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DIRECT POTENTIOMETRIC TITRATION OF 2-THIOURACIL AGAINST SILVER NITRATE USING COPPER BASED MERCURY FILM ELCTRODE

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ABSTRACT:

A simple and rapid direct potentiometric titration of and against silver nitrate is delineated. In this method, known amount of freshly prepared and 2-thiouracil in pure and tablet form is directly titrated against Silver nitrate using cheap and simple lab made Copper Based Mercury Film Electrode (CBMFE). The titration condition is optimized for determination of compounds in pure form. The precision and accuracy of the method have been assessed by the application of lack of fit test and other statistical methods. Overall mean recovery and relative standard deviations obtained was100.274 and 0.3008% respectively.

Key Works : 2-thiouracil, Copper Based Mercury Film Electrode, Direct Potentiometric Titration, Argentometric Titration.

INTRODUCTION

Pharmaceutical analysis involves analysis of thousands of diverse organic compounds which are used as medicines and raw materials employed in the production of drugs. Generally almost all drugs contain impurities. The contamination of pharmaceuticals by various admixtures may not only lower their therapeutic effect, but also cause undesirable side effects. An enormous amount of research is currently being conducted in the field of pharmaceutical analysis making use of electro analytical techniques such as polarography, amperometry, potentiometry etc., and also other techniques such as chromatography, spectroscopy etc. Electro analytical techniques are preferred to other techniques due to a high degree of sensitivity, selectivity and accuracy.

The potentiometry has drawn considerable interest over the other techniques, as the potentiometry is a simple and versatile technique making use of simple equipments. Potentiometry enables rapid, precise and accurate analysis of inorganic and organic species present in diverse samples such as biological, clinical, environmental, pharmaceutical samples etc. Although most of the potentiometric pharmaceutical analysis make use of commercially available ion-selective electrodes, lab-made inexpensive electrodes can also been used as an indicator electrode.

Recently, Copper Based Mercury Film Electrode has successfully been applied as an indicator electrode for potentiometric pharmaceutical analysis. CBMFE has been applied for the indirect titration of ascorbic acid against silver nitrate [1]. CBMFE has also been used for the direct titration of ascorbic acid in

pure and dosage forms against $CuSO_4$ as titrant [2], sulphamethoxazole [3] and isoniazid [4-5] have also been determined in pure and dosage forms using CBMFE as an indicator electrode. Copper based mercury film electrode has been studied to show potentiometric response towards some specific ions such as Cu (II), Hg (II), Hg (I) SCN^-, I^-, and Br^-. Further, CBMFE has been successfully applied as an indicator electrode for the determination of the assay of isoniazid [4, 5], ascorbic acid [2] and sulphamethoxazole [3]. Copper Based mercury film electrode (CBMFE) functions as an ion– selective electrode [1-5]. Mercury film can be easily coated over the surface a copper wire by dipping the wire in mercuric nitrate solution for few minutes. CBMFE has been shown as potentiometric sensor. It shows potentiometric response towards Cu (II), I^-, Br^- and SCN^-. It is a suitable indicator electrode for the titration involving any of these ions.

2-Thiouracil which is also chemically known as 4-hydoxy-2-mercapto-pyrimidines. 2-Thiouracil is the first thionamide anti-thyroid drug. It is employed for the treatment of hyperthyroidism, congestive heart failure and angina pectoris [6]. Many methods have been developed for the determination of 2-thiouracil based on its oxidation property [7, 8]. These methods include flow injection analysis method [9], chromatographic techniques such as high-performance liquid-chromatography [10], gas chromatographic and mass spectrometric techniques [11].

Even though several methods are available for determining 2-thiouracil, all pharmacopoeias describe visual titration procedure for its estimation. But, literature survey indicates various visual titrimetric methods and a variety of instrumental methods reported for the assay of 2-thiouracil in pure and pharmaceutical formulations.

In the current study, 2-thiouracil in alkaline medium was titrated against silver nitrate using Copper Based Mercury Film Electrode (CBMFE) as an indicator electrode. Importantly, the proposed method is simple, selective and cost-effective for the determination of 2-thiouracil.

EXPERIMENTAL:

FABRICATION OF COPPER BASED MERCURY FILM ELECTRODE (CBMFE)

A plastic sleeved copper wire (99% purity) of 15 cm length and 1 mm thickness was taken and plastic sleeve was removed at one end to expose about 1cm copper wire. Epoxy seal was applied at the junction of copper wire and plastic sleeve to impede entry of solution into the sleeve. The copper wire was cleaned well by abrasion with a fine emery paper and washed with water followed by treatment with concentrated HNO_3 for a few seconds and finally rinsed with water. The polished copper wire was coated with mercury as a thin film by dipping the wire in mercuric nitrate solution (0.2 M) containing nitric acid (1% v/v) for 10 min. The electrode surface was gently wiped with a filter paper and rinsed with water.

