The E ffect of Chitosan for Medicines

易延陵、王三郎 ; ? ; 耀國

E-mail: 9318452@mail.dyu.edu.tw

ABSTRACT

The objective of this study is to discuss about how chitosan effects on drug release by means of diverse proportions of chitosan dosage, granulating processes, and ways of chitosan dosage to compare the various results from tablet dissolution profile tests to presumably surmise how drugs release in human bodies. To figure out, during tabletting process which consists of chitosan, if there is any significant variety from parameters, such as thickness, hardness, and disintegration tests, two different kinds of drugs are chosen to be the objects of the experiment to research the roles chitosan plays in by designing prescriptions according to functions of the two drugs themselves respectively. Based on those released researches, chitosan would increase the absorption of medicine. A well-known pain reliever Acetaminophen was chitosan as one of the experimental objects to see if chitosan caused the drug release rapidly to suggest that it ease the pains in human bodies very shortly. In comparison with samples from marketable drugs, after the experiments of pain relieving, it concludes that different proportion of chitosan dosage makes different drug release rate. The principle of prescription design is to apply the character of acid-soluble chitosan. Hence, while Acetampoplien is under acid environments with the character of chitosan itself, it expectably shall come to a result of rapid medicine release. There is another choice motion sickness medicine, Meclizine HCl, for some long journey travelers, they need to retake medicine because it merely lasts for about 3 to 4 hours if they take regular motion sickness relief. If they don''t, they may suffer from indisposition, vomit, and drowsiness caused by motion sickness during the rest of the journey. Consequently, the experiments indicated that different proportions of chitosan dosages minimize the drug release to extend the time in the stomach to keep its availability longer respectively, because chitosan forms colloid coating after absorbing water. Therefore, we can make chitosan work its best via prescription designs according to its various characters on different drugs.

Keywords : Chitosan ; Dissolution profile ; Control Release ; Rapid Release ; Delay Release ; Acetaminophen ; Meclizine HCl

