ABSTRACT

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Application of non-separation flow techniques in pharmaceutical analysis

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Flow techniques are a branch of instrumental techniques in chemical analysis based on the handling of the sample in a tubing manifold. Since the introduction of what is recognized nowadays as modern flow techniques in the early seventies, this analytical approach gained popularity among scientist thanks to their main principles. Controlled dispersion and precise timing due to the programming enable full automation of a variety of analytical procedures.

Flow methods were employed in a multiple different applications: simple sample measurement, chemical reactions, kinetic studies, sample pretreatment, separation, and others in an automated way. They are especially valued for automation, decrease of chemicals consumption and thus lower cost and waste production, and shortening of the analysis time.

This dissertation presents new contributions to the field of flow techniques. It is divided into a theoretical part and an experimental part, the latter one listing five publications and one manuscript submitted for publication.

The theoretical part comprises three main chapters: sample pretreatment methods, flow methods, and selected sample handling methods in flow techniques. An overview is given on sample pretreatment and related procedures, and especially modern microextraction techniques are emphasised here. Both liquid and solid phase-based methods are discussed further.

The definition and basic instrumentation of flow techniques is described in the following section, highlighting the ones applied in the experimental works. The main features of each technique are briefly discussed including the technical differences and performance.

The third chapter is devoted to the applications of flow techniques in several sample handling procedures, applied in analysis of pharmaceuticals in their formulation or in a biological sample, or in analysis of other biologically active substances. It includes applications of enzymatic reactions and use of irradiation as well as the possibility of automation of selected microextraction techniques in a flow manifold.

The experimental part comprises five publications and one manuscript currently submitted for publication. Each of the attached publications is accompanied by a short comment clarifying the most

interesting features of the respective work, the method development, and a discussion about the novelty of the presented methods.

The first experimental work is focused on the execution of a reaction catalysed by an enzyme in a sequential injection system with spectrophotometric detection. The method is applied to the determination of an anaesthetic drug propofol in emulsion and compared to a simple flow method with fluorimetric detection.

The second experimental work studies the use of a Sequential Injection Analysis system for the automation of a liquid-liquid microextraction and a modified method for dispersive liquid-liquid microextraction of thiocyanates in human saliva samples.

In the third experimental work, a novel mode of head-space single drop microextraction performed in an In-syringe system applied to the determination ethanol as a model volatile analyte is described.

The fourth experimental work deals with solid phase based microextractions carried out on-line. A use of a flow-batch system for SPE, UV-photodegradation and a fluorimetric determination of the pesticide metsulfuron methyl is presented as an application from the field of environmental analysis that corresponds to the scope of cooperation with the Department of Chemistry at the University of the South in Bahía Blanca, Argentina.

The fifth experimental work was focused on the study of conditions influencing fluorescence of two model substances in a sequential injection system.

The last, sixth experimental work shows a novel mode of automation of microextraction by packed sorbent coupled directly to separation in a low pressure sequential injection chromatographic system. The method was applied to the determination of betaxolol in human urine samples and the work is presented as a manuscript submitted for a publication in a scientific journal with impact factor.