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Research article

Development and validation of a high-performance liquid chromatography-tandem mass spectrometry assay for the quantification of Dexamphetamine in human plasma

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Highlights

- A LC-MS/MS assay is described for the quantification of dexamphetamine in plasma.
- The method is a new combination of simplicity, high sensitivity and full validation.
- The developed method is fast, easy-to-use and economic.
- Low m/z measuring problems in the clinical setting problems are briefly addressed.
- Applicability of the method for clinical studies was shown.

Abstract

Dexamphetamine is registered for the treatment of attention deficit hyperactivity disorder and narcolepsy. Current research has highlighted the possible application of dexamphetamine in the treatment of cocaine addiction. To support clinical pharmacologic trials a new simple, fast, and sensitive assay for the quantification of dexamphetamine in human plasma using liquid chromatography tandem mass spectrometry (LC-MS/MS) was developed. Additionally, it is the first reported LC-MS assay with these advantages to be fully validated according to current US FDA and EMA guidelines.

Human plasma samples were collected on an outpatient basis and stored at nominally -20 °C.

The analyte and the internal standard (stable isotopically labeled dexamphetamine) were extracted using double liquid-liquid extraction (plasma-organic and organic-water) combined with snap-freezing. The aqueous extract was filtered and 2 µL was injected on a C18-column with isocratic elution and analyzed with triple quadrupole mass spectrometry in positive ion mode.

The validated concentration range was from 2.5-250 ng/mL and the calibration model was linear. A weighting factor of 1 over the squared concentration was applied and correlation coefficients of 0.997 or better were obtained. At all concentrations the bias was within ±15% of the nominal concentrations and imprecision was ≤15%. All results were within the acceptance criteria of the latest US FDA guidance and EMA guidelines on method validation.

In conclusion, the developed method to quantify dexamphetamine in human plasma was fit to support a clinical study with slow-release dexamphetamine.

Keywords Dexamphetamine; HPLC-MS/MS; Plasma; Validation; GLP.

Abbreviations

MTBE	methyl *tert*-butyl ether
MF	Matrix factor

Introduction

Dexamphetamine (dextroamphetamine, *S*-amphetamine) (figure 1.) is a powerful central nervous system stimulant [1]. It exerts its pharmacological action through the rapid increase of dopamine levels in the striatum and noradrenaline levels in the prefrontal cortex [2].

In Europe, dexamphetamine is used in the therapy of attention-deficit hyperactivity disorder (ADHD) for children between the ages of 6 and 17 years where methylphenidate and atomoxetine were not