

Voltammetric determination of a novel 1-(3-Fluoro-benzenesulfonyl)-5-{3-[5-(3-methoxy-phenyl)-2-methyl-2H-[1,2,4]triazol-3-yl]-phenyl}-1H-indole using glassy carbon electrode in a Britton- Robinson buffer

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Abstract

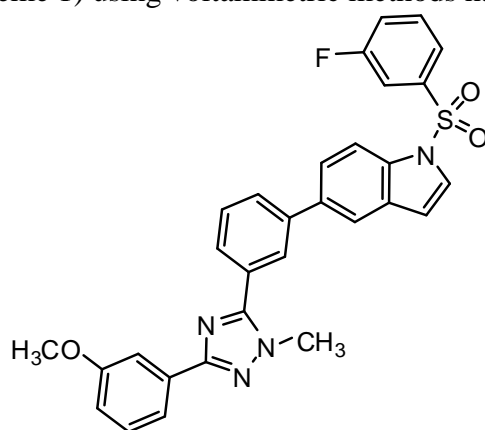
The voltammetric behavior of 1-(3-Fluoro-benzenesulfonyl)-5-{3-[5-(3-methoxy-phenyl)-2-methyl-2H-[1,2,4] triazol-3-yl]-phenyl}-1H-indole (**FB**) has been investigated in Britton Robinson buffer (B-R) at pH 7.0 using differential pulse voltammetric (DPV), anodic stripping voltammetric (ASV) and cyclic voltammetric (CV) techniques on the glassy carbon electrode in presence of Ag/AgCl reference electrode. The preliminary observation for **FB** was investigated using DPV technique in B-R buffer and pH 7, an obvious differential pulse voltammetric oxidation peak was observed at $E_a = 0.65V$. The voltammetric oxidation process has been shown to be irreversible and the diffusion is controlled with adsorption characteristics. The developed anodic stripping voltammetry (ASV) was used to study some optimized experimental conditions such as time and potential of accumulation, frequency, pulse amplitude, scan rate, convection rate and some working electrodes. A calibration curve for **FB** was studied from 2×10^{-6} to $3 \times 10^{-5} M$ (correlation coefficient = 0.994, $n=8$) under optimum conditions and the detection limit was $8 \times 10^{-8} M$. The used anodic stripping voltammetric method shows a good reproducibility ($n=8$) for **FB** with relative standard deviation RSD% of 0.54% and a good stability. An accuracy of the developed ASV was evaluated via the mean recovery of $97\% \pm 1.0$. Some interference present in pharmaceutical compounds has been also evaluated by ASV technique. The voltammetric application of the developed ASV technique was used for the forthwith determination of **FB** in medical preparations and biological fluids.

Keywords: Suzuki reaction, anodic stripping voltammetry, cyclic voltammetry, biological fluids.

1. Introduction

In general, stripping voltammetry is considered a sensitive electroanalytical technique for the determination of trace metals, organic and inorganic compounds in solutions. The technique contains three steps: the first step; analyte is deposited onto a working electrode; during this step, the solution is stirred to maximize the amount of analyte deposited. The second step which called the rest step; stirring is stopped so that the

