Int. J. Electrochem. Sci., 7 **(2012)** 7235 - 7252

International Journal of
ELECTROCHEMICAL
SCIENCE
www.electrochemsci.org

Carbon Nanotubes Modified and Conventional Selective Electrodes for Determination of Selegiline Hydrochloride and Its Pharmaceutical Preparations

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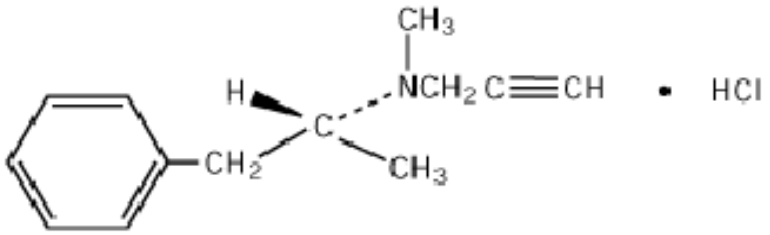
Received: 25 June 2012 / *Accepted:* 17 July 2012 / *Published:* 1 August 2012

The construction and performance characteristics of selegiline (Sel) carbon paste (CPEs) and plastic membranes electrodes are described. The cited electrodes are based on the ion associates selegiline phosphomolybdate (Sel-PMA) or phosphotungstate (Sel-PTA). Matrix composition of each electrode is optimized on the basis of effects of type and concentration of the ionophore as well as influence of the selected plasticizers. Carbon nanotubes (CNTs) have a good conductivity which helps the transduction of the signal in carbon paste electrode, so the addition small quantity of multi-wall carbon nanotubes (MWCNTs) particles to the composition of carbon paste electrode gave a better performance characteristics for Sel-electrodes with Nernstion slope of 59.50 and 58.20 mV at 25°C for Sel-PMA and Sel-PTA ion associates, respectively within a linear concentration range from $1.0x10^{-5}$ to $1.0x10^{-2}$ M for MWCNTs modified paste electrodes. The mean recovery of the amounts taken of pure and pharmaceutical preparations ranged from 95.2 to 103.5% with RSD = 0.2–0.8%. While for urine and plasma samples, the recovery values ranged from 96.2 to 103.5% with RSD =0.2-0.7%, with limit of detection (LOD), ranged from 1.52 to 21.26 µg/L, while the limit of quantification (LOQ) ranged from 1.52 to 20.36 µg/L for the studied electrodes.

Keywords: Selegiline; potentiometry; PVC membrane; carbon nanotubes.

1. INTRODUCTION

Selegiline hydrochloride (SelCl), [CAS number 14611-52-0], is [(R)-(-)-N, 2-dimethyl-N-2-propynylphenethylamine hydrochloride] of molecular formula $C_{13}H_{18}ClN$. Scheme (1) represents the structural formula of selegiline hydrochloride.



Scheme 1. Structural formula of selegiline.

Selegiline (also known as l-deprenyl, Eldepryl) is a drug used for the treatment of early-stage Parkinson's disease, depression and senile dementia and has a low oral bioavailability, which increases to moderate when ingested together with a high-fat meal (the molecule being liposoluble) [1-3]. Limited number of methods has been reported for the determination of SelCl including high performance liquid chromatography (HPLC) [4–7]; gas chromatography [8-9] and capillary electrophoresis [10-11]. No potentiometric methods have been yet given in literature for the determination of SelCl.

Ion-selective electrodes (ISEs) had found wide applications for drug quality control [12–14]. Carbon paste electrodes possess many advantages as long operational lifetime, short response time, low Ohmic resistance, easer fabrication and regeneration besides no need for internal solution [15–17]. The carbon paste usually consists of graphite powder dispersed in a non-conductive mineral oil. Although a considerable attention has been given to the preparation of carbon paste electrodes, their applications have been focused on pre-concentration followed by voltammetric determination of the analyte [18] and just few of these electrodes have been used as potentiometric sensors [19].

Recently, carbon nanotubes (CNTs) have also been used in carbon paste electrodes [20, 21]. CNTs have very interesting physicochemical properties, such as ordered structure with high aspect ratio, ultra-light weight, high mechanical strength, high electrical conductivity, high thermal conductivity, metallic or semi-metallic behavior and high surface area [22, 23]. The facility of electron transfer between the electro-active species and the electrodes offers great promise for fabricating electrochemical sensors and biosensors. The combination of these characteristics makes CNTs unique materials with the potential for diverse applications [24–26].

The present study describes preparation, characterization and application of simple potentiometric sensors for determination of SelCl in its pure solution, pharmaceutical formulations, spiked human urine and plasma samples. Both carbon paste electrodes and plastic membranes electrodes were fabricated besides studying the effect of addition multi-wall carbon nanotubes (MWCNTs) to graphite, for constructing carbon nanotubes modified paste electrodes, and all the prepared electrodes are optimized to select the electrode possessing the most favorable analytical characteristics. The developed sensors were then applied in the potentiometric determination of SelCl using standard additions and potentiometric titration in its analytical grade solutions; pharmaceutical formulations and biological samples.

2. MATERIALS AND METHODS

2.1. Reagents

All of the chemicals used were of analytical grade. Bi-distilled water was used throughout all experiments. Pure-grade selegiline hydrochloride was provided by ACAPI pharmaceutical Co., Egypt, while its pharmaceutical preparation (Tonus® 5mg/ tablet) was purchased from local market. Phosphotungstic acid (PTA), phosphomolybdic acid (PMA), tetrahydrofuran (THF), dioctylphthalate (DOP), dioctyladipate (DOA), dibutylphthalate (DBP) and polyvinyl chloride (PVC) of high relative molecular weight are purchased from Fluka (USA), high purity of graphite powder (1-2 micron) and multi-wall carbon nanotubes powder (DXL 110-170 nm x 5-9 μm) are from Aldrich (USA).

2.2. Apparatus

Potentiometric and pH measurements were carried out using a digital Schott Gerate pH meter, Model JENWAY 3010 (England). A circulator thermostat model HAAKE type N2, B (Germany) was used to control the temperature of the test solutions. Packed saturated calomel (SCE) (Sentek, UK) was used as an external reference, while an Ag/AgCl electrode was used as an internal reference. The electrochemical system of the conventional electrode may be represented as follows: Ag/AgCl/filling solution/membrane/ test solution//KCl salt bridge//saturated calomel electrode. While for carbon paste electrodes and carbon nanotubes modified paste electrodes may be represented as: CPEs or CNTs modified paste electrodes /test solution//KCl salt bridge//saturated calomel electrode, where the internal solution is a mixture of $1.0x10^{-2}$ M solutions of the drug and NaCl.

