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Enhancement of Chitosan Nanoparticle and Cyclosporine Tolerance for Future Applications

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Abstract

APPLICATIONS for cancer treatment widely use reliable cyclosporine compounds combined with the organic polymer chitosan nanoparticles. The surface chemical characteristics of the chitosan/cyclosporine nanoparticles were investigated using X-ray diffraction (XRD), Fourier transform infrared spectroscopy (FTIR), and particle size (PS) measurements. Field-emission scanning microscopy (FESM) was used to obtain morphological images of the composite materials. The homogenous composition and interaction between chitosan and cyclosporine performed well for future studies, supporting this study are its nanoparticle applications. The proposed chitosan nanoparticle manufacturing process is simple, low-cost and environmentally friendly. Moreover, these advantages indicate the possibility of using interesting samples for cancer treatment applications in advanced biomedical and practical fields.

Keywords: chitosan nanoparticles, biomedical, drug delivery, nanomaterials.

Introduction

Researchers have investigated the use of biological and synthetic covering materials to reduce the risk of thrombosis and restenosis after implantation. Chitosan (Ch) has been suggested as a promising material for improvingt implant surface coating biocompatibility with surrounding tissues [1,2]. The biocompatibility of chitosan is mostly reliant on its source, extraction technique, and purity because it is made by N-deacetylation of chitin, a naturally occurring polymer found in the exoskeletons of insects and arthropods, as well as in crustacean shells and the cell walls of some fungi [3,4]. One amino group and two hydroxyl groups were found in the repeated glucoside residues of chitosan, a polycationic polymer[5]. The polymer acquires mucoadhesive properties from the interaction of positively charged amino groups with the negatively charged mucous layer[6,7]. Chitosan is considered a safe material of choice for drug-delivery applications and is one of the most investigated materials in the biomedical industry[8]. Chitosan is a suitable cationic biopolymer for ocular applications because of its biocompatibility, biodegradability, and lack of potential for accumulation or retention in the body [8,9].

Cyclosporine is one of the best medications for immunosuppression. T-lymphocyte function, which is crucial for triggering the an immunological response, is inhibited. Immune reactions typically occur following organ transplants, including bone marrow, kidney, and liver transplantion [10]. In contrast, cyclosporin A is an 11-amino acid cyclic peptide that is weakly soluble in water. The low bioavailability, limited therapeutic window, nephrotoxicity, hepatotoxicity, and neurotoxicity of cyclosporine, A are among the drawbacks that restrict its use[11].The first documented use of cyclosporine as an immunosuppressive drug was in adult humans to prevent renal allograft rejection[12,13]. Since then, cyclosporine has emerged as the mainstay of organ transplant immunosuppression [14,15].

The U.S. The Food and Drug Administration (FDA) authorized cyclosporine in 1983 for the management and avoidance of transplant rejection in human health [16,17]. Si the FDA approved Novartis Animal Health's Atopica, an oral cyclosporine capsule, for the treatment of canine atopy [18,19].

Material and Aim of work

Raw Materials & Characterization

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Chitosan (deacetylation grade 0.85, MW 110 kDa), calcium nitrate ($Ca(NO3)_2.4H2O$) tetrahydrate, and diammonium hydrogen phosphate ($(NH4)_2HPO4$ were purchased from Avonchem Ltd, UK. All solvents and reagents were used without additional purification[20,21]. The morphology and diameter of cyclosporins and/or CS/cyclosporins were examined using Field Emission Scanning Electron Microscopy (Model Quanta 200FEG), which is configured to operate at 120 kV and various magnification levels. The crystallinity and crystal phase of cyclosporin and/or CS/cyclosporin were studied using with Rigaku X-ray diffractometer (6000, Shimadzu, Japan). FTIR [FTIR 8400S,Shimadzu, Japan] and UV-Vis spectroscopy [AA 6300, Shimadzu, Japan] characterized the physical properties and chemical structure antimicrobial tests were performed in vitro.

Method

First, the procedure used to prepare chitosan nanoparticles was performed according to our previous study[22]. In summary, chitosan nanoparticles (Csn) were obtained for use in acid function control at pH 11. Ultrasound was used to study the effect of particle size; cyclosporine was mixed with chitosan nanoparticles, followed by sonication for 1 min. Subsequently, a 1:4 (5:20) loading ratio of cyclosporine to chitosan was obtained by slowly distilling 250 mg of cyclosporine in 1 ml of distilled water with continuous stirring on a heated plate stirrer for 30 min at 900 rpm. Subsequently, the mixture was sonicated for a minute. The solution was continuously stirred, and 10 ml using tripolyphosphate solution (TPP) (0.25%) was added at a ratio of 5:1 by progressive distillation, and stirring was continued for 30 min to allow the cyclosporine to adsorb on the surface of the chitosan particles [23,24].

