Original Research Paper

JIC *Journal of Industrial Catalysis*
Vol. 1, No. 2, 2024, 60-65

Formulation and Evaluation of Chitosan-Based Nanoparticles for Enhanced Transdermal Delivery of Niacinamide

Nasrin Haftabadi[1], Rahele Zhiani[1*], Malihesadat Hosseiny[1]

1Department of Chemistry, Ne.C., Islamic Azad University, Neyshabur, Iran.
* E-mail: Zhiani@iau.ac.ir

Received 20 July 2025; accepted 14 September 2025

Abstract

The Topical delivery of hydrophilic compounds such as niacinamide had consistently faced challenges due to the complex structure and inherent permeability limitations of the skin. Niacinamide, a water-soluble vitamin with sebum-regulating, anti-inflammatory, brightening, and anti-aging properties, was widely used in the treatment of dermatological conditions. However, its limited chemical stability and skin penetration hindered its optimal therapeutic efficacy. In this study, chitosan nanoparticles were employed as drug carriers due to their biocompatible structure, mucoadhesive properties, and positive surface charge, aiming to enhance stability, enable controlled release, and improve transdermal penetration of niacinamide. Chitosan nanoparticles were synthesized using the ionic gelation method, and the resulting niacinamide-loaded nanocapsules (CS/NIA) were thoroughly characterized. Structural features of the nanoparticles were examined via FT-IR and SEM analyses, confirming the presence of amide bonds, ether groups, and pyridine rings. SEM images revealed particle sizes predominantly in the range of 65 to 120 nanometers, which was favorable for epidermal penetration and minimizing systemic accumulation. In vitro drug release studies in simulated physiological conditions demonstrated that the nanocarrier system provided a stable and controlled release profile of niacinamide over a 300-minute period, whereas the pure form of the drug did not exhibit comparable performance.

Keywords: *Chitosan nanoparticles, Niacinamide, Skin delivery, Drug delivery, Controlled release*

1. Introduction

The skin, the largest and most complex organ in the human body, functions as the primary physiological barrier against both external and internal factors. Due to its multilayered architecture (epidermis, dermis, and hypodermis), it imposes substantial restrictions on the permeability of therapeutic compounds [1–3]. Topical drug delivery, particularly for hydrophilic molecules such as niacinamide (vitamin B3), presents considerable challenges because the stratum corneum exhibits intrinsically limited permeability toward such compounds. Over the past decade, niacinamide has received increasing attention as a key ingredient in therapeutic and cosmetic formulations. This water-soluble molecule has been shown to exert a wide spectrum of biological effects, including skin brightening, anti-inflammatory activity, sebum regulation, anti wrinkle properties, and protection against oxidative stress. Consequently, it demonstrates therapeutic potential in the management of various dermatological conditions, such as acne, hyperpigmentation, rosacea, melanoma, and premature skin aging [6–9]. However, its clinical applications remain limited owing to poor skin penetration, instability under environmental conditions, and susceptibility to both chemical and enzymatic degradation [10–12]. In recent years, nanotechnology has emerged as a promising approach to address the challenges associated with dermal permeation and stability [13–15]. Among different nanocarrier systems, biocompatible polymeric nanoparticles particularly chitosan-based formulations have gained substantial attention. Due to their biodegradability, low toxicity, positive surface charge, and mucoadhesive properties, chitosan nanoparticles are highly suitable for dermal delivery [16–18]. Through electrostatic interactions with the negatively charged phospholipids of cell membranes and keratinocytes, chitosan can facilitate drug penetration across the stratum corneum. Moreover, their nanostructure enables controlled drug release and provides protection against degradation. Recent studies have highlighted the critical influence of nanoparticle size and surface charge on dermal absorption. Typically, particles smaller than 200 nm with a positive charge exhibit superior penetration into epidermal tissues and improved local accumulation, while simultaneously reducing systemic absorption and minimizing adverse effects [22–24]. Furthermore, surface modifications such as coating with peptides,

