How to Cite:
Sreedevi, G., Chakravarthy, E., & Reddy, N. R. (2022). A simple spectrophotometric method for the determination of haloperidol from pharmaceutical formulations. *International Journal of Health Sciences*, *6*(S3), 7532–7538. https://doi.org/10.53730/ijhs.v6nS3.7700

A simple spectrophotometric method for the determination of haloperidol from pharmaceutical formulations

G. Sreedevi
Department of Chemistry, Rayalaseema University, Kurnool, (A.P)-518002, India

E. Chakravarthy
Department of Chemistry, Rayalaseema University, Kurnool, (A.P)-518002, India

N. Rami Reddy
Department of Chemistry, K.V. R. Government College, Kurnool, (A.P)-518002, India

***Abstract*---**A simple, sensitive, rapid, accurate and cost effective spectrophotometric method has been developed and validated for the estimation of haloperidol in bulk drug and for its pharmaceutical formulations. The proposed method is based on the formation of chloroform extractable ion pair complex of haloperidol with bromothymol blue. The absorbance of the coloured extractable ion pair complex is measured at the wavelength of maximum absorbance 420 nm against the reagent blank. Beer's law is obeyed over a concentration range of 20 to 100 µg/ml of haloperidol, for a linear calibration curve. Results are statistically validated and found to be reproducible.

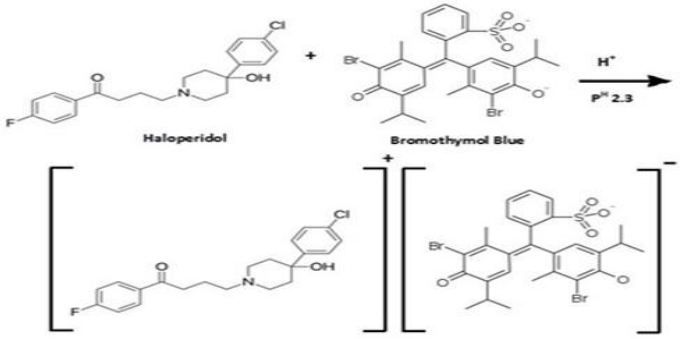
***Keywords*---**spectrophotometry, haloperidol, bromothymol blue, pharmaceutical formulations.

Introduction

Haloperidol is the first of the butyrophenone series of major antipsychotics. The chemical designation is 4-[4-(p-chlorophenyl) -4- hydroxypiperidino]-4-fluorobutyrophenone. Haloperidol is used to treat psychotic disorders like schizophrenia, to control motor (movement) and verbal (for example, Tourette's syndrome) and is used to treat severe behavior problems in children. Haloperidol is also available as a sterile parenteral form for intramuscular injection. Various methods have been reported in literature for the determination of haloperidol, which includes Spectrophotometric methods[1-7],

RP-HPLC[8-10], HPLC[11-12], Gas chromatography[13], Spectrofluorimetry[14], Adsorption ratio method[15], Stripping voltametry[16], Thermodynamic method[17]. In the present communication, a simple spectrophotometric method has been developed for the determination of haloperidol in pharmaceutical formulations. Spectrophotometric technique is a most preferred method for routine analytical work due to its simplicity and reasonable sensitivity with significant economical advantage.

The present method is based on the formation of chloroform extractable ion pair complex of haloperidol with bromothymol blue in methol medium. The absorbance of the coloured extractable ion pair complex is measured at 420 nm using optimized experimental conditions. The aim of present research work is to develop the simple spectrophotometric method for the determination of haloperidol in dosage forms without interference of excipients. The reaction sequence of haloperidol and bromotymol blue ion-pair complex is shown in the scheme .1.



Scheme 1. Reaction scheme of Haloperidol with Bromothymol blue

Experimetal

All reagents and solvents used were analytical grade. Haloperidol drug is supplied by Rhyme Organics and Chemicals Ltd.

Instrument

All experimental measurements are taken by using Milton Roy 1001 spectrophotometer with 10 mm quartz cuvettes.

