

PROJECT REVIEW

“Qualitative and Quantitative Determination of Insulin-Like Growth Factor-I (IGF-I) or Synthetic Analogues in Human Plasma”

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Insulin-like growth factors (IGFs) are circulating peptides that are involved in the regulation of cell proliferation, differentiation and apoptosis. In particular IGF-I has been found to be a critical modulator of skeletal muscle growth when administered locally rather than systemically. The infusion of IGF-I into target tissues such as selected skeletal muscles results in a significant increase in total protein and DNA content, an effect that is highly desirable for athletic performance in various sports disciplines. Owing to the growth promoting properties of IGF-I it belongs to the prohibited list of the World Anti-Doping Agency, and the determinations of its abuse or corresponding synthetic derivatives is of paramount importance. The amino acid composition of recombinant IGF-I is identical to that of endogenously produced IGF-I, and preliminary approaches to reveal IGF-I misuse are based on its quantification. By means of mass spectrometry, a precise determination of IGF-I amounts in human plasma is aspired in addition to an unambiguous identification of this peptide. Moreover, synthetic analogues such as R³-IGF-I and long IGF-I are commercially available, and strategies enabling the detection of three structurally related compounds are required. A selective isolation of IGF-I and analogues from human plasma is possible by means of immunoaffinity extraction and subsequent liquid chromatography coupled to mass spectrometry provides substantial data allowing a qualitative and quantitative determination of target analyses.

Results and Conclusions

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Human IGF-1 is a promising part of a strategy to reveal the abuse of human growth hormone by serving as a biomarker. Therefore, it is of paramount importance to quantify the plasma level of IGF-1 in order to be able to compare the results with valid reference ranges and thus to distinguish between ‘normal’ and ‘abnormal’ concentrations. The definition of such reference values is still ongoing because there are many parameters to consider. Regarding the IGF-1 analogues as a possible threat in sports and doping control analysis, there is a lack of information because pharmacological data in humans are currently not available. Recent investigations in the internet have, however, shown that LONGTMR³IGF-1 in particular is already in use. Although it is not approved for the use in humans, it is probably favoured due to its increased potency (e.g. prolonged half-life). Based on its higher biological activity the administered doses and, hence the costs, are much lower than expected for an application of recombinant human IGF-1. Thus, an assay enabling the determination in athletes’ plasma specimens is required. The described procedure allows the valid quantification of human IGF-1 as well as the unequivocal identification of its analogues LONGTMR³IGF-1 and des(1-3)IGF-1. The combination of immunoaffinity isolation and purification with LC-ESI-MS/MS provides utmost specificity for the analysis of banned peptides as recently demonstrated¹. It enables absolute quantification without distortion caused by, e.g., cross-reactions.

PUBLICATIONS

- Quantification of human insulin-like growth factor-1 and qualitative detection of its analogue in plasma using liquid chromatography/electrospray ionisation tandem mass spectrometry. Bredehöft M, Schänzer W, Thevis M. Rapid Commun Mass Spec, (2008) 22:477.