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A Review on Cationic Lipids with Different Linkers for Gene Delivery

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ABSTRACT:

Cationic lipids have become known as one of the most versatile tools for the delivery of DNA, RNA and many other therapeutic molecules, and are especially attractive because they can be easily designed, synthesized and characterized. Most of cationic lipids share the common structure of cationic head groups and hydrophobic portions with linker bonds between both domains. The linker bond is an important determinant of the chemical stability and biodegradability of cationic lipid, and further governs its transfection efficiency and cytotoxicity. Based on the structures of linker bonds, they can be grouped into many types, such as ether, ester, amide, carbamate, disulfide, urea, acylhydrazone, phosphate, and other unusual types (carnitine, vinyl ether, ketal, glutamic acid, aspartic acid, malonic acid diamide and dihydroxylbenzene). This review summarizes some research results concerning the nature (such as the structure and orientation of linker groups) and density (such as the spacing and the number of linker groups) of linker bond for improving the chemical stability, biodegradability, transfection efficiency and cytotoxicity of cationic lipid to overcome the critical barriers of *in vitro* and *in vivo* transfection.

Keyword: gene delivery; cationic lipid; linker; transfection efficiency; cytotoxicity

1. Introduction

Gene therapy has gained significant attention over the past three decades as a potential method not only in the treatment of diseases with hereditary diseases, but also in the development of strategies for treatment and prevention of a broad variety of different acquired diseases such as cancer, cystic fibrosis and AIDS [1-3]. One major challenging issue for successful application of gene therapy to human diseases is how to find a suitable vector for the delivery of genetic materials into a wide variety of cells, tissues and whole organs. Broadly, the present vectors used for gene therapy are divided into two main categories: viral and non-viral vectors [4-6].

Although viral vectors have become an important research avenue for clinical applications due to highly efficient gene delivery [7, 8], they bring about a number of disadvantages, inducing adverse immunogenic responses, high cost, and so forth. Compared to their viral counterparts, non-viral vectors can offer several advantages, including lower immunogenicity and toxicity, and greater gene packaging capacity [9-15]. Among non-viral vectors [4, 11, 13, 16-28], the use of cationic lipid as gene delivery system has attracted great attention of worldwide formulators due to their distinct advantages, such as simplicity of preparation, good repeatability and biodegradability, and potential commercial value [29, 30].

Cationic lipids are amphiphilic small molecules which can be easily designed and synthesized