

Preparation of Atorvastatin-loaded Polylactide-Poly(ethylene glycol)-Polylactide Tri-block Copolymer Polymersomes and Evaluation of Drug Release Behaviors *in vitro*

H. Danafar^{1,2,*}, K. Rostamizadeh², S. Davaran¹, M. Hamidi³

¹Department of Medicinal Chemistry, School of Pharmacy, Tabriz University of Medical Sciences, Tabriz, Iran ²Department of Medicinal Chemistry, School of Pharmacy, Zanjan University of Medical Sciences, Zanjan, Iran ³Department of Pharmaceutics, School of Pharmacy, Zanjan University of Medical Sciences, Zanjan, Iran

Background and Aims: In the recent years there has been increased interest in the use of Biodegradable and biocompatible polymeric nanoparticles for drug delivery application. Atorvastatin calcium (AC) is a second-generation of 3-hydroxy-3-methylglutaryl-CoA reductase inhibitor approved for clinical use as a lipid lowering agent. AC, the world's best selling drug is associated with poor oral bioavailability and serious adverse effects like rhabdomyolysis on chronic administration. The objective of the present research work is to design and evaluate polymeric nanoparticles for controlled release of AC in order to improve the efficacy and safety of AC. **Methods:** Polylactide-Poly(ethylene glycol)-Polylactide (PLA-PEG-PLA) copolymers with various molar ratios of lactic to polyethylene glycol with molecular weight of 6000 Da were synthesized by ring-opening polymerization using stannous octoate as catalyst. The copolymer structure was confirmed by NMR, DSC, FT-IR, and GPC. A nanoprecipitation method was used to prepare the nanoparticles. The nanoparticles were characterized by dynamic light scattering. The release behavior of obtained Polymersomes were examined by

UV spectrophotometery at λ max=238.

Results and discussion: The copolymer structure was confirmed by NMR, DSC, FT-IR. The molecular weight of copolymer was found to be 29000 Da by GPC technique. Results showed that the mean diameters of the nanoparticles were less than 177 nm. The drug entrapment efficiency was more than 89%. The nanoparticles showed a sustained release profile for a long time.

Conclusions: Polymersomes are able to encapsulate hydrophobic drugs. The drug release experiments indicated that the atorvastatin-loaded polymersomes possessed sustained release characteristics.

Keywords: PLA-PEG-PLA; Polymersomes; Atorvastatin