Chitosan-based Nanocarriers for Delivery of Micro-RNAs Inducing Cardiac Regeneration

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Background:

Ischemic heart disease is the leading cause of death in developed countries and one of the biggest causes of death and disease burden in developing countries, yet no cure is available. A therapeutic intervention requires regeneration of the heart by inducing controlled cardiomyocyte proliferation in the infarcted region. Some miRNAs seem well suited for this ground-breaking-therapeutics class as they locally induce cardiac regeneration. However, to deliver miRNA efficiently, nanocarriers are required to protect it from rapid cleavage and ensure delivery to cardiomyocytes. Ideally, these vehicles should be formulated with safe components via green processes and feature a long shelf life to ensure simple conditions of storage and distribution.

Methods:

We developed a green process based on chitosan (a biodegradable biocompatible cationic polysaccharide) formulated by polyelectrolyte complexation; a process carried out at room temperature using no organic solvent nor high shear. Different parameters were varied to check for optimal physicochemical characteristics. To ensure scalability and reproducibility, a microfluidic system was used to reproduce our formulation. A proof-of-concept genetic material was used first to prove the suitability of our formulation to genetic material loading. Later, the intended therapeutic miRNA has been tested as well and a targeting agent has also been investigated for decorating nanoparticles' surface. In vitro and in vivo testing of safety and efficacy are commencing.

Results:

Depending on the formulation conditions, different sizes [100-300nm] of nanoparticles were obtained. They were colloidally stable for 1 year at room temperature, steam-sterilized, and we could also reproduce them using specific conditions of microfluidics. The incorporation yield of a model nucleic acid was up to 75% for chitosan/dextran sulfate nanoparticles and up to 40% for chitosan/nucleic acid nanoplexes. Moreover, a targeting agent (TA) was successfully bound to the nanoparticles' surface to ensure specificity to the heart's infarcted region.

Conclusions:

Using a green process as polyelectrolyte complexation for the formulation of colloidally stable chitosan nanocarriers was proven suitable for encapsulation of genetic material and surface association with a targeting agent.