Abstrakt v anglickém jazyce

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Angiogenesis, or the formation of new blood vessels from existing ones, is currently one of the processes targeted by cancer therapy, as the formation of new blood vessels is a prerequisite for successful tumor growth and eventual expansion in the body in the form of metastasis. One of the receptors involved in signalling leading to angiogenesis is endoglin (CD105). This receptor is also targeted by the chimeric monoclonal antibody carotuximab.

The aim of this thesis was to perform indirect labelling of the monoclonal antibody carotuximab with the radionuclide gallium-67 using the bifunctional chelator 1,4,7-triazacyclononane,1-glutaric acid-4,7-acetic acid (NODAGA). During the labelling process, the NODAGA:carotuximab molar ratio was optimized (1:20, 1:50 and 1:100). The prepared radiopharmaceutical [^{67}Ga]Ga-NODAGA-carotuximab was subsequently determined for its radiochemical purity by HPLC with radiometric detection. This was followed by *in vitro* binding experiments on human renal tumor cell culture involving internalization, saturation and competition studies. In particular, the kinetic parameter of the equilibrium dissociation constant (K_D), which expresses the affinity of the antibody for the CD105 receptor, was evaluated. Furthermore, the inhibitory concentration (IC_{50}) value was determined, which also indirectly determines the affinity of the ligand for the receptor.

Optimization of the molar ratio of the NODAGA chelator conjugated to the antibody resulted in the most suitable ratio of 1:20. The results of the radiochemical purity analysis followed by radiolabelling confirmed the suitability of the chelator and the method of conjugation and radiolabelling of the antibody for the preparation of the diagnostic radioimmunoconjugate [^{67}Ga]Ga-NODAGA-carotuximab at the

pharmacopoeia-required purity (≥ 95%). The prepared radiopharmaceutical was subsequently tested in *in vitro* studies. The most suitable incubation time (150 to 180 minutes) was found for internalization, and a lower rate of internalization of ^{67}Ga-labeled carotuximab was also observed, because a larger fraction remained bound on the cell receptors than was internalized. From the *in vitro* saturation study, an equilibrium dissociation constant of K_D = 225 (±6.6) nM was determined, which is significantly lower compared to the unlabelled antibody but still significant. In a competitive study, IC_{50} = 140.4 (±0.4) nM was determined, which again confirmed the significant affinity of labelled carotuximab to the CD105 receptor.

In conclusion, we were able to prepare a potential diagnostic radiopharmaceutical [^{67}Ga]Ga-NODAGA-carotuximab, which retained affinity to the target receptor, but it was lower compared to the native form of the antibody. A potential reason for this could be the higher number of chelators bound to the antibody (5.4 NODAGA molecules per molecule of carotuximab). However, the binding of the ^{67}Ga-labelled antibody to CD105 is still sufficient and therefore *in vivo* biodistribution studies with mouse xenografts could be pursued in the next phase of preclinical testing.