

Formulation and Evaluation of Telmisartan-Loaded Nanosponge-Based Drug Delivery System for Antihypertensive Therapy

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ABSTRACT :

Telmisartan is an angiotensin II receptor antagonist widely used in the treatment of hypertension. However, its poor aqueous solubility and limited bioavailability pose significant challenges to its therapeutic effectiveness. The present study was aimed at formulating and evaluating Telmisartan-loaded nanosponges to improve drug release and enhance formulation performance. Nanosponges were prepared using a suitable polymer and evaluated for various physicochemical parameters. Preformulation studies including organoleptic evaluation, melting point determination, solubility studies, UV spectrophotometric analysis, and Fourier Transform Infrared (FTIR) spectroscopy were performed to assess the characteristics and compatibility of the drug with excipients. The prepared nanosponges were characterized for particle size, zeta potential, entrapment efficiency, surface morphology, in vitro drug release, and stability studies. SEM analysis confirmed the formation of porous and nearly spherical nanosponges. The optimized formulation (F4) exhibited a particle size of 149 nm, zeta potential of -32.20 mV, and entrapment efficiency of 91.27%. In vitro drug release studies demonstrated a maximum cumulative drug release of 98.10% within 8 hours, indicating enhanced drug release behavior. Stability studies conducted for three months under various storage conditions revealed that the formulation remained stable with minimal changes in drug release characteristics. The results suggest that Telmisartan-loaded nanosponges are a promising drug delivery system capable of enhancing drug release, improving stability, and potentially increasing the bioavailability of Telmisartan. Further in vivo studies may be conducted to establish their therapeutic efficacy.

Keywords: *Telmisartan, Nanosponges, Drug Delivery System, Entrapment Efficiency, In Vitro Drug Release, Stability Studies.*

I. INTRODUCTION

Nanosponges are an advanced class of nanostructured drug delivery systems characterized by a porous, three-dimensional network capable of encapsulating a wide variety of drug molecules. These systems are generally formed by cross-linking polymers, resulting in nanosized cavities that can effectively entrap both hydrophilic and lipophilic drugs. Due to these unique structural features, nanosponges have emerged as promising carriers for enhancing the delivery of poorly water-soluble drugs. One of the major challenges in pharmaceutical formulation is the poor aqueous solubility and low bioavailability of many therapeutic agents. Nanosponges help to overcome these limitations by improving drug solubility, protecting the drug from chemical and enzymatic degradation, and providing controlled and sustained drug release. The porous structure of nanosponges allows them to adsorb drug molecules into their internal cavities, thereby enhancing dissolution rate and therapeutic efficacy. Nanosponges are commonly synthesized using polymers such as cyclodextrins, ethyl cellulose, and other biodegradable materials through cross-linking methods. Among these, cyclodextrin-based nanosponges are extensively studied due to their biocompatibility, non-toxicity, and ability to form inclusion complexes with hydrophobic drugs. These nanosponges can be incorporated into various dosage forms including oral, topical, and parenteral formulations. In addition to improving solubility, nanosponges offer several advantages such as targeted drug delivery, reduced side effects, enhanced stability, and prolonged drug release. Their nanoscale size and high surface area promote better interaction with biological membranes, leading to improved absorption and bioavailability.

II. EXPERIMENTAL WORK

Telmisartan was procured from Synpharma Research Labs, Hyd. Poloxamer, B-Cyclodextrin, Ethyl

cellulose, PVA and Methanol were obtained from Synpharma Research Labs, Hyderabad. Other chemicals and the reagents used were of analytical grade.

Drug excipient compatibility study:

The compatibility between Telmisartan and the selected excipients was evaluated using Fourier Transform Infrared (FT-IR) spectroscopy. The FT-IR spectra were recorded using a Shimadzu FT-IR spectrophotometer to identify any possible chemical interaction between the pure drug and the excipients in the solid state. Samples were prepared by the potassium bromide (KBr) pellet method. Approximately 1 mg of the sample was thoroughly mixed with 100 mg of dry, IR-grade potassium bromide (KBr) using a mortar and pestle. The homogeneous mixture was compressed into a transparent pellet using a hydraulic press. The prepared pellet was placed in the sample holder, and the spectrum was recorded over the wavenumber range of 4000–400 cm^{-1} . The obtained spectra of the pure drug, excipients, and their physical mixture were compared to assess the presence or absence of any significant interaction.

