PhytoSolve® – an innovative way to increase bioavailability of nutrients: studies and application

In a series of papers we introduced the PhytoSolve®-system (previously: Nanosolve) in the dietetic as well as in the cosmetic field[1,2,3,12].

PhytoSolve® represents a technique to produce transparent emulsions which are able to solubilize lipids or lipophilic actives for dietetic applications in a smart, gentle and environmentally friendly manner[4]. What distinguishes the PhytoSolve® -system is the strict philosophy of working only with natural substances. One of the key components of PhytoSolve® are purified phospholipids. Phospholipids are the functional ingredients of lecithins. Lecithins are widely used, highly functional standard additives for food. Their phospholipid composition is of great relevance for their technological and even more for their physiological properties.

Utilizing sophisticated techniques and special formulations result in transparent emulsions with lipid concentrations up to 40%. The PhytoSolve®- principle is not restricted to a special lipid but comprises a broad variety of hydrophobic substances including the very popular actives coenzyme Q10, omega-3 fatty acids, lutein and phytosterols.

Transparency could be achieved by choosing an appropriate matrix and by generating small particle sizes. Particle size is a primary determinant of bioavailability. The smaller the particle size the better the absorption. Besides this, phospholipids are also considered to work as a sorption promoter, hence PhytoSolve® is the ideal candidate for a powerful naturally based carrier system[5,6].

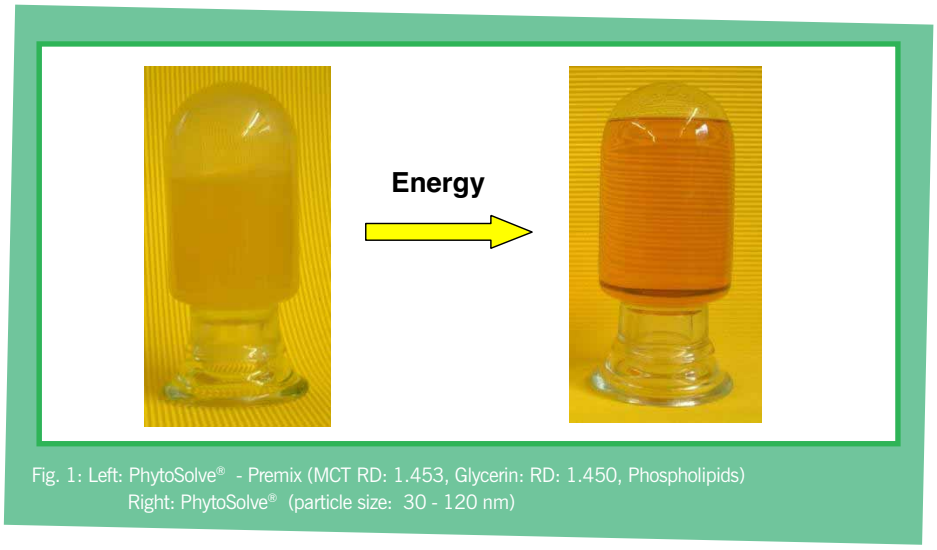

Fig. 1: Left: PhytoSolve® - Premix (MCT RD: 1.453, Glycerin: RD: 1.450, Phospholipids)
Right: PhytoSolve® (particle size: 30 - 120 nm)

Transparent emulsions

There are several ways to produce transparent emulsions. Microemulsions, mixed micelles and refractive index matching are well-known methods for producing transparent products[7,8,9].

For **PhytoSolve®** we use a combination of refractive index matching and small particle production (see Fig.1). Refractive index matching requires at least two phases with a more or less identical refractive index. Compared to water as continuous phase polyols have some remarkable advantages in the field of o/w-emulsions. The influence on the interface between oil and polyol/water leads to a reduced interfacial tension and hence to lower diameters of the oil droplets compared to a pure water phase.

PhytoSolve® - principle

Highly concentrated solutions of polyols or carbohydrates are able to solubilize large quantities of lipids in the presence of phospholipids. The results are clear transparent or translucent emulsions with honey-like to gel-like consistency and a droplet size between 30 - 120 nm. Tiny oil droplets combined with an appropriate refractive index are the key for transparency as well as stability of these emulsions.

PhytoSolve® is a very unique principle because it works exclusively with natural ingredients.

A great variety of lipophilic candidates are suitable for this system whereby coenzyme Q 10, vitamins E, A, D, K, omega-3 fatty acids, lutein and phytosterols are the most well-known candidates in the dietetic area.

The focus of a dietetic product should always be

a) to make the nutrient available and to reduce the concentration of technologically necessary excipients (surfactants, emulsifiers,...) to the lowest possible and
b) to refrain from synthetic emulsifiers/ surfactants as well as alcohol for nutritional and physiological reasons.

