

## Clinical and Experimental Dermatology: Polymeric nanospheres for topical delivery of adapalene

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### Abstract

**Introduction:** Hair follicles are considered as alternative pathway for topical and transdermal delivery. They can contribute to absorption and uptake of large molecules and nanoparticles. Therefore, Nano carriers can potentially be an effective drug delivery system targeting at hair follicle-related diseases, such as acne and alopecia<sup>1</sup>. Adapalene is a third generation retinoid and a highly lipophilic drug ( $\log P=8.2$ ), which is commercially available in forms of topical gel and lotion for treatment of mild to moderate acne<sup>2</sup>. In these commercial products adapalene exists as microcrystals dispersed in the formulations. Skin irritation has been reported with topical adapalene products due to direct contact of adapalene microcrystals containing acid groups (-COOH) with stratum corneum (SC), as well as presence of alcohols and surfactants in the formulation<sup>3</sup>. We have developed a platform technology to encapsulate hydrophobic drugs in tyrosinederived nanospheres (TyroSphere) and to facilitate skin delivery<sup>4</sup>. In this study, the applicability of TyroSphere for targeted delivery of adapalene into hair follicles is assessed. **Experimental Methods:** Adapalene was loaded in the TyroSphere according to a previously reported protocol<sup>4</sup> and the final formulation was in form of liquid dispersion or a gel. Adapalene loaded-nanosphere (Ada-TyroSphere) dispersion were characterized for their particle size, particle morphology, drug-polymer binding efficiency, drug sebum/water and stratum corneum/water partition coefficients, and drug's crystallinity. Adapalene aqueous solubility was measured in presence of different amount of surfactant and was compared with TyroSphere formulations. HPLC technique was used for all the quantification purposes. Skin distribution of adapalene formulated in TyroSphere (gel and suspension) and marketed lotion (Differin®) was examined on human cadaver and porcine ear skin. Fluorescent microscopy was used to visualize adapalene delivery to epidermis and hair follicles. **Results & Discussion:** The average particle size of TyroSphere was approximately 70 nm ( $PDI<0.22$ ), which is suitable for follicular uptake. TyroSphere provided substantial enhancement in the solubility of adapalene in phosphate buffer saline (PBS) pH=7.4. In X-Ray diffraction diagram, the crystalline peaks of adapalene were absent in Ada-TyroSphere, suggesting absence of adapalene microcrystals. Sebaceous glands are part of pilosebaceous unit and they produce and secrete sebum into follicular orifice. In order to

target hair follicles it is critical to understand drug/formulation partition properties into human sebum<sup>5</sup>. The average partition coefficient of adapalene -in form of Ada- TyroSphere in PBS- into sebum after 15 h was  $39.5\pm 7.1$ , while this parameter for SC partitioning was  $18.6\pm 1.5$ . Following 12 h application of 0.5 ml Ada-TyroSphere aqueous dispersion (0.02% drug w/w) on dermatome human cadaver skin, adapalene extracted from epidermis was measured as  $3.43\pm 1.14 \mu\text{g}/\text{cm}^2$ , while 100 mg Differing® lotion (0.1% drug w/w) delivered  $1.25\pm 1.28 \mu\text{g}/\text{cm}^2$  of drug into the epidermis ( $n=8$ ). Moreover, results of another permeation study on porcine skin showed that there was no significance difference in delivery of adapalene to SC among Ada-TyroSphere gel formulations (0.025 % drug w/w) and Differin® (0.1% drug w/w). Figure 1 depicts fluorescent images of porcine skin treated topically with Ada-TyroSphere for 24 h (blue fluorescence coming from adapalene). Clearly, adapalene was delivered to upper epidermal layers and hair follicles

### Biography

Bozena Michniak-Kohn is a tenured Professor of Pharmaceutics at the Ernest Mario School of Pharmacy, and Founder /Director of the Center for Dermal Research CDR at Rutgers- The State University of New Jersey, Piscataway, NJ. She is also the Director of the Laboratory for Drug Delivery of the New Jersey Center for Biomaterials (NJCBM). Her main focus is topical, transdermal and buccal drug delivery. She has over 35 years experience in design & optimization of topically applied formulations and transdermal patches. She holds patents for novel drug carrier approaches for dermatologicals. She is a member of graduate programs at Rutgers in Pharmaceutical Sciences, Biomedical Engineering, Chemical and Biochemical Engineering, Chemistry and Chemical Biology as well as the RWJ Graduate School of Biomedical Sciences. She received her BSc (Honors) in Pharmacy and PhD in Pharmacology from the UK. She has directed over 50 PhD and Masters Students and the work resulted in over 120 peer-reviewed manuscripts, over 420 abstracts, 2 books, and 35 book chapters.

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