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Synthesis of metal nanoparticles modified with carbosilane dendrons as antitumoral agents

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Transport of NP across endothelial barrier

- There are several routes for NPs transport across the endotelial barier .One type of transport is the formation of intercellular spaces through the interaction of cadherin with NPs.
- **Creation of NP with positively charged groups at the chain ends of PEG (polyethylene glycol) to reduce the interaction of NP with cadherin.**

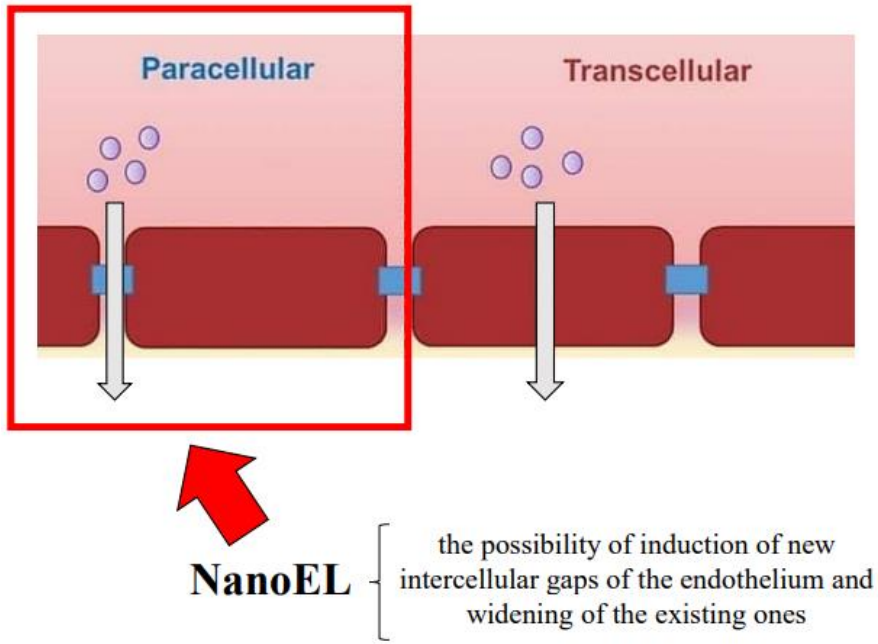


Fig. 1 Types of transport across endothelial barrier [4].

NanoEL effect (research problem)

- Toxicity of metal nanoparticles on the endothelial barrier.
- The interaction of NPs with cadherin causes the formation of gaps between endothelial cells (toxic effect).
- Creation of NPs with attached ligands to eliminate the gaps effect.
- PEG (polyethylene glycol) chains to **reduce cytotoxicity and that NH3 groups are attached not directly to the NP surface but through PEG chains.**