solution will become quiet and stable. The third step, the analyte deposit is stripped from the electrode by scanning of the potential. The recorded current during the stripping step can be related to the amount of the analyzed material in solution. The stripping step may contain a positive or a negative potential, creating either an anodic or cathodic peak respectively. So, stripping voltammetric technique is included anodic stripping voltammetry (ASV) and cathodic stripping voltammetry (CSV). ASV and CSV are differed in the direction of the scan of potential. On the other hand, the linear sweep voltammetry (LSV) is considered a simplest technique which recorded the potential in linear scanning as a function of time. Differential pulse voltammetry (DPV) is also another commonly applied technique which has a lower limit of detection than LSV. The differential pulse voltammetry is contained a pulsed waveform which measured the current in pulses by doing two measurements and recording the difference values in the potential. This approach can be helped to reduce the background current [1]. Now, anodic stripping voltammetry (ASV) is widely recognized as a powerful tool for analysis of metal ions and organic compounds in solutions. Additionally the advantages of stripping voltammetric method include the capability for simultaneous multielement determination and relatively cheap instruments compared to that required for the spectrophotometric and chromatographic techniques. There are many articles have been published to investigate the anodic stripping voltammetric behavior for the determination of several pharmaceutical compounds such as propranolol [2], cefixime [3], domperidone [4], lansoprazole [5], methotrexate [6], pantoprazole [7], resveratrol [8] and metoclopramide [9]. In addition, the voltammetric techniques were used to analysis other triazole and indole compounds, for example: square wave adsorptive stripping voltammetric (SWAdSV) technique to determine non-ionic 1,2,4-triazole surfactants on HMDE [10], and other electrochemical voltammetric methods [11-15]. The present work was performed to evaluate the behavior of voltammetric techniques for 1-(3-Fluorobenzenesulfonyl)-5-{3-[5-(3-methoxy-phenyl)-2-methyl-2H-[1,2,4]triazol-3-yl]-phenyl}-1H-indole (**FB**) as an experimental and new compound in order to improve and develop a sensitive and an effective of the used voltammetric techniques for determination **FB** in pharmaceutical and biological samples. To the best of our knowledge, no analysis of **FB** (scheme 1) using voltammetric methods has been reported in the literature.



Scheme 1. 1-(3-Fluoro-benzenesulfonyl)-5-{3-[5-(3-methoxy-phenyl)-2-methyl-2H-[1,2,4]triazol-3-yl]-phenyl}-1H-indole (**FB**)

2. Experimental part

2.1. Instrumentation

All voltammetric studies were carried out by 797 AV instrument (Metrohm company, Switzerland) controlled by VA computrace 2.0 software. The voltammogram peaks were printed via a hp printer; laserjet

CP1215. Three electrochemical electrodes; glassy carbon (GCE) working electrode, Ag/AgCl reference electrode and Pt auxiliary electrode were used for the determination of **FB**. A pH 211; Hanna instrument (made in Romania) was used to regulate pH values. Moreover, the micropipettes (Ireland) 100 - 1000 μL ; oxford adjustable, were used to inject the volumes of standard solutions and the studied samples. A 200 labofuge instrument (Heraeus Sepatech, German Made) was used to shake and centrifuge the biological samples to be suited for a voltammetric determination.

2.2. Chemicals

Stock solution of a novel indole compound (**FB**; of 1×10^{-3} M) was prepared by dissolving the appropriate amount of **FB** in THF and H_2O solvents in a 50 ml volumetric flask and it was stored in the dark. The lower concentrations of standard solutions of **FB** were prepared by diluting the stock solution with solvents analysis by analysis. All supporting buffers such as britton-robinson (B-R), phosphate, acetate and carbonate were prepared to be suitable and ready for the voltammetric determinations of analyte [16].

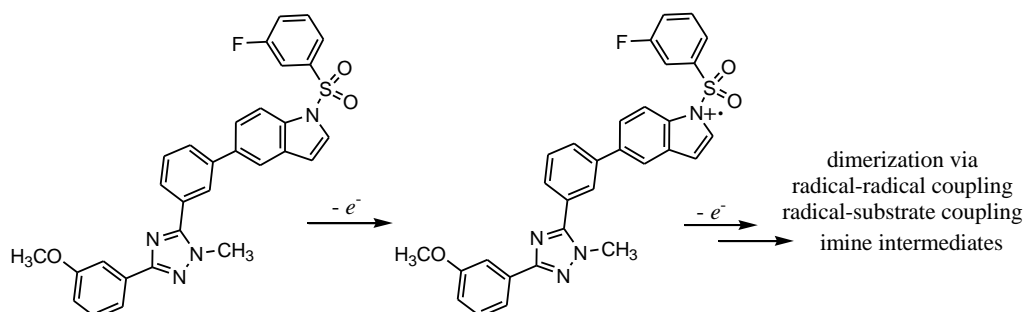
2.3. Procedure

The instrumental procedure which used for obtaining all voltammograms was carried out as follows: 10 ml of B-R buffer (pH 7) was placed in a clean and dry voltammetric cell to be ready to electrochemically study the **FB** compound. The buffer solution was purged with a nitrogen gas for 300 seconds, and stirred. The accumulation potential of +0.2 volt vs. Ag/AgCl reference electrode, was applied to analysis **FB** on a glassy carbon electrode (GCE). The oxidation scans were monitored over the range 0.0 - 1000 mV. Finally, the oxidation voltammetric determination was carried out at room temperature.

