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DETERMINATION OF TRIPROLIDINE-HCl BY SPECTROPHOTOMETRIC METHOD IN PURE AND PHARMACEUTICAL PREPARATIONS USING DICHLORONITROBENZENE AS A NEW CHROMOGENIC REAGENT

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Abstract: In the present study it is demonstrated that H_1- blockers such as triprolidine–HCl can be determined by a very simple, sensitive and accurate spectrophotometric procedure. The method consisted of interaction of triprolidine-HCl with dichloronitrobenzene in alkaline medium. Absorbance of resulting orange colour was measured at 440 nm .The reaction turned out to be selective for triprolidine –HCl with 0.005 $mgml^{-1}$ as the visual limit of identification and provided a basis for a new spectrophotometric determination. The reaction obeyed Beer's law from 0.05 mg to 0.15 $mgml^{-1}$ for triprolidine–HCl and the relative standard deviation was 0.60 %. The quantitative assessment of other drugs was also studied.

Keywords: Triprolidine–HCl determination, dichloronitrobenzene, colour stability, analytical pharmacy

Introduction

Triprolidine hydrochloride (Fig.1) is a pyridine derivative with the properties of antihistamine. It is a potent histamine H_1-receptor antagonist (H_1-blocker), with a rapid onset and long duration action, almost up to 12 hours. It is probably effective for the symptomatic treatment of seasonal and perennial allergic rhinitis, vasomotor rhinitis, allergic conjunctivitis due to allergens, foods and prevention of allergic reactions to blood or plasma [1]. The most common side effects are sedation, dizziness, incoordination, gastrointestinal disturbances, nausea, vomiting and diarrhea. It may also produce blurred vision, dryness of mouth, tightness of chest, blood disorders including agranulocytosis and haemolyticanaemia [2].

In view of the importance of antihistamine considerable analytical work has been carried out. In the reversed phase HPLC [3,4] and HPLC photodiode procedures [5], 12.5 cm Nucleosil 100 $t-5C_{18}$ bonded phase column with a mobile phase consisting of methanol acetonitrile was used. A 0.01M potassium dihydrogen phosphate solution was employed to adjust the pH to 6.8 [3] and UV detection was carried out at 254 and 280 nm [4]. In another HPLC method different UV absorption characteristics of triprolidine hydrochloride have been used to facilitate its determination in a mixture [6]. A wavelength switching programme has to be employed in this procedure. In the micro extraction capillary GC procedure [7] headspace solid-phase extraction was carried out followed by capillary gas chromatography with flame ionization detection. The recoveries in blood extraction were 4 - 51 folds lower than those in urine extraction. In the capillary electrophoresis procedures [8,9] the quality of separation was dependent upon the sample diluent used [8] and only basic drugs are screened from blood [9] while most of the spectrophotometric

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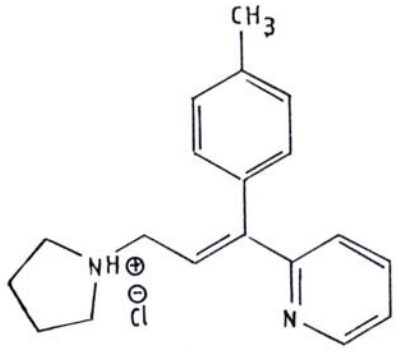
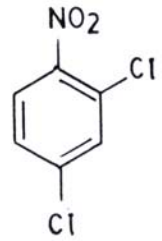


Triprolidine hydrochloride



2, 4- dichloronitrobenzene

Fig. 1. Structural formula of triprolidine hydrochloride and 2, 4-dichloronitrobenzene.

procedures [10-13] are carried out in the UV region. Long and tedious procedures are involved in chemiluminescent nitrogen detection in conjunction with reversed phase HPLC, UV and MS [14] and TLC/MS [15] exhibiting an average error of ± 10 over the entire linear range of absorbance [14]. Triprolidine (trip) ion selective electrodes of three types, i.e. conventional polymer membrane, graphite coated and carbon pasted based on the ion pair of triprolidine hydrochloride with sodium tetraphenylborate were also employed [16]. A kinetic method based on the alkaline oxidation of triprolidine with $KmnO_4$ has also been reported [17].

