HPLC-MS/MS によるラット血漿中リバスチグミンおよびその代謝物の同時測定法の開発

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High performance liquid chromatography coupled with mass spectrometry for simultaneous determination of rivastigmine and its metabolite in rat plasma

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ABSTRACT At present, there is no quantitation method that is highly sensitive and can be applied to simultaneous monitoring of the pharmacokinetics of rivastigmine and its metabolites (NAP 226-90) in rat plasma. No methods fulfilling the assay validation requirements was also established. Therefore, this study developed a quantitative method for measuring rivastigmine and NAP 226-90 concentrations using high-performance liquid chromatography and tandem mass spectrometry, examining plasma samples after rivastigmine administration. The methods for measuring rivastigmine and NAP 226-90 concentrations showed good fit over wide ranges of 1–100 ng mL^{-1} and 0.5–50 ng mL^{-1}, with lower limits of quantification at 1 ng mL^{-1} and 0.5 ng mL^{-1}, respectively. The plasma concentrations of rivastigmine and NAP 226-90 in six healthy rats were successfully determined, demonstrating the feasibility of applying the developed method. Thus, this research has successfully developed a sensitive, selective method, to simultaneously quantify rivastigmine and NAP 226-90 concentrations in rat plasma and be applicable to a pharmacokinetic study.

抄録　認知症治療薬リバスチグミンとその代謝物（NAP 226-90）のラット血漿中濃度について、アッセイバリデーションの要件を満たす同時測定法は現在まで開発されていない。本研究では HPLC-MS/MS 法を用いてその測定法を開発した。リバスチグミンおよび NAP 226-90 の検量線はそれぞれ 1–100 ng mL^{-1} と 0.5–50 ng mL^{-1} の範囲で良好な直線性を示し、定量下限値はそれぞれ 1 ng mL^{-1} と 0.5 ng mL^{-1} であり、感度および選択性も良好であった。さらに本法はリバスチグミンを投与したラットで測定することができ、今後の薬物動態研究に適用できることが明らかとなった。

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