

## The Cellular Internalization Mechanisms of Cationic Niosomes/DNA Complex in HeLa Cells

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**Abstract :** Cationic niosomes formulated with Span20, cholesterol and novel synthesized spermine-cationic lipids (2-hydrocarbon tail and 4- hydrocarbon tail) in a molar ratio of 2.5:2.5:1 can mediate high gene transfection in vitro. However, the uptake mechanisms of these systems are not well clarified. In the present study, effect of endocytic inhibitors on the transfection efficiency of niosomes/DNA complexes was determined on a human cervical carcinoma cell line (HeLa cells) using the inhibitors of macropinocytosis (wortmannin), clathrin- and caveolae-mediated endocytosis (methyl- $\beta$ -cyclodextrin), clathrin-mediated endocytosis (chlorpromazine), caveolae-mediated endocytosis (genistein and filipin), cytosolic transfer (ammonium chloride) and microtubules polymerization (nocodazole). The transfection of niosomes with 2-hydrocarbon tail lipid was blocked by nocodazole, genistein, ammonium chloride and filipin, respectively, whereas, the transfection of niosomes with 4-hydrocarbon tail lipid was blocked by nocodazole, genistein, ammonium chloride, methyl- $\beta$ -cyclodextrin and filipin, respectively. It can be concluded that these niosomes/DNA complexes were internalized predominantly by endocytosis via clathrin and caveolae-independent pathway.

**Keywords :** cellular internalization, cationic niosomes, gene carriers, spermine-cationic lipids

**Conference Title :** ICPBE 2014 : International Conference on Pharmaceutical and Biotechnological Engineering

**Conference Location :** Rome, Italy

**Conference Dates :** September 18-19, 2014