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Synthesis of New Phospholipid Biocompatible Textile Finishing Agent

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Abstract— A methacrylate monomer having phospholipid polar group and cell membrane structure is known as highly biocompatible. Based on these properties, new biocompatible multi-functional textile finishing agent was developed using phospolipid copolymer. 2-Methacryloyloxyethyl phosphorylcholine (MPCE) was synthesized using 2-hydroxyethyl methacrylate (HEMA), 2-chloro-2-oxo-1,3,2-dioxaphospholane (COP) and triethylamine (TEA), and then polymerized to prepare MPCE copolymer by radical polymerization using azobisisobutyronitrile(AIBN). The structures of MPCE was characterized by FT-IR and ^{1}H NMR and will be evaluated as textile finishing agent in further study.

Keywords: *phospholipid, biocompatible, finishing agent, skin care, MPC, MPCE*

1. Introduction

Environmental technology (ET) is already one of the most important technology area throughout the world and the demand of environmental friendly and biocompatible products are continuously increasing. Also in textile industry, lots of functional eco products such as antimicrobial, skin aging, atopy prevention and moisturizing are continuously developed and introduced. Especially, biocompatible moisture finishing products for skin protection such as squalene, collagen, chitosan, and hyaluronic acid are very widespread in cosmetics or medical care area. However, in textile industry, these materials were not so popular since the performance was unsatisfactory when applied to synthetic fibers. In case of skin care products using natural materials, continuous stability was indicated with problem, and not only functionality of products but also durability were unsatisfactory. In this regards, binder treatment was attempted but it was not used widely since the performance of finishing agent itself was markedly reduced. Also the product development using microcapsules for complement of stability was progressed, but productivity decrease due to additive process and cost performance were unsatisfactory, and materials for capsulation and binder were indicated with problem like rough touch.

The main component of phospholipid polymer known as lipidure is 2-Methacryloyloxyethyl phosphorylcholine (MPC) shown in Fig. 1, MPC consists of hydrophilic phosphoric acid parts and hydrophobic lipid parts forming fats. It was already verified that they have functions of moisturizing, anti skin aging, antimicrobial and excellent stability since they have similar structures to cell membrane[1-3]. Recently these phospholypid was developed extensively for textile finishing agent, but product research and application were very few in the country[4-8].

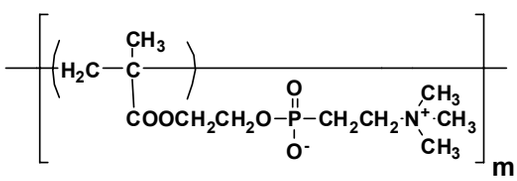

Fig. 1. The structure of MPC.

In this study, new phospholipid compound as 2-Methacryloyl oxyethyl Phosphoryl Choline (MPCE) in which the terminal methyl group of MPC was substituted with ethyl group was synthesized and polymerized with biocompatible materials such as 2-hydroxyethyl methacrylate (HEMA) and N-isopropyl acrylamide (NIPAM). At this point, 7 types of copolymers were synthesized by varying biocompatible monomers and polymerization ratio.

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The chemical structure in each synthetic process was characterized by ^{1}H NMR and FT-IR spectroscopy, and biocompatibility of synthesized polymers were verified by single-dose patch test and skin barrier function recovery test.

These results demonstrate the synthesis of new biocompatible muti-functional textile finishing agents based on phospholipid MPCE copolymer and expect to provide important information for preparing and application to finishing agent for textile.

2. Experimental

2.1 Materials

2-hydroxyethyl methacrylate (HEMA), triethyl amine (TEA), N-isopropylacrylamide (NIPAM) and amminopropanoic acid were obtained from Aldrich, 2-chloro-2-oxo-1,3,2-dioxaphospholane (COP) and acryloyl chloride were obtained from TCI, and azobisisobutyronitrile (AIBN) was obtained from JUNSEI. All chemicals are extra pure reagent quality and used without purification.

Tetrahydrofuran (THF) and acetonitrile (AN) were purified by distillation using sodium and calcium chloride to eliminate extent oxygen.

