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IR INTERPRETATION, DERIVATIVE UV SPECTRA AND VALIDATED UV SPECTROSCOPY METHOD FOR THE ESTIMATION OF HALOPERIDOL IN TABLET DOSAGE FORM

R.K. Sangeetha[1*], T. Sudhakaran[1], T.K. Ravi[1], M. Mahendra Raja[2]

[1]College of Pharmacy, Sri Ramakrishna Institute of Paramedical Sciences, Coimbatore -641044, Tamil Nadu, India.
[3]Sunglow Pharmaceuticals, Kurumbapet, Pondicherry, India.

ABSTRACT

A simple, accurate and rapid UV method was validated with derivative spectra for the estimation of haloperidol in tablets. The drug is soluble in 0.1 N methanolic sulphuric acid and all the solutions were prepared using the same. Infra-red spectral interpretation by attenuated total reflectance method was done to confirm the structure of haloperidol. The peaks obtained at 1594 cm $^{-1}$, 1869 cm $^{-1}$, 600-800 cm $^{-1}$, 1312 cm $^{-1}$, 1681 cm $^{-1}$ confirm the presence of functional groups like tertiary amine, fluorine, chlorine, hydroxyl and ketone group present. The drug has maximum absorption at 243 nm with a linearity range of 10-50 µg/ml. The %RSD values of accuracy and precision was found to be less than 1.The limit of detection and limit of quantitation were calculated statistically based on the slope of the curve and was found to be 3.8 and 10.6µg/ml respectively. The solution of haloperidol was found to be stable for 8 h after which there was decrease in absorbance. The first, second and third derivative spectra revealed that the peak obtained with the formulation has no interference from other ingredients present. The present study was validated according to ICH guidelines. The proposed analytical method was found to be accurate, precise, and reproducible.

Keywords: Haloperidol, UV spectroscopy, IR interpretation, Derivative spectra.

INTRODUCTION

Haloperidol is chemically 4-[4-(4-chlorophenyl)-4-hydroxy-1-piperidyl]-1-(4-fluorophenyl)-butan-1-one and white or light yellow crystalline powder insoluble in most of the solvents like DMF, chloroform, methanol, ethanol, acetone, acetonitrile but soluble in slight acidic pH[1,6] like 0.1 N methanolic sulphuric acid. The drug was found to be sensitive to light. Haloperidol is a dopamine antagonist of the typical antipsychotic class of medications. It is a butyrophenone derivative and has pharmacological effects similar to the phenothiazines.

Haloperidol is an older antipsychotic used in the treatment of schizophrenia and acute psychotic states and delirium. Haloperidol is stable in its formulations for a longer period of time [6]. The literature survey reveals the analysis of haloperidol by capillary zone electrophoresis [2], HPTLC [3], spectrofluorometric [4] and HPLC [5, 8] methods.

INSTRUMENTS AND MATERIALS

The measurements were made from Jasco - V-530 spectrophotometer with 10 mm matched quartz cells and Jasco FT/IR- 4100 spectrophotometer. Weighing was done using Shimadzu AY220 – Analytical single pan balance. The methanol and acid used are of analytical grade procured from S.D.fine chemicals Ltd., Mumbai. The pure drug was procured commercially. The tablets were procured from the local market.

IR Interpretation of Haloperidol

The sampling for infra red spectrum was done by attenuated total reflectance by directly placing the sample powder onto the sample holder. The interpretation was done to check the structure of haloperidol with the reference structure in Indian Pharmacopoeia. The peaks obtained at 1681cm[1] for ketone group, 1594 and 1360 cm^{-1}

Corresponding Author:- R.K. Sangeetha Email:- geetkaran@gmail.com

for tertiary amine group, 1492 cm $^{-1}$ for C=C stretching, 1410 cm^{-1} for tertiary amine methylene, 1312 cm^{-1} for hydroxyl group, 1219 cm $^{-1}$ for OH bend augmented with CH in plane bend, 1046.19 cm^{-1} for in plane CH bend, 996, 960 and 614 cm^{-1} for aromatic group, 790 cm^{-1} for alkenes out of plane CH bend, 739 cm^{-1} for out of plane CH bend, 1869 cm^{-1} for fluorine group and 800 cm^{-1}for chlorine group confirm the presence of the functional groups in haloperidol.

