

## Porous polymeric monoliths: design and preparation towards environmental applications

Ahmed M. Khalil<sup>1</sup><sup>1</sup>Photochemistry Department, National Research Centre, El-Buhouth St., Dokki - 12622, Giza, Egypt\*corresponding author e-mail address: [akhalil75@yahoo.com](mailto:akhalil75@yahoo.com)

## ABSTRACT

Polymeric monoliths are porous substrates comprised of suitable monomer(s) beside a crosslinking agent and a radical initiator. The polymerization reaction may be thermally or radiation initiated in a mold. They take the shape of continuous rods or columns upon preparation. These materials are porous substrates used to overcome some deficiencies that arose from using the corresponding traditional monoliths such as ceramic and metallic ones. Increasing the efficiency of the monolith can be achieved via grafting the surface. Functional groups on the monolithic surface can be introduced to boost the performance of the monolith. Immobilizing nanoparticles; mainly the metallic ones onto the surface of the polymeric monolith enhances the efficiency of these columns and expands their application fields. Depositing the metal nanoparticles takes place via *in-situ* reduction of metal nanoparticles from their precursor salts or via *ex-situ* loading of previously prepared nanoparticles. There are various applications for polymeric monoliths; separation of proteins, small and large molecules can be mentioned. Monoliths are used in chromatographic separation applications beside catalytic implications. These monoliths represent the stationary phase. For expanding the separation application, polymeric monoliths can be applied in electrochromatographic separations. Besides, catalytic reactions can take place inside these monolithic rods.

**Keywords:** Monolith, porous polymer, metal nanoparticles, chromatography, separation, catalysis, polymerization.

## 1. INTRODUCTION

A monolith is a geological structure consisting of a single huge stone such as some mountains or rocks. It is derived from the word *monolithus*, from the ancient Greek word meaning stone. The natural monolith encouraged scientists to design and prepare such structures by using polymeric substrates. This is performed by adjusting the features of the prepared monoliths and directing them towards specific applications. The monolithic rod (column) has to offer a continuous pathway for reactants to transfer through, ending with the products at the terminal of the column; as shown in Figure 1. Some conventional monoliths like ceramic and metallic monoliths that contain iron, aluminum or chromium showed some drawbacks due to deficiencies in the geometry and the composing materials. Hence, scientists moved to other alternatives which can be easily tailored to be convenient for specific applications with acceptable characteristics. Polymeric materials attracted the attention to build up these new materials that cope with the required applications. Polymer monoliths can be synthesized via free radical polymerization to provide a crosslinked porous polymeric network structure [1-5]. The aforementioned structure is close to the functionalized silica which has been prepared via sol-gel methods previously [6-10]. These two major types (polymeric and silica based monoliths) have flourished since at the end of the twentieth century and turned to be effective commercial substrates in separation applications. Polymer monolithic materials go parallel with silica based monoliths stationary phases in separating small molecules in various elution procedures. Macroporous polymeric monoliths are suitable in the separation of large molecules [11-14]. There are some developments in both of these major branches of monolithic column technology that arose in the past few years. Many researches were directed to develop polymer monolithic substrates and use them in separating small and large molecules. Some of the

used pathways to develop the monoliths are the early termination of the polymerization reaction [15-18], the kind of the used crosslinkers [19-21], introducing nanoparticles in the internal porous structures, either *in-situ* or post polymerization [22-24].



**Figure 1.** Reactants entering through a monolith column and coming out as products.

Polymeric monoliths present distinctive properties compared to the traditional chromatographic stationary phases based on (porous) adsorbent particles. It is observed that some chemical methods aim to characterize and focus on the scaffold formation of the monolith. Although the use of polymer monoliths as chromatographic materials continues to attract researchers. Meanwhile, more applications such as extraction [1, 25] and catalysis [26-28] are growing rapidly.

### 1.1. Free volume of the monolithic matrix.

In polymeric substrates, the unoccupied spaces lying inside are known as the free volume. The volume of a polymer consists of both the occupied volume by the polymer molecules and the free volume surrounding the polymer. Characterizing this free volume is possible. Experimental methods by using specific probe molecules such as nitrogen based on the probe's size are followed. Hence, various experiments can estimate the amounts of free volume [29]. Methods to assess free volume often make use of positronium parts with measuring their lifetimes [30]. The free volume is influenced by temperature, as various temperatures originate thermal vibrations in the occupied volume of the polymer. Moreover, crosslinked polymers are affected by the solvent by generating an increase in the free volume. This results

in the swollen polymer and its nanoscale solvation. Consequently, the specific solvated-state equilibrium depends on the experimental conditions. This feature is based on originating permanent microporosity in polymers. The surplus free volume contacting the solvent can be reduced upon removing the solvent from the polymeric matrix [29].

The present free volume is formed due to a crosslinked polymeric network within the solvent in addition to binding labile polymer chains together. Upon removal of solvents, physical aging may arise, with a microporous material in the dry state [31]. These polymeric substrates can swell even in poor solvents due to the existing stress on the polymer chains providing microporosity. For instance, hyper crosslinked polystyrene tends to swell slightly even in a poor solvent like water [30]. Upon using polymer monoliths in certain implementations, it is important to monitor the swelling volume of the used crosslinked polymer. When a crosslinked polymer is subjected to water, acetonitrile, tetrahydrofuran (THF) or their mixtures, swelling takes place leading to a nanoscale structure in the polymeric monolith. A particular volume and interchain space are generated in the solute will be established, known as (gel porosity) [32]. Changing the kind of the solvent and mixing it with others will vary the nanoscale swelling of the polymer [33].

Some experiments for determining monomer-specific conversions from *in-situ* prepared porous polymer monoliths have been carried out to show the changes in the polymerization mixture for both methacrylate-based [16,33] styrene/divinylbenzene [34] and related crosslinking systems [18]. These results suggest that some compositional nanostructural heterogeneity arose. These changes have been recognized by atomic force microscopy (AFM) [34]. The heterogeneity can be correlated to some conversions in the monomer. Some amounts of the pendant functional groups in the monomer are unable to proceed in the polymerization process and crosslinking like others [35]. The matrix consists of thick cross-linked inner cores and less cross-linked peripheral parts. Similar results have been found for styrene/divinylbenzene monoliths [34]. At the beginning of the polymerization process of porous polymer monoliths, crosslinked nuclei with different sizes are formed, directing to a phase separation in the polymer [36]. In most applications, this phase separation is uncontrollable [16]. The phase separated polymer swells in the solvent, leading to progress in polymerization and crosslinking with forming the new polymer monolith. Some heterogeneous globular structure of phase-separated polymer may emerge, with some aggregates in the mold with various sizes, shapes and morphology [16,17,36]. Though, the formed pores permit the flow of the mobile phase. It was not easy to determine the pore space, so some techniques were developed to assess and characterize polymer monoliths. Confocal Raman spectroscopy imaging assisted in defining the inter-spaces between polymer and solvents [34]. Water was noticed in the micrometer-sized flow-through pores, acetonitrile was even present within globular features. Using confocal Raman imaging clarified some observations about hierarchical length scales. The solvent is spread in the crosslinked polymer with different interspaces.

