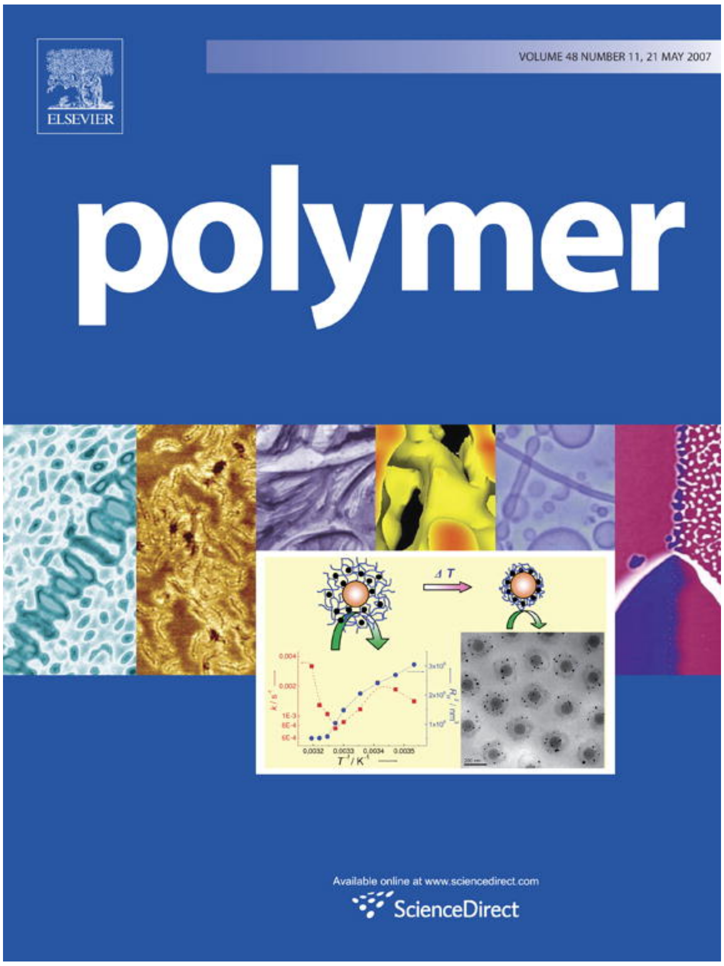
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Poly(2-hydroxyethyl acrylate-*co*-ethyleneglycol dimethacrylate) monoliths synthesized by radiation polymerization in a mold

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Abstract

Copolymer monoliths of diethyleneglycol dimethacrylate and 2-hydroxyethyl-acrylate were prepared by using the advantage of radiation initiated polymerization over the thermally initiated polymerization, namely, that it is sufficient to use only a monomer and a porogenic solvent and no initiator is needed. Besides, the reaction can take place at any desired temperature in a mold of suitable size and shape.

The results showed that increase of the HEA content in the comonomer mixture (up to 18 vol%) resulted in monoliths with increased pore size and hydrophilic character. The specific surface area of these monoliths was in the order of 1 m^2/g. The porous properties could be fine-tuned by changing the solvent.

Flow rate measurements for several eluents indicated that these monoliths could be useful as chromatographic columns. This is illustrated by separation of several amino acids.

Keywords: Polymer monoliths; Radiation polymerization and crosslinking; Chromatography

1. Introduction

Porous polymer blocks, usually called monoliths, came to the front of the research and applications in the early 1990s when Svec and Fréchet prepared them by polymerization and crosslinking inside of a mold [1]. Such porous polymer rods proved to be a useful alternative to columns packed with polymeric beads or particles [2], because monolith columns can be connected to various chromatographic systems [3] immediately after the synthesis, eliminating most of the problems related to the tedious column packing procedure. Monoliths are characterized by a system of interconnected pores with a bimodal distribution: the small pores provide the desired surface area required for the specific interactions, while the larger channels allow a high flow rate at moderate pressures. Therefore, additional advantages of using such monoliths in chromatography would be increased speed, capacity and resolution.

The most widely used method for synthesis of polymer monoliths is the free radical polymerization in a mold, where the column is filled with the mixture of monomers, porogenic solvents, initiators and crosslinker, and the polymerization and crosslinking start by the decomposition of the initiators. The decomposition of the initiator in radical polymerization is usually induced thermally at a specific temperature [4,5]. Another possibility is the photo-induced initiation [6–10]. Drawback of the thermally induced process is that the pore size depends on the temperature, and the UV initiated polymerization is limited by the transparency of the mold and the polymerization mixture, and in some cases also by the diameter of the column [7,8].

We have shown previously that it is also possible to prepare molded monoliths by initiating the polymerization by ionizing

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radiation [11–14]. By this method, the above-mentioned drawbacks of the classical methods can be eliminated. The porous structure of the monoliths can be influenced with the monomer concentration, type of porogenic solvent, temperature, irradiation dose and dose rate [13,14].

