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Novel Disposable Potentiometric Sensor for Determination of Granisetron in Surface Water Samples and Pharmaceutical Formulations

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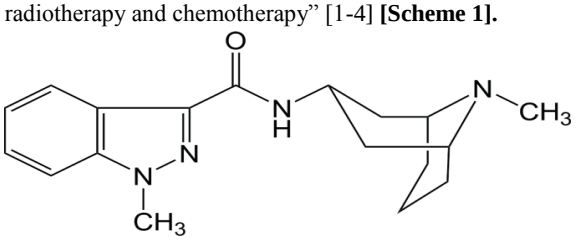
Abstract

Herein, the fabrication and characterization of novel granisetron (GST) disposable screen-printed potentiometric sensors was described. Different fabrication protocols were introduced including; incorporation of different ions of pairing agents or GST- ion associatesas electroactive sensing materials. For sake of simplicity, the dummy blank sensors can be soaked in the GST- ion associates aqueous suspension, where ion associates were extracted within the electrode matrix by the membrane plasticizer. Deep and comprehensive investigations were performed regarding the sensing matrices compositions including the influence of modifier nature and content, plasticizer, and the fabrication protocol. Incorporation of the electrode matrix with SWCNTs improved the sensor performance. Sensors modified with phosphotungstic acid showed Nernstian compliance for the GST concentration range from 10^{-6} to 10^{-2} mol L^{-1}, adequate operational shelf lifetime (6 weeks) and fast response time (4s). Moreover, the electrode potential was pH-independent in wide range with improved selectivity. The developed sensors were introduced for GST quantification in surface water samples and pharmaceutical formulations under flow injection analysis (FIA), standard addition and potentiometric titration conditions.

Keywords: Granisetron Hydrochloride; Disposable screen-printed potentiometric sensors; Pharmaceutical preparations; Surface water samples

1. Introduction

Granisetron hydrochloride (GST) [1-Methyl-*N*-[(1*R*, 3*r*, 5*S*)-9-methyl-9-azabicyclo [3.3.1] non-3-yl]-1*H*-indazole-3- carboxamide hydrochloride] is a serotonin 5-HT3 receptor antagonist used as a potent and effective drug for treatment of nausea and vomiting that may accompany radiotherapy and chemotherapy" [1-4] **[Scheme 1].**



Scheme 1: Chemical structure of granisetron.

The main effect of this drug is reducing the vagus nerve activity which is responsible for vomiting center in the medulla oblongata [5]. GST showed better tolerability profile, fewer side effects and weaker drug interaction risks with longer action duration compared to other 5-HT3 receptor antagonists [4, 6].

Spectrophotometric and chromatographic tools are the most common techniques found in the research literature for determination of granisetron. High-performance liquid chromatographic (HPLC) methods with different detectors including RP-HPLC [7-10], HPLC- tandem mass spectrometry [11], and HPLC with DAD detection [12] were reported for determination of GST in the literature. Derivative spectrophotometry technique was suggested for the estimation of granisetron hydrochloride in presence of other degradation products [13]. Sensitive visible spectrophotometric analysis protocols were introduced for determination of GST including the formation of a chloranilic acid (CA)-GST charge-transfer complex with high molar absorptivity. Moreover, the formation of GST-I_2charge transfer complex was suggested as a simple and fast analysis protocol for GST [14]. Among different drugs, GST was determined by the oxidative indirect spectrophotometric method through reaction with N-Bromo succinamide (NBS), where the excess was assayed using methyl orange dye at λ_{max} 508 nm [15].

Although these techniques are sensitive, they have many drawbacks such as poor selectivity, application of toxic organic solvents, requirements of sophisticated and expensive equipments, expensive apparatus, and high technician required. Electroanalytical techniques offer the advantages of rapid and low-cost operation, wide linear

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range and good selectivity with the property of being portable, which introduce these techniques as promising candidates for the quality control of pharmaceutical formulations [16-21]. Regarding GST potentiometric sensors, Ganjali et al. [22] proposed PVC membrane sensors incorporated with GST-tetraphenylborate ion associates. Nernstian slope was achieved within the working range between 10^{-5} to 10^{-2} mol L^{-1} and a relative longer response time about 35 s. Following, all-solid-state senor was introduced for GST quantification in pharmaceutical formulations [23].

