Available online at www.derpharmachemica.com

Scholars Research Library

Der Pharma Chemica, 2012, 4(5):1883-1886
(http://derpharmachemica.com/archive.html)

ISSN 0975-413X
CODEN (USA): PCHHAX

Extractive Spectrophotometric estimation of Eplerenone using Acid dyes in Tablet dosage forms

P. Saifulla Khan*[1], P. Raveendra Reddy[1], V. Krishana Reddy[1] and N. Appalaraju[2]

[1]Department of Chemistry, Sri Krishanadevaraya University, Anantapur-515003.
[2]Department of Pharmaceutical Chemistry, Sultan-ul-Uloom College of Pharmacy, Banjara Hills, Hyderabad-500034.

ABSTRACT

Three simple, accurate, rapid and sensitive methods (A, B and C) have been developed for the estimation of Eplerenone in its pharmaceutical dosage forms. The methods A, B and C are based on extraction of colored ion-association complex in chloroform formed between Eplerenone and BTB, BCG and BPB in potassium hydrogen phthalate buffer (pH-2.4). Which shows λ_{max} at 410nm 414nm and 425nm respectively. Beer's law is obeyed in the concentration range of 1.25-55µg/mL of Eplerenone for method A, 5-45µg/mL for method B, and 2.5-45µg/mL for method C. Results of analysis for all the methods are validated statistically and by recovery studies. The proposed methods are economical, sensitive and can be used for routine analysis of Eplerenone in bulk and tablet formulation.

Key Words: UV-Visible Spectrophotometry, Eplerenone, BromoThymol Blue (BTB), BromoCresol Green (BCG), Bromo Phenol Blue (BPB), Potassium hydrogen phthalate buffer, Chloroform, Methanol.

INTRODUCTION

Eplerenone has the chemical name Pregn-4-ene-7, 21-dicarboxylic acid, 9, 11-epoxy-17-hydroxy-3-oxo, γ-lactone, methyl ester (7α, 11α, 17α). It is off-white, crystalline powder with a molecular formula of $C_{24}H_{30}O_6$ and a molecular weight of 414.50.The structural formula is shown in Fig.1.

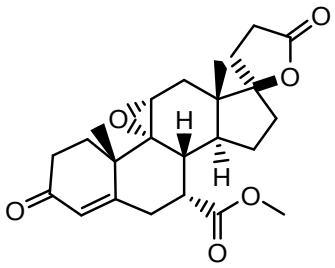


Fig.1. Structure formula of Eplerenone

Eplerenone is an aldosterone antagonist used as an adjunct in the management of chronic heart failure [1-3]. It is clinically used as antihypertensive and diuretic. Literature survey indicated that LC-MS Methods have been reported for its estimation from human plasma and urine [4-5], two spectrophotometric methods have been reported for the estimation of eplerenone in bulk and pharmaceutical dosage forms [6-7] .The present study describes simple, sensitive and economical spectrophotometric methods A, B and C for the estimation of Eplerenone in tablet dosage forms.

MATERIALS AND METHODS

Instrument: Shimadzu UV-1700 Pharmaspec with 1cm matched quartz cell was used for spectral measurements. Digi Sun Digital pH-meter was used for pH measurements.

Reagents:
All the chemicals used were of analytical grade reagents.
1. Bromo Thymol Blue (0.1%w/v): Dissolve 100mg of bromo thymol blue in the mixture of 4.0mL NaOH and 20.0mL Ethanol (95%).After the solution was made up to 100mL with distilled water.
2. Bromo Cresol Green (0.1%w/v): Dissolve 100mg of bromo cresol green in the mixture of 4.0mL NaOH and 20.0mL Ethanol (95%).After the solution was made up to 100mL with distilled water.
3. Bromo Phenol Blue (0.1%w/v): Dissolve 100mg of bromo phenol blue in the mixture of 4.0mL NaOH and 20.0mL Ethanol (95%). After the solution was made up to 100mL with distilled water
4. Potassium hydrogen phthalate buffer (pH-2.4): 4.1gm of potassium hydrogen phthalate was dissolved in 100mL of distilled water. To 25mL of above solution, 21.0mL of 0.2M HCl were added and diluted up to 100mL with distilled water to obtain a buffer solution of pH-2.4.

Experimental
A standard stock solution of the drug was prepared by dissolving 10mg of Eplerenone in 10mL of water: methanol (1:1) to get a concentration of 1000 µg/mL. This was further diluted to get the working standard solutions of 100µg/mL.

