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From first concepts to production and broad application of CIM monoliths for separation of macromolecules and nanoparticles and for continuous enzymatic conversion

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First Czechoslovak/Russian patents about production of “porous methacrylate membranes for chromatography”, followed by corresponding USA patents were published 1987 and 1989, followed by first publication about application of these membranes for very fast separation of standard proteins [1]. Interestingly, parallel paper about use of stocked up membranes packed in cartridges was published in the same year [2]. In early 90-ies, followed further development of methacrylate monolithic supports especially towards their application for separation of proteins from complex biological samples and for fast “in flow” enzymatic conversion [3,4], and their experimental use in our laboratory [3,4]. Experiments that were performed this time gave first hints about tremendous advantage of monoliths – almost complete absence of diffusion as a limited factor in separation of large molecules. Further technical solutions like sample distribution and construction of separation cartridge enabled the first commercial use of monolithic columns, that were named CIM columns [5]. Construction of cylindric columns and their use in radial flow was further important step for use of CIM columns in preparative chromatography [6, 7]. Further giant step in the right direction was demonstration of use of “Short monolithic columns for purification of proteins, DNA and viruses” [8] followed by broad use of CIM monoliths for analytical and preparative separation of nanoparticles, namely viruses, plasmids, large nucleic acid molecules, lipoproteins and large protein multimers and extracellular vesicles [9,10]. These applications are now in the focus of interest, but the use of CIM monoliths for fast enzymatic conversion [11] and isolation of biologically active biopolymers, with the focus of human plasma fractionation [12] and removal of pathological macromolecules from biological fluids will be presented.

References

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