

Study on the Preparation of Hydroxypropyl Chitosan and its Optimal Reaction Conditions

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Abstract

In order to solve poor water solubility of chitosan, it was modified by C₆ hydroxyl groups. Hydroxypropyl chitosan with good water solubility was prepared by using chitosan as raw material, propylene oxide as an etherifying agent and isopropanol as a solvent in an alkaline environment. The suitable conditions for the etherification reaction were determined by single factor experiments. The results showed that the optimum conditions for the synthesis of hydroxypropyl chitosan were as follows: under the alkaline environment of 55°C, the amount of chitosan was 2 g, the amount of isopropanol and propylene oxide was 25 g, and the reaction time was 7 h. Under these conditions, the yield and grafting ratio of hydroxypropyl chitosan was 25.65% and 68.81% respectively.

Keywords: Chitosan, Modification, Hydroxypropyl Chitosan, Water solubility

1. Introduction

Chitin is a kind of natural polymer with abundant sources, which mainly comes from crustaceans, invertebrates, insects and microorganisms[1]. Chitosan, also known as deacetylated chitin, can be obtained from chitin by heating and removing part of N-acetyl groups under the alkaline condition[2]. It is the only alkaline polysaccharide in nature and has many excellent characteristics, such as film-forming ability, biodegradability, biocompatibility, non-toxicity, adsorption[3] and anti-bacteria activity[4, 5], so it has broad application prospects in food[6], medicine[7, 8], water treatment[9-11], cosmetics[12], cultural relics protection[13] and many other fields. However, the solubility of chitosan is very poor, which is insoluble in water, alkaline solution and general organic solvents, so its application scope is greatly limited[14]. Fortunately, there are a large number of hydroxyl and amino groups on the chitosan skeleton, which are easy to undergo modification reactions such as alkylation[15], acylation[16], esterification, crosslinking[17] and graft copolymerization[18] with other compounds to improve its solubility. Therefore, this paper intends to conduct etherifying modification of chitosan to prepare hydroxypropyl chitosan and improve its water solubility. The effects of the amount of etherifying agent and solvent, reaction time and reaction temperature on the yield and grafting ratio of hydroxypropyl chitosan were also studied by a series of single factor experiments.

2. Materials and Methods

2.1 Experimental reagents

The main reagents of the experiment are shown in Table 1.

2.2 Experimental instruments

The main instruments and equipment of the experiment are shown in Table 2.



Table 1. Main reagents for the synthesis of hydroxypropyl chitosan

| Reagent | Specification | Manufacturer |
|-------------------|---|---|
| Chitosan | Degree of deacetylation $\geq 95\%$ AR | Shanghai Macklin Biochemical Technology Co., Ltd. |
| Isopropanol | AR | Tianjin Kemiou Chemical Reagent Co., Ltd. |
| Sodium hydroxide | AR | Saen Chemical Technology Co., Ltd. |
| Propylene oxide | AR | Saen Chemical Technology Co., Ltd. |
| Hydrochloric acid | AR | Luoyang Chemical Reagent Factory |
| Acetone | AR | Shanghai SSS Reagent Co., Ltd. |

Table 2. Main experimental instruments for the synthesis of hydroxypropyl chitosan

| Instrument and equipment | Type | Manufacturer |
|---|------------|--|
| Multi-function electron balance | JY-3002 | Shanghai Equitable Instrument and Meter Factory |
| Heat collecting magnetic agitator with constant temperature | DE-101S | Henan Baize Instrument Co., Ltd. |
| Circulating water multi-purpose vacuum pump | SHZ-D | Henan yuhua Instrument Co., Ltd. |
| Low temperature thermostatic reaction bath | DFY-5/25°C | Zhengzhou Yuxiang Instrument and Equipment Co., Ltd. |
| Electric blast drying oven | FXB101-3 | Shanghai Shuli Instrument and Meter Co., Ltd. |

2.3 Synthesis principle of hydroxypropyl chitosan

Chitosan has a large number of highly reactive hydroxyl and amino groups, on which reactions can take place. The amino group is alkaline and has a larger reactivity in an acidic medium, so the reaction sequence under acidic conditions is usually as follows: amino > primary hydroxyl > secondary hydroxyl. However, this reaction occurs in an alkaline environment, so the reactivity of the primary hydroxyl groups of chitosan is higher than that of the amino groups. During the alkalization treatment, the crystalline regions in the molecular structure of chitosan are destroyed, after which chitosan can fully expand. On the other hand, sodium hydroxide can bond with C₆-OH to form active centers. In the reaction stage of hydroxypropylation, nucleophilic substitutions take place as the active centers contact with propylene oxide to produce hydroxypropyl chitosan. The reaction equation of hydroxypropyl chitosan is shown in Fig.1.

