以聚?胺酸水溶嬌吸附Hydralazine HCl進行釋放之研究

陳憶馨、張耀南 ; 吳建一

E-mail: 9417915@mail.dyu.edu.tw

摘 要

本研究以味丹企業股份有限公司所提供三種聚麩胺酸(高、低分子量Na型γ-PGA與水膠Na型 γ-PGA，分別以H-PGA、L-PGA與 HG-PGA簡稱之)進行其對Hydralazine HCl (HA-HCl)藥物釋放之探討。實驗結果顯示，L-PGA、H-PGA或HG-PGA對HA-HCl藥物之釋放率分別可達到98% (0.039 g/L)、89% (0.036 g/L)或96% (0.038 g/L)，而且隨著PGA添加濃度增加，HA-HCl藥物釋放的效率亦提高到約89%以上。HA-HCl藥物釋放之斜率將隨著PGA添加濃度增加而下降，但HA-HCl藥物釋放的T1/2(釋放藥物最大濃度之－半所需時間)卻隨著PGA添加濃度增加而延長，T1/2釋放時間大小依序為HG-PGA>H-PGA>L-PGA。不論添加1.0 g/L PGA與否，HA-HCl藥物在pH 2.2之磷酸緩衝溶液(phosphate buffer solution; PBS)中釋放速率皆比較在pH 7.4之PBS中釋放速率為快，由於PGA與HA-HCl在酸性環境下不易離子性的鍵結，再加上PGA與透析膜在酸性環境下易酸解，且造成透析膜孔徑變大，使HA-HCl藥物快速釋放出。PGA分子量對HA-HCl藥物釋放亦有影響，結果顯示HA-HCl藥物釋放時間T1/2將隨著PGA分子量增大而增加，由此可知，不同分子量與不同型式PGA，以及磷酸緩衝液之酸鹼值皆對PGA和HA-HCl的鍵結強弱有不同之影響，此可能由於不同型式PGA有不同化學結構所造成。

關鍵詞 : 聚麩胺酸 ; Hydralazine HCl ; 藥物釋放

目錄

參考文獻

1.財團法人 編著。1989。藥物控制釋放劑型技術與市場分析。第54-56頁。財團法人文教基金會。台北，臺灣。 2.呂文凱。2003。利用回應曲面法尋求苔蘚桿菌生產聚麩胺酸之培養基最適化:第17-18頁。大葉大學碩士論文。彰化。 3.行政院衛生署中華藥典編修委員會 編著。2000。中華藥典第五版。第1011-1013頁。行政院衛生署。台北，臺灣。 4.李安榮、鄒台黎 編著。2000。新編藥物學。第38頁。永大書局有限公司。台北，臺灣。 5.李建蓉、公瑞煜。1998。以親水凝膠為載體的藥物控制釋放體系。大理醫學院學報 7 (1) :42-45。 6.邱紫與。2003。利用苔蘚桿菌生產聚麩胺酸之搖瓶饋料批式培養探討:第四頁。大葉大學碩士論文。彰化。 7.吳禮光、劉茉娥、朱長東、潘祖仁。1994。控制釋放技術，應用化學中文期刊 11 (3) :1-10。 8.徐銅文、王紹亭。1994。擴散型高分子藥物緩釋機理的研究現狀。國外醫學生物醫學工程分冊 17 (4) :187-191。 9.徒二中彥、中野真汎。1986。聚合物在藥物釋放上的應用。化學工業 37 (288) :24-32。 10.陳長安 編著。2002。常用藥物治療手冊。第617-618頁。全國藥品年鑑雜誌社。台北，臺灣。 11.陳建州。2003。聚麩胺酸之生物絮凝性質的研究:第13-14頁。大葉大學碩士論文。彰化。 12.傅杰、李世普。1999。生物可降解高分子材料及其在醫學領域的應用(II)*。武漢工業大學學報 21 (5) :19-22。 13.葉淑芬。2003。幾丁聚醣電解產物於藥物釋放控制之探討:第10頁。大葉大學碩士論文。彰化。 14.蔡靖彥、蔡百欣、蔡百榮 編著。2001。常用藥品手冊。第402-403頁。杏欣出版社。嘉義，臺灣。 15.蕭聰明、朱康杰。2000。可控生物降解釋藥

