

**NOTE****Microdetermination of 4-Chlorophenol and 5-Chloro-8-Hydroxyquinoline with Bromine Chloride and Its Application to Pharmaceutical Preparations**

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A simple titrimetric method for the microdetermination of 4-chlorophenol and 5-chloro-8-hydroxyquinoline in acetic acid medium is described. The proposed method can be successfully applied for the assay of methyl dopa and halquinol in pharmaceutical preparations.

It has been established that the bromination of bromine chloride takes place with rapidity as compared to the conventional bromate-bromide mixture. Pioneer work on the use of BrCl as an analytical reagent has been done by Schulek and coworkers<sup>1</sup>. Schulek and Burger used BrCl as a halogenating agent in the determination of antipyrine, phenol and fluorescein. Other compounds which have been determined with BrCl include hypophosphite<sup>2</sup>, hydroxylamine<sup>3</sup>, maleic and fumaric acids<sup>4</sup>, formic acid<sup>5</sup>, hydrazine<sup>6</sup>, thiocyanate, urea and thiourea<sup>7</sup>, isoniazid, triphenylphosphine, phosphorothiate, trithionates, xanthates, dithiocarbamates, reineckates, oxine and metallic oxinates<sup>8</sup>, phloroglucinol, thymol and pyrogallol<sup>9</sup>. The inherent usefulness of BrCl for the quantitative determination of a few more organic compounds<sup>10</sup> led to the investigation of its applicability to 5-chloro-8-hydroxyquinoline (CHQ) and 4-chlorophenol (CP) and to some pharmaceutical preparations such as methyl dopa used as an antihypertensive drug and halquinol used for antifungal, antiprotozoal and antibacterial treatment. The reported method offers the advantages of rapidity, simplicity, sensitivity and reproducibility.

A stock solution of sodium thiosulphate (12.4160 g in 1000 mL distilled water) was prepared and standardised using potassium dichromate iodometrically. Bromine chloride was prepared by dissolving potassium bromide (1.9835 g) and potassium bromate (1.3917 g) in distilled water (125 mL), cooled in ice and then concentrated hydrochloric acid (100 mL) was added and the solution was made up to 500 mL in a volumetric flask. Potassium iodide (10%) and starch solution (2%) were used for the study.

**Determination of Stoichiometry:** The stoichiometry of the reaction was first determined by dissolving the sample (2–10 mg) in glacial acetic acid-water and allowing it to react with known excess of BrCl for about 15–20 min in an ice bath. The excess reagent was back titrated against Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> iodometrically. A blank was also run under identical conditions.

**Microdetermination:** An aliquot containing 2–10 mg of the sample was taken in a 100 mL iodine flask, 5 mL glacial acetic acid and 5 mL of BrCl were added

and the reaction mixture after mixing well was cooled in an ice bath for about 15–20 min. 10 mL of 10% potassium iodide solution were then added, allowed to stand for 2 min with gentle shaking and the contents of the flask were titrated against standard  $\text{Na}_2\text{S}_2\text{O}_3$  solution using starch indicator. A blank was also run under identical conditions.

The stoichiometry of the reaction was examined before applying the procedure for quantitative determination. The experimental results reveal that the CP and methyl dopa require 2 moles of BrCl whereas CHQ and halquinol require 1 mole of BrCl. The results of the microdetermination of these compounds are summarised in Table-1. The results indicate that they are precise and the maximum deviation is about 0.74. The low value of coefficient of variation indicates that the proposed method is reproducible (98–99%). The proposed method was successfully applied for the determination of methyl dopa and halquinol in pharmaceutical preparations. The excipients such as lactose, magnesium stearate, gelatin, talc etc. did not interfere in the assay tablets. The reactivity of BrCl is found to be higher in polar solvents and hence acetic acid was used as the medium for the determination. The results improved when the estimations were carried out at low temperatures.

TABLE-1  
DETERMINATION OF COMPOUNDS USING BrCl

Compound	Weight taken (mg)	Weight found (mg)	Standard deviation*	Relative error (%)
CP	2.05–10.30	2.01–10.45	0.42	1.78
CHQ	2.08–10.60	2.03–10.82	0.68	1.96
Halquinoi	2.21– 8.08	2.15– 8.15	0.74	1.84
Methyl dopa	2.04–10.62	2.01–10.54	0.48	1.38

\*For determinations in each case.

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