Kinetics of hyaluronic acid-protamine nanoparticles under intravenous injection, and targeted delivery of anti-cancer drug directed by radiation

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Abstract

The particles consisted from hyaluronic acid (HA) and Protamine (P), which release carboplatin with response to radiation, were generated and encapsulated into Coatsome EL-010. And their ability to targeted delivery to tumors, to increase antitumor effect and to reduce adverse effect was tested IN VIVO in C3He/N mice.

Hyaluronic acid and Protamine were mixed into the solution, containing carboplatin, and placed in room temperature for 30 minutes. Finally, solution of the generated particles was injected into vial bottle of Coatsome EL-010, and placed in room temperature for 30 min. In this way, particles for tumor treatment were generated. Those particles were intravenously injected through tail vein of C3He/N mice with MM 48 tumor in the left hind leg. The kinetics of particles were evaluated basing on the Pt contamination in tumors, liver, brain, lungs, and spleen, which was measured by PIXE. Nine hours after injection, single doses of 10 or 20 Gy 140 KeV soft X-rays was given to the tumors. The release of carboplatin was measured by means of Pt contamination, using PIXE. The antitumor effect was tested by measuring tumor diameter, and strength of adverse effect was tested by alteration of weight of kidneys.

The particles were accumulated to the tumor on nine hours after injection. The particles released carboplatin with response to irradiation. The released carboplatin gradually passed through membrane of coatsome EL 010 and reached to tumor, which increased antitumor, synergistically with radiaton. The localization of carboplatin by particles with coatsome EL-010 decreased adverse effect. Our encapsulated particles led to increased anti-tumor effect and decreased adverse effect.