RECOMMENDED READING

Ashrafi, H. et al. (2013). "Nanostructure L-asparaginase-fatty acid bioconjugate: Synthesis, preformulation study and biological assessment." *Int J Biol Macromol* 62:180–187.

The present study aims to develop a novel L-asparaginase fatty acid bioconjugates and characterize their applicability for intravenous delivery of L-asparaginase. These bioconjugates were achieved by covalent linkage of fatty acids having different chain lengths (C12, C16 and C22) to the native enzyme. To determine the optimum conditions of bioconjugation, the effect of lipid:protein ratios, reaction time and medium composition on enzyme activity and conjugation degree were evaluated. The native and bioconjugates have been characterized by activity, conjugation degree, particle size, and zeta potential. The results showed that bioconjugated L-asparaginase were more resistant to proteolysis, more stable at different pH, and had prolonged plasma half-life, compared to the native form. From partition coefficient study, the modified enzymes showed approximately 15-fold increase in hydrophobicity. Secondary structure analysis using circular dichroism revealed alteration after lipid conjugation. In addition, the Michaelis constant of the native enzyme was 3.38 mM, while the bioconjugates showed the higher affinity to the substrate L-asparagine. These findings indicate that new lipid bioconjugation could be a very useful strategy for intravenous delivery of L-asparaginase.

Beg, S. et al. (2015). "QbD-based systematic development of novel optimized solid self-nanoemulsifying drug delivery systems (SNEDDS) of lovastatin with enhanced biopharmaceutical performance." *Drug Deliv* 22(6):765–784.

Of late, solid self-nanoemulsifying drug delivery systems (S-SNEDDS) have been extensively sought-after owing to their superior portability, drug loading, stability and patient compliance. The current studies, therefore, entail systematic development, optimization and evaluation (in vitro, in situ and in vivo) of the solid formulations of (SNEDDS) lovastatin employing rational quality by design (QbD)-based approach of formulation by design (FbD). The patient-centric quality target product profile (QTPP) and critical quality attributes (CQAs) were earmarked. Preformulation studies along with initial risk assessment facilitated the selection of lipid (i.e. Capmul MCM), surfactant (i.e. Nikkol HCO-50) and co-surfactant (i.e. Lutrol F127) as CMAs for formulation of S-SNEDDS. A face-centered cubic design (FCCD) was employed for optimization using Nikkol-HCO50 (X1) and Lutrol-F127 (X2), evaluating CQAs like globule size, liquefaction time, emulsification time, MDT, dissolution efficiency and permeation parameter. The design space was generated using apt mathematical models, and the optimum formulation was located, followed by validation of the FbD methodology. In situ SPIP and in vivo pharmacodynamic studies on the optimized formulation carried out in unisex Wistar rats, corroborated superior drug absorption and enhanced pharmacodynamic potential in regulating serum lipid levels. In a nutshell, the present studies report successful QbD-oriented development of novel oral S-SNEDDS of lovastatin with distinctly improved biopharmaceutical performance.

Beg, S. et al. (2015). "Positively charged self-nanoemulsifying oily formulations of olmesartan medoxomil: Systematic development, in vitro, ex vivo and in vivo evaluation." *Int J Pharm* 493(1–2):466–482.