Synthesis and Characterization of Inulin Derivatives Bearing Urea Groups with Promising Antifungal Activity

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The toxicity concerns associated with chemical fungicides currently on the market have resulted in an increased demand for alternative ecofriendly fungicides. As a biodegradable and biocompatible dietary fiber, inulin shows potential as such a compound, given its lack of toxicity. In the current study, seven novel inulin derivatives with promising antifungal activity (BUCAIL, 2CBUCAIL, 3CBUCAIL, 4CBUCAIL, 3,4CBUCAIL, 2FBUCAIL, and 2BBUCAIL) are synthesized via condensation reactions of chloroacetyl inulin (CAIL) with urea groups bearing 4-amino-pyridine. Their structures are confirmed using FT-IR, $^1$H NMR, $^{13}$C NMR, and elemental analysis. Their antifungal activity against three kinds of phytopathogen (Fusarium oxysporum f. sp. niveum, Phomopsis asparagus, and Fusarium oxysporum f. sp. cucumeribrium Owen) is evaluated using the mycelial growth rate in vitro at concentrations of 0.10, 0.25, 0.50, 0.75, and 1.0 mg mL$^{-1}$. Results reveal that all seven inulin derivatives show improved antifungal activity compared with unmodified inulin, and two obvious inhibition rules are found: 3,4CBUCAIL > 4CBUCAIL > 3CBUCAIL > 2CBUCAIL > BUCAIL > CAIL > inulin and 2FBUCAIL > 2BBUCAIL > BUCAIL > CAIL > inulin. Thus, the introduction of urea groups into inulin derivatives could be key to increasing the antifungal activity of such compounds.

1. Introduction

Inulin, which comprises linear chains of β-(2,1) fructose units terminating in a glucose unit at the reducing end, is a water-soluble storage polysaccharide belonging to a group of nondigestible carbohydrates called fructans.[1–3] Inulin is mainly extracted from $\approx$36,000 species of plants, such as chicory, leek, garlic, Jerusalem artichoke, banana, and rye, with barley and chicory roots being the main source.[4–6] Inulin is used in a variety of foods, but cannot be digested or absorbed in the human digestive tract; instead, it is fermented in the colon by bacteria, with beneficial effects on overall health.[7,8] However, there are few reports on applications of antifungal agents of inulin because of its low bioactivity. Chemical modification is a useful method that can improve the bioactivity of inulin by grafting it with active groups with high antifungal activity. Various publications have reported the improved biological activity of inulin derivatives after chemical modification.[9–11] Thus, this approach could provide a new way of preparing environmentally friendly antifungal compounds.

Urea, with the structure −NH–CO–NH−, is an organic compound with a range of biological activities.[12] Urea derivatives have favorable biological properties that enable their use as antiproliferative, anticancer (against renal, colon, lung, prostate, and breast cancers), anticonvulsant, antidiabetic, analgesic, anti-HIV, antifungal, and antibacterial agents.[13,14] For example, hydroxylurea is an effective component in the treatment of solid tumors as well as acute and chronic leukemia.[15] Furthermore, N-phenyl-N-(2-chloroethyl) urea and heterocyclic urea derivatives have also been reported to show good anticancer activity because of their inhibitory activity against receptor tyrosine kinases.[16] In addition, synthetic urea derivatives have also attracted interest as antioxidant, fungicidal, herbicidal, and antibacterial agents. Thus, in the current study, a series of urea groups were synthesized and grafted onto inulin to investigate their effects on the antifungal activity of this compound.

Plant fungicidal diseases are one of the main causes of damage to agricultural crops, with resulting economic impacts. The most commonly used approach for inhibiting fungal growth is the large-scale use of chemical fungicides, although their use can cause significant environmental pollution.[17,18] Given their low environmental toxicity, the current study investigated the potential of a series of inulin derivatives for use as antifungal agents. The chemical structures of the inulin derivatives were characterized using FT-IR, $^1$H NMR, and $^{13}$C NMR. Meanwhile, the degrees of substitution (DS) of inulin derivatives were analyzed by elemental analysis. Furthermore, three common phytopathogenic fungi, including Fusarium oxysporum f. sp.
niveum (F. oxysporum f. sp. niveum), Phomopsis asparagus (P. asparagus), and Fusarium oxysporum f. sp. cucumebrium Owen (F. oxysporum f. sp. cucumebrium Owen) were selected to evaluate the antifungal properties of inulin and inulin derivatives. We also discuss the relationship between the structure and antifungal activities of inulin derivatives suggested by our data.

