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QUANTIFYING THERAPEUTIC PEPTIDES IN HUMAN PLASMA BY MASS SPECTROMETRY: OUR EXPERIENCE APPLIED TO PHARMACOKINETIC STUDIES IN CLINICAL TRIAL

Ania Cabrales Rico
Center for Genetic Engieneering and Biotechnology, Cuba

Mass spectrometry (MS) has impressive capabilities in terms of sensitivity, resolving power, mass accuracy and different scan-modes versatility. Either alone or in combination with liquid chromatography, it is the analytical tool of choice for synthetic therapeutic peptide characterization. Nevertheless, for peptide quantitation in human plasma or other biological samples, the design of the internal standard (IS) and the optimization of the sample processing and LC-MS analysis are also key elements for a successful outcome. In consequence, all strategies involving the peptide quantitation in biological fluids are still a challenge and need to be tailored. We present here our recent experiences in the development and validation of customized bioanalytical methods applied to pharmacokinetic studies included in phase I clinical trials. For the absolute quantitation of these three therapeutic peptides, alternatives to the AQUA® methodology were used. However, the design of the IS, sample processing and mass spectrometry techniques were optimized case by case for CIGB-500, CIGB-300 and CIGB-814 candidates. IS for CIGB-500 and CIGB-814 were synthetic peptides labeled with stable isotopes (13C and/or 15N) in specific residues within the amino acids sequence, instead of IS for CIGB-300 that was a N-terminus acetylated peptide. Sample processing, mainly based on plasma proteins organic or acid precipitation was adapted according to the peptide recovery. In the particular case of CIGB-300, no liquid chromatography separation was needed before MS analysis by MALDI-TOF MS. For CIGB-500 it was applied LC-MS analysis with simultaneous ion monitoring (SIM) in full scan mode. For CIGB-814 it was used LC-MS analysis in single reaction monitoring mode (SRM). The three bioanalytical methods were fully validated and applied to pharmacokinetic (PK) analysis in a phase I clinical trials. It was possible to obtain PK profiles and main PK parameters for all of the assessed candidates.

Biography

Ania Cabrales Rico is working as a Research Assistant at the Center for Genetic Engineering and Biotechnology (CIGB), Cuba. She graduated from University of Havana and got her PhD in Pharmaceutical Sciences in 2015 when she was promoted to Head of Purification and Analytics group, from the Physicochemical Characterization Department, in Biomedical Research. She has been working with synthetic peptides for many years, but particularly in the field of bioanalytical methods based on mass spectrometry (MS), since 2008. This multidisciplinary work allowed her to gain expertise in: (1) isotope labeled internal standards design, (2) sample processing previous to LC-MS analysis, (3) peptide quantitation by MS, (4) bioanalytical method validation and (5) pharmacokinetic analysis. Peptides are quite diverse regarding to their physicochemical properties, so the bioanalytical methods needs to be tailored, becoming each experience in unique opportunity to overcome an analytical challenge in a successful outcome.

ania.cabrales@cigb.edu.cu