



INFLUENCE OF SODIUM SACCHARIN IN BLOOD MEDIUM USING CYCLIC VOLTAMMETRIC METHOD AT NANO-SENSOR

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Abstract: Several chemical compounds were used as an alternative of natural sugar for diabetic patients such as sodium saccharin (NaSc). This compound has unknown side effects so far on human health especially on the blood components as oxidative or anti-oxidative reagents, so the study is very important in this field. In this study, it was used a high-precision sensor (glassy carbon electrode GCE modified with carbon nanotubes CNT) in detection of electrochemical properties for sodium saccharin compound in the blood medium by cyclic voltammetric technique. It was found that NaSc has oxidation-reduction current peaks in blood medium at 450 and -900 mV respectively; different concentration, scan rates and pH. Also, the study was included the determination each of current ratio (I_{pa}/I_{pc}), potential peak separation (ΔE) and diffusion coefficient (D_f) value on the preparation nano-sensor. In application study of NaSc in blood medium, it was found the effect of each of vitamin E, ascorbic acid (AA) and folic acid (FA) on the redox current peaks of NaSc in the blood medium at different concentrations.

Keywords: Sodium saccharin, cyclic voltammetry, blood medium, CNT/GCE

Introduction: In the first time has been studying the effect of the chemical compounds in diluted blood media as an electrolyte using cyclic voltammetric technique to finding the oxidation-reduction current peaks effective on

the blood component [1-5]. Previous studies did not address the use of alternative compounds of natural sugar with sodium saccharin for the diabetic patients.

Saccharin has been found to possess an anti-prothrombin effect in vitro, but it is inert to thromboplastin and to thrombin. Lithium ferriheme shows an antithrombic and anticoagulant action. Saccharin administered orally had no effect on prothrombin time and showed no antagonism or synergism with dicoumarol [6]. Oxidation-reduction behavior of

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copper-saccharin was studied using the cyclic voltammetric technique. It was found that the adsorption process suppresses the Faradaic process of the copper-saccharin and the heterogeneous charge transfer rate constant was found for the complex [7]. The cathodic and anodic current peaks of uncoordinated Fe(III)/Fe(II) in saccharin was studied at platinum electrode with legends. It was found the process is reversible and to be quasi-reversible in nature with diffusion control [8].

The subacute toxicity of sodium saccharin was studied with different compounds in animals (dog and rats). Parameters determined for treated animals, including growth, food consumption, hematologic profiles, clinical blood chemistry studies, urinalyses, organ weight and ratio data, and both gross and microscopic pathologic evaluation were not significantly different from control values. It was suggested that there is little toxicologic hazard associated with ingestion of the derivatives of sodium saccharin [9]. A novel Schiff-base was synthesized by the reaction of saccharin with tryptophan. The voltammetric behavior of Schiff-base was studied on the hanging mercury drop electrode (HMDE) by using Square-Wave Voltammetry (SWV) and Cyclic Voltammetry. The voltammograms of the Schiff-base exhibited two irreversible cathodic peaks in buffer solution (pH 7.0-10.0) for the potential range from 0.0 V to -1.4 V. These peaks which appeared at more positive potentials than the cathodic peaks of tryptophan and saccharin was assigned to the reductions of $C-N^+$ and $>C=N^-$ moieties of Schiffbase [10].

In this work, NaSc was studied in blood medium to find the electrochemical and physical properties using high sensitive modified working electrode by carbon nanotubes on GCE.

Experimental

Materials: Sodium saccharin (purity 98% from china company), carbon nanotubes (purity 99%) supplied from Fluka company (Germany), and other chemical used in the experiment in high

pure materials from SCRC (china), healthy human blood samples from center medicine of Baghdad City. Deionize water was used for the preparation of aqueous solutions. All solutions which used in the cyclic voltammetric cell were treated with nitrogen gas for 10-15 minutes prior to oxygen free from the solutions.

Apparatus: The instrument EZstat series (Potentiostat/Glvanostat) NuVant Systems Inc. (made in USA). The Electrochemical Bio-analytical cell was connected with potentiostat device and monitoring through the special program that has been installed on the personal computer to perform cyclic voltammetry (CV). The silver-silver chloride reference electrode (Ag/AgCl in 3M NaCl) and Platinum wire (1 mm diameter) was used as a reference and counter electrodes respectively. The glassy carbon working electrode (GCE) modified with CNT was used in this study after cleaning by polishing with alumina solution and treated with ultrasonic path water for ten minutes.

