Comparability of biosimilar products: Insulin as a model

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Introduction: Government initiatives at several nations have motivated the development of biosimilar products. In contrast to generics, biosimilar regulations require comparative preclinical and clinical data because of uncertainties regarding the level of characterization achievable, and the possible clinical consequences of differences in physical–chemical characteristics, such as amount of impurities. Protein therapeutics are a class of products which have a complex three-dimensional structure in solution whose integrity determines the biological activity, clinical efficacy, and safety. Thus, it is highly desirable that products from this class meet well-defined requirements for structural integrity. The characterization of conformational and oligomeric distribution of proteins is of paramount importance.

Methodology: We have studied regular acting, wild-type human insulin, and insulin analogues from different pharmaceutical products directly from their final finished formulation by the combined use of mass spectrometry, dynamic light scattering, small-angle X-ray scattering, nuclear magnetic resonance, single-crystal protein crystallography and electrospray ionization-mass spectrometry coupled to ion mobility spectrometry with the aim to analyze structural information.

Findings: We have made the combined use of modern state-of-the-art structural techniques for the detailed characterization of the chemical and structural integrity, accessing the correct folding through the evaluation of the secondary, tertiary and quaternary structural arrangement of the human insulin and insulin analogues.

Conclusion & Significance: These structural methods are currently well-established, and they can be accessed in most countries, in special those for the main pharmaceutical markets, the Americas, Europe and Japan. It could be used in routine evaluation of structural integrity and identity, as a part of current or evolving methods aiming the minimization of animals' requirement in routine quality control, in the development of novel insulin products, or in future protocols for a thorough comparability exercises between follow-on protein product and a reference product.

Speaker Biography

Maely Pecanha Favero-Retto is graduated in Pharmacy from the Federal University of Rio de Janeiro (1995), Master in Biological Chemistry from UFRJ (1999) and PhD in Pharmaceutical Sciences from UFRJ (2013). She is specialist in Hospital Pharmacy (2007) and Clinical Pharmacy (2015) by SBRAFH, with Executive MBA by the COPPEAD Institute (2008). She is currently a Technologist in Hospital Pharmacy at the National Cancer Institute and at the Hospital Municipal Miguel Couto. She is Professor of the Multiprofessional Residency in Oncology at INCA and postgraduate courses and President of the Brazilian Society of Hospital Pharmacy and Health Services (SBRAFH). She has experience in the field of biological metrology with emphasis on the study of biosimilar products.

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