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INDIRECT ELECTROCHEMICAL DETERMINATION OF RIBOFLAVIN (VB_2) USING 1, 4-BENZAQUINONE MODIFIED CARBON PASTE ELECTRODE

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Abstract: Herein, simple voltammetric sensor based on 1,4-benzaquinone modified carbon paste electrode (1,4-BQCPE) is demonstrated for detection of riboflavin (VB_2). The detection method is established on the decline of 1,4-benzoquinone redox peak current on adding VB_2. Cyclic voltammetric (CV) and linear sweep voltammetric (LSV) methods were used for the study. The 1,4-BQCPE displayed a distinct peak with consistent peak current values for repeated determinations; and exhibited a decrease in redox peak current value with rise in VB_2 concentration. Two linear range ranges were observed between 0.5 μM - 10 μM and 20 μM - 200 μM, with a limit of detection (LOD) of about 0.087 μM and 14.51 μM, respectively. As compared to bare carbon paste electrode, 1,4-BQCPE showed superb sensitivity. Moreover, good reproducibility, stability and recovery for the detection of VB_2 was obtained with the proposed votammetric sensor and successfully applied for detection of VB_2 in pharmaceutical tablet.

Keywords: Electrochemical determination; riboflavin; carbon paste electrodes; 1, 4-benzaquinone

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Introduction

Riboflavin (7,8-dimethyl-10-ribityl-isoalloxazine) also known as vitamin B_2 (VB_2), is a water soluble vitamin present in different kind of foods and pharmaceutical products.[1-3] VB_2 is an important component of diet and pharmaceutical substance and has significant roles in our human body.[4] It plays a vital role in normal functioning of essential mineral metabolism, hemoglobin synthesis and upkeep of the visual function of an eye.[4-7]

Since VB2 cannot be produced by human body, it has to be supplemented through ingestion via other sources since its deficiency in humans can lead to several diseases.[8-9] Therefore, development of fast, selective and sensitive methods is vital for determination of VB_2.

Various analytical methods have been reported for detection of VB_2 in foods and pharmaceuticals. These include chromatographic techniques[10-12], fluorescence[13-14] and spectroscopy[15]. However, the expensiveness of the instrumentation and tedious procedures are the shortcomings[16]. Since VB_2 is an electroactive species, electroanalytical methods are the possible alternative for electroanalysis of VB_2. As it is well known, electrochemical methods are usually described by inexpensiveness, possess better sensitivity and selectivity and fast analysis.[5,17]

Carbon paste electrodes (CPEs) and chemically modified carbon paste electrodes (CMCPEs) are extensively utilized in different fields of electrochemistry because of their low background current and noise, simplicity to fabricate, wide potential window, rapid surface renewability by simple polishing, stability, robustness in aqueous media and inexpensiveness. Furthermore, CMCPEs commonly prepared by introducing various modifying substances to the bulk of CPEs so as to enhance sensitivity, selectivity, and rapidity of detection.[18-21] Quinones are a class of compounds consisting of conjugated cyclic diketone organic systems. They are one of the most used mediators which serve as electron acceptors in mediated biosensors.[22-23] Benzoquinone have been found important modifying agent for the preparation of modified carbon paste electrodes.[24-25]

Therefore, in this work, we demonstrated electroanalytical technique using 1,4-BQCPE for electroanalysis of VB_2. The electrochemical determination of VB_2 is possible due to its electro-reduction at the electrode. In general, it is believed that electro-reduction of VB_2 is a reversible process involving two electrons and two protons (Figure 1).[3]

Accurate detection of VB_2 in pharmaceuticals established the capability 1,4-BQCPE in the electroanalysis of VB_2 in real samples. Therefore, the demonstrated sensor may possibly be used for selective and sensitive determination of the target analyte in pharmaceuticals. So, 1,4-BQCPE has been successfully used for quantification of VB_2 in a tablet with satisfactory recovery.

