Synthesis and Characterization of Alkyl Methacrylate-based Microgels by Experimental Design Method

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In this work, alkyl methacrylate-based microgels were synthesized by an experimental design method, and their sebum absorption characteristics were investigated. The results of fractional factorial experimentation indicated that the cross-linking agent content, solvent content, and stirring speed were the main parameters in the synthesis of the microgels. The suitable synthesis conditions were determined by the response surface design method. Through a study of the monomer and solvent effects, it was confirmed that the microgel shows the highest sebum absorption ratio when *t*-butyl methacrylate is used as a monomer or when acetone is used as a solvent. The optimal microgel synthesis conditions for cosmetic application were determined, and the resulting microgel had a mean particle size of 4.7 μm and a sebum absorption ratio of 435%.

Key Words : Microgels, Synthesis, Alkyl methacrylate, Sebum absorption ratio, Experimental design method

Introduction

Microgels are cross-linked polymer particles with good dispersion stability and processing characteristics as well as various porosities, particle compositions, and cross-linking densities. Microgels are easy to functionalize by preparation methods and the introduction of functional groups, and have a high-ratio surface area, which qualities make them suitable for many industrial applications such as chromatographic media, surface coatings for metal panels, and fibers for cosmetics.[1-6]

Generally, polymer microgels are synthesized by seed-swelling polymerization, emulsion polymerization, precipitation polymerization, and dispersion polymerization. According to the polymerization method, the particle size, particle distribution, and molecular weight of the resulting polymer microgel differs. Among those methods, dispersion polymerization is simple in its process, and can produce microgels that are constituted of spherical particles below 5 μm in diameter.[7-11]

Fisher in 1920 created the experimental design that is still extensively used in industrial and agricultural applications. The design includes fractional experimentation, fractional factorial experimentation, response surface design, and mixture design.[12]

Sebum is the fatty, wax-like substance exuded by the sebaceous glands. In the duct of the gland, sebum is liquid, but it solidifies at skin temperatures and covers the skin in a thin semi-solid layer. The sebum absorption ratio determines the efficiency of cosmetics. Thus the sebum absorption ratio is the critical parameter in a cosmetic additive.

In the current study, in order to obtain a cosmetic additive boasting a high sebum absorption ratio, alkyl methacrylate-based microgels were synthesized by dispersion polymerization using *iso*-butyl methacrylate as a monomer and hydroxypropylmethylcellulose and acacia gum as dispersive stabilizers in an isopropyl alcohol/water medium. The effect of the reaction parameters on the sebum absorption ratio and the mean particle size was investigated by fractional factorial experimentation and response surface design. The relationship between monomer or solvent type and the sebum absorption ratio or mean particle size was also studied.

Experimental

Materials. The monomers used in this study were *n*-butyl methacrylate (*n*-BMA), *iso*-butyl methacrylate (*iso*-BMA), *t*-butyl methacrylate (*t*-BMA), and cyclohexyl methacrylate (CHMA), all purchased from Junsei Chem. The monomers were washed with 10% NaOH solution and evaluated under a nitrogen atmosphere before use. Ethyleneglycol dimethacrylate (EGDMA, Wako Pure Chem.), 2,2'-azobis(isobutylronitrile) (AIBN, Junsei Chem.), hydroxypropylmethylcellulose (HPMC, Sumsung Pure Chem.), and acacia gum (Shinyo Pure Chem.) were used as a cross-linking agent, an initiator, a dispersive stabilizer, and a co-stabilizer, respectively. Solvents including isopropyl alcohol (IPA), acetone, ethyl acetate, *n*-butanol, and ethyl alcohol were used as received.

Synthesis of polymer microgels. The optimal synthesis conditions for synthesis of polymer microgels were determined using fractional factorial experimentation. *iso*-BMA (content: 20 wt%) was used as a monomer. IPA (wt%), calcium phosphate (wt%), AIBN (mole%), acacia gum (wt%), EGDMA (mole%), HPMC content (wt%), and stirring speed (rpm) were chosen as the reaction parameters.

