迅速作用的 Sildenafil 微乳劑之鼻噴劑型發展研究

Development of Sildenafil Microemulsion for Rapid-Onset Nasal Spray

中文摘要

利用微乳劑發展出 sildenafil 之鼻腔內迅速傳輸藥物系統。微乳劑主要以油酸 (oleic acid) 爲基劑；Cremophor EL 或 Tween 系列爲非離子界面活性劑；輔助界面活性劑則以短鏈的單元醇、PEG 600 或 PG，進行鼻噴劑之發展研究。觀察此微乳劑系統的物化性質和溶解藥物能力，並討論 sildenafil 微乳劑型在活體兔子內鼻腔吸收的情況。由不同比例的界面活性劑與輔助界面活性劑所發展出的相圖中形成單一均質相的區域稱爲微乳劑。隨著界面活性劑比例的增加，相圖中形成微乳劑的區域會越小，但是黏度則會變大。Sildenafil 本身雖然屬於難溶性藥物，但是當微乳劑系統組成爲 40 % 油酸、10 % 水和 50 % 的界面活性劑系統，其中界面活性劑系統中 Tween 80 與 ethanol 比例爲 1:4，藥物的溶解度可達到 124 mg/ml。鼻腔內投予此 sildenafil 微乳劑型後，可以快速的被吸收，當給予 10 mg 的噴鼻劑量後，會立即達到最低有效濃度且作用時間持續超過 3 個小時。由本研究的結果顯示，oleic acid、Tween 80、ethanol 和水組成的微乳劑可快速地將 sildenafil 經由鼻腔傳輸達到最低有效濃度來治療勃起功能障礙。

英文摘要

An oleic acid-based microemulsion system with Cremophor EL or Tween series as surfactants, and short-chain alcohol, PEG 600 or PG as cosolvents was developed for rapid-onset intranasal delivery of sildenafil. Phase behavior and solubilization capacity of the microemulsion system were characterized and in vivo nasal absorption of sildenafil from microemulsion formulations was investigated in rabbits. A single isotropic region, which is considered as a microemulsion, was found in the pseudo-ternary phase diagrams developed at various surfactants : cosolvents ratios. With the higher weight percentage of surfactant, the region area of microemulsion in the phase diagram decreased whereas the viscosity of microemulsion increased. Sildenafil, a water-insoluble drug, displayed a high solubility of 124 mg/ml in a microemulsion consisting of 40 % oleic acid, 10 % H2O, and 50 % Tween 80:ethanol (at 1:4 weight ratio). Nasal absorption of sildenafil from this microemulsion was found to be fairly rapid. At 10 mg dose, the onset of action was arrived instantly follow administrating the IN formulation and the duration was over 3 hours. These results suggest that the microemulsion system composed of oleic acid, Tween 80, ethanol and water may be a useful approach for the rapid-onset delivery of sildenafil with the erectile dysfunction.