Ind. J. Pharm. Edu. Res., 2025; 59(2s):s454-s463.
https://www.ijper.org

Original Article

Formulation and Characterization of Chitosan Based Oral Nanoparticles of Poorly Water-Soluble Drug Lurasidone Hydrochloride

Purushottam Gangane[1,*], Pallavi Ingle[1], Vijaya Rabade[2], Harigopal Sawarkar[3]

[1]Department of Pharmaceutics, Dadasaheb Balpande College of Pharmacy, Besa, Nagpur, Maharashtra, INDIA.
[2]Department of Pharmacognosy, Dadasaheb Balpande College of Pharmacy, Besa, Nagpur, Maharashtra, INDIA.
[3]Department of Pharmaceutical Chemistry, Rajendra Gode College of Pharmacy, Amravati, Maharashtra, INDIA.

ABSTRACT

Aim: The purpose of research was to refine the solubility and dissolution assessment of lurasidone hydrochloride, a poorly water-soluble drug with a pH dependent solubility, by preparing chitosan-based nanoparticles using the ionic gelation process with sodium Tripolyphosphate (TPP) as a conjoin factor. **Background:** The poor water solubility and moderate oral bioavailability of anti-psychotic medications provide a significant challenge in their oral distribution. The hydrophobic medication lurasidone hydrochloride revealed a limited therapeutic effect when compared to traditional drug delivery systems. To enhance the restorative effectiveness while reducing the adverse effects of traditional treatment, it is also necessary to investigate and develop new drug delivery systems. **Materials and Methods:** A modified ionotropic gelation process was used to make lurasidone hydrochloride loaded chitosan nanoparticles. **Results:** The prepared Formulation (F1) had a particle size of 222.2 nm and 85.32% drug entrapment efficiency. The maximal drug loading was determined and it was 82% in formulation F1, while the cumulative drug release was found to be 84.37%. **Conclusion:** Due to the maximal solubility of lurasidone HCl at pH 7.4 phosphate buffer solution, it formed expanding cores and merged into nanoparticles. Based on the findings, it was determined that expanding chitosan nanoparticle is a viable method for enhancing the solubility and dissolution rate of Lurasidone HCl.

Keywords: Lurasidone HCl, Chitosan, Nanoparticles, Solubility.

Correspondence:
Dr. Purushottam Gangane
Associate Professor, Department of Pharmaceutics, Dadasaheb Balpande College of Pharmacy, Besa, Nagpur-440037, Maharashtra, INDIA.
Email: p.gangane@gmail.com

Received: 05-04-2023;
Revised: 17-07-2024;
Accepted: 17-12-2024.

INTRODUCTION

In comparison with alternate course of administration like intramuscular, intravenous and pulmonary routes, oral drug distribution is a popular, convenient and widely used since it gives benefits such as painless administration and better patient acceptance. Despite this, due to poor oral absorption and bioavailability, a number of drugs are useless and have been phased out of research and development.[1] By low aqueous solubility, less permeability and P-glycoprotein (P-gp) efflux oral absorption is restricted.[2,3] An orally administered drug, water solubility is a critical parameter to determine that how rapidly it will dissolve in the gastrointestinal tract. Hydrophobic drugs that are taken orally have poor absorption, dosage proportionality and excess of adverse effects.[4,5] The rate of dissolution in Gastrointestinal fluids (GI) and the permeability between biological membranes are the most important elements in limiting the bioavailability of orally ingested drugs.[6]

During the therapy of schizophrenia in 2010 US Food and Drug Administration permitted lurasidone hydrochloride.[7] Lurasidone hydrochloride is a non-inventive thiazole azapirone that is used to treat mental problems and acts as an absolute antagonist against the D2 and serotonin 5HT2A receptors.[8] The slow dissolving rate of lurasidone hydrochloride, a biopharmaceutical classification system class-II medication with pH dependent solubility, explains for its low oral bioavailability, which ranges from 9 to 19%.[9] In the biopharmaceutical classification system because of its high lipophilicity and low water solubility, it is classed as a class II medicine.

According to the literature review, many solubility enhancement tactics, such as solid dispersion, micronization, insinuate problems and others, appeared to be examined during the development of solubility and hence an increased oral bioavailability of Lurasidone HCl. Traditional dosage forms have shown an increase in therapeutic effectiveness, but only to a limited extent, due to limitations like over or under medicament, deficient

DOI: 10.5530/ijper.20253872

patient compliance, dosing recurrence, complicated procedure, high cost, poor stability, etc.[10] The nanotechnology-based drug delivery method, on the other hand, provides a practical means of enhancing the therapeutic effect of lipophilic drug. The use of Chitosan-based oral nanoparticles to boost the dissolving rates and oral bioavailability of less water-soluble drug is promising method.[11] Nanoparticles are extremely small particles with sizes ranging from 1 to 100 nm. Nanoparticles are large chunks with a diameter of up to 500 nm that have the advantages of increased medication loading, food import depletion, enhanced bioavailability and long-term stability.[12]

Chitosan was substantially considered as a biopolymer in the expansion of, medication delivery systems because of its biocompatibility, biodegradability and benign nature. Chitin, a protein found in crab shells, is deacetylated to form chitosan, a natural polymer.[13]

To make chitosan-based nanoparticles coacervation phase separation, nanoprecipitation, emulsion solvent evaporation, ionic gelation with cross-linking agents such as tripolyphosphate or glutaraldehyde and emulsion solvent evaporation are only a few of the processes used. One of the most extensively used procedures for nanoparticle manufacturing is ionic gelation, which requires mild conditions without using organic solvents or elevated temperatures. The ionic gelation approach uses TPP (a multivalent polyanion) since it is non-toxic, less costly and easier to handle. The cationic chitosan and anionic tripolyphosphate were used to make ionic contact at room temperature (hydroxyl and phosphoric ions). The intermolecular and intramolecular interactions formed by the negatively charged tripolyphosphate and the electrically charged amino group of chitosan complete the gelation process. TPP and chitosan have variable charge densities depending on the pH of the solution, which influences how these oppositely charged species interact.[14-16]

MATERIALS AND METHODS

Materials

Loba Chem, Mumbai, India, provided Chitosan (CS) as an offering sample. Emcure Ltd., Pune, provides lurasidone HCl as a gift sample. Sodium Tripolyphosphate (TPP) provided by Loba Chem, Pvt. Ltd., (Mumbai, India).

