Synopsis of Original Research Paper

Understanding the change in physical forms of nanoparticles exposed dermally and proposing test methods for appropriate analysis and prediction of their toxicity

Kazuya Nagano

School of Pharmaceutical Sciences, Wakayama Medical University

To ensure the safe usage of silver nanoparticles (nAgs) in cosmetics, it is necessary to reveal the physical forms of nAgs inside the skin, as these forms may change during the process of percutaneous absorption. In this respect, we have previously established an analytical system based on single-particle inductively coupled plasma mass spectrometry (sp-ICP-MS) to determine the physical forms of nAgs in the skin. Here, we analyzed the physical forms of nAgs inside the mouse skin. Furthermore, we tried to propose an appropriate test system, to understand the kinetics of nAgs after dermal exposure in a simple and detailed manner.

We evaluated the quantity as well as the physical forms of Ag in the epidermis and dermis of mice after exposing nAgs with 100 nm diameters (nAg100) or Ag^+ to the skin. Sp-ICP-MS analysis indicated that nAg100 could be absorbed and distributed into the deeper layers in the ionized form, whereas Ag+ was absorbed and distributed without a change in physical forms. This data suggested that it is essential to consider the distribution and particle size of not only nAgs but also Ag^+ released from nAgs into the skin, to understand the skin response following exposure of nAgs. Next, we focused on a three-dimensional skin culture model as an animal-substitute *in vitro* test system from the viewpoint of animal welfare, and analyzed the distribution of nAg100 (epidermal and dermal layer) and the amount and physical form of nAg100 in each layer. Sp-ICP-MS analysis showed that nAg100 could be also absorbed and distributed into the deeper layers in the ionized form, as well as *in vivo* studies. The data suggested that a three-dimensional skin culture model could be a useful *in vitro* test system for understanding the kinetics of nAgs after dermal exposure in a simple and detailed manner.