Preparation of Nanosponges:

Table: 1 Formulation table of Telmisartan loaded nanosponges

S.No.	Ingredients (mg)	F1	F2	F3	F4
1	Telmisartan	50	50	50	50
2	Ethyl Cellulose	0.1	0.15	0.2	0.25
3	β -cyclodextrin	0.1	0.15	0.2	0.25
4	Poloxamer	0.05	0.05	0.05	0.05
5	PVA(1% w/v) (mL)	100	100	100	100
6	Methanol (ml)	10	10	10	10
7	Water (ml)	Q.S	Q.S	Q.S	Q.S

Method of Preparation of Nanosponges by solvent Evaporation method:

Telmisartan-loaded nanosponges were prepared by the solvent evaporation method using β -cyclodextrin, ethyl cellulose, poloxamer, and polyvinyl alcohol as formulation components by solvent evaporation method. Disperse phase consisting of Telmisartan dissolved in 10 ml solvent (methanol) was slowly added to a definite amount of PVA in aqueous continuous phase, prepared by using magnetic stirrer. The reaction mixture was stirred at 1000 rpm on a magnetic stirrer for 2 hours and kept on hot plate upto complete removal of organic solvent from the formulation. The nanosponges formed were collected by filtration through whatman filter paper and dried.

Evaluation parameters of Nanosponges:

Particle Size Analysis

Particle size was determined using Dynamic Light Scattering (DLS). The nanosponge dispersion was diluted with distilled water and analyzed using a particle size analyzer at 25°C. Measurements were performed in triplicate and the mean particle size was recorded.

Scanning electron microscopy

The morphological characteristics of the prepared nanosponges were examined using Scanning Electron Microscopy (SEM). A small quantity of the dried nanosponge sample was mounted on an aluminum stub using double-sided adhesive carbon tape and coated with a thin layer of gold under vacuum using a sputter coater. The samples were then observed under the scanning electron microscope at different magnifications to evaluate their surface morphology, shape, and particle characteristics.

Zeta Potential

The zeta potential of the prepared nanosponge formulation was determined using a Zeta Potential Analyzer (e.g., Malvern Zetasizer Nano ZS) at room temperature. The nanosponge dispersion was diluted appropriately with distilled water or deionized water to avoid multiple scattering effects. The diluted sample was transferred into a disposable zeta cell, and the zeta potential was measured based on the electrophoretic mobility of the nanoparticles. The measurements were performed in triplicate, and the average value was recorded.

In-vitro Drug Release Studies

The in-vitro drug release study of Telmisartan-loaded nanosponges was carried out using a Franz diffusion cell apparatus. A pre-soaked dialysis membrane was mounted between the donor and receptor compartments of the diffusion cell. The receptor compartment was filled with phosphate buffer solution (pH 6.8), which served as the dissolution medium and was maintained at a temperature of $37 \pm 0.5^\circ\text{C}$ throughout the study. The medium was continuously stirred using a magnetic stirrer to maintain uniform distribution of the drug. An accurately weighed quantity of Telmisartan-loaded nanosponge formulation equivalent to the required dose of Telmisartan was placed in the donor compartment. At predetermined time intervals, aliquots of the receptor medium were withdrawn and replaced immediately with an equal volume of fresh phosphate buffer (pH 6.8) maintained at the same temperature to maintain sink conditions. The collected samples were suitably diluted and analyzed using a UV-Visible spectrophotometer at the predetermined λ_{max} of Telmisartan. The cumulative percentage drug release was calculated and plotted against time to evaluate the drug release pattern from the nanosponge formulations.

Stability studies:

The optimized nanosponge formulation of Telmisartan was subjected to accelerated stability studies to evaluate its physical and chemical stability. The prepared nanosponges were wrapped in aluminium foil and packed in airtight glass vials to protect them from light and environmental factors. The samples were stored in a stability chamber maintained at $25 \pm 2^\circ\text{C} / 60 \pm 5\% \text{ RH}$, $30 \pm 2^\circ\text{C} / 65\% \text{ RH}$ and $40 \pm 2^\circ\text{C} / 75 \pm 5\% \text{ RH}$ for a period of 3 months as per ICH guidelines. During the stability study, samples were withdrawn at predetermined time intervals (0, 1, 2, and 3 months) and evaluated for changes in physical appearance and in-vitro drug release.

