# Novel Nano-biomaterials for Protein and Gene Delivery

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A new approach for attaining sustained release of water-soluble macromolecules is introduced, involving a pore-closing process of preformed porous PLGA microspheres. Highly porous biodegradable poly(D,L-lactic-co-glycolic acid) (PLGA) microspheres were fabricated by a single water-in-oil emulsion solvent evaporation technique using Pluronic F127 as an extractable porogen. The pore size and its volume in the microspheres were readily controlled by adjusting the relative amount of Pluronic F127 and PLGA. The pores, having a uniform distribution, were highly interconnected throughout the bulk phase and to the surface of the microspheres. Various macromolecular drugs were incorporated into porous microspheres by a simple solution dipping method. For their controlled release, the porous microspheres containing various drugs were treated with water-miscible solvents in aqueous phase for production of pore-closed microspheres. The aqueous pore-closing process resulted in nonporous microspheres which exhibited sustained release patterns over an extended period. However, the drug loading efficiency was extremely low due to rapid dissolution and diffusion of entrapped drug molecules into the aqueous phase during the pore-closing process. To overcome the drug loading problem, the pore-closing process was performed in an ethanol vapor phase using a fluidized bed reactor. Porous microspheres, loaded with recombinant human growth hormone (rhGH), were treated with ethanol vapor to produce nonporous microspheres. The resultant pore-closed microspheres maintained high protein loading amount through the vapor phase pore-closing process and showed sustained rhGH release profiles over an extended period. The released rhGH exhibited structural integrity after the ethanol vapor treatment.