During the studies it was found that triprolidine-HCl reacts with dichloronitrobenzene in alkaline media to give an orange colour having maximum absorbance at 440nm. The reaction obeys Beers Law and has 0.005 $mgml^{-1}$ as visual limit of identification. The colour reaction has not been reported in the literature. The present method is simple, accurate, precise and sensitive. Percentages of other drugs have also been studied.

Materials and Methods

Apparatus and reagents

Cecil CE-2041 spectrophotometer with 1cm Quartz cell was used to measure the absorbance and graduated pipettes were employed. Analytical grade chemicals and doubly distilled water were used. Triprolidine-HCl (Glaxo Wellcome, Karachi, Pakistan) standard solution (w/v) (1.0$mgml^{-1}$) was prepared by dissolving triprolidine HCl (100mg) in ethyl alcohol (20 ml) (BDH) and the volume was made up to 100ml with distilled water to give a stock solution, which was diluted further as required. A 1% (w/v) dichloronitrobenzene (BDH) was prepared in ethyl alcohol and 1.0 N sodium hydroxide was prepared in distilled water.

General procedure

To an aliquot of triprolidine-HCl containing 0.005 mg to 0.15 $mgml^{-1}$ was added 2 ml of 1% dichloronitrobenzene, 1ml of 1.0N of sodium hydroxide and the contents were heated for 45 s in a water bath at 65°C, cooled and the volume was made up to 10 ml with ethyl alcohol. The resulting absorbance of the orange colour was measured 440 nm, employing all reagents except triprolidine-HCl as a blank. The experiment was repeated with different volumes of standard triprolidine-HCl solution and a calibration curve was prepared (Fig.2). The colour reaction obeys Beer's Law from 0.005 to 0.15 mg/ml^{-1} of triprolidine-HCl.

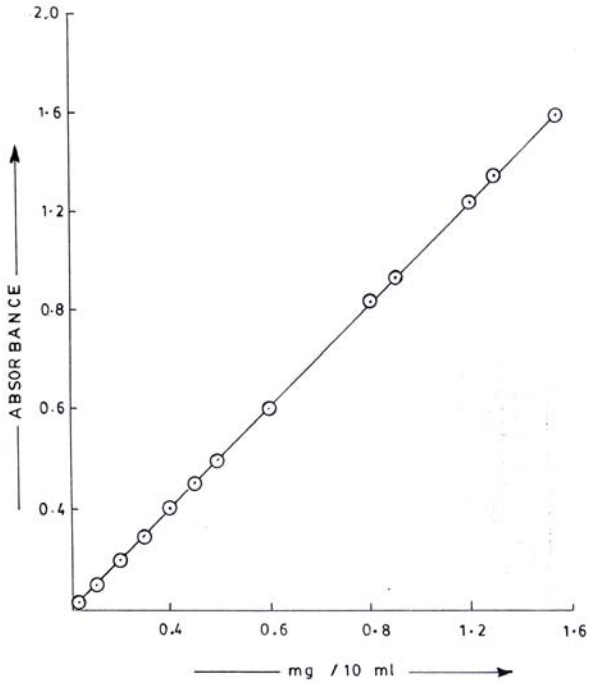


Fig. 2. Calibration curve of triprolidine — HCl with dichloronitrobenzene.

Procedure for studying the interfering compounds

To an aliquot containing 1.0 $mgml^{-1}$ of triprolidine-HCl, different amounts of various compounds (1.0 $mgml^{-1}$) were added individually until the solution showed the same(± 0.01) absorbance as that of pure triprolidine-HCl solution without the addition of the organic compound, under experimental conditions, as described in the general procedure. The value was calculated as the percentage of organic compound with respect to the amount of triprolidine-HCl.

Procedure for the determination of triprolidine-HCl in pharmaceautical preparations

Tablets containing 1.25, 1.5 and 2.5mg of triprolidine-HCl were powdered, weighed, dissolved in ethyl alcohol and filtered. The filtrate was diluted with distilled water to get a 1 mg/ml^{-1} solution of triprolidine-HCl. An aliquot containing 0.005 to 0.15 $mgml^{-1}$ was taken and the procedure was followed as described above and the absorbance was measured at 440 nm. The quantity per tablet was calculated from the standard calibration curve.