Preparation of chitosan based Lurasidone HCl nanoparticles

A modified ionotropic gelation process was used to make lurasidone hydrochloride loaded chitosan nanoparticles.[17] Chitosan solution of different concentrations like 0.05, 0.10, or 0.15% w/v was prepared in a 2% acetic acid solution. To the mentioned solution add 40 mg of lurasidone hydrochloride with the help of magnetic stirrer and add drop wise aqueous TPP solution (chitosan: TPP: 3:1) during 60 min with continuous stirring at 1000 rpm. The nanoparticles were segregated by centrifugation (Remi Cool Equipment) at 15,000 rpm for 40 min at 0°C, emerging in nanoparticles. To avoid particle agglomeration, the supernatant solution was collected for drug entrapment efficiency and the leftover suspension was lyophilized with mannitol as a cryoprotectant.

Nanoparticle Characterization and Evaluation

Particle Size, Zeta Potential and Polydispersity Index

Among energetic light scattering, the particle dimension dispensation of generated chitosan nanoparticles was examined using Photon Cross-Correlation Spectroscopy (PCCS). By clearing the particles with a laser light and monitoring the intensity variations in the dispersed using (Model: Malvern Instruments Ltd.,) with a sensitivity range of 1 nm to 10 μM, Brownian motion of molecules disseminates in liquid and is associated to particle size. A Dynamic Light Scattering (DLS), zeta potential, additionally a nanoparticle analyser (Model: Malvern Instruments Ltd.,) among a zeta potential assortment of 200 to +200 mV and the polydispersity index, were used to evaluate the Zeta Potential (ZP) of chitosan nanoparticles.

Drug content

Nanoparticles equivalent to 10 mg of lurasidone HCl were weighed; dissolving them in 10 mL of methanol and stirring the mixture were used to determine the amount of drug in each formulation. Using 0.45 μ membrane filter solution was filtered and properly diluted before the absorbance was measured spectrophotometrically at 231 nm using methanol as a blank. The drug content of nanoparticles was calculated.

Drug Entrapment Efficiency (DEE)

After centrifugation of Lurasidone hydrochloride nanoparticles at 15,000 rpm for 40 min, the supernatant was formed, filtered through 0.22 μM membrane filter and the amount of medication contained was measured utilizing a UV-visible spectrophotometer set to 231 nm. The quantity of medication in the supernatant was determined utilizing the formula y=0.0164x+0.0076 (R2=0.996), where x represents the concentration in micrograms per millilitre and y expresses the absorbance. By subtracting the total amount of medication given from the amount of medicine in the supernatant, DEE was computed.[17]

Drug loading

A weighted quantity of nanoparticles from one preparation batch were treated in methanol and left to extract Lurasidone HCl overnight before filtering via Whatmann filter paper. Dilute 1 mL in 10 mL methanol to make this solution.[18] UV spectrophotometer set to 231 nm was used to check for drug loading with methanol as a blank and calculate percent drug loading.

Fourier Transforms Infrared (FTIR) spectroscopy

The FTIR is carried out to check if the polymers chitosan and TPP could be utilised in conjunction with Lurasidone HCl. It also helps in determining the appropriateness of polymers for nanoparticle production. A Shimadzu FTIR spectrometer (IR Affinity 1Model, Japan) was used to analyse the FTIR spectra.[19] The sample of pure drug and physical combinations such as Lurasidone HCl with chitosan and TPP were separated using KBr and kept in desiccators after drying in a hot air oven for about 1 hr before scanning the spectra between 4000 and 500 cm^{-1}.

Differential Scanning Calorimetry Studies

Chitosan nanoparticles and medicament were studied using a differential scanning calorimeter that had already been calibrated. A nitrogen gas flow rate of 50 mL/min was applied to the specimen and it was hermetically sealed in an aluminium pan. The thermograms were acquired at a heating rate of 10°C/min with a scanning temperature extent of 50-250°C. Before each run, a baseline correction was performed. Chitosan, lurasidone hydrochloride and chitosan-based lurasidone hydrochloride nanoparticles were subjected to DSC thermograms.[19]

Saturation Solubility Studies

The saturated solubility of lurasidone HCl pure drug was performed in 0.1 N and 0.01 N HCl, acetate buffer solutions of pH 3 and 4 and Phosphate Buffer Solution (PBS) of pH 5, 6, 6.8, 7 and 7.4. The solutions were agitated using the mechanical shaker for 48 hr, at 200 rpm. The supernatant was filtered through a membrane filter (0.45 µ). 1 mL of this filtrate, after appropriate dilutions, was assayed using a UV-visible spectrophotometer at 231 nm wavelength.[13]

X-ray Diffraction

X-ray diffractometer was utilized to record the X-ray diffraction design of the pure drug, empty nanoparticles and drug-loaded chitosan-based nanoparticles. The samples were bombarded with monochromatized Cu-K radiation at temperatures ranging from 3 to 60°C and evaluated. 40 kV and 35 mA were employed as the voltage and current, respectively.[13]

Scanning Electron Microscopy

It was utilized to explore the morphological characters of nanoparticles. The nanoparticle powder was dusted to a thickness of 4 A° on double-sided tape on an aluminium remnant and gold cover in a SEM chamber among a cold sputter coater, followed by photomicrographs among a 20 kV electron beam. At magnifications of 500x and 7000x, the photomicrographs were examined.[13]

Transmission Electron Microscopy

The morphology of optimized nanoparticles was planned utilizing TEM. A 2% (w/v) phosphotungstic acid solution was used to stain the nanoparticle powder in a negative manner on a carbon-coated copper grid. Allow the grid to dry at room temperature. A TEM with an accelerating voltage of 80 kV was utilized to investigate the stained film, which was placed on a holder.

In vitro Dissolution Studies

The solubility of Lurasidone HCl pure drug and chitosan-based nanoparticles preparation *in vitro* was investigated using dissolving test sample on equipment, USP type II. In a 900 mL dissolution media rotated at 50 rpm and maintained at 37±0.5°C in a pH 7.4 phosphate buffer solution, the study was carried out using a muslin cloth with a formulation quantity corresponding to a single dosage of Lurasidone HCl. At time intervals of 15, 30, 45, 60, 75 and 90 min, aliquots of 5 mL dissolving media were withdrawn. An equivalent amount of the same medium was replaced in the meanwhile. Spectrophotometric examination of filtered dissolution samples was done at 231 nm using 0.22 µ filters.[2]

RESULTS AND DISCUSSION

Particle size, Zeta Potential and Polydispersity Index

Lurasidone HCl nanoparticles made from chitosan were measured between 222.2 nm and 348.5 nm. The particle size of chitosan-based Lurasidone HCl nanoparticles is intent by the concentration of chitosan in the combination. The polymer concentration decreases, the mean particle size of chitosan-based Lurasidone HCl nanoparticles decreases (F1). Because of the higher polymer content, the particle size was increased from F2 (231.1 nm) to F3 (231.1 nm) (348.5 nm). The best particle size for chitosan-based Lurasidone HCl nanoparticles was found to be 222.2 nm due to the less concentration of chitosan in the F1 formulation (Figure 1).

