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The Potential of Sucrose Esters to be used as Oral Absorption Enhancers

L. KIS [1,2], A. SZŰTS [2], N. OTOMO [3], P. SZABÓ-RÉVÉSZ [2], M. A. DELI [1]

[1] Laboratory of Molecular Neurobiology, Institute of Biophysics, Biological Research Center, Hungarian Academy of Sciences, Szeged, Hungary
[2] Department of Pharmaceutical Technology, University of Szeged, Szeged, Hungary
[3] Mitsubishi-Kagaku Foods Corporation, Tokyo, Japan

E-mail: kisslori@brc.hu (L. Kis)

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Overcoming biological barriers, including the gastrointestinal epithelial barriers, is a great challenge for pharmaceutical research. There is a need for new absorption enhancers with more favorable profile. Sucrose esters are widely used in the food and cosmetic industry, and there are reports on their potential use in pharmaceutical formulations as excipients [1, 2], however no data are available on their toxicity profile and their usefulness as absorption enhancers in epithelial models.

We tested three water soluble sugar esters having HLB value of 16, laurate (L-1695), myristate (M-1695), palmitate (P-1695) esters, with 12, 14 and 16 carbon fatty acid chains, respectively, on human Caco-2 epithelial monolayers, a widely used model for the human intestinal epithelial barrier. Cremophor RH40 and Tween 80 were used as reference absorption enhancers. For toxicity tests cells were cultured in 96-wells, and MTT dye conversion and lactate dehydrogenase relase were determined after treatments. For permeability tests cells were cultured on Millipore CM inserts (hydrophilic PTFE membranes, pore size: 0.4 µm, surface 4.2 cm^2) in 6-well plates for 3 weeks to reach stationary phase and barrier properties. Fluorescein was selected as a marker of paracellular permeability. Untreated monolayers formed a good barrier as reflected by a transepithelial resistance of $722 \pm 80\ \Omega\ cm^2$ and positive immunostaining for tight junction proteins claudin-4 and ZO-1. Sucrose esters showed 50 % cytotoxicity (1 h treatment) at 300 µg/ml, while cell death was measured at concentrations above 1 000 µg/ml. The reference molecules were only toxic at doses above 10 000 µg/ml. L-1695 in non-toxic concentrations reduced TEER and increased permeability for fluorescein in Caco-2 monolayers indicating an absorption enhancer property.

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