin Science*, R. H. Chen, and H. C. Chen, (Ed.), Vol. 3, pp.328-333. Rita Advertising Co., ROC.

169. Jeon, Y. J., and Kim, S. K. 2000a. Continuous production of chitooligosaccharides using a dual reactor system. *Process Biochem.* 35:623-632.

170. Jeon, Y. J., and Kim, S. K. 2000b. Production of chitooligosaccharides using an ultrafiltration membrane reactor and their antibacterial activity. *Carbohydr. Polym.* 41:133-141.

171. Jing, S. B., Li, L. S., Ji, D. X., Takiguchi, Y., and Yamaguchi, T. 1997. Effect of chitosan on renal function in patients with chronic renal failure. *J. Pharmacy & Pharmacology.* 49 (7):721-723.

172. Kaaks, R. and Riboli, E. 1995. Colorectal cancer and intake of dietary fibre. A summary of the epidemiological evidence. *Eur. J. Clin. Nutr.* 49 (3) :S10-S17.

173. Kanauchi, O., Deguchi, K., Imasato, Y., and Kobayashi, E. 1994. Increasing effect of a chitosan and ascorbic acid mixture on fecal dietary fat excretion. *Biosci. Biotechnol. Biochem.* 58:1617-1620.

174. Kanauchi, O., Deguchi, K., Imasato, Y., Shizukuishi, M., and Kobayashi, E. 1995. Mechanism for the inhibition of fat digestion by chitosan and for the synergistic effect of ascorbate. *Biosci. Biotech. Biochem.* 59 : 786-790.

175. Kawase, K., Suzuki, T., Kiyosawa, I., Okonogi, S., Kawashima, T., and Kuboyama, M. 1981. Bifido- bacteria Microflora. 2:25-31.

176. Kay, R. M. and Strasberg, S.

M. 1978. Origin, Chemistry, Physiological effects and clinical importance of dietary fiber. *Clin. Invest. Med* 1:9- 24. 177. Kelsay, J. L., Behall, K. M., and Prather, E. S. 1978. Effect of fiber from fruits and vegetables on metabolic responses of human subjects. I. Bowel transit time, number of defecation, fecal weight, urinary excretion of energy and nitrogen and apparent digestibilities of energy, nitrogen and fat. *Am. J. Clin. Nutr.* 31:1149-1153. 178. Kendar, D. F. and Hadwiger, L. A. 1984. Characterization of the smallest chitosan oligomer that is maximally antifungal to *Fusarium solani* and elicits pisatin formation in *Pisum sativum*. *Exp. Mycol.* 8:276-281. 179. Kennedy, R., Costain, D. J., McAlister, V. C., and Lee, T. D. 1996. Prevention of experimental postoperative peritoneal adhesion by N, O-carboxymethyl chitosan. *Surgery.* 120:866-870. 180. Kim, Y. S., Taso, D., Siddiqui, B., Whitehead, J. S., and Arnstein, P. 1980. Effect of sodium butyrate and DMSO on biochemical properties of human colon cancer cells. *Cancer* 45:1185-1192. 181. Kirby, R. W., Anderson, J. A., Sieling, B., Rees, E. D., Chen, W. L., Miller, R. E., and Kay, R. M. 1981. Oat bran selectively lowers serum low-density lipoprotein cholesterol concentrations of hypercholesterolemic men. *Am. J. Clin. Nutr.* 34:824-829. 182. Klaver, F. A. M. and Meer, R. V. D. 1993. The assumed assimilation of cholesterol by *Lactobacilli* and *Bifidobacterium bifidum* is due to their bile salt-deconjugating activity. *Appl. Environ. Microbiol.* 59:1120-1124. 183. Klokkevold, P. R., Lew, D. S., Ellis, D. G., and Bertolami, C. N. 1991. Effect of chitosan on lingual hemostasis in rabbits. *J. Oral Maxillofac. Surg.* 49:858-863. 184. Klokkevold, P. R., Vandemark, L., Kenney, E. B., and Bernard, G. W. 1996. Osteogenesis enhanced by chitosan in vitro. *J. Peri-odont.* 67:1170-1175. 185. Klurfeld, D. M. 1992. Dietary fiber-mediated mechanisms in carcinogenesis. *Cancer Res.* 52:2055s-2059s. 186. Knorr, D. and Betschat, A. A. 1981. Water absorption and loaf volume of protein fortified breads. *Food Sci. Technol.* 14:306-312. 187. Knorr, D. 1983. Dye binding properties of chitin and chitosan. *J. Food Sci.* 48:36. 188. Knorr, D. 1984. Use of chitinous polymers in food. A challenge for food research and development. *Food Technol.* 38:85-97. 189. Kobayashi, T., Otsuka, S., and Yugari, Y. 1979. Effect of chitosan on serum and liver cholesterol levels in cholesterol-fed rats. *Nutr. Rep. Int.* 190. Kobayashi, M., Watanabe, T., Suzuki, S., and Suzuki, M. 1990. *Microbiol. Immunol.* 34:413-426. 190. Koide, S. S. 1998. Chitin-chitosan: properties, benefits and risks. *Nutrition Research* 18:1091-1101. 191. Kratz, G., Amander, C., Swedenborg, J., Back, M., Falk, C., Gouda, I., and Larm, O. 1997. Heparin-chitosan complexes stimulate wound healing in human skin. *Scandinavian J. Plastic & Reconstructive Surgery & Hand Surgery.* 31:119-123. 192. Kratz, G., Back, M., Amander, C., and Larm, O. 1998. Immobilized heparin accelerates the healing of human wounds in vivo Scandinavian. *J. Plastic & Reconstructive Surgery & Hand Surgery.* 32:381-385. 193. Kritchevsky, D. and Story, J. A. 1974. Binding of bile salts in vitro by non nutritive fibre. *J. Nutr.* 104:458-464. 194. Lakesmanan, M. R., Nepokroeff, C. M., Nes, G. C., Dugan, R. E., and Porter, J. W. 1973. Stimulation by insulin of rat liver -OH- -methylgluteryl CoA reductase and cholesterol synthesizing activities. *Biochem. Biophys. Res. Commun.* 50:704-710. 195. Landes, D. R. and Bough, W. A. 1976. Effect of chitosan in the diets of rats on growth and liver and blood composition. *Bull. Environ. Contam. Toxicol.* 15:555-536. 196. Lehoux, J. G. and Grondin, F. 1993. Some effect of chitosan on liver function in the rat. *Endocrinol.* 132:1078-1084. 197. Lim, B. O., Yamada, K., Nonaka, M., Kuramoto, Y., Hung, P., and Sugano, M. 1997. Dietary fibers modulate induces of intestinal immune function in rats. *J. Nutr.* 127:663-667. 198. Linder, M. C. 1985. Nutritional biochemistry and metabolism with clinical applications. pp.28- 31. Eksevier, New York. 200. Livesey. 1990. *Am. J. Clin. Nutr.* 51:617-637. Lupton, J. P., Coder, D. M., and Jacobs, L. R. 1988. Long-term effect of fermentable fiber on rat colonic pH and epithelial cell cycle. *J. Nutr.* 118:840-845. 201. Maeda, M., Murakami, H., Ohta, H., and Tajima, M. 1992. Stimulation of IgM production in human-human hybridoma HB4C5 cells by chitosan. *Biosci. Biochem.* 56:427-431. 202. Maezaki, Y., Tsuji, K., Nakagawa, Y., Kawai, Y., Akimoto, M. 1993. Hypocholesterolemic effect of chitosan in adult