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Spectrophotometric Estimation of Eplerenon in Bulk Drug and Tablets

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Abstract: The present paper describes a simple, precise and economical spectrophotometric method which has been developed and validated for the estimation of Eplerenone (EPL) in bulk and pharmaceutical formulations. The method involves absorbance measurement at 242.5 nm in methanol-water (80:20) and Estimation of EPL is done by using A (1 %, 1 cm), interpolation method on calibration curve, regression equation and comparison with standard. Results of the analysis are validated statistically and by recovery studies and were found to be satisfactory.
Key words: Eplerenone, Interpolation method on calibration curve, Regression equation, comparison with standard.

Introduction:[1, 2]

EPL is clinically used as antihypertensive and diuretic as it binds to the mineralocorticoid receptors and blocks the binding of aldosterone, a component of the renin-angiotensin-aldosterone system. Chemically EPL is 9α,11α-Epoxy-7α-methylcarboxy-3-oxo-17α-pregn-4-en-21,17β-carbolactone. It is clinically used as antihypertensive and diuretic.

It is not official in any of the pharmacopoeias. It is listed in The Martindale. Literature survey reveals that no analytical methods are reported for estimation of Eplerenon in tablet dosage form. Hence it was planned to develop quantitative analytical method by using spectrophotometer with good accuracy, simplicity, precision and economy by using spectrophotometer.

Materials and Method:

Pure sample of EPL was obtained from MSN Lab. Pvt. Ltd. Medak as a gift sample. Shimadzu UV-1700 UV/VIS spectrophotometer was used with 1 cm matched quartz cells. Tablets of 25 mg strength were procured from local pharmacy of commercial brands Eptus 25 (Glenmark Pharmaceutical Ltd.). Methanol and water of HPLC grade were procured from Merck Co., Mumbai.

Spectrophotometric method:

Accurately about 50 mg of the pure drug was weighed and dissolved in 40 ml of methanol and volume was made up to 50.0 ml with distilled water to give standard stock solution 1000.0 µg/ml.

The aliquot portion of standard stock solution was appropriately diluted with methanol-water 80:20 solution to get the final concentration 10.0 µg/ml of EPL. The solutions were scanned in the spectrum mode from 400 nm to 200 nm wavelength range as shown in *Figure 1*. The λ_{max} of Eplerenon was found to be at 242.5 nm. The drugs followed the Beer-Lamberts law in the range of 0 to 45 µg/ml.

Tablet powder equivalent to 50.0 mg of EPL was weighed and dissolved in 40.0 ml of methanol and shaken for 15 min. Then volume was made up to 50.0 ml with water and the solution was filtered through Whatman filter paper no. 41 to get stock solution of concentration 1000.0 µg/ml. Aliquot portions of this solution were diluted with methanol-water 80:20 solution to produce 10.0 µg/ml working sample solution. The absorbance's of working standard solution and working sample solution was measured at 242.5 nm against the blank. Estimation of EPL was done by using following formulae's.

a. Using A (1 %, 1 cm)

$$\text{Estimated amount} = \frac{A_u \times d}{A\ (1\ \%, 1\ cm)} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots(1)$$

b. Interpolation method on calibration curve

$$\text{Estimated amount} = \text{Concentration } (\mu g/ml) \times d \times 10^{-4} \quad \ldots\ldots(2)$$

c. Regression equation

$$\text{Absorbance} = 0.0514 \times \text{Concentration} + 0.0059 \quad \ldots\ldots\ldots\ldots\ldots(3)$$

$$\text{i.e., Estimated amount} = \frac{\text{Absorbance} - 0.0059}{0.0514} \times d \quad \ldots\ldots\ldots(4)$$

d. Comparison with standard

$$\text{Estimated amount} = \frac{A_u}{A_s} \times C_s \quad \ldots\ldots(5)$$

Further percent labelled claim was calculated by using formula.

$$\text{Labelled claim (\%)} = \frac{\text{Amt estimated} \times \text{Avg weight of tablet}}{\text{Weight taken} \times LC} \times 100 \quad \ldots\ldots(6)$$

Where, A_u = Absorbance of tablet working solution

A_s = Absorbance of standard working solution

A (1%, 1 cm)= 518.10

C_s = Weight of standard (g)

d = dilution factor

LC = Labelled claim

The result of estimation is shown in **Table 1.**

Table 1: Studies of results of estimation of marketed tablet formulation

Serial No.	Labelled claim (%)			
	A (1 %,1 cm)	Interpolation method	Regression equation	Comparison with standard
1	99.79	99.34	99.34	99.96
2	99.28	98.80	98.80	98.86
3	100.13	99.73	99.73	100.04
4	99.64	99.21	99.21	99.18
5	99.54	99.14	99.14	99.64
Mean	99.67	99.24	99.24	99.53
SD	0.2813	0.3015	0.3015	0.4535
RSD	0.0028	0.0030	0.0030	0.0045
RSD (%)	0.2822	0.3038	0.3038	0.4556
s_x	0.1258	0.1348	0.1348	0.2028

Table 2: Accuracy studies

Serial No.	Wt of tablet powder (g)	Concentration of tablet + standard (µg/ml)	Absorbance	Recovery (%)
1	0.1562	10 + 2	0.594	100.98
2	0.1559	10 + 4	0.689	100.52
3	0.1571	10 + 6	0.792	100.31
Mean				100.60
SD				0.2798
RSD				0.0028
RSD (%)				0.2781
s_x				0.1614

Average weight of tablet is 0.0823 g

Validation of method [3, 4, 5,]

The proposed method was validated on the basis of parameters namely accuracy, precision, specificity, ruggedness and linearity and range.

