EXPLORING THE ENCAPSULATION OF NAPHTHOQUINONE IN NANOCHITOSAN FOR ANTIMICROBIAL ACTIVITY

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Introduction

Chitosan stands out among natural polymers with applications in the pharmaceutical field, being primarily obtained from the deacetylation of chitin, a biological polymer of marine origin, mainly found as a structural component of the exoskeletons of arthropods. In addition to being considered a biocompatible, biodegradable, and non-toxic biopolymer, chitosan also possesses well-documented antimicrobial properties. This antimicrobial effect is even more pronounced when chitosan is used in nanoparticle form, due to the increased surface area, which enhances interaction with microorganisms. This can lead to cell membrane rupture, interference in DNA transcription and translation, and inhibition of cellular respiration.[1] Thus, the use of chitosan as an encapsulation method emerges as a promising technique in drug formulation, gaining relevance due to its unique properties. When associated with other active substances, this technique can represent an effective approach for developing controlled drug delivery systems. Therefore, the antimicrobial potential of chitosan nanoparticles has become a subject of great interest among researchers.[2] Quinones form a group of natural metabolites found in plants, bacteria, and fungi, standing out for their potential to exhibit synthetic versatility and have a significant medicinal impact. 1,4-naphthoquinones comprise a group of quinones, and their biological activities and structural properties make these structures extremely useful in medicinal chemistry. However, their low solubility in water limits their topical application through conventional formulations, and their therapeutic applications require attention due to their toxicity to biological systems.[3] An innovative approach to overcome these limitations is the development of nanostructured therapeutic formulations, using biocompatible and biodegradable nanocapsules (**Figure 1**) capable of transporting and releasing quinones into the bloodstream and intracellular aqueous environments.

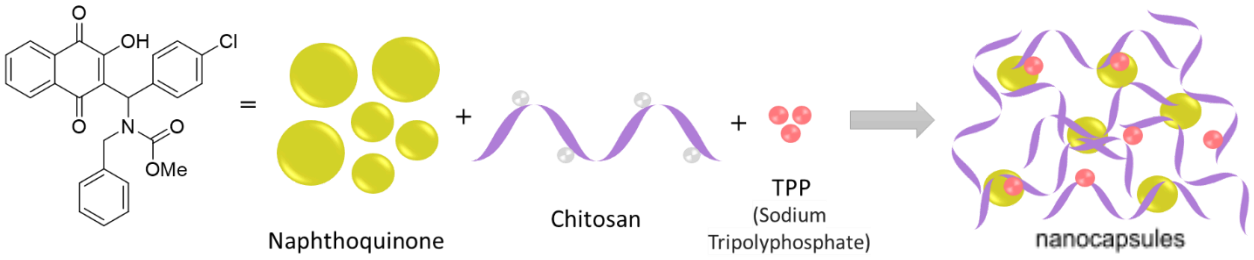

Figure 1. Planning for obtaining chitosan nanocapsules loaded with naphthoquinone.

Material and Methods

Herein, the naphthoquinone methyl benzyl((4-chlorophenyl)(3-hydroxy-1,4-dioxo-1,4-dihydronaphthalen-2-yl)methyl)carbamate (NQ) was successfully obtained through a multicomponent reaction between lawsone, benzylamine, and benzaldehyde, using anhydrous THF as the solvent. After 1 hour of reaction, DBU was added, followed by the addition of methyl chloroformate 15 minutes later. The reaction was stirred for 24 hours at room temperature. After this period, the NQ was isolated and purified by column chromatography, yielding a red solid with a 77% yield. The structural characterization of the NQ was confirmed through infrared spectroscopy and ^{1}H NMR analysis.[4]

Subsequently, NQ was nanoencapsulated into chitosan (CNP) using the ionotropic gelatinization technique, using sodium tripolyphosphate (TPP) as the crosslinking agent. The process began with the preparation of chitosan (0.2%) and TPP (0.4%) solutions, with chitosan being solubilized in 1% acetic acid under intense stirring for 24 hours, and TPP dissolved in water with constant stirring until complete solubilization. Once the solutions were prepared, the NQ, solubilized in DMSO, was added dropwise to the chitosan gel, followed by the slow addition of the TPP solution by drop wise 1mg/min. After 40 minutes of constant stirring, the CNP were obtained as a gel. The solution was then centrifuged and resuspended in Milli-Q water for DLS analysis, where the nanocapsules showed an average size of approximately 206nm and a zeta potential ranging from +23.23mV to +25.63mV.[5]

Conclusion

The naphthoquinone (NQ) was successfully synthesized and characterized, followed by its encapsulation in chitosan, resulting in particles approximately 200nm in size. The nanoparticles were analyzed by DLS, obtaining the polydispersity index (PDI) and the zeta potential as well.

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