Preparing the modification of GCE with CNT (CNT/GCE): A mechanical attachment technical method was used to preparation the CNT/GCE working electrode and employed to fabrication of nano-sensor [11,12]. The method was included abrasive application of multiwall carbon nanotubes (MWCNT) at the clean surface of GCE, forming an array of MWCNT as MWCNT/GCE and replaced in 10 ml of electrolyte in the cyclic voltammetric cell.

Scanning electron microscopy (SEM) study: SEM analysis was carried out to investigate nano articles for carbon nano tubes (CNT). Samples were dehydrated for 45 min before being coated with gold particle using SEM coating unit. SEM was used to examine the morphology of CNT by mechanical attached technique on a graphite electrode surface before and after electrolysis with NaSc by cyclic voltammetry using blood medium as an electrolyte. Figure (2-1a) is SEM of CNT attached basal plane graphite electrode which electrolysis in blood medium and exhibited an array of microcrystal with 0.1-2 μ m diameter.

Figure 2-1b is SEM of the modified with after electrolysis with NaSc using cyclic voltammetry with slightly enlarged size range of 0.1-3µm

diameter indicating presence of solid to solid conversion and that the film appears stable even after 10 potential cycling.

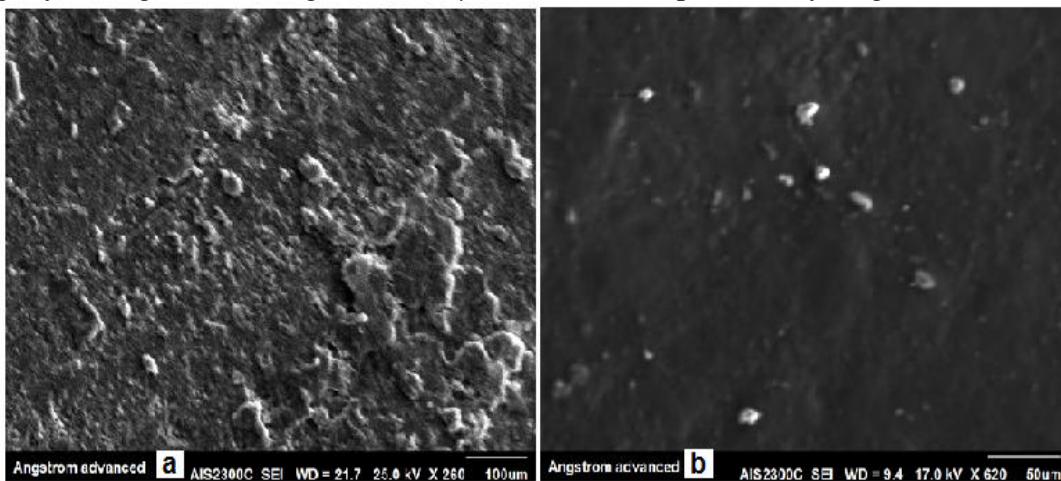


Figure (2-1) Scanning Electron Microscopy (SEM): (a) of CNT attached via mechanical method on to basal plane graphite electrode after electrolysis in blood medium. (b) SEM of CNT after electrolysis of NaSc in blood medium by cyclic voltammetry.

Results and Discussion: One of the alternative compounds of the sugar is sodium saccharin which was used by diabetic disease patients. The effect of sodium saccharin in blood medium was studied to using cyclic voltammetric technique on nano-sensor (CNT/GCE) at the following different studies:

Effect varying pH

The influence of both alkaline and acidic medium in blood medium for sodium saccharin was studied using modified GCE with CNT (CNT/GCE) as working electrode and Ag/AgCl as reference electrode. It was observed that the oxidation-reduction current peaks of Sodium Saccharin in blood medium at different pH have a strange phenomenon as shown in table 3-1,

Figure 3-1 and 3-2. It was found from the results that high value of cathodic current peak of NaSc at acidic pH=5 as in Figure 3-1, but the high value of anodic current peak in media pH=5 as in Figure 3-2. So, it can be say that NaSc in acidic blood medium is more oxidative effected on the blood component, and more anti-oxidative in acidic media at pH=4.

Also, it was found from table (3-1) the current ratio (I_{pa}/I_{pc}) value of NaSc at different pH in the range of 0.4 to 0.9, this ratio values means that redox reaction of NaSc is reversible process in both acidic and alkaline media [13]. The mechanism of the redox process of NaSc was described in the following equations no.1 and 2 [14].



Figure 3-3 shows the effect of different pH on the redox current peaks of NaSc in blood medium especially at pH 5 and 11. The cyclic voltammogram of reduction current peak at

acidic pH=5 was enhanced more than at alkaline pH=11, so all studies were used the blood medium at pH=5.

