

# Study on biomimetic phospholipid modification of aliphatic polyester biomaterials

Xiaomin ZHANG<sup>1</sup>, Jin DENG<sup>2</sup>

<sup>1</sup> The First Affiliated Hospital of Hebei North University, Zhangjiakou 075000, China;

<sup>2</sup> College of Science, Hebei North University, Zhangjiakou 075000

## ARTICLE INFO

Received: 6 June 2023

Accepted: 17 August 2023

Available online: 2 September 2023

<http://doi.org/10.59400/eco.v3i1.27>

Copyright © 2023 author(s).

Licensed under the Creative Commons Attribution-NonCommercial 4.0 International License (CC BY-NC 4.0).  
<https://creativecommons.org/licenses/by-nc/4.0/>

**ABSTRACT:** It is low feasibility using plasma energy particles to excite, ionize and break bonds molecules on the surface of aliphatic polyester biomaterials to produce new topological structures. The biomimetic phosphatidylcholine modification technology of aliphatic polyester biomaterials was studied. The phosphatidylcholine monomer [2 (methacryloxy) ethyl]phosphatidylcholine was synthesized by reaction of 2 chloro 1, 3, 2 dioxaphosphoric heterocyclic pentane with different raw material solutions; the phosphatidylcholine[2 (methacryloxy) ethyl]phosphatidylcholine, acrylonitrile and water were copolymerized to form PANCMPC; the phosphatidylcholine [2 (methacryloxy) ethyl]phosphatidylcholine was replaced by PANCMPC, and PANCHEMA was obtained by repeated copolymerization. PANCHEMA was reacted with 2 chloro 2 oxygen 1, 3, 2 dioxophosphorus heterocyclic pentane, and then opened with trimethylamine to form biomimetic phospholipid modified PLCANCP. Experiments show that the proposed technology has good hydrophilicity.

**KEYWORDS:** Aliphatic polyester; Biomaterials; Surface; Biomimetic phospholipidization; Modification technology; Biocompatibility

## 1 Introduction

Aliphatic polyester-based biomaterials are new high-tech functional materials that can diagnose and treat human diseases and regulate and replace damaged tissues and organs in order to enhance their functions<sup>[1]</sup>. Since the surface of aliphatic polyester biomaterials is the first to come into contact with human tissues during their placement in the human body, the biophilicity, biocompatibility, and resistance to contamination of the material surface play a decisive role in whether they are accepted by the human body<sup>[2]</sup>. To improve the biocompatibility of aliphatic poly-

ester-based biomaterials, the material itself is usually changed<sup>[3]</sup>, therefore, it is particularly important to investigate an efficient surface modification technique for aliphatic polyester-based biomaterials.

Currently, when changing the surface properties of aliphatic polyester-based biomaterials, plasma modification techniques are mostly used<sup>[4]</sup>, where aliphatic polyester-based biomaterials are placed in a plasma cavity in the presence of a non-polymeric atmosphere, and plasma energy particles are used to excite, ionize, and break bonds on the surface molecules of aliphatic polyester-based biomaterials, resulting in new topology.

However, such techniques are more difficult and enhance the surface properties of the material poorly<sup>[5,6]</sup>. In this study, we propose a surface biomimetic phospholipid modification technique to

enhance the surface biocompatibility of aliphatic polyester-based biomaterials.

## 2 Biomimetic phospholipid modification of aliphatic polyester-based biomaterial surfaces

Taking acrylonitrile as an example, the biomimetic phosphorylation modification technique was specified: Aqueous phase precipitation polymerization was used to produce acrylonitrile copolymers by co-acrylonitrile and hydroxyethyl methacrylate<sup>[7]</sup>, and the acrylonitrile copolymers were reacted with 2-chloro- 2-oxo-1, 3, 2 -dioxaphospholane and then reacted with trimethylamine to achieve surface bionic phosphorylation of acrylonitrile copolymer.

### 2.1 Experimental materials

The main instrumentation required for the surface bionic phospholipidation modification process of aliphatic polyester-based biomaterials is shown in **Table 1**.

The main chemical raw materials required for the surface biomimetic phospholipidation modification process of aliphatic polyester-based biomaterials are shown in **Table 2**.