Table 1. Polymerization recipes for poly(*iso*-BMA-co-EGDMA) microgels using fractional factorial experimentation

Sample code	IPA/Water (wt%)	Calcium phosphate (wt%)	AIBN (mol%)	EGDMA (mol%)	Acacia (wt%)	HPMC (wt%)	Stirring speed (rpm)
MG-1	5	0.9	1.0	2.0	0.5	0.7	500
MG-2	10	0.9	4.0	8.0	0.5	0.7	900
MG-3	5	1.5	1.0	8.0	0.9	0.7	900
MG-4	5	0.9	4.0	2.0	0.9	1.3	900
MG-5	10	1.5	1.0	8.0	0.5	0.7	500
MG-6	10	0.9	4.0	2.0	0.5	1.3	500
MG-7	10	0.9	1.0	2.0	0.9	0.7	900
MG-8	5	0.9	4.0	8.0	0.9	0.7	500
MG-9	10	1.5	4.0	2.0	0.9	0.7	500
MG-10	5	1.5	4.0	8.0	0.5	1.3	500
MG-11	5	0.9	1.0	8.0	0.5	1.3	900
MG-12	10	1.5	1.0	2.0	0.5	1.3	900
MG-13	10	1.5	4.0	8.0	0.9	1.3	900
MG-14	10	0.9	1.0	8.0	0.9	1.3	500
MG-15	5	1.5	4.0	2.0	0.5	0.7	900
MG-16	5	1.5	1.0	2.0	0.9	1.3	500

The polymerization recipes are shown in Table 1.

Typical dispersion polymerization was conducted as follows. The determined HPMC and acacia gum were dissolved in 80 °C distilled water, and then IPA, monomer, EGDMA, and AIBN were added to the mixture. The mixture was placed under a nitrogen atmosphere to eliminate oxygen. Then, dispersion polymerization was carried out at 80 °C for 90 min. The resulting products were put in acetone, and the deposit was washed with acetone several times. Finally, the microgels were dried at 100 °C for 4 h.

The suitable synthesis conditions were further investigated using the Box Wilson method (the method of steepest ascent). The experiments were carried out according to the sequence followed in the dispersion polymerization, and the resultant polymerization recipes are shown in Table 2.

After the fractional factorial experimentation and the application of the method of steepest ascent, IPA, stirring speed, and EGDMA were chosen as the main parameters in order to perform experiments by response surface design.

Table 2. Polymerization recipes for poly(*iso*-BMA-co-EGDMA) microgels using two-way factorial design and method of steepest ascent

Sample code	IPA/Water (wt%)	Stirring speed (rpm)
MG-17	10	500
MG-18	5	900
MG-19	10	900
MG-20	5	500
MG-21	7.5	700
MG-22	11.25	850
MG-23	15	1000
MG-24	18.75	1100

Synthesis conditions: calcium phosphate = 1.1 wt%, acacia gum = 0.9 wt%, HPMC = 1.3 wt%, AIBN = 1.0 mole%, EGDMA = 1.0 mole%.

The experiments were carried out according to the sequence followed in the dispersion polymerization, and the polymerization recipes are shown in Table 3.

The effect of monomer type (including *n*-BMA, *iso*-BMA, *t*-BMA, and CMA) on the sebum absorption ratio and mean particle size, under the suitable synthesis conditions, was investigated. The experiments were carried out according to the sequence followed in the dispersion polymerization, and the polymerization recipes are shown in Table 4.

The effect of solvent type (including IPA, acetone, ethyl acetate, *n*-butanol, and ethyl alcohol) on the sebum absorption ratio and mean particle size, under the suitable synthesis conditions, was also investigated. The experiments were carried out according to the sequence followed in the dispersion polymerization, and the polymerization recipes

Table 3. Polymerization recipes for poly(*iso*-BMA-co-EGDMA) microgels using response surface design

Sample code	Std No.	Run No.	Blocks	IPA (wt%)	Stirring speed (rpm)	EGDMA (mole%)
MG-25	13	1	1	15	1000	2.5
MG-26	10	2	1	15	1100	2.0
MG-27	1	3	1	10	900	2.5
MG-28	8	4	1	20	1000	3.0
MG-29	12	5	1	15	1100	3.0
MG-30	4	6	1	20	1100	2.5
MG-31	6	7	1	20	1000	2.0
MG-32	3	8	1	10	1100	2.5
MG-33	11	9	1	15	900	3.0
MG-34	5	10	1	10	1000	2.0
MG-35	9	11	1	15	900	2.0
MG-36	7	12	1	10	1000	3.0
MG-37	2	13	1	20	900	2.5

Synthesis conditions: calcium phosphate = 1.1 wt%, acacia gum = 0.9 wt%, HPMC = 1.3 wt%, AIBN = 1.0 mole%.