2.3. Procedures

2.3.1.Construction of plastic membranes electrodes, carbon paste electrodes and carbon nanotubes modified paste electrodes

2.3.1.1. Preparation of ion associates

The ion associate selegiline phosphomolybdate [Sel_3PMA] and selegiline phosphotungstate [Sel_3PTA] were prepared by mixing of 50 mL of $1.0x10^{-2}$ M of each of phosphomolybdic acid (PMA) or phosphotungstic acid (PTA) with 150 mL of $1.0x10^{-2}$ M of selegiline hydrochloride (SelCl). The resulting precipitates were left in contact with their mother liquor over night to assure complete coagulation, then the precipitates were filtered and washed thoroughly with distilled water till chloride free (tested using $AgNO_3$ solution) and left to dry at room temperature for at least 3 days.

$$3\ SelCl + PTA \rightarrow Sel_3PTA \quad (1)$$

$$3SelCl + PMA \rightarrow Sel_3PMA \quad (2)$$

2.3.1.2. Preparation of plastic membranes electrodes

The membrane composition was studied by mixing varying percentages (w/w) of the ion associate, polyvinyl chloride PVC and dioctyladipate (DOA), (ratio PVC to plasticizer 1:1 (w/w)) into Petri dish "5 cm" diameter until the optimum composition that exhibits the best performance characteristics was obtained. The mixture was dissolved in THF and stirred for 15 min. After 48 hr of slow evaporation of solvent, a master membrane with 0.12 mm thickness was obtained which was mounted on the softened end of the PVC tubing with the help of adhesive solution prepared by dissolving PVC in THF. The electrode body was filled with inner solution that is $1.0x10^{-2}$ M for drug solution and NaCl. The fabricated electrodes were soaked in $1.0x10^{-3}$ M drug solution before used.

2.3.1.3. Preparation of carbon paste electrodes and carbon nanotubes modified electrodes

The carbon paste electrodes were prepared, by mixing the required amount of the ion associate with spectroscopic graphite powder (Aldrich, 1–2 micron) and dioctyladipate (DOA) as a pasting liquid (ratio of graphite powder to pasting liquid was 60:40 (w/w)) of total weight of components 0.35 gram in a mortar until it was uniformly wetted. This matrix was thoroughly mixed in the mortar and the resulting paste was used to fill a Teflon electrode body. A fresh surface was obtained by gently pushing the stainless-steel screw inside the electrode body forward and polishing the new carbon-paste surface with filter paper to obtain a shiny new surface [27].

The effect of addition multi-wall carbon nanotubes (MWCNTs) powder, on the performance characteristics of carbon paste electrode (CPE), was studied for both ion associates Sel-PMA and Sel-PTA by adding variable percentages of carbon nanotubes to the optimum composition obtained for the carbon paste electrode. After the mixture homogenization, the paste was then packed carefully into the end of the hole of Teflon holder of the electrode body [28]. The external electrode surface was smoothed with soft paper until it had a shiny appearance and the electrode became ready to use directly for potentiometric measurements.

2.3.2. Sample analysis

2.3.2.1. Standard additions method

SelCl was determined using the prepared electrodes by the standard additions method **[29].** Small increments of standard SelCl solution ($1.0x10^{-2}$ M) were added to 50 mL aliquot of samples of various concentrations (at the appropriate pH value). The change in potential (at 25°C) was recorded for each increment and used to calculate the concentration of SelCl in the sample solution.

2.3.2.2. Potentiometric titration

An aliquot of SelCl, pure or sample (tablets) solution containing 6.71–33.56 mg SelCl was transferred into a100-mL titration vessel and diluted to about 50 mL with water, then titrated

potentiometrically with a standard solution of $1.0x10^{-2}$ M PMA or PTA depending on the type of the electrode. The volume of the titrant at equivalence point was obtained using the differential method.

2.3.2.3. Analysis of SelCl in pharmaceutical formulations

For sampling of tablets, (Tonus®, 5 mg/tablet), fifty tablets were accurately weighed and finely powdered. The required amount of powder was weighed, dissolved in about 30 mL bi-distilled water, filtered in a 50 mL-volumetric flask and after pH adjustment, volume was completed with bi-distilled water. The standard additions and potentiometric titration methods were then applied.

2.3.2.4. Determination of SelCl in biological samples

Different amounts of SelCl (6.71–33.56 mg) were added to 1 mL human plasma or 5 mL human urine of a healthy person then transferred to 50 mL measuring flask and completed to the mark with $1.0x10^{-4}$ M HCl to give solutions of pH (within the optimum pH range of the electrodes); the standard additions method was then applied for SelCl determination.

3. RESULTS AND DISCUSSION

3.1. Electrodes performance

Table 1. Optimum composition of different Sel-electrodes and slopes of the corresponding calibration graphs.

Sensor	Matrix composition	Slope	Linear Concentration range	Response Time	Detection limit	Correction Coefficient
	(W/W%)	(mV)	(M)	(s)	(µg/L)	**(r)**
Sel-PMA(I)	5.0%Sel-PMA, 47.5% PVC and 47.5% DOA	60.6	$5.0x10^{-6}$ - $1.0x10^{-2}$	35	1.52	**0.9998**
Sel-PMA(II)	5.0%Sel-PMA, 57.5% graphite powder and 37.5% DOA	56.2	$1.0x10^{-5}$ - $1.0x10^{-2}$	10	21.26	**0.9995**
Sel-PMA(III)	5.0%Sel-PMA, 52.5% graphite powder, 5.0% MWCNTs and 37.5% DOA	59.5	$1.0x10^{-5}$ - $1.0x10^{-2}$	5	2.46	**0.9997**
Sel-PTA(I)	5.0%Sel-PTA, 47.5% PVC and 47.5% DOA	59.8	$1.0x10^{-5}$ - $1.0x10^{-2}$	30	2.69	**0.9998**
Sel-PTA(II)	5.0% Sel-PTA, 57.5% graphite powder and 37.5% DOA	57.0	$1.0x10^{-5}$ - $1.0x10^{-2}$	12	1.77	**0.9996**
Sel-PTA(III)	**5.0% Sel-PTA, 56.5% graphite powder, 1.0% MWCNTs and 37.5% DOA**	**58.2**	**$1.0x10^{-5}$ - $1.0x10^{-2}$**	**7**	**3.58**	**0.9994**

Many trials were made with different compositions and ratios of ion-associate, PVC and plasticizer, the best composition and performance for the studied electrodes are indicated in table 1.

The electrodes showed near Nernestian responses over the concentration range $5.0x10^{-6}$-$1.0x10^{-2}$ to $1.0x10^{-5}$-$1.0x10^{-2}$ M with slope values ranging from 60.2 to 56.2 mV where,

$$\text{Slope } S = dE/mV \,/d \log[Sel]/M \quad (3)$$

These compositions were used for all the subsequent measurements made for unknown SelCl concentrations.

On comparing the performance of the carbon nanotubes modified paste electrodes with the conventional electrodes and the traditional carbon paste electrodes as given in table 1, it clear that the three different types are of comparable working range, and have more or less similar Nernestian slopes, the main significant behavior noticed was the fast response time of the electrodes, and in accordance, the shorter time need for measurements and in turn sampling rates and this can be favorable in case of quality control assays.

This is mainly because CNT;s similar to other nano-structured materials tend to have non faradic transduction mechanisms and accordingly, faster equilibrium is attained, also, being hydrophobic hinders accumulation of water particles on the surface of the electrode which will ease the diffusion of the sensed ions through the electrode surface [22, 24]. Representative calibration graphs for carbon paste electrodes performance of Sel-PMA (II) electrode and Sel-PMA (III) electrode (containing 5% MWCNTs in its composition) are illustrated in figure 1.

