ISSN 1061-9348, Journal of Analytical Chemistry, 2010, Vol. 65, No. 10, pp. 1035–1040. © Pleiades Publishing, Ltd., 2010.

ARTICLES

# Poly(aniline) Solid Contact Ion Selective Electrode for Udenafil[1]

**Won-Sik Han[a], Jang-Ki Kim[a], Koo-Chun Chung[b], Joo-Yeon Hong[c], Jong-Ki Hong[c], Jeong-Hoon Kim[d], and Tae-Kee Hong[a]**

[a] *Department of Chemistry, Hanseo University Seosan, Chungnam, 356-820 Korea*

[b] *Department of Chemistry, Konkuk University, Seoul, 143-701 Korea*

[c] *College of Pharmacy, Kyunghee University, Seoul, 130-701 Korea*

[d] *Research Laboratory, Dong-A Pharmaceutical Company Limited, Yongin, Kyunggi-Do, 446-905 Korea*

Received 1 July, 2009; in final form, March 16, 2010

**Abstract**—Udenafil is an oral agent for treating male erectile dysfunction. The poly(aniline) solid contact selective electrodes for udenafil have been fabricated from PVC cocktail solutions with three ion selective ion pairs. This solid contact electrode contains three layers of Pt/electro-conductive poly(aniline) polymer/PVC film with an ionophore with a thickness of $2.5 \pm 0.1$ mm. We compared the slopes of EMF responses and the response range of a solid contact electrode based on Udenafil-TmCIPB ion pair with those based on Udenafil-PMA and Udenafil-TPB ion pairs and showed that the response slopes were influenced by plasticizers. The EMF response slopes of Udenafil-TmCIPB-based solid contact electrodes equalled 58.0 mV/decade (at $20 \pm 0.2$°C) and their linear response dynamic ranges were $1.0 \times 10^{-2}$~$1.0 \times 10^{-5.85}$ M ($r^2 = 0.9984$). When electrodes with 6 different plasticizers based on Udenafil-TmCIPB were compared, as the dielectric constant of PVC plasticizer increased, so was the response slope at the same time. Having applied the electrodes to artificial serum directly, we could get same satisfactory results [Nernstian slope: 60.3 mV/decade, dynamic range: $1.0 \times 10^{-2}$~$1.0 \times 10^{-5.78}$ M ($r^2 = 0.9978$) in artificial serum]. Solid contact electrodes with Udenafil-TmCIPB have shown the best selectivity, reproducibility of EMF, long-term stability, and short response time (< 20 s).

**Key words**: solid contact electrodes, udenafil, poly(aniline)

**DOI:** 10.1134/S1061934810100084

Phosphodiesterase type 5 (**PDE5**) inhibitors are vasoactive drugs that have been developed for the treatment of erectile dysfunction [1]. PDE5 inhibitors act by blocking the degradation of cGMP, which is increased in the vascular smooth muscle cells in the endothelium by 1—arginine in the presence of NO synthase, leading to relaxation of the vessels [2]. It was reported that zaprinast enhances the endothelium—dependent, NO—mediated vasodilation in an intact lamb with experimental pulmonary hypertension [3]. Halcox et al. reported that sildenafil citrate, which was the first PDE—5 inhibitor approved for treating erectile dysfunction, dilated the epicardial coronary arteries, improved the endothelial dysfunction, and improved the physiologic coronary vasomotion in patients with coronary artery disease (**CAD**) [4, 5]. Udenafil (5-[2-propyloxy-5-(1-methyl-2-pyrollidinylethylamidosulphonyl)phenyl]-1-methyl-3-propyl-1,6-dihydro-7-H-pyrazolo(4,3-d)pyrimidin-7-one) is also a potent and selective PDE5 inhibitor developed by the Dong-A Pharmaceutical Company in Korea as an oral agent for treating male erectile dysfunction (Fig. 1). For these drugs, few reports appeared describing accurate spectrochemical, chromatographic and electroanalytical techniques for their quantification [6, 7]. However, most of these methods are expensive, suffer from lack of selectivity and require careful control of conditions and considerable time for routine analysis [8, 9]. Therefore, precise and simple methods for the quantification of udenafil in pharmaceutical preparations are required. Recent years have seen an upsurge of interest in the application of ion sensors in the field of medicinal analysis. These instruments provide fast, accurate, reproducible and selective determination of various species [10, 11]. Solid contact electrodes have especially great advantages of mechanical flexibility, possibilities of miniaturization and microfabrication. The solid membranes are easy to construct and better suited for multi-ion sensors because they can be miniaturized and are not restricted to one side of the electrode. Therefore, these are gaining popularity in medical, biotechnological, pharmaceutical and environmental fields [12]. The solid contact electrodes exhibit good performance, such as better stabilization of the base potential, reproducibility, selectivity, wide response range, and fast response time. We have recently developed and reported such solid contact electrodes for hydrogen ion and many other ions based on conducting polymers of poly(aniline) and poly(pyrrole) in PVC with various carriers [13, 14]. In the last paper, we described

[1] The article is published in the original.

