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H-bond in Chitosan-based Hydrogels

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Summary: N-alkyl chitosan derivatives, including N-ethyl, butyl, heptyl and lauryl forms were prepared via Schiff's base intermediates. The study of H-bonds in chitosan-based hydrogel was performed by DSC, NMR, XRD and PALS. The content of unfrozen bound water increases with increasing length of the alkyl side chain and the degree of substitution. The X-ray diffraction peak centered at $2\theta = 26.5°$ is sensitive to water. The free volume enhances in the order, chitosan (CS) < N-ethyl CS < N-butyl CS < N-heptyl CS << N-lauryl CS. Moreover the free volume of the derivatives decreases as water content rises but the situation of chitosan is opposite. The dynamic properties of water molecules within the networks were studied through the variation of the proton line width in the ^{1}H-NMR spectrum. The proton line width of the water peak of N-alkyl chitosan increases in the sequence, N-ethyl CS < N-butyl CS < N-heptyl CS < N-lauryl CS. The same results arise from the spin-lattice relaxation time (T_1) for these N-alkyl chitosan derivatives.

Keywords: alkylation; chitosan; free volume; hydrogen bond; water

Introduction

Chitosan, derived from chitin by partial deacetylation is a unique basic polysaccharide. Chitosan hydrogel has some advantages of non-toxicity, bio-compatibility, biodegradation and drug-absorption enhancement.[1-2] Chitosan-based hydrogels have promising perspectives for applications as carriers in drug delivery systems and scaffold in tissue engineering. To extend the adaptive ability of the matrix for drug release, N-alkyl chitosan derivatives, including N-ethyl, butyl, heptyl and lauryl forms were prepared via Schiff's base intermediates as shown in Scheme 1.

The property of the matrix material of drug carriers is determined by the polymer network and the water contained in it. In previous papers,[3-4] our group studied the swelling behaviour and water states in cross-linked chitosan and chitosan-based hydrogels. In present work we apply

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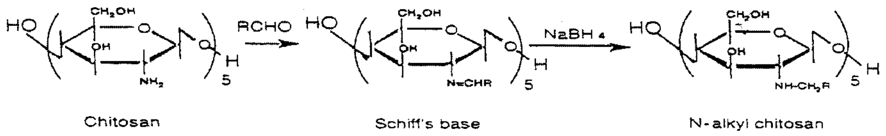
DSC, NMR, XRD and PALS techniques in order to explore the role of the hydrogen bond within N-alkyl chitosan hydrogels.



Scheme 1. Synthesis of N-alkyl chitosan.

Experimental

N-alkyl chitosan was synthesized and its substitution degree was calculated according to reference [6]. The gel samples of chitosan and its derivatives were prepared as follows: cast 4 % chitosan or its derivative solution in 1 % acetic acid on a clean plate. The cast film was dried in an air oven at 60 °C for 24 h. The gel samples can be easily separated from the glass surface and were immersed in 5 % NaOH solution to remove residual acid. The gel samples were repeatedly washed with several portions of distilled water and were stored in de-ionized water until use. The density of chitosan and its N-alkyl derivatives was measured by the flotation method using a mixture of benzene and tetrachloromethane at 25°C. The DSC, NMR, XRD and PALS measurements were carried out as in references [3-5].

Results and Discussion

The effect of modification of chitosan on density and swelling degree can be seen from Table 1 The state of water absorbed in N-alkyl chitosan derivatives was investigated using differential scanning calorimetry. The content of unfrozen bound water increases with increasing length of the alkyl side chain and their degree of substitution (see Table 2). It is worth noting that the X-ray diffraction peak centred at $2\theta = 26.5°$ is sensitive to water and modification of chitosan (see Figure 1). Its intensity weakens with increasing water content (see Figure 2). This implies that modification of chitosan can change its structure and influence its supramolecular interaction with water due to hydrogen bond.

Table 1. Effect of modification of chitosan on density and swelling degree.