Table (3-1) current, potential and peak potential separation values of oxidation-reduction peaks of 0.1mM NaSc in different pH at CNT/GCE.

pH	Ipa μA	Ipc μA	Epc mV	Epa mV	Epa - Epc	Ipa/Ipc
4	5.603	9.966	765.6	327.3	438.3	0.562212
5	12.01	13.88	1.497	241.4	239.903	0.865274
3	7.325	12.95	787.6	297.6	490	0.565637
7	6.956	13.88	1.513	105.4	103.887	0.501153
8	6.53	15.32	1.521	317.2	315.679	0.42624
9	11.44	21.53	1.53	217.5	215.97	0.531352
10	9.425	14.8	1.548	199.4	197.852	0.636824
11	10.79	18.27	679	103.3	575.7	0.590586

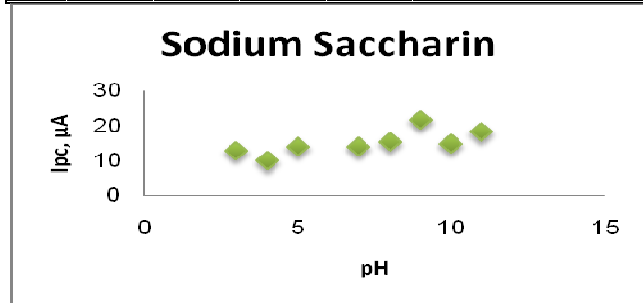


Figure (3-1) plot redaction current against the pH (3-11) of 0.1mM NaSc in blood at CNT/GCE.

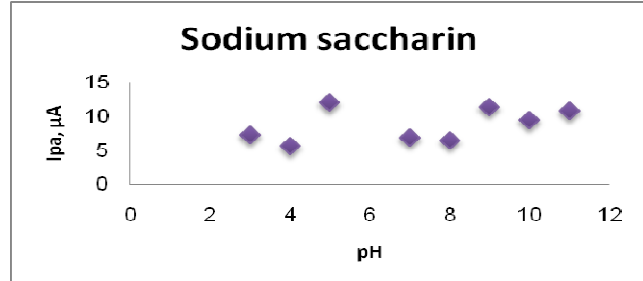


Figure (3-2) plot oxidation current against the pH (3-11) of 0.1mM NaSc in blood at CNT/GCE.

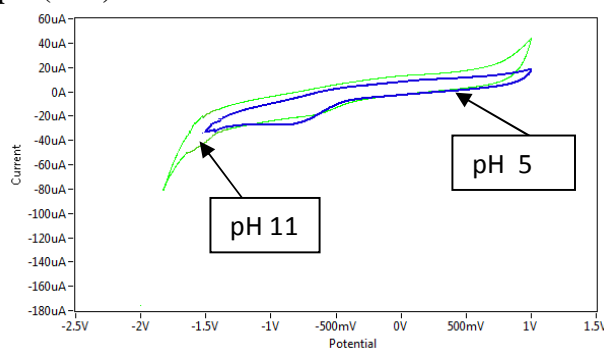


Figure (3-3) Cyclic voltammogram of 0.1mM NaSc at different pH (5 and 11) on CNT/GCE,

scan rate 100 mV sec⁻¹ versus Ag/AgCl as reference electrode.

Effect varying concentrations: Figure (3-4) and (3-5) shows the calibration curve of different concentration (0.01-0.1mM) of oxidation-reduction current peaks of NaSc in blood medium respectively. The detection limit for the low concentrations of NaSc analysis at the CNT/GCE of 10⁻³mM with oxidation current sensitivity of close to 308.52 μA/mM which observed with curvature being detected at a concentration of greater than 10⁻³ mM and reduction current sensitivity of close to 470.07 μA/mM. The calibration plot at Figure 3-4 and 3-5 were performed at the CNT/GCE in the NaSc with a good linearity of anodic and cathodic current as described by the equation: y = 71.444x + 3.0429, R² = 0.9845 and y = 28.509x + 13.274, R² = 0.9379 respectively. Table (3-2) was represented values of the different concentration of NaSc, cathodic and anodic current peaks expression of the reaction rate, which depended on the electrode area, A [cm²] as shown in table 3-2 [15].

$$\text{Rate} = \frac{I}{nAF} \dots \dots \dots (1)$$

- I: current.
- F: number of faradays.
- A: area of electrode.
- n: number of electrons transfer

Figure 3-6 and 3-7 show the cathodic and anodic rate reaction of NaSc was proportional to the different concentration 0.01-0.1 mM in both oxidation and reduction process. The redox rate reaction was increased against to the increasing the concentration of NaSc in blood medium [16]. From table 3-2, it can be seen the reaction rate at anodic and cathodic electrodes of different concentration (0.01-0.1 mM) of NaSc in blood medium. The relationship between the reaction rate and the concentration of NaSc on the anodic and cathodic electrodes to be increased the rate with increasing the concentration as shown in Figure 3-6 and 3-7 respectively. So, the oxidation reaction rate at the anodic electrode was increased against to

increasing of the concentration of NaSc in the electrolyte which depended on the reduction

reaction rate at the cathode electrode as shown in the following equation [17].

