Voltammetric Sensor Based on Nano TiO$_2$ Powder Modified Glassy Carbon Electrode for Determination of Dopamine

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Abstract: Synthesis of TiO$_2$ nanopowder *via* a low cost ultrasonic spray pyrolysis technique is reported and the nanopowder is used for the surface modification of glassy carbon electrode. The structural characterization of nanopowder by high temperature XRD clearly shows the phase transformation from anatase to rutile phase on increasing temperature. The morphological structure is characterized by field emission scanning electron microscope and high resolution transmission electron microscope. The modified electrode is used for the determination of dopamine in the presence of excess of ascorbic acid/ uric acid using square-wave voltammetry. The voltammograms obtained during the oxidation studies revealed that nano TiO$_2$ exhibits better catalytic function towards the oxidation of dopamine and ascorbic acid/uric acid. The overlapping voltammetric response of all the biomolecules at the bare electrode gets resolved into well defined voltammetric peaks with lowered oxidation potential and enhanced oxidation currents. Linear calibration curves for dopamine are obtained over the concentration range 75 nM - 2.5 µM in 0.1M phosphate buffer solution at pH 7.2 with a correlation coefficient of 0.9940 and the detection limit (3σ) is estimated to be 13.8 nM.

1. INTRODUCTION

TiO$_2$ is n-type, wide-band gap semiconductor and shows excellent optical transmittance in the visible and near infrared regions [1, 2]. TiO$_2$ has been widely used as a model transition-metal oxide because of its rather simple electronic structure, which is characterized by a filled valence band and an empty conduction band [3]. It is relatively inexpensive, nontoxic, and biocompatible in nature and exhibits a high photostability in adverse environments. The biocompatibility of TiO$_2$ is highly important in medicinal biology because the TiO$_2$ layers on Ti and Ti alloys are in direct contact with biological tissue in hip or dental implants [4, 5]. The desirable surface properties of TiO$_2$ make it a potential interface for the immobilization of biomolecules and its application in photochemistry [6], electrochemistry [7-9] and sensor technology [10, 11]. TiO$_2$ has been used for the destruction of toxic organic compounds and microorganisms such as bacteria and viruses and hence been used in purification of polluted air and wastewaters [12, 13]. The most actively pursued applied research on TiO$_2$ is its use for photo-assisted degradation of organic molecules.

TiO$_2$ exists in seven different polymorphic forms, four of which are found in nature. The three common natural crystalline forms are: anatase, rutile, and brookite which consist of octahedrally coordinated Ti cations arranged in edge-sharing chains, but differ in the number of shared edges and corners [14]. Traditionally, the rutile phase has been investigated most extensively due to availability of good single crystals for characterization and also because of the comparatively simple crystal structure. Recently, however, experimental investigations have also focused on the anatase phase, because of its promising efficiency for photocatalytic applications [15]. Rutile and anatase are both tetragonal, containing 6 and 12 atoms per unit cell, respectively. The third form of TiO$_2$, brookite has a more complicated structure.

Various synthesis techniques such as hydrolysis [16], sol-gel route [17, 18], microemulsion or reverse micelles [19] and hydrothermal [20] have been used to prepare the nanoparticles of titanium dioxide. In liquid-phase synthesis, nanopowders can be produced with relatively narrow size distribution; however, such processes often produce nanopowders that contain chemical residues. In contrast, gas-phase condensation processes can avoid some problems encountered in the liquid phase processes. The requirement of high vapor pressure precursors also limits operation flexibility and sometimes poses environmental problems. The capability to produce an aerosol with narrow size distribution is of critical importance. Such ultra-fine, liquid atomization enables the use of any soluble precursor without concern for its vapor pressure. By adjusting solution concentrations and constituents, wide range of experimental compounds can be formed quickly and easily. Spray pyrolysis technique is an economical technique to produce nanopowder. It takes the advantage of inexpensive and environmental friendly precursors dissolved in suitable organic or inorganic solvents which can also act as combustible fuel [21].

