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Lamivudine-poly-E-caprolactone conjugate based particles for targeted drug delivery, synthesis and characterization

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Poly-E-caprolactone (PCL) is biodegradable, nontoxic polyester synthesized mainly in ring-opening polymerization (ROP) of E-caprolactone (CL). PCL alone or in blends was utilized in numerous medical applications, such as scaffolds, implants, nano- and micro- drug carriers. It is characterized by slow degradation of polyester chains in hydrolytic mechanism. Lamivudine (LV), as well as other antiretroviral drugs used in HIV-1 treatment, targets infected immune system cells, mainly CD4+ T helper cells. However, other infected cells like macrophages, monocytes, dendritic cells are found through whole body, including lungs and central nervous system. This cells halflife, measured in weeks/years, is dramatically longer in comparison to CD4+ T helper cells, which is counted in hours/days. Such cells are often recognized as reservoirs of retroviruses, especially these which are found in sites hardly available for drug substances, so called "sanctuaries". The aim of this study was to design a process of poly-E-caprolactone-lamivudine conjugate (PCL-LV) synthesis, and forming it into microspheres. Due to extremely slow hydrolytic degradation, phagocytosis would be main mechanism of intravenously administered particles clearance. Suggested mechanism of ROP includes formation of bond between initiator and polymer backbone. Drug bound covalently to oligomeric chain would not be released from polymeric matrix in to plasma, therefore whole administered dose would eventually achieve phagocytic cells, i.e., HIV-1 infected macrophages, monocytes or dendritics cells. Conjugate structure was confirmed by the proton nuclear magnetic resonance and electro-spray ionization time of flight mass spectroscopy. Further stage of study included microsphere forming in a variant of solvent evaporation method. Shape and size of obtained particles was determined by scanning electron microscopy, light microscopy and dynamic light scattering. Average molecular weight of obtained polymers was 5400 Da, size of prepared particles varied from nanometric to micrometric dimensions.

Biography

Tomasz Urbaniak is a Pharmacist and Research Assistant in Physical Chemistry Department of Faculty of Pharmacy, Wroclaw Medical University. His activity includes evaluation of polymerization methods, structural analysis of polymeric materials on molecular and bulk level, and examination of drug release from nanometric and micrometric particles. Also, utilization of quantum chemistry calculations in the field of pharmaceutical science is in scope of his interests. Interdisciplinary approach is the way he thinks and acts in his work.

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