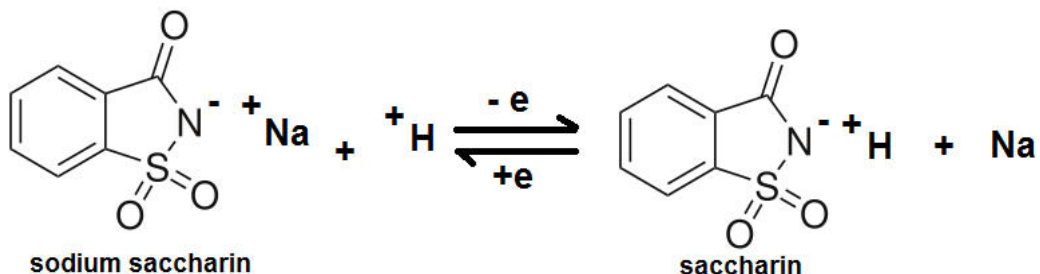


Table (3-2) different concentration (0.01-0.1 mM) of NaSc in blood at cathodic and anodic current peaks by CNT/GCE.

Concentration mM	Ipa μA	Epa mV	Ipc μA	Epc mV	Epa-Epc mV	Ipa/Ipc	anodic rate $\times 10^{-3}$	cathodic rate $\times 10^{-3}$
0.01	3.673	259.5	13.43	875.4	-615.9	0.273	0.5	1.97
0.02	4.737	265.6	13.53	879.7	-614.1	0.350	0.6	1.985
0.03	5.415	261.6	14.55	879.6	-618	0.372	0.7	2.134
0.04	5.987	235.3	14.64	866.5	-631.2	0.408	0.8	2.147
0.05	6.263	245.7	14.8	856.9	-611.2	0.423	0.9	2.171
0.06	6.957	247.7	14.9	875.5	-627.8	0.466	1	2.185
0.07	7.983	291.3	15.17	879.7	-588.4	0.526	1.1	2.225
0.08	8.856	263.5	15.34	874.5	-611	0.577	1.2	2.25
0.09	9.228	263.7	15.78	879.7	-616	0.584	1.3	2.315
0.1	10.624	275.5	16.28	875.4	-599.9	0.652	1.5	2.388

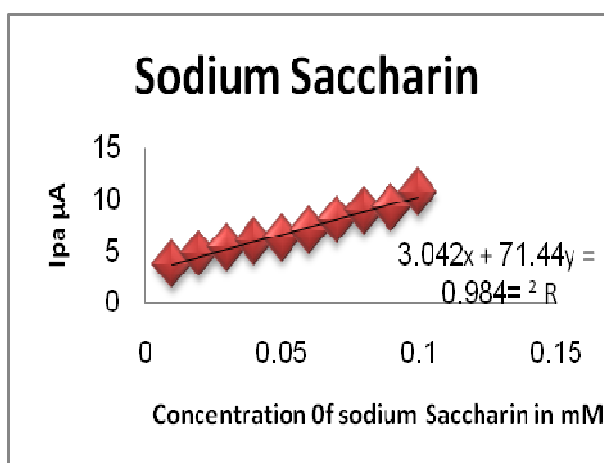


Figure (3-4) plot of oxidation current against different concentration of NaSc in blood at CNT/GCE.

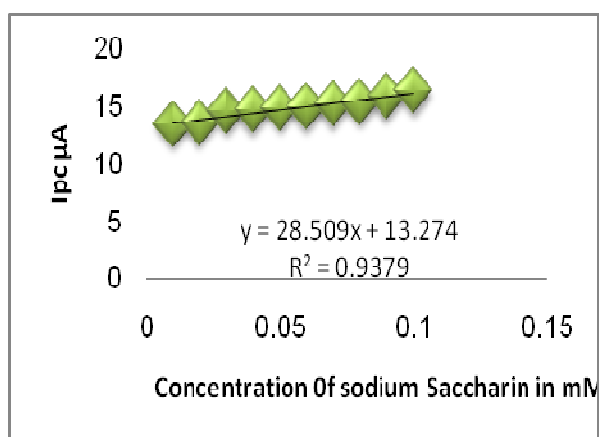


Figure (3-5) plot of reduction current against different concentration of NaSc in blood at CNT/GCE.

