H. Bodugoz-Senturk and O. Güven / Hacettepe J. Biol. & Chem., 2014, 42 (1), 81–88

Preparation of porous and non-porous poly(iso-butyl methacrylate) microspheres by suspension polymerization

Suspensiyon polimerizasyonu ile gözenekli ve gözeneksiz poli(iso-bütil metakrilat) mikrokürelerinin hazırlanması

Research Article

Hatice Bodugoz-Senturk[1,2]* and Olgun Guven[3]
[1]Massachusetts General Hospital, Department of Orthopaedic Surgery, Boston, MA, USA
[2]Harvard Medical School, Orthopaedic Surgery, Boston, MA, USA
[3]Hacettepe University, Department of Chemistry, Ankara, Turkey

ABSTRACT

Porous and non-porous Poly(isobutyl methacrylate) (PiBMA) microspheres were synthesized by suspension polymerization technique in aqueous medium to remove light petroleum derivatives from sea water. Influence of the crosslinking agent, porogen and reaction parameters on the solvent uptake, porosity and networks structure of the PiBMA spheres were investigated. Gasoline and small aliphatic hydrocarbons (pentane, hexane and heptane) were used as model solvents. Swelling behavior and network properties were found to be dependent on the crosslinking density of the sphere, crosslinking agent, porosity and solvent. Highest solvent uptake for both porous and non-porous PiBMA spheres was observed in gasoline. PiBMA microsphere shown to be good candidates for the removal of light petroleum derivatives and they preserved their uptake capacity and shape over several usages.

Key Words
Microspheres, gamma radiation, poly(isobutyl methacrylate), suspension polymerization.

ÖZET

Deniz suyundan hafif petrol türevlerinin uzaklaştırılması amacıyla suspensiyon polimerizasyonu tekniği ile sulu ortamda gözenekli ve gözeneksiz poli(izo-butilmetakrilat) (PiBMA), mikro küreleri hazırlanmıştır. Çapraz bağlayıcı, gözenek yapıcı ve reaksiyon parametrelerinin, mikro kürelerin sıvı tutma kabiliyetlerine, gözenek yapısına ve ağ yapısına olan etkileri incelenmiştir. Benzin ve küçük hidrokarbonlar (pentan, hekzan ve heptan) model çözücüler olarak kullanılmıştır. Mikrokürelerin çözücü içinde şişme davranışı ve ağ yapı özellikleri, çapraz bağlanma yoğunluğuna, çapraz bağlayıcı türüne, gözenek yapısına ve çözücü türüne bağlı olduğu tespit edilmiştir. Hem gözenekli hem gözeneksiz kürelerde en yüksek sıvı tutma kapasitesi benzinde gözlenmiştir. Genel olarak PiBMA mikroküreleri deniz suyundan hafif petrol türevlerinin uzaklaştırılmasında etkili oldukları ve birden fazla kullanım sırasında hem kapasitelerini hem de şekillerini yitirmedikleri gözlenmiştir.

Anahtar Kelimeler
Mikrokureler, gamma radyasyonu, poli(izo-butil metakrilat), suspensiyon polimerizasyonu.

Article History: Received October 31, 2013; Revised November 11, 2013; Accepted November 11, 2014; Available Online: February 5, 2014.

Corresponding author: : H. Bodugoz-Senturk., Harris Orthopaedic Laboratory Massachusetts General Hospital 55 Fruit Street, GRJ-1102 Boston, MA 02114

Tel: (617) 724-6780 (voice) Fax: (617) 643-2521 (fax) E-Mail: hsenturk@partners.org

INTRODUCTION

Polymeric microspheres have found large applications in the medical and industrial field. In medicine, alone or coated with antibodies, antigens and proteins they have been used for immobilization of enzymes, for the encapsulation of mammalian cells, for immunochemical studies, for the controlled release of pharmaceuticals and as molecularly imprinted selective agent [1-5]. Unmodified polymer spheres also find extensive use as standards for instrument set-up and calibration [6]. Microspheres have been used as sorbents to remove some metal ions [7]. This large application field prompted us to study these useful beads for the environmental application and we prepared both porous and non-porous poly(iso-butyl methacrylate, PiBMA) microspheres for the oil removal from sea water. In an earlier communication we published our data on preparation of non-porous PiBMA microspheres and investigated their uptake capacity and swelling behavior in various light molecular weight hydrocarbons (pentane, hexane, and heptane) and gasoline [8]. We produced microspheres with 800-1500mm diameter range and having different crosslinking densities by suspension polymerization technique. We chose the suspension polymerization over emulsion polymerization due to size of the particles, higher purity, reaction conditions and less post reaction maintenance.