UV spectroscopy

Standard stock solutions were prepared by dissolving in 0.1 N methanolic sulphuric acid and further dilutions were made using the same solvent. Aliquot portions of the stock solutions were diluted to give a concentration range of 10-50 µg/ml. The resultant solutions were scanned in UV range (400-200 nm) in 1.0 cm cell against solvent blank. The drug has maximum absorption at 243 nm with a linearity range of 10-50 µg/ml. The correlation coefficient was found to be 0.99203 with a slope of 0.021785 and a slope intercept form of 0.021785+ - 0.09145.The % RSD for interday precision was found to be 0.1183 and 0.0892, 0.0669, 0.0307 for day1, day 2, day 3 respectively. The recovery studies had a recovery of 99.97± 0.645% with a % RSD of 0.1199.The drug is reported for its resistance to degradation by WHO expert committee [7]. The stability of drug was checked for every one hour and was found to be stable for 8 hours after which there was decrease in the absorbance. The derivative spectra were found to show no interference by the excipients present in the formulations. The present study was validated according to ICH guidelines.

Derivative UV Spectroscopy

The absorption spectra thus obtained were derivatized from first to third order. The solutions were prepared in 0.1 M methanolic sulphuric acid. The zero order spectrum with maximum absorption at 243 nm was derivatized using mathematical calculations. But the data points at the beginning and end of the wavelength range are lost in the derivative spectrum. If three data points are used for the process then one data point will be lost at each end of the range for first derivative order. If five points are used then two points will be lost and so on. An unwanted effect of the derivatization process is that the signal –to-noise ratio decreases as higher order of derivatization are used. This follows from the discrimination effect and the fact that noise always contains the sharpest feature of the spectrum. Thus if the spectral data used is 2 nm interval, then noise has 2 nm bandwidth [9].

The first order spectrum passes through zero at the lambda maximum 243 nm of the drug with positive and negative bands on the both sides of the same wavelength as the inflection point in the absorbance band. This bipolar function is the characteristic of all odd order derivatives.

The second derivative spectra give the maximum absorption at the negative region with two positive satellite bands on both the sides. The most characteristic feature of second order derivative is the negative band at the maximum on the zero order bands. The number of bands observed is equal to the derivative order plus one [10-15]. The third order derivative at the maxima of the zero order band of the drug gives the maximum absorbance with two negative bands and two positive bands on both sides.

