S. Sambamurty Raju, Actapharmica (2015) Vol.2 (1) 107-111 ISSN 2386-8937

Validated UV and Visible Spectrophotometric Methods for the quantification of Haloperidol in Pharmaceutical dosage forms

S. Sambamurty Raju[1]*, P. Naga Raju[2], R. Ashok Babu[3], & A. Anjani Devi[4]
PG Department of Chemistry, K.V.R, K.V.R & M.K.R College, Khajipalem, A.P., India

Abstract:
Simple and cost effective UV and Visible spectroscopic methods were described for the estimation of Haloperidol in Phamaceutical dosage forms. Visible method was based on the formation of organic solvent extractable ion association complex with ARS dye. In both methods the solutions showed maximum absorption at 248nm, 495nm; also obeyed Beer's law in the concentration range of 25-250 µg/mL and 2-14 µg/mL for UV and ARS methods respectively. The absorbance was found to increase linearly with increasing concentration of Haloperidol with correlation coefficient of 0.995 and 0.992 for both methods respectively. The optimum experimental parameters for the reaction have been studied. The validity of the described procedure was assessed. Statistical analysis of the results has been carried out revealing high accuracy and good precision. The proposed methods were successfully applied for the determination of Haloperidol in pharmaceutical formulations.
Keywords: Antipsychotic; haloperidol; UV spectroscopy method; Alizarin Red Dye.

1.0 Introduction:

Haloperidol is an antipsychotic. Haloperidol is in a group of medications called conventional antipsychotics that works by decreasing abnormal excitement in the brain. It helps in restoring the balance of certain natural substances in the brain (neurotransmitters). Haloperidol is used to control motor tics (uncontrollable need to repeat certain body movements) and verbal tics (uncontrollable need to repeat sounds or words) in adults and children who have Tourette's disorder (condition characterized by motor or verbal tics).

It occurs as a white crystalline powder. The chemical designation is 4-[4-(p-chlorophenyl)-4-hydroxypiperidino] 4'-fluorobutyrophenone and its structural formula is given in Figure 1.

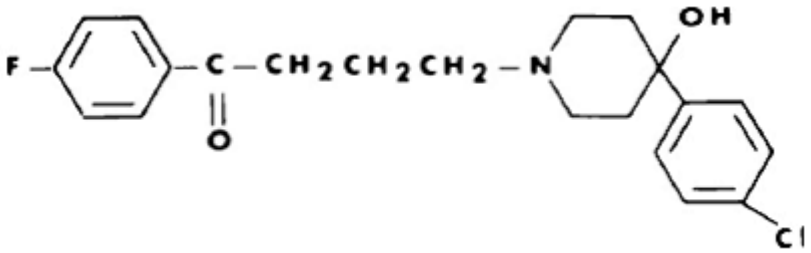

Figure 1: Structure of Haloperidol

Haloperidol is used in the control of the symptoms of Schizophrenia [1], acute psychosis, hyperactivity, aggression, hallucinations in alcohol withdrawal [2]. Common dosage forms are tablets and injections. Side

effects related to Haloperidol are extra pyramidal including acute dystonic reactions, akathisia syndrome, drug induced Parkinsonism, bradykinesia and tardive dyskinesia [3]. Haloperidol is stable in its formulations for a longer period of time.

The literature survey reveals that very few determination methods are available for Haloperidol [4-9]. This article describes a simple and sensitive spectrophotometric method for the determination of Haloperidol in pharmaceutical preparations. The proposed methods are based on the direct UV and ion-pair complex formation between Haloperidol and ARS dye as per International Conference on Harmonization (ICH) guidelines [10].

2.0 Materials and Methods:

2.1 Instrument:

TECHCOMP double beam UV visible spectrophotometer with HITACHI software was used for the spectral analysis. Standard cuvetts made of quartz with 10mm path length were used for holding solutions. Elico pH meter, Ultrasonic bath sonicator are used.

