

PHYSICAL FORM:**TECHNOLOGY TYPE:****1) What are mixed micelles?**

Mixed micelles are aggregates of at least two different surfactants in water. Though a variety of combinations are possible experimentally, in practice the most common mixed micelles contain lecithin (phospholipid) and a bile salt. These mixed micelles are typically less hemolytic compared to single component micelles. This is beneficial for intravenous administration because the nasty effects of hemolytic surfactants can be reduced.

2) Which administration route is our Mixed Micelles technology suitable for?

The formulations can be administered orally and parenterally. This versatility is nicely illustrated by the pediatric formulation Konakion® (Roche) which is licensed for both oral and injection (intramuscular) administration.

3) Which types of compound are suited to mixed micelles?

Mixed micellar solubilization is suitable for poorly soluble lipophilic compounds such as oils or compounds with greasier properties which fit well into the structures. The pharmaceutical forms may be liquids or dry powders.

4) How do mixed micelles increase bioavailability?

No dissolution of the poorly soluble compound is required before absorption because the drug is solubilized. When administered orally, mixed micelles behave in a similar way to natural bile that is secreted by the gall bladder into the intestinal tract. Mixed micelles can increase the aqueous solubility of poorly soluble compounds (compared to water alone) and assist with the diffusion of the drug (compared to a solid particle) towards the surface of the intestines. The lecithin component of the mixed micelles is digested by enzymes present in the small intestine.

5) Which Phares services use the Mixed Micelle technology?

Mixed micelles are explored during the Survey and Icebreaker services.

They can be used in our Speed service for tox formulation studies providing the fit between the drug and mixed micelles is satisfactory.

6) Advantages and disadvantages of mixed micelles

Advantages

- Compared to single component surfactants, the formulations are relatively well tolerated across many different pre-clinical species
- Relatively high concentrations can be administered

Disadvantages

- The behaviour of the colloidal particles is considerably more complicated than mono component systems. The QC of the products is correspondingly more complicated
- Complexing the drug with the mixed micelles may be challenging

7) Scale-up of mixed micelles

In most cases, standard liquid processing equipment can be employed. However, the difficulty of the production will be dependent on the ease of complexing the drug with the mixed micelles and the resulting stability of the complex (which may have to be lyophilized).

8) Phares mixed micelle expertise

We have developed a variety of different mixed micelle formulations for poorly soluble compounds and understand the challenges likely to be faced when developing these types of formulations. Physical characterization, long term stability and change in performance after dilution are just some of the critical parameters that have to be monitored and controlled.

9) Mixed micelle products

An example of a mixed micelle formulation for parenteral administration is Cernevit® (Baxter). This is a lyophilised cake licensed in EU and US for vitamin malabsorption.

KEY SERVICES:

