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Extended Abstract

Inspired by Nature: Redox Modulators and Natural Nanoparticles †

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Abstract: Numerous secondary metabolites found in edible plants modulate intracellular redox processes and are suggested to prevent certain diseases, especially in ageing organisms. Since such nutraceuticals provide the basis for new and innovative designer diets and therapies, extracting these substances and their potential from plants has become a focus of research, with nanotechnology and natural nanoparticles at the centre of some of these developments.

Keywords: nanoparticles; prevention; redox modulation; secondary metabolites

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In recent decades, it has become apparent that Oxidative Stress (OS) plays a major role in the formation and progression of many human diseases, in particular those related to ageing and the elderly population. Traditionally, medications have been administered to prevent or slow down these ailments. In societies affected by demographic changes, such (poly-)medication is not always feasible and, in any case, places a massive burden on the individual, the society, the environment and the economy.

Nutrition provides a promising alternative. Plants and mushrooms tend to be rich in phytochemicals and many secondary metabolites, including Reactive Sulfur Species (RSS) and Reactive Selenium Species (RSeS), are able to modulate intracellular redox processes [1–3]. Compounds such as allicin and polysulfides found in many *Allium* plants, for instance, can interact with the "cellular thiolstat" [4]. Such agents are moderately reactive, affect numerous cellular processes, exhibit pronounced antioxidant and also cyto-toxic activities and, therefore, have been linked to certain preventive or even therapeutic actions [5–10]. Together, a balanced cocktail of such biologically active nutritional components may provide a promising and also more applicable alternative to extensive medication. Additionally, the global market place—for food—also implies that it is now possible to design diets which may address specific needs, for instance for specific sub-populations and age groups.

Despite these advantages, there are still some challenges associated with this strategy. One major obstacle, for example, is the low solubility and hence bioavailability of many secondary metabolites, such as polyphenols. Rather than simply consuming the relevant food, complicated extraction and formulation methods are required to produce adequate food supplements. Here, nanotechnology provides potential solutions. It is now possible to produce nanoparticles of the relevant plant materials with comparable ease, for instance by milling or fermentation. These nanosized materials are entirely "natural" as far as their chemical composition is concerned, and often exhibit an amazing release profile for active ingredients and therefore also considerable biological activity [11–14]. Nanosized plant materials rich in biologically active ingredients may therefore unlock the considerable potential of many food items, and possibly also of materials which so far have been considered as "waste", such as the spent coffee ground, grape seeds and various shells, leftovers and peels [15]. At the same time, nanoscopic particles of sulfur and selenium generated by and in microorganisms may represent interesting preparations for agricultural applications [16–18].

In both cases, the combination of phytochemistry and nanotechnology promises access to new biological activities and innovative applications in various areas, from nutrition and medicine to agriculture and cosmetics.

