Safety of antimicrobial nanoparticles on in vitro models of the skin

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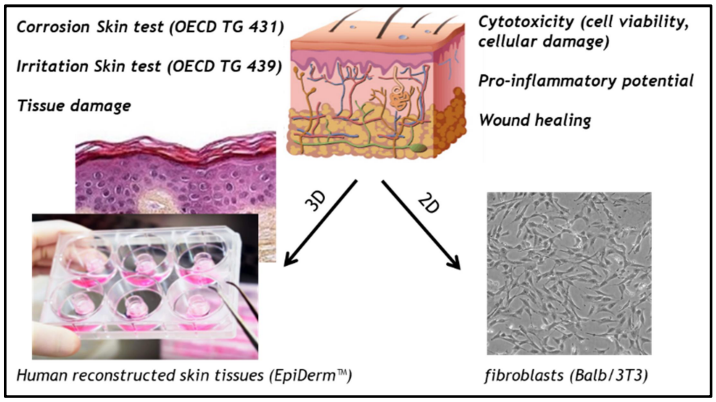
Nanomaterials (NMs), including metal oxide (MeO) nanoparticles (NPs) and polymeric NPs, has been largely used for the production of nanoenabled products (NEPs), such as catheters, textiles for bed sheets, gowns and bandages, water and air filter membranes, in order to functionalize them with antimicrobial properties [1]. Consequently, together with the massive production and use of NMs in many fields of applications, it has arisen a growing concern about NMs safety towards humans, especially through skin contact, which is one of the major route of exposure. Since nosocomial infections are a dramatic worldwide issue, and considering that during the COVID-19 pandemic it has been further highlighted that the persistence of viruses on surfaces could contribute to the spread of infections [2], there is a urgent need to develop new safe materials in order to overcome the request of effective antibacterial agents. In this work, the toxicological effects of already characterized antimicrobial NMs, including different types of MeO (CuO, ZnO, and hybrid SiO_2/TiO_2) and polymeric (Polypyrrole) NPs and extracts from NEPs (e.g. coated textiles), has been investigated on in vitro model of skin barrier (EpiDerm™, MatTek) following standardized OECD protocols (TG. 431, TG. 439) and ISO guidelines (ISO/TC 194/WG 8 for MD extracts). The impact of MeOs on epidermis was assessed at different artificial sweat pHs, to demonstrate the toxicological behaviour of these NMs in conditions similar to the physiological ones. Morphological observations of the skin tissue and quantification of the inflammatory cytokine interleukin-8 production in response to these NMs were performed to evaluate the skin damage induced by the extracts derived from the different NEPs. The cytotoxicity of the antimicrobial products has been also tested on cells representative of the dermal layer, Balb/3T3 fibroblasts, and wound healing assay has been also performed in order to understand the toxicity potential of NPs on a damaged skin model. From the data obtained, four principal key messages were identified:



1. Antibacterial MeO-NPs (CuO and ZnO) are safe on intact epidermis, unless ions dissolution from NPs occurs in acidic conditions, while SiO2/TiO2 hybrid-NPs are safe on intact epidermis unrelatedly of ions release
2. Polypyrrole NPs and respective NEPs are safe on intact epidermis
3. Antibacterial NMs may affect dermal cells, when eventually achieved through skin lesions or though skin permeation
4. During the development of nano-based antimicrobial coatings for skin contact applications, it would be worthwhile to implement stringent safe-by-design strategies, such as changing NPs surface properties, in order to prevent NPs toxicity

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Abstract

References

[1] M. Cloutier M. et al. Antibacterial Coatings: Challenges, Perspectives, and Opportunities. Trends in Biotechnology, 2015, 33: 637-652

[2] Chia, P.Y., Coleman, K.K., Tan, Y.K. *et al.* Detection of air and surface contamination by SARS-CoV-2 in hospital rooms of infected patients. *Nat Commun* 11, 2800 (2020). https://doi.org/10.1038/s41467-020-16670-2