Synthesis, characterization and safety evaluation of gold nanoparticles

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Gold nanoparticles (AuNPs) are known to present outstanding potential for biomedical applications [1,2]. The physical-chemical properties of AuNPs, in particular their shape, seem to be critical for the biological effects of AuNPs. Gold nanostars have interesting optical properties that make them highly attractive [3]. Nevertheless, the information on their nanotoxicological properties is still very scarce. The current work aimed at synthesizing and characterizing MUA-capped star-shaped AuNPs and sphere-shaped AuNPs of similar diameter (50-60 nm), and further assessing the influence of shape on their toxicological effects. AuNPs characterization was performed using transmission electron microscopy (TEM), dynamic light scattering (DLS), UV-Vis spectrophotometry, and graphite furnace atomic absorption spectrometry (GFAAS).The toxicity, cellular uptake and permeability of the AuNPs were evaluated in vitro in non-differentiated human hepatoma HepaRG cells , primary rat hepatocytes, human epithelial colorectal adenocarcinoma Caco-2 cells and the human blood-brain barrier hCMEC/D3 cells. Viability assays as the (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) tetrazolium (MTT) reduction and neutral red (NR) incorporation assays were performed after 4 and 24 hour incubations. When toxicity was detected, other assays as the integrity of the cytoplasmic membrane by the lactate dehydrogenase (LDH) release assay and the oxygen reactive species production were included into the study. The HepaRG cells proved to be the most resistant model, while the hCMEC/D3 were the most sensitive. Overall, gold nanostars demonstrated higher toxicity and distinct cellular uptake compared to their spherical counterparts. None of the AuNPs were able to cross in vitro intestinal and/or blood brain barrier. In respect to their toxicity, these results suggest that the shape of gold nanomaterials greatly influence their interaction with the biological environment and their toxicological effect, that should be taken into consideration for biomedical applications.

REFERENCES

[1] Liu, Y., Yuan, H., Fales, A. M., Register, J. K., & Vo-Dinh, T, Frontiers in chemistry, *3*-51 (2015).
[2] Bibikova, O., Haas, J., López-Lorente, Á. I., Popov, A., Kinnunen, M., Ryabchikov, Y., ... & Mizaikoff, Analytica chimica *a*cta, 990 (2017) , 141-149.
[3] Favi, P. M., Gao, M., Johana Sepúlveda Arango, L., Ospina, S. P., Morales, M., Pavon, J. J., & Webster, T. J., Biomedical Materials Research Part A, 103 (2015), 3449-3462.

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FIGURES

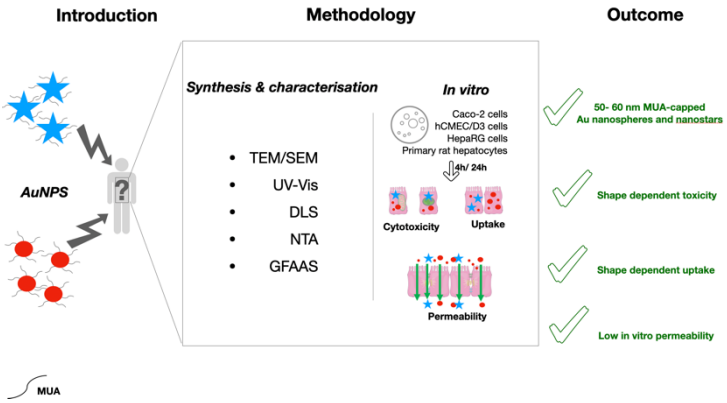

Figure 1: Graphical abstract for the shape-dependent study of AuNPs.