Table of Contents

REFERENCES

1. 97.Zhao, F., Y. Yin, W. W. Lu, J. C. Leong, W. Zhang, M. Zhan王三郎(2000)，水產資源利用學，高立圖書公司。 2. 王三郎(1998)，應用微生物學，高立圖書出版社。 3. 王三郎(1999)，海洋未利用生物資源之回收再利用-幾丁質及幾丁聚醣，生物資源 生物技術, 1:1-8。 4.王正一、林峰輝(2000)，生醫材料概論，教育部醫學工程科技教育改進計劃，台北，44-45。 5.王啟浩(1999)，利用細菌發酵農水產廢棄物生產生物製劑之研究.大葉大學食品工程研究所碩士論文。 6.田福助(1988)，電化學基本原理與應用，五洲出版社，台北，11-20。 7.生物技術產業資訊叢書(1989)，藥物控制釋放劑型技術與市場分析，財團法人生物產業資訊叢書。 8.呂明洲(1994)，Pseudomonas aeruginosa K-181 所產幾丁質分解酵素之探討.大葉工學院食品工程研究所碩士論文。 9.李安榮、鄒台黎(2000)，新編藥物學，永大書局有限公司，台北，38。 10.邱少華(2000)，幾丁聚醣在藥物控制釋放上的應用以及其微膠囊製備的技術，生物資源 生物技術，2(3)，19-23。 11.林佳姣、張曉婷、吳柏昇、林睿哲(2001)，幾丁聚醣於生醫材料之應用與特性，化工，48(2)，84-91。 12.林錫杰(2000)，幾丁質在環保方面之應用，食品技術，32(7)，27-33。 13.林睿哲，莊文喜(2000)，血液相容性高分子生醫材料，化工技術，8(10)，230-240。 14.吳永志、陳松青、林宥欣、梁祥發、糜福龍、宋信文(2003)，水溶性幾丁聚醣酸鹼應答型水膠之製備及其蛋白質藥物包覆與制放行為探討，第二十六屆高分子研討會。 15.吳襄、林坤偉(1994)，生理學大綱，藝軒圖書出版社，台北，44-45。 16.洪敏元、劉良慧、林育娟、何明聰、賴明華(2000)，當代生理學，華杏出版股份有限公司，台北，41-42。 17.莊仲揚(2002)，幾丁聚醣於生醫產業上的應用，化工資訊，16(4)，46-50。 18.陳美惠、莊淑惠、吳志津(1999)，幾丁聚醣的物化特性，食品工業月刊，31(10)，1-6。 19.陳美惠(2000)，幾丁聚醣之抑菌作用，食品工業月刊，32(4)，29-38。 20.陳慶鴻圖(2000)，幾丁聚醣在藥物運送系統上之應用，食品工業月刊，32(4)，18-28。 21.楊禎明、林浩慈(2001)，含肝素的改質熱可塑性橡膠在血液相容性的研究，化工，48(2)，78-83。 22.張根源(2001),智慧型料之生物醫學應用,化工,48(2),53-61。 23.劉興華、陳思萍(1996)，簡明藥物學，華杏出版社，台北，11-12。 24.蘇遠志(2001)，幾丁質與幾丁聚醣之機能及其有效利用，生物資源 生物技術，3(2)，6-19。 25.闕山璋(1998)，淺談骨科生醫材料之展望，工業材料，4(136)，81-84。 26.Akbuga J. and Durmaz, G.(1994) Preparation and evaluation of crosslinked chitosan microspheres containing furosemide. Int. J. Pharm. 100: 257-261. 27.Akbuga J. and Durmaz, G.(1994) Preparation and evaluation of crosslinked chitosan microspheres containing furosemide. Int. J. Pharm. 111: 217-222. 28.Allan, G. G.(1985) US patent No. 4,532,267. Vision correctionlens made from an aminopolysaccharide compound or an ether or ester thereof. Board of Regents, University of Washington,Seat-tle, Washington. 29.Araki,Y.and Ito,E.(1975) A pathway of chitosan formation inMucor rouxii. Enzymatic deacetylation of chitin. Eur. J.Biochem.56:669-674. 30.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. (ends.). p16-24. Eisevier Applied Science. London and New York. 31.Borah. G.,Scott,G. and Wortham, K(1992)Bone induction by chitosan in endochondra! Bones of the extremities. In“ Advance in chitin and chitosan ”. Brine, C. J.,Sandford, P. A. and Zikakis. J. P. (eds.), p47-53. Eisevier Applied Science, London and New York. 32.Brine, C. J.(1989) Controlled release pharmaceutical applications of chitosan. In“ Chitin and Chitosan ”. Skjak-Braek, G.. Anthonsen, T. and Sandford, P. (eds.),p679-691. Eisevier Applied Science. London and New York. 33.Calvo,P., R.L. Carmen,L. V. J. Jose,and J. A. Maria (1997),Chitosan and Chitosan/Ethylene Oxide-Propylene Oxide Block Copolymer Nanoparticles as Novel Carriers for Proteins and Vaccines, Plenum Publishing Corporation,14 431-1436. 34.Calvo-Mendze, C. andRuiz-Herrera, J.(1987) Biosynthesis of chitosan in membrane fraction from mucor rouxii by the concerted action of chitin synthetase and a particulate deacetylase. Exp.Mycol. 11:123-140. 35.Chandy, T. and Sharma, C. P.(1992) Chitosan beads and granules for oral sustained delivery of nifedipine: in vitro studies. Biomaterials. 13: 949-952. 36.Chandy, T. and Sharma, C. P.(1993) Chitosan matrix for oral sustained delivery of ampicillin. Biomaterials. 14: 939-944. 37.Collinge, D. B., Kragh, K. M., Mikkslesen, J. D., Nielsen, K. K., Rasmussen, U. andvad, K. (1993)Plant Chitinase. J, Plant, 3:31-40 38.Corroad D. A. and Tom, R. A. (1978) Bioconversion of shellfish chitin waste : process conception and selection of microorganism. J. Food Sci ., 43: 1158-1164. 39.Cosio, I. G., Fisher, R. A. and Carroad , D. A. (1982) Bioconversion of shellfish chitin waste: waste pretretement , enzyme production, process design , and economic analysis. J. Food Sci ., 47: 901-905. 40.Eicin, Y. M. Dixit, V., Lewin, K., and Gitnick. G. (1999) Xenotransplantation of fetal pocrine hepatocytes in rats using a tissue engineering approach. Artifical Organs 23:146-152. 41.Eicin, Y. M.. Dixit, V., Lewin, K., andGitnick. G. (1999) Xenotransplanation of fetal porcine hepatocytes in ratsusing a tissue engineering approach.Artifical Organs 23:146-1521999.

