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

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1st STSM Conference

16th March 2022

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NANO2CLINIC
CANCER NANOMEDICINE - FROM THE BENCH TO THE BEDSIDE

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STSM
February 2019

Host Institution

Laboratory for Nanomedicine
The Division of Biophysics
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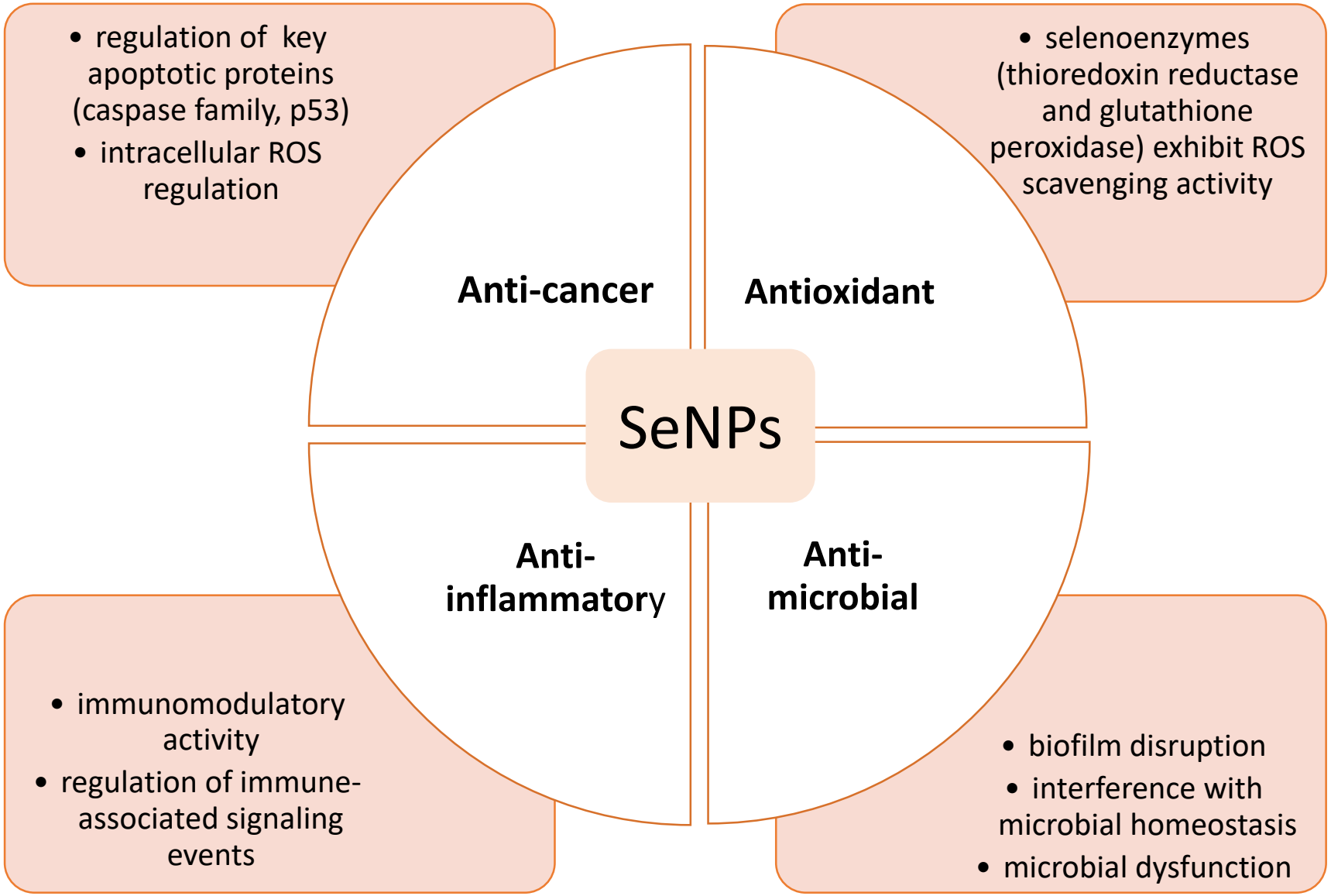
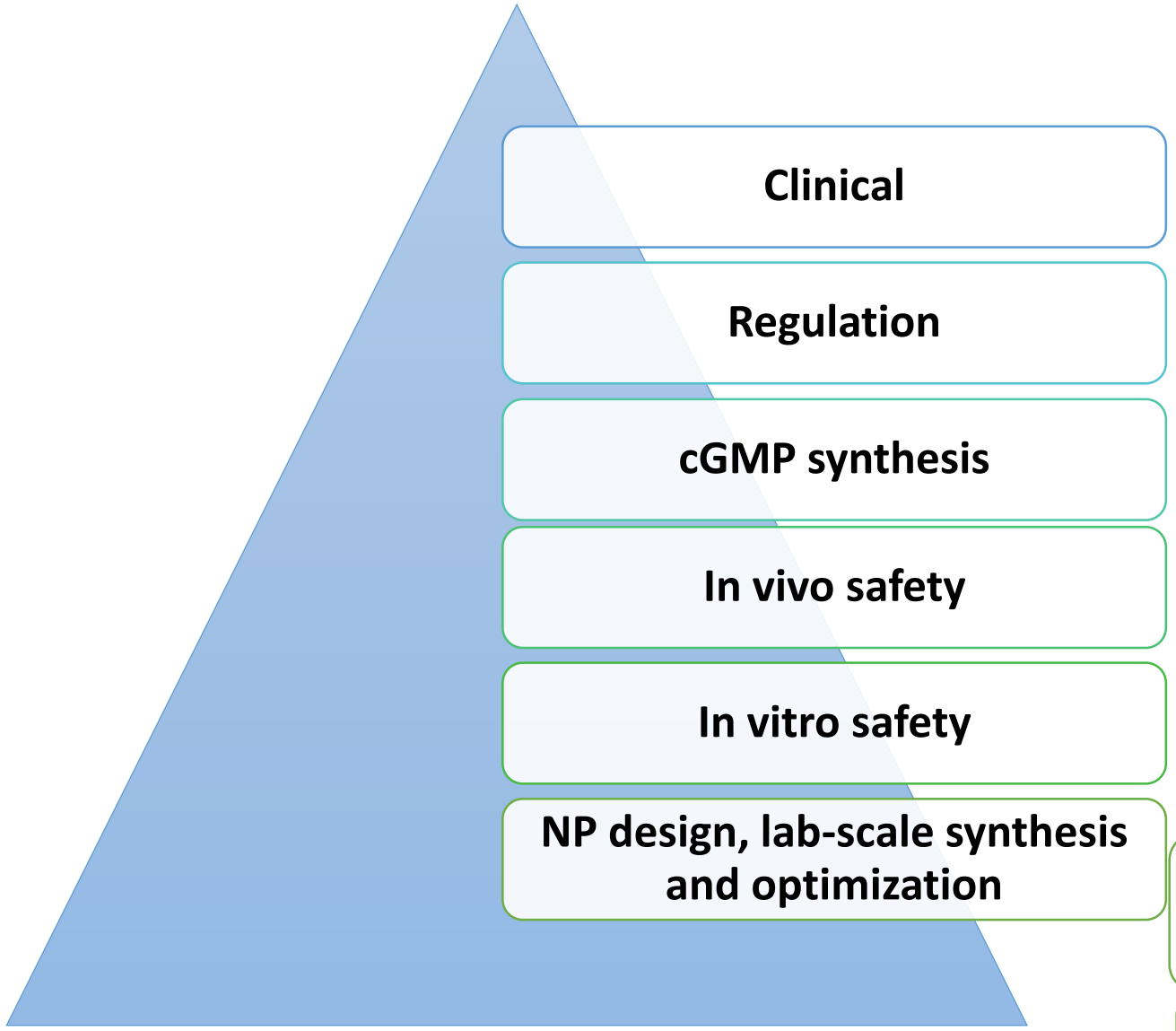
Introduction

