2.1 Preparation and Standardization of Potassium ditelluratocuprate(III) Reagent:

Preparation of Cu(III) solution has been reported by many workers\textsuperscript{1,3,4,5,13}, usually by the oxidation of Cu(II) solution with suitable oxidants in the presence of complexing ligands in alkaline medium. In most of the cases persulphate was used as an oxidant but very meagre attention was paid towards its removal from the resulting Cu(III) solution. Chandra and Yadava\textsuperscript{14} suggested a method to prepare potassium ditelluratocuprate (III) \([\text{K}_4\text{H}_4\text{Cu(TeO}_6)_2]\) solution free from persulphate by boiling the solution for about an hour. In the present work, this fact has been taken into consideration. As organic compounds are estimated with excess of Cu(III) reagent followed with iodimetric method, the complete removal of the unused persulphate is very important to rule out the possibility of any side reaction with persulphate and organic compound sought for. Moreover, some part of the telluratocuprate(III) forms an insoluble brown precipitate if boiled for longer time. This tendency is enhanced with the removal of persulphate and with concentration of potassium hydroxide with boiling. It was, therefore, very essential to frequently test the presence of persulphate in
the proximity of its complete removal, and also to restrict the increase of the concentration of potassium hydroxide due to boiling in order to ensure the higher yield of the fairly stable reagent, potassium ditelluratocuprate (III), in the solution form.

Accordingly, following procedure lias been followed for the preparation of potassium ditelluratocuprate(III) solution.

A mixture of 1.56 g of copper sulphate (E. Merck), 3.17 g potassium tellurite (BDH), 4.22 g of potassium persulphate (BDH) and 8.0 g of potassium hydroxide (E. Merck) was dissolved in 80 nil of water and then heated on a hotplate. In about 20 minutes, the boiling mixture became intense red due to conversion of Cu(II) into Cu(III) form. The boiling is continued for another 20 minutes for completion of the reaction. It is then cooled and filtered through a G-4 jena sintered-glass crucible and finally diluted to 100 ml distilled water and stored in a polyethylene bottle at cool and dark place.

It is to be borne in mind that the amount of persulphate taken should be just sufficient to oxidize Cu(II) to Cu(III) and tellurite to tellurate only. In case it is taken in excess, the contents may be boiled for another one hour for its complete decomposition.
The absence of persulphate in the prepared solution of Cu(III) was tested by acidifying about 1 ml of reagent solution with dil H$_2$SO$_4$ till the red colour of the solution is completely changed due to Cu(III) conversion into Cu(II). It was treated with 5 ml of 0.5 M NaHCO$_3$ and 2 ml of 5% KI solution and allowed to stand for a couple of minutes. The nondevelopment of blue colour after addition of 2-3 drops starch indicator indicates the absence of persulphate.

The final concentration of KOH in the prepared solution essentially remains ~ 0.7 M to impart the stability of Cu(III) in alkaline media for several months.

Several methods for standardization of Cu(III) solution have been described in the literature. For instance, Beck$^5$ standardized potassium ditelluratocuprate (III) solution against glucose by visual titration method. However, this was found erroneous by Keyworth and Stone$^{13}$. Chandra and Yadava$^{14}$ also reported that Beck's method cannot be used for the standardization of Cu(III). A titrimetric method for the standardization of ditelluratocuprate(III) called the arsenite method$^{14}$, was recommended by these workers.

Accordingly, an aliquot of Cu(III) solution (5 ml) was mixed with approximately large excess volume (10 ml) of sodium arsenite solution (0.02 M, prepared by the usual method and standardized against iodine solution) and allowed to stand for 3-4 minutes and then acidified with requisite amount of 0.5
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M-H$_2$SO$_4$ till the green suspension disappears. It was then treated with 5 ml of 0.5 M sodium bicarbonate solution. The unused arsenite was back titrated with standard iodine solution* (0.01 M) using starch as an indicator. A blank was also run simultaneously. The process was repeated with different aliquots of Cu(III) solution. The solution of potassium ditelluratocuprate (III) thus formed had a strength of 0.03 5 M.

