“Elimination profile of orally administered phenylethylamine”

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Project Overview

Phenylethylamine (PEA) is a naturally occurring modulator in the human central nervous system which also represents the core structure of different stimulants and psychoactive drugs. Because of the presumed effects on mood and body weight, PEA is widely sold as nutritional supplement. However, the oral bioavailability of the primary amine is very limited as it undergoes an extensive first-pass metabolism. The main metabolite of PEA is phenylacetic acid and its urinary concentrations were found to be significantly affected by physical exercise, stress, and mental disorders. The misuse of PEA in sports is prohibited in competition and the drug is classified as specified stimulant in the World Anti-Doping Agency (WADA) Prohibited List. But as the compound is naturally excreted into urine, a tool is required to differentiate between the renal elimination of endogenous PEA and an illicit administration of the drug. In 2015, the results of a pilot elimination study were published, which showed that orally administered PEA has only a minimal effect on urinary PEA levels. Moreover, a promising metabolite (M1 = 2-(3-hydroxyphenyl)acetamide sulfate) was identified which can potentially be used to verify PEA misuse.

Within this research project, two elimination studies with single and multiple doses of PEA will be conducted to evaluate whether the ratio of M1/PEA can be used as biomarker for an oral PEA administration. Reference material for PEA will be synthesized and comprehensively characterized, and 100 blank urine samples collected from healthy volunteers will be analyzed by means of liquid chromatography – tandem mass spectrometry (LC-MS/MS) as reference population to suggest a cut-off level for the stimulant. The results of this project will help doping control laboratories to clarify atypical PEA observations.

Results and Conclusions

Offering analytical strategies to detect the misuse of substances naturally produced in the human body remains crucial in the fight against doping in sport. Investigating the metabolism of prohibited substances in sport drug testing is a key element, in order to find efficient markers for their detection, prolong detection windows or even enable the discrimination between the abuse of substances from the consumption of contaminated food or their natural occurrence in the human body. Within this study, new insights could be provided concerning the renal elimination of 2-phenylethylamine and two of its respective metabolites on the basis of human administration studies. Given the rapid metabolism and thereby low impact of PEA ingestion on its urinary concentrations, threshold levels for PEA in doping control deemed inadequate. Evaluating the concentration ratio of M1 and PEA to detect potential misuse seemed promising at first, but respecting the large inter-individual variation within the calculated ratios, the establishment of a cut-off level for this marker proved difficult. However, assessing the urinary levels of M1 and a second major metabolite, PAG, combined by means of logistic regression analysis presents a novel approach to distinguish endogenous PEA from a potential misuse. In regard to the natural presence of both metabolites in the human body and the large variability observed within urinary levels, further research into potential confirmation methods, i.e. isotope ratio mass spectrometry, seems advisable in order to clarify potential suspicions of PEA administration