### 2.2 Phosphatidylcholine synthesis

#### 2.2.1 Synthesis of 2-chloro-1, 3, 2-dioxaphospholane

A three-neck flask with a capacity of 1000 mL was selected. a condensation reflux tube containing CaCl<sub>2</sub> desiccant, a stirrer, and a dropping funnel were fixed to the flask. Purified dichloromethane and phosphorus trichloride were added to the flask at 450 and 200 mL, respectively, and stirred using a stirrer. Anhydrous ethylene glycol was gradually added dropwise during stirring to a volume of about 126 mL, generating a large amount of hydrogen chloride gas. To remove the residual dichloromethane<sup>[8]</sup>, distillation of the reactants in the flask was performed immediately after the feedstock was placed into the reaction, and reduced-pressure distillation of the formation in the flask after distillation was performed<sup>[9]</sup> to

**Table 1** Main instruments and equipment

| Instrument name                           | Model               | Place of origin                         |
|-------------------------------------------|---------------------|-----------------------------------------|
| SEM Scanning Electron Microscopy          | S-570               | Stender Testing Center                  |
| Speed-controlled multi-purpose oscillator | HY-2                | Background Zhongke Huxin Technology Co. |
| Electronic tension test machine           | AGS-500ND           | Shimadzu Corporation                    |
| Visible spectrophotometer                 | UV-1601PC           | Japan                                   |
| Nuclear Magnetic Resonance Instrument     | ADVANCE-DMX500      | BRUKER, Switzerland                     |
| Contact angle measuring instrument        | OCA20 - Dataphysics | Germany                                 |
| Infrared spectrophotometer                | BRUKER VECTOR-22    | BRUKER Switzerland                      |

**Table 2** Main chemical raw materials

| Chemical material name | Purity specifications | Chemical material name         | Purity specifications |
|------------------------|-----------------------|--------------------------------|-----------------------|
| Benzene                | Analysis of pure      | Sodium metal                   | Chemically pure       |
| Bovine serum albumin   | B. R                  | Dichloromethane                | Analysis of pure      |
| Oxygen                 | General               | Phosphorus trichloride         | Analysis of pure      |
| Nitrogen               | General               | Sodium hydroxide               | Chemically pure       |
| Acetonitrile           | Analysis of pure      | Anhydrous ethanol              | Analysis of pure      |
| Acrylonitrile          | Chemically pure       | Dimethyl sulfoxide             | Analysis of pure      |
| Ethylene glycol        | Analysis of pure      | Calcium chloride for sewage    | Analysis of pure      |
| Triethylamine          | Analysis of pure      | Phosphorus pentoxide           | Analysis of pure      |
| Trimethylamine         | Analysis of pure      | Potassium dihydrogen phosphate | Analysis of pure      |
| Glutaraldehyde         | Analysis of pure      | Disodium hydrogen phosphate    | Analysis of pure      |
| Calcium hydroxide      | Chemically pure       | Tetrahydrofuran                | Analysis of pure      |
| N, N dimethylformamide | Analysis of pure      | Hydroxyethyl methacrylate      | Analysis of pure      |

obtain 2-chloro-1, 3, 2-dioxaphosphorane at 46 ~ 46.5 °C/15 mm-Hg.

### ***2.2.2 Synthesis of 2-chloro-2-oxo-1, 3, 2-dioxaphosphorus heterocyclopentane***

A three-necked flask with a capacity of 500 mL was selected, and 2-chloro-1, 3, 2-dioxaphosphorus heterocyclopentane and benzene solutions were added to the flask in the amounts of 45 g and 90 mL, respectively, and the flask was fed with dry oxygen for 6.5 h. To remove the residual benzene solution, distillation was performed on the reactants in the flask, and the formation in the flask after distillation was distilled under reduced pressure to obtain 2-chloro-2-oxo-1, 3, 2-dioxaphosphorus heterocyclopentane at 70°C/0.3 mmHg.

### ***2.2.3 Synthesis of 2-(methacryloyloxy)ethyl-2-oxo-1, 3, 2-dioxaphospholane***

A three-necked flask with a capacity of 500 mL was selected and a thermometer, a drying tube and a dropping funnel were fixed to the flask. Tetrahydrofuran, hydroxyethyl methacrylate and triethylamine were added to the flask in the amounts of 180 mL, 18 g and 14 g, respectively, and the temperature of the reaction solution was lowered to 20°C by stirring the three ingredients. About 20 g of 2-chloro-2-oxo-1, 3, 2-dioxaphospholane was dissolved in 90 mL of dry tetrahydrofuran, and the mixture was gradually added dropwise to the reaction solution in the flask with stirring until the end of the dropwise addition, and the reaction state was maintained for 3 h at a temperature of about -25°C. The triethylamine salt and residual tetrahydrofuran<sup>[10]</sup> produced in the flask were removed to obtain clear and viscous 2-(methacryloyloxy)ethyl-2-oxo-1, 3, 2-dioxaphospholane.