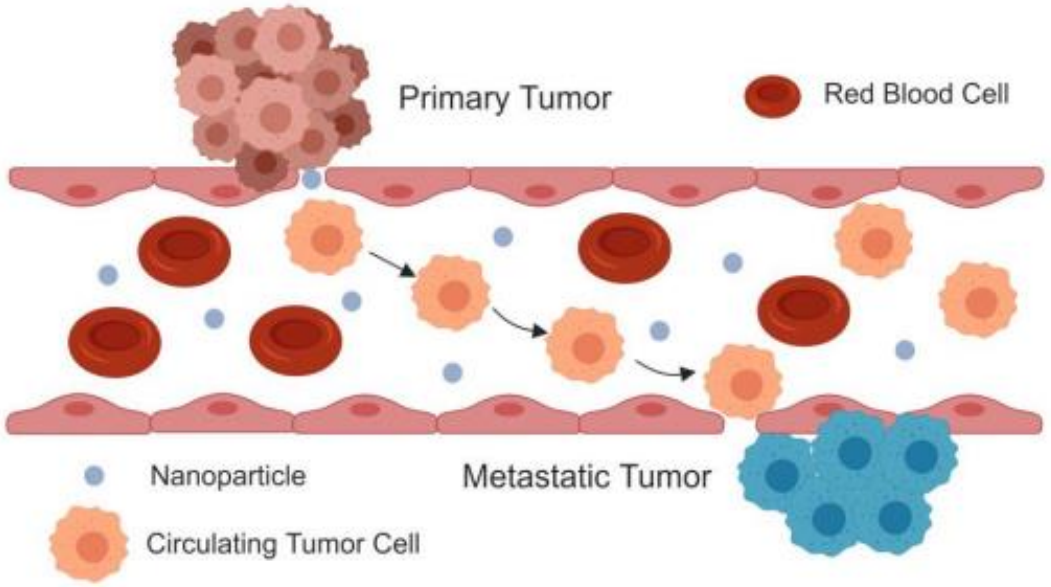


Fig. 2 Schematic diagram showing the role of nanoparticles in the formation of tumor metastasis , *[4]*.