lipids, or polyethylene glycol have been reported to enhance the ability of nanoparticles to traverse cutaneous barriers. The incorporation of niacinamide into chitosan nanocarriers has attracted growing attention. Evidence indicates that encapsulation of niacinamide within chitosan nanoparticles not only stabilizes the compound and protects it against chemical transformation, but also enables sustained and controlled release, thereby markedly enhancing its topical absorption and therapeutic efficacy [27–30]. Experimental and animal studies have confirmed these benefits, reporting improved wound healing, reduced inflammation, inhibition of lipid peroxidation, and regulation of collagen synthesis [31–33]. Beyond niacinamide, a variety of chitosan-based nanocarriers have been investigated for the delivery of other bioactive compounds with dermatological applications. Favorable outcomes including enhanced penetration, reduced irritation, and improved antioxidant activity have been observed in formulations containing retinol, azelaic acid, curcumin, and vitamin E [34–37]. Additionally, hybrid systems that combine chitosan nanoparticles with nanogels, nanoemulsions, or composite hydrogels have introduced significant innovations in optimizing topical drug delivery [38–40].Taken together, chitosan nanoparticle systems loaded with niacinamide represent a promising and emerging strategy to overcome the limitations of permeability and stability associated with this molecule. Systematic evaluation of their structural characteristics, stability, release profile, and skin penetration is essential for fully assessing their therapeutic efficacy and safety. Such investigations will pave the way for the rational design of advanced pharmaceutical and cosmetic formulations.

2- Experimental method

2-1- Chemicals:

Chitosan (degree of deacetylation 75–85%) was purchased from Merck, Germany.Acetic acid (glacial, ≥99%) was obtained from Merck, Germany.Sodium hydroxide (NaOH, pellets, ≥98%) was supplied by Merck, Germany.Sodium tripolyphosphate (TPP, ≥95%) was purchased from Sigma-Aldrich, USA.Niacinamide (≥99%) was obtained from Merck, Germany.All other chemicals used were of analytical grade and sourced from Merck, Germany or Sigma-Aldrich, USA.

2-2- Instruments:

pH meter (Metrohm, Switzerland) was used for monitoring and adjusting the pH of solutions.Magnetic stirrer (IKA, Germany) was employed for continuous and uniform stirring.Centrifuge (Hettich, Germany) was used for separation of nanoparticles.UV–Vis spectrophotometer (Shimadzu, Japan) was applied to evaluate the in vitro release of niacinamide at 765 nm.Fourier-transform infrared spectrometer (FTIR) (Bruker, Germany) was used for functional group characterization.Scanning electron microscope (SEM) (ZEISS, Germany) was employed to investigate the morphology and size of nanoparticles.Dynamic light scattering (DLS) and zeta potential analyzer (Malvern Zetasizer Nano ZS, UK) was used to determine particle size, polydispersity index (PDI), and zeta potential.Incubator shaker (Memmert, Germany) was used for in vitro release studies under simulated body fluid (SBF) conditions at 37 °C.

2-3-Synthesis of Chitosan Nanoparticles (CS) via Ionic Gelation Method

To prepare the chitosan solution, 1 gram of chitosan powder was dissolved in 100 mL of 1% (v/v) acetic acid solution. The mixture was placed on a magnetic stirrer at 800 rpm and was stirred continuously until a homogeneous clear or slightly opalescent solution was obtained. The dissolution process took several hours; to accelerate it, the temperature was maintained between 40°C and 60°C. The pH of the chitosan solution was then adjusted using a pH meter (or pH paper if a meter was unavailable). A 1 M sodium hydroxide (NaOH) solution was added dropwise to the chitosan solution under continuous stirring until the pH reached the range of 4.6–4.8. It was critical not to exceed this pH range, as chitosan tended to precipitate at higher pH values.

2-4- Preparation of Tripolyphosphate (TPP) Solution (0.25 mg/mL)

To prepare the TPP solution, 25 mg of sodium tripolyphosphate (TPP) was dissolved in 100 mL of deionized water. The solution was stirred thoroughly using a magnetic stirrer to ensure complete and uniform dissolution of TPP.

2-5- Formation of Chitosan Nanoparticles (CS) via Ionic Gelation Method

The TPP solution was slowly added dropwise to the chitosan solution using a micropipette or burette, maintaining a volumetric ratio of 1:3 (i.e., one part TPP to three parts chitosan). For instance, 30 mL of TPP solution was added to 90 mL of chitosan solution. The mixture was stirred on a magnetic stirrer at 800 rpm for 45 minutes at room temperature. During this process, chitosan nanoparticles gradually formed, resulting in a turbid suspension.