Results and Discussion

Cyclic Voltammetric Study of Unmodified Carbon Paste Electrode (UCPE) and 1,4-BQCPE in Buffer and in the Presence of VB_2

CV was first used to examine the electrochemical properties of the UCPE and 1,4-BQCPE in the absence and presence of VB_2. As shown in Figure 2A, curve a, the CV recorded in BR buffer (pH 1.5) at UCPE, no redox peaks were observed. Whereas the CV recorded at 1,4-BQCPE in BR buffer (pH 1.5) showed two peaks at potentials of about 0.3 V and 0.56 V (Figure 2B, curve a). The Figure shows that the electrochemical reaction of 1,4-BQ is reversible.

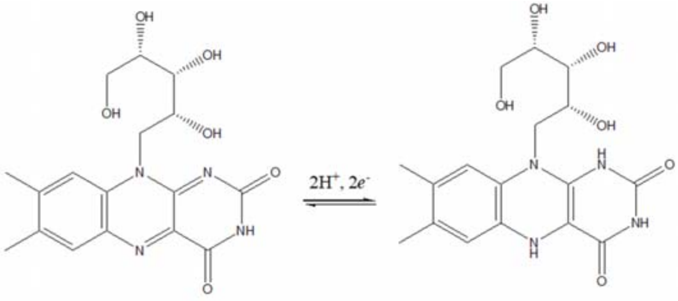

Figure 1. The electro-reduction mechanism of VB_2.

CV for the redox behavior of VB_2 at the UCPE and 1,4-BQCPE at pH 1.5 is shown in Figure 2A and 2B, curve b. As can be observed in Figure 2A, curve b, VB_2 shows two redox peaks at about 0.62 V and 0.1 V which is corresponding to its oxidation and reduction, respectively. However, the intensities of the two redox peaks are very weak as compared to 1,4-BQCPE. The electrochemical redox behavior of 1,4-BQCPE in the presence of VB_2 was shown in Figure 2B, curve b. The 1,4-BQCPE peak current declined when VB_2 was added to the buffer solution. The decrease in redox peak current helps to determine VB_2 by analyzing the decrease in peak current up on addition of different concentration of VB_2.

As observed in the CV, when the concentration of VB_2 increases, the redox peak current of 1,4-BQ decreases. The decline in redox peak current of VB_2 was found to be directly correlated with the concentration of VB_2.

The LSV for 1,4-BQCPE in the presence of VB_2 revealed a distinct peak at the same potential as seen in the CV, and it was observed a reduction in peak current up on increasing the concentration of VB_2， the reason for which is unclear. A similar phenomenon has been reported by Akililu *et. al.*[25]

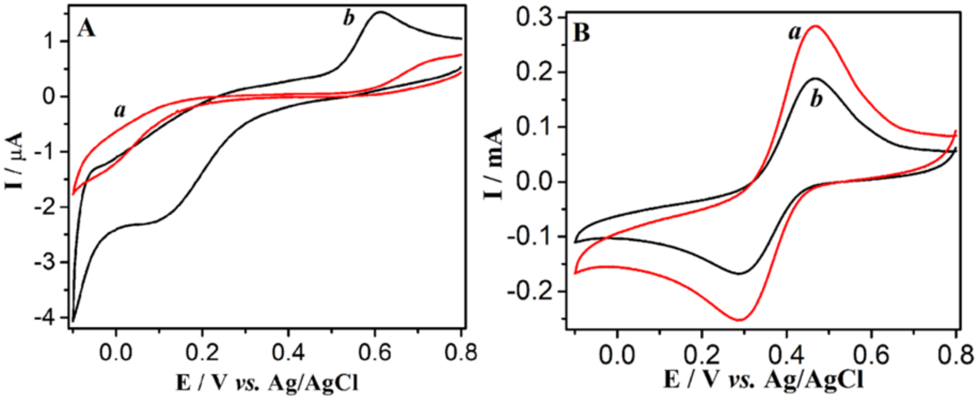

Figure 2. CV of a) BR buffer pH 1.5 b) 5 µM VB$_2$ (pH 1.5) at UCPE (A) and 1, 4 BQCPE (B); scan rate 50 mVs^{-1}.

Herein, we examined different assumptions for the possible reason for the decline in redox current up on rising the concentration of VB$_2$. We expected an electroactive complex formation at the electrode surface because of adsorption of VB$_2$ on to the electrode surface, which may result competitive surface adsorption resulting in the variation of electrochemical parameters. This assumption was carefully studied by varying scan rate using 1,4-BQCPE in the presence of VB$_2$. The result showed that the peak current of VB$_2$ linearly increases with the square root of scan rate which shows diffusion controlled mechanism (Figure 3). Therefore, competitive surface adsorption is not a reason for the decrease in peak current up on successive addition of different concentrations of VB$_2$.

