Title: Dermal absorption behavior of fluorescent molecules in nanoparticles on human and porcine skin models

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<AT>Dermal absorption behavior of fluorescent molecules in nanoparticles on human and porcine skin models.
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<ABS-HEAD>Abstract
<ABS-P>The percutaneous passage of poorly skin absorbed molecules can be improved using nanocarriers, particularly biodegradable polymeric nanospheres (NSs) or nanocapsules (NCs). However, penetration of the encapsulated molecules may be affected by other factors than the nanocarrier properties. To gain insight information on the skin absorption of two fluorescent cargos, $DiIC_{18}(5)$ and coumarin-6 were incorporated in NSs or NCs and topically applied on various human and porcine skin samples. 3D imaging techniques suggest that NSs and NCs enhanced deep dermal penetration of both probes similarly, when applied on excised human skin irrespective of the nature of the cargo. However, when *ex vivo* pig skin was utilized, the cutaneous absorption of $DiIC_{18}(5)$ was more pronounced by means of PLGA NCs than NSs. In contrast, PLGA NSs noticeably improved the porcine skin penetration of coumarin-6, as compared to the NCs. Furthermore, the porcine skin results were reproducible when triplicated whereas from various human skin samples, as expected, the results were not sufficiently reproducible and large deviations were observed. The overall findings from this comprehensive comparison emphasize the potential of PLGA NCs or NSs to promote cutaneous bioavailability of encapsulated drugs, exhibiting different physicochemical properties but depending on the nature of the skin.

<KWD>Abbreviations: AUC, area under curve; CLSM, confocal laser scanning microscope ; Cryo-TEM, cryo-transmission electron microscopy ; DHEA, dehydroepiandrosterone; MCT, mid-chain triglyceride ; NC, nanocapsule; NP, nanoparticle ; NS, nanosphere; PDI, polydispersity index ; PLC, poly(ε-caprolactone) ; PLGA, poly(lactic-co-glycolic acid); PTA, phosphotungstic acid ; Rhod B, rhodamine B; TEM, transmission electron microscopy ; TEWL, transepidermal water loss

<KWD>Keywords: Human;;;; porcine; skin; penetration; nanospheres; nanocapsules.
<H1>1. Introduction