2. Experimental Section

2.1. Materials

Inulin with average DP of 20 fructosyl fructose units was supplied by weide biological Corp. (Beijing, P. R. China). Iodomethane (product code 80084117), chloroacetyl chloride (product code C104559), aniline (product code A112122), o-chloroaniline (product code C103931), m-chloroaniline (product code C103948), p-chloroaniline (product code C103934), 3, 4-dichloroaniline (product code D113551), 2-fluoroaniline (product code F107841), 2-bromoaniline (product code B108449), and 4-amino-pyridine (product code A78403) were purchased from the Sigma–Aldrich Chemical Corp. The other reagents such as N-Methyl pyrrolidone (NMP) (product code 30121518), dimethyl sulfoxide (DMSO) (product code 30072428), etc., were supplied by Sinopharm Chemical Reagent Co., Ltd., Shanghai, China and used without more purification.

2.2. Analytical Methods

2.2.1. Fourier Transform Infrared (FT-IR) Spectroscopy

FT-IR spectra were used on a Jasco-4100 Fourier Transform Infrared Spectrometer (Japan, provided by JASCO China, Co., Ltd., Shanghai, China) at 25 °C. The samples were mixed with KBr disks at a weight ratio of 1/100 mg for testing and all spectra were scanned in the range of 4000–400 cm⁻¹ with resolution of 4.0 cm⁻¹.

2.2.2. Nuclear Magnetic Resonance (NMR) Spectroscopy

1H Nuclear Magnetic Resonance spectrometer (¹H NMR) and ¹³C Nuclear Magnetic Resonance spectrometer (¹³C NMR) spectra were measured using a Bruker AVIII-500 Spectrometer (500 MHz, Switzerland, provided by Bruker Tech. and Serv.

Scheme 1. Synthesis routes for inulin derivatives.
Co., Ltd., Beijing, China) and using D₂O or (CD₃)₂SO as solvents.

2.2.3. Elemental Analysis

The elemental analyses (C, H, and N) were performed on a Vario Micro Elemental Analyzer (Elementar, Germany) and they can be used to evaluate the degrees of substitution of inulin derivatives. The degrees of substitution (DS) of inulin derivatives were calculated on the basis of the percentages of carbon and nitrogen according to the following equations:

\[
DS = \frac{n_1 \times M_C + n_2 \times M_C \times DS_{CAIL}}{n' \times M_N \times W_{C/N} - n_3 \times M_C}
\]

where \(DS\) represents the urea groups in inulin derivatives (BUCAIL, 2CBUCAIL, 3CBUCAIL, 4CBUCAIL, 3,4CBUCAIL, 2FBUCAIL, or 2BBUCAIL); \(DS_{CAIL}\) represents the chloroacetyl group in inulin derivative (CAIL), which is estimated on the basis of the integral values in \(^{13}\text{C}\) NMR spectrum; \(M_C = 12, M_N = 14; n_1, n_2, \) and \(n_3\) are the number of carbon of inulin, chloroacetyl group, and urea group, \(n_1 = 6, n_2 = 2, n_3 = 12; n'\) is the number of nitrogen of urea group, \(n' = 3; W_{C/N}\) represents the mass ratio between carbon and nitrogen in inulin derivatives.