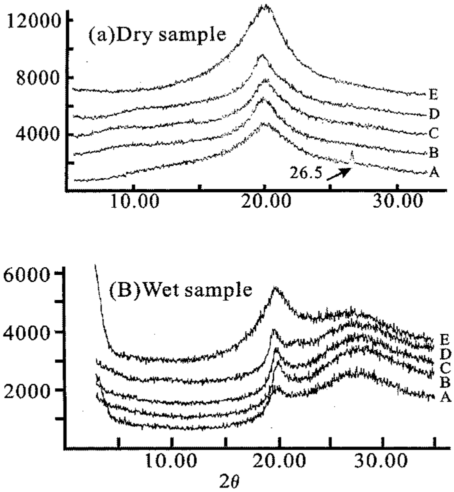
Sample	DS(mol%)	D(g/cm^3)	Sw(100%)
Chitosan	—	1.45	4.75
N-ethyl chitosan	2.15	1.43	3.47
N-butyl chitosan	2.21	1.41	2.89
N-heptyl chitosan	2.04	1.40	2.23
N-lauryl chitosan	6.56	1.35	1.48

DS: degree of chitosan substitution; D: density; Sw: swelling degree.

Table 2. Water state in chitosan and its N-alkyl derivative.

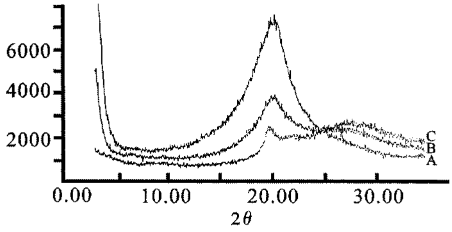
Sample	DS(mol%)	Water Content	Frozen water	Bound water	Bound water in total water
		g/dry polymer, g			
Chitosan	—	3.750	3.111	0.639	17%
N-ethyl chitosan	2.15	2.471	1.731	0.740	30%
N-butyl chitosan	2.21	1.885	1.194	0.691	37%
N-heptyl chitosan	2.04	1.226	0.706	0.520	42%
N-lauryl chitosan	6.56	0.483	0.000	0.483	100%

DS: degree of substitution



A: chitosan, B: N-ethyl chitosan, C: N-butyl chitosan, N-heptyl chitosan, E: N-lauryl chitosan.

Fig. 1. X-ray diffraction spectrum of Chitosan and its N-alkyl derivatives.



A: dry state; B: less water; C: more water. D:

Fig. 2. X-ray diffraction spectrum of N-lauryl chitosan in the different water contents.

The free volumes of chitosan and its N-alkyl derivatives were measured by the positron annihilation lifetime spectrum (PALS) technique. Table 3 and Figure 3 show that the free volume of sample increases in the order, chitosan (CS) < N-ethyl CS < N-butyl CS < N-heptyl

CS << N-lauryl CS. Moreover the experiment found that the variation of free volume of chitosan as a function of water content was opposite to that of its N-alkyl derivatives. The former increases with increasing swelling degree, but all the latter decrease. This variation may have some relationship with the hydrophobicity of the materials.

Table 3. Free volume V_f of dry and wet sample measured by PALS.

Sample	$V_{f,d}(cm^3/g)$	$V_{f,w}(cm^3/g)$
Chitosan	0.1006	0.1307
N-ethyl chitosan	0.1353	0.1320
N-butyl chitosan	0.1410	0.1327
N-heptyl chitosan	0.1454	0.1340
N-lauryl chitosan	0.2209	0.2024

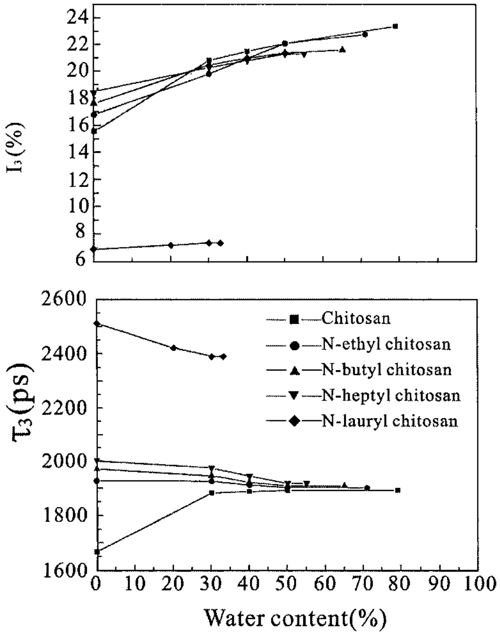


Fig. 3. Effect of water content on o-Ps lifetime (τ_3) and strength (I_3) of chitosan and its derivatives.

Table 4. Spin-lattice relaxation time (T_1) of chitosan and its derivatives.