The Polydispersity Index (PDI) of F1 batch was found to be 1.0. The Particle size Distribution Index (PDI) is a measure of a particle size distribution's width, spread, or fluctuation. The PDI value of mono-dispersed samples is lower, whereas the PDI value of poly-dispersed samples is higher. The F1 preparation's zeta potential was found to be -13.3 mV as shown in Table 1. The zeta potential in the range of -13 to -18 mV indicates good stability of formulation (Figure 2).

Fourier-Transform Infrared Spectroscopy (FTIR)

In FTIR spectra, the absorption peak of Lurasidone HCl correlates to the frequency of vibrations between the bonds inside a molecule. The magnitude of the peak in each spectrum is directly related to the amount of material available within each specimen. The N-H extension may be assigned to the band at 3433.35 cm^{-1} in the FTIR spectra of lurasidone HCl (Figure 3).

		Size (d.nm):	% Intensity	Width (d.nm):
Z-Average (d.nm): 1569	Peak 1:	222.2	100.0	19.34
PdI: 1.000	Peak 2:	0.000	0.0	0.000
Intercept: 1.32	Peak 3:	0.000	0.0	0.000
Result quality : Refer to quality report				

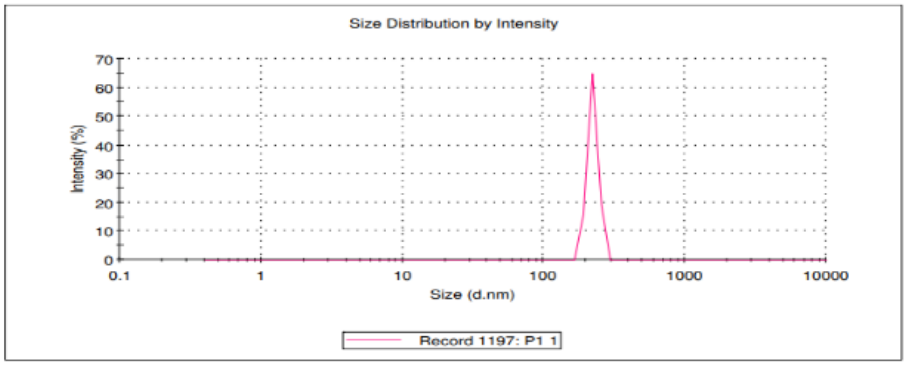

Figure 1: Particle Size Distribution of batch F1.

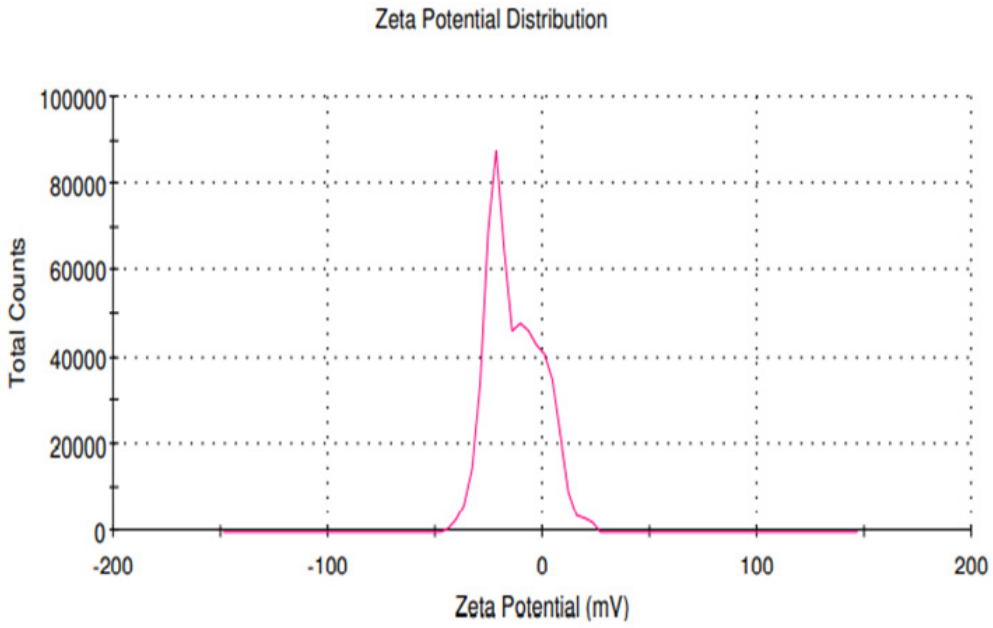

Figure 2: Zeta Potential of batch F1.

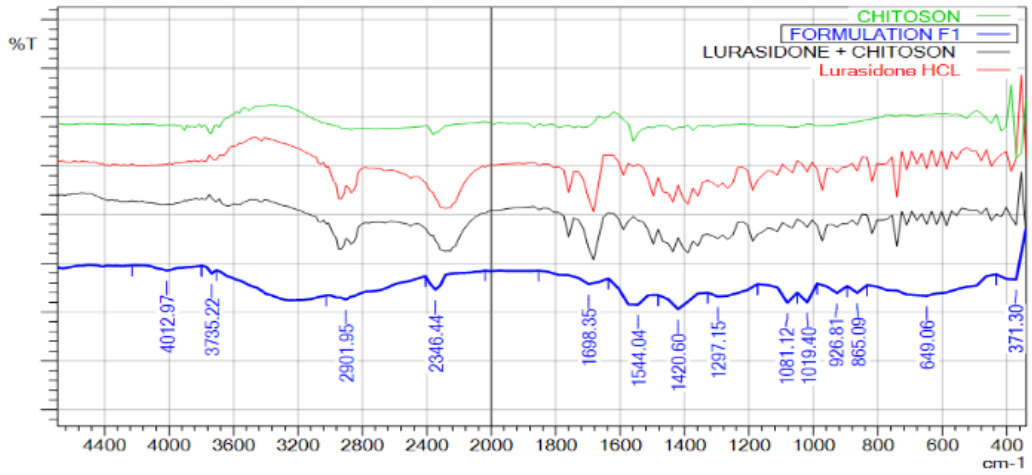

Figure 3: Overlay of FTIR.

