



Multi-walled carbon nanotube modified glassy carbon electrode as a voltammetric nanosensor for the sensitive determination of anti-viral drug valganciclovir in pharmaceuticals

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ABSTRACT

Valganciclovir hydrochloride (VAL) is an antiviral drug active compound which is used for the treatment of the cytomegalovirus infections. The voltammetric oxidation of VAL was investigated at multi-walled carbon nanotubes modified glassy carbon electrode using cyclic and differential pulse voltammetry over a wide pH range. The results revealed that the oxidation of VAL is an irreversible pH-dependent process in an adsorption-controlled mechanism. The results show that the oxidation signal was remarkably enhanced to provide down to the ultra trace levels. Operational parameters have been optimized. The calibration curve was linear in the concentration range of 7.50×10^{-9} – 1.00×10^{-6} M with the detection limit of 1.52×10^{-9} M. The reproducibility of the peak current was found 2.07% ($n = 5$) relative standard deviation (RSD) value in pH 4.0 Britton–Robinson (BR) buffer for the modified electrode. The modified electrode showed good stability and reproducibility, and also it was successfully applied to the sensitive and selective determination of VAL in its dosage forms.

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1. Introduction

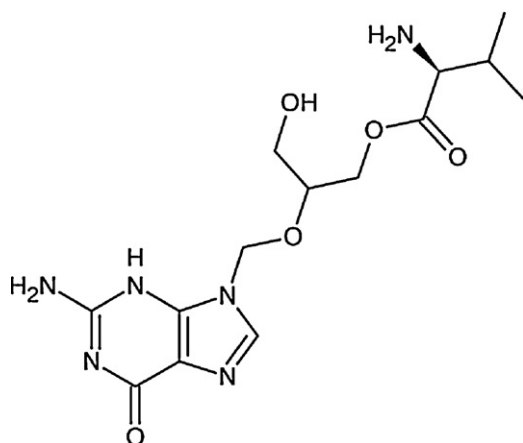
VAL is a pro-drug of ganciclovir which has been developed for the treatment of cytomegalovirus retinitis in patients with AIDS (Scheme 1). After oral administration, it is rapidly converted to ganciclovir by intestinal and hepatic esterase. Ganciclovir is a synthetic analog of 2'-deoxy-guanosine [1–3]. Oral bioavailability is approximately 60%. It takes about 2 h to reach maximum concentration in the serum. Also VAL is eliminated as ganciclovir in the urine, with a half-life of about 4 h in people with normal kidney function. Only a few analytical methods for the determination of VAL are described in the literature. Some methods based on the use of chromatographic techniques such as HPLC [4] and LC/MS [5–7] have been reported for the determination of VAL. Electroanalytical methods are widely used for the determination of a wide range of drug compounds due to their low cost, less buffer consumption, sensitivity, selectivity and relatively short analysis time interval it is also not required extraction, evaporation or complicated preparation procedure when compared to other techniques. Furthermore, the knowledge of the electrochemical properties of a drug is an important pharmaceutical tool because it can be showed the way for better understanding to its metabolic fate or in vivo redox processes and pharmacological activity.

These methods appear time consuming, owing to the re-extraction procedure and the use of expensive instrumentation. Also, until now official pharmacopeias have not yet been reported in any monograph about VAL and no official analysis method is available in its dosage form.

The interest in developing electrochemical sensing devices for use in clinical assays and in environmental monitoring is growing rapidly. Electrochemical sensing based on carbon nanotubes (CNTs) is a newly developed research field on the drug assay. Since the rediscovery of CNTs by Iijima in 1991, CNTs have been the subject of numerous investigations in chemical, physical and materials areas. The extraordinary electrochemical features of CNTs make them suitable for use in Faradaic processes or in non-Faradaic processes. Due to the presence of the cloud of electrons surrounding CNT walls can accept or withdraw charges from or to molecules in their nearest chemical environment [8–10]. Electrocatalytic activity defined as the capability to increase the electron-transfer kinetics. Therefore to reduce the over potential, toward many electrochemical processes of analytical significance, and anti-fouling capability are key properties of CNT-modified electrodes that are widely used in electroanalysis [11]. Also the modification of the electrodes with multi-walled carbon nanotubes (MWCNTs) for use in analytical sensing has been documented to result in low detection limits and high sensitivities. The oxidation of carbon surfaces is known to generate not only more hydrophilic surface structures but also more oxygen containing functional groups and to increase the ion-exchange capacity [12]. The specific surface area and pore

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Scheme 1. Structure of valganciclovir.

specific volume of CNTs increase after oxidation process. Multi-walled carbon nanotubes functionalized with carboxylic acid group (MWCNTs-COOH) have high dispersion quality, binding activity for molecular recognition and redox activity of carboxylic acid groups on the surface of MWCNTs [13].

