Electrochemical Determination of Pitavastatin Calcium As Bulk Drug by Voltammetry Techniques

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Abstract— : **Pitavastatin calcium, a lipid lowering drug whose electrochemical behavior was studied in aqueous acid medium at glassy carbon electrode by cyclic voltammetry. Cyclic voltammetric analysis of pitavastatin calcium showed one well defined reduction peak at -1.25 V in phosphate buffer (pH 6). The effect of scan rate, pH, supporting electrolytes and concentration of pitavastatin calcium were tested. The plausible reaction mechanism involved in the reduction of pitavastatin calcium was proposed. The electrochemical reduction of pitavastatin calcium occurred on the electrode surface was diffusion controlled process rather than surface confined one. Under optimum conditions, the reduction current of pitavastatin calcium is proportional to its concentration in the range of 50 µM with a correlation coefficient of 0.9951 and the detection limit was found to be 50 µM (S/N = 3). The proposed method based on glassy carbon electrode is simple, easy and cost effective which implies the usage of the proposed sensor in pharmaceutical analysis.**

Key Words: Pitavastatin Calcium, Cyclic Voltammetry, Differential Pulse Voltammetry..

I. INTRODUCTION

The lipid lowering drugs (statins) are playing major role in the treatment of cardio vascular disease by reducing cholesterols. [1] The statins reduce the 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase which helps to suppress cholesterol biosynthesis in human body. [2] Goldstein et al reported as, these drugs emerged as the most effective means of reducing elevated levels of plasma cholesterol. [3, 4] There are currently nine statins available and they are lovastatin, mevastatin, simvastatin, pravastatin, fluvastatin, atorvastatin, rosuvastatin, cerivastatin and pitavastatin.[5,6] First-generation statins, such as lovastatin and mevastatin, were isolated from fungi, and the first generation statins having a decalin ring and an aliphatic side chain. However, second- and third- generation statins have been developed by either modification of first-generation statins or chemical synthesis in the laboratory and the second- and third- generation statins having several aromatic rings and an aliphatic fatty acid side chain in their chemical structure. Pitavastatin calcium [PTV], mono calcium bis {(3R, 5S, 6E)-7-[2-cyclopropyl-4-(4-flurophenyl)-3-quinolyl]-3-5-dihydroxy-6-heptenoate} (figure.1), is a lipid-lowering agent , used in hyperlipidemia.[7,8] Literature survey reports that PTV has been analysed by several analytical techniques such as, Jian-wei Deng et.al estimated PTV by LC/MS and HuaLv et.al estimated PTV by LC-ESIMS/MS/MS.[9-10]

PTV was determined by Liquid chromatography technique, reported by Sathishkumar et.al and Panchal et.al.[11,12] Bakyalakshmi et.al have reported the determination of PTV by high performance thin layer chromatography (HPTLC) technique.[13]

PTV has also been determined by spectrophotometric technique that was reported by Maruthuvamsi Krishna et.al, Virupaxappa et.al and GamzeErgin et.al. Gomes et.al have reported the stability of PTV determined by ultra-pressure liquid chromatography (UPLC) technique.[14-17] However, some of these methods require expensive equipment and are time-consuming. In some cases, the methods entail an extraction and derivatization procedures due to their relatively low sensitivities. Hence, a more rapid and simpler method for identification and determination of Pitavastatin Calcium at trace levels is highly desirable. Drug analysis has an extensive impact on public health. So far the literature survey reports clearly that still no electrochemical technique has been used to determine PTV. Electrochemical techniques have been used for the determination of the drug's electrode mechanism. The redox properties of drugs can provide insight into their metabolic fate, their invivo redox processes and their pharmacological activity.[18] Glassy carbon electrode has been very popular because of its excellent electrical and mechanical properties, wide potential range, extreme chemical inertness and relatively reproducible performance. [19-26]

Fig.1 Pitavastatin calcium chemical structure

II. EXPERIMENTAL

A. Reagents

The stock solution of the Pitavastatin Calcium (1 mM) was prepared by dissolving it in 0.1M HCl and kept in the dark under refrigeration to avoid any degradation of the drug. Freshly prepared solutions were used in each experiment. All chemicals were of analytical grade quality and were used without further purification. Other dilute standard solutions were prepared by appropriate dilution of stock solution in water.