The development of electrochemical sensors for dopamine (DA), which is an important neurotransmitter and plays a crucial role in the function of central nervous, hormonal, renal and cardiovascular systems, has received

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much interest in the last decade [22, 23]. Determination of catecholamines in body fluids is of great significance in the investigation of physiological functions and the diagnosis of Parkinsonian syndrome, senile dementia, and schizophrenia etc [24]. Since the major hurdle in the determination of DA is the coexistence of high levels of ascorbic acid (AA) and uric acid (UA), several methods have been reported for the determination of dopamine in presence of AA and UA. A variety of modified electrodes have been proposed to determine the concentration of dopamine in the presence of excess of ascorbic acid [25-37]. In the present studies the surface of glassy carbon electrode is modified with nano TiO_2 in the expectation that such modification will improve the current response of the electrode and thus will increase the detection limit of dopamine.

Several groups have also studied the formation of TiO_2 *via* ultrasonic spray pyrolysis, but most of them have worked on the thin films preparation and its characterization [38-41], about the modeling of droplet formation mechanism and particle genesis [42] and the antibacterial activity of the doping titania powder [43]. In this paper the structural and morphological characterization of TiO_2 nanopowders are reported and their electrochemical sensing properties for the determination of dopamine in the presence of excess of ascorbic acid (AA)/ uric acid (UA) by means of the osteryoung square wave voltammetric technique are presented.

2. MATERIALS AND METHODOLOGY

2.1. Reagents

Dopamine hydrochloride was purchased from Sisco Research Laboratory, Mumbai (India) and titanium trichloride (purity > 99%), uric acid and ascorbic acid were obtained from Sigma Aldrich, (USA). Other solvents and chemicals used were of analytical grade. All the chemicals were used as received without further purification. Freshly prepared solutions of DA and AA/UA were prepared in double distilled water each day.

2.2. Apparatus

The crystallinity of the powder was studied using Bruker AXS D-8 advance diffractometer with high temperature attachment in θ-2θ geometry. The high temperature stage allows samples to be measured at tightly controlled temperatures from room temperature to $1600^{\circ}C$ in open air, under vacuum, or in a purge gas. The surface topography and microstructure were studied using field emission scanning electron microscope (FESEM, Quanta 200f). The micrographs and diffraction pattern of nanopowder were studied using high resolution transmission electron microscope (Tecnai-20).

The electrochemical experiments were carried out using computerized BAS (Bioanalytical Systems, West Lafayette, USA) CV-50W voltammetric analyzer. Electrochemical studies were performed using a conventional three electrode glass cell with a platinum wire as an auxiliary electrode and Ag/AgCl electrode as reference (model MF- 2052 RB-5B). The bare or nanopowder modified glassy carbon electrode was used as the working electrode. For the study of pH effect on the peak current (peak potential) the phosphate buffers in the pH range 2.0 to 9.00 (ionic strength, μ = 0.1 M) were

prepared according to the method reported by Christian and Purdy [44]. The pH of the phosphate buffer solutions was measured using a Century India Ltd. Digital pH-meter (Model CP-901). Phosphate buffer of pH 7.2 (μ = 0.1M) was used for recording voltammograms. All potentials were measured at an ambient temperature of 20 ± 2 $^{\circ}C$.

2.3. Preparation of TiO_2 Nanopowder Modified Electrode

A modified ultrasonic spray pyrolysis set up was used for the preparation of TiO_2 nanopowders in a cost effective way. The details of the setup used for the UM-CVD have been described earlier [37, 45]. To prepare TiO_2 nanopowder, titanium trichloride was used as precursor. The solution was prepared by dissolving the metal chloride in double distilled water to a concentration of 0.1 M. The aqueous titanium trichloride solution was delivered into the reactor by liquid atomization at a flow rate of 10 ml h^{-1}. The atomized droplets containing the precursor were passed through the reactor maintained at the temperature of $500^{\circ}C$ and the nanopowder was collected on a special geometry which was kept at room temperature. The detailed condition is summarized in Table **1**.

Table 1.   Optimized Spray Parameters for Titanium Dioxide Nanopowder

Spray mode	Ultrasonic nebulizer
Carrier gas	Air
Ultrasonic frequency (MHz)	1.7
Droplet size (μm)	2.89
Solution flow rate (ml h^{-1})	10
Solvent	double distilled water
Precursor	Titanium trichloride
Concentration (mol L^{-1})	0.1
Reactor temperature ($^{\circ}C$)	$500^{\circ}C$
Deposition temperature	Room temperature

The as-synthesized TiO_2 nanopowder was dispersed in acetone by ultrasonic agitation for 15 min to give 1 mg/mL stable homogenous suspension which was then poured on the GCE surface in order to modify the electrode surface. Prior to modification, the GCE was polished with alumina slurry to a mirror-like finish, then rinsed and sonicated in double distilled water. For the preparation of electrode, 20 μL of nano-TiO_2 colloid was dropped onto the GCE and left to evaporate. The modified electrode was then used for studying the electrochemical oxidation of dopamine solution.

