

## DIFFERENT INORGANIC NANOPARTICLES AS ENHANCERS FOR DERMAL DELIVERY OF PROTEINS IN PHARMACEUTICAL AND COSMETIC PRODUCTS

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### ABSTRACT

**Objectives:** In last decades, dermal delivery of drugs has attracted a great interest. In this study, calcium phosphate nanoparticles (CaP-NPs), zinc oxide nanoparticles (ZnO-NPs) and some organic solvents were used as combination enhancers for dermal delivery of albumin.

**Methods:** Formulations contained albumin, solvent, CaP-NPs and/or ZnO-NPs. Permeation of albumin was determined by an *ex vivo* (animal skin) method. Distribution of the NPs in the skin layers was depicted by optical microscopic method.

**Results:** Among solvents, liquid paraffin (LP) showed the greatest increase in albumin permeation (total permeation of 384 mg). CaP-NPs and ZnO-NPs also increased the albumin permeation (19 and 22 mg, respectively). Combination of these NPs and LP further increased the albumin permeation (470 and 487 mg, respectively).

**Conclusion:** All solvents increased albumin permeation while LP showed a dramatic increase. CaP-NPs or ZnO-NPs also increased the permeation. Enhancing mechanism of the NPs was attributed to their deposition through skin layers shown by images. Using a combination of CaP-NPs and/or ZnO-NPs with LP caused synergistic permeations following by a saturation at a high dose of the NPs. The study suggests simultaneous use of proper doses of such inorganic NPs with LP to considerably enhance dermal delivery of albumin or other proteins.

**Keywords:** Albumin; Calcium phosphate nanoparticles; Organic solvents; Skin permeation, Zinc oxide nanoparticles.

### INTRODUCTION

Dermal route of drug administration possesses several advantages. Its advantages over oral administration are decreased or total avoidance of first-pass drug metabolism, bypassing absorption steps, effects of pH and enzymes and transit time. Its advantages over injection and other routes are non-invasive and controlled delivery and termination<sup>1</sup>.

The most important barrier for transdermal drug delivery is the skin's horny layer or *stratum corneum* (SC). This layer must be altered for penetration of drugs through the skin. This topic has been the subject of research for pharmaceutical scientists especially during the two recent decades<sup>2</sup>. Extensive research on chemical penetration enhancers (CPEs) has been performed which form the main strategy of formulation-design approaches for dermal and transdermal drug delivery<sup>3</sup>. It is now well known that formulation components can improve the quantity and rate of transdermal absorption of drugs<sup>4</sup>. Permeation of a drug through the skin in the presence of a CPE is related to physico-chemical characteristics of the CPE and the drug<sup>5-7</sup>. Therefore, skin permeation of drugs varies in the presence of different CPEs. Thus each pair of drug-CPE should be examined separately. In this case, CPEs should

construct a situation to make new skin microstructures. More than two hundred CPEs have been shown to enhance skin permeation of drugs<sup>3</sup> mainly including aliphatic acids, fatty acids, esters, alcohols, oils and terpenes<sup>1</sup>.

One group of the CPEs are hydrophobic nanoparticles (NPs) made from lipids or hydrophobic polymers. The drug is trapped inside these NPs. The polymeric NPs should be evaluated in terms of safety, biocompatibility and especially degradation kinetics. Therefore, they should be accurately designed to become suitable for use in medications<sup>8-10</sup>, such as designing their preparation methods in order to obtain suitable NP size, surface charge, and degradation mechanisms. Lipid NPs have similar steps.

Another group is inorganic NPs. Among them, titanium dioxide NPs have been introduced as dermal enhancer and its physicochemical optimization as an enhancer was investigated<sup>11</sup>. In this study inorganic NPs including calcium phosphate nanoparticles (CaP-NPs) and zinc oxide nanoparticles (ZnO-NPs) were used as enhancers. CaP with molecular weight (MW) of 310.176 g/mol is a safe and inexpensive natural chemical containing calcium and phosphate which are essential nutrients<sup>12</sup>. It has excellent biocompatibility because of

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