B. Apparatus

Electrochemical measurements were carried out with a model CHI 1103A (CHI instruments) a three electrode system was employed. The glassy carbon electrode (GCE) is used as working electrode, saturated calomel electrode (SCE) as reference electrode and the platinum electrode as auxiliary electrode for all experiment.

III. RESULT AND DISCUSSION

A. *Electrochemical behavior of pitavastatin calcium at gce*

Cyclic voltammetric technique was utilized to investigate the electrochemical behavior of Pitavastatin Calcium on GCE [Fig.2b] and in blank solution containing phosphate buffer solution (pH 6) [Fig.2a]. GCE showed one reduction peak at -1.22 V with a peak reduction current of -7.45 µA. No oxidation peak was observed at this potential in the reverse scan, suggesting that the electrochemical reaction is a totally irreversible process. This statin drug shows significant electrochemical reduction on bare GCE in phosphate buffer pH=6 solution. The number of electron transfer involved in the reduction of pitavastatin calcium is two.

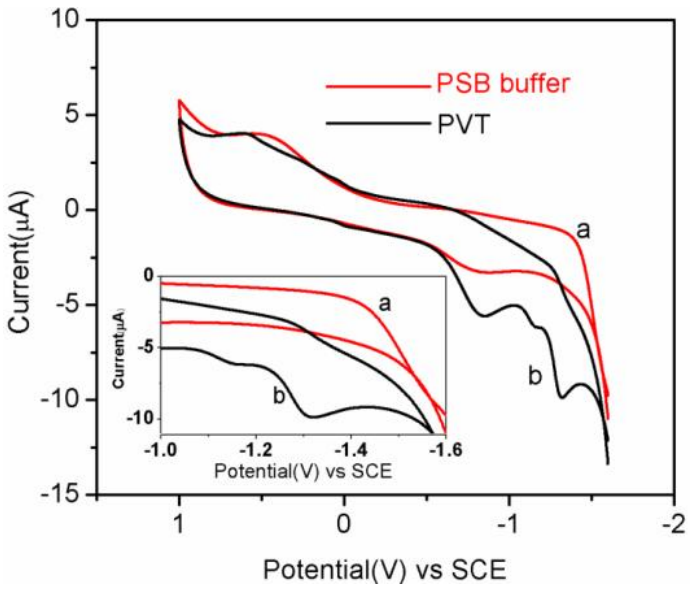

FIG.2. CYCLIC VOLTAMMETRIC RESPONSE OF (A) BARE ELECTROLYTE (0.1 MM PHOSPHATE BUFFER) ON GCE (B) 0.2 MM PVT ON GCE

C. Effect of supporting electrolytes

The electrochemical reduction of Pitavastatin Calcium was studied in various supporting electrolytes such as KCl, NaOH, $NaNO_3$, NaH_2PO_4-Na_2HPO_4. Pitavastatin Calcium yielded a single reduction peak in the entire above supporting electrolyte. However, the best results were obtained with NaH_2PO_4 -Na_2HPO_4.The cyclic voltammograms of 1 mM PVT with the varying supporting electrolytes on the surface of GCE.

D. Effect of scan rate

The effect of scan rates on the electrochemical response of 0.2 mM PVT at GCE was studied between the range of 10 to 100 mV/s and the cyclic voltammograms were shown in Fig. 4A. From Fig. 4B, it was found that the reduction peak current increases linearly with the increase in scan rate with a correlation coefficient of 0.9927 and slope of 0.1046, which indicates diffusion controlled process occurring at the GCE. However linearity was also obtained for the plot of square root of scan rate vs. the reduction peak current with a correlation coefficient of 0.9931.

