嘉南學報第二十八期
第196～207頁，民國九十一年
CHIA-NAN ANNUAL BULLETIN
VOL. 28, PP. 196－207, 2002

評估Alginate/Pluronic複合配方做為原位成膠輸送眼藥用載體之可行性

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摘 要

一般市面用液體眼藥製劑常因滴入眼睛時，受到經常性的淚液分泌及鼻淚管的快速排液，因此呈現很低的生體可用率(Bioavailability)，此缺點可用原位成膠(In-situ gel formation)輸送系統來加以改善。本文分別製備Pluronic、Alginate及Pluronic/Alginate高分子溶液做爲輸送眼睛載體，藉由這些載體在非生理狀態轉變到生理狀態時會產生相轉移(Phase transition)，來延長藥劑在前角膜的滯留時間，進而增加眼睛的生體可用率。本文首先尋找三種系統之最適合配方，發現14% Pluronic、2% Alginate與14% Pluronic/0.1% Alginate爲在單獨配方或複合配方中最適合輸送眼藥之系統，由流變行爲(Rheological behavior)觀察得知複合配方之凝膠強度優於單獨配方。本文並將治療青光眼的藥劑(Pilocarpine hydrochloride)加入各種配方內，探討藥物在生理狀態下對配方之影響，結果發現藥物會使單獨配方之凝膠強度下降，而複合配方之凝膠強度則反而增強。由此更加證明14% Pluronic/0.1% Alginate複合配方優於單獨配方，可做爲輸送眼藥(Ophthalmic delivery)的原位成膠載體，進而提高眼睛的生體可用率。本實驗目前正在進行活體外(In vivo)與活體內(In vitro)試驗，以評估此輸送系統之藥理反應(Pharmacological response)。

關鍵詞：生體可用率、原位成膠、相轉移流變行爲、眼藥輸送

緒 言

根據文獻報導，液體眼藥製劑在滴入眼睛時，大約只有1~10%的生體可用率[1]。爲了達到療效，需增加藥劑的量與次數，因而造成眼睛負擔與使用上的不便利。爲了克服此問題，很多研究學者

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ABSTRACT

Evaluation of Using Alginate/Pluronic Solution as an In Situ Gelling System for Ophthalmic Drug Delivery

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ABSTRACT

The commercialized liquid ophthalmic formulation is eliminated from the precorneal area immediately upon instillation because of lacrimal secretion and nasolacrimal drainage. This results in very low ocular bioavailability. The problem can be conquered by in situ gelling system for ophthalmic drug delivery. In this study, a series of polymer solutions including Pluronic, Alginate, and Pluronic/Alginate solutions were prepared and used as in situ gelling vehicles for ophthalmic drug delivery. The phase transition of these vehicles occurs once their exposure environment is switched from non-physiological to physiological condition, which can prolong the residence times of the drug in the eye and improve the ocular bioavailability. It was found that the optimum concentrations for the in situ gel system were 14% Pluronic, 2% Alginate, and 14% Pluronic/0.1% Alginate, respectively. From rheological behavior, it demonstrated that the gel strength of Pluronic/Alginate mixture was greater than that of Pluronic or Alginate solutions alone. The effects of pilocarpine hydrochloride on the rheological behaviors of the polymer solutions were also investigated in this study. It was found the gel strength of the drug-containing individual polymer solution was decreased, but that of the mixture was increased. This further indicates that the rheological behavior of the 14% Pluronic/0.1% Alginate solution was better than that that of Pluronic or Alginate solutions alone. The results demonstrated that this polymer mixture can be used as an in situ gelling vehicle to enhance the ocular bioavailability. In addition, the study of in vitro pilocarpine release and in vivo pilocarpine pharmacological response of various drug-containing polymer solutions are carrying on in our lab.

Key words: Bioavailability, In situ gel formation, Phase transition, Rheological behavior, Ophthalmic delivery system.