2.3. Synthesis of Inulin Derivatives

2.3.1. Synthesis of the Ureas of 4-Amino-Pyridine

Firstly, 5 mmol triphosgene (BTC) and 10 mmol aniline, o-chloroaniline, m-chloroaniline, p-chloroaniline, 3,4-dichloroaniline, 2-fluoroaniline, or 2-bromoaniline were mixed in 15 mL of acetic ether at 25 °C for 1 h. Then, the reaction mixture was refluxed to clarify at 60 °C and four different isocyanates were obtained under the condition of reduced pressure at 50 °C. Subsequently, a solution of 10 mmol 4-aminopyridine and 15 mL of acetone was added dropwise into the flask that containing isocyanate. The mixture was stirred at room temperature (r.t.) for 2 h and refluxed at 60 °C for an additional 0.5 h. After reflux reaction, several unsymmetrically substituted ureas were synthesized after distilling solvents. And the products were purified by crystallization from the solvent that the ratio of water and ethanol was 1:1.

2.3.2. Synthesis of Inulin Derivative CAIL

Chloracetyl inulin (CAIL) was synthesized according earlier method. 10 mmol inulin was dissolved in 100 mL H₂O and 0.02 mol chloracetyl chloride was then added. After continuous stirring for 12 h at room temperature (r.t.), the solution was concentrated under the condition of reduced pressure. The concentrated solution was poured into acetone to obtained the product. Subsequently, it was precipitated by the addition of excess acetone and the precipitant was filtrated. Finally, CAIL was obtained after being washed with acetone for three times and dried at 60 °C for 12 h.

A solution of 1 mmol CAIL and 3 mmol synthesized urea groups was stirred for 24 h at 60 °C in 20 mL of N, N-dimethylformamide (DMF). Upon reaction completion, the solution was precipitated in acetone. Then the precipitate was filtered and washed with ethanol to extract the unreacted ureas and other outgrowth. Finally, the inulin derivatives were obtained by freeze-drying overnight in vaccum.

2.4. Antifungal Assay

Antifungal assays were performed by the following plate growth rate method described by Luan. Briefly, the compounds were dissolved in water at a concentration of 5.0 mg mL⁻¹. Triadimefon solution with the same concentration was used as a positive control. Then, each solution was added to Fungi Medium to give final concentrations of 0.10, 0.25, 0.50, 0.75, and 1.0 mg mL⁻¹ and they were poured into sterilized Petri dishes. After the mixture was...
cooled in the plate, 5.0 mm diameter of fungi mycelium was transferred to the test plate and incubated at 27 °C for 3 days. When fungi mycelium in control plate (without samples) reached edges, the antifungal index was calculated as follows:

Antifungal index (%) = \( (1 - \frac{D_a}{D_b}) \times 100 \)

where \( D_a \) is the diameter of the growth zone in the test plates and \( D_b \) is the diameter of the growth zone in the control plate.

2.5. Statistical Analysis

All the experiments were performed in triplicate and the data were expressed as means ± the standard deviation (SD, \( n = 3 \)).

Figure 2. \(^1\)H NMR spectra of inulin and inulin derivatives.
Figure 3. \(^{13}\text{C}\) NMR spectra of inulin and inulin derivatives.
Table 1. The yields and the degrees of substitution of inulin derivatives with urea groups.

| Compounds | Yields [%] | C   | N   | H   | C/N | Degrees of substitution |
|-----------|------------|-----|-----|-----|-----|-------------------------|
| BUCAIL    | 72.3       | 47.002 | 8.207 | 4.945 | 5.73 | 1.01                    |
| 2CBUCAIL  | 69.8       | 48.149 | 6.998 | 5.606 | 6.88 | 0.68                    |
| 3CBUCAIL  | 70.3       | 47.387 | 7.468 | 4.560 | 6.46 | 0.77                    |
| 4CBUCAIL  | 67.5       | 48.478 | 7.572 | 5.413 | 6.40 | 0.78                    |
| 3CBUCAIL  | 70.3       | 47.387 | 7.486 | 4.560 | 6.46 | 0.78                    |
| 2CBUCAIL  | 69.8       | 48.149 | 7.008 | 5.606 | 6.88 | 0.68                    |
| BUCAIL    | 72.3       | 47.002 | 8.207 | 4.945 | 5.73 | 1.01                    |

Significant difference analysis was determined using Scheffe’s multiple range test. A level of \( p < 0.05 \) was considered statistically significant.

