# Development and Evaluation of Dapagliflozin-Loaded Chitosan Nanoparticles for Oral Delivery in Diabetes Mellitus

**Anuradha Pannu[1], Asha Rani M[2], Diksha N. Jadhav[3], Kasturi Vishwanathasetty Veerabhadrappa[4], Dr. P. Poornima[5]*, Dr. Parag Arun Kulkarni[6]**

1. Assistant Professor, Department of Pharmaceutical Sciences, Maharishi Dayanand University, Rohtak, Haryana 124001, India Email: anuradhapannu@gmail.com
2. Assistant Professor, Visveswarapura Institute of Pharmaceutical Sciences, 22nd Cross Road, Siddanna Layout, Banashankari Stage II, Basavanagudi, Bengaluru, Karnataka 560070, India Email: asharani_m@yahoo.com
3. Assistant Professor, Department of Pharmacology, PRES's College of Pharmacy for Women, Chincholi, Taluka Sinner, District Nashik, Maharashtra, India Email: dikshajadhav215@gmail.com
4. Associate Professor, Kampala International University (Western Campus), Ishaka, Bushenyi, P.O. Box 71, Uganda and Raghavendra Institute of Pharmaceutical Education and Research (RIPER), Autonomous, KR Palli Cross, Chiyyedu, Anantapur, Andhra Pradesh 515728, India Email: kasturibadri73@gmail.com
5. Professor, Department of Pharmaceutics, Siddhartha Institute of Pharmacy, Narapally, Korremula Road, Ghatkesar Mandal, Medchal-Malkajgiri 500088, Telangana, India Email: pamupoornima@gmail.com
6. Professor, Department of Pharmaceutics, Shastry Institute of Pharmacy, Erandol, Maharashtra, India Email: kparag4@yahoo.com

***Corresponding Author:** Dr. P. Poornima, Professor, Department of Pharmaceutics, Siddhartha Institute of Pharmacy, Narapally, Korremula Road, Ghatkesar Mandal, Medchal-Malkajgiri -500088, Telangana, India Email: pamupoornima@gmail.com

**Abstract**

The present study aimed to develop and evaluate Dapagliflozin-loaded chitosan nanoparticles for enhanced oral delivery in the management of diabetes mellitus. Nanoparticles were prepared using the ionic gelation technique employing chitosan as the polymer and sodium tripolyphosphate (TPP) as the cross-linking agent. Five formulations (F1–F5) were prepared by varying the concentrations of chitosan and TPP and were evaluated for particle size, polydispersity index (PDI), zeta potential, entrapment efficiency, drug loading, FTIR, DSC, SEM, in vitro drug release, release kinetics, and stability. The optimized formulation (F4) exhibited a particle size of 296.1 ± 9.4 nm, PDI of 0.271 ± 0.03, zeta potential of +32.7 ± 1.5 mV, entrapment efficiency of 87.8 ± 2.1%, and drug loading of 18.4 ± 0.8%. FTIR and DSC studies confirmed the compatibility of Dapagliflozin with formulation excipients and successful drug encapsulation within the chitosan matrix. SEM analysis revealed predominantly spherical nanoparticles with smooth surfaces and minimal aggregation. The optimized formulation demonstrated a sustained drug release profile with 92.4 ± 1.8% cumulative drug release over 24 hours. Release kinetic analysis indicated diffusion-controlled drug release following the Higuchi model with anomalous transport behavior. Stability studies demonstrated minimal changes in physicochemical properties over a three-month storage period. The findings suggest that Dapagliflozin-loaded chitosan nanoparticles represent a promising oral drug delivery system for sustained antidiabetic therapy.

**Keywords:** Dapagliflozin; Chitosan Nanoparticles; Ionic Gelation; Oral Drug Delivery; Diabetes Mellitus; Sustained Release.