These stringent criteria can only be met by means of the PhytoSolve® technology.

Advantages of PhytoSolve®

PhytoSolve's® specific composition and sophisticated technology contributes to its advantages:

- **PhytoSolve®** is free of preservatives and self-preserving because of its low water activity.
- **PhytoSolve®** is hydrophilic and can be mixed with water in any ratio.
- **PhytoSolve®** contains physiologically safe phospholipids and polyols of vegetable origin.
- **PhytoSolve®** has not to be labeled as GMO according to the new directive EC 1829/2003 and 1830/2003.
- **PhytoSolve®** contains the solubilized nutrients always in an excess to the phospholipids.
- **PhytoSolve®** allows an increased bioavailability of insoluble nutrients.
- **PhytoSolve®** is free of alcohols.
- **PhytoSolve®** displays an outstanding stability compared to conventional emulsions

Bioavailability

Bioavailability is a measure of the uptake of an ingested substance by the body as assessed by its concentration in the blood. The rate and extent of its appearance in the blood are important determinants of bioavailability. Relative bioavailability involves a comparison of the test substance with a reference product, whereas absolute bioavailability refers to a comparison of its kinetics with that of a reference product administered intravenously[6].

Coenzyme Q10 is a naturally-occurring, vitamin-like substance which is found in every cell. It is vital for the production of energy and was first isolated from the mitochondria of bovine hearts.

Coenzyme Q10 is insoluble in water and poorly soluble in oil so that the efficiency of absorption and bioavailability can be expected to be poor. Peak plasma levels are attained within 5-10 hours following oral administration[10].

Absorption is dependent on the presence of fat in the gastrointestinal tract. Therefore, the importance of product formulation was recognized early in the development of

coenzyme Q10 preparations[11]. It is well known that in the case of poorly soluble drugs, the surface area of the particles is directly related to bioavailability. The smaller the particle size the better is the absorption. Thus particle size becomes the primary determinant of bioavailability in both solid and liquid dosage forms of coenzyme Q10[6].

Uptake of PhytoSolve® Q10 and vitamin E-acetate in rabbits and humans

In previous papers we presented two studies on the bioavailability of coenzyme Q10 and Vitamin E-acetate respectively[2, 3, 12].

In a first study we compared the bioavailability of **PhytoSolve®** Q10 (solubilized form) with a non-solubilized Q10 powder in rabbits. Either test formulations contained the same amount of coenzyme Q10 (35 mg/kg bw). Both test samples have been administered orally.

Compared to the non-solubilized form (coenzyme Q10 powder) the plasma concentration of coenzyme Q10 in **PhytoSolve®** was significantly higher (Cmax: 100 %). Even the AUC (area under the curve) shows an increase of 68 % when coenzyme Q10 is administered in form of PhytoSolve®.

A second study has been carried out with human subjects in a randomized, one day kinetic after a single dose. It was a cross-over design study with 23 volunteers and the improved bioavailability of a **PhytoSolve®** formulation with coenzyme Q10 and a **PhytoSolve®** formulation with vitamin E-acetate was proven in comparison to the pure products (powder-filled and liquid-filled capsules respectively). The aim of the trial was the characterization of the bioavailability according to pharmacokinetic parameters in plasma. Healthy volunteers were given the same concentration of coenzyme Q10 and vitamin E-acetate in form of **PhytoSolve®** as well as in the pure non-solubilized form.

The plasma coenzyme Q10 concentration peaked after 6 hours post application of the pure material (capsules) and returned nearly to baseline within 14 hours. Whereas after the intake of **PhytoSolve®** formulation a two peak pattern of coenzyme Q10 was visible. After 14 h coenzyme Q10 levels were still raised above baseline (see Fig. 2). After the intake of pure vitamin E –acetate (capsules) the total concentration time curves showed negative profiles, indicating a very poor absorption. In contrast, after supplementation with **PhytoSolve®**, the peak maximum was achieved at 6 hours with rising levels from 2 hours on. Within 14 hours vitamin E concentration did not return to baseline (see Fig.3). According to the pharmacokinetic parameter Cmax (maximum concentration) Tmax (time at which Cmax is achieved) and AUC (area under the curve) the **PhytoSolve®** formulation demonstrated a significant faster and higher increase in comparison to control preparation (capsules). Also the AUC-values substantiated a significant higher bioavailability (5-fold for coenzyme Q10 and 10-fold for vitamin E-acetate) with **PhytoSolve®** in comparison to capsules based on haematocrit corrected data.