3. Results and discussion

3.1. Differential pulse voltammetric behavior of FB

The first investigation of the compound **FB** indicates that it was deposited onto the glassy carbon electrode (GCE) and it was analyzed by DPV after scanning of the potential in the oxidative direction; from 0.0 to 1000 mV. The DPV depositing of 5×10^{-5} M **FB** solution for 30 sec in B-R buffer pH 7.0, yielded a well oxidation signal at 650 mV and 284 nA, as shown in figure 1. The differential pulse voltammetric signal is approximately resulted from the oxidation process of indole moiety of **FB** which is shown in scheme 2.



Scheme 2. Suggested DP voltammetric oxidation of the indole moiety of **FB**

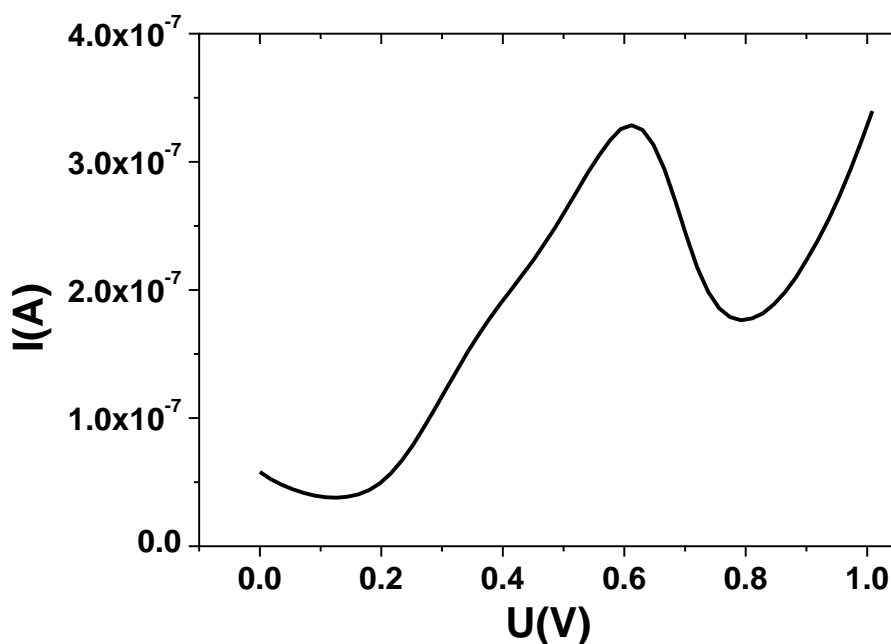


Figure 1. Differential pulse voltammogram of **FB** in B-R buffer pH7

3.2. Cyclic voltammetric behavior of **FB**

Cyclic voltammetry method confirmed the irreversible nature of the anodic oxidation process of **FB** ($C=5 \times 10^{-5} \text{M}$) in B-R buffer, pH 7 and 50 mV/s scan rate, as shown in figure 2 which showed no reduction signal. In addition, the multi-cyclic voltammograms of $5 \times 10^{-5} \text{M}$ of **FB** in B-R buffer and pH 7 given in figure 3 show that the surface of the glassy carbon electrode was saturated by the analyte from start of oxidation sweeps, resulting in gradual decrease in anodic current values. On the other hand, $5 \times 10^{-5} \text{M}$ of **FB** in B-R buffer and pH 7 was studied by CV method at different scan rates, resulting in anodic current increase over the range of scan rates 10 – 100 mV/s. A linear relationship between the logarithm of oxidation current ($\log i$) and logarithm of scan rate ($\log v$) was produced as shown in figure 4, with a slope value of 0.84. This value is nearly 1.0, confirming the diffusion controlled to analysis **FB** onto GCE [17].

