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Determination of Glucose using Flow Injection Analysis and Borate Selective Electrode

Duygu Uner-Bahar[1*], *And Ibrahim Isildak*[2]

[1] Istanbul Gelisim University, Vocational School of Health Services, Biomedical Device Technology Department, Istanbul, Turkey,
[2] Yildiz Technical University, Faculty of Chemical and Metallurgical Engineering, Bioengineering Department, Istanbul, Turkey.
[*]E-mail: duygu.uner1@gmail.com

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This study focuses on the development of a flow injection analysis method that performs nonenzymatic glucose measurement. It is aimed to develop a more economical blood glucose monitoring system by measuring the instant blood glucose level indirectly with borate based ion selective electrode. A non-enzymatic electrode based on carbon nanotube-silver borate (CNT-SB) composite electrode was developed and integrated into a flow injection analysis system as a detector, and glucose measurement was performed. Potentiometric measurement was made with this detection chamber. Heights of potentiometric peaks obtained were used for the determination of the amount of glucose in blood samples. Repeated injections were tested by using a mini-sized separation column as stationary phase and successful results were obtained. In addition, boronic acid solution was used as a carrier solution in the system, and it is predicted to be more accessible and simple method than the present non-enzymatic methods as it has ability at neutral pH conditions. The developed glucose measurement system was simple, economic and fast.

Keywords: Borate Sensor, Diabetes Diagnosis, Economic Blood Glucose Measurement, Health quality, Sustainability.

1. INTRODUCTION

Diabetes is a metabolic disease and regular glycemic control is required to prevent the progression of the complications of the disease. Glycemic control is achieved by daily fasting glucose measurements or by measuring glycosylated proteins (HbA1c and fructosamine) [1]. Instantaneous blood glucose readings reflect the current glycemic level [2]. Achieving glucose sensing at a neutral pH is essential as human blood pH is usually varies between 7.35 and 7.45. Long-term complications of diabetes develop gradually, and the less controlled a person's blood sugar levels are, the higher the risk of complications. Eventually, diabetes complications may be disabling or even life-threatening, as excess sugar may injure the walls of the capillaries nourishing the nerves, damage the glomeruli blood vessel clusters in the kidneys, and affect the blood vessels of the retina, potentially leading to blindness.

Glucose measuring devices are therefore crucial for patients and clinicians. Hence many methods have been developed to measure blood sugar. Currently, the amount of glucose in serum or plasma is often determined by the enzymatic electrochemical and optical methods (glucose oxidase and glucose dehydrogenase methods) in the last 10 years to monitor glucose [3-8]. Amperometric nonenzymatic glucose sensors, which rely on direct electrochemical oxidation of glucose, are also widely used today [9]. The major advantage of the amperometric nonenzymatic glucose measurement method over the enzymatic method is that it eliminates the stability problem arising from the structure of the enzymes. Many metal materials such as noble metals (such as Au and Pt) and their composites are widely used as electrode materials in nonenzymatic glucose detection due to their high electrocatalytic properties, high sensitivity and good selectivity for the electrooxidation of glucose [9],[10]. Generally, amperometric non-enzymatic glucose sensors offer less analytical selectivity than amperometric enzymatic glucose sensors. Because these electrocatalytic substances cannot work as specific as enzymes in catalyzing glucose oxidation [9]. However, it provides a faster and more economical operation for the nonenzymatic detection of glucose directly based on glucose electrochemistry (oxidation or reduction) [3],[4],[8]. In a different glucose sensor study published in 2017, the non-enzymatic potentiometric glucose sensor was developed by bonding a molecularly imprinted polymer to a conductive polymer layer to determine glucose at micromolar level in saliva. In this study, a screen-printed carbon electrode precipitated with benzoic acid functionalized poly (terthiophene) was used with the formation of amide bonds on gold nanoparticles, and successful results in the measurement of glucose in saliva were reported with potentiometric graphics similar to this study [11]. In another potentiometric sensor study, a polymeric liquid membrane electrode (PLME) was developed for highly selective and non-enzymatic glucose detection based on diboronic acid. The potentiometric performance of PLME at different glucose concentrations was evaluated similar to that in this study, and it has been reported that it can be used as a glucose-selective sensor when optimum conditions are met [12]. In addition, different non-enzymatic electrochemical biosensors have been developed to detect glucose in the blood but these had different methods and contents. In a study conducted in 2018, a non-enzymatic sensor was developed using nanopore Pt particles instead of enzymes to detect glucose in the blood. A highly sensitive electrode measurement to glucose has been reported [13]. In another study conducted in 2019, an amperometric biosensor was designed by developing the Au foam electrode. The precise glucose detection level obtained has revealed that Au foam electrodes can be used in blood glucose determination[14].

In an electrochemical sensor developed by Qian et al in 2020, the ZnO-CeO_2 electrode was developed and a voltammetric system was designed. According to the results of the study, it has been reported that nanocomposite electrodes are an ideal method for non-enzymatic glucose measurement[15].

This study focuses on the development of a novel potentiometric flow injection analysis measurement system that can measure glucose levels indirectly using borate selective electrode. In the flow injection analysis system, there was a detection chamber comprising the borate selective electrode as glucose can be attached to borate in the electrode membrane. Potentiometric measurements were made by this detection chamber. Detailed data on the characterization of borate-selective electrode by using scanning electron microscope, x-ray diffraction and fourier transform infrared spectrophotometer analysis were performed in order to study for structural and morphological characteristics of the borate-selective electrode membrane. In addition, Turkey has the largest share of the world boron reserves (73%) [16]. Therefore, boron-based methods developed are considered a priority for Turkey and more affordable / accessible systems are considered as an opportunity to produce.

2. METHODS

0.1 M silver nitrate and 0.1 M sodium tetra borate were mixed and precipitated using a homogenizer and dried in the oven for 3 days to prepare of the synthesis of silver borate. Ag_2S (Silver sulfide) and Cu_2S (Copper (I) sulfide) Sigma brand were used. Prepared using 50 % graphite, 35 % epoxy, 15 % hardener, and a few drops of THF (tetrahydrofuran) / acrylic to make solid contact. Purified tetrahydrofuran (THF) was used. Glucose solution (dextrose monohydrate) was prepared in 5 different concentrations to be 1.0×10^{-5}-1.0×10^{-1} M.