## 1.2. Structure and relevant mass transport.

The mass transport of the polymeric monolith is an essential feature to study the dispersion of traces due to heterogeneity in the flow through monolithic pores [37,38]. A practical determination for mass transport behavior is performed via pulse experiments. Pump probe spectroscopy is used, as a narrow pulse of a probe is introduced at the inlet of the column. This pulse spreads to make a macroscopic response in the form of a peak eluting at a certain time with a specific shape and width. This authorizes to utilize different probes with different sizes through adsorption mechanism to interact with the stationary phase. In polymer monoliths including polar or hydrophilic materials, they are able to conserve the polar analytes in mobile organic phases. Consequently, the more polar mobile phase component moves easily while the less polar species show lower mobility. So, the moving components as polar ones affect the transport of hydrophilic solutes in separation applications. The development of polymer monoliths as engineering materials was explained by fast-gradient liquid chromatography separations of large polymers. Various novel materials were prepared with concentrating on a wide range of molecules beside chromatographic applications, like hydrophobic, hydrophilic, or ion exchange chromatography [17,39]. Further important fields of applications deal with the enhanced physical structure of polymer monoliths are the ones which depend on aqueous size exclusion chromatography of biomolecules [40,41] and hydrodynamic chromatography of synthetic polymers [42]. Eluting large biomolecules including proteins, is considered as one of the main applications for polymer monolithic columns. It is important for the chromatography of large proteins. This is due to the dependence of protein retention on mobile phase composition [38]. Under isocratic conditions, it was noticed that a low elution efficiency take places with low retention time. This is due to slow pore fluid gel interphase diffusion as protein is adsorbed and moves slowly [38]. Upon taking this point in consideration, enhancing micro-scale separations of proteins is interesting. The developments focus on using a minute or trace amounts of the sample by improving the sensitivity of mass spectrometry [16]. The experiments explored applying high pressure by utilizing small flow through tiny sized monolithic structures [43]. Experimental data showed that a decrease in pore size with an increase in the applied pressure enhances the performance of the used monolithic column under equilibrium conditions [33,38]. Separating low-molecular weight biomolecules; less than 500 g/mol is regarded as an interesting field for applying polymer monoliths [44,45]. Hence, polymer based monoliths coincide with the analytical domain of conventional silica-based monoliths in separation implementations.

Extraction is a promising and extending field of application for polymeric monoliths. This domain has attracted attention due to the facility in preparing polymer monolithic materials in molds of various sizes and shapes (e.g., capillary tubes and chips). In this case, a material with high chromatographic efficiency has to be selected with having sufficient capacity for solutes. The mass

transport has to be effective. The efficiency of these materials depends on the gel structure for a given analyte under given experimental conditions. The rate of diffusion during the transport process in the solvent for the analytes has to be taken into consideration. Treating this process is interesting with suitable postulates in assessing the mass transfer step with a suitable reference for adsorption capacity. In most of the studies, this reference that will be used for comparison may be the surface area

for monolithic materials, which was estimated by dry-state estimations and confirmed by chromatographic measurements [6,11,37]. Nowadays, porous monolithic materials in columns or rod forms can be introduced as novel and efficient substrates for separation or extraction. They are prepared in a simple way. The process takes place in a mold; via preparing a mixture based on vinyl monomers with an inert solvents.

## 2. PREPARATION OF POROUS POLYMERIC MONOLITHS

### 2.1. Components of porous monoliths.

Polymeric monoliths comprise the merits of porous materials including rigidity and keeping the porous format in any solvent as well as in dry form. These porous matrices are synthesized via copolymerization in suspension. These materials are prepared easily from a homogeneous polymerization mixture, including an appropriate monomer such as [monovinyl monomer(s) and polyfunctional monomer(s)] with a crosslinker and a radical initiator and porogenic solvent [46] in a mold. Figure 2 represents the stages of synthesizing porous polymeric monoliths.

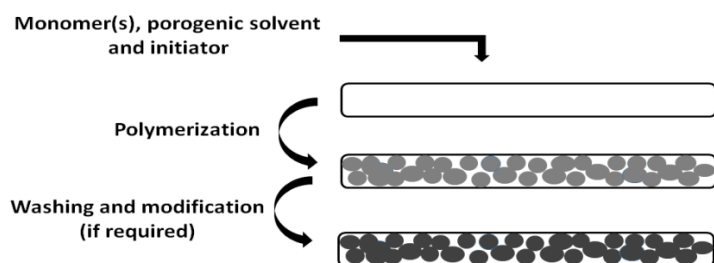


Figure 2. Different steps for preparing polymeric monoliths.

As soon as the polymer is formed in the mold, the functional groups on the monolithic surface are able to control the performance of the monolith. Consequently, these groups can be managed for immobilizing biological catalysts or certain ligands to be used in separation through high performance liquid chromatography (HPLC) of small and large molecules. Generally, glass tubes loaded with the polymerization ingredients are used as molds. These tubes are kept at specific temperatures where the reactions take place. The polymerization process starts with thermal initiators that decompose to produce free radicals. Some procedures are initiated by ultraviolet radiation and redox reactions [46,47]. Glass tubes or fused silica capillaries are employed. Some processes comprise radiation by using Co-60 gamma-source [48] or by atom transfer radical polymerization (ATRP) [49]. The experimental procedures can be designed and tailored to suit the application where the monolith will be used. Tubes of different substrates and sizes like glass, stainless steel [35,50], poly(ether ether ketone) (PEEK), and silica capillaries [11] are processed as molds. The monolith components are flushed inside the mold by applying certain pressure.

### 2.2. Originating pores in polymeric monoliths.

The pores are formed during polymerization reactions with monomers in an inert porogenic solvent and a radical initiator. The polymer chains will be then produced in solution then precipitate

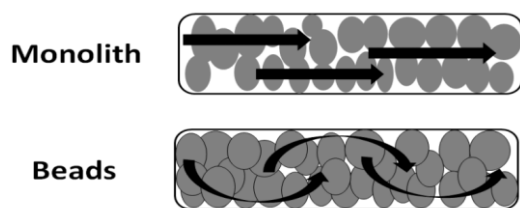
due to the crosslinking density of the polymeric network. During this step, the monomers contribute in dissolving a part of the formed polymer besides the porogenic solvent. Therefore, the precipitated insoluble gel nuclei dissolve by the present monomers in the solvent around these nuclei. The solvent continues to be allocated in the pores of the crosslinked polymer. Then, polymerization extends in the solution or with the swollen parts inside [50]. In addition, the branching chains in the solution will be trapped with the growing nuclei leading to an increase in size. Then, large nuclei gather to form clusters. These polymeric clusters are spread in the solution with continuous growth. They have a big size permitting them to compose an interconnected matrix in the medium. Eventually, this matrix will provide a porous polymeric substrate. It is convincing to investigate the pore size of the polymers via their spread in the solution. However, changing the polymerization method leads to variation in the pore distribution. The interfacial tension between monomers and the solvent has an essential aspect informing the required polymer. Upon performing suspension polymerization, surface tension leads to decrease in the size of the solvent droplet. This will contribute to reducing the pore size in the monolith. The size diminishes due to induced shrinking during the polymerization process. The interfacial tension exerts pressure on the surface of the drop of the solvent, with keeping its shape as a sphere.

### 2.3. Boosting the mass transfer via convection.

Using large-pores polymeric monoliths demonstrated that mass transfer increases by convection [51]. The mobile phase elevates the mass transfer of solutes. However, many polymers exhibit pores up to 100 nm, do not suit convective transport. Then, new materials for having bigger spaces have been developed. Porous poly(styrene-codivinylbenzene) poly(Sty-co-DVB) particles with pores of approximately 400 nm were employed in separating biopolymers. The eluent passes between the inter-particle voids since the transport that occurs by convection [51,52] is only 2% of the total amount. This low percentage besides the increase in pore volume is adequate to enhance separating biopolymers. The main characteristic of these novel polymer monolithic materials is raising the mass transfer by convection. The mobile phase has to cross the separation medium with a dynamic binding capacity. They are independent on the flow rate. The path of crossing the mobile phase through columns loaded with polymer monoliths in comparison with beads is illustrated in Figure 3.

Polymeric monolithic columns create a single continuous pathway filling the whole column. Hence, a series of continuous

pores form a connected passage. It is composed of attached holes that compose flow channels with a specific size [53]. The polymer monolithic column creates interconnected channels in the porous matrix with high permeability. The inner surface area increases leading to decrease the back pressure than that in the traditional columns with separate pores. In addition, the presence of channels provides good contact between the components inside the monolith [54]. Monoliths with micro-sized pores are able to carry out convective flow. Monoliths with soft gels based on poly(acrylamide) (polyAAm) were developed in 1989 for separating proteins [55,56]. Thereafter, polymer monolith materials were prepared by Tennikova and Svec [57] from organic monomers, in a tubular mold. Cartridges were used to keep these polymeric substrates to be applied in separating high molecular weight materials. Svec and Frechet [1] developed the monoliths which have been previously prepared to be utilized as columns. They were synthesized via *in-situ* polymerization inside tube having micro-sized diameter. Moreover, Tanaka [58] and Sestak [59] worked on employing sol-gel method to enhance the performance of porous silica monoliths. These research studies were performed to achieve an enhancement in the features and efficiencies of the prepared monoliths. Moreover, these improved substrates show effective and functional alternatives when compared with polymeric beads applied in various applications.