2.2 Materials:

Haloperidol standard drug was obtained from the Sun Pharmaceutical Industries Ltd, Hyderabad. Laboratory reagent grade methanol and chloroform was purchased from Merck chemicals, Mumbai, India and double distilled water was used for preparation of solutions.

2.3 Preparation of reagents:

Alizarin red solution (ARS): 200 mg of ARS Reagent is dissolved in 100ml of distilled water.

1N HCL Solution: Diluted 8.6 ml of concentrated hydrochloric acid to 1000ml with double distilled water.

2.4 Preparation of standard drug solution:

An mg /ml solution was prepared by dissolving accurately weighed 10mg of standard drug in 10ml methanol. Sonicated the solution for 10 minutes in Ultrasonicator bath. The obtained concentration is 1000 µg/ml and this is marked as stock solution and stored for further use. At the time of work, working standard solutions were prepared from this stock solution.

2.5 Preparation of working standard solution:

Working standard solutions like 25, 50, 75.....250 mg/ml solutions and 2, 4, 6...14 mg/ml solutions for UV and ARS visible methods were prepared from the standard stock solution by proper dilution respectively.

2.6 Preparation of sample solution:

10 tablets of Haloperidol (Agidol 20) was taken and finely ground and from the tablet powder, an amount of powder equivalent to 10mg of drug (Haloperidol) was weighed accurately and was dissolved in 10ml Methanol. The content were mixed well and then filtered to get a clear drug solution. From this a concentration of 100 µg/ml was prepared by selected dilution. This solution was used as sample solution.

3.0 Methods:

3.1 UV method:

To determine the specific wavelength, a solution was scanned from 400-200 range of UV, and obtained maximum absorbance was found to be at 248nm. Series of aliquots were taken and absorbance was measured at 248nm using same diluents as blank. The wavelength scanning spectra was shown in the figure 2.

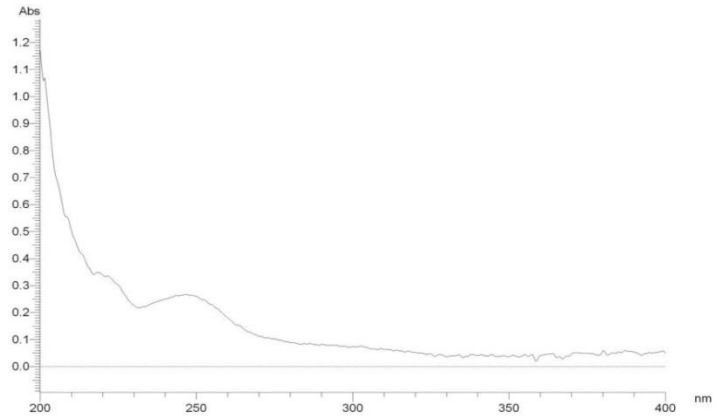

Figure 2: Wavelength scanning spectra for Haloperidol in UV Method

3.2 ARS method:

A series of 125 ml separating funnels containing aliquots of standard drug solution was taken. To this 6ml of 1N HCl solution and 2ml of dye solutions were added successively. The total volume of the aqueous phase in each separating funnel was adjusted to 15ml with distilled water. To each separating funnel 10ml of Chloroform was added and the contents were shaken for 2 min. the two phases were allowed to separate and the absorbance of the separated chloroform layer was measured at 495nm against a similar reagent blank.