Reagents

Hydrochloric acid (1.0 N):

10 g of 36% HCl (Merck) is dissolved in 100 ml of distilled water.

Potassium Hydrogen Phthalate (0.1 M)

It is prepared by dissolving 2.0422 grams of potassium hydrogen phthalate (Fischer Scientific) in 100 ml of distilled water.

Buffer solution (pH 2.3)

It is prepared by mixing 100 ml of 0.1 M potassium hydrogen phthalate (20.422 gm of potassium hydrogen phthalate (Fischer scientific) in 1000 ml of distilled water) in 91.6 ml of 0.1M HCl (10 g of 36% HCl (Merck) is dissolved in 1000 ml of distilled water) and pH of the solution is adjusted to pH 2.3.

Bromothymol blue (BTB) (100µg/ml)

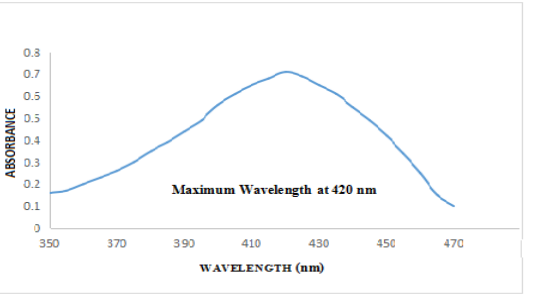
It is prepared by dissolving 10 mg of bromothymol blue (Fischer scientific) in 100 ml of methanol.

Preparation of standard stock solution of Haloperidol

An accurately weighed 50 mg of haloperidol is dissolved in methanol. The volume is adjusted to 50 ml with methanol in 50 ml standard flask. One ml of this solution contains 1 mg/ml. The stock solution is further diluted to get desired concentration 100 µg/ml.

Spectrum of Haloperidol with bromothymol blue

Haloperidol with tertiary amino group reacts with bromothymol blue at pH 2.3 to give ion association complex. It is extracted into chloroform layer and absorbance of the yellow coloured ion association complex is determined from absorption spectrum and from the calibration curve amount of haloperidol is estimated. The absorbance of extractable ion pair complex is measured at 420 nm against reagent blank. Absorption spectrum is shown in the fig .1.



Scheme 1. Absorption spectrum of Haloperidol

Calibration curve for Haloperidol drug

Various amounts of haloperidol drug solution ranging from 0.2 to 1.0 ml are taken into different flasks and to each of these flasks 1.0 ml of bromothymol blue dye solution, 1.0 ml of buffer solution pH 2.3 are added and made up to the mark with distilled water. The reaction mixture is shaken well for 5 minutes and allowed to stand for 5 minutes. The reaction mixture in the flasks is taken into a series of separating funnels and extracted with 5 ml aliquots of chloroform three times and the combined chloroform layers are extracted in to 25 ml standard flask

and contents are made up to the mark with pure chloroform. The yellowcoloured chloroform solution is used to measure the absorbance against the reagent blank (reaction mixture without drug) at 420 nm of λmax. The calibration curve is drawn by plotting absorbance against the concentration of haloperidol in µg/ml. It is a linear curve which is obtained over a concentration range of 20 to 100 µg/ml of haloperidol. The amount of haloperidol present in the sample is estimated by using calibration curve represented by fig .2.