Syrup containing 0.25 $mgml^{-1}$ of triprolidine-HCl was weighed, dissolved in distilled water and filtered. If turbidity persisted, the contents were centrifuged until a clear supernatant was obtained. After filtration a 1.0 $mgml^{-1}$ solution of triprolidine-HCl was prepared. An aliquot containing 0.005 to 0.15 $mgml^{-1}$ was taken, the above procedure was followed and the absorbance was measured at 440 nm. The quantity of triprolidine-HCl per 5 ml of syrup was calculated from calibration curve.

Results and Discussion

Absorption spectrum of the coloured complex

Triprolidine-HCl reacts with dichloronitrobenzene when heated for 45s at 65°C in basic media to give an orange complex, the absorption spectra of which under optimum condition lies at 440 nm (Fig. 3).

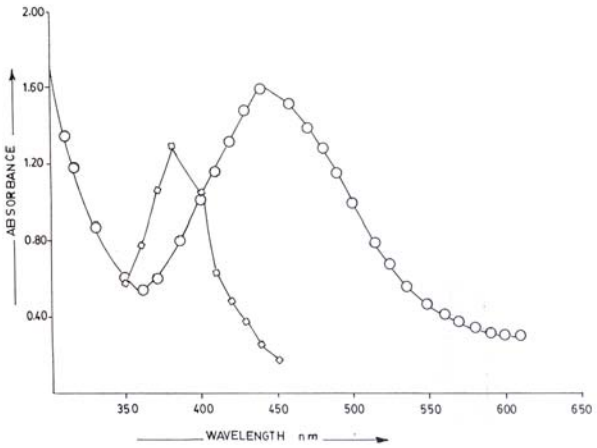


Fig. 3. ○ Absorption spectrum of triprolidine hydrochloride with 2, 4-dichloronitrobenzene.
□ Absorption spectrum of reagent blank.

Effect of colour producing reagent

Dichloronitrobenzene was used as a colour producing reagent. It was found that 2.2 mgml^{-1} of dichloronitrobenzene gave maximum colour (Fig. 4), above and below this concentration the colour intensity diminished and the colour became unstable. Effect of pH is shown in Fig. 5. Maxium colour intensity was obtained at pH 13.6. This pH was maintained by the addition of 1ml of 0.1N sodium hydroxide. The probable mechanism (Fig. 8) of the colour reaction is that on addition of sodium hydroxide, pyridine moiety is generated thus furnishing a pair of electrons for interaction with electron deficient dichloronitrobenzene. A charge transfer complex is formed having a $\ddot{e}_{max}$ at 440nm. Charge transfer complexes are formed by interaction between the basic N of antihistamine as electron donor and the electron acceptor in this case dichloronitrobenzene [18].

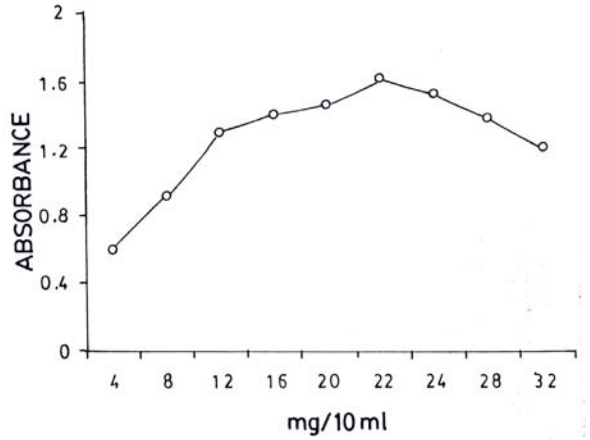


Fig. 4. Effect of reagent.

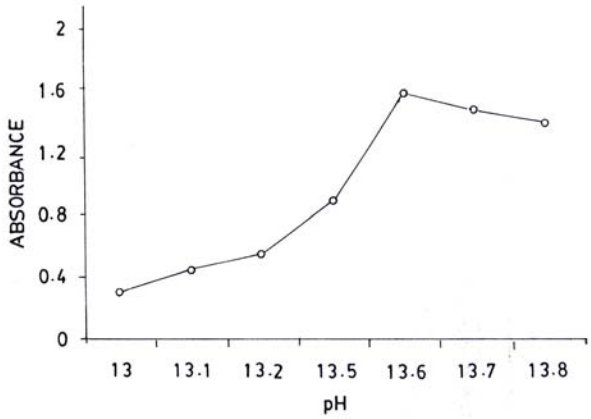


Fig. 5. Effect of pH.

