

Enantioselective analysis of ketamine and other common drugs of abuse using supercritical fluid chromatography tandem mass spectrometry (SFC-MS/MS): Investigation of fundamental aspects

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Supercritical Fluid Chromatography (SFC) is a powerful separation technique. This technique offers certain advantages in terms of separation efficiency, analysis speed, sensitivity and is environmentally friendlier compared to high-performance liquid chromatography (HPLC). The use of supercritical carbon dioxide as the major component of a mobile phase provides low viscosity and high diffusion coefficient, enabling achieving higher theoretical plates at higher flow rates compared to HPLC. Furthermore, the combination of carbon dioxide with polar mobile phases (organic modifiers) allows the technique to effectively analyze both polar and non-polar compounds simultaneously.

SFC coupled with tandem mass spectrometry (MS/MS) is one of the most powerful techniques in modern science for both separation and identification, as the minimal amount of polar mobile phase used significantly increases sensitivity compared to other chromatographic methods.

Additionally, SFC is better compatible with electrospray ionization (ESI) techniques, as the use of carbon dioxide in the mobile phase facilitates the desolvation of droplets generated in the ion source, increasing the likelihood of ionization. SFC coupled with tandem mass spectrometry does not require basic or acidic additives to enhance ionization efficiency, as the use of methanol (and also ethanol and isopropanol) in the mobile phase leads to a reaction between the organic modifier and carbon dioxide, resulting in the formation of methoxycarbonyl acid(s), which represents good proton donor, thus ensuring effective ionization without the need of additives.

This study explores a comparison between HPLC and SFC in the analysis of ketamine and its metabolites in human saliva samples, evaluating separation efficiency, sensitivity, and various fundamental aspects of these techniques.