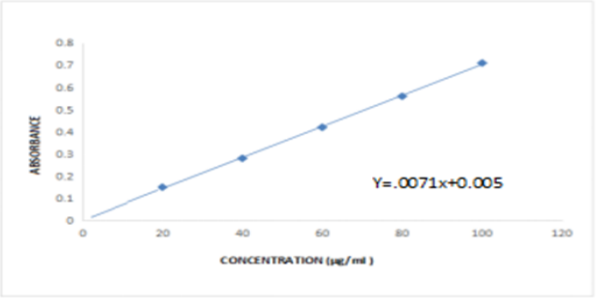


Fig.2. Calibration curve of Haloperidol

Assay of Haloperidol in pharmaceutical formulations

For the analysis of tablet formulations 20 tablets of haloperidol were weighed and finely powdered. 50 mg of accurately weighed powdered haloperidol drug is transferred into a 50 ml volumetric flask containing 25 ml of methanol. The solution is filtered using whatmann filter paper No: 41 into another 50 ml volumetric flask and the solution is made up to the mark with methanol. The concentration of drug solution is 1 mg/ml. The stock solution is further diluted with methanol to get the working concentration and absorbance values are recorded as per the procedure described for calibration curve. The amount of drug present in haloperidol was estimated from the predetermined calibration curve and the experimental results are statically validated.

Statistical analysis of results

The optical characteristics for haloperidol - bromothymol blue ion pair complex, like λmax, Beer's law limit, molar absorptivity and Sandell's sensitivity are estimated and presented in table .1. The molar absorpitivity and Sandell's sensitivity values indicates sensitivity of the method. Regression analysis is done by least square method, by taking different concentrations of drug. This helps to calculate intercept (a), slope(b) and correlation (r). The data is tabulated in the table .1. The correlation coefficient value of 0.9993 shows the good linearity of calibration curve. In table .2. %RSD values obtained are less than 2% indicates the excellent reproducibility. Low standard deviation value obtained indicates reproducibility and also high accuracy of the method followed. The t-test is used to give the perfect precision of the said method. The experimental values obtained in this are compared with theoretical value of 2.78. During the total process of ion association complex method there is no effect of additives and excipients like starch, glucose and calcium lactose present in different concentrations of general pharmaceutical formulations.

Table 1
Optical characteristics

Optical parameters	Experimental / Calculated values
λmax (nm)	420
Beer's law limit (µg/ml)	20-100
Molar absorptivity (lit. $mole^{-1}$ cm^{-1})	$2.81x10^4$
Sandell'sensitivity(µg cm^{-2} / 0.001 absorbance unit)	0.0354
Regression equation (Y = bx+a)	Y=0.0071X+0.005
Slope (b)	0.0071
Intercept (a)	0.005
Correlation coefficient (r)	0.9993

Y = bx+a where Y is the absorbance and X concentration in µg/ml

Table 2
Assay of Haloperidol in pharmaceutical formulations

Tablets	Labeled amount(mg)	Amount found (mg)±S.D	% label claim	%RSD	t–test value
Tablet 1	10	9.91±0.0024	99.1	0..60	0.232
Tablet 2	10	9.90±0.0023	99.0	0.55	0.250
Tablet 3	10	9.92±0.003	99.2	0.70	0.095

Average of five determinations based on label claim

Conclusion

The proposed spectrophotometric method for the assay determination of selected drug is simple, sensitive, rapid, and low cost and gives precise, and accurate results. Hence the present proposed method can be successfully applied for the routine analysis of haloperidol in bulk samples and in pharmaceutical formulations.

Acknowledgments

The author would like to thank prof.I.E. Chakravarthy and Dr.N. Rami Reddy for their guidance and continuous support and also Rhyme Organics and Chemicals Ltd for providing necessary drugs.