III. RESULTS AND DISCUSSION

Drug-excipient compatibility studies (FT-IR)

The compatibility between the drug and other excipients was evaluated using FTIR peak matching method. There was no appearance or disappearance of peaks in the drug-polymer mixture, which confirmed the absence of any chemical interaction between the drug, polymer and selected excipients.

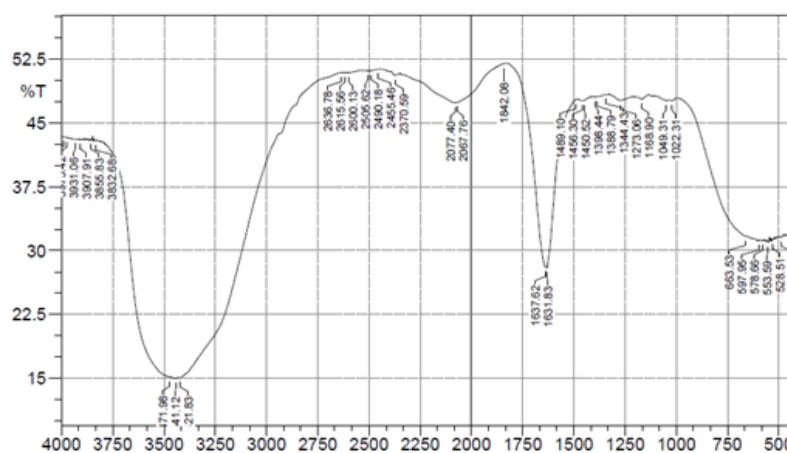


Fig-1: FTIR Studies of Telmisartan

Table-2: Characteristic Peaks for Telmisartan

S. No.	Characteristic Peaks	Frequency range (cm-1)	Frequency (cm-1)
1	OH stretching	4000-3500	3907.65
2	OH Bending	1500-1000	1481.39
3	C-H stretching	3000-2500	2633.85
4	C=O stretching	2000-1500	1635.73

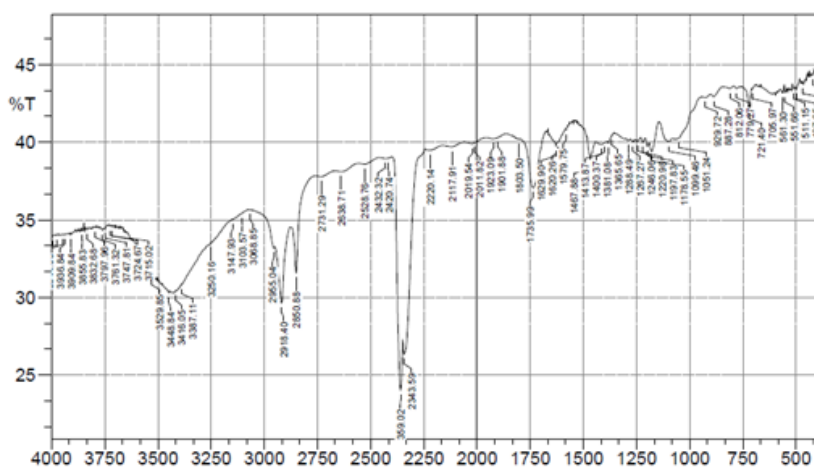


Fig-2: FTIR Studies of optimized formulation

Table-3: Characteristic Peaks for optimized formulation

S.No.	Characteristic Peaks	Frequency range (cm-1)	Frequency (cm-1)
1	OH stretching	4000-3500	3400.75
2	OH Bending	1500-1000	1204.65
3	C-H stretching	3000-2500	2839.31
4	C=O stretching	2000-1500	1599.93

Scanning Electron Microscopy:

The surface characteristic of prepared crystal was studied by SEM (ZEISS Electron Microscope, EVO MA 15). Powder samples were mounted onto aluminum stubs using double-sided adhesive tape and sputter-coated with a thin layer of gold under 10 Torr vacuum before examination. The specimens were scanned with an electron beam of acceleration potential of 20 kV and the images were collected as secondary electron mode.

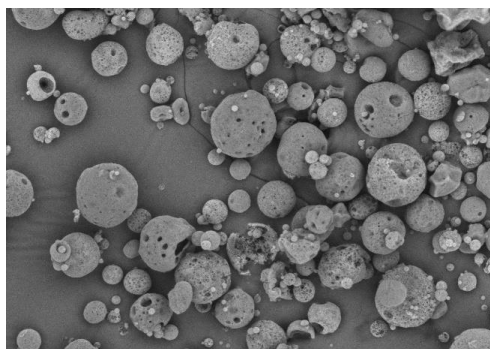


Fig-3: SEM Analysis of Nanosponges

SEM analysis revealed that the prepared Telmisartan nanosponges possessed a porous and sponge-like surface morphology with nearly spherical particles. The porous structure confirms the successful formation of nanosponges and supports efficient drug entrapment and controlled drug release.

