323e Nanostructured Polymeric Materials for Biomedical Applications

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The rapid evolution of nanotechnology is aiming to fulfill the goal of optimal drug delivery and selective recognition through the development of nanostructured targeted drug carriers (e.g., liposomes, polymeric nanoparticles and molecularly imprinted polymers (MIP)) with increased circulation lifetimes. Targeted drug delivery requires drug-loaded particles, which preferentially localize to the sites of injury and avoid uptake into uninvolved tissues. In addition, selective recognition requires the introduction of a molecular memory into a polymer matrix in order to make it capable of rebinding an analyte with a very high specificity. Among other drug delivery systems, liposomes offer several advantages, including biocompatibility, control of biological properties via modification of physical properties and several modes for drug delivery to cells (e.g., absorption, fuse, endocytosis, phagocytosis). In addition, polyalkylcyanoacrylates (PACA) and poly(lactide-co-glycolide) (PLGA) have attracted much attention as colloidal drug carriers due to their ease of preparation, long-term safety in humans, biodegradability and biocompatibility properties. In the present study, PLGA microparticles containing multilamellar liposomes (MLVs), polymethylcyanoacrylate (PMCA) nanocapsules and MIP nanoparticles were synthesized to be employed as drug carriers and synthetic receptors respectively. MLVs were synthesized using hydration, followed by sonication and extrusion. Various types of phospholipids (e.g., Phospholipon 80, 80H, 90 and 90H) and cholesterol were employed for the synthesis of the liposomes. Hydroquinone, a hydrophilic drug used for skin whitening was employed as the active ingredient. The morphology of the MLVs after the hydration step was examined by means of optical microscopy and their size distribution was measured by dynamic light scattering. The size of the MLVs was found to depend on the preparation method the type of the phospholipid and the pore size of the membrane used during the extrusion process. The hydroquinone-loaded MLVs were subsequently encapsulated in PLGA microparticles employing a complex solvent evaporation process. Simple PLGA particles containing hydroquinone were also prepared using the same technique. An aqueous solution of hydroquinone or of hydroquinone-loaded liposomes was added to a PLGA solution in dichloromethane resulting in the formation of a w/o emulsion. The latter was then added to an aqueous PVA solution leading to the formation of a w/o/w emulsion. Simple and composite, spherical PLGA microparticles were formed by solvent evaporation from the w/o/w emulsion at increased temperature. The release rate of hydroquinone from the composite PLGA microparticles was compared to that from the simple ones and was found to be significantly retarded. PMCA nanocapsules containing benzyl benzoate/tea-tree oil were prepared by interfacial polymerization. The oil phase consisted of a solution of methylcyanoacrylate and benzyl benzoate/tea tree oil in acetonitrile whereas, the aqueous phase consisted of a solution of the surfactant Tween 80. The organic phase was slowly injected, into the aqueous phase and subjected to homogenization. Polymerization occurred at the oil/water interface of the droplets and the nanocapsules were formed immediately. The colloidal suspension was then concentrated, allowing the organic solvent to evaporate. The loading capacity of the produced PMCA nanocapsules was determined employing UV spectroscopy. The effect of various process parameters on the synthesis of the PMCA nanocapsules (e.g., drug/monomer volume ratio, pH, type of solvent) was examined. The average diameter of the produced nanocapsules was found to increase with an increase in the monomer concentration and a decrease in the pH. Regarding the effect of the type of solvent on the synthesis of the PMCA nanocapsules, it was shown that when ethanol was used as a solvent, the polymerization took place initially in the organic solution, leading to the formation of nanospheres along with nanocapsules, whereas, when ethanol was replaced by acetonitrile, no formation of nanospheres was observed. MIP nanoparticles were synthesized by precipitation polymerization to be used as synthetic receptors selective for theophylline. The template molecule was added in acetonitrile in a borosilicate glass tube equipped with a screw cap followed by the addition of the functional monomer, methacrylic acid, the crosslinker, EGDMA and the initiator, AIBN. The polymerization was induced by placing the tube in a preheated water bath. The resultant polymeric nanoparticles were collected by

centrifugation and were subsequently washed (x five times) with methanol containing 10% (v/v) acetic acid to remove the template species. Non-imprinted polymeric (NIP) nanoparticles were also prepared using the same technique. UV spectroscopy was employed to measure the affinity and selectivity of the MIP particles. A small amount of MIP/NIP particles (e.g., 0.03g MIP or NIP / ml solution) were incubated at room temperature in theophylline, caffeine / acetonitrile solutions of known concentrations (e.g., 1ìmole theophylline or caffeine /ml solvent). The surface examination of the MIP and NIP polymeric particles revealed that they exhibit a rough, porous surface indicating that the presence of the template does not influence significantly the polymer morphology. It was shown that the MIP particles rebind 3.63 ìmole of theophylline per 1gr of polymer whereas the NIP particles bind 1.49 ìmole of theophylline per 1gr of polymer. Competitive analysis was also performed employing caffeine, an analyte which is chemically-related to theophylline, in order to examine the selectivity of the theophylline imprinted polymeric receptors. It was shown that the MIP nanoparticles adsorb 0.48 ìmole of caffeine per 1gr of polymer thus, proving the selectivity of the artificial receptors towards the template molecule.