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# Selenium-Carbon Bifunctional Nanoparticles for the Treatment of Malignant Mesothelioma – Online Supporting Information

By *Love Sarin*, *Vanesa C. Sanchez*, *Aihui Yan*, *Agnes B. Kane* and *Robert H. Hurt**

[*] Prof. R. H. Hurt, Dr. L. Sarin
Division of Engineering, Brown University
Providence, RI 02912 (USA)
Email: Robert_Hurt@brown.edu

V. C. Sanchez, Prof. A. B. Kane
Department of Pathology and Laboratory Medicine
Brown University, Providence, RI 02912 (USA)

A. Yan
Department of Chemistry, Brown University
Providence, RI 02912 (USA)

## Experimental Details

During nano-selenium synthesis, the addition of fixed volume of sodium hydroxide was performed quickly to obtain a narrower size distribution of particles. Lysosomal (pH = 4.5) buffer solution was prepared by mixing glacial acetic acid (25.5 ml, 0.2M) and potassium acetate (24.5 ml, 0.2 M), followed by a dilution to 100ml total volume and pH adjustment to desired value. Physiological (pH = 7.4) buffered solution was prepared by mixing monobasic potassium phosphate ($H_2KPO_4$, ACS, Acros) (9.5 ml, 0.2 M) and dibasic potassium phosphate ($K_2HPO_4$, ACS, AcrosOrganics) (40.5 ml, 0.2 M), followed by a dilution to 100ml total volume and pH adjustment to desired value. A new method was developed for ICP-AES, which involved calibration with the relevant media to control matrix effects, and acidification of all the solutions up to 2% nitric acid concentration to prevent any elemental precipitation. The dry sample for FE-SEM was coated in Au-Pd sputter (PS-2 coating unit, International Scientific Instruments) for 30 seconds to minimize charging under the electron beam.

## Additional Information on Selenium Biochemistry

As an essential trace element, selenium plays a fundamental role in multiple metabolic functions. It is involved in the maintenance of the immune system,[1-6] improvement of sperm motility,[7] and activation of the thyroid hormone.[8, 9] Selenite has been reported to induce p53- independent apoptosis of chemoresistant sarcomatoid more effectively than epithelioid MM cells.[10, 11] Inhibition of the SEP15 gene, which encodes a 15-kDa selenoprotein, makes mesothelial cells further resistant to selenium, underlying one of the possible mechanism of the effect of selenium.[12] Nano-selenium toxicity to A375 human melanoma cells, has been attributed to mitochondrial pathway induced apoptosis showing upregulation of ROS generation in cells in a dose dependent manner.[13]

In biological environments, selenide may be generated from elemental nano-selenium by (i) oxidation of normally stable thiols with low reduction potential[14, 15] or (ii) reduction by lactate.[16] It is noteworthy that some cancer cells have high concentrations of lactate[17-20] and high metabolic utilization of oxidized form of lactate, acetate,[21-23] that could facilitate this reduction.

## Cell Delivery Mechanisms

The enhanced delivery itself is consistent with the high cellular affinity for these supramolecular nanocarbons[24] but may also be aided by favorable "particokinetics",[25] which are colloidal dynamic phenomena that determine the local rate of particle collision with the cell surface through Brownian diffusion and gravitational settling. Our cell viability assays have an average particle path length of 3 mm (1/2 the depth of the cell culture dish) giving a mean diffusion times ($L^2/D$) using the Stokes-Einstein equation of 50 hours for nSeBSA and 1000 hours for CNPnSe. In contrast, the Stoke's law settling times are 800 hours for nSeBSA and 3 hours for CNPnSe. Stoke's sedimentation is thus likely to contribute to the transport

mechanism for the CNPnSe nanocomposite and increase the cellular dose rate, especially at short incubation times.

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