Table 4. Polymerization recipes for poly(*iso*-BMA-co-EGDMA) microgels according to monomers

Sample code	Monomer
MG-38	*n*-BMA
MG-39	*iso*-BMA
MG-40	*t*-BMA
MG-41	CHMA

Synthesis conditions: calcium phosphate = 1.1 wt%, acacia gum = 0.9 wt%, HPMC = 1.3 wt%, AIBN = 1.0 mole%, EGDMA = 2.5 mole%, IPA = 14 wt%, stirring speed = 1000 rpm.

Table 5. Polymerization recipes for poly(*iso*-BMA-co-EGDMA) microgels according to solvents

Sample code	Solvent
MG-38	isopropyl alcohol
MG-42	acetone
MG-43	ethyl acetate
MG-44	*n*-butanol
MG-45	ethyl alcohol

Synthesis conditions: calcium phosphate = 1.1 wt%, acacia gum = 0.9 wt%, HPMC = 1.3 wt%, AIBN = 1.0 mole%, EGDMA = 2.5 mole%, stirring speed = 1000 rpm, solvent/water = 14 wt%.

are shown in Table 5.

Characterization and measurements. The microgel powder was dissolved in methanol, after which the solution was evenly dispersed on glass surfaces. The particle size and morphology were observed using a scanning electronic microscope (SEM, Hitachi S570).

Polymer microgel (1 g) was dissolved in distilled water (100 mL) using an ultrasonic generator. The particle size distribution was obtained using a particle size analyzer (Marvern Autosizer-II).

Polymer microgel or face powder (0.3 g) was placed in a Millicell for 10 h in order to absorb sebum. Then, the polymer microgel or face powder was placed on tissue to eliminate the over-absorbed sebum. The sebum absorption ratio was calculated from the following equation:

$$\text{Sebum absorption ratio} = \frac{W_f - W_i}{W_i} \times 100 \qquad (1)$$

where W_i is the initial weight of the polymer microgels, and W_f is the weight of the polymer microgels after absorption. The sebum absorption ratio was calculated by a new equation, as follows:

Sebum absorption ratio (New method)
$= -0.0037 + 1.18 \times$ sebum absorption ratio (JIS method).

Results and Discussion

Fractional factorial experimentation. The conditions for synthesis of polymer microgels were determined using fractional factorial experimentation.[9] To study the effect of the reaction parameters on the sebum absorption ratio and the mean particle size of the poly(*iso*-BMA-co-EGDMA) microgel, IPA (wt%), calcium phosphate (wt%), AIBN (mole%), acacia gum (wt%), EGDMA (mole%), HPMC (wt%), and stirring speed (rpm) were chosen as the parameters for synthesis by the dispersion polymerization method. The IPA content in the IPA/water medium varied from 5 to 10 wt%, the calcium phosphate content from 0.9 to 1.5 wt%, the AIBN content from 1.0 to 4.0 mole%, the HPMC content from 0.7 to 1.3 wt%, the acacia gum content from 0.5 to 0.9 wt%, and the stirring speed varied from 500 to 900 rpm.

To reduce the test frequency, the experimental conditions were designed for fractional factorial experimentation, and the synthesis conditions are shown in Table 1. The experiment was carried out according to the sequence followed in the dispersion polymerization. The sebum absorption ratio and the mean particle size of the poly(*iso*-BMA-co-EGDMA) microgels were measured using the new sebum absorption ratio measurement method.

As can be seen, the effect of the EGDMA content on the sebum absorption ratio was most significant. The effects of the IPA content and the stirring speed were greater than those of the other parameters and lesser than that of EGDMA, whereas neither the calcium phosphate content, the AIBN content, the HPMC content, nor the acacia gum content significantly affected the sebum absorption ratio. The effect of the stirring speed on the mean particle size was the greatest. The effect of the HPMC content was greater than those of the other parameters and lesser than that of the stirring speed. Neither the calcium phosphate content, the AIBN content, the EGDMA content, the IPA content, nor the acacia gum content affected the mean particle size.[13]

According to these results, it can be confirmed that EGDMA, IPA, and stirring speed are the main parameters for synthesis of poly(*iso*-BMA-EGDMA) microgels. The other parameters are 1.5 wt% calcium phosphate, 1.0 mole% AIBN, 1.3 wt% HPMC, and 0.9 wt% acacia gum.