Purpose of the STSM

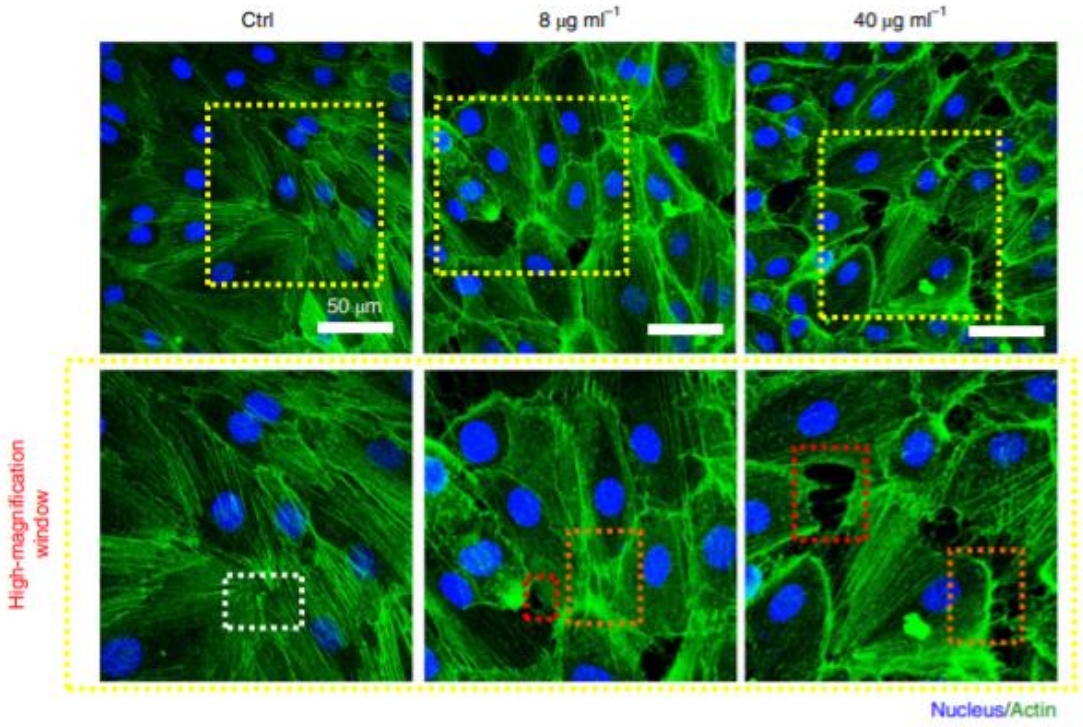


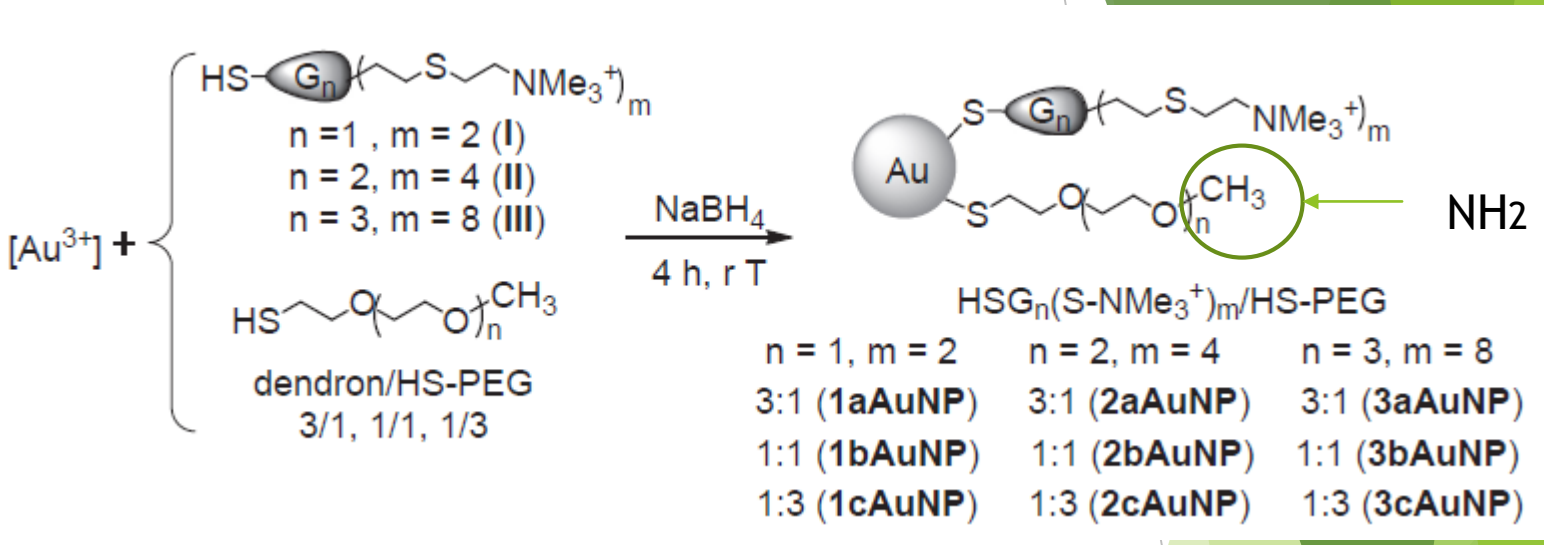
Fig. 3 Intracellular stress fibres, Formation of gaps (black points) between endothelial cells caused by the interaction of cadherin with NPs of metals (green fields - cadherin, blue circles – cell nuclei) [4].

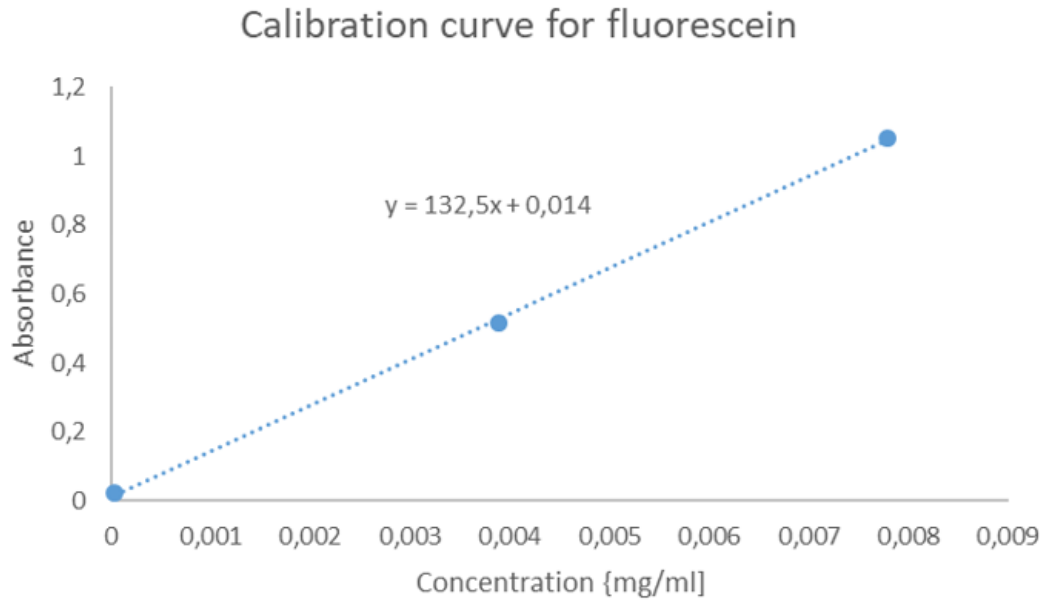
Preparation of positively charged nanoparticles to reduce their interaction with cadherin.

