Formulation design can be described as the creation of a drug product, a dosage unit including a certain amount of drug substance, to assure the ‘dosage and administration’ for a certain period of time. The biggest goal to design drug products with high quality is neither more nor less than to control pharmacokinetics of drug substance in human. More drug substance are not biopharmaceutical class I (high solubility and high permeability) recently due to ‘drug-like’ optimization of specific binding to target receptors or enzymes and high-throughput screening of drug substance. It has led to issues, especially for oral dosage products, including non-linear pharmacokinetics, intra- and inter-individual absorption variability, it will also lead increased cost of not only the final drug product but also the pharmaceutical development itself. Therefore, increased interest in pharmacokinetics based formulation design has been expressed.

In a development at pharmaceutical companies, the speed of the development is very important to provide patients of excellent drug products with a right time, and it is desirable to supply clinical trial materials over a short term. Generally, quality target product profile (QTPP) sets for a final drug product. Also, in each development stage, quality target formulation profile (QTFP) should be set to ensure a desirable pharmacokinetics. At pre-clinical and early clinical stage of the development, it is mainly focused on increase in exposure amount of drug substance with dose proportionality to investigate the safety and toxicity of drug substances. Solubilization technology become therefore important through the use of various pharmaceutical technologies at early stage of formulation design. But it becomes sometime not necessary at late clinical stage or final drug product since those target dose strength becomes lower than at early stage. At late stage or for final drug product, manufacturability and ease of administration for patient would be added into QTFP and QTPP. The formulation at each development stage is different, however, constancy of the purpose of each formulation is ‘pharmacokinetics control’.

In case of a design of modified release formulation, it is important to set the target pharmacokinetics for the benefit for the better safety and efficacy of drug product by the control of peak and trough ratio of drug concentration. Moreover, the detail information of drug absorption become important for the formulation design, such as regional drug absorption, existence of absorption transporters, food effect, and so on. Input of the information to pharmaceutical scientist in early timing will be effective to reflect to formulation design in considering the preparation period of clinical trial materials.

The main purpose of this lecture is to discuss what role pharmacokinetics control play in the design of formulation during pharmaceutical development and to feel that both formulation design and pharmacokinetics control work cooperatively to the assurance of drug product quality and ‘dosage and administration’.

Biography

1986- Pharmaceutical Research Labs., Yamanouchi Pharmaceutical Co., Ltd.
2003- Director, Drug Delivery, Yamanouchi Pharmaceutical Co., Ltd.
2005- Senior Director, Drug Delivery, Astellas Pharma Inc.
2008- Senior Director, Oral Formulation Development, Astellas Pharma Inc.
2005- Associate Professor, Faculty of Pharmaceutical Science, Kyushu University
2007- Professor, Faculty of Pharmaceutical Science, Kyushu University