**How to cite this article:** Pannu A, Rani MA, Jadhav DN, Veerabhadrappa KV, Poornima P, Kulkarni PA. Development and Evaluation of Dapagliflozin-Loaded Chitosan Nanoparticles for Oral Delivery in Diabetes Mellitus. Int J Drug Deliv Technol. 2026;16(64s):317-323. DOI: 10.25258/ijddt.16.64s.34

## 1. Introduction

Diabetes mellitus is a chronic metabolic disorder characterized by persistent hyperglycemia resulting from defects in insulin secretion, insulin action, or both. The prevalence of diabetes has increased significantly worldwide, posing a major public health challenge due to its associated complications, including cardiovascular diseases, nephropathy, neuropathy, and retinopathy [1]. Among the various therapeutic agents used for the management of type 2 diabetes mellitus, Dapagliflozin, a sodium-glucose co-transporter 2 (SGLT2) inhibitor, has gained considerable attention owing to its ability to reduce blood glucose levels by promoting urinary glucose excretion independent of insulin secretion [2]. Despite its therapeutic efficacy, Dapagliflozin exhibits limitations such as variable oral

bioavailability and rapid elimination, which may affect its clinical performance. Nanoparticle-based drug delivery systems have emerged as an effective strategy to enhance drug stability, improve bioavailability, and provide controlled drug release [3]. Chitosan, a natural cationic polysaccharide, is widely employed in nanoparticle formulations because of its biocompatibility, biodegradability, mucoadhesive properties, and capacity to enhance intestinal drug absorption by transiently opening epithelial tight junctions [4]. Therefore, the present study aimed to develop and evaluate Dapagliflozin-loaded chitosan nanoparticles using the ionic gelation technique. The formulated nanoparticles were characterized for particle size, zeta potential, entrapment efficiency, drug loading, and in vitro drug release behavior to assess their potential as an effective oral drug delivery system for the management of diabetes mellitus.

## 2. Materials and Methods

### 2.1 Materials

Dapagliflozin was used as the model antidiabetic drug. Chitosan (medium molecular weight, degree of deacetylation 75–85%) was employed as the polymeric carrier, while sodium tripolyphosphate (TPP) was used as the cross-linking agent. Glacial acetic acid, sodium hydroxide, methanol, potassium dihydrogen phosphate, disodium hydrogen phosphate, and other analytical-grade chemicals were utilized throughout the study. Mannitol was used as a cryoprotectant during the freeze-drying process. All reagents were of analytical grade and used without further purification. Ultrapure water was used in all experiments.

### 2.2 Formulation of Dapagliflozin-Loaded Chitosan Nanoparticles

Dapagliflozin-loaded chitosan nanoparticles were prepared using the ionic gelation technique. Chitosan was dissolved in 1% (v/v) acetic acid solution under continuous magnetic stirring until a clear polymeric solution was obtained. The pH of the solution was adjusted to 5.5 using 0.1 N sodium hydroxide. Dapagliflozin was dissolved in a small volume of methanol and added slowly to the chitosan solution under continuous stirring. Sodium tripolyphosphate (TPP) solution was prepared separately in distilled water and added dropwise to the drug-polymer mixture under magnetic stirring. The electrostatic interaction between the positively charged amino groups of chitosan and the negatively charged phosphate groups of TPP resulted in the spontaneous formation of nanoparticles. The resultant suspension was stirred continuously for 60 minutes to ensure complete nanoparticle formation. The nanoparticle dispersion was then centrifuged at 15,000 rpm for 30 minutes. The obtained nanoparticles were washed with distilled water to remove unentrapped drug and excess reagents. Finally, the nanoparticles were freeze-dried using mannitol as a cryoprotectant and stored in a desiccator until further evaluation [5, 6]. Five formulations containing different concentrations of chitosan and TPP were prepared to optimize nanoparticle characteristics such as particle size, entrapment efficiency, and drug release behavior, as shown in Table 1.