2.2 Synthesis of OPEMA

Into a 500 ml double walled vessel equipped with constant low temp circulator and dropping funnel under dry nitrogen atmosphere, 15.6g (0.154mol) of TEA and 20g (0.154mol) of HEMA were dissolved to 200ml of dry THF. The reaction mixture was kept at 0℃, since COP is very reactive and the reaction generated a large amount of heat, 24.1g (0.186mol) of COP in 100ml of dry THF were added dropwise to the stirred solution. The mixture was warm up to room temperature after 1hr and maintained for 4hrs. Then, the precipitate was filtered off to remove triethylammonium chloride salt and the filtrate was evaporated under reduced pressure. To the residue, THF and diethyl ether were added to precipitate a small amount of salt by filtration. By evaporation of filtrate under reduced pressure, colorless liquid compound, 2-(2-oxo-1,3,2-dioxaphospholoyloxy) ethyl methacrylate (OPEMA) was obtained (yield : 34.9%). ^{1}H NMR ($CDCl_3$): δ=1.95 (-CH_3, 3H), 4.12～4.40 (-CH_2-, 8H), 5.61 (-CH=, 1H), 6.18 (-CH=, 1H).

2.3 Synthesis of MPCE

Into a 500 ml flask equipped with oil bath and condenser under dry nitrogen atmosphere, 35.0g (0.148mol) of OPEMA was dissolved to 200ml of dry acetonitrile and stirred for 20 min. After 30.0g (0.296g) of TEA was added to stirred solution, the flask was sealed. The reaction mixture was warm up to 60℃ and maintained for 3 days and evaporated under reduced pressure. Dry acetonitrile were added to the residue and evaporated to give colorless liquid product, 2-Methacryloyloxyethyl phosphorylcholine (MPCE) (yield : 36.9g). ^{1}H NMR($CDCl_3$): δ= 1.30 (-CH_3 in $N^+(CH_2CH_3)_3$, 9H), 1.95 (-CH_3, 3H), 3.05 (-CH_2 - in $N^+(CH_2CH_3)_3$, 6H), 4.00～4.50 (-CH_2-, 8H), 5.60 (-CH=, 1H), 6.18 (-CH=, 1H). IR(cm^{-1}): 1716 (C=O), 1635 (C=C), 1238 (O^--P=O), 1200～1000 (P-O-C), 970 (N^{+}-$(CH_2CH_3)_3$). [Fig. 2]

2.4 Polymerization of MPCE

The desired amount of MPCE was dissolved to 50ml of methanol(MeOH)-THF mixture (3:7, v/v), and 1 mol% AIBN for monomer was added to reaction mixture.

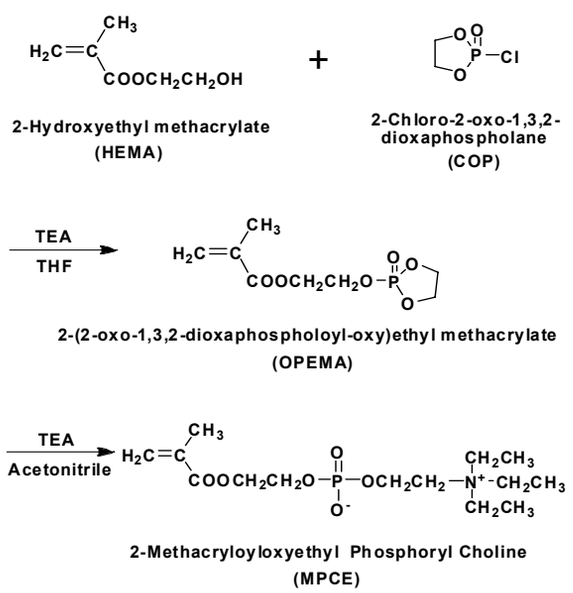

Fig. 2. Synthesis of MPCE.

To eliminate oxygen in the flask, dry nitrogen was bubbled and the flask was sealed. After it was heated at 60℃ for 48 hr, the reaction mixture was precipitated by pouring into diethyl -ether. The precipitate was filtered and dried in vaccum oven and MPCE homopolymer was obtained. IR(cm^{-1}): 1731 (C=O), 1240 (O^--P=O), 1200～1000 (P-O-C), 983 ($N^+(CH_2CH_3)_3$). [Fig. 3]

