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SENSORS

Determination of 2',3'-Dideoxyinosine Using Iron (II) Phthalocyanine Modified Carbon Paste Electrode

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ABSTRACT

An amperometric sensor, based on carbon paste impregnated with iron (II) phthalocyanine complex (FePc), has been constructed for the assay of anti-HIV agent dideoxyinosine (didanosine, DDI). Using chronoamperometry ($E = +1.04$ V versus Ag/AgCl) technique, the amperometric sensor can be used reliably for dideoxyinosine assay at pH 7.4 phosphate buffer in the 1.5–9.5 nmol/L concentration range with a detection limit of 5.7×10^{-10} mol/L. The surface of the electrode can easily be regenerated by simple polishing, obtaining a fresh surface ready for use in a new assay. The new amperometric sensor proved to be highly reliable

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for the assay of dideoxyinosine purity in raw material as well as for the uniformity content test of Videx[®] tablets.

Key Words: Amperometric sensor; Iron (II) phthalocyanine; 2',3'-Dideoxyinosine.

INTRODUCTION

2',3'-Dideoxyinosine (Didanosine, DDI) (Fig. 1) is a dideoxypurine-nucleoside analog that potently inhibits the replication of the human immunodeficiency virus (HIV), the virus that causes acquired immunodeficiency syndrome (AIDS).^[1,2] Among dideoxynucleosides, dideoxyinosine was approved for the treatment of adults and children with advanced HIV infection, especially for those patients who are intolerant or resistant to azidothymidine (AZT) therapy or whose health have been deteriorated by AZT use.^[3]

To date, most published analytical methods for the assay of DDI are based on high performance liquid chromatography,^[4-8] capillary electrophoresis-electrospray ionization tandem mass spectrometry,^[9] and liquid chromatography-tandem mass spectrometry.^[10] Electrochemical techniques can be a good alternative for the chromatographic methods by offering advantages such as simplicity, high efficiency, and low-cost of instrumentation over other analytical techniques.^[11]

Among metallophthalocyanines (MPcs), iron (II) phthalocyanine (FePc) (Fig. 2) and its analog complexes have been recognized as very good electrocatalysts in chemically modified electrodes.^[12-16] MPc-based carbon paste

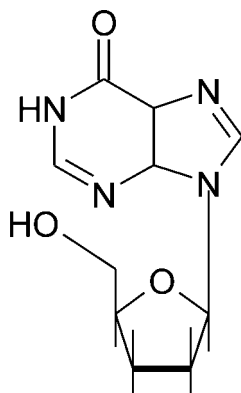


Figure 1. 2',3'-Dideoxyinosine.

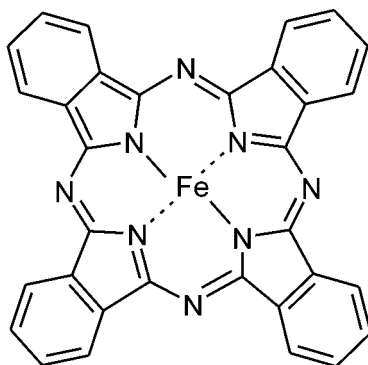


Figure 2. Iron (II) phthalocyanine (FePc) complex.

electrodes have found several applications in the determination and quantification of a wide range of chemical substances.^[13–15,17–19]

The aim of the present study is to develop an amperometric sensor based on FePc (Fig. 2) complex impregnated on carbon paste matrix and to explore its application for the determination of the purity of DDI—raw material as well as for the content uniformity test of Videx[®] tablets.

EXPERIMENTAL

Reagents and Materials

2',3'-Dideoxyinosine was obtained from Sigma-Aldrich (St. Louis, MO, USA). Iron (II) phthalocyanine and graphite powder (1–2 μm , synthetic) were supplied by Aldrich. Paraffin oil was supplied by Fluka (Buchs, Switzerland). Videx[®] tablets were obtained from Bristol-Myers Squibb. Deionized water obtained from a Modulab system (Continental Water Systems, San Antonio, TX, USA) was used for the preparation of all solutions. All solutions were buffered with phosphate buffer solution of pH 7.4.