Precise balance, ultrasonic homogenizer (ultrasonic cell crusher), water bath, magnetic stirrer, centrifuge, oven and ultrapure water device were used in the preparation of solutions and composites. The pH of the studied solutions was measured by Microcomputer pH / Conductivity / Temp Meter 6307 pH meter. The potentiometric measurements of the developed composite ion selective electrode were performed with MEDISEN brand four channel potentiometer. Acer laptop was used with ISEMS software. Ag/AgCl reference electrode HANNA INSTRUMENTS brand was used for potentiometric measurements in stationary phase. A mini Ag/AgCl reference electrode developed by Prof. Dr. İbrahim IŞILDAK (Medisen R&D) was prepared in flow injection analysis system in appropriate dimensions and attached to the cell. Global FIA Valco brand peristaltic pump was used in flow injection system. (Vici Miligat Pump model CP-DSM). Multiple valve Global FIA Valco Vici brand was used for sample injection in mobile environment. The computer program we used to set the valve parameters was commercial software and branded as FlZF. XRD, FTIR and SEM analyzes were performed for structural and morphological characteristics of the composite borate selective electrode membrane. Scanning electron microscope (SEM) analyses was used for dimensional analysis of the composite borate selective electrode membrane and branded Zeiss EVO® LS 10, PERKIN ELMER brand Fouirer Transform Infrared Spectrophotometer (FTIR) was used to determine the presence and binding sites of functional groups in the borate selective electrode membrane to demonstrate its presence. Malvern PANalytical brand X'Pert^3 MRD XRD (X Ray Diffraction) system was used to demonstrate the chemical composition of the the composite borate selective electrode matrix.

2.1. CNT-SB Composite electrode development

CNT-SB composite electrode developed was similar to our previous borate-selective electrode [17]. In this study, the borate-selective electrode was prepared in the same way at different compositions. Table 1 shows the CNT-SB composite electrode compositions selected. Series with free silver borate and carbon nanotube (series 1-103) were prepared beforehand. However, since the desired potentiometric performance could be achieved, CNT-SB was synthesized and added to form compositions.

Table 1. CNT-SB composite electrode compositions (*Mixtures with better results were decided based on their repeated potentiometric behavior against 1.0×10^{-1}-1.0×10^{-5} M standard sodium tetraborate solutions.)

Composition Number	CNT (g)	CNT-Ag_3BO_3 (g)	Ag_2S (g)	Cu_2S (g)	Epoxy (g)
40*	0.1	0.01	0.08	0.01	0.8
81*	0.01	0.01	0.08	0.01	0.6
84*	0.1	0.01	0.08	0.03	0.3
88*	0.1	0.01	0.08	0.03	0.2
90*	0.1	0.01	0.08	0.03	0.2
102*	0.1	0.01	0.08	0.03	0.2
103*	0.1	0.01	0.08	0.03	0.1

Each mixture shown in Table 1 was filled into catheter tubes and compressed in a vise and allowed to dry for an average of three weeks at room temperature. Sections of appropriate length were taken from the dried composites and placed into the plastic tubing of appropriate size to the flow cell. The end of the pipe was covered with ring-shaped liquid adhesive to prevent liquid escape. It was then bonded to the end of copper wire using a solid contact. The remaining openings in the adhered parts and the solid contact material were isolated with an adhesive and the preparation of CNT-SB composite electrodes was completed. The electrodes were saturated in 1.0×10^{-1} M standard sodium tetraborate solution overnight and made ready for potentiometric measurement.

3. RESULTS AND DISCUSSION

3.1 Structural characterization of the composite electrode membrane

For the characterization of the composite material developed in the study, XRD, FTIR and SEM images were first taken by using the instruments. The XRD diffractogram of the CNT-SB Composite electrode membrane is given in Fig.1. The analyzed composite borate selective electrode membrane content was: CNT, CNT-SB, Ag_2S, Cu_2S and epoxy. The XRD analysis results indicated the presence of these contents in the borate selective electrode membrane.