- essential micronutrient
- vital role in various biological processes
- incorporated in selenoproteins → regulating immune cell functions and response
- narrow window between therapeutic and toxic effects → SeNPs
- SeNPs – lower toxicity than bulk Se forms


• regulation of key apoptotic proteins (caspase family, p53)
• intracellular ROS regulation
• selenoenzymes (thioredoxin reductase and glutathione peroxidase) exhibit ROS scavenging activity
Anti-cancer
Antioxidant
SeNPs
Anti-inflammatory
Anti-microbial
• immunomodulatory activity
• regulation of immune-associated signaling events
• biofilm disruption
• interference with microbial homeostasis
• microbial dysfunction



establishment of a framework for redesign and optimization of efficient and safe SeNPs as a medical delivery vehicle

optimization of synthetic protocols for two differently coated SeNPs following Safe-by-Design concepts

Workflow for the development of nanomedicine from bench to bedside

Aim

- **synthesis and characterization of SeNPs coated with PVP and PEG**

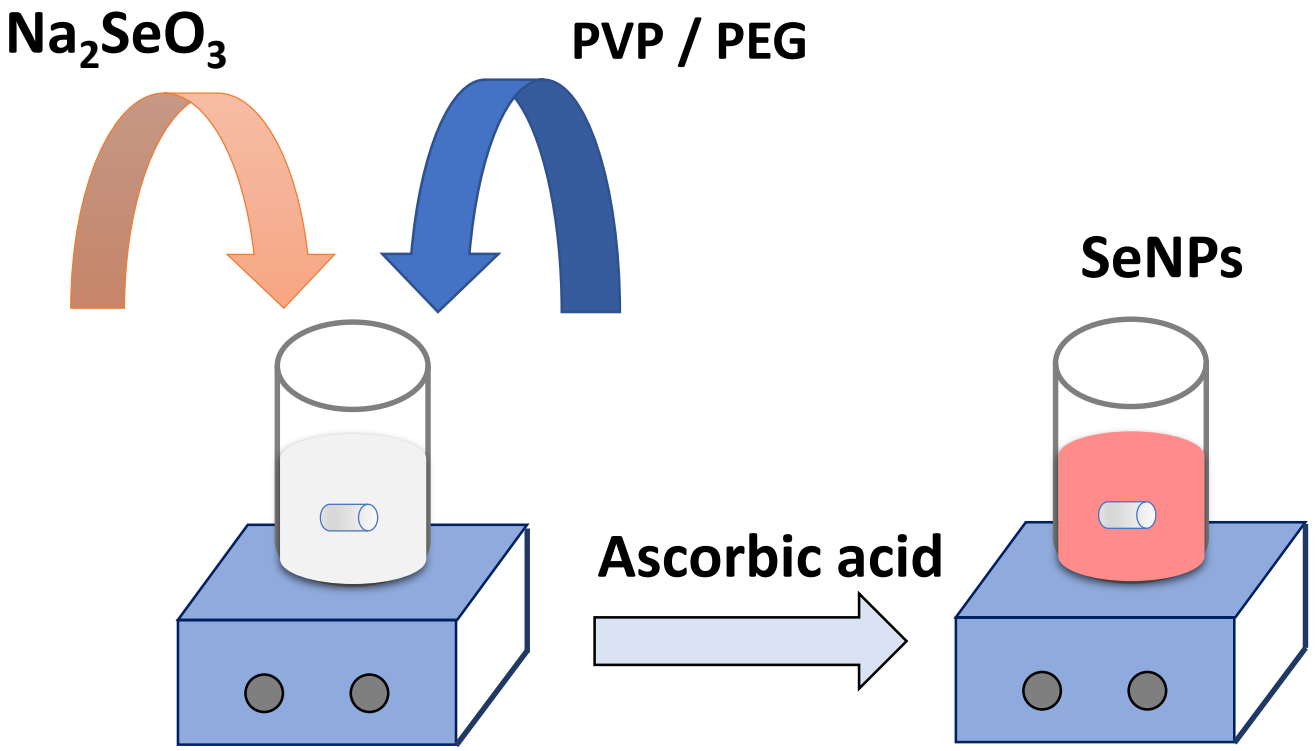
- PVP: water-soluble, inert, non-toxic, temperature-resistant, pH-stable, biocompatible, biodegradable polymer → encapsulate both hydrophilic and lipophilic drugs

