In vivo predictive dissolution: relevant gastrointestinal factors and methodological approaches:

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In-vivo predictive dissolution methods (iPD) should incorporate the physiologically relevant characteristics of the "gold standard dissolution beaker" i. e. the human gastrointestinal (GI) tract. To design iPD methodologies, it is necessary to observe directly in-vivo drug dissolution. We have observed in vivo Ibuprofen levels on the GI tract after the administration of an oral immediate release ibuprofen product to human volunteers by using a specialized manometric catheter with 4 sampling ports that allowed the measurement intestinal drug concentrations, pH values as well as intestinal wall motility. Ibuprofen formulation was administered with a solution of Phenol Red (PR) as a non-absorbable marker. The relationship of GI variables (as luminal pH and GI motility) with Ibuprofen absorption rates has been explored. Results show that Ibuprofen luminal concentration is determined principally by the luminal pH and the GI Ibuprofen profiles follow closely the pH versus time fluctuations. In addition the modelling of PR concentrations has allowed the characterization of the range of gastric emptying profiles and their variability. All the in vivo modelled parameters have been incorporated in the Gastrointestinal simulator (GIS), a physiological based multi-compartment dissolution device. Examples of application of GIS dissolution experiments to discriminate non bioequivalent formulations of desketoprofen trometamol and etoricoxib will be presented. These results demonstrate the relevance of the gastrointestinal variables, pH and motility in oral absorption. iPD methodologies incorporating these variables in combination with mass transport computational methods will be an invaluable tool for formulation optimization.

References:

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Biography . Marival Bermejo, Pharm.D. PhD. Universidad Miguel Hernández, Elche, Spain
Marival Bermejo is Full Professor at the University Miguel Hernández, Spain. She earned her Ph.D degree at the University of Valencia in 1992. She got a position as Assistant Professor in 1994 and was promoted to Associate Professor in 1998. In 2008 she was appointed at University Miguel Hernández to coordinate the Area of Pharmacy in the Department of Engineering. She performed two post-doctoral research stages at the Institute of Topology and System Dynamics in Paris VII University, with Prof. Christiane Mercier and at the University of Michigan, with Prof. Gordon Amidon. Dr. Bermejo research is centered on developing in vitro models of biological barriers and predictive dissolution methods. She has been co-author of more than 100 papers, 10 books chapters and is co-author with Gordon Amidon of the English and Spanish versions of Modern Biopharmaceutics, a CD-Rom teaching tool. In 2001 she received the Research Prize of "Liconsa-Chemo Ibérica" for her work on fluoroquinolones absorption. She is member of the Board of Directors of the Drug Delivery Foundation and external assessor of the Spanish Agency of Medicines and EMA. Dr Bermejo has been nominated foreign member of the Chilean Academy of Sciences for her contribution to Pharmaceutical Scientists education and corresponding member of the Academy of Pharmacy of Valencia. She was awarded with a Fulbright scholarship for a 4-month sabbatical period at the University of Michigan in 2015 working on in vivo predictive dissolution with Prof. Amidon as local host and has been appointed as visiting research scholar in 2016-19 summer periods.