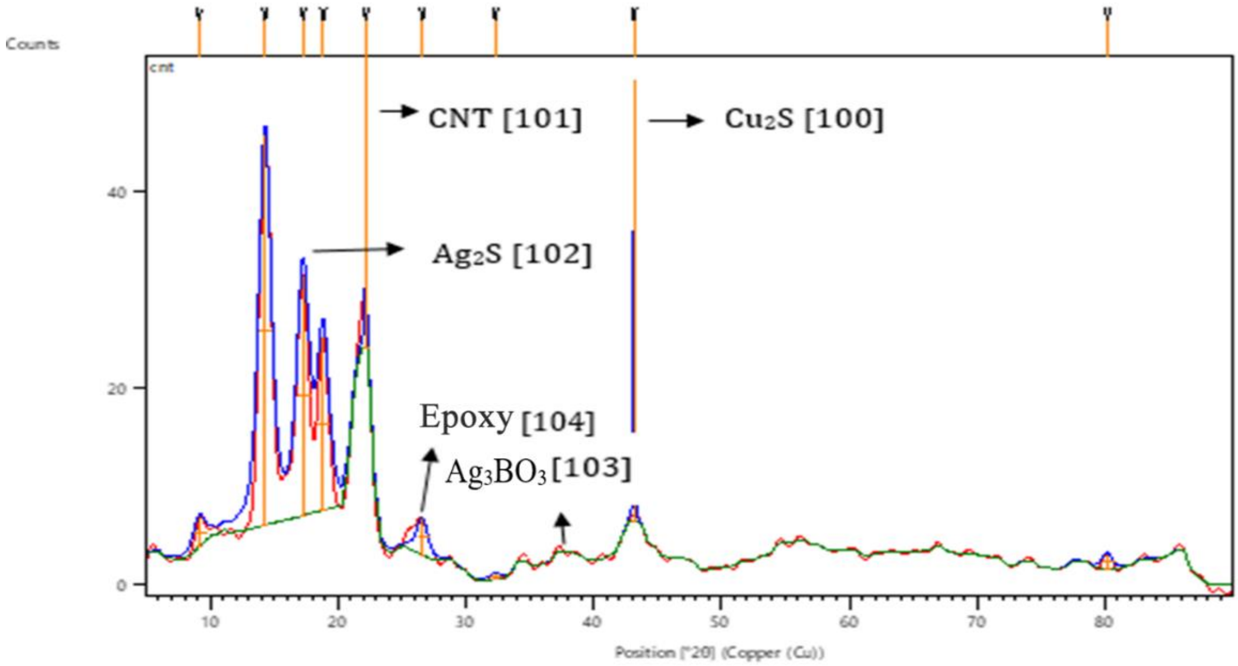

Figure 1. CNT-SB composite XRD diffractogram

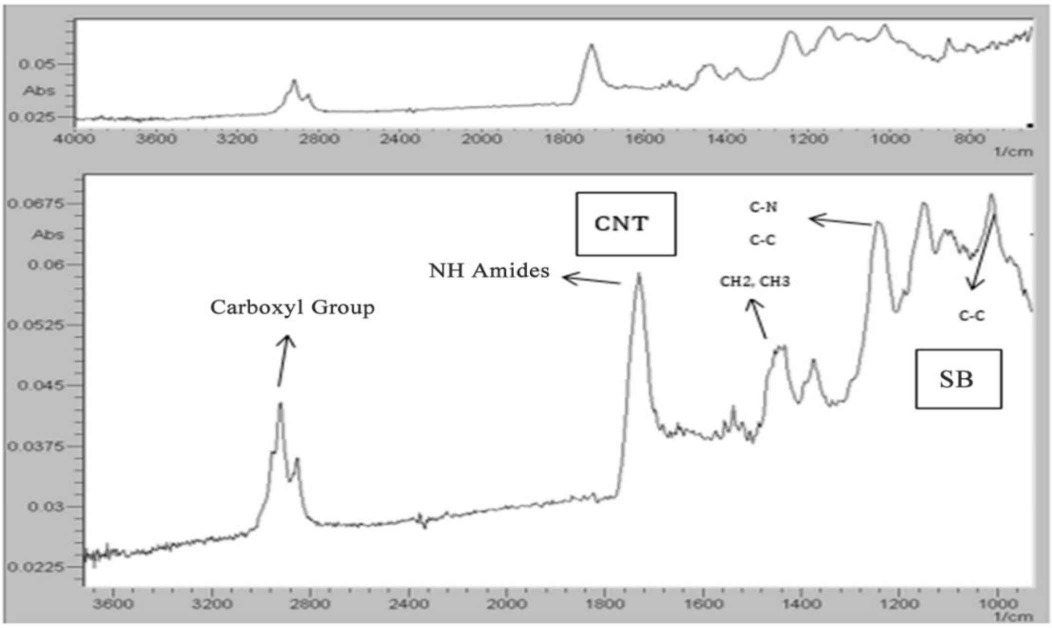

Figure 2. FTIR Analysis of CNT-SB Composite Electrode Membrane

The CNT-SB Composite FTIR analysis is given in Fig.2. All FTIR analyzes were evaluated according to the approximate infrared absorption frequency data of different groups and were marked on Fig.2. These results indicated that the presence and binding sites of functional groups in the borate selective electrode membrane.

The CNT-SB Composite SEM images are given in Fig.3-4. It is thought that CNT-SB is attached to the regions indicated by the arrow.

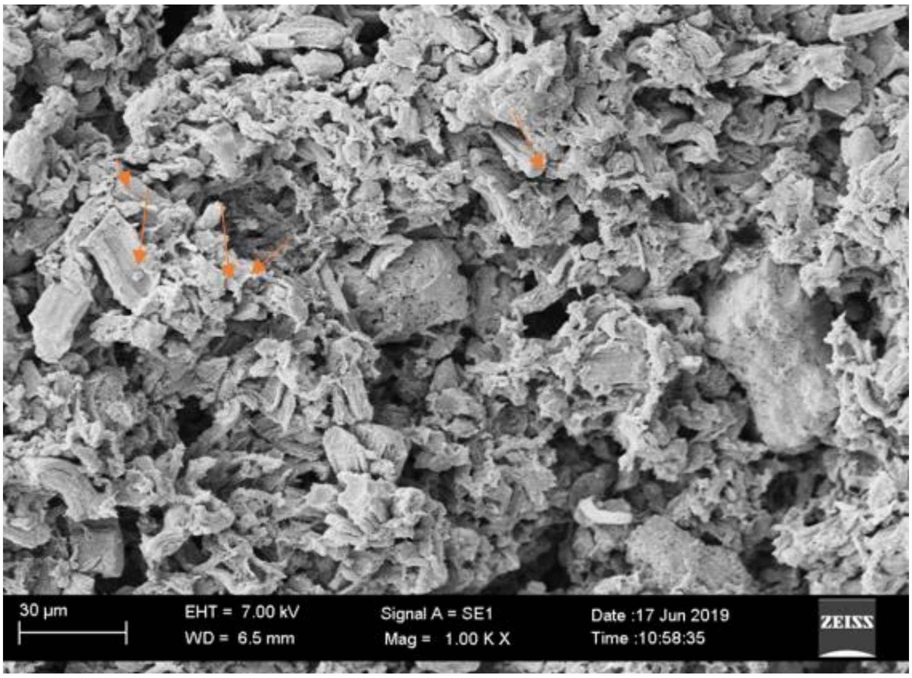

Figure 3. SEM images of the CNT-SB Composite Electrode Membrane (30 µm)

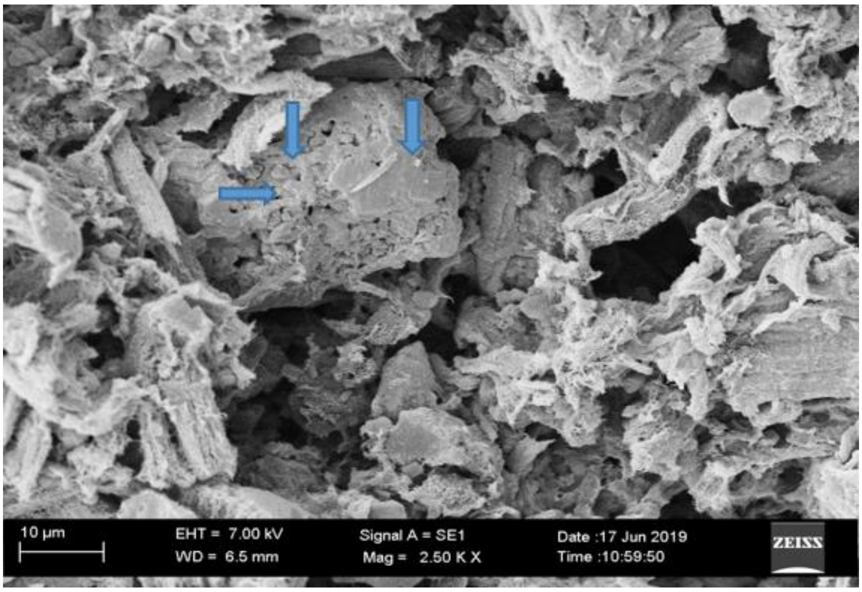

Figure 4. SEM images of the CNT-SB Composite Electrode Membrane (10 µm)

3.2. Potentiometric performance characteristics of composite electrodes

Potentiometric behavior of CNT-SB composite electrodes against standard sodium tetraborate ($B_4O_7^{2-}$) solutions in between 1.0×10^{-1}-1.0×10^{-5} M was investigated. At the end of the measurements, it was decided that the composition showing the best potentiometric performance was 102-103 series. Potentiometric behavior of electrode 102 against borate ions is given in Fig.5.