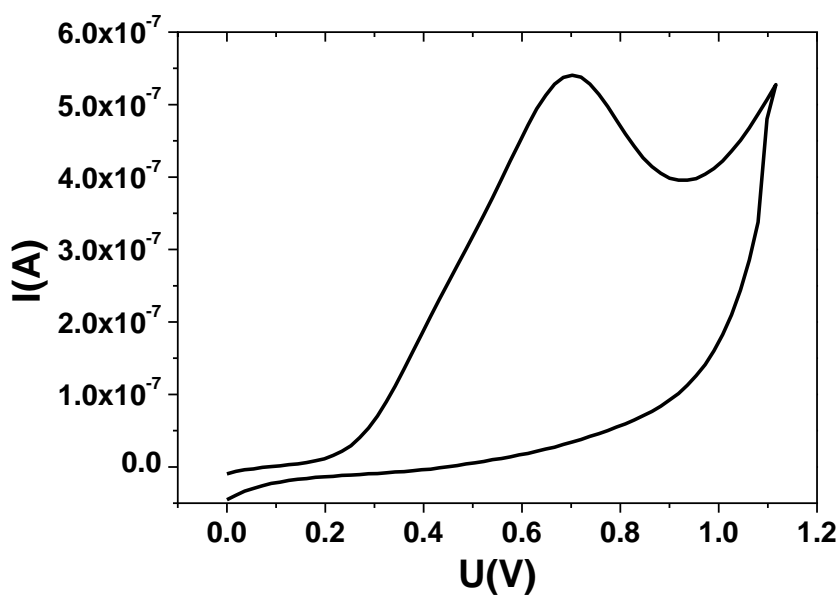


Figure 2. Cyclic voltammogram of **FB** ($c=5 \times 10^{-5} \text{M}$) in B-R buffer pH7 using GCE and 50 mV/s

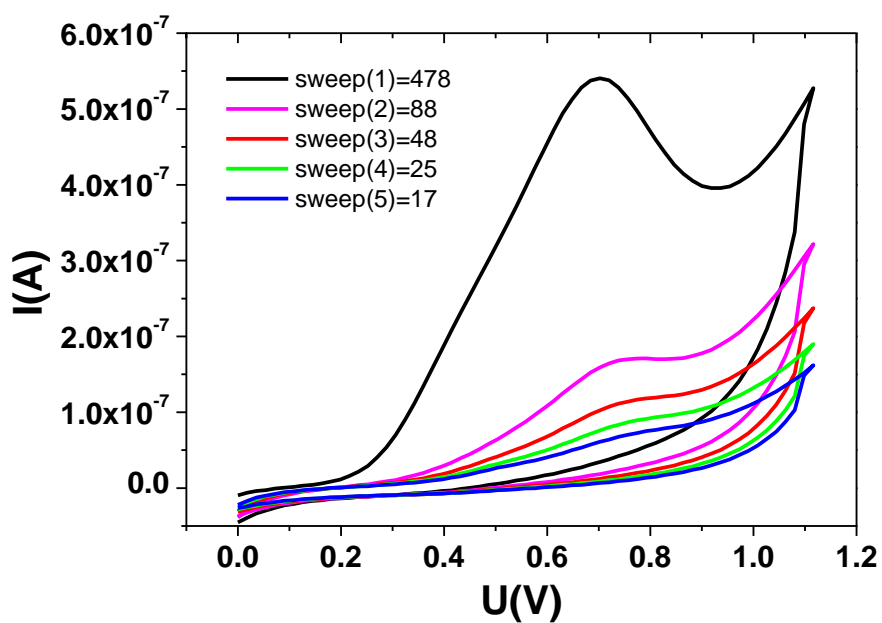


Figure 3. Multi-Cyclic voltammograms of **FB** ($c=5 \times 10^{-5} \text{M}$) in B-R buffer pH7 using GCE and 50 mV/s

