Research Note

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Determination of Phenylpropanolamine in Pharmaceutical Preparations by Second Derivative Spectrophotometry

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ABSTRACT

Phenylpropanolamine (PPA) hydrochloride used as nasal decongestant agent was determined by second derivative spectrophotometry after derivatization with 2-hydroxynaphthaldehyde. The absorbance was measured between minimum-maximum of 386 nm-392 nm. The linear calibration range was obtained within 0.5~2.0 μg/mL. The method was applied for the determination of phenylpropanolamine from pharmaceutical preparations Tavegyl-D and Sinutab with coefficient of variation of 0.8~1.6%. Paracetamol present together with phenylpropanolamine could also be determined by spectrophotometry in aqueous phase after extraction of PPA in chloroform.

Key words: phenylpropanolamine (PPA), second derivative spectrophotometry, paracetamol

INTRODUCTION

Phenylpropanolamine HCl (PPA·HCl) is a sympathomimetic agent with vascoconstriction and decongestant effect on inflammed mucous membranes. It is also reported as an appetite suppressant. Recently, considerable interest in PPA·HCl has arisen due to the serious side effects accompanied its use including hemorrhage stroke, arrhythmis and hypertension[1-2]. A number of analytical methods have been reported for the determination of PPA based on spectrofluorimetry[3], room temperature phosphorescence[4], fluroammuno assay[5], radioenzymatic assay[6], Raman spectroscopy[7], capillary zone electrophoresis[8], thin layer[9], gas[9-11] and liquid chromatography[12-18]. The spectrophotometer methods are simple and required sensitivity could be achieved by employing suitable derivatizing reagent. The spectrophotometric methods for PPA are based on the measurement of absorbance within UV region, or recording the absorbance in visible region after derivatization[19-27]. Tan and Kolmonpunpon[28] reported second-derivative spectra with maxima at 260 and minima at 257 nm with calibration range within 20~350 μg/mL. The present work examines a sensitive method for PPA, based on second-derivative spectrophotometry after derivatization with 2-hydroxynaphthaldehyde (HN).

MATERIALS AND METHODS

Phenylpropanolamine HCl (Novartis, Pak.), paracetamol (Pharmatec (Pvt) Ltd. Karachi), 2-hydroxynaphthaldehyde (HN) (Fluka), methanol, chloroform (E. Merck) and sodium hydroxide (Fluka) were used. Spectorphotometric studies were carried out using Hitachi 220-spectrophotometer.

I. *Spectrophotometric Determination*

An aqueous solution containing 12.5 to 50 μg of PPA·HCl and 1.625 to 8.125 mg of paracetamol were transferred to separating funnel and sodium hydroxide solution (0.5 mL of 0.2% w/v) was added. Chloroform (4 mL) was added and contents were thoroughly mixed. The layers were allowed to separate and the organic layer was collected in 25-mL volumetric flasks. The extraction was repeated with chloroform (4 mL) and to the combined extract was added 2-hydroxynaphthaldehyde (HN) (2 mL, 0.3% w/v in methanol) and acetic acid (0.5mL). The contents were heated on water bath at 70~75°C for 10 min and its volume was adjusted to mark with methanol. Second derivative absorption spectrum was recorded in the range: 430 nm to 250 nm against reagent blank with scan speed: 60 nm/min, chart speed: 20 nm/cm and response time: 1 sec, slit width: 2 nm and scale: 0~1 A. The quantitation was carried out by measuring the amplitude of peaks obtained between maxima at 392 nm and minima at 386 nm.

The aqueous layer remaining in the separating funnel was collected in another volumetric flask (25 mL) and the volume was adjusted with water. The absorbance of the solution was measured against water at 291 nm.

II. *Determination of Phenylpropanolamine and Paracetamol in Pharmaceutical Preparations*

Ten tablets each of Tavegyl-D (Sandoz (Pak.) Ltd. Karachi) and Sinutab (Park-Davis & Co. (Pak) Ltd. Karachi) were ground. An amount of 0.51 g from Travergl D and 0.0475 g Sinutab tablets were separately dissolved in water on water bath at 70~80°C. The solution was

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filtered and the final volume was adjusted to 50 mL with distilled water. A solution (1.0 mL) of Travegl-D or (2.0 mL) from Sinutab tablets was transferred to a separating funnel and the procedure was followed as above. For the determination of paracetamol from the Sinutab tablets (10.0 mL) of solution was taken and procedure was followed as above. The amounts of PPA and paracetamol from the pharmaceutical preparations were evaluated from the calibration curves.

RESULTS AND DISCUSSION

Phenylpropanolamine hydrochloride (PPA·HCl) in aqueous solution absorbs in UV region at 210 nm and 256 nm with molar absorptivities of 3778 and 156 $L \cdot mole^{-1} \cdot cm^{-1}$. In order to increase the spectrophotometric sensitivity for the determination of PPA, the derivatization with HN was carried out.

The drug PPA·HCl is soluble in water, but is insoluble in organic solvents (chloroform, ethyl ether and ethyl acetate), while the derivatizing reagent HN is readily soluble in the organic solvents, but is insoluble in water. The drug was first treated with sodium hydroxide solution and the free base was quickly extracted in chloroform. The derivatization reaction was carried out in chloroform-methanol media, in the presence of glacial acetic acid.