2.5 Copolymerization of MPCE and HEMA

MPCE and HEMA were dissolved to 50ml of methanol(MeOH)-THF mixture (3:7, v/v). At this time, monomers were added at the molecular ratio of each 1:5 and 1:1. Other processes are the same as the above. IR(cm^{-1}): 3430 (-OH), 1728 (C=O), 1241 (O^--P=O), 1200～1000 (P-O-C), 966 ($N^+(CH_2CH_3)_3$). [Fig. 4]

2.6 Copolymerization of MPCE and NIPAM

MPCE and NIPAM were dissolved to 50ml of methanol(MeOH)-THF mixture (3:7, v/v). At this time, monomers were added at the molecular ratio of each 1:5 and 1:1. Reaction was kept for 5 days, and other processes are the same as the above. IR(cm^{-1}): 3300 (-NH- stretch), 1728 (C=O), 1652 (CONH), 1243 (O^--P=O), 1200～1000 (P-O-C), 966 ($N^+(CH_2CH_3)_3$). [Fig. 5]

2.7 Copolymeriztion of MPCE and NIAPM-COOH

To synthesis the NIPAM that carboxylate was substituted, 33.85g(0.38mol) of aminopropanoic acid and 50.00g(0.88mol) of calcium hydroxide were dissolved to 580ml of water into a 500ml flask equipped with ice bath. [Fig. 6, Table 1]

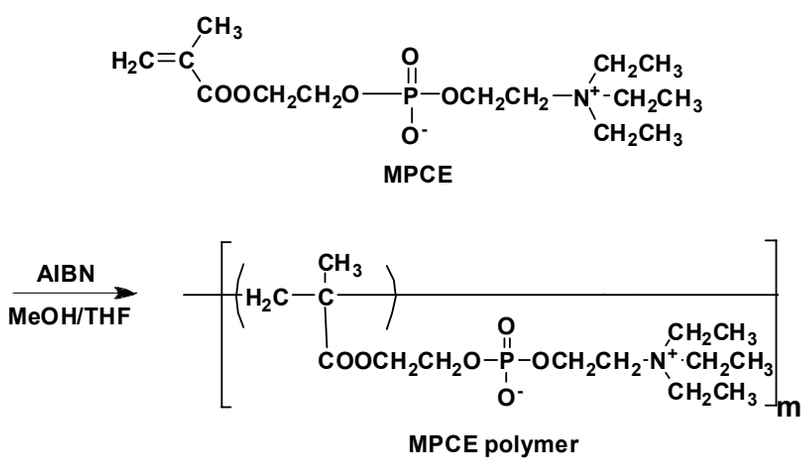

Fig. 3. Synthesis of MPCE homopolymer.

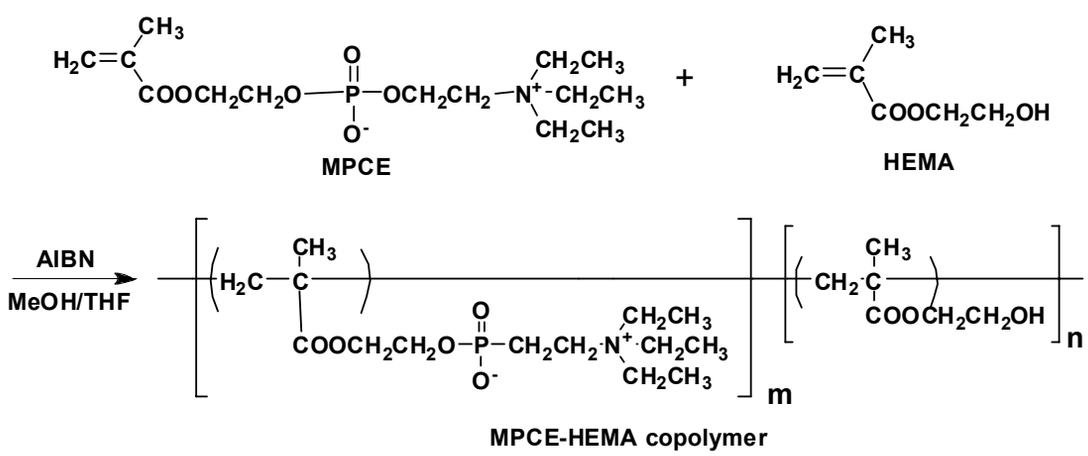

Fig. 4. Synthesis of MPCE-HEMA copolymer.