### ***2.2.4 Synthesis of [2-(methacryloyloxy)ethyl] phospholipid phosphatidylcholine***

A pressure flask with a volume of 200 mL was selected. 2-(methacryloyloxy)ethyl-2-oxo-1, 3, 2-dioxaphospholane and purified acetonitrile were placed in the pressure flask in volumes of 4.5 g and 27 mL, respectively. After setting the temperature to -20°C, the pressure flask was added with

After the temperature was set to -20°C, 1.8 mL of anhydrous trimethylamine was added to the pressure flask, and the flask was quickly sealed. The temperature was raised to 60 °C for 14.5 h, and then the temperature was lowered to -20°C again to crystallize the product in the pressure flask and obtain a white precipitate.

The white precipitate was placed in dry argon for filtration and cycled using acetonitrile<sup>[11]</sup> to finally obtain the phospholipid monomer [2-(methacryloyloxy)ethyl]phosphatidylcholine.

## **2.3 Phospholipid phosphatidylcholine copolymer synthesis**

A three-necked flask with a capacity of 1000 mL was selected and filled with fixed amounts of acrylonitrile, [2-(methacryloyloxy)ethyl]phosphatidylcholine and water in turn. Nitrogen was introduced into the flask and kept for 20 min. After setting the temperature to the reaction temperature, the redox initiator was placed into the flask and the co-polymerization reaction was started with stirring under the protection of nitrogen. After the reaction, the precipitate was removed and the product was washed several times in deionized water and ethanol. To remove unreacted monomer and soluble ethyl]phospholipid phosphatidylcholine copolymer (PANCMPC). PANCMPC was experimentally shown to have good hydrophilicity, resistance to protein adsorption, and hemocompatibility.

## **2.4 Synthesis of PANCMPC and acrylonitrile copolymer**

The [2-(methacryloyloxy)ethyl] phospholipid phosphatidylcholine in section 2.3 was replaced with PANCMPC and the copolymerization process was repeated to obtain PANCHEMA, a copolymer of PANCMPC and acrylonitrile.

## **2.5 Synthesis of biomimetic phospholipid modified PLCANCP**

In order to introduce functional groups of phospholipids with biological properties into the side chains of the copolymer molecules<sup>[13]</sup>, PANCHEMA was reacted with 2-chloro-2-oxo-1,

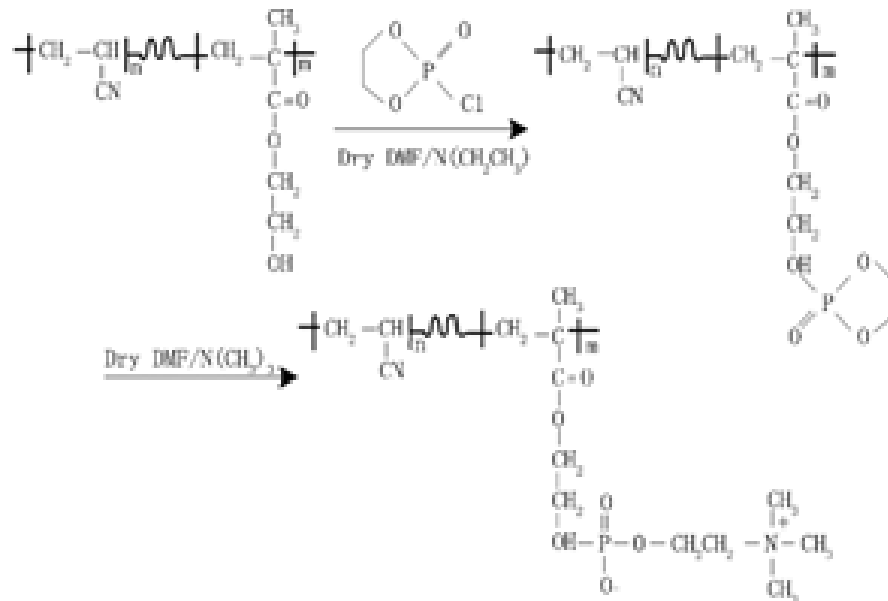


Figure 1 PLCANCP generation path

3, 2-dioxaphosphorane and then ring-opening reaction was performed with trimethylamine to generate the biomimetic phospholipid modified PLCANCP, the pathway of which is shown in Figure 1.