3. RESULTS AND DISCUSSION

3.1. Structural and Morphological Characterization of Prepared Nanopowder

Among the three crystallographic allotropes of nanocrystalline titania (rutile, anatase and brookite), anatase exhibits the greatest potential for a variety of applications, especially in the area of catalysis and sensors, and is known to be the low temperature (300- 550 $^{\circ}C$) form of TiO_2. However, with rutile being thermodynamically the most stable phase, anatase tends to transform into rutile on heating

in the range of 500°C to 700 °C. Several efforts have been made to stabilize the anatase phase at higher temperatures by doping with metal oxides. But it suffers from the problems of having a large amorphous content on synthesis as well as the formation of secondary impurity phases. Recent studies have suggested that the as-synthesised phase composition, crystallite size, initial surface area and processing conditions greatly influence the anatase to rutile transformation temperature. In this study nanocrystalline titania was synthesised in the anatase form by ultrasonic spray pyrolysis method using titanium trichloride as a precursor in the presence of atmospheric oxygen. The synthesized material exhibited traces of anatase phase even at elevated temperatures (up to 900 °C) during vacuum annealing [46].

Fig. (**1**) presents the high temperature XRD (HT-XRD) of as-deposited TiO₂ nanopowder performed in vacuum in the temperature range from room temperature to 1000 °C. It was observed that TiO₂ nanopowder exhibited dominant anatase phase along with rutile phase at room temperature. The crystallinity along anatase phase was found to increase with increase in temperature up to 500°C, while rutile phase became dominant as the temperature increased to 600 °C. Up to 900 °C, the mixed phase i.e. anatase and rutile was observed, while at 1000 °C the reflection corresponded to rutile phase only.
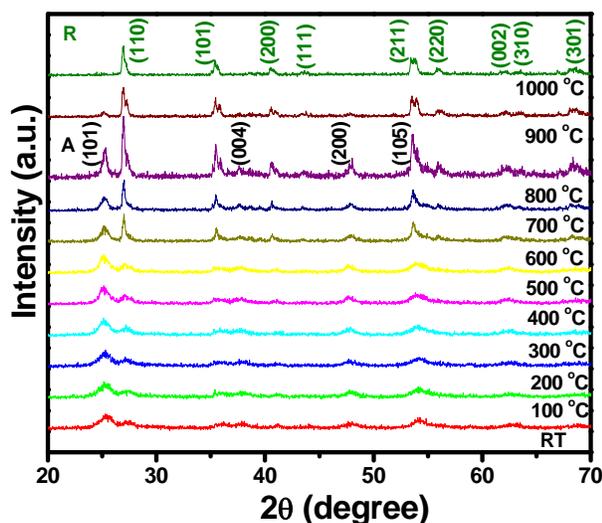

Fig. (1). *In situ* high temperature X-ray diffraction pattern of TiO₂ nanopowder at various temperatures.

The crystallite sizes of prepared titania nanopowder were estimated from XRD line broadening along anatase (101) and rutile (110) reflections using Scherrer's equation and are listed in Table **2**. The crystallite size was found to increase with the increase in hot stage temperature, which could be due to merging of the smaller particles into larger ones according to Ostwald ripening. The merging of the particles is the result of potential energy difference between small and large particles and can occur through solid state diffusion.

In order to confirm the crystallinity and particle size, TEM measurements were performed at room temperature. It can be concluded from the obtained diffraction pattern that the nanopowder exhibited polycrystalline nature as show in Fig. (**2**). The average crystallite size calculated from TEM

micrograph was found to be approximately 10 nm which is higher than that calculated from XRD results. This can be explained on the basis of the fact that Scherrer's equation gives the average or ''apparent'' crystallite size, since peak broadening in diffraction pattern, is affected by different factors such as microstrains, crystalline domain size, and domain size distribution. The advantage of TEM is the direct observation of the samples, which allows straightforward deduction of particle size distribution and morphology.