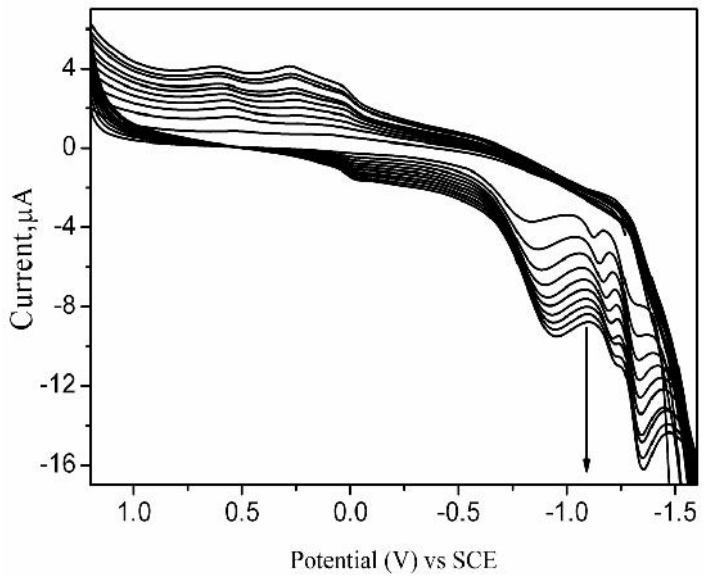

Fig.4A. Cyclic voltammograms of 0.2 mM PVT at bare GCE in Na_2HPO_4-NaH_2PO_4 buffer in with scan rates 10 to 100 mV/s.

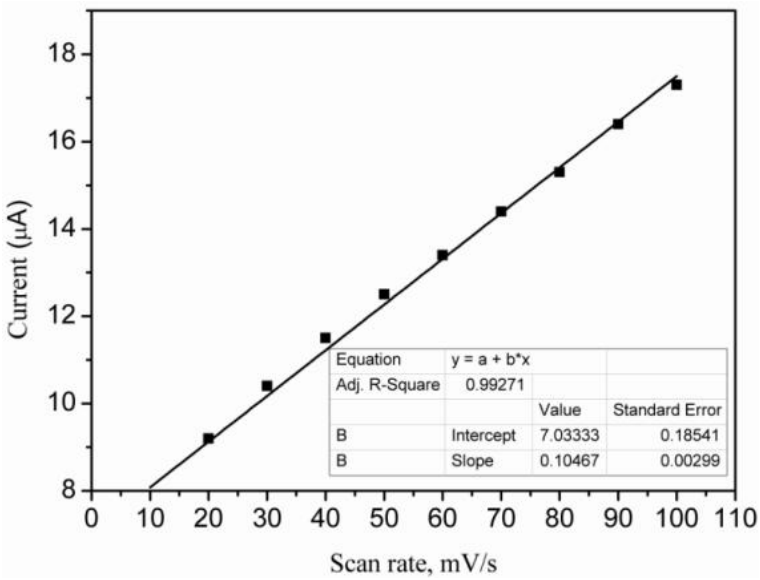

Fig.4B. The plot of reduction peak currents vs. scan rates at bare GCE (r= 0.9927)

E. Effect of pitavastatin calcium concentration

The variation of concentration of PVT was studied at GCE at a scan rate of 50 mV/s. shows the cyclic voltammograms of PVT at GCE. The plot of I_{pc} versus concentration of PVT showed the linear relationship between the cathodic peak current I_{pc} and the PVT concentration in the range of 67 to 130 µM with a correlation coefficient of 0.9951 Fig. 5.

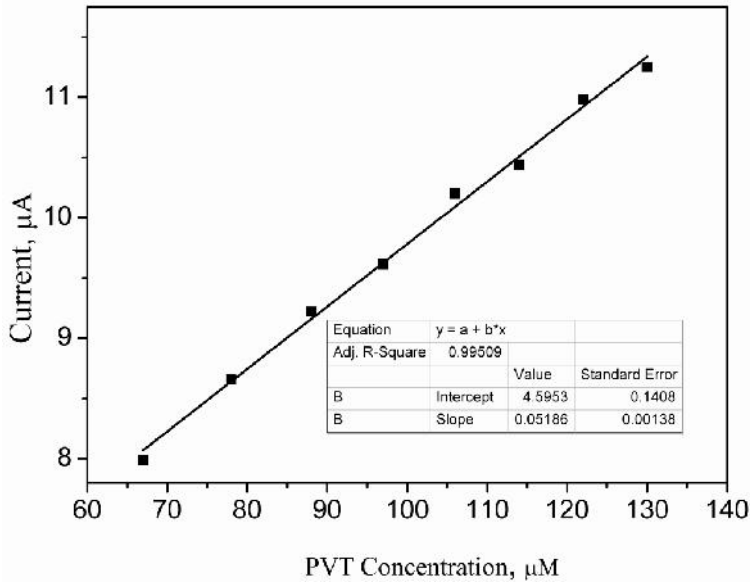

Fig.5. Plot of reduction peak current vs. PVT concentration on GCE (r= 0.9951)