CNT modified electrodes have also been used to develop very sensitive adsorptive stripping methods. Adsorptive stripping pulse voltammetric techniques are effective and rapid electroanalytical techniques with well-established advantages including low detection limits and good discrimination against background currents with high sensitivities [14].

The VAL is an electroactive molecule, but nothing seems to have been published concerning neither its electrochemical behavior nor the electroanalytical applications to pharmaceutical dosage forms. The aim of the present study is to investigate the detailed voltammetric behavior and sensitive assay of VAL at MWCNTs modified glassy carbon electrode (GCE) using cyclic voltammetry (CV) and adsorptive stripping differential pulse voltammetry (AdSDPV). The resulted nanosensor exhibits high sensitivity, rapid response and good reproducibility. This nanosensor is used for the sensitive and selective analysis of VAL in its dosage forms. As a comparison method, already published LC method [8] has been used for the determination of VAL in pharmaceutical dosage forms.

2. Experimental

2.1. Reagents and chemicals

Multi-walled carbon nanotubes produced through chemical vapor deposition (CVD). They are purified to remove free amorphous carbon deposits and catalyst metallic particles. They are purified to more than 95% carbon. They have an average diameter of 10 nm and an average length of 1.5 μm . COOH group functionalized multi-walled carbon nanotubes (MWCNTCOOH) was measured by XPS and was found approximately as 5%. They were obtained from DropSens and used as is. VAL and its pharmaceutical dosage forms Valcyte[®] tablets were kindly supplied by Roche Pharm. Ind. (Istanbul, Turkey). A stock solution of VAL (2.50×10^{-3} M) was prepared with distilled water. The different supporting electrolytes; acetate (0.2 M CH_3COOH ; pH 3.5–5.5), phosphate (0.2 M H_3PO_4 ; 0.2 M $\text{NaH}_2\text{PO}_4 \cdot 2\text{H}_2\text{O}$; 0.2 M Na_2HPO_4 ; pH 2.0–8.0) and Britton–Robinson buffers (BR) (0.04 M H_3BO_3 ; 0.04 M H_3PO_4 , and 0.04 M CH_3COOH ; pH 2.0–10.0) were used for electrochemical measurements. Other reagents were of analytical grade, and their solutions were prepared with bi-distilled water.

2.2. Apparatus

The voltammetric experiments were performed using AUTOLAB-PGSTAT 30 (Eco Chemie, Utrecht, The Netherlands) electrochemical and electroanalytical instrument having General Purpose Electrochemical Software (GPES) 4.9 software. The utilized electrodes were: a bare glassy carbon ($\Phi = 3.0$ mm) or MWCNTs modified glassy carbon as a working electrode; a platinum wire as a counter electrode and an Ag/AgCl (BAS; 3 M KCl) as a reference electrode. All pH measurements made using a pH meter Model 538 (WTW, Austria) with a combined electrode (glass electrode–reference electrode) with an accuracy of pH ± 0.05 .

DPV conditions were given as follows; step potential: 0.00795 V; modulation amplitude: 0.0505 V; modulation time: 0.05 s; interval time: 0.5 s. Average baseline correction defined using a 'peak width' of 0.01 V. Optimum AdSDPV conditions were; accumulation potential: 0 V and accumulation time: 180 s.

2.3. Preparation of the MWCNT modified glassy carbon electrode

The MWCNT suspension was prepared by dispersing 0.5 mg of MWCNTs in 1 ml N,N-dimethylformamide (DMF) during 2 h using ultrasonic bath. Before the modification, the surface of bare GCE was polished on a polishing cloth with alumina slurry, then washed with bi-distilled water and dried. Different volumes of MWCNTs suspension between 5 and 20 μl was dropped to electrode surface and dried overnight.

2.4. Analytical procedure

Until stable voltammograms were obtained, the prepared MWCNTs modified GC electrode was scanned in pH 4.00 BR buffer by successive cyclic voltammetric sweeps between 0.0 and 1.5 V potential range using 100 mV s^{-1} . When the current became steady, a certain volume of VAL standard solution was added into the electrochemical cell. After an accumulation using 180 s at 0 V with stirring, the differential pulse voltammograms were recorded between 0.20 and 1.50 V.

