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Enantioseparation of 3-chloromethcathinone by liquid chromatography at the milligram scale

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Abstract

Background: The most prominent synthetic cathinone (SCAT) is 3-chloromethcathinone (3-CMC), accounting for 34% and 63.41% of the total seized new psychoactive substances (NPS) in Europe in 2021 and 2022, respectively [1, 2]. Over the latest years, since the first identification on the European drug market in September 2014 in Sweden, 3-CMC has gained significant popularity among the younger drug users [3]. Moreover, 3-CMC is chiral and its enantiomers can show different biological activity, highlighting the importance of the enantioselectivity studies in clinical, forensic and ecotoxicological context. **Objective:** The aim of this study was to optimize a chromatographic method for the enantiomeric separation of 3-CMC at the milligram scale for further use in *in vitro* and ecotoxicity assessments. **Methods:** The enantioseparation as well as the enantiomeric purity evaluation of the 3-CMC were performed by liquid chromatography coupled to the ultraviolet-visible detector (UV/Vis), using a CHIRALPAK® AD-H 10 x 250 mm, 5 µm, a semi-preparative column. A Dionex Ultimate 3000 automated fraction collector was used for fractions collection. Data was analyzed by Chromeleon 7.0 software. For method conditions optimization, a solution at 100 µg mL^{-1} of 3-CMC in ethanol with diethylamine was used. **Results:** The optimized method allowed the separation of the enantiomers of 3-CMC at final concentration of 3.7 mg mL^{-1}, with an enantiomeric purity of 98 % and 95 % for the first and second eluted enantiomer, respectively. The determination of the absolute configuration of the enantiomers is ongoing by electronic circular dichroism. **Conclusions:** The isolated enantiomers will be used for the enantioselective evaluation of the 3-CMC ecotoxicity. The determination of the absolute configuration of the enantiomers will enable correlating the ecotoxicity of each enantiomer.

Keywords: 3-chloromethcathinone; enantioseparation; synthetic cathinones

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