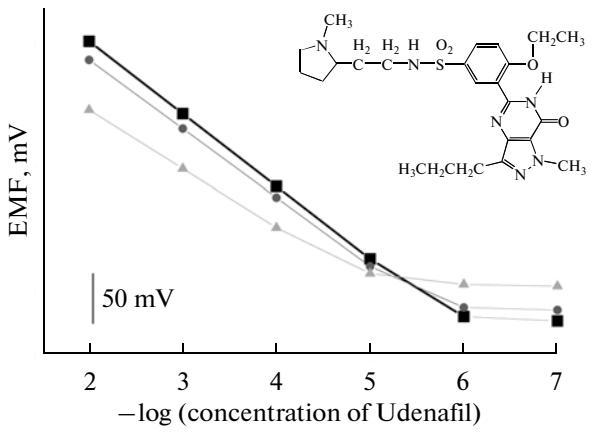


**Fig. 1.** Formula of udenafil and response characteristics of udenafil solid contact electrodes with various plasticizer in pH 4.5 acetate-buffered udenafil solution. ■, (Udenafil-TmCIPB) ion pair 0.050 : PVC 0.19 : NPOE 0.35 : KTpCIPB 0.001; ●, (Udenafil-PMA) ion pair 0.010 : PVC 0.19 : NPOE 0.35 : KTpCIPB 0.001; ▲, (Udenafil-TPB) ion pair 0.010 : PVC 0.19 : DOP 0.45 : KTpCIPB 0.001.

the application of two developed ion selective solid contact electrodes for udenafil determination in pharmaceutical preparations using the ion-association complex of udenafil with the electroactive phase containing sodium tetraphenylborate (**TPB**) or phosphomolybdic acid (**PMA**) in a poly vinyl chloride (**PVC**) matrix over a wide concentration range. The slopes of EMF responses showed, respectively, 55.0, 47.0 mV/decade, and the linear response dynamic ranges were $1 \times 10^{-2}$~$1 \times 10^{-5.73}$ M for PMA based solid contact electrodes and $1 \times 10^{-2}$~$1 \times 10^{-5.04}$ M for udenafil-TPB based solid contact electrodes [15]. The proposed methods are successfully applied for the determination of udenafil in the presence of other components.

In this work, we describe the poly(aniline) solid contact electrode with Udenafil-TmCIPB ionophore dissolved in *o*-nitrotoluene for udenafil ion detecting. Various plasticizers (DOS, NPOE, DOP, TEHP, DOA, DBP) were tested for best response. General physical properties of these electrodes such as responsibility, effect of interfering ions, response time, and stabilization time and the application of these properties to the analysis of an artificial serum were studied.

## EXPERIMENTAL

**Reagents.** Aniline and tetrahydrofuran (**THF**) were purified by vacuum distillation. For all experiments, analytical grade chemicals and doubly distilled and demineralized water were used. The membrane matrix high molecular weight poly(vinylchloride) (PVC, $n = 1$, 100), the anionic additive potassium tetrakis(4-chlorophenyl) borate (**KTpClPB**), the plasticizers 2-nitrophenyl-octylether (*o*-**NPOE**), tris(ethylhexyl)phosphate **(TEHP)**, bis(2-ethylhexyl)adipate **(DOA)**, dioctylphthalate (**DOP**), and bis(2-ethylhexyl)sebacate (**DOS**), the solvent THF, sodium tetraphenylborate (**TPB**), phosphomolybdic acid (**PMA**), and aniline were from Aldich Co.

**Polymerization** [16]. Electrochemical experiments were performed in a conventional cell with three electrodes. A saturated calomel electrode was used as the reference electrode and all potentials were recorded and reported with respect to this electrode. Platinum wires (1 mm in diameter, 50 mm in length) were used as the working and counter electrodes. Electro-polymerization was carried out at the one end of a platinum wire by cyclic voltammetry in $3.0 \times 10^{-2}$ M aniline and $6.0 \times 10^{-2}$ M HCl solution. Cyclic voltammograms were recorded using a potentiostat (EG & G 273A). For electrochemical polymerization of aniline, the potential was swept between 0.0 and 1.0 V at scan rate of 100 mV/s. The potential cycling was repeated up to 30 cycles and stopped at 1.0 V. After electrodeposition, the poly(aniline) was washed with distilled water and then dried for 24 h in an 80°C oven. Then the part of the Pt in Pt-poly(aniline) electrode was covered with a thermocontractive insulation tube.