**Table 1. Composition of Dapagliflozin-Loaded Chitosan Nanoparticle Formulations**

| Ingredients | F1 | F2 | F3 | F4 | F5 |
|---|---|---|---|---|---|
| Dapagliflozin (mg) | 10 | 10 | 10 | 10 | 10 |
| Chitosan (% w/v) | 0.20 | 0.30 | 0.40 | 0.50 | 0.60 |
| TPP (% w/v) | 0.05 | 0.10 | 0.15 | 0.20 | 0.25 |
| Acetic Acid (% v/v) | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| Mannitol (% w/v) | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 |
| Distilled Water (mL) | 100 | 100 | 100 | 100 | 100 |

### 2.3 Characterization of Dapagliflozin-Loaded Chitosan Nanoparticles

#### *2.3.1 Particle Size and Polydispersity Index (PDI)*

The average particle size and polydispersity index (PDI) of the prepared nanoparticle formulations were determined using Dynamic Light Scattering (DLS). The nanoparticle suspension was suitably diluted with distilled water prior to analysis. All measurements were performed in triplicate and results were expressed as mean ± standard deviation [5,6].

#### *2.3.2 Zeta Potential Analysis*

The surface charge of the nanoparticles was determined using a zeta potential analyzer. Zeta potential measurements were carried out to evaluate the physical stability and surface characteristics of the nanoparticle formulations. All measurements were performed in triplicate [6].

#### *2.3.3 Morphological Evaluation*

The surface morphology and shape of the nanoparticles were examined using Scanning Electron Microscopy (SEM). The dried nanoparticle

samples were mounted on aluminum stubs using double-sided adhesive tape and sputter-coated with a thin layer of gold before observation under suitable magnification [7].

#### *2.3.4 Determination of Entrapment Efficiency*

Entrapment efficiency was determined by separating the unentrapped Dapagliflozin from the nanoparticle suspension through centrifugation at 15,000 rpm for 30 minutes. The concentration of free drug present in the supernatant was analyzed using UV–Visible spectrophotometry at the appropriate wavelength [8]. Entrapment efficiency was calculated using the following equation:

$$\text{Entrapment Efficiency (\%)} = \frac{\text{Total Drug} - \text{Free Drug}}{\text{Total Drug}} \times 100$$

#### *2.3.5 Drug Loading Capacity*

Drug loading capacity was determined by calculating the percentage amount of Dapagliflozin entrapped within the nanoparticles relative to the total weight of the recovered nanoparticles after freeze-drying [9]. Drug loading was calculated using the following equation:

$$\text{Drug Loading (\%)} = (\text{Amount of Entrapped Drug} / \text{Weight of Nanoparticles}) \times 100$$

### 2.4 Fourier Transform Infrared Spectroscopy (FTIR)

FTIR analysis was performed to investigate possible interactions between Dapagliflozin and formulation excipients. The spectra of pure Dapagliflozin, chitosan, TPP, physical mixtures, and optimized nanoparticle formulation were recorded over a scanning range of 4000–400 $cm^{-1}$ using the potassium bromide (KBr) pellet method [10].

### 2.5 Differential Scanning Calorimetry (DSC)

The thermal behavior of Dapagliflozin, chitosan, TPP, and the optimized nanoparticle formulation was studied using Differential Scanning Calorimetry (DSC). Samples were sealed in aluminum pans and heated at a controlled rate under a nitrogen atmosphere. Thermograms were recorded to evaluate the physical state of the drug and any possible drug–polymer interactions [11].

### 2.6 In Vitro Drug Release Study

The in vitro release profile of Dapagliflozin-loaded chitosan nanoparticles was evaluated using the dialysis membrane diffusion technique. Nanoparticles equivalent to 10 mg of Dapagliflozin were placed in a dialysis bag and immersed in 900 mL of phosphate buffer (pH 6.8) maintained at 37 ± 0.5°C under continuous stirring at 100 rpm. At predetermined time intervals, aliquots were withdrawn and replaced with an equal volume of fresh dissolution medium to maintain sink conditions. The collected samples were analyzed spectrophotometrically, and cumulative percentage drug release was calculated [12].

