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SPECTROPHOTOMETRIC DETERMINATION OF METHYLDOPA IN PHARMACEUTICALS DOSAGE FORMS BY BROMINATION METHOD

***Dr. Mallapu. E. Rani**

*Head of the Dept of Chemistry, Rayalseema University, Kurnool, Andhra Pradesh, India.

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***Correspondence for Author:**

Dr. Mallapu.E.Rani
Head of the Dept of Chemistry, Rayalseema University, Kurnool, Andhra Pradesh, India..
drmerani@gmail.com

ABSTRACT

A Spectrophotometric method is described for assay of Methyldopa in tablets. In this method, the Methyldopa was brominated with bromate – bromide mixture under strong acidic condition. After bromination, the excess brominating mixture is treated with methylene blue; the stable grass green coloured complex was formed. The absorbance of the grass green colour was measured at 670 mm against the blank solution. Results of analysis were validated statistically and by recovery studies. The proposed method is successfully applied to the determination of Methyldopa in tablets.

Key Words: Spectrophotometric, Methyldopa, methylene blue.

INTRODUCTION

Methyldopa chemically, 2 – amino-3-(3, 4-dihydroxy phenyl) -2- methyl – propanoic acid. It is used as control Hypertension. It is commercially called as Alfodopa. The structure of Methyldopa is represented in figure -1. It is used in the treatment of Anti Hypertensive.

Survey of Literature reveals that various Method's were reported for the estimation of Methyldopa in its pharmaceutical formulations.

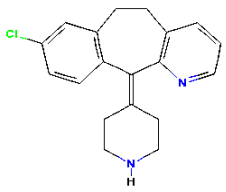

Fig : 1. Methyldopa

This drug describes a flow-injection spectrophotometric method, for assay in tablets and a simple colorimetric estimation of Methyldopa based on its conversion to a nitroro derivative is described and also kinetic method for the determination of Methyldopa in pharmaceutical Preperation.

A wide range of chromoto graphic techniques such as spectrophotometric method for the estimation of derivative of Methyldopa in pharmaceutical formulation are describe other techniques include UV-spectrophotometry, Kinetic spectrophotometry, the present investigation was under taken with the developing simple, rapid and accurate method. This method is based on the oxidation-bromination reaction of the drug by bromine generated by the action of acid on a bromate bromide mixture.

EXPERIMENTAL

Apparatus

A Specronics 1001 Spectrophotometer with 10 mm Matched quartz cuvettes used for absorbance values of the drug solution.

Reagents

All employed chemicals were of analytical grade, and all solutions were freshly prepared in double distilled water.

Bromate – bromide mixture (0.1NKBro3-0.1NKBr)

Prepared by dissolving 0.278 g of K Bro_3 and 1.5g of K Br dissolved in 100 ml distilled water.

Hydrochloric acid solution (4N)

Hydrochloric acid solution (4N) is prepared by diluting the requisite volume of concentrated AR hydrochloric acid (Ranbaxy make) i.e.36.36 ml of concentrated AR hydrochloric acid diluting 100 ml of double distilled water.

Methylene Blue solution (1%)

1g of AR methylene Blue is dissolved in double distilled water and the resulting solution is made up to the mask in the 100 ml standard flask with distilled water.

Standard solution of Methyldopa

50 mg of Methyldopa was dissolved in methanol and the volume was adjusted to 50ml with methanol in 50 ml standard flask. Then 10 ml drug solution was made up to the mask in the 50 ml standard flask with methanol, to give a working concentration of 200 µg / ml .

Spectrophotometric Method

This method was applied to the estimations of the drug dosage forms were purchased from local commercial sources and subjected to analysis. The contents of tablets were accurately weighed and ground into a fine powder. A quantity of the powder equivalent to 50mg standard flask five minutes. This solution is filtered into 50 ml with methanol to get concentration of 1 mg/ml. The stock solution was further diluted to obtain working concentration of 200µg / ml.

Different aliquots of 1 ml, 2ml, 3ml, 4ml of the working drug solution are transferred into a series of 25 ml volumetric standard flasks. To each flask 2 ml of 4N Hydrochloric acid and 2 ml of 0.02N brominating mixture (or) bromate – bromide mixture are added. The contents in each flask are thoroughly mixed and allowed to stand for five mixtured at room temperature for complete bromination orange coloured solution was formed. Then 1 ml of 1% methylene blue solution was added each flasks and the resultant solution was diluted with methanol and mixed thoroughly to get a solution of uniform light grass green colour. After '5' minutes in each absorbance of the light at 670 mm against blank solution. A calibration curve was plotted between the absorbance values and amount of the drug in micrograms. The calibration curves are presented in figure -2.

