

Cellular Uptake Mechanism of Paclitaxel Nanocrystals

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Therapeutic options for metastasized human cancer in current practice remain limited and, sadly, there is no cure for metastatic cancer. The typical approach, chemotherapy, has both low efficacy due to poor drug solubility, and cytotoxic side effects to healthy tissue when delivered indiscriminately. To address both of these issues, we are pursuing the use of nanocrystal formulations of current chemotherapeutic agents as delivery platforms. Herein, we have studied cellular uptake mechanisms in cancer cells of nanocrystals of a chemotherapeutic agent, paclitaxel. Our goal in this study is to determine whether the nanocrystals can be taken up via endocytosis, especially when the surface is conjugated by ligand molecules that target cancer cells. As such, we cultured KB cells with various formulations of paclitaxel nanocrystals, including crystals treated with fluorescent dyes for imaging purposes, and with various polymer coatings for examining their effect on cellular drug uptake. We examined the incubated cells using confocal microscopy in order to identify how the nanocrystals are being taken up. In addition, we measured IC_{50} values for each nanocrystal formulation. Our results suggest the presence of an endocytotic uptake mechanism, as, in cell samples treated with either of the conjugated nanocrystals, we see some overlap of the nanocrystal and the lysosome imaging agents within the cells. Future work will utilize electron microscopy imaging to confirm cellular uptake mechanisms identified here. These data will offer important insight for developing novel chemotherapeutic systems that are more effective and safe.