C=O stretching resulted in intensities of 1688.71 cm^{-1}, while C=C stretching resulted in values of 2257.72 cm^{-1}. Another array was observed at 1269.80 cm^{-1}, which was linked to C-N stretching. The drug's FT-IR spectra were interpreted and it was discovered that all of the characteristic peaks pertaining to the functional group present in Lurasidone HCl's molecular structure were placed within the reference range, confirming its identity.

The positions of typical absorption bands and linkages between distinct functional groups in the medication did not differ considerably. This observation clearly reveals that when Lurasidone HCl is physically mixed, its properties do not alter much. The FTIR spectra revealed the interaction between the drug lurasidone HCl and polymer chitosan.

Differential Scanning Calorimetric analysis (DSC)

The DSC thermogram of Lurasidone HCl, Chitosan, TPP and formulation batch F1 are shown in Figure 4.

Differential scanning calorimetry was utilized to assess the thermal analysis of pure drug, chitosan, TPP and F1 formulations. Lurasidone HCl has an endothermic peak temperature of roughly 273.08°C (Figure 4a). Figure 4b shows that chitosan has a strong endothermic peak at 90.39°C that also happens to be its melting point. The DSC thermogram (Figure 4c) of TPP shows endothermic peaks at 134.70°C. The two endothermic peaks of drug-loaded chitosan nanoparticles at 49.16°C and 200.71°C respectively were seen (Figure 4d).

Determination of drug content

Lurasidone HCl nanoparticles made with chitosan had a drug content ranging from 29.80 to 35.06%. As the chitosan concentration grew, the medication content decreased. Due to the less concentration of chitosan in the F1 formulation, the highest drug content of chitosan-based Lurasidone HCL nanoparticles was determined to be 35.06% show in Table 2.

Determination of Drug loading

The drug loading of chitosan-based Lurasidone HCl nanoparticles showed a range between 75% and 80%. With a chitosan concentration of 0.05% in the F1 formulation, the maximal drug

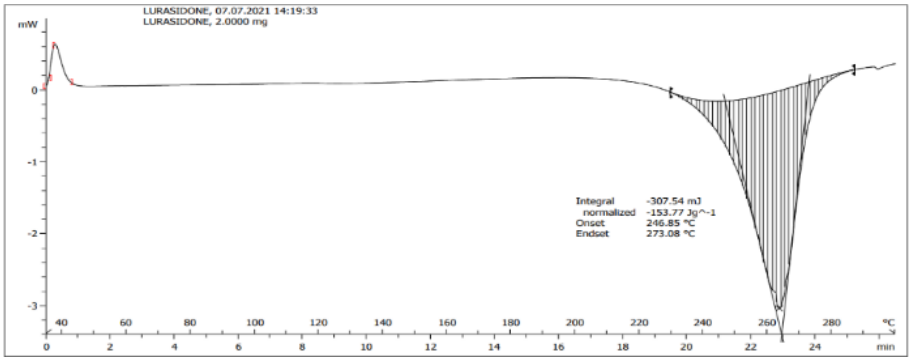

Figure 4a: DSC thermogram of Lurasidone HCl.

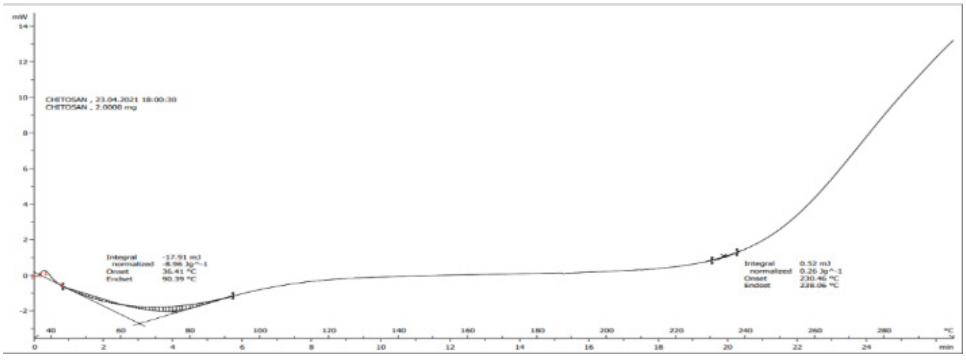

Figure 4b: DSC thermogram of Chitosan.

Table 1: Particle's size, Zeta potential, Polydispersity index.

Sl. No.	Formulation Code	Particle Size	Zeta Potential	Polydispersity Index
1	F1	222.2 nm	-13.3 mV	1.000
2	F2	231.1 nm	-12.4 mV	0.581
3	F3	348.5 nm	-18.8 mV	0.642

Table 2: Drug content, Drug loading and Entrapment efficiency.

Sl. No.	Formulation Code	Drug Content (%)	Drug Loading (%)	Entrapment Efficiency (%)
1	F1	36.06	82	82.32
2	F2	32.10	77	86.07
3	F3	29.80	75	87.90

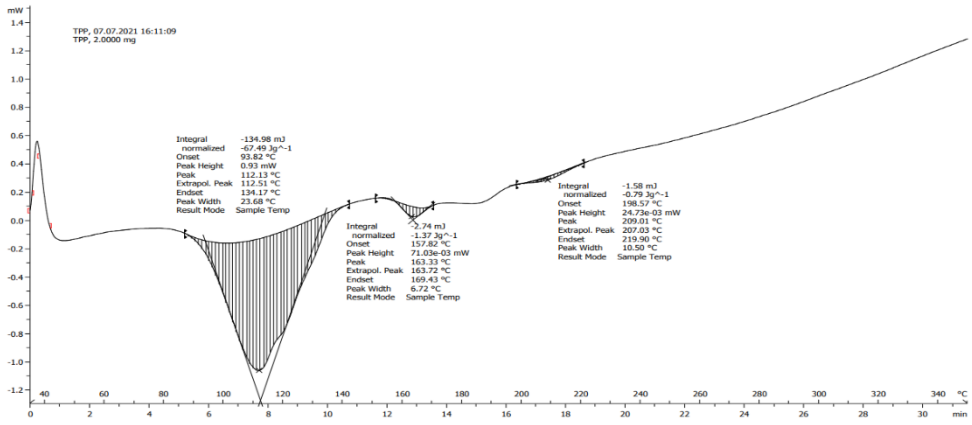

Figure 4c: DSC thermogram of TPP.