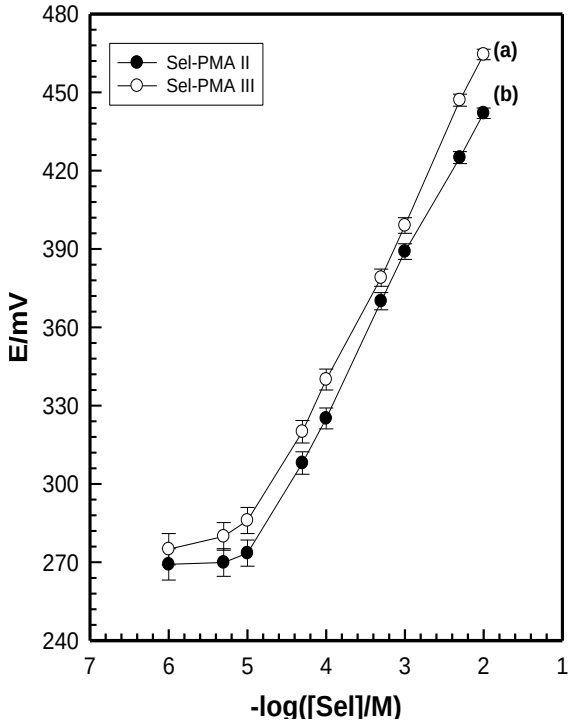


Figure 1. Calibration curves for Sel-PMA (III) electrode (a) and Sel-PMA (II) electrode (b).

The influence of the plasticizer choice on the electrode performances has been studied as the electrode plasticized with dioctyladipate (DOA) is compared with those plasticized with dibutylphthalate (DBP) and dioctylphthalate (DOP) as given in Table 2.

Table 2. Effect of plasticizer type on the slopes of the calibration graphs of Sel-electrodes.

Slope			
mV			
Plasticizer	Sel-PMA(I)	Sel-PMA(II)	**Sel-PMA(III)**
DOA	60.2	56.2	**59.5**
DBP	53.3	50.9	**52.4**
DOP	56.4	53.4	**53.1**
Plasticizer	Sel-PTA(I)	Sel-PTA(II)	**Sel-PTA(III)**
DOA	59.78	57.0	**58.2**
DBP	52.4	53.2	**52.6**
DOP	**55.7**	**54.2**	**55.6**

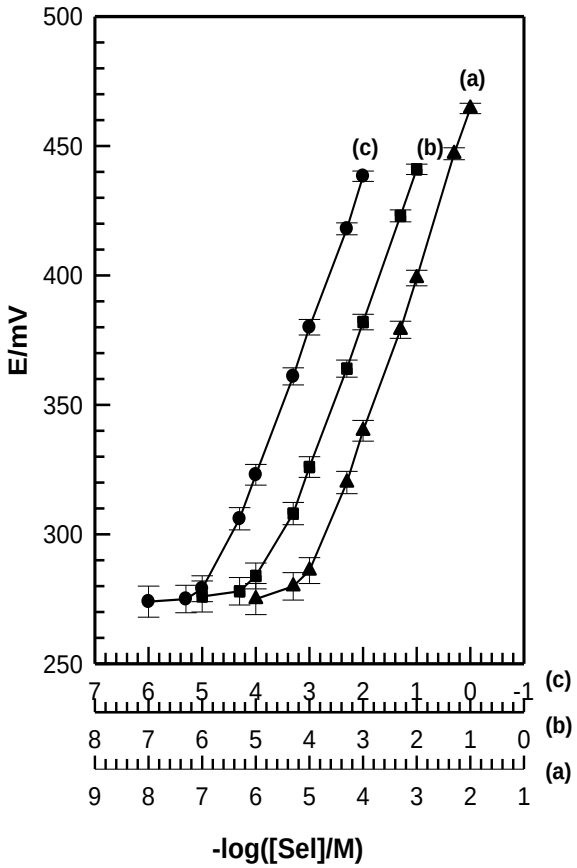


Figure 2.Variation of slopes of the Sel-PMA (I) (A), Sel-PMA (II) (B), Sel-PMA (III) (C) electrodes with soaking time.

From the three tested plasticizers, DOA shows the highest total potential change and shortest response time compared with other electrodes which is reflected on the total time required to achieve stable potential readings. This may be because DOA has a greater polarity and less lipophilicity that make it more suitable for the plastic membrane electrodes and carbon paste electrodes [30, 31]. Representative curve for the response of for Sel-PMA (III) electrode, carbon nanotubes modified paste electrode, with the three plasticizers (DOA, DBP and DOP) is shown in figure 2.

3.2. Effect of soaking

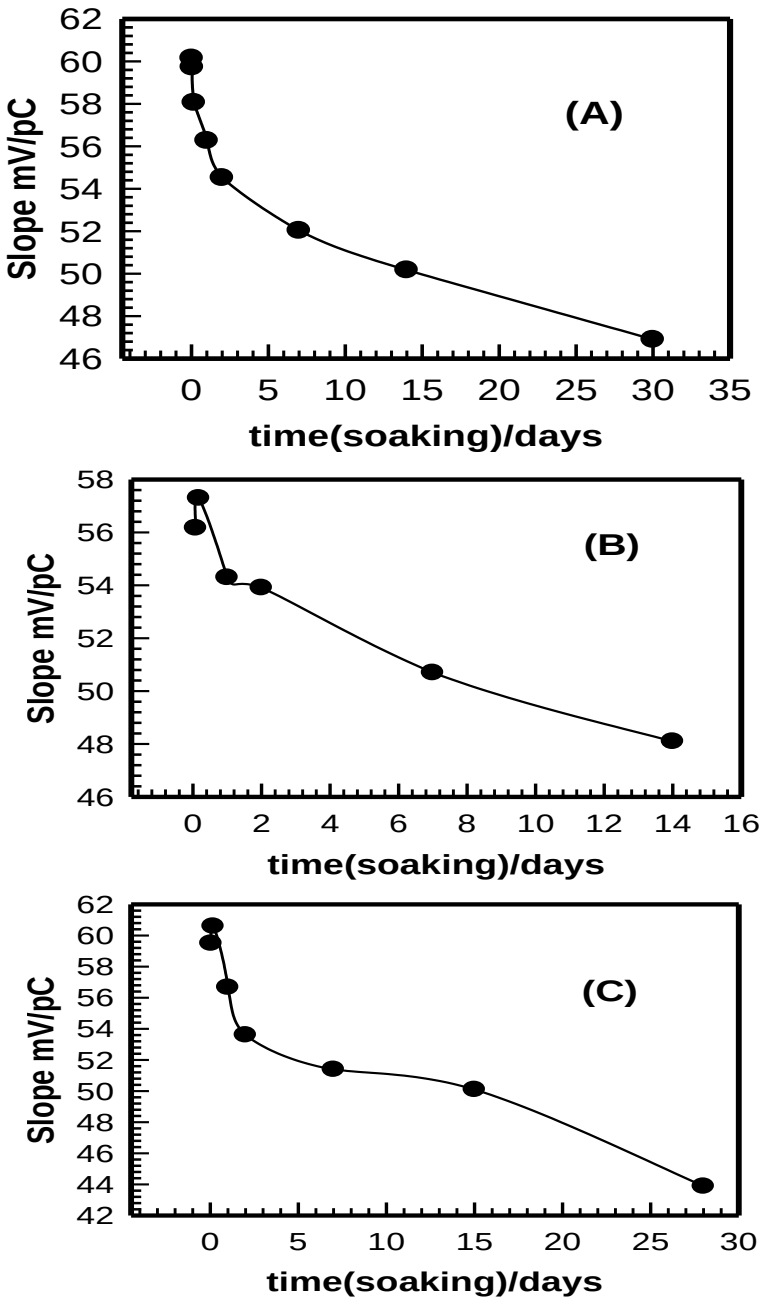


Figure 3. Dynamic response time plot of Sel-PMA (III) electrode.

