EFFECTS OF CITRUS JUICES ON THE FUNCTION OF HUMAN ORGANIC ANION TRANSPORTING POLYPEPTIDE OATP-B (OATP2B1)

Hiroki Satoh, Fumiaki Yamashita, Masayuki Tsujimoto, Hisakazu Ohtani and Yasufumi Sawada
Graduate School of Pharmaceutical Sciences, Kyushu University, 3-1-1 Maidashi, Higashi-ku, Fukuoka 812-8582, Japan

**Purpose:** Organic anion transporting polypeptides (OATPs) transport various anionic compounds. Recently, some fruit juices have been shown to inhibit the function of human OATP-A (OATP1A2) *in vitro*, and to decrease the intestinal absorption of fexofenadine in human. However, human intestinal epithelial cells express OATP-B (OATP2B1) but not OATP-A. The purpose of this study is to examine the effects of citrus juices on the function of human OATP-B. **Methods:** We investigated the effects of citrus juices on the uptake of estrone-3-sulfate (E1S), typical OATP-B substrate, into HEK293 cells stably expressing human OATP-B. **Results and Discussion:** Extracellular pH (5.5–7.4) did not affect the OATP-B-mediated E1S uptake. Although this finding is inconsistent with previous reports, the reason of this disagreement remains unknown. Both grapefruit juice and orange juice (pH adjusted to 7.4) inhibited the OATP-B-mediated E1S uptake at a concentration range from 1 to 5%. Lineweaver-Burk plot revealed that grapefruit juice (pH 7.4) competitively inhibited the OATP-B-mediated E1S uptake. Since human OATP-B is expressed on the luminal membrane of intestinal epithelial cells, inhibition of OATP-B by citrus juices might result in a decrease in the drug absorption. Moreover, glibenclamide was first identified as substrate of human OATP-B, and then citrus juices inhibited the OATP-B-mediated glibenclamide uptake. We are presently investigating pravastatin, which was previously reported as substrate of human OATP-B. **Conclusion:** Intestinal OATP-B may be partially responsible for the interactions between drugs and citrus juices.