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The Adsorption and Desorption Effects of Nylon-6-Resin with Epothilone B

Myongchol Ho, Inchol Ri*, Gyonghak Cho, Gwangsu Kim, Hyegyong Ri

Institute of Microbiology, The State Academy of Sciences, Pyongyang, DPR Korea

Email address:

ric1966@star-co.net.kp (Inchol Ri)

*Corresponding author

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Abstract: In recent years, as the mortality from cancer is increasing in the world, the development of anticancer drugs is considered as one of the most important research. Epthilones appear as new anticancer agents that can inhibit tumor, therefore many people in the world are interested in it. Epthilones are mainly obtained through the process of biosynthesis by the strain *Sorangium cellulosum*- one kind of myxobacteria. In the production and manufacturing process of Epothilones, Amberlite XAD-16 that can effectively adsorb Epothilones is widely used, previous results of investigations show that it plays a very important role in the adsorption of Epothilones produced in the fermentation. However, because of high cost and a large amount consumption of XAD-16, the porous adsorption resin XD-5 replaces Amberlite XAD-16 in China. The porous adsorption resins such as Amberlite XAD-16 and polyamide resin are being used in the adsorption, separation and purification of various natural products such as flavonoids. In this paper we mentioned the data on the the adsorption and desorption effect of porous Nylon-6-resin with Epothilone B, compared to the effect of Amberlite XAD-16 and porous adsorption resin XD-5 resin. The result showed that the adsorption and desorption rate of Nylon-6-resin were similar to that of Amberlite XAD-16 and porous adsorption resin XD-5 in Epothilone B standard solution. And the effect of the sort and concentration of elution agent, elution time and extract number were examined in the desorption of Nylon-6-resin with Epothilone B. In conclusion, Nylon-6-resin can be used effectively for the purification of Epothilone B in the future.

Keywords: Epothilone B, Nylon-6-Resin, Adsorption, Desorption, Amberlite XAD-16, XD-5 Resin

1. Introduction

Epothilones are secondary metabolites which are biosynthesized by myxobacteria *Sorangium cellulosum* in the soil [3, 9-11]. Epothilones are anticancer agents similar to paclitaxel in their mechanism of killing tumor cell but they show higher activity and fewer side effect compared to pacilitacxel [6, 12]. Because Epothilones have the high effect on cancer disease tolerant to various anticancer drugs such as paclitaxel, Epothilones are gaining great interest to many researchers [7].

Epothilones can be obtained by both chemical and microbiological methods, but they are mainly biosynthesized microbiologically because of drawbacks of chemical synthesis such as complicated synthetic routes, high cost of separation and purification and lower yield [1, 2].

The biosynthesis of Epothilones is a reversible reaction, so that Amberlite XAD-16 resin which can adsorb Epothilones is generally added in order to raise the yield. The yield of Epothilones can increase ten times higher when this resin is added than when is not added [5, 6]. In China, the porous adsorption resin XD-5 is used in the synthesis of Epothilones and the productive yield of Epothilones by the porous adsorption resin XD-5 is smilar to that by Amberlite XAD-16 [5]. Several reports show that the yield is about two times higher when cyclodextrin is added than when is not added [8]. Therefore, a large amount of researches are being carried out in order to increase yield and improve the effect of separation and purification by using porous resins.

On the other hand, polyamide resin as well as Amberlite XAD-16 is widely used in the adsorption and separation of flavonoids [14, 15].

In this paper, we compared the adsorption and desorption effects of Nylon-6-resin, a kind of polyamide resins, with

Epothilone B to that of Amberlite XAD-16 resin and porous adsorption resin XD-5 and examined several factors that affect the desorption of Epothilones.

2. Material and Methods

2.1. Experimental Material

Sorangium cellulosum strain So ce90 was used as Epothilone B producing strain. The Epothilone B standard sample and the Amberlite XAD-16 resin were purchased from Germany Rohm & Haas Company; the porous XD-5 resin was obtained from Hubei Kewode Chemical Industry Co., Ltd. and Nylon-6-resin was supplied by Tianjin Bohong Resin Technology Co., Ltd.