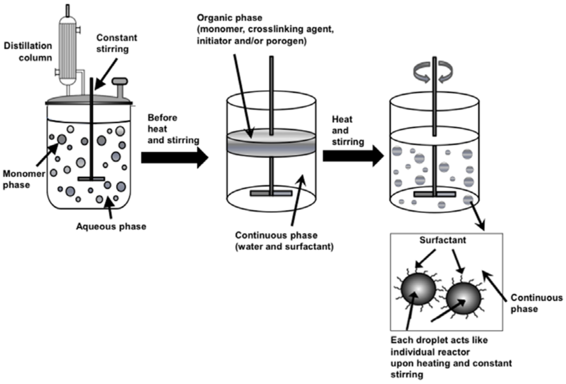

Figure 1. Suspension polymerization.

The suspension polymerization process is typically carried out in well stirred batch reactors (Figure 1) [8-12]. All the reactants (monomer, initiator, etc.) reside in the organic (or oil) phase [13]. The organic phase is dispersed in the continuous phase which is commonly water in the presence of surface active (surfactant) agents (inorganic or/and water-soluble polymers) and agitation. The polymerization occurs in the monomer droplets that are progressively transformed into rigid, spherical polymer particles. Suspension polymerization has important advantage compared to the bulk process and emulsion based polymerization such as control of the reaction temperature due to the presence of the dispersion medium (water), milder reaction conditions, product homogeneity, and higher purity than those produced by emulsion polymerization. In earlier study we published our findings on the polymerization conditions for the preparation of non-porous PiBMA spheres by suspension polymerization technique [8]. We studied the effect of crosslinking agent concentration (0.03, 0.05, 0.07, 0.1 weight percent of monomer) and molecular weight (ethylene glycol dimethacrylate (EGDMA) and butanediol dimethacrylate) on the solvent uptake in pentane, heptane, hexane and gasoline along with the network and diffusion parameters. The study revealed that even with a small increase in the crosslinking agent chain length, the equilibrium swelling was increased in all solvents (Figure 2-3) [8-10]. Also the increase in the crosslinking agent concentration reduced the maximum swelling value regardless the chain length. For the solvent with higher molecular weight we observed more solvent uptake due to the similarities between the solvent parameter of PiBMA spheres and the solvents studied (the solubility parameters for pentane, hexane, heptane and PiBMA are 7.0, 7.3, 7.4 and 8.5–11.

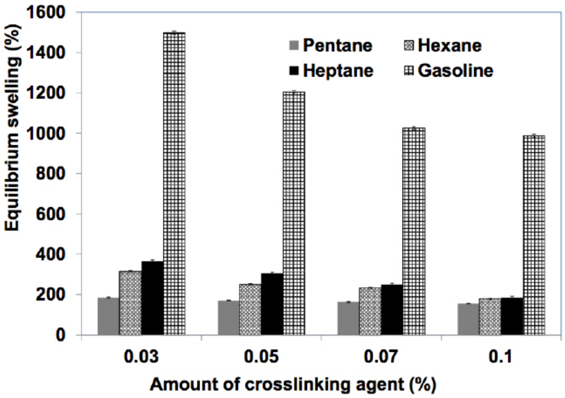

Figure 2. Equilibrium swelling of non-porous PIBMA spheres crosslinking with EGDMA.

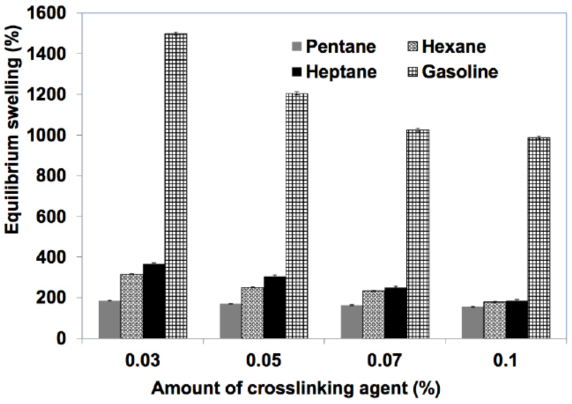

Figure 3. Equilibrium swelling of non-porous PIBMA spheres crosslinking with BDDMA.

