J. King Saud Univ., Vol. 11, *Science* (1), pp. 53-60 (A.H. 1419/1999)

A Novel Method for the Determination of Isoprenaline in a Pharmaceutical Preparation by Differential-pulse Voltammetry

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(Received on 12/11/1997; accepted for publication 3/5/1998)

Abstract. A differential-pulse voltammetric procedure is described for the determination of low concentrations of isoprenaline in pure form in a pharmaceutical preparation. At pH 0.5 and with 0.1 M potassium nitrate as the base electrolyte, the electrode response was linearly proportional to the concentration of isoprenaline in the range 10^{-5}-10^{-2} M. The detection limit was 1×10^{-6} M and the relative standard deviation (n=10) was 1.2% at 4×10^{-4} M isoprenaline. The degree of interference from some excipients, added to the pharmaceutical product, on the differential pulse voltammetric signal for isoprenaline was evaluated. No matrix separation is required.

Introduction

Isoprenaline[1-(3,4-dihydroxyphenyl)-2-isopropylaminoethanol; or Isopropyl-noradrenaline] is a sympathominetic agent which acts almost exclusively on beta-adrenergic receptors. It stimulates the central nervous system, has a powerful stimulating action on the heart and increases cardiac output, excitability, and rate. It is used for the symptomatic relief of bronchial asthma, in the treatment of bradycardia in patients with heart block [1].

The quantitative determination of isoprenaline and other catecholamine drugs is complicated by their intrinsic susceptibility to oxidation and the need for their stabilization with antioxidants. Isoprenaline determination was reported in the literaure by using colorimeteric methods in which they used 0-phenylene diamine. Most methods reported

for isoprenaline determination are colorimetric involving the use of o-phenylenediamine dihydrochloride[2], an organic brominating agent such as bromine-T [3], sodium metaperiodate in an aqueous alcoholic medium[4] also, a flow-injection system coupled to a colorimetric reaction based on the oxidation of isoprenaline with sodium metaperiodate [5]. Most of the colorimetric methods are limited in heir specificity and involve tedious and time-consuming manipulations. Other analytical studies made on isoprenaline involve nonaqueous titrimetry[6], spectrofluorimetry[2], high performance liquid chromatography (HPLC)[7], and chemiluminescence [8, 9].

Differential pulse voltammetry is a useful technique in pharmaceutical analysis, agrochemical bioregulators, toxicology, biochemicals, waste treatment and disposal. Samples such as amino acids [10], diethylamino [11], mitozantrone [12], paracetamol [13], and aconitine [14], have been determined using such a technique.

A literature survey shows that almost no work has been done so far on the determination of isoprenaline using a glassy carbon electrode. Therefore, the present investigation is conducted to develop a novel rapid, accurate and specific electrochemical study of isoprenaline using a glassy carbon electrode. The proposed method was applied to the determination of isoprenaline in samples of pharmaceutical preparation in the presence of exipients and other substances that are usually encountered in such formulation. The method obviates the need for extraction or other tedious manipulations inherent in most published procedures.

Experimental

Apparatus

A metrohm polarecord Model 626(Metrohm, Herisau, Switzerland) was used to record all differential pulse voltammograms. All measurements were carried out at room temperature (ca.25 °C) using a pulse amplitude of 100 mV and scan of 10 mV s^{-1}. The pH was measured with a metrohm E 510 pH meter. The solutions were purged with oxygen - free nitrogen for 3 min before recording voltammograms.

Electrodes and electrochemical cell

The polarographic detector was a double-walled three electrode cell (Metrohm) with a Metrohm 6.0805.010 glassy carbon working electrode, a Metrohm 6.0332.000 platinum auxiliary electrode and saturated calomel reference electrode.

Reagents and solutions

All chemicals used were of analytical-reagent grade. Isoprenaline sulphate was obtained from Sigma (97%). Stock solution (0.01 M) of isoprenaline sulphate was prepared by dissolving the compound in 0.1 M potassium nitrate and diluted as required. The working solutions were adjusted to pH 0.5 using hydrochloric acid.

Determination of isoprenaline

A 50-ml volume of the sample solution was placed in polarographic cell and deaerated for a few min with nitrogen. Measurements were made in 0.1 M potassium nitrate (pH=0.5) with potential scans between 0.0 and 0.8V at 10 mV s^{-1}, a 100 mV pulse amplitude and 0.5 s repetition time.

