

SITE-SELECTIVE CARBOXYMETHYLATION OF CHITOSAN UNDER HETEROGENEOUS CONDITIONS

(Penentuan Tapak bagi Proses Pengkarboksimetil pada Kitosan dalam Keadaan Heterogen)

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Abstract

The substitution sites on chitosan are affected by the presence of a base. Herein, the effects of pH on the site-selective carboxymethylation of chitosan were investigated. Carboxymethyl chitosan was synthesized by reacting chitosan with monochloroacetic acid at different pH under heterogeneous conditions. Fourier transform infrared-attenuated total reflectance (FTIR-ATR) spectroscopy confirmed that carboxymethylation was successful, with the appearance of peaks around 1326-1320 cm^{-1} (C–N groups) and 1257-1253 cm^{-1} (C–O–C groups) and allowed differentiation between the carboxymethyl substitution sites on chitosan. Additionally, the peaks at approximately 3.28 and 4.12 ppm in the ^1H nuclear magnetic resonance (NMR) spectra confirmed that substitution occurred at amine and hydroxyl groups, respectively. Overall, the carboxymethylation of chitosan under heterogeneous conditions at pH 8.5-11 gave O-substitution, at pH 12-13 gave N,O-substitution, and at pH 14 gave N-substitution. This pH dependence of the site-selective substitution of chitosan is important for polymer electrolyte application.

Keywords: carboxymethyl chitosan, pH effect, substitution site, heterogeneous conditions

Abstrak

Tapak penggantian kitosan dipengaruhi oleh kehadiran bes. Dalam kajian ini, kesan pH terhadap tapak penggantian pengkarboksimetil kitosan telah dikaji. Karboksimetil kitosan disintesis melalui tindak balas

kitosan dengan asid monokloroasetik pada pH berbeza dalam keadaan heterogen. Spektroskopi inframerah transformasi Fourier (ATR-FTIR) mengesahkan bahawa karboksimetilasi telah berjaya dilakukan dengan kemunculan puncak sekitar 1326–1320 cm^{-1} (kumpulan C–N) dan 1257–1253 cm^{-1} (kumpulan C–O–C), yang menunjukkan perbezaan tapak penggantian karboksimetil pada kitosan. Selain itu, puncak sekitar 3.28 dan 4.12 ppm dalam spektrum resonans magnetik nukleus (^1H NMR) mengesahkan bahawa penggantian berlaku pada kumpulan amina dan hidroksil. Secara keseluruhan, karboksimetilasi kitosan dalam keadaan heterogen pada pH 8.5–11 memberikan penggantian pada tapak O, pH 12–13 memberikan penggantian pada tapak N dan O, dan pH 14 memberikan penggantian pada tapak N. Kebergantungan tapak pemilihan untuk penggantian kitosan dengan pH ini adalah penting untuk aplikasi elektrolit polimer.

Kata kunci: karboksimetil kitosan, kesan pH, tapak penggantian, keadaan heterogen

References

1. Zhao, D., Yu, S., Sun, B., Gao, S., Guo, S. and Zhao, K. (2018). Biomedical applications of chitosan and its derivative nanoparticles. *Polymers*, 10(4): 462.
2. Wang, W., Meng, Q., Li, Q., Liu, J., Zhou, M., Jin, Z. and Zhao, K. (2020). Chitosan derivatives and their application in biomedicine. *International Journal of Molecular Sciences*, 21(2): 487.
3. Kalliola, S., Repo, E., Srivastava, V., Zhao, F., Heiskanen, J. P., Sirvio, J. A., Liimatainen, H. and Sillanpää, M. (2018). Carboxymethyl chitosan and its hydrophobically modified derivative as pH-switchable emulsifiers. *Langmuir*, 34(8): 2800–2806.
4. Rayung, M., Aung, M. M., Azhar, S. C., Abdullah, L. C., Su'ait, M. S., Ahmad, A., and Jamil, S. N. A. M. (2020). Bio-based polymer electrolytes for electrochemical devices: Insight into the ionic conductivity performance. *Materials*, 13(4): 838.
5. Zhang, E., Xing, R., Liu, S., Li, K., Qin, Y., Yu, H., and Li, P. (2017). Comparison in docetaxel-loaded nanoparticles based on three different carboxymethyl chitosans. *International Journal of Biological Macromolecules*, 101: 1012–1018.
6. Aranaz, I., Acosta, N., Civera, C., Elorza, B., Mingo, J., Castro, C., Gandía, M. D. L. L. and Caballero, A. H. (2018). Cosmetics and cosmeceutical applications of chitin, chitosan and their derivatives. *Polymers*, 10(2): 213.
7. Jimtaisong, A. and Saewan, N. (2014). Utilization of carboxymethyl chitosan in cosmetics. *International Journal of Cosmetic Science*, 36(1): 12–21.
8. Zhong, H., He, A., Lu, J., Sun, M., He, J. and Zhang, L. (2016). Carboxymethyl chitosan/conducting polymer as water-soluble composite binder for LiFePO_4 cathode in lithium ion batteries. *Journal of Power Sources*, 336: 107–114.
9. Sun, S. and Wang, A. (2006). Adsorption kinetics of Cu(II) ions using N,O-carboxymethyl-chitosan. *Journal of Hazardous Materials*, 131(1–3): 103–111.
10. Mi, Y., Su, R., Fan, D., Zhu, X. and Zhang, W. (2013). Preparation of N,O-carboxymethyl chitosan coated alginate microcapsules and their application to *Bifidobacterium Longum* BIOMA 5920. *Materials Science and Engineering: C*, 33(5): 3047–3053.
11. Muzzarelli, R. A. A., Tanfani, F., Emanuelli, M. and Mariotti, S. (1982). N-(carboxymethylidene) chitosans and N-(carboxymethyl)chitosans: Novel chelating polyampholytes obtained from chitosan glyoxylate. *Carbohydrate Research*, 107(2): 199–214.
12. Nudga, L. A., Plisko, E. A. and Danilov, S. N. (1973). N-alkylation of chitosan. *Zhurnal Obshchei Khimii*, 43(12): 2756–2760.
13. An, N. T., Dung, P. L., Thien, D. T., Dong, N. T. and Nhi, T. T. Y. (2008). An improved method for synthesizing N,N'-dicarboxymethylchitosan. *Carbohydrate Polymers*, 73(2): 261–264.
14. An, N. T., Dung, P. L., Thien, D. T., Dong, N. T. and Nhi, T. T. Y. (2009). Water-soluble N-carboxymethylchitosan derivatives: preparation, characteristics and its application. *Carbohydrate Polymers*, 75(3): 489–497.
15. Nikmawahda, H. T., Sugita, P., and Arifin, B. (2015). Synthesis and characterization of n-

