ABSTRACT (EN)

This dissertation thesis contains scientific results achieved in the field of analytical chemistry, particularly liquid chromatography. The major part of the results has been published in prestigious international journals in five papers. In addition to that, relevant yet unpublished results have been included as well.

In general terms, the work presented here contributed to the concerted efforts to tackle the current lack of novel antibiotics. Specifically, high-performance liquid chromatography (HPLC) and ultra high-performance liquid chromatography (UHPLC) techniques coupled to a variety of detection systems have been employed for analysis of antibiotics and actinomycete secondary metabolites.

The first thematic part describes the development of liquid chromatography methods for analysis of lincomycin precursors, lincomycin precursor analogues, and lincomycin derivatives. The methods have been applied to study lincomycin biosynthetic pathway and obtain improved lincomycin derivatives by mutasynthesis.

The second thematic part aims at investigating alternative approaches for analysis of antibiotics. Firstly, the core-shell particle and the sub-2 μm particle chromatographic columns were compared. The core-shell particle columns compatible with HPLC proved to be a convenient alternative to the sub-2 μm particle columns compatible only with UHPLC. However, it applies only for analysis of tetracyclines under acidic conditions, not for analysis of macrolides under alkaline conditions. Secondly, the compatibility of a condensation nucleation light-scattering detector and the UHPLC system was investigated under both isocratic and gradient conditions. Also, the limits of detection for several macrolides were found to be significantly lower with this detector than with an ultraviolet detector.

The third thematic part focuses on the development and application of a universal fingerprinting method for secondary metabolites in cultivation broth of actinomycetes. The method is based on UHPLC with diode-array ultraviolet detection and provides two 3D fingerprints of secondary metabolites for a sample. The fingerprints contain physico-chemical information on the fingerprinted analytes, which can be used for further statistical evaluation.