

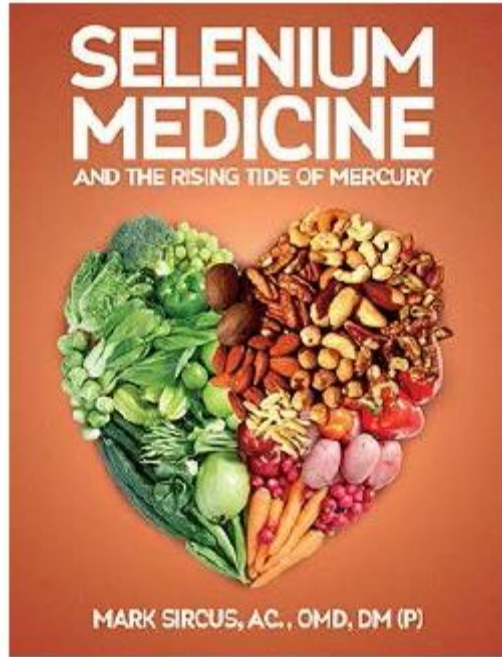
The role of selenium nanoparticles to dampen the metastatic potential of aggressive cancers

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Selenium: Health Interest



Ex: brazil nuts 19 μ g/g,
seafood 1.5 μ g/g,
pork 0.52 μ g/g

Main sources for humans : (Fordyce 2013)

- **Food** (cereals, rice, meat, eggs, fish, vegetables and fruits, milk, wine!)
- Water
- Air

Selenium: Element trace, different forms

- Food : few μ g/g (ppm) or μ g/kg (ppb)
- Healthy human body: few μ g/g

Physiological importance :
Antioxidant and anti-inflammatory
Protective action



Selenium in Cancer Therapy

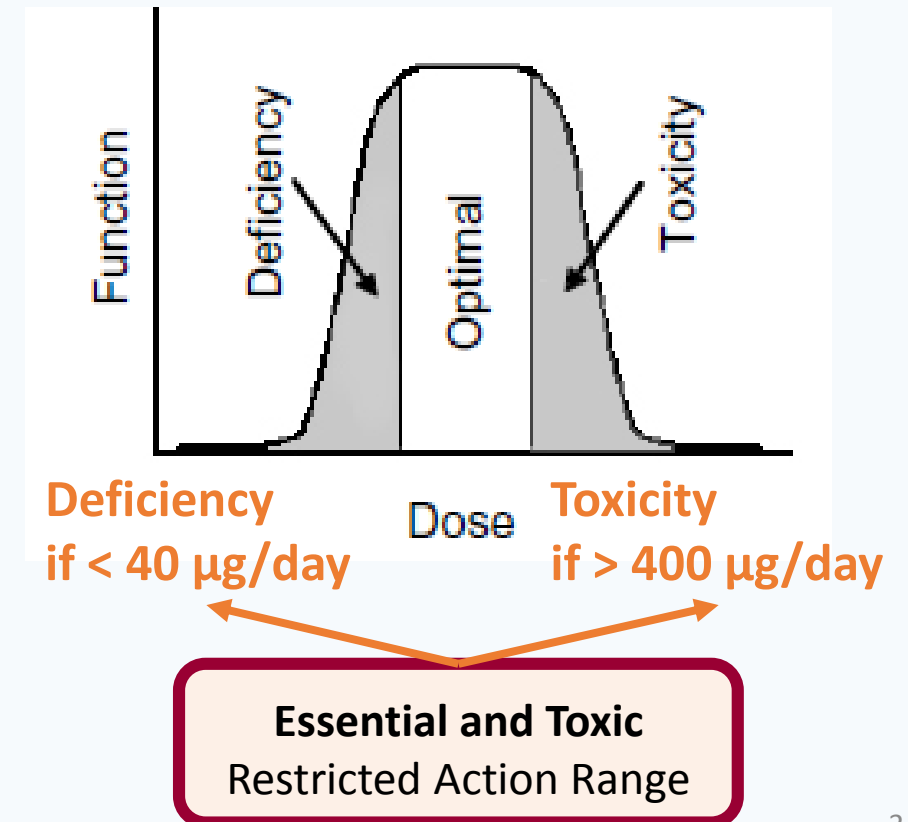
Double-edged sword element

Selenium:

