Micellation - Encapsulation at Nano-Level

A transport system according to Nature's principle as a prerequisite for the absorption and digestion of lipids

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Physiological mixed micelles - fundamental for lipid resorption

The digestion and absorption of nutritional fats (principally triglycerides) in human beings is a process which is characterized by a number of different steps. The first step in fat digestion is the formation of an emulsion of the disperse lipids. In the stomach the hydrolysis (lipolysis) of the triglycerides in free fatty acids, monoglycerides and glycerol then follows through gastric lipases. About 20 - 30% of the complete lipolysis of nutritional fats occurs in the stomach. The lipolysis is terminated in the small intestine (duodenum and upper part of the jejunum) by the influence of the pancreatic lipase and co-lipase. The lipolysis products which are insoluble in water are released in the form of water-soluble mixed micelles to the cells of the small intestine for absorption. The water-soluble mixed micelles are molecular aggregates of fatty acids, monoglycerides, cholesterols, phospholipids, fat-soluble vitamins, antioxidants and conjugated bile acids. They are formed when the concentration of the conjugated bile acids is higher than their "critical micelle formation concentration" (CMC). The physiological micelle facilitates the transport and the release of the water-insoluble products of the lipolysis and of other fat-soluble molecules via the so-called "unstirred water layer", which is located on the luminal cell membrane of the small intestine, to the point of resorption.

Limiting factors in the efficient formation of a physiological micelle are primarily the availability of conjugated bile acids. If the duodenal concentration of the conjugated bile acids is below their CMC, substantial disturbance to the micellation occurs. Reduced availability of pancreatic lipases, variations in the intraduodenal pH value and a reduced supply of bile liquid can prevent the optimum physiological micellation. Under some circumstances this may lead to essential fat-soluble vitamins and antioxidants being poorly ingested or not ingested at all.

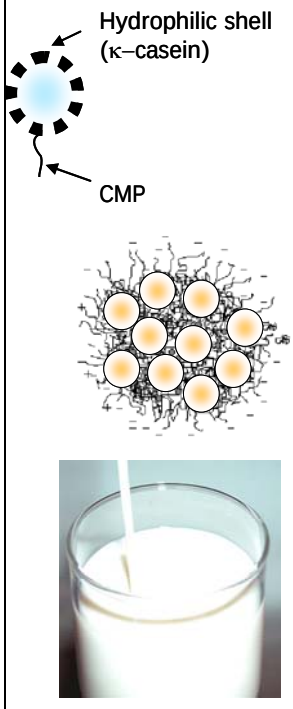
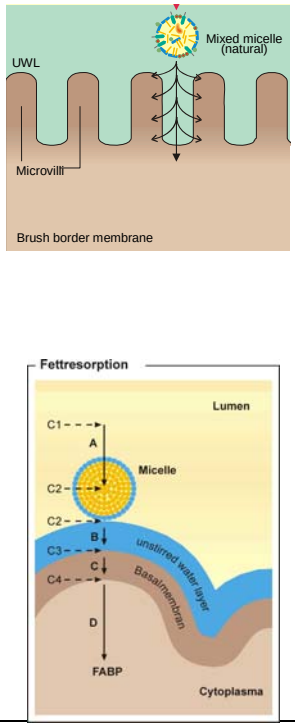
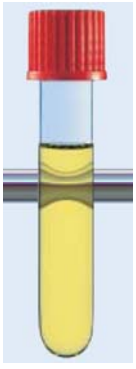
The product micelle (see below) is not subject to these physiological variations and can thus be regarded as a natural "smart transport and delivery system" or one that is analogous to the natural principle. Micellar structures on the nanoscale are found, for example, in foodstuffs such as milk (casein submicelle with a diameter between 10 - 20 nm) or the hen's egg (LDL and HDL cholesterol micelle with a diameter between 20 - 60 nm).

A remarkable property of the micelle is the capability of encapsulating non-polar lipids, antioxidants and fat-soluble vitamins in order to transport them in this manner in an aqueous medium (e.g. in the gastrointestinal fluid). Thus, water-insoluble organic compounds can be rendered water-soluble with the aid of micelles.

Micellar structures
- all-pervasive principle of nature

Micelles are spherical particles with a diameter of 10 - 200 nanometers. They are found in:

1. natural foodstuffs, such as milk,
2. natural foodstuffs, such as the hen's egg,
3. the natural, human, physiological mixed micelle,
4. the product micelle.

1	2	3	4
Milk: **Casein Micelle and Casein submicelle**	Hen's egg: **LDL micelle**	Human being: **Physiological micelle**	Solubilisate: **Product micelle** (e.g.. Vitamin E)
		 	 
D = 50 – 250 nm / D = 10 – 20 nm	D = 20 – 60 nm	D = ≤ 50 nm	D ≈ 30 nm
Prof. Dr.-Ing. U. Kulozik, TU München / Schmidt, 1980; Walstra und Jennes, 1984; Fox, 1989	Prof. Dr.-Ing. U. Kulozik, TU München	Dr. Evelyn Back, Prof. H. K. Biesalski, (Taschenatlas der Ernährung, Uni Hohenheim)	AQUANOVA, TU Darmstadt

The product micelle
- implementing the natural principle in products

The structure of the product micelle, with a size of appr. 30 nm, is similar to the structure of the naturally formed physiological mixed micelle containing water-insoluble compounds in its core which is enclosed by ambiphilic molecules. The chemical or molecular structures of the micellized ingredients are fully retained in the product micelle. The product micelle is chemically and mechanically stable and is also stable in gastric acid. It releases the ("transported") fat-soluble compound enclosed in it chemically unmodified to the luminal cell membranes of the small intestine for absorption. That the transported fat-soluble compounds (vitamins & antioxidants) remain completely unchanged in the product micelle is shown by determining the content in the solubilisate itself (HPLC analysis) and the concentration of these unchanged compounds. The higher bioavailability, which is obtained by the product micellation, is based on the independence of this transport system from the limiting parameters in the formation of the physiological mixed micelle. It is important to appreciate the product micelle's character as an "encapsulation and transport medium". This must not be confused with "nanoparticles" which are often spoken about in nanotechnology and which, for example, are used in sun lotions or technical applications such as surface sealing. In contrast to these substances, the substances encapsulated in the product micelle are a natural object of metabolism or physiological processing in the human body. In addition, no new types of substances or nanoparticles are used in the formation of the product micelle.

Conclusion

Nanostructures in the form of micelles have great potential in improving the efficiency of the transport, release and absorption of nutraceuticals and bioactive compounds in functional foods (smart transport and delivery system). In principle the micelle can increase the controlled release and the bioavailability of the enclosed bioactive compounds.

Due to the solubilization of lipophilic raw materials and active ingredients, such as vitamin E, ß-carotene or coenzyme Q10, so-called product micelles can be produced, which are similar in the size, shape and functionality to the natural, physiological micelle. In this respect the molecules of the micellated (encapsulated) raw materials and active ingredients are not modified. Since the natural micelle formation, hence Nature, is mimicked by the solubilization, the requirement of a toxicological reassessment of a solubilisate is in no way required. The components of the product micelle have been assessed individually and do not change their toxicological profile due to the micellation.