Determination of Zeta potential:

Zeta potential is a measure of charge present on the vesicle surface. It was determined by using phase analysis light scattering with Malvern zetasizer at field strength of 20V/cm in distilled water and based on electrophoretic mobility of charged particles present in the nanocarrier system. Charged particles migrated towards electrodes of opposite charge when an electric field was applied.

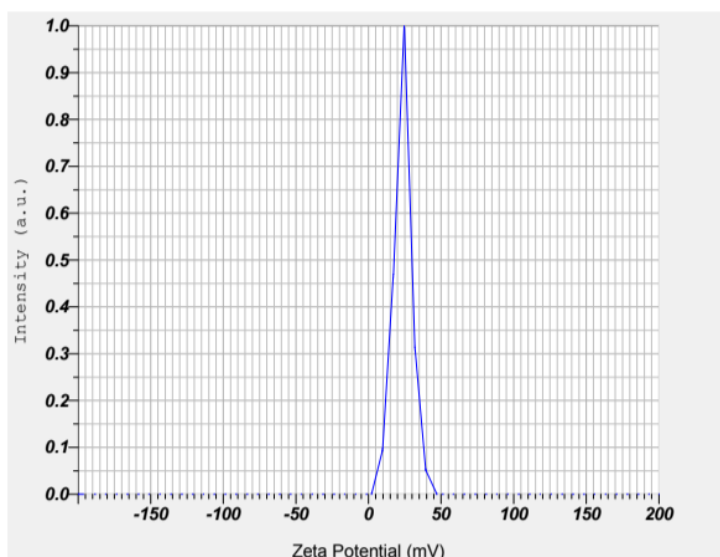


Fig-4: Zeta potential of Optimized formulation

The optimized formulation F4 exhibited a zeta potential of -32.20 mV, indicating good electrostatic stability. Values greater than ± 30 mV generally suggest sufficient repulsive forces between particles, thereby preventing aggregation and ensuring colloidal stability.

Particle size

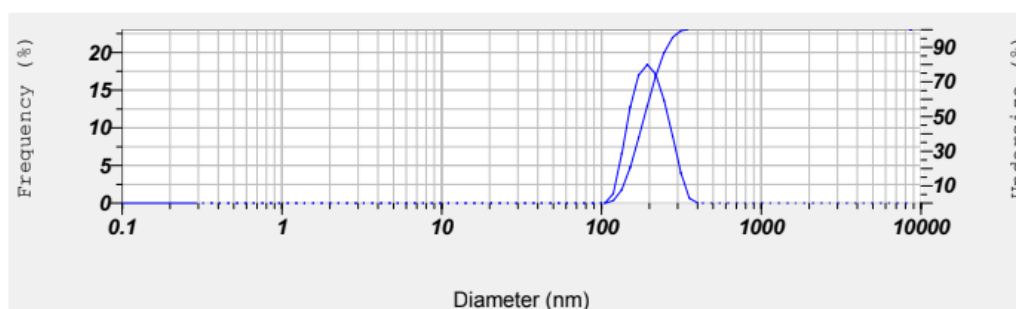


Fig-5: Particle size of optimized formulations

Particle size analysis revealed that the nanosponges were in the nanometer range. Formulation F4 exhibited the smallest particle size of 149 nm, which may contribute to enhanced drug dissolution and bioavailability.

Characterization of Nanosponges of Telmisartan

Table-4: Evaluation Studies of particle size Nanosponges

F. no	Particle size (nm)	Entrapment Efficiency (%)	Zeta Potential(mV)
F1	196	90.28	-33.72
F2	183	87.25	-30.10
F3	215	87.93	-34.52
F4	149	91.27	-32.20

Entrapment efficiency

The drug entrapment efficiency of all four formulations was evaluated. Among all formulations, F4 showed the highest entrapment efficiency of 91.27%, indicating effective incorporation of Telmisartan into the nanosponge matrix. The high entrapment efficiency may be attributed to the optimal polymer-to-drug ratio used during formulation.