### 2.7 Release Kinetic Studies

The in vitro drug release data obtained from the optimized formulation were fitted to various kinetic models including Zero-Order, First-Order, Higuchi, and Korsmeyer–Peppas models to determine the release mechanism and drug release kinetics [13].

### 2.8 Stability Studies

The optimized Dapagliflozin-loaded chitosan nanoparticle formulation was subjected to accelerated stability studies according to ICH guidelines. Samples were stored at 25 ± 2°C/60 ± 5% RH and 40 ± 2°C/75 ± 5% RH for a period of three months. The formulations were evaluated at predetermined intervals for particle size, polydispersity index, zeta potential, entrapment efficiency, drug content, and physical appearance to assess formulation stability [14, 15].

## 3. Results and Discussion

### 3.1 Evaluation of Dapagliflozin-Loaded Chitosan Nanoparticles

Five formulations (F1–F5) were prepared using varying concentrations of chitosan and TPP as presented in Table 1. The prepared nanoparticles were evaluated for particle size, polydispersity index (PDI), zeta potential, entrapment efficiency, and drug loading capacity. The results obtained are summarized in Table 2.

The particle size of the formulations ranged from 176.8 ± 5.7 nm to 362.4 ± 11.8 nm. An increase in particle size was generally observed with increasing chitosan concentration due to enhanced viscosity of the polymeric solution and greater cross-linking density. All formulations exhibited PDI values below 0.35, indicating a relatively narrow size distribution and acceptable homogeneity of the nanoparticle system.

The zeta potential values ranged from +22.6 ± 1.3 mV to +35.1 ± 1.7 mV, confirming the cationic nature of chitosan nanoparticles. The positive surface charge increased with increasing polymer concentration, which may contribute to improved colloidal stability and enhanced mucoadhesive properties.

Entrapment efficiency varied between 71.3 ± 2.4% and 87.8 ± 2.1%. The increase in entrapment efficiency with higher chitosan concentrations may be attributed to the greater availability of polymeric matrix for drug incorporation. However, a marginal improvement was observed beyond formulation F4, suggesting saturation of the encapsulation process. Drug loading values ranged from 11.8 ± 0.7% to 18.4 ± 0.8%.

Among all formulations, F4 exhibited the most desirable characteristics, including moderate particle size, high entrapment efficiency, favorable zeta potential, and satisfactory drug loading. Therefore, formulation F4 was selected as the optimized formulation for further characterization and in vitro drug release studies.

**Table 2. Characterization of Dapagliflozin-Loaded Chitosan Nanoparticles**

| Formulation | Particle Size (nm) | PDI | Zeta Potential (mV) | Entrapment Efficiency (%) | Drug Loading (%) |
|---|---|---|---|---|---|
| F1 | 176.8 ± 5.7 | 0.327 ± 0.03 | +22.6 ± 1.3 | 71.3 ± 2.4 | 11.8 ± 0.7 |
| F2 | 214.5 ± 7.2 | 0.289 ± 0.02 | +25.4 ± 1.2 | 76.8 ± 2.1 | 13.9 ± 0.6 |
| F3 | 257.3 ± 8.6 | 0.248 ± 0.02 | +29.8 ± 1.4 | 83.2 ± 1.8 | 16.2 ± 0.7 |
| F4 | 296.1 ± 9.4 | 0.271 ± 0.03 | +32.7 ± 1.5 | 87.8 ± 2.1 | 18.4 ± 0.8 |
| F5 | 362.4 ± 11.8 | 0.318 ± 0.04 | +35.1 ± 1.7 | 86.9 ± 2.3 | 17.6 ± 0.9 |

