Department of Applied Pharmaceutics and Pharmacokinetics

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Research Projects:

With the aging of the population, the disease pattern is changing, and medical care is becoming increasingly complex. Although pharmaceuticals have been contributing significantly to the health care, medications for patients in clinical practice are variable among patients, depending on their genetic background, living environment, and health conditions. Therefore, even if it is a drug whose efficacy and safety are guaranteed through clinical trials, unexpected problems often occur such as its limited efficacy, side effects due to drug-drug or drug-food interactions, and idiosyncratic side effects. In order to reduce the risk of such problems arising, it is of extreme importance to establish the risk assessment method in drug development, to develop pharmaceutical technology for risk mitigation and avoidance, and to establish a clinical medication design and monitoring method. From these points of view, our laboratory is currently working on the following research.

1) Development of tissue/intracellular targeted drug delivery systems using biomolecular recognition mechanisms

When administered to the body a drug distributes nonspecifically throughout vascular and interstitial tissues, nonspecific tissue distribution. However, if specific molecular recognition mechanisms of endogenous substances are available, it is possible to selectively deliver the drug to the site of action. We are developing a targeted drug delivery system in which vesicles composed of lipids and synthetic polymers are used as drug carriers and the vesicle surface is modified with receptor recognition molecules. Specifically, the drug is efficiently taken up into the target cells using a sugar chain that recognizes E-selectin expressed in inflammatory blood vessels, and a peptide that binds to transferrin receptor highly expressed in cancer cells. We are trying to control intracellular dynamics and enhance pharmacological effects by using molecular recognition related to endoplasmic reticulum transport.

2) Development of pharmacokinetics and toxicity evaluation systems using the microfluidic devices

In order to understand the pharmacokinetics of candidate substances in drug discovery research, in vitro pharmacokinetic tests using cultured cells are usually conducted. At this time, with the ideal of reflecting the function of the cells used to human beings, expectations for human iPS cells have recently increased. Currently, we are developing a system that can evaluate the pharmacokinetics and toxicity of human tissues on a chip by seeding cells on a microfluidic device and performing perfusion culture in a 2D or 3D environment.

3) Information analysis of adverse event databases and its application to risk assessment

The side effects of medicines impose not only a clinical burden on patients in which they occur but a social and economic burden on medical practice and pharmaceutical companies. By epidemiologically analyzing large-scale data on post-marketing safety information, it is possible to find feature quantities in the occurrence of side effects and to formulate an action plan for risk reduction and avoidance. Currently, we are conducting researches on comprehensive searches for drugs with hepatotoxicity, their biomarkers, and applications to risk assessment.

4) Molecular dynamics and pharmacological analysis of adverse reaction and research on development for prevention and treatment

The side effects of medicines are a frequent problem in the clinical setting, which reduces the quality of life of patients and interferes with treatment. By clarifying the mechanism of its expression from the pharmacokinetics and pharmacological aspects, it is possible to cope with the side effects, which can lead to the prevention of the occurrence and the alleviation of the symptoms. At present, we are conducting researches on pharmacokinetic control factors in anti-HIV drugs and selection of appropriate anti-HIV drugs for controlling the onset of HIV-related neurocognitive disorders, and on mechanism analysis of taste disorders, which are side effects generated during cancer chemotherapy.

Recent publications

- Babazada H, Yanamoto S, Hashida M, Yamashita F. Binding and structure-kinetic relationship analysis of selective TLR4-targeted immunosuppressive self-assembling heparin nanoparticles. Int J Pharm. 552(1-2):76-83, 2018.
- Tsuda M, Otani Y, Yonezawa A, Masui S, Ikemi Y, Denda M, Sato Y, Nakagawa S, Omura T, Imai S, Nakagawa T, Hayakari M, Matsubara K. Analysis of glycoforms and amino acids in infliximab and a biosimilar product using new method with LC/TOF-MS. Biol Pharm Bull. 41(11):1716-1721, 2018
- Yamashita F, Fujita A, Sasa Y, Higuchi Y, Tsuda M, Hashida M. An evolutionary search algorithm for covariate models in population pharmacokinetic analysis. J Pharm Sci. 106(9):2407-2411, 2017.