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SPECTROPHOTOMETRIC DETERMINATION OF HALOPERIDOL WITH 2,3 DICHLORO 5,6 DICYANO – 1,4 BENZOQUINONE

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ABSTRACT

We present the validation of a developed a new spectro photometric method on a charge transfer complexation reaction. In this method, the reaction of Haloperidol with 2,3 dichloro 5,6 dicyano 1,4 benzo quinone (DDQ) in chloroform mixture to form an light orange colour charge transfer complex. The light orange colour solution was stable for more than 24 hrs and was used to determine the haloperidol spectrophotometrically. The absorbance of the light orange colour solution was measured at 470 nm, against the reagent blank Beer's Law was obeyed for 50-250 µg/ml of haloperidol. Results of analysis were validated statistically evaluated. The procedures described were successfully applied to the determination of haloperidol in tablets.

KEYWORDS: DDQ Method by spectrophotomethically, Haloperidol Method of validation.

INTRODUCTION

Haloperidol chemically, 4-[4-(4-chlorophenyl)-4-hydroxy piperidin -1-yl] -1(4-fluorophenyl) butan -1-one. Haloperidol is soluble in chloroform. It is used in the treatment of psychoses, restlessness and confusion. Survey of Literature reveals that various methods were reported for the determination of Haloperidol in pharmaceutical formulations. Which includes HPTLC Method, HPLC method and spectrophotometric method.

The Present investigation was under taken with the aim of developing new, simple, rapid and accurate method Hence this spectrophotometric method based on a charge transfer complexation reaction.

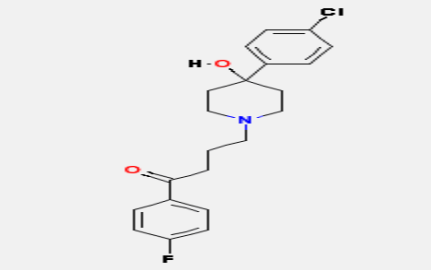


Fig: 1 Structure of haloperiodol.

EXPERIMENTAL

Apparatus

1. Elicouv: visible double beam spectrophotometer with 10 nm matched quartz cuvettes used for absorbance values of the drug solution. This instrument provides a unique monochromatic design and a variety of micro process controlled features to give fast and accurate spectrophotometric measurements.

Reagnets

All chemicals used were of analytical reagent grade, chloroform was used through out the investigation.

1. Standard solution of DDQ i.e. 2,3 dichloro 5, 6 dicyano -1,4 Benzoquinone

DDQ Solution (100 μ g/ml) 50 mg was dissolved in chloroform and the resulting solution was made up to the mark in the 50 ml standard flask with chloroform.

2. Haloperidol Solution: An accurately weighed 50 mg of Haloperidol was dissolved in chloroform. The volume was made up to the mark in the 50 ml standard flask with chloroform. The stock solution was further diluted to get working concentration of 50 μ g/ml.

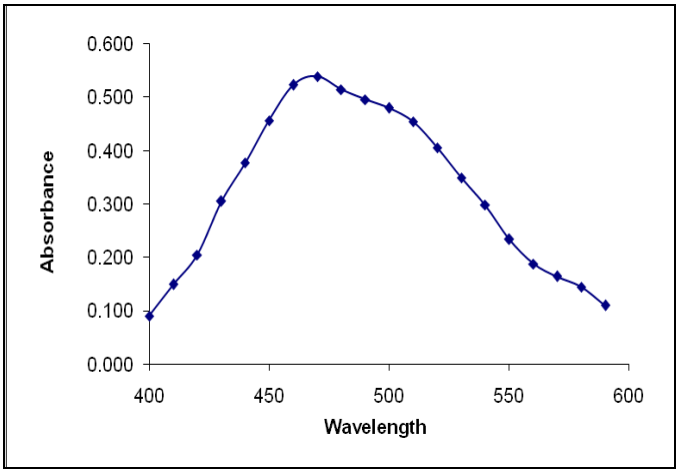
Spectrophotometry

The estimation of haloperidol by DDQ Method In this method was based on the reaction of Haloperidol with 2,3-dichloro 5,6 dicyano-1, 4 - benzoquinone (DDQ) to form an light orange colour charge transfer complex solution. The light orange colour solution was stable for more than 24 hrs and was used to determine the haloperidol spectrophotometrically. The absorbance of the light orange colour solution was measured at the wave length range 400-600 nm, against the reagent blank solution. The blank were prepared for this study, the reagent blank containing optimum concentrations of the reagents expect drug.

The absorbance was found to decrease linearly with increasing concentrations of haloperidol and this forms the basis for the determination of drug, Finally the estimation of the drug was made through the calibration curve.

PROPOSED ASSAY PROCEDURE

A series of 25 ml of volumetric flasks, 0.5 ml, 1 ml, 1.5 ml and 2.0 ml 2.5 ml of the working standard solution of the drug was pipetted into each flask. To each flask, were varying amount of 0.5 -2.0 ml of DDQ reagent solution are added to produce light orange colour solution. The final volume was brought to 10 ml with chloroform. The reaction mixture in each flask was well shaken and allowed to stand for 5 minutes for complete the reaction the absorbance of the light orange colour solution was measured at 470 nm, against the reagent blank solution. The Absorption spectrum of haloperidol is presented in figure -2.