PVC membrane based sensors are mechanically complicated bulky sensors with a relative short operational lifetime due to leaching of the ion associates from the sensing PVC matrix to the inner filling or the bathing solutions. Solid contact kind electrodes showed relatively potential drift due to the poor adhesion and formation of undefined layer between the sensing membrane and the metal conductor [24].

Moreover, these sensors are usually inconvenient for biomedical analysis due to the difficulty of sterilization and miniaturization. Therefore, fabrication of disposable planer electrochemical sensors with prolonged shelf-lifetime applying screen printing technology is welcomed. This methodology supports sensor miniaturization with portable devices and establishes its route from "lab-to-market" for a plethora of sensors [25-32].

The present work focuses on the fabrication and performance characterization of granisetron disposable screen-printed sensors with different fabrication protocols with incorporated with single-wall carbon nanotubes (SWCNTs) as transducer. The proposed sensors will be introduced as sensitive and selective analytical tool determination of granisetron in surface water samples and pharmaceutical formulations under batch and flow injection modes.

2. Experimental

2.1. Reagents

Anionic ion pairing agents were used for preparation of different GST ion associates including sodium tetraphenylborate (NaTPB), potassium tetrakis (4-chlorophenyl) borate (KTCPB), ammonium reineckate (RNC), phosphomolybdic acid (PMA), and phosphotungstic acid (PTA) were purchased from Fluka.

Membrane plasticizers with different polarities were applied including; *o*-nitrophenyloctylether (*o*-NPOE, Sigma), dibutylphthalate (DBP, Aldrich), dioctylsebacate (DOS, Avocado), dioctylphthalate (DOP, Sigma) and tricresylphosphate (TCP, Fluka). The printing ink was prepared using relative high molecular weight poly vinylchloride (PVC, Aldrich) andsynthetic graphite powder (Aldrich). Nano carbonaceous materials namely; single-wall carbon nanotubes (SWCNTs, Aldrich), multi-wall carbon nanotubes (MWCNTs, Aldrich), and graphene nanosheet (Gr, Sigma) were used.

2.2. Standard sample

Granisetron hydrochloride ($C_{18}H_{25}ClN_4O$, 348.9 g mol^{-1} with purity 99.5±1.2%) standard sample was provided from Standard Laboratory, National Organization for Drug Control and Research, Egypt. Appropriate amount of the standard drug sample was dissolved in water for the preparation of stock solution.

2.3. Stress degradation products

Degradation studies were performed by refluxing 200 mg GST in 50 mL of 1.0 mol L^{-1} HCl or 0.5 mol L^{-1} NaOH for a reaction period of 12h [33]. The degradation reaction was followed spectrophotometrically at 290 nm till the disappearance of the GST peak. The resulting solution was neutralized and used in interference studies.

2.4. Samples

Four tablets of Granitryl hydrochloride tablets (2mg GST/tablet; EGY pharma, Egypt) were grinded, weighed, dissolved in 10 ml bidistilled water and filtered.

Surface water samples (Nile River, Giza Governorate) were treated with citrate buffer to the pH value of 3.1 and spiked with different aliquots of GST standard solution.

2.5. Instrumentation

46-Range Digital Multimeter with PC interface (Radiosack, China) was applied for the potentiometric measurements and 692-pH meter (Metrohm, Switzerland) accompanied with pH glass electrode was used for adjusting the pH. Flow injection system was constructed with a continuous flow cells adapted for the fabricated disposable sensors as described in details elsewhere [34].

