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# AN OPTIMIZED PEPTIDE-BASED SYSTEM FOR NUCLEIC ACID DELIVERY FOR UTERINE FIBROID GENE THERAPY

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**Introduction:** Uterine fibroids are prevalent health concern affecting women of reproductive age [1]. Their development is influenced by both genetic predisposition and environmental factors. Due to their precise localization and accessibility, uterine fibroids represent a promising target for in situ gene therapy. This approach aims to deliver therapeutic genes directly to the fibroid tissue, potentially offering targeted treatment and minimizing systemic side effects. However, a key challenge in gene therapy lies in developing safe and effective delivery methods. Viral vectors, widely employed as vehicles for gene therapy delivery, carry risks of immune response and insertional mutagenesis [2]. Non-viral vectors offer a safer alternative, but their transfection efficiency is often lower. Consequently, a significant focus of current research is on modifying non-viral carriers to enhance their ability to overcome extracellular and intracellular barriers of DNA transport, ultimately improving their potential for therapeutic applications. Development of stable DNA-peptide carrier complexes with a reduced packaging volume has a great potential to improve non-viral transfection efficiency. While a sufficient packaging volume is required for stable complex formation with some vectors, excessive carrier administration damages transfected tissues and negatively impacts the recipient's tissues. Another modification of non-viral complexes aimed to improve their stability is addition of polyanions to change surface zeta-potential.

**Main Body:** The primary goal of the study was to optimize the packaging volume of DNA-peptide complexes and test their stability in a solution containing a polyanion. Additionally, the aim was to determine the degree of binding efficiency of these complexes to DNA and the efficiency of their transfection. To achieve these objectives, we synthesized cationic and anionic peptides and studied formation of complexes with plasmid DNA carrying the β-galactosidase or green fluorescent protein gene. Then stability of DNA-peptide carrier complexes was evaluated using the ethidium bromide displacement assay. We have found that in the presence of dextran sulfate, the formed complexes are stable and do not release DNA over an extended period of time. Transfection experiments, including assessment of the toxic properties of the complexes using Alamar Blue dye, were carried out in the PANC-1 cell line. Transfection activity was evaluated using *gfp* marker gene. The Alamar Blue test demonstrated the maintenance of cell viability after adding the complexes. The transfection results showed a high percentage of GFP-positive cells, indicating effective DNA delivery by these carriers. Then we performed the plasmid DNA delivery directly to uterine fibroids *ex vivo*. We found significant *gfp* gene expression detected in cryostat sections of uterine fibroid tissue.

**Conclusion:** An analysis of the DNA transfection efficiency by peptide carriers was performed. Reduction in packaging volume has no negative impact on DNA binding efficiency, the complexes transfection activity and viability of PANC-1 cells. Additionally, successful delivery of *gfp* gene to uterine fibroid tissue was demonstrated.

**Список использованных источников**:

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