This article appeared in a journal published by Elsevier. The attached copy is furnished to the author for internal non-commercial research and education use, including for instruction at the authors institution and sharing with colleagues.

Other uses, including reproduction and distribution, or selling or licensing copies, or posting to personal, institutional or third party websites are prohibited.

In most cases authors are permitted to post their version of the article (e.g. in Word or Tex form) to their personal website or institutional repository. Authors requiring further information regarding Elsevier’s archiving and manuscript policies are encouraged to visit:

http://www.elsevier.com/copyright
The use of nanoparticles as drug delivery vectors is presently undergoing intense scrutiny. The topical–transdermal route of drug administration has not escaped the attention of the nanoparticle community, initially because of potential toxicity concerns resulting from exposure to such structures in sunscreens, for example. Subsequently, the drug delivery community recognized a more positive opportunity and several studies have appeared in which improved skin penetration/permeation of active substances associated with nanoparticle-containing formulations have been reported. These results have led to claims that nano-sized objects are, somehow, able to make their way across this most resilient of membranes. These claims were made despite the acknowledged, superlative nature of the skin's barrier function to the ingress of just about any small drug, let alone even the tiniest of particles.

In this issue, Professor Richard Guy and his colleagues[1] objectively assess the disposition of nanoparticles on mammalian skin after prolonged topical application. The paper focuses particular attention on the interface between the applied nanoparticle formulations and the outermost layer of the skin, the stratum corneum. The over-riding function of the thin layer (on average only 10–20 μm) of stratum corneum is to constrain the outward transport of water from inside the body. To address the conflicting points of view in the literature about nanoparticle transport across skin, Professor Guy and his team have used laser scanning confocal microscopy to track the fate of fluorescently-labeled polystyrene beads ranging in diameter from 20 to 200 nm. Aqueous suspensions of these particles have been applied to mammalian skin for periods of up to 16 h before microscopic examination. Experiments have been performed both on normal, intact skin and on skin from which several layers of the stratum corneum were first removed by the repeated application of adhesive tape. The latter approach is recognized to remove both the stratum disjunctum (the most exterior layer of the stratum corneum that is in the final process of desquamation) as well as, progressively, the functional component of the barrier itself.

Importantly, the analysis of the confocal images obtained has been undertaken in an objective and statistical manner so as to minimize or indeed eliminate investigator bias. Specifically, regions of interest were selected as coordinates from fields of view using true random numbers generated from atmospheric noise. At least three random regions of interest were recorded for each skin sample, thereby preventing selection bias towards those offering the most attractive images. The entire acquired image was analyzed and a profile of the fluorescence distribution emanating from the nanoparticles (which, individually, were too small to resolve optically) was generated. This process required essentially no human decisions, and thus, the subjectivity inherent in image interpretation was considerably decreased. Consequently, the profiles from independent skin samples could be compared to assess whether the nanoparticles could actually penetrate beyond the skin surface or not.

Confocal imaging permits the effect of an uneven skin surface to be visualized unambiguously, and the apparent “deep” penetration of particles that have, in fact, been deposited into an invagination of the sample to be interpreted correctly. The results show clearly that polymeric nanoparticles (of diameters from 20 to 200 nm) only penetrated into the surface layers (to a depth of 2–3 μm) of the stratum corneum, suggesting simple infiltration along fissures in the stratum disjunctum. The quantitative assessment of bulk particle location could be compared to assess whether the nanoparticles could actually penetrate beyond the skin surface or not.

This over-riding function of the thin layer (on average only 10–20 μm) of stratum corneum is to constrain the outward transport of water from inside the body. To address the conflicting points of view in the literature about nanoparticle transport across skin, Professor Guy and his team have used laser scanning confocal microscopy to track the fate of fluorescently-labeled polystyrene beads ranging in diameter from 20 to 200 nm. Aqueous suspensions of these particles have been applied to mammalian skin for periods of up to 16 h before microscopic examination. Experiments have been performed both on normal, intact skin and on skin from which several layers of the stratum corneum were first removed by the repeated application of adhesive tape. The latter approach is recognized to remove both the stratum disjunctum (the most exterior layer of the stratum corneum that is in the final process of desquamation) as well as, progressively, the functional component of the barrier itself.

Importantly, the analysis of the confocal images obtained has been undertaken in an objective and statistical manner so as to minimize or indeed eliminate investigator bias. Specifically, regions of interest were selected as coordinates from fields of view using true random numbers generated from atmospheric noise. At least three random regions of interest were recorded for each skin sample, thereby preventing selection bias towards those offering the most attractive images. The entire acquired image was analyzed and a profile of the fluorescence distribution emanating from the nanoparticles (which, individually, were too small to resolve optically) was generated. This process required essentially no human decisions, and thus, the subjectivity inherent in image interpretation was considerably decreased. Consequently, the profiles from independent skin samples could be compared to assess whether the nanoparticles could actually penetrate beyond the skin surface or not.

Confocal imaging permits the effect of an uneven skin surface to be visualized unambiguously, and the apparent “deep” penetration of particles that have, in fact, been deposited into an invagination of the sample to be interpreted correctly. The results show clearly that polymeric nanoparticles (of diameters from 20 to 200 nm) only penetrated into the surface layers (to a depth of 2–3 μm) of the stratum corneum, suggesting simple infiltration along fissures in the stratum disjunctum. The quantitative assessment of bulk particle location could be compared to assess whether the nanoparticles could actually penetrate beyond the skin surface or not.

Reference

Kinam Park
Purdue University, Department of Biomedical Engineering and Pharmaceutics, West Lafayette, IN, USA
Kyung Hee University, Department of Maxillofacial Biomedical Engineering, Seoul, Republic of Korea
E-mail address: kpark@purdue.edu

5 May 2012