2.6. Procedures

2.6.1. Preparation of ion associates

Different GST ion associates were precipitated via drop wise addition of NaTPB, RNC, PMA, or PTA solutions to the GST solution. The precipitated ion associates were filtered and dried at 50°Cfor 24 h. The chemical formula of the formed ion associates were analyzed (Elemental analysis, Viro EL. Elementar, Germany).

2.6.2. Sensor construction

Both reference and working electrodes were printed on a PVC sheet through pushing of the Ag/AgCl and graphite-based inks through the stainless steel mesh as described in details elsewhere [35]. For soaked electrodes, the sensing matrix cocktails composed of 360 mg *o*-PNPE and 240 mg PVC dissolved in 6 mL THF were drop casted on the working electrode surface and left to dry at 50 °C for 24 h. Prior to application for potentiometric measurements, the printed sensors were soaked in different freshly GST-ion associates suspensions for 24 h. Otherwise, modified sensors were printed using sensing cocktail matrix containing 7.5 mg GST-PTA or 2.5 mg PTA, 240 mg of *o*-PNPE and 240 mg PVC powder in 6 mL THF. After drying at 50 °C for 24 h, the printed sensors were soaked in 10^{-3} $molL^{-1}$ GST for 2 h prior measurement.

2.6.3. Calibration of sensors

Sensor calibration was performed through immersing the bielectrode strip in the granisetron solutions with in the concentration range from 10^{-7} to 10^{-2} mol L^{-1} at 25°C. The recorded potential values were plotted against the logarithmic scale of concentration [36]. Under FIA conditions, 50 µL of the GST standard solutions were injected in the system at flow rate 12.6 mL min^{-1}. For each injection, the recorded maximum peak heights were plotted against GST concentration.

2.6.4. Analysis of GST sample

Using the fabricated sensors, the GST contents in surface water samples and pharmaceutical formulations were estimated potentiometrically under the standard addition, potentiometric titration, and flow injection conditions compared with the spectrophotometric measurements.

The sample solutions were spiked with known increments of the GST standard solution and the recorded electrode potentials were used to calculate GST concentration in the sample solution [37].

GST sample solution containing 3.314 to 15.67 mg GST, were titrated potentiometrically against the standardized NaTPB solution applying the fabricated GST sensor as indicator electrode. The stable electrode potentials after each addition were plotted against the titrant volume to estimate the equivalence points [38]. For FIA measurements, 50 µL of the unknown sample solution were injected in the carrier stream and the recorded peak height was compared to those obtained via injection of the standard GST solutions.

2. Result and Discussion

Granisetron cation has the ability to form water insoluble ion associates with oppositely charged lipophilic anionic species including NaTPB, KTCPB, PTA, PMA, or RNC. Elemental analysis data revealed the formation of 1:1 ion associate (GST: reagent) with NaTPB, KTCPB and RNC, while with PTA and PMA forms 3:1 stoichiometric ratios. These ion associate complexes can be applied as electroactive materials in granisetron potentiometric sensors.

3.1. Optimization of the sensing matrix

To achieve the highest performance, different senor fabrication protocols were carried out including; direct modification with the precipitated ion associates, in situ modification with ion pairing agents, and finally modification through soaking the bare sensor in the ion pair

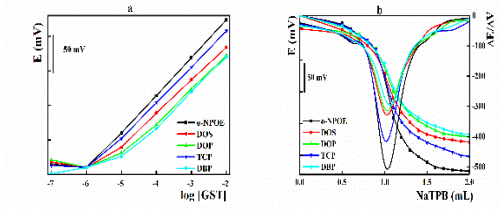

Fig. 2:a) Performance of GST sensor fabricated with different plasticizers; **b)** effect of membrane plasticizer on the potentiometric titration of GST against NaTPB solution.

suspension solution. For each modification mode, the nature of the modifier, plasticizer and nanomaterials were investigated.