The other assumption is, there might be the formation of an electro inactive complex of 1,4-BQ with VB$_2$. The experimental evidences found from UV-Vis measurement shown no proof for any complex formation between VB$_2$ and 1,4-BQ. However, in depth investigations and studies are needed.

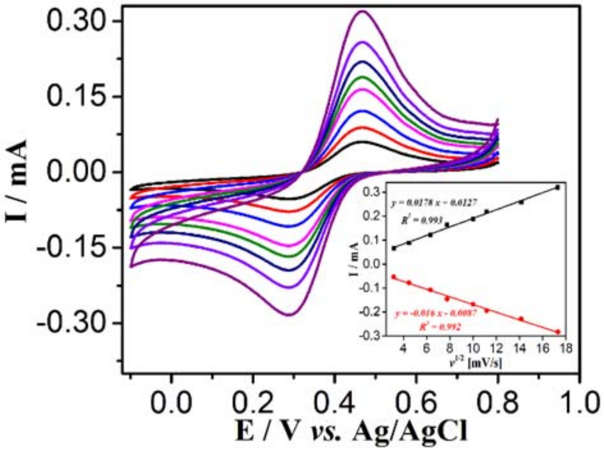

Figure 3. CV of 5 μM VB_2 at 1,4-BQCPEs in BR buffer at pH 1.5 at different scan rates, from 10-300 mVs^{-1} (Inset : The plot of I_{pa} and I_{pc} *vs.* $\upsilon^{1/2}$).

Optimization of Experimental Parameters

To obtain the best experimental conditions, some parameters were optimized for CV and LSV determination of VB_2 at 1,4-BQCPE.

Effects of pH

In order to improve the performance of 1,4-BQCPE, the pH of supporting electrolytes on the redox current of VB_2 at 1,4-BQCPE studied. Therefore, the influence of the pH of supporting electrolyte on the 1,4-BQCPE redox current was tested in the range from 1.5 to 6.0, and shown in Figure 4.

As observed from the Figure 4, both the oxidation and reduction current decreases with rise in pH of the buffer. This can be described by the protonation-deprotonation phenomenon of VB_2 during the redox reaction. With rise in pH value, the peak current of VB_2 declines because VB_2 undergoes deprotonation process which hinders the redox process and hereafter leads to the decline in the redox current.[17, 26-27]. Since the peak current is decreasing with increase in pH, pH of 1.5 was used for further study.

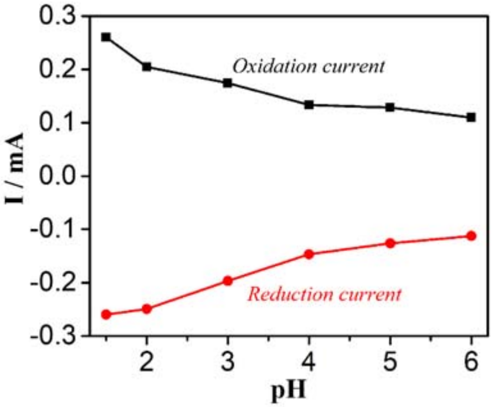

Figure 4. The relationship between the redox peak current of VB_2 and buffer pH values.

Effects of Composition of Modifiers

The amount of 1,4-BQ on the voltammetric response of the 1,4-BQCPE was examined by changing the amount of 1,4-BQ, graphite powder and paraffin oil.

As shown on Figure 5, the maximum peak current was observed at 20% (w/w) composition of 1,4-BQ in the carbon paste. The peak current decreased when the amount of 1,4-BQ is higher than 20% (w/w). The decrease in peak currents of the electrode is because of the reduction of the electric conductivity as a result of decrease in the graphite content in the paste. The best composition for the electrode was found to be, 20% (w/w) 1,4-BQ, 60% (w/w) graphite powder and 20% (w/w) paraffin oil.

