PROJECT REVIEW

"Characterization and detection of Growth Hormone Releasing Peptides and their Metabolites using in-vitro and in-vivo approache

M. Thevis, A. Thomas, P. Delahaut (German Sport University, Cologne, Germany)

Besides the widely assumed misuse of growth hormone as performance enhancing drug, a new class of compounds has received much interest in doping controls. Recent findings of growth hormone releasing peptides (GHRP) in nutritional supplements have shown the urgency to develop detection methods for these substances. To date the knowledge of the metabolic fate of these agents after oral application are only barely described. In the planned study different GHRPs will be synthesized, chemically characterized by liquid chromatography and mass spectrometry and metabolic products will be identified after in-vitro metabolism and animal feeding experiments. Finally, these metabolites will also be synthesized and a sensitive determination method by means of LC-MS/MS will be established.

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Results and Conclusion:

Growth hormone releasing peptides (GHRP) have received considerable attention in modern doping controls due to widespread availability of these compounds via internet-based (black-market) providers even as nutritional supplements.

These mostly non-approved substances offer, in addition to the potentially performance-enhancing boost of the endogenous growth hormone (hGH) production and release, also a masking effect due to negatively influencing the routine hGH assay. Eight different peptide candidates are known, but the metabolic fate of these small peptidic drugs after administration is largely unknown; consequently, a comprehensive in-vivo and in-vitro study was conducted in order to establish sufficient target analytes for doping control screening methods.

The substances were administered orally and intravenously to laboratory rodents and for each known GHRP at least three metabolites were identified in urine samples over a period of 12-24 hours. The formation of these metabolites was mainly due to peptidase activities, and experiments allowing for the comparison of animal in vivo with human in vitro data supported the applicability of animal model results to human doping control samples and authentic urine test scenarios.

For the identified and characterized metabolites a fast and efficient sample preparation procedure and sensitive and specific liquid chromatographic/mass spectrometric detection was developed, enabling the analysis of these compounds by commonly employed routine instrumentation.