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HPLC Estimation of Perindopril Erbumine in Tablet Dosage Form

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In the present investigation, a simple method for estimation of coversyl has been developed with a simple mobile phase (Hypersil, C8, 250 × 4.6 mm, 5 µm column). Mobile phase was made up of heptane sulphonic acid buffer (pH 2.0) and acetonitrile in ratio of 60:40. Detector used was a UV detector and detection was carried out at 215 nm. Linearity was determined at five levels over the range of 60 to 140 % of working concentration.

Key Words: Perindopril erbumine, Coversyl, HPLC.

INTRODUCTION

Perindopril erbumine is a prodrug which, following oral administration, is hydrolyzed to its active metabolite perindoprilat. Perindopril acts as an angiotensin converting enzyme inhibitor (ACE-inhibitor) thereby reducing angiotensin II generation. The structure of perindopril erbumine is shown in Fig. 1. It is official in European Pharmacopoeia[1]. Perindopril erbumine is a white, crystalline powder with a molecular weight of 368.47 (free acid) or 441.61 (salt form). It is freely soluble in water (60 % w/w), alcohol and chloroform.

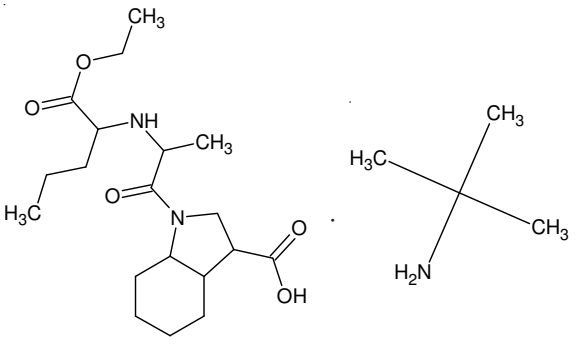

Fig. 1. Perindopril erbumine

A few spectrophotometric[2,3], HPLC[4] and LC-MS[5] methods were reported earlier for the determination of perindopril in bulk and pharmaceutical dosage form. The objective of this study is to develop new, sensitive reversed phase high performance liquid chromatographical method for perindopril erbumine in pharmaceutical dosage form and validation of method as per ICH guidelines[6].

EXPERIMENTAL

Acetonitrile was used as mobile phase. Heptane sulphonic acid sodium salt, perchloric acid and triehylamine were taken for preparation of buffer of 2.0 ± 0.5 pH as mobile phase. All the reagents used were of analytical grade and all of work was done with milli-Q water. Instruments used were HPLC of Shimadzu corporation with hypersil, C8, 250 × 4.6 mm, 5 µm column, UV detector of model number UV-2450 of Jasco. pH meter of labonia, balance of sartorious of make BP110S. Karl-Fischer autotitrator of metrohm-titrino. Dissolution apparatus, disintegration apparatus and centrifuge used in the study were of electrolab corporation.

UV spectrophotometeric method for perindopril: Stock solution of perindopril (Coversyl tablets; Servier Labs, U.K.) was prepared by dissolving 10 mg of drug in 10 mL of methanol (1000 µg/mL). From this 5 mL solution was taken and diluted up to 50 mL with simulated gastric fluid (SGF). Further dilutions (1 to10 µg/mL) were prepared and absorbances were measured at 215 nm. Concentrations were prepared 2, 4, 6, 8, 10 µg/mL and absorbances were found to be 0.241, 0.496, 0.735, 0.966 and 1.204, respectively. Calibration curve as shown in Fig. 2 shows that absorbance of perindopril is proportional to its concentration.

RESULTS AND DISCUSSION

A reverse phase high performance liquid chromatographic method was developed using HPLC of Shimadzu corporation

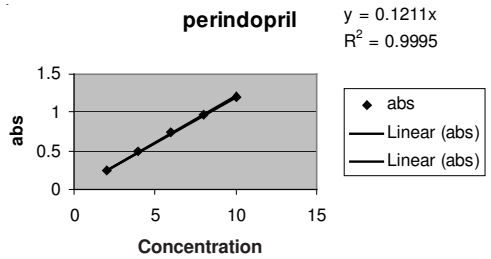

Fig. 2. Calibration curve for perindopril

with hypersil, C8, 250 × 4.6 mm, 5 µm column, with a variable wavelength programmable UV detector of model number UV-2450. Mobile phase selected was acetonitrile and buffer of pH 2.0 ± 0.5 system. Flow rate of the mobile phase was maintained at 1.5 mL/min oven temperature kept was 60 ºC. The quantity injected was 50 µL and the λ_{max} was fixed to be 215 nM.

Assay of pharmaceutical preparation:

Standard preparation: 500 µg of standard solution of perindopril erbumine was prepared in mobile phase. Further 5 mL of this solution was diluted to 25 mL with mobile phase to obtain working concentration.

Sample preparation: Five coversyl tablets were taken along with mobile phase and were sonicated and volume was made up to 200 mL. 10 mL of this solution was centrifuged for 15 min at 3500 rpm and supernatant was used.

Percentage assay for perindopril tablets was calculated (Table-1) and their respective chromatograms are shown in Figs. 3 and 4.

