S12-6 Manipulation of intestinal influx transporters which are responsible for glucose absorption by polymer conjugates bearing glucose moieties

◯Shinji SAKUMA[1], Shinji YAMASHITA[1], Ikumi TAMAI[2], Toshiyuki KIDA[3], Mitsuru AKASHI[3]
[1]Setsunan Univ. Faculty of Pharm. Sci., [2]Kanazawa Univ. Faculty of Pharmacy, [3]Osaka Univ. Grad. Sch. of Engineering

Many scientists have investigated the potential of conjugation of drugs with biocompatible polymers as a technology that eliminates pharmacokinetic and/or physicochemical disadvantages of original drugs and often confers unique properties to the drugs that they do not originally possess. We have been also investigating the conjugation with the aim of developing a novel strategy for the treatment of systemic diseases through the manipulation of diverse molecules on the intestinal membranes. Orally administered polymer-drug conjugates with high-molecular weights are not absorbed logically through the intestinal membranes. This character limits the application of the conjugates as oral medicines, but non-absorption of the conjugates may result in high safety and a low incidence of drug-drug interactions when compared with conventional low-molecular weight drugs that are absorbed systemically. Polymer-drug conjugates appear to be suitable for oral medication against patients with life style-related diseases who are required to take several drugs concomitantly for a long period. For the treatment of diabetes, it is essential to maintain the blood glucose level appropriately. Carbohydrates in the diet are hydrolyzed by digestive enzymes. The resulting monosaccharides are absorbed from the small intestine mainly via Na+/glucose cotransporter 1 (SGLT1) expressed at the apical membranes of intestinal epithelial cells. We have successively obtained several polymer conjugates bearing glycosides that reduce SGLT 1-mediated glucose absorption in vitro and in vivo. In this symposium, our recent findings will be discussed.