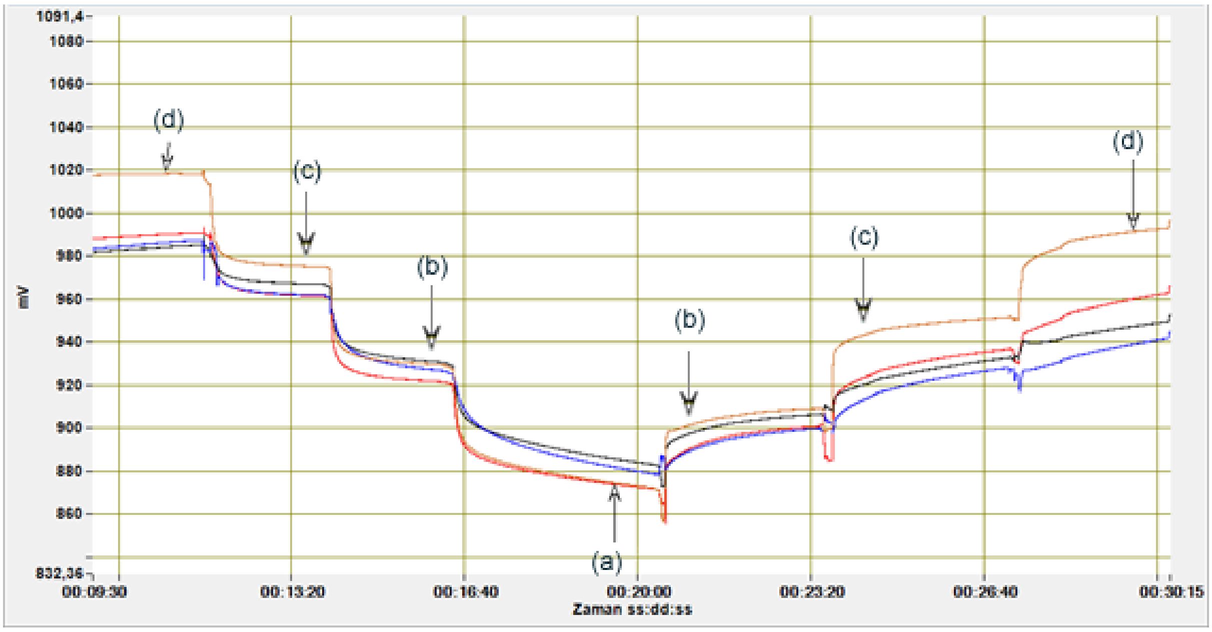

Figure 5 Potentiometric response of electrode series 102 against $B_4O_7^{2-}$ ions. [(a): 1.0×10^{-1} M $B_4O_7^{2-}$, (b): 1.0×10^{-2} M $B_4O_7^{2-}$(c): 1.0×10^{-3} M $B_4O_7^{2-}$, (d): 1.0×10^{-4} M $B_4O_7^{2-}$]

Potentiometric behavior of CNT-SB composite electrode against standard anion solutions (prepared using sodium salts) between 1.0×10^{-1}-1.0×10^{-5} M by direct immersion. During the transition from one solution to another, care was taken to thoroughly wash the electrodes with ultra-pure water. The selectivity coefficient, determination limit, working life, response time, reproducibility, pH working range and reproducibility behavior of the electrodes were investigated. The potentiometric behavior of the developed electrode against glucose in both inert and mobile environments was investigated. As a result of potentiometric measurements using CNT-SB composite electrode, it was observed that the electrode showed linear response to standard $B_4O_7^{-2}$ ions between 1.0×10^{-4}-1.0×10^{-1} M. It was observed that the electrode produced a potential difference of approximately 35 mV with each 10 fold concentration change in the linear operating range. As seen in Fig.5, it was determined that the linear working range was in the range of 1×10^{-1}-1×10^{-4} M.

The reproducibility of the borate selective electrode developed was studied with 1×10^{-2} M and 1×10^{-3} M borate solutions. The results obtained show that the electrode exhibits reproducible behavior as seen in Fig.6.

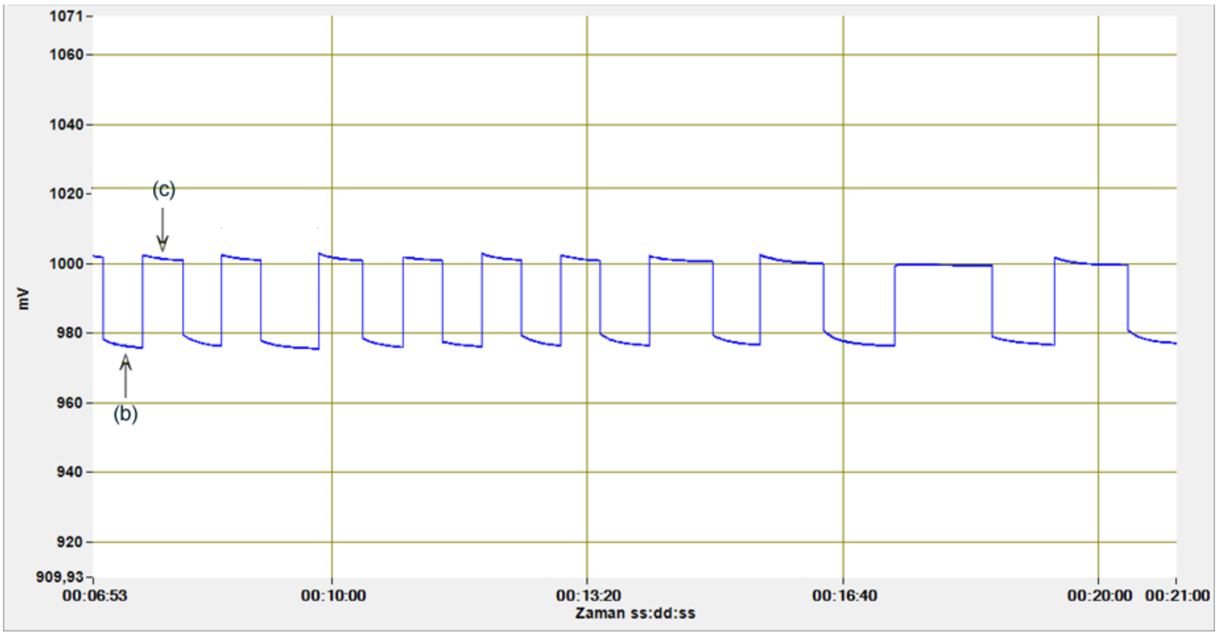

Figure 6. Repeatability test of electrode 102. [(b): 1.0×10^{-2} M $B_4O_7^{2-}$, (c): 1.0×10^{-3} M $B_4O_7^{2-}$]

The selectivity coefficients of the electrode against possible interfering ions were calculated according to the separate solution method. For this purpose, 1.0×10^{-1}-1.0×10^{-4} M standard $B_4O_7^{2-}$ solutions were prepared. The potential changes of CNT-SB composite electrode against $B_4O_7^{2-}$ solutions were investigated with the prepared solutions. The CNT-SB composite electrode was found to exhibit selective behavior against borate ion. Selectivity coefficients for tested ions are given in Table 2.