TABLE-1
ASSAY OF PERINDOPRIL ERBUMINE
TABLET (4 mg) DOSAGE FORM

Test No.	% Assay found by the proposed method
1	100.73
2	100.02
3	101.72
4	98.52
5	99.95
6	99.38
7	99.69

Validation parameters

Specificity

Interference from placebo: No interference was observed from blank and placebo at retention time of perindopril. Peak purity index for perindopril peak was found above 0.99 in standard and sample preparation which is well under specified acceptance criteria.

Interference from degradation impurity: Forced degradation studies were done and satisfied results were obtained as degradation impurities in all degraded sample preparations were well separated from main peak. Peak purity index for perindopril for all the studies was found above 0.99 in degraded preparation and sample preparation. Peak purity results are given in Table-2.

Linearity: Linearity was determined at five levels over the range of 60 to 140 % of working concentration. The areas obtained were directly proportional to the concentration of

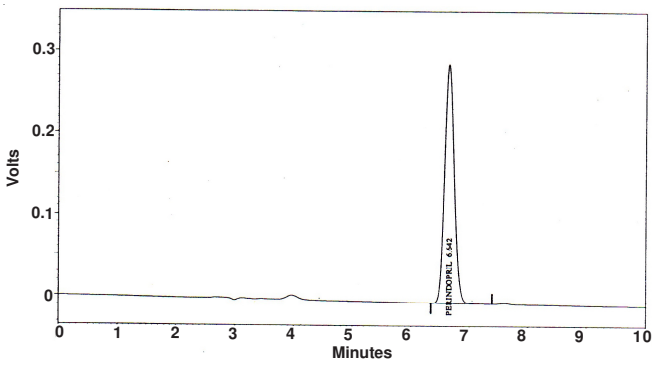

Fig. 3. Chromatogram of standard test preparation

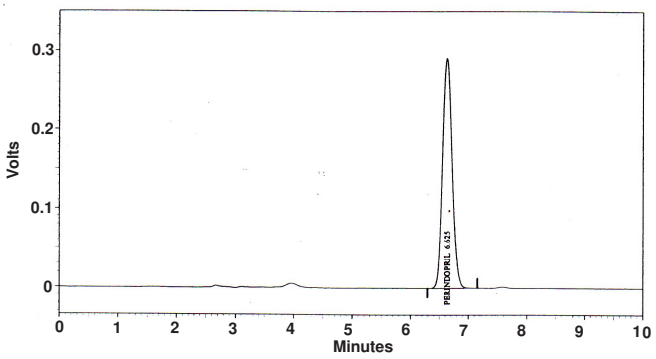

Fig. 4. Chromatogram of test preparaiton

TABLE-2
PURITY INDEX FOR SAMPLE PREPARATION
OF PERINDOPRIL ERBUMINE

Sample	Purity index
API preparation	1.00
Standard preparation	1.00
Sample preparation	1.00

analyte in solution. The linearity was confirmed by correlation coefficient which was 0.9994, representing good fit of the line over the points. Results of linearity are shown in Table-3.

TABLE-3
OBTAINED LINEARITY PARAMETERS FOR
PERINDOPRIL ERBUMINE

Correlation coefficient (R^2)	0.99840
Slope of regression line	28741
Y-intercept	2252.8
Residual sum of squares	3995476329.3

Accuracy: Accuracy was determined over the same range as that on which the linearity is established, *i.e.*, 60 to 140 %. Calculated amount of perindopril was added in placebo to obtain 60, 100 and 140 % of sample concentration. Recovery at each level and percentage mean recovery should be between 98 to 102 and % RSD should not be more than 2.0. Reported recovery was 98.5 to 101.8. And % RSD at each level was found within acceptance criteria. Results of accuracy are given in Table-4.

Method precision (repeatability): Method precision was established by assaying six test preparations under same conditions. Six replicates of sample were prepared at test concentration and analyzed on the same day. Individual % assay, % RSD and 95 % confidence interval were calculated. Method

TABLE-4
OBTAINED ACCURACY DATA FOR PERINDOPRIL ERBUMINE

% Concentration	Mean % recovery	% RSD
60	100.7	1.10
100	99.4	0.71
140	98.7	0.18

is said to be précised if the % RSD of six replicates are not outside 2 %. % RSD of six replicates of sample was found to be 0.72 % which is well under limits. Results of accuracy are shown in Table-5.

TABLE-5
OBTAINED DATA FOR METHOD PRECISION OF PERINDOPRIL ERBUMINE

Mean	% RSD	95 % confidence interval
98.7	0.92	97.7-99.6

Intermediate precision (ruggedness): Intermediate precision was done by doing different analysis using a different HPLC system, repeating the procedure which was been followed for method precision on a different day using same lot of sample. The mean assay value was calculated and compared with the mean assay value obtained in the method precision study. The differences of the mean assays obtained were calculated. Here, for a method to be said as précised, difference in the mean assay value obtained in intermediate precision study should not be more than 2.0 % as well as % RSD of six replicates of sample should not be more than 2.0 %. results of intermediate precision are shown in Table-6.

TABLE-6
OBTAINED DATA FOR INTERMEDIATE PRECISION OF PERINDOPRIL ERBUMINE

Mean	% RSD	95 % confidence interval	Difference
98.5	0.72	97.8-99.3	0.2

Conclusion

It is, thus, concluded that the proposed method is simple, cost-effective, safe, accurate and precise. This method can be successfully employed in the routine analysis of perindopril in tablet dosage form.

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