(cal/cm^3)$^{1/2}$ respectively) [14]. The highest swelling was observed in gasoline for both BDDMA and EGDMA; although no solubility parameter value is available for gasoline in the literature, one would assume since gasoline [8] is composed of a mixture of many organic aliphatic and aromatic compounds which are likely to interact well with PiBMA.

The diffusion parameters; diffusion coefficient, *D* and diffusional exponent, *n* for the non-porous PiBMA (Table 1-2) indicated that the diffusion coefficient was inversely proportional to the molecular weight of the penetrant. As the mesh size of crosslinked network was reduced through higher concentrations of crosslinking agents, the diffusion coefficient of all three solvents showed considerable decreases. The network parameters were also highly dependent on the crosslinking agent (Table 3); the increase in the percentage of the crosslinking agent caused a decrease in molecular weight between crosslinks, $\overline{M}_c$. Also, the $\overline{M}_c$ values which were determined for the BDDMA have higher values than that of EGDMA [8]. The reason for this observation is the relatively longer chain length of BDDMA.

Using same method we also prepared porous PiBMA spheres to decrease uptake time. For the production of porous microspheres we introduced an inert porogens (toluene and heptane/dioxane mixture) into polymerization medium which could be easily removed upon polymerization. In this publication while summarizing the findings of earlier work we reported the effect of crosslinking agent concentration along with porogen type and amount on the porosity, swelling behavior and network parameters of PiBMA microspheres.

Table 1. Variation of diffusion coefficient, D, with the amount of crosslinking agent (EGDMA and BDDMA) and type of solvent.

$Dx10^{5}$ (cm^{2}/min)								
Amount of crosslinking agent (wt%)	Pentane		Hexane		Heptane		Gasoline	
	EGDMA	BDDMA	EGDMA	BDDMA	EGDMA	BDDMA	EGDMA	BDDMA
0.03	5±0.5	5±1	4±1	5±0.3	4±0.6	4±1	10±1	10±0.3
0.05	3±0.3	5±1	3±0.2	4±0.2	3±0.7	4±1	9±0.7	10±1
0.07	3±0.2	3±0.4	2±0.2	2±0.4	2±0.2	2±0.5	9±0.7	9±0.4
0.1	2±0.4	3±0.2	2±0.5	2±0.1	2±0.1	2±0.7	7±1	8±1

Table 2. Variation of diffusional exponent, n, with the amount of crosslinking agent (EGDMA and BDDMA) and type of solvent.

n								
Amount of crosslinking agent (wt%)	Pentane		Hexane		Heptane		Gasoline	
	EGDMA	BDDMA	EGDMA	BDDMA	EGDMA	BDDMA	EGDMA	BDDMA
0.03	0.6±0.2	0.5±0.2	0.7±0.1	0.5±0.1	0.7±0.3	0.6±0.2	0.7±0.1	0.6±0.1
0.05	0.8±0.1	0.6±0.2	0.8±0.2	0.6±0.1	0.9±0.2	0.7±0.2	0.9±0.1	0.8±0.1
0.07	0.9±0.1	0.7±0.1	0.9±0.1	0.7±0.3	0.9±0.1	0.8±0.1	0.9±0.1	0.9±0.2
0.1	0.9±0.1	0.7±0.1	0.9±0.2	0.8±0.3	1.0±0.1	0.9±0.1	1.0±0.2	1.0±0.1

Table 3. Variation of network structure parameters with the amount of crosslinking agent (EGDMA and BDDMA); values are averages of the values calculated for each solvent (pentane, hexane, heptane and gasoline).

