6 SUMMARY

The aim of the present work was to accomplish a synthetic contribution for the application of dendrimers as carriers for anticancer-therapy. A synthetic concept had to be developed, which allows peripheral functionalization of poly(amidoamine)-dendrimers with pharmacologically relevant motifs. The dendrimers were to be equipped with chelating ligands for Pt^{2+}-complexation and were intended to have enhanced solubility in water through OEGs. In order to further optimize the carrier-concept, initial structure/ toxicity correlations were to be evaluated by *in vitro* cytotoxicity essays.

A set of molecules for surface-modification of amino-terminated G0- and G1-dendrimers was synthesized. G0-dendrimers were made accessible, which were based on a trifunctional core moiety. The well-defined construction of *bi*- (hetero-) functional G1-dendrons and G1-dendrimers was achieved by optimized reaction conditions for the synthesis of *tris*-orthogonally protected branching units.

The compounds with selectively addressable functional groups and monodisperse OEGs (“caps”) were equipped with chelating malonic acid or ethylene-diamine ligands or with a fluorescence tag. Their acid group offered the possibility for assembly with dendritic building blocks by employing amide coupling-protocols. The enhanced solubility of “caps” in water was ensured by 12 repeating units of ethylene glycol.

The applied coupling protocols made G0-dendrimers **78**, **81**, **82**, **84** and **115** accessible in very good yields and high purity. These molecules served as “models” for this pharmacologically oriented project.

The G1-Dendrimers **99** und **100** with ethylene-diamine ligands were obtained in excellent yields in a quasi-convergent approach. Dendrimer **113**, carrying fluorescence tag and malonic acid ligands, was readily available and was synthesized in a divergent approach.

Dendrimers **81** and **113** are very promising, because they offer free malonic acids for hydrolytically reversible Pt^{2+}-binding.

Initial experiments were done to complex these dendrimers with Pt^{2+}. ^{1}H- and ^{13}C-NMR spectroscopy as well as UV-spectra of the obtained compounds, give reason to

believe in a successful platination. Unfortunately, corresponding ^{195}Pt-NMR spectrocopic measurements were of minor success, as of yet.

Results from cytotoxicity essays on human breast cancer cell lines MCF-7 lead to preliminary, but not generally established structure/ toxicity correlations. None of the dendrimers tested in this context proved to be cytotoxic. In consequence, neither the applied surface-functionalization nor the intrinsic structure of dendrimers of both generations seemed to play a significant role.

This can be considered an encouraging signal for the continued development of the described strategy on the generation of new drug-carriers.