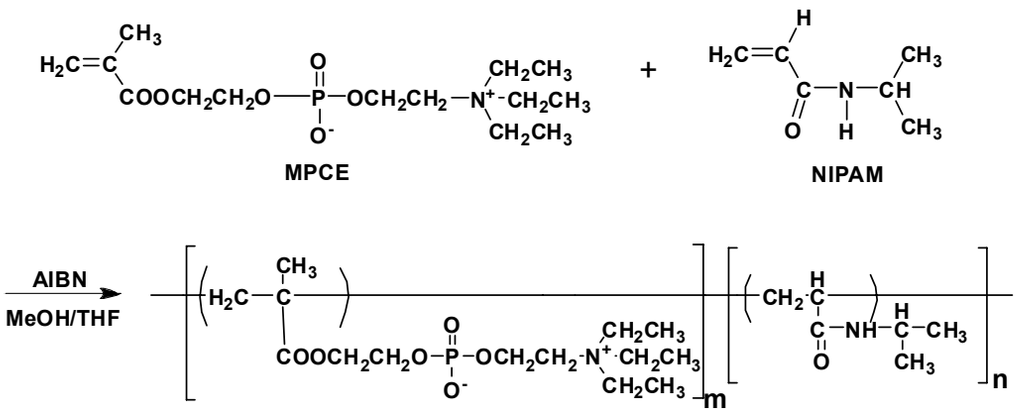

Fig. 5. Synthesis of MPCE-NIPAM copolymer.

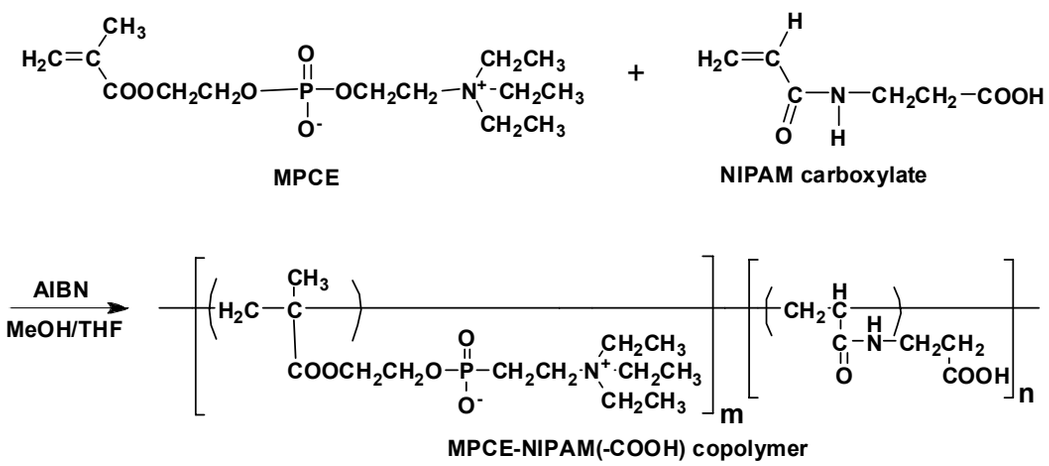

Fig. 6. Synthesis of MPCE-NIPAM(-COOH) copolymer.

Table 1. Copolymerization of MPCE

Polymer	Composition (g)		AIBN (mg)	Solvent (MeOH/THF)	Time (days)	Yield (%)
	MPCE	Monomer				
MPCE	10.0	-	49	3 / 7	3	82.7
MPCE / HEMA (1:5)	1.7	3.2	49	3 / 7	3	72.3
MPCE / HEMA (1:1)	5	1.9	49	1 / 1	3	76.3
MPCE - NIPAM (1:5)	1.7	2.8	49	3 / 7	5	64.5
MPCE - NIPAM (1:1)	5	1.7	49	1 / 1	5	72.8
MPCE - NIPAM(-COOH) (1:5)	1.7	3.5	49	3 / 7	5	76.1
MPCE - NIPAM(-COOH) (1:1)	5	2.1	49	1 / 1	5	73.6

The reaction mixture was kept at 0℃ and 38.99g(0.43mol) of acryloyl chloride was added dropwise to the stirred solution and kept for 2hrs. After stirring, the reaction mixture was filtered off to remove calcium hydroxide, and acidity of filterate was maintained at pH 1～2 using aqueous hydrochloric acid. Then, solution was saturated by sodium chloride and dissolved to ethyl acetate. After mixture was treated using separatory funnel 3～4 time, it was evaporated under reduced pressure. The remaining substance was recrystallized with ethyl acetate, and white crystal product was

obtained. ^{1}H NMR($CDCl_3$): δ=2.48 (CH_2 in CH_2COOH, 2H), 3.30 (CH_2 in -$NHCH_2$-, 2H), 5.55 (CH in CH_2=, 1H), 6.03 (CH in CH_2=, 1H), 6.20(CH in =CHCO-, 1H), 8.17 (-NH-, 1H), 12.24 (-OH, 1H).