3.1.1. Modification with ion pair

3.1.1.1. Type and content of the ion associate

Following this fabrication mode, the sensing matrix cocktails were directly modified with different GST-IPs prepared as described in **sec 2.6.1.** The recorded results declared that dummy electrodes fabricated without incorporation of electroactive material gave lower Nernstian response towards GST (30.1±1.1 mV decade^{-1}). On the other hand, sensors incorporated with different GST-IPs showed improved responses related to the type of ion associate. Among the tested ion pairs, GST-PTA possessed the highest Nernstian cationic slope of 51.8±1.5 mV decade^{-1} within the GST concentration range from 10^{-6} to 10^{-2} mol L^{-1} **(Fig. 1a)**. Moreover, potentiometric titration of GST against standardized NaTPB was performed using sensors based on different GST-IPs. Sensors based on GST-PTA showed the highest potential jump and potential break at the inflexion point **(Fig. 1b)**. The recorded ΔE values were 167,204, 189, 229 and for the blank, NaTPB, RNC, PMA, PTA based ion pairs, respectively.

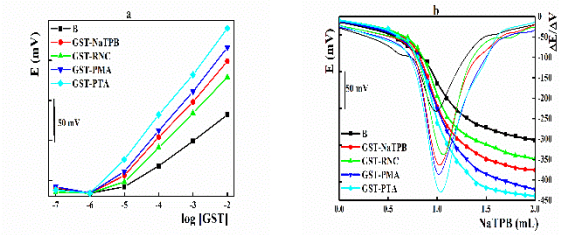

Fig. 1: a) Performance of granisetron sensors incorporated with different ion associate complexes; **b)** Effect of the ion associate on the potentiometric titration of GST against NaTPB solution.

Consequently, the content of the selected GST- PTA ion associate incorporated in the sensing matrix was varied from 0 to 15 mg. The results showed that addition of 7.5 mg GST-PTA produce the highest performance (**S 1a**) with a proper ionic exchange process at the membrane gel layer–test solution interface that is responsible for the membrane potential. Similar concept was achieved applying the potentiometric titration process **(S1b).**

3.1.1.2. Influence of the membrane plasticizer

For potentiometric sensors, the nature of the membrane plasticizer showed major role controlling the performance of sensors through improving of the mobility of the sensing element and decreasing the overall membrane resistance [39, 40]. Herein, different membrane plasticizers having different dielectric constants were studied namely; DPB, DOP, DOS, TCP, and *o*-NPOE (ΔE =3.8, 4.2, 5.2, 17.6 and 24.3, respectively). Plasticizer with high polarity (TCP, and *o*-NPOE) showed enhanced sensor performance indicated by higher Nernstian compliance (50.1±2.2 and 55.6 ±0.4 mV decade^{-1}, respectively) compared with other less polar plasticizers (**Fig. 2a**).

In a parallel study, the performance of the potentiometric titration process expressed by the total potential change (ΔE) and the potential break at the inflexion point ($\Delta E_{mV}/\Delta V_{mL\ titrant}$) were influenced by the polarity of the applied plasticizer [38, 40-43]. The recorded total potential jump values were 245, 222, 199, 191 and 187 mV for *o*-NPOE, TCP, DOS, DOP, DBP, respectively **(Fig. 2b).**

3.1.1.3. Effect of carbon nanomaterials

Nanostructures with their unique characteristics and high mass/volume ratio accelerate the conversion of the chemical signal into electrical signal, which in turn enhances the sensor performance [44, 45]. Different carbonaceous nanostructures including SWCNTs, MWCNTs, or rG were tested. Both SWCNTs and MWCNTs showed higher Nernstian response (slope values were 57.1±0.3 and 56.1±0.7 mVdecade^{-1}, respectively) (**Fig. 3a**). Unexpectedly, the reduced graphene nanosheets showed lower performances which may be attributed to the presence of some function on the sheet surface make a disturbance with potentiometric measurements. Under the potentiometric titration conditions, both MWCNTs and SWCNTs showed improved potential jump compared with the PVC membrane and rG (**Fig. 3b**).

