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# Recent Developments in Analytical and Preparative Scale Enantioseparations

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Field of enantioseparations represents one of the actual topics of chemistry. Significant, in some cases dramatic differences in a desired activity as well as in toxic properties of enantiomers of chiral drugs, food additives, agrochemicals, cosmetic products, etc. represents a driving force in this field. The enantiomers of all chiral bioactive compounds have to be isolated and to be tested. Besides the ethical or environmental reasons for developing single enantiomers, it may be a real therapeutic benefit and in some cases, it has been used as a strategy for extending patent life.

Separation science offers attractive possibilities for both, obtaining of enantiomerically pure chiral compounds on a preparative and product scale, as well as for analytical determination of the enantiomers during the process of their production, storage, examination and use. Two trends can be noted in the recent years in the field of separation science: One the one hand, the size of a separation chamber (columns, pumps, etc.) is becoming larger for a cost-effective production of enantiomerically pure compounds. On the other hand the size of a separation chamber is reducing significantly in analytical applications in order to make the analytical process more cost effective, efficient, to increase analytical troughput and protect the environment from hazardous exposition. Both of these trends will be discussed in this presentation.

The chromatographic separation of enantiomers on a preparative scale has been recognized as a powerful technique of supplying pure enantiomers of bioactive compounds and chiral synthons [1]. From these techniques a classical column (batch) chromatography, recycling chromatography, countercurrent chromatography and simulated-mouving bed (SMB) chromatography have been established for isolation of enantiomerically pure chiral compounds. A decision which of these techniques must be used can be made depending on a development stage of the product, required amounts, available time, equipments, stationary phases, money, etc. Alternative techniques such as enantioselective synthesis, crystallysation, etc. must be also considered. The aspects regarding a selection of the separation technique, chiral stationary phase, etc. will be addressed in this talk.

Major techniques available for analytical enantioseparations such as high-performance liquid chromatography (HPLC), gas chromatography (GC), super/sub-critical fluid chromatography (SFC), capillary electrophoresis (CE), capillary electrochromatography (CEC) and lab-on-chip based approaches will be compared based on the criteria such as universality, efficiency, selectivity, method development and application time, automation, costs, etc. HPLC still represents the most widely used enantioseparation technique in industrial laboratories but CE already became a more established technique for the same purpose in academia and is entering industrial environment [2, 3]. The most important advantages of this rapidly developing technique in comparison with chromatographic techniques is inherently high peak efficiency, flexibility in adjustment of separation selectivity, miniaturization, short method development time, low costs, etc. Together with CE, a heritage of HPLC and CE, known as CEC shows promises in the field of enantioseparations. This technique combines high separation efficiency of CE with the advantages of a stationary bed of HPLC [4]. It is interesting to note, that GC, SFC and CE (together with free-flow electrophoresis) previously considered as the techniques suitable only for analytical scale enantioseparations, appear promising also for micropreparative enantioseparations.

Highly efficient enantioseparation techniques are attractive not only for isolation or quantitative determination of enantiomers but also for invetigation of stereochemical effects in noncovalent intermolecular interactions. From this viewpoint CE appears to be especially useful technique and it can be applied in combination with NMR spectroscopy, mass spectrometry, X-ray crystallography and molecular modeling techniques. Some examples of these studies will be also presented.

**References:**


[1] E. Francotte, Enantioselective chromatography as a powerful alternative for the preparation of drug enantiomers, J. Chromatogr. A, 906 (2001) 379-397.

[2] B. Chankvetadze, Capillary Electrophoresis in Chiral Analysis, Wiley&Sons, Chichester, UK, 1997, 555 pp.

[3] B. Chankvetadze, G. Blaschke, Enantioseparations in capillary electromigration techniques: recent developments and future trends, J.Chromatogr. A, 906 (2001) 309-363.

[4] S. Fanali, P. Catarcini, G. Blaschke, B. Chankvetadze, Enantioseparations by capillary electrochromatography, Electrophoresis, 22 (2001) 3131-3151.