材料的設計與研究，高分子材料科學與工程學報 16 (6) :175-177。 16.龔育胺。2004。聚麩胺酸的鎘、鉛重金屬吸附性質探討:第24-26頁。大葉大學碩士論文。彰化。 17.羅毅。1996。藥物控制釋放方法。高分子通報 1 :18-27。 18.Mopper, B. 1987. Ultraviolet spectrophotometric determination of Hydralazine Hydrochloride in tablets following derivatization with Nitrite. J. Assoc. Off. Anal. Chem. 70(1): 42-46. 19.Mopper, B. Cape, C. C. Eeverett, R. L. Fleming-Jones, M. E. McCarthy, J. P. and Ting, S. 1988. UV spectrophotometric determination of Hydralazine Hydrochloride in tablets: Collaborative study. J. Assoc. Off. Anal. Chem. 71(6): 1121-1122. 20.Bhattacharya, D. Hestekin, J. A. Brushaber, P. Cullen, L. Bachas, L. G. and Sikdar, S. K. 1998. Novel poly-glutamic acid functionalized microfiltration membranes for sorption of heavy-metals at high capacity. J. Memb. Sci. 141(1): 121-135. 21.Cheng, C., Asada, Y. and Aida, T. 1989. Production of γ -polyglutamic acid by Bacillus subtilis A35 under denitrifying conditions. Agric. Biol. Chem. 53: 2369-2375. 22.Chun, L. Yu, D. F. Newman, A. F. Cabral, C. Stephens, N. Hunter, L. Milas, and S. Wallace, 1998. Complete regression of well-established tumors using novel water-soluble poly(L-glutamic acid)-paclitaxel conjigate. Cancer Res. 58: 2404-2409. 23.Chun, L. Price, J. E. Milas, L. Hunter, N. R. Ke, S. Tansey, W. Charnsagavej, C. and Wallace, S. 1999. Antitumor activity of poly(L-glutamic acid)-paclitaxel on syngeneic and xenografed tumors. Clin. Cancer Res. 5: 891-897. 24.Daninippon Parmaceutical Co. Ltd. 1972. Ice cream stabilizer. 19735. Japanese Patent. 25.Donbrow, M. and Friedman, M. 1975. Timed release from polymeric films containing drugs and kinetics of drug release. J Pharm. Sci. 64(1): 76-80. 26.Goto, A. and Kunioka, M. 1994. Biosynthesis of poly (γ -glutamic acid) from L-glutamic acid, citric acid, and ammonium sulfate in Bacillus subtilis IFO3335. Biosci. Biotechnol. Biochem. 56: 1031-1035. 27.Knuth, K. 1993. Hydrogel delivery systems for vaginal and oral applications(for mulations and biological considerations). Adv. Drug Deliv. Rev. 11(3): 148-156. 28.Konno, A. Taguchi, T. and Yamaguchi, T. 1989. New use of polyglutamic acid for foods. European Patent Application EPO284386A1. 29.Kunioka, M. 1995. Biosynthesis of poly (γ -glutamic acid) from L-glutamine, citric acid and ammonium sulfate in Bacillus subtilis IFO3335. Appl. Microbiol. Biotechnol. 44: 501-506. 30.Kunioka, M. 1997. Biosynthesis and chemical reactions of poly(amino acid)s from microorganisms. Appl. Microbial. Biotechnol. 47: 469-475. 31.Kurane, R. and Matsuyama, H. 1994. Production of a bioflocculant by mixed culture. Biosci. Biotech. Biochem. 58: 1589-1594. 32.Kurane, R. Takeda, K. and Suzuki, T. 1986. Screening and characteristics of microbial flocculants. Agric. Biol. Chem. 50: 2301-2307. 33.Kurane, R. and Nohata, Y. 1991. Microbial flocculation of waste liquids and oil emulsion by a bioflocculant from Alcaligenes latus. Agric. Biol. Chem. 55: 1127-1129. 34.Kydonieus, A. F. 1980. Controlled release technologies: Methods, theory and applications. Boca Raton. 1: 17-22. 35.Lee, S. H. Lee, S. O. Jang, K. L. and Lee, T. H. 1995. Microbial flocculant from Arcuadendron sp. TS-49. Biotech. Lett. 17: 95-100. 