RESULTS

Synthesis of the nanoparticles

- To check how many of PEG chains with amine groups was anchored to the metal surface the Kaiser method was carried out.
- Calibration curve was created by means of a fluorescent marker (fluorescein) that binds to NH2 groups, and then the amount of attached NH2 groups to the analyzed nanoparticles was calculated (figure next to).
- Obtained results: NH_2 groups – **98.6 mmol / ml**

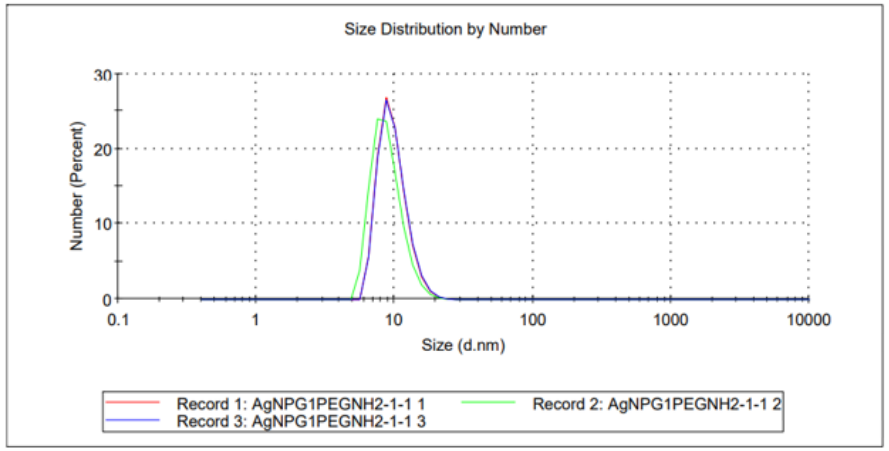




The results obtained with the DLS and Zeta potential methods

DLS

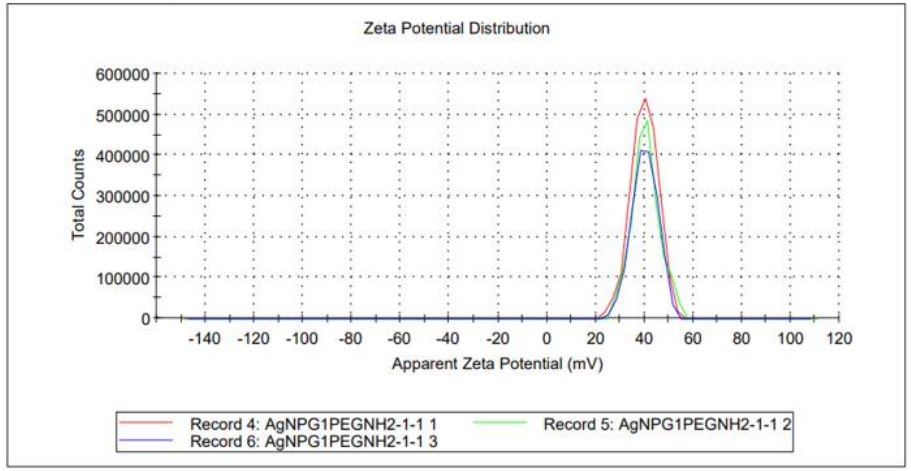
			Size (d.n...	% Number:	St Dev (d.n...
Z-Average (d.nm):	36,10	Peak 1:	9,865	100,0	2,454
PdI:	0,490	Peak 2:	0,000	0,0	0,000
Intercept:	0,858	Peak 3:	0,000	0,0	0,000
Result quality	Refer to quality report				



The average size was around 9.865 nm in diameter.

