Study on Hydralazine HCl Release from Poly(γ -glutamic acid) Hydrogel

陳憶馨、張耀南 ; 吳建一

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

ABSTRACT

In this study, the effects of addition concentration of various poly- γ -glutamic acid (γ -PGA) and pH of phosphate buffer solution (PBS) on the release properties of hydralazine HCl (HA-HCl) from PGA was investigated. Three types of PGA, high molecular weight (MW) Na+- γ -PGA (H-PGA), low MW Na+- γ -PGA (L-PGA), hydrogel-Na+- γ -PGA (HG-PGA), were donated by the Vedan Enterprise Co., Taichung County, Taiwan. It was found that the drug release percentage (%) of HA-HCl from L-PGA, H-PGA or HG-PGA was up to 98% (0.039 g/L) , 89% (0.036 g/L) or 96% (0.038 g/L), respectively, while the release percentage (%) increased up to 89% or higher as increasing the addition concentration of PGA. The drug release slope of HA-HCl decreased and the release time T1/2 increased when the addition concentration of PGA increased. No matter when PGA was added in PBS (phosphate buffer solution) or not, the drug release rate of HA-HCl at pH 2.2 of PBS was faster than that at pH 7.4 of PBS. This result may be due to the degradation of PGA and dialysis membrane, the large pore size of the dialysis membrane, and the weak ionic binding bonds between PGA and HA-HCl at much acidic PBS condition. The drug release time T1/2 of HA-HCl increased as the molecular weight of PGA, which was added in PBS, increased. The drug release rate (slope) or time of HA-HCl could be affected by the various type and MW of PGA, and pH of PBS. This may be due to the chemical structure of the various type of PGA.

Keywords : poly- γ -glutamic acid (PGA) ; Hydralazine HCl ; drug release

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REFERENCES

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.龔育朌。2004。聚麩朌酸的鎘、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.