During the generation of mimetic phosphatidylated modified acrylonitrile copolymers, the implementation of the reaction with 2-chloro-2-oxo-1, 3, 2-dioxaphospholane by copolymer PANCHEMA was able to moderate the reaction process, while the use of excess 2-chloro-2-oxo-1, 3, 2-dioxaphospholane and trimethylamine allowed the hydroxyl group on the side chain of the copolymer molecule and the 2-chloro-2-oxo-1, 3, 2 dioxaphospholane react as a whole and convert all of them to phospholipid functional groups<sup>[14]</sup>.

## 2.6 Performance evaluation method design

The main parameters used for the evaluation of the surface properties of aliphatic polyester-based biomaterials after bionic phospholipidation modification, mainly for their biocompatibility, are water hydrophilicity and protein retention<sup>[15]</sup>. Equation (1) is the hydrophilic equation:

$$J = \frac{Y}{B\Delta t} \quad (1)$$

where  $Y$ ,  $B$  and  $\Delta t$  denote the permeable liq-

uid volume, effective surface area and operation time in L,  $m^2$  and h, respectively.

Equation (2) is the compatibility formula:

The homopolymer was purified using deionized water and dried under vacuum at  $60^\circ\text{C}$  to obtain acrylonitrile/[2-(methacryloyloxy)

$$E (\%) = \left(1 - \frac{x_p}{x_f}\right) \times 100 \quad (2)$$

Where  $x_p$  indicates the concentration of bovine serum albumin in the permeate and  $x_f$  indicates the concentration of bovine serum albumin in the raw material solution, both units are  $\text{mg/mL}$ .

The adhesion ratio  $E_{FE}$  of aliphatic polyester-based biomaterials after bionic phospholipidation modification was analyzed and calculated as:

$$E_{FE} = \frac{J_{w2}}{J_{w1}} \quad (3)$$

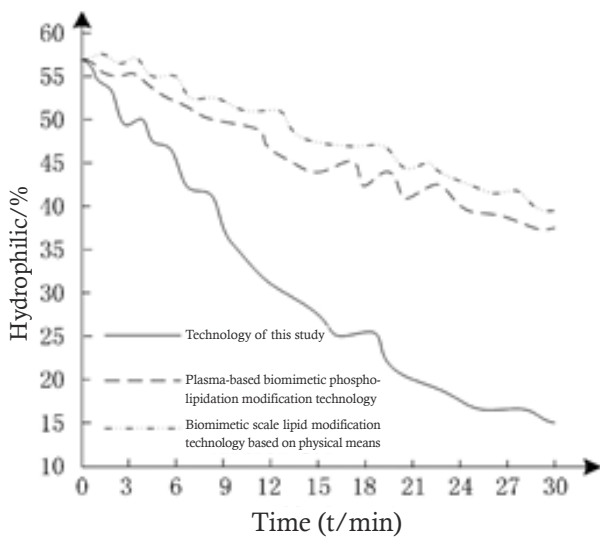
Where  $J_{w1}$  indicates the initial water flux, and  $J_{w2}$  indicates the water flux after cleaning the material surface.  $J_{w1}$  and  $J_{w2}$  can be obtained by equation (1), and then the EFE can be derived.

## 3 Experimental analysis

### 3.1 Comparative hydrophilic analysis

In order to test the clearness of the bionic

phospholipidization modification technique on the surface of aliphatic polyester biomaterials proposed in this study, the present technique, plasma-based bionic phospholipidization modification technique on the surface of aliphatic polyester biomaterials and the bionic phospholipidization modification technique on the surface of aliphatic polyester biomaterials based on physical means were used to The results of the bionic phospholipid modification experiments are shown in **Figure 2**.



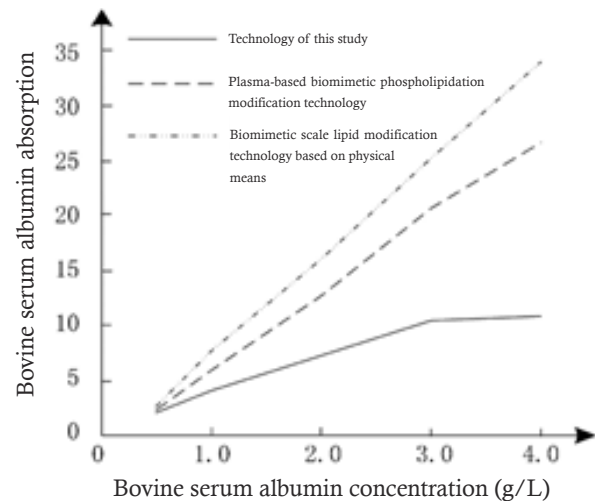
**Figure 2** Hydrophilicity of different technologies