Initially the absorptiometric studies were carried out using zero order spectrophotometry, but some difficulties were encountered in the reproducibility of the determination because the derivatizing reagent also indicated some absorbance at the wavelength of maximum absorbance of the derivative. The derivative spectrophotometry was then examined within 430~250 nm against reagent blank. Second derivative spectrophotometry gave reproducible results with improvement in the sensitivity of determination. The spectrum was recorded and amplitude was measured between two wavelengths 392 nm and 386 nm (Figure 2). Linear calibration curve was obtained within 0.5~2.0 μg/mL PPA·HCl with the coefficient of determination (r^2) 0.9998 and regression equation y = 0.4385x. The reproducibility of the response with 1 μg/mL PPA·HCl was measured (n = 6) and coefficient of variation was obtained 1.2%.

The effect of heating time and concentration of derivatizing reagent were examined. The heating timing at 70~75°C was varied from 5~25 min at an interval of 5 min. A similar absorbance was observed after the heating of 5 min and heating time of 10 min was selected. The reagent HN concentration was varied between 1~5 mL (0.3% w/v in methanol) at an interval of 1 mL and a similar response was obtained with 1~3 mL and addition of 2 mL proved satisfactory for quantitative derivatization.

PPA·HCl is present in pharmaceutical preparations in combination with paracetamol, phenyltoloxamine citrate, clemestine hydrogen fumarate and pheniramine maleate, hence their possible interfering effects on the determination of PPA·HCl was investigated. The study was performed at

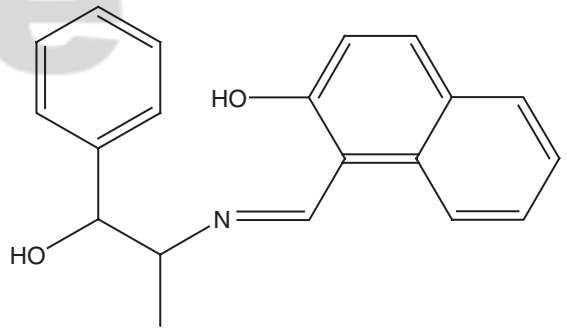

Figure 1. Structural diagram of 2-hydroxynaphthaldehyde derivative of phenylpropanolamine.

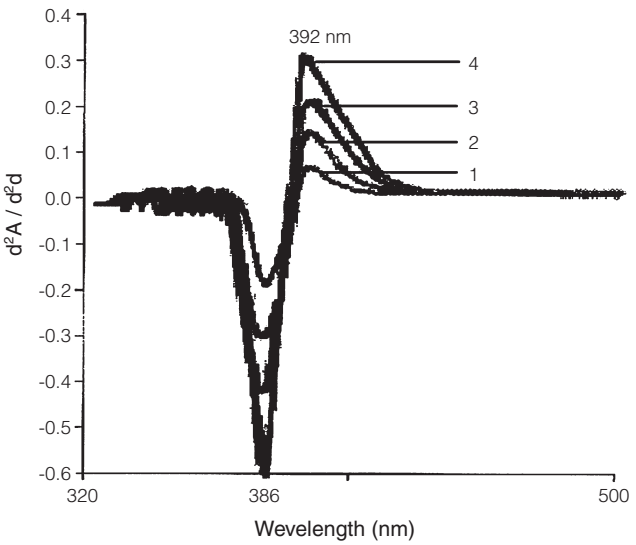

Figure 2. Second derivative absorption spectra of derivative of phenylpropanolamine against reagent blank. Concentrations: (1) 0.5, (2) 1.0, (3) 1.5 and (4) 2.0 μg/mL phenylpropanolamine.

the same concentration and 10 times the concentration to that of PPA·HCl. PPA is selectively extractive in organic solvent prior to derivatization; therefore, these drugs do not affect the determination of PPA·HCl, with the change in absorbance within 3%. Similarly, possible additives, such as lactose, gum accacia, methylparabin, propylparabin, sorbitol, propylene glycol do not affect the quantitative response of PPA when added at the concentration of 10 times of that PPA·HCl.

After the extraction of PPA in chloroform, paracetamol was determined in aqueous phase in alkaline medium. A linear calibration curve was obtained, which obeyed the Beer's law, in the range of 65~325 μg/mL at 291 nm, with the coefficient of determination (r^2) 0.9981, y= 0.001x. The analysis of test solutions of paracetamol together with PPA indicated relative error within ±3%.

Finally the method was applied for the determination of PPA·HCl and paracetamol from pharmaceutical preparations — Tavegyl-D, Sinutab and Panadol tablets. The results (Table 1) obtained indicated the relative deviation of 3.2~4.8% for both PPA and paracetamol from

Table 1. Analysis of phenylpropanolamine hydrochloride and paracetamol by second derivative spectrophotometry

Name of preparation	Compound present	Amount reported by manufacturer mg/tablet	Amount found mg/tablet (CV%, n=3)	Relative deviation (%) from reported values
Tavegel-D	Clemestine (as hydrogen fumarate)	1	—	—
	Phenylpropanol-amine hydrochloride)	75	72.6 (1.3)	3.2
Sinutab	Paracetamol	325	311 (1.6)	4.3
	Phenylpropanol-amine hydrochloride	25	23.8 (0.8)	4.8
	Phenyltoloxamine citrate)	22	—	—
Panadol	Paracetamol	500	480.5 (0.9)	3.9

the reported values by the manufacturer with the coefficient of variation (CV) in the range of 0.8~1.3%.

CONCLUSIONS

A simple second derivative spectrophotometric procedure has been suggested for the determination of PPA·HCl after derivatization with HN, with the observed linear calibration within 0.5~2.0 μg/mL. After extraction of PPA in chloroform, the paracetamol remaining in aqueous solution having alkaline medium could also be determined by spectrophotometry. The CV for to analysis of PPA·HCl and paracetamol from pharmaceutical preparations was observed within 0.8~1.3%.

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