# Reinvigorating cosmetic dermatology with the nanoparticle revolution

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It is said by many that cosmetic dermatology has hit a glass ceiling, meaning that few novel ingredients are being introduced for topical application, oral ingestion, or intradermal injection. Many new topical ingredients from mushrooms to salmon caviar to sea urchin spines to green algae to knotweed have been placed in complex antiaging formulations. The problem is that they are all functioning as antioxidants. They are simply variants of the same old theme purporting that when antioxidants found in nature are applied to the skin surface, they can decrease dermal oxidative damage and prevent collagen destruction by highly energetic oxygen radicals. Whether topical antioxidants can prevent oxidative damage has never been demonstrated in a real-time, controlled, human study. Other popular topical cosmeceutical ingredients are vitamins, but they too have a long use history. Even the new injectables for facial rejuvenation are hyaluronic acid based with subtle differences. This begs the question, ''Is any new is really happening in cosmetic dermatology?'' The answer is ''yes.''

If new chemical entities cannot be discovered, then it is possible to rediscover old chemicals in new forms. For example, the oldest quest of man has been to find gold. This drove Columbus to the new world in search of riches to transport back to Spain. Columbus was looking for a metal with a golden color, which is the familiar appearance of elemental gold. However, if gold is ground into nanoparticles of 100 nm or less, the gold will actually appear red. A gold slab melts at 1064 °C, while 2.5-nm nanoparticle gold melts at 300 °C. Would Queen Isabella have been happy with Columbus if he brought her back red nanoparticle gold? Probably not, but nanoparticle gold may be the future of affordable solar-generated power because the solar radiation absorption in gold photovoltaic cells is much higher with discontinuous gold nanoparticles as opposed to continuous gold film sheets.

When well-known substances are ground into nanoparticles, they display completely different properties and can behave in an unpredictable manner. This means that nanoparticles could reinvent the properties of substances currently used in cosmetic dermatology creating new chemical entities from old chemical entities. Are nanoparticles new? No. Nanoparticles were invented when man discovered fire! The first identified use of nanoparticles was in ninth century when the Mesopotamians used them in clay pot glitter. The nanoparticles in the pot glaze are still present in museums today. Silver and copper salts were mixed with vinegar, ocher, and clay and heated in a kiln to 600 °C to produce these iridescent pots. The high temperature results in nanoparticle formation.

A modern view of nanoparticles was first described in 1857 when Michael Faraday published a paper on the optical properties of nanometer-scale metals. Further work by Turner observed that thin leaves of gold or silver underwent a change around 500 °C with a discontinuity of the metallic film and increase in electrical resistance. Indeed, one of the major uses of nanoparticles today is in electronics, as physical material properties change at the nanoscale level in unexpected ways. The properties of metals and other elements change as the percentage of atoms at the surface increases in relation to the bulk of the material affecting melting points, magnetic potential, and electrical conductivity, for example. New medical imaging beyond CT and MRI scans uses injectable nanoparticles less than 10nm, known as quantum dots, in a magnetic field. These quantum dots are also being studied for their ability to deliver targeted drugs to cancerous tissue and for their ability to make microsized digital computers.

Nanoparticle skin care products are already entering the market and changing the way cosmeceutical ingredients interact with the skin. In 2005, 54 nanoparticle products were in the worldwide marketplace compared with 1015 in 2009; however, concerns are being voiced. The Swedish FDA banned 10 companies making nanoparticle zinc oxide sunscreens, and the EU has passed legislation requiring the word ''nano'' placed in brackets on the label of products containing nanoparticles. Furthermore, the EU is requiring companies to notify of the intent to release nanoparticle products as of November 2013.

Environmental concerns regarding nanoparticles have given rise to a new field known as nanotoxicology. Nanotoxicologists are concerned about the introduction of nanoparticles in the water supplies of the world. One of the more common uses of nanoparticles is in inorganic sunscreens. Nanoparticle zinc oxide is used to provide an invisible film of photoprotection on the skin surface. What happens when the nanoparticle zinc oxide is removed when swimming in the ocean? Where do the nanoparticles go? They go into the water supplies of the world, and as far as we know, they stay there for forever. Nanoparticle zinc oxide is actually antimicrobial and toxic to certain aquatic organisms. The long-term effects of nanoparticles in the oceans of the world are not currently known.

Yet, nanoparticles could be the next frontier in cosmetic dermatology. One of the biggest challenges with cosmeceutical ingredients is that they just sit on the stratum corneum and do nothing but moisturize the skin. Nanoparticles, with their high surface area-to-volume ratio, create an increased driving force for diffusion. This means that nanoparticles could be effectively used to deliver cosmeceuticals to the skin surface with enhanced penetration. Their small particle size, four to seven times smaller than the wavelength of light, also makes them invisible. This is the value of nanoparticles in inorganic sunscreen filters, such as zinc oxide and titanium dioxide. Finally, nanoparticle pigments can be used to create unusual topical skin effects for camouflaging and minimization of wrinkles and dyspigmentation.

The ability of nanoparticles to reinvigorate cosmetic dermatology depends on their ability or inability to penetrate the skin. This remains controversial; however, most of the early studies on nanoparticle penetration were carried out on pig skin. It now appears that pig skin is more permeable than human skin to nanoparticles because of the presence of more terminal hair follicles. The organization of the stratum corneum is key to human skin nanoparticle penetration. Human stratum corneum is made of alternately layers of protein-rich corneocytes and intercellular lipids. It appears that based on this stratum corneum organization, nanoparticles must be smaller than 13 nm to penetrate the skin. Further, 25-nm nanoparticles can penetrate into the upper 3–5 layers of the stratum corneum. This means that not all nanoparticles are equal. Nanoparticles of 14–100 nm do not penetrate the skin, while nanoparticles of 13 nm or less may penetrate. Further, nanoparticles do not tend to remain as single nanoparticles in emulsions. They tend to clump together or aggregate, meaning that the penetration kinetics are altered. Much more remains to be done on nanoparticle technology.

Nanoparticles have the potential to break the glass ceiling in cosmetic dermatology creating topical cosmeceutical formulations that behave in ways that enable better penetration of active skin ingredients. Someday in the not too distant future, we may be using nanoparticle therapy, nanoemulsions, polymeric nanoparticle spheres, and nanoliposomes to improve the appearance of the skin. Nanotechnology may allow old ingredients to exhibit new skin effects advancing the science of cosmetic dermatology.

  