MPCE and NIPAM carboxylate were dissolved to 50ml of methanol(MeOH)-THF mixture (3:7, v/v). At this time, monomers were added at the molecular ratio of each 1:5 and 1:1. Reaction was kept for 5 days, and other processes are the same as the above.

2.8 Single-dose patch test of MPCE treated fabric

The primary irritation of MPCE polymer for human skin was evaluated by 48hr single-dose patch test. The testing solution was prepared by concentraion of 0.5% MPCE polymer in water and test area were washed and dried by 70% ethanol. After 20㎕ of testing MPCE solution was droped in IQ Ultra TM chamber (Chemotechnique Diagnostics AB, Sweden), it was attached and fastened at the back of test subject. Patch was kept for 48 hrs, and erythema was observed after 30 min and 24hrs after removal. [Table 2]

Table 2. MPCE polymer solution for Single-dose patch test

No.	MPCE polymer solution (0.5% MPCE)
control	-
1	MPCE homopolymer
2	MPCE-HEMA 1:1
3	MPCE-NIPAM 1:1
4	MPCE-NIPAM(-COOH) 1:1

2.9 Skin barrier function recovery test

Skin barrier function recovery test was carried out to clarify the effect of skin function recovery by MPCE polymer. Generally, since skin surface is roughen and increased surface area by skin irritation, water loss per time is relatively increased. Consequently, skin fuction recovery effect was evaluated by trans-epidermal water loss. For this test, test area was artificially damaged by 10% aqueous SDS(sodium dodesyl sulfate) solution, and the water loss was measured by Tewameter TM 300 when contacted with MPCE treated and untreated fabric. Selected and tested polymers were MPCE homopolymer and MPCE-NIPAM carboxylate copolymer. [Fig. 7, Table 3]

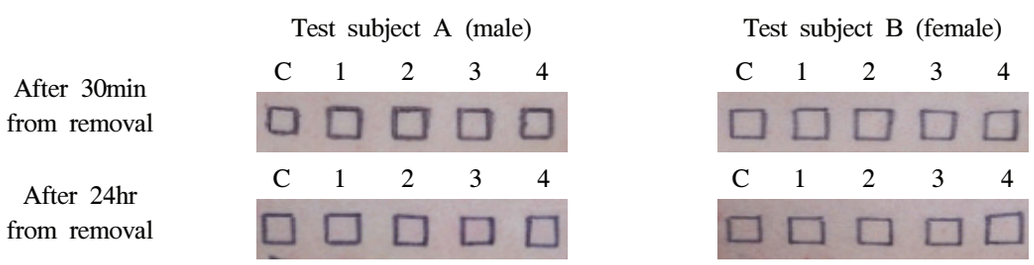

Fig. 7. Erythema measurement after removal of MPCE treated patch.

Table 3. Trans-epidermal water loss by Tewameter

Test subject	MPCE polymer		Before SDS treatment	After SDS treatment	After removal	Recovery ratio
Male	MPCE homopolymer	untreated	12.8	27.3	21.1	42.8
		treated	12.6	32.4	21.6	54.5
	MPCE-NIPAM (-COOH)	untreated	19.5	37.2	25.8	64.4
		treated	13.8	36.8	21.8	65.2
Female	MPCE homopolymer	untreated	19.3	34.6	21.9	83.0
		treated	17.3	30.9	19.1	86.8
	MPCE-NIPAM (-COOH)	untreated	19.7	27.6	25.5	26.6
		treated	17.3	30.3	18.3	92.3

