SUMMARY OF THE DOCTORAL DISSERTATION

Designing of linear and grafted biofunctional polymers with the use of "click" reaction for applications in transdermal therapy

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In this work, new biofunctional linear and grafted methacrylic polymers were designed, synthesized and characterized, with potential application in biomedicine or cosmetology in the form of micellar carriers or conjugates. The key in the proposed research was the introduction of biofunctionalities into the obtained systems, which were achieved through the use of new "bio"initiators for atom transfer radical polymerization (ATRP). For this purpose, bromoester derivatives of retinol or 4-*n*-butylresorcinol were synthesized, which were characterized by very good efficiency in initiation of the polymerization reaction, constituting an alternative to standard ATRP initiators, and moreover, they enabled the introduction of the biologically active unit into the polymer at the stage of its synthesis. As a result of the ATRP reaction, well-defined linear and graft copolymers were obtained using monomers such as methyl methacrylate (MMA), polyethylene glycol monomethyl ether methacrylate (MPEGMA), 2-hydroxyethyl methacrylate (HEMA), as well as an alkyne derivative of HEMA (AlHEMA).

Copolymers with AlHEMA units were subjected to a "click" reaction with polymers (*grafting onto*), i.e. polyethylene glycol (PEG), poly (ε-caprolactone) (PCL) or polydimethylsiloxane (PDMS) to obtain grafted or heterografted copolymers, as well as with selected bioactive compounds which led to conjugates. An important issue was the possibility of giving the final copolymer certain properties, i.e. hydrophilicity, and film-forming properties resulting from the type of grafted chain, as well as potential anti-aging activity. The efficiency of the "click" reactions were dependent on the type of grafted chain, the topology and hydrophilicity of the copolymer, as well as the proportion and distribution of alkyne units in the copolymer.

The amphiphilicity of linear and grafted copolymers, including heterografted ones obtained as a result of the "click" reaction, enabled their self-assembling leading to micellar structures and the encapsulation of selected active substances with anti-wrinkle, antioxidant and discoloration reducing properties. The hydrodynamic diameters of the micelles formed by the copolymers were primarily influenced by their topology and degree of grafting, but also by the type and chemical nature of the encapsulated substance. In turn, the efficiency of the encapsulation process was mainly determined by the hydrophilic-hydrophobic balance of the copolymer, the distribution of hydrophilic units, the ability of the encapsulated substance to dissolve in water and in the case of PCL copolymers, also the length of the grafted chain. The process of the release of active substances from micelles has shown that a significant part of the compound was released usually in the first hour of the experiment. The amount of active substance released and the release rate was influenced by the pH of the buffer (medium), the topology and hydrophilicity of the micelle-forming copolymer, but the acidity of the active substance was also crucial. Another group of polymer carriers was conjugated with ferulic acid or lipoic acid, whose kinetics of the release process was slightly different from micellar systems. A large content of the hydrophobic fraction in the conjugate was associated with a high burst of the released substance immediately after the initiation of the release process in the case of systems with lipoic acid, while ferulic acid was characterized by an extended release time from 2 to 4 hours.

Biological tests, including tests of permeability through an artificial membrane imitating skin, initially indicated the possibility of use of the obtained systems in products applied to the skin. Both the cytotoxicity test and the tests determining the cell cycle, the type of cell death that occurs, and the aging tests showed no negative effect of carrier solutions of various concentrations on skin cells.

The study confirmed that the obtained copolymers can be used as effective carriers of cosmetic substances in products delivering them transdermally for a short application time, i.e. masks, eye pads.