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RESEARCH PAPER



# Simultaneous Determination of Pseudoephidrine HCl (PSE) and Terfanidine (TER) from Formulations by Reversed-Phase Ion Pair High-Performance Liquid Chromatography (RP-HPLC)

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**ABSTRACT**

*A new simple, precise, rapid, and selective reversed-phase ion pair high-performance liquid chromatography (RP-HPLC) method has been developed for the simultaneous determination of pseudoephidrine (PSE) and terfanidine (TER) from tablets using 60:15:25 acetontrile:methanol:water (v/v) containing 2.9 g sodium lauryl sulfate/liter, pH adjusted to 3.1 using phosphoric acid as a mobile phase and $C_{18}$ Spherisorb ODS 2 (3 μm, 5 cm × 4.6 mm i.d.) as stationary phase. Detection was carried out using a UV detector at 254 nm. A constant flow of 1.0 ml/min was maintained throughout the analysis. Retention times for PSE and TER were 1.90 and 7.35 min, respectively. Linearity range and percentage recoveries for PSE and TER were 24–1200 and 12–600 μg/ml, and 100.01 and 100.4%, respectively.*

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## INTRODUCTION

Pseudoephidrine hydrochloride (PSE) is a direct and indirect acting sympathomimetic agent. It is a stereoisomer of ephidrine having similar action but stated to have less pressor activity and central nervous system effects. Pseudoephidrine and its salts are given by mouth for the symptomatic relief of nasal congestion.

Terfanidine (TER) is an antihistamine that does not generally cause sedation or antimuscarinic effect. Ventricular arrhythmias have been associated with raised blood concentration of TER and the recommended dose should not be exceeded.

There are currently few combination dosages of these two drugs on the market. These are used for treatment of allergic cold.

PSE and TER are determined from active substances by titrimetric method (1–3). In tablets either alone or in combination with various drugs they are determined by HPLC (4–8) or spectophotometry (9,10). George et al. has reported a method for the individual determination of these two drugs from the combined dosage form by HPLC using two different columns and mobile phases (11).

An attempt was therefore made to develop a new, rapid, and sensitive method for the simultaneous determination of PSE and TER. The results are discussed and presented in this paper.

## EXPERIMENTAL

### Instrumentation

A liquid chromatographic system from Waters comprising an autoinjector, quarternary gradient low-pressure pump, and UV-visible variable-wavelength detector connected to Millenium software for controlling the instrumentation as well as processing the data generated, were used.

### Reagents and Chemicals

Sodium lauryl sulfate and phosphoric acid were of AR grade and acetonitrile and methanol were HPLC grade, supplied by S.D. Fine Chemicals, Tarapur, Thane, Maharashtra, India.

Reference standards pseudoephidrine hydrochloride and terfanidine were obtained from M/S Merind Ltd., Bhandup, India. Purity of PSE and TER standards was found to be 99.80 and 99.14%, respectively, by USP method.

### Chromatographic Conditions

Mobile phase consisted of a mixture of 60:15:25 acetonitrile:methanol:water (v/v) containing 2.9 g sodium lauryl sulfate/liter, pH adjusted to 3.1 using phosphoric acid. $C_{18}$ Spherisorb ODS 2 (3 μm, 5 cm × 4.6 mm i.d.) column was used as stationary phase. A constant flow of 1.0 ml/min was maintained throughout the analysis. Detection was carried out using a UV detector at 254 nm.

### Standard Preparation

#### Standard Stock Solution

Standard stock solutions of 3.0 mg/ml of PSE and 1.5 mg/ml of TER were prepared by dissolving 300 mg of standard PSE and 150 mg of standard TER in 100 ml of mobile phase.

#### Working Standard Solution

Ten milliliters of each standard stock solution was diluted to 50 ml with mobile phase. This gave working concentrations of 600 μg/ml of PSE and 300 μg/ml of TER, which were used as working standards.

### Sample Preparation

Twenty tablets were weighed and crushed to fine powders. Powder samples equivalent to 60 mg of PSE and 30 mg of TER were weighed in a 100 ml volumetric flask. Fifty milliliters of mobile phase was added; after sonication for 10 min, the solution was cooled and diluted up to the mark with mobile phase. The solution was centrifuged and the supernatant was used for the analysis.

### Calibration

From the above stock solutions, various aliquots were pipeted out into different 50 ml volumetric flasks. These were diluted to the mark with the mobile phase to provide solutions of 24–1200 μg/ml of PSE and 6–600 μg/ml of TER.