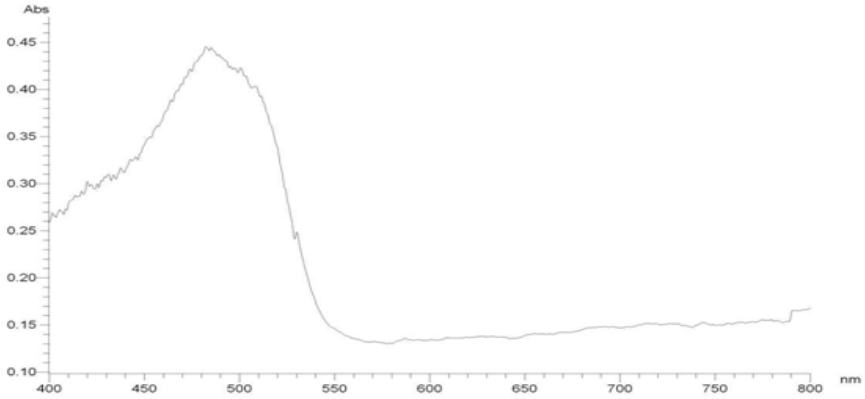

Figure 3: Wavelength scanning spectra for Haloperidol in ARS Method

4.0 Method Validation:

4.1 Linearity:

To determine the linearity, serial dilutions of the standard drug solutions in the range of 25-250µg/ml solutions for UV method and 2-14µg/ml solutions were prepared and absorbance was taken at 248 nm and 495nm respectively. Linearity was plotted by taking absorbance on Y-axis and concentration on X- axis. Linearity was determined by its regression equation i.e., y = 0.002x + 0.020 and y = 0.020x + 0.053.

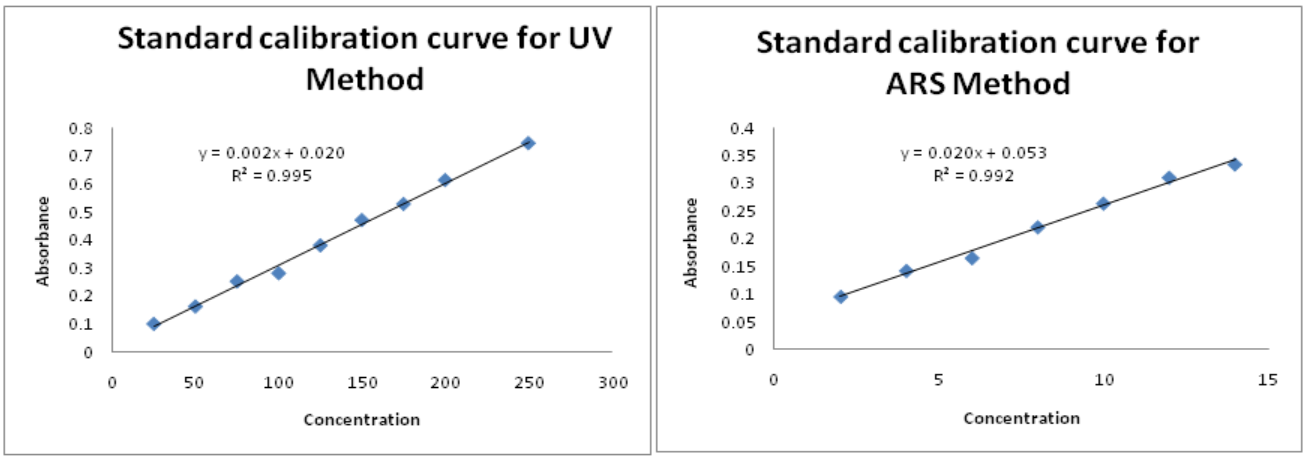

Figure 4: Calibration curves for Haloperidol

S.NO	UV method		ARS method	
	Concentration in µg/ml	Absorbance at 248nm	Concentration in µg/ml	Absorbance At 495nm
1	25	0.101	2	0.095
2	50	0.163	4	0.142
3	75	0.252	6	0.165
4	100	0.281	8	0.221
5	125	0.38	10	0.264
6	150	0.47	12	0.311
7	175	0.527	14	0.335
8	200	0.612		
9	250	0.743		
	Slope **Intercept** **R^2**	**0.002** **0.020** **0.995**	**Slope** **Intercept** **R^2**	**0.020** **0.053** **0.992**

Table 1: Calibration curve results for Haloperidol in the proposed method

4.2 Precision:

The Precision was determined at two levels intra-day precision and inter-day precision in triplicates. The intra-day precision results are 0.87 and 1.28 whereas inter-day precision shows 0.79 and 1.17 for the UV and ARS method respectively. The % relative standard deviation was calculated for absorbance to obtain the intra-day variation and inter-day variation.