2-6- Preparation of Chitosan–Niacinamide Nanoparticles (CS/NIA) via Ionic Gelation

To prepare chitosan–niacinamide nanoparticles (CS/NIA), chitosan solutions were prepared following the previously described procedure, except that the final pH was adjusted to 4.7 in order to provide optimal conditions for electrostatic interactions between the

polycationic chitosan and the polyanionic TPP. Subsequently, 5 mL of niacinamide solution was gradually added to 15 mL of the chitosan solution, and the resulting mixture was gently stirred to ensure homogeneity. Thereafter, 2 mL of sodium tripolyphosphate (TPP) solution was introduced dropwise into the system to initiate the ionic gelation process, allowing nanoparticles to gradually form. The obtained suspension was subjected to centrifugation at 500 rpm for 30 minutes at room temperature to facilitate particle separation and improve uniformity. Finally, the pH of the CS/NIA nanoparticle suspension was measured to be 5.9, confirming the stable formation of nanoparticles under the experimental conditions.

2-7- In Vitro Niacinamide Release from Chitosan Nanoparticles

The release study was conducted by dispersing 25 mg of the CS/NIA sample in 35 mL of simulated body fluid (SBF) with a pH of 7.40. The mixture was incubated at 37 °C and stirred at 100 rpm for 5 hours (300 minutes). At predefined time intervals, 0.5 mL aliquots were withdrawn for analysis of niacinamide concentration. The release profile of niacinamide was monitored using a UV-Vis spectrophotometer at a wavelength of 765 nm over the 5-hour period.

3- Results

3-1- FTIR Spectrum of Chitosan Nanoparticles (CS)

A broad absorption band observed in the range of 3200–3400 cm^{-1} corresponds to the stretching vibrations of O–H and N–H functional groups. The characteristic peaks at approximately 1650 cm^{-1} and 1580 cm^{-1} are attributed to the presence of amide groups within the chitosan structure. Additionally, the absorption band detected in the range of 1020–1070 cm^{-1} is indicative of ether linkages (C–O–C) in the chitosan backbone.

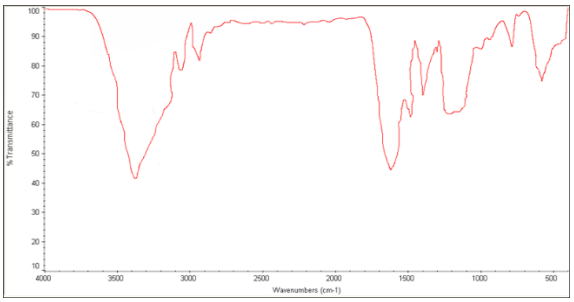

Figure 1. FT-IR spectrum of chitosan nanoparticles (CS).

3-2- FTIR Spectrum of Niacinamide-Loaded Chitosan Nanoparticles (CS/NIA)

The broad absorption band observed in the range of 3200–3400 cm^{-1} corresponds to the stretching vibrations of N–H and O–H groups. The sharp peak between 1650–1680 cm^{-1} is attributed to the C=O stretching vibration, indicative of niacinamide's carbonyl structure. The absorption bands in the range of 1230–1320 cm^{-1} correspond to C–N stretching vibrations, while the peaks observed in the region of 1500–1600 cm^{-1} are associated with C=C stretching within the pyridine ring of niacinamide.

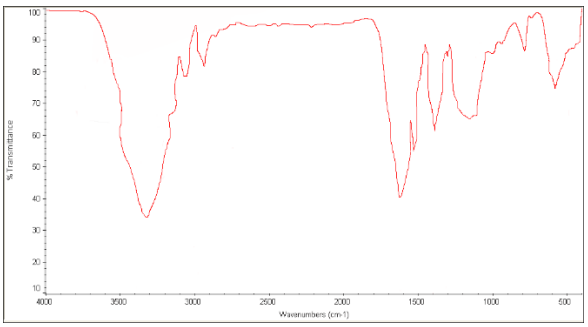

Figure 2. FT-IR spectrum of niacinamide-loaded chitosan nanoparticles (CS/NIA).

