Spectrophotometric Estimation of Piperazine in Dosage forms using Dichlone and Acetaldehyde as Reagent

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A simple spectrophotometric method for the determination of Piperazine Citrate in bulk drug and dosage forms is described. The method is based on the reaction between piperazine and 2,3- dichloro-1,4-naphthoquinone in presence of acetaldehyde to give a violet colored product having λmax at 580 nm. The results are comparable with those obtained by official method.

PIPERAZINE and its salts are widely used in the treatment of round worms and thread worms infections in humans and animals. Piperazine salts are estimated by titrimetric and gravimetric procedures in the official compendia[1,3]. Various other methods for the estimation of piperazine salts include polarographic[4] and colorimetric[5-12] procedures. Sodium tetraphenyl borate,[5] ammonium reinecket[5-7], folinciocalteu reagent,[9] sodium-1,2-naph-thoquinone-4- sulphonate[10], 3,5-dichlorobenzoquinone chlorimide[11] and chloranil[12] have been used earlier for colorimetric estimation of piperazine.

In the present work, a new spectrophotometric method for the determination of piperazine is described.

EXPERIMENTAL

Apparatus

Double beam Beckman Model 25 Spectrophotometer with 1 cm. matched cells.

Materials and Reagents

Piperazine Citrate IP, Piperazine Hexahydrate IP, 2,3-dichloro- 1,4-naphthoquinone (National),

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Dimethyl sulphoxide (SD's), Dioxane (SD's), Acetaldehyde (freshly prepared), Methanol (BDH), Acetonitrile (E.Merck), Dimethyl formamide (SD's), Benzene (BDH), and double distilled water were used in the study.

Formulations of piperazine citrate were procured from the local market.

Dichlone Reagent

Dichlone (300 mg) was weighed accurately and dissolved in dimethylsulphoxide (50.0 ml). Acetaldehyde (8.0 ml) was added, mixed and diluted to 100 ml with the same solvent. Freshly prepared reagent was used in the study.

Preparation of Acetaldehyde

Acetaldehyde was prepared by known literature method involving the oxidation of ethanol with potassium dichromate and dilute sulfuric acid.

Preparation of standard Piperazine hexahydrate or Piperazine citrate solution

Piperazine hexahydrate (75 mg) or piperazine citrate (100 mg) was weighed accurately and dissolved in water and diluted to 100 ml with water.

The resulting solution (5.0 ml) was diluted further to 100 ml with dimethylsulphoxide. The final solution contained 37.5 mcg of piperazine hexahydrate and 50 mcg of piperazine citrate per ml of the solution.

Calibration curve

An aliquot of piperazine citrate solution (0.25 to 1.50 ml) was transferred to 25 ml volumetric flasks. Reagent solution (3.0 ml) was added to it slowly with constant shaking and the reaction mixture was allowed to stand for 30 minutes. The volume was adjusted to the mark with methanol. The absorbance of the reaction mixture was measured at 580 nm against blank.

Analysis of Piperazine citrate or (Piperazine hexahydrate) powder

Piperazine citrate (or Piperazine hexahydrate) solution (1.0 ml) was transferred into a 25 ml volumetric flask and analyzed as described above.

The amount of drug was computed from calibration curve.

Analysis of Piperazine Citrate Tablets

Twenty tablets were weighed and powdered. The powder equivalent to ca 100 mg piperazine citrate was weighed accurately and treated with water (50 ml) and filtered through Whatman No. 40 filter paper. The residue was washed thoroughly with water. The filtrate and washings were combined in a 100 ml volumetric flask and diluted to the mark with water. The solution (5.0 ml) was diluted further to 100 ml with dimethyl sulphoxide. The dilute solution (1.0 ml) was analyzed as described above.