After each measurement, for removing the adsorbed compound, the MWCNTs modified GCE was regenerated by successive cyclic voltammograms (number of scans=5) in pure supporting electrolyte (pH 4.00 BR buffer). All electrochemical experiments were performed at room temperature.

2.5. Sample preparation

Ten Valcyte[®] tablets were weighed and ground to a homogenous fine powder in a mortar. A portion equivalent to stock solution of a concentration of about 2.50×10^{-3} M was accurately weighed and transferred into a 10.0 ml calibrated flask and completed to the volume with distilled water. The contents of the flask were sonicated for 60 min. Appropriate solutions were prepared by taking suitable aliquots of the liquid from clear supernatant and diluting them with the pH 4.00 BR buffer solutions.

To study the accuracy of the proposed method and to check the interferences from excipients used in the dosage form, recovery experiments were carried out. The concentration of VAL was calculated using standard addition method. For these experiments, known amount of pure VAL was added to the previously analyzed tablet samples.

The nominal content and recovery of VAL was calculated using the regression equation that was previously obtained from calibration plot.

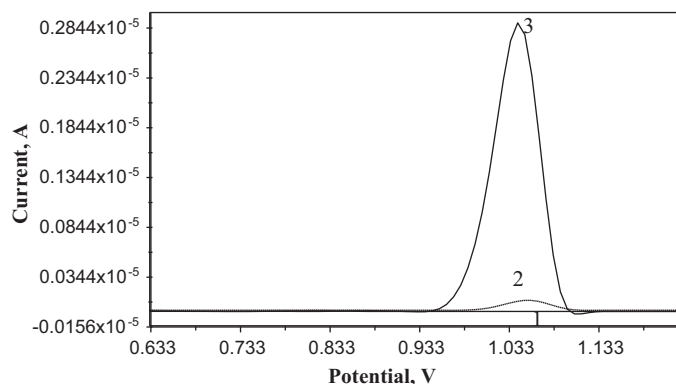


Fig. 1. Differential pulse voltammograms in pH 4.0 BR buffer only (1); 1.0×10^{-6} M VAL on bare GCE (2) and MWCNTs modified GCE (3). Accumulation potential: 0.0 V and accumulation time: 180 s.

3. Results and discussion

No previous electrochemical studies were available neither concerning the electrode behavior nor the sensitive electroanalytical determination of VAL in its dosage forms. To demonstrate the benefits of the MWCNTs modified GCE for the determination of VAL, which may offer advantages for the use of such electrodes as nanosensors, voltammetric behavior of VAL on MWCNTs modified GCE was investigated in details.

3.1. CNT amount optimization

Different volumes of MWCNTs suspension between 5 and 20 μ l was dropped to electrode surface and dried overnight. The 10 μ l volume was chosen as the optimum coated amount for the better peak current response. After 20 μ l of suspension amount, the peak current was decreased. The cleaned GCE was coated with 10 μ l of the black suspension of MWCNTs and dried in air for further studies.

The surface area of bare and MWCNT modified GC electrode were calculated for determining the efficacy of surface modification procedure. For this purpose, the electroactive areas of the electrodes were obtained using 1.0×10^{-3} M $K_3Fe(CN)_6$ as a probe at different scan rates by cyclic voltammetry. For a reversible process, the following Randles–Sevcik equation can be used [15,16];

$$ip_a = (2.69 \times 10^5) An^{3/2} D_R^{1/2} C_0 \nu^{1/2}$$

where ip_a refers to the anodic peak current in ampere, A is the surface area of the electrode in cm^2 , n is the electron transfer number, D_R is diffusion coefficient, C_0 is the concentration of $K_3Fe(CN)_6$ in M and ν is the scan rate in $V s^{-1}$. At 1.0×10^{-3} M $K_3Fe(CN)_6$ in 0.1 M KCl electrolyte, and for $n = 1$, $D_R = 7.6 \times 10^{-6} cm^2 s^{-1}$, from the slope of the plot of ip_a versus $\nu^{1/2}$, relation, the electroactive areas can be calculated. For bare GCE and MWCNTs modified electrode surfaces were found as $5.28 \times 10^{-5} cm^2$ and $8.82 \times 10^{-5} cm^2$, respectively. The modified electrode surface was nearly 2.0 times greater than that of bare GCE surface.