**Figure 3.** The pathway of the mobile phase in a monolith and beads.

Recently, monoliths are *in-situ* prepared and shaped in any geometry form such as disks, rods and capillary columns. Their sizes range from liters down to a few microliters in the channel of the monolithic column [60]. On the other hand, Svec [36,48] and Wu [61] determined the progress in enhancing the monolithic stationary phases. They concentrated on micro-sized chromatographic separations. Moreover, Svec determined to utilize the polymeric monoliths in solid phase extraction beside the designed capillaries for gas chromatographic separations [62].

Svec prepared continuous rods known as monoliths [1]. Polymerization took place by employing glycidyl methacrylate (GMA) as monomer and ethylene glycol dimethacrylate (EGDMA) crosslinking agent. The setup of this process was thermally in the presence of cyclohexanol and dodecanol as porogenic solvents and azo-bis-isobutyro-nitrile (AIBN) as initiator. In the preliminary experiments, applying these monoliths was not encouraging upon being subjected to separation implications. The experiment lasted for more than half an hour to separate proteins like myoglobin and cytochrome C. This was correlated to the formed pores inside the monolith which was

### 3. SOME APPLICATIONS OF POLYMERIC MONOLITHS

There are several applications for polymeric monoliths. Among these applications, separation can be determined including chromatographic and electrochromatographic ones beside catalytic applications.

prepared by suspension polymerization [63]. The main cause is the difference in porosity between monoliths and polymeric beads prepared via suspension polymerization that led to making a change in the interfacial tension [64]. The monolithic column is composed of interconnected globules with diameter. These microglobules were originated in the polymerization process to build up the monolith. An enormous number of molecules were formed and connected together. These interconnected nuclei have small sizes, with tiny pores leaving a little pore volume in-between.

#### 2.4. Factors affecting the efficiency of polymeric monoliths.

**2.4.1. Polymerization temperature.** The polymerization kinetics are highly affected by temperature [65,66]. The half-time to decompose azo-bis-isobutyro-nitrile (AIBN) in styrene is 5.7 hours at 70 °C. Upon increasing the temperature to 110 °C, the decomposition time is about 3.2 minutes. The quick degradation of initiator provides a lot of expanding polymer chains [65,66]. The quantity and the polarity of the porogenic solvent plays a role in determining the pore size inside the monolithic column. The perfect solvent assists in forming interconnected pores while the poor one leads to scattered pores. The interconnected pores are spaces inside the monolithic column that conserves the structure for a continuous phase of the polymer. As a consequence, polymeric aggregates results in a non-uniform structure.

**2.4.2. Porogenic solvents.** Poor solvent in the absence of crosslinking agent leads to a glassy and fragile monolithic structure. In this aspect, selecting a porogen depends on the polarity of both the monomer and the crosslinker. Raising the amounts of alcohols provides the monolithic columns with larger pores. Acrylamide/N,N'-methylene-bisacrylamide monoliths have been prepared by using a mixture of dimethyl sulfoxide (DMSO) and 2-heptanol solvents [64]. Non-polar styrene/divinylbenzene (DVB) monoliths are synthesized in the presence of a mixture of decanol and tetrahydrofuran (THF) [67]. Nonpolar norborn-2-ene and cyclo-octene monoliths [62,63,68] are prepared in the presence of mixtures of 2-propanol and toluene. CO<sub>2</sub> has been selected as a promising porogen in preparing ethylene glycol dimethacrylate or trimethylolpropanetri-methacrylate polymer monoliths [69]. The specific surface area depends on the exerted CO<sub>2</sub> pressure [70].

**2.4.3. Functionalization.** Acrylate based monolithic substrates are ideal materials for separation. Functionalization is significant to implement polymer monoliths systems in specific applications. They are used in separation and catalysis. To obtain successful functionalization, the following conditions have to be considered : 1) The copolymerization of functional monomers. 2) Secondary functionalization or grafting [71]. Functionalization takes place by means of grafting mercapto, amino or surface carboxylic groups of the monolith. These groups can act as chelating agents. They facilitate surface depositing metal nanoparticles. Hence, more efficiency can be provided to the prepared monoliths.

#### 3.1. Chromatographic separation.

Researchers paid a lot of efforts to improve novel techniques to reach a high level and advanced results in separating polar nuclei [17,22,45,72]. They focused on separating immiscible

mixture in chromatographic investigations. Developing these methods depends on preparing and using efficient and permeable substrates as stationary phases. In the coming section, some studies will be discussed which are interested in preparing and using hydrophilic polymeric monoliths polymers. These monolithic stationary phases are applied in chromatographic and electro-chromatographic domains. The stationary phase allows interacting sites to separate analytes with generating electro-osmotic flow in the monolithic capillary tube. Hydrophilic polymer monoliths are prepared by utilizing water soluble monomer. N,N'-dimethyl- N-methacryloxyethyl-N-(3-sulfopropyl) ammonium betaine as a hydrophilic monomer was polymerized with ethylene dimethacrylate after applying pressure in the capillary tube. The resulting polymer is a hydrophilic permeable monolith with an electrostatic interacting surface with proteins. Preparing monolithic columns was carried out for separating pyrimidic nuclei [73]. Primarily, N-acryloxy-succinimide (NAS) was copolymerized in the presence of ethylene dimethacrylate (EDMA) as crosslinker. A hydrophilic polymer monolith was then formed after the polymerization process. This was followed by surface grafting of alkyl-diamine through aminolysis while the remaining N-hydroxysuccinimide groups were hydrolyzed. The produced primary amine and carboxylic acid moieties offered charges on the surface. These charges depend on the pH of the mobile phase. The hydrophilic nature of the monoliths is related to the length of the aliphatic segment (hexa-methylene against ethylene) in the alkyldiamine. Among the commonly used negatively charged polymers, methacrylic acid-containing polymers are mentioned [74]. Poly methyl methacrylate (MAA) - *co*- ethylene dimethacrylate (EDMA) prepared in acetonitrile as a polar solvent is regarded as an efficient monolithic capillary in chromatographic separations [75]. The tendency of the monolith to possess a hydrophilic nature does not rely upon the amount of MAA and EDMA only. It relies on the behavior of the solvent as well. Polymeric monoliths using a porogenic solvents of dimethyl sulfoxide and poly(ethylene glycol) (PEG) showed a potent hydrophilic behavior when compared with monolith prepared in the presence of hydrophobic solvents such as toluene and dodecanol. This monolith was used in separating bovine serum albumin. Some studies reported copolymerizing 2-dimethyl aminoethyl methacrylate (DMAEMA), hydroxyethyl methacrylate (HEMA) and ethylene dimethacrylate (EDMA) [76]. The monolith showed surface functionality for anion exchange and mixed separation. N-acryloxy-succinimide (NAS) based monoliths give successful porous polymeric columns [77]. Hydrophilic monoliths were prepared via surface functionalization of poly(NAS-*co*-EDMA) in a two-step process [78]. The primary step occurs through surface grafting of allylamine providing surface grafted thiol-sensitive alkene molecules. Then, a radical addition of oligo ethylene glycol with thiol end-functionality. The resulting monolithic column can interact efficiently with poly-hydroxylated aromatic molecules.