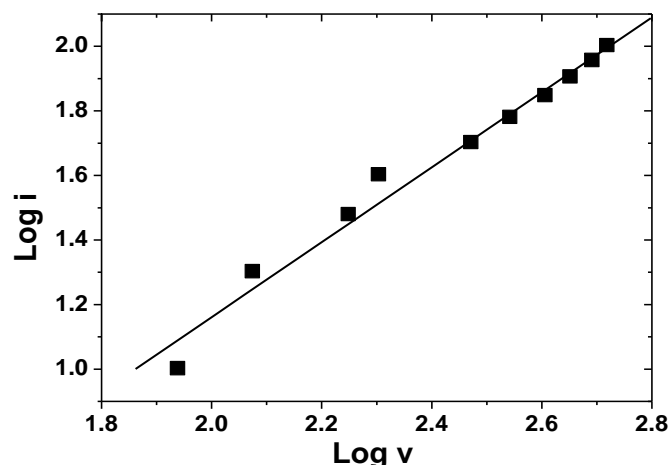


Figure 4. Relationship between logarithm of oxidation currents and logarithm of scan rates of **FB** ($c=5 \times 10^{-5}$ M) in B-R buffer pH 7.0

3.3. Anodic stripping voltammetric behavior of FB

A concentration range from 2×10^{-6} to 3×10^{-5} M of **FB** ($n=8$) were analyzed using ASV technique in B-R buffer, pH7 and successfully accumulated on GCE over the positive potential range 0.0 – 1.0 V under optimum conditions which gave well-recorded anodic signals, as shown in figure 5.

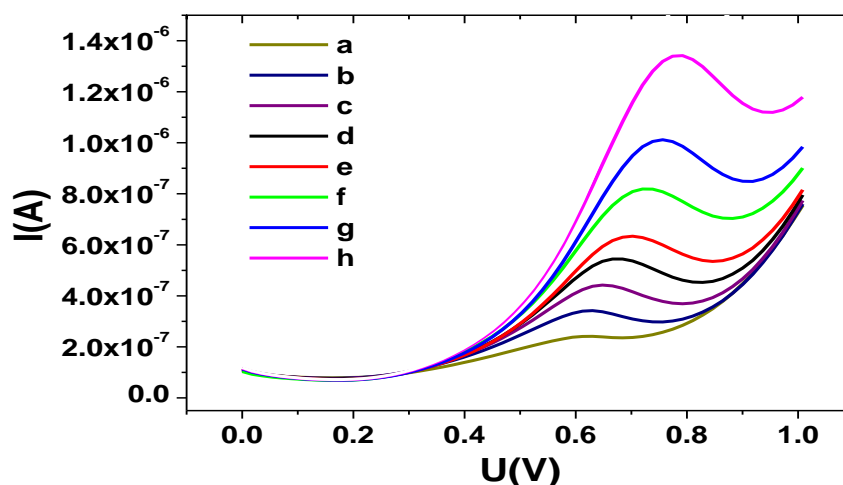


Figure 5. Anodic stripping voltammograms of **FB** in B-R buffer pH7 onto GCE over the concentration range ($a=2 \times 10^{-6}$, $b=4 \times 10^{-6}$, $c=6 \times 10^{-6}$, $d=8 \times 10^{-6}$, $e=10 \times 10^{-6}$, $f=1.5 \times 10^{-5}$, $g=2 \times 10^{-5}$ and $h=3 \times 10^{-5}$ M)

3.4. Optimization of some significant parameters

3.4.1. Effect of supporting electrolyte and pH

The supporting electrolytes and pH values were considered as a very important parameters for the electrochemical determinations and they defined the effect of the current voltammetric evaluation. In this study, **FB** ($c=5 \times 10^{-6}$ M) was analyzed by ASV technique in Britton-Robinson, acetate, phosphate and carbonate supporting electrolytes at 30 sec and 0.0 V accumulation time and potential. Britton-Robinson

(B-R) recorded a high current and anodic stripping response. As a result, B-R buffer (pH7) was selected as the optimum parameter for the future work. While the effect of pH values on the anodic signals was studied over the range 5-9 as shown in figure 6. A pH=7 gave a high current and was selected as the optimum pH value for future voltammetric work.

