Yoshihiro Takatsu, J Pharm Drug Deliv Res 2017, 6:3 (Suppl)
http://dx.doi.org/10.4172/2325-9604.C1.018

Chonylation™ : A new drug delivery technology for improving the therapeutic efficacy of proteins and peptides utilizing naturally-occurring sugar polymer chondroitin (CH) as an alternative to polyethylene glycol

Yoshihiro Takatsu
Seikagaku Corporation, Japan

PEG has become the gold standard polymer extending the circularly stability of conjugated therapeutics. However, repeated administration of PEGylated proteins to animals has in some cases been associated with cellular vacuolation of macrophages, histiocytes, renal tubular cells and choroid plexus ependymal cells. In addition, immune responses to PEG itself have been recognized and have caused a loss of therapeutic efficacy. CH is the naturally-occurring biodegradable sugar chain which consists of repeated disaccharide units of D-glucuronic acid and N-acetyl-D-galactosamine. We found that i.v.-injected CH circulated surprisingly for a long period as well as PEG in mice. Consequently, we have been developing chonylation™ technology comprising conjugation of CH to protein and peptide therapeutics. CH-conjugated asparaginase (CH-Asp) showed a good pharmacokinetic profile ($T_{1/2}$=35.2 hours, MRT=48.7 hours) although asparaginase (Asp) itself disappeared from the circulation within 24 hours. Similarly, chonylation™ improved pharmacokinetics of various kinds of protein and peptide, including ovalbumin, interferon α, growth hormone, GLP-1 and insulin. To evaluate the influence of chonylation™ to the immunogenesity of foreign protein, Asp, PEGylated Asp (oncaspar®) and CH-Asp were repeatedly injected via the intramuscular route. Asp-treated group induced high immune responses against Asp. Oncaspar®-treated group induced immune responce to PEG but not to Asp. In contrast, CH-Asp induced no immune responces, neither to Asp nor to CH. Chonylation™ technology will be a new generation drug delivery system for protein and peptide therapeutics with significantly improved pharmacological profiles.

Biography

Yoshihiro Takatsu has completed his PhD at Hokkaido University. After working for Takeda Pharmaceutical Company Limited as a Principal Research Scientist for nine years, he moved to Seikagaku Corporation and has been developing Chonylation™ technology as a Associate Chief Researcher in Glyco Research Department in Central Research Laboratory.

yoshihiro.takatsu@seikagaku.co.jp

Notes: