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ARGENTOMETRIC TITRATION OF 6-PROPYL-2-THIOURACIL AGAINST SILVER NITRATE USING COPPER BASED MERCURY FILM ELECTRODE

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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 6-propyl-2-thiouracil in pure 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 both compounds in pure and tablet 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 was 1.023% respectively. No interference was caused by other excipients present in pharmaceutical dosage forms.

Key Works : 6-propyl-2-thiouracil, Copper Based Mercury Film Electrode, Direct Potentiometric Titration, Argentometric Titration.

Introduction:

6-propyl-2-thiouracil is a thionamide anti-thyroid drug. It is employed for the treatment of hyperthyroidism[1], congestive heart failure[2], plaque psoriasis [3] and angina pectoris [4]. Even though several methods are available for determining 6-propyl-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 6-propy-2-thiouracil in pure and pharmaceutical formulations. Most of the official methods of analysis are visual titrations and spectrophotometric methods [5-6] which suffer limitations in the analysis of turbid and opaque pharmaceuticals preparations. The other methods mostly involve either sophisticated instruments or time consuming process. Since versatility of potentiometry is well known, it was contemplated to develop a potentiometric method for the determination of 6-propy-2-thiouracil. Potentiometry, being a simple technique has widely been applied to monitor the variety of species contained in samples such as pharmaceutical, clinical, biological and also in food stuffs. Potentiometry methods mostly make use of ion selective electrodes [7-9] which are either costly or not readily available, particularly in developing countries. So, there is a need to develop lab made inexpensive electrode which can be used 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 ascorbic acid [10], sulphamethoxazole [11] and isoniazid [12,13].

In the current study, 2-thiouracil and 6-propyl-2-thiouracil in alkaline medium was directly 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 both 2-thiouracil and 6-propy-2-thiouracil.

Experimental :

FABRICATION OF COPPER BASED MERCURY FILM ELECTRODE (CBMFE)

A plastic sleeved copper wire (99% purity) of 10 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 prevent entry of solution into the sleeve. The copper wire was cleaned well by abrasion using a fine emery paper and treated with concentrated HNO_3 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

Unless and otherwise specified all the chemicals used were of Analytical Reagent grade. De-ionized and twice distilled water was used throughout the present investigation. The inorganic/organic substances such as 6-propy-2-thiouracil, silver nitrate, sodium hydroxide, nitric acid, Tris buffer and mercuric (II) nitrate were used

6-propyl-2-thiouracil solution (0.003 M)

It was prepared by dissolving 0.125 g of 6-propy-2-thiouracil in 250 ml standarad flask and made up to the mark by using 0.01M of sodium hydroxide [15] solution and standardized by potentiometric titration with iodine [15].

Silver nitrate 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 [16].

Triethanolamine-nitrate buffer [Tris buffer]

It was prepared by diluting 0.726g of the triethanolaminein 60 ml water and then pH was adjusted to reqiured pH in the of range of 7 to 8 with the addition of 0.5M nitric acid and 0.5M sodium hydroxide.

Equipment

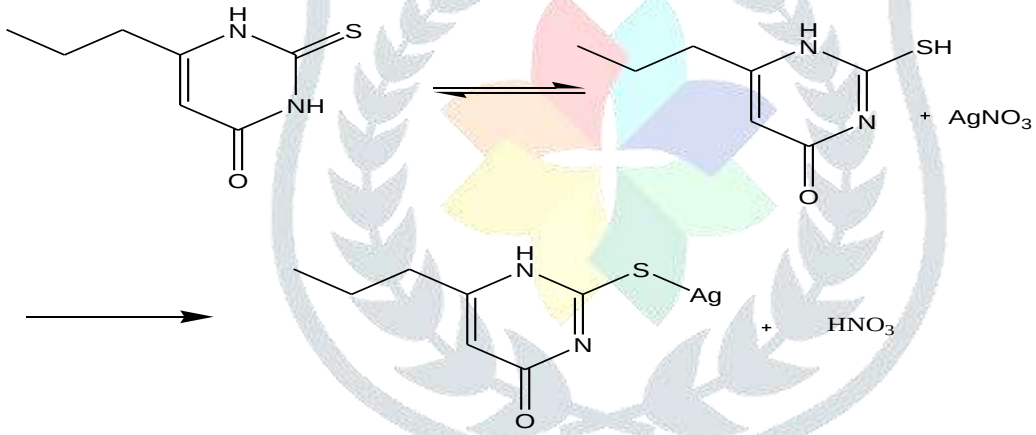
A digital multimeter was used to measure potential and pH. Saturated calomel electrode (SCE) was used as a reference electrode. To measure potential, saturated calomel electrode is coupled with CBMFE in the titration cell. To measure pH of solution, saturated calomel electrode is coupled with glass electrode.