Results and Discussion

The nanoparticles were obtained from chitosan nanoparticles using an ultrasonic technique. Fig. 1. shows the morphology of chitosan. The obtained chitosan solution contains almost spherical particles with a narrow size distribution. The average size of the chitosan particles was approximately 30 nm, as shown in Fig. 1. The FE-SEM images indicate individual spheres with agglomeration and porosity. the homogeneous composition and distribution of CS nanoparticles are due to the high level of association between ultrasound and the chitosan nanoparticle molecule[25,26]. Fig. 2 shows the transmission electron microscopy (FE-SEM) images of CS/cyclosporine. The shape of the prepared material was, in the form of homogeneous chitosan nanoparticles distributed over cyclosporine. The original cyclosporine was a complex particle. two reasons explain why the diameter of chitosan is smaller than that of cyclosporine because it is a nanomaterial. First, the mass was formed by cyclosporine molecules. Second, the CS-cyclosporine complex before gel formation indicates that cyclosporine is relatively dispersed over a wide area in the CS matrix. The fluorescence results of cyclosporine were suggested to be homogeneously incorporated with CS/Cyclosporine .The average size of chitosan particles is approximately 30-50 nm, as shown in Fig. 2. [27,28].

The nanoparticle density was chosen as the criterion for analyzing the results. The preparation of chitosan nanoparticles was studied, and the optimum particle size for chitosan alone was obtained at 36.6 nm. However, mixing chitosan nanoparticles with cyclosporine yielded better results. This result was attributed to the large size of the cyclosporine molecules, and the result of mixing was 202.8 nanometers. Knowing that cyclosporine alone gave the highest results 731.8 nm, as shown in Figs. 3,4, and 5 [29,30].

The XRD patterns of the CS and CS/Cyclosporine with samples are summarized in Fig. 6,7. The XRD result was confirmed by energy diffraction, which indicated that the broad diffraction peak observed around 20° corresponded to chitosan alone or in combination with cyclosporine. The sharp peaks observed at approximately 12.5° and 25° were specific to cyclosporine (12.5°, 25°). The XRD patterns indicated peaks for both chitosan and cyclosporine with almost no change in the (2θ) angle position [31,32].

The FTIR spectra indicated that the absorption bands at 3489.07, 2924.59, 1664.04, 1575.64, and 1422.79 cm^{-1} for chitosan nanoparticles and at 3470 and 3570 cm^{-1} correspond to the stretching and vibration of the lattice of OH ions in chitosan nanoparticles and cyclosporine [33,34]. The bands at 631 cm^{-1} were assigned to the ν1 mode of the PO4-3 characteristic bands, and the absorption bands at 1093/1040 cm-1 were observed for the symmetric PO ν3 stretching vibration. The absorption bands of HPO4-2 appeared at 1393 cm-1 and 1460 cm^{-1} as shown in Fig.8,9, and 10. These results indicate the presence of cyclosporine in the chitosan samples, as confirmed by the XRD results [33,35].

Conclusion

The synthesis of chitosan nanoparticles with uniform spherical particles, approximately 35 nm in size, in an aqueous solution in the presence of cyclosporine was achieved by particle size using FESEM equipment. The particles also demonstrated a compositional hierarchy from the inorganic material of cyclosporine to the organic material of chitosan, suggesting potential applications in the medical field due to its efficacy in treating cancer, especially for cyclosporine. This is further enhanced and supported by nanotechnologies such as drug delivery devices, hybrid tissue engineering, and

scaffolds. The XRD and FTIR spectra correspond to the structures of the composite materials. The efficacy of cancer treatment was found to be highly dependent on the concentration of the nanoparticles, as demonstrated in the tests.

These results indicate that the CS/cyclosporine nanoparticle biomaterials exhibit strong potential for medical treatments, especially in longer treatment periods for cancer."

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Conflict of interest

There are no conflicts of interest to be declared.

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Author contributions

Conceptualization, study design and sample collection Essa D Alhtheal. Data analyses, Manuscript drafting, and Manuscript finalization: Sufian Saleh Salman.

Ethical approval

It was granted through the local committee of the animal care and use at the College of Veterinary Medicine/University of Baghdad (Number 314/P.G. at 13/2/2024).