Assay procedure:
In a set of different 25mL separatory funnels, variable volumes (0.5 to 5.0mL) of Eplerenone (100µg/mL), 1.0mL of suitable acid dye (0.1%w/v) and 1.0mL of potassium hydrogen phthalate buffer (pH-2.4) were mixed. To this 10mL of distilled chloroform were added and the contents were equilibrated for 5minutes and allowed for the separation of two layers. The yellow colored organic layer were then removed and dried by adding small amount of anhydrous sodium sulphate. The chloroform layers were finally transferred quantitatively in to 10mL volumetric flasks and made up to the mark with chloroform. The absorbance of the extracted layers was then measured at λ_{max} values and plotted against the amount of Eplerenone.

The methods were extended for the determination of Eplerenone in tablet formulations (EPITUS® 25mg). Ten tablets were accurately weighed and powdered. Tablet powder equivalent to 50 mg of Eplerenone was dissolved in 50 mL of water: methanol (1:1) in volumetric flasks. 5 mL of the above solution was diluted to 50 mL to get the working sample solution contains of 100µg/mL Eplerenone and analyzed as given under the assay procedure for bulk samples. The analysis procedure was repeated three times with tablet formulations and the results of analysis are shown in Table-2.

Recovery studies:
To ensure the accuracy and reproducibility of the results obtained, adding amounts of pure drug to the previously analyzed formulated samples and these samples were reanalyzed by the proposed method and also performed recovery experiments. The percentage recoveries thus obtained were given in Table-2

RESULTS AND DISCUSSION

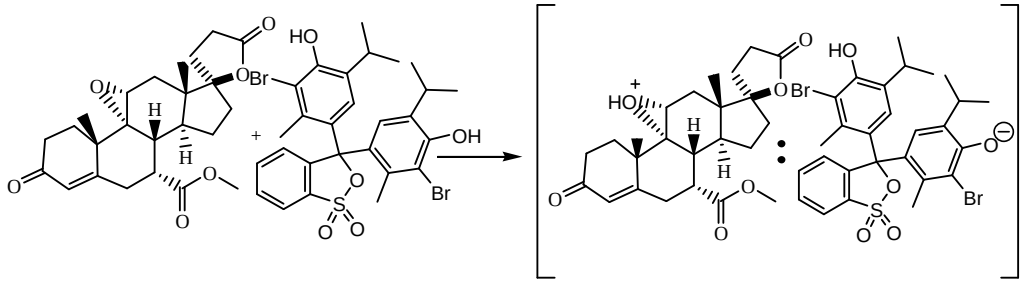
In the present study all the three acid dyes bromo thymol blue (BTB), bromo cresol green (BCG) and bromo phenol blue (BPB) form yellow colored soluble species with Eplerenone in potassium hydrogen phthalate buffer solution of pH 2.4, which are quantitatively extractable in to chloroform. The extracted species showed absorption maxima in the wave length range410-425nm. The effect of pH on the color formation was studied in the range 2.0 to 4.0. It was

noticed that all the colored species exhibited maximum absorbance at pH 2.4 which was chosen for analytical studies. The stabilities of the yellow colored species were evaluated by measuring the absorbance of the experimental solutions for 8 hours with 15 minutes time interval. It was observed that the color was stable up to 5 hours and then gradually decreased.

The acid dyes, BTB, BCG and BPB are acid-base indicators and at low pH they undergo deprotonation forming $H^+$and In^- species. The drug, Eplerenone possesses an epoxy linkage which may be undergoing protonation in acid buffer solution converting in to positively charged species as shown in the structure. Thus , the cationic drug species and anionic acid dye combine forming ion-association complexes, the potential analytical species, whose absorbance is measured at 410nm,414nm and425nm for BTB,BCG and BPB respectively Fig.2.