- PEG: non-ionic hydrophilic, reduces the tendency of particles to aggregate by steric stabilization → producing formulations with increased stability during storage and application, prolonged blood circulation time

- **characterization** – morphology, size and zeta potential
- **stability studies** – behaviour in various media with different complexity

Experimental

Synthesis



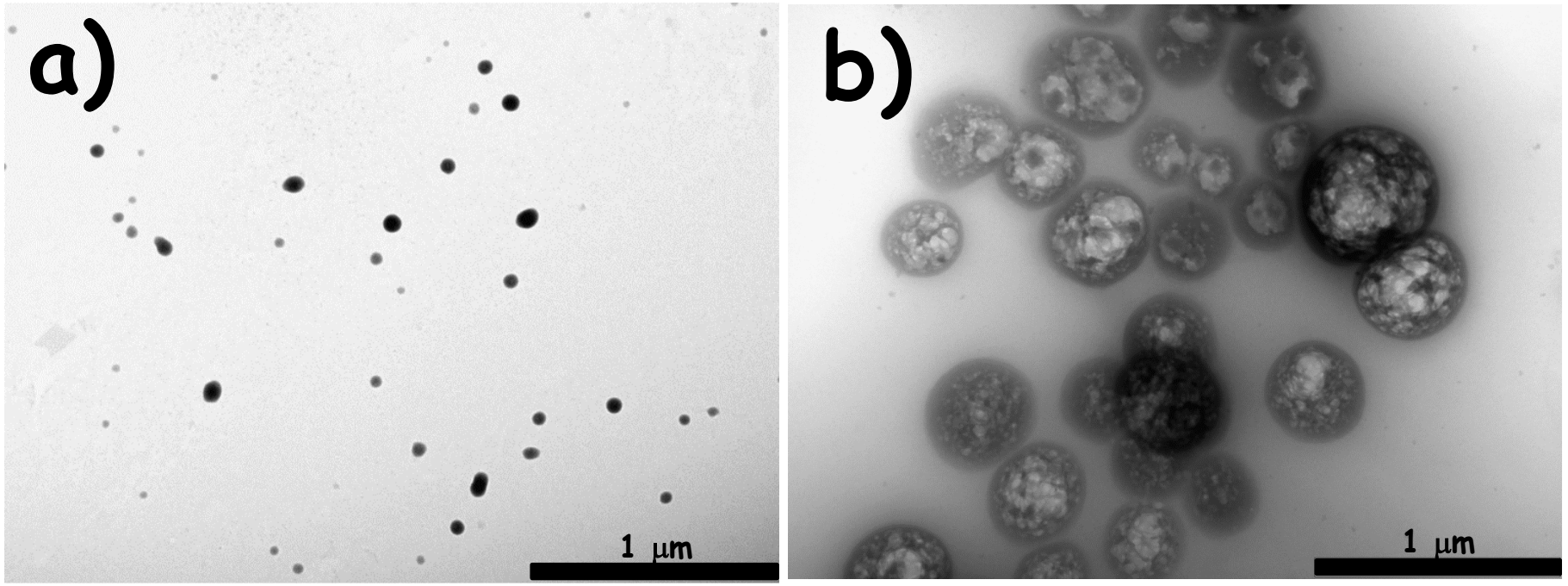
Characterization

- Se concentration → Atomic Absorption Spectrometry
- Se morphology and size → TEM
- Se morphology and size → DLS and NTA