Results and Discussion

Electrolyte and pH: The influence of several electrolytes such as potassium nitrate, potassium chloride, potassium phosphate and potassium citrate on the analytical signal was studied to obtain the best voltammograms. It was found that with $1+10^{-4}$ M isoprenaline and a scan rate of 10 mVs^{-1} the best results were achieved with a solution containing potassium nitrate.

The differential-pulse voltammograms of the isoprenaline were investigated at various pH values . The results shown in Table 1 indicate that the peak potential is appreciably dependent on the pH. The results also show the effect of pH on peak current. At high pH values (pH=12.0) the oxidation peak of isoprenaline becomes poorly defined.

Table 1. Effect of pH on 1.0×10^{-4} M isoprenaline (in 0.1 M KNO_3) peak current and peak potential: scan rate=10 mVs^{-1}

pH	Peak potential (Ep) mV	Peak current mA
0.49	700	10.5
1.0	700	10.5
1.5	680	9.75
2.0	660	8.35
2.5	680	7.35
3.0	670	6.0
4.08	570	5.5
6.0	520	5.5
8.1	510	5.15
10.0	500	2.75

Figure 1 shows cyclic voltammgrams obtained on glassy carbon electrode for a solution of isoprenaline in potassium nitrate. Only one oxidation peak was observed at 0.7 V which indicates the irreversible character of the oxidation processes. This result was confirmed by applying different criteria to d.c. polarograms.

Figure 2 presents differential-pulse voltammograms for solutions of isoprenaline of increasing potassium nitrate concentration (pH 0.5). Linearity between the peak current and the isoprenaline concentration over the range $2\text{-}8\times10^{-4}$ M was obtained (slope=3.212

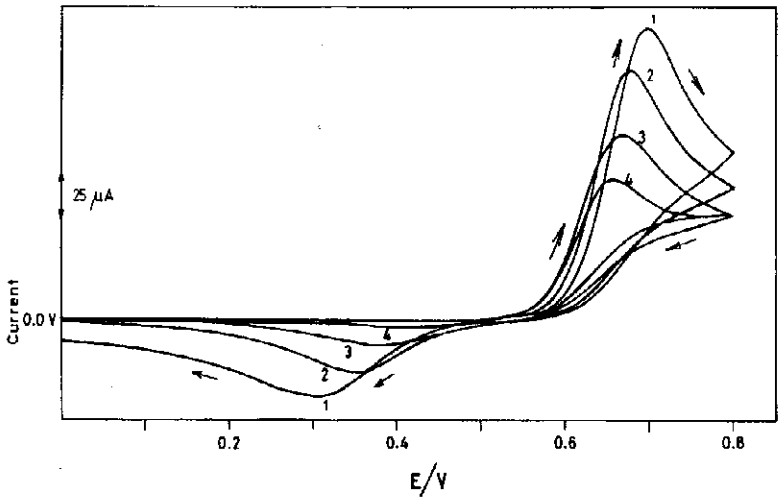

Fig. 1. Cyclic voltammograms of 1 x 10^{-2} M isoprenaline in 0.1 M KNO_3; pH=0.5 at different sweep rates: (1) 15 mV S^{-1}; mV S^{-1}; (2) mV S^{-1}; (3) mV S^{-1}; (4) 3 mV S^{-1}.

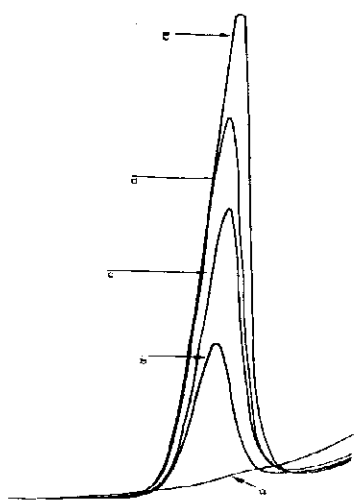

Fig. 2. Calibration graph for solutions of isoprenaline 0.1 M KNO_3, pH = 0.5, 100 mV/cm, 10 mV/s and and 0.05 μA/mm; a) blank (electrolyte); b) 2 x 10^{-4} M; c) 4 x 10^{-4} M; d) 6 x 10^{-4} M; e) 8 x 10^{-4} M.

nA/ml and correlation coefficient = 0.995). The detection limit under the conditions of the experiment was 2 μg ml^{-1}.