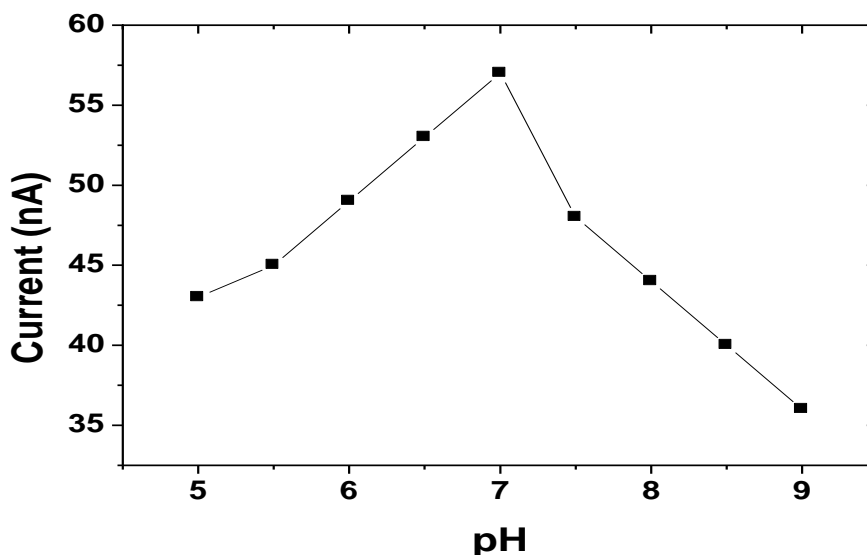


Figure 6. The effect of pH on anodic voltammogram of **FB** ($c=5 \times 10^{-6}$ M) with B-R buffer

3.4.2. Effect of accumulation time and potential

The study of deposition time and potential of the analyte was considered important for a sensitive determination and voltammetric analysis of **FB** on GCE. The anodic voltammetric current of **FB** ($c=5 \times 10^{-6}$ M) was monitored over the range 0.0 – 90 sec, yielded, the 30 sec accumulation time gave a high anodic current and was selected as optimum value for a future study. On the other hand, when accumulation potential was monitored over the range -0.2 to +0.8 for the same concentration of **FB**, $E_{aac} = +0.2$ was recorded as the high current and it was considered as an optimum result for the next analysis.

3.4.3. Effect of scan rate

Scan rate was also classified as an important parameter to obtain anodic stripping voltammetric current of analyte. In this experimental part, compound **FB** ($c=5 \times 10^{-6}$ M) was studied over the range 30 – 300 mV/s ($n=9$), and gave high current (180 mV/s). This result was selected as optimum scan rate for the next step.

3.4.4. Effect of frequency

The influence of frequency on the anodic stripping current was studied over the range 5.0-30 Hz ($n=6$) for **FB** ($c=5 \times 10^{-6}$ M). 10 Hz was produced high current and it was adopted as optimum value.

3.4.5. Effect of pulse amplitude

The influence of pulse amplitude on the anodic voltammetric signal was evaluated for 5×10^{-6} M of **FB** over the range 10-120 mV. The results showed that the anodic current gradually increased to 80 mV then gradually decreased. A 80 mV was selected for further work.

3.4.6. Effect of convection rate and working electrodes

The voltammetric signal depends on the convection rate to obtain a sensitive analysis. The convection rate was monitored over the range 0 – 3000 rpm for 5×10^{-6} M of **FB** as shown in figure 7, yielded, 1600 rpm high anodic current and it selected as optimum value for a voltammetric analysis. On the other hand, the varying of working electrode was also evaluated. Glassy carbon, platinum, gold and graphite electrodes were used to monitor the anodic signal for analyte where the glassy carbon electrode recorded the highest current, and this was selected as working electrode to determine the studied compound.