Calibration Plot for Riboflavin

The 1,4-BQCPE displayed a distinct peak with consistent cathodic current readings for repeated measurements; and indicated a decline in reduction current reading with rise in VB_2 concentration. The result shows two linear ranges between 0.5 μM and 10 μM and 20 μM and 200 μM, with regression equations:

$y = 0.0157\,x - 0.284$ (x concentration in μM), $R^2 = 0.997$

$y = 0.0005\,x - 0.11$ (x concentration in μM), $R^2 = 0.987$, respectively (Figure 6).

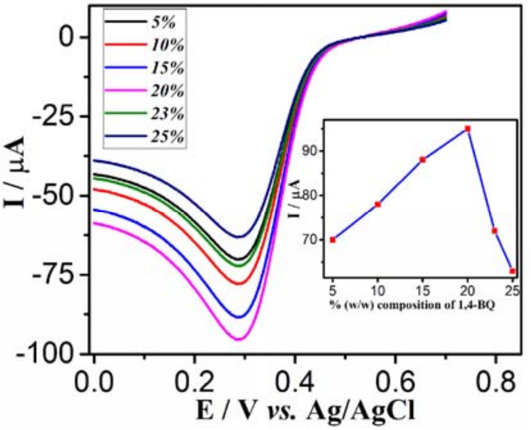

Figure 5. LSV of VB_2 at 1,4-BQCPE with different composition of 1,4-BQ (Inset: Effect of composition of 1,4-BQ on the reduction peak current; Note: the y-axis in the inset is the absolute value of cathodic current).

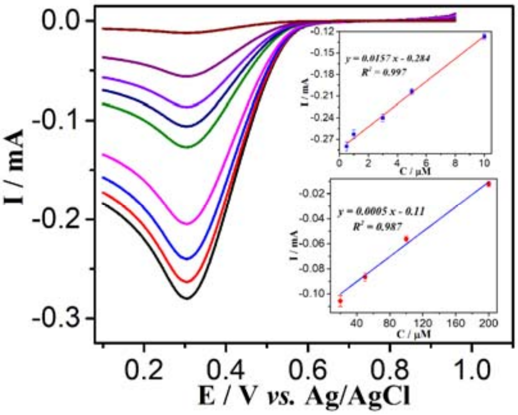

Figure 6. LSV of 1,4-BQCPE at different VB_2 concentrations (Inset: The corresponding calibration curve from 0.5 – 10 μM and from 20 – 200 μM).

A limit of detection of 0.087 µM and 14.51 µM ($3\sigma/m$), respectively for the two linear ranges (σ is the standard deviation of the blank and m is the slop of the calibration curve).

The analytical performance of the demonstrated electrode was compared with previously reported sensors and results are shown in Table 1. It can be realized from the Table that the proposed electrode herein are comparable in terms of linear range, sensitivity and reproducibility to those attained with other electrodes used for the detection of VB_2.

Table 1. Comparison between the proposed sensor and other electrodes.

Electrode	Modifier	Method	LOD (µM)	Linear range (µM)	Ref.
Carbon paste electrode	Zeolite	CV	0.71	1.7 - 34	6
Glassy carbon electrode	MnO_2	DPV	0.0015	0.02 - 9	9
Copper electrode	Bi	SWAdSV	0.1 and 1.1	0.3 - 0.8 and 1.0 - 9.0	28
Rotating disk glassy carbon	Hematite (α-Fe_2O_3)	SWV	8.4	1.3 - 100	29
Carbon paste electrode	1,4-BQ	LSV	0.087 and 14.51	0.5 - 10 and 20 -200	This work

Repeatability, Reproducibility and Stability of 1,4-BQCPE

The repeatability of 1,4-BQCPE was obtained by estimating the percent relative standard deviation (%RSD) of triplicate determination of a solution of 5 µM VB_2. The %RSD were obtained to be 4.7%.

Three different electrodes were used to determine the reproducibility between 1,4-BQCPEs and the calculated %RSD was about 7.7% in a solution of 5 μM VB_2. This result showed that the repeatability and reproducibility of the 1,4-BQCPE was satisfactory.

The stability of modified electrode was studied by measuring the current response of 5 μM VB_2 at 1,4-BQCPE after the electrode kept at room temperature for 14 days. It was observed that, the current response conserved almost 95.4 % of its initial value.

