以包覆型賦形劑作為間質性控釋劑型之材質

Coated Excipients as Matrixs for Controlled Release Dosage Forms

中文摘要

以直接壓錠法製造間質性控釋劑型是最經濟且簡便的方法。在本研究第一部份中，應用簡易的噴霧法製備包覆型賦形劑作為直接壓錠的材質。包覆的聚合物包括：Eudragit RS 30D，Eudragit RL 30D 以及乙基纖維素。乳糖和磷酸二鈣則是所使用的賦形劑。以流變性的性質與打錠特性測試不同包覆量的包覆型賦形劑。結果顯示包覆型賦形劑皆比原始賦形劑有較佳的流動性與壓縮性。對錠片的要求而言，大部份錠片的脆度皆小於 1%，除了以包覆較低量的乙基纖維素與無包覆的乳糖所製得的錠片，抗張強度與錠片厚度的變化說明脆度的結果。所有的測試建議，原本就用於打錠的賦形劑，可經由修飾而提供佳的物理物質作為直接壓錠的間質性材質。

圓粒膠囊劑型因具多樣懷而提高治療的安全性與有效性並在製造流程與處方設計上擁有許多優點。在藥廠製造圓粒的方法應用最廣泛的有：擠壓搓圓法（Extrusion and Spheronization）、溶液或分散液層覆法（Solution or LSuspension Layering）、粉末層覆法（Powder Layering）的攪圓法（Mixing Pelletization）。在本研究第二部份中，使用擠壓搓圓法製備圓粒，探求不同包覆材質賦形劑添加不同比例的微晶纖維素（MCC），在不同的轉速與添加水量下，對圓粒大小及圓度的影響。搓圓所需的水量與起始物質的選擇息息相關。含較高比例的 MCC 需要較多的水量方足以形成適當大小的圓粒。相對於乳糖，磷酸二鈣需要較多的水量形成圓粒。磷酸二鈣添加 10%的微晶纖維素（MCC）無法搓出適當的顆粒，但包覆型磷酸二鈣添加 10%的微晶纖維素（MCC）就可搓出適當的顆粒。通常，在較低的搓圓速度下，易產生較大且不規則的圓粒，而在較高的搓圓速度下，可得較小且較圓的圓粒。更近一步地，選擇兩種不同溶解度的藥物：易溶於水 Captopril 與不溶於水的 Nifedipine 作為模式藥物測試溶離的特性。無論包覆物質的有無或不同的賦形劑，所製成的含藥顆粒，顯示相似的溶離狀態，擴散機轉主要是控制在藥物本身的溶解度。

英文摘要

Direct compression is an economical and simplest way to manufacture a matrix-type controlled released release dosage form. In the first part of this study, a simple spraying method was applied to prepare a new coated excipient as the direct compression diluent. The coating polymers include: Eudragit RS 30D, Eudragit RL 30D, and ethylcellulose. Lactose and dicalcium phosphate(DCP) were used as the excipient. Rheological properties and tabletting characteristics of the coated excipient with various amount were measured. Results showed that coated granules posses

better flowability and compressibility compared to the original uncoated granules. Most tablets exhibit friability less than 1% except for low concentration of ethylcellulose coated lactose and the uncoated lactose tablets. The changes of tensile strength and tablet thickness were in good agreement with the friability results. This investigation suggests that the excipients. originally utilized in tabletting could be modified to provide better physical properties for direct compression as matrix materials.

Pellet capsule dosage form has shown many advantages and flexibility in the way of enhancing the therapeutic safety and potency or in term of processing and formulation design. The most widely used pelletization processes in the pharmaceutical industry are extrusion/spheronization, solution/suspension layering, powder layering, and melting pelletization. In the second part of this study, pellets were prepared using extrusion and spheronization method.

Basically, the effect of different ratio of excipients (lactose, dicalcium phosphate (DCP), and their coated powders (manufactured in the first study) to microcrystalline cellulose (Avicel PH 101), water content, and spheronization speed on the size and sphericity of pellets were investigated. The amount of water required for spheronization depended on the type and proportion of staring materials. A higher proportion of Avicel required correspondingly a greater amount of water to form spheroids of a certain mean size. DCP also required a greater amount of water to produce spheroids. Generally, a larger and irregular shape of pellet was obtained at lower spheronization speed, whereas a smaller and round shape of pellet was produced at higher spheronization speed. Further, a examine the dissolution Captopril and a water insoluble drug of Nifedipine were selected as model drugs to examine the dissolution characteristics. All level of coated amount for both excipients show a similar pattern of dissolution profile. The diffusion mechanism is mainly controlled by the solubility of drugs.