Apparatus

A 663 VA stand (Metrohm, Herisau, Switzerland) connected to a PGSTAT 100 and a Eco-Chemie software ver. 4.9 were used for all electrochemical (cyclic voltammetry and amperometry) measurements. A platinum electrode and a Ag/AgCl (0.1 mol/L KCl) electrode served as counter and reference electrodes in the cell, respectively.

Amperometric Electrode Design

Graphite powder and FePc (4% based on the weight of graphite powder) were first ground together to ensure uniform dispersion of the phthalocyanine complex. This was followed by mixing paraffin oil and graphite-FePc mixture in a ratio of 1 : 4 (w/w). A certain quantity of graphite paste free of FePc was prepared and placed into a plastic pipette peak leaving 3 to 4 mm empty in the top to be filled with carbon paste that contains the FePc. The diameter of the amperometric sensor was 3 mm. Electric contact was obtained by inserting a Ag/AgCl wire into the carbon paste. The internal solution was 0.1 mol/L KCl. The surface of the electrode was wetted with deionized water and polished with alumina paper (polishing strips 30144-001, Orion) before use. When not in use, the amperometric sensor was stored in a dry state at room temperature.

Recommended Procedure

Direct Amperometric Assay

The technique used for direct amperometry was chronoamperometry. The potential applied was +1.04 mV versus Ag/AgCl. The applied potential gave the best current response in cyclic voltammetric experiment. The working temperature was 25°C. Different aliquots of stock DDI solution ($C = 10^{-4}$ mol/L) were added to generate a series of concentration steps.

Content Uniformity Test of Videx[®] Tablets

Each of ten Videx[®] tablets (100 mg DDI/tablet) was placed in a 100 mL volumetric flask and dissolved in phosphate buffer. The apparatus cell was filled with the prepared solution and the current developed was measured. The unknown concentration was determined from the calibration graph.

RESULTS AND DISCUSSION

Electrode Response

The electrode response was determined using chronoamperometric technique ($E = +1.04$ V versus Ag/AgCl). The calibration equation obtained for the amperometric sensor is:

$$I = -5.16 + 6.87C; \quad r = 0.9953$$

where I is the current intensity (nA), C is the concentration of the DDI (nmol/L), and r is the regression coefficient. All the values are the average of ten measurements performed during one month. The proposed electrode was highly stable and reproducible over a month test period (RSD for the current intensity $<1\%$). The limit of detection for the amperometric sensor was 5.70×10^{-10} mol/L, with a working concentration range in the region of 10–60 nmol/L. The response time of the sensor is 2 minutes. The low limit of detection, high reliability, and stability of the new amperometric sensor are due to the high electrocatalytic and thermal stability properties of the iron (II) phthalocyanine complex.

Analytical Application

The amperometric sensor proved to be useful for the purity tests of the DDI raw material using chronoamperometric ($E = +1.04$ V versus Ag/AgCl) technique with an average recovery of 99.91 ± 0.05 ($n = 10$). The results obtained for the uniformity content test (Table 1) indicate that dideoxyinosine can be reliably assayed from its pharmaceutical formulation, Videx[®] tablets with an average recovery of 99.82 ± 0.05 ($n = 10$). The results are in good agreement and within the range given in the United States Pharmacopoeia XXIV,^[20] 90 to 110% per tablet.

Table 1. Uniformity content of Videx[®] tablets (100 mg dideoxyinosine/tablet) using amperometric sensor based on iron (II) phthalocyanine complex. All measurements were made at 25°C. All values are averages of ten measurements performed during one month.

Tablet sample	Recovery of DDI, mg
1	99.85 ± 0.05
2	99.79 ± 0.06
3	99.82 ± 0.05
4	99.86 ± 0.05
5	99.78 ± 0.06
6	99.81 ± 0.05
7	99.87 ± 0.04
8	99.80 ± 0.05
9	99.84 ± 0.04
10	99.82 ± 0.05

CONCLUSIONS

This paper has shown that the construction of amperometric sensor based iron (II) phthalocyanine using carbon paste matrix is simple and reproducible. The reliability of the analytical information is assured by the RSD (%) values obtained in the recovery tests. The proposed amperometric sensor is suitable for the assay of 2',3'-dideoxyinosine raw material as well as from its pharmaceutical formulation. The main advantage of the proposed method over the other methods described for its assay is the possibility of the direct determination of the active compound, without prior separation, with high precision, rapidity, stability, and low consumption of sample and buffer.

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