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Design And Characterization of Chitosan Nanoparticles Containing Telmisartan for Controlled Drug Delivery System

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Abstract

This study aimed to formulate and evaluate Telmisartan-loaded chitosan nanoparticles using the ionic gelation technique to enhance drug solubility, bioavailability and achieve sustained drug release. Telmisartan-loaded chitosan nanoparticles were prepared by ionic gelation using chitosan as the polymer and sodium tripolyphosphate (STPP) as the cross-linking agent. Formulations were optimized by varying polymer concentration and sonication time. The prepared nanoparticles were characterized for particle size, zeta potential, morphology, drug entrapment efficiency and in vitro drug release. Drug–polymer compatibility was assessed using Fourier Transform Infrared (FTIR) spectroscopy. The optimized formulation exhibited a mean particle size of approximately 180 nm, a positive zeta potential indicating good colloidal stability and an entrapment efficiency exceeding 85%. The in-vitro drug release profile demonstrated a sustained, controlled release following zero-order kinetics with a non-Fickian diffusion mechanism. *In vitro* release studies demonstrated sustained drug release over 24 hours with improved dissolution compared to the marketed formulation.

Keywords

Telmisartan, Chitosan nanoparticles, Ionic gelation, Sustained drug release.

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INTRODUCTION:

Hypertension is one of the leading contributors to cardiovascular morbidity and mortality worldwide and remains a major public health challenge despite the availability of effective antihypertensive therapies. Persistent elevation of blood pressure significantly increases the risk of stroke, myocardial infarction, heart failure and chronic kidney disease. Although several classes of antihypertensive drugs are available, inadequate therapeutic response is often associated with poor medication adherence, low oral bioavailability and fluctuations in plasma drug concentrations. Therefore, the development of advanced drug delivery systems capable of improving therapeutic efficacy and patient compliance has become an important area of pharmaceutical research (1,2).

Telmisartan is a widely prescribed angiotensin II receptor blocker (ARB) used for the management of hypertension and cardiovascular disorders. It selectively blocks the angiotensin II type-1 receptor, resulting in vasodilation, reduced aldosterone secretion and improved cardiovascular protection. However, telmisartan belongs to the Biopharmaceutics Classification System (BCS) Class II, characterized by poor aqueous solubility and high membrane permeability. Its limited solubility leads to slow dissolution in gastrointestinal fluids, resulting in variable absorption and an oral bioavailability of approximately 40–60%. These limitations reduce its

therapeutic efficiency and necessitate the exploration of novel drug delivery strategies (3,4).

Nanotechnology-based drug delivery systems have emerged as promising approaches for enhancing the solubility, stability, bioavailability and controlled release of poorly water-soluble drugs. Polymeric nanoparticles provide protection against drug degradation while enabling sustained drug release and improved tissue distribution. Among the various polymers investigated, chitosan has attracted considerable attention because of its excellent biocompatibility, biodegradability, nontoxicity and mucoadhesive properties. The cationic nature of chitosan facilitates interaction with negatively charged biological membranes, enhances epithelial permeability and promotes prolonged gastrointestinal residence time, thereby improving oral drug absorption (5).

Chitosan nanoparticles prepared by ionic gelation have demonstrated significant potential as carriers for controlled drug delivery owing to their simple preparation, mild processing conditions and ability to encapsulate both hydrophilic and hydrophobic drugs. The physicochemical characteristics of these nanoparticles, including particle size, zeta potential, encapsulation efficiency and drug release profile, play crucial roles in determining their therapeutic performance. Consequently, the design and characterization of chitosan nanoparticles containing telmisartan may provide an effective platform for sustained drug release, improved bioavailability and enhanced antihypertensive efficacy while minimizing dosing frequency and adverse effects.

Therefore, the present study focuses on the formulation and evaluation of Telmisartan-loaded chitosan nanoparticles using the ionic gelation method to enhance solubility, bioavailability and provide controlled drug release.

MATERIALS AND METHODS:

Materials:

Telmisartan was procured from Medopharm, Kolar, India. Chitosan (85% degree of deacetylation, molecular weight 50 kDa, viscosity 50 centipoise) was obtained from the Central Institute of Fisheries Technology, Cochin,India. Glacial acetic acid and sodium tripolyphosphate (STPP) were purchased from S.D. Fine Chem. Ltd., Mumbai, India. HPLC-grade water was supplied by Merck Pvt. Ltd., Mumbai, India. All chemicals and reagents used in the study were of analytical reagent (AR) grade and were used without further purification.

METHODS:

Compatibility Studies:

Preformulation studies were performed to evaluate the physicochemical compatibility between Telmisartan and the selected excipients before the development of the nanoparticle formulation. These studies are important to identify any possible interactions that may influence the stability, efficacy, or performance of the final dosage form. Drug–polymer compatibility was investigated using Fourier Transform Infrared (FTIR) spectroscopy.