Accuracy of the proposed method was ascertained by carrying out recovery studies using standard addition method. The results are shown in Table 2.

Precision of an analytical method is expressed as SD or RSD of a series of measurements. It was ascertained by replicate estimation of drug by the proposed method.

For specificity an accurately weighed 50.0 mg equivalent of tablet powder was stored for 24 h under following different conditions.

- At room temperature (normal)
- At 50^0 after addition of 1.0 ml of 0.1 N NaOH (alkali)
- At 50^0 after addition of 1.0 ml of 0.1 N HCl (acid)
- At 50^0 after addition of 1.0 ml of 3 % H_2O_2 (oxide)
- Heat at 50^0

After 24 hours, the contents of the flask were subjected to same procedures as previously described.

Test for ruggedness was carried out by repeating the procedure under different conditions, i.e., on different days, at different time and by different analysts.

Linearity and range study was done by preparing concentration in the range of 80 -120 % of test concentration and absorbance values were recorded at 242.5 nm. The plot of linearity and range is shown in Figure 2.

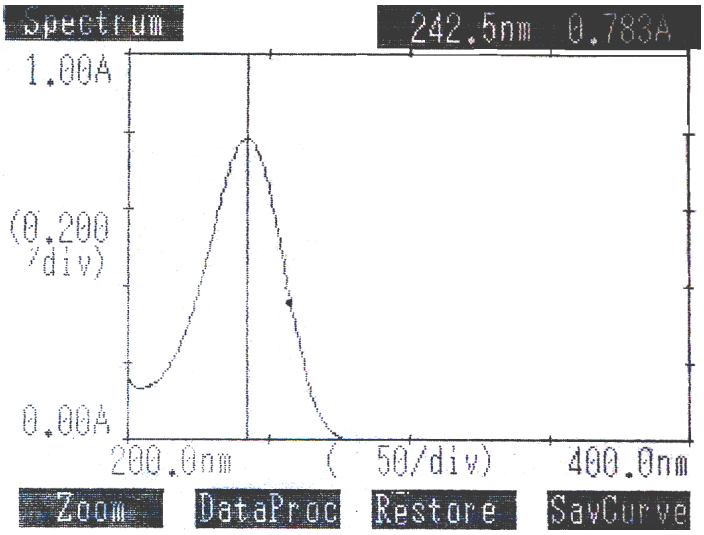

Figure 1: UV spectra of EPL

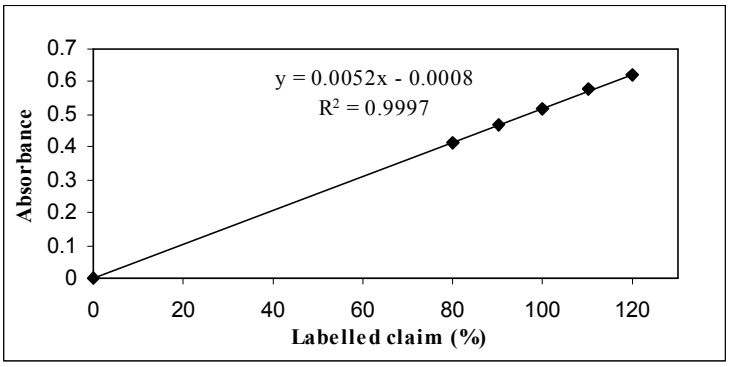

Figure 2: The plot of Linearity and Range studies

Table 3: Specificity studies

Serial No.	Environment	Wt of tablet powder (g)	Absorbance	Labelled claim (%)
1	Normal	0.1612	0.504	99.35
2	Heat	0.1579	0.491	98.81
3	Acid	0.1589	0.456	91.19
4	Alkali	0.1601	0.111	22.03
5	Oxide	0.1595	0.406	80.88

Average weight of tablet is 0.0823 g

Table 4: Results of ruggedness study

Condition	Label claim*	SD	RSD
Intraday	99.96	0.2939	0.0029
Interday	99.95	0.1569	0.0016
Different analyst	99.71	0.1821	0.0018

*Results are mean of five replicates

Results and Discussion

The methods for the estimation of EPL in tablet dosage form was found to be simple accurate and reproducible. Beer-Lambert's law was obeyed in the concentration range of 0-45 µg/ml . The method was validated as per the ICH and USP guidelines. The values of SD or RSD are within the prescribed limit of 2 %, showing high precision of method and recovery was close to 100%**.** During the linearity study it was observed that absorbance values of EPL in the marketed formulation were linear in the range of 80% to 120% of test concentration with R^2 close to one. Hence these methods can be useful in the routine analysis of EPL in bulk drug and formulations.

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