利用非對稱性膜膠囊以滲透壓方式釋放難溶性藥物之研究

Asymmetric membrane capsules for the delivery of poorly water soluble drugs by osmotic pressure

中文摘要

對於一個水不會崩散之膠囊系統而言，其膠囊殼具有非對稱性膜之結構，此結構可增加水通透性而增強滲透壓的作用，進而釋放難溶性藥物。膠囊殼是以相轉換的方式所產生，製備過程是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。此膠囊殼可以充填入不同成份的藥物或賦型劑，成爲以滲透壓釋放的控釋劑型。選擇 felodipine 和 nifedipine 兩種難溶性藥物爲模式藥物，研究非對稱性膜膠囊以滲透壓作用釋放難溶藥物的情形。

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。爲了增加難溶藥物的釋出，配方中添加了助溶劑。在 nifedipine 的滲透劑型中，影響膠囊內處方的因子包括 hydroxypropyl methylcellulose (HPMC)的黏度和添加量、sodium lauryl sulfate (SLS)的添加量和 nifedipine 的含量將被探討測試。實驗結果發現 HPMC 50cps 在處方中是一個適當的增稠劑，HPMC 和 SLS 的添加都會增加藥物的釋出，而藥物的含量並不影響藥物的釋出。在本實驗中 nifedipine 由此滲透膠囊劑型釋放的機制亦將一併討論。

英文摘要

A non-disintegrating polymeric capsule system, in which asymmetric membrane offers an improved osmotic pump effect, was used to release poorly water-soluble drug in a control manner after encapsulation. The capsule wall was made by a phase inversion process, in which 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 polymeric capsule with asymmetric membrane is then filled with a blend of the active agent and excipient for the controlled drug delivery modulated by osmotic pump effect. Two poorly water-soluble drugs of felodipine and nifedipine were selected as the model to demonstrate that the controlled release characteristics can be manipulated by the design of polymeric capsule with coating an asymmetric membrane.

The results showed that the release rate from asymmetric membrane capsule increased with increasing solubility for both 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. In order to enhance the release rate for these two poorly

water-soluble drugs, solubilization with the addition of solubility enhancers is necessary. In the osmotic system for nifedipine, the influence of core formulation variables including viscosity and amount of hydroxypropyl methylcellulose (HPMC), amount of sodium lauryl sulfate (SLS), and nifedipine loadings were examined. It was found that HPMC 50cps was suitable to be a thickening agent and both amount of HPMC and SLS showed a comparable and profoundly positive effect, whereas nifedipine loading had no influence on the drug release rate. Mechanism responsible for the controlled release of nifedipine from this system was proposed.