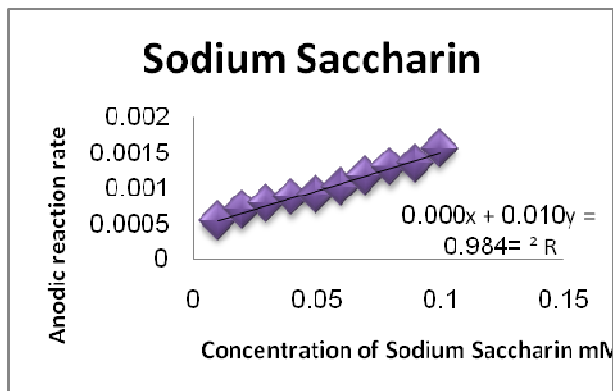


Figure (3-6) relationship between anodic reaction rate and different concentration of NaSc in blood at CNT/GCE.

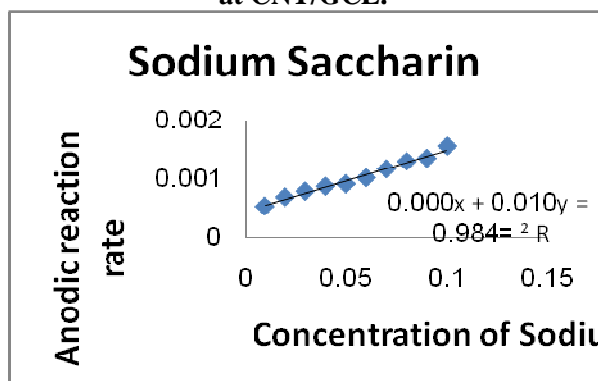


Figure (3-7) relationship between cathodic reaction rate and different concentration of NaSc in blood at CNT/GCE.

Effect varying scan rate: The voltammograms of NaSc at different scan rate in blood medium was affected on the redox current peaks of NaSc by increased the current peaks with increasing the scan rate. However, the anodic current peak of NaSc was shifted to the lower potential. In a slow scan rate the diffusion layer grows much further from the electrode in comparison to a fast scan rate as shown in the result of diffusion coefficient values in table 3-3, it was found that the rate of flux to the electrode surface is much smaller at slow scan rates than it is at faster rates. The current was depended as proportional to the flux towards to the electrode and the current intensity becomes lower at slow scan rates and higher at high scan rates. In the general process of the redox system was acted at diffusion controlled [18].

A reasonably linear dependence of reduction and oxidation current peaks of NaSc on different scan rates was described by the following equations: $y = 0.3551X + 3.5181$, $R^2 = 0.9903$ and $y = 0.8018X + 3.7904$, $R^2 = 0.9681$ respectively, which was displayed in Figure (3-8) and (3-9). It was found that current peaks ratio of anodic to cathodic was increased with increasing of scan rate at the range (0.4-0.7 mVsec^{-1}). These observations were suggested that the system in the redox current ratio of the voltammograms is recorded in Table (3-3). Figure (3-10) shows the cyclic voltammograms of NaSc in different scan rate at 0.01 and 0.1 mVsec^{-1} on CNT/GCE. Randles-Sevcik equation was described reversible redox couple of the current peaks [19].

$$I_p = (2.69 \times 10^5) n^{3/2} A C D_f^{1/2} v^{1/2} \dots \dots \dots (2)$$

Where: I_p is the current.

n is the number of moles of electrons transferred in the reaction.

A is the area of the electrode.

D_f is the diffusion coefficient.

v is the scan rate of the applied potential.

It was found the diffusion coefficient values of the redox process of NaSc at different scan rates which calculated from Randles-Sevcik equation as described in table 3-3 with values close to the values contained in references [20]. It can be seen from table 3-3 that the diffusion coefficient values at anodic electrode were increased against to increasing of scan rate, but these values were decreased versus to increasing the scan rates. The discussion of these phenomena was depended on the electrochemical catalysis of nanoparticles of CNT on the GCE which causes the enhancement of the anodic current peak at higher scan rate [21]. The average value of potential peak separation (ΔE) was more than 100 mV and I_{pa}/I_{pc} less than 1, indicating that irreversibility of the modified electrode [22].