Weight crosslinking agent (wt%)	ϕ		S		$\bar{M}_c$		q		ρ	
	BDDMA	EGDMA	BDDMA	EGDMA	BDDMA	EGDMA	BDDMA	EGDMA	BDDMA	EGDMA
0.03	0.3±0.01	0.3±0.2	3.0±0.4	3.0±0.6	2100±3	910±15	0.06±0.01	0.2±0.06	1±0.2	1±0.1
0.05	0.3±0.04	0.3±0.5	3.0±0.2	3.0±0.3	1975±4	765±12	0.07±0.01	0.2±0.04	1±0.3	1±0.3
0.07	0.3±0.1	0.3±0.3	3.0±0.8	3.0±0.3	1755±9	650±9	0.08±0.02	0.2±0.04	1±0.1	1±0.4
0.1	0.4±0.05	0.4±0.1	2.5±0.1	3.0±0.4	1450±14	588±8	0.08±0.03	0.2±0.02	1±0.1	1±0.2

Experimental

Materials and Methods

The iso- butyl methacrylate monomer, supplied from Merck was purified by passing through active alumina. The crosslinking agents (EGDMA, BDDMA) were purified by the same method. Benzoyl peroxide initiator supplied from BDH was purified by recrystalization twice from methanol before use. Poly(2-N-vinyl pyrrolidone) (PVP) and tricalcium phosphate (TCP) obtained from BDH and Merck respectively selected as suspension stabilizers and used without further purification. Toluen, heptane and dioxane were also used as received. Distilled water was used as dispersion medium.

Synthesis of porous PiBMA microspheres

In order to obtain PiBMA spheres with an average diameter of 800-1500 mm the following procedure has been applied. For the non-porous PiBMA spheres, the monomer/water ratio selected as 1/5 by volume and dispersion medium was prepared by dissolving predetermined amounts of PVP and TCP in distilled water. The initiator concentration was selected as 1g BPO / 100g i-BMA, and then crosslinking agent added to monomer phase. For the porous PiBMa microspheres varying amount of porogen (toluene or heptane/dioxane mixture (1:3 by volume) was also added to monomer phase then transferred into dispersion medium placed in a mechanically stirred (at a constant stirring rate) round bottom cylindrical reactor which was thermostatically controlled to ±1°C. All experiments were carried out at nitrogen atmosphere and 70°C. After polymerization the spheres were cleaned by several washing steps with water and ethanol then dried in a vacuum oven.

Swelling

Dynamic swelling behaviours of crosslinked spheres were determined by measuring the diameter of spheres as a function of time by an optical microscope at room temperature. All experiments were repeated with n=6 samples with same diameter. The PiBMA spheres prepared in this study had a crosslinked network structure. The following equation was used to calculate the percentage volume swelling:

$$\text{Swelling \% (volume percent)} = [(V_t - V_i)/V_i] \times 100$$
$$= (R_t^3/R_i^3)-1] \times 100$$

Here, V_i, V_t, R_i, and R_t show the volume and diameter of spheres initially and at time t, respectively. The % swelling values obtained from this equation is plotted against time and used to calculate diffusional exponent (n) and diffusion coefficient (D, in cm^2/min) ,

$$M_t / M_\infty = kt^n \text{ and } M_t/M_\infty = 6[\ Dt/\pi a^2\ ]^{1/2} - 3Dt/a^2,$$

Where M_t is the amount of solvent diffused in the spheres at time t and M_∞ is the amount of solvent at equilibrium [15]. k is the constant incorporating characteristic of the macromolecular network system and penetrant. n is the diffusional exponent which indicates the transport mechanism; D is the diffusion coefficient in cm^2/min, t is the time of diffusion and a is the radius of sphere.

To test the samples for repeatable usage, spheres swollen in gasoline were first dried in air at room temperature and then in vacuum oven were swollen in gasoline to equilibrium. Same experiment was repeated for 5, 10, 15 and 25 times.

Porosity

Mercury intrusion porosimeter (Micrometritics, 220 porosimeter) was used to determine the total pore volume and surface area of the porous spheres [16]. Scanning electron microscope (SEM) was also used for surface characterization; the microspheres were coated with a thin layer of gold in vacuum and imaged in the electron microscope with x1000 magnifications.

