Liposomes and Emulsions – Liquid Formulations for more Bioavailability

By Philipp Gebhardt

Phospholipids (lecithin) form the characteristic double layers of the cellular membranes of animal and plant cells. Because of their amphiphilic ("both-loving") character, they can mediate between water and fats, which allows many applications in food technology. Phospholipids can be used to produce emulsions and liposomes containing nutrients that provide a significantly increased bioavailability compared to the unformulated substances.

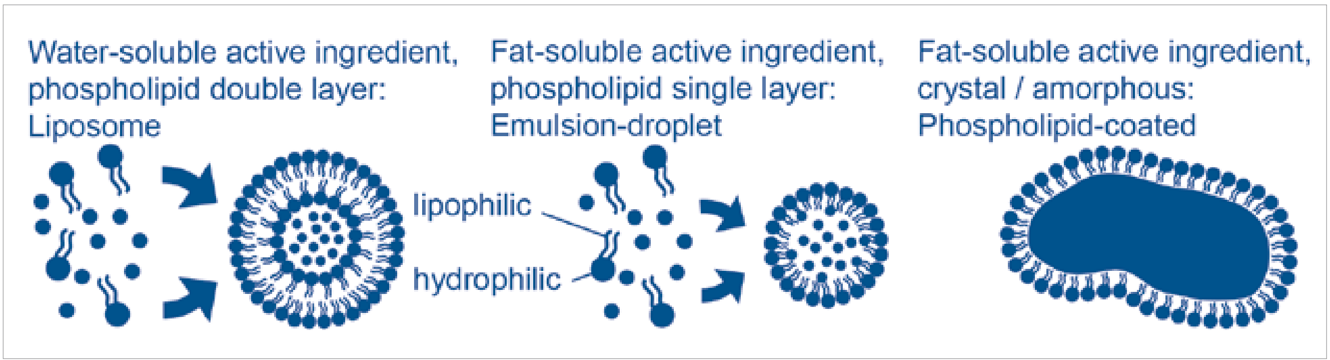
Phospholipids are polar lipids that consist of a hydrophilic ("water-loving") head and two lipophilic ("fat-loving") fatty acid chains that are linked together via a glycerol backbone. As amphiphilic ("both-loving") substances, they can combine with fat-soluble nutrients and disperse them finely in an aqueous environment. The lipophilic parts of the molecule are oriented towards the fat phase, while the polar, hydrophilic parts of the molecule are oriented towards the outside, towards the water. The resulting systems are called emulsions. They are characterized by a single-layer phospholipid shell. A prerequisite to produce emulsions is that the fat phase is in a liquid form. An example of a nutrient that can be formulated in this way is coenzyme Q10. The coenzyme has a comparatively low melting point, which is in the range of 50°C. In the production of coenzyme Q10 emulsions, homogenization processes are used similar to processes used in the dairy industry. In the process, the melting point of the coenzyme is exceeded and the nutrient is dispersed in the water phase in small droplets coated with phospholipids. The surface area of the droplets increases exponentially with their decreasing size, so that the effect of surface charge becomes increasingly relevant. Since the same charges repel each other, creaming by droplets melting together is prevented and the resulting formulations remain stable over a long time. A prerequisite to produce stable emulsions is a low melting point of the substance to be formulated. If this is too high, there are no droplets, but crystals or small fragments of amorphous substance, which are coated with phospholipids and are thus kept in suspension in an aqueous environment for a certain time. As an alternative way to formulate higher-melting, fat-soluble nutrients in this way, it is possible to dissolve the substances in oil before homogenizing. However, various nutrients have only a limited solubility, so this procedure does not always makes sense.

In the form of double layers, phospholipids also form the shell of so-called liposomes. Their lipophilic molecule parts align themselves towards each other, while the hydrophilic head groups orient themselves outwards towards the water phase and inwards towards an aqueous core. The water droplets that are contained inside can be loaded with water-soluble nutrients in order to obtain a "liposomal formulation". Due to their nature of having an aqueous core inside, these formulations are only suitable for water-soluble substances.

A fat-soluble substance could be accommodated in the area between the phospholipid layers, but the absorption capacity is very low, so that relevant concentrations usually cannot be reached. The attempt to produce a "liposomal curcumin" (the melting point of curcumin is clearly above the boiling point of water at 183° C) leads to small curcumin fragments that are coated with phospholipids and are thus kept in suspension in water for a limited time (Figure 1). Since the inside of the liposomes are lined with the polar, hydrophilic head groups of the phospholipids, a liposomal system that contains a lipophilic nutrient obviously cannot result.

The formulation with phospholipids is particularly useful for substances that

Figure 1: Liposomes (left) are characterized by a phospholipid double layer that contains an aqueous core that can be loaded with water-soluble active ingredients. In contrast, emulsion droplets have a single-layer phospholipid envelope which encloses a fat droplet or a lipophilic active ingredient. The preparation of emulsions requires a low melting point or sufficient solubility in oil. If these factors are not given, small fragments of the fat-soluble active ingredient are formed, which are coated with phospholipids and are thus kept in suspension in an aqueous environment for a limited time.