Additionally, since a broad range of monomers and porogenic solvents is available, monoliths with adjusted chemical properties and pore size for the intended utilization can be prepared. It is also possible to alter the properties of monoliths by building them from two monomers, either by copolymerization or graft polymerization, which will result in copolymers with new functional surfaces.

The most prevalent copolymer systems are glycidyl methacrylate-*co*-ethylene dimethacrylate (GMA-*co*-EDMA) and poly(styrene-*co*-divinylbenzene) monoliths. The glycidyl methacrylate-based monoliths are especially liked by many, since the epoxy groups can be easily modified according to the intended application (hydrophobic [15], ion exchange [1,16], affinity [17,18] and reversed phase separation media). A number of articles were published about the influence of the temperature and the solvents on the porous structure [4,5,19], and how the grafting alters the surface of the already existing matrix structure, for example, making the column thermally sensitive [20,21]. Svec et al. studied in detail the poly(styrene-*co*-divinylbenzene) monoliths [3–5,22].

In our previous work we showed the influence of the parameters of the radiation synthesis on the porous properties of a system consisting of one monomer, diethyleneglycol dimethacrylate (DEGDMA) in a variety of solvents. We showed the effect of monomer concentration, type of solvent, irradiation temperature, dose and dose rate [13].

Our present paper deals with the effects of the addition of a hydrophilic monomer, 2-hydroxyethyl acrylate (HEA) to DEGDMA/solvent system on the porous structure and flow characteristics of the resulting monolithic column as compared to the monolith prepared from single monomer/solvent system. HEA is easily polymerized and crosslinked into a hydrogel in the presence of minute amount of ethyleneglycol dimethacrylate as crosslinker in different solvents [23,24]. Such hydrogels have also been prepared by radiation initiated polymerization and crosslinking [25].

We have used HEA in order to increase the hydrophilicity of the monolith, and investigated the change of the pore size by introducing HEA gel into the pores. We have also investigated the possibility to use such HEA-containing chromatographic columns for separation of various amino acids by using water as the mobile phase.

2. Experimental

2.1. Materials

Diethyleneglycol dimethacrylate (DEGDMA, Aldrich) and 2-hydroxyethyl acrylate (HEA, SP^2) monomers were used for the preparation of monoliths. The solvents were methanol (AnalityCals, Carlo Erba), ethanol (Reanal), propanol (Merck) and acetonitrile (AnalityCals, Carlo Erba). For chromatographic separation, several amino acids, L-tryptophan (Trp, Merck), tyrosine (Tyr, Merck), histidine (His, Merck) and phenylalanin (Phe, Merck), and a pyrimidine nucleobase, thymine (T, Reagent) were used. All chemicals were HPLC grade and used as received.

2.2. Synthesis and characterization of the monoliths

The monoliths were prepared by an in situ radiation polymerization method. Typically two Teflon tubes (25 mm × 4 mm ID) filled with deoxygenated solution of DEGDMA and HEA in a solvent were placed in plastic bags, sealed under nitrogen and irradiated in a ^{60}Co γ-source. The irradiation conditions were temperature 25 °C, absorbed dose 30 kGy, and dose rates of 11 kGy/h and 16 kGy/h. The dose and dose rate were determined by using ethanol–chlorobenzene dosimeter solution. For each data point, the average from at least three samples prepared under identical irradiation conditions was used. After the irradiation was completed, the excess polymer outside the tube was mechanically removed, and the tube was attached to a chromatographic pump (Liquochrom Model 2010, LMIM, Hungary) via standard chromatographic fittings. Solvents were pumped through the tube to clean it and to determine the flow-through characteristics. The monolith was later removed from the tube and used for further measurements.

The conversion of the monomer into crosslinked polymer was investigated by irradiating deoxygenated solutions of monomers in selected solvents at ^{60}Co γ-source with doses up to 50 kGy, at constant 11 kGy/h dose rate. After irradiation, the obtained polymer was washed several times with the solvent in an ultrasonic bath and dried until constant weight. The conversion was calculated from the weight of the crosslinked polymer as compared to the weight of the monomer in the feed solution.

The morphology of the monoliths was characterized by a JEOL JSM 5600 LV scanning electron microscope (SEM). Thin conducting gold layer was sputtered on the surface of the monolith by using a JEOL JFCI 300AutoFine Coater instrument. The photographs were usually taken with several different magnifications between 500× and 20,000×.

The porous properties of the monoliths were determined by using nitrogen adsorption–desorption isotherms obtained at 77 K by using a Quantachrome Autosorb-1 instrument. The specific surface was calculated from the BET model. The pore-size distribution of the monolithic materials was determined using an Autopore III 9400 mercury intrusion porosimeter (Micromeritics, Norcross, GA).

For chromatographic separations, monoliths were prepared in 128 × 4 mm ID stainless steel chromatographic column. After the irradiation, the column was directly connected to a chromatograph. First the solvent was pumped through to wash the monolith and then acetonitrile, methanol or water was used as the mobile phase for measurements of the back pressure and separation of selected compounds.