Table (3-3) different scan rates, diffusion coefficient values, redox current peaks and potential of NaSc in blood medium on CNT/GCE.

Scan rate	I _{pc} μA	E _{pc} mV	E _{pa} mV	I _{pa} μA	E _{pa} -E _{pc}	I _{pa} /I _{pc}	D _f (pa) x10 ⁻⁶	D _f (pc) x 10 ⁻⁶
0.01	7.635	801.4	164.5	2.868	636.9	0.375639	2.277	16.139
0.02	9.294	872.4	169.4	4.891	703	0.526253	3.311	11.957
0.03	10.34	848.5	169.2	6.026	679.3	0.582785	3.351	9.867
0.04	11.94	847.5	169.3	7.031	678.2	0.588861	3.421	9.867
0.05	13.14	896.3	192.3	7.979	704	0.60723	3.525	9.560
0.06	14.03	894.9	190.5	8.794	704.4	0.6268	3.568	9.083
0.07	14.74	895.9	169.7	9.403	726.2	0.637924	3.497	8.593
0.08	15.3	896.4	194	10.35	702.4	0.676471	3.707	8.101
0.09	16.31	919.9	169.5	10.73	750.4	0.657879	3.541	8.183
0.1	16.91	918.6	241.4	12.01	677.2	0.710231	3.993	7.916

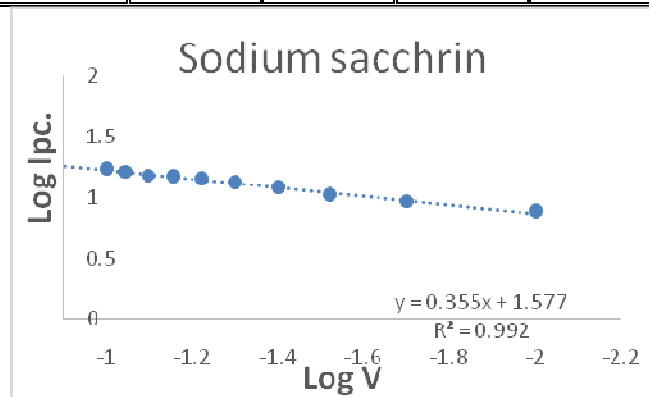


Figure (3-8) plot log I_{pc} against to Log V (scan rate) for 0.1 mM NaSc in blood and (0.1 M acetate buffer at pH 5) using CNT/GCE.

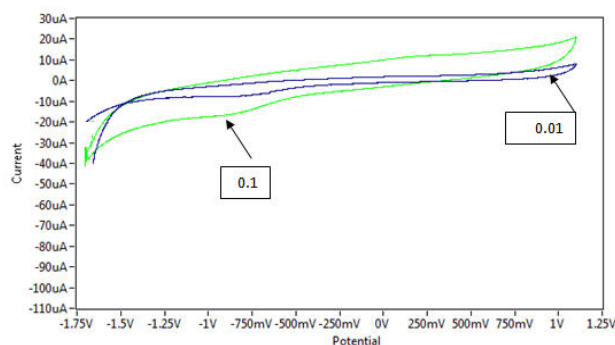


Figure (3-10) cyclic voltammogram of 0.1 mM NaSc at different scan rate 0.01 and 0.1 Vsec⁻¹ in blood on CNT/GCE electrode.

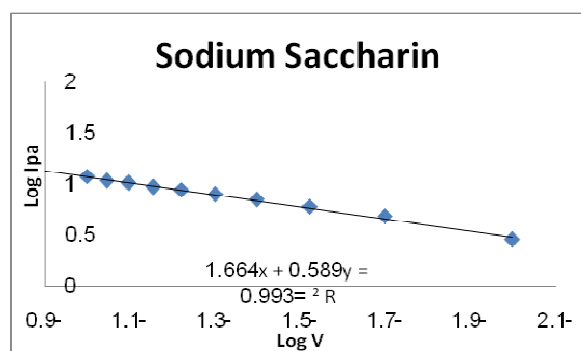


Figure (3-9) plot log I_{pa} against to Log V (scan rate) for 0.1 mM NaSc in blood and (0.1 M acetate buffer at pH 5) using CNT/GCE.

Reliability and stability of modified electrode:

The potential cycling of the oxidation-reduction current was carried out during cyclic voltammetry for the modified working electrode CNT/GCE in NaSc with blood at scan rate was 100 mVsec⁻¹. Table (3-4) illustrated the reliability of the anodic and cathodic current peaks with the relative standard deviation (RSD)= ±0.773% and ±0.522%, respectively. Figure 3-11 shows the cyclic voltammogram of redox current peaks of 0.1 mM of NaSc in blood at ten times of cyclic, which revealed a good stability of the cyclic voltammetry of the

modified GCE by overlapping of the voltammogram lines.

