Commentary

Evaluation of Skin Toxicity of Silver Nanoparticles in 3D Epidermal Model Compared to 2D Keratinocytes

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INTRODUCTION

The increasing use of nanotechnology to manufacture consumer products raises concerns about the safety risks associated with exposure to nanomaterials. Silver nanoparticles (AgNPs) are one of the most commonly used nanomaterials due to their excellent broad-spectrum antibacterial properties. Colloidal silver particles are found in many industrial and medical products such as textiles, food packaging, water disinfectants, implant coatings, catheter coatings and wound dressings. Silver nanoparticles are reported as a component of 30% of products containing nanomaterials. However, AgNP can be toxic. Therefore, it is essential to accurately assess the potential risks associated with the administration of AgNP.

The toxicity of AgNP has been extensively studied over the last few decades. Most studies used two-dimensional (2D) cell culture models or animal models to assess toxicity. However, few studies have used three-dimensional (3D) tissue models. The use of 2D monolayer cultures consisting of immortalized cell lines, stem cells, or primary cells is the most common method for assessing toxicity *in vitro*. The cell type depends on the proposed use of nanomaterials and the expected target organs *in vivo*. Two-dimensional cell cultures are easy to use for biochemical assays. However, 2D culture lacks cell-cell and extracellular matrix interactions and lacks barrier function. Therefore, current 2D cell culture models are generally unable to mimic the skin microenvironment *in vivo* and therefore provide limited information about the organism's physiological response to external stimuli such as nanoparticles.

According to studies, *in vitro* and *in vivo* data are often poorly correlated. Therefore, care must be taken when generalizing *in vitro* results to *in vivo* effects. In recent years, some new drugs have been excluded from preclinical studies because *in vitro* toxicity studies failed to detect the risks associated with these drugs. *In vivo* studies are usually performed with a series of doses based on the results of *in vitro* experiments or actual doses, which may lead to more reliable results. However, animal use can be a limiting factor in determining toxicity for cost, biosafety, and animal ethics. To reduce the gap between *in vitro* and *in vivo*, there is a strong need for a new *in vitro* model system that can be used to accurately predict *in vivo* toxicity. The ideal model would assess the adverse effects of actual doses on inflammation, Reactive Oxygen Species (ROS) formation, immune system activation, etc. *in vitro* to accurately assess the potential risks associated with nanoparticles. You can evaluate it. Cells in the 3D tissue model, unlike cells in the 2D model, can differentiate and develop cell subsets with different functional states to form tissue structures. Three-dimensional tissue models can also simulate barrier functions that mimic the absorption and distribution of substances *in vivo*. Therefore, 3D models may be able to bridge the gap between *in vitro* and *in vivo* models. *In vitro* studies of the biological effects of nanoparticles using a 3D model system may be more appropriate than using a 2D model system, as toxicity can be affected by the cellular microenvironment. Lee et al. For the first time in 2009, we evaluated the toxicity of nanoparticles using a 3D spheroid culture-based test system. They found that the toxic effects of CdTe and Au nanoparticles were significantly reduced in spheroid cell cultures compared to 2D cell cultures. In addition, several different *in vitro* 3D models have been created and used to assess the biological effects of nanoparticles. These systems include a 3D cell spheroid culture system and an EpiDerm ™ tissue model.

CONCLUSION

The rapid development of wearable textiles and medical devices, including AgNP, raises concerns that consumers may be at increased risk of adverse health effects from skin exposure to AgNP. Previous studies have shown that AgNP induces severe cytotoxicity in cultured keratinocytes, whereas *in vivo* studies have shown relatively weak toxicity. Previous reports have shown that no significant toxicological changes occurred during the 28-day AgNP inhalation study in rats. In this study, we developed a 3D epidermis model called EpiKutis, which is composed of human keratinocytes (KC) that mimic human epidermis, and used it to evaluate AgNP toxicity. A two-dimensional keratinocyte culture was used as a control. Oxidative damage and inflammation were evaluated in each model.