3. Results and discussion

The objective of our studies was to determine the relationship between the porous properties of the monoliths and preparation parameters affecting them, to investigate how the addition of a second monomer changes the pore structure of the monolith and how this is reflected in separation of selected compounds.

3.1. Conversion

By irradiating a monomer or a monomer mixture in an organic solvent, free radicals that initiate the polymerization reaction are generated homogeneously in the system. Since one of the monomers used in our monomer mixture (DEGDMA) has two vinyl groups, besides the polymerization, crosslinking will also take place [13,14]. After the formation, the crosslinked, insoluble polymer network precipitates out of the solution, thus changing the homogeneous system to a heterogeneous one. Fig. 1a shows this transformation for the DEGDMA–HEA system, and compares it with the conversion of a single monomer, DEGDMA. It can be seen that the formation of this copolymer monolith does not differ considerably from the formation of the DEGDMA-only network.

Fig. 1b compares the formation of the 18 vol% HEA + 12 vol% DEGDMA monolith in three different alcohols. The

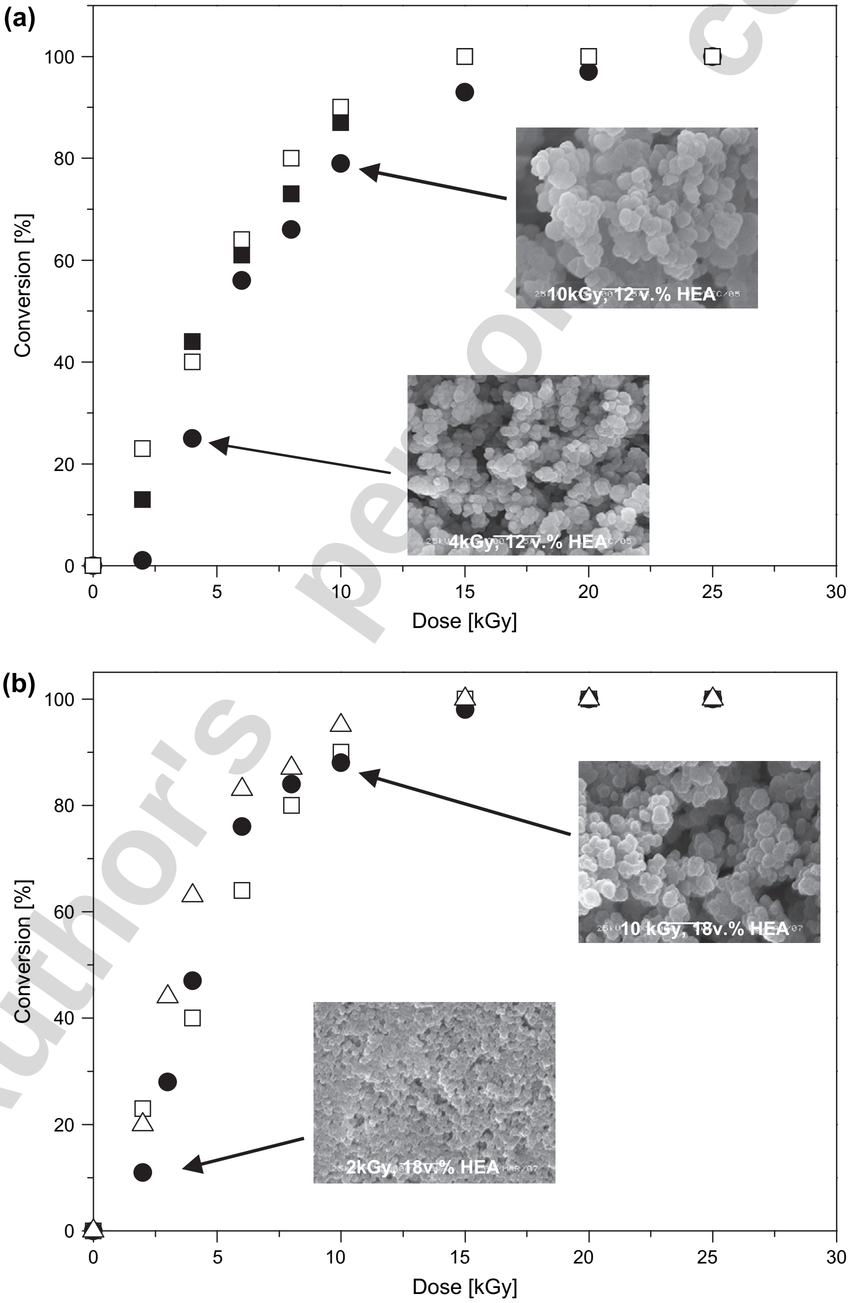

Fig. 1. Reaction kinetics of polymerization and crosslinking in solutions: (a) 30 vol% DEGDMA in methanol (■), 12 vol% HEA + 18 vol% DEGDMA in methanol (●) and 18 vol% HEA + 12 vol% DEGDMA in methanol (□); (b) 18 vol% HEA + 12 vol% DEGDMA in methanol (□), in ethanol (○) and in propanol (△). The irradiation was done at 25 °C, with the dose rate of 11 kGy/h.