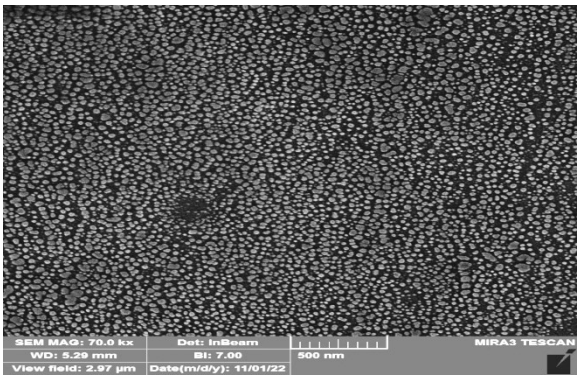

Fig. 1. FE-SEM images of chitosan nanoparticles

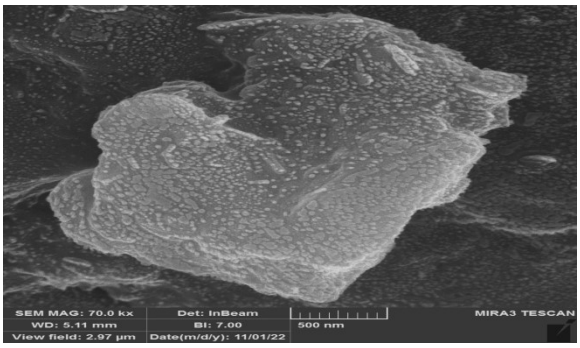

Fig. 2. FE-SEM images of cyclosporine-loaded chitosan nanoparticles

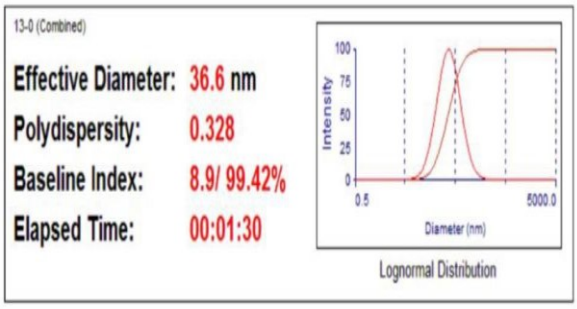

Fig. 3. Particle size analysis of chitosan nanoparticle

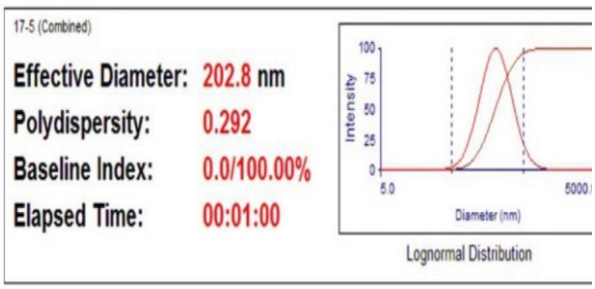

Fig. 4. Particle size analysis of chitosan nanoparticle and cyclosporine

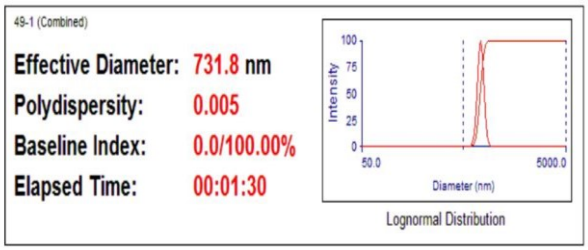

Fig. 5. Particle size analysis of cyclosporine

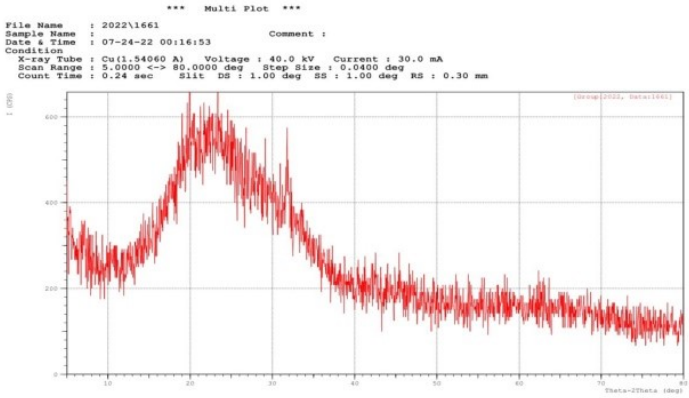

Fig. 6. XRD images of chitosan nanoparticles

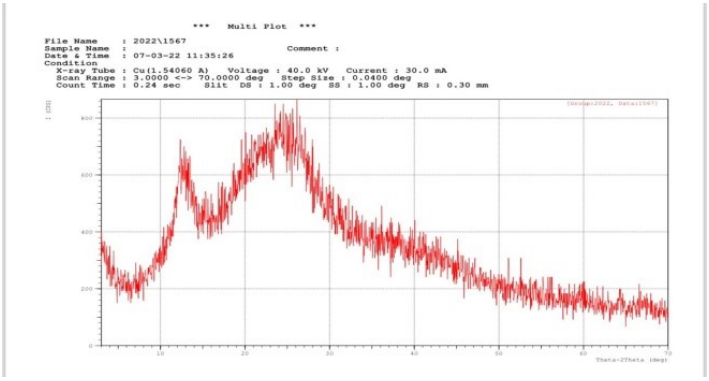

Fig. 7. XRD images of cyclosporine-loaded chitosan nanoparticles

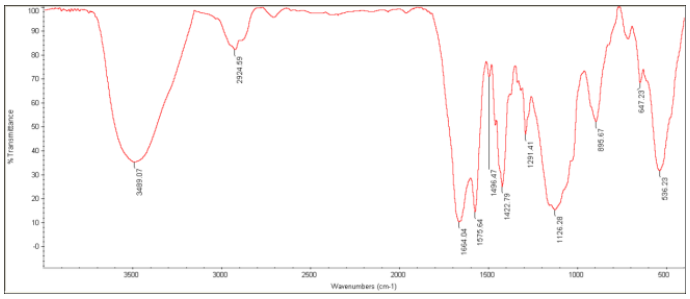

Fig. 8. FTIR spectra of chitosan nanoparticles

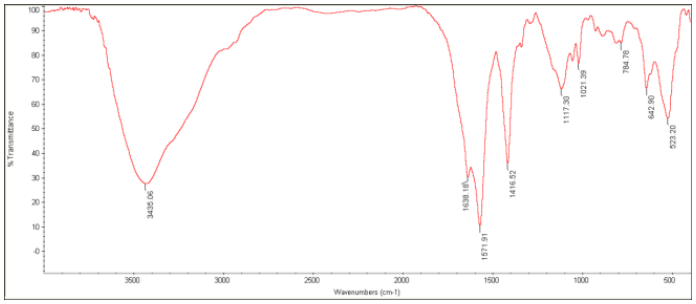

Fig. 9. FTIR of cyclosporine

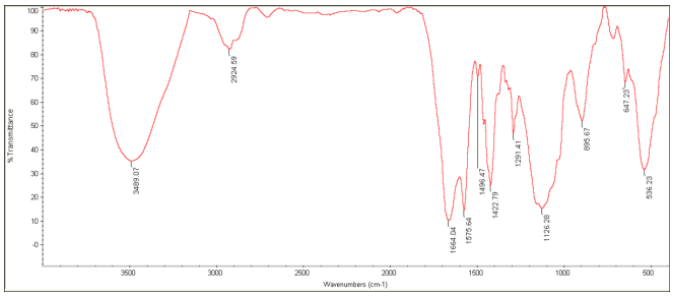

Fig. 10. FTIR of chitosan nanoparticle and cyclosporine