Xenotransplantation of fetal pocrine hepatocytes in rats using a tissue engineering approach.Artifical Organs 23:146-152. 42.Eser EIcin, A., EIcin, Y. M., and Pappas. G. D.(1998) Neuraltissue engineering: adrenal chromaffin cell attachment and viability on chitosan scaffolds.Neurological Research 20:648-654. 43.Felt, O., Furrer, P., mayer, J. M., Plazonner, B., Buri, P.,and Gurny, R. (1999) Topical use of chitosan in ophthalmology: toler-ance assessment and evaluation of precorneal retention. Interna-tional J. Pharmaceutics.180:185-193. 44.FRANK S, G. J Pharm Sci, (1975), 64(10):1585. 45.Ganza-Gonzalez,A.,Anguiano-Igea,S..Otero-Espinar,F.J.,and Blanco Mendez, J.(1999) Chitosan and Chondroitin microspheres for oral-administration controlled release of metocio-pramide. European J. Pharmaceutics & Biopharmaceutics. 48:149-155. 46.Harada, A., Higashiyama, S., Muranaka H., and Kawase, M.(1997) Effectiveness of fructose-modified Chitosan as a scaffold for hepatocyte. Biological & Pharmaceutical Bulletin 20:1290-1294. 47.Hari, P. R., Chandy, T., and Sharma, C. P.(1996) Chitosan/calcium alginate microcapsules for intestinal delivery of nitrofurantoin. J. Microencapsul. 13:319-329. 48.Hou, W. M., Miyazaki, S., Takada, M., and Komai T. (1985) Sustained release of indomethacin from chitosan granules.Chem. Pharm. Bull.33:3986-3992. 49.Jumaa, M., and Muller, B. W.(1999) Physiochemical properties of chitosan-lipid emulsions and their stability International J. Pharmaceutics 183:175-184. 50.Kawase, M., Michibayashi, N., Nakashima, N., Yagi, K.. and Mizoguchi, T. (1997) Application of glutaraldehyde-crosslinked chitosan as a scaffold for hepatocyte attachment. Biological& Pharmaceutical Bulletin 20:708-710. 51.Kawashima, Y., Handa, T., Kasai, A., Takenaka, H., and Lin, S. Y. 1985a. The effects of thickness and hardness of the coating film on the drug release rate of theophylline granules coated with chitosan-sodium tripolyphosphate complex. Chem. Pharm. Bull. 33:2469-2474. 52.Kawashima, Y., Lin, S. Y., Kasai, A., Handa, T., and Takenaka, H. (1985b) Preparation of a prolong release tablet of aspirin with chitosan. Chem. Pharm. Bull. 33:2107-2113. 53.Kawashima, Y., Yamamoto, H., Takeuchi, H., and Kuno, Y.(2000) Mucoadhesive DL-lactide/glycolide copolymer nanospheres coated with chitosan to improve oral delivery of elcatonin. Pharm. Dev. Technol. 5:77-85. 54.Khor, E., and Y. L. Lee(2003), Implantable application of chitin and chitosan,Biomaterial, 24, 2339-2349. 55.Kifune, K. (1992) Clinical application of chitin artificial skin (Beschitin W). In Advances in chitin and chitosan. Brine, C. J., Sandford, P. A. and Zikakis, J. P. (eds.),p9-13. EisevierApplied Science, London and New York.M Klokkevold, P. R., Vandemark, L.,Kenny. E.B., and Bernard,G.W.(1996)Osteogenesis enhanced by chitosan(poly-N-acetylgl-ucosaminoglycan)In vitro.J Periodontology 67:1170-1175. 56.Knapczyk, J.(1993)Chitosan hydrogel as a base for semisolid drug forms. Int. J. Pharm. 93:233-237. 57.Koizumi,T., G. C. Ritthidej, and T. Phaechamud(2001),Mechanistic modeling of drug release from chitosan coated tablets,Journal of Controlled Release, 70,277-284. 58.Kratz, G., Arnander. C., Swedenbrog, J., Back, M.. Falk, C., Gouda, I.,and Larm, O.(1997)Heparin-chitosan complexs stimulate wound healing in human skin. Scandinvian J. Plastic & Reconstructive Surgery & hand Surgery. 31:119-123. 59.Kratz, G., back, M., Arnander. C., and Larm, O.(1998)Immobilized heparin accelerates the healing of human wounds invivo.Scandinavi- an J. Plastic & Reconstructive Surgery & Hand-Surgery 32:381-385. 60.Kuang, Y., Hou, C., and Gou. S. (1998) Experomental study of the effect on growth of Schwann cell from chitin and chitosan in vitro. Chung-Kuo Hsiu Fu Chung Chien Wai Ko Tsa Chih/Chinese J. Reparative & Reconstructive Surgery 12:90-93. 