第一部份：卡普洛芬於醇類溶媒之光解反應 第二部份：以高壓液相層析法定量甲醇溶液中之那普洛辛及其方法驗證

I. Photolytic Studies of Carprofen in Alcoholic Solvents II. Quantitation of Naproxen in Methanol by HPLC and Method Validation

中文摘要

本研究分爲兩部份進行一系列光分解實驗。先將卡普洛芬(CPF)及那普洛辛(NAP)分別置於醇類溶媒中如甲醇或乙醇，以 Hanovia 200 W 高壓汞燈照射數小時下，進行光解反應。

第一部份以管柱層析法將卡普洛芬光解產物分離，共得到三種主要的光解產物，分別命名爲 CPF 10、CPF 28 及 CPF 48。藉由質譜儀、紅外線光譜儀、核磁共振氫譜及碳譜判斷：CPF 10 爲 2-(2-carbazolyl) propionic acid；CPF 28 爲 2-(2-carbazolyl) propionic acid, methyl ester；而 CPF 48 爲 2-(6-chloro-2-carbazolyl) propionic acid, methyl ester。在乙醇溶液中則發現有相當於甲醇溶媒滯留時間的 CP 11、CP 28 及 CP 56 光解產物生成。CP 56 爲乙基酯，爲酯化反應之衍生物。以上是以高效液相層析法(HPLC)於醇類溶液中監測卡普洛芬進行光解反應並以各類光譜法決定 CPF 10、CPF 28 及 CPF 48 產物構造的方法。

第二部份乃發展一個快速、敏感度高及準確的安定性指標的高壓液相層析法來定量那普洛辛。對那普洛辛的分析方法是用 Inertsil ODS-3V 管柱，移動相則採乙腈:甲醇:水=40:20:40 (v/v/v) ，UV 偵測器則設定爲 230 nm。就已發展出的分析方法，其相關統計及確效包含有高壓液相層析系統規範、波峰純度完整以及光解產物和原料藥之間的解析度，及日內、日間差異分別在 4.56%和 3.82%以內。靈敏度可偵測到極低的濃度，偵測極限(Limit of Detection；LOD)可測得之濃度爲 64 ng/mL，而定量極限(Limit of Quantitation；LOQ)可測得之濃度爲 0.29 μg/mL。由此可知，就建立的分析方法表現出良好的選擇性和特異性，適合用來作爲那普洛辛的光安定性的分析。

英文摘要

This thesis is divided into two parts. Carprofen or naproxen was placed in a polar solvent, methanol or ethanol separately, then it was exposed to a Hanovia 200 W high pressure mercury lamp.

Firstly, a series of photolytic study of Carprofen(CPF) was undertaken.The photodegradants were separated and quantified by a HPLC method. Three photolytic products, CPF 10, CPF 28 and CPF 48, were isolated by the column chromatography. By way of analyzing MS, NMR and IR spectra, their structures were characterized.

Their structures were identified as CPF 10, 2-(2-carbazolyl) propionic acid；CPF 28, 2-(2-carbazolyl) propionic acid, methyl ester；and CPF 48, 2-(6-chloro-2- carbazolyl) propionic acid, methyl ester. Similar photolytic products including CP 11, CP 28, and CP 56 were found in ethanol. CP 56, an ethyl ester of CPF 48 was found as a derivative in ethanol. High-performance liquid chromatographic assay method was used for monitoring the degradation of CPF and its degradants-CPF 10, CPF 28, and CPF 48.

Secondly, we focused on the quantitation studies of the photochemical decomposition of Naproxen (NAP). A rapid, sensitive, and accurate stability-indicating high performance liquid chromatographic assay method for determination of the degradation of NAP was developed and validated under photoirradiated conditions. The quantitation was monitored with an Inertsil ODS-3V column using a mobile phase of acetonitril : methanol : water = 40:20:40 (v/v/v). The UV detector was set at 230 nm. The related statistics of the developed methods including the system criteria, peak integrity, and resolution among the parent drug and its degradation products were calculated. The CV% of intraday and interday tests were lower than 4.56% and 3.82%, respectively. LOD (Limit of Detection) was 64 ng/mL, and LOQ (Limit of Quantitation) was 0.29μg/mL. Our established HPLC assay method shows good selectivity and specificity which is suitable for the stability measurement of NAP.