Synopsis of Original Research Paper

Development of new hyaluronan derivatives modified with metal-ion ligands and their tissue penetration

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Peritoneal metastasis is frequently found at a late stage of stomach and ovarian cancer. Recently intraperitoneal administration of anticancer drugs such as paclitaxel and cisplatin (CDDP) is expected because relatively high concentration of the drugs can be administered to disseminated cancer cells. i.p. of paclitaxel is now clinically used as an advanced medical treatment in Japan. However, the clearance of CDDP is much faster than that of paclitaxel, thus new approach to deliver CDDP to peritoneal nodules are expected. It is well known that high concentration of hyaluronan exists in peritoneum, thus hyaluronan (HA) -based drug carrier for CDDP is potentially biocompatible in peritoneum. In addition, the affinitiy between HA and CD44, which is highly expressed in cancer cells, can be utilized to delivery CDDP to cancer cells selectively. Therefore, we have developed nanogel composed of iminodiacetic acid-modified HA (HA-IDA) and CDDP. In the present research, we investigate the targeting effect of the nanogel in vitro using human disseminated stomach cancer cell line, MKN45P, and human mesothelium cell line, Met-5A. Moreover, we made stomach cancer cell spheroids of MKN74 using PDMS-bottom plate, then clarified the efficient penetration of the nanogel compared to HA-IDA without CDDP. HA has excellent water-retention ability, so is utilized widely in cosmetic industry nowdays. The knowledge from the present research will contribute not only to medical applications but also cosmetic applications.