The slopes of calibration curves were found to be 60.2, 56.2, 59.5, 59.8, 57.0 and 58.2 mV/decade of selegiline concentration after 0.5, 0.5, 2.0, 2.0, 1.0, 1.0 hr of precondi-tioning, this process requires different times depending on diffusion and equilibration at the electrode - test solution interface; a fast establishment of equilibrium is certainly a condition for a fast potential response; thus, the performance characteristics of the Sel ion- selective electrodes was investigated as a function of soaking time. It was found that the slopes start to decrease gradually with soaking time reaching about 46.9, 48.1, 43.9, 46.0, 44.9 and 46.5 mV/decade of selegiline concentration after 30, 14, 28, 27, 7 and 16 days of continuous soaking for Sel-PMA (I), Sel-PMA (II), Sel-PMA (III), Sel-PTA (I), Sel-PTA (II) and Sel-PTA (III) electrodes, respectively. This indicates the life span of conventional membrane electrodes is greater than carbon paste electrodes or carbon nanotubes modified paste electrodes but yet the latter has longer life span than carbon paste electrodes which reflect a good advantage for carbon nanotubes in improving the performance of carbon paste electrodes.

The variation of slope of Sel-PMA (I), Sel-PMA (II) and Sel-PMA (III) electrodes with the soaking time is shown in figure 3. The decrease in the efficiency of the conventional membrane electrodes on prolonged soaking may be due to diminished ion exchanger rate of the electro-active species on the membrane gel layer test solution interface which is responsible for the membrane potential [14, 32]. While is case of carbon paste and modified carbon paste, the electrodes are characterized by longer practical life time, as simply, a new surface can be easily formed by screwing the other layer of the electrode, thus the life span of these electrodes can extend to several months regardless of soaking time.

3.3. Response time, reversibility and repeatability of the electrodes

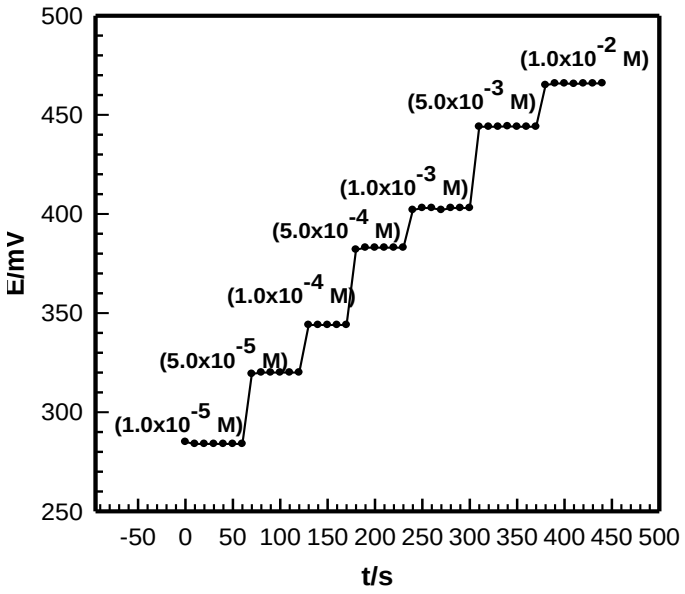


Figure 4. Dynamic response of Sel-PMA (III) electrode for several high-to-low sample cycles.

The effect of response time of the electrodes, which is the time needed for the electrodes to reach a stable potential reading, was made by recording the practical response time on measuring solutions of different Sel^+ concentration (1.0×10^{-5} to 1.0×10^{-2} M). The carbon nanotubes modified paste electrodes were found to have shorter response time in comparison to carbon paste electrodes and plastic membrane electrodes which indicates that carbon nanotubes helped in improving the performance of carbon paste electrodes [22]. Representative figure for response time of Sel-PMA (III) electrode are shown in figure 4.

To evaluate the reversibility of the electrodes, a similar procedure in the opposite direction was adopted. With measurements performed in the sequence of high-to-low sample concentrations and the results are shown in figure 5. It shows that the potentiometric responses of the electrodes are reversible and the times needed to reach the equilibrium are about 55, 15, 10, 60, 18 and 8 s for Sel-PMA (I), Sel-PMA(II), Sel-PMA (III), Sel-PTA (I), Sel-PTA (II) and Sel-PTA (III) electrodes, respectively.

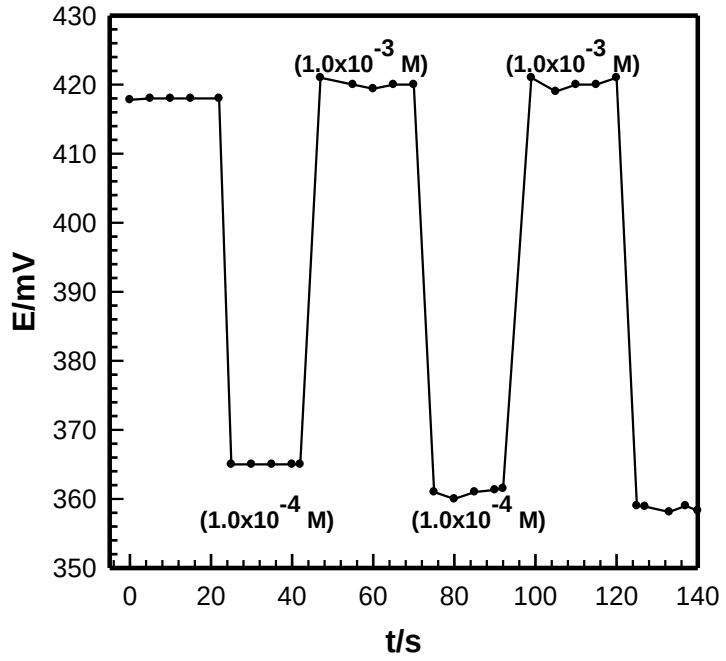


Figure 5. Calibration curves for Sel-PMA (III) electrode on using Plasticizer DOA (a), DBP (b) and DOP (c) as plasticizer, respectively.

The reproducibility of the electrodes was also examined by immersing the electrode alternatively in $1.0x10^{-4}$ and $1.0x10^{-2}$ M of selegiline hydrochloride solutions. The standard deviation of measuring e.m.f for five replicate measurements was found to be 1.12, 1.28, 1.35, 1.86, 0.95 and 0.80 for 1.0×10^{-4} M solution and 0.62, 1.08, 0.90, 0.69, 1.22 and 0.64 for 1.0×10^{-2} M solution for Sel-PMA (I), Sel-PMA (II), Sel-PMA (III), Sel-PTA (I), Sel-PTA (II) and Sel-PTA (III) electrodes, respectively. This indicates the excellent repeatability of the potential response of the electrode.

