Should nanoparticles be used in sunscreens? — a unique study

(First use of stable isotopes in nanotechnology)

Outline

• Metal oxides in sunscreens/Issues/ Previous testing
• Stable Isotope Tracing ZnO
• Human Trials ZnO
• Results blood ZnO
• Summary ZnO
• Should we be concerned?

• (TiO$_2$)
• (Products with active ingredients in Australia & US)
To minimise UV exposure, 2 types of active ingredients are used in sunscreens – “chemical” (“organic”) and “physical” (“inorganic”)

**Disadvantages of “chemical” sunscreens**
- absorption through the skin – found in breast milk/urine
- certain chemicals may cause damage to sensitive organs or hormone receptors (endocrine disruptors)
- may cause skin irritation a mixture of UV-absorbers is needed to provide full (broad) spectrum protection
- can interact & break down in sunlight (e.g. avobenzone needs octocrylene)

**Advantages of “physical” sunscreens containing metal oxide nanoparticles**
- Zinc oxide (ZnO) and titanium dioxide (TiO₂) are largely stable
- nanoparticles of ZnO and TiO₂ appear clear on the skin
- ZnO and TiO₂ provide broad spectrum protection against UVA and UVB
Nanoparticles are tiny!

Human hair
~80,000 nanometers wide

1000 nanometres

Nanoparticles in sunscreens are typically ~10-30nm

Source: Maxine McCall CSIRO
Skin absorption of nano zinc (and TiO$_2$) oxide - The Issues

- Use of nanoparticles in cosmetics is highly controversial: CC 2016 survey 13% respondents wouldn’t use sunscreen because of nanoparticles
- Friends of the Earth
  - have called for a moratorium on their use,
  - convinced the Victorian Teachers Union to ban the use of sunscreens containing NP at child-care centres
  - didn’t believe the manufacturers so carried out their own testing with NMI
Previous testing

**Diffusion** cells with skin
- Human excised
- Pig

**Tape stripping**

In Vivo rodents/pigs/rabbit
(Sadrieh et al TiO$_2$ minipigs/mice CSIRO)

Multiphoton Microscopy in vivo
Source: Andrei Zvyagin MU/ Tarl Prow/Michael Roberts
STABLE ISOTOPE TRACING
- a new approach for detection of absorbed zinc from sunscreens
Testing skin absorption - Stable Zn Isotopes

- To distinguish between Zn from sunscreen and that occurring naturally in the body (e.g. from diet), the ZnO used in sunscreens in our studies was enriched with the stable Zn isotope, $^{68}\text{Zn}$ (~18-20% w/w in oil/water “commercial” formulation) - i.e. not radioactive

- An increase in the amount of $^{68}\text{Zn}$ in blood and urine samples compared with control samples indicates Zn from sunscreen has entered the body
Human trials - Trial 1 & 2
Nanoparticle ZnO in sunscreen

Trial 1 – 2 males 51% enriched $^{68}$ZnO
1 day

Trial 2 – 51% enriched $^{68}$ZnO 5 days
Winter (July 2008)
Human trials - Trial 2

$^{68}$Zn is tracer, $^{64}$Zn is natural abundance

Blood
- Max uptake day 14
- Cleared by day 50

Urine
- Max 5 days
- Cleared by day 22
Beach Trial 3-subjects & sampling

• Two groups of various: ages, skin types, countries, BMI
• Two sunscreens tested to compare effect of particle size:
  - “Nano” group (n=11) containing 19nm ZnO particles
  - “Bulk” group (n=9) >100nm particles
• ZnO uncoated
• Venous blood samples collected:
  – at the start of the trial,
  – twice daily during the trial, and
  – at 6 days post-trial.
• Sunscreen applied to backs of volunteers twice daily for 5 days/non ZnO formulation to exposed areas
• Subjects experienced a minimum of 1 hr UV exposure in two episodes following sunscreen application
• Urine sampled minimum 3 times daily
The volunteers
Analytical methods

Multicollector inductively coupled plasma mass spectrometer (RSES ANU)

Ultraclean chemistry
- Digest samples in clean HNO$_3$
- Anion exchange resin to separate Zn

Measures changes in amount of $^{68}$Zn in samples using isotope ratios

Zn is everywhere!!
Changes in amount of zinc in blood coming from sunscreen

Bar graphs showing the ratio $^{68}\text{Zn}/^{64}\text{Zn}$ in blood from subjects receiving bulk or nano sunscreens

- Each subject acts as their own control
- The pre-exposure data (red) illustrate the uniformity in $^{68}\text{Zn}/^{64}\text{Zn}$ ratios prior to sunscreen application, reflecting the isotopic composition of naturally-occurring Zn
- Statistically significant increases in the ratio in all subjects at end of the beach exposure phase (blue) and 6 days post-exposure (purple) are due to skin absorption of $^{68}\text{Zn}$ from the sunscreens
Urine results show Zn coming from sunscreen being wee’d out

- Larger increases in tracer $^{68}\text{Zn}$ than in blood
- Peak at Day 5 (end of days at beach)
- Still some $^{68}\text{Zn}$ signal at Day 40 in some subjects but most cleared by day 14
- Females (red) who had nano sunscreen had higher uptake of $^{68}\text{Zn}$ tracer than other groups
Summary - What did we find?

- In contrast to all previous studies, small amounts of Zn from our sunscreens found their way into the blood and urine of volunteers under real-life conditions.

- The amounts of Zn entering the body over the 5 day study (mean 15µg) were miniscule – around 1/1000th of the concentration of Zn already in the volunteers’ bloodstream (~12mg), and around 1/1000th of the amount of Zn recommended in a person’s daily diet.

- Even though some of the tracer Zn entered the bloodstream either as nanoparticles or soluble Zn, tracer was excreted in urine within a month.

- Thus the overwhelming majority of applied Zn was not absorbed.
**Should we be concerned?**

- **No** – given the tiny amounts we have detected with a very sensitive method
- **No** - given the absolutely critical need for Zn and homeostasis (‘tight control’) for Zn in the body
- **No** - Zn used in topical applications (ointments) for ~100 years and no reported ill effects
- **No** - for an occasional user going to the beach at weekends or even a 3 week holiday
- **Perhaps** - for occupational user and young children, BUT more research to find out if the Zn we found is present as nanoparticles in the body although new research is encouraging
- Until we know more SLIP/SLOP/SLAP shade. not at high UV time, & sunglasses!
Acknowledgements

Other collaborators
• David Andrews EWG Washington DC
• Laura Gomez, Alan Taylor (Macquarie University)
• Brent Baxter (Baxter Laboratories)
• Gavin Greenoak (Australian Photobiology Testing Facility)
• Les Kinsley (ANU)

Funding largely from Macquarie University and CSIRO
Thank you for your attention