alkylchitosan as well as its potency as a paper coating material. *Advances in Applied Science Research*, 6(2): 141-149.

16. Sashiwa, H., Shigemasa, Y., and René, R. (2000). Novel N-alkylation of chitosan via michael type reaction. *Chemistry Letters*, 29(8): 862-863.

17. Sun, G., Chen, X., Li, Y., Zheng, B., Gong, Z., Sun, J., Chen, H., Li, J. and Lin, W. (2008). Preparation of H-oleoyl-carboxymethyl-chitosan and the function as a coagulation agent for residual oil in aqueous system. *Frontiers of Materials Science in China*, 2(1): 105-112.

18. Leong, K. H., Chung, L. Y., Noordin, M. I., Mohamad, K., Nishikawa, M., Onuki, Y., Morishita, M., and Takayama, K. (2011). Carboxymethylation of kappa-carrageenan for intestinal-targeted delivery of bioactive macromolecules. *Carbohydrate Polymers*, 83(4): 1507-1515.

19. Singh, R. K. and Khatri, O. P. (2012). A scanning electron microscope based new method for determining degree of substitution of sodium carboxymethyl cellulose. *Journal of Microscopy*, 246(1): 43-52.

20. Elomaa, M., Asplund, T., Soininen, P., Laatikainen, R., Peltonen, S., Hyvärinen, S. and Urtti, A. (2004). Determination of the degree of substitution of acetylated starch by hydrolysis, ^1H NMR and TGA/IR. *Carbohydrate Polymers*, 57(3): 261-267.

21. Aggeryd, I., and Olin, Å. (1985). Determination of the degree of substitution of sodium carboxymethylcellulose by potentiometric titration and use of the extended henderson-hasselbalch equation and the simplex method for the evaluation. *Talanta*, 32(8A): 645-649.

22. Liu, J., Zhang, X., Kennedy, J. F., Jiang, M., Cai, Q. and Wu, X. (2019). Chitosan induces resistance to tuber rot in stored potato caused by *Alternaria tenuissima*. *International Journal of Biological Macromolecules*, 140: 851-857.

23. Mobarak, N. N., Ahmad, A., Abdullah, M. P., Ramli, N. and Rahman, M. Y. A. (2013). Conductivity enhancement via chemical modification of chitosan based green polymer electrolyte. *Electrochimica Acta*, 92: 161-167.

24. Lusiana, R. A., Siswanta, D. and Mudasir, M. (2014). Modifying surface charge of chitosan membrane by N,O-carboxymethyl chitosan blended with poly(vinyl alcohol). *International Journal of Advances in Chemical Engineering and Biological Sciences*, 1(1): 16-20.

25. Hirai, A., Odani, H. and Nakajima, A. (1991). Determination of degree of deacetylation of chitosan by ^1H NMR spectroscopy. *Polymer Bulletin*, 26(1): 87-94.

26. Muzzarelli, R. A. A., Ilari, P., and Petrarulo, M. (1994). Solubility and structure of N-carboxymethylchitosan. *International Journal of Biological Macromolecules*, 16(4): 177-180.

27. Prabakaran, M. and Gong, S. (2008). Novel thiolated carboxymethyl chitosan-g- β -cyclodextrin as mucoadhesive hydrophobic drug delivery carriers. *Carbohydrate Polymers*, 73 (1): 117-125.

28. Chen, X. G. and Park, H. J. (2003). Chemical characteristics of o-carboxymethyl chitosans related to the preparation conditions. *Carbohydrate Polymers*, 53(4): 355-359.

29. Bukzem, A. L., Signini, R., Dos Santos, D. M., Lião, L. M. and Ascheri, D. P. R. (2016). Optimization of carboxymethyl chitosan synthesis using response surface methodology and desirability function. *International Journal of Biological Macromolecules*, 85: 615-624.

30. Mourya, V. ., Inamdar, N. N. and Tiwari, A. (2010). Carboxymethyl chitosan and its applications. *Advanced Materials Letters*, 1(1): 11-33.

31. Pranowo, H. D., Mulya, F., Aziz, H. A, and Santoso, G. A. (2018). Study of substituent effect on properties of platinum(II) porphyrin semiconductor using density functional theory. *Indonesian Journal of Chemistry*, 18(4): 742-748.

32. Lu, X., Xue, J. Q., Wang, Y. J., Mao, W. B., Wu, M. and Li, J. X. (2010). Theoretical studies on the chemical structure of carboxymethyl chitosan. *Advanced Materials Research*, 160-162: 1822-1827.