3.4. Effect of pH

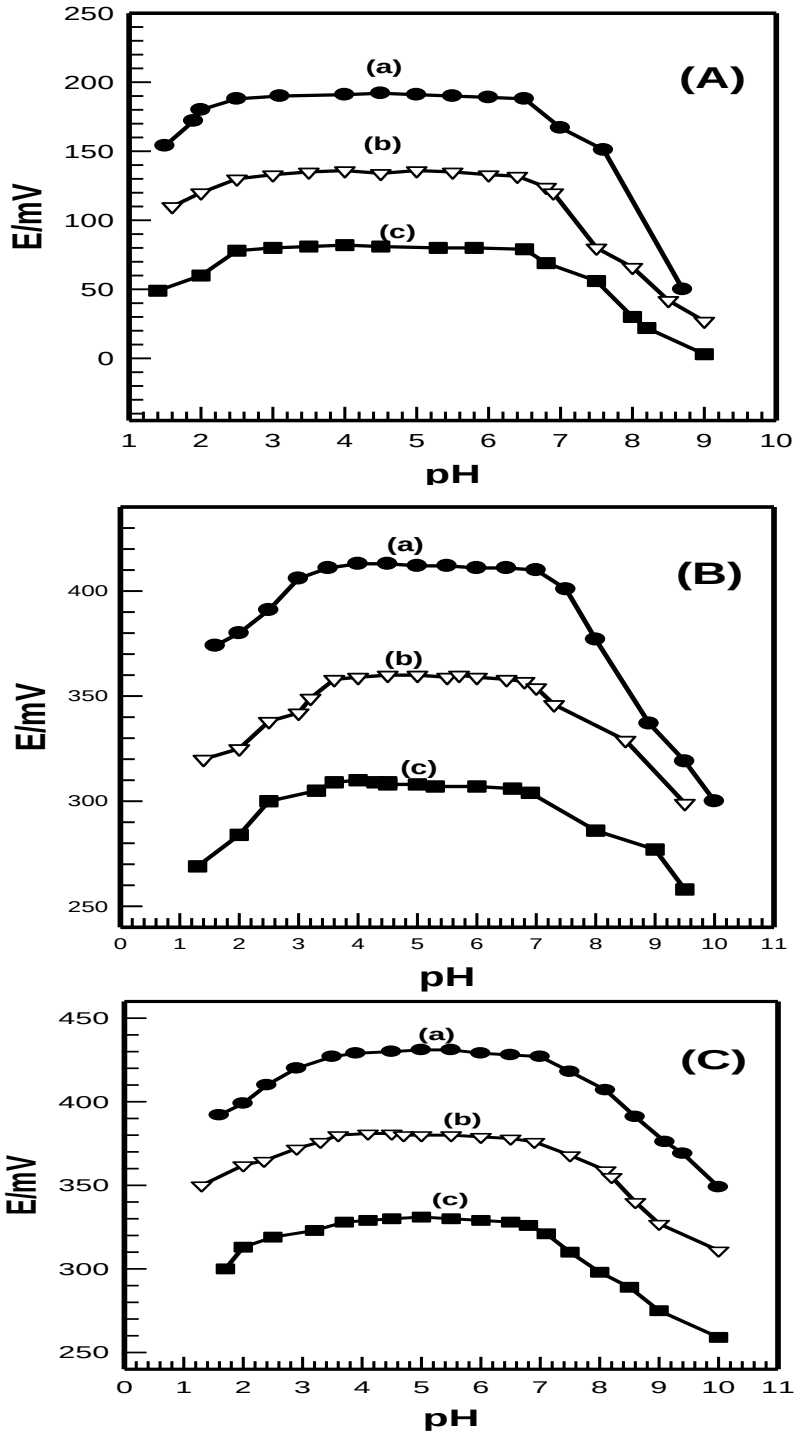


Figure 6. Effect of pH of test solution of concentrations $1.0x10^{-2}$ (a), $1.0x10^{-3}$ (b) and $1.0x10^{-4}$ (c) M on the potential response of Sel-PMA (I) (A), Sel-PMA (II) (B) and Sel-PMA (III) (C) electrodes.

The effect of pH on the potential reading of the electrodes was studied using solutions of different concentrations of SelCl ($1.0x10^{-2}$, $1.0x10^{-3}$, $1.0x10^{-4}$ M). The pH was changed by adding few increments of (0.10-1.00 M) HCl or NaOH and the change in pH were followed after each addition in

the range 1.00-14.00. Representative curves for effect of pH on Sel-PMA (I), Sel-PMA (II) electrode and Sel-PMA (III) electrodes are shown in figure 6.The result reveal that the change in pH does not affect the potential readings within the range 2.50-6.50, 3.50-7.00, 3.50-7.00, 3.00-6.00, 3.50-7.50 and 3.00-7.00 for Sel-PMA (I), Sel-PMA (II), Sel-PMA (III), Sel-PTA (I), Sel-PTA (II) and Sel-PTA (III) electrodes, respectively, so the electrodes can be used safely in these ranges for the respective determination. The potential decrease above these ranges can be attributed to the release of free base in the solution, leading to a decrease in the concentration of the detected selegiline cation [33, 34].

3.5. Effect of temperature on the test solution

Calibration graphs (electrode potential (E_{elec}) versus p [SelCl] were constructed at different test solution temperatures (25-70°C). For the determination of the isothermal coefficient (dE°/dt) of the electrode, the standard electrode potentials (E°) against the normal hydrogen electrode at different temperatures were obtained from calibration graphs as the intercepts at p[SelCl] = 0 (after subtracting the values of the standard electrode potential of the Ag/AgCl electrode at these temperatures) and were plotted versus (t−25), where t was the temperature of the test solution in °C. A straight line plot is obtained according to Antropov's equation **[35]**:

$$E°/mV = E°_{25} + [(dE°/mV)/ (dT/K)]. [(T – 25°C)] \quad (4)$$

Where $E°_{(25)}$ is the standard electrode potential at 25°C, T is the temperature in unit cellulous, the slope of the straight-line obtained represents the isothermal coefficient of the electrode (0.0014, 0.001311, 0.001267, 0.001111, 0.001356 and 0.001333 V/°C for Sel-PMA (I), Sel-PMA (II), Sel-PMA (III), Sel-PTA (I), Sel-PTA (II) and Sel-PTA (III) electrodes, respectively). The values of the obtained isothermal coefficient of the electrodes indicate that plastic membranes electrodes, carbon paste electrodes and carbon nanotubes modified paste electrodes have high thermal stability within the investigated temperature range. The investigated electrodes were found to be usable up to 70°C without noticeable deviation from the Nernestian behavior.

3.6. Selectivity

The selectivity coefficients $K^{pot}_{drug,J^{z+}}$ determined by the separate solution method (SSM) and matched potential method (MPM) (34, 36-38). The influence of some inorganic cations, sugars and amino acids on the Sel-electrodes was investigated. None of the investigated species interfered, as shown by the very small values of -log $K^{pot}_{drug,J^{z+}}$ as given in table 3.