The acidification with sulphuric acid neutralizes potassium hydroxide present in the mixture, otherwise some of the iodine added during the titration will be consumed by it. Addition of excess of bicarbonate is important as it helps instantaneous oxidation of the arsenite with iodine and its presence also prohibits the liberation of iodine by Cu(II) from potassium iodide present in the iodine solution.

2.2 Sample Preparations:

Sulphonamides (1 mg/ml):

A stock solution of sulphanilamide, sulphapyridine, sulphathiazole

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* Prepared a saturated solution of KI (4g.E. Merk) in 3 ml of distilled water by heating. Then cooled it to room temperature. The solution was then transferred to a well stoppered iodine flask. About 1.27 g of iodine (E.Merk) was introduced into the saturated solution of potassium iodide and the mixture was shaken well to dissolve iodine completely. The solution of iodine thus prepared was diluted to one litre with distilled water and stored in an amber-glass bottle. It was then standardized against the standard sodium thiosulphate solution (0.01 M), which has already been standardized with copper sulphate solution (0.01 M) iodonetrically.
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and sulphadiazine (Sigma Chemicals, USA; May and Baker Ltd, England) was prepared by dissolving known amount (~500mg) of the sample in minimum quantity of 0.05 N NaOH in a 500 ml volumetric flask and then the solution was made up to the mark with distilled water.

Antimalarials (1 mg/ml):

Stock solutions of aminoquinoline derivative antimalarials were prepared by dissolving known amount (~500mg) of chloroquine phosphate, santoquin, amodiaquine hydrochloride, pamaquine hydrochloride, pentaquine and primaquine (Parke Davis, India; Bayer India Ltd., Bombay) in distilled water in 500 ml volumetric flasks.

Analgesics (1 mg/ml):

Stock solution of analgin, aminopyrine and melubrin (Indian Drugs and Pharmaceutical Limited) was prepared by dissolving known amount (~500mg) of the sample in distilled water in a 500 ml volumetric flask.

2.3 General Procedure for Determination of the Drugs:

In all titrations, micropipettes (Least count 0.01 ml) and microburette (Least count 0.01ml) were used: aliquots containing 1-5 mg of the sample were taken in 150 ml Erlenmeyer flasks and known excess (5-10 ml) of 0.035 M Cu(III) solution was added. The contents were shaken thoroughly. The reaction
mixture heated on a boiling water bath for the prescribed reaction time. After the reaction was over, the contents were cooled to room temperature. The unused Cu(III) was determined by the following Arsenite method.

The reaction mixture was treated with excess volume (10-15 ml) of 0.02 M sodium arsenite solution, allowed to stand for 3-4 minutes and then acidified with 0.5M-H₂SO₄ till the green suspension was dissolved and a clear acidic solution was obtained. It was then treated with 5 ml of 0.5 M sodium bicarbonate solution. The unused arsenite was back titrated with a standardized iodine solution (0.01 M) using starch as indicator. A blank was also run simultaneously using all the reagents except the sample. The molar ratio of the reagent with the samples was obtained with the litre value of the reagent consumed for the sample. The recovery of the sample was calculated by the following expression:

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\text{Mass of the Sample (mg)} = \frac{M \cdot N \cdot (S - B)}{n}
\]

Where, 
- \(M\) = Relative molecular mass of the sample,
- \(N\) = Normality of iodine solution,
- \(S\) = Volume of iodine solution required for the sample experiment,
- \(B\) = Volume of iodine solution required for the blank experiment,
- \(n\) = Number of moles of Cu(III) reagent per mole of the sample.

The recommended procedure was successfully applied for the determination of some sulpha-drugs, antimalarials and analgesics at milligram level. For
evaluating results on an accurate scale and testing the utility of the sample, a large number of experiments were carried out and the effect of various parameters, e.g., reaction temperature, reaction time and the volume of the reagent were studied. Percentage error, standard deviations and coefficient of variations were calculated for each set of determinations.
References