Effect of temperature and heating time

The effect of temperature is shown in Fig. 6. With the rise of temperature the colour intensity increased and was stable at 65°C. The colour did not develop at room temperature. The absorbance of the developed colour was stable for more than 24 h. A water bath was used to carry out the temperature studies. The effect of heating time on colour intensity is shown in Fig. 7. It was found that heating for 45 s at 65°C gave maximum colour, above and below this time the colour intensity decreased and was unstable.

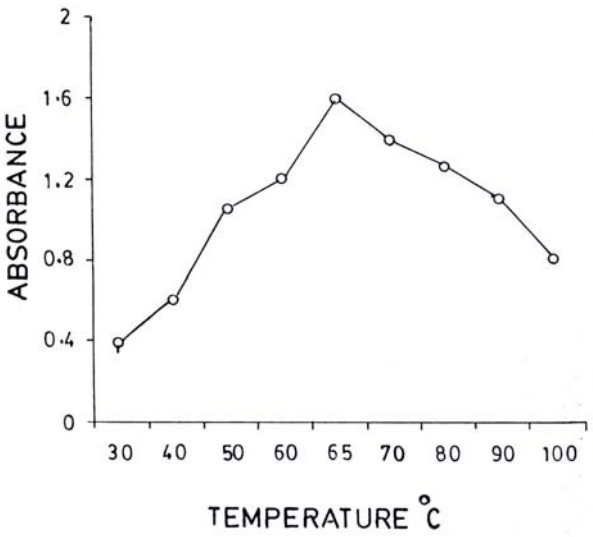


Fig. 6. Effect of temperature.

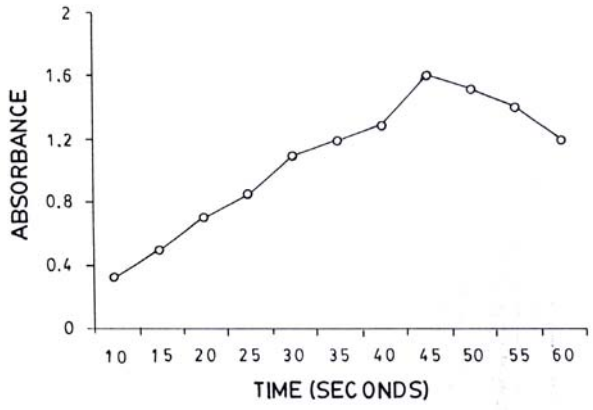


Fig. 7. Effect of heating time.

Effect of organic solvents

Different organic solvents such as choloroform, n-hexane, xylene, acetone, benzene, dichloro-methane, dioxane, formaldehyde and tetra hydrofuran, were tested for colour extraction and for stability, but none was effective and therefore no organic solvent was employed.

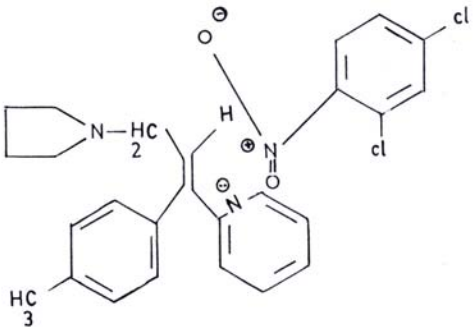


Fig. 8. Effect of pH.

Analytical Figures of Merit

The results for the determination of triprolidine-HCl are shown in Tables 1 and 2, which show the sensitivity, validity and repeatability of the method. It is also reasonably precise and accurate, as the amount taken from identical samples is known and the amount found by the above procedure does not exceed the relative standard deviation of 0.60% which is the replicate of five determinations (Table 1). The optimization has been done at lower analyte concentration. The calibration graph is linear in the range of 0.005 mg to 0.15mgml^{-1}. The apparent molar absorptivity calculated was 2.81 x 10^3 and the regression [19] was calculated by the method of least squares from ten points, each of which was the average of five determinations. The regression cofficient of determination (r^2) comes out to be 0.978.

Interferences

The quantitative assessment of tolerable amount of different organic compounds under the experimental conditions is given in Table.3. Various amounts of diverse interfering compounds were added to a fixed amount of triprolidine-HCl (Imgml^{-1}) and the recommended procedure for the spectrophotometric determination was followed. Other common interferences, like buscopan, zantac, septran, cimet,semidine and glucophage did not interfere.

