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SNEDDS is the key in a peptide protection towards luminal enzymes

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Aim: The aim of this study is the development of self-nanoemulsifying drug delivery systems (SNEDDS) with improved resistance towards pancreatic lipases andwith protective effect against luminal enzymatic metabolism using leuprorelin as model peptide drug.

Material & Methods: Hydrophobic leuprolide oleate obtained after leuprolide acetate complexation with sodium oleate was incorporated into three different SNEDDS formulations. SNEDDS stability towards pancreatic lipases was investigated utilizing a dynamic *in vitro* digestion model simulating small intestinal digestion. Protective effect of SNEDDS in respect to peptide drug stability against proteolytic enzymes, trypsin and alfa- chymotrypsin, was determined via HPLC. Leuprorelin acetate in an aqueous control solution served as control.

Results: All formulations were dispersed in a concentration of 1% (m/v) in simulated gastrointestinal fluid at pH 6.5. Results of *in vitro* digestion demonstrated that 80% of SNEDDS containing the highest amount of ester linkages was degraded within 60 min. In comparison to that, SNEDDS without ester bonds showed no degradation. With increasing oil droplets hydrolysis the remaining amount of peptide encapsulated into formulation decreased. Furthermore, after 180 min incubation with trypsin up to 33.5% and with chymotrypsin up to 60.5% of leuprolide oleate was still intact while control solution was completely metabolized by trypsin within 120 min and by α-chymotrypsin within 5 min. Protective effect in environment containing lipases was lower due to oil phase degradation, however, the amount of peptide in SNEDDS free of ester linkages was remarkably higher (48.14%) compared to control solution and SNEDDS susceptible to lipases.

Conclusion: The present study revealed that SNEDDS which are stable towards hydrolysis are able to exhibit a protective effect for oral peptide delivery.

Biography

Gintare Leonaviciute was born in Lithuania in 1987. She currently is a PhD student in Austria of University in Innsbruck (Department of Pharmaceutical Technology). Her research interests focus on the oral drug delivery systems. She finished her studies in pharmacy at The Kaunas University of Medicine.

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