3-3- SEM Analysis of Chitosan Nanoparticle (CS) Structure

Based on scanning electron microscopy (SEM) images at magnifications of 20,000× and 50,000×, it can be concluded that chitosan nanoparticles were successfully synthesized. The high-resolution images clearly reveal the shape and distribution of the particles, confirming their nanometric scale. The morphology of the particles appeared predominantly as irregular, rod-like, and occasionally sheet-like structures, which was consistent with the physical properties of chitosan and the nature of the synthesis process. A more comprehensive assessment of particle distribution across the images showed that most particles fell within the 65–120 nm range. This size range remained well within the nanoscale and was highly suitable for applications such as drug delivery, tissue engineering, and biomedical use. The observed high particle density, relatively uniform dispersion, and distinct particle boundaries suggest effective control over the nanoparticle fabrication process. Additionally, the moderately rough surface texture may contribute to an increased specific surface area, thereby enhancing the performance of the nanoparticles in various applications.
In conclusion, the evidence supports that the chitosan nanoparticle synthesis was successful, producing particles with appropriate size and desirable morphological characteristics.

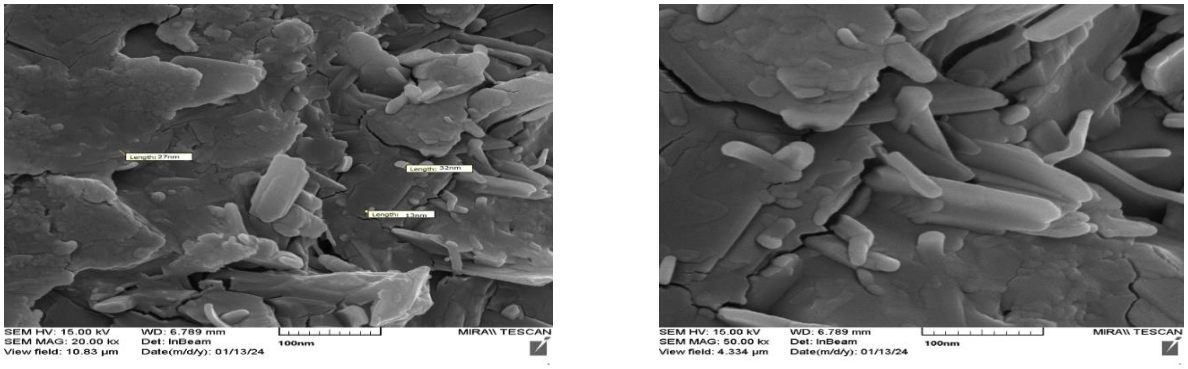

Figure 3. SEM images of chitosan nanoparticles (CS)

3-4- Comparative Evaluation of Niacinamide Release

A comparative assessment of niacinamide release under two conditions—pure niacinamide (NIA) and niacinamide incorporated into chitosan nanoparticles (CS/NIA) demonstrated a significant enhancement in release performance in the presence of chitosan. According to the release profile, the NIA sample exhibited a gradual and limited release, reaching approximately 18% after 100 minutes and remaining stable through 300 minutes. In contrast, the CS/NIA formulation showed a more rapid increase in drug release, reaching 31% at 100 minutes and maintaining approximately 32% up to 300 minutes. This marked improvement was attributed to the presence of chitosan, a biocompatible polymer known for its mucoadhesive properties, swellability, and ability to form porous matrices. These characteristics enhanced drug permeability and solubility, prolonged residence time, and facilitated more controlled and efficient drug release. Based on the observed kinetic behavior, chitosan played a critical role in enhancing both the rate and extent of niacinamide release. This supported the potential of CS/NIA systems as effective candidates for controlled-release formulations in pharmaceutical or cosmetic applications.

