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NANO2CLINIC

CANCER NANOMEDICINE - FROM THE BENCH TO THE BEDSIDE

Gottfried Schatz Research Center for Cell Signaling, Metabolism and Aging

Medical University of Graz

Stability of selenium nanoparticles as novel anticancer delivery vehicle in relevant biological media

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INTRODUCTION

Selenium nanoparticles (SeNPs) represent promising anticancer delivery vehicles due to synergistic effects of the therapeutic cargo, antioxidant and cancer inhibitory activities [1]. Recent studies claim that SeNPs are less toxic than bulk Se forms displaying better biocompatibility and bioefficacy. Moreover, many studies have shown that SeNPs have preventive and therapeutic roles in cancer [2-3].

In order to develop an efficient SeNPs-based drug delivery vehicle, the first step after preparation should be detailed evaluation of the interaction between SeNPs and biological systems, which determines uptake, fate and biological effects of SeNPs.

The aim of this study was to establish and optimize synthetic protocols for two different SeNPs architectures following Safe-by-Design concepts. For this, gathering information about dynamic and complex interactions between SeNPs and biological systems is necessary. Most relevant, physicochemical properties of the synthetic SeNPs might affect their interaction with biological systems modifying uptake, fate and biological effects. Once we understand how size, shape, and surface chemistry of SeNPs influence biological parameters, we aim to establish a framework for redesign and optimization of efficient and safe SeNPs as a medical delivery vehicle. Full characterization and stability evaluation of these SeNPs was performed in relevant biological media including ultra-pure water, phosphate buffer, cell culture media and blood plasma.

MATERIALS AND METHODS

SeNPs

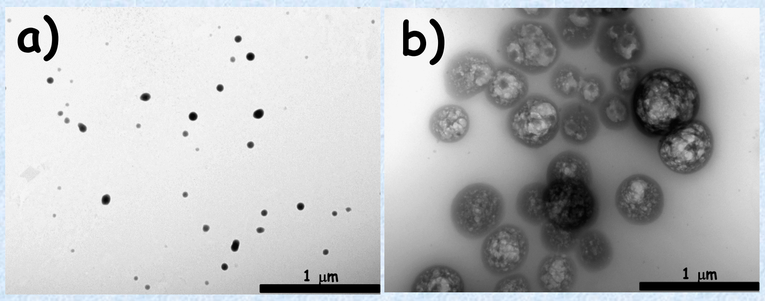
PVP = polyvinylpyrolidone
or
PEG = polyethylene glycol

