Solid phase N-terminal mono-PEGylation of recombinant interferon alpha 2a: Separation, Characterization, and Biological Activity

이병국, 이은규*
한양대학교
(eklee@hanyang.ac.kr*)

Interferon (IFN) alpha 2a plays an essential role in the treatment of chronic hepatitis C. To improve its serum circulation stability, IFN is conjugated with PEG (polyethylene glycol) moiety. For N-terminally site-specific modification, we developed a solid-phase PEGylation process based on reductive alkylation in which aldehyde mPEG of 5, 10, or 20 kDa was conjugated to the IFN immobilized to a cation exchange resin (CM-Sepharose). From this preparation the IFN mono-PEGylate was easily purified by a single chromatographic step. N-terminal amino acid sequencing and MALDI-TOF MS confirmed the N-terminal, mono-PEGylation. The PEGylate showed the reduced anti-viral activity (by cell proliferation assay) and immunogenicity (by antibody binding assay). However, the proteolytic resistance as well as thermal stability was considerably improved. The solid-phase PEGylation process was highly reproducible in site specificity. This novel conjugation method may find other applications in improving biopharmaceutical proteins' characteristics by site-specific chemical modification.