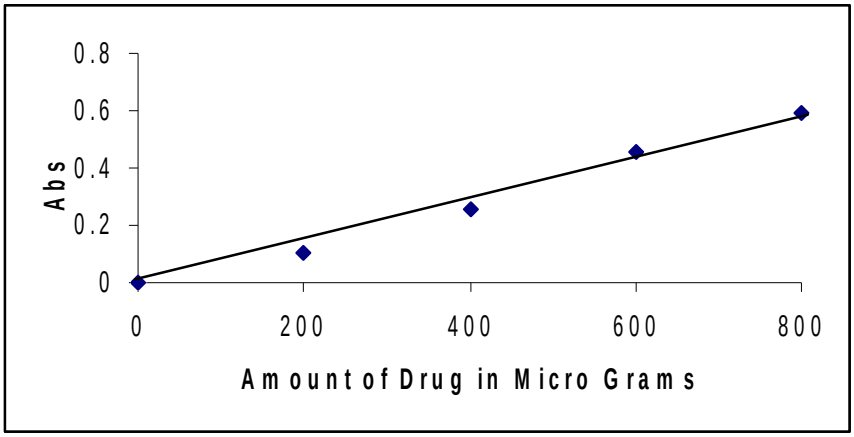

Fig:7.1.2: Calibration curve of methyldopa

Table 1: Spectral data for calibration of methyl dopa

Amount of drug (micrograms)	200	400	600	800
Abs at 670 nm	0.102	0.256	0.456	0.593

Method Validation

This method was validated in terms of linearity, accuracy and precision and reprocibility of the sample applications. A linear relation was found between absorbance and concentration in the ranges. Beer's law was obeyed in the concentration ranges.

Statistical analysis

A Statistical analysis was performed on the statistically significant variables using the statistical software. The following parameters were determined. Co-efficient of variation, standard deviation and student –t-test.

The Standard deviation and t-test of the Methyldopa was calculated from five measurements of replicate samples. The values of standard deviation and teal were shown in table -1. The values of standard deviation and coefficient variation are low, indicates high accuracy and reproducibility of the method. The calculated 't' values are less than 't' theoretical values with 4(x-1=5-1) degrees of freedom at 5-1. Level of significance, indicate that there is no significant difference between proposed method and standard method.

TABLE -1 :Statistical analysis of the determination of Methyldopa

Sample	S.D	C.V	t_{cal}^{a}	t_{tab}^{*}
Tablet – 1	0.4159	0.1663	0.2147	2.78
Tablet – 2	0.8502	0.3399	0.1578	
Tablet – 3	0.7300	0.2921	0.4901	

* Standard deviation

* * coefficient of variation

'a' calculated 't' value by proposed Method.

'b' theoretical values at 95% confidence limit.

RESULTS AND DISCUSSION

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

In the present proposed method, Methyldopa is treated with known potassium bromate-potassium bromide excess of brominating mixture in acidic medium. The drug undergoes bromination it forms uniform orange coloured solution. These contents are thoroughly mixed and allowed to stand for five minutes at room temperature for complete bromination. Then treated with 1% of methylene blue at 670 nm the standard deviation and coefficient of variation are low, indicates high accuracy and reproducibility of this method. The data gassay values of commercial formulations were subjected to statistical evaluation for student 't' test to study the proposed method. The calculated 't' values are less than 't' theoretical values. Hence the proposed assay of drug content of the sample was estimated of drug content of the sample was estimated from the calibration curve. The results are given in Table-2.

Assay of Methyldopa in tablets

Sample	Labeled amount mg/tab	Amount found mg/tab	%Recovery
Tablet – 1	250	249.96	99.6
Tablet – 2	250	250.06	100.02
Tablet – 3	250	248.84	99.93

CONCLUSIONS

The proposed spectrophotometric method was found to be simple, precise, accurate and less time consuming. Hence the assay results to demonstrate that it is possible to use a bromate-bromide solution as an oxidimetric and brominating agent for the determination of Methyldopa in pharmaceutical formulations.

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