vitamin C

Na_2SeO_3

"one pot" reduction synthesis

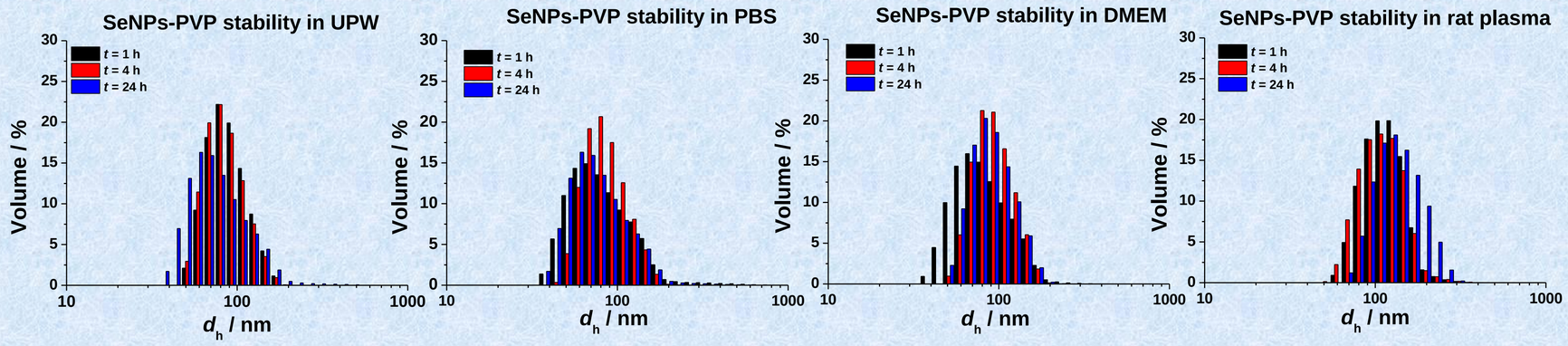
RESULTS



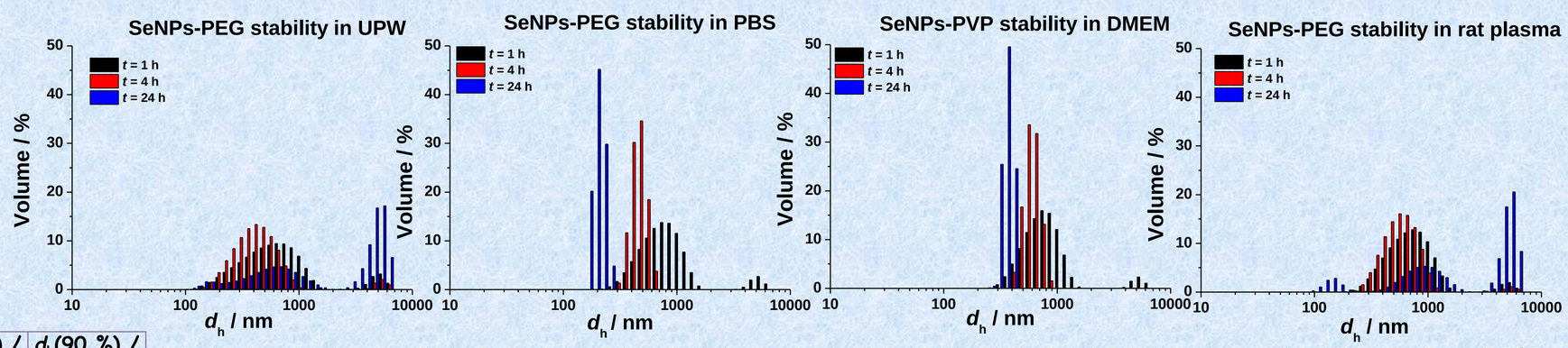
TEM micrographs of SeNPs: a) PVP coated and b) PEG coated.

SeNPs-PVP
uniform spherical nanoparticles with size 50-70 nm

SeNPs-PEG
spherical assemblies consisted of SeNPs crystals core, imbedded in the network of PEG macromolecular chains with size in range of 200-500 nm



Hydrodynamic diameter (d_h) obtained from dynamic light scattering (DLS) size volume-weighted distribution of SeNPs, coated with PVP in different medium: UPW, phosphate buffer solution (PBS), cell culture media (DMEM) and rat plasma. γ(SeNPs) = 100 ppm , ϑ = 25 °C.



Hydrodynamic diameter (d_h) obtained from dynamic light scattering (DLS) size volume-weighted distribution of SeNPs, coated with PEG in different medium: UPW, phosphate buffer solution (PBS), cell culture media (DMEM) and rat plasma. γ(SeNPs) = 100 ppm , ϑ = 25 °C.

Hydrodynamic diameter (d_h) of SeNPs, coated with PVP and PEG in different medium obtained by nanoparticle tracking analysis (NTA).

SeNPs	Media	t / h	(d_h ± SD)/ nm	d_h(10 %) / nm	d_h(50 %) / nm	d_h(90 %) / nm
PVP-coated	UPW	1	92.2 ± 14.3	77.0	90.2	104.9
		4	106.5 ± 23.9	86.6	101.9	123.2
		24	106.3 ± 26.1	83.5	94.7	114.7
	PBS	1	135.3 ± 55.0	99.1	113.6	185.4
		4	149.0 ± 75.5	95.4	112.1	270.1
		24	176.2 ± 70.7	111.7	150.0	293.4
	DMEM	1	103.7 ± 14.3	87.4	100.6	119.7
		4	126.2 ± 37.4	94.5	117.5	158.6
		24	95.8 ± 22.7	78.4	91.0	113.2
PEG-coated	UPW	1	161.0 ± 60.3	98.9	149.9	226.4
		4	177.6 ± 61.4	112.7	165.5	253.9
		24	164.0 ± 64.1	94.9	154.2	242.3
	PBS	1	173.5 ± 73.6	100.5	159.7	258.1
		4	172.2 ± 83.4	97.2	151.1	256.9
		24	172.7 ± 74.5	110.9	151.4	273.6
	DMEM	1	210.2 ± 75.8	119.6	199.1	309.7
		4	293.1 ± 122.1	147.2	263.8	444.8
		24	216.7 ± 140.7	56.6	202.2	389.3

Zeta potential (ζ) of SeNPs, coated with PVP and PEG in different medium: UPW, phosphate buffer solution (PBS), cell culture media (DMEM) and rat plasma, γ(SeNPs) = 100 ppm , ϑ = 25 °C.

SeNPs	Media	(ζ ± SD)/ mV		
		t = 1 h	t = 4 h	t = 24 h
PVP-coated	UPW	-35.1 ± 0.2	-39.7 ± 5.8	-29.0 ± 0.9
	PBS	-18.4 ± 1.1	-18.1 ± 1.5	-16.2 ± 1.7
	DMEM	-13.6 ± 0.6	-12.6 ± 0.8	-11.9 ± 1.7
	RAT PLASMA	-13.9 ± 0.5	-12.9 ± 0.3	-11.9 ± 1.0
PEG-coated	UPW	-50.3 ± 0.4	-49.2 ± 1.2	-48.4 ± 0.6
	PBS	-37.9 ± 1.7	-33.4 ± 1.6	-28.7 ± 0.7
	DMEM	-21.3 ± 1.7	-18.0 ± 1.9	-20.3 ± 1.5
	RAT PLASMA	-24.1 ± 1.1	-24.1 ± 1.2	-18.0 ± 0.8

- ✓SeNPs with two different coatings were prepared, PVP and PEG coated SeNPs
- ✓obtained results shown that the complexity of the media, *i.e.* ionic strength, pH, presence of sugars and proteins have a strong impact on the size distribution, aggregation and surface chemistry of SeNPs
- ✓the first phase for the rationale development of new potential nanotherapeutics was achieved

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