去乙醯幾丁聚醣之非對稱性膜滲透膠囊之製備與特性解析

Characterization of Osmotic Capsule with Asymmetric Membrane Using Chitosan

中文摘要

本研究主要目的是要以去乙醯幾丁聚醣(Chitosan)來當作非對稱性膠囊之材質，設計合適的滲透性控釋膠囊。非對稱性膜在膠囊化處理後可改善滲透性幫浦難溶性藥物釋放的情形。 膠囊殼乃是以交聯的方式膠化所產生，先將模具浸入含有聚合物的包覆溶液(coating solution)，再浸入到淬鍊溶液(quenching solution)，而在膜具上形成具有非對稱結構之膠囊殼。選用不同的膜衣材質，包覆溶液，浸漬溶液和浸漬時間來製作並評估非對稱結構之膠囊殼之特性。

滲透壓實驗中，薄膜釋藥孔之存在由包覆葉綠素的膠囊緩緩釋出葉綠素而得到證實。選用不同溶解度的藥物來評估對稱性膠囊的控釋效果。結果顯示藥物從非對稱性膜膠囊的釋放會因藥物的溶解度增加而增加，藥物的溶出速率與藥物溶解度成線性相關。在實用的觀點下考量製作難易度及通透效果後，選取以去乙醯幾丁聚醣與三磷酸鹽交聯三十分鐘這組膠囊為試驗膠囊。膠囊的通透率經計算而得 1.40*10-6 cm2/h-atm 於 攝氏 37.8 度，因為難溶性藥物 felodipine 及 nifedipine 不能提供足夠的滲透壓動力，於是在處方中添加助溶劑 SLS 或添加助懸劑 HPMC 以增加藥物釋放。經計算而得之複回歸方程式:

YF(drug max released %)= 32.48367-1.04456* F+0.14909 * H+ 0.23256 * S(mg)

YN(drug max released %)= 30.99458-0.95958 * N+0.12802 * H+0.21321 * S(mg)

最後，我們成功地設計出以去乙醯幾丁聚醣與三磷酸鹽 (TPP)交聯之非對稱性滲透膠囊。

英文摘要

The major purpose of the study was to devise a suitable osmotic capsule for drug release. In this study, chitosan was utilized as the matrix of asymmetric membrane capsules. Asymmetric membrane offering an improved osmotic pump effect was used to release poorly water-soluble drug in a control manner after encapsulation. The capsule wall was composed of membrane produced by gelation process, controlled by the ionic cross-linking reaction between protonated chitosan and ionized triphosphate (TPP). Asymmetric membrane was formed on stainless steel mold pins by dipping the mold pins into a coating solution containing a polymeric material followed by dipping into a quenching solution. The factors influenced the prosperities of the capsule membrane, such as the molecular weight of chitosan、the solvent、the dipping solution and the dipping time were investigated in view of the drug release.

In situ formation of a delivery orifice in the thin membrane was proven by

observation of a jet stream of chlorophyll being released from the capsule. Drugs with different solubility were selected as the model to demonstrate that the controlled release characteristics can be manipulated by the design of polymeric capsule coating an asymmetric membrane. The results showed that the release rate from asymmetric membrane capsule increased with the solubility for drugs. A correlation between drug solubility and the initial drug release rate calculated from the slope of the drug release profile was verified to be linear. From the practical viewpoint it is useful to estimate selectivity of the capsules towards the difficulty of production and permeability. The model capsule made of chitosan 500 cross-linked with triphosphate. Permeability across the selected asymmetric membrane of the C500/TPP30 capsule was determined to be 1.40*10-6 cm2/h-atm at 37.8OC for drugs with water solubilities in a moderate to high range. The poorly water-soluble drug, felodipine and nifedipine, were unable to create a sufficient osmotic effect on activating the release of drug. Solubilization either by the addition of the solubility enhancer, SLS, or by a solid dispersion with HPMC could increase the solubility of nifedipine to a sufficient extent to activate drug release. It was found that HPMC further interacted with SLS to synergistically increase the maximal percent of release amount and the release rate of felodipine and nifedipine.

The multi regression formulations of felodipine and nifedipine were “YF(drug max released %) =32.48367-1.04456*F+0.14909*H+0.23256*S(mg)” and“YN(drug max released%) =30.99458-0.95958*N+0.12802*H+0.21321*S(mg)”, respectively. Consequently, we successfully designed the osmotic capsule with asymmetric membrane which was made of chitosan and cross-linked with TPP.