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Introduction

Haloperidol is an orally administered dopamine inverse agonist of the typical antipsychotic class of medications that chemically belongs to butyrophenone group [1]. Its mechanism of action is mediated by blockade of D2 dopamine receptors in brain [2]. It is used to treat certain psychiatric conditions including schizophrenia, maniac states, medicament induced psychosis and neurological disorders with hyperkinesias [3]. Haloperidol is chemically 4-[4-(4-chlorophenyl)-4-hydroxypiperidino] 4'- uorobutyrophenone (Figure 1). e molecular formula of haloperidol is $C_{21}H_{23}ClFNO_2$ and molecular weight is 375.86 g/mol.

Author developed the solid lipid nano particles of haloperidol for nose to brain delivery (data are not given here and already published by same author). SLNs have the several advantages including targeted drug delivery and controlled release delivery, and increase bioavailability so as to reduce the dose and adverse e ects associated with drug. SLNs o er an improvement to traditional nose-to-brain drug delivery since they are able to protect the encapsulated drug from biological and/or chemical degradation and may also increase nasal retention time due to an occlusive e ect, good application properties, and adhesion of the SLNs to mucous membranes [4].

Various analytical techniques have been used for determination of haloperidol in pharmaceutical formulations. ese include high performance thin-layer chromatography (HPTLC) [5], 19F NMR spectroscopy [6], square-wave adsorptive stripping voltammetry at a mercury electrode [7], square-wave and cyclic voltammetry at hanging mercury drop electrode [8], cyclic voltammetry at multi-walled carbon nanotubes-modi ed glassy carbon electrode [9]. Non-aqueous titrimetric method has also been developed for haloperidol determination [10]. Several UV spectrophotometric assay procedures have been developed and described in o cial compendia [11-13]. e literature survey revealed that haloperidol was quantitatively assayed in pharmaceutical preparations as well as in biological uids either individually or in the presence of other drugs using HPLC (Table 1) but procedures related to detection of haloperidol in solid lipid nanoparticles are not published in literature till today. Author tried to reproduce the previously reported methods (Table 1) but due to unknown reasons none of them could reproduced. Hence, the aim of the research work was to develop and validate a new HPLC method for haloperidol. e di erent analytical performance parameters such as linearity, precision, accuracy, reproducibility, limit of detection (LOD) and limit of quanti cation (LOQ) were determined as per ICH Q2 (R1) guidelines [14,15]. e signi cance and relevance of this method was in vitro dissolution assessment of solid lipid nanoparticles. is showed sustained drug release with maximum value of 95.52 ± 5.21% in found to be 2.31 years at 4°C.

New Delhi, India. All reagents were of HPLC grade. Milli-Q grade (Millipore, Molsheim, France) water was used to prepare solutions wherever required and it was ltered before use through a 0.22 µm membrane lter.

Instruments

Bath sonicator (Multitech Pvt. Ltd., N. Delhi), Balance (AUX 220, Shimadzu Corporation, Kyoto, Japan), Magnetic stirrer (Remi Instruments Pvt. Ltd., Mumbai, India), pH meter (Hicon Scienti c Instruments, Delhi, India), Centrifuge (Remi Instruments Pvt. Ltd., India), Micro pipettes (Labnet, USA), Vortex mixture (S.M. Scienti c instruments, Pvt. Ltd, Delhi) were used for the study.

HPLC System

e HPLC system consisted of a pump (Jasco PU 2080 plus), UV/VIS detector (Jasco UV 2075 plus) and the so ware used was Jasco Borwin version (1.5, LC-Net II/ADC system). e column used was C-18 Cosmosil packed column (5.0 MS-II, 250 mm × 4.6 mm with particle size of 5.0 m). Syringe lters (Syringe-driven lters of 0.22 m, HiMedia Laboratories Pvt. Ltd., Mumbai, India) were used to lter to sample.

Preformulation studies of haloperidol: Haloperidol was received as a gi sample from Vamsi Labs Ltd Solapur, Maharashtra, India. Authenticity of haloperidol was veri ed by conducting the preformulation studies like organoleptic properties, melting point, FTIR spectral analysis, DSC study, partition coe cient determination.