curves look similar, but there is indication that the transformation from monomer to a crosslinked polymer is slightly slower in methanol than in ethanol, and is quickest in propanol. At low conversions up to about 15%, the crosslinked polymer is mechanically weak, the porous structure is not yet developed, during freeze-drying it shrinks, and the surface becomes without or with very small pores. At conversions above 20%, the pores and the channels are observable also after drying, but the matrix is soft, and such a monolith could not be used for flow rate measurements. At conversions above 80%, both the porous structure and the mechanical properties of all monoliths were suitable for chromatographic application. Since the magnitude of the dose influences significantly the conversion and in this way the porous structure, for all further experiments samples were prepared with 30 kGy dose.

3.2. Properties of monoliths

It was expected that mixing a good sphere forming monomer (DEGDMA) [26,27] with a hydrophilic monomer (HEA) in a good pore-forming solvent will result in a porous polymer, the hydrophilic character of which can be controlled with the HEA concentration. The influence of the comonomer ratio on the properties of the monoliths was investigated in the following way: the amount of the monomers (DEGDMA + HEA) was set to 30 vol% and the ratio of the 2-hydroxyethylacrylate was varied from 2 vol% up to 22 vol%, while the solvent concentration was a constant 70 vol%. The dose was 30 kGy in all cases.

The results of the porosity measurements are illustrated in Fig. 2 and summarized in Table 1. Since the most substantial contribution to the overall surface area comes from micropores and mesopores, the nitrogen adsorption measurements were used to calculate the specific surface area of the monoliths. Macropores contribute very little to the surface area, but they are essential to allow the liquid to pass through at a low pressure. Mercury intrusion porosimetry can give us the idea about the size and distribution of such pores. We have to keep in mind that all results are obtained on samples in the dry state, which might not necessarily be the same when the monolith is in a solvent.

The DEGDMA-only monoliths have rather narrow pore-size distribution with average pore size at around 3 μm, while increase of the amount of HEA in the feed solution increases the pore size, widens the distribution and with 18 vol% HEA a second peak appears at around 8 μm. In the same time, the increase of the HEA content in the comonomer mixture from 5 vol% up to 18 vol% resulted in a decrease of the surface area by half, in good agreement with the increase in the pore size. The reason for the increase in the pore size is to be found in the decreasing amount of the crosslinking monomer, DEGDMA. We have observed earlier [12–14] that in solutions with lower DEGDMA concentration the growing nuclei are more apart from each other, and as they are less crosslinked, they can swell more both in the solvent and in the remaining monomer. When the solvent used is alcohol, the nuclei will swell more in the monomer than in the solvent, therefore the polymerization will continue preferentially in the swollen nuclei growing thus to a bigger size.

The morphology of the polymer monoliths is illustrated in SEM micrographs (Fig. 3), all taken with the same magnification. These photographs show both the influence of the HEA concentration in the feed solution on the pore size when irradiated in methanol, and also the effect of three different alcohols on the porous structure of the monoliths with 18 vol% HEA. The pictures show the familiar globular structures

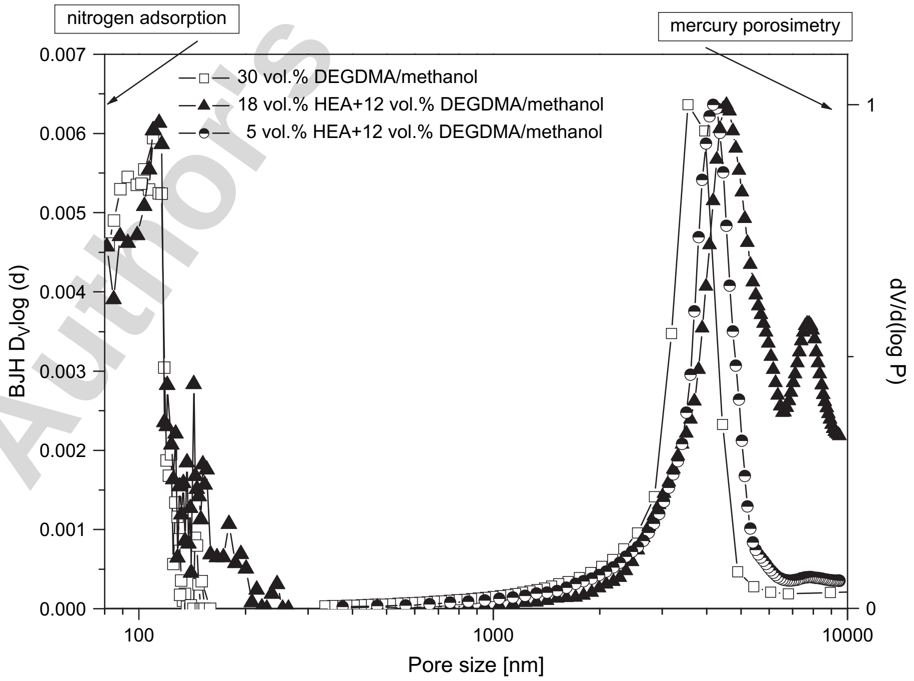

Fig. 2. Porous properties of the various HEA-*co*-DEGDMA monoliths obtained by nitrogen adsorption and mercury intrusion porosimetry measurements.