Table (3-4) The reliability of CNT/GCE as working electrode at scan rate is 100mVsec⁻¹ for anodic current peak of 0.01mM NaSc in 1M Na₂SO₃ at ten times cyclic.

Number	I _{pc} μA	I _{pa} μA	Mean I _{pa}	Mean I _{pc}	RSD I _{pc}	RSD I _{pa}
1	13.72	9.711	9.52	13.69	±0.522	±0.773
2	13.74	9.457				
3	13.7	9.47				
4	13.68	9.488				
5	13.6	9.482				
6	13.6	9.483				
7	13.6	9.487				
8	13.69	9.526				
9	13.78	9.544				
10	13.79	9.537				

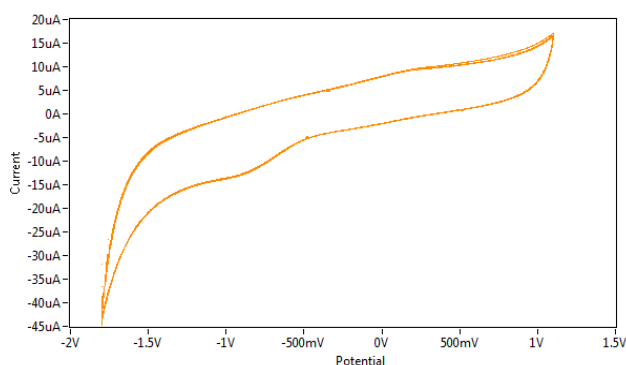


Figure (3-11) Cyclic voltammogram of redox current peaks of 0.1mM NaScin blood at ten times cyclic on CNT/GCE, scan rate 100 mVsec⁻¹ versus Ag/AgCl.

Effect of Vitamin E, AA and FA on NaSc in blood medium: The present study reveals the effect each of Vitamin E, ascorbic acid (AA) and folic acid (FA) on the NaSc in blood medium at modified working electrode CNT/GCE. It was found that the increasing of the concentration of Vitamin E leads to enhancement the oxidation current peak of NaSc in blood medium as shown in Figure 3-12, but a new phenomenon was appeared in the reduction current peak of NaSc which decreased against to increasing the concentration of vitamin E as shown in Figure 3-13, this mean that vitamin E cannot used as antioxidant

reagent with NaSc in blood medium. Also, it was noted that when using each of AA and FA with NaScin blood medium was acted for enhancement of redox process as shown in Figures 3-14, 3-15, 3-16 and 3-17, this mean that each of anti-oxidative reagent of AA and FA for using with NaSc as inhibition reagent of oxidation stress of NaSc on blood components.

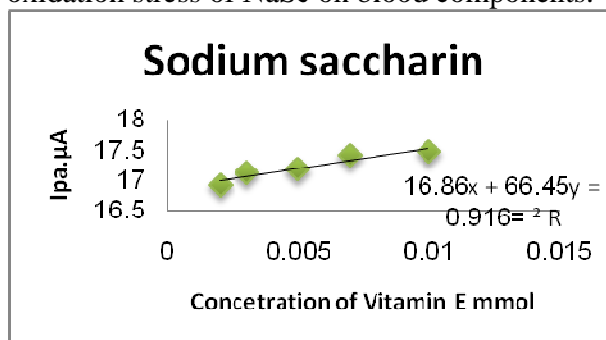


Figure (3-12) plot of cathodic current peak of 0.1 mMNaSc in blood medium against to different concentrations of Vitamin E on CNT/GCE and Ag/AgCl as reference electrode.

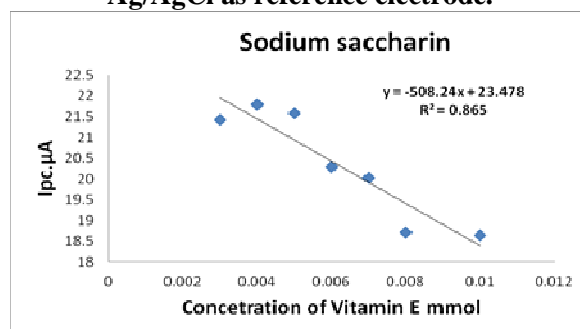


Figure (3-13) plot of cathodic current peak of 0.1 mMNaSc in blood medium against to different concentrations of Vitamin E on CNT/GCE and Ag/AgCl as reference electrode.

