含藥奈米級生物可分解性薄膜之製備及其釋放行爲探討

Fabrication and release behavior of drug-containing nano-sized biodegradable membrane

中文摘要

本研究以高分子聚合物 Poly-L-lactic acid (PLLA)、Poly butylene succinate-co-adipate (PBSA)爲溶質、利用 95% CH2Cl2 及 5% CHCl3 爲溶劑，藉電氣紡絲(electrospinning)加工步驟技術製成含藥奈米級生物可分解性薄膜，製程中並包覆四環黴素(tetracycline)作爲抑菌藥物、測試所得薄膜之物理特性，並觀察其體外藥物制放及高分子降解程度，此薄膜期望應用於藥物制放、手術縫線、組織隔離膜。用 12-16wt%PBSA、PLLA 溶劑濃度、0.019-0.238ml/min 之供液速率、10-18kV 之電場電壓、不同條件下的包覆藥物後、觀察薄膜藥物之制放行爲。結果顯示電壓強弱及供液速率爲最主要影響纖維直徑大小之原因。當電壓愈高 16kV、輸液速率愈小 0.017ml/min；所得纖維直徑愈小 1-4um、但因電壓在 14kV 時會造成 pore size 差異性大。細胞實驗中以人類牙齦纖維細胞(human gingival fibroblast)(HGF)作爲細胞毒性測試，將細胞直接培養於薄膜上、以 MTT assay 分析，結果顯示細胞生長(P>0.05)未有受明顯的抑制。PLLA 纖維直徑愈小 1um，降解情形愈快，1 小時即有藥釋物放，在 1 週時即有降解情形；在溶液條件濃度 7-8%，電壓 13-15kV，輸液速率 0.119ml/min 條件下所製出來的薄膜，纖維直徑 8-10um、所包覆藥物能力愈強、約在二小時有藥物釋放情況，本實驗結果顯示薄膜纖維之粗或細，會影響到藥物釋放的情形，進而左右高分子降解速率，所留下的孔洞促進了高分子薄膜的降解亦即較快釋出乳酸，且藥物釋放愈快、其高分子薄膜降解也愈快。也就是藉由適當控制下，可得到不同孔隙度含藥奈米級生物可降解性薄膜，並希望未來能應用於臨床上治療牙周病的引導性組織再生隔離膜，或是可吸收性之含藥傷口敷料。

英文摘要

In our study, 12-16% poly-L-lactic acid (PLLA) or/and poly butylene succinate-co-adipate (PBSA) is dissolved in 95% CH2Cl2 and 5% CHCl3 to produce drug-containing nano-sized biodegradable membrane via electrospinning process. The polymer membrane is added with 10-15% tetracycline to prohibit infection. It is also capable of applying for different purposes, such as Guided Tissue Regeneration (GTR), drug delivery and operator suture line and fracture healing. The physical feature, drug delivering efficiency in vivo depended on 12~16wt%PBSA, concentration of PLLA solution, supplying rate of PLLA solution at 0.019~0.238ml/min, supporting voltage of 10~18kV, distinct drug adding conditions, and the level of polymeric degradation have been analyzed as well.It is revealed that

voltage and supplying rate of PLLA or PBSA solution are two of the most effective parameters which determine the diameter of this biodegradable nano-fiber. The higher voltage (up to 16kV) and less supplying rate of solution (at 0.017ml/min) are applied, thus thinner the fiber (1-4um) is obtained. However, high voltage (14kV) may cause significant differences in pore size. We cultured Human gingival fibroblast cell (primary culture, HGF) on the biocomposite membrane to perform in vitro experiment and examine cell toxicity via MTT assays; nevertheless, the growing was not hindered ($P>0.05$). While the thinner fiber (1um) is applied, the drug is released faster (within the first hour) and degraded earlier (after 1 week). The membrane produced under the solution concentration of 7~8%, voltage of 13~15kV, solution input of 0.119ml/min which consists of thicker fibers (8-10um), higher accessing ability for the process of drug addition; therefore, the rate of drug releasing is slower (starting from the second hour), and the vise versa. Depending on the diameter of fibers, the efficiency of drug delivery determines the degradation of polymer. In other words, membrane with thinner fiber discharge drug faster. The pore exposed would influence the degradation of the nano-fiber. Under adequate conditions, drug-containing nano-sized biodegradable membrane with various fiber thickness features is anticipated applying on guided tissue regenerating membrane in clinical treatment of periodontal disease or biodegradable drug containing biomaterial for wound dressing.