難溶性マイトマイシンC－アルブミン結合体のザルコーマ180移植マウスにおける徐放型薬物送達系としての性質

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Properties of Water-Insoluble Mitomycin C–Albumin Conjugate as a Sustained Release Drug Delivery System in Mice Inoculated with Sarcoma 180

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In order to improve the deposition of mitomycin C (MMC) in the administered site, water-insoluble mitomycin C–albumin conjugate (MMC–G–BSA) was prepared. MMC was covalently attached to the glutarylated BSA (G–BSA) in the presence of 1-ethyl-3-(3-dimethyl-aminopropyl)carbodiimide hydrochloride (EDC) to give MMC–G–BSA. The MMC content of the conjugate (16.3 w/w %) was higher than that of water-soluble mitomycin C–albumin conjugates. MMC was liberated from MMC–G–BSA suspended in a phosphate buffer (pH 7.4, 37 ℃) with a half-life of 155.3 h. In the same buffer system containing α-chymotrypsin, MMC–G–BSA was dissolved perfectly within 24 h due to enzymatic degradation, and the liberation of MMC from the conjugate was significantly accelerated ($t_{1/2}$ = 24.5 h). After intraperitoneal injection in mice, most of the MMC–G–BSA was retained in the abdominal cavity. Furthermore, the survival time of mice inoculated with Sarcoma 180 was significantly increased by the intraperitoneal injection of MMC–G–BSA. These findings suggest that MMC–G–BSA is a biodegradable macromolecular hybrid which acts as a sustained release delivery system of MMC.

マイトマイシンC（MMC）とアルブミンの難溶性結合体を合成した。結合体は16.3 w/w %のMMCを含有し，徐放性プロドラッグとして作用した（半減期155.3 h）。∂トリプシンにより，結合体は低分子化を受けながら速やかにMMCを放出した（半減期24.5 h）。結合体はマウスの腹腔内に滞留し，ザルコーマ180 細胞を移植したマウスの平均生存日数を延長した。以上，結合体は生体内分解能を有する徐放性の局所滞留型送達系として作用することが明らかになった。