Results and Discussion

In making the non-porous PiBMA spheres the highest amount of crosslinking agent used was 0.1% for both EGDMA and BDDMA, however when preparing porous spheres in the presence of a porogen previously described amounts of crosslinking agents resulted in aggregate formation rather than well-defined spheres. Increasing the crosslinking agent by 5 fold resulted in better shaped spheres. For that reason microspheres prepared for this study has higher amounts of crosslinking agent and the effect of crosslinking agent on porosity is studied. We also had better result with EGDMA than the samples prepared with BDDMA, therefore we preferred to use EGDMA over BDDMA in porous spheres. Non-porous PiBMA spheres with 0.1%EGDMA was used as comparison.

SEM pictures of porous and non-porous PiBMA spheres showed visible difference in the morphology with porous spheres having less smooth surface and more pore like structure (Figure 4). Total pore volume of the porous spheres for the samples prepared with both toluene and heptane/dioxane mixture were higher than those prepared with no porogen (Figure 5). As expected total pore volume increased significantly with increasing crosslinking agent (EGDMA) amount for the PIBMA spheres prepared with both porogens toluene and heptane/dioxane while the samples with no porogen did not show any significant increase with increasing crosslinking agent concentration. The spheres prepared with heptane/dioxane mixture exhibited higher pore volume compared to their counterparts prepared

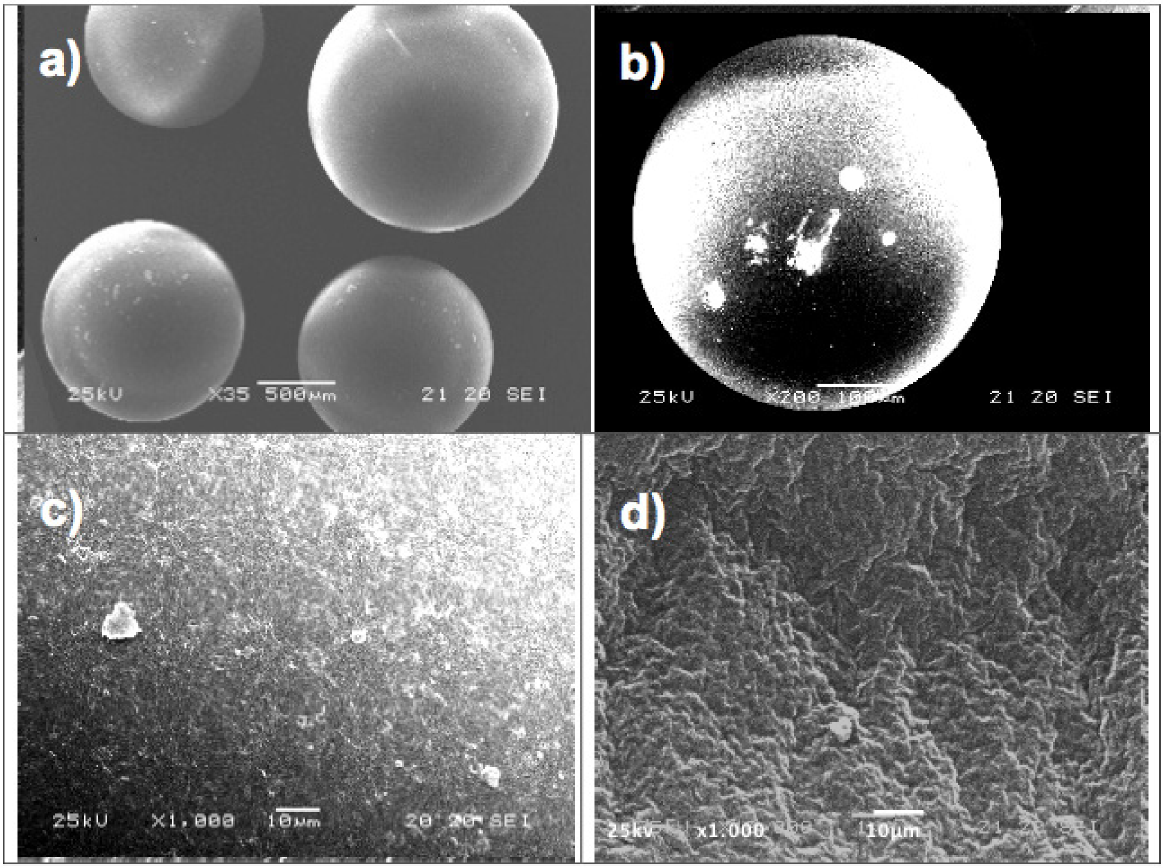

Figure 4. SEM pictures of a, c) non-porous b,d) porous PIBMA spheres prepared with 10%EGDMA and 100%toluene.

