University of Fribourg / Faculty of Science and Medicine / Department of Chemistry

The potential of cobalamin as a drug vector
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Applying recent advances in the organometallic chemistry of cobalamin

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Vitamin B_{12} (Cobalamin, Cbl) was used in this thesis to develop “drug delivery systems” for compounds with poor solubility and selectivity. The core of the following dissertation is composed of five parts (chapter 3.1 to 3.5) describing my contribution to the field.
In the first part, the β-upper ligand of Cbl was substituted with metal complexes of current medicinal interest (such as Platinum, Ruthenium and Rhenium). The anticancer activity of these derivatives was evaluated *in vitro* and their uptake mechanism elucidated. In the second part, a 17e- Re(I) complex was attached at the CNCbl β position by relying on the ability of the cyanide ligand to bridge two metal centers. The study focused on the derivatives anti-platelet activity and especially on the tuning of the carbon monoxide (CO) releasing kinetics by chemical modifications at the corrin ring of the B_{12} scaffold. The third part of the results discusses a new biomaterial (constituted of diatomaceous earth) designed for targeted delivery of poorly water-soluble inorganic anticancer drugs, with a focus on colorectal cancer. The fourth part treats about the effect of CO released inside cancer cells and its potential synergic effect with drugs, while the last one discusses the synthesis and use of antimalarial vitamin B_{12} for the *in vivo* delivery of chloroquine derivatives tested on the zebrafish model.
The results presented in this thesis demonstrate the feasibility of using a biological compound, such as cobalamin, to deliver drugs to a specific target by using a trojan horse approach. In the future, this could lead to the development of a new generation of cobalamin prodrugs.

Jury:
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