### Evaluation

Peak areas for all the peaks were recorded. From the peak areas respective amounts were computed as follows:

$$\text{Amount} = \frac{\text{Rspl} \times C \times D \times \text{ave. wt.}}{\text{Rstd} \times W}$$

where Rspl is area of PSE/TER peak in sample solution; Rstd is area of PSE/TER peak in standard solution; $C$ is concentration of standard in mg/ml; $D$ is dilution factor for sample; and $W$ is weight of tablet powder in mg.

## RESULTS AND DISCUSSION

### Chromatography

Reversed-phase LC alone of PSE and TER posed various problems. Acetonitrile and water used in different combination did not yield good peak shape. A study carried out using mobile phases of acetonitrile and buffer in the pH range of 3–5 gave very low retention time for PSE (which eluted in dead volume). Any attempt to retain PSE for longer time by increasing the aqueous content of the mobile phase resulted in very high retention times for TER. Mobile phases comprising acetonitrile and buffer above pH 6.5 retained these drugs but yielded poor and distorted peak shapes.

The use of ion pair chromatography using sodium salts of small-chain aliphatic acids did not help much in achieving good separation.

Addition of sodium lauryl sulfate to the mobile phase and adjustment of the mobile phase pH to 3.1 solved these problems, giving reasonably good retention for PSE, i.e., 1.9 ml (column dead volume 0.82 ml) and a faster elution for TER under the prescribed conditions.

PSE and TER were well-resolved in a reasonable time of 8 min. The resolution between PSE and TER was 10.3. This is a fairly good resolution by USP standards. A representative graph of the same is shown in Fig. 1. The dilution with the mobile phase helped to minimize the peak that appeared as a result of the diluent, and facilitated quantification of PSE.

### System Suitability

System suitability test was applied to a representative chromatogram to check various parameters such as column efficiency, resolution, and peak tailing. The results obtained are shown in Table 1 and are in concurrence with the USP requirements.

### Linearity

Microsoft Excel software was used to plot the peak areas versus concentrations in micrograms per milliliter.

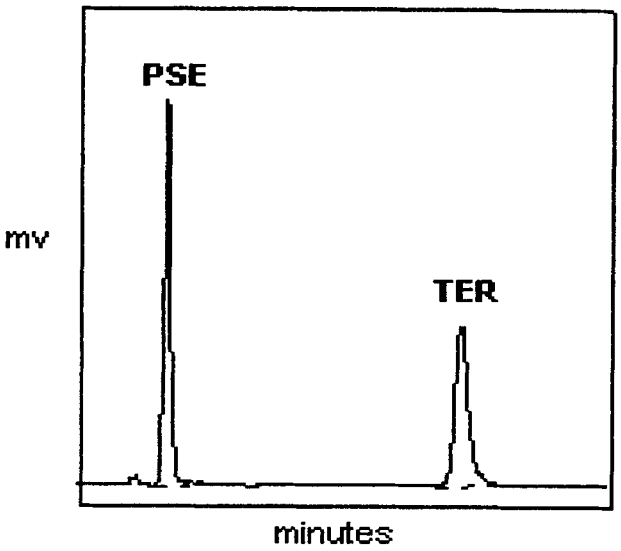


**Figure 1.** Representative chromatogram of PSE and TER.

Calibration graphs for PSE and TER are shown in Fig. 2. PSE showed linearity of response between 24 and 1200 μg/ml. TER showed linearity of response between 6 and 600 μg/ml. These linearities were represented by linear regression equations as follows:

$$\text{APSE} = 668.36x + 110.08 \qquad (r = 1)$$

$$\text{YTER} = 1184.6x - 228.24 \qquad (r = 1)$$

### Assay

The PSE and TER contents found in tablets by the proposed method are tabulated in Table 2. Low relative standard deviation (RSD) values indicate that the method is precise and accurate.