As can be seen from **Figure 2**, the difference in water contact angle between the three biomimetic phospholipidation modification techniques was small at the initial stage, and all of them were maintained at about 57%. With the extension of time, the water contact angle of all three biomimetic phospholipidation modification techniques began to show a decreasing trend in different degrees. When the time reached 30 min, the water contact angle of the modified aliphatic polyester biomaterials showed the most significant decrease, reaching about 15%; the plasma-based biomimetic phospholipidation modification technique showed a lower decrease than the present technique, reaching about 38%; the physical-based biomimetic phospholipidation modification technique showed the least decrease, reaching only 42%. The experimental results showed that the best hydrophilicity among the three biomimetic phospho-

lipidation modification techniques was due to the introduction of phospholipid groups in this study, which improved the hydrophilicity of the surface of aliphatic polyester-based biomaterials.

### 3.2 Comparative biocompatibility analysis

To test the biocompatibility of the material after the bionic phospholipidation modification of the surface of aliphatic polyester-based biomaterials by this study technique, the biocompatibility of the material after the three bionic phospholipidation modification techniques was compared based on the experimental procedure in Section 3.1, and the results are shown in **Figure 3**.



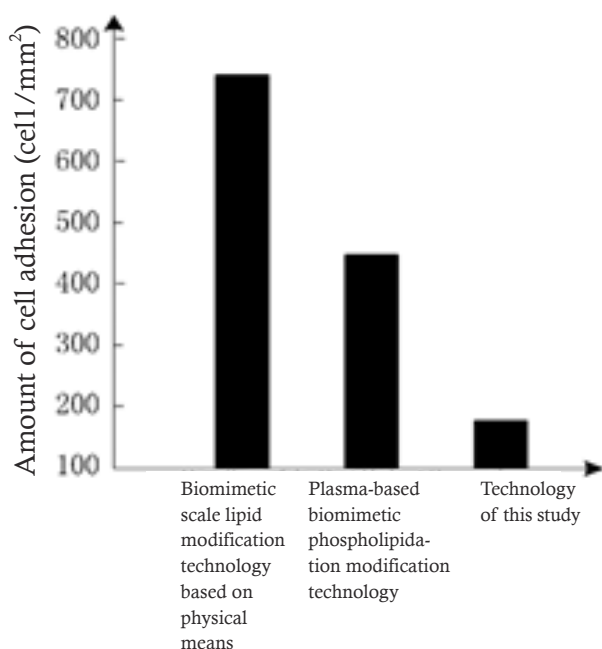
**Figure 3** Biocompatibility of different techniques

As can be seen from **Figure 3**, the absorption performance of the proteins by all three techniques of bionic phospholipidation modification was enhanced to different degrees when the concentration of bovine serum albumin was gradually increased. The surface of the aliphatic polyester-based biomaterials modified by bionic phospholipidation with this study technique showed the lowest uptake of bovine serum albumin compared with the other two techniques. The highest bovine serum albumin uptake of 10.46  $\mu\text{g}/\text{cm}^2$  was achieved by the present study technique when the concentration of bovine serum albumin reached 4.0 g/L, while the plasma-based bionic phospholipidation modified technique showed 26.66  $\mu\text{g}/\text{cm}^2$  for bovine serum albumin uptake

and the physical means-based bionic phospholipidation modified technique showed  $32.90 \mu\text{g}/\text{cm}^2$ .

### 3.3 Material adhesion ratio analysis

To test the cell adhesion performance of the techniques in this study, the cell adhesion results of the materials after comparing the three biomimetic phospholipidation modification techniques based on the experimental procedure in Section 3.1 are shown in **Figure 4**.



**Figure 4** Material adhesion contrast results of different technologies

As can be seen from **Figure 4**, there is a large difference in the cell adhesion of the three biomimetic phospholipidation modification techniques. The amount of cell adhesion per square millimeter on the surface of the polyester biomaterials using the physical biomimetic phospholipid modification technique was more than 730 cells per square millimeter, while the amount of cell adhesion per square millimeter on the surface of the material using the plasma biomimetic phospholipid modification technique was about 440 cells per square millimeter, and the amount of cell adhesion per square millimeter on the surface of the material using the present study was nearly 180 cells per square millimeter. The amount of cell adhesion per mm<sup>2</sup> on the surface of the material after this

study is less than a quarter of the amount of cell adhesion by physical means of biomimetic phospholipidation modification, which indicates that this study technique is more helpful in enhancing the hydrophilicity and biocompatibility of the surface of aliphatic polyester-based biomaterials.

