12 administration, such as insertional mutagenesis or germline transmission, are minimal.

[PE2-13] [10/18/2002 (Fri) 13:30 - 16:30 / Hall C]

Pharmacokinetics of DA-3021 (mono-PEGylated recombinant human interferon α-2a) after Subcutaneous Administrations to Experimental Animals

Jo YeongWoo°, Kim WonGeun, Choi YunKyu, Jeon HyunKyu, Kim Donghwan, Park BeomSoo, Lee SungHee, Kim WonBae, Youn YuSeok, Lee SangDeuk, Lee KangChoon, Choi EungChil

Research Laboratories, Dong-A Pharm. Co., Ltd.
College of Pharmacy, Sungkyunkwan University
College of Pharmacy, Seoul National University

Interferon has therapeutic potential for a wide range of infectious and proliferative disorders such as chronic hepatitis C and malignant melanoma. However, it has some therapeutic problems as other protein therapeutics do. A variety of approaches have been developed to circumvent these problems. Among them, the attachment of a polyethylene glycol (PEG) moiety to interferon is considered as one of the most promising solutions for its ability of extending the plasma residence time. Mono-PEGylated recombinant human interferon α-2a was prepared by conjugating reaction and then appropriate separation and purification steps. Its pharmacokinetic parameters were estimated after subcutaneous administration into SD rats, beagle dogs, and cynomolgus monkeys. Area under the plasma concentration-time curve (AUC) and the peak plasma concentration (Cmax) increased in a dose-related manner in SD rats. The time to reach the plasma peak (Tmax) was 47.8hr in rats and 72hr in both dogs and monkeys. The elimination half-life (t1/2) was 31.7hr in rats, 157.2hr in dogs, and 93.6hr in monkeys, respectively. These results indicate that DA-3021 has sustained absorption and a longer half-life than unmodified interferon yielding longer periods in the circulation. Considering these pharmacokinetic studies, we can expect that enhanced pharmacological profiles for DA-3021 would come out in clinical trials.

[PE2-14] [10/18/2002 (Fri) 13:30 - 16:30 / Hall C]

In vivo Characterization of Sustained-Release Formulation of Recombinant Human Growth Hormone in Immunosuppressed Rats and Dogs

Jo YeongWoo°, Park YongMan, Lee Ghunll, Yang HiChang, Kim MiRyang, Lee SungHee, Kwon JongWon, Kim WonBae, Choi EungChil

Research Laboratories, Dong-A Pharm. Co., Ltd.
College of Pharmacy, Seoul National University

The in vivo release characteristics of rhGH-loaded PLGA microsphere prepared using a double emulsion process from hydrophilic 50:50 poly(D,L-lactide-co-glycolide) (PLGA) polymers were analyzed. This formulation showed particle size of ca 53.1㎛ with high drug incorporation efficiency. To investigate in vivo release kinetics without the interference of formation of antibodies to rhGH in the experimental animals, the animals were immunosuppressed by treatment with Cyclosporin. When this formulation was subcutaneously administrated in immunosuppressed rats, it showed an initial burst of 4-8 hrs followed by a sustained release phase and produced serum levels above 1-5 ng/ml rhGH for 14 days and followed by a diminished release which terminated after 4 weeks. And it showed dose-dependent patterns in serum rhGH levels. When dosed every 2 weeks, this formulation showed slightly different release patterns and no accumulative effects were observed. These results suggested that this formulation would be efficacious for sustained delivery of rhGH over 14 days. In case of dogs, results obtained after administration of this formulation were similar with those of rats. This formulation showed elevation in serum rhGH levels with dose-dependent patterns for 10 days. As in case of rats, no accumulative effects were observed after consecutive administration of this formulation in dogs. These studies demonstrated the potential for a sustained release, 14-day formulation for rhGH.

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