REAGENTS

2 - Thiouracil solution (0.01 M)

It was prepared by dissolving 0.1281 g of 2-thiouracil in 100 ml graduated flask and made up to the mark by using 0.1M of sodium hydroxide solution[12].

Silver nitrate standard solution (0.05M)

It was prepared by dissolving 2.1235 g of silver nitrate in 250 ml graduated flask and made up to the mark by using distilled water and standardized volumetrically by titration with sodium chloride.

Sodium chloride solution (0.05 M)

It was prepared by dissolving 0.2922 g of sodium chloride in 100 ml graduated flask and made up to the mark.

Mercury (II) nitrate solution (0.02 M)

It was prepared by dissolving 0.34 g of mercury (II) nitrate monohydrate in 80 ml of distilled water containing 2 ml of nitric acid (2M), and diluted to 100 ml in a graduated flask [13].

Triethanolamine – nitrate buffer [Tris buffer]

It was prepared by diluting 0.669 ml of the triethanolamine in 100 ml of graduated flask and made up to the mark then pH was adjusted to reqiures pH in the of range of 8.5 to 11.0 with the addition of 0.5M nitric acid.

Equipment

A digital pH/mV meter was used to measure potential and pH. Saturated calomel electrode (SCE) was used as a reference electrode. pH meter combined with a glass electrode and standard calomel electrode was used to measure pH of the solution. CBMFE was coupled with Standard Calomel Electrode to measure the cell potential in the titration cell.

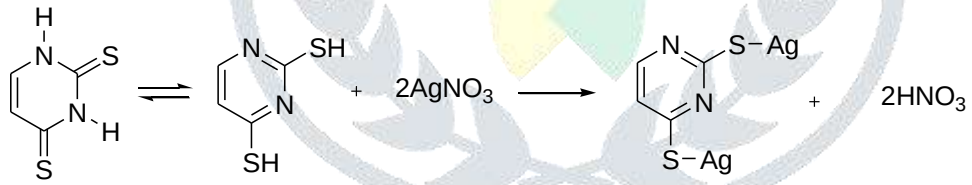
RECOMMENDED PROCEDURE FOR POTENTIOMETRIC TITRATION OF 2-THIOURACIL IN PURE FORM

An aliquot of freshly prepared 2-thiouracil (2.0-10.0 mg) solution was transferred in to a titration cell followed by the dilution with the distilled water to about 50.0 ml. The pH of the solution was adjusted to 8.5 using 0.5M nitric acid/sodium hydroxide and followed by the addition of 2.0 ml of Tris buffer (pH 8.5). The titration cell was equipped with freshly prepared CBMFE and double junction standard calomel electrode as reference electrode. Silver nitrate (0.01-0.02 M) was slowly added from 10 ml micro burette. The potential after each addition of titrant was noted. The end point was detected from the first derivative of the titration curve using software.

RESULTS AND DISCUSSION

Since Copper Based Mercury Film Electrode has been studied to show Nernstian response towards ions such as Cu (II), Hg (II), Hg (I) etc, it can be applied as an indicator electrode for direct or indirect potentiometric titration of any organic compound or a pharmaceutical which can readily form complex with any of the metal ions such as Cu (II), Hg (II), Hg (I) etc.

In the present work, a thorough investigation was carried to determine 2-thiouracil (2-TU) by direct titration against silver nitrate. 2-thiouracil, as a thiol, reacts with Ag (I), to form a complex. The reaction stoichiometry was found to be 1:2 (2-TU: $AgNO_3$), according to the reaction [52].



The thiol group being acidic, the reaction is facilitated rapidly in basic medium. In the present work, a systematic study was carried out to determine 2.0 to 6.0 mg of 2-thiouracil by direct titration with silver nitrate using the CBMFE as an indicator electrode. The required basic medium was provided by the addition of a solution of Tris buffer.

Titrations were carried out in slightly basic medium and the required pH was maintained with appropriate quantities of Tris buffer.

It has been shown that CBMFE can be successfully used as an indicator electrode for titrations involving silver ion, of concentration less than 10^{-3} M and also CBMFE can be successfully used as an indicator electrode for titrations involving silver ion in the concentration range studied [1]. During the titration of 2-thiouracil with silver nitrate, a white precipitate was formed nearly at the end of the titration.