Fourier Transform Infrared (FTIR) Spectroscopy:

The compatibility of Telmisartan with chitosan was assessed using a Shimadzu UV-Vis spectrophotometer. Approximately 1 mg of the sample was thoroughly blended with 200 mg of dry potassium bromide (KBr) and compressed into a transparent pellet under high pressure. The prepared pellets were scanned over a wavenumber range of 4000–450 cm^{-1} at a spectral resolution of 4 cm^{-1}. The characteristic absorption peaks of the pure drug, polymer and formulated nanoparticles were compared to identify any significant changes, disappearance, or shifting of peaks that could indicate drug–excipient interactions.

Estimation of Telmisartan:

The quantitative estimation of Telmisartan was carried out using a UV–Visible spectrophotometric method. The absorbance of the drug was measured at its maximum absorption wavelength (λmax) of 296 nm. Beer–Lambert's law was found to be applicable over the concentration range of 2–18 µg/mL and a calibration curve was constructed for quantitative analysis.

Preparation of Telmisartan-Loaded Chitosan Nanoparticles:

Telmisartan-loaded chitosan nanoparticles were prepared by the ionic gelation method with slight modifications to the procedure reported by Calvo et al. (1997) (6). Chitosan was dissolved in 1% (v/v) acetic acid and 100 mg of Telmisartan was dispersed in the polymer solution containing 0.5% Tween 80. The mixture was stirred at 1000 rpm for 45 minutes at room temperature. A 0.25% (w/v) aqueous sodium tri poly phosphate solution was then added drop wise under continuous stirring to induce nanoparticle formation through ionic cross-linking. The resulting suspension was sonicated for 5 minutes to obtain a uniform dispersion. The nanoparticles were separated by refrigerated centrifugation at 12,000 × g for 30 minutes and the supernatant was collected for determination of drug entrapment efficiency. The nanoparticle pellet was freeze-dried using glucose and lactose (1:2) as cryoprotectants at −40°C under 0.4 mbar for 5 hours. The dried

nanoparticles were stored in a desiccator at 4°C until further evaluation. The composition of the formulations is presented in Table 1.

Table 1: Composition of Telmisartan Loaded Chitosan Nanoparticles

Formulation Code	Drug (mg)	Chitosan (mg)	STPP (%)	Tween 80 (%)	Sonication Time (min)
F1	100	100	0.25	0.5	5
F2	100	200	0.25	0.5	5
F3	100	300	0.25	0.5	5
F4	100	400	0.25	0.5	5
F5	100	500	0.25	0.5	5
F6	100	600	0.25	0.5	5

Evaluation of Telmisartan-Loaded Chitosan Nanoparticles:

Particle Size and Zeta Potential:

The particle size and zeta potential of the prepared nanoparticles were determined using a Zetasizer 3000HS (Malvern Instruments, UK). The samples were diluted (1:1000) with the aqueous phase before analysis. Measurements were performed at 25°C with a detection angle of 90°.

Surface Morphology:

The surface morphology of the nanoparticles was examined using a Carel Zeiss EVO 18 Scanning electron microscopy (Germany). The dried samples were mounted on aluminium stubs using double-sided adhesive tape, coated with platinum and examined under high vacuum to evaluate particle shape and surface characteristics.

Entrapment Efficiency and Drug Loading:

The nanoparticle suspension was centrifuged at 12,000 × g for 30 minutes to separate the nanoparticles from the entrapped drug. The concentration of free Telmisartan in the supernatant was determined spectrophotometrically at 296 nm. Entrapment efficiency (EE) and drug loading (DL) were calculated using the following equations:

Encapsulation efficiency=Total amount of Telmisartan – Free Telmisartan/ Weight of nanoparticles x 100

***In Vitro* Drug Release Study:**

The in vitro release of Telmisartan from the prepared chitosan nanoparticles was evaluated using the dialysis bag diffusion technique. The nanoparticle suspension was separated by ultracentrifugation and redispersed in phosphate buffer (pH 7.4). The dispersion was transferred into a dialysis membrane (molecular weight cut-off: 5 kDa), which served as the donor compartment and immersed in phosphate buffer maintained at 37 ± 0.5°C under continuous magnetic stirring. At predetermined intervals, 1 mL of the dissolution medium was withdrawn and replaced with an equal volume of fresh buffer to maintain sink conditions. The collected samples were analysed at 296 nm using a UV–Visible spectrophotometer and the cumulative percentage of drug released was calculated.

Drug Release Kinetics:

The release data obtained from the in vitro study were fitted to different mathematical models to determine the drug release mechanism. The kinetic models evaluated included zero-order, first-order, Higuchi and Korsmeyer–Peppas models. The cumulative percentage of drug released was plotted against time for the zero-order model, while the logarithm of the percentage of drug remaining was plotted against time for the first-order model. The Higuchi model was evaluated by plotting cumulative drug release against the square root of time, whereas the Korsmeyer–Peppas model was obtained by plotting the logarithm of cumulative drug release against the logarithm of time. The correlation coefficient (R^2) of each model was used to identify the best-fit release kinetics and to explain the mechanism governing drug release from the nanoparticles.