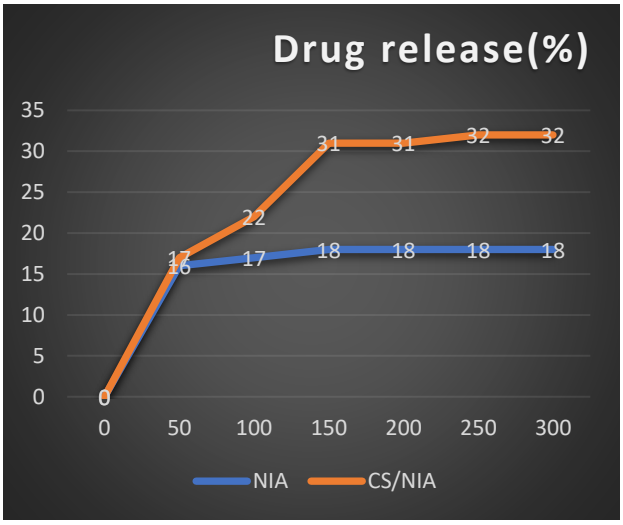

Figure 4. Comparative release profile of niacinamide: free niacinamide (NIA) vs. niacinamide-loaded chitosan nanoparticles (CS/NIA) over a period of 300 minutes in simulated body fluid (SBF) at pH 7.4 and 37 °C.

3-5- Dynamic Light Scattering (DLS), Polydispersity Index (PDI), and Zeta Potential

The physicochemical features of the prepared nanoparticles were presented in Table 1. Chitosan nanoparticles without drug (CS-NPs) displayed a mean hydrodynamic diameter of 120 ± 1.9 nm with a low polydispersity index (0.12 ± 0.02), which reflected a narrow size distribution and good colloidal uniformity. After niacinamide incorporation (CS/NIA), the average particle size was reduced to 98.2 ± 7.8 nm, while the PDI showed a modest increase (0.23 ± 0.02). Such a decrease in particle size was likely related to molecular interactions between niacinamide and the protonated amino groups of chitosan, leading to a denser packing of the polymer chains during nanoparticle formation. The

surface charge of the systems, expressed as zeta potential, was measured at +23.1 ± 0.1 mV for CS-NPs and +20.7 ± 0.8 mV for CS/NIA. Despite the slight drop in zeta potential upon drug loading, the values remained well above the ±20 mV threshold, which was generally considered sufficient for maintaining electrostatic stabilization of nanoparticle suspensions. In addition, the encapsulation efficiency of niacinamide in the chitosan matrix reached 93.4 ± 2.1%. This high value demonstrated the strong interaction between niacinamide and chitosan and confirmed the suitability of the ionotropic gelation approach for efficient drug entrapment.

Table 1. Characterization of chitosan nanoparticles (CS-NPs) and niacinamide-loaded chitosan nanoparticles (CS/NIA)

Sample	**Size (nm)**	**PDI**	**ZP (mV)**	**(%) EE**
CS-NPs	120±1.9	0.12±0.02	23.1±0.1	–
CS/NIA	98.2±7.8	0.23±0.02	20.7±0.8	93.4±2.1

4-Conclusion

The findings of this study clearly demonstrated that the use of chitosan nanoparticles as a drug delivery carrier presented a novel and effective strategy for enhancing the performance of niacinamide in transdermal applications. The physicochemical properties of chitosan, including its positive surface charge, biocompatibility, and ability to enable controlled release, contributed significantly to improved penetration, stability, and localized efficacy of the active compound. FT-IR analysis and SEM imaging confirmed the successful synthesis of nanoparticles and the chemical interactions between chitosan and niacinamide. In vitro drug release studies further indicated that the CS/NIA system provided a stable and sustained release profile, which was a key advantage over the pure form of niacinamide, as it extended the duration of action and reduced premature degradation. Moreover, the synergistic combination of chitosan's anti-inflammatory, regenerative, and antibacterial properties with niacinamide's therapeutic effects offered a promising pathway for the development of advanced skin care formulations. These innovative systems not only held great potential for treating dermatological disorders but were also highly relevant to the cosmetic industry, where efficacy, safety, and clinical appeal were essential for commercialization and standardization.