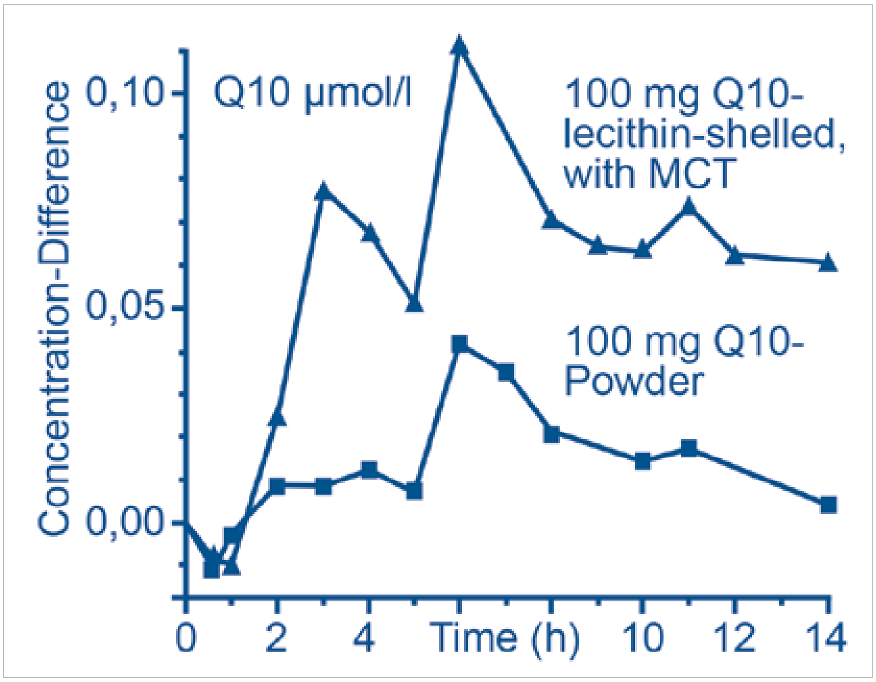


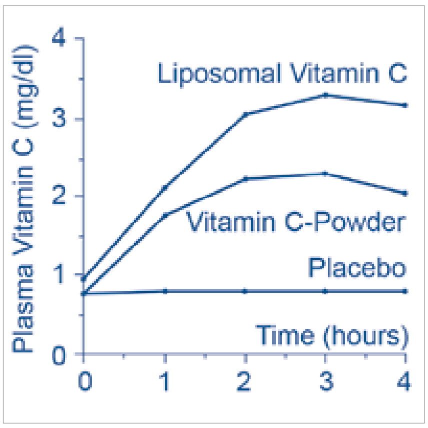
Figure 2: Mean change in the coenzyme Q10 plasma concentrations after the supplementation of 100 mg coenzyme Q10 in unformulated form or as an emulsion with phospholipids and MCT oil (according to [2]). The first peak after three hours, which can be observed with the coenzyme Q10 emulsion is probably caused by absorption through the oral mucosa.

are sparingly water-soluble and tend to agglomerate in the gastrointestinal tract. Coenzyme Q10 supplemented in the form of powder capsules is therefore only resorbed to a small extent. Only molecules on the surface of the agglomerates can be absorbed into the enterocytes of the small intestine. Emulsions in which the coenzyme is "pre-packaged" in small droplets with phospholipids contribute to a significantly higher absorption rate (Figure 2).

It could be shown that the bioavailability of corresponding coenzyme Q10 emulsions is higher by a factor of 3-4 compared to powder capsules. A further increase in bioavailability can be achieved if the coenzyme is formulated together with MCT oil. MCT ("medium-chain triglycerides") consists of fats that contain fatty acids with chain lengths between six and twelve carbon atoms and is contained to a high proportion in coconut oil. MCT can be transported through the mitochondrial membrane without the help of L-carnitine, where it is increasingly metabolized into so-called ketone bodies. Ketone bodies are a water-soluble energy source that can be used by many tissues as an alternative to glucose. MCT oil increases the absorption rate in emulsions with coenzyme Q10 and phospholipids. The improvement in bioavailability was demonstrated in a comparative crossover study with 23 participants. Compared to taking 100 mg of unformulated coenzyme Q10, the bioavailability was at least five times higher (as area under the curve) (Figure 2). [1]

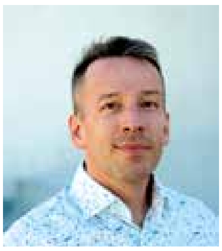
With the help of liposomes, the bioavailability of water-soluble active ingredients such as vitamin C can also be improved. After the administration of liposomally encapsulated vitamin C, significantly higher plasma levels could be measured compared to the unencapsulated form (Figure 3). [2]

Figure 3: Vitamin C plasma level after administration of 4 g of a liposomal vitamin C formulation, 4 g of uncapsulated vitamin C or placebo (according to [2]).



Conclusion

Phospholipids are characterized by their ability to mediate between water and fat. Their amphiphilic nature makes them the structure-forming components of our cell membranes, in which they are arranged in characteristic double layers. Phospholipids are also of central importance for fat metabolism, since fats can only be transported in the lecithin shells in the aqueous environment of the blood. Phospholipids open up interesting applications in the food industry. In chocolate they prevent the formation of fat ripening (so-called blooming) as a progressive accumulation of fat on the surface as a white to grayish coating by segregation. In the area of food supplements, they can significantly improve the bioavailability of nutrients. Corresponding systems are liposomes that are suitable for water-soluble nutrients and are characterized by a phospholipid double layer. The phospholipids are arranged in a single layer in emulsion droplets in order to coat a fat-soluble nutrient or oily solutions. The size of the emulsion droplets is around 60 nm which is in the range of lipoproteins (VLDL, Very Low Density Lipoprotein) formed in the body, with which fats and fat-soluble nutrients are naturally transported in the blood.



The Author
Philipp Gebhardt founded his own company specialising in products to support and protect mitochondria, the "power houses of the cell". After studying science, he gained 12 years of professional experience in the food and pharmaceutical industries, including more than five years in the development of nutritional supplements.

References:
[1] Wajda, R., Zirkel, J., et al., Journal of medicinal food, 10(4), 731-734 (2007)
[2] Davis, J. L., Paris, H. L., et al. Nutrition and metabolic insights, 9, NMI-S39764 (2016)