Comparative Study with the Marketed Formulation:

The in vitro drug release profile of the optimized Telmisartan-loaded chitosan nanoparticles formulation (F3) was compared with that of the marketed Telmisartan tablet (Cresar® 20 mg). The study was performed in phosphate buffer (pH 7.4) for 24 hours under identical experimental conditions. Since Telmisartan is conventionally administered as an oral tablet, the nanoparticles formulation were prepared to deliver an equivalent dose of 2 mg, with the objective of achieving sustained drug release suitable for once-daily administration.

Stability Studies:

Short-term stability studies were conducted on the optimized formulation (F3) following ICH guidelines. The formulation was divided into three sets and stored under different conditions, namely refrigerated temperature (4°C), room temperature

and 37°C. After 90 days of storage, the samples were evaluated by conducting an in vitro drug release study to assess the stability and release characteristics of the formulation.

RESULTS:

Compatibility Studies

Fourier Transform Infrared Spectroscopy (FTIR):

FTIR analysis was carried out to examine the compatibility between Telmisartan and chitosan in the developed nanoparticle formulation. The spectra of pure Telmisartan, chitosan and the optimized formulation F3 were compared to identify any changes in the characteristic functional group peaks. The major absorption peaks of Telmisartan were observed in the nanoparticle formulation without any noticeable shift or disappearance. No additional peaks were detected in the spectra of the formulated nanoparticles. These observations suggest that the formulation process did not alter the chemical structure of the drug and that Telmisartan remained compatible with chitosan. The FTIR spectra of pure Telmisartan, chitosan and the optimized formulations (Fig 1A, Fig 2A and Fig 3A) are shown in the respective figures.