Metal or metal oxide nanoparticles, like those of gold, silver, platinum or palladium are used as organometallic nanocatalysts. Immobilizing these nanometals on solid surfaces provides brilliant solutions for avoiding the aggregation of nanoparticles with adjusting metal distribution onto the surfaces. The metal nanoparticles have the advantage of being bio-friendly, biosafety

and biocompatibility [79]. Gold nanoparticles (GNPs) are among the important nanoparticles used to functionalize monoliths for separation applications. Some studies discussed using carbon-based nanoparticles such as carbon nanotubes and fullerene hollow spheres. These nanoparticles supply efficient separation processes [80,81]. Tailoring the surface of polymer monoliths for certain purposes via grafting thiol, carboxylic or amine chelating groups has a strong effect in distributing the gold nanoparticles homogeneously on the monolithic surfaces.

Surface functionalization strategy includes grafting of propargyl-amine by nucleophilic substitution. This is followed by radical addition of cysteamine through photo-activated radical addition. Photo-initiation of thiol-yne assisted in controlling the chelating behavior in the monolithic matrix. The adsorbed gold nanoparticles have an average size of 20 nm. The chelating properties of the amino-gold monolith [82] surface were characterized by their highly hydrophilic nature. [83,84]. Svec determined the preparation of thiol-functionalized monoliths through aminolysis of poly(glycidyl methacrylate- *co*-EDMA) with cysteamine [85]. Depositing gold nanoparticles on the monolithic surface occurred in two steps. *In-situ* reduction of chloroauric acid was the first step followed by adsorbing gold nanoparticles onto the monolithic surface. Thiol-containing molecules are able to build up strong sulphur-gold bonds on the surface. The dynamic behavior of the gold-thiol bonds facilitates various functional groups to bind with the monolithic structure. Silver nanoparticles are a good representative for metal nanoparticles to deposit on the surface of monoliths. They have immobilized on the surface of glycidyl-methacrylate based monoliths. The generated monolithic columns are able to detect proteins [86]. The used monoliths were used after polymerization process without surface treatment.

### 3.2. Electrochromatographic separation.

A hybrid inorganic-organic monolith with stellated mesoporous silica nanoparticles (SMSNs) was synthesized [87]. In the presence of acetonitrile and acetic acid as porogenic solvents at room temperature, an SMSN- monolith of poly(butyl methacrylate-coethylene glycol dimethacrylate) showed a permeable and uniform structure. To investigate the behavior of the prepared SMSN-monolith, the aforementioned monolith was compared with neat SMSN-free monolith in separating small molecules. This monolith was tested in capillary electrochromatographic experiments [88,89].

Small molecules containing alkylbenzenes, anilines, naphthalenes and phenols were selected for separation. The SMSN-monolith exhibited better results with high resolution and effectiveness when compared with the SMSN-free monolith in separating the selected materials. For alkylbenzene samples containing eight compounds, elution order was as follow acetone, 2,5-dihydroxyacetophenone, acetophenone, butyrophenone, toluene, ethylbenzene, propylbenzene, butylbenzene. On the other hand, the SMSN-free monolith showed inadequate separation with asymmetrical peaks. The baseline separation was not clearly recognized upon having the same experimental conditions. A polymeric monolith was synthesized in glass chips [90]. It was then applied in electrochromatographic implications. The monomer was introduced to the glassy mold by using a high pressure pump [91]. The monolith consists of acrylate monomer

prepared via photopolymerization. Ultraviolet (UV) initiation polymerization permits forming a polymeric monolith in the chips [92]. These monoliths were polymerized in less than 10 minutes. The monolith was employed in separating bioactive peptides and amino acids. The performance was acceptable showing rapid and efficient results. This study showed an added value which is presented in regenerating the glass chips. The removal of the used polymer was carried out by incinerating it to restore a clean glassy matrix (mold) for use in further investigations.

### 3.3. Catalytic application.

Loading metal nanoparticles onto the monolithic surfaces offered an opportunity to apply these polymeric rods in catalytic purposes. Gold nanoparticles drew the attention of the scientists due to their facile synthesis and functionalization. Monolithic polymers with chelating surface were prepared in a two steps [93]. First, a UV-induced free radical polymerization of N-acryloxy-succinimide (NAS) and ethylene dimethacrylate (EDMA). Then, surface grafting of ethylene diamine on the surface to produce a hydrophilic monolith with the chelating surface. The prepared monolith was loaded with gold nanoparticles (GNPs) through forming a complex of either commercial Au<sup>0</sup> nanoparticles or Au<sup>3+</sup> precursor salt. This was followed by *in-situ* reduction. The process took place in capillary tubes [94,95] with micro-sized diameters. The catalytic reactivity of these monolithic columns towards reducing the polluting nitrophenol isomers, namely 2-nitrophenol, 3-nitrophenol and 4-nitrophenol, and 4-nitroaniline

was evaluated by using UV-vis spectroscopic investigations. The results confirmed the reduction process as a result of forming the corresponding amino derivatives with lower polluting impact. This research emphasized that the *in-situ* reduction process for immobilizing gold nanoparticles allowed high reaction yield with preserving the permeability of the monolithic capillary. Scanning electron microscopy (SEM) illustrates the morphology for the monolithic structure of poly(NAS-co-EDMA). An ideal porous form for attached globules is observed. The morphologies of *in-situ* (a and b) and *ex-situ* (c) are compared. It shows the distribution of GNPs on the monolithic surface. The *in-situ* prepared GNPs showed homogenous distribution while the *ex-situ* (commercial) GNPs are present as aggregates [96,97]. In fact, the *in-situ* ones behaved more ideally with easier flow inside the capillary tube. This results in better performance and more efficient catalytic activity for the monolithic column. The catalytic activity of *ex-situ* and *in-situ* monolithic columns (10 cm) was compared at a flow rate of 15 mL/min. This was carried out to confirm the inhomogeneity of *ex-situ* deposited gold nanoparticles. From the results, the *in-situ* capillary column exceeds the *ex-situ* one. The *in-situ* monolith succeeded in completing the catalytic reduction of the pollutant 4-nitrophenol and changing it to 4-aminophenol which has lower pollutant effect. On the other hand, the *ex-situ* monolith did not accomplish the reduction reaction properly.

## 4. CONCLUSIONS

Porous polymeric monoliths are commonly formed as continuous rods or columns. These materials have been prepared to overcome some deficiencies that arose from using the corresponding traditional monoliths such as ceramic and metallic ones. Polymeric monoliths are commonly used in chromatographic separation applications beside catalytic implications. These monoliths represent the stationary phase. They are composed mainly of suitable monomer(s) beside a crosslinking agent and a radical initiator. The thermally or UV induced polymerization reaction can be initiated in a mold. After completing the polymerization process, the monolith is washed and dried to get rid of excess molecules to be ready for use. The porogenic solvent is an important factor for creating pores that allow the passage of the tested molecules as the mobile phase through the polymer monolithic system. During the polymerization process, the pores are formed. The solvent possesses a big volume permitting it to compose an interconnected matrix in the medium that includes voids. Eventually, this assists in constructing a porous polymeric substrate. The spreading pore sizes in the macroporous polymers can be estimated. It is possible to determine the spreading pore sizes in the macroporous polymers. The quantity of the solvent assists in determining the pore size inside the monolithic column. The distances between spaces in the polymer chains vary according to the amount of the

solvent in the polymerization solution. The perfect solvent assists in forming interconnected pores while the poor one leads to sporadic pores.

The functional groups on the monolithic surface dominate the performance of the monolith. Increasing the efficiency of the monolith can be achieved via grafting the surface. Immobilizing nanoparticles; mainly the metallic ones onto the surface of the polymeric monolith boosts the performance of these columns and expands their application fields. Depositing the metal nanoparticles takes place via *in-situ* reduction of metal nanoparticles from their precursor salts or via *ex-situ* loading of previously prepared nanoparticles.

Among the common applications for polymeric monoliths; separation of proteins, small and large molecules are determined. The flow of the tested species is affected by their polarity. To assure an easy transfer of the mobile phase through the monolithic column, convection can be introduced to facilitate the transfer of the molecules at suitable temperatures. To extend the separation application, polymeric monoliths can be applied in electrochromatographic separations. Besides, catalytic reactions can take place inside these monolithic rods. The performance of these monoliths can be enhanced by immobilizing metal nanoparticles on their surfaces to provide efficient catalytic reactions.