3. Results and Discussion

3.1. Chemical Synthesis and Characterization

Inulin derivatives bearing urea groups were synthesized as shown in Scheme 1. To graft urea groups containing pyridine onto inulin, CAIL was synthesized first by the reaction of inulin with chloroacetyl chloride, wherein polysaccharides with chloride acetyl groups attack pyridine to result in N-alkylpyridinium salts. [9,23] Then, several additional urea groups were obtained following the reaction of isocyanates, the products of the reaction of triphosgene (BTC) with aniline compounds, and 4-amino-pyridine. Finally, we prepared the target products by reacting CAIL with urea groups. The chemical structures of the resultant inulin derivatives were confirmed using FT-IR (Figure 1), \(^1\)H NMR (Figure 2), and \(^13\)C NMR (Figure 3) spectroscopy. The yields and DS of inulin derivatives with urea groups are shown in Table 1.

The FT-IR spectra illustrated in Figure 1 provided clear evidence of the structures of inulin and the inulin derivatives. The spectrum of unmodified inulin showed typical peaks of saccharide at 3405, 1029, and 848 cm\(^{-1}\).[24] The major peak at \( \approx 3405 \) cm\(^{-1} \) indicated the presence of carbohydrate hydroxyl groups (\( \text{─OH} \)). The band at \( \approx 848 \) cm\(^{-1} \) indicated the typical absorbance of polysaccharide structures with \( \text{─O─C─O} \) bonds, whereas that at \( \approx 1029 \) cm\(^{-1} \) was assigned to \( \text{─O─C─C─O} \) bonds of the inulin pyranose ring. Compared with the spectrum of inulin, CAIL appeared as a new peak at 1751 cm\(^{-1} \), resulting from its carbonyl bond (\( \text{─C=O} \)). In addition, the reaction of inulin with chloroacetyl chloride led to the appearance of peaks at \( \approx 1319 \) cm\(^{-1} \) and \( \approx 786 \) cm\(^{-1} \), which were assigned to the \( \text{─C─H} \) and the \( \text{─C─Cl} \) groups, respectively.[9,25] The appearance of the characteristic peaks of the chloroacetyl group confirmed the formation of CAIL. Following the grafting of urea onto CAIL, peaks indicating the absorbance of \( \text{─C─O} \) and \( \text{─C─Cl} \) became weaker and new peaks appeared at \( \approx 1600, \approx 1530, \) and \( \approx 750 \) cm\(^{-1} \), showing that \( \text{─C─Cl} \) bonds had been destroyed and new groups had been grafted onto CAIL.[23] The peaks at \( \approx 1600, \approx 1530, \) and \( \approx 750 \) cm\(^{-1} \) were characteristic of benzene and pyridine from the urea groups.[26] Moreover, the peak at \( \approx 1654 \) cm\(^{-1} \) increased, indicating the presence of \( \text{─NH─CO─NH} \). Therefore, these results confirmed that the new groups grafted onto CAIL were the targeted urea groups, indicating the successful synthesis of BUCAIL, 2CBUCAIL, 3CBUCAIL, 4CBUCAIL, 3,4CBUCAIL, 2FBUCAIL, and 2BBUCAIL.

To further confirm the formation of the synthesized products, \(^1\)H NMR (Figure 2) and \(^13\)C NMR (Figure 3) were also conducted. The obvious signals of all samples at 3.0–5.4 ppm (\(^1\)H NMR spectra) and 60–105 ppm (\(^13\)C NMR spectra) represented characteristic signals of inulin.[27] In terms of the NMR spectra of CAIL, the chemical shifts of the chloride acetyl groups (\( \text{─CH₂Cl} \)) appeared at 4.4 ppm (\(^1\)H NMR spectra)[26,28] and 41 ppm (\(^13\)C NMR spectra).[23] In addition, the signal at 168 ppm (Figure 3), which was related to the resonance of \( \text{─C─O} \) bonds in the chloride acetyl groups, also confirmed the formation of CAIL. After CAIL had been reacted with urea groups, changes in the NMR spectra were obvious, as were chemical shifts in the aromatic rings. The specific positions of the protons and carbons of urea groups are indicated in Figure 2.