2.2. Experimental Methods

The seed and biosynthesis cultivations of *Sorangium cellulosum* So ce90 was performed according to the procedures reported in the literature [13]. Before use, all resins were soaked with 95% methanol for 24 hours and then washed with 5% NaOH, 5% HCl solution for 5 hours, and double-distilled water till neutrality.

The Epothilone B standard solution was prepared by dissolving 60μg of Epothilone B in 30mL of water. After centrifuging the culture fluid of *Sorangium cellulosum* So ce90 at 4 000rpm for 20min, the supernatant was used as sample solution. As a result, Epothilone B content in the sample solution was 1.9μg/ml. The adsorption and desorption of Epothilone B were performed as follows: 2g of pretreated porous resin and 100mL of Epothilone B standard and sample solution were added respectively and the flasks were shaken in a shaker (120rpm) for 24 hours. After adsorption, the porous resin and the solution were separated and analyzed. And then the different resins were put into 20mL elution agent and were shaken for 2 hours, 2 times respectively, subsequently, the supernatant was added and the adsorption and desorption rate of Epothilone B were measured. On the base of examining the adsorption and desorption rate of Epothilone B, we examined the effect of the sort and concentration of the elution agent, elution time and extract number. Methanol, ethanol and ethyl acetate were used as elution agent. The adsorption and desorption rate were calculated by the following formula.

$$\text{Adsorption ratio}(\%) = [(A_0 - A_1)/A_0] \times 100$$

$$\text{Desorption ratio}(\%) = [A_2/(A_0 - A_1)] \times 100$$

Where A_0 is the amount of Epothilone B in solution before adsorption; A_1 is the amount of Epothilone B in solution after adsorption; A_2 is the amount of Epothilone B in elution agent. The Epothilone B content was analyzed by HPLC (LC-20AT). All experiments were repeated three times and the results were represented as Mean±SD (SDOM).

3. Results and Discussion

The porous adsorption resins are being applied to adsorption and desorption of various natural compounds [5, 15]. And Nylon-6-resin, one kind of polyamide resin, also exhibits adsorption and desorption effects with many materials such as flavonoids [15]. There are some reports on the adsorption and desorption effects of Amberlite XAD-16, porous adsorption resin XD-5 with Epothilone B [5, 6], but there are no data on that of Nylon-6-resin. Therefore we performed the adsorption and desorption experiments of Nylon-6-resin with Epothilone B.

In the static adsorption and desorption experiments, adsorption and desorption effects of Amberlite XAD-16, porous adsorption resin XD-5 and Nylon-6-resin were examined in Epothilone B standard solution (figure 1). The result showed that the adsorption and desorption rate of Amberlite XAD-16 were 68.42±2.7%, 71.23±3.2%, while that of porous adsorption resin XD-5 were 66.47±2.5%, 71.67±3.7%, and that of Nylon-6-resin were 65.21±3.1%, 70.61±3.5%, respectively.