These reflect high selectivity of the investigated electrodes towards Sel ion. Inorganic cations do not interfere because of the differences in ionic size, mobility and permeability as compared with Sel^+. The high selectivity of amino acids can be attributed to the differences in polarity and to the lipophilic nature of their molecules relative to Sel ion. The mechanism of selectivity is mainly based

on the stereo-specificity and electrostatic environment and is dependent on how much fitting is present between the locations of the lipophilicity sites in two competing species in the bathing solution side and those present in the receptor of the ion pair [14, 33]. The results showed that the tolerance towards glycine, glucose, fructose, maltose, L-alanine and lactose for the carbon paste electrodes or carbon nanotubes modified paste electrodes is smaller than that for plastic membranes electrodes; this due to the adsorption of these compounds on the surface of carbon paste electrode.

3.7. Analytical applications

Several methods are applied for the quantitative analysis using ion-selective electrodes. These methods comprise: i) The direct calculation of the concentration applying Nernst equation or calibration graph extrapolation and interpolation. ii) Potentiometric titration involving the use of counter ions as titrant which is more accurate depending on the use of electrode as an end point detector. iii) The standard additions method, which is frequently applied for pure solution and pharmaceutical solutions, and applied also for biological samples.

Table 3. Selectivity coefficients and tolerance values for Sel-electrodes.

	$-LogK^{pot}_{Sel,J^{z+}}$											
	Sel-PMA (I)		Sel-PMA (II)		Sel-PMA (III)		Sel-PTA (I)		Sel-PTA (II)		**Sel-PTA (III)**	
Interferent	[a]SSM	[b]MPM	[a]SSM	[b]MPM	[a]SSM	[b]MPM	[a]SSM	[b]MPM	[a]SSM	[b]MPM	[a]SSM	**[b]MPM**
Na^+	2.60	4.54	2.80	4.72	2.79	4.65	2.90	4.94	3.70	5.65	2.13	**4.12**
K^+	2.44	4.40	1.77	3.60	1.88	3.76	2.94	4.90	3.13	5.09	2.35	**4.30**
NH_4^+	2.23	4.31	2.16	4.07	2.30	4.18	3.89	5.78	2.47	4.37	1.80	**3.80**
Mg^{2+}	2.88	4.98	3.92	5.76	3.03	4.93	3.69	5.63	4.03	5.89	3.05	**4.94**
Ca^{2+}	3.06	5.13	3.44	5.32	2.59	4.50	3.07	4.95	4.83	6.67	2.68	**4.70**
Sr^{2+}	3.17	5.46	2.74	4.65	3.33	5.20	2.40	4.27	3.90	5.77	2.78	**4.67**
Ba^{2+}	2.98	5.01	1.36	3.31	1.89	5.14	2.87	4.79	4.77	6.68	2.95	**4.88**
Mn^{2+}	3.51	5.38	2.41	4.30	3.18	5.03	3.43	5.38	4.53	3.45	3.03	**5.00**
Cu^{2+}	2.92	4.92	3.79	5.69	1.56	3.45	3.30	5.27	3.53	5.50	3.48	**5.40**
Fe^{3+}	2.34	4.27	4.10	5.68	2.04	3.87	3.65	5.57	4.07	5.99	2.50	**4.45**
Al^{3+}	2.65	4.50	2.93	6.01	2.32	4.19	3.72	5.68	5.23	7.11	3.15	**5.35**
Glycine	3.44	5.33	4.14	4.87	2.87	4.70	4.10	6.02	4.13	6.37	3.40	**5.27**
L- Alanine	3.37	5.27	3.94	6.08	3.42	5.33	3.97	5.90	4.53	6.79	3.25	**4.91**
Fructose	3.62	5.52	4.31	6.17	3.11	5.01	4.13	6.13	4.97	5.54	2.93	**5.08**
Glucose	3.95	5.91	3.73	5.59	2.68	4.62	4.34	6.30	3.27	5.29	3.18	**5.04**
Maltose	3.32	5.23	3.15	5.02	3.53	5.37	4.17	6.15	3.60	5.57	3.45	**5.32**
Lactose	3.80	5.79	3.21	5.12	3.29	3.30	3.87	5.94	4.37	6.22	3.05	**4.97**

[a]SSM: Separate Solution Method.
[b]MPM: Matched Potential Method.

The results of the standard additions method were found to be in good agreement with those obtained from the official method [4]. The mean recovery of the amounts taken of pure and

pharmaceutical preparations using the Sel-electrodes is comparable and ranged from 95.2 to 103.5% with RSD = 0.2–0.8%.

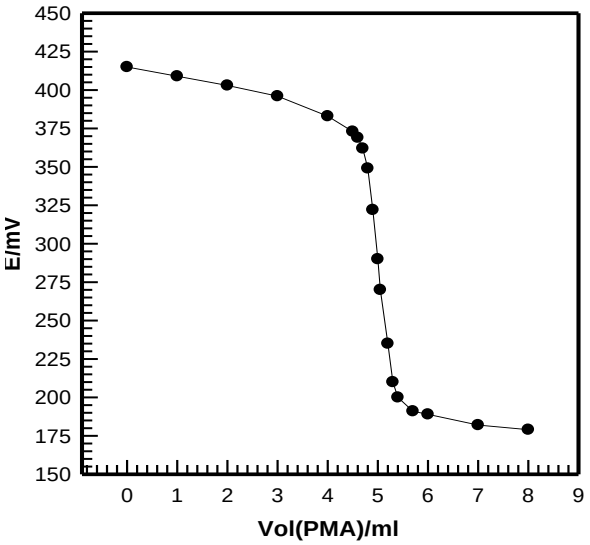


Figure 7. Potentiometric titration curve of 50 mL solution containing 33.56 mg SelCl with $1.0x10^{-2}$ M PMA solution and Sel-PMA (III) electrode.

Table 4. Determination of SelCl by applying the standard additions method.

		Sel-PMA (I)		Sel-PMA (II)		Sel-PMA (III)		Sel-PTA (I)		Sel-PTA (II)		Sel-PTA (III)	
Sample	Taken	Recovery	RSD[a]	Recovery	RSD[a]	Recovery	RSD[a]	Recovery	RSD[a]	Recovery	RSD[a]	Recovery	**RSD[a]**
	(mg)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	***(%)***
Pure solutions	6.71	99.2	0.7	100.9	0.4	97.8	0.6	98.5	0.4	95.2	0.6	97.4	**0.6**
	13.43	99.9	0.5	101.9	0.6	98.7	0.5	99.1	0.4	97.1	0.6	98.4	**0.5**
	20.14	101.8	0.3	103.6	0.7	100.0	0.4	98.8	0.5	97.4	0.6	98.2	**0.4**
	26.85	100.7	0.4	102.7	0.4	101.3	0.4	99.4	0.5	98.2	0.5	98.9	**0.5**
	33.56	101.2	0.6	102.1	0.3	99.9	0.4	100.2	0.5	99.8	0.4	99.7	**0.4**
Tonus® (5mg/ tablet)	6.71	98.5	0.5	98.6	0.6	98.2	0.5	97.2	0.8	96.5	0.5	98.8	**0.7**
	13.43	100.1	0.22	99.2	0.6	98.5	0.6	99.5	0.7	96.3	0.5	100.3	**0.4**
	20.14	102.4	0.4	100.4	0.8	97.6	0.6	101.7	0.6	98.7	0.5	99.1	**0.5**
	26.85	101.2	0.4	100.2	0.7	99.6	0.7	98.7	0.4	99.0	0.3	98.9	**0.3**
	33.56	103.5	0.6	101.4	0.6	98.3	0.5	100.6	0.6	99.2	0.4	99.6	**0.3**
Urine	6.71	98.9	0.3	101.7	0.5	97.7	0.6	98.3	0.5	96.2	0.4	98.9	**0.3**
	13.43	99.8	0.3	100.5	0.5	99.2	0.3	97.7	0.5	97.7	0.7	100.2	**0.3**
	20.14	101.1	0.4	99.2	0.3	102.1	0.5	100.5	0.4	98.2	0.3	101.4	**0.2**
	26.85	100.3	0.2	102.1	0.5	100.2	0.3	98.3	0.3	99.3	0.3	99.1	**0.2**
	33.56	99.5	0.2	101.1	0.4	101.2	0.2	99.3	0.2	99.8	0.3	100.3	**0.3**
Plasma	6.71	97.8	0.3	96.4	0.6	96.8	0.4	99.9	0.5	97.5	0.5	103.4	**0.6**
	13.43	99.7	0.4	97.9	0.6	98.3	0.5	100.5	0.4	97.9	0.4	103.5	**0.4**
	20.14	100.0	0.3	100.2	0.4	100.1	0.3	102.4	0.4	99.5	0.3	101.7	**0.4**
	26.85	100.2	0.2	99.4	0.3	99.3	0.4	99.2	0.3	98.2	0.4	101.4	**0.3**
	33.56	101.3	0.3	98.5	0.2	100. 1	0.3	101.4	0.2	98.6	0.4	100.1	**0.4**