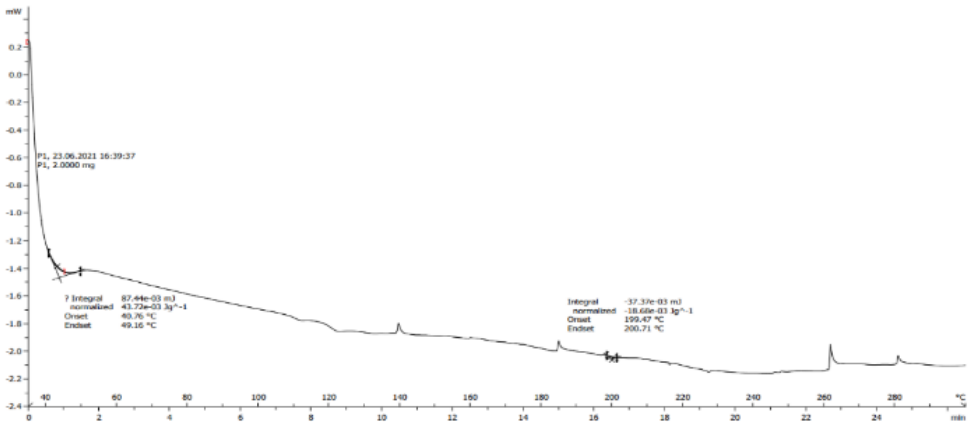

Figure 4d: DSC thermogram of F1 Formulation.

loading in chitosan-based Lurasidone HCl nanoparticles was determined to be 82% shown in Table 2.

Entrapment efficiency

The entrapment efficacy of chitosan-based Lurasidone HCl nanoparticles improved as the polymer content was increased to 0.05% chitosan. As a result, there was no discernible improvement in trapping efficiency. At the least elevated values, entrapment efficiencies were found to be 85.32% and 87.9%, sequentially shown in Table 2. Additionally, elevated entrapment effectiveness was not regarded as optimal. Using the medication content and polymer used, the best percentage efficiency was calculated. The optimum entrapment effectiveness of chitosan has been determined to be 85.32%. The Chitosan-based Lurasidone HCl nanoparticles F1 batch was chosen as the best experiment based on drug content and entrapment efficiency.

Saturation solubility study

In water and different pH buffers, the solubility of freeze-dried chitosan-based Lurasidone HCl nanoparticles was compared to the pure Lurasidone HCl (0.1 N HCl pH 1.2, Acetate buffer pH 4, Phosphate buffer pH 6.8 and 7.4). Lurasidone HCl displayed a pH-dependent solubility outline, among the highest solubility at phosphate buffer pH 7.4 because of the pH maximum impact of organic hydrochlorides. The solubility of chitosan-based lurasidone HCl nanoparticles in water and pH 1.2, 4.0, 6.8, 7.4 buffers was found to be 13.78%, 20.87%, 41.67%, 54.89% and 67.89%, respectively, which was higher than that of the pure

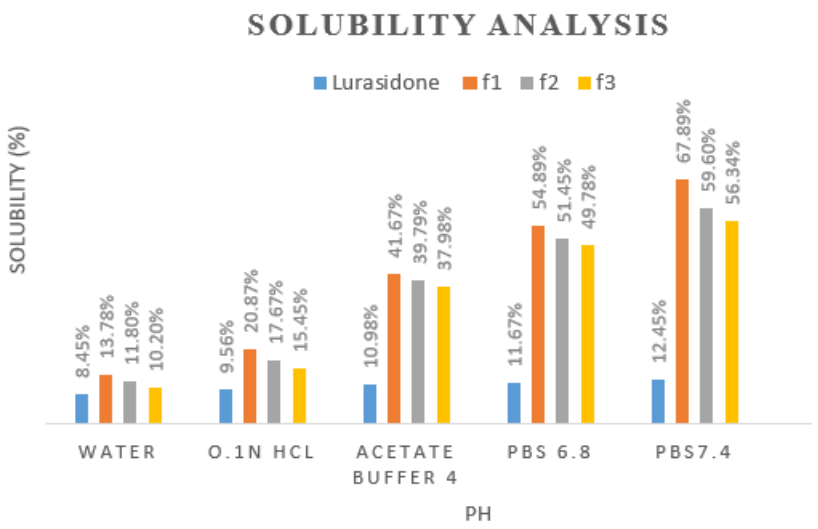

Figure 5: Solubility of Lurasidone HCl and lyophilized chitosan based lurasidone HCl nanoparticle in Water, HCl solution (pH 1.2), Acetate buffer (pH 4.0) and PBS (6.8 and 7.4).

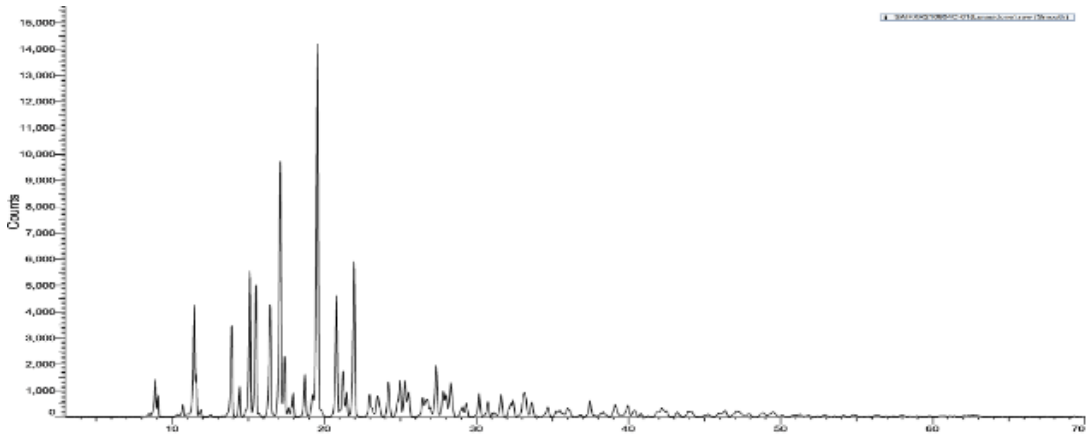

Figure 6a: XRD of pure drug Lurasidone HCl.