F. Effect of pH

The influence of pH on the reduction of 0.2 mM PVT at the GCE using NaH_2PO_4-Na_2HPO_4 buffer of pH 3 to 11 was investigated by CV. It shows that, by increasing the pH of the NaH_2PO_4-Na_2HPO_4, a negative shift was observed in the reduction peak potentials, showing that the involvement of protons in these electrode reactions [Fig. 6].

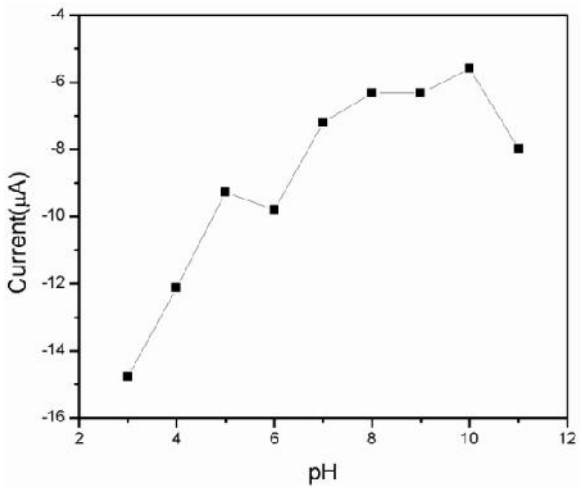

Fig.6. The plot of reduction peak currents vs. different pH

G. Differential pulse voltammetry

In order improve the sensitivity, low background current and to achieve lower the detection limit for the determination of Pitavastatin calcium on GCE differential pulse voltammetry technique was chosen. Fig. 7A showed the differential pulse voltammograms of PVT with the concentration ranging from 1.2 to 30 µM under the optimized experimental conditions. The linear regression equation was I_{pc} (µA) = 0.032 (µM) + 1.112 with a correlation coefficient of 0.9926 . The detection limit was evaluated to be 4 µM (S/N = 3).

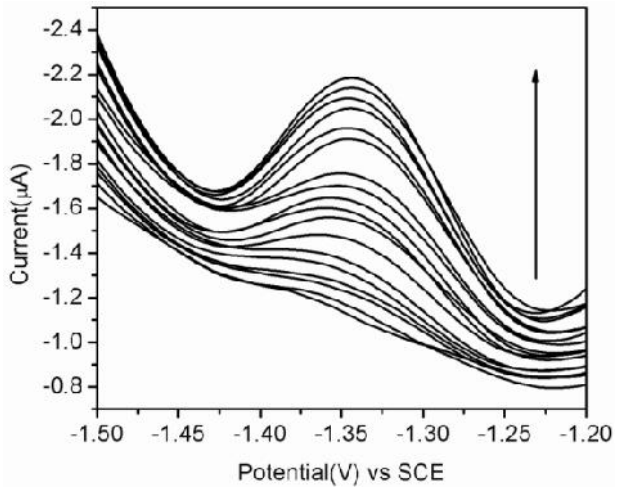

Fig.7. Differential pulse voltammograms at the GCE for PVT solutions at different concentrations.

IV. CONCLUSION

The electrochemical behavior of Pitavastatin Calcium was studied in aqueous acid medium at glassy carbon electrode by cyclic voltammetry and differential pulse voltammetry. Pitavastatin Calcium responded well the electrochemical reduction on bare glassy carbon electrode at phosphate buffer. The detection limit of Pitavastatin calcium on bare glassy carbon electrode was detected as 50 µM. The probable reaction mechanism involved in the reduction of Pitavastatin Calcium was also proposed. The proposed method was sensitive and simple. It was successfully employed to determine Pitavastatin Calcium in pharmaceutical samples.

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