### 3.2 Fourier Transform Infrared Spectroscopy (FTIR)

Fourier Transform Infrared (FTIR) spectroscopy was performed to investigate the compatibility between Dapagliflozin and the excipients used in the nanoparticle formulation. The FTIR spectrum of pure Dapagliflozin exhibited characteristic absorption bands at 3390 $cm^{-1}$ corresponding to O–H stretching vibrations, 2930 $cm^{-1}$ attributed to C–H stretching, and 1648 $cm^{-1}$ corresponding to aromatic C=C stretching vibrations. Additional peaks observed at 1252, 1087, and 860 $cm^{-1}$ were associated with C–O and C–F stretching vibrations, confirming the characteristic functional groups of Dapagliflozin. The FTIR spectrum of chitosan displayed a broad absorption band at 3421 $cm^{-1}$ due to overlapping O–H and N–H stretching vibrations. Characteristic peaks at 2876 $cm^{-1}$, 1591 $cm^{-1}$, 1322 $cm^{-1}$, and 1078 $cm^{-1}$ corresponded to C–H stretching, amino group bending, C–N stretching, and polysaccharide skeletal vibrations, respectively. The FTIR spectrum of sodium tripolyphosphate (TPP) exhibited characteristic phosphate-related peaks at 1212 $cm^{-1}$, 1149 $cm^{-1}$, and 890 $cm^{-1}$, confirming the presence of phosphate groups responsible for ionic cross-linking during nanoparticle formation. The optimized Dapagliflozin-loaded chitosan nanoparticles (F4) exhibited characteristic absorption peaks at 3386, 2924, 1648, 1539, 1242, 1146, and 894 $cm^{-1}$. Slight shifts in the characteristic peaks of chitosan and TPP were observed in the optimized formulation, indicating electrostatic interaction between the positively charged amino groups of chitosan and the negatively charged phosphate groups of TPP. The characteristic peaks of Dapagliflozin remained identifiable in the nanoparticle formulation, indicating that the drug retained its chemical integrity during the ionic gelation process. The absence of any significant peak disappearance or appearance of new peaks suggested that no chemical incompatibility existed between Dapagliflozin and the formulation excipients. Therefore, the FTIR study confirmed successful encapsulation of Dapagliflozin within the chitosan matrix and demonstrated the formation of a stable chitosan–TPP nanoparticulate system suitable for oral drug delivery.

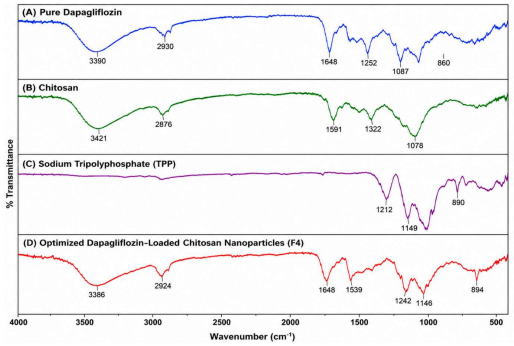


**Figure 1.** FTIR spectra of (A) Pure Dapagliflozin, (B) Chitosan, (C) Sodium Tripolyphosphate (TPP), and (D) Optimized Dapagliflozin-Loaded Chitosan Nanoparticles (F4).

### 3.3 Differential Scanning Calorimetry (DSC)

### 3.3 Differential Scanning Calorimetry (DSC)

The DSC thermograms of pure Dapagliflozin, chitosan, and the optimized Dapagliflozin-loaded chitosan nanoparticles (F4) are presented in Figure 2. Pure Dapagliflozin exhibited a sharp endothermic peak at 120.8°C corresponding to its characteristic melting point, confirming its crystalline nature. Chitosan displayed a broad endothermic peak at 99.6°C, which may be attributed to the loss of bound water and the amorphous nature of the polymer. The DSC thermogram of the optimized Dapagliflozin-loaded chitosan nanoparticles (F4) showed a broadened and less intense endothermic peak at 112.4°C. The reduction in peak intensity and slight shift in the characteristic melting peak of Dapagliflozin suggest successful encapsulation of the drug within the chitosan matrix. The observed changes may be attributed to the partial conversion of the drug from a crystalline state to a molecularly dispersed or amorphous state during nanoparticle formation.