Stability studies

- DLS and ELS

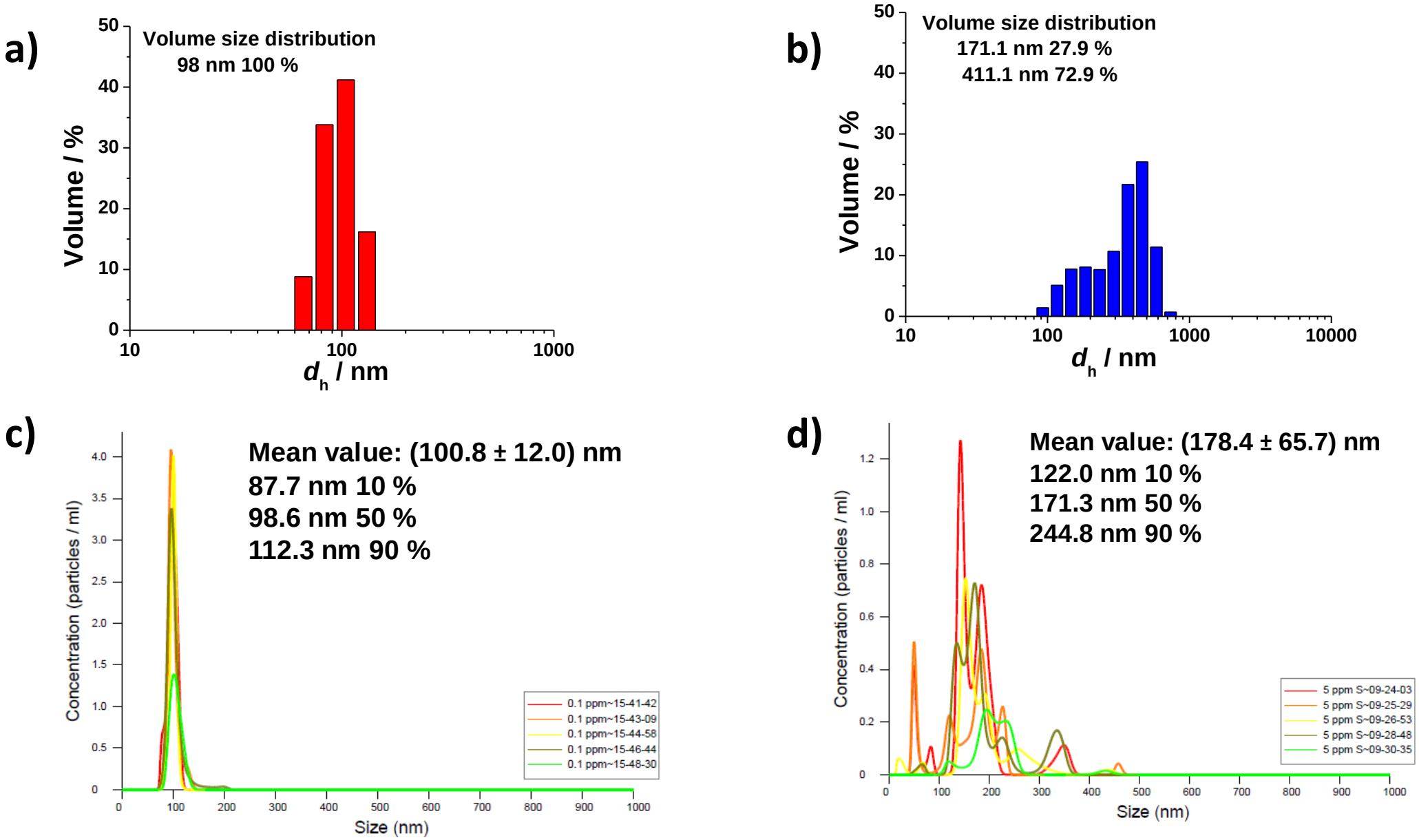
Results