Sample	chitosan(CS)	N-ethyl CS	N-butyl CS	N-heptyl CS	N-lauryl CS
T_1(S)	0.7873	1.151	1.123	1.113	1.012

There is an exchange between fractions of bound and unbound water molecules with a distribution of correlation times between chitosan-based hydrogel networks and their microenvironments. The dynamic properties of water molecules were studied through variation of proton line width in their ^{1}H-NMR spectrum. The line widths of protons of water peaks of N-alkyl chitosan increase in the sequence, N-ethyl CS < N-butyl CS < N-heptyl CS < N-lauryl CS. The order implies that N-ethyl chitosan exhibits the largest mobility for water, while N-lauryl chitosan provides the lowest (see Figure 4). The same results arise from the spin-lattice relaxation time (T_1) for chitosan and its N-alkyl derivatives. Table 4 shows that the T_1 of all N-alkyl derivatives are larger than that of chitosan and its sequence is as follows, N-ethyl CS > N-butyl CS > N-heptyl CS > N-lauryl CS.

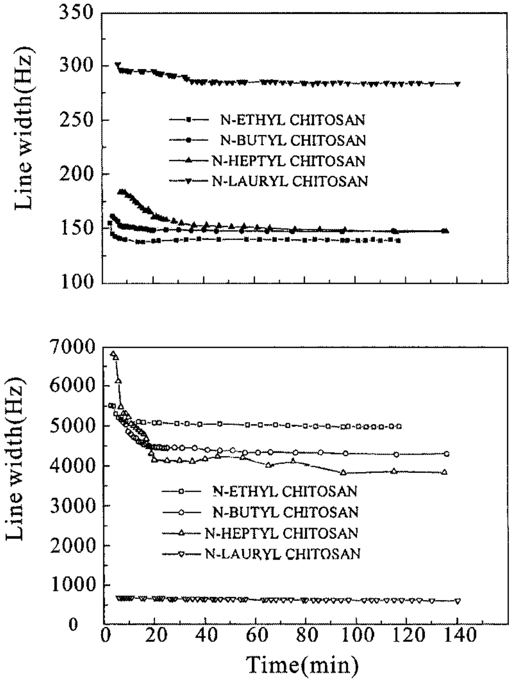
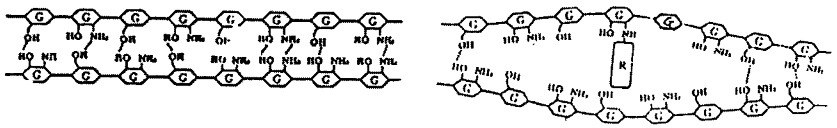


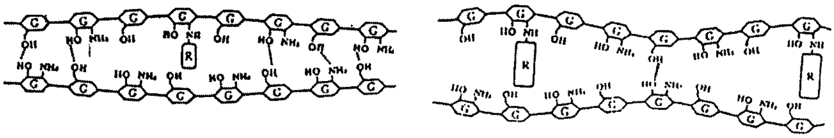
Fig. 4. Plot of proton line width of water (solid) and chitosan (open symbols) as a function of time.

We try to use the following model as Scheme 2 to explain these experimental results. In pure chitosan networks, all amine groups and hydroxyl groups are very close and they easily form inner molecular hydrogen bonds. After modification with N-alkyl hydrophobic chains, the structure of the chitosan network will become loose and weaken their inner molecular hydrogen bonds. Upon modification with large side chains and high substitution, this kind of influence will become more obvious.



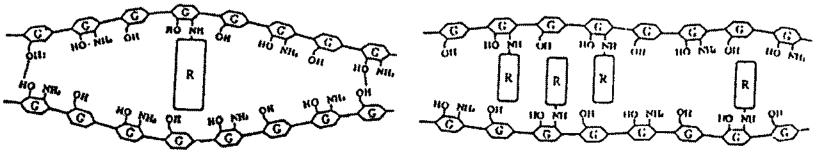
Chitosan

Low substitution



N-ethyl、butyl、heptyl Chitosan

Middle substitution



N-lauryl Chitosan

High substitution

Scheme 2. Model for structure of chitosan and its derivatives (the original model was designed by T. Uragami[6]).

Conclusion

The interaction of chitosan-based hydrogels with water, and their free volume, can be changed by N-alkylation modification. The properties of the hydrogels are determined by the polymer network and water contained. The water state and H-bond within hydrogels of chitosan and its derivatives can be investigated by DSC, XRD, NMR and PALS.

Acknowledgement

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