Table 1
Porous properties of monoliths prepared by radiation polymerization and crosslinking

Monomer		Porogenic solvent [70 vol%]	S_{BET}[a] [m^2/g]	Mean pore diameter[b] [nm]
HEA [vol%]	DEGDMA [vol%]			
–	30	Methanol	1.4	3540
5	25	Methanol	1.3	4193
12	18	Methanol	1.3	–
18	12	Methanol	0.68	4561
18	12	Ethanol	0.75	–
18	12	2-Propanol	0.75	–

[a] Nitrogen adsorption measurements.

[b] Mercury intrusion porosimetry.

with irregular voids. The clusters of globules and voids between them increase with increasing HEA content up to 18 vol%. The pores and globules of the 20 vol% HEA sample are not well defined, since the amount of HEA is double of the amount of DEGDMA, therefore the dominating structure will be of a crosslinked gel instead of a monolith. Because of such low DEGDMA concentration, the monolith is not rigid enough to be used as chromatographic column: when swollen, it slips out from the column, when dry, it shrinks.

From the above results it could be concluded that the HEA concentration influences both the pore size of the monolith and the mechanical properties of the matrix: 18 vol% HEA in the monomer mixture might be optimal.

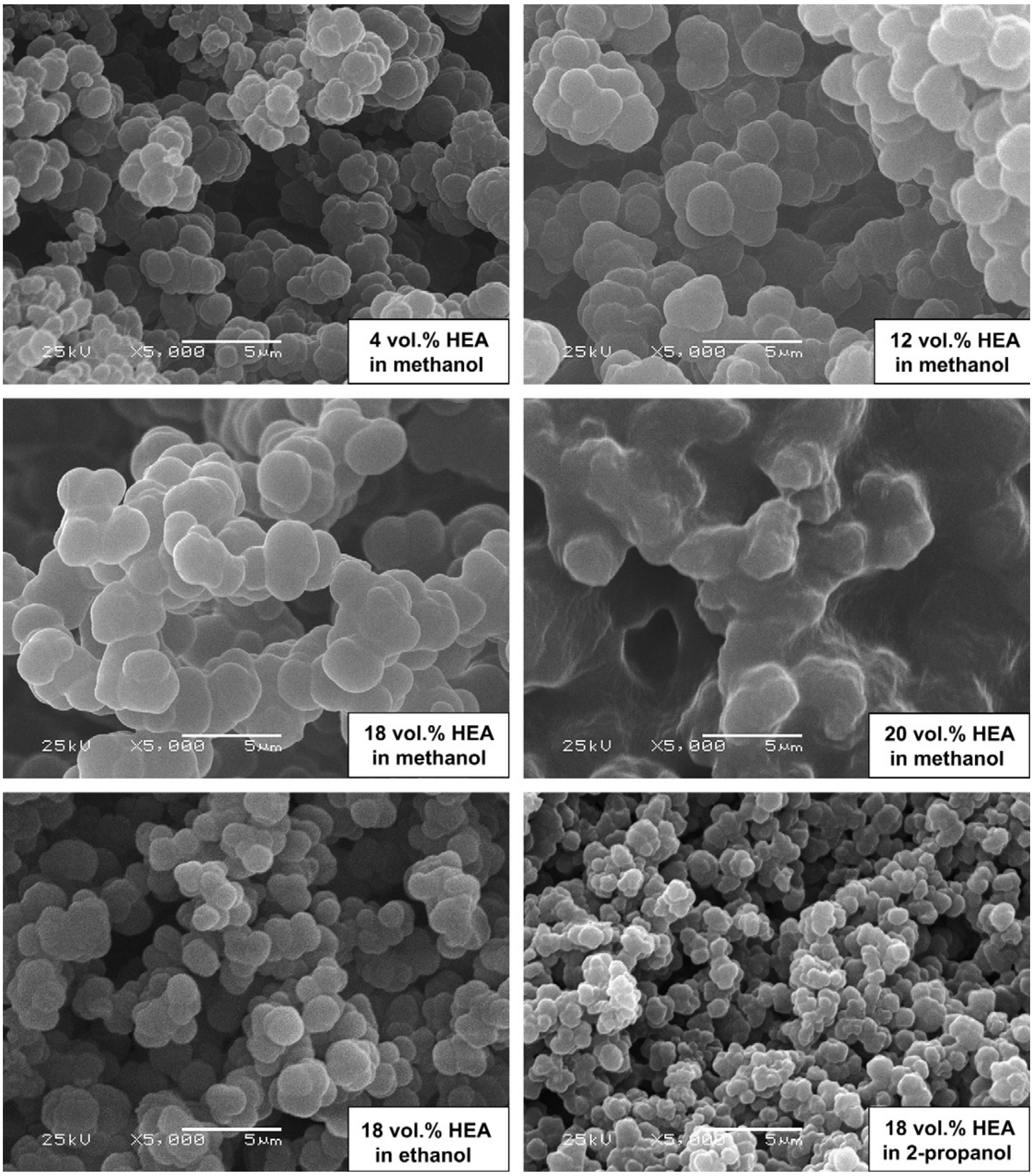

Fig. 3. SEM photographs of monoliths obtained from solutions with different HEA monomer content and different solvents. The white bar represents 5 µm. The irradiation was done at 25 °C, with the dose rate of 16 kGy/h, up to total dose of 30 kGy.