Table 1.
Determination of triprolidine - HCl from pure solution.

Triprolidine-HCl taken mg/10ml	Triprolidine-HCl found *mg/10ml	Percentage Recovery
0.100	0.102 (± 0.60)	102.0
0.150	0.151 (± 0.58)	100.6
0.200	0.203 (± 0.50)	101.5
0.300	0.290 (± 0.39)	96.6
0.500	0.504 (± 0.31)	100.8
1.000	1.042 (± 0.10)	104.2
1.200	1.210 (± 0.08)	100.8
1.500	1.515 (± 0.06)	101.1

*Every reading is an average of five independent measurements

Table 2.
Optical characteristics precision and accuracy of the proposed method.

Parameters	Values
λ_{max} (nm)	440
Molar absorptivity (mol^{-1} cm^{-1})	0.2814x 10^4
Regression equation (Y)*	
Slope (b)	0.7676
Intercept (a)	0.0021
Regression coefficient of determination (r^2)	0.978
Relative standard deviation (RSD%)**	0.60 %
% Range of error (confidence limit) at 95% confidence level	1.25+ 0.0022 %

*Y = a + bC where C is the concentration of analyte (mg/10 ml) and Y is the absorbance unit.

**Calculated from five determinations.

Table 3.
Quantitative assessment of tolerable amount of other drugs.

Drugs	Maximum Amount Not Interfering* (%)
Aspirin	200
Marzine	100
Diclofenac sodium	100
Flubiprofen	100
Avil	150
Phenytoin sodium	150
Indomethacin	200
Propranolol-HCl	150
Metamizole sodium	100
Paracetamol	100
Ibuprofen	100
Buscopan	150
Bricanyl	100
Fluoxetine-HCl	100

*The value is the percentage of the drug with respect to 1mg/ 10ml of triprolidine-HCl that causes +0.01 change in absorbance.

Application

In conclusion, the proposed method has been successfully applied for the quality control of pure triprolidine-HCl and in the pharmaceutical dosage form (Table 4). The spectrophotometric method for the determination of Triprolidine-HCl is simple, reliable, sensitive and less time consuming. The statistical analysis is in good agreement with those of the official British Pharmacopeia 1988. The colour reaction is selective for Triprolidine-HCl. The method can be successfully applied to the micro determination of Triprolidine-HCl either in pure or in pharmraceutical preparations. The colour reaction has 0.005 $mgml^{-1}$ as visual limit of identification. The advantage of the present procedure is that it does not require many solvents whereas the HPLC procedures [7-9] are long, tedious and expensive, involving many reagents and solvents showing high RSD value i.e. 12% [9] and the colour stability varied

Table 4.
Determination of triprolidine-HCl from pharmaceutical preparations.

Drug	**Trade Name**	**Pharmaceutical preparations**	**Labeled (mg)**	**Amount found* (mg)**	**Amount Percentage recovery (%)**
Triprolidine – HCl	Actidil (Glaxo Wellcome Pharmaceutics, Karachi, Pakistan)	Tablet	2.5	2.52	100.6
Triprolidine – HCl	Actified P (Glaxo Glaxo Wellcome Pharmaceutics, Karachi, Pakistan)	Tablet	1.5	1.51	100.6
Triprolidine – HCl	Actified -DM (Glaxo Wellcome Pharmaceutics, Karachi, Pakistan)	Tablet	1.25	1.24	99.2
Triprolidine – HCl	Actidil (Glaxo Wellcome Pharmaceutics, Karachi, Pakistan) Elpomide (Elite Pharama, Pakistan)	Syrup	1.25 mg/ 5ml	1.246mg/ 5ml	99.6

* Every reading is an average of five determinations

from five to sixty minutes in the TLC procedure [3]. The literature indicates that this colour reaction has not been reported previously. The present method is precise, accurate and other compounds like buscopan, zantac, septran, cimet and semidine do not interfere. A significant advantage of a spectrophotometric determination is its application to the determination of individual compounds. This aspect of spectrophotometric analysis is of major interest in the analytical pharmacy, since it offers a distinct possibility of quality control in the assay of pharmaceutical dosage formulations.

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