3.2. Electrochemical behavior of VAL

After an accumulation 180 s at 0 V with stirring, the obtained AdSDPV of VAL is shown in Fig. 1. As can be seen in this figure, the peak currents of VAL significantly increased and also peak slightly potential shifted from 1060 to 1040 mV with MWCNT modified GCE. These shifts (to less positive potentials) showed that the investigated compound was more easily oxidized on MWCNTs modified GCE than the bare GCE. These results confirm that the MWCNTs show effective enhancement to VAL, because of its specific surface

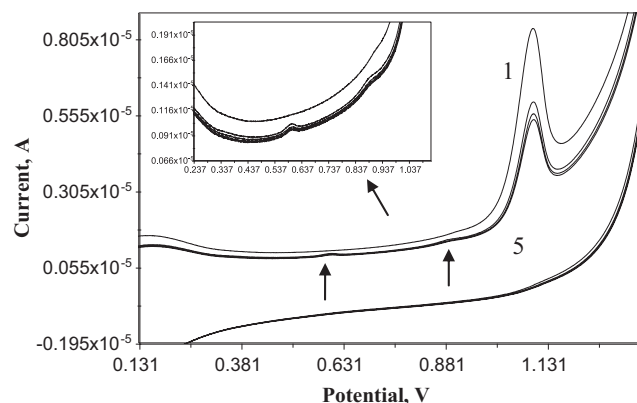


Fig. 2. Repetitive cyclic voltammograms of 3.00×10^{-5} M VAL on MWCNTs modified GCE in pH 4.00 BR buffer. Scan rate is $100 mV s^{-1}$.

area and special electrical properties, which improve adsorption capability of VAL in solution and provides enough effective reaction sites.

According to Fig. 2, no peak was observed in the reverse scan suggesting that the oxidation of VAL at MWCNTs modified GCE is irreversible. Also, after first and further cycles, two new oxidation waves at about 600 mV and 890 mV were appeared and increased while the main anodic peak was decreased (Fig. 2, inset). It may be explained as the oxidation of the intermediate products of the main oxidation group.

3.3. Effect of the accumulation potential and time

It is important to fix the accumulation potential and time when adsorption studies were undertaken. Bearing this in mind, the effect of accumulation potential and accumulation time has been studied by DPV method. Fig. 3a displays the resulting peak current versus accumulation potential for 1.0×10^{-6} M VAL in pH 4.00 BR buffer at MWCNTs modified GCE. When the accumulation potential changes between 0.0 V and 1.2 V, the anodic peak current of VAL decreases gradually (Fig. 3a). This means that VAL is accumulated mainly by electrostatic attraction on the MWCNTs modified GC electrode [16].

The influence of accumulation time ranging between 0 and 300 s is shown in Fig. 3b. The peak current increases greatly as the accumulation time is increased from 0 to 180 s. For accumulation time greater than 180 s, the peak current tends to be almost stable (Fig. 3b). Hence, 180 s was chosen as the accumulation time. Using long pre-concentration times caused problems due to the memory effect at the nanotubes-modified electrode that occurs from the accumulation of VAL at the electrode surface during the adsorptive stripping method. The unpredictable adsorption of reaction product on the MWCNTs modified GC electrode surface also implies the necessity to regeneration was the electrode after each measurement. Therefore, after each measurement, the MWCNTs modified GCE was regenerated by successive cyclic voltammograms (number of scans = 5) in pure supporting electrolyte (pH 4.00 BR buffer).

As a brief summary, using an accumulation time as 180 s at 0 V accumulation potential with stirring at 300 rpm, the DPV curves were recorded between 0.20 and 1.50 V.

3.4. Effect of pH

The pH of the supporting electrolyte has a major impact on the oxidation peak of VAL at MWCNTs modified GCE. The pH-dependent oxidation of VAL was studied systematically using various buffers (BR, phosphate, acetate) in the pH range between