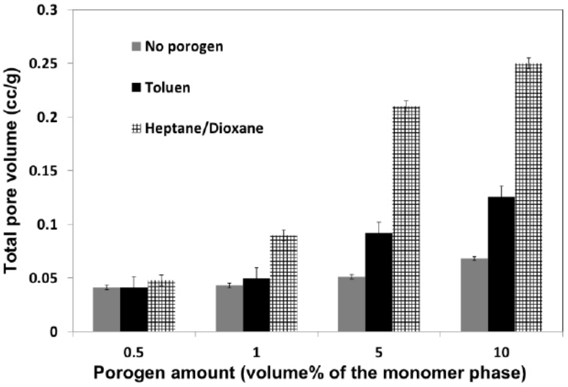

Figure 5. Total pore volume of porous and non-porous PIBMA spheres with respect to crosslinking agent prepared with 100% Toluene and 100%Heptane/dioxane (percentages are by volume of monomer phase).

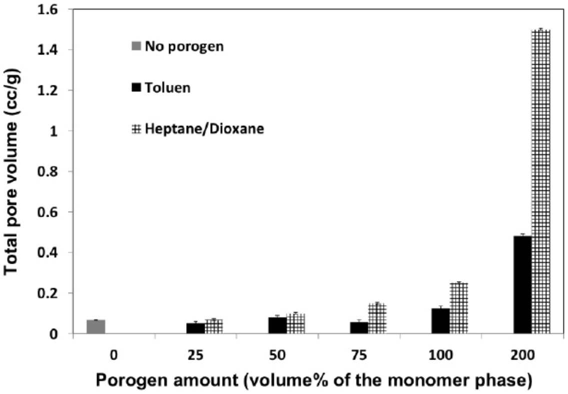

Figure 6. Total pore volume of porous and non-porous PIBMA spheres with varying porogen amount by volume of monomer phase (all samples were crosslinked with 10%EGDMA).

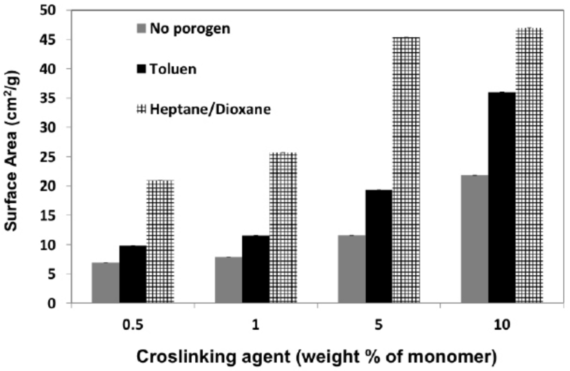

Figure 7. Surface area of porous and non-porous PIBMA spheres with respect to crosslinking agent prepared with 100% Toluene and 100%Heptane/dioxane (percentages are by volume of monomer phase).

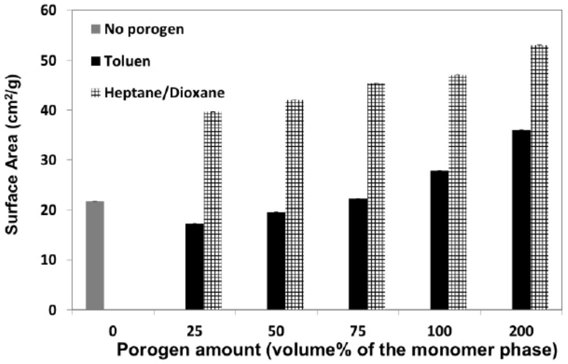

Figure 8. Surface area of porous and non-porous PIBMA spheres with varying porogen amount by volume of monomer phase (all samples were crosslinked with 10%EGDMA).

with toluene and with no-porogen. This is probably due the interaction between the monomer and porogen; solvent interaction parameter for toluene, heptane, dioxane and PiBMA as follows respectively 18.1, 7.0, 10 and 8 -11$(cal/cm^3)^{1/2}$ [14]. Clearly heptane/dioxane mixture is a better solvent for PiBMA spheres allowing them to swell easily as the reaction proceed. Also upon completion of the reaction due to the relatively lover boiling point of heptane/dioxane (98°C and 101°C) is easier to remove from the spheres than toluene (110.6°C). The amount of porogen was also effective in the pore volume of PiBMA spheres; for both toluene and heptane/dioxane but more significantly in heptane/dioxane mixture, increasing porogen amount resulted in an increase in the pore volume (Figure 6).