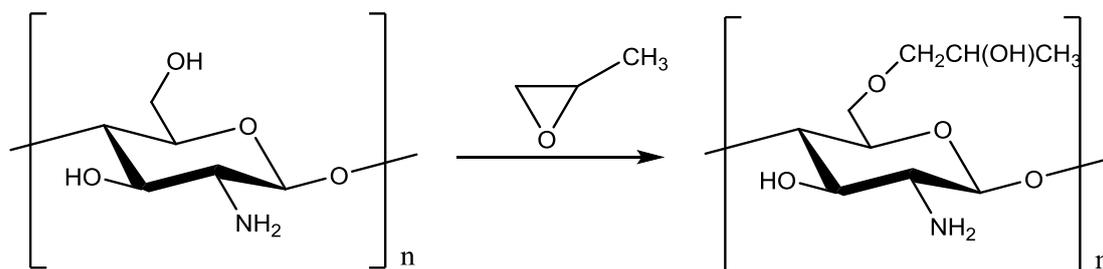


Fig.1 Reaction equation of hydroxypropyl chitosan

2.4 Synthesis process of hydroxypropyl chitosan

2 g chitosan was added into a three-mouth flask and dissolved in 25 g isopropanol and the sodium hydroxide solution, prepared by mixing 8 g sodium hydroxide and 12 g water, which was then stirred with a glass rod continuously for 5 min. A magnetic stirrer was placed into the three-mouth flask, which was then sealed with glass plugs, equipped with a thermometer and placed on a thermostatic heating magnetic stirrer to stir the

mixture for 3 h in the room temperature. Then excess propylene oxide was slowly added dropwise as it rises to the specified temperature to react for some time at the given temperature respectively. After the reaction stopped, the solution was neutralized with 1:1 hydrochloric acid and the product was transferred from the three-mouth flask to a breaker. Then 25 ml acetone was added to precipitate the product. After the precipitation was completed, the supernatant was poured into an acetone waste liquid bottle for recovery, and the precipitate was dissolved in water and then centrifuged for 2 min. The insoluble substance after centrifugation was removed, and the supernatant was poured into the breaker to precipitate again with acetone. After precipitation, the precipitate was centrifuged again for 2 min. The resultant precipitate was the product, which was then freeze-dried in a lyophilizer and weighed to calculate the yield and grafting ratio of hydroxypropyl chitosan. The synthesis process of hydroxypropyl chitosan is shown in Fig.2.