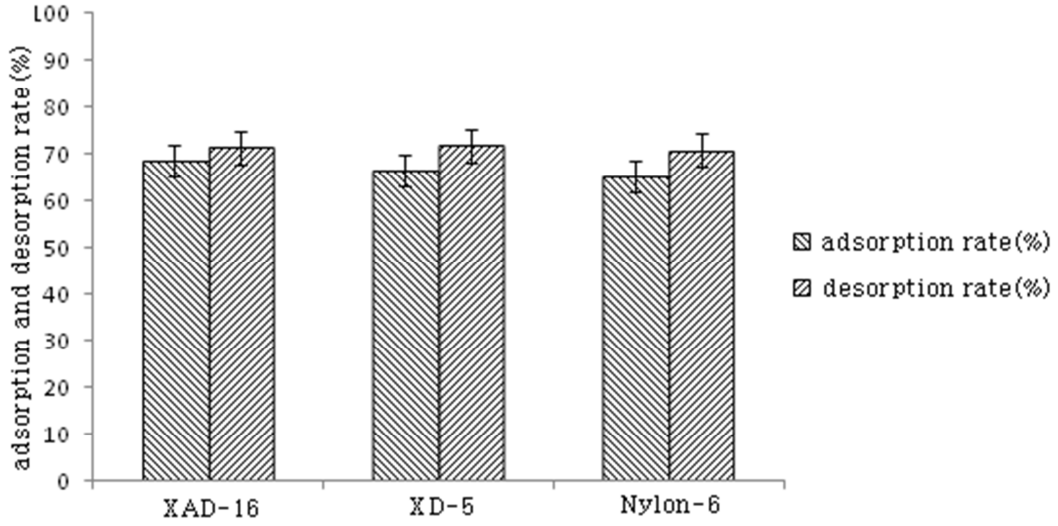

Figure 1. *The adsorption and desorption rate of various resins with Epothilone B in Epothilone B standard solution.*

As a result, the adsorption and desorption effect of these three kinds of resins with Epothilone B were similar with one another. Therefore we could find that Nylon-6-resin can be used in the adsorption and desorption of Epothilone B.

Next, Nylon-6-resin was put into Epothilone B sample solution in order to absorb Epothilone B and we examined the desorption effect of Epothilone B using methanol, ethanol and ethyl acetate as elution agent (figure 2).

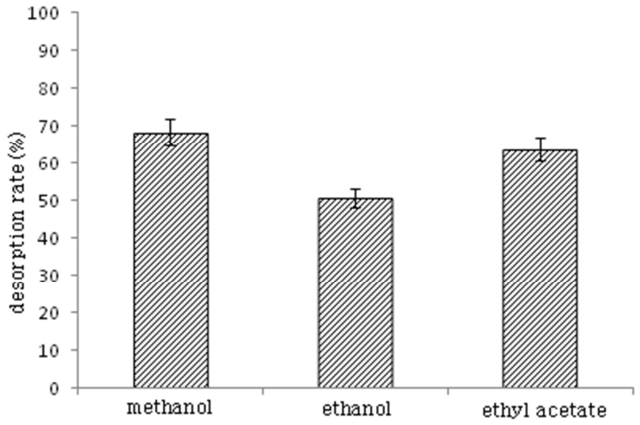

Figure 2. *The desorption effect of Epothilon B following by kinds of elution agent.*

As shown in figure 2, desorption rate by methanol was the highest as 68.18%, therefore methanol was chosen as elution agent for desorption of Epothilone B.

Next, the desorption effect of Epothilone B with the increase of the concentration of methanol for desorption of Epothilone B was tested (figure 3).

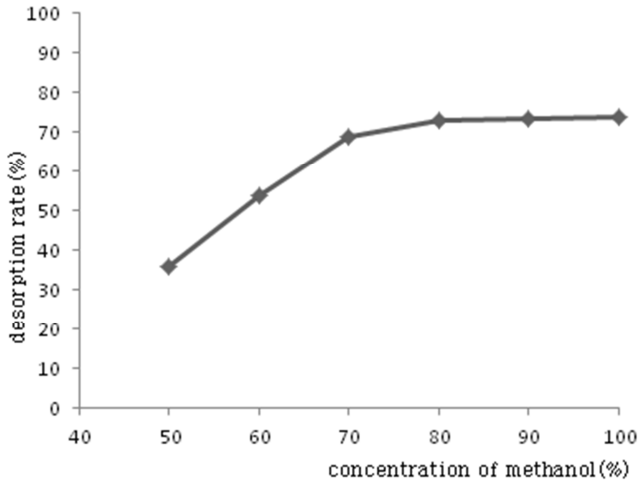

Figure 3. *The effect of the concentration of methanol on the desorption rate of Epothilon B.*

As shown in figure 3, as the concentration of methanol was increased, the desorption rate of Epothilone B was increased at first, but no obvious change was observed over 80% of methanol. Therefore optimal concentration for desorption of Epothilone B was set as 80%. Next, the effect of elution time on Epothilon B desorption from Nylon-6-resin was examined, as a result, as the desorption time increased, the desorption rate was also raised, over 3 hours the rate did not nearly change (figure 4).