The surface areas of non-porous spheres were smaller than those prepared with a porogen (Figures 7 and 8). The increasing crosslinking agent (EGDMA) amount increased the surface area of both non-porous and porous PiBMA spheres. As in the pore volume, samples prepared with heptane/dioxane mixture exhibited higher surface area compared to non-porous and spheres prepared with toluene. Similar result with pore volume with increasing porogen amount observed in the surface area measurements; increasing porogen amount resulted in an increase in the surface area more so in the samples prepared with heptane/dioxane.

Equilibrium swelling value in other words maximum gasoline intake was very much dependent on the first and foremost to crosslinking agent concentration; PiBMA spheres crosslinked with 0.1% EGDMA were swollen to 1078% of their original volume while the samples with 10%EGDMA were only swollen to 102% (Figure 9). The difference for the spheres with same amount of crosslinking agent (10% EGDMA) but prepared with a porogen was smaller; 350% for heptane/dioxane mixture and 280% for toluene. Although the porous spheres did not retain as high gasoline as 0.1% EGDMA corsslinked non-porous spheres due to their higher EGDMA content (10%), the diffusion time was significantly low in porous PiBMA. The time taken for equilibrium for porous spheres prepared with 10% EGDMA (10 min for heptane/dioxane and 20 min for toluene) was significantly lower than those for the non-porous samples prepared with 0.1% EGDMA (30 min) and 10% EGDMA (26 min) non-porous spheres. As it was confirmed with the diffusional coefficient data (Table 4), the diffusion rate was higher for porous samples in gasoline. All the samples exhibited zero order diffusion (Table 4).

Both porous and non-poorus PiBMA spheres kept their shape after several use, however the non-porous samples with least amount of crosslinking agent (0.1%EGDMA) exhibited a decrease in maximum uptake value while the maximum uptake for all other samples was not effected significantly (Figure 10).

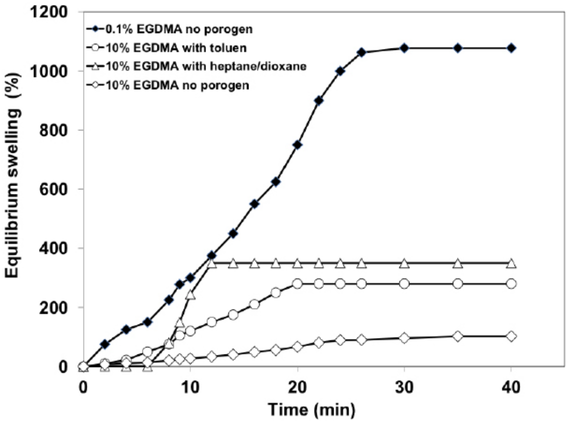

Figure 9. Equilibrium swelling of porous and non-porous PIBMA spheres crosslinking in gasoline.

Conclusion

Previously reported suspension polymerization recipe for non-porous PIBMA microspheres is modified for the preparation of porous PiBMA spheres by the addition of porogens (heptane/dioxane and toluene) to the monomer phase and increasing the crosslinking agent (EGDMA) concentration by 5 fold of earlier described 0.1%EGDMA value. The significance of crosslinking agent and porogen was clear; the results of the porosity measurement showed that when heptane/dioxane mixture used, pore volume and surface area was higher than non-porous PiBMA spheres and toluene prepared counterparts. As in the non-porous PiBMA spheres all porous samples resumed their original size and shape after swelling and de-swelling for 25 time to equilibrium value indicating that they would be highly effective for uptake of gasoline like structure from water.