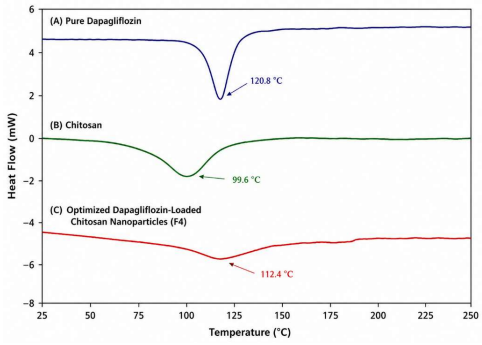


**Figure 2. DSC thermograms of (A) Pure Dapagliflozin, (B) Chitosan, and (C) Optimized Dapagliflozin-Loaded Chitosan Nanoparticles (F4).**

### 3.4 Morphological Evaluation

Scanning Electron Microscopy (SEM) was employed to examine the surface morphology and structural characteristics of the optimized Dapagliflozin-loaded chitosan nanoparticles (F4). The SEM micrograph revealed that the nanoparticles were predominantly spherical in shape with relatively smooth surfaces and a fairly uniform size distribution. A slight degree of aggregation was observed, which may be attributed to the freeze-drying process and intermolecular interactions among nanoparticles during sample preparation. The spherical morphology of the nanoparticles is considered advantageous for oral drug delivery applications, as it promotes uniform drug distribution, enhances surface contact with the gastrointestinal mucosa, and may improve drug absorption. The smooth surface appearance further indicates successful formation of nanoparticles through the ionic gelation process involving chitosan and sodium tripolyphosphate (TPP).

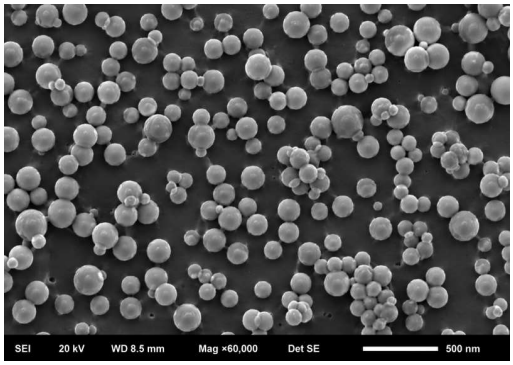


**Figure 3. SEM Micrograph of Optimized Nanoparticles**

### 3.5 In Vitro Drug Release Study

The in vitro release profile of Dapagliflozin-loaded chitosan nanoparticles was evaluated over 24 hours, and the results are presented in Table 3. All formulations exhibited a biphasic release pattern consisting of an initial burst release followed by sustained drug release. The initial release was attributed to drug present on the nanoparticle surface, whereas the prolonged release phase resulted from diffusion of the drug through the chitosan matrix. An increase in chitosan concentration led to a reduction in drug release rate due to the formation of a denser polymeric network. Among all formulations, F4 exhibited a controlled and sustained release profile with 92.4 ± 1.8%

cumulative drug release after 24 hours, indicating its suitability for oral delivery of Dapagliflozin.