[a] Relative standard deviation (four determinations).

Table 5. Determination of SelCl in pure solutions and pharmaceutical preparations applying the potentiometric titration method.

		Sel-PMA (I)		Sel-PMA (II)		Sel-PMA (III)		Sel-PTA (I)		Sel-PTA (II)		Sel-PTA (III)	
Sample	Taken	Recovery	RSD[a]	Recovery	RSD[a]	Recovery	RSD[a]	Recovery	RSD[a]	Recovery	RSD[a]	Recovery	**RSD[a]**
	(mg)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	***(%)***
Pure solutions	6.71	101.5	0.5	100.5	0.4	97.4	0.2	97.6	0.6	96.9	0.4	99.8	**0.3**
	13.43	99.3	0.6	99.3	0.5	103.3	0.3	99.5	0.5	101.1	0.3	100.7	**0.2**
	20.14	99.4	0.4	99.5	0.4	100.7	0.3	99.3	0.4	99.5	0.4	100.8	**0.3**
	26.85	100.6	0.42	99.8	0.4	99.6	0.2	101.2	0.4	101.0	0.2	102.1	**0.4**
	33.56	98.8	0.5	100.9	0.3	100.5	0.2	100.4	0.3	100.5	0.2	99.2	**0.3**
Tonus (5mg/ tablet)	6.71	96.7	0.3	99.0	0.3	101.0	0.4	99.8	0.4	99.5	0.6	95.5	**0.3**
	13.43	99.2	0.4	100.0	0.3	99.1	0.5	101.3	0.3	100.7	0.4	100.1	**0.3**
	20.14	101.1	0.6	100.2	0.3	101.5	0.5	100.2	0.3	99.3	0.4	99.7	**0.2**
	26.85	99.5	0.4	99.5	0.4	99.1	0.3	98.9	0.4	99.6	0.4	99.0	**0.6**
	33.56	100.7	0.5	100.9	0.4	99.7	0.3	99.3	0.5	99.7	0.3	100.2	**0.3**

[a] Relative standard deviation (three titrations).

Table 6. Statistical treatment of data obtained for the determination of SelCl using Sel-electrodes in comparison with the official methods.

	Sel-PMA(I)	Sel-PMA(II)	Sel-PMA(III)	Sel-PTA(I)	Sel-PTA(II)	**Sel-PTA(III)**
Pure solution						
X ± S.E[a]	100.6±0.5	102.2±0.5	99.6±0.4	99.2±0.4	97.5±0.5	**98.5±0.5**
Probability	0.10	0.025	0.10	0.01	0.001	**0.01**
F test[b]	1.08 (2.59)	0.88 (4.43)	0.77 (2.59)	0.77 (6.03)	1.12 (6.03)	**0.88 (6.03)**
Student t test	1.27 (1.40)	3.06 (3.18)	0.43 (1.64)	2.64 (2.89)	6.83 (12.94)	**2.26 (2.89)**
Tonus® tablets (5mg/tablet)						
X ± S.E[a]	101.1±0.4	99.9±0.7	98.4±0.6	99.5±0.6	97.9±0.4	**99.4±0.4**
Probability	0.10	0.50	0.01	0.10	0.01	**0.01**
F test[b]	0.64 (2.59)	1.80 (2.59)	1.39 (6.03)	1.59 (2.59)	0.71 (6.03)	**0.74 (6.03)**
Student t test	1.30 (1.39)	0.10 (0.26)	3.87 (4.54)	0.92 (1.64)	3.17 (4.54)	**2.36 (2.89)**
Urine sample						
X ± S.E[a]	99.9±0.3	100.9±0.4	100.1±0.4	99.6±0.2	98.2±0.4	**100.0±0.3**
Probability	0.50	0.10	0.50	0.05	0.05	**0.50**
F test[b]	0.34 (2.59)	0.77 (2.59)	0.38 (2.59)	0.23 (3.44)	0.41 (3.44)	**0.21 (3.62)**
Student t test	0.23 (0.26)	1.83 (1.87)	0.10 (0.26)	2.46 (2.92)	2.72 (2.92)	**0.05 (0.26)**
Plasma sample						
X ± S.E[a]	99.8±0.3	98.5±0.4	99.6±0.4	100.7±0.6	98.4±0.4	**102.0±0.4**
Probability	0.10	0.01	0.05	0.10	0.01	**0.025**
F test[b]	0.35 (2.59)	0.71 (6.03)	0.58 (3.44)	1.44 (2.59)	0.64 (6.03)	**0.67 (4.43)**
Student t test	0.32 (1.89)	2.33 (2.89)	1.43 (1.85)	1.23 (1.87)	5.03 (6.97)	**3.14 (4.30)**

[a]X±S.E.: average ± standard error.
[b]One tailed critical F-value.
N.B: for the official method (X±S.E.) = 99.3±0.5

The performance of the method was also assessed by calculation of the t- and F-values in comparison to the official method [4]. Mean values were obtained in a student's t- and F-test at 95%

confidence limits for corresponding degrees of freedom [39], and the results showed in table 6, that the calculated t- and F-values did not exceed the critical values.

Representative results of application of the standard additions method using Sel-electrodes are shown in table 4. While for urine and plasma spiked samples, the recovery values ranged from 96.2 to 103.5% with RSD =0.2-0.7%, where these data reflect the high accuracy and precision of the investigated electrodes.