## 4 Conclusion

To enhance the surface properties of aliphatic polyester-based biomaterials, it is particularly important to modify them with biomimetic phospholipidation. In this study, we propose a surface biomimetic phospholipid modification technique for aliphatic polyester biomaterials. The experimental results showed that the surface hydrophilicity, biocompatibility and material adhesion ratio of aliphatic polyester biomaterials were improved after surface biomimetic phospholipid modification by this research technique.

## References:

- [1] Wang JC, Shang XH, Wang WJ, et al. Research progress on enzyme-catalyzed synthesis of aliphatic polyesters [J]. *Chemical Progress*, 2017, 36(7):25922600.
- [2] Gao Zhaoying, Jiangnan, Liu Huifang, et al. Research progress on modification of biodegradable plastic polybutylene succinate [J]. *Engineering Plastics Applications*, 2015, 43(5):136140.
- [3] Chen J, Sun M, Dai XM, et al. Modification of petroleum asphalt with coal direct liquefaction residue based on benzaldehyde crosslinker [J]. *Journal of Fuel Chemistry*, 2015, 43(9):10521060.
- [4] Wang, Y. Q., Zhang, P. B., Jiang, P. P., et al. Study of castor oil-based polyol modified polyurethane adhesives [J]. *China Plastics*, 2015, 29(8):9197.
- [5] Bi Shuang, Zhang Qiaozhi, Ding Jian, et al. Infrared spectroscopic study of the effect of ultrasound pro-aggregation on the structure and function of soy protein phospholipids [J]. *Food*

- 
- Science, 2017, 38 (11):18–24.
- [6] Chen J., Liu L. Q.. Preparation and performance study of aliphatic modified alkali lignin water reducing agent [J]. *New Building Materials*, 2015, 42(2):6166.
- [7] Grigsby W J, Bridson J H, Lomas C, et al. Evaluating modified tannin esters as functional additives in polypropylene and biodegradable aliphatic polyester [J]. *Macromolecular Materials & Engineering*, 2015, 299(10):12511258.
- [8] Tang Q.H., Zhang H., Shen J.J., et al. Influence of compound phospholipid composition on the behavior of the active ingredients of Xiangxiang Siwu Tang through liposomal artificial skin membranes [J]. *Journal of Nanjing University of Traditional Chinese Medicine*, 2017, 33(4):371375.
- [9] Yue S. P., Lin Y. C., Xu Y. J. Study of esterified lignin for interfacial modification of PBS CTMP fiber composites [J]. *China Paper*, 2016, 35(8):1924.
- [10] Bi Shuang, Li Yang, Mao Huiting, et al. Analysis of structural and functional conformational relationships of ultrasound-treated protein phospholipid complexes [J]. *Food and Fermentation Industry*, 2016, 42 (10): 6167.
- [11] Zhang L, Hu S, Cook L, et al. Analysis of aminophospholipid molecular species by methyl- $\beta$ -cyclodextrin modified micellar electrokinetic capillary chromatography with laser - induced fluorescence detection[J]. *Electrophoresis*, 2015, 23(17):30713077.
- [12] Wu Boer, Sun Xiangdong, Li Aiyuan, et al. Research progress on C5 aliphatic and C9 aromatic copolymer petroleum resins [J]. *China Adhesives*, 2016, 25(8):5053.
- [13] Zhu Guihua, Zhu Tianhong, Hong Xiaobo, et al. On the simulation of homogeneity mixing optimization of sludge mixer [J]. *Computer Simulation*, 2017, 12:411414.
- [14] Vogel A, Scheidt H A, Baek D J, et al. Structure and dynamics of the aliphatic cholesterol side chain in membranes as studied by (2) H NMR spectroscopy and molecular dynamics simulation [J]. *Physical Chemistry Chemical Physics* Pccp, 2016, 18(5):37303738.
- [15] Zhou Ran, Song Yupin, Liu Xiaomei, et al. Study on bionic silicon-immobilized glucose oxidase with horseradish peroxidase [J]. *Food Industry Science and Technology*, 2017, 38(2):221225.