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NOTE

Spectrophotometric Determination of Hydralazine Hydrochloride in Pure Form and Pharmaceutical Formulations Using Chloranilic Acid

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A simple and selective method for the determination of Hy·HCl in pharmaceutical formulations is described. The procedure is based on the formation of coloured complex with chloranilic acid in acid medium. Different variables affecting the complex formation were studied and optimized. The method was used to determine 1.90–68 μg mL^{-1} of Hy·HCl in the final measured solution. The simplicity of the method permits rapid analysis and thus suitable for routine control.

Hy·HCl (phthalazine-lyl-hydrazine hydrochloride) is an important pharmaceutical compound used as a vasodilator in the treatment of hypertension. The Hy·HCl tablets were analyzed spectrophotometrically using ninhydrin[1]. The absorbance of the coloured solution formed was measured at 422 nm. The reaction was unaffected by other drugs that may be used in combination with Hy·HCl. Results of IR and MS studies suggested that the coloured product is the hydrazone. Studies by using UV spectrophotometry showed the dilute solutions of Hy·HCl degraded rapidly in the presence of alcohol. Jendry Czko[2] described a method for the microdetermination of Hy·HCl in blood plasma; the absorbance of the butanol extract was measured at 470 nm. Naik *et al.*[3] measured the fluorescence of Hy·HCl in conc. H_2SO_4 at 353 nm; the results agreed with those obtained by UV absorptiometric method. Mopper[4] determined Hy·HCl by treating with nitrite in 0.1 M HCl to form tetrazolo [5,1-a] phthalazine. The absorbance was obeyed for 4 to 40 μg mL^{-1} of Hy·HCl. Badawy[5] determined Hy·HCl in pure solutions and tablets by standard addition and potentiometric titrimetric methods using tetraphenylborate based ISE. Gaidukerich *et al.*[6] used 5-diethyl sulphamoyl-N-(2-methoxy phenyl) anthranilic acid in 1% sodium carbonate solution, with or without 0.05% methyl blue for determining Hy·HCl.

The solution is titrated with $K_3Fe(CN)_6$ to a dark red colour. The relative errors are ±0.26% and ±0.17%, respectively. Badair and Korany[7] determined Hy·HCl in tablets by extraction into methanol, dilution with 0.1 M HCl, and the absorbance was measured at 317 nm and the coefficient of variation was < 2% and 100.6% recovery. Ibrahim and Rizk[8] determined Hy·HCl, amidopyrine

phenazone, phenelzine sulphate and isoniazid using tetracyanoethylene spectrophotometrically. Mahrous *et al.*[9] determined Hy·HCl in tablets by extracting the free base. The absorbance was measured at 522 nm versus a reagent blank, recovery was in the range 99 to 102%. Hy·HCl has been determined amperometrically in flowing stream at glassy carbon electrode; 10 ng of Hy·HCl could be detected[10].

The absorbance measurements were recorded using a Perkin-Elmer Model λ 4B spectrophotometer.

Reagent: Analytical-reagent grade chemicals and doubly distilled water were used throughout. Hy·HCl (M.wt. = 196.64) was an Aldrich product. Apresoline ampoules (20 mg hydralazine HCl/mL) and Ser-Ap-Es tablets (25 mg Hy·HCl/tablet) (Clba, Swisspharma, Cairo, A.R.E.) 1.0×10^{-4} M solution was prepared by dissolving the calculated amount in the required volume.

1.0×10^{-3} M chloranilic acid (3,6-dichloro-2,5-dihydroxy-1,4-benzoquinone (Aldrich) was prepared in water.

General procedure: Pipette out 3.0 mL of 1.0×10^{-3} M chloranilic acid in 10 mL calibrated flask and varied amounts of Hy·HCl 0.1 mL to 3.0 mL $\times 10^{-4}$ M, add 2.0 mL of 0.05 N HCl and complete to the mark with water. Measure the absorbance at 260 nm against a blank solution prepared in the same manner.

For analysis of Hy·HCl formulatins, sampling was made by taking 0.3–4.5 mL (containing 0.24–1.85 mg) of apresoline or grinding up 20 tablets of Ser-ApEs, then dissolving the exact weight of one tablet in water into 100 mL calibrated flask.

