Niosomes as Colloidal Carriers for Targeted Glioma Diagnosis and Therapy

D. Ag Selci[1,2], V. Maurer[1,2], J. C. Porsiel[1], F. Stahl[3], T. Scheper[3], G. Garnweitner[1,2]

[1] Institute for Particle Technology (iPAT) | Technische Universität Braunschweig, 38104 Braunschweig, Germany

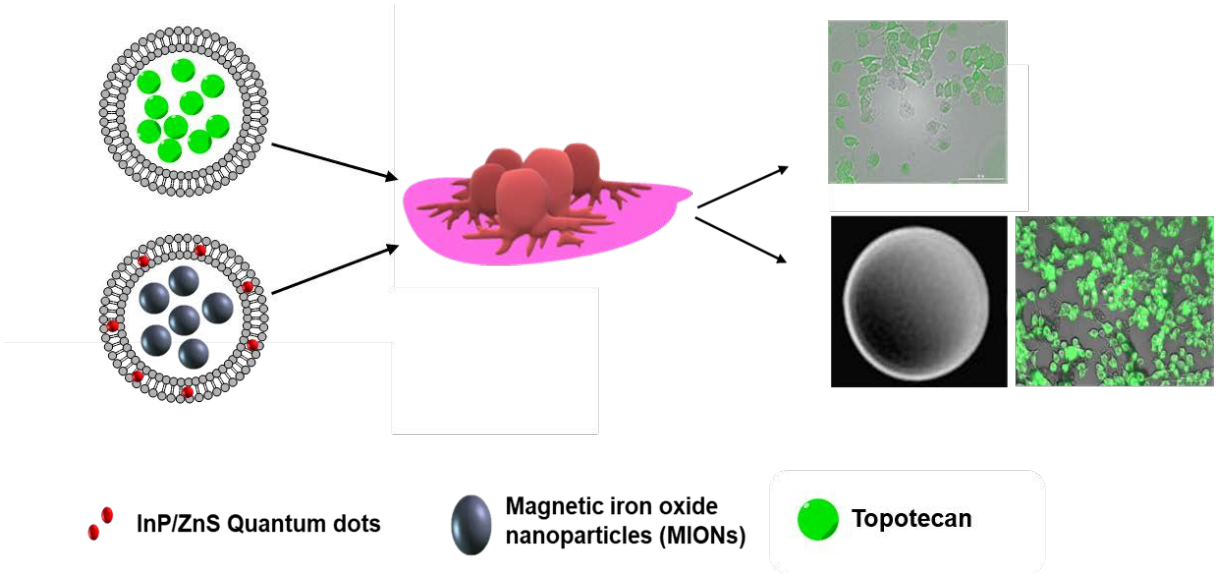
[2] Centre for Pharmaceutical Engineering Research (PVZ) | Technische Universität Braunschweig, 38106 Braunschweig, Germany

[3] Institute for Technical Chemistry | Leibniz University Hannover, 30167 Hannover, Germany

Glioblastoma is a malignant brain tumor and patients diagnosed with glioma have a median survival perspective of less than 2 years. Chemotherapy is usually the current treatment for brain cancer. However, the therapeutic efficacy of many anticancer drugs is limited by the existence of the blood-brain barrier (BBB), the blood-brain tumor barrier (BBTB), as well as a relatively weak enhanced permeability and retention (EPR) effect [Wei, 2014]. Early detection of tumor cells can prevent approximately 3.0% to 35% of cancer deaths; thus, it is essential that imaging probes be developed for the early diagnosis of glioma. Over the last decade, the advances in nanomedicine have enabled to develop novel nanocarriers for site-specific drug delivery and bioimaging to gain access to brain tumors [Hu, 2013]. Niosomes are promising carriers that have a bilayer structure and are formed by self-association of nonionic surfactants and cholesterol in an aqueous phase. They can accommodate a large number of drugs and imaging agents with a wide range of solubilities. In this work, the design of niosomal drug delivery and bioimaging systems and their applications in targeted glioma therapy and diagnosis were evaluated. To achieve this goal, two different niosomal formulations were designed involving the modification of niosomes with targeting groups as well as the incorporation of magnetic nanoparticles and quantum dots, and applied *in vitro*.

For drug delivery applications, the anti-cancer drug topotecan was entrapped in the aqueous core of polyethylene glycolated niosomes (PEGNIO) utilizing a microfluidic method. Furthermore, for bioimaging studies InP/ZnS quantum dots and citrate-stabilized iron oxide nanoparticles were synthesized and incorporated into niosomes.

Each niosomal formulation and the nanoparticles were characterized deeply via several methods such as UV/Vis and fluorescence spectroscopy, dynamic light scattering (DLS), zeta-potential measurement as well as transmission electron microscopy (TEM). Subsequently, all systems were applied to glioma cells. Fluorescence microscopy and flow cytometry analysis were used to investigate the cellular uptake and intracellular distribution of the niosomal formulations. Moreover, *in vitro* cytotoxicity studies were carried out. Our results indicate that the niosomes and in particular the multifunctional nanoparticle-containing niosomes offer promising new opportunities for the development of novel drug and imaging agent delivery platforms.



Scheme 1. Schematic representation of two different niosomal formulations with incorporated nanoparticles and topotecan, and their *in vitro* applications.

References

[Wei, 2014] Wei, X., Chen, X., Ying, M., and Lu, W., 2014, Brain tumor-targeted drug delivery strategies, Acta Pharm Sin B, Vol. 4, pp. 193-201.

[Hu, 2013] Hu, Q., Gu, G., Liu, Z., Jiang, M., Kang, D., Miao, D., Tu, Y., Pang, Z., Song, Q., Yao, L., Xia, H., Chen, H., Jiang, X., Gao, X., and Chen, J., 2013, F3 peptide-functionalized PEG-PLA nanoparticles co-administrated with tLyp-1 peptide for anti-glioma drug delivery. Biomaterials, Vol.34, pp.1135-45.