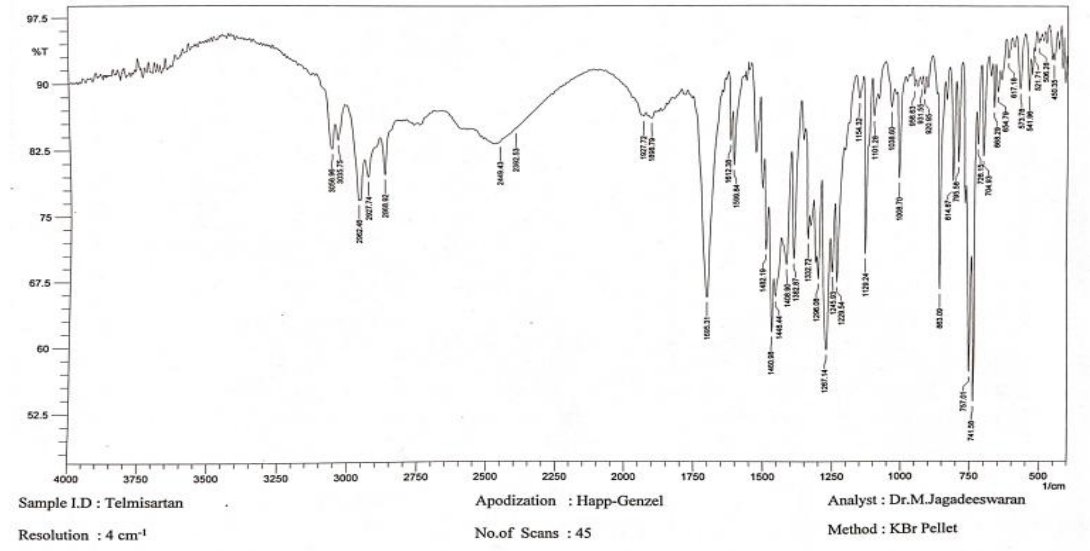


Figure 1A: FTIR of spectrum of pure Telmisartan

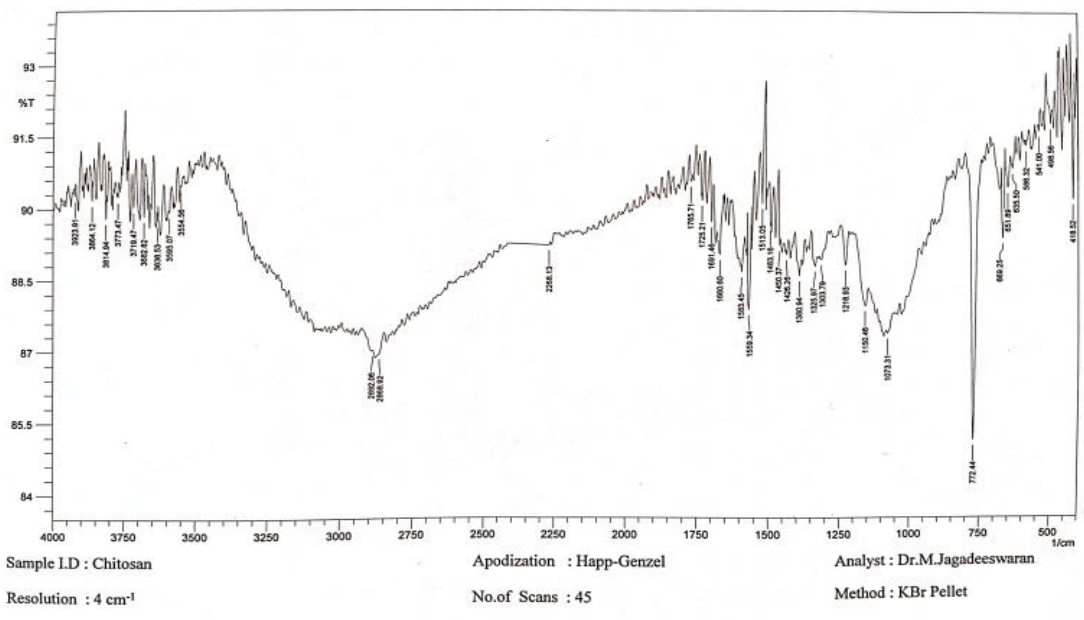


Figure 2A: FTIR of Spectrum of Chitosan

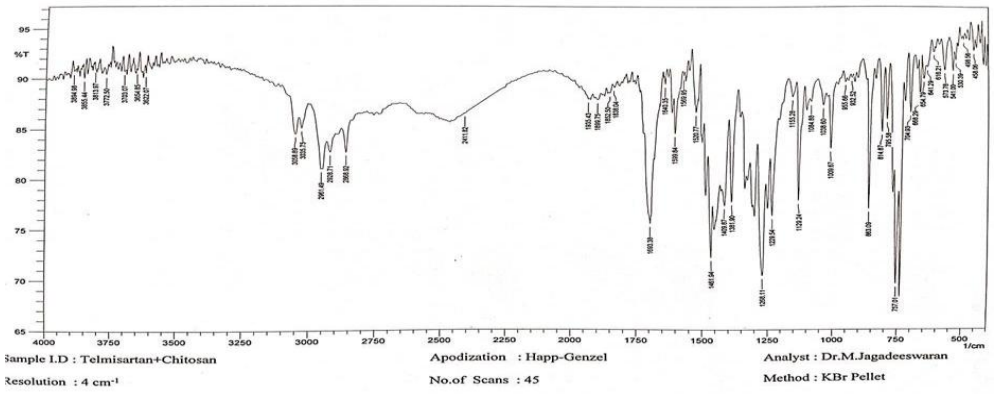


Figure 3A: FTIR of Spectrum of F3 formulation

Particle Size and Zeta Potential of Telmisartan-Loaded Chitosan Nanoparticles:

The particle size and zeta potential of the Telmisartan-loaded chitosan nanoparticle formulations (F1–F6) were determined using a Zetasizer 3000HS and the results are presented in Table 2. The particle size of the formulations ranged from 426.1 to 503.1 nm. Among the prepared formulations, F3 exhibited the smallest mean particle size 426.1 nm, whereas F2 showed the largest particle size (503.1 nm). Variations in particle size were observed with changes in the concentration of chitosan, indicating that the polymer content influenced nanoparticle formation. The particle size distribution and zeta potential of formulation F3 are presented in Figures 2A and 2B, respectively. The zeta potential values of all the telmisartan loaded chitosan nanoparticles displayed a positive surface charge ranging from +30.24 to +37.23 mV.

Table 2: Particle size and Zeta potential of Telmisartan nanoparticles

Formulation Code	Mean Particle Size (nm)	Zeta Potential (mV)
F-1	475.2	+37.23
F-2	503.1	+31.41
F-3	426.2	+33.57
F-4	432.8	+30.24
F-5	483.3	+31.91
F-6	498.2	+34.85