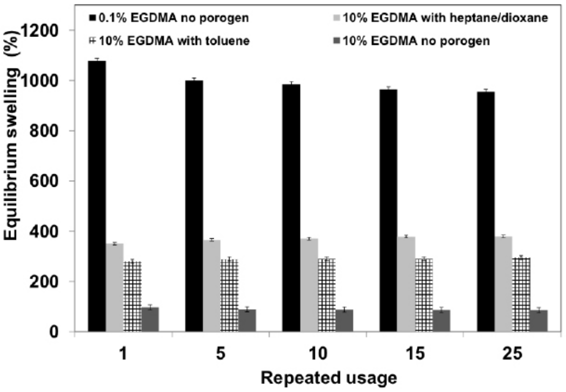

Figure 10. Equilibrium swelling with repeated usage, samples were swollen in gasoline and dried at in air at room temperature then in vacuum oven before tested each time.

Table 4. Variation of diffusion coefficient, *D*, *and* diffusional exponent, *n*, with the amount of crosslinking agent (EGDMA and BDDMA) and type of porogen.

Porogen	Crosslinking agent EGDMA (%)	Diffusion Coefficient $Dx10^5$ (cm^2/min)	*n*
None	0.1	7±1	0.9±0.01
None	10	3±0.2	1.1±0.01
Toluene (100% of monomer phase)	10	9±1	1.2±0.1
Heptane/Dioxane (100% of monomer phase)	10	12±1	1.2±0.1

References

1. J. Cejkova, F. Stepanek, Compartmentalized and internally structured particles for drug delivery - a review. Current Pharm. Design, 19 (2013) 6298.
2. M. Paulis, J.R. Leiza, Polymer/clay nanocomposites through emulsion and suspension polymerization. Advances in Polymer Nanocomposite Technology, ed. V. Mittal. (2010) 53-100.
3. D.R. Kryscio, Peppas, Critical review and perspective of macromolecularly imprinted polymers. Acta Biomater., 8 (2012) 461.
4. D.L. Elbert, Liquid-liquid two-phase systems for the production of porous hydrogels and hydrogel microspheres for biomedical applications: A tutorial review. Acta Biomater., 7 (2011) 31.
5. B.N. Kolarz, Reactive multiacrylic copolymers prepared by suspension polymerization. Polimery, 44 (1999) 637.
6. A. Nasser, U. Mingelgrin, Mechanochemistry: A review of surface reactions and environmental applications. Appl. Clay Sci., 67-68 (2012) 141.
7. T. Caykara, S.S. Alaslan, M. Gürü, H. Bodugoz, O. Güven. Preparation and characterization of poly(isobutyl methacrylate) microbeads with grafted amidoxime groups. Radiat. Phys. Chem., 76 (2007) 1569.
8. H. Bodugoz, O. Guven, The synthesis of nonporous poly(isobutyl methacrylate) microspheres by suspension polymerization technique and investigation of their swelling properties. J. Appl. Polym. Sci., 83 (2002) 349.
9. M.J. Zohuriaan-Mehr, K. Kabiri, Superabsorbent polymer materials: A review. Iranian Polym. J., 17 (2008) 451.
10. G.H. Ma, Control of heterogeneous structure of porous polymer microspheres prepared from polymerization system and preformed polymer system. Colloid Polym. Sci., 291 (2013) 53.
11. P.J. Dowding, B. Vincent, Suspension polymerisation to form polymer beads. Colloid Surf. A-Physicochem. Eng. Aspect., 161 (2000)259.
12. F. Askari, S. Nafisi, H. Omidian, S. A. Hashemi. Synthesis and characterization of acrylic-based superabsorbents. J. Appl. Polym. Sci., 50 (1993) 1851.
13. B.W. Brooks, Suspension polymerization processes. Chem. Eng. Technol., 33 (2010) 1737.
14. J. Brandrup, E.H. Immergut, Polymer Handbook,. Vol. Third ed.; 1989, New York: Wiley. VII/517, V/126.
15. N.A. Peppas, P. Colombo, Analysis of drug release behavior from swellable polymer carriers using the dimensionality index. J. Control. Release, 45 (1997) 35.
16. S. Bryant, G. Mason, D. Mellor, Quantification of spatial correlation in porous media and its effect on mercury porosimetry. J. Colloid Interface Sci., 177 (1996) 88.