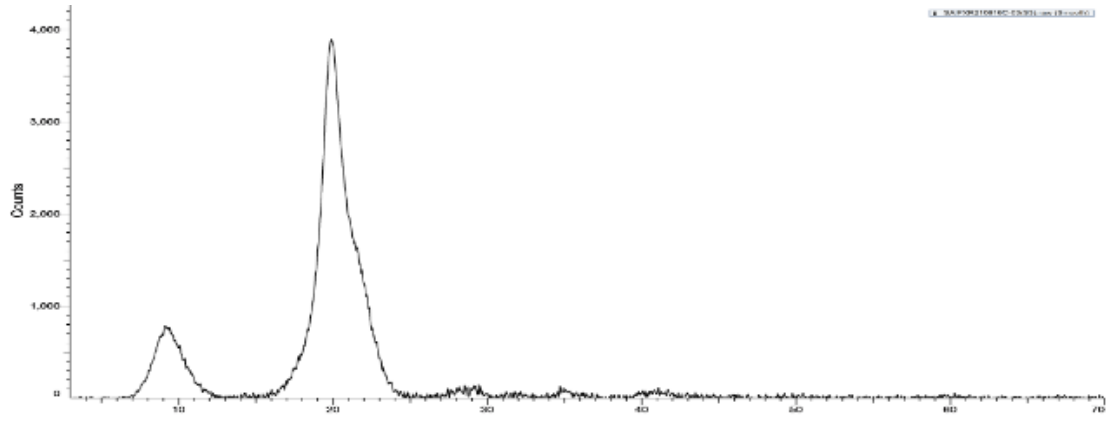

Figure 6b: XRD of chitosan.

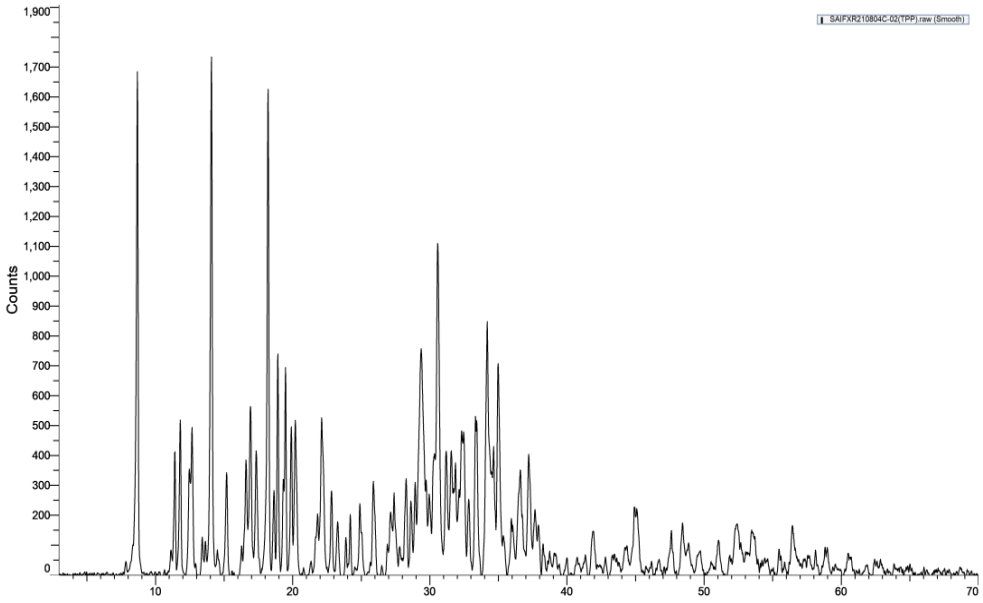

Figure 6c: XRD of TPP.

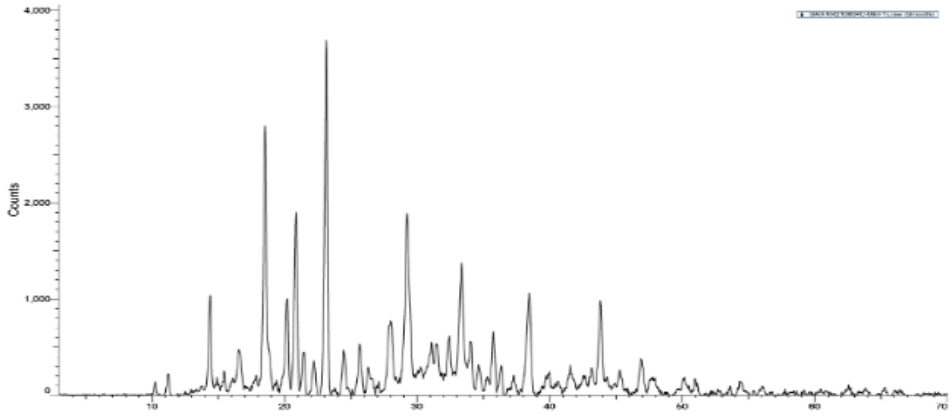

Figure 6d: XRD of drug loaded chitosan nanoparticles.

Lurasidone HCl. This was connected to a reduction in particle size on the nanoscale scale. The formulation F1 had an elevated solubility in phosphate buffer solution pH 7.4 than the other batches and the phosphate buffer solution pH 7.4 had a higher solubility than the other buffers shown in Figure 5.

X-ray Diffraction study (XRD)

An X-ray diffractometer was utilized to record the X-ray diffraction patterns of pure Lurasidone HCl, chitosan-based Lurasidone HCl loaded nanoparticles and both polymers, chitosan and TPP. On a scale of one to two, the drug's distinct sharp peaks were visible at diffraction angles of 10.897º, 11.452º and 17.714º shown in Figure 6a demonstrating the drug's regular crystalline shape. The large peak of 20.862º on the nanoparticles indicated that the polymer was amorphous (Figure 6b). It was presumed that the drug had dispersed molecularly throughout the polymer and become amorphous because there were no crystalline peaks in drug-loaded nanoparticles (Figure 6c and Figure 6d).

Scanning Electron Microscopy

SEM was utilized to explore the exterior of the F1 formulation. The F1 Formulation was scanned at 5,000x, 15,000x and 3000x, as illustrated in Figure 7.

SEM image shows elongated and irregular shape particles may be due to aggregation of particles and incomplete drying before evaluation. Particle size was found in the range of 0.84 µM to 1.11 µM.

Transmission Electron Microscopy

TEM was retained in studying the morphology of F1 after it was placed on a copper grid. The particle size was found around 50 nm.