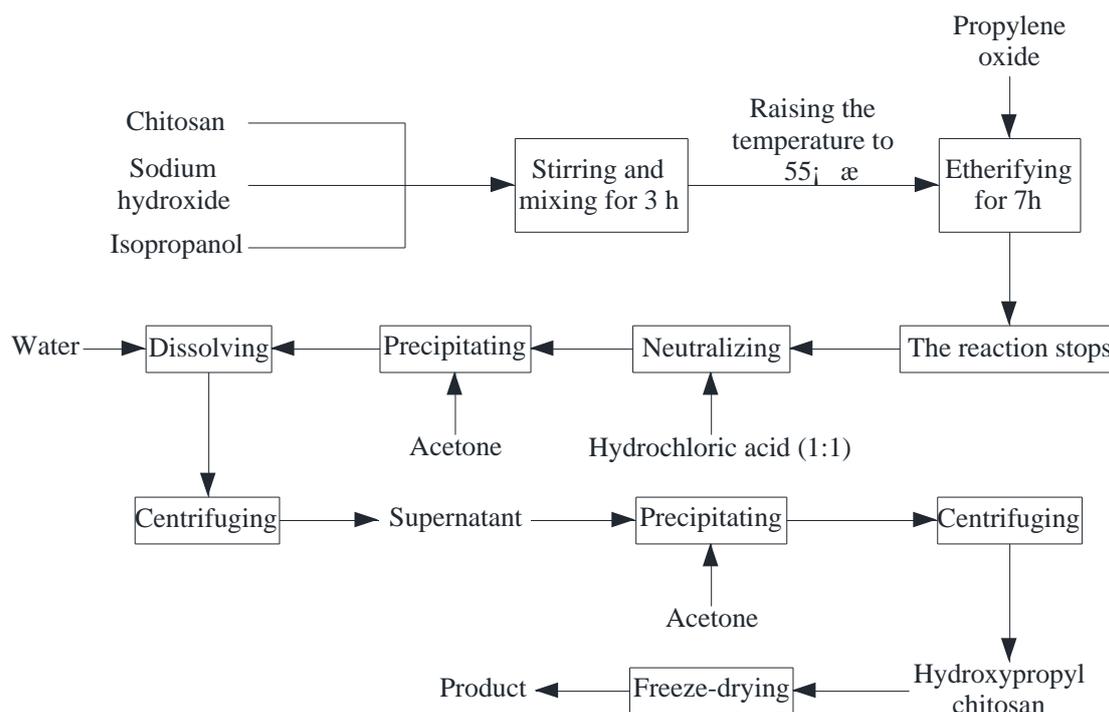


Fig.2 Synthesis process of hydroxypropyl chitosan

2.5 Calculation of yield and grafting ratio

The yield and grafting ratio of hydroxypropyl chitosan are calculated as follows:

$$\text{Yield} = \frac{\text{The mass of final product (g)}}{\text{The mass of reactant (g)}} \times 100\% \quad (2.1)$$

$$\text{Grafting ratio} = \frac{m_{\text{HPCS}} - m_{\text{CS}}}{m_{\text{CS}}} \times 100\% \quad (2.2)$$

In which: m_{HPCS} represents the mass of obtained hydroxypropyl chitosan, g m_{CS} represents the mass of chitosan, g

3. Results and Discussion

3.1 The effects of the amount of etherifying agent on the yield and grafting ratio

The effects of the amount of etherifying agent on the yield and grafting ratio of hydroxypropyl chitosan are shown in Table 3.



Table 3. The effects of the amount of etherifying agent on the yield and grafting ratio

| Mass of chitosan/g | Mass of propylene oxide/g | Yield/% | Grafting ratio/% |
|--------------------|---------------------------|---------|------------------|
| 2 | 10 | 13.74 | 12.43 |
| 2 | 15 | 15.71 | 18.57 |
| 2 | 20 | 21.87 | 40.59 |
| 2 | 25 | 20.14 | 51.85 |
| 2 | 30 | 16.95 | 42.38 |

As can be seen from Table 3, the yield and grafting ratio of hydroxypropyl chitosan are very low when the amount of propylene oxide is 10 g, which indicates that the reactivities of chitosan and propylene oxide are also very low when the amount of etherifying agent is too small. After increasing the amount of propylene oxide, the yield and grafting ratio are obviously increased. This is because there are enough raw materials to react with the active groups of chitosan when the amount of reactant is increased. At the same time, the speed of the diffusion of reaction reagents to the interior of chitosan is greatly accelerated, which increases the probability of the collision between reagents and the active groups of chitosan, thus improving the grafting ratio of the product. However, the yield and grafting ratio will decrease when the amount of etherifying agent exceeds a certain value, among which the grafting ratio will change a lot while the change of the yield is relatively small. When the dosage of etherifying agent is about 20 g, the yield reaches the maximum, but the grafting ratio is only 40.59%. When the amount of propylene oxide is increased to 25 g, the grafting ratio reaches about 50% and the yield doesn't decrease significantly.

Therefore, based on the above analysis, the optimal amount of the etherifying agent is finally determined to be 25 g, at which time the yield is 20.14% and the grafting ratio is 51.85%.

3.2 The effects of the amount of solvent on the yield and grafting ratio

The effects of the amount of solvent on the yield and grafting ratio of hydroxypropyl chitosan are shown in Table 4.

Table 4. The effects of the amount of solvent on the yield and grafting ratio

| Mass of chitosan/g | Mass of isopropanol/g | Yield/% | Grafting ratio/% |
|--------------------|-----------------------|---------|------------------|
| 2 | 15 | 17.43 | 53.21 |
| 2 | 20 | 22.85 | 57.58 |
| 2 | 25 | 23.99 | 59.13 |
| 2 | 30 | 20.38 | 56.75 |
| 2 | 35 | 16.89 | 53.47 |

It can be seen from Table 4 that the yield and grafting ratio of hydroxypropyl chitosan are very low when the amount of isopropanol is small, while the yield and grafting ratio gradually increase with the amount of isopropanol. The reason may be that isopropanol is an inert organic solvent and a good dispersant. Alkalization in the system containing isopropanol can ensure the uniform dispersion of the solution. In addition, the heat released in the process of alkalization is easy to be transferred out, which reduces the reverse reaction of the hydrolysis of alkalized chitosan, thus more uniform alkalized chitosan can be obtained. And the solubility of alkali in alcohol solvent is lower than that in water, for which more alkali can be adsorbed by chitosan. However, it doesn't mean that the more isopropanol is used, the higher the yield and grafting ratio of the product will be. When the mass of the solvent is 25 g, the yield and grafting ratio reach the maximum, after which the yield and grafting ratio are reduced with the increase of the amount of isopropanol.