Response surface design. The suitable synthesis conditions, which include a high sebum absorption ratio and an appropriate particle size (3-5 μm), were determined using the main parameters, that is, EGDMA, IPA, and stirring speed, according to the response surface design method. Accordingly as the sebum absorption ratio increases with deceasing EGDMA content, the EGDMA content was established as 0.02-0.03 mole%. The IPA content and the stirring speed were varied from 5 to 10 wt% and from 500 to 900 rpm, respectively. According to the results of two-way factorial design and the method of steepest ascent, the sebum absorption ratio of the microgels exhibited a maximum value at 1100 rpm stirring speed and 15 wt% IPA. Thus, we expanded the experimental range to 900-1100 rpm stirring speed and 10-20 wt% IPA.[14]

The experiments were carried out according to the Box Benhken design, and the sebum absorption ratio and the mean particle size were expressed as functions of EGDMA, IPA, and stirring speed, according to the second-order model.

$$Y_1 = b_0 + b_1X_1 - b_2X_2 + b_3X_3 + b_{12}X_1X_2 + b_{13}X_1X_3 + b_{23}X_2X_3 + b_{11}X_1X_1 + b_{22}X_2X_2 + b_{33}X_3X_3 \quad (2)$$

$$Y_2 = c_0 + c_1X_1 + c_2X_2 + c_3X_3 + c_{12}X_1X_2 + c_{13}X_1X_3 + c_{23}X_2X_3 - c_{11}X_1X_1 + c_{22}X_2X_2 + c_{33}X_3X_3 \quad (3)$$

where Y_1 and Y_2 are the sebum absorption ratio and the mean particle size, X_1, X_2, and X_3 are the IPA content, stirring speed, and EGDMA content, b_0 and c_0 are the initial sebum absorption ratio and mean particle size values, and b_n and c_n are the sebum absorption ratio and the mean particle size regression coefficients, respectively.

According to the results of the regression analysis, it was confirmed that the sebum absorption ratio depends more on a square formula than a linear formula. Between the EGDMA content and the stirring speed or between the IPA content and the stirring speed, there is an alternating action. The sebum absorption ratio can be calculated according to following equation.

$$Y_1 = 7914.6 + 85.5X_1 + 13.6X_2 + 540.9X_3 + 1.9X_1X_2 + 0.007X_1X_3 + 0.06X_2X_3 - 1.9X_1X_1 + 0.007X_2X_2 - 215.3X_3X_3 \quad (4)$$

When the stirring speed was 1000 rpm, the microgel showed a maximum value of sebum absorption ratio at 14 wt% IPA and 2.6 mole% EGDMA. When EGDMA was 2.5 mole%, the microgel exhibited a maximum value at 14 wt% IPA and 1100 rpm stirring speed. When the IPA content was 15 wt%, the microgel showed a maximum value at 2.6 mole% EGDMA and 1100 rpm stirring speed. According to these results, the suitable conditions can be determined to be the following: 14.4 wt% IPA content, 1016 rpm stirring speed, and 2.6 mole% EGDMA. Under these conditions, the microgel showed a sebum absorption ratio of 282.4%.

The determination of the synthesis conditions for the particle size can be approached similarly to the determination of the synthesis conditions for the sebum absorption ratio. Those conditions are 14.0 wt% IPA content, 1000 rpm stirring speed, and 2.5 mole% EGDMA, under which the microgel has a particle size of 3.5 μm.

The synthesis conditions were determined by synthetically considering the sebum absorption ratio and the mean particle size, and are 14.0 wt% IPA content, 1000 rpm stirring speed, and 2.5 mole% EGDMA, under which the microgel shows a particle size of 3.5 μm and a sebum absorption ratio of 282%. An SEM micrograph of the microgel is shown in Figure 1.

Effect of monomer type. The effect of the monomer type on the sebum absorption ratio and the mean particle size were investigated. Figure 2 shows the relationships between the monomers, that is, *n*-BMA, *iso*-BMA, *t*-BMA, and CMA, and the sebum absorption ratio and the mean particle size. As can be seen, the mean particle size of the microgels was not significantly affected by the change of monomer. Poly(*n*-BMA-co-EGDMA) microgel showed the highest sebum absorption ratio (198%), whereas poly(CMA-co-EGDMA) microgel exhibited the lowest value (77%). The sebum absorption ratio order was poly(*n*-BMA-co-EGDMA) > poly(*iso*-BMA-co-EGDMA) > poly(*t*-BMA-co-EGDMA) > poly(CMA-co-EGDMA). This result can be attributed to the fact that the hydrodynamic volume in the linear large-side-chain-containing structure was larger than that in the ramification chain-containing structure.[15]