36.Li, C. Yu, D. F. Newman, R. A. Cabral, F. Stephens, L. C. Hunter, N. Milas, L. and Wallace, S. 1998. Complete regression of well-established tumors using a novel water-soluble poly(L-glutamic acid)-paclitaxel conjugate. Cancer Research 58: 2404-2409. 37.Mitsuiki, M. Mizuno, A. Tanimoto, H. and Motoki, M. 1998. Relationship between the antifreeze activities and the chemical structures of oligo- and poly(glutamic acid)s. J. Agric. Food Chem. 46(3): 891-895. 38.Multani, A. S. Li, C. Ozen, M. Yadav, M. Yu, D. F. Wallace, S. and Pathak, S. 1997. Paclitaxel and water-soluble poly(L-glutamic acid)-paclitaxel, induce direct chromosomal abnormalities and cell death in a murine metastatic melanoma cell line. Anticancer Research. 17: 4269-4274.? 39.Otani, Y. Tabata, Y. and Ikada, Y. 1996a. Anew biological glue from gelatin and poly (L-glutamic acid). J. Biomed. Mater. Res. 31: 157-166. 40.Otani, Y. Tabata, Y. and Ikada, Y. 1996b. Rapidly curable biological glue composed of gelatin and poly (L-glutamic acid). Biomater. 17(14): 1387-1391. 41.Otani, Y. Tabata, Y. and Ikada, Y. 1998a. Effect of additives on gelation and tissue adhesion of gelation poly (L-glutamic acid) mixture. Biomater. 19: 2167-2173. 42.Otani, Y. Tabata, Y. and Ikada, Y. 1998b. Hemostatic capability of rapidly curable glues from gelatin poly (L-glutamic acid) and carbodiimide. Biomater. 19: 2091-2098. 43.Otani, Y. Tabata, Y. and Ikada, Y. 1999. Sealing effect of rapidly curable gelatin-poly(L-glutamic acid) hydorgel glue on lung air leak. Ann. Thorac. Surg. 67: 922-926. 44.Peppas, N. A. 1993. Preparation, struture and diffusion albehavior of hydrogels in controlled release. Adv. Drug Deliv. Rev. 11(2): 130-137. 45.Salehizadeh, A. and Shojaosadati, S. A. 2001. Extracellular biopolymeric flocculants: Recent trends and biotechnological importance. Biotech. Adv. 19: 371-385. 46.Suh, H. Kwon, G. S. Lee, C. H. Kim, H. S. Oh, H. M. and Yoon, B. D. 1997. Characterization of bioflocculant produced by Bacillus sp. DP-152. J. Ferment. Bioeng. 84(2): 108-112. 47.Takeda, M. Koizumi, J. Matsuoka, H. and Nakamura, I. 1991. A protein bioflocculant produced by Rhodococcus erythropolis. J. Ferment. Bioeng. 74: 408-409. 48.Takeda, M. Koizumi, J. Matsuoka, H. and Hikuma, M. 1992. Factors affecting the activity of a protein bioflocculant produced by Nocardia amarae. Agric. Biol. Chem. 55: 2663-2664. 49.Toeda, K. and Kurane, R. 1991. Microbial flocculant from Alcaligenes cupidus KT201. Agric. Biol. Chem. 55: 2793-2799. 50.Troy, F. A. 1993. Chemistry and biosynthesis of the poly(γ -D-gluramy)capsule in Bacillus subtilis, 1. Properties of the membrane-mediated biosynthetic reaction. J. Biol. Chem. 48: 305-315. 51.Wang, Z. Wang, K. and Xie, Y. 1995. Bioflocculant-producing microorganisms. Acta Microbiol. Sin. 35(2): 121-129. 52.Yokoi, H. Arima, T. Hirose, J. Hayashi, S. and Takasaki, Y. 1996. Flocculation properties of poly(γ -glutamic acid) produced by Bacillus subtilis. J. Ferment. Bioeng. 82(1): 84-87. 53.Yokoi, H. Natsuda, O. Hirose, J. Hayashi, S. and Takasaki, Y. 1995. Characteristics of biopolymer flocculant produced by Bacillus sp. PY-90. J. Ferment. Bioeng. 79: 378-380. 54.Yoshida, R. 1993. On-off regulation of drug release using gel surface as a switch. Adv. Drug Deliv. Rev, 11(4): 185-193.