## The Potential of Dried Saliva Spots for Antidepressant Drugs Monitoring

Soares S.<sup>1, 2</sup>, Rosado T.<sup>1,2,3</sup>, Barroso M.<sup>4</sup>, Gallardo E.<sup>1,2,3\*</sup>

## ORIGINAL ARTICLE

## ABSTRACT

**Introduction:** Portugal has one of the highest rates of mental illness in Europe, and the consumption of antidepressants amongst its population has doubled between the years 2013 and 2016. Approximately 30 million packs of medication are prescribed and dispensed annually in this country to treat major depressive disorders<sup>1</sup>. Therapeutic Drug Monitoring (TDM) is a practice established for a small number of drugs, for which there is a direct relationship between concentration and pharmacological effect at the site of action. Commonly, TDM involves measuring drug concentrations in serum, plasma or blood, being complemented with clinical observation measures to assess patient's condition, support the individualization of therapy, detect changes in the patient 's pathophysiological status or the modification of the drug pharmacokinetics, but also to assess adherence to therapy.

**Methodology:** The present work describes a methodology with great potential for TDM purposes, allowing the determination of antidepressants (fluoxetine, venlafaxine, citalopram, sertraline, paroxetine and metabolites) using 100  $\mu$ L of oral fluid with dried saliva spots (DSS) and analysis by gas chromatography-tandem mass spectrometry (GC-MS/MS).

**Results:** For both sampling and extraction with DSS, several parameters were optimized using the statistical tool Design of Experiments (DoE), namely: drying and extraction times, extraction solvent and volume. The final optimized conditions were: 1 hour of drying, 1 mL of methanol and 5 minutes of extraction. The method was validated showing linearity within the adopted therapeutic ranges, with limits of detection and quantification between 10 and 100 ng/mL. All validation parameters were assayed according to the SWGTOX guidelines.

**Discussion:** This is the first work that uses DSS to extract antidepressants from oral fluid samples, proving to be a sensitive, simple and fast alternative to conventional techniques and samples used in TDM (solid phase extraction based procedures and plasma samples). It also reveals potential to be routinely applied in TDM and forensic toxicology purposes, as it has been successfully applied to the analysis of authentic patient samples<sup>2</sup>.

Keywords: antidepressants, DSS, drug monitoring.

\*Corresponding author: egallardo@fcsaude.ubi.pt.

<sup>&</sup>lt;sup>1</sup> Centro de Investigação em Ciências da Saúde, Faculdade de Ciências da Saúde da Universidade da Beira Interior (CICS-UBI), Covilhã, Portugal.

<sup>&</sup>lt;sup>2</sup> Laboratório de Fármaco-Toxicologia UBIMedical, Universidade da Beira Interior, Covilhã, Portugal.

 <sup>&</sup>lt;sup>3</sup> Centro Académico Clínico das Beiras (CACB) – Missão de Problemas Relacionados com Toxicofilias, Covilhã, Portugal.
<sup>4</sup> Serviço de Química e Toxicologia Forenses, Instituto Nacional de Medicina Legal e Ciências Forenses-Delegação do Sul, Lisboa, Portugal.

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