RECOMMENDED PROCEDURE FOR POTENTIOMETRIC TITRATION AND 6-PROPYL-2-THIOURACI IN PURE FORM

An aliquot of freshly prepared 6-propy-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 7-8 using 0.5M nitric acid/sodium hydroxide and followed by the addition of 1.0 ml of Tris buffer (pH 7-8). 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

In the present work, a thorough investigation was carried to determine 2-thiouracil (TU) and 6-propy-2-thiouracil (PTU) by direct titration against silver nitrate. Both 2-thiouracil and 6-propy-2-thiouracil, as a thiol, reacts with Ag (I), to form a complex. The reaction stoichiometry was found to be 1:1 (TU/PTU: $AgNO_3$), according to the reaction.



The thiol group being acidic, the reaction is facilitated rapidly in basic medium.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 systematic study was carried out to determine 2.0 to 10.0 mg of 6-propy-2-thiouracil by direct titration with silver nitrate using the CBMFE as an indicator electrode. The required neutral and slightly basic medium was provided by the addition of a solution of Tris buffer.

Titrations were carried out in neutral and 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 6-propy-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 1.92 mg of 6-propy-2-thiouracil. Various basic buffers were tested to maintain the required pH. Quantitative recovery of 6-propy-2-thiouracil by replicate analyses in the presence of Tris buffer indicated it as suitable buffer for the titration. The pH 7-8 was found to be optimum for the quantitative precise recovery of 6-propy-2-thiouracil. Below the pH 7, the reaction was slow as indicated by the more response time needed to establish equilibrium potential during the titration. Above pH 8.0, 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 1.92 mg of 6-propy-2-thiouracil, an end point break at -71 mV was observed for the addition of 0.5 ml of 0.0035M silver nitrate(Fig.1). For the titration of 3.84 mg of 6-propy-2-thiouracil, an end point break at -102 mV was observed for the addition of 0.5 ml of silver nitrate (fig. 2). For the titration of 2.0-10.0 mg of 6-propyl-2-thiouracil against silver nitrate, titration curves obtained were developed [Fig. 1-5].

Precision and accuracy

Six standard solutions of 6-propy-2-thiouracil of different concentration were prepared. Six 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 thirty determinations was 1.023 %. It indicated that the proposed method is precise and free from random errors. Over all standard analytical error for thirty determinations was 0.0048. The overall mean recovery was 99.75 % 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 2.57 at 5% level of significance and five 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.

Table-I

Results of six replicate titration of 6-propy-2-thiouracil with silvernitrate 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 ($s/\sqrt{n}$)	Student's t-value $t = \lvert\mu - x\rvert / (s/\sqrt{n})$
1.	1.920	1.915	0.0233	1.216	99.740	0.0095	0.5263
2.	3.840	3.835	0.0427	1.113	99.870	0.0174	0.2870

3.	5.760	5.741	0.0541	0.942	99.671	0.0220	0.8630
4.	7.680	7.622	0.0753	0.987	99.245	0.0307	1.8890
5.	9.600	9.620	0.0829	0.861	100.21	0.0330	0.6060
Mean				1.023	99.747	0.0225	0.8343

CONCLUSION

Although 6-Propyl-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 6-propy-2-thiouracil assay can be applied successfully for 6-propy-2-thiouracil assay in tablets. The proposed argentometric titration of 6-propy-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.

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