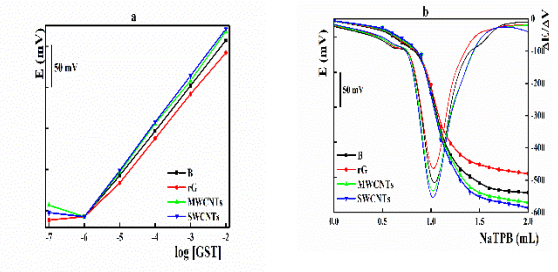

Fig. 3: a) Nanomaterial impact on the sensor performance**; b)** effect of the nanomaterial on potentiometric titration of GST against NaTPB solution.

3.1.2. Insitu modification

3.1.2.1. Nature of the modifier

Via incorporation of the sensing membrane with a suitable ion pairing agents following by soaking in GST solution, the GST–ion associates will be precipitated on the membrane/aqueous solution interface which consequently be extracted into the electrode bulk by the plasticizer which act as organic solvent [40-42, 46-48].Thus, there is no need for precipitation of ion pair complex which safe time and chemical consumption. Herein, different types of ion pairing agents were tested including: NaTPB, RNC, KTCPB, PTA and PMA **(Fig. 4a)**. The obtained results referred that the highest sensitivity was given in case of incorporation of KTCPB and PTA into the electrode matrix (52.3±2.2and 51.6±2.3 mV decade^{-1}, respectively). Sensors incorporated with different ion pairing agents and soaked in GST solution were tested for potentiometric titration of GST. The results revealed the priority of PTA which showed higher potential jump and the potential change at the inflexion point compared with other modifiers **(Fig. 4b)**. Next, from different PTA ranged from 2.5 to 20.0 mg, addition of 2.5mg of PTA to the electrode matrix was the most proper (**S 2**).

3.1.2.2. Influence of the membrane plasticizer

In case of insitu modification mode, the membrane plasticizer extracts the formed ion associates into the electrodes matrix; therefore, the sensor performance in presence of five different plasticizers was studied. Among the tested plasticizers (**S3**), *o*-NPOE exhibited the highest performance (Nernstian slopes value of 55.1± 0.9 mV decade^{-1} and the highest potential jump).

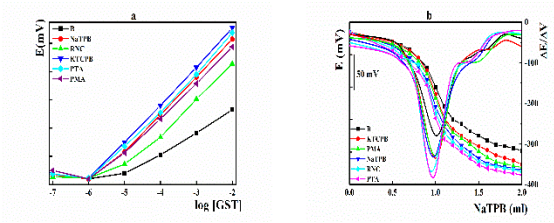

Fig. 4: a) Performance of granisetron sensors incorporated with different ion pairing agents; **b)** Effect of the ion pairing agents on potentiometric titration of GST against NaTPB solution.

3.1.2.3. Effect of nanomaterials

Moreover, trials to improve the sensor performance were employed via incorporation of selected carbonaceous nanomaterials within the electrode matrix (**S4**). It was obvious that both SWCNTs and MWCNTs impacted the sensitivity under direct potentiometric measurements and titration process.

3.1.3. Modification by soaking

3.1.3.1. Effect of the modifier content

In addition to the above fabrication protocols, more reliable and simple modification protocol could be conducted through immersing the blank electrodes (fabricated without incorporation of a modifier) in the ion-associates aqueous suspension, where the membrane plasticizers acts as organic solvents which extract by ion associates to the sensing membrane [41-43]. The obtained results revealed the highest sensitivity for sensors soaked in the GST-PTA suspension compared with other ion associates (45.3±0.8, 46.1±1.0, 45.3±1.2 and 49.1±0.5 mV decade^{-1}, for GST-TPB, GST-RNC, GST-PMA and GST-PTA, respectively).