61.Kurita, K. (1998), Chemistry and Application of chitin and chitosan, Polymer Degradation and Stability,59,117-120. 62.LACH JL and PAULI W A,J Pharm Sci , (1966),55(1):32~38 63.Lee,J. Y., S. H. Nam, S. Y. Im, Y. J. Park, Y. M. Lee, Y. J.Seol, C. P. Chung,and S. J. Lee (2002), Enhanced bone formation by controlled growth factor delivery from chitosan-based biomaterials,Journal of Controlled Release,78,187-197. 64.Leroiix, L., Hatim, Z., Freche, M., and Lacout, J. L.(1999)Effects of various adjuvants (lactic acid, glycerol, and chitosan)on the injectab- ility of a calcium phosphate cement. Bone 25 (2Suppl) : 31 S —34S. ift6Markey, M. L.. Bowman,L. M., and Bergamini, M. V. W.(1992) Contact lenses made of chitosan. In ” Advance in chitin and chitosan ” . Brine, C. J..Sandford, P. A. and Zikakis, J. P. (eds.),p713-717. Eisev- ier Applied Science, London and New York. ZfiMeyer, S. P., and Chen H. M. 1985.Process for the utilizationof shellfish waste. U. S. Patent 4, 505,936. 65.Lorenzo, L. M. L., R. L. Carmen, L. V. J. Jose, and J. A. Maria(1998),Design of microencapsulated chitosan microspheres for colonic drug delivery, Journal of Controlled Release,52,109-118. 66.Liu, L. S., Liu, S. Q., Ng, S. Y., Froix, M., Ohno, T., and Heller, J. (1997) Controlled release of interleukin-2 for tumor immunotherapy using alginate/chitosan porous microspheres. J. Control. Rel. 43: 65-74. 67.Macleod, G. S., Fell, J. T., Collett, J. H., Sharma, H. L., and Smith, A.M.(1999) Selective drug deliver to the colon using pectin: chitosan: hydroxypropyl methylcellulose film coated tabnets. Int. J. Pharm. 187: 251-257. 68.Majeti, N. V., and R. Kumar (2000),The review of chitin and chitosan applications ,Reactive & Function Polymers,46,1-27. 69.Mi,F. L., S. S. Shyu, Y. B. Wu, S. T. Lee, J. Y. Shyong,and R. N. Huang(2001),Fabrication and characteriation of a spong-like asymmetric chitosan membrane as a wound dressing, Biomaterial, 22,165-173. 70.Mi, F. L., Y. B. Wu, S. S. Shyu, A. C. Chao, J. Y. Lai,and C. C. Su(2002),Asymmetric chitosan membrane prepared by dry/wet phase separation: a new type of wound dressing for controlled antibacterial release, Journal of membrane Science,212,237-254. 71.Mi, F. L., Wong, T. B., and Shyu, S. S.(1997) Sustained-release of oxytrtracycline from chitosan microspheres prepared by interfacial acylation and spray hardening methods. J. Microencapsulation 14:577-591. 72.Miwa, A., Ishibe, A., Nakano, M., Yamahira, T., Itai, S., and Kawa- hara,H.(1998) Development of novel chitosan derivatives as micellar carriers of taxol. Pharmaceutical Research 15:1844-1850. 73.Miyazaki, S., Ishii, K., and Nadai, T.(1981) The use of chitin and chitosan as drug carriers. Chem. Pharm. Bull. 29:3067-3069. 74.Miyazaki, T., Komuro, T., Yomota, C., and Okada, S.(1990) Usage of chitosan as a Pharmaceutical Material: efrfectiveness as an addit- ional additives of sodium alginate. Eisei Shikenjo Hokoku 108:95-97. 75.Miyazaki, S., Nakayama, A., Oda, M., Takada, M., and Attwood, D. (1994) Chitosan and sodium alginate based bioadhesivetablets for intraoral drug delivery. Biol. Pharm. Bull. 17:745-747. 76.Muzzarelli, R.(1992) Role of lysozyme and N-acetly-/3-D- glucoami -nidase in the resorption of wound dressings. In “ Advance in chitin and chitosan ” . Brine. C. J., Sandford. P. A. and Zikakis, J. P. (eds.), p25-p33. Eisevier Applied Science , London and New York. 77.Narayani, R. and Panduranga R. K.(1995) pH-Responsive Gelatin Microspheres for Oral Deliver of Anticancer Drug Methotrexate. J. Appl. Polym. Sci. 58:1761-1769. 78.Nigalaye, A. G., Adusumilli, P.,

