Stability, liposome interaction, and in vivo pharmacology of ghrelin in liposomal suspensions - DTU Orbit (02/01/2019)

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Ghrelin is an appetite-stimulating peptide hormone. It is a pharmacologically interesting peptide because of its involvement in e.g. appetite and metabolism, but it has a very short half-life in the body. Ghrelin carries a Ser-3-octanoyl group, and it has previously been suggested that acylated peptides can bind to or be incorporated into liposomes. Therefore, neutral dipalmitoylphosphatidylcholine (DPPC) liposomes and phosphatidylcholine:cholesterol (PC:Chol) (70:30) liposomes as well as negatively charged dipalmitoylphosphatidylcholine:dipalmitoylphosphatidylcholine:dipalmitoylphosphatidylserine (DPPC:DPPS) liposomes (70:30) were prepared, and ghrelin was added. The chemical and physical stability of ghrelin was examined. Affinity capillary electrophoresis (ACE) revealed an interaction between ghrelin and the negatively charged (DPPC:DPPS) liposomes, whereas only very small affinities were discerned in the other liposomal formulations of ghrelin. Differential scanning calorimetry showed no changes in phase transitions (T-m). In vivo pharmacokinetics following subcutaneous administration of ghrelin in buffer and in the liposomal formulations was examined in rats. The PC:Chol formulation had a longer-lasting effect as compared to the ghrelin buffer solution and the other two liposomal formulations. The prolonged effect of the PC:Chol formulation is suggested not to be caused by association between ghrelin and the liposome. (C) 2009 Elsevier B.V. All rights reserved.

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