It was shown in the literature that the solvent has a significant effect on the porous structure of monoliths, providing another tool for tuning the pore size without changing the chemical properties of the matrix. The effect of the use of ethanol and propanol as solvents was investigated on the monolith with 18 vol% HEA. From the SEM photos (Fig. 3) it is clearly seen that the pores are smaller when ethanol was used as the solvent instead of methanol, similarly to the effects observed and explained for the DEGDMA-only system [12–14] earlier.

From the application point of view, monoliths intended for use in various chromatographic separation and purification processes must allow liquid to permeate through the pores at a pressure as low as possible. Fig. 4a shows the effect of the HEA monomer concentration on the flow rate. It can be seen that until 20 vol% of HEA, higher the monomer percentage, higher the permeability. However, no measurable flow was observed for the columns prepared with HEA monomer concentrations above that value even at increased pressure of 0.4 MPa. The values obtained for monoliths with 18 vol% HEA synthesized in ethanol and propanol are also included, showing decreased flow, confirming once again that the pores of these monoliths are smaller.

Fig. 4b shows the effect of flow rate on back pressure for a 128 × 4 mm ID column containing a monolith prepared with 5 vol% and 18 vol% HEA solution in methanol. Methanol and water were used as the mobile phase. These solvents were pumped through the monolith with several different pressures during which the flow rate was recorded, and finally all data were recalculated to the pressure of 0.1 MPa. The linear fit confirms both incompressibility of the monolith and high permeability to flow for both solvents used as the mobile phase. A much lower pressure drop corresponds to the same flow rate on the 18 vol% HEA monolith than on the 5 vol% one, confirming the earlier results that the former has larger pores and higher hydrophilicity.

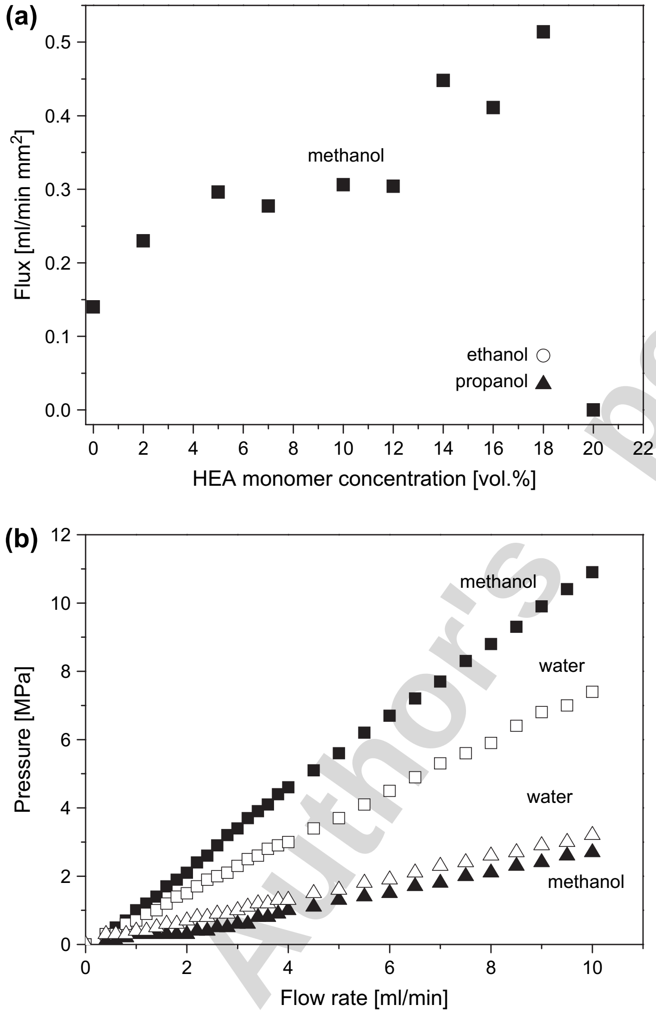

Fig. 4. (a) Flux dependence on the HEA monomer ratio in the feed solution containing 30 vol% monomer (HEA and DEGDMA) when acetonitrile was used as the mobile phase; (b) Pressure response at increasing flow rate for a monolith synthesized by irradiating a 5 vol% HEA + 25 vol% DEGDMA (□) and 18 vol% HEA + 12 vol% DEGDMA (△) in methanol solution in a stainless steel column (128 × 4 mm i.d.). The irradiation was done at 25 °C, with the dose rate of 11 kGy/h, up to total dose of 30 kGy. Two different eluents, methanol and water were used.

