Dermal absorption of ZnO particles from sunscreens applied to humans at the beach

Brian Gulson1,2, Maxine McCall3, Laura Gomez1, Michael Korsch4, Phil Casey4, Les Kinsley5

1Graduate School of the Environment, Macquarie University, Sydney NSW 2109, Australia
2CSIRO Exploration and Mining, North Ryde NSW 2113, Australia
3CSIRO Future Manufacturing Flagship, North Ryde NSW 2113, Australia
4CSIRO Future Manufacturing Flagship - Clayton VIC 3168, Australia
5Research School of Earth Sciences, Australian National University, Canberra ACT 2601, Australia

I. INTRODUCTION

The incidence of skin cancer is increasing globally. The use of sunscreens is advocated to reduce the risk of skin cancer by filtering ultraviolet radiation when people are outdoors, either for recreational or occupational activities. Advances in formulation using nanotechnology have seen incorporation of ultraviolet (UV) absorbers titanium dioxide (TiO2) and zinc oxide (ZnO) into commercial sunscreens at amounts ranging from 4% to 30% w/w. These micronised sunscreens coat the skin as a transparent film and work primarily by reflecting and scattering light. The Australian Therapeutic Goods Administration stated that there are almost 400 sunscreen products, with many containing nanoparticulate TiO2 and/or ZnO, commercially available in Australia.

Dermal penetration of metal oxide nanoparticles from personal care products remains controversial and there is ongoing media attention. Most investigations were in vitro using diffusion cells or animal models with very few in vivo human studies. Several reviews and some more investigations in recent years have concluded that nanoparticles do not penetrate the stratum corneum although they can lodge in hair follicles and sweat glands. The most comprehensive review to date of the use of nanoparticles in personal care products is by the Environmental Working Group [1], a US-based NGO, and they concluded after peer-review of more than 400 documents that: “zinc and titanium-based formulations are among the safest, most effective sunscreens on the market based on available evidence” and of 16 studies on skin absorption, “nearly all showing no absorption of small-scale zinc and titanium sunscreen ingredients through healthy skin”.

II. METHODS

Concerns about dermal absorption and penetration of nanoparticles can be addressed with the approach of isotopic tracing [2], whereby an enriched stable isotope of the element of interest is incorporated into the product allowing any transfer to be detected using high resolution inductively coupled plasma mass spectrometry (ICP-MS), multi-collector ICP-MS or thermal ionization mass spectrometry.

This paper describes the use of stable isotopes of Zn for tracing potential absorption of Zn from ZnO nanoparticles in sunscreen applied to human skin under conditions of normal use. Zinc has 5 stable isotopes. One stable isotope 68Zn has a natural abundance of 18.8%. The ZnO particles used in this study were enriched with 68Zn to either 51% or >99%. Therefore increases in levels of 68Zn in blood and urine samples would indicate dermal absorption of Zn from sunscreens. The sensitivity of the stable isotope method allows for detection of <0.1% absorption of Zn.

Three trials have been undertaken to evaluate the dermal absorption of ZnO particles from sunscreens in human volunteers. The first trial involved 2 male subjects with two applications to their backs of a formulation containing ZnO nanoparticles (with diameters of ~30nm) enriched to 51% with 68Zn. Several blood and urine samples were collected throughout the day and for a number of days post trial. The second trial involved the same two males, and a female. The same formulation was applied twice daily for 5 days. Subjects experienced limited UV exposure as this trial was carried out in winter. Blood was sampled 3 times daily and urine at least 3 times daily and post trial for up to 126 days. These trials formed the basis and protocol refinement for the main beach trial in which particles of ZnO enriched to >99% with 68Zn were incorporated into a different formulation. Two groups, each consisting of 10 people of various ages, skin classifications, and race, participated in the study at a Sydney beach in March 2009 (Figure 1). One group of 10 volunteers was tested with a sunscreen containing nanoparticles of 68ZnO (~20nm) – the “nanoparticle” group (NP) -and the other group was tested with particles of 68ZnO >100nm – the “bulk” group (Figure 2). Sunscreen was applied to the backs of the volunteers twice daily for a period of 5 days and the subjects experienced a minimum of 1 hour UV exposure in two episodes following sunscreen application. Blood was sampled twice daily and urine three times daily. Blood and urine samples were also supplied before the 5-day beach exposure and in a follow-up period.

Zinc was purified from blood and urine samples by ion exchange procedures. Changes in the isotopic abundance of 68Zn of the purified samples, measured by multi-collector
inductively-coupled plasma mass spectrometry (MC-ICP-MS), were used to evaluate the dermal absorption of Zn from the sunscreens.

III. RESULTS AND DISCUSSION

Changes in the isotopic abundances are commonly expressed as ratios, in this case the enriched tracer $^{68}\text{Zn}$ divided by the naturally occurring $^{64}\text{Zn}$, i.e. $^{68}\text{Zn}/^{64}\text{Zn}$. Alternatively they can be presented as Wt% $^{68}$ tracer in the sample. In this instance we present the results as ratios.

**Pilot Trials** -

Results from the first two trials showed changes in the isotope ratios of <0.1% and it is estimated that this limits the dermal absorption to be <0.1%.

**Beach Trial** -

Changes in the $^{68}\text{Zn}/^{64}\text{Zn}$ ratio in blood samples for the NP group range from 0.1 to 0.8% at the end of the beach trial. Surprisingly all subjects showed significant increases in the abundance of $^{68}\text{Zn}$ 6 days after the completion of the trial (post-trial).

Changes in blood samples for the bulk group are similar to those for the NP group and also show the same trend of increased abundance of $^{68}\text{Zn}$ 6 days after the completion of the trial.

Excluding the data for 2 outliers, there is no statistically significant difference in dermal absorption for the volunteers in the NP and the bulk groups; the mean increase is about 0.4%.

Urine samples show larger increases in abundance of $^{68}\text{Zn}$ over the same time intervals but there is no simple relationship with changes in blood for the same volunteers.

IV. CONCLUSIONS

These results provide the first conclusive evidence that Zn from ZnO particles in sunscreen penetrates healthy skin and is observed in blood and urine. Whether the Zn is present as particles or soluble Zn ions is unknown at this stage.

These studies have been approved by human ethics committees at Macquarie University and CSIRO.

ACKNOWLEDGMENTS

We thank: David Ellis of Ellis and Associates and Brent Baxter of Baxter Pharmaceuticals for preparation of the sunscreen formulations; Gavin Greenouk for measuring the SPF on the “beach” formulations, assessment of skin types for the volunteers, and providing ongoing encouragement and advice; Mary Salter for phlebotomy; the North Curl Curl Surf Life Saving Club and Macquarie University Medical Centre and Aquatic Centre for use of their facilities; Yalchin Oytam in measuring UV levels for the beach trial; Malcolm McCulloch and Julie Trotter for mass spectrometer assistance in the earlier trials; Dianne Gulson as the applicator and assistance with logistics.

We thank the CSIRO Flagship Collaboration Scheme and Macquarie University for partial funding of these trials.

REFERENCES
