MOLECULAR WATER INTERACTION IN LIPID-BASED FORMULATIONS AND CAPSULE COMPATIBILITY

INTRODUCTION

Lipid-based formulations (LBF) have become increasingly important for oral delivery of poorly soluble drugs [1]. These delivery systems typically improve solubility, dissolution and absorption of these challenging drugs. An example of LBF are systems comprising mixtures of surfactant and oil, so-called self-emulsifying drug delivery systems (SEDDS), that result in a fine emulsion upon aqueous dispersion in vivo.

Lipid-based formulations are commonly filled in both, soft and hard-shell capsules [2]. Although soft capsules have been widely used for this purpose, liquid-filling of hard capsules provides an attractive alternative dosage form [3, 4].

When designing the formulation and the final dosage form, it is very important to foresee potential incompatibility issues between the fill mass and the capsule shell material. One of the key factors to consider is the extent of water exchange between the formulation and the shell. Hyperswollen formulations can remove water from the capsule shell leading to brittleness, whereas formulations with relatively high amounts of water may lead to over-hydration of the shell with its consequent capsule softening [5].

In this study, we investigated the phase behaviour of the LBF system, Kolliphor EL and Miglyol 812 (60:40, w/w). When diluted 1:100 (v/v) in water, this forms emulsions with a droplet size of ~90 nm, and it is thus classified as a self-nanoemulsifying drug delivery system (SNEDDS). The present study aimed at better understanding of how water interacts with the formulation and possible effects on capsule compatibility by using time-domain nuclear magnetic resonance (TD-NMR).

EXPERIMENTAL SECTION

MATERIALS

Kolliphor® EL (Macrogolglycerol ricinoleate) was provided by BASF (Germany) and medium-chain triglycerides, Miglyol 812, were obtained from the local supplier Hürner (Waterloo, Switzerland). The reagent for coulometric Karl Fischer titration, Hydranal Hänseler (Switzerland). The reagent for coulometric Karl Fischer titration, Hydranal (Switzerland).

DETERMINATION OF RESIDUAL AMOUNTS OF WATER

To determine the initial amount of water in the components and thus to know the amount of water determined.

LBFs were prepared by mixing the surfactant with oil (60:40, w/w) and increasing the amount of water determined.

Sample of known weight of the dried surfactants was injected into the KF solution and the amount of water determined.

LIPID-BASED FORMULATION PREPARATION

LBFs were prepared by mixing the surfactant with oil (60:40, w/w) and increasing.

RESULTS AND DISCUSSION

Figure 1 shows that the conductivity remained almost negligible for samples with low water content. When approaching 5% (w/w) of water in the formulation, a pronounced increase in the conductivity was observed. As the conductivity of oil is negligible, this increase seems to correspond to the formation of water continuous channels in the formulation (Figure 2). This could indicate, for the given system, that encapsulation of samples with water content above 5% may harm the capsule shell.

Figure 3 shows that above 5% (w/w) water in the formulation, the water activity becomes higher than 0.6. Relative humidity values above ca. 60% have been reported to lead to softening of the hard capsule shell [5].

These findings of water activity were therefore in agreement with the results of conductivity measurements regarding potential capsule shell softening using formulations containing water amounts above 5% (w/w).

CONCLUSIONS

The results obtained indicate that different types of water exist in a lipid-based formulation containing increasing amounts of water, which could be differentiated regarding capsule compatibility. In the system studied, 5% (w/w) was identified as the potential concentration to trigger changes in the capsule shell. Further research will include mechanical testing of capsules to determine compatibility with water levels determined using these methods.

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REFERENCES