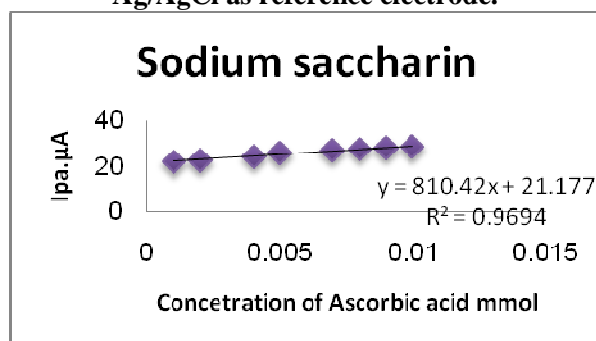


Figure (3-14) plot of anodic current peak of 0.1 mMNaSc in blood medium against to different concentrations of Ascorbic acid on CNT/GCE and Ag/AgCl as reference electrode.

different concentrations of AA on CNT/GCE and Ag/AgCl as reference electrode.

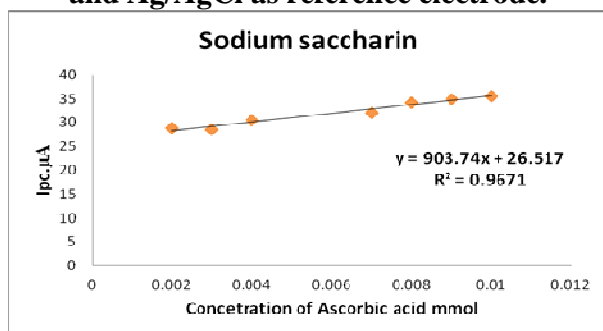


Figure (3-15) plot the cathodic current peak of 0.1 mMNaSc in blood medium against to different concentrations of AA on CNT/GCE and Ag/AgCl as reference electrode.

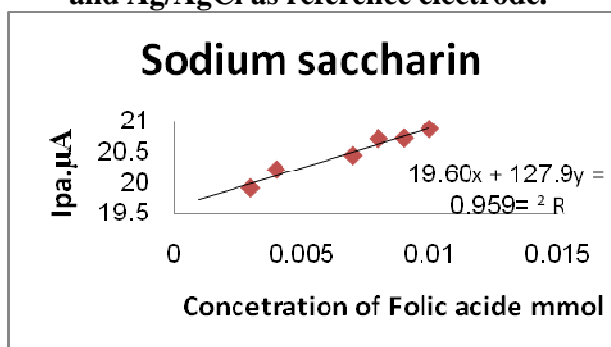


Figure (3-16) plot the anodic current peak of 0.1 mMNaSc in blood medium against to different concentrations of FA on CNT/GCE and Ag/AgCl as reference electrode.

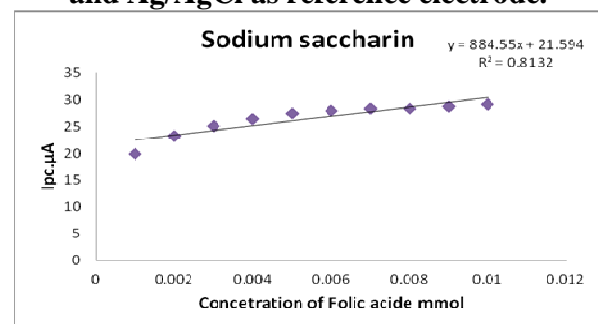


Figure (3-17) plot of cathodic current peak of 0.1 mMNaSc in blood medium against to different concentrations of FA on CNT/GCE and Ag/AgCl as reference electrode.

Conclusion: It can be concluded from this work, the using of the alternative chemical compound which taking by diabetic patients of sodium saccharin (NaSc) that affected on the

blood component. Cyclic voltammetric technique was used at modified GCE with CNT as good nano-sensor. The study was included results of different concentration of NaSc, different pH of blood medium, and different scan rates. It was found that the better pH of blood medium is 5 that give enhancement of redox current peaks of NaSc, so pH=5 of blood medium were depended in all study. Through the study at different scan rates were obtained that the redox reaction of NaSc in blood medium is irreversible. Also, the diffusion coefficient values were determined from Randles-Seveik equation at the modified working electrode (CNT/GCE) which given an increasing conductivity of the nano-sensor by increasing the scan rates in blood medium. The use of certain antioxidants such as vitamin E, AA and FA to prevent oxidative stress factor in NaSc in blood medium were used in this study, all anti-oxidative reagents inhibition the effect of NaSc in blood component.

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