Polythiophene based Carbon Dots for siRNA delivery and PDT: Application to Atopic Dermatitis

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Résumé

This research project aims to synthesize photosensitive "Carbon Dots" (CDs) for the delivery of therapeutic small-interfering RNA (siRNA) in the treatment of Atopic Dermatitis (AD). The objective is to provide a non-invasive alternative to currently available treatments, which are often costly, require frequent dose administration, and are commonly associated with undesirable side-effect.(1)

The proposed strategy involves delivering siRNA into the cells to regulate the immune response. However, using siRNA poses certain challenges: it struggles to enter cells and is rapidly degraded by the nucleases. To overcome these limitations, siRNA can be delivered using nanoparticles.(2) The use of nanoparticles allows to both protect the siRNA from the nuclease and facilitate cellular uptake. For this research project, it was decided to work on carbon-based nanoparticles called "Carbon Dots" (CDs), specifically on **polythiophene based CDs**. These kinds of nanoparticles offer several advantages, including high stability, biocompatibility, low toxicity and their good solubility in aqueous solution.(3) Additionally, they often exhibit very interesting photoluminescence properties.

The CDs used in this project are synthesized via a monowave pyrolysis of cationic polythiophene polymers. The polymers, obtained from aromatic building blocks, contain both ammonium functional groups and amine functional groups, allowing further post-functionalization. The pyrolysis is carried out in an acidic aqueous solution. Both the polymers and the resulting CDs are characterized using Dynamic Light Scattering (DLS) to determine their size and their zeta potential (charge). The aim is to obtain small (below 100 nm) and positive particles (around 20 mV). The photophysical properties of the particles are also analyzed, including absorbance, emission and excitation spectra, as well as their fluorescence quantum yield and their singlet oxygen quantum yield. The particles should be able to produce singlet oxygen, as similarly structured CDs are already used in Photo-Dynamic Therapy (PDT) applications.(4) Singlet oxygen production is crucial, as it enables the siRNA-CD complex to escape endosomal vesicles upon light irradiation, mimicking the PDT mechanism. Additionally, a possible functionalization of the amine function on the polymer/CDs is the addition of singlet oxygen sensible cationic linker. These linkers are inspired by the reactivity of β-amino-acrylate with singlet oxygen.(5) Their presence is a key feature, as they facilitate siRNA release upon singlet oxygen generation, thereby increasing cytosolic siRNA concentration.

*Intervenant

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