References

1. Yasir and U. V. S. Sara, (2014) Development and Validation of UV Spectrophotometric Method for the Estimation of Haloperidol, British Journal of Pharmaceutical Research, 4(11), 1407-1415.
2. C. V. N. Prasad, Chandrika Parihar, T. Rama Chowdhary, Suresh Purohit and P.Parimoot, (1998)Simultaneous Determination of Atenolol-Amlodipine and Haloperidol-Trihexyphenidyl in Combined Tablet Preparations by Derivative Spectroscopy , Pharm. Pharmacol. Commun.,4(1), 325-330.
3. Nafisur Rahman, Shahroora Sameen & Mohammad Kashif, (2016) Spectroscopic Study on the Interaction of Haloperidol and 2,4-Dinitrophenylhydrazine and its Application for the Quantification in Drug Formulations, Analytical Chemistry Letters , 3(6), 874-885 .
4. Ghufran Kawas, Oussama Mansour, Malek Okdah,Amir AlHaj
5. Sakur(2016) Spectrophotometric Determination of Haloperidol in Pure Form and Pharmaceutical Formulation using Calcon and Amido Black, Research J. Pharm. and Tech., 9(2), 119 – 124.
6. S. P. Wate and A. A. Borkar,(2010) Simultaneous Spectrophotometric Estimation of Haloperidol and Trihexyphenidyl in Tablets, Indian J Pharm Sci., 72(2), 265–267.
7. Doungdaw, Chantasart, PrisadaRakkaew,(2019)Preparation and characterization of dry β-cyclodextrin-based ternary complexes of Haloperidol and Lactic acid for drug delivery, Journal of Drug Delivery Science and Technology, 20(3), 73-82.
8. Ghufran Kawas, Dr. Malek Okdah, Dr. Amir Alhaj Sakur, (2010) Spectrophotometric Determination of Haloperidol in The Pharmaceutical Preparations Using Calcon Dye, Tishren University Journal of Research and Scientific Studies, 2(32), 199-211.
9. A K Jain, B K Dubey, Salaj Khare, Amit Joshi, M Ahirwar, P Jain, (2018) Comparision of RP-HPLC and UV Spectrophotometric Methods for Estimation of Haloperidol in Pharmaceutical Formulation, Journal of Drug Delivery and Therapeutics, 8(5), 277-282.
10. Ramesh Raju Rudra Raju and Srikantha dammalapati, (2014) A RP – HPLC Method for Simultaneous Determination of Haoperidol and Trihexyphenidyl Hydrochlorie in Tablet dosage form, Asian Journal of Pharmaceutical and Clinical Research, 79(7), 14-18.
11. M. Syamala, S Angalaparameswari, T. VimalakKannan, C. Sumanjali, T. Jyotshna, (2019) Stability indicating method development and validation for the determination of Haloperidol and Benzhexol by RP-HPLC,International Journal of Research In Pharmaceutical Chemistry and Analysis, 1(2), 52-58

12. Mohd Yasir, Udai Vir Singh Sara, Iti Som, (2017) Development of a new HPLC method for *in vitro* and *in vivo* studies of Haloperidol in solid lipid nanoparticles, Braz. J. Pharm. Sci., 53(2), 1-13.
13. H Trabelsi, S Bouabdallah, K Bouzouita, F Safta, (2002) Determination and degradation study of Haloperidol by high performance liquid chromatography, Journal of Pharmaceutical and Biomedical Analysis, 299(4), 20 , 649-657.
14. A. Forsman, E. Mårtensson, G. Nyberg, R. Öhman, (1974) A gas chromatographic method for determining Haloperidol, Naunyn-Schmiedeberg's Archives of Pharmacology, 286(2), 113–124.
15. Nafisur Rahman and Sana Siddiqui, (2010) Development and validation of spectrofluorimetric method for determination of Haloperidol in pharmaceutical dosage forms, Drug Testing and Analysis, 2(5), 252-258.
16. S.P. Wate,A.A. Borkar ,(2009) Absorption Ratio Method for Simultaneous Estimation of Haloperidol and Trihexyphenidyl in Tablet, Research Journal of Pharmacy and Technology, 2(3), 603- 604.
17. H.S.El-Desoky, M.M.Ghoneim, (2005) Assay of the anti-psychotic drug Haloperidol in bulk form, pharmaceutical formulation and biological fluids using square-wave adsorptive stripping voltammetry at a mercury electrode, Journal of Pharmaceutical and Biomedical Analysis, 38(3), 543-550 .
18. Anthony Amaechi Attama, Petra Obioma Nnamani, Michael Umale Adikwu, Florence Obianuju Akidi, (2004) Thermodynamic Consideration of the Charge Transfer Interaction of the Donor: Acceptor Type between Chloranilic Acid and Haloperidol, Chemical and Pharmaceutical Bulletin, 52 (3), 303-306.