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Electrochemical study of primaquine Diphosphate in Presence of uranyl nitrate in aqueous media.

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Abstract : Interactions of uranium metal with primaquine diphosphate were investigated by differential pulse and differential current voltammetry. Measurements were performed is sodium acetate buffer at pH 4.00 in aqueous solutions under physiological ionic strength (0.1 mol/dm^3). The electrochemical behavior of complexes of U(II) with primaquine diphosphate were studied for determination of the corresponding stability constant ([M^{2+}])=9 into 10^{-5} mol/dm^{-3}, pH=4.00; total concentration of primaquine diphosphate from $1x10^{-5}$ to $1x10^{-4}$ mol/dm^{-3}). It was observed that primaquine diphosphate forms 1:1, 1:2, complexes with U (II) respectively. The stability constants of the U (II) primaquine diphosphate and complexes were evaluated with the Deford-Hume procedure at different ligand concentrations and they were calculated from the dependence of the shift of metal peak potential and decrease in peak current on the free primaquine diphosphate ion concentration.
Keywords: Electrochemistry; primaquine diphosphate; Uranyl Nitrate; voltammetry.

INTRODUCTION AND EXPERMENTAL :

The electrochemical methods have shown to be of great use in the quantitaive determination, as well as in the study of action mechanism of drugs. The voltammetric behaviour study of primaquine here in described constitutes the first step toward the evaluation of the delivery and action mechanisms of its respective synthesized prodrugs [1,2]. Besides, it can contribute to the understanding of the redox process involved, since little information is available in the literature on the electrochemical behaviour of primaquine diphosphate in aqueous medium.[3]. Different methods of analysis had been reported such as spectrophotometry [4,6], Flurimetry [7,8], HPLC [9] and gas chromatography [10]. Most of them are complicated and time consuming and need sophisticated instruments such as HPLC or gas chromatography or voltammetry. Primaquine a well known antimalarial affecting asexual blood forms of human malaria parasite [11-12] belongs to a therapeutically important group of 8-aminoquinolines, being a potential chelating agent, like other derivatives of this group [13-15], primaquine interact with metal ion presents in the biological system and thereby affects their concentration and/or role in the biochemical reaction pathways. The chelating behavior of primaquine

may be of interest to pharmacologists, specifically with reference to (a) diseases caused by metal ion deficiency, (b) supply of metal ion to the deficient part and (c) its role in metabolic pathways. Further, information on the structure and nature of the complexes formed is helpful in understanding the therapeutic and toxic effects of the drug. The studied drug Primaquine salts have high electron density sites, so they may act as powerful electron donors.

In the present work the formation of complexes have been examined by differential pulse and differential current voltmmetric study. The overall stability constant of the Uranyl complexes of primaquine diphosphate in aqueous medium was determined by shift in peak potential.

REAGENTS AND SOLUTIONS :

The following chemical reagents were used for all volumetric experiments CH_3COOH (Merck), primaquine diphosphate (Aldrich), Uranyl Nitrate (Merck). All the chemicals used in voltammetric measurements were of analytical grade. Double distilled, deionized water was used for preparation of all solutions. The stock solutions of primaquine diphosphate (10^{-2} mol dm^{-3}), Uranyl Nitrate ($9x10^{-5}$ mol dm^{-3}) were prepared in sodium acetate buffer at PH = 4.00. The solutions were kept in darkness at 4^0 c and were found to be stable over a period of several weeks. Diluted solutions of primaquine diphosphate were prepared from the stock just prior to analysis pure nitrogen (99.99%) was used to degass the solutions.

APPARATUS AND MEASURMENTS

Electrochemical measurement were carried out using a computerized multipurpose system consisting of AUTOLAB (Eco Chemie, Utrecht, The Netherlands), a personal computer (486 DX2-80 MHz32 Mb RAM) and a static Mercury drop Electrode Assembly (SMDE) PAR 303 A (Princeton Applied Research, Princeton, USA) with a homemade holder of electrode comprising saturated calomel electrode system comprising saturated calomel electrode as a reference electrode, carbon electrode as a counter electrode and multimode mercury electrode as a working was used. The electrochemical instrument was controlled by a computer with the following software packages. Eas (Electro Analytical System) and GPES 4.5 (general Purpose Electrochemical System) The capillary of drop size 04 with the surface are of 0.04mm2 was used. Before each measurements steam of pure nitrogen degass (oxygen free) the solution. The time of purging was 1805 and the time of equilibrations was 20s.

A known volume of supporting electrolyte 0.15 M KCL in buffer solution pH 4.00 was taken in sample cell and polarogram was run as a blank. To this solution the metal solutions were prepared to get desired working solution. A known volume of working solution was taken in cell and polarogram was run. Then a step by step increase in concentration of primaquine diphosphate drug was made using a micropipette the total concentration of the drug was opproximately thrice the concentration of metal. The potential scans were recorded using polarographic technique at scan rate of $10mVs^{-1}$ad pulse amplitude of primaquine diphosphate with uranyl ions in aqueous medium are given in TABLE 1.

