Multidimensional Optimum Performance Laminar Chromatography (OPLC) in Combinatorial Chemistry

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The recent combinatorial approach in synthetic organic chemistry started a new age in drug discovery. The introduction of a new drug to the market requires at least ten years and a budget of more than 500 million dollars. Application of the combinatorial approach makes possible the significant reduction in time and cost of the drug discovery process. The generation of libraries of peptides, peptoids, peptidomimetics or other small organic molecules in combination with high-throughput screening has become the method of choice for the production of new pharmacological leads for chemical optimization. Due to the well-established methodologies of solid-phase peptide chemistry, there is no technical difficulty in the production of large number of compounds. However, characterization and separation of such pool of compounds have been lagging behind the synthetic and screening methodologies. Moreover, proteomics, an emerging area of research for the new millennium, requires a plethora of high resolution analytical techniques. For the efficient analysis of complex mixtures, synthetic or natural libraries, an integrated application of the “classical” (e.g. two-dimensional polyacrylamide gel electrophoresis, capillary electrophoresis, high performance reversed-phase chromatography) and novel methodologies would be highly desirable. However, by using conventional chromatographic and electrophoretic methods based on column technologies, the number of samples routinely analyzed during a normal working day is confined to about 20–40. Optimum performance laminar chromatography (OPLC), however, allows the simultaneous separation of the same number of samples within minutes. Thus, daily analysis of hundreds of samples can easily be performed. Using commercially available, fine particle HTSorb HP plates, OPLC might be the method of choice for the separation of complex mixtures of stereoisomers and structurally highly related compounds. By using the latest generation of the OPLC instrumentation (OPLC 50, Bionisis, France) our paper shows the application of this robust, high-throughput analytical technique for the rapid characterization of peptide libraries obtained by the split–mix and tetrazine libraries any of the parallel synthetic methods. This work was supported by the Hungarian Scientific Research Fund (OTKA 25829 and NKFP 1/047 research grants).