## 5. REFERENCES

1. Svec, F.; Frechet, J.M. Continuous rods of macroporous polymer as high-performance liquid chromatography separation media. *Analytical Chemistry* **1992**, *64*, 820-822, <https://doi.org/10.1021/ac00031a022>.
2. Viklund, C.; Nordstrom, A.; Irgum, K.; Svec, F.; Frechet, J.M. Preparation of porous poly(styrene-co-divinylbenzene) monoliths with controlled pore size distributions initiated by stable free radicals and their pore surface functionalization by

- grafting. *Macromolecules* **2001**, *34*, 4361-4369, <https://doi.org/10.1021/ma001435+>.
3. Rohr, T.; Yu, C.; Davey, M.H.; Svec, F.; Frechet, J.M. Porous polymer monoliths: simple and efficient mixers prepared by direct polymerization in the channels of microfluidic chips. *Electrophoresis* **2001**, *22*, 3959-3967, [https://doi.org/10.1002/1522-2683\(200110\)22:18<3959::AID-ELPS3959>3.0.CO;2-5](https://doi.org/10.1002/1522-2683(200110)22:18<3959::AID-ELPS3959>3.0.CO;2-5).
4. Yu, C.; Xu, M.; Svec, F.; Frechet, J.M. Preparation of monolithic polymers with controlled porous properties for microfluidic chip applications using photoinitiated free-radical polymerization. *Journal of Polymer Science Part A: Polymer Chemistry* **2002**, *40*, 755-769, <https://doi.org/10.1002/pola.10155>.
5. Tsujioka, N.; Hira, N.; Aoki, S.; Tanaka, N.; Hosoya, K. A new preparation method for well-controlled 3D skeletal epoxy resin-based polymer monoliths. *Macromolecules* **2005**, *38*, 9901-9903, <https://doi.org/10.1021/ma051409h>.
6. Minakuchi, H.; Nakanishi, K.; Soga, N.; Ishizuka, N.; Tanaka, N. Octadecylsilylated porous silica rods as separation media for reversed-phase liquid chromatography. *Analytical chemistry* **1996**, *68*, 3498-3501, <https://doi.org/10.1021/ac960281m>.
7. Cooper, A.I.; Wood, C.D.; Holmes, A.B. Synthesis of well-defined macroporous polymer monoliths by sol-gel polymerization in supercritical CO<sub>2</sub>. *Industrial & engineering chemistry research* **2000**, *39*, 4741-4744, <https://doi.org/10.1021/ie000159k>.
8. Kanamori, K.; Yonezawa, H.; Nakanishi, K.; Hirao, K.; Jinnai, H. Structural formation of hybrid siloxane-based polymer monolith in confined spaces. *Journal of separation science* **2004**, *27*, 874-886, <https://doi.org/10.1002/jssc.200401816>.
9. Dulay, M.T.; Quirino, J.P.; Bennett, B.D.; Kato, M.; Zare, R.N. Photopolymerized Sol-Gel Monoliths for Capillary Electrochromatography. *Analytical chemistry* **2001**, *73*, 3921-3926, <https://doi.org/10.1021/ac0100749>.
10. Feinle, A.; Elsaesser, M.S.; Huesing, N. Sol-gel synthesis of monolithic materials with hierarchical porosity. *Chemical Society Reviews* **2016**, *45*, 3377-3399, <https://doi.org/10.1039/C5CS00710K>.
11. Causon, T.J.; Nischang, I. Critical differences in chromatographic properties of silica-and polymer-based monoliths. *Journal of Chromatography A* **2014**, *1358*, 165-171, <https://doi.org/10.1016/j.chroma.2014.06.102>.
12. Urban, J.; Svec, F.; Frechet, J.M. Efficient separation of small molecules using a large surface area hypercrosslinked monolithic polymer capillary column. *Analytical chemistry* **2010**, *82*, 1621-1623, <https://doi.org/10.1021/ac100008n>.
13. Arrua, R.D.; Talebi, M.; Causon, T.J.; Hilder, E.F. Review of recent advances in the preparation of organic polymer monoliths for liquid chromatography of large molecules. *Analytica Chimica Acta* **2012**, *738*, 1-12, <https://doi.org/10.1016/j.aca.2012.05.052>.
14. Lubbad, S.H.; Buchmeiser, M.R. Highly cross-linked polymeric capillary monoliths for the separation of low, medium, and high molecular weight analytes. *Journal of separation science* **2009**, *32*, 2521-2529, <https://doi.org/10.1002/jssc.200900188>.
15. Trojer, L.; Bisjak, C.P.; Wieder, W.; Bonn, G.K. High capacity organic monoliths for the simultaneous application to biopolymer chromatography and the separation of small molecules. *Journal of Chromatography A* **2009**, *1216*, 6303-6309, <https://doi.org/10.1016/j.chroma.2009.07.010>.
16. Nischang, I.; Bruggemann, O. On the separation of small molecules by means of nano-liquid chromatography with methacrylate-based macroporous polymer monoliths. *Journal of Chromatography A* **2010**, *1217*, 5389-5397, <https://doi.org/10.1016/j.chroma.2010.06.021>.
17. Karbarz, M.; Khalil, A.M.; Wolowicz, K.; Kaniewska, K.; Romanski, J.; Stojek, Z. Efficient removal of cadmium and lead ions from water by hydrogels modified with cysteine. *Journal of environmental chemical engineering* **2018**, *6*, 3962-3970, <https://doi.org/10.1016/j.jece.2018.05.054>.
18. Koeck, R.; Fischenaller, M.; Bakry, R.; Tessadri, R.; Bonn, G.K. Preparation and evaluation of monolithic poly (N-vinylcarbazole-co-1, 4-divinylbenzene) capillary columns for the separation of small molecules. *Analytical and bioanalytical chemistry* **2014**, *406*, 5897-5907, <https://doi.org/10.1007/s00216-014-8007-1>.
19. Liu, K.; Tolley, H.D.; Lee, M.L. Highly crosslinked polymeric monoliths for reversed-phase capillary liquid chromatography of small molecules. *Journal of Chromatography A* **2012**, *1227*, 96-104, <https://doi.org/10.1016/j.chroma.2011.12.081>.
20. Santora, B.P.; Gagne, M.R.; Moloy, K.G.; Radu, N.S. Poregen and cross-linking effects on the surface area, pore volume distribution, and morphology of macroporous polymers obtained by bulk polymerization. *Macromolecules* **2001**, *34*, 658-661, <https://doi.org/10.1021/ma0004817>.
21. Kanamori, K.; Nakanishi, K.; Hanada, T. Rigid macroporous poly (divinylbenzene) monoliths with a well-defined bicontinuous morphology prepared by living radical polymerization. *Advanced Materials* **2006**, *18*, 2407-2411, <https://doi.org/10.1002/adma.200601026>.
22. Maya, F.; Svec, F. A new approach to the preparation of large surface area poly (styrene-co-divinylbenzene) monoliths via knitting of loose chains using external crosslinkers and application of these monolithic columns for separation of small molecules. *Polymer* **2014**, *55*, 340-346, <https://doi.org/10.1016/j.polymer.2013.08.018>.
23. Augustin, V.; Jardy, A.; Gareil, P.; Hennion, M.C. In situ synthesis of monolithic stationary phases for electrochromatographic separations: Study of polymerization conditions. *Journal of Chromatography A* **2006**, *1119*, 80-87, <https://doi.org/10.1016/j.chroma.2006.02.057>.
24. Gusev, I.; Huang, X.; & Horvath, C. Capillary columns with in situ formed porous monolithic packing for micro high-performance liquid chromatography and capillary electrochromatography. *Journal of Chromatography A* **1999**, *855*, 273-290, [https://doi.org/10.1016/S0021-9673\(99\)00697-4](https://doi.org/10.1016/S0021-9673(99)00697-4).
25. Potter, O.G.; Hilder, E.F. Porous polymer monoliths for extraction: Diverse applications and platforms. *Journal of separation science* **2008**, *31*, 1881-1906, <https://doi.org/10.1002/jssc.200800116>.
26. Cantillo, D.; Kappe, C.O. Immobilized Transition Metals as Catalysts for Cross-Couplings in Continuous Flow—A Critical Assessment of the Reaction Mechanism and Metal Leaching. *ChemCatChem* **2014**, *6*, 3286-3305, <https://doi.org/10.1002/cctc.201402483>.
27. Nagaki, A.; Hirose, K.; Moriwaki, Y.; Takumi, M.; Takahashi, Y.; Mitamura, K.; Matsukawa, K.; Ishizuka, N.; Yoshida, J. I. Suzuki-Miyaura Coupling Using Monolithic Pd Reactors and Scaling-Up by Series Connection of the Reactors. *Catalysts* **2019**, *9*, 300, <https://doi.org/10.3390/catal9030300>.
28. Anderson, E.B.; Buchmeiser, M.R. Catalysts immobilized on organic polymeric monolithic supports: from molecular

