Employing Pickering emulsions as carrier system for retinol palmitate and α-tocopherol acetate

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INTRODUCTION

Pickering emulsions were introduced at the early beginning of the 20th century. In contrast to classical formulations, Pickering emulsions employ small solid particles instead of emulsifiers to stabilise the oily phase in an aqueous environment [1]. Recently, it has been shown that Pickering emulsion can also be coated onto substrates (e.g. tablets). These formulations present some moisture protective features due to the distinct amount of lipophilic excipients contained in the coat applied [2].

The idea of this work was to use the lipophilic components of the Pickering emulsion as a carrier system for lipophilic substances (e.g. retinol palmitate and α-tocopherol acetate). In this feasibility study the general applicability of this idea was evaluated.

MATERIALS AND METHODS

The following oily components were used to formulate the Pickering emulsion: α-tocopherol acetate (vitamin E 98%, BASF), retinol palmitate (vitamin A palmitate 1.0 mio IE/g, BASF), and medium-chain triglycerides (Kollisolv® MCT 70, BASF). As surfactants stearic acid (Kolliwax® S Fine, BASF) and precipitated calcium carbonate (Sigma Aldrich) were employed. Hypromellose (HPMC 2910 (6 cP), Pharmacoat® 606, Shin-Etsu) was used as matrix/film-former. Additionally, purified water constituted the hydrophilic phase. Eventually, the Pickering emulsion was coated onto cross-linked poly(vinyl pyrrolidon) (crospovidone, Kollidon® CL-SF).

In general, all Pickering emulsions were prepared according to the schema indicated below (Figure 1), followed by a more detailed description.

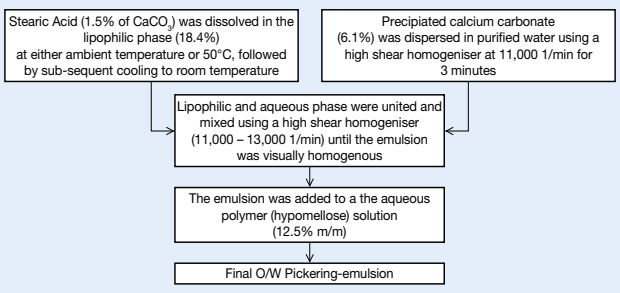

Figure 1. General preparation of the O/W-Pickering emulsion.

Preparation of the retinol palmitate emulsions

Firstly, 0.3 g stearic acid was dissolved in 60 g retinol palmitate at ambient temperature. Secondly, 20 g precipitated $CaCO_3$ was dispersed in 110 g purified water using a high shear homogeniser (Ultra-Turrax®, IKA) at 11.000 rpm for 3 minutes. After gaining two homogeneous systems, both phases were united and homogenised at 11,000–13,000 rpm until appearing visually consistent. The emulsion was then added to 135 g aqueous hypromellose solution (12.5%, m/m) which was prepared simultaneously.

Preparation of the α-tocopherol acetate emulsion

Firstly, 0.3 g stearic acid was dissolved in a mixture of 45 g α-tocopherol acetate and 15 g medium-chain triglycerides at ambient temperature. Secondly, 20 g precipitated $CaCO_3$ was dispersed in 110 g purified water (see previous preparation). After gaining two homogeneous systems, both phases were united, homogenised, and then added to 135 g aqueous hypromellose solution (12.5%, m/m).

Preparation of the retinol palmitate and α-tocopherol acetate emulsion

Firstly, 0.3 g stearic acid was dissolved in a mixture of 10.9 g retinol palmitate, 37.1 g α-tocopherol acetate and 12.0 g medium-chain triglycerides at 50°C followed by a subsequent cooling to room temperature. Secondly, 20 g precipitated $CaCO_3$ was dispersed in 110 g purified water (see previous preparation). After gaining two homogeneous systems, both phases were united, homogenised, and then added to 135 g aqueous hypromellose solution (12.5%, m/m).

