Micronization of hyaruronic-protamine particles by encapsulation into lipid capsules

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Abstract

Purpose: Micronization of Hyaluronic acid-Protamine particles were tested by encapsulating them into lipid capsules, aiming to reduce their trapping to lungs, kidneys, brain, and spleen in order to increase their delivery to tumors to be treated.

Materials & Methods: 1.6 mg protamine and 1.28 mg hyaluronic acid were added to 2.0 ml of 1mg/ml solution of carboplatin (Pt containing anticancer drugs), then reacted for 30 min in room temperature. The particles were generated by electrostatistical reaction between protamine and hyaluronic acid. 1.0 ml -solution of these particles was mixed in the ample of coatsome 01-EL-1 (Nichiyu corporation) and placed for 15 min. Finally, encapsulated particles were centrifuged for 1500 rpm for 20 min, and resuspended in 1.0 ml of distilled water. In this way, we got the solution of encapsulated particles.
The solution was injected intravenously through tail vein of C3He/N mice, associated with MM46 tumors in their left hind leg. Injected particles were allowed to circulate in mice for six hours, then their lungs, kidneys, brain, spleen, and tumors were excised. These tissues were digested by heated nitrogen-acid and dropped onto the Mylar-film and dried in room temperature, then used as targets for PIXE study. The trapped particles into lungs, kidneys, brain, spleen, and tumors were assessed in the contamination of Pt, which was contained in carboplatin in particles.

Results: By encapsulating hyaluronic acid-protamine particles into lipid capsules, the average size of particles was significantly reduced, which was 574 ± 23 nm. The downsizing of particles resulted in decreased trapping of particles into lungs, kidneys, brain, spleen, and increased delivery of those in tumors.

Conclusion: The downsizing of particles by encapsulating hyaluronic acid-protamine particles into lipid capsules will lead to better delivery of particles under the intravenous injection to body.