Table 2. Crystallite Sizes of TiO₂ Nanopowder Observed at Different Temperatures

Temperature (°C)	Crystallite Size (nm)	
	(Along A (101) Peak)	(Along R (110) Peak)
RT	5.6	6.0
6.0		6.2
6.5	6.4	
6.9	6.6	
7.5	8.6	
8.4	9.1	
10.7	28.2	
12.6	30.3	
15.9	31.9	
17.7	28.9	
1000	--	28.8

The FESEM image of the TiO₂ nanopowder modified GCE and its EDX spectra are shown in Fig. (**3**). The surface of the electrode becomes rougher due to the deposition of porous and compact film of TiO₂ with particle size of 50-100 nm. At % of carbon was found to be less at the surface of the modified electrode as shown by the EDX spectrum, which suggest that major portion of the electrode, is covered by the nano-powder. The structure consisted of a three-dimensional porous interspace formed by randomly connected particles. This structure is believed to be very attractive for the development of electrochemical sensors and is expected to enhance the electrocatalytic reaction between the electroactive species and the electrode surface.

3.2. Electrochemical study

3.2.1. Voltammetric Response of Dopamine

The electrochemical study of the TiO₂ modified glassy carbon electrode revealed that there was a significant promoting effect for the oxidation of dopamine with enhanced peak current and the lowered peak potential. Fig. (**4**) shows the Osteryoung square wave voltammograms (OSWV) at the bare glassy carbon electrode and the modified TiO₂/GCE in the presence of 0.25 mM dopamine (DA) solution in 0.1 M phosphate buffer (pH 7.2). At the bare electrode, the electrooxidation of DA occurs at ~320 mV and the peak obtained is rather broad, suggesting slow electron transfer kinetics. However, a well-defined oxidation peak was obtained at the modified electrode. The oxidation peak potential shifted negatively to ~148 mV and the peak
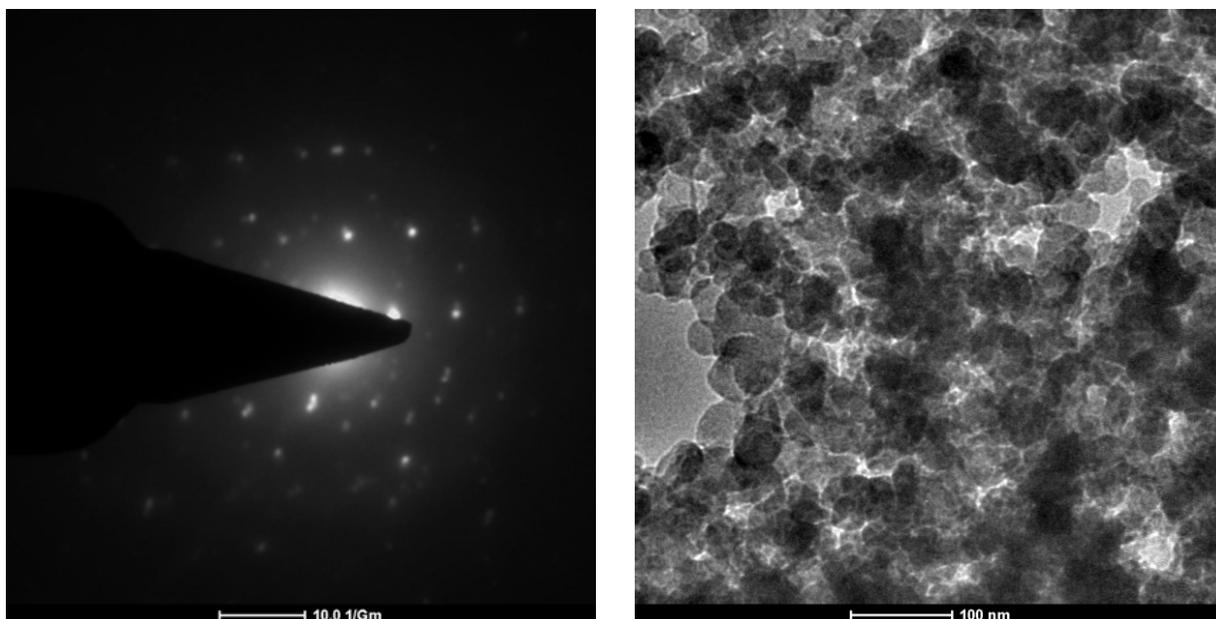
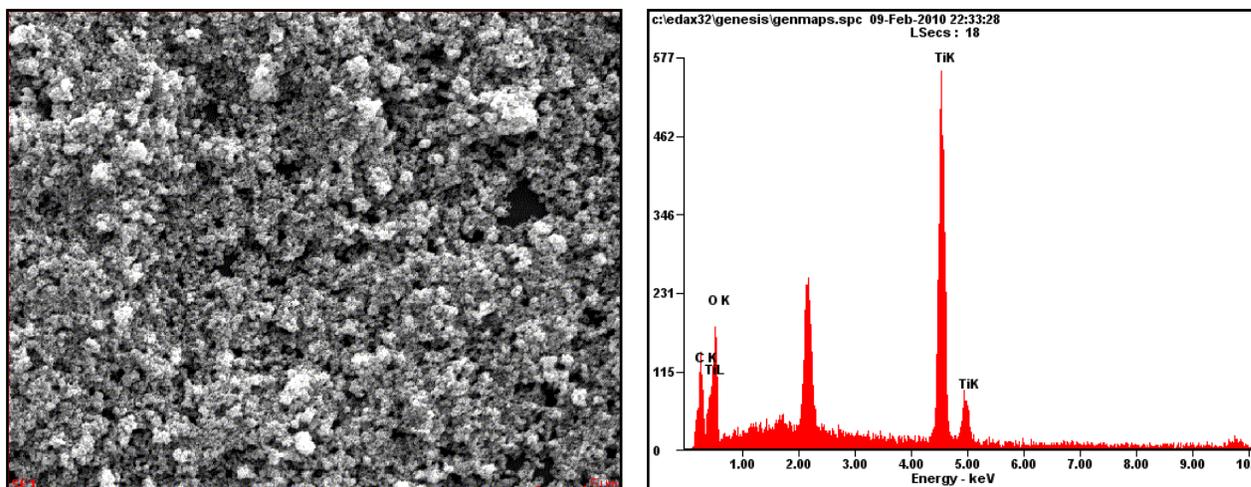**Fig. (2).** Observed TEM image and diffraction pattern of prepared TiO_2 nanopowder.

