報 告 書

医薬品医療機器レギュラトリーサイエンス
Pharmaceutical and Medical Device Regulatory Science
Vol. 41, No. 12, 971～982 (2010)

平成20年度「日本薬局方の試験法に関する研究」研究報告[*5]

近赤外分光法を用いた医薬品の規格・基準の設定に関する研究 その3[†]

―結晶レジボア型経皮吸収テープの品質評価法への応用と含量試験に用いる検量モデルの構築法に関する一例―

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Application of NIR Spectroscopy/Macroscopic Mapping as a Quality Evaluation Tool of Crystal Reservoir-type TDDS Tapes, and an Approach to High-precision Qualitative Prediction of API by NIR Spectroscopy

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Summary

Transmittance-reflectance near-infrared (NIR) spectroscopy/mapping was employed for non-destructive detection of a crystalline active pharmaceutical ingredient (API) in transdermal drug delivery system (TDDS) tapes employing a crystal-reservoir system. Tulobuterol, which is used as a bronchodilator (β_2-blocker) to treat bronchial asthma, was selected for this study, and the absorption at 6430 cm^{-1} of TBR crystals was detected. Moreover, mapping analysis using the focused NIR beam (3 mm diameter) provided a chemical map of the whole tape in a short time. These results support the value of NIR spectroscopy as a non-destructive quality evaluation tool for TDDS tapes with a crystal-reservoir system.

We also constructed a high-precision calibration model for quantitative prediction of API by NIR spectroscopy. Experimental design and practical sample numbers for precise and robust calibration were evaluated using model tablets containing theophylline as the API. The characteristic absorption of N-H was selected for quantitative prediction and partial least-squares (PLS) calibration models were calculated using various pre-processed data. The calibration models were evaluated using the relative standard errors between the NIR values and the reference (HPLC) values, and the correlation coefficients of the calibration curves. The calibration models obtained from two sample sets (5 levels × 6 samples set and 30 levels × 1 sample set) showed no significant difference concerning the evaluation items. These results suggest that small numbers of samples can provide comparatively high precision, if a suitable experimental design and data pre-processing are used.

Key words

NIR, Transdermal tapes, Macroscopic mapping, Calibration models, PLS, data pre-processing