Table 2. Study of effect of interferences.

Interferences	Change in reduction currents (%)
Ascorbic acid	- 0.91
Glucose	1.78
Uric acid	1.3
VB_1	1.1
VB_6	-8.2

Interference Study

The effect of interference for the detection of VB_2 at 1,4-BQCPE was evaluated by studying the selectivity using possible interfering agents. Various possible interfering species were added into the solution containing 1 μM of VB_2. The result was shown in Table 2. The change in reduction current was taken as the difference between the reduction current of 1 μM VB_2 alone and the reduction current after adding 10 μM interferences. Percentage in change in reduction current was calculated by Eq. (1). It was observed that 0.1 mM ascorbic acid (AA), uric acid (UA), glucose (GL), and VB_1 have negligible interference with the determination of 1 μM VB_2. But 8.2% of the reduction current of VB_2 was decreased by adding 10 μM VB_6.

$$\Delta i(\%) = \frac{i_{VB_2 - i_{mix}}}{i_{VB_2}} \times 100 \qquad (1)$$

Real Sample Analysis and Recovery Study

For practical applicability of 1, 4-BQCPE for the detection of VB_2, VB_2 in content in pharmaceutical tablets was used. This sample was prepared as described in experimental section. Briefly, the tablet from Ningbo Shuangwei Pharm. Co., Ltd. was weighed and powdered in a mortar and pestle. 0.18 g of the powdered tablet was dissolved in to 100 mL volumetric flask and diluted with BR buffer. It was labeled that one multivitamin tablet contains 10 mg of VB_2. Therefore, the concentration corresponding to 10 mg of VB_2 in the tablet in 100 mL is 0.266 mM. The diluted solution was directly analyzed by proposed method. Finally, 20 µL of tablet sample solutions was diluted in 10 mL BR buffer. Triplicate of LSV was measured and the mean values were recorded. Also three different solutions of VB_2 solutions were prepared by mixing 20 µL of tablet sample solution with 1.00 µM, 3.00 µM and 6.00 µM standards of VB_2 and the % recovery was calculated. The determination of VB_2 in the tablet was taken place using the regression equation of the calibration curve. The percent recovery was performed to evaluate the accuracy of the method and the results are presented in Table 3 and 4.

Table 3. Amount of VB_2 detected in the multivitamin tablet with the demonstrated method.

Expected (µM)	**Detected**		**Labeled value (mg/tablet)**	**% recovery**
	In µM	**mg/tablet**		
0.54	0.53	9.82	10.00	98.15

Table 4. Recovery study of VB_2 in real sample.

Present (μM)	Added (μM)	Expected (μM)	Found (μM)	%Recovery	%RSD
0.54	1.00	1.54	1.59	103.25	4.50
	3.00	3.54	3.61	101.98	4.91
	6.00	6.54	6.52	99.69	5.21

Experimental

Chemicals

VB_2 (Sigma Aldrich), 1,4-benzaquinone (Meric), paraffin oil (Fulka, Switzerland), graphite powder (BDH, UK), H_3BO_3 (Techno Pharmachem), HCl, 37% (Riedel de Haen), NaOH (LeSOL laboratory reagent), H_3PO_4, 85% (Riedel de Haen), CH_3COOH, 100% (BDH), VB_2 tablet (Ningbo Shuangwei Pharm. Co., Ltd) and distilled water was used to prepare all aqueous electrolyte solutions throughout the study.

Instruments

The electrochemical measurement was performed by using Epsilion EC-Ver 1.40.67 voltammetric analyzer (Bioanalytical System, USA), using a standard cell with three electrodes. The three electrode system consists of UMCPE or 1,4-BQCPE which was used as working electrode, Ag/AgCl as a reference electrode and a platinum wire as a counter electrode.

Procedure for Preparation of Solution

Buffer solution

Britton–Robinson (BR) buffer was prepared by dissolving 0.004 M H_3BO_3, 0.004 M H_3PO_4 and 0.004 M CH_3COOH in distilled water and adjusting to the required pH value with dilute hydrochloric acid solution 0.1 M HCl and 0.1 M NaOH.