![Figure 4](image-url)
and 3. In particular, the characteristic signal of $-\text{COCH}_2\text{Cl}$ at 4.4 ppm was weaker and new signals appeared at 6.8–8.7 ppm, confirming the existence of aromatic nuclei. Generally, the peaks at around 6.8–8.3 ppm were related to the protons on the pyridine and benzene rings. The peaks at 8.5 ppm and 8.7 ppm could be assigned to the protons on $-\text{NH}$ on the urea groups. Furthermore, the $^{13}$C NMR spectra of the synthesized products (BUCAIL, 2CBUCAIL, 3CBUCAIL, 4CBUCAIL, 3,4CBUCAIL, 2FBUCAIL, and 2BBUCAIL) exhibited peaks at 110–175 ppm (carbons of pyridine ring, benzene ring, and CO), also confirming the presence of urea groups. Hence, these data indicated that inulin derivatives had been synthesized successfully.

The DS for the inulin derivatives are shown in Table 1. The DS of CAIL was 1.08, evaluated on the basis of the integral values in the $^{13}$C NMR spectrum because of the absence of nitrogen from the chloride acetyl group. Given that the chloroacetylation reaction occurs on the hydroxyl group at position 3 and 4, it is relevant that the DS of CAIL was $>$1. The DS of the seven final products (BUCAIL, 2CBUCAIL, 3CBUCAIL, 4CBUCAIL, 3,4CBUCAIL, 2FBUCAIL, and 2BBUCAIL) were calculated on the basis of the percentages of carbon and nitrogen according to elemental analysis. After calculation, the DS of BUCAIL and 3,4CBUCAIL were 1.01 and 0.88, respectively, whereas the DS of the other derivatives were all around 0.77.

### 3.2. Antifungal Activity

The antifungal activities of inulin and inulin derivatives against three phytopathogenic fungi ($F.\text{ oxysporum}$ f. sp. niveum, $P.\text{ asparagus}$, and $F.\text{ oxysporum}$ f. sp. cucumebrium Owen) are shown in Figure 4. Their antifungal indices and rules are discussed below.

Figure 4 shows the inhibitory indices of inulin and inulin derivatives against $F.\text{ oxysporum}$ f. sp. niveum. All the samples inhibited the growth of $F.\text{ oxysporum}$ f. sp. niveum and the inhibitory rates increased with increasing concentrations of the compounds. For instance, the inhibitory rates of 3CBUCAIL were 23.29%, 25.69%, 35.18%, 40.12%, and 56.97% for the corresponding concentrations of 0.10%, 0.25%, 0.50%, 0.75%, 1.00%, respectively.
and 1.00 mg mL$^{-1}$. Compared with inulin, all inulin derivatives showed better antifungal activity as a result of the grafted urea groups. For example, whereas inulin showed an inhibitory rate of 10.11% at 1.0 mg mL$^{-1}$, the inhibitory rates of BUCAIL, 2BUCAIL, 3CBUCAIL, 4CBUCAIL, 3,4CBUCAIL, 2FBUCAIL, and 2BBUCAIL were 31.21%, 42.48%, 56.97%, 66.11%, 88.72%, 46.11%, and 40.97%, respectively. This confirmed that the introduction of urea groups had a key role in enhancing the antifungal activity of inulin. The order of the inhibitory activity of all samples was 3,4CBUCAIL > 4BUCAIL > 3CBUCAIL > 2CBUCAIL > BUCAIL > CAIL > inulin (Figure 4a), which suggested that their antifungal ability was affected by the number and position of chlorine atoms on the urea groups. An additional order of inhibitory activity was 2FBUCAIL > 2BUCAIL > 2BBUCAIL > BUCAIL > CAIL > inulin (Figure 4b), which was identical to the order of the electronegativity ($-F > -Cl > -Br$) of groups substituted by halogens in the inulin derivatives. The relationship between the structure of the compounds and their antifungal activity is briefly discussed subsequently.

