Green synthesis of Chitosan Nanoparticles as Locked Nucleic Acid Delivery Systems

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Nanoparticle delivery systems, such as chitosan nanoparticles (Ch-NPs), hold great potential for enhancing therapeutic efficacy and safety. Ch-NPs, derived from the natural polysaccharide chitosan, offer several benefits, including increased stability, improved cellular uptake, and superiori ability for targeted delivery. Ch-NPswere synthesized via the ionic gelation method, with tripolyphosphate (TPP) acting as a cross-linker obtaining a size between 150 and 300 nm. Successively, Ch-LA were functionalized with hyaluronic acid (HA). This synthesis involved encapsulating negatively charged locked nucleic acid (LNA) oligonucleotides targeting miR-210 (LNA-210) through ionic interactions with the polymeric components. The resulting NPs exhibited high entrapment efficiency of LNA-210 and provide effective protection of the genetic material from RNAse degradation. Ch-NPs loaded with LNA-210 were biocompatible without intracellular reactive oxygen species (ROS) production in cardiosphere-derived cells (CDCs). Moreover, treatment with Ch-LNA did not result in any detectable alterations in the organization of cortical actin fibers and mitochondria morphology. Additionally, no significant changes were observed in cell area or nuclear circularity. These groundbreaking findings unlock new opportunities for research and innovation, setting the stage to fully harness the potential of Ch-NPs in revolutionizing targeted drug delivery and advancing precision medicine.