References

1 M.R. Prausnitz, R. Langer, Nat. Biotechnol. 26 (2008) 1261–1268. https://doi.org/10.1038/nbt.1504

2 R. Neupane, S.H.S. Boddu, M.S. Abou-Dahech, R.D. Bachu, D. Terrero, R.J. Babu, et al., Pharmaceutics 13 (2021) 960. https://doi.org/10.3390/pharmaceutics13070960

3 T.W. Prow, J.E. Grice, L.L. Lin, R. Faye, M. Butler, W. Becker, et al., Adv. Drug Deliv. Rev. 63 (2011) 470–491. https://doi.org/10.1016/j.addr.2011.01.012

4 G. Cevc, U. Vierl, J. Control. Release 141 (2010) 277–299. https://doi.org/10.1016/j.jconrel.2009.10.016

5 B. Zhao, X. Li, Y. Kong, W. Wang, T. Wen, Y. Zhang, et al., Front. Bioeng. Biotechnol. 10 (2022) 1010724. https://doi.org/10.3389/fbioe.2022.1010724

6 W. Gehring, J. Cosmet. Dermatol. 3 (2004) 88–93. https://doi.org/10.1111/j.1473-2130.2004.00115.x

7 C. Marques, F. Hadjab, A. Porcello, K. Lourenço, C. Scaletta, P. Abdel-Sayed, et al., Antioxidants 13 (2024) 425. https://doi.org/10.3390/antiox13040425

8 J. Levin, S.B. Momin, J. Clin. Aesthet. Dermatol. 3 (2010) 22–41. PMID: 20725560; PMCID: PMC2921764

9 Zhen A.X., Piao M.J., Kang K.A., Fernando P.D.S.M., Kang H.K., Koh Y.S., Yi J.M., Hyun J.W., Biomol. Ther. (Seoul) 27 (2019) 562–569. https://doi.org/10.4062/biomolther.2019.061

10 L. Zhao, J. Chen, B. Bai, G. Song, J. Zhang, H. Yu, et al., Front. Pharmacol. 14 (2024) 1333986. https://doi.org/10.3389/fphar.2023.1333986

11 Y.C. Boo, Antioxidants 11 (2022) 1663. https://doi.org/10.3390/antiox11091663

12 F. Iliopoulos, B.C. Sil, A.S.M. Monjur Al Hossain, D.J. Moore, R.A. Lucas, M.E. Lane, Int. J. Pharm. 579 (2020) 119137. https://doi.org/10.1016/j.ijpharm.2020.119137

13 C. Zhu, Z. Ji, J. Ma, Z. Ding, J. Shen, Q. Wang, Pharmaceutics 13 (2021) 940. https://doi.org/10.3390/pharmaceutics13070940

14 C.S. Amrutkar, S.B. Patil, Indian J. Ophthalmol. 71 (2023) 2355–2366. https://doi.org/10.4103/ijo.IJO_1893_22

15 K. Jafernik, A. Ładniak, E. Blicharska, K. Czarnek, H. Ekiert, A.E. Wiącek, A. Szopa, Molecules 28 (2023) 1963. https://doi.org/10.3390/molecules28041963

16 N. Desai, D. Rana, S. Salave, R. Gupta, P. Patel, B. Karunakaran, A. Sharma, J. Giri, D. Benival, N. Kommineni, Pharmaceutics 15 (2023) 1313. https://doi.org/10.3390/pharmaceutics15041313

17 A. Stefanache, I.I. Lungu, N. Anton, D. Damir, C. Gutu, I. Olaru, A. Plesea Condratovici, M. Duceac, M. Constantin, G. Calin, L.D. Duceac, M. Boev, Polymers 17 (2025) 1453. https://doi.org/10.3390/polym17111453