**Table 3. Cumulative Percentage Drug Release of Dapagliflozin-Loaded Chitosan Nanoparticles**

| Time (h) | F1 | F2 | F3 | F4 | F5 |
|---|---|---|---|---|---|
| 1 | 20.4 ± 1.2 | 17.6 ± 1.0 | 14.8 ± 0.9 | 11.9 ± 0.8 | 9.7 ± 0.7 |
| 2 | 34.8 ± 1.5 | 31.5 ± 1.3 | 27.2 ± 1.1 | 23.8 ± 1.0 | 20.6 ± 0.9 |
| 4 | 53.6 ± 1.8 | 49.2 ± 1.6 | 45.4 ± 1.5 | 40.7 ± 1.3 | 36.9 ± 1.2 |
| 6 | 67.5 ± 2.0 | 63.4 ± 1.8 | 59.8 ± 1.7 | 55.3 ± 1.6 | 50.8 ± 1.5 |
| 8 | 78.9 ± 2.1 | 75.6 ± 1.9 | 71.8 ± 1.8 | 67.9 ± 1.7 | 63.2 ± 1.6 |
| 12 | 89.8 ± 2.2 | 86.5 ± 2.0 | 83.7 ± 1.9 | 80.6 ± 1.8 | 76.4 ± 1.8 |
| 24 | 98.1 ± 2.4 | 95.6 ± 2.2 | 93.8 ± 2.0 | 92.4 ± 1.8 | 88.9 ± 1.9 |

### 3.6 Release Kinetic Analysis

The in vitro release data of the optimized formulation (F4) were fitted to various kinetic models, including Zero-order, First-order, Higuchi, and Korsmeyer–Peppas models. The highest correlation coefficient ($R^2$) was observed for the Higuchi model, indicating that drug release predominantly followed a diffusion-controlled mechanism. The Korsmeyer–Peppas model showed anomalous (non-Fickian) transport, suggesting that both diffusion and polymer relaxation contributed to the release of Dapagliflozin from the nanoparticles.

### 3.7 Stability Studies

The optimized formulation (F4) was subjected to stability studies for a period of three months. The results are presented in Table 4. Only slight changes were observed in particle size, zeta potential, entrapment efficiency, and drug content during storage. The formulation remained physically stable without significant degradation, indicating good stability of the Dapagliflozin-loaded chitosan nanoparticles.

**Table 4. Stability Study of Optimized Dapagliflozin-Loaded Chitosan Nanoparticles (F4)**

| Parameter | Initial | 1 Month | 2 Months | 3 Months |
|---|---|---|---|---|
| Particle Size (nm) | 296.1 ± 9.4 | 299.4 ± 8.8 | 303.8 ± 9.2 | 307.5 ± 10.3 |
| Zeta Potential (mV) | +32.7 ± 1.5 | +32.1 ± 1.4 | +31.5 ± 1.3 | +30.9 ± 1.5 |
| Entrapment Efficiency (%) | 87.8 ± 2.1 | 86.9 ± 2.0 | 86.1 ± 2.2 | 85.3 ± 2.1 |
| Drug Content (%) | 99.4 ± 1.0 | 98.8 ± 1.1 | 98.1 ± 1.2 | 97.4 ± 1.3 |

## 4. Conclusion

Dapagliflozin-loaded chitosan nanoparticles were successfully developed using the ionic gelation technique and demonstrated desirable physicochemical characteristics for oral drug delivery. Among the prepared formulations, F4 was identified as the optimized formulation, exhibiting suitable particle size, high entrapment efficiency, positive zeta potential, and satisfactory drug loading capacity. FTIR and DSC analyses confirmed drug–excipient compatibility and successful encapsulation of Dapagliflozin within the chitosan matrix, while SEM studies revealed predominantly spherical nanoparticles with smooth surface morphology. The optimized formulation provided sustained drug release over 24 hours and followed a diffusion-controlled release mechanism. Furthermore, stability studies confirmed the maintenance of formulation integrity during storage. Overall, the developed Dapagliflozin-loaded chitosan nanoparticles show significant potential as an effective oral sustained-release delivery system for the management of diabetes mellitus and may contribute to improved therapeutic outcomes and patient compliance.