Fig. (3). FE-SEM image and EDX spectra of TiO_2 nanopowder modified GCE.

current increased nearly three times that could be assigned to larger surface area of the nanometer sized particles which may enhance the catalytic activities of the electrode and adsorb DA more easily as compared to smaller exposed surface area [47]. In addition a layer of hydroxyl groups formed on the outermost surface of the oxide film [48] may also cause strong interaction through N-H bonds.

Thus, the nanoparticles of TiO_2 film appear to act as a promoter by lowering the potential of DA oxidation with a negative shift in its anodic peak with increase in peak current. The square wave voltammograms of different concentrations of DA are presented in Fig. (**5A**). Under the optimized conditions, the i_p (peak current) increased with increase in DA concentration. The peak current versus concentration plot exhibited two linear segments. In the

concentration range 75 nM - 2.5 µM and 2.5 to 20 µM (Fig. **5B**), the linear dependence obeyed the following equations:

$$i_p = 0.551 \ C; \ (R^2 = 0.9949) \tag{1}$$

$$ip = 0.262 \ C + 0.7291 \ (R^2 = 0.9992) \tag{2}$$

where i_p is in µA and C is the concentration in µM. The detection limit (3σ/slope) of DA at the modified electrode is estimated to be 13.8 nM and the observed sensitivity is 0.551 µA /µM.

The effect of change in pH on peak potential of dopamine was investigated in the range 2.0 - 9.0. The E_p shifted to less positive potential with increase in pH. The variation of peak potential (E_p) with pH is linear and obeys the relation:

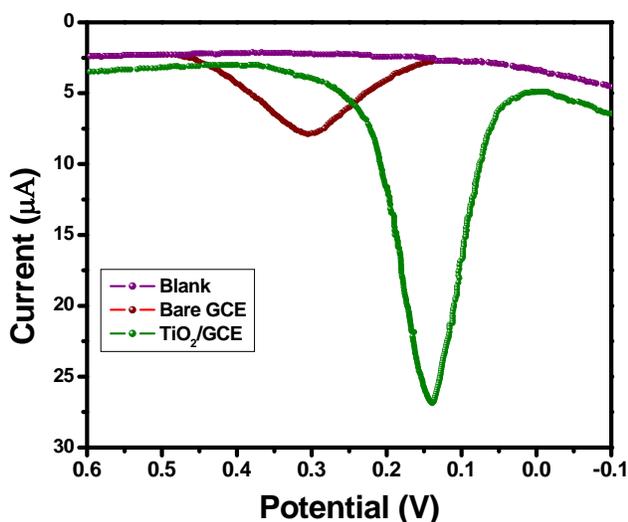$$E_p = 5337.3 - 58.29 \ pH; \ (R^2 = 0.9490) \tag{3}$$

Fig. (4). Voltammetric response of dopamine (0.25 mM) at bare GCE and on TiO$_2$ modified glassy carbon electrode.
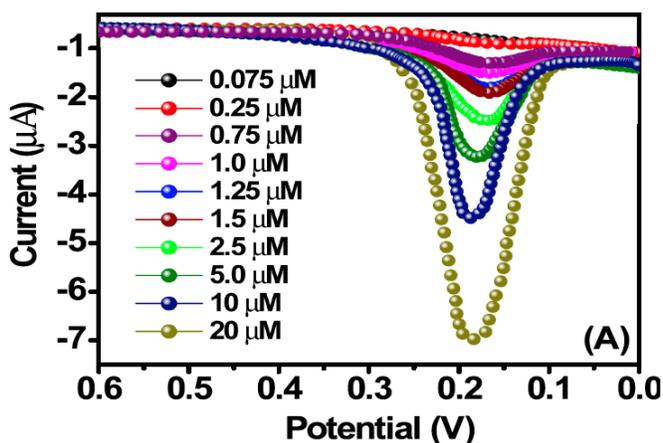

Fig. (5A). Voltammetric response of various concentrations of dopamine on TiO$_2$ modified glassy carbon electrode.
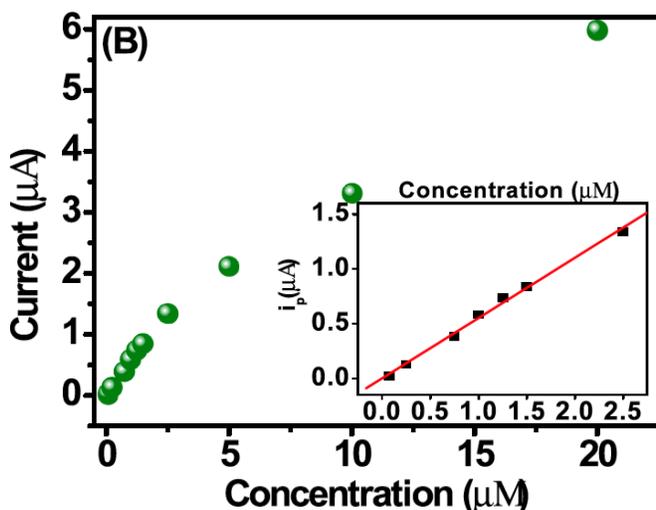

Fig. (5B). Linear relation observed between peak current (i$_p$) *vs* Concentration of DA.

The dEp/dpH slope of 58 mV/pH suggests that same number of electrons and protons are involved in the oxidation process.

The effect of square wave frequency on the peak current and peak potential of DA was investigated in the range 5 to 180 Hz. The oxidation peak current of DA shows a linear relationship with the scan rate in the range (5- 180 Hz) and the dependence of i$_p$ *vs* frequency can be represented by the equation:

$$i_p = 0.081\,f - 0.404; (R^2 = 0.9940) \tag{4}$$

This behavior suggests that the electrode process is adsorption-controlled [49]. The adsorbed compound was removed from the electrode surface by applying the potential of -100 mV for 60 sec. in the time base mode. This process is repeated atleast thrice after each run in order to assure full desorption of the compound. The peak potential of dopamine also shifted to more positive potential with increase in square wave frequency. The dependence of peak potential on the square wave frequency can be represented by the equation given as

$$E_p = 23.32 \log f + 125.4; (R^2 = 0.984) \tag{5}$$

Thus, it is clear that modified TiO$_2$/GCE can be successfully used for the determination of biomolecules.