In vitro drug release studies

Table-5: In vitro drug release studies of all formulations

Time (hr)	F1	F2	F3	F4
0	0	0	0	0
1	15.86	16.79	17.49	18.10
2	23.40	25.79	26.78	27.84
3	34.49	35.83	36.81	37.49
4	42.10	47.49	48.13	49.53
5	61.23	62.28	63.19	65.43
6	73.58	75.49	73.46	75.10
7	82.63	83.69	85.10	86.92
8	94.15	95.61	96.59	98.10

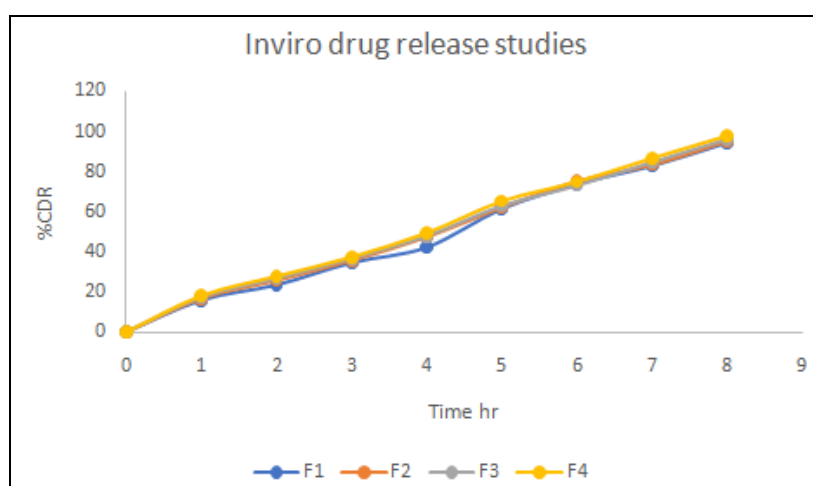


Fig-6: In vitro drug release studies of (F1-F4) formulations

The drug release studies of all formulations of Telmisartan Nanosponges were conducted by means of diffusion apparatus for a time period of 8 hrs. From the drug release studies as depicted in Figure, the results showed that Formulation F4 exhibited the highest cumulative drug release of 98.10% at the end of 8 hours, indicating its suitability as the optimized formulation.

Stability studies:

Accelerated stability studies were performed on the optimized formulation F4 according to ICH guidelines. The formulation showed only a slight decrease in cumulative drug release during the three-month study period under different storage conditions. However, the drug release remained above 94%, which is within acceptable limits, indicating good stability of the formulation.

Table-6: Stability studies of Optimized formulations F4

F.no	Parameters	Initial	1 st Month	2 nd Month	3 rd Month	Limits as per Specifications
F-4	25°C/60%RH % Release	98.10	96.89	95.58	94.65	Not less than 85 %
F-4	30°C/65% RH % Release	98.10	96.80	95.64	94.48	Not less than 85 %
F-4	40°C/75% RH % Release	98.10	96.75	95.54	94.35	Not less than 85 %

CONCLUSION

The present study was successfully carried out to formulate and evaluate Telmisartan-loaded nanosponges for improving drug release and enhancing formulation performance. The prepared nanosponges were evaluated for various physicochemical parameters including particle size, zeta potential, entrapment efficiency, in vitro drug

release, and stability studies. Preformulation studies confirmed the purity and suitability of Telmisartan for formulation development. FTIR studies demonstrated the compatibility of the drug with the selected excipients, indicating the absence of any significant chemical interaction. SEM analysis revealed the formation of porous and nearly spherical nanosponges, confirming successful nanosponge preparation. Among all the formulations, F4 was identified as the optimized formulation as it exhibited the smallest particle size (149 nm), highest entrapment efficiency (91.27%), satisfactory zeta potential (-32.20 mV), and maximum cumulative drug release (98.10% at 8 hours). The optimized formulation showed sustained and enhanced drug release behavior compared to the other formulations. Furthermore, stability studies performed under different storage conditions demonstrated that the optimized formulation remained stable over a period of three months, with no significant changes in drug release characteristics. The cumulative drug release remained above 94%, indicating good physical and chemical stability of the formulation. Therefore, it can be concluded that Telmisartan-loaded nanosponges represent a promising drug delivery system capable of improving drug release and stability. The developed nanosponge formulation may serve as an effective approach for enhancing the therapeutic performance of Telmisartan and could be explored further through in vivo studies and clinical investigations.

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