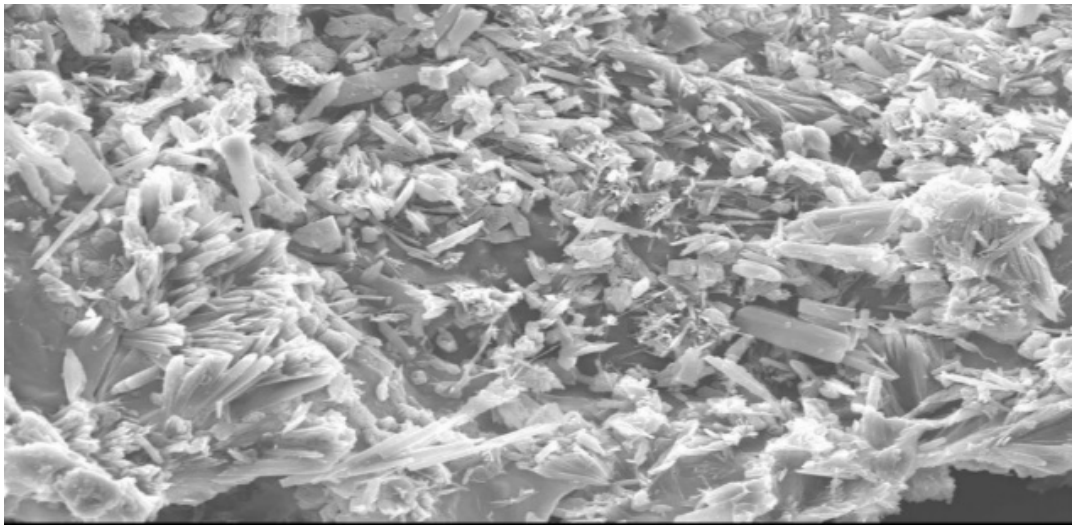

Figure 7: SEM image of the chitosan based Lurasidone HCl nanoparticles of batch F1.

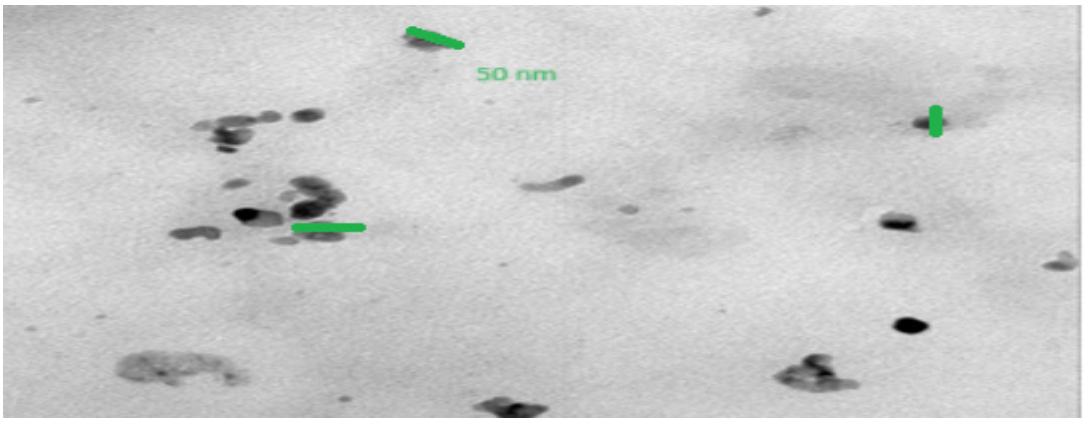

Figure 8: TEM image of the chitosan based Lurasidone HCl nanoparticles of batch F1.

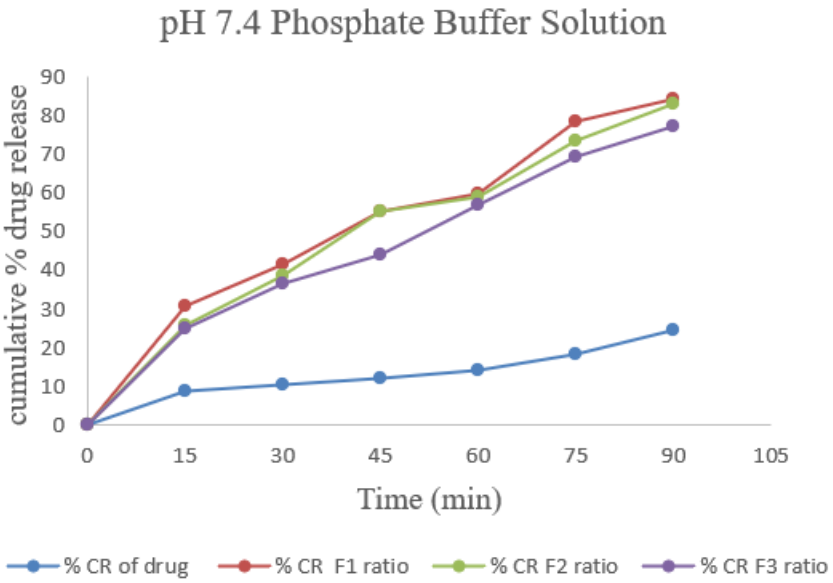

Figure 9: Comparative *In vitro* drug release study of pure Lurasidone HCl and formulation batches F1, F2 and F3.

As shown in Figure 8, TEM was utilized to determine the morphological features of chitosan-based nanoparticles. In the specified nanoparticles, spherical shapes with specific diameters were detected. Covalent crosslinking had no effect on the shape, or globular form, of the resultant chitosan-based lurasidone HCl nanoparticles.

In vitro dissolution study

During the dissolution study it was observed that the concentration of polymer had an impact on drug release. In all formulations, increased polymer concentration resulted in significant decrease in drug release. The drug was rapidly released due to the less polymer concentration (0.05% chitosan) in batch F1. During the initial 90 min of dissolution study, batch F1 released maximum drug. The percentage cumulative drug release of F1 in pH 7.4 phosphate buffer was measured to be 84.37%. According to the results of an *in vitro* drug release investigation, all batches of chitosan-based Lurasidone HCl nanoparticles have better drug release rates than pure drug (Figure 9).

CONCLUSION

Ionic gelation with sodium tripolyphosphate serves as a cross-linker Chitosan nanoparticles containing lurasidone HCl were produced. When constant dose forms are established, various obstacles arise due to the medication's restricted solubility. As a result, nanoparticulate drug delivery methods are gaining traction and these chitosan-based Lurasidone HCl nanoparticles demonstrate improved drug solubility and dissolution rates. The generated NPs had good zeta potential, particle size, drug loading and drug entrapment. In simulated intestinal fluid, the chitosan-based Lurasidone HCl nanoparticles dissolve faster than the Lurasidone HCl raw material (pH 7.4 phosphate buffer solution). Using chitosan nanoparticles to improve the solubility and dissolution rate of Lurasidone HCl could be a potential technique based on these findings.