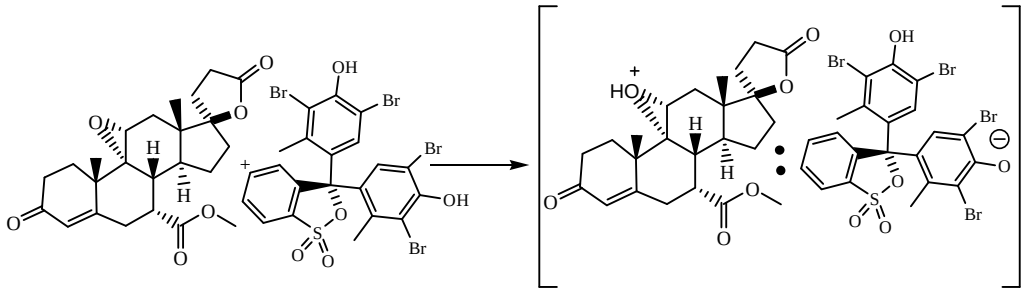
CHEMISTRY OF COLORED SPECIES

Method A



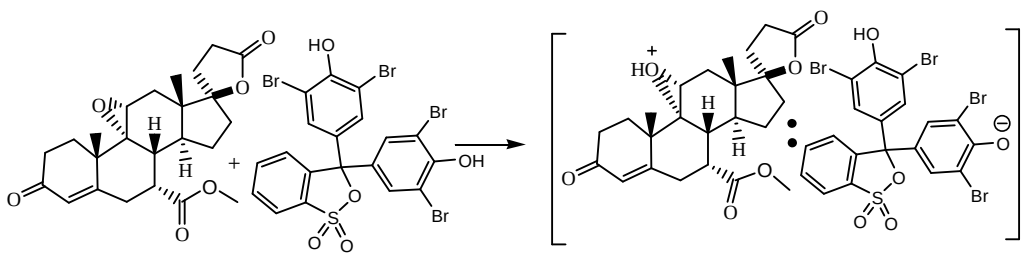
Eplerenone Bromo Thymol Blue Ion-association complex

Method B



Eplerenone Bromo Cresol Green Ion-association complex

Method C



Eplerenone Bromo Phenol Blue Ion-association complex

Fig.2. Formation of Ion-Association complexes between Eplerenone and Acid dyes

The measured absorbance values were found to be linear giving straight line in the concentration range of 1.25-55µg/mL, 5-45µg/mL and 2.5-45µg/mL of the drug with BTB, BCG and BPB respectively. The optical

characteristics such as absorption maxima, Beer's law limits, molar absorptivity and sandell's sensitivity are presented in Table-1. The regression analysis using the method of least squares was made and the slope (m), intercept(c) and the correlation coefficient of the regression plots are summarized in Table-1. The reproducibility and precision of the methods are very good as shown by the values of % RSD. The mean percentage recovery value of 99.95% for Method A, 98.59% for Method B and 99.69% for Method C, indicate non-interference from the excipients present in the powder for injection. All the validated parameters are summarized in Table-2

Table-1: OPTICAL CHARACTERISTIC AND PRECISION DATA.

Parameters	Method A	Method B	Method C
λ_{max} (nm)	410	414	425
Beer's law limits(µg/mL)	1.25-55	5-45	2.5-45
Molar Absorptivity(Lt/mole/cm)	$1.036x10^4$	$7.875x10^3$	$9.119x10^3$
Sandell's Sensitivity (µg/cm^2 /0.001 absorbance unit)	0.040	0.052	0.045
Regression Equation* (Y= mx +c)			
Slope(m)	0.0173	0.0185	0.0216
Intercept(c)	0.0042	0.0023	0.0064
Correlation Coefficient (r)	0.9998	0.9990	0.9993
Precision(% RSD)	0.395	0.850	0.550

Table-2: ASSAY OF OLOPATADINE IN TABLET FORMULATIONS.

S.No	Labeled Amount(mg)	*Amount obtained by proposed method (mg)			** % Recovery by the proposed method		
		Method A	Method B	Method C	Method A	Method B	Method C
1	25	24.96	24.95	24.94	100.22	98.81	99.3
2	25	24.98	24.85	24.83	99.89	99.05	99.69
3	25	24.95	24.24	24.90	99.76	97.95	100.1

** Average three determinations.* *** After spiking the sample.*

CONCLUSION

The proposed methods are simple, sensitive, accurate and economical for routine analysis of Eplerenone in bulk and its parenteral formulations. Based on molar absorptivity data and Beer's law range, it may be concluded that among the proposed methods, method A is more sensitive than method C which in turn is more sensitive than the method B.

Acknowledgement
The author acknowledges M/s Vishnu Chemicals Limited, Hyderabad for the supply of Eplerenone as gift sample for providing the necessary facilities to carry out the research work.

REFERENCES

[1] Inspra, **2003**. Eplerenone (Product Information). Pfizer Pharmaceuticals.
[2] W.B.White, D.Duprez and M.A.Weber, *Hypertension*, **2003**,41,1021.
[3] M.h.Weinberg, B.roniker and R.J.Weiss *Am.J.Hypertens.* **2002**, 15,709.
[4] J.Y.Zhang, D.M.Fast and A.P.Breau *J.Chromatogr. B Analyt.Technol.Biomed. Life Sci*., **2003**,787,333.
[5] J.Y.Zhang, D.M.Fast and A.P.Breau *J.Pharm.Biomed.Anal*.**2003**,31,103.
[6] V.S.Banode,P.B.Khedekar and P.S.Tartye, *International Journal of Chem. Tech Research* , **2011**,3(1),398-402.
[7] A.L.Ganure, M.H.G.Dehghan, D.S.Patel and J.N.Sangshetti, *Der Pharma Chemica*, **2011**,3(1),420-425