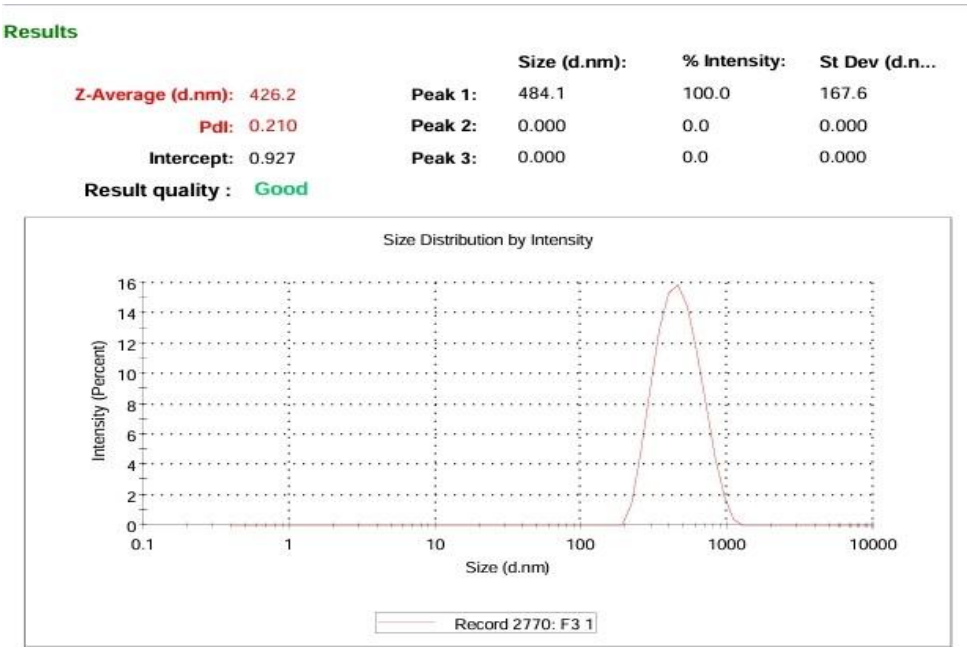


Figure 1B: Particle size of formulation F3 nanoparticles

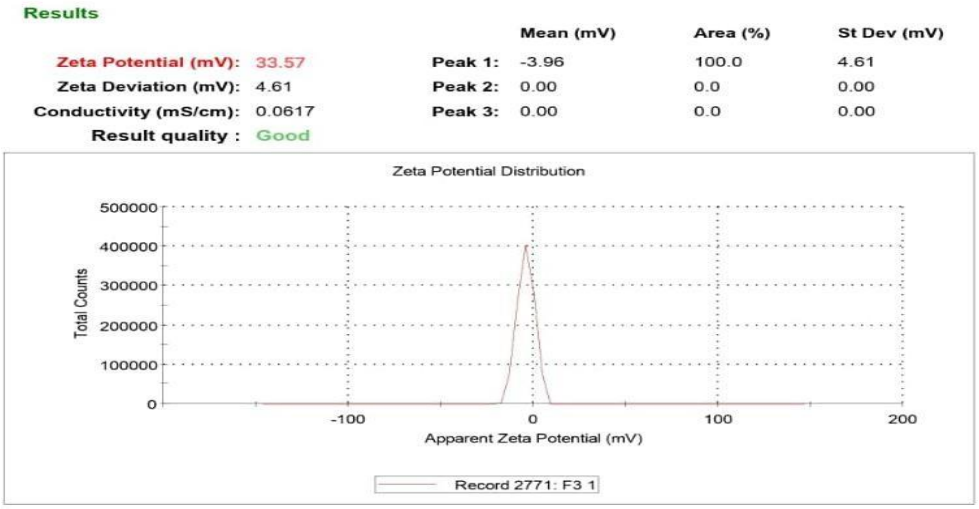


Figure 2B: Zeta potential of formulation F3 nanoparticles

Surface Morphology by Scanning Electron Microscopy:

The surface morphology of the Telmisartan-loaded chitosan nanoparticles was examined using scanning electron microscopy (SEM). The SEM images showed that all formulations (F1–F6) produced nanoparticles with a nearly spherical shape and smooth surface morphology. The particle size observed in the micrographs was within the nanometer range, which was consistent with the particle size analysis. Among the prepared formulations, F3 exhibited uniformly distributed spherical nanoparticles with minimal aggregation, indicating successful nanoparticle formation. The SEM image of the optimized formulation (F3) is presented in Fig 3.

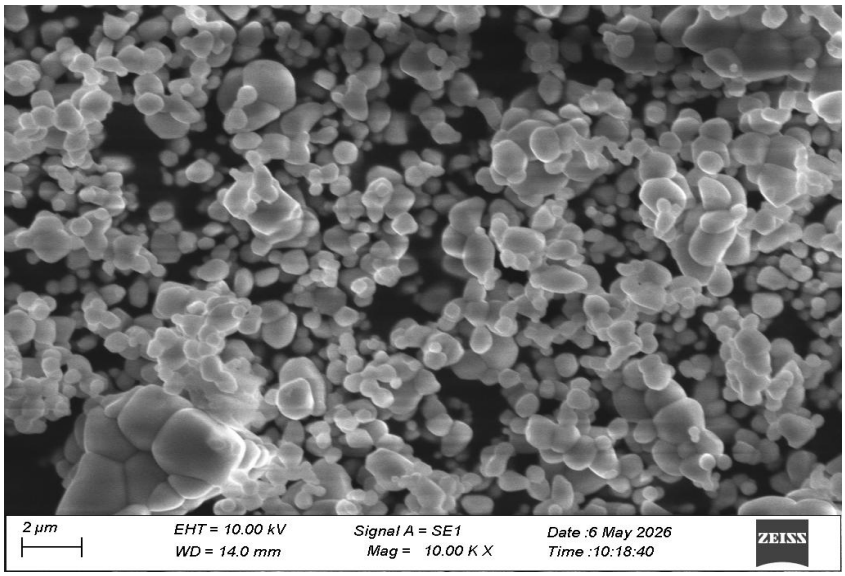


Figure 3: SEM Photograph of formulation F-3

Telmisartan Encapsulation Efficiency and Drug Loading:

The encapsulation efficiency and drug loading of the Telmisartan-loaded chitosan nanoparticle formulations (F1–F6) are shown in Table 3. The encapsulation efficiency of the formulations ranged from 75.72% to 90.81%. An increase in chitosan concentration resulted in improved drug encapsulation, with formulation F6 exhibiting the highest encapsulation efficiency (90.72%), while F1 showed the lowest value (75.7%). In contrast, drug loading decreased with increasing polymer concentration and varied between 40.58% and 25.22%. The highest drug loading was observed in F1, whereas the lowest was recorded for F6. These findings indicate that polymer concentration plays a significant role in determining both the

encapsulation efficiency and drug loading of the prepared nanoparticles.

