Byung Hwa Jung et al., Madridge J Pharm Res. 2018
http://dx.doi.org/10.18689/2638-1591.a2.003

madridge CONFERENCES
International
Pharma Conference and Expo
May 2-4, 2018 Rome, Italy

Identification of Metabolite for mTOR Inhibitor, AZD8055 in Rats after a Single Oral Administration using Ultra-Performance Liquid Chromatography and Mass Spectrometry

Byung Hwa Jung[1]*, Md Mamunur Rashid[1], Hyunbeom[1] and **Hyun-A Oh[1, 2]**
[1]Korea Institute of Science and Technology, Republic of Korea
[2]Konkuk University, Republic of Korea

Metabolite identification of AZD8055, which is an ATP-competitive specific dual mTOR inhibitorand exhibited potent antitumor activity on several types of solid tumors, was performed using ultra high-performance liquid chromatography-ion trap mass spectrometry (UHPLC-IT-MS) through both in vitro and in vivo approaches using rat liver microsomes (RLMs) and rat plasma, urine and feces, respectively. A total of eight putative metabolites (five phase I and three phase II) were identified, and a tentative metabolic pathway was suggested for the first time. Considering the accurate mass and mass fragmentations of the detected metabolites, their plausible structures were suggested. Demethylation, hydroxylation, oxidation and morpholine ring opening were the major biotransformation processes for the phase-I metabolism, while phase-II metabolites were merely generated by the glucuronide conjugation reaction. The cumulative excretion of AZD8055 in urine and feces was 0.13% and 1.11% of the dose, respectively. When the semi-quantitative analysis of the metabolites was performed using UHPLC-MS/MS (ultra-performance liquid chromatography tandem mass spectrometry) to evaluate the overall trend of metabolites formation and excretion, AZD8055 was excreted more in the form of the metabolites than itself and their formation was very fast. Therefore it was presumed that biotransformation was playing a crucial role in its elimination. Ultimately, this study provides novel insights regarding the in vitro and in vivo bio transformations of AZD8055. Further investigations of metabolites of this potent anti-cancer compound could be beneficial for the antitumor drug design and development process

Biography:

Byung Hwa Jung has her expertise in metabolomics and DMPK (drug metabolism and pharmacokinetics). She has developed analytical methods for the quantitative and qualitative determination of endogenous metabolites and xenobiotics (drugs). The platforms for the non-targeted metabolomics and lipidomics using LC-MS for the evaluation of metabolic change in in vivo and in vitro systems were already established in her lab. Along with these systems, the quantitative analytical platforms for more than 170 metabolites and several drugs were also set up. The mechanisms and biomarkers for disease generation and development, and drug effect and adverse effects are studied with those systems.