# Colorimetric Method for the Determination of Piperazine in Pharmaceutical Formulations

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Piperazine and its salts are reacted with alcoholic p-benzoquinone and buffered at pH 5.4 to give a coloured product with maximum absorption at 516 nm. The piperazine base has a molar absorptivity of $0.96 \times 10^4$ 1/mol/cm, and Beer's law is obeyed in the range of 4-20 µg/ml. When applied to two commercial preparations, the proposed method gave mean recoveries within 1%, and relative standard deviation was less than 1%.



Piperazine and its salts have been determined by gravimetric[1], spectrophotometric[2,3] and complexometric[4] methods. The aim of present investigation was to develop an improved colorimetric method with greater precision and accuracy. The colour reaction with p-benzoquinone was first reported by Foucy[5] and later developed into a quantitative method[6–8] based on heating the reaction mixture. This reaction with p-benzoquinone seems to be general for amines, and Benson and Spillane[9] have described its use for determination of a wide range of amines (aliphatic, primary and secondary, alicyclic and heterocyclic amines), again by conducting the reaction at elevated temperature. The condensation may take place between an amine and p-benzoquinone at position 2 or position 2 and 5.

This paper presents a simpler direct method for the determination of piperazine by reaction with p-benzoquinone at room temperature without prior separation of the free base. The method is very suitable for routine analysis and can replace the official gravimetric method[1], which is based on precipitating as dipicrate salt. A Shimadzu 1601 UV/Vis spectrometer with 1 cm matched quartz cells was used for all absorbance measurements. All other chemicals used were analar grade. P-benzoquinone solution (1% w/v) in 95% ethanol and buffer solution (pH 5.4) were freshly prepared. Stock solution of piperazine citrate was prepared by dissolving 100 mg in 100 ml of distilled water. The stock solution was further diluted to get a working standard solution containing 80 µg/ml. In a series of 20 ml volumetric flasks, 1.0 ml to 5.0 ml of standard piperazine citrate solution was transferred separately; and to each flask, 2 ml of buffer solution (pH 5.4) and 2 ml of p-benzoquinone solution were added. This was allowed to stand for 30 min and diluted to volume with distilled water. The absorbance of the coloured solutions was measured at 516 nm against reagent blank. The method was applied to the determination of piperazine of two commercial preparations (piperazine citrate syrup, Burroughs Welcome and Antipar; piperazine phosphate tablet, Glaxo Pharmaceuticals). An accurately weighed amount of tablets, 500 mg; and an accurately measured volume of piperazine syrup, 750 mg/5 ml, which is equivalent to 100 mg, were transferred into a 100 ml standard flask separately and the volume was made up to the mark. Thereafter, 20 ml of the above solution was transferred into a 50 ml volumetric flask and diluted to 50 ml with distilled water. From the above stock, 4 ml of the solution was transferred into a 20 ml volumetric flask, which gave final concentration of 80 µg/ml; and 2 ml of buffer solution (pH 5.4) and 2 ml of p-benzoquinone solution were added and allowed to stand for 30 min and then diluted to volume 20 ml with distilled water. Absorbance was measured at 516 nm against reagent blank.

Two grams of standard piperazine citrate was added to previously analyzed tablets and syrup and solution so obtained was treated as described above. Absorbance of the coloured solution (80 µg/ml) was measured at 516 nm at intervals of 5 min till the end of 30 min. The effect of pH of the buffer used has been examined, and optimum pH for high sensitivity, minimal blank reading and high stability was found to be 5.4. The colour

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**TABLE 1: ESTIMATION OF PIPERAZINE IN PHARMACEUTICAL FORMULATIONS**

| Pharmaceutical formulations | Labeled amount of piperazine citrate (mg) | Amount of piperazine citrate found (mg)* | Recovery studies | | |
|---|---|---|---|---|---|
| | | | Amount added (mg)* | Amount found (mg)* | % recovery |
| Piperazine citrate syrup | 750 / 5 ml | 738 | 2 | 735 | 97.7 |
| Antipar tablets | 500 | 490 | 2 | 501 | 99.8 |

*Average of six readings

**TABLE 2: COMPARISON OF RECOMMENDED PROCEDURE WITH THE OFFICIAL BP METHOD**

| Sample | Recovery ± S.D., % | |
|---|---|---|
| | Official method | P-Benzoquinone method* |
| Piperazine citrate syrup | 97.2±0.5 | 97.7±0.6 |
| Antipar tablets | 99.2±0.4 | 99.8±0.6 |

*Average of six readings

reaches maximum intensity in 30 min and remains stable for 2 h. The optical characters such as Beer's law were found to be obeyed over the concentration range of 4-20 µg/ml. Apparent molar absorptivity was found to be 2.97 (l/mol/cm) × $10^3$, while Sandell's sensitivity was found to be 0.961 µg/$cm^2$/0.001 absorbance unit. The regression equation gave a slope of 0.006 with an intercept at 0.0653. The precision and accuracy of the method was established by measuring six replicate samples of the drug in commercial formulations. The percentage recovery was found to be 97.0-99.8 (Table 1). The results obtained from the commercial formulations were compared with those obtained by the official gravimetric method[1] (Table 2). A recovery study reveals that there is no significant difference in precision and accuracy between the proposed and the official methods. The official gravimetric method[1] was also applied to ascertain purity of piperazine citrate used in the work. The method has the advantage over the previous methods[4-6], viz., no heating is required. Since p-benzoquinone reacts with primary, secondary and cyclic and heterocyclic amines[6], any of these compounds, if present, might interfere with the determination. However, application of the molar ratio and continuous variation methods under the conditions given in this paper showed the reaction ratio of p-Benzoquinone to piperazine to be 4:1.



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