- prevent transformation of normal cells to malignant cells (Schrauzer *et al.* Cell Mol. Life Sci. (2000))
- could be an effective chemopreventive and chemotherapeutic agent

Bioavailability and side effects:
related to Se chemical species
(organic/inorganic/metallic)

Necessity vs. Toxicity



Selenium Nanoparticles in Cancer Therapy

Selenium Nanoparticles (Se-NPs) :

- high bioavailability,
- excellent low toxicity (towards non cancerous cells),
- novel therapeutic properties,
- **anti-proliferative properties**

Wang H, et al. (2007) Free Radic Biol Med.42:1524–1533

Zhang J, et al. (2008) Toxicol Sci.101:22–31

Suggestions:

Se-NPs might have potential applications as chemotherapeutic agents for the management of human cancers

Potential therapeutic agent & drug carrier

Polysaccharide coated Se-NPs:

- Regulation of cell cycle
- Stimulation of apoptosis
- Inhibition of cancer cells growth and migration
- Impact on biomechanical properties of cancer cells

Kong L, et al. (2011). Biomaterials 32: 6515-6522.

Vekariya KK, et al. (2012) Nanomedicine 8: 1125-1132.

Project

Mechanism by which Se-NPs exert their anti-metastatic activity is still misunderstood

HYPOTHESIS:

Impact of Se-NPs could lead to significant alterations to the physicochemical forces that drive proliferation, differentiation, and migration of studied cancer cells.

NEED:

Unveil targeted intracellular compartmentalization and biotransformation of Se-NPs.
Nanomechanics to investigate the in-situ cellular biomechanical effects of Se-NPs
Detailed study of the formation, recognition and repair of DSB induced by Se-NPs

OBJECTIVE:

Integrative work to try to better understand how Se-NPs can prevent cancer cell migration

Get important information regarding the chemopreventive effects of Se-NPs - therapeutic approaches.

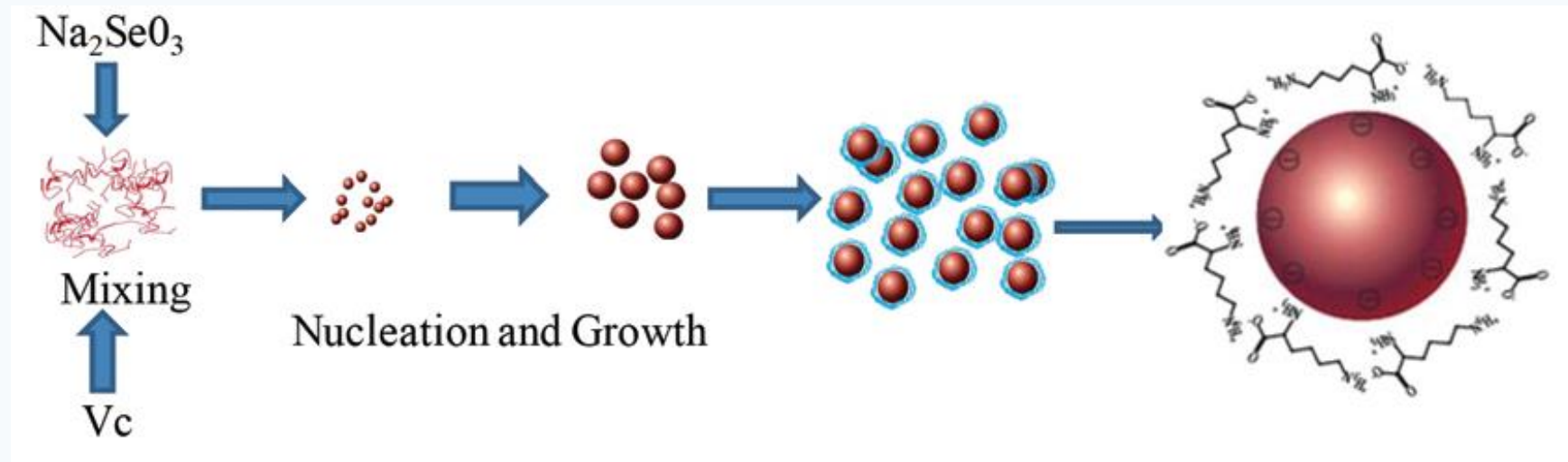
Synthesis and Physical characterization of Se-NPs and their interactions with model surfaces