- heterogeneous catalysis to biocatalysis. *ChemCatChem* **2012**, *4*, 30-44, <https://doi.org/10.1002/cctc.201100086>.
29. Kupgan, G.; Abbott, L.J.; Hart, K.E.; Colina, C.M. Modeling amorphous microporous polymers for CO<sub>2</sub> capture and separations. *Chemical reviews* **2018**, *118*, 5488-5538, <https://doi.org/10.1021/acs.chemrev.7b00691>.
30. He, Y.; Benedetti, F.M.; Lin, S.; Liu, C.; Zhao, Y.; Ye, H.Z.; Voorhis, T.V.; De Angelis, M.G.; Swager, T.M.; Smith, Z.P. Polymers with side chain porosity for ultrapermeable and plasticization resistant materials for gas separations. *Advanced Materials* **2019**, *31*, 1807871, <https://doi.org/10.1002/adma.201807871>.
31. Huang, J.; Turner, S.R. Hypercrosslinked polymers: a review. *Polymer Reviews* **2018**, *58*, 1-41, <https://doi.org/10.1080/15583724.2017.1344703>.
32. Brooijmans, T.; Okhuijsen, R.A.; Oerlemans, G.M.M.; Pirok, B.W.J.; Schoenmakers, P.J.; Peters, R.A.H. Heterogeneity analysis of polymeric carboxylic acid functionality by selective derivatization followed by size exclusion chromatography. *Analytical chimica acta* **2019**, *1072*, 87-94, <https://doi.org/10.1016/j.aca.2019.04.051>.
33. Nischang, I. On the chromatographic efficiency of analytical scale column format porous polymer monoliths: Interplay of morphology and nanoscale gel porosity. *Journal of Chromatography A* **2012**, *1236*, 152-163, <https://doi.org/10.1016/j.chroma.2012.03.017>.
34. Laher, M.; Causon, T.J.; Buchberger, W.; Hild, S.; Nischang, I. Assessing the nanoscale structure and mechanical properties of polymer monoliths used for chromatography. *Analytical chemistry* **2013**, *85*, 5645-5649, <https://doi.org/10.1021/ac401303k>.
35. Tripathi, A.K.; Tsavalas, J.G.; Sundberg, D.C. Monte Carlo simulations of free radical polymerizations with divinyl cross-linker: pre-and postgel simulations of reaction kinetics and molecular structure. *Macromolecules* **2014**, *48*, 184-197, <https://doi.org/10.1021/ma502085x>.
36. Svec, F.; Frechet, J.M. Kinetic control of pore formation in macroporous polymers. Formation of "molded" porous materials with high flow characteristics for separations or catalysis. *Chemistry of materials* **1995**, *7*, 707-715, <https://doi.org/10.1021/cm00052a016>.
37. Hormann, K.; Tallarek, U. Mass transport properties of second-generation silica monoliths with mean mesopore size from 5 to 25 nm. *Journal of Chromatography A* **2014**, *1365*, 94-105, <https://doi.org/10.1016/j.chroma.2014.09.004>.
38. Nischang, I. Impact of biomolecule solute size on the transport and performance characteristics of analytical porous polymer monoliths. *Journal of Chromatography A* **2014**, *1354*, 56-64, <https://doi.org/10.1016/j.chroma.2014.05.053>.
39. Kip, C.; Erkakan, D.; Gokaltun, A.; Celebi, B.; Tuncel, A. Synthesis of a reactive polymethacrylate capillary monolith and its use as a starting material for the preparation of a stationary phase for hydrophilic interaction chromatography. *Journal of Chromatography A* **2015**, *1396*, 86-97, <https://doi.org/10.1016/j.chroma.2015.04.005>.
40. Li, Y.; Tolley, H.D.; Lee, M.L. Preparation of polymer monoliths that exhibit size exclusion properties for proteins and peptides. *Analytical chemistry* **2009**, *81*, 4406-4413, <https://doi.org/10.1021/ac900364d>.
41. Mizuno, S.; Asoh, T.A.; Takashima, Y.; Harada, A.; Uyama, H. Cyclodextrin cross-linked polymer monolith for efficient removal of environmental pollutants by flow-through method. *Polymer degradation and stability* **2019**, *160*, 136-141, <https://doi.org/10.1016/j.polymdegradstab.2018.12.014>.
42. Catala-Icardo, M.; Torres-Cartas, S.; Meseguer-Lloret, S.; Simo-Alfonso, E.F.; Herrero-Martinez, J.M. Photografted fluoropolymers as novel chromatographic supports for polymeric monolithic stationary phases. *Talanta* **2018**, *187*, 216-222, <https://doi.org/10.1016/j.talanta.2018.05.026>.
43. Vaast, A.; Novakova, L.; Desmet, G.; de Haan, B.; Swart, R.; Eeltink, S. High-speed gradient separations of peptides and proteins using polymer-monolithic poly (styrene-co-divinylbenzene) capillary columns at ultra-high pressure. *Journal of Chromatography A* **2013**, *1304*, 177-182, <https://doi.org/10.1016/j.chroma.2013.07.040>.
44. Koeck, R.; Bakry, R.; Tessadri, R.; & Bonn, G.K. Monolithic poly (N-vinylcarbazole-co-1, 4-divinylbenzene) capillary columns for the separation of biomolecules. *Analyst* **2013**, *138*, 5089-5098, <https://doi.org/10.1039/C3AN00377A>.
45. Wang, Y.; Ma, S.; Chen, Y.; Zhang, L.; Ou, J.; Shen, Y.; Ye, M. Thiol-radical-mediated polymerization for preparation of POSS-containing polyacrylate monoliths in capillary liquid chromatography. *Talanta* **2018**, *190*, 62-69, <https://doi.org/10.1016/j.talanta.2018.07.061>.
46. Gu, B.; Armenta, J.M.; Lee, M.L. Preparation and evaluation of poly (polyethylene glycol methyl ether acrylate-co-polyethylene glycol diacrylate) monolith for protein analysis. *Journal of Chromatography A* **2005**, *1079*, 382-391, <https://doi.org/10.1016/j.chroma.2005.02.088>.
47. Tan, A.; Benetton, S.; Henion, J.D. Chip-based solid-phase extraction pretreatment for direct electrospray mass spectrometry analysis using an array of monolithic columns in a polymeric substrate. *Analytical chemistry* **2003**, *75*, 5504-5511, <https://doi.org/10.1021/ac030196w>.
48. Safrany, A.; Beiler, B.; Laszlo, K.; Svec, F. Control of pore formation in macroporous polymers synthesized by single-step  $\gamma$ -radiation-initiated polymerization and cross-linking. *Polymer* **2005**, *46*, 2862-2871, <https://doi.org/10.1016/j.polymer.2005.02.024>.
49. Kanamori, K.; Hasegawa, J.; Nakanishi, K.; Hanada, T. Facile synthesis of macroporous cross-linked methacrylate gels by atom transfer radical polymerization. *Macromolecules* **2008**, *41*, 7186-7193, <https://doi.org/10.1021/ma800563p>.
50. Okay, O. Macroporous copolymer networks. *Progress in polymer science* **2000**, *25*, 711-779, [https://doi.org/10.1016/S0079-6700\(00\)00015-0](https://doi.org/10.1016/S0079-6700(00)00015-0).
51. Smits, W.; Nakanishi, K.; & Desmet, G. The chromatographic performance of flow-through particles: A computational fluid dynamics study. *Journal of Chromatography A* **2016**, *1429*, 166-174, <https://doi.org/10.1016/j.chroma.2015.12.019>.
52. Maier, R.S.; Schure, M.R. Transport properties and size exclusion effects in wide-pore superficially porous particles. *Chemical engineering science* **2018**, *185*, 243-255, <https://doi.org/10.1016/j.ces.2018.03.041>.
53. Arrua, R.D.; Strumia, M.C.; Alvarez Igarzabal, C.I. Macroporous monolithic polymers: preparation and applications. *Materials* **2009**, *2*, 2429-2466, <https://doi.org/10.3390/ma2042429>.
54. Svec, F.; Huber, C.G. Monolithic materials: promises, challenges, achievements *Analytical Chemistry* **2006**, *78*, 2100-2107, <https://doi.org/10.1021/ac069383v>.
55. Vlach, E.G.; Tennikova, T.B. Applications of polymethacrylate-based monoliths in high-performance liquid



