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Dedicated to the memory of
Professor Candin Liteanu on his 100th anniversary

ON THE HPLC/MS-MS ASSAY OF EPHEDRINES IN URINE: AN EXPERIMENTAL APPRAISAL

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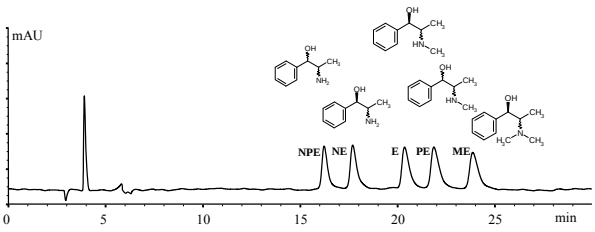
Chromatographic separation of ephedrines faces the imperative discrimination among the diastereoisomeric pairs ephedrine/ pseudoephedrine and norephedrine/norpseudoephedrine, respectively. Additionally, specific elution mechanisms and/or conditions are required to adequately control the peak symmetry. A discussion about the necessary experimental conditions to fulfil such goals is presented. Three alternatives were selected for the assay at sub-ppm level of ephedrines in urine through HPLC/MS-MS: i) ion pair reversed phase liquid chromatography with a perfluorinated ion pair agent; ii) reversed phase liquid chromatography on a phenyl modified silicagel as a stationary phase; iii) on-line solid phase extraction and reversed phase liquid chromatography under alkaline elution conditions. These alternatives were comparatively discussed with respect to their quality specifications.



INTRODUCTION

Ephedrines are commonly used as stimulants, decongestants, and appetite suppressants. Ephedrines belong to the alkaloids class, acting through the increase of noradrenaline on adrenergic receptors. Due to their increased ability to cross the blood brain barrier, they are acting as central nervous system stimulants, similar to amphetamines. Ephedrines are usually isolated from plants (Ephedraceae family). Analytical applications involving ephedrines refers to their assay in materials of natural origins,[1,2] in pharmaceutical formulations or dietary supplements,[3-5] forensic studies[6-9] (*i.e.* assay in human plasma, urine, or hair for anti-doping control) and monitoring in waste water.[10] The congeners of this class are (see Fig. 1): ephedrine (E), pseudoephedrine (PE), norephedrine (NE), norpseudoephedrine (NPE), and N-methyl ephedrine (ME). The pairs E/PE and NE/NPE are diastereoisomers. Consequently, their chromatographic reciprocal resolution is expressly needed, as long as, even mass spectrometry (MS), with its intrinsic tunable selectivity, is unable to discriminate among them. Certainly, relating to ephedrines, the chiral discrimination on adequate chiral selectors represents another major topic, often discussed in the literature.[11-13]

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through application of the three alternative methods on the incurred samples, although some of the experimental values exceeded the upper limit of quantitation (ULOQ) determined during validation.

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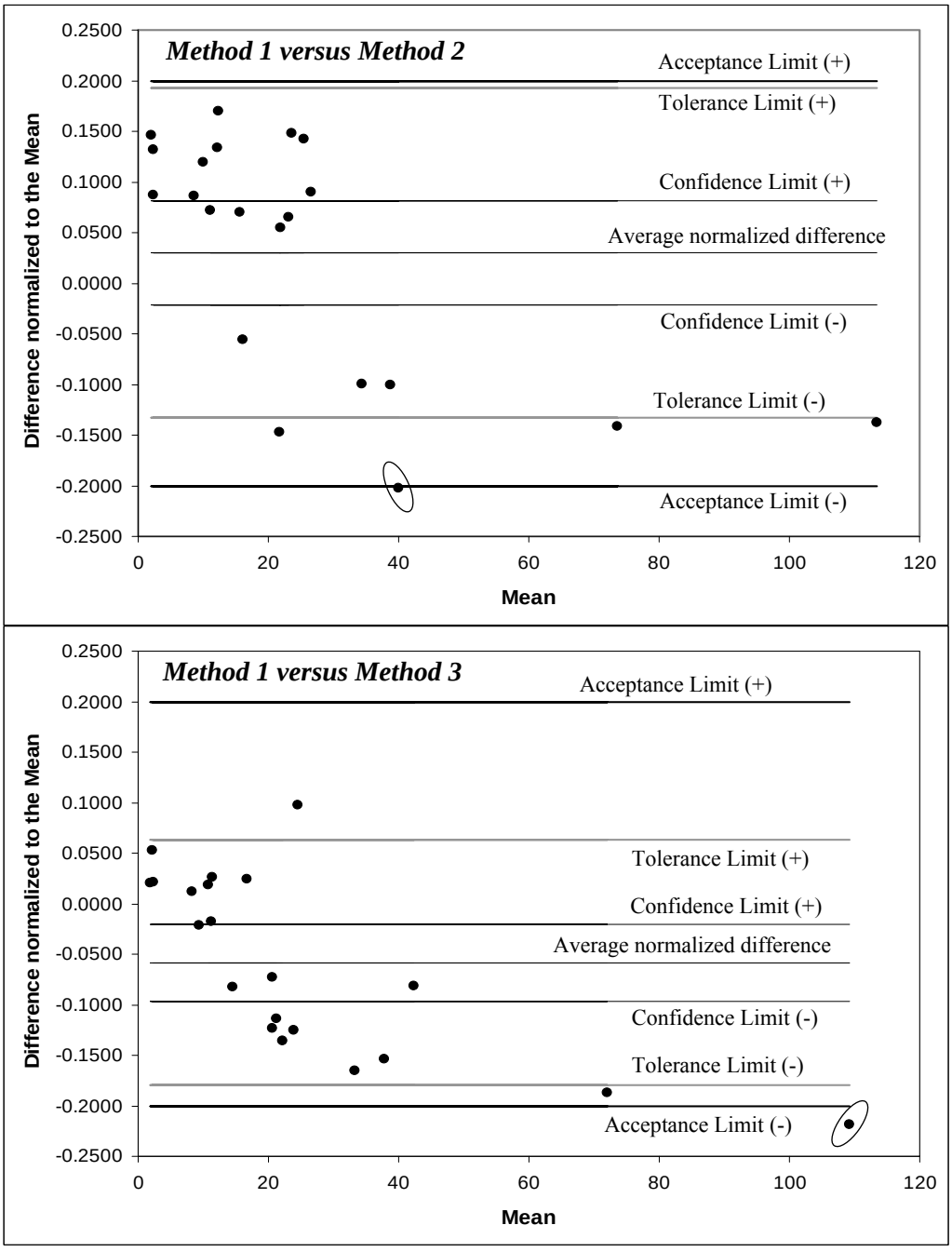

Fig. 8 – Bland-Altman plots for comparison of **Method 1** to **Method 2** and **3** respectively, illustrating the reciprocal good fitting between experimental results referring to the analyte Ephedrine (E) in incurred urine samples.

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