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Optimization of the derivatization procedure for the separation of the stereoisomers of 1,3-dimethylamylamine (1,3-DMAA) by gas chromatography - preliminary data

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Abstract

Background: 1,3-Dimethylamylamine (1,3-DMAA), also known as methylhexanamine, is a central nervous system stimulant with structural similarities with amphetamines and therefore presenting overlapping biological and detrimental effects [1]. Despite being banned, the presence of 1,3-DMAA in doping controls and dietary supplements continues to be of significant concern. This molecule has two stereogenic centres and thus four stereoisomers [2]. It is widely recognized that enantiomers may exhibit different biological activity, including pharmacokinetics, pharmacodynamics, and toxicity. Consequently, the development of analytical methods for enantioselective separation of 1,3-DMAA is crucial for an accurate determination of the risks associated with each of these stereoisomers. **Objective:** To develop an indirect method by gas chromatography coupled to mass spectrometry (GC-MS) for the separation and identification of the stereoisomers of the 1,3-DMAA. **Methods:** 1,3-DMAA was regenerated with sodium hydroxide, extracted with 0.1% triethylamine in hexane and then derivatized using the enantiomeric pure reagent (*R*)-(-)-α-methoxy-α-(trifluoromethyl)phenylacetyl chloride ((*R*)-MTPA-Cl). Subsequently, the sample was evaporated, reconstituted in anhydrous ethyl acetate, and analyzed by GC-MS. The chromatographic conditions were established using a capillary column containing 5% diphenyl-95% dimethylpolysiloxane (30 m × 0.25 mm × 0.25 µm), an injector temperature set to 280 ºC, with a temperature ramp starting at 140 ºC and increasing up to 215 ºC at a flow rate of 1 mL/min to a total run of 12.32 min. **Results:** As preliminary data indicate, the derivatization procedure allowed the formation of 4 diastereomers of 1,3-DMAA. The chromatographic conditions were optimised, allowing for the separation of the four diastereomers within 12 min. **Conclusions:** Derivatization and chromatographic conditions were established for enantioselective separation of 1,3-DMAA by GC-MS. Further validation of the method will be crucial for understanding the diastereomers' differential pharmacokinetics and pharmacodynamics, and consequently, the perils associated with their presence in food supplement samples.

Keywords: enantioselectivity; dietary supplements; chromatographic analysis

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