- chromatography. *Journal of Chromatography A* **2009**, *1216*, 2637-2650, <https://doi.org/10.1016/j.chroma.2008.09.090>.
56. Hjerten, S.; Liao, J.L.; Zhang, R. High-performance liquid chromatography on continuous polymer beds. *Journal of Chromatography A* **1989**, *473*, 273-275, [https://doi.org/10.1016/S0021-9673\(00\)91309-8](https://doi.org/10.1016/S0021-9673(00)91309-8).
57. Tennikova, T.B.; Svec, F.; Belenkii, B.G. High-performance membrane chromatography. A novel method of protein separation. *Journal of Liquid chromatography* **1990**, *13*, 63-70, <https://doi.org/10.1080/01483919008051787>.
58. Svec, F. Porous polymer monoliths: amazingly wide variety of techniques enabling their preparation. *Journal of Chromatography A* **2010**, *1217*, 902-924, <https://doi.org/10.1016/j.chroma.2009.09.073>.
59. Sestak, J.; Moravcova, D.; Krenkova, J.; Planeta, J.; Roth, M.; Foret, F. Bridged polysilsesquioxane-based wide-bore monolithic capillary columns for hydrophilic interaction chromatography. *Journal of Chromatography A* **2017**, *1479*, 204-209, <https://doi.org/10.1016/j.chroma.2016.11.062>.
60. Eeltink, S.; Wouters, S.; Dores-Sousa, J.L.; Svec, F. Advances in organic polymer-based monolithic column technology for high-resolution liquid chromatography-mass spectrometry profiling of antibodies, intact proteins, oligonucleotides, and peptides. *Journal of Chromatography A* **2017**, *1498*, 8-21, <https://doi.org/10.1016/j.chroma.2017.01.002>.
61. Wu, R.A.; Hu, L.; Wang, F.; Ye, M.; Zou, H. Recent development of monolithic stationary phases with emphasis on microscale chromatographic separation. *Journal of Chromatography A* **2008**, *1184*, 369-392, <https://doi.org/10.1016/j.chroma.2007.09.022>.
62. Svec, F. Less common applications of monoliths: Preconcentration and solid-phase extraction. *Journal of chromatography B* **2006**, *841*, 52-64, <https://doi.org/10.1016/j.jchromb.2006.03.055>.
63. Dziomba, S.; Araya-Farias, M.; Taverna, M.; Guerrouache, M.; Carbonnier, B.; Tran, N.T. Microscope-assisted UV-initiated preparation of well-defined porous polymer monolithic plugs in glass microchips for peptide preconcentration. *Analytical and bioanalytical chemistry* **2017**, *409*, 2155-2162, <https://doi.org/10.1007/s00216-016-0161-1>.
64. Xie, S.; Svec, F.; Frechet, J.M. Preparation of porous hydrophilic monoliths: Effect of the polymerization conditions on the porous properties of poly (acrylamide-co-N, N'-methylenebisacrylamide) monolithic rods. *Journal of Polymer Science Part A: Polymer Chemistry* **1997**, *35*, 1013-1021, [https://doi.org/10.1002/\(SICI\)1099-0518\(19970430\)35:6<1013::AID-POLA4>3.0.CO;2-5](https://doi.org/10.1002/(SICI)1099-0518(19970430)35:6<1013::AID-POLA4>3.0.CO;2-5).
65. Svec, F.; Frechet, J.M. Temperature, a simple and efficient tool for the control of pore size distribution in macroporous polymers. *Macromolecules* **1995**, *28*, 7580-7582, <https://doi.org/10.1021/ma00126a044>.
66. Viklund, C.; Svec, F.; Frechet, J.M.; Irgum, K. Monolithic, "molded", porous materials with high flow characteristics for separations, catalysis, or solid-phase chemistry: control of porous properties during polymerization. *Chemistry of materials* **1996**, *8*, 744-750, <https://doi.org/10.1021/cm950437j>.
67. Mayr, B.; Holzl, G.; Eder, K.; Buchmeiser, M.R., Huber, C.G. Hydrophobic, pellicular, monolithic capillary columns based on cross-linked polynorbornene for biopolymer separations. *Analytical chemistry* **2002**, *74*, 6080-6087, <https://doi.org/10.1021/ac025919a>.
68. Lubbad, S.; Steiner, S.A.; Fritz, J.S.; Buchmeiser, M.R. Metathesis polymerization-derived monolithic membranes for solid-phase extraction coupled with diffuse reflectance spectroscopy. *Journal of Chromatography A* **2006**, *1109*, 86-91, <https://doi.org/10.1016/j.chroma.2005.11.082>.
69. Cooper, A.I.; Holmes, A.B. Synthesis of molded monolithic porous polymers using supercritical carbon dioxide as the porogenic solvent. *Advanced Materials* **1999**, *11*, 1270-1274, [https://doi.org/10.1002/\(SICI\)1521-4095\(199910\)11:15<1270::AID-ADMA1270>3.0.CO;2-E](https://doi.org/10.1002/(SICI)1521-4095(199910)11:15<1270::AID-ADMA1270>3.0.CO;2-E).
70. Hebb, A.K.; Senoo, K.; Bhat, R.; Cooper, A.I. Structural control in porous cross-linked poly (methacrylate) monoliths using supercritical carbon dioxide as a "pressure-adjustable" porogenic solvent. *Chemistry of materials* **2003**, *15*, 2061-2069, <https://doi.org/10.1021/cm020979j>.
71. Guyot, A.; Bartholin, M. Design and properties of polymers as materials for fine chemistry. *Progress in Polymer Science* **1982**, *8*, 277-331, [https://doi.org/10.1016/0079-6700\(82\)90002-8](https://doi.org/10.1016/0079-6700(82)90002-8).
72. Guerrouache, M.; Khalil, A.M.; Kebe, S.; Le Droumaguet, B.; Mahouche-Chergui, S.; Carbonnier, B. Monoliths bearing hydrophilic surfaces for in vitro biomedical samples analysis. *Surface Innovations* **2015**, *3*, 84-102, <https://doi.org/10.1680/sufi.14.00011>.
73. Guerrouache, M.; Pantazaki, A.; Millot, M.C.; Carbonnier, B. Zwitterionic polymeric monoliths for HILIC/RP mixed mode for CEC separation applications. *Journal of separation science* **2010**, *33*, 787-792, <https://doi.org/10.1002/jssc.200900681>.
74. Wang, X.; Lu, H.; Lin, X.; Xie, Z. Electrochromatographic characterization of methacrylate-based monolith with mixed mode of hydrophilic and weak electrostatic interactions by pressurized capillary electrochromatography. *Journal of Chromatography A* **2008**, *1190*, 365-371, <https://doi.org/10.1016/j.chroma.2008.02.106>.
75. Chen, M.L.; Li, L.M.; Yuan, B.F.; Ma, Q.; Feng, Y.Q. Preparation and characterization of methacrylate-based monolith for capillary hydrophilic interaction chromatography. *Journal of Chromatography A* **2012**, *1230*, 54-60, <https://doi.org/10.1016/j.chroma.2012.01.065>.
76. Allah, A., Pyell, U. Preparation of cationic mixed-mode acrylamide-based monolithic stationary phases for capillary electrochromatography. *Chromatographia* **2018**, *81*, 1325-1336, <https://doi.org/10.1007/s10337-018-3564-7>.
77. Guerrouache, M.; Carbonnier, B.; Vidal-Madjar, C.; Millot, M.C. In situ functionalization of N-acryloxysuccinimide-based monolith for reversed-phase electrochromatography. *Journal of Chromatography A* **2007**, *1149*, 368-376, <https://doi.org/10.1016/j.chroma.2007.03.039>.
78. Tijnelyte, I.; Babinot, J.; Guerrouache, M.; Valincius, G.; Carbonnier, B. Hydrophilic monolith with ethylene glycol-based grafts prepared via surface confined thiol-ene click photoaddition. *Polymer* **2012**, *53*, 29-36, <https://doi.org/10.1016/j.polymer.2011.11.014>.
79. Lu, J.; Ye, F.; Zhang, A.; Wei, Z.; Peng, Y.; Zhao, S. Preparation and characterization of silica monolith modified with bovine serum albumin-gold nanoparticles conjugates and its use as chiral stationary phases for capillary electrochromatography. *Journal of separation science* **2011**, *34*, 2329-2336, <https://doi.org/10.1002/jssc.201100102>.
80. Chambers, S.D.; Holcombe, T.W.; Svec, F.; Frechet, J.M. Porous polymer monoliths functionalized through copolymerization of a C60 fullerene-containing methacrylate monomer for highly efficient separations of small molecules.