Fig 1. Structure of Haloperidol

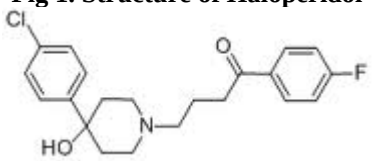

Figure 2. Zero order spectrum – Haloperidol

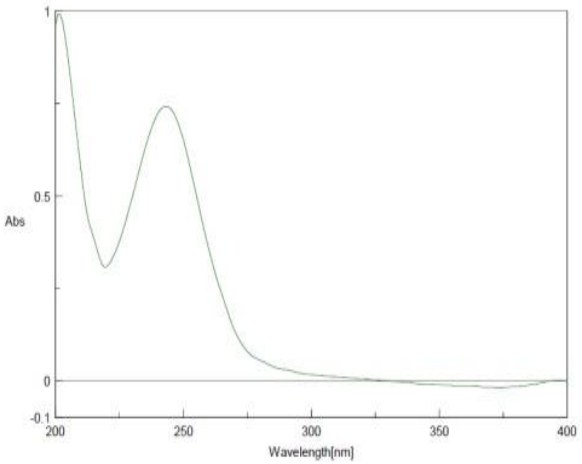

Figure 3. First order spectrum – Haloperidol

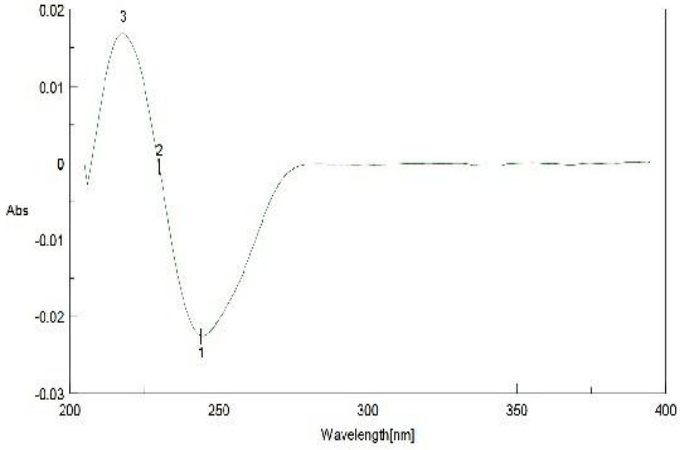

Figure 4. Second order spectrum - Haloperidol

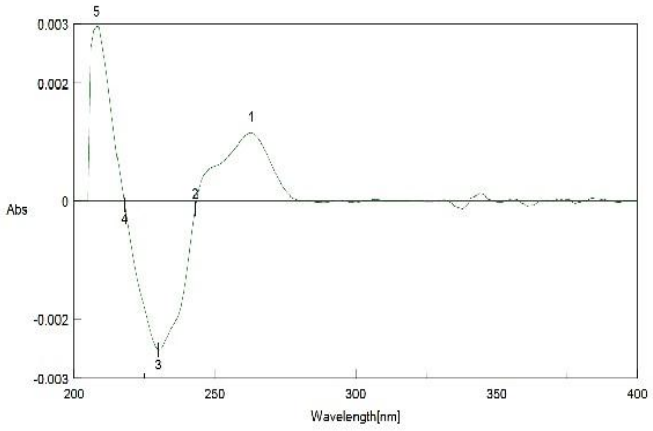

Figure 5. Third order spectrum - Haloperidol

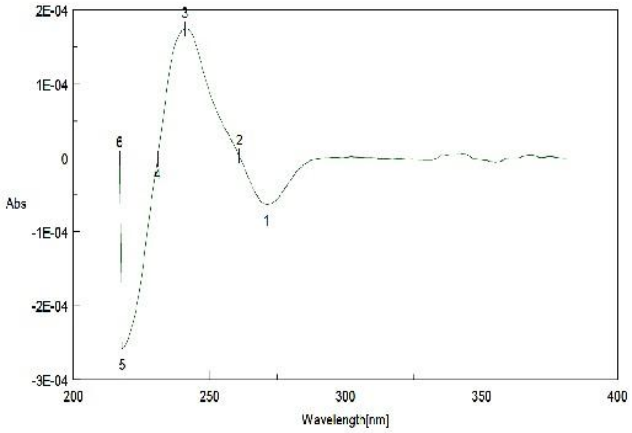

Table 1. – Linearity and Range

S.No	Concentration(µg/ml)	Absorbance
1	10	0.1264
2	20	0.4284
3	30	0.6510
4	40	0.8300
5	50	0.9978

Table 2. Precision studies

Precision	Absorbance	Average	SD	% RSD
Intra day	0.6515 0.6498 0.6501 0.6510 0.6514	0.6507	0.0077	0.1183
Interday Day 1	0.6511 0.6511 0.6507 0.6498 0.6512	0.6507	0.00058	0.0892
Day 2	0.6514 0.6511 0.6509 0.6503 0.6513	0.6510	0.0064	0.0669
Day 3	0.6512 0.6511 0.6511 0.6507 0.6509	0.6510	0.0002	0.0307

CONCLUSION

The drug Haloperidol is a butyrophenone derivative having the functional groups like Fluorine, chlorine, hydroxyl, ketone, tertiary amine with two benzene rings. The infrared interpretation was done for the structural confirmation by comparing with the reference spectra in Indian Pharmacopoeia 2007. The peaks obtained at 1681 cm^{-1} for ketone group, 1594 and 1360 cm^{-1} for tertiary amine group, 1492 cm^{-1} for C=C stretching, 1410 cm^{-1} for tertiary amine methylene, 1312 cm^{-1} for hydroxyl group, 1219 cm^{-1} for OH bend augmented with CH in plane bend, 1046.19 cm^{-1} for in plane CH bend, 996, 960

and 614 cm^{-1} for aromatic group, 790 cm^{-1} for alkenes out of plane CH bend, 739 cm^{-1} for out of plane CH bend, 1869 cm^{-1}, for fluorine group and 800 cm^{-1} for chlorine group confirm the presence of the functional groups in haloperidol.

The literature survey reveals the analysis of haloperidol by capillary zone electrophoresis [2], HPTLC [3], spectrofluorometric [4] and HPLC [5, 8] methods. The present study was validated according to ICH guidelines for validation of analytical procedure .The linearity range was found to be 10-50 50µg/ml with correlation coefficient of 0.99203. The % RSD was found to be less than 1 .The drug solution was found to be stable for 8 hours. So the method was found to be precise and accurate for the routine analysis of haloperidol in tablet dosage form.

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