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Targeted PLGA-Microparticles as a Novel Concept for Treatment of Lactose Intolerance

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Background: Lactose intolerance is the inability to metabolize lactose because of the absence of the enzyme lactase. It is estimated that 75–90% of birth lactase levels are lost by most people after weaning. The prevalence of lactase deficiency ranges widely with the ethnic background from 2–15% among Northern Europeans to 95–100% among Asians [1]. Nowadays, lactose intolerance is usually controlled by strict adherence to a loactose-free or lactose-reduced diet. Moreover, as an alternative, capsules or tablets containing microbial-derived ß-galactosidase are available. However, this treatment is inconvenient for patients since these formulations have to be administered immediately before or together with lactose-containing diet because of their short-acting effect.

Aim: Therefore, the present work is aimed to develop an innovative long-acting peroral formulation for the treatment of lactose intolerance.

Methods: Biodegradable and biocompatibale polymeric microcarriers (2.78±1.05µm in diameter) were manufactured from poly(D,L-lactide-co-glycolide) (PLGA) using spray-drying. They were functionalized with β-galactosidase from *Kluyveromyces lactis* and targeted with wheat germ agglutinin (WGA), which might prolong the residence time of particles in the small intestine. The particle-bound enzyme activity, the mucoadhesive as well as the cytoadhesive properties were assessed.

Results: The highest particle-bound enzyme activity (1470 U ß-galactosidase per gram PLGA) was obtained with hexamethylene diamine as a spacer using carbodiimide method representing a 6-fold increase as compared to particles without spacer. Surface immobilisation of WGA enhanced considerably the particle binding to porcine mucin layer (mucoadhesion) and Caco-2 cell monolayers (cytoadhesion).

Conclusions: PLGA-microparticles, surface-modified with active ß-galactosidase as enzyme substitute and WGA as a targeter, are able to bind to enterocytes and thereby to prolong the intestinal residence time. It is a promising approach towards a promising approach towards a more convenient therapy of lactose deficiency and intolerance.

[1] Harrington LK, Mayberry JF. A re-appraisal of lactose intolerance. Int J Clin Pract. 2008; 62: 1541–1546. doi:10.1111/j.1742-1241.2008.01834.x