BSA and Chitosan coated Se-NPs

Size Characterization: DLS/HR-TEM/SEM/HE-XRD-PDF

Charge & Electro-physical interactions: NanoZetaSizer/XPS

formulation, type of Se-NPs

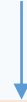


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Human cell lines:

human prostate cancer cell lines with high (PC-3) and low (LNCaP) metastatic potential

human ovarian cancer, high grade serous (UACC) and low-grade endometrioid (TOV112D)

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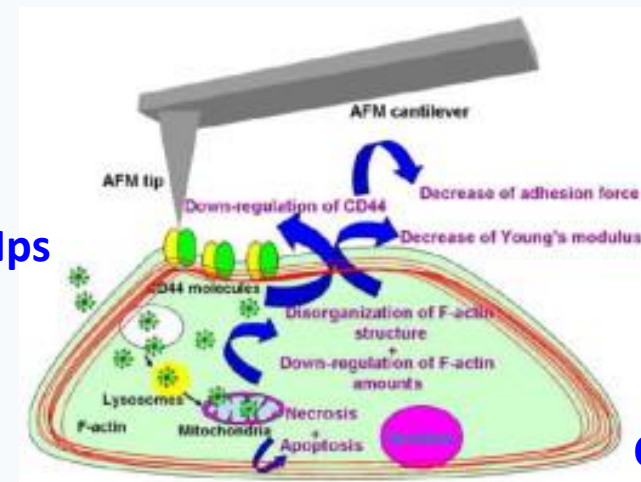
in-situ cellular and Matrix biomechanical effects of Se-NPs

AFM characterization: Adhesion force (nanindentation) & Young's Modulus investigation

Confocal on Cytoskeleton: actin, microtubules...

Alteration of biomechanical properties of the cell-adhesion by Se-NPs treatment

Se- Nps



Ji. P. et al. Bioorganic & Medicinal Chemistry Letters, Volume 23, Issue 23, 2013, 6296–6303

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**in-situ cellular and
Matrix biomechanical
effects of Se-NPs**

**Se chemical imaging
and speciation of the
effects of Se-NPs on
human cancer cells**

**Se-NP intracellular distribution/
released Se chemical species**
(dependent on NPs formulation)

SR-XRF

Effect of type and concentration of Se-NPs on
intracellular location and distribution

HR-HERFD-XAS

Evolution of elemental NPs and chemical
states/speciation

Se-NPs chemical form to unveil targeted intracellular
compartmentalisation and biotransformation of Se-
NPs: XRF vs. **Fluorescence labeling**

Cytotoxicity and proliferation tests

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**in-situ cellular and
Matrix biomechanical
effects of Se-NPs**

**Se chemical imaging
and speciation of the
effects of Se-NPs on
human cancer cells**

**ATM-dependent molecular and
cellular pathways of Se-NPs-
induced DNA damage recognition
and repair on human cancer cells**

**Resultant genotoxic effects of the Se-NPs
– mathematical model
(Bodgi and Foray. Int. J. Radia. Bio. (2016))**

Merci pour votre attention.