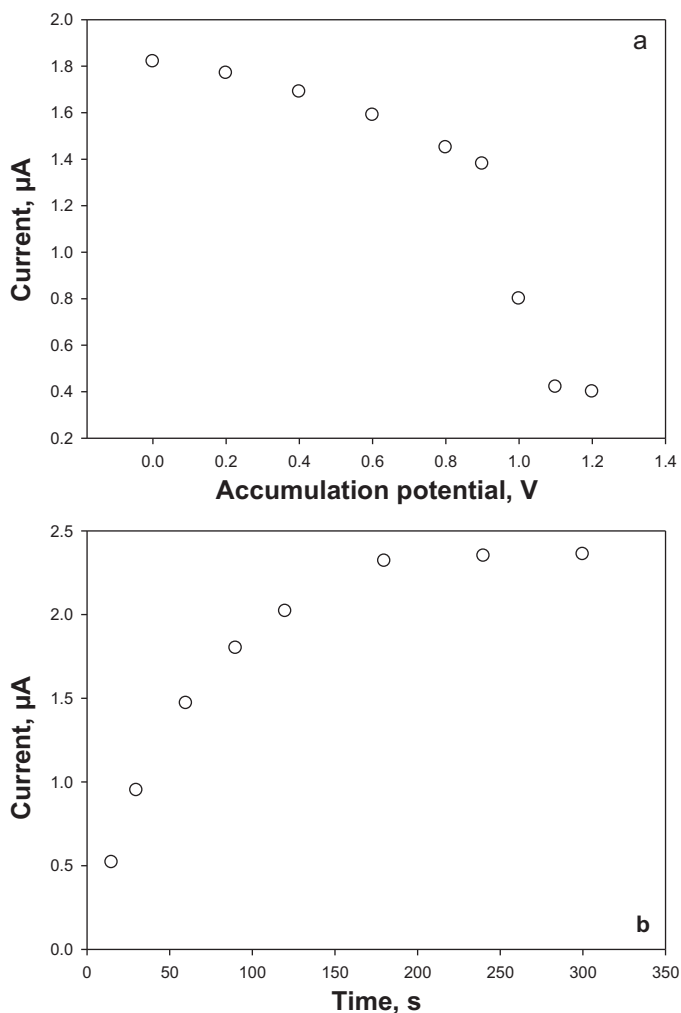


Fig. 3. (a) Effect of the accumulation potential on the peak current with 60 s of accumulation time. (b) Effect of accumulation time on the peak current, with an accumulation potential at 0.0 V for 1.00×10^{-6} M VAL in pH 4.00 BR buffer using AdSDPV method on MWCNTs modified GC electrode.

2.00 and 12.00 by DPV. The voltammetric peak potentials for VAL display a negative shift with increasing pH (Fig. 4a and b).

The plot of the peak potential (E_p) versus pH showed two straight lines (Fig. 4b), which can be expressed by the following equations:

$$E_p = 1182.5 - 31.10 \text{ pH}; \quad r = 0.991 \quad (\text{pH } 2.0 - 8.0) \quad (1)$$

$$E_p = 1360.6 - 56.5 \text{ pH}; \quad r = 0.995 \quad (\text{pH } 8.0 - 12.0) \quad (2)$$

The intersection of the E_p -pH curves is located around pK_a values of drugs. The pK_a value of VAL was reported in the literature as 7.6 [17]. As can be seen in the above equations, intersection point of about pH 8.0 is close to the pK_a value of VAL. This break could be due to a change in protonation-deprotonation process of purine ring of the molecule. At $\text{pH} < pK_a$, the conjugate base must be formed by a rapid dissociation of the protonated form.

The slope of above equation (between pH 2.0 and 8.0) is found as -31.10 mV/pH . According to the obtained slope value of this equation, 3.79 (~ 4.0) electrons and 4 protons are involved in the rate-determining step based on Nernst equation [18].

The peak current of VAL was increased at pH 4.0, and then decreased continuously. Therefore, pH 4.00 BR buffer where peak current reached a maximum was chosen as the optimum working media for the determination of VAL.