Table 3: Encapsulation efficiency and Loading capacity of the nanoparticles

Formulation Code	Encapsulation Efficiency (%)	Drug Loading Capacity (%)
F-1	75.72	40.58
F-2	81.50	35.90
F-3	86.91	30.84
F-4	87.35	29.76
F-5	89.22	25.42
F-6	90.81	25.22

***In Vitro* Drug Release:**

The in vitro release profile of Telmisartan from the chitosan nanoparticle formulations (F1–F6) was evaluated over a period of 24 hours and the results are presented in Fig 4. The release pattern demonstrated that polymer concentration influenced the rate of drug release. Formulations containing higher concentrations of chitosan exhibited a slower release profile, which may be attributed to the formation of a denser polymeric matrix that restricted drug diffusion. During the first hour, the cumulative percentage of drug released from formulations F1, F2, F3, F4, F5 and F6 was 13.5%, 15.2%, 17.9%, 12.9%, 14.6% and 16.2%, respectively. After 24 hours, the cumulative drug release was 72.30% (F1), 78.42% (F2), 93.56% (F3), 76.94% (F4), 71.72% (F5) and 82.85% (F6). Among all the formulations, F3 showed the highest cumulative drug release (93.56%) and exhibited a sustained release profile throughout the study period. Based on these findings, formulation F3 was considered the optimized formulation for further evaluation.

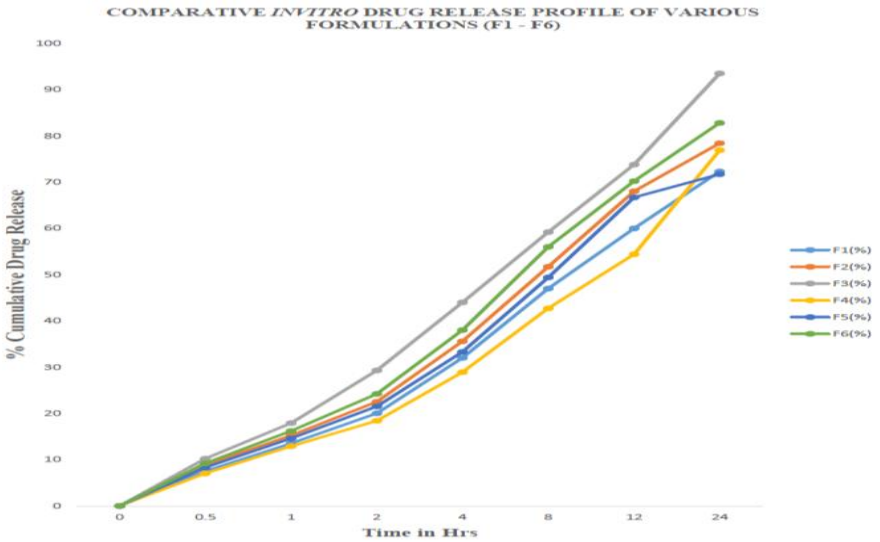


Figure 4: Comparative *in vitro* drug release profile of various formulations (F1 - F6)

Comparative in Vitro Drug Release Study of the Optimized Nanoparticles and the Marketed Formulation:

The in vitro drug release profile of the optimized Telmisartan-loaded chitosan nanoparticle formulation (F3) was compared with that of the marketed Telmisartan tablet (Cresar® 20 mg) in phosphate buffer (pH 7.4) for 24 hours. The nanoparticle formulation was designed to provide a sustained release of an equivalent dose of 2 mg of Telmisartan for once-daily administration. The optimized formulation (F3) exhibited an initial release of the drug followed by a gradual and sustained release throughout the study period. At the end of 24 hours, the cumulative drug release from formulation F3 was 93.56%, whereas the marketed formulation released 52.11% of the drug under the same experimental conditions. The improved release profile of the nanoparticle formulation may be attributed to the enhanced dispersion of the drug within the chitosan matrix and its controlled diffusion from the polymeric network. The comparative in vitro release profiles of the optimized formulation and the marketed product are presented in Fig5.

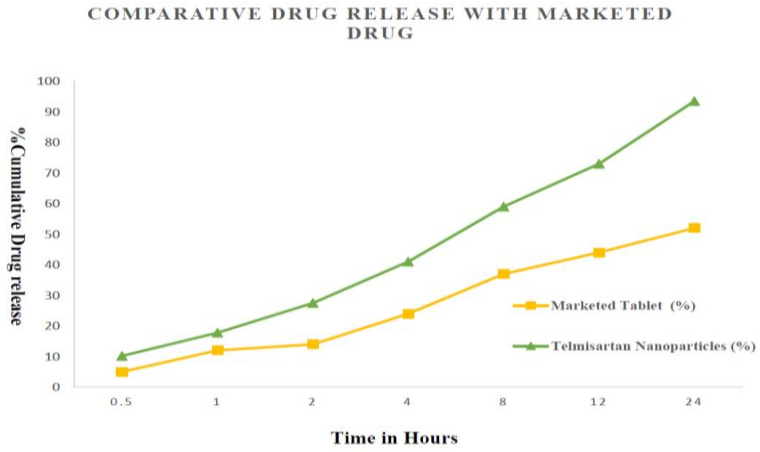


Figure 5: Comparative *in-vitro* drug release of F-3 and marketed formulation

Drug Release Kinetics:

