

Topical absorption and safety of nanomaterials applied to human skin

Michael S. Roberts^{1,2}, Yousuf H. Mohammed², Amy Holmes¹, Ivan Kempson³, Tarl W. Prow³, Andrei V Zvyagin⁴, Zahra Khabir⁴, Zhiping Xu⁵, Heather A.E. Benson⁶ and Jeffrey E. Grice²*

¹ Therapeutics Research Group, School of Pharmacy and Medical Science, University of South Australia, Basil Hetzel Institute for Medical Research, Woodville, South Australia

² Therapeutics Research Centre, Diamantina Institute, University of Queensland, Translational Research Institute, Woolloongabba, Queensland, Australia

³ Future Industries Institute, University of South Australia, Mawson Lakes, South Australia

⁴ ARC Centre of Excellence in Nanoscale BioPhotonics. Macquarie University, Sydney, New South Wales

⁵ Australian Institute for Bioengineering and Nanotechnology, University of Queensland, St Lucia, Queensland, Australia

⁶ School of Pharmacy and Biomedical Sciences, Curtin University, Perth, Western Australia

First and corresponding author email: m.roberts@uq.edu.au

The talk describes our journey of assessing the safety of topically applied nanoparticles. A particular focus is on those applied to the skin for cosmetic, consumer protection and therapeutic purposes. This work has involved the assessment of nanoparticle exposure and hazard using various techniques, including electron microscopy, multiphoton fluorescence lifetime imaging microscopy, laser ablation inductively coupled plasma mass spectrometry and synchrotron X-ray fluorescence microscopy in both the x,y and x,z planes in both *ex vivo* and *in vivo* human skin. Our studies have focused on the absorption, disposition and effects of nano zinc oxide, zinc pyrithione, nano silver, zinc ions and quantum dots in human epidermal cells, in animals, in excised human skin, in volunteers and in psoriatic patients.

Our key findings are that, whilst all nanoparticles have the potential to be toxic, especially in cell cultures, the larger nanoparticles now used in consumer products are safe because they are intrinsically not hazardous in the formulations used and are rarely absorbed intact after application to human skin. These findings apply for a range of application conditions, including occlusion, massage, flexing, repeated exposure and different skin types. However, zinc ions released after the application of nano zinc oxide and zinc pyrithione to the skin are absorbed into the viable epidermis and can enter into the systemic blood and excreted into the urine. However, this systemic exposure is less than the normal levels of zinc ions found in the body arising from the ingestion of food from various sources.

The importance of our work is that it shows that various nanoparticles can be safely used in a number of consumer products to meet various needs and that the products may assist in minimizing adverse sequelae such as actinic keratosis, skin cancer and other conditions that may arise when they are not used.

References

- Holmes AM, Lim J, Studier H, Roberts MS. Varying the morphology of silver nanoparticles results in differential toxicity against micro-organisms, HaCaT keratinocytes and affects skin deposition. *Nanotoxicol.* 2016 **Dec**;10(10):1503-1514.
- Holmes AM, Kempson I, Turnbull T, Paterson D, Roberts MS. Imaging the penetration and distribution of zinc and zinc species after topical application of zinc pyrithione to human skin. *Toxicol Appl Pharmacol.* 2018 **Mar** 15;343: 40-47.
- Mohammed YH, Holmes A, Haridass IN, Sanchez WY, Studier H, Grice JE, Benson HAE, Roberts MS. Support for the Safe Use of Zinc Oxide Nanoparticle Sunscreens: Lack of Skin Penetration or Cellular Toxicity after Repeated Application in Volunteers. *J Invest Dermatol.* 2019 **Feb**;139(2):308-315.