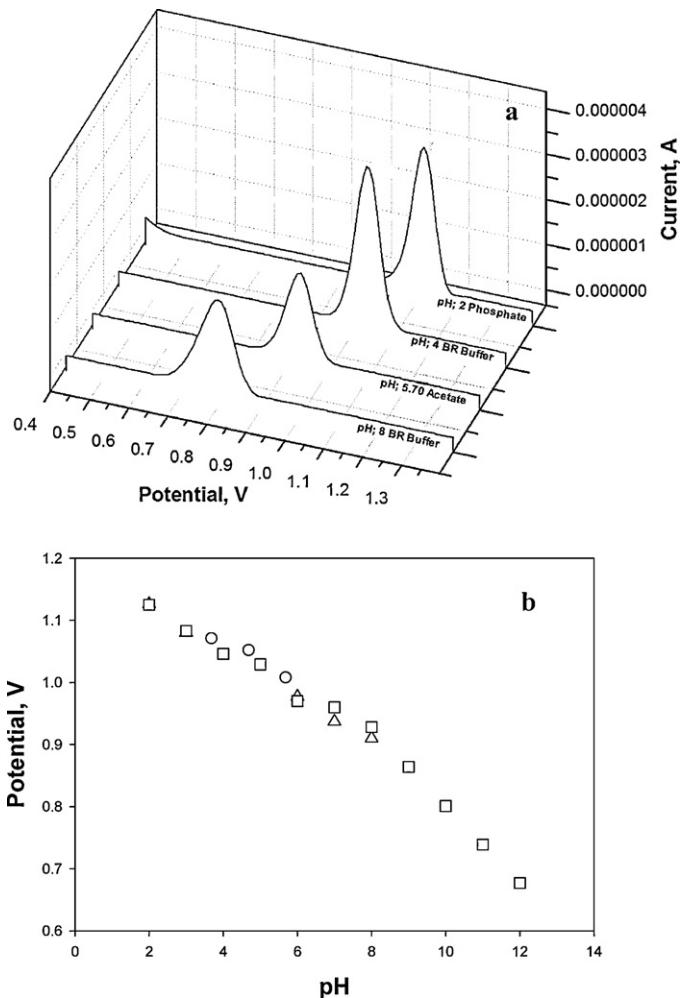


Fig. 4. (a) AdSDP voltammograms of 3.00×10^{-5} M VAL on MWCNTs modified GC electrode. (b) Effect of pH on 3×10^{-5} M VAL anodic peak potential (○) acetate buffer, (□) BR buffer and (Δ) phosphate buffer.

3.5. Effect of scan rate

The influence of scan rate (ν) on the voltammetric peak is investigated in the range from 5 to 100 mV s^{-1} . Useful information involving electrochemical mechanism usually can be acquired from the relationship between the peak current and the scan rate. Scan rate studies were carried out whether the processes on MWCNTs modified GCE were under diffusion or adsorption-controlled in 3.0×10^{-5} M VAL solutions. It is found that the anodic peak current of VAL is linear to the scan rate according to the following equation:

$$ip(\mu\text{A}) = 52.20 \nu(\text{V s}^{-1}) + 0.5527, \quad r = 0.993 \quad (n = 6) \quad (3)$$

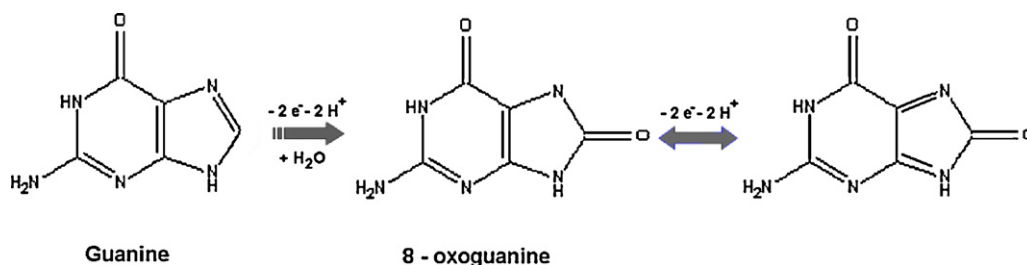
reflecting the feature of an adsorption-controlled system.

A plot of logarithm of peak current versus the logarithm of scan rate gave a straight line with a slope of 0.75. The obtained equation is:

$$\log ip(\mu\text{A}) = 0.75 \log \nu(\text{V s}^{-1}) + 1.50, \quad r = 0.999 \quad (n = 6) \quad (4)$$

A plot of the $\log ip$ versus $\log \nu$ is linear, with a slope of 0.5 for a diffusion peak and a slope of 1 for an adsorption peak. But the intermediate value of the slope is observed, suggesting a mixed diffusion-adsorption peak [18].

Also, the peak potential of the oxidation was shifted to more positive values, with increasing of the scan rates. The linear



Scheme 2. Possible oxidation pathway of guanine [22].

relation between peak potential and the logarithm of scan rate can be expressed as;

$$E_{p_a} = 1.1247 + 0.0308 \log \nu; \quad r = 0.998 \quad (n = 6) \quad (5)$$

This behavior was consistent with the electrochemical nature of the reaction in which the electrode reaction is coupled with an irreversible follow-up chemical reaction step [19]. The plot of E_p versus $\log \nu$ gives a straight line with a slope of 30.8 per decade which indicates that the rate of control is a first order step following electron transfer [20].