In order to fix the optimum pH for the titration, replicate titrations were carried out with 1.28 mg of 2-thiouracil. Various basic buffers were tested to maintain the required pH. Quantitative recovery of 2-thiouracil by replicate analyses in the presence of Tris buffer indicated it as suitable buffer for the titration. The pH 8-9.5 was found to be optimum for the quantitative precise recovery of 2-thiouracil. Below the pH 8, the reaction was slow as indicated by the more response time needed to establish equilibrium potential during the titration. Above pH 9.5, silver ion got hydrolyzed in the basic medium.

During the titration, equilibrium potential was established rapidly after the each addition of the titrant. In the vicinity of the end point the potential raised significantly. A wait of 2-3 min was necessary at the end point for the equilibrium potential to be established.

For the titration of 1.28 mg of 2-thiouracil, an end point break at 117 mV was observed for the addition of 0.05 ml of 0.00854 M silver nitrate. For the titration of 5.12 mg of 2-thiouracil, an end point break at 141 mV was observed for the addition of 0.05 ml of 0.0174 silver nitrate

Precision and accuracy

Five standard solutions of 2-thiouracil of different concentration were prepared. Five replicate analyses were carried out on each of these in order to assess the precision and accuracy of the proposed method. The results obtained are presented in Table-1. The overall percentage relative deviation (co-efficient of variations) for twenty five determinations was 0.3008 %. It indicated that the proposed method is precise and free from random errors. Over all standard analytical error for twenty five determinations was 0.0048. The overall mean recovery was 100.27 % which indicated the proposed method to be accurate.

Student's t-test to detect systematic error.

In order to detect any systematic error associated with the analysis, two tailed t-test was applied on the experimental data given in Table 1. The amount taken for analysis (μ) at each concentration level was compared with the amount found x by Student's t-test. The Student's t-value was calculated at each concentration level using equation $|\mu - x| / (s/\sqrt{n})$. **The hypothesis considered for the testing was that the amount found by five replications of analysis did not differ significantly from the amount (μ) taken**. The mean value of Student's t-value calculated for five concentrations was 2.07 which was less than the critical value of 2.78 at 5% level of significance and four degrees of freedom. Thus **the hypothesis was retained to make decision that amount found by the analysis did not differ from that taken.** It also indicated that the proposed method is free from any systematic error.

CONCLUSION

Although 2-thouracil has been determined by a number of analytical techniques reported earlier, the most of the methods require sophisticated instruments or time consuming for the process or involve various stages which may increase the risk of errors. The need to develop a method making use of simple instrument always prevails, particularly in developing countries.

The proposed method is simple, rapid and require simple instrument which is commonly available in any laboratory. The proposed potentiometric method of 2-thiouracil assay can be applied successfully for 2-thiouracil assay in tablets.

Remarkable Features of argentometric titration of 2-thiouracil

The proposed argentometric titration of 2-thiouracil makes use of a multi- meter of pH meter which is commonly available in any laboratory.

The copper based mercury film electrode which has been used as an indicator can be easily fabricated in the laboratory making use of commercially available copper wire. It is very much inexpensive lab-made electrode.

The method is a direct potentiometric titration which offers sharp detection of end point with a sufficiently large potential break near the end point.

The proposed method can be adopted for 2-thiouracil assay in any pharmaceutical dosage form. The method does not require sophisticated instruments nor a skilled person to carry out the analysis.

The frequency of analysis is also high, since a titration requires, less time. The proposed method is also sensitive to determine the presence of 1.5 mg per aliquot taken for the analysis.

Table – 1

Results of five replicate determination of 2-thiouracil with silver nitrate and statistical analysis of the data.

Serial Number	Amount Taken (μ) mg	Amount Found ($\bar{x}$) mg	Standard Deviation(s)	RSD (%)	% mean recovery	Standard Analytical error	Student's t-value $t = \|\mu - x\| / (s/\sqrt{n})$
1.	1.2815	1.2876	0.0047	0.3650	100.47	0.0021	2.9050
2.	2.5630	2.5710	0.0047	0.1813	100.31	0.0021	3.8090
3.	3.8445	3.8450	0.0057	0.1488	100.01	0.0025	0.2000
4.	4.4853	4.5052	0.0162	0.3596	100.44	0.0072	2.7639
5.	5.1260	5.1190	0.0230	0.4493	100.14	0.0103	0.6796
Mean				0.3008	100.274	0.0048	2.0716

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