Novel prolonged release particulate system for transdermal delivery of water-insoluble antifungal drug

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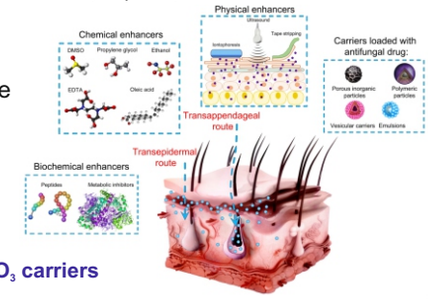
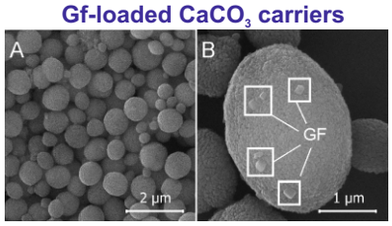
The concept of the study

Delivery of antifungals to affected regions of skin and effective drug concentration are of high importance for treatment of superficial mycoses. Penetration of conventional dosage forms into the skin is often limited. This encourages the development of various nano/microparticle-based antifungal formulations. The research is focused on the particulate drug delivery system for topical antifungal therapy aimed to improve therapeutic efficiency of low-bioavailable drugs.
Griseofulvin (Gf) was used as a model antifungal drug.



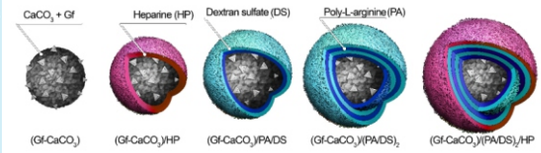
Gf-loaded $CaCO_3$ carriers



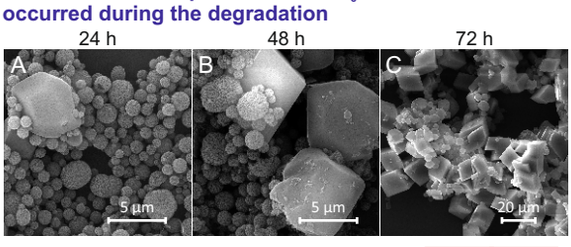
Layer-by-Layer complex polyelectrolyte shells assembling on $CaCO_3$ carriers

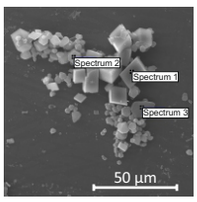
The Gf-$CaCO_3$ carriers were modified with LbL coatings consisted of various combinations of polyectrolyte layers (polyarginine (PA) and dextran sulfate (DS)) and protein (heparin (Hp)) molecules.

Such a complex PE shell allows inhibition of Gf-$CaCO_3$ carriers degradation and prolongation of Gf release



The characteristic phases in $CaCO_3$ carriers occurred during the degradation





	C, W%	O, W%	Cl, W%	Ca, W%
Spectrum 1 Calcite particle	14.72	24.27	0.80	60.21
Spectrum 2 Gf particle	57.43	34.55	5.86	2.15
Spectrum 3 Gf particle	65.22	19.86	10.97	3.95

Degradation of Gf-loaded $CaCO_3$ carriers

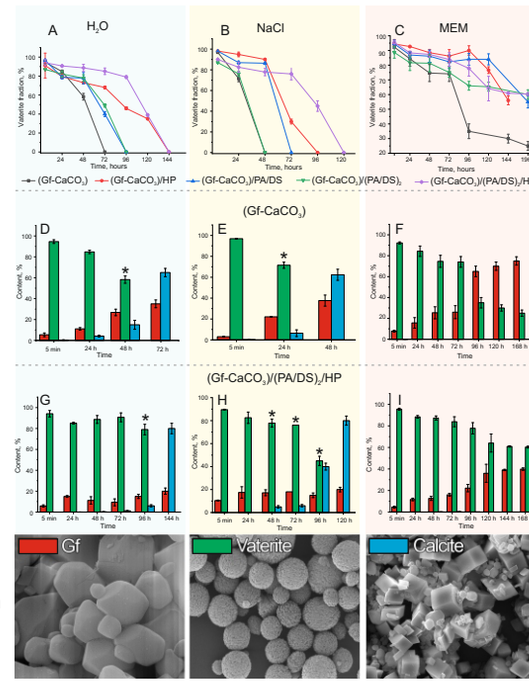
The carriers with $(PA/DS)_2$/HP shell results in most efficient inhibition of Gf-$CaCO_3$ carriers degradation. The vaterite phase in (Gf-CaCO3) with this shell was observed up to 96 h in water, as compared with unmodified carriers (48 h).

Cell viability for all the studied carriers was above 70 %, which indicates the absence of a cytotoxic effect of the developed Gf-formulation.