The results of the antifungal activity of inulin and inulin derivatives against P. asparagus are shown in Figure 5. Generally, the aforementioned rules were also appropriate for the antifungal activity of samples against P. asparagus. The inhibitory indices of all samples were concentration dependent and the antifungal potential was correlated positively with concentration. For instance, the inhibitory rates of 4CBUCAIL were 23.65%, 47.63%, 62.29%, 65.32%, and 72.29% at concentrations of 0.10, 0.25, 0.50, 0.75, and 1.00 mg mL$^{-1}$, respectively. The inhibitory indices of BUCAIL, 2BUCAIL, 3CBUCAIL, 4CBUCAIL, 3,4CBUCAIL, 2FBUCAIL, and 2BBUCAIL were 25.88%, 47.46%, 49.80%, 74.70%, 89.54%, 64.70%, and 37.46% at 1.00 mg mL$^{-1}$, respectively, compared with the inhibitory rates of inulin and CAIL of 7.36% and 25.87%, respectively. Therefore, all inulin derivatives bearing urea groups showed better antifungal activity compared with both inulin and CAIL. Furthermore, the rules of antifungal activity were 3,4CBUCAIL > 4BUCAIL > 3CBUCAIL > 2BUCAIL > BUCAIL > CAIL > inulin and 2BBUCAIL > 2CBUCAIL > CAIL > BUCAIL > CAIL > inulin, as also reported for F. oxysporum f. sp. niveum.

The antifungal trends of all samples against F. oxysporum f. sp. cucumber were similar to those against P. asparagus (Figure 6). For example, the synthesized products showed improved inhibitory properties compared with inulin and CAIL and their inhibitory indices were also concentration dependent. These results further confirmed that the introduction of urea groups into inulin contributed significantly to the antifungal action of the synthesized compounds.

According to the foregoing results, the antifungal activities of products against F. oxysporum f. sp. niveum, P. asparagus, and F. oxysporum f. sp. cucumber were generally in the order 3,4CBUCAIL > 4BUCAIL > 3CBUCAIL > 2BUCAIL > BUCAIL > CAIL > inulin. There are various reasons for this consistency. Given the positive effect of urea groups on antifungal activity, the inhibitory indices of BUCAIL, 2BUCAIL, 3CBUCAIL, 4CBUCAIL, and 3,4CBUCAIL were higher than those of CAIL and inulin. Thus, one can hypothesize that the greater the number of chlorine atoms in the inulin derivatives, the better their antifungal activity was. Chlorine atoms show strong electronegativity and have a key role in inhibiting the growth of fungi by disrupting cell walls and cytoplasmic membranes, resulting in fungal death.$^{[32,33]}$. These results were in agreement with those of Tan et al.$^{[34]}$ who also reported that the antifungal potential of compounds was associated with the electronegativity of the substituted groups, with the antifungal activity of samples increasing with increasing electronegativity. In samples with the same number of chlorine atoms, the different positions of those atoms could have different effects on their antifungal activity, given the order 4CBUCAIL > 3CBUCAIL > 2BUCAIL. Generally, the degree of substitution of products increased with the decrease in the steric hindrance resulting from the urea groups; therefore, the degree of substitution of inulin derivatives directly affected their antifungal activities. The more functional groups the inulin derivatives carried, the stronger the antifungal activity they presented. Thus, 4CBUCAIL, with the lowest steric hindrance and highest degree of substitution, showed the highest antifungal activity among 4CBUCAIL, 3CBUCAIL, and 2BUCAIL.

