[*Yakugaku Zasshi*, **121**, 441-450 (2001)] [Lab. of Pharm. Engineering]

Preparation of a Gel-Forming Ointment Base Applicable to the Recovery Stage of Bedsore and Clinical Evaluation of a Treatment Method with Different Ointment Bases Suitable to each Stage of Bedsore.

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A novel ointment base suitable for the treatment of bedsore at the recovery stage was developed by the use of HM-HPMC modified on the basis of the hydrophobicity. A considerable sustained release of drug (minocycline hydrochloride) formulated to the ointment was attained with a macrogol ointment mixed with the HM-HPMC and Carbopol (CP) of the formulating ratio of 3:7. It was also found that a change in the formulating ratio of HM-HPMC and CP lead to a change in the drug release rate. We clinically evaluated the effectiveness of the bedsore treatment, in which different ointment bases were applied to patients at different stages of the bedsore. In comparison of the clinical results with the healing index, we ascertained that the latter method was significantly more efficacious than the conventional one. The effectiveness was emphasized in treating the intractable bedsore classified into the grades IV and V.

[*J. Pharm. Sci. Technol., Japan*, **61**, 86-96 (2001)] [Lab. of Pharm. Engineering]

Surface Modification of Liposomes with Various Hydrophilic Polymers Bearing Hydrophobic Anchors and Their Circulation Properties.

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The objective of this study was to confirm the feasibility of polymer coating of liposomes with various hydrophilic polymers bearing hydrophobic anchors (HPMC-R, PVP-R, PVA-R) for designing injectable drug carriers for passive targeting of drugs. The formation of a thick polymer layer with HPMC-R and PVA-R on the surface of the liposomes was confirmed by comparing the particle size and zeta potential of the liposomes before and after polymer coating. The coating layer formed with PVP-R was not as thick as that of HPMC-R or PVA-R. The HPMC-R coated liposomes showed a significantly improved circulation compared to that of non-coated ones as had been observed for the PVA-R coated liposomes, while no significant improvement was observed for the PVP-R coated ones. It was concluded that a thick and flexible coating layer on the surface of liposomes with HPMC-R or PVA-R could prolong the circulation time of the liposomes and that PVP-R could not form such a steric coating layer owing to its molecular structure

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Evaluation of the anti-tumour activity of liposomal doxorubicin coated with hydrophilic polymers in tumour-bearing mice.

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The purpose of this study was to evaluate the effectiveness of polymer-coated liposomes as a carrier of the anticancer drug, doxorubicin, via intravenous administration. The size-controlled doxorubicin-loaded liposomes (egg phosphatidylcholine/cholesterol 1/1 in molav ratio) were coated with hydrophilic polymers having a hydrophobic moiety in the molecules (PVA-R, HPMC-R). The therapeutic efficiency of the drug encapsulated into the polymer-coated liposomes was evaluated by measuring the tumour size and the mean survival time in Ehrlich ascite carcinoma-bearing mice. A significant improvement in the therapeutic efficacy of the drug was observed with the PVA-R- and HPMC-R-coated liposomal formulation. We ascertained that polymers having a hydrophobic moiety in the molecule such as PVA-R and HPMC-R are suitable materials for modifying the surfaces of the doxorubicin-loaded liposome to enhance the therapeutic efficacy of the drug.

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Formulation Design of Ointment Base Suitable for Healing of Lesions in Treatment of Bedsores.

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We intended to develop a desired ointment base suitable for treatment of bedsores including the proliferation of granulation and epidermis. The main bedsore bacteria detected in our hospital were S. aureus and P. aeruginosa. The macrogol ointment (MO) was found to have bactericidal effects on these bacteria. To improve the properties of the ointment base, co-formulating effects of various additives to MO were evaluated. The sustained release function of the ointment base was obtained by adding hydrophilic petrolatum (HP) to MO. MO containing 5% of hydroxypropyl cellulose (HPC) showed both the humidity regulating and the controlled drug releasing properties. The card tension meter tests for the ointments prepared with the various polymers showed that the MO-HPC base, which showed the highest sustained drug releasing property, was found to have the highest hardness. This result means that HPC formulated into the base forms the most rigid gel structure to resist the erosion of the ointment and to control the drug release.