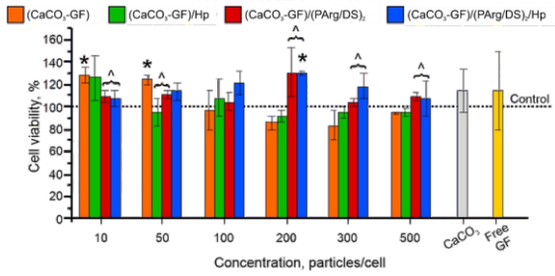
Successfulness of the carrier delivery into hair follicles was proved by SEM images demonstrated the filling of the follicular sacs with the carriers.

As seen from the photographs of the rat back, no skin damaging, inflammatory state or erythema was being registered during the experiment.

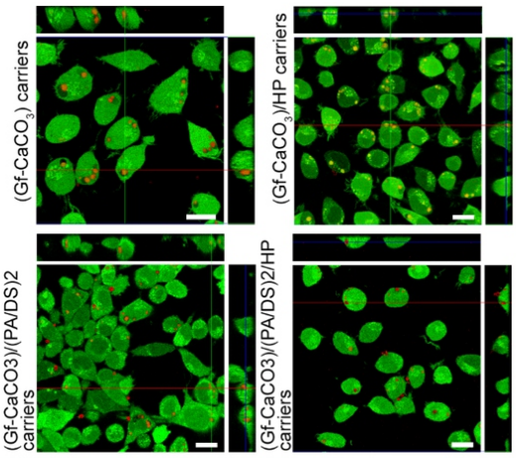
So, the developed system allows enhancing the bioavailability of water-insoluble drug Gf for topical applications. The complex PE shell on carriers surface moderates the rate of carriers degradation and drug sustaining in hair follicles. The technique presented can be adapted for wide range of drugs with low solubility and low bioavailability.



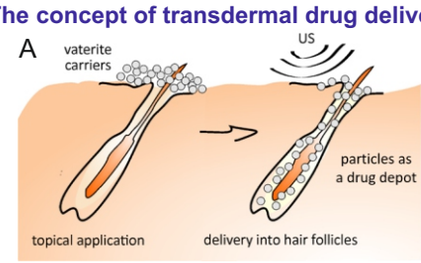
Cytotoxicity of PE-modified carriers incubated with NHDF cells

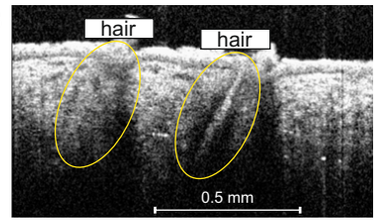


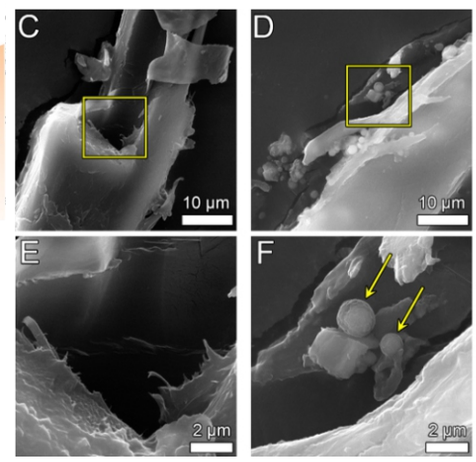
Internalization of PE-modified carriers by L929 cells



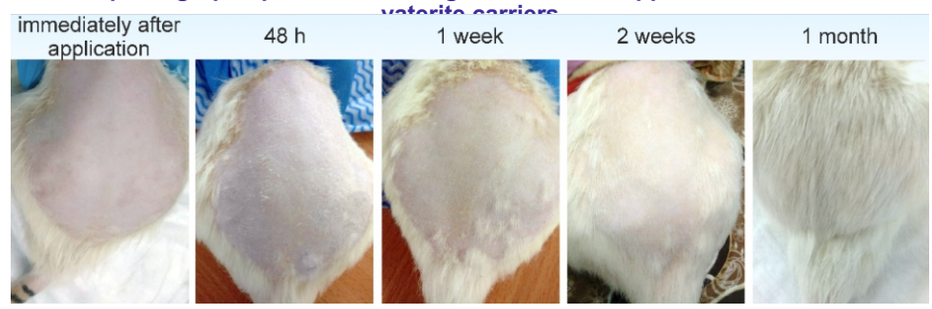
The concept of transdermal drug delivery of $CaCO_3$ carriers via skin appendages







Rat back photographs performed during 1 month after application of the Gf-loaded vaterite carriers



Conclusions

- $CaCO_3$ carriers loaded with antimycotic drug were obtained, the loading efficiency was 25% (w/w).
- $(PA/DS)_2$/HP shell provided the prolongation of carrier degradation and griseofulvin release.
- Carriers allowed efficient accumulation of griseofulvin in hair folliclesof rat *in vivo.*

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