4.3 Recovery Studies:

The accuracy of the proposed methods was checked by recovery studies with the addition of standard drug solution to pre analyzed sample solution at three different concentration levels [50%, 100% and 150%], within the range of linearity for the drug. The recovery values for Haloperidol ranged from 98-102 % for both the methods. Hence the methods were found to be accurate.

4.4 Application to Analysis of Commercial Sample:

The proposed procedures were applied to determine the content of Haloperidol in commercially available tablets. The results obtained for the Haloperidol in the proposed two methods – Direct UV method and visible method were shown in the following table 2.

S.NO	Method	Formulation	Amount prepared	Amount found	% Assay
1	UV	Agidol 20	50µg/ml	49.245	98.49
2	ARS	Agidol 20	4µg/ml	3.985	99.63

Table 2: Formulation Analysis

S.NO	Parameter	UV method	ARS Method
1	Wavelength Maxima	248nm	495nm
2	Linearity Range	25-250µg/ml	2-14 µg/ml
3	Correlation coefficient	0.995	0.992
4	Slope	0.002	0.020
5	Intercept	0.020	0.053
6	RSD of Precision	0.87,0.79	1.28,1.17
7	Average recovery*	99.46	99.78
8	LOD	2.0µg/ml	0.5µg/ml
9	LOQ	7.0 µg/ml	2.0µg/ml
10	% Assay of Formulation	98.49	99.63

**mean of five determinations*

Table 3: Summery results for Haloperidol in the proposed methods

5.0 Conclusion

We can conclude now that the proposed UV and Visible spectroscopic methods are simple, easier, rapid, precise, accurate and inexpensive. Therefore, these methods can be used in direct quantitative and extractive determinations of Haloperidol in the pharmaceutical formulation analysis.

5.1 References

1. "Haldol Official FDA information, side effects and uses". Drugs.com. Retrieved 2013-10-03.
2. Schuckit, MA (27 November 2014). "Recognition and management of withdrawal delirium (delirium tremens).". The New England journal of medicine 371 (22): 2109–13.
3. Rahman N, Khatoon A, Rahman H. Studies on the development of spectrophotometric method for the determination of haloperidol in pharmaceutical preparations. Quim. Nova. 2012; 35(2):392-397.
4. Paul JAW Demoen. Properties and analysis of haloperidol and its dosage forms. Journal of Pharmaceutical Sciences, 50(4), 1961, 350–353.
5. Wu SM, Ko WK, Wu HL, Chen SH. Trace analysis of haloperidol and its choral metabolite in plasma by capillary electrophoresis. J Chromatogr A, 846(1-2), 1999, 239-43.
6. Mennickent S, Pino L, Vega M, Godoy CG, de Diego M,"Quantitative determination of haloperidol in tablets by high performance thin-layer chromatography. Sep Sci, 30(5), 2007, 772-7.

7. Mohd Yasir and U. V. S. Sara developed and validated a UV Spectrophotometric Method for the Estimation of Haloperidol. British Journal of Pharmaceutical Research 4(11): 1407-1415, 2014.
8. Nafisur Rahman; Asma Khatoon; Habibur Rahma, "Studies on the development of spectrophotometric method for the determination of haloperidol in pharmaceutical preparations". Química Nova.
9. International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use, ICH Harmonized Tripartite Guideline, Validation of Analytical Procedures: Text and Methodology, Q2(R 1), Complementary Guideline on Methodology dated 06 November 1996, incorporated in November 2005, London.