

Abstract

As the development of cancerostatic drugs progresses it is becoming necessary to contemplate the question of how to deliver these drugs, which themselves tend to exhibit carcinogenic properties, effectively and accurately to the affected tissues and thus to circumvent their destructive effects upon the healthy parts of the organism. One approach to delivering drugs selectively to cancerous tissues is to make use of some of the specific properties which these tissues tend to possess, one of which being the so-called enhanced permeability and retention effect (EPR effect). This effect, which will be further discussed within this thesis, allows for macromolecules that are too massive to pass from the bloodstream into healthy tissue, to exit the blood vessels of cancerous tissue and to accumulate there. Therefore, a drug molecule can specifically enter cancerous tissue along with a suitable macromolecule, to which it is conveniently attached. If, moreover, the given drug is connected to the carrier molecule via an enzymatically cleavable spacer, it is possible to make use of lysosomal proteases (such as cathepsin B, which is overexpressed in some cancer cells) in order to attain its detachment from the carrier molecule and its subsequent activation. This bachelor thesis focuses on describing the structure and function of various polymeric drug delivery systems along with the cancerostatic drugs themselves. The experimental section of this thesis further details the synthesis of some of these polymeric conjugates (consisting of a carrier molecule, a spacer and a drug molecule) and their characterisation. The results obtained include a set of polymeric conjugates of doxorubicin and pirarubicin cancerostatics with three different peptide spacers and a body of data acquired by measuring drug release rates, determining the cytotoxicity of the conjugates and by characterising them by means of standard analytical procedures.

Keywords: drug delivery systems, EPR effect, cancerostatic drugs, polymers, cathepsin B

(In Czech)