Is the future of antioxidants mineral? Nanozymes and other nanotechnology solutions

Victor Puntes[1,2,3,4]

[1] Vall d'Hebron Research Instiute (VHIR), 08035 Barcelona, Spain
[2] Instiut Català de Nanociència I Nanotecnologia (ICN2), CSIC, The Barcelona Institute of Science and Technology (BIST), Campus UAB, Bellaterra, 08193 Barcelona, Spain
[3] Institució Catalana de Recerca I Estudis Avançats (ICREA), 08010 Barcelona, Spain
[4] Networking Research Centre for Bioengineering, Biomaterials, and Nanomedicine (CIBER-BBN), Instituto de Salud Carlos III, Madrid, Spain

Victor.puntes@vhir.org

The role of antioxidants in biology became popular in the second half of the 20th century at times when Linus Pauling (1954 and 1962 Nobel laureate) worked on the so called orthomolecular medicine, based on nutritional supplementation and high doses of ascorbic acid. It bumped again in the 90s, as consequence of a large human study suggesting that vitamin E supplements could be associated with a reduced risk of heart diseases. During these years, other works, basically pre-clinical and epidemiological, also reported beneficial effects of antioxidant substances in chronic inflammation, neurodegeneration, and cancer. As a consequence of that, antioxidant therapies were evaluated in placebo-controlled trials involving tens of thousands of patients and, despite pathophysiologic, epidemiologic, and mechanistic compelling evidence, these clinical trials have been, to date, mostly negative. This has given rise to a pessimistic view on antioxidant therapies. This has been attributed to the non-drug-likeness of available antioxidant compounds. These compounds have high unspecific uncontrolled reactivity, poor solubility, and hence limited absorption profiles, low bioavailability and low concentrations at the target site. During this time, nanomaterials has been proposed for use in treating human diseases, primarily as drug delivery agents, showing potential benefits in terms of pharmaceutical flexibility, selectivity, dose reduction, and minimization of adverse effects. Thus, efforts have been made towards loading antioxidant molecules such us coenzyme Q10, vitamin E and vitamin A, resveratrol and polyphenols, curcumin, lycopene, silymarin, and superoxide dismutase in nanocarriers such as liposomes, polymeric NPs, lipid NPs, and self-emulsifying systems. More recently, nanotechnology has shown us how rare earth mineral antioxidant NPs, especially cerium oxide NPs, nanoceria[1], are powerful antioxidant and consequent anti-inflammatory agents that can treat many inflammation-related diseases. This is a new paradigm, where the nanoparticle itself, thanks to its nanometric form and high concentration of oxygen vacancies at its surface, is the active principle, not a vehicle. Interestingly, nanoceria is safe, xenobiotic, and highly traceable material.

References

[1] Lena Montana-Ernst and Victor Putes Frontiers in immunology, 2022 (13), 750175

Figures

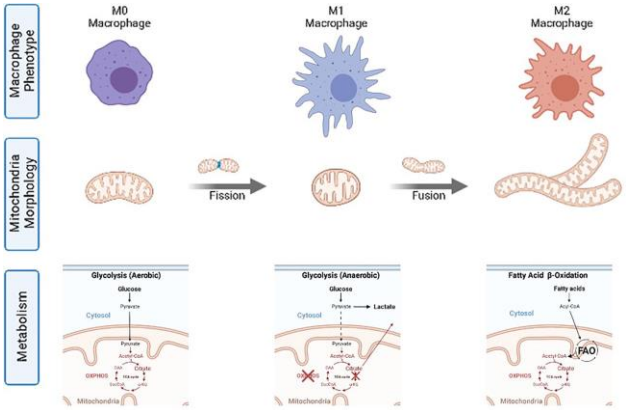

Figure 1. Macrophage phenotypes, mitochondria morphology and corresponding catabolic pathways