3.2.2. Voltammetric Response of Dopamine in the Presence of Ascorbic Acid

The presence of ascorbic acid (AA) causes major interference in the voltammetric determination of dopamine. Therefore, it is necessary to determine DA in the presence of AA. Fig. (**6**) shows the SWVs of DA and AA coexisting in a 0.1 M phosphate buffer at the TiO$_2$ modified glassy carbon electrode. The bare GCE was unable to separate the responses of DA and AA. A rather broad oxidation peak was obtained and the oxidation peak potentials of the analytes were indistinguishable. This behavior is similar to the one reported in the literature [50]. On the other hand, at the modified electrode, two separate oxidation peaks were obtained. This may be due to the different polarity of DA and AA which would cause different extent of adsorption on the electrode surface and thus oxidized the biomolecules at different potentials. The peak at 165 mV corresponds to oxidation peak of DA and other at -98 mV corresponds to AA. These peaks are at almost the same potentials as those obtained for the individual oxidation of DA and AA. Fig. (**6**) depicts the voltammograms obtained upon varying the concentration of dopamine (keeping the concentration of ascorbic acid constant in large excess). The oxidation peak current of dopamine increased systematically without any change in the voltammetric peak response of ascorbic acid.

3.2.3. Voltammetric Response of Dopamine in the Presence of Excess of Uric Acid

The voltammograms shown in Fig. (**7**) represent the voltammetric study of 0.5 µM DA in the presence of 1.0mM UA in 0.1 M phosphate buffer solution of pH 7.2 at TiO$_2$ modified GCE. Two well-defined separate peaks were obtained at peak potentials of 310 mV and 160 mV corresponding to UA and DA respectively. The determination of DA in the presence of UA is performed at the modified electrode, by varying the concentration of DA, whereas, the concentration of the UA is kept constant in large excess. The results are shown in Fig. (**8**). It can be seen that the peak current of DA is increasing with the increase in

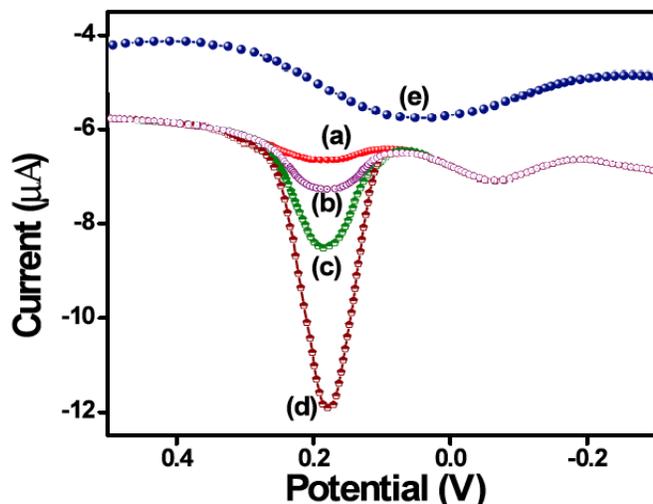its concentration keeping the concentration of UA at 0.5 mM.

Fig. (6). Square-wave voltammograms of various concentrations of DA at a fixed concentration of AA ([AA] =0.5mM; [DA]: (a) ions = 0.1, (b)= 1.0, (c)= 7.5, (d)= 20.0 µM) at TiO$_2$ nanopowder modified electrode and (e) [AA] = 0.5 mM & [DA] = 1.0 µM at bare GCE.
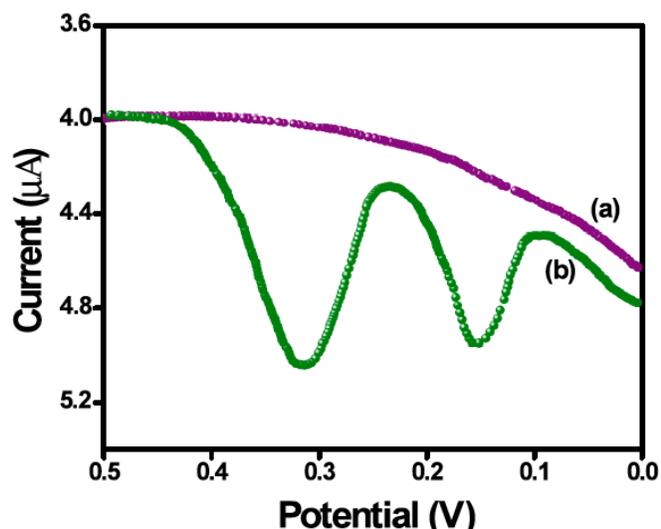

Fig. (7). Square-wave voltammogram of DA (1.0 µM) and UA (0.5 mM) at TiO$_2$ modified GCE in 0.1 M phosphate buffer (pH 7.2). Curve 'a' is the background.

