RESEARCH PAPER

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New colorimetric and photometric titration procedures for the determination of Dimercaprol in injections

B.C. VERMA, V.S. JAMWAL, B.S. SAMBRA AND D.K. SHARMA*
Dept. of Chemistry, Himachal Pradesh University, Summer hill, Shimla - 171 005.

Simple and rapid colorimetric and photometric titration procedures for the determination of dimercaprol in injection have been developed. They are based on the formation of yellowish brown colour instantaneously, on mixing dimercaprol with cobalt(II) acetate in dimethylformamide.

DIMERCAPROL (2,3-dimercapto-1-propanol) is an effective

CH_2——CH——CH_2OH
SH SH

antidote for poisoning with arsenic, gold, antimony, mercury and perhaps other heavy metals. The clinical use of dimercaprol has prompted the appearance of many methods for its analysis. Most of the methods available in literature for the determination of dimercaprol are volumetric involving oxidimetric tirations of the compound with iodine or iodine monochloride in different solvent media[1-4]. The end-points have been detected visually[1], potentiometrically[2,3] or amperometrically[4]. A blank titration needs to be performed in most cases to make necessary correction. The above methods are based on the oxidation of thiol group to disulphide group (2RSH ——RSSR + $2H^+$ + 2e). However, in literature doubts have frequently been expressed over the stoichiometry of the above reaction and it is mentioned that the oxidation could proceed beyond disulphide stage[5-9]. In view of this, these methods lack specificity. Though cobalt(II) forms a coloured complex with dimercaprol, no serious attempt appears to have been made to develop a colorimetric method for the analysis of this compound. Even, otherwise, most of the colorimetric methods which are available in literature[10,11] for the determination of mercaptans, have been developed primarily for the determination of mercapto group in biological materials and to a limited extent for mercaptan-based drugs. That dimercaprol reacts with cobalt (II) in demethylformamide in 2:1 molar ratio forming an intense yellowish brown complex (playsibly I) showing λ_{max} at 475 nm has been made the basis of sensitive colorimetric as well as photometric titration methods for the analysis of this compound. The colour which develops instantaneously on mixing the reagents is stable for atleast 5 hrs. Both the colorimetric and photometric titration methods have been applied for the analysis of dimercaprol injections.

$$2C_3H_8OS_2 + Co^{2+} \longrightarrow [Co(C_3H_6OS_2)_2]^{2-} + 4H^+ \quad (I)$$

It may be mentioned here that the formation of above type of complexes (I) as a result of the reaction of 1,2-dithiols and related compounds with cobalt(II) is well known[12,13]. Further support to this stoichiometry is provided by the photometric titrations which are marked by a well-defined intersection at drug to reagent molar ratio of 2:1.

*For correspondence

EXPERIMENTAL

Reagents:

Dimethylformamide (BDH) was purified before use.

Dimercaprol: The compound 2,3-dimercapto-1-propanol (Merck) was used as received. The purity of the sample was checked by reported method[1].

Cobalt (II) acetate tetrahydrate, standard solution in dimethylformamide, was prepared by a known method[14].

All the chemical used were of analytical grade.

Apparatus: Bausch and Lomb spectrophotometer (Spectronic 20D) with 1 cm matched glass cells was used for all absorption measurements.

Procedures

Direct colorimetric procedure Preparation of calibration graph: Dimercaprol standard solution was prepared by dissolving 5 mg of the pure compound in dimethylforamide and diluting it to 100 ml with the same solvent. The solution contains 50 μg ml^{-1} of dimercaprol. Each aliquot of this solution was diluted to 5 ml prior to absorption measurements.

Aliquots (0.2-2.0 ml) of standard solutions of pure dimercaprol in dimethylformamide were added to cobalt (II) acetate (0.5 ml, 0.005N in DMF) and the volume was made upto 5 ml with dimethylformamide. The absorbance of resulting solution was measured at 475 nm against a reagent blank and the calibration curve was prepared. Beer's law is obeyed upto 24.6 μg ml^{-1} of dimercaprol.

Spectrophotometric titrimetric procedure: Aliquots of solution of dimercaprol in dimethylformamide were taken and volume was made upto 5 ml with the same solvent. Each solution was titrated photometrically at 475 nm at room temperature (~ 24°) with standard cobalt (II) acetate. Dilution corrections were applied and titration curve plotted in the usual way. An inverted L-shaped titration curve was obtained. The end-point was found by extrapolation of two straight lines.

Drug analysis: A single large sample of dimercaprol injection was weighed and dissolved in known volume of tert.- butanol-dimethylformamide (1:1) mixed solvent. Aliquots of this solution were processed for direct colorimetry and photometric titrations in the manner as given above for pure compound. The results are recorded in **Table 1.**

Results and Discussion

The proposed colorimetric method for the determination of dimercaprol involving cobalt (II) acetate is extremely sensitive and can be employed for the determination as little as 0.2 μg ml^{-1} of dimercaprol. The molar absorptivity of dimercaprol-cobalt(II) complex (on the basis of dimercaprol content) is 7.0×10^3 l mol^{-1} cm^{-1}. Dimercaprol in the range 2-22 μg could be determined with maximum relative standard deviation (RSD) of 1.0% both by direct colorimetric as well as photometric titration procedure. When applied to a commercial drug formulation viz. injection containing 50 mg ml^{-1} of active ingredient content, the recoveries were in the range 98.8-100.1% of the nominal content with RSD's in the range 0.5-0.7% using direct colorimetry procedure and the same using photometric titration procedure were in the range 99.0-99.8% of the nominal content with RSD's in the range 0.3-0.5% (Table 1).

The proposed colorimetric methods for the determination of dimercaprol are simple rapid and sensitive and do not involve any extraction. The methods are therefore. recommended for the routine analysis of above drug. The excellent solution stability of the reagent in dimethylformamide and that of the coloured complex as well as the well-established stoichiometry of the colour reaction are some of the special attributes of the proposed methods.

Table 1: Assay of dimercaprol injection containing 50 mg ml^{-1}+ active ingredient.

Nominal amount taken, µg	Found*, µg	
	Direct colorimetric procedure	Photometric titrimetric procedure
2.5	98.8 ± 0.7	99.0 ± 0.5
5.0	99.7 ± 0.5	99.8 ± 0.3
10.0	99.6 ± 0.7	99.5 ± 0.4
20.0	100.1 ± 0.5	99.6 ± 0.3
25.0	98.8 ± 0.7	99.0 ± 0.5

*Values are mean of three determinations with standard deviation (±).
+Maker's specification established separately by I.P. Method[1].'

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