Investigations were carried out to elucidate the most favourable conditions for the formation of the reaction product between chloranilic acid and Hy·HCl for the spectrophotometric determination of Hy·HCl. The absorption spectra indicate that chloranilic acid has no absorbance at 260 nm while the product of the reaction between chloranilic acid and Hy·HCl has maximum absorbance at 260 nm.

Effect of solvent: The type of solvent employed affects both wavelength and intensity of the maximum absorption. The effect of some water miscible solvents *e.g.* methanol, ethanol, propan-1-ol, acetone, DMSO and DMF was investigated. The results showed that methanol and ethanol decrease the absorbance values, while other solvents do not affect the formation of the complex.

Effect of pH: The effect of pH was investigated by using different buffer solutions. The results indicate that the complex is best formed in acid media of 0.05 N HCl.

Effect of time and temperature: The coloured complex of chloranilic acid with Hy·HCl is formed instantaneously and the complex was found to be stable for more than 72 h. Raising the temperature up to 50 to 100°C has no influence on the complex.

Nature of the complex: The stoichiometry of the complex formed between chloranilic acid and Hy·HCl was investigated by the molar ratio and continuous variation methods. The results indicate that the formed compound has molecular ratio 1:1.

Quantification: A linear correlation was found between absorbance and concentration in the range 1.9 to 68 μg mL^{-1} of Hy·HCl. The linear regression

equation derived using the least squares method was applied, r = 0.9998. The validity of the derived regression equation was assessed in the determination of the drug in tablets and ampoules. The apparent molar absorptivity of the resulting coloured product was 1.83×10^4 L mol^{-1} cm^{-1}, whereas Sandell sensitivity amounts to 0.01 μg cm^{-2}. For more accurate analysis Ringbom optimum concentration range was calculated and found to be from 1.9–3.8 μg mL^{-1}. The mean of six replicates analysis of solution of Hy·HCl at concentration of 19 μg mL^{-1} gave a standard deviation value of 0.021.

This level of precision is adequate for the quality control analysis of pharmaceutical preparations. The accuracy of the method was tested by applying the recommended method using chloranilic acid. The recoveries of different amounts tested determined from the calibration curve amounted to 99.3%. The performance of the suggested method was judged through calculation of t-values at 95% confidence level. The corresponding value was 2.60 which is less than the tabulated value indicating the absence of determined error, F-value was calculated (Table-1) for the present method and the method reported by Issa *et al.*[12] indicating that there is no difference between the two methods.

TABLE-1
ANALYTICAL DATA FOR Hy·HCl USING THE PROPOSED SPECTROPHOTOMETRIC PROCEDURE

Validity of Beer's Law μg mL^{-1}	1–68
Ringbom optimum concentration range μg mL^{-1}	1.9–38
Molar absorptivity L mol^{-1} cm^{-1}	1.8×10^4
Specific absorptivity	0.00940
Sandell senstivity μg cm^{-2}	0.021
Correlation coefficient	0.9998
Calculated t-value	4.24
Calculated F-value	3.66

TABLE-2
RESULTS OF DETERMINATION OF PHARMACEUTICAL PREPARATIONS CONTAINING HYDRALAZINE

Sample	Taken (mg)	Mean recovery (%)	Mean relative error (pph)	Mean RSD (%)
Hy·HCl	0.19–1.96	100.02	0.02	0.98
Apresoline ampoules	0.24–1.85	100.05	0.05	1.03
Ser-Ap-Es tablets	0.20–1.60	100.30	0.30	1.22

Interferences: The influence of concomitant compound of Hy·HCl was studied and each compound tested was mixed to obtain samples containing 19 μg mL^{-1} of Hy·HCl and various concentrations of the foreign compounds. The ratio of each foreign compound taken as a 50 folds gave no error in absorbance

of the formed complex like starch, glucose, sucrose, lactose, galactose, glycine, valine, cystine, sodium chloride; while 100 folds interfered.

Conclusion

The above results indicate that Hy·HCl which has no characteristic spectrophotometric groups in its molecular form, can be determined by complex formation with chloranilic acid. The spectrophotometric procedure developed for Hy·HCl allows its determination in pharmaceutical preparations. The recommended procedure offers considerable economy as regards reagent consumption and time required for the analysis without any loss of precision. The proposed procedure is useful for quality control of Hy·HCl in pharmaceutical dosage forms.

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