



Neuroscience Center of Excellence

LSU Health Sciences Center School of Medicine, New Orleans SEMINAR

Medusa: A Polymer-based Sustained Release Delivery Technology for Proteins and Peptides

Kenneth Lundstrom, Ph.D.
Director of Research, Flamel Technologies
Vénissieux, France

Delivery of protein- and peptide-based drugs has been hampered by high immediate drug release and short-term effect. This has limited the drug dosage, enhanced side effects and required frequent repeated drug administration. To circumvent these problems, the Medusa[®] slow release system based on polymer technology has been developed. Two different polymer formulations have been applied. One formulation based on an amphiphilic block polymer consisting of two amino acids (L-leucine and L-glutamate) is called Medusa I[®]. In Medusa II[®] the polymer backbone is composed of poly L-glutamate with hydrophobic α -tocopherol (vitamin E) molecules grafted on the glutamate units, which creates a colloidal suspension of nanoparticles in water in the size range of 10 to 50 nm. Sustained drug release is achieved through the presence of hydrophobic nanodomains within the nanoparticles. Studies have demonstrated that when Medusa[®] nanoparticles are subcutaneously (s.c.) injected the therapeutic protein associated with the polymer in the polymer-protein complexes is displaced by endogenous proteins present in physiological fluids. This leads to a slow release of the therapeutic drug and a dramatic decrease in C_{max} values and extended protein release for at least one week based on studies in animal models and in humans.

The Medusa[®] technology has been applied to several therapeutic proteins. The Medusa I[®] formulation has been applied to insulin (Basulin[®]) and compared favorably to conventional insulin delivery especially when the second generation Basulin[®] microparticle formulation was applied. The pharmacokinetic profile of IL-2 XL (Medusa II[®] extended release formulation) was compared to Proleukin[®] (the commercially available immediate release form of IL-2) in three animal models (Sprague-Dawley rats, Beagle dogs and Cynomolgus monkeys). In all three species a delayed pharmacokinetic serum profile due to sustained release of IL-2 was observed for IL-2 XL. The peak concentration (C_{max}) values of IL-2 were also significantly decreased and extended release of IL-2 XL found in rats, dogs and monkeys. A phase I/II clinical trial was conducted on 10 renal cancer patients with a single injection of IL-2 XL (10.6 million IU/m²) to monitor safety, pharmacokinetics and biological activity. Preliminary results demonstrated a clear sustained release pharmacokinetic profile and with a 2-fold decrease in C_{max} compared to Proleukin[®] and extended presence (7 days) in serum and superior bioavailability. Another protein drug that has been applied to the Medusa II[®] technology is interferon alpha (IFN- α). Animal studies and preliminary clinical data suggest similar safety and efficacy profiles for IFN- α .

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