Zeta potential

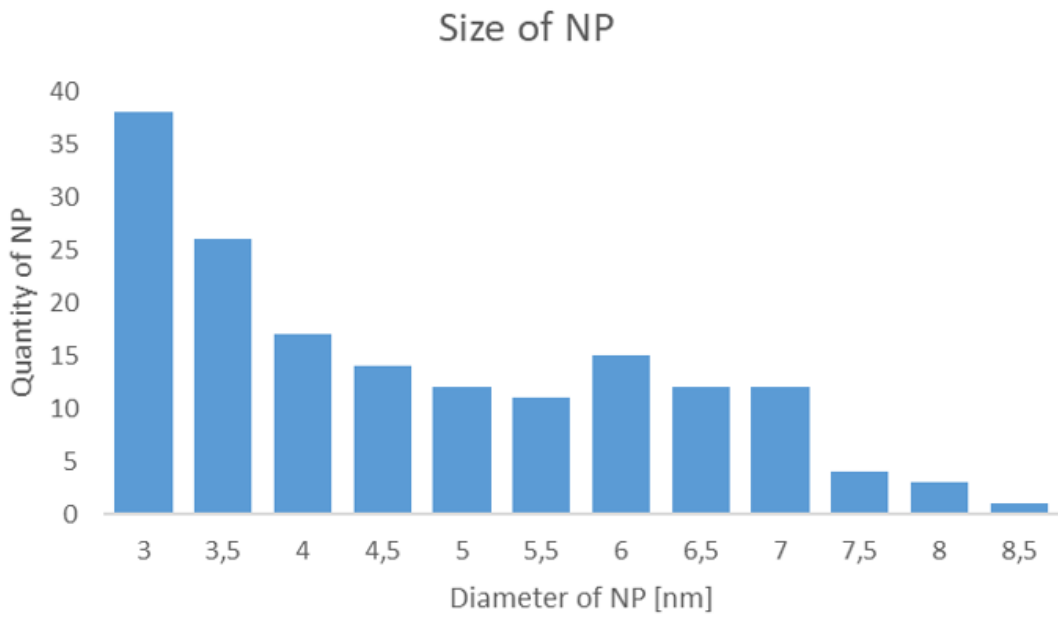
			Mean (mV)	Area (%)	St Dev (mV)
Zeta Potential (mV):	40,1	Peak 1:	40,1	100,0	5,26
Zeta Deviation (mV):	5,26	Peak 2:	0,00	0,0	0,00
Conductivity (mS/cm):	0,0525	Peak 3:	0,00	0,0	0,00
Result quality	Good				



The Zeta potential was around 40 mV.
This indicate a very stable homogenic sample.

The size of NPs distribution by TEM microscopy

- The size distribution was determined by TEM microscopy and the size of NP was analyzed with ImageJ.
- As the results showed, using this method of metal nanoparticle synthesis, we obtain **nanoparticles in the size range of 3-10 nm.**



Future plans

- The synthesized nanoparticles will be used for biochemical studies on the endothelial barrier
- The NH2 moieties at the PEG end will let us to attach another ligand eg. anticancer drugs. We are also planning to carry out experiment about influence of these type of nanoparticles on epithelial cells barrier disruption what is very common in anticancer drug treatment (the leakage of cancer cells from tumor to blood).
- The knowledge about what type of modifications of dendronized metal nanoparticles should be used to avoid this nanotoxicological effect will be very useful.

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