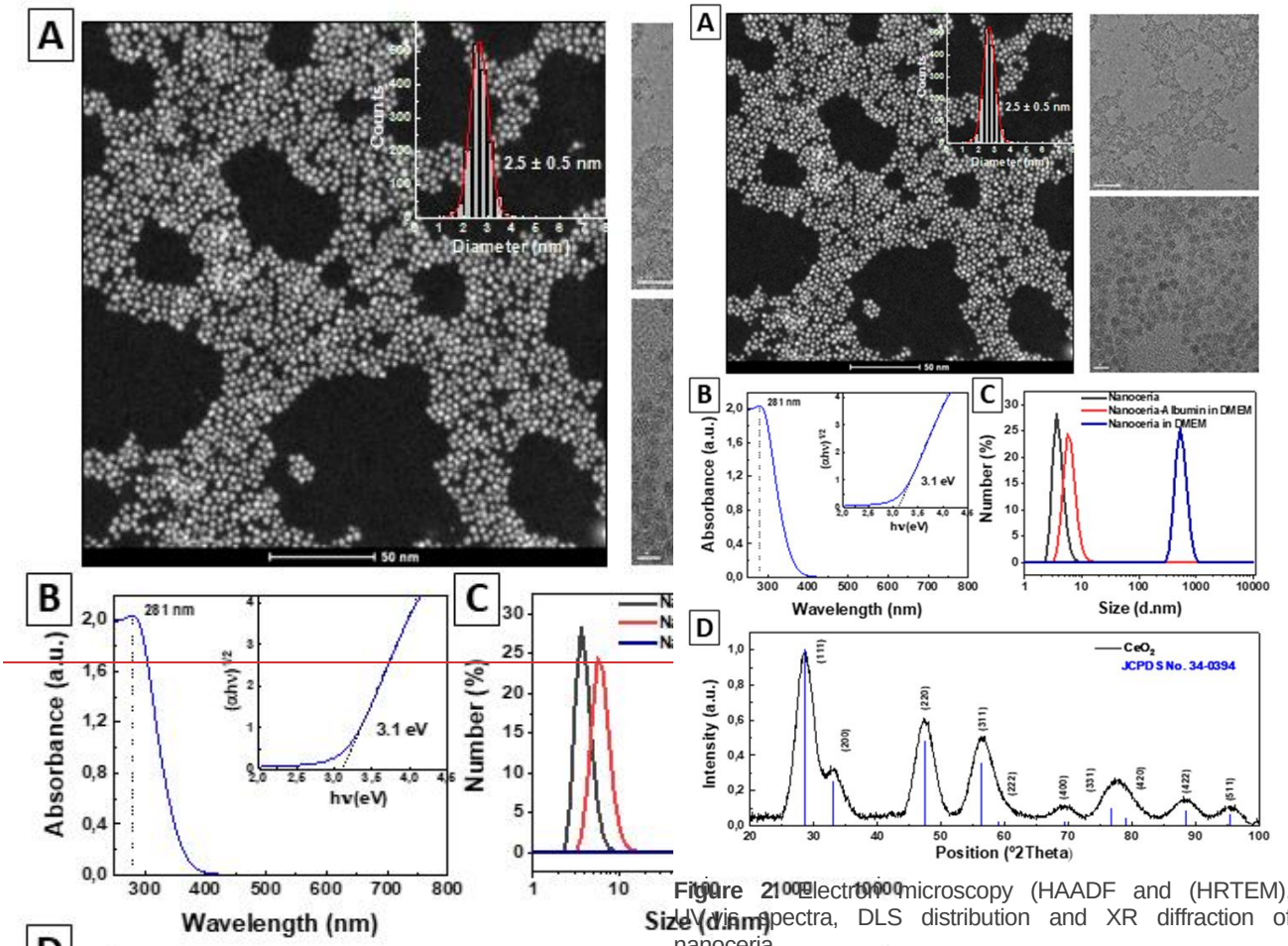

Figure 21 Electron microscopy (HAADF and (HRTEM), UV-vis spectra, DLS distribution and XR diffraction of nanoceria.