Table 2. Selectivity coefficients of borate selective electrodes (Separate solution method)

Cations	**($K_{i,J}$)**	**-log ($K_{i,J}$)**
Cl	-0.00233	2.63
SO_4	-0.00297	2.52
HCO_3	-0.00125	2.90
NO_3	-0.00295	2.52

At the end of these calculations, it was observed that borate-selective electrode made by CNT-SB composite was highly selective in the presence nitrate, chlorate and sulfate and bicarbonate ions in the measurements. To determine the pH measurement range of the electrode, we prepared sodium phosphate buffer solutions, arranged to pH 7.4 to pH 8.72 and to pH of 5.96 by addition of 0.1 M NaOH and 0.01 M HCl. The lifetime of the composite borate selective electrode was found to be approximately

8 months. The electrode developed were found to have a response time less than 20 seconds depending on the concentration.

3.2.1. Potentiometric responses to standard glucose solutions ın stationary phase

Potentiometric response behavior of the electrode to glucose solutions in stagnant medium were evaluated. Fig.7 shows the potentiometric response by adding glucose at different quantity to 3 mL of 5×10^{-3} M borate solution. Potentials were observed to change consistently in a positive direction. This shows that the developed CNT-SB composite electrode works selectively against glucose by quenching.

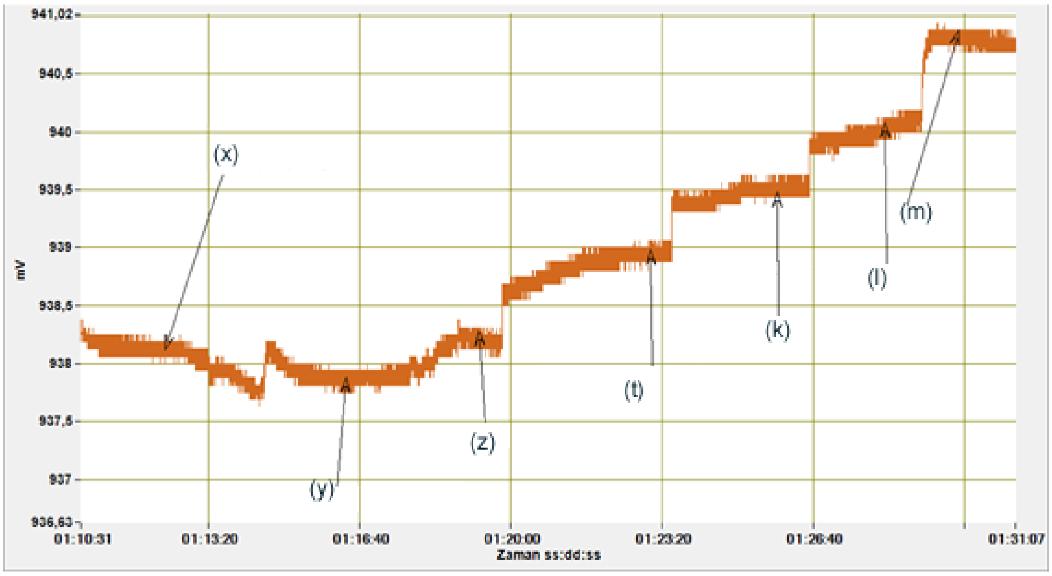

Figure 7. Potentiometric response by adding 1×10^{-2} glucose to a 5×10^{-3} M borate solution in stationary phase. [(x): 5×10^{-3} M borate +900 µL1×10^{-2} M glucose, (y): 5×10^{-3} M borate +1100 µL1×10^{-2} M glucose, (z): 5×10^{-3} M borate +2 mL 1×10^{-2} M glucose, (t): 5×10^{-3} M borate +3 mL 1×10^{-2} M glucose, (k): 5×10^{-3} M borate +4 mL 1×10^{-2} M glucose, (l): 5×10^{-3} M borate +5 mL1×10^{-2} M glucose, (m): 5×10^{-3} M borate +6 mL 1×10^{-2} M glucose.]

In another study, a non-enzymatic electrochemical method was developed for sensing glucose by using a glassy carbon electrode modified with 3-aminophenylboronic acid (APBA) immobilized on polyethyleneimine (PEI)-coated gold nanoparticles. The respective calibration plot, established at open circuit potential (vs. Ag/AgCl) covers the 5×10^{-4}–5×10^{-2} M glucose concentration range, which makes it suitable for blood glucose assays [18]. In 2018, a new non-enzymatic glucose sensor based gold nanoparticle (AuNp)-chitosan (Ch/AuNp) was developed in 2018 by Celik et al. Gold nanoparticle surfaces were modified with 4-mercaptophenyl boronic acid, and 1-decanethiol for being sensitive to glucose. It was found that linear working range is 5×10^{-4}–3×10^{-2} M, while limit of detection is 3×10^{-4} M for the glucose measurement of the prepared potentiometric sensor [19]. These results were consistent with the detection range we obtained in our study.

3.3. Potentiometric responses to standard glucose solutions in FIA system

Dynamic studies were performed through the flow injection analysis (FIA) system designed. The system contained a peristaltic pump for a continuous flow, a valve unit for a controlled sample injection, and a detection chamber (mini flow cell) in which the developed electrodes were placed. The mini flow cell was designed for the use of CNT-SB composite electrode as detector in the flow injection analysis system. This mini-flow cell consisted of 2 parts, one injection chamber and one detector chamber. A flow path was opened into a plexy mold of 1 cm×0.5 cm×0.5 cm with an equal diameter with the electrode surface. A housing for the reference and working electrode included in the upper part of the flow path was formed to contact these electrode membranes with the solutions passing through the flow path. The designed injection chamber was created on a similar principle. The flow path was opened into the plexy mold of similar dimensions to be of suitable diameter to the flow pipes. The sample injection was introduced into the flow path with a tube connected to the valve by opening a cavity at the top of the mold.

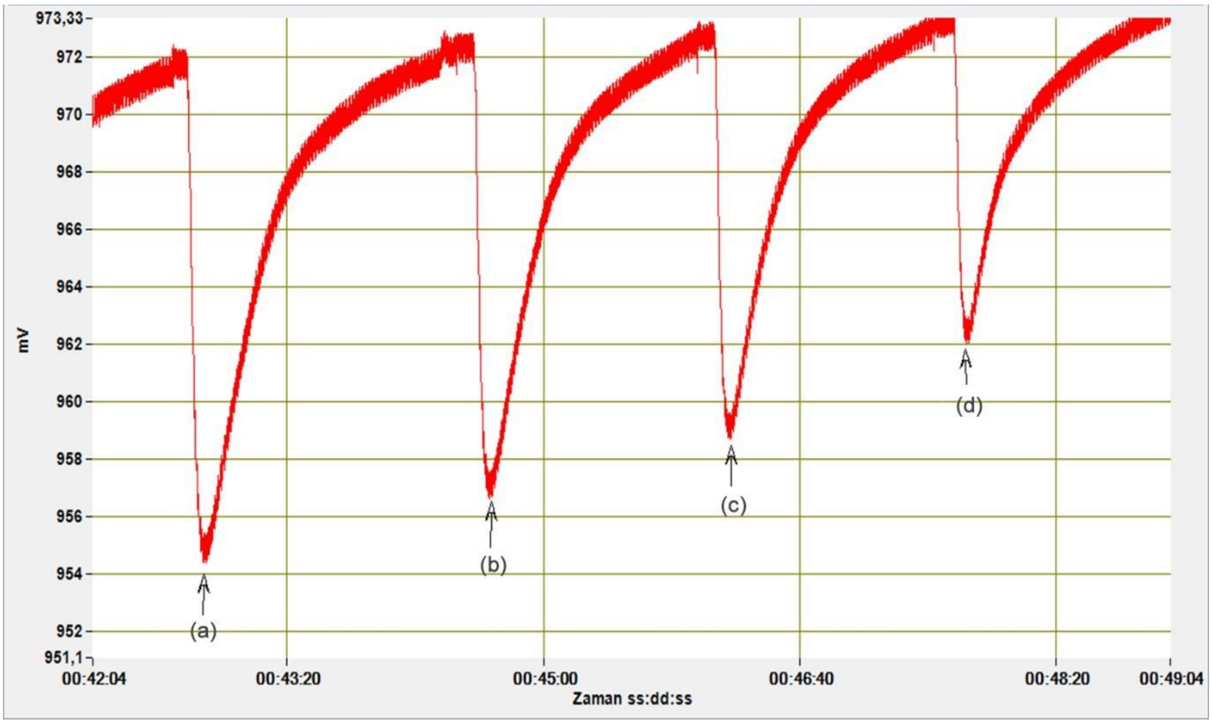

Figure 8 Potentiometric responses of CNT-SB composite electrodes to varying $B_4O_7^{2-}$ ion concentrations in the flow injection system. [(a): 1.0×10^{-1} M $B_4O_7^{2-}$, (b): 1.0×10^{-2} M $B_4O_7^{2-}$ (c): 1.0×10^{-3} M $B_4O_7^{2-}$, (d): 1.0×10^{-4} M $B_4O_7^{2-}$]

For the optimization of the FIA system, firstly, the mobile phase concentration and flow-rate parameters were tested, and then optimum flow parameters were determined. At flow rates applied, injection volumes were tested in the designed flow injection analysis system. During the optimization study, the injected 1×10^{-1} M-1×10^{-3} M borate solutions were kept constant with a volume of 15 µL and the flow rate of the mobile phase (5×10^{-5} M borate solution) was changed in the range of 2-30 µL/s.

Subsequently, the mobile phase was fixed at a flow-rate of 14 µL/s and 1×10^{-1} M-1×10^{-4} M borate solutions were injected by changing the injection volume in the range of 5-100 µL to evaluate potential changes. As a result of the measurements, the optimum flow-rate was decided to 14 µL/s and the injection volume was decided 25 µL. In the flow injection analysis system, potentiometric behavior of CNT-SB composite electrode as detector for 1.0×10^{-5} M-1.0×10^{-1} M standard $B_4O_7^{2-}$ solutions were examined. The peak height values of the obtained data were plotted to concentrations, the corrected equation was established, and the limit of determination of the CNT-SB composite electrode in the flow injection analysis system was determined. The mobile phase concentration was adjusted to 5×10^{-5} M $B_4O_7^{2-}$, and potentiometric results obtained against the varying $B_4O_7^{2-}$ concentrations in the flow injection analysis system are shown in Fig.8.

The linear operating intervals and calibration graphs of the developed borate-selective electrode were determined based on peak heights. As a result of potentiometric measurements made in flow injection analysis system, it was observed that the electrode exhibited a linear response to standard $B_4O_7^{2-}$ions. The linear operating range of the CNT-SB composite electrode as detector in the flow injection system was 1.0×10^{-4}-1.0×10^{-1} M. The limit of detection of the electrode against borate ion in the flow injection analysis system was determined to be 1.0×10^{-4} M. Linear equation giving the potential concentration relationship at linear working range in flow injection analysis system was found as $Y=-5\times(B_4O_7^{2-})+12.5$ and R^2 was 0.9921.

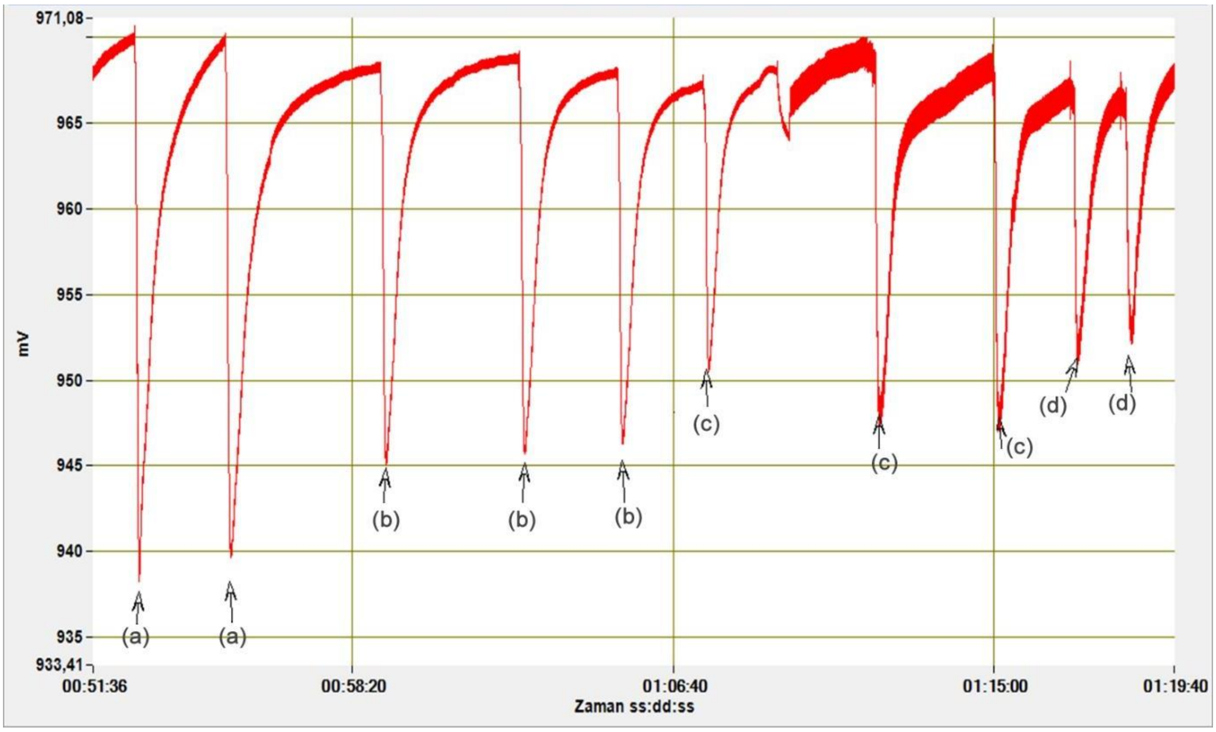

Figure 9. Repeatability of CNT-SB composite electrodes in flow injection system. [(a): 1.0×10^{-1} M $B_4O_7^{2-}$, (b): 1.0×10^{-2} M $B_4O_7^{2-}$(c): 1.0×10^{-3} M $B_4O_7^{2-}$, (d): 1.0×10^{-4} M $B_4O_7^{2-}$]