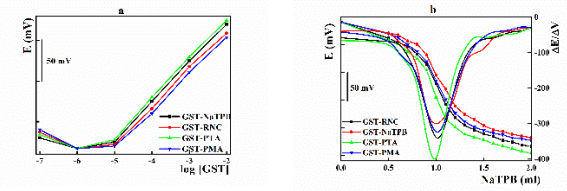

Fig. 5: a) Performance of granisetron sensors soaked in different ion pair complexes suspension solution; **b)** potentiometric titration of GST against NaTPB.

The variation in the sensor performances may be correlated to the ion associates solubility products and their extractability within the membrane matrix (Fig.5 a, b). For potentiometric titration, soaking in GST-PTA improved both the total potential change and potential break at the end point compared with other ion associates.

3.1.3.2. Influence of the membrane plasticizer

The extraction of the ion associates from the bulk solution to the electrode matrix represents the critical step

controlling the sensor performance. Among five tested plasticizers, *o*-NPOE with the highest dielectric constant showed the best performance with the highest potential jump under potentiometric titration conditions (**S5**). This phenomenon is mainly based on the extraction ability of the membrane plasticizer based on the polarity which expressed in the form of dielectric constants values.

3.1.3.3. Effect of nanomaterials

Reaching the final study, the impact of different carbon nanomaterials on the sensor performance was tested. These nanostructure carbon materials increased the Nernstian slope values with about 2-3 mV decade^{-1} and improved the titration curves compared with the blank PVC membrane (**S6**).

3.2. Performances of the fabricated sensors

The performances of the different granisetron disposable sensor were evaluated following the IUPAC recommendations [36]. Different sensitivities were recorded where the insitu modification with PTA offers the highest performance with Nernstian cationic slope 59.6±0.8mV decade^{-1} in the granisetron concentration ranged from 1.0×10^{-6} to 1.0×10^{-2} mol L^{-1} **(Table 1 , Fig. 6).**

Due to the solid state nature of the fabricated sensors with the absence of internal filling solution, long storage lifetime of 6 weeks was recorded with slight variation of the Nernstian slopes (±1 mV decade^{-1}). Wherever, the soaked electrodes showed operational lifetime for 2 weeks only, but reactivation can be performed via soaking in the GST-PTA ion pair suspension for 24 h to compensate the sensing materials that leached from the membrane during measurements.

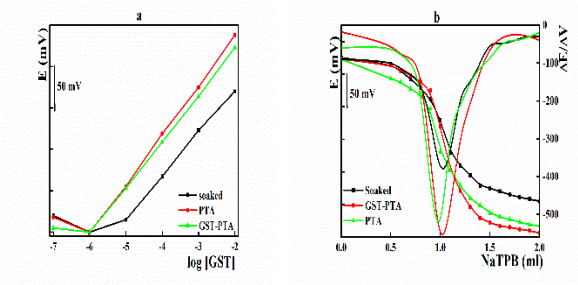

Fig.6: a) Performance of different granisetron senor, **b)** potentiometric titration of GST against NaTPB.

Table 1: Analytical performances of different granisetron disposable sensors

Parameter	GST-PTA	PTA	Soaked
Linear range (mol L^{-1})	10^{-6}-10^{-2}	10^{-6}-10^{-2}	10^{-5}-10^{-2}
Nernstian Slope (mV decade^{-1})	55.7±0.6	59.6±0.8	52.1±1.2
Correlation coefficient	0.9998	0.9997	0.9995
LOD (mol L^{-1})	1.0×10^{-6}	1.0×10^{-6}	3.0×10^{-6}
Response time (s)	4	4	8
Shelf lifetime (weeks)	6	6	2
Potential jump for 3.13 mg GST (mV)	220	267	266
Working pH range	2-6	2-6	2-6

*Average of five calibration graphs.

Although, the fabricated sensors were disposable; the same sensor operated continuously up to 20 successive measurements without diminishing the performance. Moreover, the sensor fabrication applying screen printing technology was characterized by the possibility of large scale production with high fabrication reproducibility. Within the same batch, the average Nernstian slope values for insitu mode were 60.5±1.1 mV decade^{-1}.