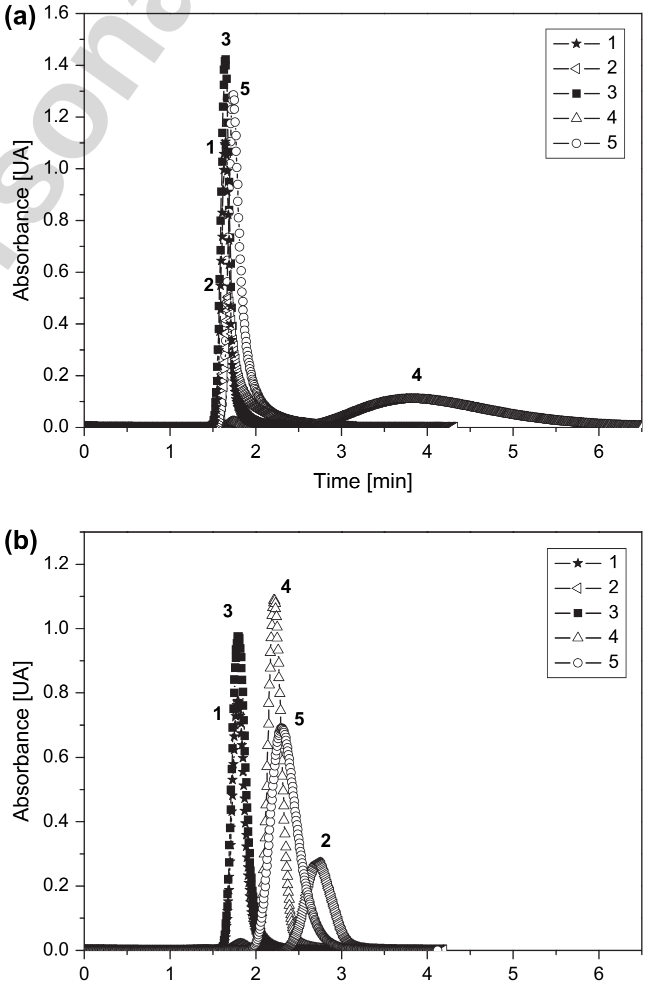

Fig. 5. Overlay of separation of Phe (1), His (2), Tyr (3), T (4), and Trp (5) injected individually using (a) a 30 vol% DEGDMA monolithic column; and (b) an 18 vol% HEA + 12 vol% DEGDMA monolithic column. Conditions: column 128 × 4 mm i.d.; mobile phase 100% water; flow rate 0.8 ml/min; UV detection 200 nm.

3.3. Behavior of the monoliths as liquid chromatography columns

One large application area of polymer monolith is in chromatography. We expected our monolithic column to be used in such separation and purification application as well. As the first trial we have selected several amino acids and one nucleobase.

Fig. 5 shows the overlay of separation of Phe (1), His (2), Tyr (3), T (4), and Trp (5) injected individually on the DEGDMA-only (5a) and on the 18 vol% HEA containing copolymer monolith (5b). The DEGDMA-only monolith could not separate these components, while the copolymer monolith showed promising results. The crosslinked HEA when swollen in water introduces not only hydrophilic character to the monolith surface, but also a new set of pores, only available in the swollen state, that may aid the separation. The possibility to use this 18 vol% HEA containing monolith column for separation was further studied by investigating the effect of various mobile phases on the separation efficiency when solutions containing various combinations of two compounds were injected (Fig. 6).

Fig. 6 shows that by using water as the mobile phase some of the amino acids could be quickly and well separated. Mixing water with small amount of acetonitrile or methanol as the mobile phase also showed good results, but high methanol or acetonitrile content resulted in poor separation. Since the sizes of the compounds separated decrease in the order of Trp > Tyr > Phe > His > T, it is seen that the separation is not based on simple size exclusion. When comparing the two best separable amino acids, Phe and His, we find that their sizes are nearly the same, but if comparing the polarity, we find that Phe is the most hydrophobic amino acid (hydropathy index 2.8), while His is the most hydrophilic one (hydropathy index −3.2). Therefore, we conclude that the improved separation of the amino acids on the column containing 18 vol% HEA as compared to the DEGDMA-only column is the results of several effects: introduction of HEA that will swell in water and therefore make the column more hydrophilic, but in the same time the pores of the swollen gel introduce a kind of sieving as well. The compounds would therefore be separated by combination of size exclusion, gel sieving and reversed phase chromatography.