For the irreversible electrode process, the relationship between the oxidation peak potential and scan rate is described by the following equation [21]:

$$E_p = E^0 + \left(\frac{2.303RT}{\alpha nF} \right) \log \left(\frac{Rt k^0}{\alpha nF} \right) + \left(\frac{2.303RT}{\alpha nF} \right) \log \nu \quad (6)$$

where E^0 is the formal potential, T is the temperature (298 K), α is the transfer coefficient, k^0 the standard heterogeneous rate constant of the reaction (s^{-1}), n the number of electrons transferred in the rate determining step, ν is the scan rate and F is the Faraday constant ($96,480 \text{ C mol}^{-1}$), R is the universal gas constant ($8.314 \text{ J mol}^{-1} \text{ K}^{-1}$). Herein, the slope is 0.0308 and αn was calculated to be 1.92. Generally, α is assumed to be 0.5 in totally irreversible electrode process. Therefore, the value of $n = 3.84$ (~ 4) was obtained for the oxidation peak which is in agreement with the results in previous report [22] (Scheme 2).

3.6. Possible mechanism of VAL

Voltammetric methods especially cyclic voltammetry are the most suitable methods for investigating the redox behavior of the new pharmaceutical compound; that can give insights into its metabolic fate [23]. The anodic oxidative behavior of VAL is comparable to those of guanine or guanosine oxidations that were reported in our previous study and literature assay [22,24–29]. To support the working hypothesis that the oxidation occurs on the guanine structure of in VAL, the anodic behavior of anodic peak of VAL was compared with those of some model compounds. As the model substances for oxidation of guanine and guanosine structure, were studied using different compounds namely guanine, guanosine, ganciclovir, acyclovir and valacyclovir. The electrooxidation of the guanine moiety of all compounds have already been reported [22,24–29]. Our obtained results revealed a good agreement with the redox mechanism postulated that guanine is oxidized by an initial $2e^- - 2H^+$ attack at the $N(7)=C(8)$ to give 8-oxyguanine [22]. Guanine has been reported to be oxidized in a two-electron step, forming 8-oxyguanine which can be further oxidized in a second two-electron step resulting in a quinonoid-diimine species [24]. Totally $4e^-$ were transferred on the electrode reaction (Scheme 2).

3.7. Analytical application and validation

As can be seen in Table 1, the intra-day precision of the method was evaluated by repeating five experiments on the same day and in the same solution of $1 \times 10^{-6} \text{ M}$ VAL and the RSD of the peak current was found as 0.82%. As to the inter-day precision, the same modified electrode was used, the response of the modified electrode was examined for three consecutive days and the RSD of the peak current was obtained as 1.68%. Hence, the reproducibility of the modification can be shown. Owing to the adsorption of VAL onto the electrode surface; if the current response of the prepared electrode decreases after successive use, the electrode should be prepared again. More significant reproducibility was also obtained between each renewed modified electrodes. The electrode-to-electrode reproducibility of the proposed method was also examined on five MWCNTs-modified GC electrodes constructed individually and the RSD of the five average peak currents of 2.07%. The long-term stability of MWCNTs-modified GCE was investigated by measuring the current response at a fixed VAL concentration of $1 \times 10^{-6} \text{ M}$ over a period of 5 days. The modified electrode was used daily and stored in air. The experimental conditions show that the current response only deviates by 4.9%.

According to the obtained results, it is possible to apply this technique to the quantitative analysis of VAL. The pH 4.0 BR buffer solution was selected as the supporting electrolyte for the quantification of VAL as it gave maximum peak current. AdSDP voltammograms obtained with increasing amounts of VAL showed that the peak current increased linearly with the increase in concentration, as shown in Fig. 5. Using the optimum conditions, linear calibration curves were obtained for VAL in the range of 7.5×10^{-9} – $1.0 \times 10^{-6} \text{ M}$. The developed techniques were fully validated and the results are summarized in Table 1. The precision (repeatability and reproducibility) of the method was investigated by repeatedly measuring peak current of VAL and these results were given as the RSD% values in Table 1. The limit of detection (LOD) and limit of quantification (LOQ) were calculated from the equations of $\text{LOD} = 3.3 \text{ s/m}$ and $\text{LOQ} = 10 \text{ s/m}$ [23,30–32] using the standard

Table 1
Regression data of the calibration lines for the determination of VAL by AdSDPV.