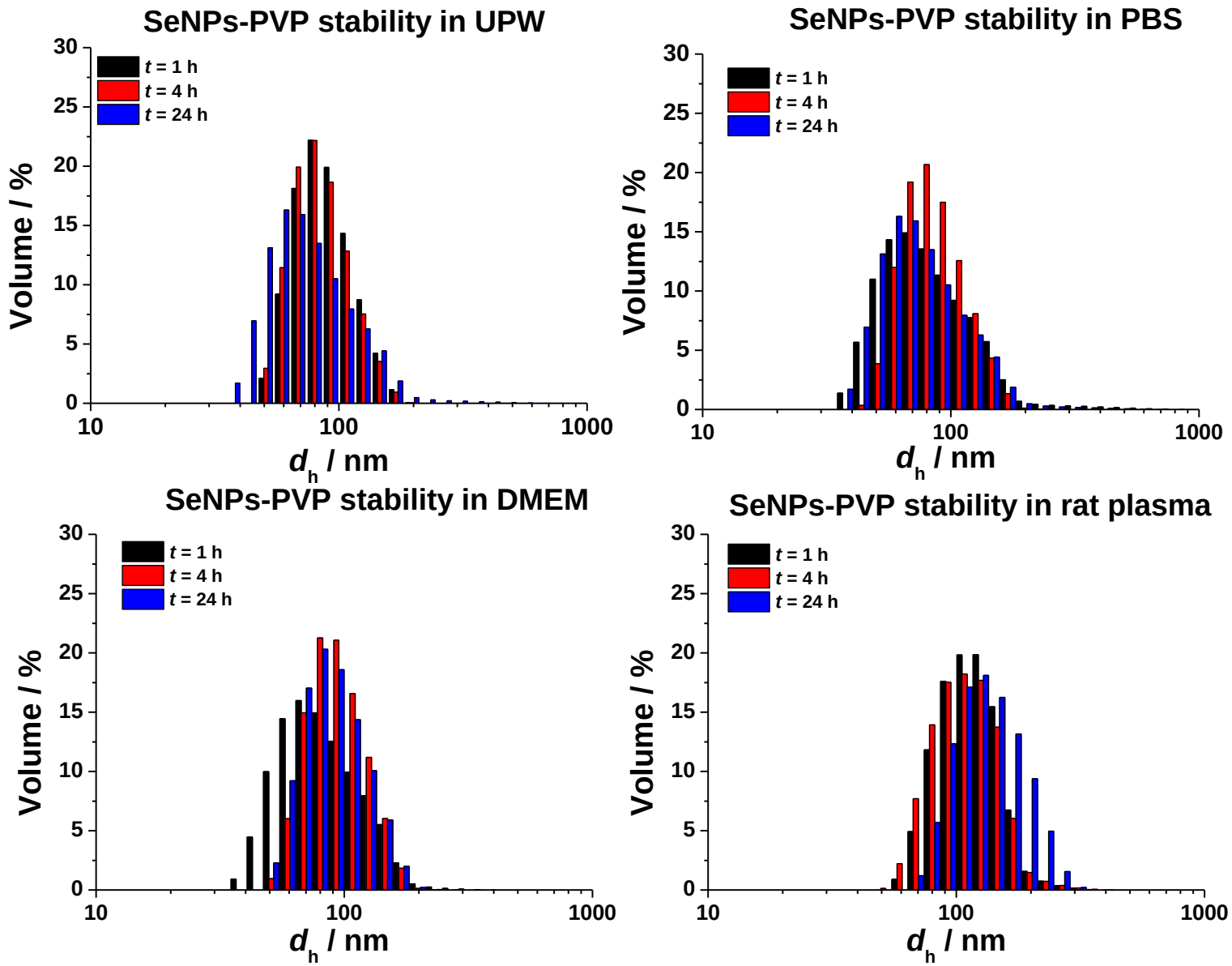
TEM micrographs of SeNPs: a) PVP coated and b) PEG coated.