The in vitro drug release data of the optimized Telmisartan-loaded chitosan nanoparticles were fitted to various kinetic models, including zero-order, first-order, Higuchi and Korsmeyer–Peppas models, to determine the mechanism of drug release. The release rate constants and correlation coefficients (R^2) were calculated from the respective plots and the results are presented in Table 4. Among the models evaluated, the Higuchi model showed the highest correlation coefficient, indicating that drug release was predominantly governed by diffusion through the polymer matrix. The release data also exhibited a good fit to the zero-order model, suggesting a sustained and controlled release pattern. The release exponent (n) obtained from the Korsmeyer–Peppas model was between 0.5 and 1.0, indicating a non-Fickian (anomalous) diffusion mechanism. These findings suggest that the release of Telmisartan from the chitosan nanoparticles was controlled by a combination of diffusion and polymer matrix relaxation, resulting in sustained drug release over 24 hours.

Table 4: Kinetic analysis of Telmisartan released from different formulation

Formulation Code	Zero-Order (R^2)	First-Order (R^2)	Higuchi Model (R^2)	Korsmeyer–Peppas Model (R^2)	Release Exponent (n)
F-1	0.9653	0.9172	0.9941	0.9956	0.9981
F-2	0.9698	0.8956	0.9976	0.9980	0.7801
F-3	0.9701	0.8881	0.9867	0.9875	0.9864
F-4	0.9776	0.8265	0.9952	0.9867	0.9899
F-5	0.9980	0.9508	0.9978	0.9976	0.9734
F-6	0.9892	0.8672	0.9856	0.9954	0.7271

Stability Studies:

Based on the results of the in vitro drug release study, formulation F3 was selected for short-term stability evaluation. The optimized formulation was stored under different storage conditions for 90 days and its release profile was compared with the initial release data to assess formulation stability. After the storage period, formulation F3 exhibited cumulative drug releases of 92.23% at 4°C, 92.54% under ambient conditions and 93.05% at 37°C after 24 hours. These values were comparable to the initial drug release of 93.56%, indicating that no significant changes occurred during storage. The slight variation in drug release observed after storage may be due to minor changes in the polymer matrix over time. Overall, the optimized formulation remained stable under the tested storage conditions and retained its sustained-release characteristics throughout the study period.

DISCUSSION:

The present study successfully developed telmisartan-loaded chitosan nanoparticles using the ionic gelation technique, demonstrating favorable physicochemical properties, high encapsulation efficiency, sustained drug release and improved in vitro performance. These findings are in good agreement with several previously published studies. The FTIR analysis of the optimized formulation confirmed the absence of any significant chemical

interaction between telmisartan and chitosan, indicating excellent drug–polymer compatibility. Similar compatibility between chitosan and hydrophobic drugs has been reported by Calvo et al., who demonstrated that ionic gelation preserves the structural integrity of encapsulated drugs without affecting their functional groups. Likewise, Agnihotri et al. reported that chitosan is a chemically compatible polymer suitable for sustained drug delivery systems (7). Particle size analysis revealed that nanoparticle size varied with polymer concentration, with formulation F3 exhibiting the smallest particle size among all formulations. The increase in particle size with increasing chitosan concentration is consistent with observations reported by Fan et al., who demonstrated that higher polymer viscosity results in larger nanoparticles due to increased intermolecular interactions during ionic gelation (9). Gan et al. also reported that chitosan concentration is one of the primary determinants influencing nanoparticle diameter [9].The optimized nanoparticles exhibited positive zeta potential values ranging from +30.24 to +33.57 mV, indicating good colloidal stability.

Mohanraj and Chen further emphasized that nanoparticles possessing zeta potentials greater than ±30 mV generally exhibit satisfactory physical stability during storage (10). Scanning Electron Microscopy demonstrated that the nanoparticles possessed smooth, spherical morphology with a dense surface. Similar morphological characteristics have been reported by Grenha et al., who prepared chitosan nanoparticles exhibiting spherical geometry and smooth surfaces suitable for controlled drug delivery applications (11).

The spherical morphology contributes to uniform drug distribution and predictable release behavior. The encapsulation efficiency obtained in the present study (75.7–90.7%) increased with increasing polymer concentration. Comparable encapsulation efficiencies have been reported by Hu et al., who achieved drug entrapment efficiencies above 80% using chitosan nanoparticles prepared by ionic gelation (12). In vitro drug release studies demonstrated an initial burst release followed by sustained drug release over 24 hours, with formulation F3 showing the highest cumulative release (93.56%). Similar biphasic release behavior has been widely reported for chitosan nanoparticles. Calvo et al. attributed the initial burst effect to surface-associated drug molecules, whereas the sustained release phase resulted from gradual diffusion of drug entrapped within the polymeric matrix.