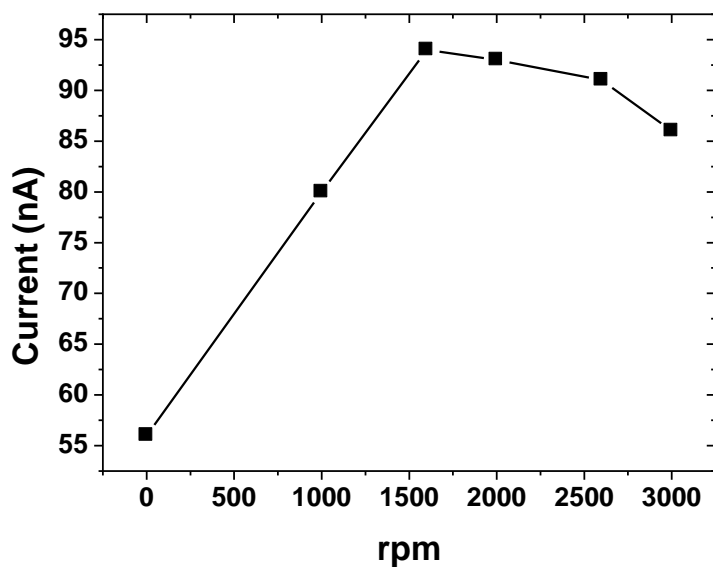


Figure 7. The effect of convection rate on anodic voltammogram of **FB** ($c=5 \times 10^{-6}$ M) at B-R buffer and pH7

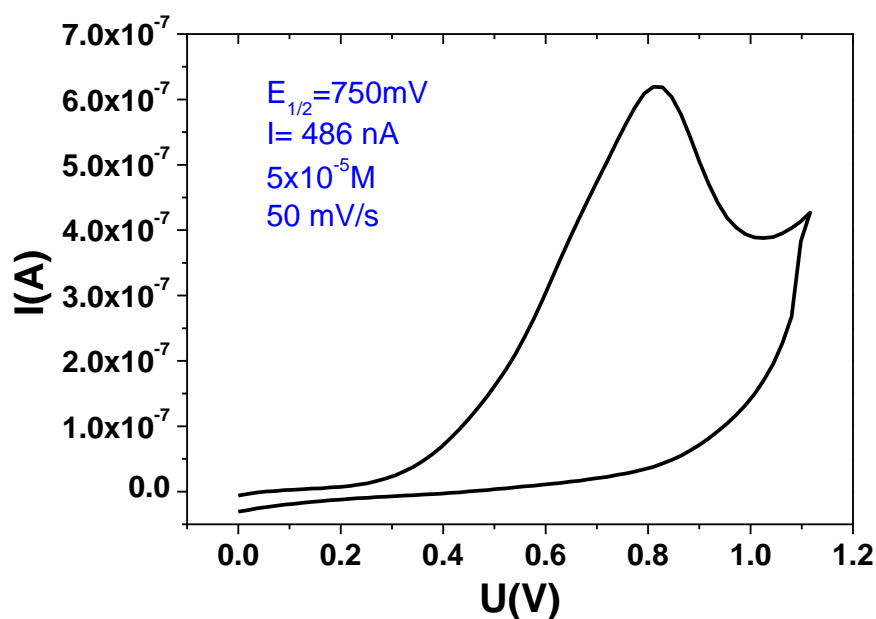


Figure 8. Cyclic voltammogram for 5×10^{-5} M indole under FB optimum conditions

On the other hand, the CV method was used to analyze the indole, in order to compare it with the studied voltammetric methods for **FB**. The anodic cyclic voltammetric current for 5×10^{-5} M indole was observed at 750 mV and 486 nA as shown in figure 8

4. Method Validation

Regarding the suitable electrochemical conditions and instrumental parameters which were already studied for the determinations of **FB** to perform and estimate the anodic stripping voltammetry technique. The analytical characteristics of the developed method should be studied in the following conditions.

4.1. Reproducibility and recovery

The study of reproducibility and recovery has been given more information about the sensitivity and accuracy of the analytical method. If the analytical technique has an excellent reproducibility and recovery, it is confirmed that the analyte has high sensitivity and accuracy. A 5×10^{-6} M of **FB** was analyzed and the measurements were repeated eight times. The results with relative standard deviation (RSD%) was 0.54%, confirming the precision of anodic stripping voltammetry method. On the other hand, the accuracy of the studied method was known by calculating the recovery of 5×10^{-6} M of **FB** in B-R buffer pH 7 under the optimum conditions, where the recovery was $97\% \pm 1.0$.

