SL01 Physiological effects of exogenous carbohydrates on gastrointestinal epithelia

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Diseases of the gastrointestinal system are often related with pathological changes of mucous membranes. In an *ex-vivo* system based on porcine colonic tissue various neutral and acidic polysaccharides were tested concerning their bioadhesive potential in order to form artificial mucin layers on colon epithelial membranes. Rhamnogalacturonans with a low degree of esterification and linear oligogalacturonids showed significant bioadhesion against colonic mucous membranes. In contrast highly esterified pectins and neutral polysaccharides were ineffective. Within a structure-activity relationship linear, strongly acidic homogalacturonides were shown to be most adhesive agents. Esterification, branching or non-linear backbone structures will reduce the adhesive properties. The bioadhesive effects were concentration-dependent. Polysaccharide layers, located exclusively on the apical membrane surface of colonic tissue, were visualized by fluorescent microscopy. The adhesion of the exogenous galacturonides on the tissue surface was mediated by interaction with the endogenous mucin, for the release of the endogenous mucines with a mucolytic agent resulted in a decreased bioadhesion of exogenous galacturonides. Additionally, mucin-galacturonide synergism was shown by rheological methods. The artificial mucin layers provide protective effects on colonic mucous membranes against toxic agents as shown by incubation of the tissue with TritonX100.

Tests performed on other gastrointestinal membranes (ileum, gastric membranes, buccal epithelia) showed different behaviour against exogenous polymers: while gastric and buccal membranes could be coated with polysaccharide layers, no such effects were seen using ileum material. The respective differences between the physiological material and the bioadhesive structures are discussed.

Further experiments indicated an other class of chitin-derived oligosaccharides to be strong stimulants of endogenous mucin secretion, leading to an increased mucin-layer on colonic membranes. This effect was shown to be similar with mucin secretion induced by steroids (cortison). The potential positive influence of our oligosaccharides within the treatment of inflammatory diseases is discussed.

SL02 Modified algal and fungal polysaccharides as potential new antiinflammatory drugs

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The adhesion of cells to the endothelium plays an important role in leukocytes recruitment during inflammation. The initial adhesive event is mediated by selectins which bind to oligosaccharide structures. There is large interest to develop inhibitors of this step as new antiinflammatory drugs. However, up to now none of the synthesized molecules proved to be successful. Besides, heparin (H) was shown to interfere with this process. But its high anticoagulant activity is opposed to a therapeutic use in inflammation and its isolation from animal material implicates several disadvantages such as poly-dispersity, contamination risk, shortage of resources. As an alternative approach we are using neutral polysaccharides from algae or fungi as starting material to obtain structurally defined sulfated polysaccharides by chemical modification.

In the presented study, the inhibitory influence on the selectin-mediated cell adhesion of a new class of partial synthetic glucan sulfates (GS) was compared with that of H and structure-activity relationships were established. In adhesion assays, the GS inhibit the L- and P-, but not the E-selectin-mediated cell adhesion. Their activity depends not only on the degree of sulfation and the molecular weight but also on the sulfation pattern of the glucose units. Further, the basic polysaccharide structure was shown to play an important role, e.g. the GS are considerably more active than H.

These results obtained under static conditions correlate well with the effects observed in a flow chamber model. The latter examines the influence of the test compounds on the interactions of selectin expressing cells with a vascular surface imitate containing Sialyl Lewis X under shear flow. H turned out to be inactive in this dynamic test system. However, the GS structure-dependently reduce the number of adhering cells and prolong the rolling velocity of the cells.

In conclusion, the cell adhesion inhibitory potency of GS is suggested to contribute to their in vivo observed antiinflammatory activity. Since their efficacy-risk ratio is much better than that of H, they may be promising candidates for the development of new anti-inflammatory drugs.