Release kinetic analysis indicated that the optimized formulation followed zero-order release with excellent correlation and exhibited Higuchi diffusion characteristics. The Korsmeyer–Peppas release exponent ($n > 0.5$) suggested a non-Fickian diffusion mechanism involving both diffusion and polymer relaxation. These findings closely resemble those reported by Ritger and Peppas, who described anomalous transport in polymeric matrices where drug release occurs through a combination of diffusion and matrix erosion (13) Higuchi also demonstrated that diffusion from polymer matrices generally follows square-root time-dependent kinetics under controlled conditions (14). The optimized formulation (F3) showed significantly higher cumulative drug release (93.56%) than the marketed telmisartan tablet (52.11%) over 24 hours. Similar improvements in dissolution and bioavailability of poorly water-soluble drugs using chitosan nanoparticles have been reported by Bernkop-Schnürch and Dünnhaupt, who highlighted the mucoadhesive nature of chitosan and its ability to enhance drug permeation across biological membranes (15). Sarmento et al. further demonstrated that chitosan nanoparticles improve oral delivery of poorly soluble drugs through enhanced intestinal residence time and permeability (16). Short-term stability studies conducted over 90 days showed no significant changes in the drug release profile of the optimized formulation, indicating satisfactory formulation stability.

CONCLUSION:

The developed telmisartan-loaded chitosan nanoparticles demonstrated efficient drug incorporation, indicating that the chitosan matrix is a suitable carrier for controlled drug delivery. Variations in polymer concentration influenced the physicochemical characteristics of the nanoparticles, including particle size, surface morphology, surface charge, drug encapsulation efficiency and drug-loading capacity. In vitro drug release studies revealed a sustained release pattern over the study period, with the optimized formulation best fitting the zero-order kinetic model, suggesting a nearly constant drug release rate. Analysis using the Korsmeyer–Peppas model indicated a non-Fickian diffusion mechanism, implying that drug release was governed by a combination of diffusion and polymer matrix relaxation.

ACKNOWLEDGMENTS

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CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

REFERENCES:

1. World Health Organization. Guideline for the pharmacological treatment of hypertension in adults. Geneva: World Health Organization; 2021.
2. International Society of Hypertension. 2020 International Society of Hypertension Global Hypertension Practice Guidelines. Hypertension. 2020;75(6):1334–57.
3. Britt H, Nabi S. Telmisartan: Pharmacology, pharmacokinetics and clinical efficacy. Clin Pharmacokinet. 2001;40(9):647–64.
4. Amidon GL, Lennernäs H, Shah VP, Crison JR. A theoretical basis for a biopharmaceutic drug classification: The correlation of in vitro drug product dissolution and in vivo bioavailability. Pharm Res. 1995;12(3):413–20.
5. Dash M, Chiellini F, Ottenbrite RM, Chiellini E. Chitosan—A versatile semi-synthetic polymer in biomedical applications. Prog Polym Sci. 2011;36(8):981–1014.
6. Calvo P, Remuñán-López C, Vila-Jato JL, Alonso MJ. Novel hydrophilic chitosan–polyethylene oxide nanoparticles as protein carriers. J Appl Polym Sci. 1997;63(1):125–32.
7. Agnihotri SA, Mallikarjuna NN, Aminabhavi TM. Recent advances on chitosan-based micro- and nanoparticles in drug delivery. J Control Release. 2004;100(1):5–28.
8. Fan W, Yan W, Xu Z, Ni H. Formation mechanism of monodisperse, low molecular weight chitosan nanoparticles by ionic gelation technique. Colloids Surf B Biointerfaces. 2012; 90:21–7.
9. Gan Q, Wang T. Chitosan nanoparticle as protein delivery carrier—Systematic examination of fabrication conditions. Colloids Surf B Biointerfaces. 2007;59(1):24–34.
10. Mohanraj VJ, Chen Y. Nanoparticles – A review. Trop J Pharm Res. 2006;5(1):561–73.
11. Grenha A, Seijo B, Remuñán-López C. Microencapsulated chitosan nanoparticles for lung protein delivery. Eur J Pharm Sci. 2005;25(4–5):427–37.
12. Hu B, Pan C, Sun Y, Hou Z, Ye H, Hu B, et al. Optimization of fabrication parameters to produce chitosan–tripolyphosphate nanoparticles for delivery of tea catechins. J Agric Food Chem. 2008;56(16):7451–8.
13. Ritger PL, Peppas NA. A simple equation for description of solute release II. Fickian and anomalous release from swellable devices. J Control Release. 1987;5(1):37–42.
14. Higuchi T. Mechanism of sustained-action medication. Theoretical analysis of rate of release of solid drugs dispersed in solid matrices. J Pharm Sci. 1963;52(12):1145–9.
15. Bernkop-Schnürch A, Dünnhaupt S. Chitosan-based drug delivery systems. Eur J Pharm Biopharm. 2012;81(3):463–9.
16. Sarmento B, Ferreira D, Veiga F, Ribeiro A. Characterization of insulin-loaded alginate nanoparticles produced by ionotropic pre-gelation through DSC and FTIR studies. Carbohydr Polym. 2006;66(1):1–7.