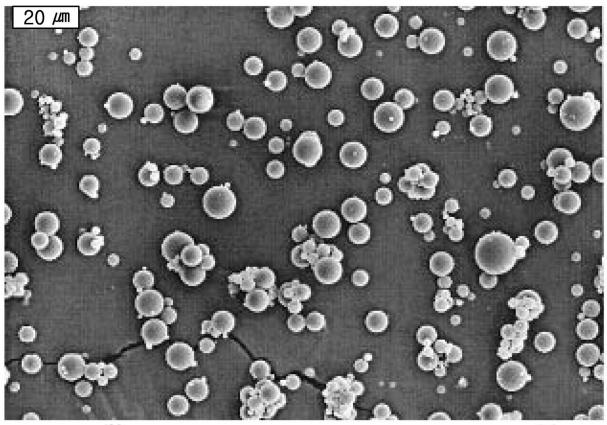

Figure 1. Particle shape of poly(*iso*-BMA-co-EGDMA) microgels.

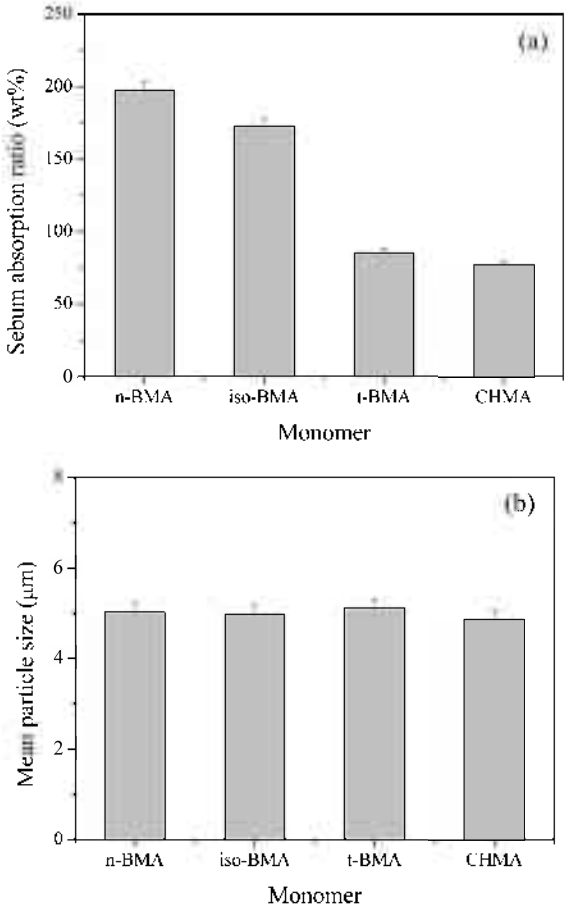

Figure 2. Sebum absorption ratio (a) and mean particle size (b) of polymer microgels prepared from various monomers.

Effect of solvents. The effect of solvent in organic solvent/water systems on the sebum absorption ratio and the mean particle size of poly(*iso*-BMA-co-EGDMA) microgel was studied using IPA, acetone, ethyl acetate, *n*-butanol, and

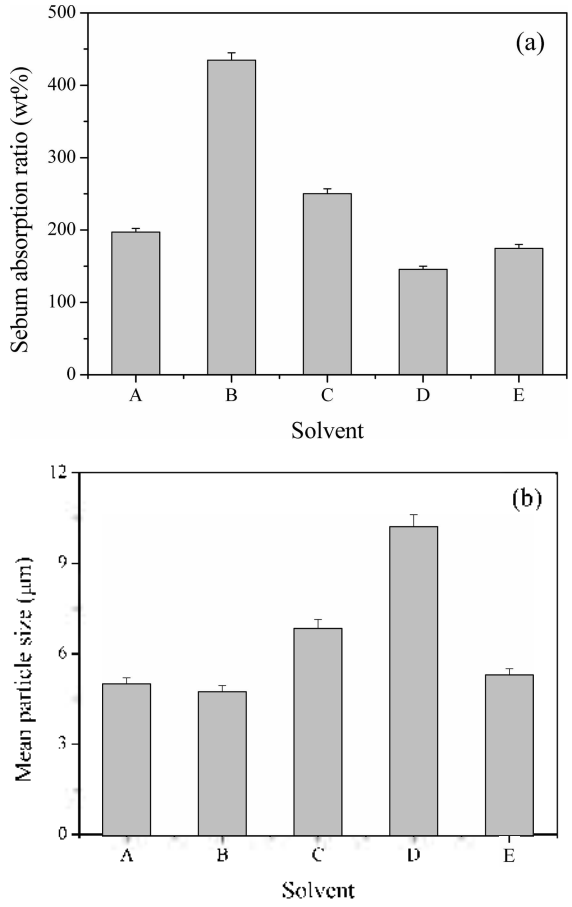

Figure 3. Sebum absorption ratio (a) and mean particle size (b) of poly(*iso*-BMA-co-EGDMA) microgels prepared from various solvents (A: IPA, B: acetone, C: ethyl acetate, D: *n*-butanol, E: ethyl alcohol)