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References

1. Giles, G.I.; Jacob, C. Reactive sulfur species: An emerging concept in oxidative stress. *Biol. Chem.* **2002**, *383*, 375–388.
2. Giles, G.I.; Nasim, M.J.; Ali, W.; Jacob, C. The reactive sulfur species concept: 15 years on. *Antioxidants* **2017**, *6*, E38.
3. Jawad Nasim, M.; Ali, W.; Dominguez-Alvarez, E.; da Silva Junior, E.N.; Saleem, R.S.Z.; Jacob, C. Reactive selenium species: Redox modulation, antioxidant, antimicrobial and anticancer activities. In *Organoselenium Compounds in Biology and Medicine: Synthesis, Biological and Therapeutic Treatments*; The Royal Society of Chemistry: Croydon, UK, 2018; Chapter 10, pp 277–302.
4. Jacob, C. Redox signalling via the cellular thiolstat. *Biochem. Soc. Trans.* **2011**, *39*, 1247–1253.
5. Czepukojc, B.; Viswanathan, U.M.; Raza, A.; Ali, S.; Burkholz, T.; Jacob, C. Tetrasulfanes as selective modulators of the cellular thiolstat. *Phosphorus. Sulfur.* **2013**, *188*, 446–453.
6. Saidu, N.E.B.; Abu Asali, I.; Czepukojc, B.; Seitz, B.; Jacob, C.; Montenarh, M. Comparison between the effects of diallyl tetrasulfide on human retina pigment epithelial cells (ARPE-19) and HCT116 cells. *BBA Gen. Subj.* **2013**, *1830*, 5267–5276.
7. Saidu, N.E.B.; Touma, R.; Abu Asali, I.; Jacob, C.; Montenarh, M. Diallyl tetrasulfane activates both the EIF2 α and NRF2/HO-1 pathways. *BBA Gen. Subj.* **2013**, *1830*, 2214–2225.
8. Allah, D.R.; Schwind, L.; Abu Asali, I.; Nasim, J.; Jacob, C.; Gotz, C.; Montenarh, M. A scent of therapy: Synthetic polysulfanes with improved physico-chemical properties induce apoptosis in human cancer cells. *Int. J. Oncol.* **2015**, *47*, 991–1000.
9. Yagdi Efe, E.; Mazumder, A.; Lee, J.Y.; Gaigneaux, A.; Radogna, F.; Nasim, M.J.; Christov, C.; Jacob, C.; Kim, K.W.; Dicato, M.; et al. Tubulin-binding anticancer polysulfides induce cell death via mitotic arrest and autophagic interference in colorectal cancer. *Cancer Lett.* **2017**, *410*, 139–157.
10. Grman, M.; Nasim, M.; Leontiev, R.; Misak, A.; Jakusova, V.; Ondrias, K.; Jacob, C. Inorganic reactive sulfur-nitrogen species: Intricate release mechanisms or cacophony in yellow, blue and red? *Antioxidants* **2017**, *6*, 14.
11. Griffin, S.; Tittikpina, N.K.; Al-marby, A.; Alkhayer, R.; Denezhkin, P.; Witek, K.; Gbogbo, K.A.; Batawila, K.; Duval, R.E.; Nasim, M.J.; et al. Turning waste into value: Nanosized natural plant materials of *Solanum incanum* L. And pterocarpus erinaceus poir with promising antimicrobial activities. *Pharmaceutics* **2016**, *8*, 11.
12. Griffin, S.; Masood, M.I.; Nasim, M.J.; Sarfraz, M.; Ebokaiwe, A.P.; Schafer, K.H.; Keck, C.M.; Jacob, C. Natural nanoparticles: A particular matter inspired by nature. *Antioxidants* **2017**, *7*, E3.
13. Griffin, S.; Alkhayer, R.; Mirzoyan, S.; Turabyan, A.; Zucca, P.; Sarfraz, M.; Nasim, M.; Trchounian, A.; Rescigno, A.; Keck, C.; et al. Nanosizing cynomorium: Thumbs up for potential antifungal applications. *Inventions* **2017**, *2*, 24.

14. Sarfraz, M.; Griffin, S.; Gabour Sad, T.; Alhasan, R.; Nasim, M.J.; Irfan Masood, M.; Schafer, K.H.; Ejike, C.; Keck, C.M.; Jacob, C.; et al. Milling the mistletoe: Nanotechnological conversion of african mistletoe (*Loranthus micranthus*) intoantimicrobial materials. *Antioxidants* **2018**, *7*, E60.
15. Griffin, S.; Sarfraz, M.; Farida, V.; Nasim, M.J.; Ebokaiwe, A.P.; Keck, C.M.; Jacob, C. No time to waste organic waste: Nanosizing converts remains of food processing into refined materials. *J. Environ. Manag.* **2018**, *210*, 114–121.
16. Estevam, E.C.; Griffin, S.; Nasim, M.J.; Denezhkin, P.; Schneider, R.; Lilischkis, R.; Dominguez-Alvarez, E.; Witek, K.; Latacz, G.; Keck, C.; et al. Natural selenium particles from staphylococcus carnosus: Hazards or particles with particular promise? *J. Hazard Mater.* **2017**, *324*, 22–30.
17. Griffin, S.; Sarfraz, M.; Hartmann, S.F.; Pinnapireddy, S.R.; Nasim, M.J.; Bakowsky, U.; Keck, C.M.; Jacob, C. Resuspendable powders of lyophilized chalcogen particles with activity against microorganisms. *Antioxidants* **2018**, *7*, E23.
18. Schneider, T.; Baldauf, A.; Ba, L.A.; Jamier, V.; Khairan, K.; Sarakbi, M.B.; Reum, N.; Schneider, M.; Roseler, A.; Becker, K.; et al. Selective antimicrobial activity associated with sulfur nanoparticles. *J. Biomed. Nanotechnol.* **2011**, *7*, 395–405.