Interference was investigated by determining 1×10^{-4} M solution of isoprenaline in the presence of 10 fold (by weight) concentration of potential interference. The responses were compared with those obtained from pure isoprenaline. No effect was observed from most excipients present in the pharmaceutical preparation as shown in Table 2, although riboflavin and carbowax, added to the drugs, showed appreciable interference. This might arise from the fact that these compounds can be oxidized to a little extent. These interferences could be eliminated by the use of a standard addition method when such excipients are present. Copper, zinc and mercury, when present, caused significant interferences. All these excipients have less effect on the potential peak. Isoprenaline down to 1×10^{-6} M can be determined very conveniently by differential-pulse voltammetry with a glassy carbon electrode. This indicates that the method is as precise as the usual spectrophotometric method where many degradation and additives interfere.

Table 2. Effect of interference (each 1×10^{-3} M) on the analytical signal for isoprenaline (1×10^{-4} M) in 0.1 M KNO3 at pH = 0.5 and scan rate 10 mVs^{-1}

Interferent	Peak current (ip) (μA)	Recovery (%)*
Pure	2.70	100
Ca^{2+}	2.70	100
Cd^{2+}	2.76	102.2
Co^{2+}	2.61	96.7
Mg^{2+}	2.45	90.7
Ni2+	2.70	100
Pb2+	2.60	96.3
Zn2+	2.22	82.2
Hg2−	2.30	85.2
Fructose	2.65	98.1
Glucose	2.50	92.6
Nicotinamide	2.7	100
Riboflavin	2.95	109.3
Magnesium stearate	2.60	96.3
Carbowax	3.05	113.0

*Average of three determinations.

The proposed voltammetric method was tested by analyzing a commercial formulation of isoprenaline (an injection). It was considered of interest to compare the figures of merit for this proposed procedure with those of a flow injection spectrophotometric assay for isoprenaline[15], which involves reacting the isoprenaline with potassium hexacyanoferrate(III) to form the red N-isopropylnoradrenochrome at (max 520 nm). Statistical

analysis of the results obtained revealed that there is no significant difference between the two methods as shown in Table 3.

Table 3. Determination of isoprenaline in commercial formulation with polarographic (dpp) and Betteridge (B) *et al.* [7] methods

Formulation	Amount of isoprenaline (μg) Found*			Recovery ± S.D. (%)	
	Claimed	dpp	B	dpp	B
Isoprenaline injection (1mg/5ml) (Elkins-Sinn)					
Sample 1	16	15.98	16	99.9±0.68	100.0±0.45
Sample 2	20	20.6	20.3	101.0±0.78	101.5±0.35
Sample 3	25	25	24.6	100±0.95	98.4±0.85

*Average of four determinations per sample.

In conclusion, the proposed method is simple, quick and could find a wide application in routine analysis compared to other spectrophotometric methods. It has the advantage of being relatively free of interferences.

Acknowledgement. We are thankful to Dr. Mohammed Abul Hassan for his useful discussion of the manuscript.

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طريقة حديثة لتقدير الايزوبرينالين في التحضيرات الصيدلانية بواسطة الفولتاميتري النبضية التفاضلية

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ملخص البحث. يصف البحث طريقة فولتاميترية نبضية تفاضلية لتقدير تراكيز ضئيلة من الايزوبرينالين كمركب نقي في التحضيرات الصيدلانية. فعند آس هيدروجيني مقداره ٥,٠ واستخدام نترات البوتاسيوم كمحلول الكتروليتي وجد أن إشارة القطب العامل تتناسب طرديا مع تركيز الايزوبرينالين في المدى الواقع بين 10^{-9} و 10^{-2} مولار وأن معامل الانحراف المعايري القياسي لـ ١٠ قراءات يساوي ٢,١٪ عند تركيز مقداره 1×10^{-4} مولار ايزوبرينالين، وأن درجة التداخل من بعض المواد المساعدة المضافة للتحضيرات الصيدلانية على الإشارة التحليلية للدواء قد تم تقييمها وان الدواء لا يحتاج إلى استخلاص قبل تقديره.