At first, trans-epidermal water loss of normal condition was measured before SDS treatment, and SDS treated textiles were applied on the back of human subjects and sealed for 24hrs. Then, textiles were taken off from the back and remeasured trans-epidermal water loss. After test area were patched by MPCE treated textile for 1hr, trans-epidermal water loss was measured immediately after removal. At this point, recovery ratio was calculated by comparing before and after SDS treatment with patching MPCE treated textiles.

$$Recovery\,rate(\%) = \frac{T_1 - T_2}{T_1 - T_0} \times 100$$

T_0 : water loss before SDS treated
T_1 : water loss after SDS treated
T_2 : water loss after removal of MPCE treated textile

3. Result and discussion

3.1 Synthesis of phospholipid

Recently, lots of biocompatible textile finishing method were proceeded actively and various products were released because of the demand of skin-care product. 'Lipidure' developed by NOF Co. showed up skin-care effects such as anti-microbial, water retention, skin irritation activity, antistatic, and hygroscopic successfully by using phospholipid having various biocompatible materials. This phopholipid was synthesized using 2-Methacryloyl oxyethyl Phosphoryl Choline (MPC) by standard method, and it has similar structure to cell membrane consisting of hydrophilic phosphoric acid parts and hydrophobic lipid parts forming fats. Also, it has advantage of polymerization due to having reactive double bond.

The MPC was synthesised by reaction of 2-(2-oxo-1,3,2-dioxaphopsoloyloxy)ethyl methacrylate (OPEMA) and trimethyl amine (TMA). TMA was difficult to use since it is colorless toxic gas at room temperature having low boiling point (2.87 °C). In practical synthesis process, it had to be controlled in strict condition which were equiped with pressure vessel and the temperature should be maintained lower than -20°C. But triethyl amine (TEA) is simple to control compared with TMA because of very lower toxicity and relatively high boiling point (89.7°C). So, MPCE could be synthesized easily when replace TMA with TEA, and MPCE have multi functionality because of similar structure to MPC.

3.2 Polymerization of MPCE

2-Hydroxyethyl methacrylate (HEMA) is hydrophilic materials and verified iocompatibility, since it is already used in medical, cosmetics and healthy foods. Actually it is the main ingredient for contact lens and intraocular lens because of high water contents and great optical penetrability[9]. Due to its biocompatibility, HEMA is also used in wound dressing[10]. In this respect, if HEMA which was verified hydrophilicity and biocompatibility is polymerized with MPCE, it can invest hydroxy group in copolymer. Hydroxy group can form hydrogen bond to form film with hydrophobic interaction of lipid parts. So polymerization with HEMA is not only investing hydrophilicity and biocompatibility but also forming film.

N-isopropylacrylamide (NIPAM) is also used in medical industry as biocompatible meterial. Usually it is applied hydrogel formation and used in drug delivery system for medicine polymer[11,12]. Therefore, copolymer preparing polymerization with MPCE and NIPAM also have biocompatibility. In addition, it is expected to have greater hygroscopic property and water retention by substituting terminal group of NIPAM with carboxylate.

3.3 Biocompatibility of MPCE polymers

The results of single-dose patch test are shown in Fig. 7. The erythema was not detected in both cases compared with control sample using pure water with MPCE solution. Also every MPCE polymers were not induced erythema when observed by naked eyes after 30min and 24hrs after removal.

Consequently, it was confirmed that MPCE polymers were biocompatible.

Table 3 shows the results of skin barrier function recovery test after SDS treatment. The recovery rate was calculated by the equation above after measurement of each skin barrier function recovery test, and it showed that the degree of skin function recovery by wearing of MPCE treated textile. From the results of the test when MPCE treated textile were applied, the recovery rate was increased more than the control textiles. Especially, in the case of woman having sensitive skin type, results showed high recovery rate about 90%. Therefore, although it showed difference according to skin type or sex, it can be confirmed that MPCE polymers were effective in skin recovery function. Consequently, it was verified that MPCE polymers are biocompatible through single-dose patch test and skin barrier function recovery test.

4. Conclusion

Phospholipid is very biocompatible since they have similar structures to cell membrane. The MPC which is used in some company had problems such as low temperature condition and toxicity of reactant in synthetic process. But MPCE which is described in this study overcomes the disadvantage of MPC and have advantage of milder synthetic condition. From this research, seven types of MPCE polymer were synthesized by polymerization with HEMA and NIPAM, and their skin recovery function and biocompatibility was confirmed.

Acknowledgement

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