Standard preparation

VB_2 was prepared by dissolving 1.882 g of the component into 100 mL of distilled water. The solution was then stored in reagent bottle and covered with aluminum foil to prevent degradation on contact to light. Working solutions of VB_2 standards were prepared daily by diluting the stock solutions in supporting electrolyte to the required concentrations.

Preparation of Electrodes

Preparation of UCPE

The a mixture of 70% (w/w) graphite powder and 30% (w/w) paraffin oil was mixed and homogenized for 30 min with mortar and pestle. Then, 0.1 g of this paste was filled and pressed into 3 mm diameter and 7 mm deep Teflon tube and kept overnight at room temperature. For electrical contact a copper wire was put in from the backside of the Teflon tube. Finally, the electrode surface was flattened and smoothed against a clean smooth white paper until a polished shiny surface was appeared.

Preparation of 1,4-BQCPE

First, 20 mg of 1,4-BQ and 60 mg of graphite powder were added in a mortar and pestle and mixed for 5 min. To this mixture 20 mg of paraffin oil was added and carefully homogenized for 30 min. 0.1 g of the obtained paste was packed into 3 mm diameter and 7 mm deep Teflon tube and kept overnight at room temperature. For electrical contact a copper wire was introduced from the backside of the Teflon tube. Then, the electrode surface was flattened and smoothed against a clean smooth white paper until a polished shiny surface was appeared before electrochemical measurements.

Procedure of Reproducibility, Repeatability and Stability Study of 1,4-BQCPE

To study the reproducibility of the 1,4-BQCPE, three modified electrodes were used to measure the same concentration of VB_2 on three successive days (three measurements on each day). Then, the %RSD was calculated for the measured current signal to estimate the reproducibility between 1,4-BQCPEs.

For the repeatability study, the 1,4-BQCPE was prepared and the concentration of VB_2 was measured three times in one day at 1,4-BQCPE. Then, the %RSD of the readings was calculated to evaluate the repeatability of the measurements.

To examine the stability of the modified electrode, three 1,4-BQCPE were prepared on the same day. The reduction current of VB_2 was recorded on different days. On each day, triplicate measurements were taken and the average current signals of day one were compared to those of the last day to evaluate the stability of 1,4-BQCPE.

Interference Study

For the applicability of the 1,4-BQCPE for the detection of VB_2 was evaluated by studying the selectivity of the method for the determination of VB_2. Various possible interfering species such as, 0.1 mM ascorbic acid (AA), uric acid (UA), glucose (GL), Vitamin B_1 (VB_1) and Vitamin B_6 (VB_6) were added into the solution containing 1 μM of VB_2. Then the percent change in the reduction current of VB_2 was calculated up on addition of these interfering substances.

Procedures of Real Sample Preparation

VB_2 tablets were purchased from local drug store (Ningbo Shuangwei Pharm. Co., Ltd.) and it was weighed and powdered in a mortar and pestle. 0.18 g of the powdered tablet was dissolved in to 100 mL volumetric flask and diluted with BR buffer. It was labeled that one multivitamin tablet contains 10 mg of VB_2. Therefore, the concentration corresponding to 10 mg of VB_2 in the tablet in 100 mL is 0.266 mM. The diluted solution was directly analyzed by proposed method. Finally, 20 µL of tablet sample solutions was diluted in 10 mL BR buffer. Triplicate of LSV was measured and the mean values were recorded. Also three different solutions of VB_2 solutions were prepared by mixing 20 µL of tablet sample solution with 1.00 µM, 3.00 µM and 6.00 µM standards of VB_2 and the %recovery was calculated. The determination of VB_2 in the tablet was taken place using the linear regression equation obtained for the calibration curve.

Conclusions

In summary, in this work 1,4-BQCPE was used for the voltammetric determination of VB_2. The demonstrated method is simple, sensitive and cost effective. It can thus be concluded that the performance of 1,4-BQCPE is comparable with other carbon paste electrode based voltammetric analysis of VB_2. The linear working range for the first one is very lower and the detection limit was enhanced to allow a sensitive detection of VB_2.The developed sensor showed a low limit of detection, good repeatability and appropriate selectivity. Moreover, the proposed method successfully used for determination of VB_2 in pharmaceutical tablets.

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