For practical applications, the response time for a newly fabricated electrode is quite important. Following the IUPAC recommendations, the response time of the present potentiometric sensor was evaluated by monitoring the interval needed to achieve a steady state potential reading (within ±1 mV) after sudden tenfold increase in the GST concentration. The fabricated GST sensors exhibited fast response time ranging between 4 and 6 s.

In general, the performance characteristics of the fabricated sensors were compared with those reported in literature with the advantages of possibility of miniaturization, application of flow injection analysis and potentiometric titration mode **(Table 2).**

Table 2: Characteristic performance of GST disposable sensors compared with other fabricated sensors

Parameter	Present work	Ref [22]	Ref [23]
Linear range (mol L^{-1})	10^{-6}-10^{-2}	10^{-5}-10^{-2}	10^{-6}-10^{3}
Nernstian Slope (mV decade^{-1})	59.6±0.8	59.5	58.1±0.2
Correlation coefficient	0.9997	0.9988	0.9982
LOD (mol L^{-1})	1.0×10^{-6}	7.8×10^{-6}	7.0×10^{-7}
Response time (s)	4	35	25
Preconditioning time (h)	2	24	24
Shelf lifetime (weeks)	6	8	8
Potentiometric titration	Included	------	--------
Flow injection analysis	Included	------	---------
Possibility of miniaturization	Included	------	---------

For assaying of pharmaceutical compounds in their formulations and biological samples, the working pH range was regarded as main operating factors. The fabricated sensors showed stable and reasonable potential readings within the working pH range from 2 to 6. At higher pHs, the electrode potential dramatically decreased due to the formation of the deprotonated species and precipitation of GST base (**S7**).

Selectivity represents one of the most critical future characteristics of the potentiometric sensors. Since it measures the sensitivity to the target ion over interferents and hence determines the electrode reliability and applicability to sample measurement is possible or not. Selectivity coefficient describes the ion discrimination ability and depends upon the nature and content of each electrode component including the recognition element, solvent and the plasticizer [49, 50]. In the present study, the

selectivity of the fabricated GST sensor was evaluated by the Matched Potential Method (MPM).

Table 3: Selectivity coefficient for granisetron sensors

Interferent	-log $K_{A,B}$		
Li^+	2.70	Maltose	4.00
NH_4^+	2.15	Starch	4.23
Ca^{2+}	1.80	Sucrose	3.92
Mg^{2+}	2.12	Glucose	4.33
Ni^{2+}	1.60	Fructose	4.05
Co^{2+}	1.73	Glycine	2.14
Phosphate	3.60	Caffeine	2.65
Citrate	3.44	Cysteine	2.75

Improved selectivity toward GST against additives and fillers that commonly present in pharmaceutical formulations (such as glycine, caffeine, citrate, maltose, sucrose, and starch) as well as inorganic cations, (Na^+, K^+, Li^+, Ca^{2+}, Mg^{2+}, and NH_4^+)was reported (Table 3).

The interference of the GST degradation products was also investigated. None of these products showed obvious interference with the parent GST moiety

3.3. Analytical applications

3.3.1. Potentiometric titration

Contrary to direct potentiometric measurements which required tedious optimization of the measuring conditions, operating the potentiometric titration approach showed high precision and accuracy [38]. Performing the titration process of granisetron against NaTPB using the insitu modified sensors, symmetrical with a well-defined potential jump titration curves were achieved indicating the high sensitivity of the electrode. High total potential jumps (ΔE ranges between 230 to 275 mV) were recorded allowing the determination of 3.314 mg GST **(Fig. 7).**

