

Development of Hollow Fibers for the Controlled Release of Drugs

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The development of a new type of reservoir device for the controlled release of highly active drugs based on hollow fibers made of biodegradable polymers was recently reported(1, 2). These fibers can be fabricated continuously and reproducibly, can be injected subdermally and can be removed-if necessary by a small incision. In principle zero order drug release rates can be obtained and the membrane permeability can be adjusted to achieve optimal release rates for a wide variety of drugs. After release of the drug the fiber should degrade *in situ* without the formation of toxic products.

Hollow fibers(o.d. 0.7 mm; i.d. 0.6 mm) with various membrane structures and permeabilities were obtained by using a dry/wet coagulation spinning process varying the process parameters.

In vitro release studies using fibers made of poly-L-lactic acid filled with ³H-levonorgestrel micronized in castor oil showed that depending on the type of the hollow fibers used release rates of 0, 1-10 μg per cm fiber

per day could be obtained for the release in ethanol/water mixtures(e.g. 4/6 w/w). A zero order release of levonorgestrel was found for periods ranging from 2 months to more than 3 months.

To test the properties of the fibers *in vivo* a rat model has been set up. Fibers are implanted subcutaneously using a syringe with a hollow needle. Changes in molecular weight of the poly-L-lactic acid, the mechanical properties of the fibers and the structure of the fiber wall were studied as a function of time. In addition, light-, scanning- and transmission electron-microscopy were used to evaluate cellular infiltration and to quantify the tissue reaction. Drug release rates *in vivo* were compared with those obtained *in vitro*.

(1) J.H.M. Albers, J.C. Rieke, J. Olijslager, P.J. Greidanus, M.J.D. Eenink, J. Feijen, Subdermal drug delivery with a biodegradable hollow fibre device, *Proceedings International Symposium on Controlled Release Bioactive Materials*, 11(1984) 80~81.

(2) M.J.O. Eenink, J.H.M. Albers, J.C. Rieke, J. Olijslager, P.J. Greidanus and J. Feijen, Biodegradable hollow fibers for the controlled release of drugs, *Proceed. Intern. Symp. Control. Rel. Bioact. Mater.*, 12(1985) 49~50.

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