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Stability and skin compatibility of an adapalene-loaded solid lipid microparticle dispersion

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Introduction: A novel adapalene-loaded solid lipid microparticle dispersion consisting of 13.93% hydrogenated palm oil, 5.97% lecithin, 0.1% adapalene, 12% poloxamer 407, 3% polyethylene glycol 12000, 0.2% potassium sorbate, 0.1% citric acid, and 64.7% water (all by weight) exhibits potential for follicular penetration and targeted drug delivery and release in sebum [1,2]. In the present study, the stability regarding particle size, melting behavior, and drug content at different storage temperatures of 4°C, 23°C, and 40°C was monitored for 4 weeks. Furthermore, skin compatibility was evaluated by an MTT test in comparison to the commercial cream formulation Differin® after incubation of various dilutions in Dulbecco's Modified Eagle Medium (supplemented with 10% fetal calf serum, 2 mM l-glutamine and antibiotics) on a HaCaT monolayer under standardized culture conditions.

Results: The particle size determination revealed an increase of the mean particle size from about 3.7 to 4.2 µm after 4 weeks of storage at 23°C, whereas the size slightly decreased to about 3.5 µm at 4°C and increased significantly to 4.7 µm at 40°C. Higher storage temperatures may promote an Ostwald ripening. The particle size distribution displayed a second mode in the nanometer range after storage at 40°C potentially due to the preferential leakage of lecithin into the aqueous phase. At 23°C and 40°C, a slight increase of the melting temperature from approximately 55°C to 56°C and 57°C, respectively, was detected, whereas the initial melting at 55°C remained nearly constant during storage at 4°C. The drug content of 0.1% was stable and the pH value remained in the range of about 5.4 for 4 weeks.

The MTT test showed a cell viability of about 80-90% referred to medium control for the 1:10, 1:100, and 1:1000 dilutions of the novel lipid particulate dispersion. In contrast to that, the cell viability of the HaCaT monolayer decreased to about 11% in the case of the 1:10 dilution of the Differin® cream. The less concentrated dilutions of 1:100 and 1:1000 still featured lower cell viabilities of 27% and 69%, respectively. This significant difference might be caused by crucial constituents of the Differin® cream such as polyethylene glycol methyl glucose sesquistearate since cell toxicity on HaCaTs depends on the type of the surfactant [3]. Methyl paraben may also decrease the cell viability [4]. On the other hand, hard fat and lecithin as components of the solid lipid microparticle dispersion do not negatively affect HaCaT cells [5].

Conclusion: The chemical stability of adapalene is independent of the storage temperature of the formulation while the physical stability of the formulation is high at 4°C and limited at 40°C. Furthermore, the novel formulation is milder to HaCaT cells and may feature less irrita-

tion potential than the cream. The latter might be a benefit in topical retinoid therapy.

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