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Modification of chitosan to improve its biophysical properties for gene delivery applications

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Background and Aims: Although genomic researches have opened up new avenues for therapeutic interventions based on genetic therapy, it would not be possible to realize the potential of these new therapies until the issue of gene delivery has been resolved. Since the application of viral vectors was restricted due to their problems such as toxicity and immunogenicity, the tendency to use non-viral vectors such as polymers has increased. Among all the available polymers, ''Chitosan'' is highly recommended due to its excellent biological and mechanical properties, such as biocompatibility, biodegradability, non-toxicity and bioadhesivity. However, it suffers from a poor solubility in water and low transfection efficacy, which needs appropriate chemical modifications. On the other hand, the ultimate goal of transferring plasmid DNA into the cell is to deliver it to cell nucleus. Tetra iodo tyronin (thyroxine), can eventually bind to its receptors in nucleus. Furthermore, it has recently been notified that thyroxine also indicate cell surface receptor too, that shows qualities of a family of structural membrane proteins (integrins) and T4 is more active than T3 in stimulating this receptors. So, T4-chitosan vector can act as an efficient carrier in gene delivery.
Methods: In this study, thyroxine has been bound to chitosan with two different conjugation degrees and characterized by instrumental methods such as ^{1}H-NMR and IR. Measurment of the buffering capacity, zeta potential and particle size, proton sponge effect and forming nano-sized particles were investigated. The ethidium bromide exclusion assay was done to show the condensation ability of the modified polymer, too.
Results: Thyroxine conjugation to chitosan yields nanocarriers with optimal biophysical properties. The ethidium bromide exclusion assay showed the ability of modified chitosan in condensing plasmid DNA efficiency.
Conclusions: These results confirm that conjugation of levothyroxine could be used to improve chitosan for gene delivery application.

Keywords: Non-viral gene delivery; Nanoparticle; Chitosan; Levothyroxine