靈芝纖維作爲錠片賦形劑之功能性評估

Functionality evaluation of Ganoderma fiber as tabletting

中文摘要

雖然現今賦形劑的種類非常多，但是以天然植物作爲開發製藥賦形劑的原料卻未曾間斷過，這些賦形劑廣泛使用於各種劑型上，尤其是錠劑劑型。靈芝（Ganoderma）爲傳統使用之中藥材，其子實體纖維屬於多醣體（fungal polysaccharide）之一類，截至目前爲止，均無有害成份之報告。本研究則是在於探討靈芝纖維是否可以成爲錠片賦形劑之原料。第一部份實驗中，在於研究靈芝纖維於不同條件下處理所得之粉末其流動性質與壓錠性質。靈芝纖維（Ganoderma fiber）分別於三種條件下浸泡 3 小時《A：蒸餾水/室溫、B：蒸餾水/85℃、C：1N NaOH 溶液/85℃》後，以 sodium hypochlorite 將粗纖維漂白乾燥所得之粉末（modifiedGanoderma）皆具有良好之流動性質；但其錠片結構強度則以鹼處理所得之粉末具有較佳之結合性質（低脆度與高硬度）。靈芝粉末與 Acetaminophen（ACT）依 1：1、1：2 及 1：3 等三種比例混合，於 5 種打錠壓力（0.5、1.0、1.5、2.0 及 3.0 噸）下壓製所得之錠片具有高硬度、低脆度與速崩散之性質。所有處方錠片硬度隨著打錠壓力的增加而增加，但是藥物溶離速率及溶離量則不受打錠壓力所影響；於 5 分鐘內藥物溶離釋出量均可達 80%以上，10 分鐘內幾乎可完全釋出。第二部份實驗則是在於探討靈芝纖維與微晶纖維素（microcrystalline cellulose，MCC）共同乾燥所得粉末之流動性質與壓錠性質。經鹼處理所得之 modified Ganoderma 與 MCC 依 1：1、1：3、1：5 及 1：10 等四種比例混合，經共同乾燥（codrying）所得之粉末皆具有極佳之流動性質。粉末於各打錠壓力下壓製所得之錠片其崩散度不受打錠壓力所影響，但會隨著 modified Ganoderma 含量的增加而提高。除了以 1：1 之比例混合之處方錠片硬度小於 10 Kp 外，其餘處方錠片硬度皆高於 10 Kp。第三部份實驗中，則是在於探討 ACT 與 modified Ganoderma 和 MCC 之混合物共同乾燥所得之粉末壓錠性質與藥物釋放情形。經鹼處理所得之 modified Ganoderma 和 MCC 之水凝膠與固定含量之 ACT（95%含量）共同乾燥所得之粉末於各打錠壓力下壓製所得之錠片硬度會隨著打錠壓力的增加而增加，但是在超過 2 噸壓力時所得之錠片硬度會急劇下降。在 0.5 噸打錠壓力下壓製所得之錠片，其藥物溶離速率與溶離量會隨著 modified Gnoderma 含量的增加而增加；但在超過 1 噸壓力所得之錠片，其溶離速率及溶離量則不受打錠壓力及處方組成所影響。1 噸壓力下壓製所得之錠片於溶離試驗結果顯示錠片具有緩釋（sustained release）之效果，藥效可達 24 小時以上，且藥物釋放速率及釋放量會隨著 modified Ganoderma 含量的增加而提高。崩散劑的添加有助於錠片之崩散，藥物釋放速率及釋放量會隨著其添加量的增加而提高；崩散能力爲 Primojel>Crospovidone>Starch 1500。

英文摘要

Development of pharmaceutical excipient from natural plants is a continuing process. These new excipients were used widely in various dosage forms, especially tablet dosage form. The fiber obtained from the fruiting body of Ganoderma, which is a traditional Chinese medicine, belongs to fungal polysaccharide. There has no report about it's toxicity till now. In this study, the possible uses of Ganoderma fiber as tabletting excipient were examined. In the first part, the effect of treated conditions on the physical characteristics of Ganoderma powder was compared. Ganoderma fiber was treatedfor 3 hours under three different conditions: in distilled water at ambient temperature (A), in hot distilled water at 85℃ (B) and 1N NaOH solution at 85℃. After processing, the fiberwas bleached with Clorox (sodiumhypochlorite) and then tray-dried in a hot air oven. All the drying products, named modifed Ganoderma, possess good flowability. But only the powder obtained from condition C shows better compactibility. These modified Ganoderma powders were physically mixed with acetaminophen(ACT) in three different ratios (1/1, 1/2 and 1/3) and then compressed into tablets with five compaction forces(0.5, 1.0, 1.5, 2.0 and 3.0 ton). All the tablets have high crushing strength,low friability and instant disintegration properties. The crushing strength ofall tablets increases as compaction force increases, but the rate of drug released was not affected by compaction force. Most shows that more than 80 %of drug was released at 5 minutes, and dissolution was completed within approximate 10 minutes. In the second part, the physical characteristics of codried powder ofmodified Ganoderma (treated with alkaline solution) and microcrystalline cellulose (MCC) at different ratios (1:1, 1:3, 1:5 and 1:10) and the resulting tablets were examined and compared. No matter what ratio was between modified Ganoderma and MCC the flowability of powder was demonstrated to be fair. The disintegration of tablet was not affected by compaction force,but increases with the increasing content of modified Ganoderma. The crushing strength ofall tablets is higher than 10 Kp except for the tablets prepared with an 1:1 ratio of modified Ganoderma to MCC. In the third part, the tabletting characteristics of ACT by codrying with amixture of modified Ganoderma and MCC was tested. The crushing strength of most ACT tablets made with codried powder containing modified Ganoderma (treatedwith alkaline solution) and MCC increases as compaction force increases. Butthere shows rapiddecline when compressed tablets at a force higher than 2 tons. The drug releaserate from the tablets compressed at 0.5 ton increases as modified Ganoderma content increases. But when compaction force was over 1 tonthe release rates were not influenced by compaction force as well as by the content of modified Ganoderma. However, the dissolution of ACT from these tablets compressed at 1 ton could be sustained to longer than 24 hours. The extent of drug release was

shownto be increased with increasing amount of modified Ganoderma in the codried mixture. The addition of disintegrants could further accelerate the drug released from tablet. It was also dependent on the amount and kind of disintrgrant added. The disintegration rate was in the following order : Primojel > Crospovidone > Starch 1500.