Endocytosis and intracellular trafficking of Solid Lipid Nanoparticles gene delivery system in HEK cells

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INTRODUCTION. Plasma membrane is selectively permeable, which makes it impermeable for most of nanomaterials. Therefore, nanomaterials must exploit endocytic pathways to gain entry into the cell. Determining the specific endocytic pathway of the nanoparticles is important to understand the mechanisms involved in their intracellular fate, biological effect and possible toxicity. **OBJECTIVE:** We aim to determine the endocytic pathway and intracellular trafficking solid lipid nanoparticles as gene delivery system in HEK cells. **MATERIAL AND METHODS:** We used labeled nanoparticles in presence of inhibitors to determine the internalization pathway. Co-localization of nanoparticles with lysosomal-associated membrane protein 1 (LAMP1) was performed using confocal microscopy. Finally, we used chloroquine, a lysosomotropic agent that prevents endosomal acidification, to test the endosomal acidification in DNA release mechanism. **RESULTS AND DISCUSSION**: Internalization in presence of inhibitors showed that chlorpromazine, inhibitor of clathrin-mediated endocytosis, significantly decreased the uptake and the transfection efficiency of solid lipid nanoparticles in HEK cells. Co-localization with LAMP1 reached the higher levels after 6h of treatment. The lysosomotropic agent dropped significantly the transfection efficiency, indicating that endosomal acidification could be associated to DNA release mechanism. **CONCLUSION:** Solid lipid nanoparticles gained access into HEK cells mainly via clathrin-mediated endocytosis. Nanoparticles were driven to lysosomal compartment within 6h. Finally, the acidification can be vital for DNA release, as indicated by transfection in presence of chloroquine.

Keywords: solid lipid nanoparticles, transfection, gene delivery, intracellular trafficking, endocytosis

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