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

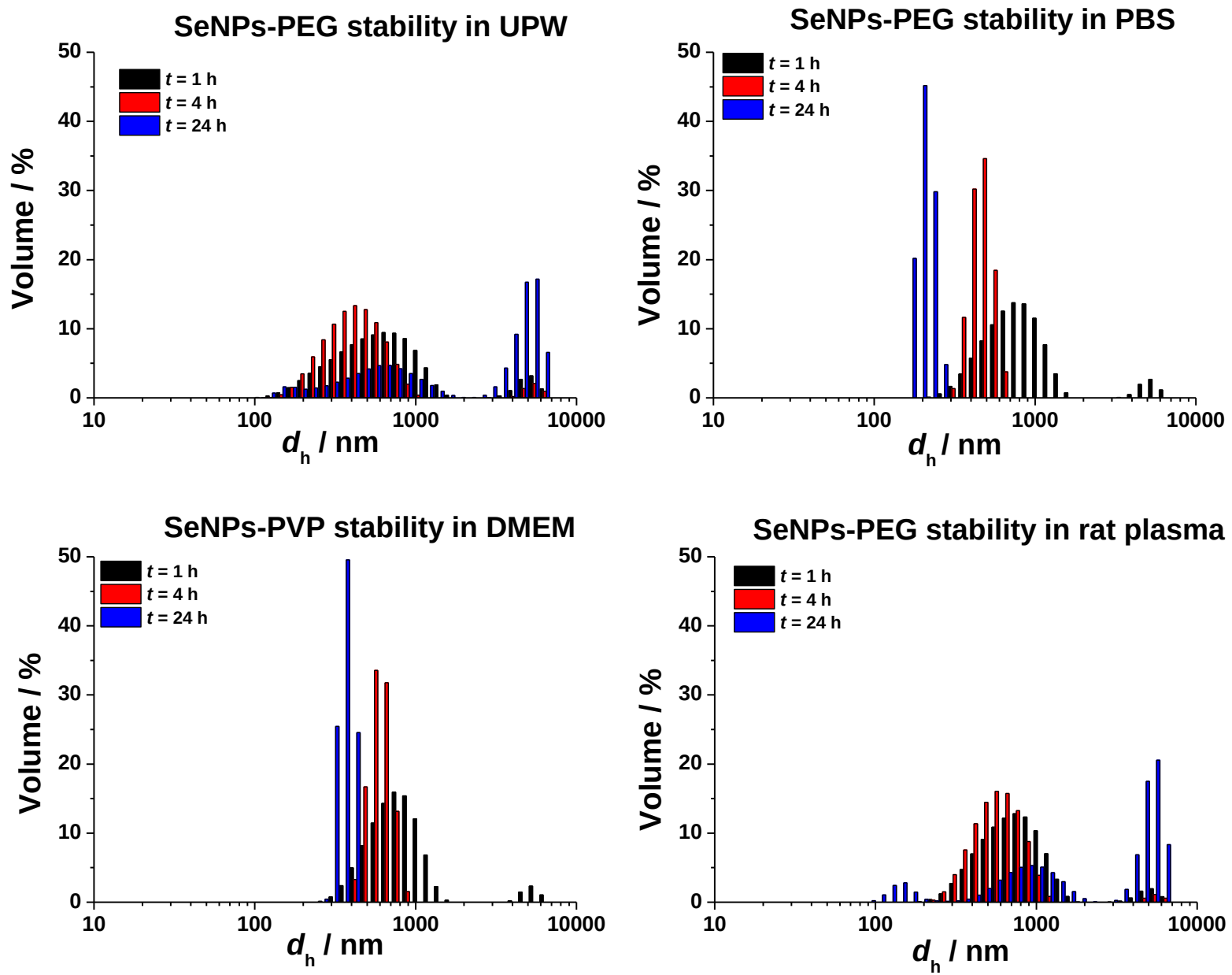
SeNPs-PEG
spherical assemblies consisted of SeNPs crystals core, imbedded in the network of PEG macromolecular chains with size in range of 200-500 nm



DLS (a, b) and NTA (c, d) measurements for SeNPs (a, c) PVP coated and (b, d) PEG coated dispersed in ultra-pure water. γ(SeNPs-PVP) = 0.1 ppm , γ(SeNPs-PEG) = 10 ppm , ϑ = 25 °C.



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

Conclusions

- ✓ **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**

Acknowledgement

Laboratory for Nanomedicine
The Division of Biophysics
Gottfried Schatz Research Center for Cell Signaling, Metabolism and Aging
Med Uni Graz

Assoc. Prof. Dr. Ruth Prassl

MPharm. Ivan Vidakovic

Dr. Chris Hill

Analytical Toxicology and Mineral Metabolism Unit
Institute for Medical Research and Occupational Health

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