SELF-ASSEMBLIES OF AMPHIPHILIC CYCLODEXTRINS.

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It has been shown that a high diversity of structure such as vesicles, micelles or even mixed phospholipides/cylodextrin derivatives films can be obtained depending on the structure of the cyclodextrin (CD). For this purpose, a novel class of amphiphilic derivatives based on CDs was considered. They were prepared from a pure phospholipid (DMPE) grafted onto the cyclodextrin core through a spacing arm leading to the phospholipidyl-CDs. On the other hand, peptidolipidyl-cyclodextrins (P-CDs) were designed to induce a very large versatility depending on the nature of the amino-acid, the number and the length of the aliphatic chains and the nature of the cyclodextrin moiety.

The purpose of this study is to find out a relationship between the molecular structures of such derivatives and their capacity to interact with model lipid membranes as well as to form supramolecular self-organized structures. Physical characterization of the self-assemblies and interactions of these compounds with membrane systems were investigated using several methods (CMC, light scattering, ^{31}P and ^{2}H NMR, small-angle X-ray scattering). Biological evaluations have been performed by a new approach making use of novel immuno-enzymatic assays.

The methylated phospholipidyl derivatives were shown to self-organize in water with low CMC to form fluctuating micellar fibers retaining the inclusion capacity of the cyclodextrin cavity. Methylated phospholipidyl-CDs can form fairly stable films by themselves, the presence of a matrix is not required. These films consist of a highly hydrated bilayers of modified cyclodextrins wich are remarkably thick due to their abundant hydration core.

Their ability to cross over the blood brain barrier was shown by a new approach making use of novel immuno-enzymatic assays. Investigations performed on a model system showed that methylated phospholipidyl-CDs can cross over the barrier without destructing it. To our knowledge, this is the very first example of an amphiphilic cyclodextrin able to go through this barrier without breaking its integrity. These methylated phospholipidyl derivatives were also tested for dermatological delivery of xenobiotics

Investigations performed by dynamic light scattering (DLS), optical density measurement (OD) techniques, and ^{2}H NMR experiments allowed to establish whether some of the novel peptidolipidyl-CD derivatives have detergent properties and may solubilize the lipid membrane, or they behave as co-lipids and may insert into biological membranes leading to the formation of lipids micro-domains within the bilayer, through finely-turned intermolecular headgroup interactions at the membrane interface. Insertion into artificial membranes has been monitored by ^{2}H NMR spectroscopy using peptidolipidyl-CDs (mixed bilayer phases: CDs surrounded by four phospholipids).

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