ethyl alcohol as solvents. Figure 3 shows the relationship between the solvents and the sebum absorption ratio and the mean particle size. When acetone was used as the solvent, the microgel showed the highest sebum absorption ratio (435 wt%) and a mean particle size of 4.7 μm, as shown in Figure 3. When *n*-butanol was used as the solvent, by contrast, the microgel showed the lowest sebum absorption ratio (146 wt%) and a mean particle size of 10.2 μm. The sebum absorption ratio order was acetone > ethyl acetate > IPA ≥ ethyl alcohol > *n*-butanol.

These results can be explained according to the molecular weight between cross-links ($\overline{Mc}$). $\overline{Mc}$ is an important characteristic of polymers, and is related to cross-linking density. In this study, $\overline{Mc}$ was measured using Flory-Rehner's equilibrium swelling method, as follows:[16]

$$\overline{Mc} = -V_1\rho_p(\phi_p^{1/3} - \phi_p/2)/[\ln(1-\phi_p) + \phi_p + x_1\phi_p^2] \quad (5)$$

where V_1 is the solvent mole volume, ρ_p is the polymer density, x_1 is the Flory-Huggins polymer-solvent interaction parameter, and ϕ_p is the ratio of microgels volume in the swelling state to microgels volume in the drying state.

$$\text{Swelling rate } (S) = 1/\phi_p \quad (6)$$

Table 6. Variation of network structure parameters and sebum absorption ratio of the microgels prepared from various solvents

Solvent (14 wt% in water)	ϕ_p	S	$\overline{Mc}$	q	ρ_p	Sebum absorption ratio (wt%)
IPA	0.43	2.30	669	0.21	0.99	173 ± 5
acetone	0.20	5.12	2286	0.06	0.98	435 ± 10
ethyl acetate	0.31	3.27	1081	0.13	0.98	250 ± 7
n-butanol	0.47	2.15	603	0.24	1.00	146 ± 4
ethyl alcohol	0.43	2.34	669	0.21	0.99	175 ± 5

The cross-linking density (q) is the ratio of molecular weight per unit to molecular weight between cross-links.

$$q = M_o/\overline{Mc} \quad (7)$$

The results for $\overline{Mc}$, S, q, ϕ_p, and the sebum absorption ratio for the poly(*iso*-BMA-co-EGDMA) microgels obtained from the various solvents are shown in Table 6. They indicate that the sebum absorption ratio of the microgels was increased by increasing the molecular weight between the cross-links.

According to these results, then, the optimal synthesis conditions for the microgels are MG-42, that is, 1.1 wt% calcium phosphate, 0.9 wt% acacia gum, 1.3 wt% HPMC, 1.0 mole% AIBN, 2.5 mole% EGDMA, 1000 rpm stirring speed, and 14 wt% acetone/water. Under these conditions, the microgel has a particle size of 4.76 μm and a sebum absorption ratio of 434.8%.

Conclusions

Alkyl methacrylate-based microgels were synthesized by dispersion polymerization, and their sebum absorption characteristics were investigated. In the course of fractional factorial experimentation, EGDMA content, IPA content, and stirring speed were chosen as the main parameters for synthesis of poly(iso-BMA-co-EGDMA) microgel. Through response surface design, the suitable synthesis conditions were determined, the resulting microgel exhibiting a particle size of 3.5 μm and a sebum absorption ratio of 282%. The sebum absorption ratio order for monomer effects was determined to be *n*-BMA > *iso*-BMA > *t*-BMA > CMA, whereas that for solvent effects was acetone > ethyl acetate > IPA ≥ ethyl alcohol > *n*-butanol. The optimal microgel synthesis conditions for cosmetics were determined to be 1.1 wt% calcium phosphate, 0.9 wt% acacia gum, 1.3 wt% HPMC, 1.0 mole% AIBN, 2.5 mole% EGDMA, 1000 rpm stirring speed, and 14 wt% acetone/water. Under these conditions, the microgel had a particle size of 4.7 μm and a sebum absorption ratio of 435%.

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