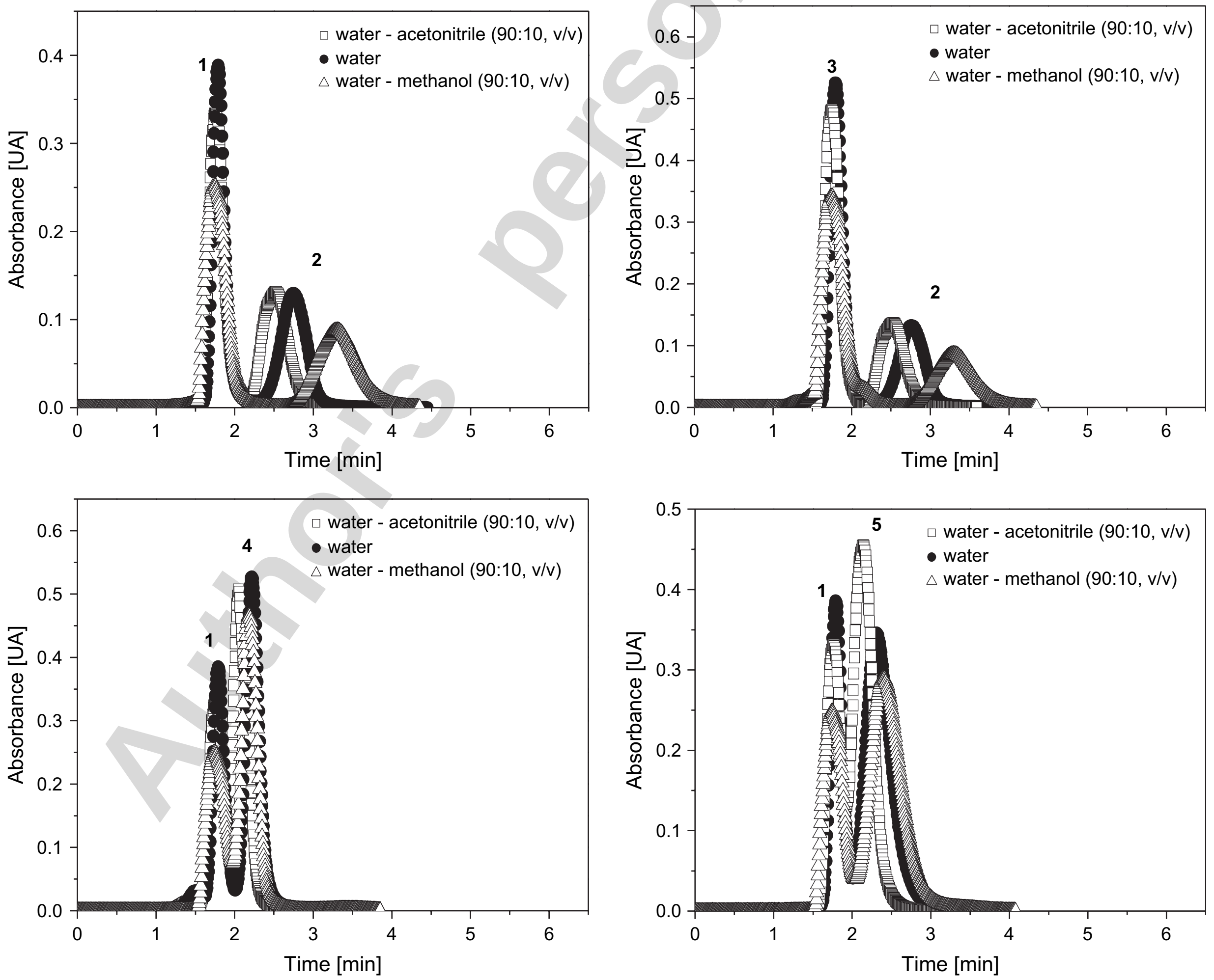

Fig. 6. Comparison of the separation of Phe (1), His (2), Tyr (3), T (4), and Trp (5) from different two-component systems on an 18 vol% HEA + 12 vol% DEGDMA monolithic column by using different mobile phases. Conditions: column 128 × 4 mm i.d.; flow rate 0.8 ml/min; UV detection 200 nm.

It should be noted that throughout this work only a simple separation method was used to show the possibility of application of the radiation-synthesized copolymer monoliths as chromatographic columns. Further refinement of the separation method, such as the use of various column conditioning methods as well as a gradient method might improve the column performance further. The investigation of the column length on the separation efficiency is also in progress.

4. Conclusion

In this work, radiation initiated polymerization and crosslinking was used for the synthesis of poly(2-hydroxyethylacrylate-*co*-diethyleneglycole dimethacrylate) monoliths. The influence of monomer concentration and type of the solvent on the porous structure was investigated. The characterization of monoliths was performed by electron microscopy and porosity measurements. The increase of the HEA monomer content in the comonomer mixture (up to 18 vol%) resulted in monoliths with bigger pore size and increased hydrophilic character. However, further increase of the HEA monomer concentration transformed the monolith into soft gel. The monoliths with adequate porous and mechanical properties were tested as chromatographic columns, and were found suitable for quick separation of selected amino acids.

An important advantage of the separation by using this copolymer monolith is its environmental friendly character, since water instead of organic solvent was used in the course of separation.

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