HPLC method

Several methods have been developed for the determination of haloperidol in pharmaceutical preparation.

e concentration of haloperidol had been earlier determined by HPLC method using methanol-water (63:37, v/v) containing 0.2 M ammonium acetate as mobile phase and diphenylamine as internal standard [21]. e method used here was slightly modi ed in the terms of mobile phase. e mobile phase consisted of 100 mM/L potassium dihydrogen phosphate-acetonitrile-TEA (10:90:0.1, v/v/v) and the pH was adjusted with o-phosphoric acid to 3.5. It was sonicated for 15 min and ltered through 0.22 m membrane lter. Flow rate of mobile phase was maintained at 2 mL/min and eluents were monitored at 230 nm. e samples were injected using a 20 L HPLC injector. All determinations were performed at ambient temperature for a run time of 5 min [22].

Preparation of calibration curve: e 1.0 mg/mL stock solution of haloperidol was prepared in mobile phase. An appropriate volume of stock solution was further diluted with mobile phase to obtain a standard solution having a nal concentration 100 g/mL. Di erent concentrations (1-60 g/mL) were made for the preparation of calibration curve from the prepared standard solution [23]. e prepared dilutions were injected serially (20 L) and area under peak was recorded for each dilution. e calibration curve was constructed by plotting the concentration of haloperidol on X-axis and peak area on Y-axis.

Method validation

HPLC method for Haloperidol was validated as per the ICH guidelines Q2 (R1) for linearity, precision, accuracy, repeatability, LOD and LOQ.

Linearity: ra

Application of HPLC Method in *in- i o* drug release study

Haloperidol loaded solid lipid nanoparticles (HP-SLNs) were prepared by modi ed solvent emulsi cation–di usion technique and optimised by Boxbehken design [13].

e in vitro dissolution studies were carried out to evaluate the release of drug form optimized HP-SLN formulation and comparing it with the pure drug.

An accurate amount of freeze dried HP-SLNs and aqueous haloperidol suspension, each containing drug equivalent to 10 mg was transferred to a dialysis bag and sealed at both ends. e sealed bag was then suspended in a beaker containing 100 mL of dissolution medium (Phosphate bu er pH 7.4, corresponding to cerebrospinal uid pH) and stirred at a constant speed at 37 ± 0.5°C. Aliquots were withdrawn at predetermined time intervals up to 24 h from receiver compartment (beaker) and replaced with an equal volume of fresh medium to maintain sink condition. e samples were analyzed by HPLC using the selected mobile phase. Comparison between release pro le of drug suspension and optimized HP-SLN formulation was made by student's t test at $p< 0.05$.

Analysis of haloperidol by HPLC method for the determination of shelf life

e shelf life of optimized HP-SLNs was determined by

% of standard spiked to the sample	Concentration			% drug recovered	% RSD	SE

Conc. (µg/ mL)	Repeatability (intraday precision)			M pB ó			

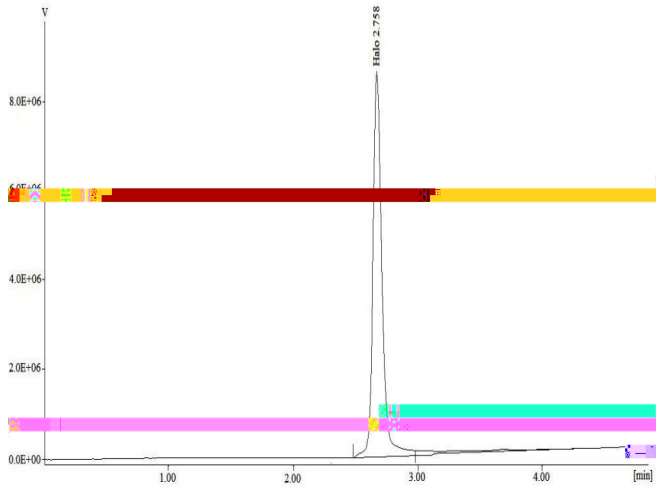

Figure 5: HPLC chromatogram of haloperidol.

References

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