In contrast to direct potentiometric measurements requiring careful calibrations of measuring cells, the potentiometric titration techniques offer the advantage of high accuracy and precision; although the cost of increased time and consumption of reagents used as titrants. Under the optimum conditions, the resulting titration curve is shown in Figure 7 with well-defined potential jumps, 150-600 mV, indicating the high sensitivity of the electrode. The results from table 5 reveal that, recovery values ranged from 95.5 to 103.0% with coefficient of variation ranging from 0.2 to 0.7%. The limit of detection of the studied electrodes (LOD), defined as the Sel concentration corresponding to the intersection of the extrapolation of the linear part of the calibration curve, ranged from 21.26 to 1.52 µg/L, while the limit of quantification (LOQ), defined as the last point corresponding to the intersection of the liner part of the calibration curve, was ranged from 1.52 to 20.36 µg/L for the studied electrodes.

4. CONCLUSIONS

In the present study, plastic membrane electrodes, carbon paste electrodes and carbon nanotubes modified electrodes were used for the simultaneous determination of SelCl in pure solution, tablets and biological samples. The carbon nanotubes modified paste electrodes investigations showed better potential response and faster response time compared to other electrodes and besides having longer life span compared to unmodified carbon paste electrodes; high sensitivity and selectivity, and very low detection limit with the ease of preparation and surface regeneration of the electrodes and reproducibility of the electrodes responses makes the proposed electrodes very useful for accurate determination of SelCl in pure solution, pharmaceutical preparations and in spiked plasma and urine samples.

ACKNOWLEDGMENTS
The authors would like to appreciate the efforts done by Dr. Emad Safwat (Production Manger of ACAPI Co., Badr City, Egypt) for providing the raw material of the drug and quality control information used in the assay and comparison with the proposed electrodes.

References

1. W.G. Ondo, C. Huntera, S.H. Isaacsonb, D.E. Silver, R.M. Stewart, J.W. Tetrud and A. Davidson, *Parkinsonism & Related Disorders* 17 (2011) 117-118.

2. Y.J. Zhao, H.L. Wee, W.L. Au, N. Luo and L.C.S. Tan, *Parkinsonism & Related Disorders* 17 (2011) 299-300.
3. C.A. Braga, J.L. Silva and D. Foguel, *J. Mol. Biol*. 405 (2010) 254-273.
4. P.D. Tzanavaras , D.G. Themelis , A. Zotou, J. Stratis, B. Karlberg, *J. Pharm. Biomed Anal*. 46 (2008) 670-675.
5. K. Nishida, S. Itoh, N. Inoue, K. Kudo and N. Ikeda, *J. Anal Toxicol*. 30 (2006) 232-7.
6. M. Katagi, M. Tatsuno, A. Miki, M. Nishikawa, K. Nakajima, *J. Chromatogr*. B 759 (2001) 125.
7. H. Mascer, B. Gud, C. Kikuta, J. Liq. *Chrom. & Related Tech*. 20 (1997) 797-809.
8. Y. Fujita, K. Takahashi, M. Takei, Y. Aoki, Y. Inoue and S. Endo, Yakugaku Zasshi 128 (2008) 1507-1512.
9. A.Kuriki, T. Kumazawa, C. Hasegawa, M. Kawamura, O. Suzuki and Sato K, *J. Chromatogr*. *B* 844 (2006) 283-291.
10. Y. Heo, Y. Whang, M. Kyo and L. Kong-Joo, *J. Chromatogr. B: Biomed. Appl*. 741 (2000) 221-230.
11. S. Juraj, S. Zdenek, B.A. Ingelse and K. Lemr, *J. Pharm. Biomed. Anal.* 14 (1996) 1089-1094.
12. N. El-Gohary, R.M. El-Nashar and H.Y. Aboul-Enien, *Anal. Lett*. 44 (2011) 241-257.
13. E. Hussien, F. Abdel-Gawad and Y.M. Issa, *J. Biochem. Eng*. 53 (2011) 210-215.
14. N.T. Abdel-Ghani and S.H. Hussein, *Anal. Lett*. 43 (2010) 582- 602.
15. Y. Wang, W.Z. Wei, X.Y. Liu, X.D. Zeng, *Michrochim. Acta* 160 (2008) 253-260.
16. M. Javanbakht, S.E. Fard, M. Abdouss, A. Mohammadi, M.R. Ganjali, P. Norouzi, L. Safaraliee, *Electroanal*. 20 (2008) 2023–2030.
17. M. Javanbakht, M.R. Ganjali, P. Norouzi, A. Hashemi-Nasa, A.R. Badei, *Electroanal.* 19 (2007) 1307–1314.
18. M. B. Gholivand and M. Torkashvand, *Talanta* 84 (2011) 905-912.
19. A.Ejhieh and N. Masoudipour, *Anal. Chim. Acta* 658 (2010) 68-74.
20. Balan, I. G. David, C. Mihailciuc, I. Stamatin and A. Ciucu, *J. Electroanal. Chem*. 654 (2011) 8-12.
21. M. Mazloum-Ardakani, H. Beitollahi, B. Ganjipour, H. Naeimi and M. Nejati, *Bioelectrochem.* 75 (2009) 1–8.
22. Jordi Riu, J.M. Pingarron and F.X. Rius, *Trends Anal. Chem*. 29 (2010) 939-953.
23. J. Li, A. Cassell, L. Delzeit, J. Han, and M. Meyyappan, *J. Phys. Chem*. B 106 (2002) 9299–9305.
24. R.N. Goyal, M. Oyama, V.K. Gupta, S.P. Singh, R.A. Sharma, *Sens. Actuators* B 134 (2008) 816–821.
25. G. Li, H. Xu, W.J. Huang, Y. Wang, Y.S. Wu, R. Parajuli, *Meas. Sci. Technol*. 19 (2008) 165-203.
26. B. Rezaei, S. Damiri, *IEEE Sens*. 8 (2008) 1523–1529.
27. E. Khaled, H.N. Hassan, G. Mohamed and A.A. Seleim, *Talanta* 81 (2010) 510-515.
28. B. Csoka, Z. Mekhalif, *Electrochim. Acta* 54 (2009) 3225.
29. E. Baumann, *Anal. Chim. Acta* 42 (1986) 127-132.
30. N.T. Abdel Ghani, R.M. El Nashar, A.A. Bioumy, *Anal. Lett*. 37 (2004) 3237-3254.
31. S.M. Ghoreishi, M. Behpour, M. Nabi, *Sens. Actuators* B 113 (2006) 963.
32. M.N. Abbas, E. Zahran, *J. Electroanal. Chem*. 576 (2005) 205.
33. G. Mohamed, T. Ali, M.F. El-Shahat, A. Al-Sabagh, M. Migahed and E. Khaled *Anal. Chim.Acta* 673 (2010) 79-87.
34. R.M. El-Nashar, M. S. Rizk, N. T. Abdel Ghani and S.M. Hamed, *J. Pharm. Chem*. 41 (2007) 49-56.
35. U. Oesch, D. Ammann and W. Simon, *Clin. Chem*. 38 (1986) 1448-1459.
36. N.T. Abdel-Ghani, S.H. Hussein, *J. Appl. Electrochem*. 40 (2010) 2077-2090.
37. H.A. Wagdy, R.M. El-Nashar, *Sensor Lett*. 8 (2010) 838-847.
38. R. M. El-Nashar, *J. Auto. Meth. Manag. Chem.*, Article ID 586310, 2008.

39. J. C. Miller and J. N. Miller, Statistics and Chemometrics for Analytical Chemistry, 4th edition, Ellis Horwood, Chichester, U.K, 2001.