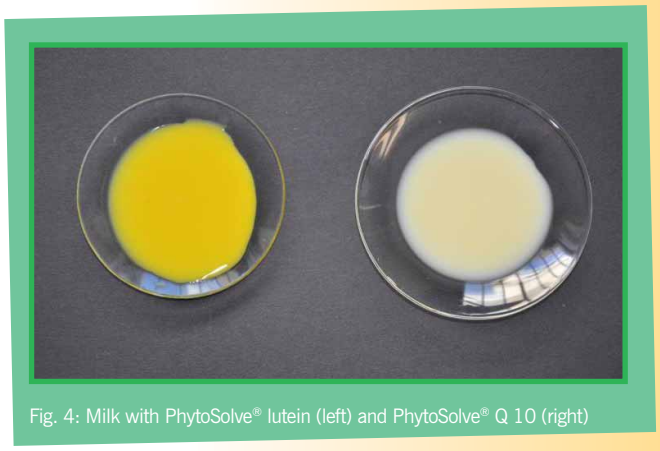

Fig. 4: Milk with PhytoSolve® lutein (left) and PhytoSolve® Q 10 (right)

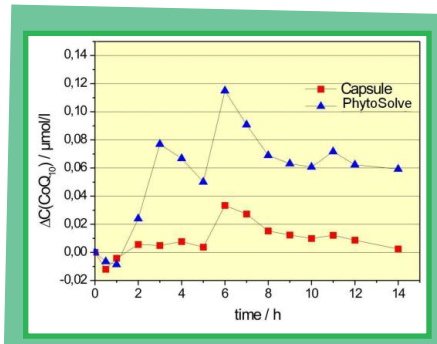

Fig.2: Coenzyme Q 10 - concentration time curves[12]

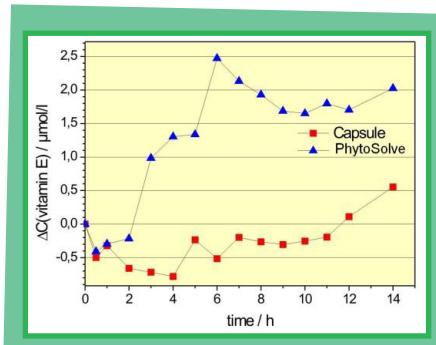

Fig.3: Vitamin E-acetate - concentration time curves[12]

Stability of PhytoSolve® at low pH

Emulsions in general tend to phase separation when subjected to low pH. Especially ionic or zwitterionic emulsifiers are sensitive to variation in pH. Zwitterionic phospholipids from soybeans are used to stabilize the **PhytoSolve®** - system so that one might expect instabilities after the oral uptake of **PhytoSolve®** preparations while passing the stomach with its low pH between 1-2. To mimic the situation in the human stomach we diluted **PhytoSolve®** Q10 with hydrochloric acid of different molarities and hence, different pH values (pH 0.7 and pH 1.5) and measured the change in particle size distribution at distinct times. The observation period of the change in particle size was limited to 3 hours. Within this time an orally administered **PhytoSolve®** should have passed the stomach leaving the critical pH region behind.

The results show without doubt only a slight increase in particle size distribution of **PhytoSolve®** during the hold-up time of 3 hours at different pH values[2]. No phase separation could be observed. The criteria for an improved bioavailability – small particle size and hence, large surface area of the particles – are still valid.

Application

PhytoSolve® can be used in different ways:

- As a nutrient-enriched concentrate which is dissolved in beverages shortly before usage.
- As a high caloric sports gel which contains a high density of energy (more than 1000 kcal/100 g).
- To enrich dairy products like milk, yoghurt or Kefir with essentials like coenzyme Q10 or lutein.

Fig. 4 shows milk which contains **PhytoSolve®** Q10 and **PhytoSolve®** lutein. Other dairy products like Kefir or yoghurt can also be supplemented with these formulations. They are stable over a period of 8 weeks at the recommended storage temperatures.

Conclusion

PhytoSolve® allows for the preparation of a physiologically safe, hydrophilic, natural, and preservative free basis for a variety of lipids and lipophilic actives.

PhytoSolve® is stable when exposed to pH values similar to those in stomach juice.

Due to the small particle sizes of the solubilized actives in **PhytoSolve®** Q10 the bioavailability of coenzyme Q10 in rabbits and also in humans could be increased clearly compared to a non-solubilzed powder form. With vitamin E-acetate the difference in bioavailability between solubilized and non-solubilized vitamin in humans is even higher than with coenzyme Q10.

From the first introduction of **PhytoSolve®** in 2004 till today this principle enjoys a great interest and is used in a broad variety of food supplements.

Literature

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