The amount of drug was computed from the calibration curve.
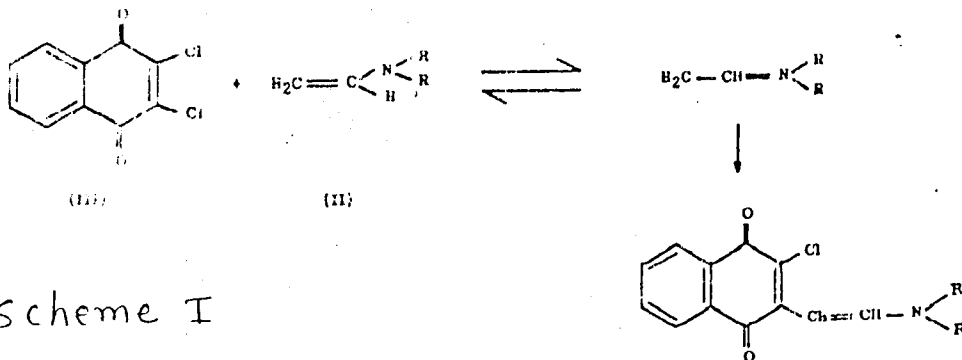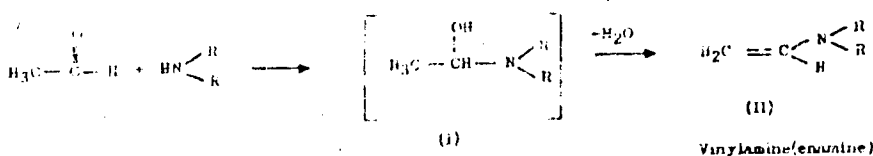
Analysis of Piperazine Citrate Syrup

The syrup equivalent to piperazine citrate (100 mg) was measured accurately and transferred to 100 ml volumetric flask, mixed with water (50.0 ml) and diluted to the mark with the same solvent. The resulting solution (5.0 ml) was diluted further to 100 ml with dimethyl sulphoxide. The dilute solution (1.0 ml) was analyzed as described above.

RESULT AND DISCUSSION

Secondary amines are known to react with acetaldehyde to form an intermediate (I), which loses a molecule of water to give a vinylamine[13](II). Vinylamine can act as anionic carbon nuclophile14.

Vinylamine (II), a stronger nucleophile probably displaces chloro group from dichlone to give a colored product(IV), having maximum absorbance at 580 nm.The rate of formation of vinylamine and its condensation with dichlone is much higher than the rate of reaction between secondary amine and dichlone.[15] Further, SN_2 reaction in protic solvents like DMSO, go as much as million times faster than in protic solvents like methanol, methanol-water mixture.[14] Therefore the SN_2 reaction between anionic carbon nucleophile, vinylamine and dichlone is further enhanced. Hence, probability of direct reaction between the amine and dichlone in the presence of acetaldehyde in DMSO is negligible.[15]

In the preliminary experiment, the reagent was prepared by using different solvents (DMF, DMSO, Dioxane, MeOH, Benzene, Acetonitrile etc.). Better results were obtained by using DMSO as a solvent, as it increase nucleophilicity of a nucleophile. DMF can also be used, but on decomposition, it gives dimethylamine and it interferes in the reaction. Final volume was adjusted in methanol, because in aqueous media the reagent precipitates out. The method of least square is employed to fit the mathematical equation to the analytical data. The Lambert-Beer's law is obeyed in the concentration range of 0.5 to 3.0 mcg/ml for piperazine citrate (r=0.999). The

$H_3C - C - H + HN < \frac{R}{R} \longrightarrow \left[H_3C - CH - N < \frac{R}{R} \right] \xrightarrow{-H_2O} H_2C = C < \frac{N < \frac{R}{R}}{H}$

(i)   (II)

Vinylamine(enamine)

Scheme I

Sandell's sensitivity of 0.0244 mcg cm^{-1} absorbance unit is obtained in the determination of piperazine citrate.

Pure samples of piperazine salts were analyzed by the proposed method. The results are in good agreement with those obtained by pharmacopoeial method.[3]

The proposed method was applied to assay piperazine tablets and syrup. The percentage recovery of piperazine in its dosage forms was found to be 98.07 to 100.20%. This indicates that the commonly used excipients do not interfere in the proposed procedure.

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