Given the previous inhibiting rules, the reasons for the order of 2FBUCAIL > 2BUCAIL > 2BBUCAIL > BUCAIL > CAIL > inulin are also clear. The reason why the antifungal activities of 2FBUCAIL, 2BUCAIL, and BUCAIL were stronger than those of CAIL and inulin was because of the introduction of urea groups to the former compounds. Given the strong electron-attracting properties of halogens, 2FBUCAIL, 2BUCAIL, and BUCAIL, which contained chlorine, bromine, and chlorine, respectively, showed better antifungal properties compared with BUCAIL. Furthermore, the order of the antifungal activity, 2BUCAIL > 3CBUCAIL > BUCAIL > CAIL > inulin and 2BBUCAIL > 2CBUCAIL, was also consistent with the electron-attracting properties ($-F > -Cl > -Br$) of the different substituted atoms of the urea groups. Thus, the structure of the urea groups grafting onto inulin derivatives was a significant factor influencing the antifungal activities of those compounds.

4. Conclusions

In the current study, we introduced urea groups with high biological activity into chloroacetyl inulin, resulting in a novel series of inulin derivatives. We tested the antifungal activity of the resulting compounds against F. oxysporum f. sp. niveum, P. asparagus, and F. oxysporum f. sp. cucumber in vitro. All of the inulin derivatives exhibited higher antifungal activity compared with inulin. The antifungal activities of the inulin derivatives were influenced by the different types, positions, and quantities of halogens on the urea groups. Thus, this study suggests that such compounds could be used as eco-friendly alternatives to currently available fungicides. Further comprehensive studies both in vivo and in vitro are required to fully determine their use in terms of the structure and antifungal activities of these derived compounds.

**Abbreviations**

$^{1}$H NMR, $^{1}$H Nuclear Magnetic Resonance spectrometer; 2BBUCAIL, 2-(4-(2-bromin benzylureido)-pyridyl)acetyl inulin chloride; 2CBUCAIL,
2-(4-(2-chlorobenzylureido)-pyridyl)acetyl inulin chloride; 2FBUCAIL, 2-(4-(2-fluorobenzylureido)-pyridyl)acetyl inulin chloride; 2FBUCAIL, 2-(4-(3,4-dichlorobenzylureido)-pyridyl)acetyl inulin chloride; 4CBUCAIL, 2-(4-(4-chlorobenzylureido)-pyridyl)acetyl inulin chloride; 4CBUCAIL, 2-(4-(3-chlorobenzylureido)-pyridyl)acetyl inulin chloride; 3CBUCAIL, 2-(4-(2-fluorobenzylureido)-pyridyl)acetyl inulin chloride; 2FBUCAIL, 2-(4-(benzylureido)-pyridyl)acetyl inulin chloride; CAIL, chloracetyl inulin; FT-IR, Fourier Transform Infrared spectroscopy.

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Conflict of Interest

The authors have declared no conflicts of interest.

