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Nanoparticulate complexation of gadopentetic acid and chitosan for neutron-capture therapy of cancer

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Galonium neutron-capture therapy (Gd-NCT) is currently under development as a potential radiation therapy of cancer. Several researchers have evidenced the potential of Gd-NCT in recent years by using gadolinium-based MRI contrast agents such as Magnevist[®]. However, *in vivo* performance in Gd-NCT has not been sufficiently established yet, because of the luck of tumor-specific affinity of such commercially available Gd agents. In this context, we developed novel gadopentetic acidloaded chitosan nanoparticles (Gd-nanoCP) as an injectable delivery system of Gd. The primary idea to achieve the improved accumulation of Gd in tumor using Gd-nanoCPs relies on the use of chitosan with bioadhesive, biocompatible and biodegradable natures in the nanoparticulate form. The Gd-nanoCPs could be prepared by a newly developed emulsion coalescence technique. The particle size and Gd content can be controlled in the range of 150-750 nm and 7-23 wt%, respectively. The *in vitro* cellular accumulation studies of Gd-nanoCPs revealed that the amounts of Gd associated with tumor cells were approximately 100-200 times higher in comparison to Magnevist[®] (as a reference). The *in vivo* Gd-NCT trial was carried out as follows: Gd-nanoCPs were intratumorally injected twice to mice bearing subcutaneous B16F10 melanoma, and subsequently the thermal neutron with the fluence of 6.32 x 10¹² neutrons/cm² was irradiated to the tumor site. The results demonstrated that the tumor growth in the Gd-nanoCPs administered mice was significantly suppressed by the thermal neutron irradiation due to the long-term, higher accumulation of Gd in the tumor while no effect was observed in the Magnevist[®] administered mice.

Biography

Hideki Ichikawa received his Ph.D. degree in Pharmaceutics from Kobe Gakuin University (Japan) in 1994. Currently he is a Professor of Pharmaceutical Technology Laboratory and the Director of Division of Physical Pharmacy at Kobe Gakuin University. His research interest is nanoparticle technology for controlled drug delivery. He has published more than 70 papers in peer-reviewed international journals and is serving as an editorial board member of Advanced Powder Technology. His research is supported by a grant from the Japanese MEXT-supported program for the Strategic Research Foundation at Private Universities, 2012-2016.

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