Therefore, based on the above analysis, the optimal amount of isopropanol is finally determined to be 25 g, at which time the yield is 23.99% and the grafting ratio is 59.13%.

3.3 The effects of the reaction temperature on the yield and grafting ratio

The effects of the reaction temperature on the yield and grafting ratio of hydroxypropyl chitosan are shown in Table 5.

Table 5. The effects of the reaction temperature on the yield and grafting ratio

| Mass of chitosan/g | Reaction temperature/°C | Yield/% | Grafting ratio/% |
|--------------------|-------------------------|---------|------------------|
| 2 | 40 | 18.36 | 47.90 |
| 2 | 45 | 20.71 | 52.65 |
| 2 | 50 | 28.32 | 65.28 |
| 2 | 55 | 25.65 | 68.81 |
| 2 | 60 | 19.28 | 48.27 |

As can be seen from Table 5, both the yield and grafting ratio of hydroxypropyl chitosan are very low at a low temperature. With the increase of reaction temperature, the yield and grafting ratio increase continuously and reach the maximum value between 50°C and 55°C. After that, if the temperature continues to rise, the yield and grafting ratio will decrease. When the temperature is low, the reaction cannot take place sufficiently. While increasing the reaction temperature will promote the permeation between reactants, which can make the contact and collision between propylene oxide and active groups of chitosan more sufficient, thus accelerating the speed of hydroxypropylation reaction. However, other side reactions also occur as the hydroxypropylation is carried out. For example, the reaction at high temperatures is accompanied by the degradation of the molecular chains, and the higher the temperature is, the more violent the degradation reaction is. Moreover, propylene oxide has a low boiling point and is volatile, so the yield and grafting ratio of the product will be reduced when the temperature is too high.

Therefore, based on the above analysis, the optimal reaction temperature is finally determined to be 55°C, at which time the yield is 25.65% and the grafting ratio is 68.81%.

3.4 The effects of the reaction time on the yield and grafting ratio

The effects of the reaction time on the yield and grafting ratio of hydroxypropyl chitosan are shown in Table 6.

Table 6. The effects of the reaction time on the yield and grafting ratio

| Mass of chitosan/g | Reaction time/h | Yield/% | Grafting ratio/% |
|--------------------|-----------------|---------|------------------|
| 2 | 4 | 19.49 | 53.16 |
| 2 | 5 | 19.63 | 53.78 |
| 2 | 6 | 19.67 | 55.01 |
| 2 | 7 | 23.31 | 63.17 |
| 2 | 8 | 17.69 | 38.78 |
| 2 | 9 | 16.50 | 22.82 |
| 2 | 10 | 13.58 | 8.34 |

It can be seen from Table 6 that the yield and grafting ratio of hydroxypropyl chitosan are relatively low when the reaction time is too short. With the increase of reaction time, the yield and grafting ratio will increase, both of which can reach the maximum when the reaction time is about 7 h. The reaction between chitosan and propylene oxide is a heterogeneous reaction between solid and liquid phases. The initial stage of the reaction is the diffusion and permeation of propylene oxide and the homogeneous mixing of alkalinized chitosan, followed by the reaction of propylene oxide with the active groups on chitosan. With the extension of time, the reaction proceeds from the outside to the inside. Propylene oxide can diffuse to the active groups through the action of water and reacts with them, which can improve the degree of substitution of the products. However, it doesn't mean that the longer the reaction time is, the higher the yield and grafting ratio will be,



because the etherification is carried out in a concentrated alkali system, in which the molecular chains of chitosan are easy to degrade. Therefore, when the reaction time is too long, the degradation degree of chitosan is large, and the yield and grafting ratio will drop sharply.

Therefore, based on the above analysis, the optimal reaction time is finally determined to be 7 h, at which time the yield is 23.31% and the grafting ratio is 63.17%.

4. Conclusions

After hydroxypropyl chitosan was prepared by a series of steps, four groups of single factor experiments on the amount of etherification agent and solvent, reaction temperature and reaction time were designed. Finally, the optimal reaction conditions for the synthesis of hydroxypropyl chitosan were determined: the amount of chitosan was 2 g, the amount of isopropanol and propylene oxide was 25 g, and the etherification was carried out at 55°C for 7 h. At this time, the yield and grafting ratio of the product were the highest, 25.65% and 68.81% respectively. This research also has a certain reference value for the application of water-soluble chitosan in paper reinforcement.

Conflicts of Interest

The author declares no conflict of interests regarding the publication of this paper.

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