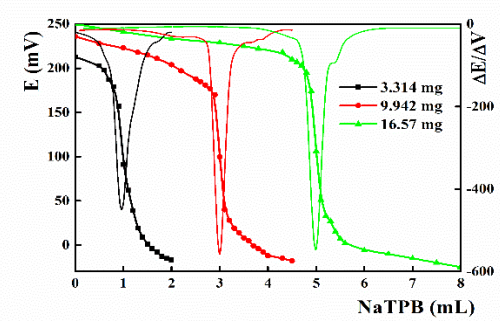

Fig. 7: Potentiometric titration of granisetron using disposable sensors insitu modified with PTA

3.3.2. Sensor performance under flow injection analysis conditions

Incorporation of the electrochemical sensors in flow injection systems represents one of their promising futures offering the automation with high sampling output [51-53]. Herein, the performance of the fabricated sensor was tested via injection of different GST solutions within the concentrations range from 10^{-6} to 10^{-2} mol L^{-1} **(Fig. 8).**

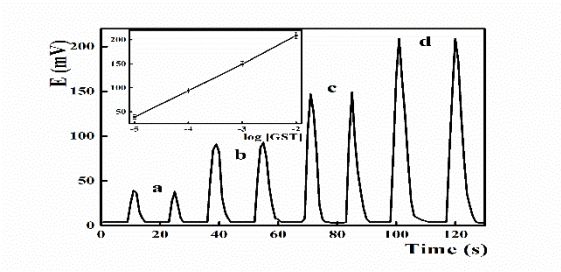

Fig. 8: Performnce of the fabricated granisetron sensors under the flow injection conditions

As the fabricated GST sensors exhibited fast response, stable potential readings and improved sensitivity, under FIA system, fast residence time and high sampling output (60 samples h^{-1}) was achieved. Calibration graphs exhibited Nernstian slopes value of 56.5±0.8 mV $decade^{-1}$ with the linear range from 10^{-5} to 10^{-2} mol L^{-1}.

3.3.3. Analysis of granisetron samples

The fabricated granisetron disposable sensors possessed satisfactory selectivity and sensitivity; therefore, it can be suggested as a promising tool for quantification of GST in water samples and pharmaceutical formulations (Table 4).

Table 4: Analysis of granisetron content in pharmaceutical and surface water samples

	Taken (mg)	Found							
		Official method		Proposed potentiometric method					
				Standard addition		Titration		FIA	
		Recovery [a]	RSD [a]	Recovery	RSD	Recovery	RSD	Recovery	RSD
Granitryl	0.1657	98.70	2.30	99.0	1.55			101.0	0.80
	1.657	99.70	2.18	98.3	1.70			102.3	1.12
	3.314	100.40	1.78	101.2	1.25	101.8	1.17		
Surface Water	0.1657	95.60	2.43	96.80	1.98			97.6	1.90
	1.657	96.80	2.19	98.70	1.90			98.2	2.11
	3.314	99.30	1.71	99.4	1.24	96.4	2.52		

[a]**Mean recovery and relative standard deviations of four determinations**

3. Conclusion

Herein, the fabrication of novel granisetron disposable sensors incorporated with granisetron ion associates or with different anionic lipophilic reagents was described. Different fabrication protocols were employed including modification with GST-PTA ion pair, incorporation of phosphotungstic acid within the electrode matrix or immersing the blank electrode in the aqueous GST-PTA ion-associate suspension. Different cationic Nernstian compliances were achieved in the GST working concentration range from 10^{-6} to10^{-2} mol L^{-1} with fast response time (4 s) and long storage lifetime. Superior performance was reported compared with those reported in literatures regarding the improved sensitivity, selectivity and fast response time with the possibility of miniaturization. The proposed sensors were introduced for analysis of granisetron in pharmaceutical and surface water samples with average recoveries agreeable with the standard methods. Moreover, as the fabricated sensors operate with low-cost measuring equipments, the developed analysis protocol allows the small laboratories with limited resources to run granisetron analysis in different samples. Screen printing technology offers mass production of sensors and supports sensor miniaturization with portable devices and establishes its route from "lab-to-market" for a plethora of sensors.

Conflicts of interest

"There are no conflicts to declare".

Formatting of funding sources

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