MODIFICATION OF THE METHOD FOR PREPARING OLIGOMERS FROM HIGH MOLECULAR WEIGHT CHITOSAN

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Chitosan is a natural polymer with huge structural possibilities for chemical modifications to generate novel properties for the application in different spheres, especially in biomedical and pharmaceutical ones. The biomedical utilization of high molecular weight chitosan is restricted by its water insolubility. Nevertheless, its biocompatibility, biodegradability, and non-toxicity combined with its antimicrobial activity and low immunogenicity point to reveal the immense potential for future development. Low molecular weight chitosan and, especially chitosan oligomers do not only have the same beneficial biological features as high molecular weight chitosan, but their solubility in water makes them the attractive pharmaceutical ingredients [1,2].

Chitosan is a random linear copolymer of (1-4)-linked 2-acetamido-2-deoxy-β-D-glucan (GlcNAc) and 2-amino-2-deoxy-β-D-glucan (GlcN) units in varying proportions. It is usually obtained by degradation and deacetylation of natural polymer chitin found in the exoskeletons of insects, the cell walls of fungi, and certain hard structures in invertebrates and fish. For example, chitin is the main building component of crustacean shells [3].

Traditionally, low molecular weight chitosan is synthesized by different enzymatic and chemical depolymerization methods. The enzymatic methods are based on the usage of specific enzymes. Although they were found to be efficient in the depolymerization of chitosan, their usage is restricted by the cost of these enzymes and their availability. Moreover, this method can not be applied on a broad scale in the industry [1]. The objective of this study was to perform an experiment in a way it can be represented as commercially available.

One of the most reliable ways to obtain chitosan oligomers is acid hydrolysis by hydrochloric acid. Our procedure is distinguished by the usage of a cheap ion exchange resin to remove chloride ion from the solution instead of the ultrafiltration cell. We based our research on the famous data [4]. Acid hydrolysis of chitosan was performed by mixing chitosan with concentrated HCl in a glass reactor. The suspension was stirred for a while in the thermostated bath. Then the mixture was cooled by cold water. The obtained solution was evaporated under vacuum, the residue was dissolved in water, and evaporated again. This stage was performed repeatedly to remove most of the HCl used for synthesis. After the evaporating, the products were dissolved in water one more time and the pH of the obtained solution was adjusted by the ion exchange resin that is capable of replacing chloride anions by hydroxide ions in the solution. After passing the solution through the ion-exchange resin, high molecular weight chitosan precipitated. Then it was filtered and concentrated under vacuum. The obtained solution was treated by isopropanol. The salt remained in the aqueous phase, while low molecular chitosan precipitated. This two-phase system was separated by filtration through a glass filter. The obtained solution was evaporated to dryness under vacuum and partially dissolved in isopropanol. The solubility of chitosan oligomers in isopropanol allowed to extract it from by-products. The resulting solution was evaporated under vacuum to obtain chitosan oligomers.

The determination of the molecular weight of the obtained samples was measured by viscosity measurement using an Ubbleohde capillary viscometer. Molecular weights were calculated using the classic Mark-Houwink equation, Eq. (1):

$$[\eta] = k \times M^{\alpha} \quad (1)$$

The main advantage of our method is that we have not used any specific and expensive equipment and compounds that were used to treat our products are widely used. Nevertheless, the obtained low molecular weights chitosan and oligomeric chitosan are water-soluble. The optimized procedure can be considered as cost-effective, practical, and potentially suitable for the industrial production of low molecular weight chitosan

[1] Aljbour, N. D., Beg, M. D. H. & Gimbun, J. Acid Hydrolysis of Chitosan to Oligomers Using Hydrochloric Acid. Chem. Eng. Technol. 42, 1741–1746 (2019).
[2] Pillai, C. K. S., Paul, W. & Sharma, C. P. Chitin and chitosan polymers: Chemistry, solubility and fiber formation. Progress in Polymer Science (Oxford) 34, 641–678 (2009).
[3] Ibrahim, K. et al. Preparation of Chito-Oligomers by Hydrolysis of Chitosan in the Presence of Zeolite as Adsorbent. Mar. Drugs 14, 43 (2016).
[4] Trombotto, S., Ladavière, C., Delolme, F. & Domard, A. Chemical Preparation and Structural Characterization of a Homogeneous Series of Chitin/Chitosan Oligomers. Biomacromolecules 9, 1731–1738 (2008).