**Monolithic supports in chromatography and down-stream processing**

**– a 30 years long history and an encouraging future development**

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Isolation of complex biomolecules, especially of macromolecular biopolymers was for long time a very frustrating job. We were looking for materials for fast separation of biologically active proteins, hydrophobic membrane (glyco)proteins and nucleic acids. We tried to overcome the problems of non-specific interactions and low recovery that we had with particle based chromatographic supports by use of cellulose membranes that were modified with different ligands, however, with limited success. Both the pressure drop and non-specific interactions on these separation units were much lower, and a fast separation of biologically active macromolecules was possible. However, the lifetime was very short, because of the low mechanical stability of such devices [1]. Few years later, these problems were solved, and separation devices based on multi membrane layers are now broadly used [2]. Monolithic supports were the other alternative, and their development started at the same time, at the end of 80’s, when Švec and Tennikova [3] and Hjertén's group [4] developed polymer based monolithic supports, firstly called «macroporous membranes» [3] or «continuous polymer beds» [4]. They are porous structures that contain channels and that bear different ligands. Both groups demonstrated their successful use for chromatographic separations of standard proteins. The main driving force for development of new chromatographic supports was the necessity for isolation and separation of physiologically active biopolymers and their use for therapeutic purposes. Our first work at this field started one year later, and first papers about use of monoliths for biopolymer separations and immobilization of enzymes were published already one year later. After this short overview, recent developments in monolithic technology and the use of these supports for the separation of biopolymers, immobilization of enzymes and fast conversion of substrates on both analytical and preparative scale, as well as for the isolation and separation of viruses, plasmids, and other nanoparticles. The possibility for using these supports in sample displacement mode opened new possibilities for fast and simple fractionation of macromolecules and nanoparticles. Newly, separation of microvesicles and exosomes rapidly gained on importance and it is one of interesting future for applications of specially tailored monolithic supports with large pore sizes. With the increasing production and use of these cellular products for diagnostic and therapeutic purposes, this development will be accompanied with increasing use of monoliths for their isolation, in-process control, and both quality control and quality assurance.

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