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The Functional Characteristics of HM30181A as a MDR1 Inhibitor

Sung Hee Lee[1], Jin O Kwak[1], Ji Hyun Lee[1], Maeng Seop Kim[2], Min Goo Lee[1]

[1]Department of Pharmacology, Yonsei University College of Medicine, [2]Hanmi Pharmaceutical Co. Ltd.

MDR1 (multidrug resistance protein 1, P-glycoprotein, P-gp, *ABCB1*) is famous for its role in the multidrug resistance. In addition to anticancer drugs, a lot of drugs like antiviral agents, antibiotics and psychotrophic drugs are substrates of MDR1. Therefore, MDR1 in gastrointestinal tract can be an important barrier in pharmacokinetic aspect of p.o. medication. For example, paclitaxel, a well-known substrate of MDR1, is well known for its poor oral absorption and should be used by parenteral administration. Although MDR1 inhibitors, such as cyclosporine A, have been tried to reduce MDR1 activity, their systemic side effects and lower selectivity for MDR1 inhibition were more hazardous. HM30181A was presented as a MDR1 inhibitor. When HM30181A is administered orally, negligible amount is detectable in the systemic circulation. Therefore, it has advantages in combination therapy with oral drugs of which absorption is interfered by MDR1. We have investigated the characteristics of HM30181A as a MDR1 inhibitor using membrane vesicular ATPase assay and FACS assay. Our results show that HM30181A is superior to other MDR1 inhibitor like cyclosporine A, XR9576 and GF120918 in MDR1 inhibition for paclitaxel transport. Furthermore, HM30181A has more specific selectivity for MDR1 than other ABC transporters, for example, MRP1, MRP2, MRP3 and BCRP. Further studies of HM30181A are in progress and will be presented.