- Analytical chemistry* **2011**, *83*, 9478-9484, <https://doi.org/10.1021/ac202183g>.
81. Fresco-Cala, B.; Carrasco-Correa, E.J.; Cardenas, S.; Herrero-Martinez, J.M. Carbon nanostructures incorporated on methacrylate monoliths for separation of small molecules by nano-liquid chromatography. *Microchemical Journal* **2018**, *139*, 222-229, <https://doi.org/10.1016/j.microc.2018.03.003>.
82. Guerrouache, M.; Mahouche-Chergui, S.; Chehimi, M.M.; Carbonnier, B. Site-specific immobilisation of gold nanoparticles on a porous monolith surface by using a thiol-ene click photopatterning approach. *Chemical Communications* **2012**, *48*, 7486-7488, <https://doi.org/10.1039/C2CC33134A>.
83. Connor, E.E.; Mwamuka, J.; Gole, A.; Murphy, C.J.; Wyatt, M.D. Gold nanoparticles are taken up by human cells but do not cause acute cytotoxicity. *Small* **2005**, *1*, 325-327, <https://doi.org/10.1002/sml.200400093>.
84. Navarro-Pascual-Ahuir, M.; Lerma-Garcia, M.J.; Ramis-Ramos, G.; Simo-Alfonso, E.F.; Herrero-Martinez, J.M. Preparation and evaluation of lauryl methacrylate monoliths with embedded silver nanoparticles for capillary electrochromatography. *Electrophoresis* **2013**, *34*, 925-934, <https://doi.org/10.1002/elps.201200408>.
85. Terborg, L.; Masini, J.C.; Lin, M.; Lipponen, K.; Riekolla, M.L.; Svec, F. Porous polymer monolithic columns with gold nanoparticles as an intermediate ligand for the separation of proteins in reverse phase-ion exchange mixed mode. *Journal of advanced research* **2015**, *6*, 441-448, <https://doi.org/10.1016/j.jare.2014.10.004>.
86. Lin, X.; Li, Y.; Xu, D.; Yang, C.; Xie, Z. Rapid capillary electrochromatographic profiling of phytohormones on a hydrophilic interaction/strong anion-exchange mixed-mode monolith. *Analyst* **2013**, *138*, 635-641, <https://doi.org/10.1039/C2AN36354B>.
87. Aydogan, C.; El Rassi, Z. Monolithic stationary phases with incorporated fumed silica nanoparticles. Part II. Polymethacrylate-based monolithic column with "covalently" incorporated modified octadecyl fumed silica nanoparticles for reversed-phase chromatography. *Journal of Chromatography A* **2016**, *1445*, 62-67, <https://doi.org/10.1016/j.chroma.2016.03.083>.
88. Wang, B.; Chai, W.; Ding, G. The application of functional silica nanoparticles to fulfill the rapid and improved enantioselective capillary electrophoresis separation of amino acid derivatives. *Journal of separation science* **2015**, *38*, 332-338, <https://doi.org/10.1002/jssc.201401016>.
89. Abbott, A.P.; El Ttaib, K.; Frisch, G.; Ryder, K.S.; Weston, D. The electrodeposition of silver composites using deep eutectic solvents. *Physical Chemistry Chemical Physics* **2012**, *14*, 2443-2449, <https://doi.org/10.1039/C2CP23712A>.
90. Throckmorton, D.J.; Shepodd, T.J.; Singh, A.K. Electrochromatography in microchips: reversed-phase separation of peptides and amino acids using photopatterned rigid polymer monoliths. *Analytical Chemistry* **2002**, *74*, 784-789, <https://doi.org/10.1021/ac011077o>.
91. Bedair, M.F.; Oleschuk, R.D. Fabrication of porous polymer monoliths in polymeric microfluidic chips as an electrospray emitter for direct coupling to mass spectrometry. *Analytical chemistry* **2006**, *78*, 1130-1138, <https://doi.org/10.1021/ac051457o>.
92. Deverell, J.A.; Rodemann, T.; Smith, J.A.; Canty, A.J.; Guijt, R.M. UV initiated formation of polymer monoliths in glass and polymer microreactors. *Sensors and Actuators B: Chemical* **2011**, *155*, 388-396, <https://doi.org/10.1016/j.snb.2010.11.020>.
93. Khalil, A.M.; Georgiadou, V.; Guerrouache, M.; Mahouche-Chergui, S.; Dendrinou-Samara, C.; Chehimi, M.M.; Carbonnier, B. Gold-decorated polymeric monoliths: *In-situ* immobilization strategies and flow through catalytic applications towards nitrophenols reduction. *Polymer* **2015**, *77*, 218-226, <https://doi.org/10.1016/j.polymer.2015.09.040>.
94. Connolly, D.; Twamley, B.; Paull, B. High-capacity gold nanoparticle functionalised polymer monoliths. *Chemical Communications* **2010**, *46*, 2109-2111, <https://doi.org/10.1039/B924152C>.
95. Hu, W.; Hong, T.; Gao, X.; Ji, Y. Applications of nanoparticle-modified stationary phases in capillary electrochromatography. *TrAC Trends in Analytical Chemistry* **2014**, *61*, 29-39, <https://doi.org/10.1016/j.trac.2014.05.011>.
96. Lv, Y.; Alejandro, F.M.; Frechet, J.M.; Svec, F. Preparation of porous polymer monoliths featuring enhanced surface coverage with gold nanoparticles. *Journal of Chromatography A* **2012**, *1261*, 121-128, <https://doi.org/10.1016/j.chroma.2012.04.007>.
97. Wu, C.; Liang, Y.; Zhao, Q.; Qu, Y.; Zhang, S.; Wu, Q.; Liang Z.; Zhang, L.; Zhang, Y. Boronate affinity monolith with a gold nanoparticle-modified hydrophilic polymer as a matrix for the highly specific capture of glycoproteins. *Chemistry-A European Journal* **2014**, *20*, 8737-8743, <https://doi.org/10.1002/chem.201402787>.



© 2019 by the authors. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (<http://creativecommons.org/licenses/by/4.0/>).