Functional Co-polymers Designed for Protein Micelle Preparations

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Like nucleic-acid drugs, protein drugs that contain such cytokine as interferon (IFN-α), interleukin, granulocyte colony stimulating factor (G-CSF) and growth factor also need to have stability in the bloodstream in order to have therapeutic efficacy. With micellar nanoparticles technology, NanoCarrier aims to develop protein micelles that have longer half-life in bloodstream (slow release), improved therapeutic efficacy and lower side effects. Particle size and release rate of drugs can be optimized to meet each application needs.

The scope of this abstract is to introduce a number of copolymers developed at NanoCarrier that could increase the half-life and the loading of various proteins. Copolymers developed by NanoCarrier comprised of a hydrophilic moiety (PEG) as well as hydrophobic one (polyamino acid derivatives). The length of the hydrophilic part as well as the number of amino acid groups could be varied. In order to increase the suitability of the copolymer with a correspondent protein, several chemical modifications have been conducted. The most prominent modification was the introduction of different hydrophobic groups that lead to prevention of the burst effect. The introduced groups are C8 or Bn groups. The encapsulation of the proteins could be achieved without the use of organic solvents.

Table 1 summarizes a number of copolymers synthesised that were used for encapsulation of different proteins. The loading rate of each protein was provided in this table.

Table 1. Summary of the copolymers used for the encapsulation of various proteins.

Polymer	Protein	Loading
PEG-PBLA (12-50 65%Bn)	IgG	>90%
PEG-PBLA (12-50 65%Bn)	Lysozyme	>90%
PEG-PBLA(12-40 65%Bn)	Papain	30%
PEG-POLA (12-40 65%C8)	IgG	>90%
PEG-PBLG (12-40 65%Bn)	IgG	80%
PEG-POLG (12-40 65%C8)	Lysozyme	50%

Figure 1 shows the pharmacokinetic profiles of two proteins (INF-α and G-CFS). The data shows that high concentrations of those proteins could be maintained for a long time in the blood stream.

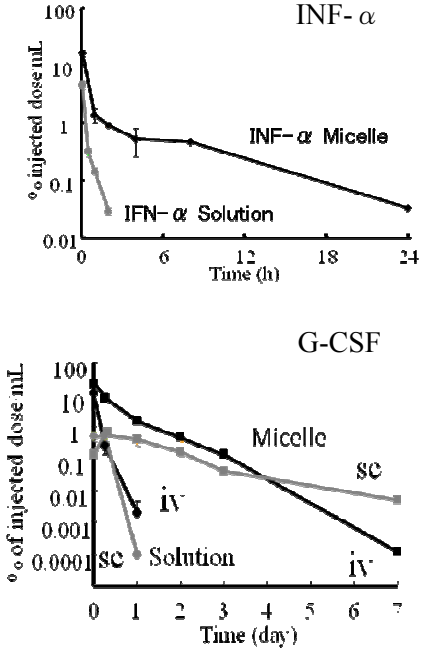

Figure 1. PK profile of INF (iv) and G-CFS (iv and sc) injected in rats

The results suggest that the copolymers synthesized by NanoCarrier could be successfully used for encapsulation of various proteins in order to either increase plasma AUCs or to reduce the number of administrations for highly potent drugs.

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