Abstract

In this thesis the anticancer drug vandetanib was studied. Vandetanib is a tyrosine kinase inhibitor affecting signalling of vascular endothelial growth factor receptor (VEGFR), epidermal growth factor receptor (EGFR) or RET protooncogene (REarranged during Transfection). It is primarily used for the treatment of advanced tumors of the thyroid gland. Unfortunately, the usage of vandetanib in the cancer treatment is significantly limited by its toxicity and cardiotoxicity (one of the adverse effects is connected with long QT interval). One way, how to minimize these side effects, is binding a drug into a suitable transporter. Apoferritin and liposomes were used as a transport nanoparticles in this study.

The aim of this thesis was to study the stability of the complex of nanoparticle apoferritin with vandetanib molecules (ApoVan) and to study the effect of pH on the release of inhibitor from the ApoVan form. Experiments have shown that ApoVan complex is relatively stable after its storage at 4 °C and – 20 °C for up to 8 weeks. Unfortunately after monitoring the effect of pH on the release of vandetanib from ApoVan, it was found that vandetanib is gradually released from its ApoVan form into the neutral environment at pH 7,4 as well as into the acidic environment at pH 6,5 and the way ApoVan is prepared does not have any impact on it. Next, the difference between the effect of alone vandetanib and ApoVan on UKF-NB-4 cell line and thyroid carcinoma cell line was studied. Unfortunately, a minimal difference was observed and thus we assume that vandetanib might not be encapsulated into the cavity of apoferritin, but instead bonds to its surface. Therefore, the next part of the thesis was focused on the preparation of liposome nanoparticles with molecules of vandetanib. The effect of the DLPC concentration and the vandetanib concentration on the preparation of the vandetanib encapsulated into liposome complex (LipoVan) were studied. LipoVan was prepared in three different ways. Using a stock solution of vandetanib in DMSO, ethanol and using the so-called injection method. The usage of a stock solution of vandetanib in ethanol did not result in the formation of LipoVan at all as DLPC are soluble in ethanol and thus do not form liposomes. The remaining two experiments used for the preparation of LipoVan did not show effective complex preparation. The formed amount was so low that the preparation process would be inefficient.

Key words: *cancer, nanoparticle, apoferritin, liposomes, vandetanib, targeted treatment*