Table 1 Results on Voltammetric measurements of Uranyl –Primaquine Diphosphate complexes for the determination of the stability constants Log (K ML^{n+}) by shift in peak potentials and reduction in peak current

Concentration [M] x 10^{-5} M	Concentration [L] x 10^{-5} M	Ep (V)	Ip (A)
9.00	-	-0.261	-2.97×10^{-8}
9.00	4.00	-0.270	-2.75×10^{-8}
9.00	9.00	-0.272	-2.45×10^{-8}
9.00	12.00	-0.272	-1.39×10^{-8}
9.00	18.00	-0.274	-5.28×10^{-9}
9.00	20.00	-	-

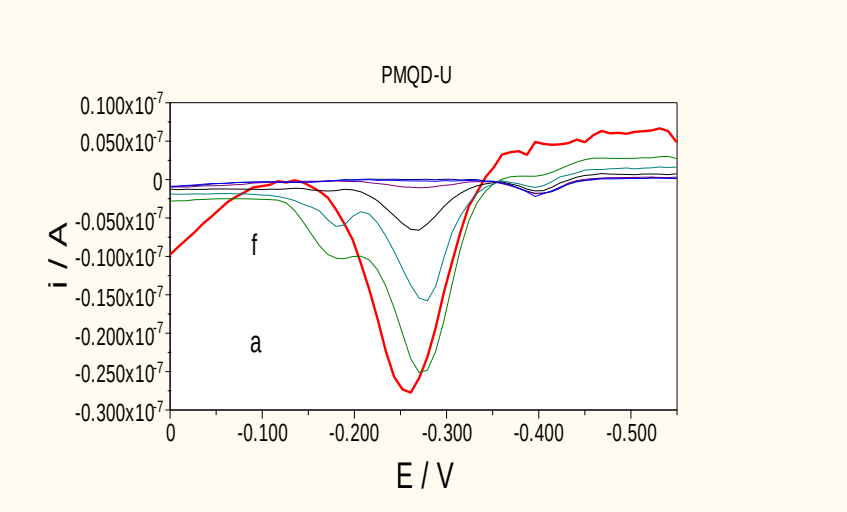

Figure 1 DPP of 9 x 10^{-5} M Uranyl with increasing concentration of Primaquine diphosphate (4.00 x 10^{-5} M to 20.00 x 10^{-5} M) in buffer solution of pH 4.00
a = 9 x 10^{-5} M pure Uranyl [-] in buffer solution
Ligand: b = 4.00 x 10^{-5}, c = 9.00 x 10^{-5}, d = 12.00 x 10^{-5}, e = 15.00 x 10^{-5}, f = 18.00 x10^{-5}, g = 20.00 x10^{-5}, h = 24.00 x 10^{-5}

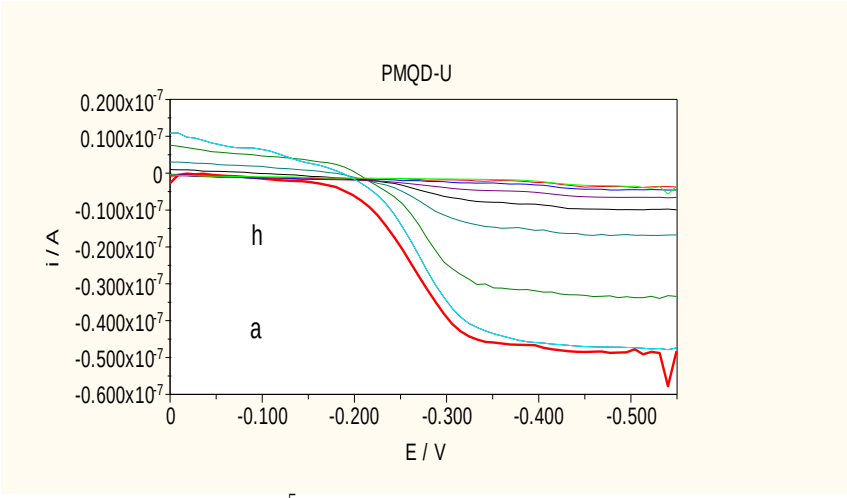

Figure 2 DC of 9 x 10^{-5} M Uranyl with increasing concentration of Primaquine diphosphate (4.00 x 10^{-5} M to 20.00 x 10^{-5} M) in buffer solution of pH 4.00
a = 9 x 10^{-5} M pure Uranyl [-] in buffer solution
Ligand: b = 4.00 x 10^{-5}, c = 9.00 x 10^{-5}, d = 12.00 x 10^{-5}, e = 15.00 x 10^{-5}, f = 18.00 x10^{-5}, g = 20.00 x10^{-5}, h = 24.00 x 10^{-5}

RESULTS AND DISCUSSION:

Complexation of Primaquine Diphosphate with Uranyl ions by differential pulse voltammetry and differential current voltammetry:

The DPP and DC for the complexation of Primaquine Diphosphate with Uranyl (IV) in pure water are given in Figure 1.and Figure 2. For DPP U (IV) shows a single reduction peak at -0.261V. On gradually increasing the concentration of Primaquine Diphosphate from 4 x10^{-5} to 20 x 10^{-4} mol dm^{-3} in the cell containing 9 x 10^{-5} mol dm^{-3} U (IV) metal solution, result in the shift in peak potential towards more negative side with simultaneous decrease in peak current. With continuous decrease in current, the peak disappears completely when ligand concentration is almost doubles to that of metal, indicating that the complex has 1:2 (metal: ligand) stiochiometry.

The stability constant was calculated from shift in potential and found to be 2.335.

CONCLUSION:

The complexation reaction occurring between metal ions i.e. Uranyl (IV) and Primaquine Diphosphate can be followed by using DPP and DC ,which allow the identification of complexes formed as well as the determination of stability complexes of 1:1 and 1:2 complexes with Primaquine Diphosphate respectively.

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