### Accuracy and Precision

Precision of the method was studied by making seven injections of the same standard solutions, with concen-

*Table 1*

*System Suitability Parameters*

| No. | Parameters | PSE | TER |
|---|---|---|---|
| 1 | Theoretical plates | 877 | 1721 |
| 2 | Resolution factor | - | 10.23 |
| 3 | Tailing factor | 1.02 | 1.40 |
| 4 | SD | 0.96 | 0.74 |

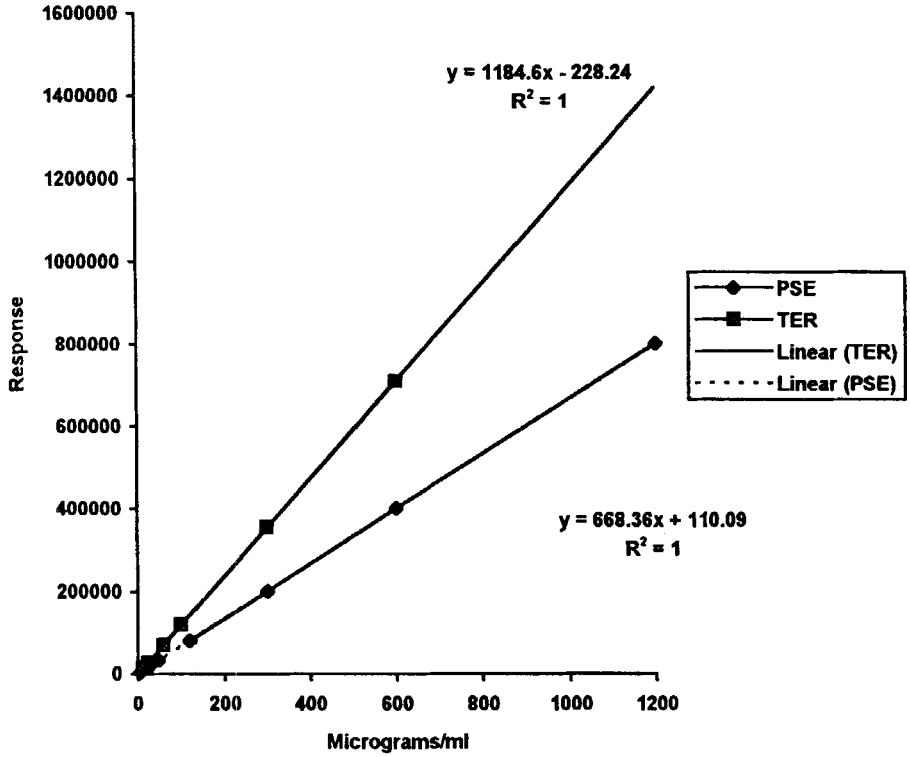


**Figure 2.** Linearity of PSE and TER.

trations close to expected concentration in the samples, and determining the standard deviation.

Recovery experiments were carried out by spiking the already analyzed samples of tablets with three different known concentrations of standard PSE and TER.

*Table 2*

*Results of HPLC Analysis of Tablets*

| | Sample No. | PSE (%) | TER (%) |
|---|---|---|---|
| Lot 1 | 1 | 99.45 | 98.14 |
| | 2 | 98.40 | 98.64 |
| | 3 | 99.12 | 98.89 |
| | 4 | 99.16 | 98.47 |
| | 5 | 98.54 | 99.12 |
| | Mean | 98.93 | 99.12 |
| | RSD | 0.44 | 0.38 |
| Lot 2 | 1 | 100.14 | 99.14 |
| | 2 | 99.67 | 98.76 |
| | 3 | 99.43 | 99.95 |
| | 4 | 99.09 | 99.00 |
| | 5 | 100.62 | 99.19 |
| | Mean | 99.79 | 99.21 |
| | RSD | 0.60 | 0.44 |

These results are summarized in Table 3. The percent recoveries for PSE range from 99.77 to 100.96% and from 99.57 to 101.39% for TER.

## Stability of Sample Solution

Sample solution injected after 12 hr did not show any appreciable change.

*Table 3*

*Results of Recovery Analysis*

| | Amount Present (mg/100 ml) | Amount Found (mg/100 ml) | Percent Recovery |
|---|---|---|---|
| PSE | 63.14 | 63.75 | 100.96 |
| Lot 1 | 66.44 | 65.98 | 99.30 |
| | 69.66 | 69.50 | 99.77 |
| Average | | | 100.01 |
| TER | 31.56 | 31.98 | 101.39 |
| Lot 1 | 33.14 | 33 | 99.57 |
| | 34.68 | 34.76 | 100.24 |
| Average | | | 100.40 |

## CONCLUSION

The proposed method is fast, accurate, and precise for the determination of PSE and TER from the tablets. Hence it can be employed for the routine quality control of tablets containing these two drugs.

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