It was observed that CNT-SB composite electrodes gave reproducible results in flow injection analysis system. Firstly standard $B_4O_7^{2-}$ solutions of 1.0×10^{-1}, 1.0×10^{-2}, 1.0×10^{-3} M and 1.0×10^{-4} M were prepared to measure reproducibility. The carrier solution was set to 5×10^{-3} M $B_4O_7^{2-}$ when taking the measurements. 25 µL standard sample solutions of borate was injected into the mobile phase at a flow rate of 14 µL/s and the resulting potential change values at negative direction were recorded. Their peak heights were measured and evaluated. Fig.9 shows the reproducibility study of CNT-SB composite electrodes at different borate concentrations.

3.3.1 Glucose measurement results in FIA

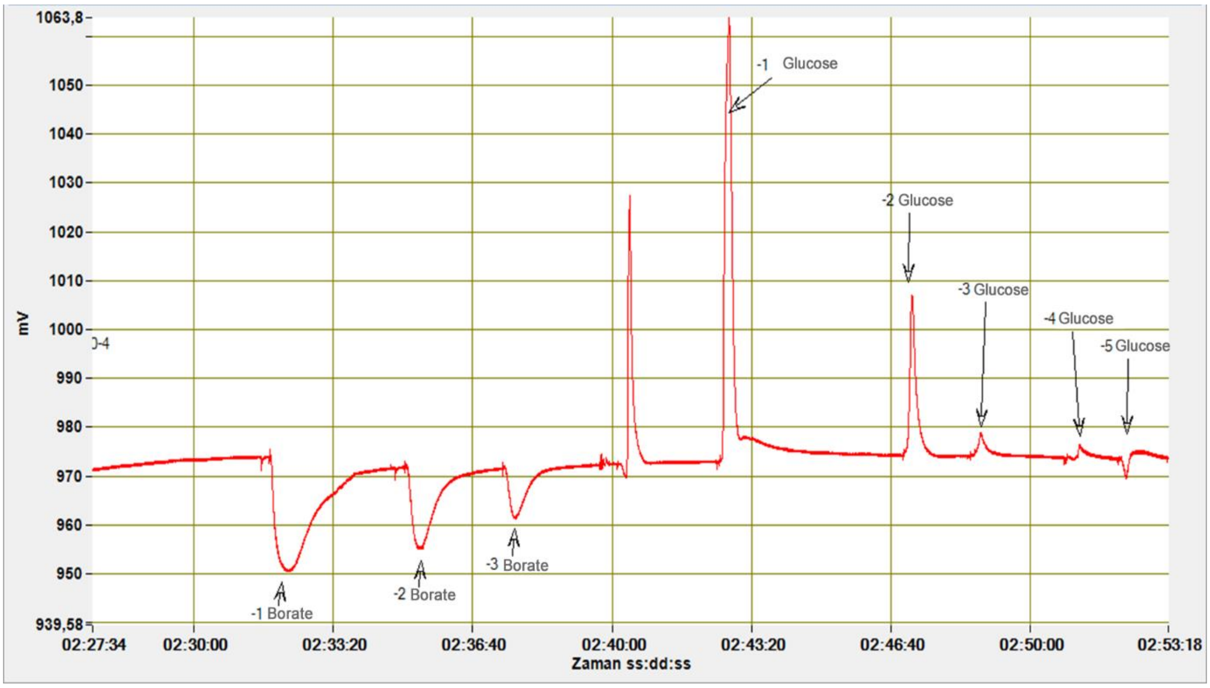

Figure 10. Potentiometric response by injecting standard glucose solutions into the FIA system. [(-1 Borate):1.0×10^{-1} M $B_4O_7^{2-}$, (-2 Borate): 1.0×10^{-2} M $B_4O_7^{2-}$, (-3 Borate): 1.0×10^{-3} $B_4O_7^{2-}$, (-1 Glucose): 1.0×10^{-1} glucose, (-2 Glucose): 1.0×10^{-2} glucose, (-3 Glucose): 1.0×10^{-3} glucose]

Firstly, in order to evaluate the potentiometric behavior of CNT-SB composite electrode against standard glucose solutions in flow injection analysis system at concentrations 1.0×10^{-1}, 1.0×10^{-2}, 1.0×10^{-3} M, 1.0×10^{-4} M, 1.0×10^{-5} M were prepared. Each of these standard glucose solutions were delivered to the flow injection system at a volume of 25 µL at a rate of 14 µL/s, and potentiometric response was measured. As expected, CNT-SB composite electrode developed exhibited a positive response when glucose solutions were injected into the system while in the negative direction against $B_4O_7^{2-}$ ions. Fig.10 shows the potentiometric response obtained by injecting standard glucose solutions into the flow injection system.

In Fig.11, the reproducibility of the CNT-SB composite electrode in the glucose measurement was evaluated. It was determined that CNT-SB composite electrode gave repeated results against different glucose concentrations as injected.

