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Multimodal Low Voltage Transmission Electron Microscopy Analysis of Iodine Nanoparticles for Stroke Theranostics

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Background incl. aims

Ischemic stroke stands as the second leading cause of mortality globally, necessitating innovative approaches for its diagnosis and treatment. This project delivers a validated pipeline for assessing the kinetics and dynamics of iodine nanoparticles (IoNPs) within the organism, specifically targeting critical areas like the brain, blood-brain barrier, blood, and organs like the spleen.

Understanding thrombus characteristics, including size, composition, and origin, holds significant promise in guiding treatment strategies not only for stroke but also for related cardiovascular diseases. Current imaging modalities are limited in their ability to visualize various clot types effectively, hindering precise diagnosis and tailored treatment.

Biodegradable IoNPs have the potential to become the basis of a modern theranostics (therapy and diagnostics) approach to improve the treatment. The afore-mentioned IoNPs made of monomer MAOETIB (2-(Methacryloyloxy)ethyl-2,3,5-triiodobenzoate) have been described as desired contrasting agents. Furthermore, they can be used as drug carriers.

Methods

The essential method for the characterization of nanoparticles is undoubtedly electron microscopy, offering intricate insights into nanoparticle behavior within tissue matrices. LVEM operates at significantly lower accelerating voltages compared to conventional TEM, typically below 25 kV. This lower voltage regime offers several distinct advantages, including increased contrast and gentle electron-sample interaction.

Low voltage provides improved contrast mechanisms, which are particularly invaluable for samples composed of light elements. The reduced electron energy results in increased electron scattering, enhancing image contrast and revealing finer details within specimens. This capability is especially important in imaging biological sections and generally low-contrast materials, where conventional TEM techniques may yield limited contrast.

The application of LVEM in nanoparticle characterization involves various aspects, including morphology, size distribution, crystallinity, surface properties, and interparticle interactions. Through advanced imaging techniques such as dark-field imaging and electron diffraction, LVEM facilitates a deeper understanding of NPs structure and behavior at the nanoscale level.

The unique combination of TEM, STEM, and SEM imaging modes in LVEM instruments provides researchers with a comprehensive toolkit for investigating nanoparticles integrated into the tissue structure. Furthermore, LVEM's versatility extends beyond imaging, offering advanced analytical capabilities such as energy-dispersive X-ray Spectroscopy (EDS) and Electron Diffraction.

Results

Utilizing a multimodal approach, comprehensive insights were gathered regarding the characteristics and behavior of IoNPs, spanning from initial nanoparticle characterization and quality assessment post-fabrication to their dynamics within blood circulation and targeted organs. A rat served as the model organism in this study, providing a relevant and translational platform for investigating IoNPs interactions in vivo. Nanoparticles were imaged throughout their entire lifecycle, starting from their presence in a native solution, followed by intravenous injection into the bloodstream, and subsequently deposited within the relevant organs. The examination of nanoparticles using low-voltage transmission electron microscopy was integrated to a comprehensive characterization utilizing various analytical methods.

Conclusion
The integration of LVEM into nanoparticle research promises to advance our understanding of nanoparticle behavior within biological systems. LVEM's unique imaging capabilities, particularly well-suited for biological sections, make it an invaluable tool for the development of theranostic strategies and personalized treatments. With its multimodal capabilities, LVEM emerges as a pivotal technology for the comprehensive analysis of biodegradable iodine nanoparticles, aiming towards improved healthcare outcomes.

Keywords:

Low-Voltage Electron Microscopy, Stroke theranostics