	MWCNTs modified GCE
Measured potential (V)	1.027
Linearity range (M)	7.50×10^{-9} – 1.00×10^{-6}
Number of point	11
Slope ($\mu\text{A M}^{-1}$)	2.97×10^6
Intercept (μA)	–0.0086
SE of slope	1.78×10^4
SE of intercept	6.29×10^{-3}
Correlation coefficient	0.999
LOD	1.52×10^{-9}
LOQ	5.08×10^{-9}
Repeatability of peak current (RSD%)	0.82
Reproducibility of peak current (RSD%)	1.68
Between modified electrode reproducibility of peak current (RSD%)	2.07

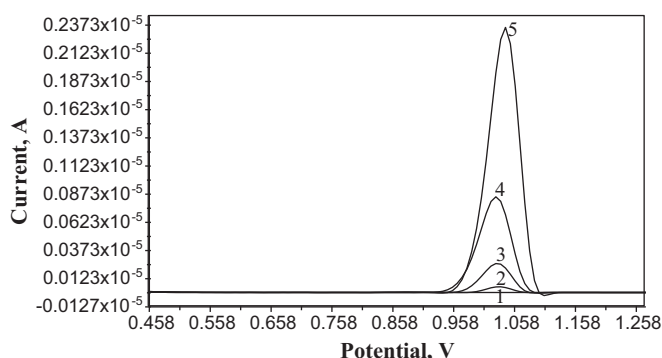


Fig. 5. AdSDP voltammograms on MWCNTs modified GC electrode in pH 4.00 BR buffer for the determination of VAL; (1) blank, (2) containing 2.5×10^{-8} M, (3) 1.0×10^{-7} M, (4) 5.5×10^{-7} M and (5) 1.0×10^{-6} M.

deviation of response (s) and the slope of the calibration curve (m). LOD and LOQ values also confirmed the sensitivity of the proposed method, as shown in Table 1.

3.8. Pharmaceutical analysis

The proposed DP voltammetric technique using MWNTs modified GCE were applied to the assay of VAL in Valcyte® tablet dosage form, using the obtained calibration lines. The samples were used after adequate dilutions without any sample extraction, evaporation or filtration and used only after adequate dilutions. Table 2 shows that the content values determined by the proposed method for the commercial dosage form are very close to the claimed amount.

The proposed method was compared with the already published LC method [8]. Table 2 compares the results of the analyses of VAL between proposed and literature method. The results obtained from the two methods were statistically compared with each other at the 95% confidence level with the aid of Student's t - and F -tests. The F - and Student's t -tests were carried out on the data and statistically examined the validity of the obtained results by LC method. According to the Student's t - and variance ratio F -test, the calculated t and F values were less than the theoretical tabulated values in either test at the 95% confidence level. These indicate that there are no significant differences between the performances of the proposed and LC method with regards to accuracy and precision (Table 2).

The accuracy of the proposed method was determined by its recovery studies using spiked experiments. Recovery studies were carried out after addition of known amounts of the pure drug to analyzed coated tablet formulation of VAL using the proposed method. According to the obtained results, the excipients, such as sodium

benzoate, fumaric acid, povidone K-30, sodium saccharin, mannitol, tutti-frutti flavoring [33] presented in tablets do not interfere with the analysis (Table 2). These results showed that the proposed method had adequate precision and accuracy.

Under the optimum experimental conditions, the effects of potential interferences on the voltammetric response of 1.0×10^{-6} M VAL were evaluated. The experimental results showed that 10-fold of uric acid, dextrose and dopamine did not interfere with the voltammetric signal of VAL.

4. Conclusions

In this work, MWCNTs modified GC electrode has been successfully used for the oxidation and electroanalytical studies of VAL. Based on the study, influence of several chemical parameters such as pH, scan rate, accumulation potential and time, concentration were investigated. A probable reaction mechanism is discussed. The electrochemical process is irreversible and presents the feature of the diffusion under adsorption-controlled system. The modified electrode shows excellent electrocatalytic activity and remarkably enhances the peak current. The quantitative evaluation of the compound was carried out in the range between 7.50×10^{-9} and 1.00×10^{-6} M with a detection limit of 1.52×10^{-9} M. The electrode can be regenerated and reused; it exhibits good repeatability and stability. The usefulness of the method was demonstrated by applying it to the analysis of pharmaceutical preparations of VAL.

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Table 2

Results obtained from VAL determination in pharmaceutical dosage form using MWCNTs modified GCE and comparison HPLC method.

	MWCNTs modified GCE	HPLC method [8]
Labeled claim (mg)	450.00	450.00
Amount found ^a (mg)	450.78	450.69
RSD%	0.61	0.61
Bias%	–0.17	–0.15
Calculated t value	0.96	$t_{\text{theoretical}}$: 2.31
Calculated F value	0.98	$F_{\text{theoretical}}$: 2.60
Added VAL (mg)	10.00	
Found VAL ^a (mg)	10.06	
Average recovery%	100.64	
RSD% of recovery	0.63	
Bias%	–0.64	

^a Each value is the mean of five experiments.

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