The above results, thus, suggested that the modified electrode can be used successfully for the determination of DA even in the presence of excess of AA or UA.

CONCLUSIONS

An inexpensive, easy and reproducible method for the synthesis of titanium oxide nanopowders was successfully developed. The prepared method affords stable anatase nanopowder. High temperature XRD studies revealed the presence of anatase phase even up to 900 ^{o}C, which can be used for its catalytic properties even in vigorous reaction conditions at higher temperatures. The anatase gets fully transformed to rutile phase at 1000 ^{o}C. The studies of SEM and TEM micrographs revealed the highly aggregated
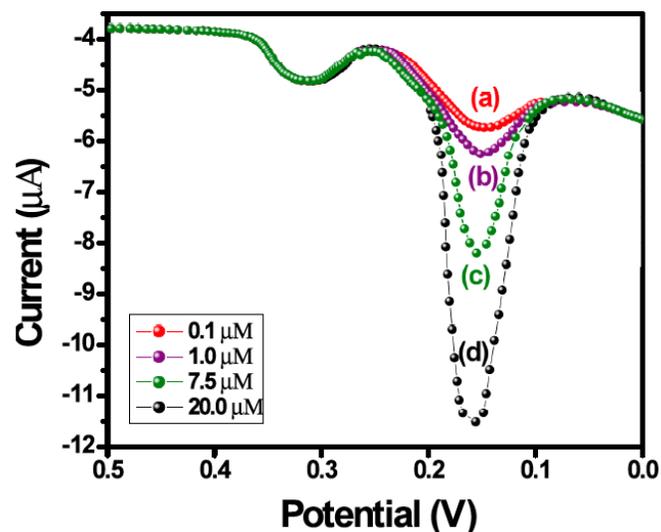

Fig. (8). Square-wave voltammograms of various concentrations of DA at a fixed concentration of UA ([UA] = 0.5mM; [DA]: a= 0.1, b= 1.0, c= 7.5, d= 20.0 µM).

particles with dia in the range of 50-100 nm and showed the porous interspace formed by randomly connected particles. Such structures are attractive for the development of electrochemical sensors and have been found to enhance the electrocatalytic activity of the electrodes. In addition, the electrochemical studies revealed that the prepared TiO$_2$ nanopowder modified GCE enhance the catalytic activity of electrode in the determination of dopamine in presence of AA/ UA under physiological conditions. A comparison of present method has also been made with reported in literature. The detection limit (3σ/slope) of DA observed in present studies (13.8 nM) is lower than reported at many other electrodes which are listed in Table **3**. In spite of the fact that lower detection limit for dopamine (~ 2 nM), than

Table 3.   Comparative Study of Detection Limit of Proposed Method with Other Reported References

S. No.	Reference	Concentration Range (µM)	Detection Limit (µM)	Real Sample
1	28	0.1-80	20	Serum/urine
2	29	0.37-36	0.2	No
3	30	5-125	1.2	No
4	31	2-1500	1.0	Serum/urine
5	32	6-384	2.31	No
6	33	15-400	0.03	Injection
7	34	5-30	0.2	No
8	35	0.5-50	0.15	No
9	36	5-25	30	No
10	37	0.33 - 160	0.142	No
11	49	2-20	0.0095	Injection
12	50	0.001- 5	0.0026	Pharmaceuticals
13	Proposed method	0.075-2.5	0.0138	No

observed in the present studies has also been reported in literature [51], the present detection limit is well below the concentration of dopamine normally present in blood serum and urine. In addition the advantage is that interference of ascorbic acid and uric acid even at 1000 times higher concentration level is observed, whereas in the earlier studies [51] the interference of uric acid was observed only up to 10 times higher concentration and of ascorbic acid up to 100 times concentration. The present method is simple, sensitive and shows the capability of nanoTiO₂ modified glassy carbon in sensing biomolecules.

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