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تعزيز جسيمات الشيتوزان النانوية وتحمل السيكلوسبورين للتطبيقات المستقبلية

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الخلاصة

تُستخدم مركبات السيكلوسبورين الموثوقة مع جسيمات البوليمر الشيتوزان النانوية العضوية على نطاق واسع في تطبيقات علاج السرطان. تم دراسة التوصيف الكيميائي السطحي للجسيمات النانوية الشيتوزان/السيكلوسبورين باستخدام قياسات حيود الأشعة السينية (XRD) واختبار فوريه للطيف بالأشعة تحت الحمراء (FTIR) ، والحجم الحبيبي للجسيمات النانوية (PS) والفحص المجهري الماسح (FESM) مورفولوجية للمواد المركبة. كان أداء التركيب المتجانس والتفاعل بين الشيتوزان والسيكلوسبورين جيدًا للدراسات التجريبية المستقبلية، ودعم هذه الدراسة هو تطبيقات الجسيمات النانوية. إن عملية تصنيع جسيمات الشيتوزان النانوية المقترحة بسيطة ومنخفضة التكلفة وصديقة للبيئة. وتشير جميع المزايا المذكورة أعلاه إلى إمكانية استخدام عينات مثيرة للاهتمام في تطبيقات علاج السرطان في المجالات الطبية الحيوية والعملية المتقدمة.

الكلمات المفتاحية: جسيمات الشيتوزان النانوية، الطب الحيوي، توصيل الأدوية، المواد النانوية.