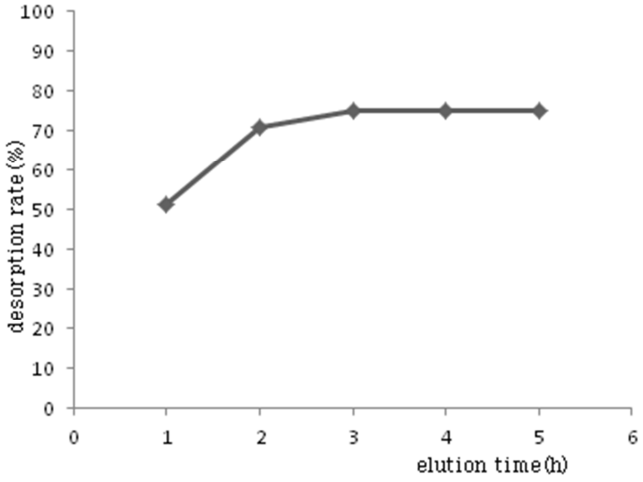

Figure 4. *The effect of elution time on the desorption rate of Epothilone B.*

Next, the effect of the extract number on Epothilone B desorption from Nylon-6-resin was examined (figure 5).

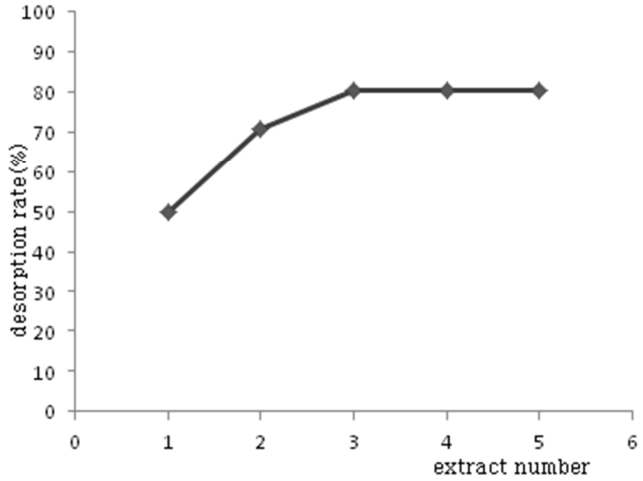

Figure 5. *The effect of the extract number of the elution agent on the desorption rate of Epothilone B.*

As shown in figure 5, with the extract number increase, the desorption rate was also raised. When the extract number was 3, the desorption rate was the highest as 80.18%, and it did not change and stayed the same above the extract number of 3.

4. Conclusion

Epothilones, as naturally biosynthesized materials, have much higher activity than any other anticancer materials such as paclitaxel and vinblastine, therefore many of researchers are interested in this material. In the present study, the adsorption and desorption effect of the porous Nylon-6-resin with Epothilone B were compared with that of Amberlite XAD-16 resin and porous resin XD-5, and the effect of several factors on the desorption with Epothilone B were

examined.

The adsorption and desorption effect of the porous Nylon-6-resin with Epothilone B is similar to that of Amberlite XAD-16 resin and porous resin XD-5.

The optimum condition to desorb Epothilone B from Nylon-6-resin with Epothilone B was as follows: the elution agent was 80% of methanol, the elution time was 3 hours and the extract number was 3. The desorption rate of Epothilone B was 80.18%.

To our knowledge, this is the first report that uses the porous Nylon-6-resin for biosynthesis of Epothilone B. In conclusion, we think that Nylon-6-resin will be widely used in the future research for biosynthesis of Epothilones.

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Conflicts of Interest

The authors declared no conflict of interest.

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