and Bolton, S.(1990) Investigation of prolonged drug release from matrix formulations of chitosan. Drug Devel. Ind. Pharm. 16:449-467. 79.Nishioka, Y., kyotani, S., Okamura, M., Miyazaki, M., Okazaki, K., ohnishi, S., Yamamoto, Y., and Ito, K. 1990. Release characteristics of cisplatin chitosan microspheres and effects of containing chitin. Chem. Pharm. Bull. 38:2871-2873. 80.Okhamafe, A. O., Amsden, B., Chu, W., and Goosen, M. F. A. (1996)Modulation of protein release from chitosan-alginate microca- psules using the pH-sensitive polymer hydroxypropyl methylcellulose acetate succinate. J. Microencapsul.13:497-508. 81.Park, Y. J., Y. M. Lee, S. N. Park, S. Y. Sheen, C. P. Chung, and S. J. Lee (2000), Platelet derived growth factor releasing chitosan sponge for periodontal bone regeneration, Biomaterials, 21, 153-159. 82.Polk, A., Amsden, B., De Yao, K., Peng, T., and Goosen, F. A.(1994) Controlled release of albumin from chitosan-alginate microcapsules. J. Pharm. Sci. 83: 178-185. 83.Ramanathan, S., and L. H. Block(2001), The use of chitosan gels as matrices for electrically-modulated drug delivery, Journal of Controlled Release, 70, 109-123. 84.Remunan-Lopez, C. and Bodmeier, R.(1996) Effect of formulation an process variables on the formation of chitosan-gelation coacervates. Int. J. Pharm. 135:63-72. 85.Rentel, C. O., Lehr, C. M., Bouwstra, J. A. Luessen, H. L., and Junginger,H.E.(1993)Enhanced peptide absorption by the mucoad- hesive polymers polycarbophil and chitosan. Proceed Intern. Symp. Control. Rel. Bioact. Mater. 20:446-447. 86.Ruel, G. E., G. Leclair, P. Hildgen, A, Gupta, J. C. Leroux (2002), Thermosentive chitosan-based hydrogel containing liposomes for the delivery of hydrophilic molecules,Journal of Controlled Release ,82, 373-383. 87.Sawayanagi, Y., Nambu, N., and Nagai,T.(1982a). Directl compre- ssed tablets containing chitin or chitosan in addition to lactose or potato atarch.Chem. Pharm. Bull. 30:2935-2940. 88.Soane, R. J., M. Frier, A. C. Perkins, N. S. Jones, S. S. Davis, and L. I11um (1999), Evaluation of the clearance characteristics of bioad- hesive systems in humans, International Journal of Pharmaceutics, 178, 55-65. 89.Sundararajan V. M., and W. T. M. Howard (1999), Porous chitosan scaffolds for tissue engineering, Biomaterials, 20, 1133-1142. 90.Takayama, K., Hirata, M., Machida, Y., Masada, T., Sannac, T., and Nagai, T.(1990) Effect of interpolymer complex formation on bioadhesive property and drug release phenomenon of compressed tablets consisting of chitosan and sodium hyaluronate. Chem. Pharm. Bull. 38:1993-1997. 91.Takeuchi, H., Yamamoto, H., Niwa, T. Hino, T., and Kawashima Y. 1996. Enteral absorption of insulin in rats from mucoadhesive chitosan-coated liposomes. Pharm. Res.13:896-901. 92.Thanoo, B. C., Sunny, M. C., and Jayakrishnan,A.(1992) Crosslinked chitosan microshheres: preparation and evaluation as a matrix for the controlled release of pharmaceuticals. J Pharm Pharmacol. 44:283-286. 93.Tozaki, H., Komoike, J., Tada, C. Maruyama, T., Terabe, A.,Suzuki, T., Yamamoto, A., and Muranishi, S. (1997) Chitosan capsules for colon-specific drug delivery: improvement of insulin absorption from the rat colon. J. Pharm. Sci. 86:1016-1021. 94.Upadrashta, S. M., Katikaneni, P. R., and Nuesste, N. O. (1992) Chitosan as a tablets binder. Drug Devel. Ind. Pharm. 18:1701-1708. 95.Vandenberg, G. W., C. Drolet, S. L. Scott, and J. D. L. Noue(2001),Factors affecting Protein release from alginate-chitosan coacervate microcapsules during production and gastric/intestinal simulation, Journal of Controlled Release,77,297-307. 96.Wang, X, H., W. J. Wang, Q. L. Feng, F. Z. Cui, Y. X. Xu, X. H. Song, and V. D. W. Mark(2003), Crosslinked collagen/chitosan matrix for artificial livers, Biomaetrials , 24, 3231-3220. g, and K. Yao(2002), Preparation and histological evaluation of biomimetic three-dimensional hydroxyapatite/chitosan-gelatin newwork compo- site scaffolds, Biomaterials, 23, 3227-3234.