ACKNOWLEDGEMENT

The authors are thankful to the Management and the Principal of Dadasaheb Balpande College of Pharmacy, Nagpur for providing the research facility.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

FTIR: Fourier Transform Infrared Spectroscopy; **DSC:** Differential Scanning Calorimetry; **SEM:** Scanning Electron Microscopy; **TEM:** Transmission Electron Microscopy; **XRD:** X-ray Diffraction; **CS:** Chitosan; **TPP:** Tripolyphosphate; **HCl:** Hydrochloride; **PBS:** Phosphate Buffer Solution.

REFERENCES

1. Agrawal U, Sharma R, Gupta M, Vyas SP. Is nanotechnology a boon for oral drug delivery? Drug Discover Today. 2014;19(10):1530-46. doi: 10.1016/j.drudis.2014.04.011, PMID 24786464.
2. Khadka P, Ro J, Kim H, Kim I, Kim JT, Kim H, *et al.* pharmaceutical particle technologies: an approach to improve drug solubility, dissolution and bioavailability. Asian J Pharm Sci. 2014;9(6):304-16. doi: 10.1016/j.ajps.2014.05.005.
3. Arzani G, Haeri A, Daeihamed M, Bakhtiari-Kaboutaraki H, Dadashzadeh S. Niosomal carriers enhance oral bioavailability of carvedilol: effects of bile salt-enriched vesicles and carrier surface charge. Int J Nanomedicine. 2015;10:4797-813. doi: 10.2147/IJN.S84703, PMID 26251598.
4. Wang XQ, Zhang Q. pH-sensitive polymeric nanoparticles to improve oral bioavailability of peptide/protein drugs and poorly water-soluble drugs. Eur J Pharm Biopharm. 2012;82(2):219-29. doi: 10.1016/j.ejpb.2012.07.014, PMID 22885229.
5. Li H, Zhao X, Ma Y, Zhai G, Li L, Lou H. Enhancement of gastrointestinal absorption of quercetin by solid lipid nanoparticles. J Control Release. 2009;133(3):238-44. doi: 10.1016/j.jconrel.2008.10.002, PMID 18951932.
6. Lipinski CA, Lombardo F, Dominy BW, Feeney PJ. Experimental and computational approaches to estimate solubility and permeability in drug discovery and development settings. Adv Drug Deliv Rev. 2001;46(1-3):3-26. doi: 10.1016/s0169-409x(00)00129-0, PMID 11259830.
7. Citrome L, Ketter TA, Cucchiaro J, Loebel A. Clinical assessment of lurasidone benefit and risk in the treatment of bipolar I depression using number needed to treat, number needed to harm and likelihood to be helped or harmed. J Affect Disord. 2014;155:20-7. doi: 10.1016/j.jad.2013.10.040, PMID 24246116.
8. Khan S, Gangane PS, Mahapatra DK, Mahajan NM. Natural and synthetic polymers assisted development of lurasidone hydrochloride intranasal mucoadhesive microspheres. Indian J Pharm Educ Res. 2019;54(1):213-22. doi: 10.5530/ijper.54.1.25.
9. Fornaro M, De Berardis D, Perna G, Solmi M, Veronese N, Orsolini L, *et al.* Lurasidone in the treatment of bipolar depression: systematic review of systematic reviews. BioMed Res Int. 2017; 2017:3084859. doi: 10.1155/2017/3084859, PMID 28573138.
10. Qian S, Heng W, Wei Y, Zhang J, Gao Y. Coamorphous lurasidone hydrochloride-saccharin with charge-assisted hydrogen bonding interaction shows improved physical stability and enhanced dissolution with pH-independent solubility behavior. Cryst Growth Des. 2015;15(6):2920-8. doi: 10.1021/acs.cgd.5b00349.
11. Patwekar SL, Baramade MK. Controlled release approach to novel multiparticulate drug delivery system. Int J Pharm Sci. 2012;4(3):757-63.
12. Pawar VK, Singh Y, Meher JG, Gupta S, Chourasia MK. Engineered nanocrystal technology: *in vivo* fate, targeting and applications in drug delivery. J Control Release. 2014;183:51-66. doi: 10.1016/j.jconrel.2014.03.030, PMID 24667572.
13. Yu P, Lu S, Zhang S, Zhang W, Li Y, Liu J. Enhanced oral bioavailability and diminished food effect of lurasidone hydrochloride nanosuspensions prepared by facile nanoprecipitation based on dilution. Powder Technol. 2017;312:11-20. doi: 10.1016/j.powtec.2017.02.038.
14. Zhang HL, Wu SH, Tao Y, Zang LQ, Su ZQ. Preparation and characterization of water-soluble chitosan nanoparticles as protein delivery system. J Nanomater. 2009;(3)1:23-30.
15. Morris GA, Castile J, Smith A, Adams GG, Harding SE. The effect of prolonged storage at different temperatures on the particle size distribution of tripolyphosphate (TPP)-chitosan nanoparticles. Carbohydr Polym. 2011;84(4):1430-4. doi: 10.1016/j.carbpol.2011.01.044.
16. Fan W, Yan W, Xu Z, Ni H. Biointerfaces Formation mechanism of monodisperse, low molecular weight chitosan nanoparticles by ionic gelation technique. Colloids Surf B Biointerfaces. 2012;90:21-7. doi: 10.1016/j.colsurfb.2011.09.042, PMID 22014934.
17. Yadav M, Parle M, Sharma N, Dhingra S, Raina N, Jindal DK. Brain targeted oral delivery of doxycycline hydrochloride encapsulated Tween 80 coated chitosan nanoparticles against ketamine induced psychosis: behavioural, biochemical, neurochemical and histological alterations in mice. Drug Deliv. 2017;24(1):1429-40. doi: 10.1080/10717544.2017.1377315, PMID 28942680.
18. Torchilin VP. Targeted polymeric micelles for delivery of poorly soluble drugs. Cell Mol Life Sci. 2004;61(19-20):2549-59. doi: 10.1007/s00018-004-4153-5, PMID 15526161.
19. Hangman N, Sinsuebpol C. Dry powder inhalation formulation of chitosan nanoparticles for co-administration of isoniazid and pyrazinamide. Pharm Dev Technol. 2020;01(8):20.

Cite this article: Gangane P, Ingle P, Rabade V, Sawarkar H. Formulation and Characterization of Chitosan Based Oral Nanoparticles of Poorly Water-Soluble Drug Lurasidone Hydrochloride. Indian J of Pharmaceutical Education and Research. 2025;59(2s):s454-s463.