4.2. Calibration curve, detection limit and stability studies

An excellent linear relationship between the anodic stripping voltammetric signal and concentrations of analyte was recorded over the concentration range 2×10^{-6} - 3×10^{-5} M of **FB** under the optimum conditions as illustrated in the previous voltammograms in **figure 5**. Least-square study of the calibration curve resulted in the following regression equation:-

$$I_a \text{ (nA)} = 56 + 1.7 \times 10^7 C \quad r^2 = 0.994, \quad n = 8$$

where i_a is the anodic stripping current, C is the analyte molarity concentration and r^2 is the correlation coefficient.

The detection limit is defined as the lowest concentration of analyte based on the signal-to-noise ratio ($S/N=3$). For this determination, it was calculated 8×10^{-8} M of **FB** compound. On the other hand, the stability of the anodic signal was evaluated by monitoring the current values for an hour. The anodic electrochemical signal was approximately fixed within this period of time.

4.3. Interferences study

The influence of interference substances on the analyte current was studied to evaluate the selectivity of the developed ASV procedure. The interferences can be found by co-existing surface-active materials able to compete with the analysed compound of interest for the adsorption site on the working electrode surface, resulting in a decrease or increase in the voltammetric current. The competitive co-adsorption substances were evaluated in the presence of some compounds usually added in the pharmaceutical formulations such as starch, sucrose, lactose, glucose and maltose which were found at different concentrations (one, 5-fold and 20-fold) higher than the **FB** concentration, (5×10^{-6} M). All interferences had negative effects at high concentrations on the **FB** anodic current.

5. Anodic stripping voltammetric applications

While **FB** contains triazole and indole moieties, the proposed ASV method was applied for the determination of **FB** in some pharmaceutical formulations which consisted of triazole and indole groups such as Eletriptan Hydrobromide and Sumatriptan pharmaceutical tablets, and biological samples. These contents of commercially available drugs were directly analysed by ASV technique after the dissolution and filtration processes. Relpax tablet contains 40 mg of Eletriptan Hydrobromide (manufactured by Pfizer manufacturing Deutschland GmbH a subsidiary of the pfizer group, Illertissen, Germany). Imigran tablet contains 50 mg of sumatriptan as the succinated (Glaxo Saudi Arabia Ltd. " member of the GlaxoSmithkline group" of companies). These tablets included indole group, as in the proposed mechanism of **FB**, showed the same anodic behavior in terms of potentials and peaks. The developed ASV method used to measure the relpax and imigran tablets, yielded five concentrations at average $5 \times 10^{-6} \text{ M} \pm 0.74 \text{ SD}$ and $7 \times 10^{-7} \text{ M} \pm 0.86 \text{ SD}$, respectively, in almost $E_a = 720 \text{ mV}$ (anodic potential). In addition, the anodic voltammetric technique was used to analysis **FB** in biological samples and evaluated by recording its recovery from spiked human urine and plasma.

Table 1. Recovery analytical results of **FB** from biological human samples

	Spiked Urine	Spiked Plasma
	% FB Recovery	% FB Recovery
Added FB $3.0 \times 10^{-6} \text{ M}$	105	93
	107	91
	108	92
	106	93
	107	91
Mean	106.6	92.0
Standard Deviation	± 1.14	± 1.00

The biological sample was pretreated and prepared by adding a small amount of 5.0% of $\text{ZnSO}_4 \cdot 7\text{H}_2\text{O}$ solution, NaOH and MeOH to the urine and plasma samples and by centrifuging this mixture to eliminate the interfering organic substances as the proteins [18]. As can be seen from table 1, the ASV procedure allowed the determination of **FB** ($3 \times 10^{-6} \text{ M}$) in spiked urine and plasma with mean recoveries $106.6\% \pm 1.14$ and $92.0\% \pm 1.00$, respectively.

6. Conclusion

The voltammetric study of 1-(3-Fluoro-benzenesulfonyl)-5-{3-[5-(3-methoxy-phenyl)-2-methyl-2H-[1,2,4]triazol-3-yl]-phenyl}-1H-indole (**FB**) indicated the irreversibility nature of the anodic oxidation process. The DPV, CV and ASV techniques were also used to analysis **FB**. In this study, a simple, selective, accurate and precise ASV method developed to determine a new **FB** compound in the pharmaceutical and biological samples.

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