INTRODUCTION
Perindopril[11] is chemically H-indole-2-carboxylic acid, AND a competitive inhibitor of angiotensin-converting enzyme (ACE). It is used as a diuretic in treatment of hypertension, as well as in cardiac failure. Indapamide[6-12] is chemically 4-chloro-N-(2-methyl-2,3-dihydroindol-1-yl)-3-sulfaamyl-benzamide a thiazide-like diuretic.[6] The combination of perindopril and indapamide is used in the management of hypertension.[1-12] There are few HPLC[13] and HPTLC methods have been reported for individual determination of these drugs. Fixed dose combination containing perindopril and indapamide is available in tablet form in the market. Few methods have been reported so far for simultaneous estimation of these drugs, but aim of this work was to develop a simple accurate, rapid, and precise reverse phase HPLC method for determination of perindopril and indapamide in solid dosage form.

MATERIALS AND METHOD

Instruments
High performance liquid chromatograph, Jasco high performance liquid chromatograph (LC-10AT), Ultra-Visible (UV-VIS) detector, Class-VP software. A BDS Hypersil C₁₈ column (25cmx4.6mm, 5 µm) in Jasco M-530 UV spectrophotometer was used.

Chemicals and Reagents
Tablet formulation (Coversyl plus by Surdia pharmaceuticals) containing 4 mg perindopril and 6.25 mg of idapamide was procured from market. Acetonitrile HPLC grade and diluted with mobile phase such that the final concentration of perindopril and indapamide was found to be in the linear range 20-160 µg/ml and 15-50 µg/ml respectively with detection at 210 nm. Separation was complete in less than 15 min. The method was validated for linearity, accuracy, precision, and specificity.

Working Standard Solution
5 ml of standard stock solution from (I) and 5 ml from (II) were taken in a 25 ml volumetric flask and diluted up to mark with mobile phase.

Sample Solution
Twenty tablets of perindopril plus indapamide, locally available, were crushed and powdered material. A portion of it which was equivalent to 25 mg perindopril and 6.25 mg of idapamide was placed in to a 250 ml volumetric flask containing about 50 mL of mobile phase. Powder was allowed to dissolve and sonicated for 5 mins. made up the volume with mobile phase mixed well and filtered through 0.45 µm PVDF filter (80 mcg/ml of perindopril and 25 µg/ml of indapamide). Filtrate was collected by discarding the first few ml of the filtrate.

Instrumentation and Chromatographic Conditions
Chromatographic separation was performed on Jasco high performance liquid chromatograph, equipped with variable wavelength detector. A double-beam spectrophotometer (Jasco-M530) was used for scanning and selecting the detection wavelength. Selected wavelength of detection was 210 nm. A reverse-phase BDS Hypersil C₁₈ column (25cmx4.6mm, 5 µm) was used for analysis. The mobile phase comprising of mixture of potassium dihydrogen phosphate buffer (pH 2.6) and acetonitrile (65:35) at a flow rate of 1.5 ml min⁻¹ with detection at 210 nm.

Assay (Precision)
10 µL of mixed working standard and sample solution (n=6) were injected into injector of HPLC and peak were recorded. From the peak area (response factor) of perindopril and indapamide the amount of drug samples (n=6) were calculated. The values are given in table I.

Method Validation
As per ICH[13] guidelines the method was validated, following parameters were evaluated and are given in the table II.

Linearity and Calibration
Standard stock solution from I and II were taken in different volumetric flask and diluted with mobile phase such that the final concentration of perindopril were in the range of 20-160 µg/ml and indapamide in the range of 15-50 µg/ml. Evaluation of two drugs was performed with UV detector at 210 nm. Peak area was recorded for all the peaks. The plot of response factor (peak area) versus the respective concentrations of perindopril and indapamide were found to be in the linear range 20-160 µg/ml and 15-50 µg/ml respectively with coefficient of correlation (r=0.9997) and (r=0.9992) respectively.

Recovery Study
To insure the reliability and accuracy of the method recovery studies were carried out by mixing a known quantity of standard drug with pre analyzed samples and contents were reanalyzed by proposed method. The mean recoveries of perindopril and indapamide were 99.66 and 99.60 respectively any positive or negative interference of excipients was not observed in the analysis of tablets.
Accuracy of the method was checked by recovery studies. Precision of the method was studied by analysis of multiple samplings of homogeneous sample.

System suitability
System suitability tests were carried out on freshly prepared working standard solution of perindopril and indapamide. 10 µl of working standard solution was injected into the chromatograph under the proposed chromatographic conditions and following parameters were studied to evaluate the suitability of system.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Perindopril</th>
<th>Indapamide</th>
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<tbody>
<tr>
<td>Number of Theoretical Plates</td>
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<td>Resolution</td>
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<td>Calibration Range</td>
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<td>Retention Time</td>
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RESULT AND DISCUSSION
This method resulted in a good separation between perindopril and indapamide. The high sensitivity of the method is confirmed by LOQ values. The detection range was found to be in the range from 20-160 µg/ml for perindopril and 15-50 µg/ml for indapamide in the proposed method no positive or negative interference of excipients present in the formulation was observed.

CONCLUSION
The proposed HPLC method was found to be highly accurate, sensitive and precise. Therefore this method can be applied for the routine analysis of perindopril and indapamide in its tablet dosage form as well as in bulk drugs.

REFERENCES

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