18 R. Biswas, S. Mondal, M.A. Ansari, T. Sarkar, I.P. Condiuc, G. Trifas, et al., Molecules 30 (2025) 1297. https://doi.org/10.3390/molecules30061297
19 M.H. Rahman, M.I.H. Mondal, Heliyon 10 (2024) e39879. https://doi.org/10.1016/j.heliyon.2024.e39879
20 S. Nasr, M. Rady, I. Gomaa, T. Syrovets, T. Simmet, W. Fayad, et al., Int. J. Pharm. 568 (2019) 118528. https://doi.org/10.1016/j.ijpharm.2019.118528
21 J. Al-Shadidi, S. Al-Shammari, D. Al-Mutairi, D. Alkhudhair, H.E. Thu, Z. Hussain, Int. J. Nanomed. 19 (2024) 8373–8400. https://doi.org/10.2147/IJN.S472433
22 S. Heydari, M. Barzegar-Jalali, M. Heydari, A. Radmehr, A.C. Paiva-Santos, M. Kouhsoltani, et al., Bioimpacts 14 (2024) 30243. https://doi.org/10.34172/bi.2024.30243
23 S.A. Coulman, A. Anstey, C. Gateley, A. Morrissey, P. McLoughlin, C. Allender, et al., Int. J. Pharm. 366 (2009) 190–200. https://doi.org/10.1016/j.ijpharm.2008.08.040
24 X. Zhou, Y. Liu, X. Wang, X. Li, B. Xiao, Colloids Surf. B Biointerfaces 187 (2020) 110880. https://doi.org/10.1016/j.colsurfb.2020.110880
25 Y. Wang, P. Li, L. Kong, AAPS PharmSciTech 14 (2013) 585–592. https://doi.org/10.1208/s12249-013-9943-3
26 T. Zhang, X. Luo, K. Xu, W. Zhong, Adv. Drug Deliv. Rev. 203 (2023) 115139. https://doi.org/10.1016/j.addr.2023.115139
27 K. Yu, Y. Wang, T. Wan, Y. Zhai, S. Cao, W. Ruan, et al., Int. J. Nanomed. 13 (2017) 129–142. https://doi.org/10.2147/IJN.S150319
28 Hu Q., Luo Y., Int. J. Biol. Macromol. 179 (2021) 125–135. https://doi.org/10.1016/j.ijbiomac.2021.02.216
29 Cao Y., Tan Y.F., Wong Y.S., Liew M.W.J., Venkatraman S., Mar. Drugs 17 (2019) 381. https://doi.org/10.3390/md17060381
30 H. Liu, Y. Li, X. Zhang, M. Shi, D. Li, Y. Wang, Can. Respir. J. (2022) 1–13. https://doi.org/10.1155/2022/8509396
31 H.L. Loo, B.H. Goh, L.H. Lee, L.H. Chuah, Asian J. Pharm. Sci. 17 (2022) 299–332. https://doi.org/10.1016/j.ajps.2022.04.001
32 L. Cremar, J. Gutierrez, J. Martinez, L. Materon, R. Gilkerson, F. Xu, et al., Nanomed J. 5 (2018) 1–10. https://doi.org/10.22038/nmj.2018.05.002
33 X. Deng, M. Gould, M.A. Ali, J. Biomed. Mater. Res. 110 (2022) 2542–2573. https://doi.org/10.1002/jbm.b.35086
34 A. Zamboulis, S. Nanaki, G. Michailidou, I. Koumentakou, M. Lazaridou, N.M. Ainali, et al., Polymers 12 (2020) 1519. https://doi.org/10.3390/polym12071519
35 V.V.S.R. Karri, G. Kuppusamy, S.V. Talluri, S.S. Mannemala, R. Kollipara, A.D. Wadhwani, et al., Int. J. Biol. Macromol. 93 (2016) 1519–1529. https://doi.org/10.1016/j.ijbiomac.2016.05.038
36 M. Karayianni, T. Sentoukas, A. Skandalis, N. Pippa, S. Pispas, Pharmaceutics 15 (2023) 1849. https://doi.org/10.3390/pharmaceutics15071849
37 X. Chen, J. Gu, L. Sun, W. Li, L. Guo, Z. Gu, et al., Bioact. Mater. 6 (2021) 3025–3035. https://doi.org/10.1016/j.bioactmat.2021.02.028
38 R. Ye, S. Liu, W. Zhu, Y. Li, L. Huang, G. Zhang, et al., Polymers 15 (2023) 2482. https://doi.org/10.3390/polym15112482
39 E.B. Souto, A. Cano, C. Martins-Gomes, T.E. Coutinho, A. Zielińska, A.M. Silva, Bioengineering 9 (2022) 158. https://doi.org/10.3390/bioengineering9040158
40 P. Gupta, S. Sharma, S. Jabin, S. Jadoun, Int. J. Biol. Macromol. 254 (2024) 127660. https://doi.org/10.1016/j.ijbiomac.2023.127660