

Investigating nanoparticle interactions with the human blood-brain barrier in vitro

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Background

Transporting currently used and potentially anticipated active substances to tissues through drug carrier systems, particularly nanocarrier systems or nanoparticles (NPs), is feasible. The unique properties of NPs facilitate increasing the concentration of active substances in the bloodstream, extending their half-life, and optimizing dosing frequency to enhance active substance solubility and stability. Moreover, NPs may enhance treatment efficiency in systemic applications by accelerating the passage of active substances through biological barriers such as the blood-brain barrier (BBB), thus potentially improving therapeutic outcomes. There is a growing body of research on NPs crossing the BBB, although most studies are conducted on experimental animals, particularly rodents. Therefore, understanding the interaction of nanoparticles with the human BBB is crucial for advancing biomedical applications.

Methods

The Brust-Schiffirin method was utilized to synthesize gold nanoparticles (AuNPs) for cell imaging purposes. These AuNPs, acting as markers, were subsequently encapsulated within human serum albumin (HSA) and bovine serum albumin (BSA) nanoparticle structures using the desolvation method. Another nanoparticle formulation employing AuNPs as markers is the nano lipid carrier (NLC), synthesized via hot homogenization. Furthermore, Zr-based metal-organic framework (MOF) structures were utilized as markers in cell imaging, with Zr nanoparticles encapsulated within Polylactide-co-glycolide (PLGA) nanoparticles. A concentration dose of 62.5 µg/ml of these NPs was administered to primary human microvascular endothelial cells (10h BMECs) and human brain vascular pericytes (HBVPs) for 3 hours. Subsequently, the cells were subjected to light microscopic and transmission electron microscopy (TEM) analysis.

Results

NP formulations of HSA, BSA, and PLGA were observed within cells by light microscopic analysis using the silver enhancement method. In contrast, no NP uptake was observed for NLC formulations in both 10h BMECs and HBVPs after a 3-hour incubation period. Furthermore, TEM analysis of 10h BMEC revealed no significant ultrastructural alterations following NP applications. Moreover, NLCs were not detected under TEM, whereas the other NP formulations were observed within the cells, consistent with the findings from light microscopic analysis. Interestingly, HSA was found within some autophagic vacuoles, randomly associated with myelin figures, and within numerous vesicles, particularly at the peripheral region of the cytoplasm.

Conclusion

There are various types of NP formulations showing promise as potential solutions to enhance drug transport to the BBB. However, their interactions within the cells of the human BBB are poorly understood. Therefore, it is crucial to comprehend the mechanisms and behavior of NPs within the human BBB.

Keywords:

Nanoparticle, BBB, Endothelial cells, Pericytes