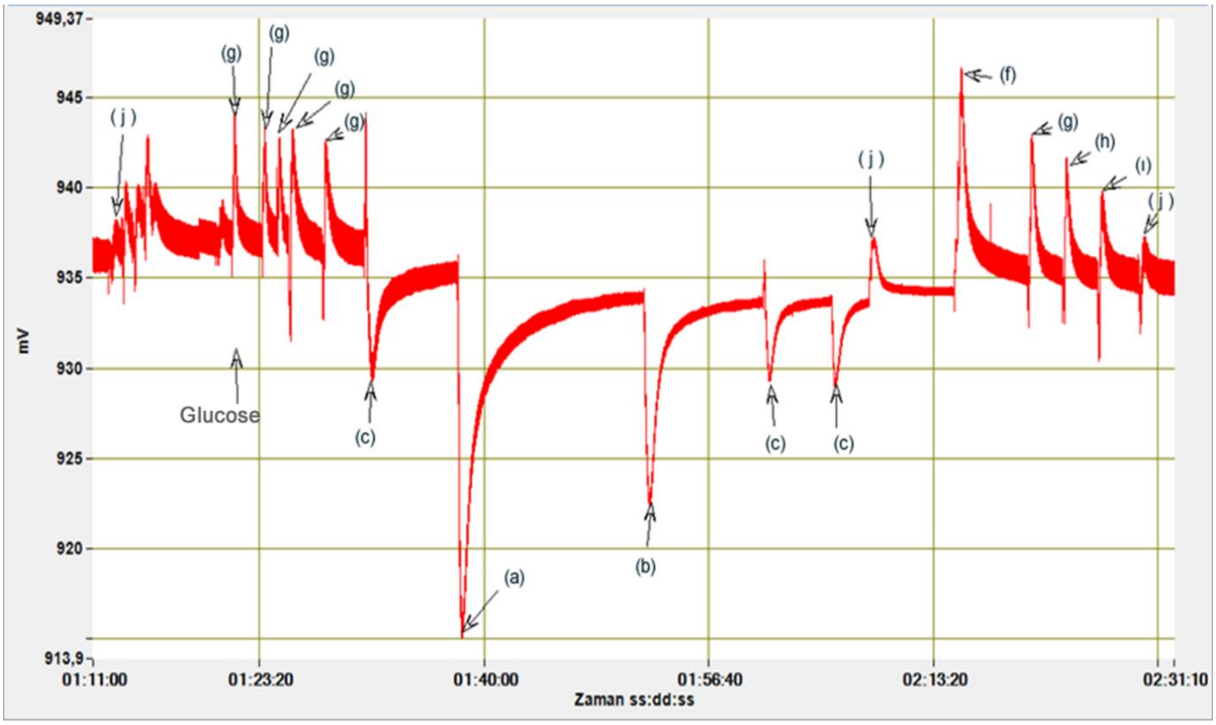

Figure 11 Repeatability of the CNT-SB composite electrode in glucose measurement. [(a): $1.0x10^{-1}$ M $B_4O_7^{2-}$, (b): $1.0x10^{-2}$ M $B_4O_7^{2-}$, (c): $1.0x10^{-3}$ $B_4O_7^{2-}$, (f): $1.0x10^{-1}$ glucose, (g): $1.0x10^{-2}$ glucose, (h): $1.0x10^{-3}$ glucose, (ı): $1.0x10^{-4}$ glucose, (j): $1.0x10^{-5}$ glucose.]

Potentiometric behavior of CNT-SB composite electrodes in 1.0×10^{-4}-1.0×10^{-1} M glucose solutions was evaluated. Table 3 shows peak heights obtained for standard glucose solutions and retention time values of the CNT-SB composite electrode as detector in the flow injection system.

Table 3. Glucose peak elevation and retention time values of the CNT-SB composite electrode in the FIA system.

logC (mol/L)	Peak elevation (mV)	Retention time (s)
-4	2	15
-3	5	17
-2	32	17
-1	82	20

The correct equation was created by plotting the calibration curve with the glucose peak height values obtained from Table 3. The linear equation that gives the potential-concentration relationship in the linear working range in the flow injection analysis system was found as E = 38.5×(glucose)-75.883 and R^2 was 0.9711. Potentiometric measurements in the flow injection analysis system using CNT-SB-borate composite electrode showed a linear response to glucose between 1.0×10^{-4} M-1.0×10^{-1} M. The glucose detection limit of the electrodes in the flow injection analysis system was also found around 1.0×10^{-4} M for a 25 µL injection volume.

In a study conducted in 2013, an amperometric flow system for blood glucose determination using an immobilized enzyme magnetic reactor was developed by Hernandez et al. The detector was improved by using a modified screen printed electrode with [Fe(tris(3,5-dimetyl-1-pyrazolyl)borate)2]+[FeCl4]$^-$. Under optimal conditions, the calibration curve of glucose sample was linear between 0.24 and 6.00 mM, and with a limit of detection of 0.08 mM [20]. In another similar study, flow injection analysis with electrochemical detection at fe(iii)-(tris(3,5-dimethyl-1-pyrazolyl)borate)2 modified electrode was improved to detect glucose in blood. Under optimal conditions, detection limits of 15 µM and 0.5 mM for H_2O_2 and glucose, respectively, were obtained in this study. The method was validated by comparing the obtained results to those provided by the enzymatic spectrophotometric method; no significant differences were observed. [21]. When compared considering that these are an enzymatic method, these results were consistent with the results we obtained in our study. This limit of detection and linear range were suitable for application in the glucose determination in real blood serum.

4. CONCLUSION

In this study, direct potentiometric measurement of glucose, one of the diabetic parameters in the blood, can be performed with flow injection analysis system by using carbon nanotube-silver borate (CNT-SB) based electrode as detector. First of all, CNT-SB composite electrode was developed as a borate selective electrode. Then it was applied as a detector in flow injection analysis system to detect blood glucose. The potentiometric performance characteristics of CNT-SB composite electrodes were determined. The electrodes were found sensitive to the tetra borate form of boron and exhibited selective behavior. A micro volume flow cell was prepared and glucose analysis was performed in the Flow Injection Analysis (FIA) system. It was observed that CNT-SB composite electrodes gave reproducible results for glucose in the FIA system. The CNT-SB based borate selective electrode was found to be highly sensitive to glucose in borate mobile phase environment. Measurement performances were examined by injection glucose samples into mobile phase in the FIA. The results obtained from the system were showed consistency with each other. It has been observed that the electrode can be used for a long time by taking a thin section from the surfaces. Furthermore, the developed electrode have important advantages such as requiring no enzyme, being economical, easy to prepare and simple to use. It is important to reduce the detection limits of the electrodes to a lower level and to further reduce the response times in order to be able to determine the lower levels with the developed electrodes. It is thought that the failure to determine levels of less than 1×10^{-5} M with the developed electrodes is due to the dissolution of silver borate salt used as active material in the electrode structure. In this context, it is planned that the active materials used in the structure of the electrodes will be tested in different compositions and dried for a longer period by applying higher pressure. For this purpose, the electrode content and preparation method must be improved: more efficient drying, better compression, better mixing, etc. Studies on different active phase concentrations are needed to obtain more effective results. Studies on carrier phase flow rate optimization can be extended. The flow conditions (flow rate, carrier concentration, injection volume and concentration) must be carefully monitored and adjusted in order to obtain regular and repeated potentiometric signals. On the other hand, direct analysis of glucose, HbA1c (glycated hemoglobin) and g-HSA (glycated human serum albumin) is planned in CNT-SB composite electrodes with potentiometric performance characteristics. Comparing the results of these planned analyzes with those obtained from biochemistry laboratories and evaluating the results will be useful in demonstrating the effectiveness of the present study.

ABBREVIATIONS

CNT-SB: Carbon nanotube-silver borate
FIA: Flow injection analysis
THF: Tetrahydrofuran
XRD: X Ray Diffraction
FTIR: Fourier Transform Infrared Spectrosopy
SEM: Scanning Electron Miscroscope
M: Molarity
K: Selectivity coefficient
mV: milivolt
s: second
L: liter
C: Consantration
µL: microliter

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