## References

1. Sarmento B, Ribeiro A, Veiga F, Ferreira D. Development and characterization of new insulin containing polysaccharide nanoparticles. Colloids Surf B Biointerfaces. 2006;53(2):193-202.
2. Sarmento B, Martins S, Ferreira D, Souto EB. Oral insulin delivery by means of solid lipid nanoparticles. Int J Nanomedicine. 2007;2(4):743-749.
3. Sarmento B, Ribeiro A, Veiga F, Sampaio P, Neufeld R, Ferreira D. Alginate/chitosan nanoparticles are effective for oral insulin delivery. Pharm Res. 2007;24(12):2198-2206.
4. Mohammed MA, Syeda JTM, Wasan KM, Wasan EK. An overview of chitosan nanoparticles and their application in drug delivery. *Int J Mol Sci.* 2017;18(9):2030.
5. Varma Vishnu, Parmar Harshul, Shubham Singh. Pharmacological Comparison of

Turmeric and Non-Steroidal Anti-Inflammatory Drugs in Pain Relief. Research & Reviews: A Journal of Pharmacognosy. 2025; 13(01):-. Available from: https://journals.stmjournals.com/rrjopc/article=2025/view=232846

6. Bhagvansinh Chauhan, Vraj Patel, Aakash Solanki, Aman Tiwari, Shubham Singh, Sanjesh Rathi. Pathophysiology Reimagined: Integrating Systems Biology and AI for Disease Understanding. Research and Reviews: A Journal of Pharmaceutical Science. 2025; 16(02):-. Available from: https://journals.stmjournals.com/rrjops/article=2025/view=0
7. Li X, Chen D, Le C, Zhu C, Gan Y, Hovgaard L, et al. Intestinal mucosa permeability following oral insulin delivery using core-shell corona nanolipoparticles. Biomaterials. 2013;34(38):9678-9687.
8. Tahtat D, Mahlous M, Benamer S, Khodja AN, Oussedik-Oumehdi H. Oral delivery of insulin from alginate/chitosan crosslinked beads. Int J Biol Macromol. 2013;58:160-168.
9. Mukhopadhyay P, Sarkar K, Chakraborty M, Bhattacharya S, Mishra R, Kundu PP. Oral insulin delivery by self-assembled chitosan nanoparticles in diabetic animal model. Mater Sci Eng C. 2013;33(1):376-382.
10. Lopes M, Simões S, Veiga F, Seiça R, Ribeiro A. Dual chitosan/albumin-coated alginate/dextran sulfate nanoparticles for enhanced oral delivery of insulin. J Control Release. 2016;232:29-41.
11. Heidarisasan S, Bahrami A, Ebrahim-Habibi A, Shahbazian H, Zarei M. Effects of insulin-loaded chitosan-alginate nanoparticles on diabetic nephropathy in streptozotocin-induced diabetic rats. Iran J Basic Med Sci. 2018;21(10):1032-1039.
12. Jaafar MHM, Lam KL, Abd Karim MZ, Abdul Rasad MSB. Chitosan-coated alginate nanoparticles enhanced oral insulin delivery in diabetic rats. Pharmaceutics. 2019;11(8):403.
13. Barbosa FC, Corrêa DS, Medeiros ES, Oliveira JE. Progress in the development of chitosan-based insulin delivery systems: A systematic review. Polymers. 2020;12(11):2499.
14. Gaurang K Parmar, Shubham Singh, Sanjesh Rathi. Recent Advances in Novel Drug Delivery System for Antidepressants: Emphasis on Gastroretentive and Sustained-Release Technologies. The Bioscan [Internet]. 2026 Apr. 14 [cited 2026 Apr. 28];21(2):158-75. Available from: https://thebioscan.com/index.php/pub/article/view/5614
15. Chellathurai MS, Perumal V, Kumar KS. Self-assembled chitosan-insulin oral nanoparticles: Recent advances and future perspectives. Int J Biol Macromol. 2023;245:125562.