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Oral peptide delivery by a novel lipid-based system

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Bioavailability of peptide drugs is very low after oral administration. Only very few products are on the market, like immunosuppressive cyclosporine A (Sandimmun Neoral®) or antidiuretic desmospressin (Minirin®). Most other peptide drugs are given by i.v or s.c. injection of peptide solutions, s.c. administration of drug loaded polymeric implants or microparticles or by nasal administration.

In the present study we developed a liposomal system based on a combination of standard lipids and membrane spanning tetraether lipids, which are extremely stable biomolecules. The shape of the liposomes was characterized by light scattering and electron microscopy. Liposomes had an average diameter of 200-250 nm. The absorption behavior was studied in vivo in rats in absence and presence of various absorption enhancers (cetylpyridinium chloride, phenylpiperazin, sodium caprate). The liposomes containing tetraether lipids resulted in a significantly increased absorption compared to the compound alone or standard liposomes. The bioavailability of several model peptides including the cyclic octapeptide octreotide (Sandostatin®) and human growth hormone (hGH) was determined after administration of peptide loaded liposomes to rats via gavage. Blood samples were taken, and the plasma concentration of absorbed peptide was determined by specific radioimmunoassays. The absolute bioavailability (BA) of octreotide was increased by a factor of 25-30 after administration of tetraether lipid liposomes, the BA of hGH was increased by a factor of 360, indicating that formulation in such liposomes is a feasible approach to increase the bioavailability of peptide drugs after oral administration. The formulation can be further optimized by incorporation of the liposomes into a jelly matrix, thus generating a semi-solid dosage form, from which liposomes can be released in the GI-tract without loss of shape and loading capacity.

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