The haloperidol curve was obtained by plotting absorbance values against the amount of standard drug. The amount of haloperidol present in the sample was computed from the calibration curve are presented in figure -3 and the result is given in Table -1.

Table 1: Spectral data for calibration curve.

Amount of Drug solution	Absorbance at 470 nm
0.5ml	0.248
1ml	0.548
1.5ml	0.756
2 ml	1.020
2.5 ml	1.311

Calibration graph was obtained by plotting absorbance values against the concentration of haloperidol solution. The calibration curve was found to be linear over a concentration range

of 50-250 μg/ml of haloperidol. The linearity of the curves obtained indicates that it obeys Beer's law The amount of haloperidol present in the sample was read from the calibration graph. The results are presented in figure -3.

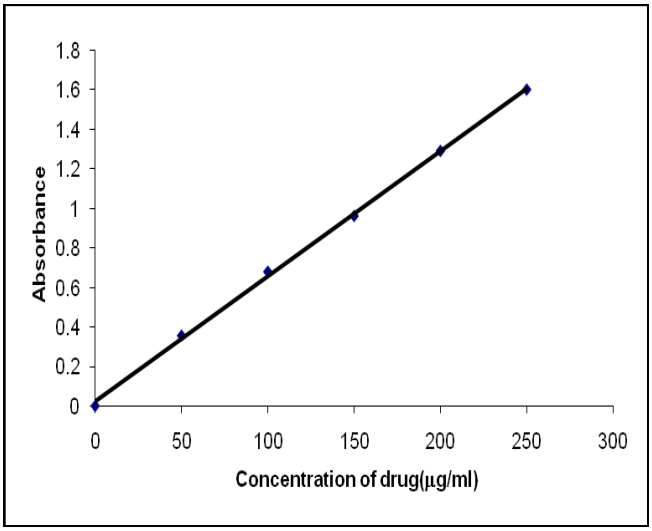


Fig 3: Calibration curve of doxazosin.

Validation of the Method

This method was validated interms of linearity accuracy, precision, specificity and reproducibility of the sample applications. The linearity of this method was investigated by serially diluting the stock solutions of haloperidol and measured the absorbance value at 470 nm by spectrophotometer. Calibration curves were constructed by plotting the absorbance difference values against the amount of drug in µg/ml.

Statistical analysis: A statistical analysis was performed on the statistically significant variables using the statistical software. The following parameters were determined, standard deviation (SD) Relative standard deviation (RSD) student t-test, F-test.

The standard deviation and relative standard deviation (RSD%) and student t-test, and F-test of variation of the haloperidol was calculated from five measurements of replicate samples. And the results are summarized in Table -2 statistical analysis of the determination of haloperidol.

Table 2: Assay of haloperidol in tablets.

Sample	Labelled amount (mg)	*Amount found by proposed method ± S.D	% of Label claim	RSD%*	t^*_{cal}	F*	*Amount found by Reference method ± S.D
Tablet1	10	9.966 ± 0.0272	99.66	0.2729	0.5401	0.1736	9.972 ± 0.0113
Tablet2	10	9.958 ± 0.0279	99.58	0.2807	1.1638	0.1645	9.972 ± 0.0113
Tablet3	5	4.963 ± 0.033	99.26	0.6804	0.8209	0.0930	4.974 ± 0.0103

***Average of six determination based on label claim.**

S.D. : standard deviation

RSD : Relative standard deviation

A: calculated ‘t’ value by proposed method

* f calculated ‘f’ value by proposed method

The values of standard deviation and relative standard deviation are low, indicated high accuracy and reproducibility of this method.

The data of assay values of commercial formulations was subjected to statistical evaluation for student ‘t’ test to study the proposed method. The calculated ‘t’ values are less than ‘t’ theoretical values with 4(n-1=5-1) degrees of freedom at 5% level of significance indicate that there is no significant difference between proposed method and standard method.

RESULS AND DISCUSSION

The present study was carried out to develop a simple, rapid, sensitive, precise, reproducible and accurate spectrophotometric method for the estimation of haloperidol in pharmaceutical dosage forms.

In this method the drug react with DDQ solution to form light orange charge complex. The light orange coloured charge complex solution formed is measured at 470 nm against reagent blank (prepared in same manner omitting drug solution). The amount of drug is read from calibration curve. The calibration curve is linear over the range of 50-250 µg/ml of haloperidol. The values of Standard deviation, RSD%, t_{cal}, F test, are shown in Table.5.2.4. The values of standard deviation, RSD%, are low, indicates high accuracy and reproducibility of the method. The data of assay values of commercial formulations is subjected to statistical evaluation for student ‘t’ test to study the proposed method. The calculated t’ values are less than‘t’ theoretical values with 4 (n-1= 5-1) degrees of freedom at 5% level of significance

indicate that there is no significant difference between proposed method and standard method.

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