Keywords

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[1] C. V. Stevens, A. Meriggi, K. Booten, Biomacromolecules 2001, 2, 1.
[2] A. C. Apolinário, E. M. de Carvalho, B. P. G. de Lima Damasceno, P. C. D. da Silva, A. Converti, Jr., AP, J. A. da Silva, Ind. Crop Prod. 2017, 108, 355.
[3] L. Wang, T. Barclay, Y. Song, P. Joyce, I. G. Sakala, N. Petrovsky, S. Garg, Vaccine 2017, 35, 4382.
[4] T. M. Rogge, C. V. Stevens, A. Colpaert, B. Levecke, K. Booten, Biomacromolecules 2007, 8, 485.
[5] S. Kralj, C. Leelefang, E. I. Sierra, B. Kempinski, V. Alkan, M. Kolkman, Carbohydr. Polym. 2018, 179, 350.
[6] M. A. Mensink, H. W. Frijlink, K. van der Voort Maarschalk, W. L. Hinrichs, Carbohydr. Polym. 2015, 130, 405.
[7] Q. Yu, J. Zhao, Z. Xu, Y. Chen, T. Shao, X. Long, Z. Liu, X. Gao, Z. Rengel, J. Shi, J. Zhou, J. Funct. Foods 2018, 40, 187.
[8] V. Castel, A. C. Rubiolo, C. R. Carrara, Food Res. Int. 2018, 103, 76.
[9] Z. Guo, Q. Li, G. Wang, F. Dong, H. Zhou, J. Zhang, Carbohydr. Polym. 2014, 99, 469.
[10] J. Ren, J. Liu, F. Dong, Z. Guo, Carbohydr. Polym. 2011, 83, 1240.
[11] F. Dong, J. Zhang, C. Yu, Q. Li, J. Ren, G. Wang, G. Gu, Z. Guo, Bioorg. Med. Chem. Lett. 2014, 24, 4590.
[12] F. Asghar, A. Badshah, B. Lal, I. S. Butler, S. Tabassum, M. N. Tahir, Inorg. Chim. Acta 2016, 439, 82.
[13] M. Gemili, H. Sari, M. Ulger, E. Sahin, Y. Nural, Inorg. Chim. Acta 2017, 463, 88.
[14] S. A. Khan, N. Singh, K. Saleem, Eur. J. Med. Chem. 2008, 43, 2372.
[15] F. Fujita, M. Fujita, H. Inaba, T. Sugimoto, Y. Okuyama, T. Taguchi, Jpn. J. Cancer Chem. 1991, 18, 2263.
[16] Z. Su, H. Li, Y. Li, F. Ni, Chem. Biol. 2007, 14, 1273.
[17] F. Lagrouth, N. Dakka, Y. Bakri, J. Mycol. Med. 2017, 27, 303.
[18] E. Lukowska-Chojnacka, J. Mierzejewska, M. Milner-Krawczyk, M. Bondaryk, M. Staniszewska, Bioorg. Med. Chem. 2016, 24, 6058.
[19] W. Tan, Q. Li, F. Dong, J. Zhang, F. Luan, L. Wei, Y. Chen, Z. Guo, Carbohydr. Polym. 2018, 182, 180.
[20] A. K. Jain, V. Sood, M. Bora, R. Vasita, D. S. Katti, Carbohydr. Polym. 2014, 112, 225.
[21] Y. Chen, J. Zhang, W. Tan, G. Wang, F. Dong, Q. Li, Z. Guo, Stärke – Stärke 2017, 69, 1700046.
[22] F. Luan, Q. Li, W. Tan, L. Wei, J. Zhang, F. Dong, G. Gu, Z. Guo, Int. J. Biol. Macromol. 2018, 107, 595.
[23] J. Zhang, W. Tan, Q. Li, F. Dong, F. Luan, Z. Guo, Stärke – Stärke 2017, 69, 1600350.
[24] J. Ren, P. Wang, F. Dong, Y. Feng, D. Peng, Z. Guo, Carbohydr. Polym. 2012, 87, 1744.
[25] P. Silku, S. Özkanlı, Z. Öztürk, A. Asan, D. A. Köse, J. Mol. Struct. 2016, 1116, 72.
[26] Y. Hu, J. Zhang, C. Yu, Q. Li, F. Dong, G. Wang, Z. Guo, Int. J. Biol. Macromol. 2014, 70, 44.
[27] T. M. Rogge, C. V. Stevens, Biomacromolecules 2004, 5, 1799.
[28] R. Li, Z. Guo, P. Jiang, Carbohydr. Res. 2010, 345, 1896.
[29] Q. Z. Zheng, K. Cheng, X. M. Zhang, K. Liu, Q. Jiao, H. Zhu, Eur. J. Med. Chem. 2010, 45, 3207.
[30] T. Xu, M. Xin, M. Li, H. Huang, S. Zhou, J. Liu, Carbohydr. Res. 2011, 346, 2445.
[31] A. S. Gurjar, V. Andreisano, A. D. Simone, V. S. Velingkar, Bioorg. Chem. 2014, 57, 90.
[32] E. Aktan, A. B. Gündüzalp, Ü. Ö. Özmen, J. Mol. Struct. 2017, 1128, 775.
[33] J. S. Lv, X. M. Peng, B. Kishore, C. H. Zhou, Bioorg. Med. Chem. Lett. 2014, 24, 308.
[34] W. Tan, Q. Li, F. Dong, L. Wei, Z. Guo, Int. J. Biol. Macromol. 2016, 92, 293.