LYMPHATIC ABSORPTION OF NARINGIN AND NARINGENIN IN RATS

Tung-Hu Tsai\textsuperscript{1,2}, Yung-Jen Tsai\textsuperscript{1}, I-Lin Chen\textsuperscript{1}, Lie-Chwen Lin\textsuperscript{3}

\textsuperscript{1}Institute of Traditional Medicine, School of Medicine, National Yang-Ming University, Taipei 112, Taiwan
\textsuperscript{2}Department of Education and Research, Taipei City Hospital, Taipei, Taiwan
\textsuperscript{3}National Research Institute of Chinese Medicine, Taipei, Taiwan

Absorption of drug molecules through the portal vein results in direct transport to the liver for additional biotransformation, however, lymphatic absorption results in delivery of the drug molecules to non-hepatic systems to avoid the first-pass effect. We hypothesize that lipophilic compounds will be primarily absorbed through the lymphatic system. The aim of study is to investigate the portal vein and lymphatic absorption of naringin and naringenin in Sprague-Dawley rats. A mesenteric lymphatic/duodenum- cannulated rat model was used to investigate the lymphatic absorption of naringin and naringenin with intra-duodenal administration. Our data demonstrated that these polyphenols could be found in both the systemic circulation and lymphatic system after naringin or naringenin was given intro-duodenally. The maximum concentrations of naringin and naringenin in plasma were higher than those in the lymph. The presence of naringin and naringenin in lymph demonstrated that both substrates could be absorbed by the mesenteric lymph system. Furthermore, narigenin, the aglycone of naringin, is more lipophilic and would be more easily absorbed into the lymphatic system.

THE ESTABLISHMENT OF HUMAN ABSORPTION PREDICTION SYSTEM BY MINI-USSING CHAMBER USING HUMAN INTESTINAL TISSUES

Masateru Miyake\textsuperscript{1,2}, Nobuhiko Kamada\textsuperscript{1}, Mina T. Kitazume\textsuperscript{1}, Hajime Toguchi\textsuperscript{2}, Tadashi Mukai\textsuperscript{2}, Susumu Okamoto\textsuperscript{1} and Toshifumi Hibi\textsuperscript{1}

\textsuperscript{1}Division of Gastroenterology, Department of Internal Medicine Keio University School of Medicine, Shinnanomachi 35 Shinjyuku-ku, Tokyo 160-8582, Japan.
\textsuperscript{2}Formulation Research Institute, Otsuka Pharmaceutical Co. Ltd., Ebisuno 224-18 Hiraishi Kawauchi-cho, Tokushima 771-0182, Japan.

[Purpose] We aimed to establish a human absorption prediction system with high reproducibility by using human intestinal tissues. Additionally, we designed our system to distinguish between non-permeable and low-permeable markers so that the system that we are developing will be able to assess drugs that are less than 50% absorbable by human intestines. [Methods] Human tissues from were taken from patients with Ulcerative colitis (UC), Crohn’s disease (CD) and cancer with the permission of the patients in accordance with the rules of the Ethical Committee in Keio University Hospital. Tissues were mounted in a Mini-Ussing chamber and a transport study was performed to investigate drug absorption. As model drugs, FD-4 was used as a non-permeable marker, Rebamipide as a low-permeable marker and Cilostazol as a high-permeable marker. The tissue viability after transport was confirmed by histopathological examination. [Results and Discussion] The respective permeabilities of FD-4 and Rebamipide with about 20% absorption bioavailability could be distinguished by considering mass balance and the total amounts of permeated and accumulated drug concentrations. The reproducibility of the ranking order of the absorptions of FD-4, Rebamipide and Cilostazol was confirmed more than 50 times, even where human tissues from UC and CD were used instead of healthy ones. [Conclusions] We could finally establish that the new human absorption prediction system produces highly reproducible results, even for low permeable drugs which have less than 50% absorption in human gut. The electrophysiological parameters such as potential differences (PD) were measured in order to confirm the tissue viability in the transport study.