Preparing isolated films of the Pickering-emulsions

In order to evaluate formed coats of Pickering emulsions visually, isolated films were prepared using an automated film-casting device (Erichsen® Coatmaster 509 MC/1). The cast films were dried for 60–90 minutes at 45°C.

Coating of the Pickering emulsions onto crospovidone

The latter emulsion was coated (1,100 g) onto the substrate (400 g) using a fluid bed coater (Glatt® GPCG 3) with 5 l container and top-spray set-up (Table 1).

Table 1. Processing parameters, fluid bed coating.

Parameter	Setting
Spray rate	20 g/min
Nozzle orifice	Ø 1.0 mm
Atomisation air pressure	1.0 bar
Inlet air volume	88 m³/h
Inlet air/product temperature	40°C/23°C
Filter cleaning	5 s/25 s

Compression of the coated substrate

The compression was carried out using a single punch press (Intrinsic®-press) equipped with biplane punches (Ø 20.0 mm). To evaluate the mechanical stability of the coat, up to 800 PSI were applied onto 800 mg powdery material.

RESULTS AND DISCUSSION

In all three variants, the Pickering emulsion could be prepared as a temporarily stable emulsion (Figure 2).

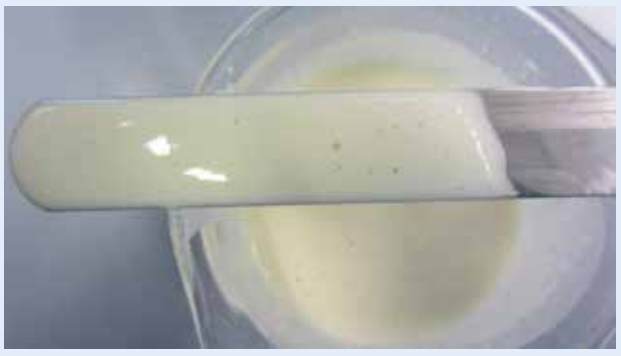

Figure 2. Appearance of the Pickering emulsion containing both retinol palmitate and α-tocopherol acetate.

Evaluation of isolated films

Isolated films appeared as turbid but homogeneous system presenting a non-oily surface (Figure 3). The elasticity of the film was moderate. Exposure of oil could be observed around cracks, suggesting that the oil phase was originally embedded in the hypromellose matrix.

Figure 3. Cast Pickering emulsion containing both retinol palmitate and α-tocopherol acetate.

Coating process and compressing

The coating process of the Pickering emulsion onto the substrate was easy. The sponge-like crospovidone allowed comparatively high spray rates without negative effects on the process. Relevant amounts of emulsion could be applied within 55 minutes spraying time, resulting in a free flowing powder (Figure 4). However, product temperature had to be kept below 30°C to avoid spilling of the oily phase.

Figure 4. Crospovidone coated with Pickering emulsion.

Compression of the coated material

The coated substrate can easily be transferred into a tablet. Even at high compression pressures exposure of oil couldn't be observed. However, the low bulk density of the powdery material presented some concerns.

Redispersion of emulsions from coated substrate

A redispersion of the Pickering emulsion was readily feasible. After presenting the coated substrate to water (while stirring), the oily phase got emulsified. The formulation formed a turbid, but stable emulsion without any accumulation of oil on its surface.

Optimisation of the preparation method

A cold preparation method appeared to offer a more robust and less stressful preparation for both vitamins. However, emulsifying the lipophilic and hydrophilic phase was a very crucial step. Applying too much shear stress (either speed or time) led to emulsions showing irreversible phase-separation. Pickering emulsions prepared without the treatment of heat where found to be more robust also during the emulsification step.

CONCLUSION

Pickering emulsions can be employed as a carrier system for lipophilic substances such as retinol palmitate or α-tocopherol acetate. The preparation was simple and similar to classical o/w emulsions. The liquid formulation could easily be transferred into a solid state (e.g. coating onto a substrate). On the other hand redispersion was easy and quick, leading to emulsions which were stable for some time.

REFERENCES

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