J. Pharm. Pharmacol. 1998, 50 (Supplement): 14

Lipid-based nanoparticles as drug delivery systems

P. ESPOSITO*, I. COLOMBO, N. COCEANI, D. DEL CURTO AND E. CHIELLINI

Vectopharma International SpA, Business Innovation Center, Via del Follatoio 12, 34148 Trieste, Italy

**Present address and correspondence: Instituto di Ricerca Cesare Serono, Drug Delivery Systems Department, Bioindustry Park, 10010 Colleretto Giacosa, Turin, Italy*

In the recent years, studies investigating the potential of nanoparticles as oral delivery systems for peptides have been reported extensively. Several factors are considered influential on particles uptake: materials type, particles size, particles stability in the GI tract, surface charge, surface hydrophobicity, or the presence of specific ligands bound to the particles(Florence 1997).

The use of lipids as materials for nanoparticulate carriers manufacturing has gained considerable interest: they are in general GRAS of low or medium cost, low toxicity, and high biocompatibility. When given orally, lipid nanoparticles may be absorbed by the normal lipid absorption route (enterocytes) or the GALT (as very small particulates).

Solid lipid nanoparticles for oral delivery of peptide drugs are manufactured using blends of different lipidic and amphiphylic materials, according to a microemulsion-dispersion technique. Materials such as fatty acids, phospholipids, triglycerides, PEG-oylated glycerides are used. An oil/water microemulsion is prepared at $T > T_{melting}$ of lipid components; subsequently, the microemulsion is dispersed in an aqueous medium, under controlled conditions. After solidification, nanoparticles suspensions are washed by ultrafiltration to eliminate excess surfactants and non-incorporated drug.

The main objectives of this study are:

to characterize the surface and bulk properties of the lipidic blends used for nanoparticles preparation

to study how such characteristics would affect the nanoparticles' properties

to investigate the potential of lipid nanoparticles as a carrier for peptide drugs

The surface properties of thin films of lipidic blends were characterized by contact angle method: surface free energy, surface polarity or surface fractions of components were calculated, according to Gibbs or Cassie-Baxter methods (Canal et al 1993). Phase diagrams of significant blends were constructed by DSC analysis, supported by hot stage microscopy observations. Lipid nanoparticles were prepared from the characterized blends. Particle size (measured by photon correlation spectroscopy) varied between 180 and 400 nm. The zeta-potential values were linearly related to the surface parameters of lipidic blends, such as surface polarity or surface fraction of components. Surface microviscosity of particles was also studied by means of polarized light spectrofluorimetry. TEM analysis evidenced the differences in nanoparticles morphology, confirming the existence of a composite structure.

Salmon calcitonin (sCT) was incorporated into nanoparticles prepared using lipidic blends of different properties. Incorporation efficiency, resulting approximately between 10 and 14%, was determined by HPLC and by fluorimetric methods. sCT-nanoparticles suspensions were orally administered in-vivo to Rhesus monkeys, at a single dose of 80 int. units kg^{-1}. Aqueous suspensions of sCT and nanoparticles components were used as controls. Significant peptide amounts were found in plasma up to 7 h after dosing, with corresponding reductions in total and ionized calcium concentrations.

The results show that the oral absorption of a peptide drug can be favoured by incorporating it into solid lipid nanoparticles. The modification of the surface properties of nanoparticles towards the decrease of total surface free energy, and the increase of surface polarity seems to enhance the absorption of salmon calcitonin.

Florence A.T. (1997) Pharm. Res. 14: 3

Canal T., Colombo I., Lovrecich M., J. (1993) Contr. Rel. 27: 19–26