**Preparation of cocktail solutions and fabrication of solid contact electrode.** Typical cocktail solution consists of ion-pair 0.010–0.100 : PVC 0.30–0.40 : plasticizer 0.50–0.70 : KTpCIPB 0.001–0.010. All components were dissolved in THF. The solid contact electrodes were produced by dipping the Pt–poly(aniline) electrode directly into the cocktail solution to coat it with a thin film. The resulting solid contact electrode contains three layers of Pt/electroconductive polymer/PVC film with an ionophore with a thickness of $2.5 \pm 0.1$ mm.

**EMF measurements.** The emf values were measured at $20 \pm 0.2$°C using a model 355 Ion-analyzer (Mettler-Toledo Ltd., England). In all experiments, the pH measurements of the sample solutions were determined with a Mettler-Toledo InLab 412 glass electrode. The external reference electrode was a double-junction calomel electrode Orion 90-20-00 (Orion Research, U.S.A.). The standard deviation arising from this equipment was < 0.1 mV for a single determination. Before use, the electrodes were conditioned in distilled water for at least 2 h.

**Measurements of stabilisation time and respons time** [17]. Time required for stabilization of the electrode was measured in $1.0 \times 10^{-3}$ M pH 4.5 acetate buffer udenafil solution with an ion analyzer (Orion Model 720A). The dry electrode was placed in udenafil-acetate buffer solution to attain a stable potential for 4 hours. Then 10.00 mL of $1.0 \times 10^{-2}$ M udenafil-pH 4.5 acetate buffer solution was added while the solution was vigorously stirred magnetically to measure the potential change and time required for the stabilization of the potential in terms of time required/unit concentration change. Electrode response was considered stable when $\Delta E/\Delta t$ became less than 0.1 mV/min.

**Udenafil standard sample solution.** A stock solution ($1.0 \times 10^{-2}$ M) of udenafil at pH 4.5 was prepared by dissolving 0.5167 g of udenafil in 100 mL of water adjusted with acetate buffer (pH 4.5) or dilute NaOH and/or HCl. Dilute solutions ($1.0 \times 10^{-2} - 1.0 \times 10^{-6}$ M) of udenafil were freshly prepared by diluting the stock solution with doubly distilled water and acetate buffer of pH 4.5.

**Synthesis of ion-pair [18].** Stock solution ($2.0 \times 10^{-2}$ M) of udenafil were prepared by dissolving an accurate weight of the reagent in 20 mL of pH 4.5 acetate buffer solution. Dissolve $2.0 \times 10^{-2}$ M of ammonium tetrakis-*m*-chlorophenyl borate (TmCIPB) in 20 mL of pH 4.5 acetate buffer solution and mix the resulting two solution. Extract the resulting heavy precipitate of (Udenafil-TmCIPB) into 10.00 mL of *o*-nitrotoluene. Filter the organic layer through a filter paper containing 1–2 g of anhydrous sodium sulfate. The filtrate should be clear and light yellow. This solution is approximately $2.0 \times 10^{-2}$ M in (Udenafil-TmCIPB) and is almost saturated.

The ionic exchangers, (Udenafil-PMA) and (Udenafil-TPB), were prepared by a precipitation reaction between 100 mL of a $2.0 \times 10^{-2}$ M udenafil solution and 100 mL of a $2.0 \times 10^{-2}$ M PMA solution or 100 mL of a $2.0 \times 10^{-2}$ M NaTPB solution. These precipitation products were (Udenafil-PMA) and (Udenafil-TPB) ion exchangers, respectively. The resulting precipitates were filtered, thoroughly washed with water, dried, and kept in a dark flask inside a desiccator to prevent alterations caused by light and humidity.

**Selectivity of the developed sensors.** Aliquots (10 mL) of $1.0 \times 10^{-3}$ M udenafil solution were adjusted to pH 4.5 with acetate buffer the udenafil sensor was immersed in the test solution and the potential was measured. The potentials of $1.0 \times 10^{-3}$ M solutions of the interferents adjusted to pH 4.5 were measured. The selectivity coefficients $K^{\text{pot}}_{\text{Udenafil, M}}$ were determined employing separate solution method (**SSM**) with the rearranged Nicolsky equation

$$\log K^{\text{pot}}_{\text{Udenafil, M}} = (E_1 - E_2)/S + (1 + z_1/z_2) \times \log(a),$$

where, $E_1$ is the potential measured in $1.0 \times 10^{-3}$ M udenafil, $E_2$ the potential measured in $1.0 \times 10^{-3}$ M of the interfering compound, $z_1$ and $z_2$ are the charges of the udenafil and interfering species M, respectively, and $S$ is slope of the electrode calibration plot.

## RESULT AND DISCUSSION

In Fig. 1, we compared the Nernstian slopes and response ranges of solid contact electrode based on Udenafil-TmCIPB ion pair with those of Udenafil-PMA and Udenafil-TPB ionophore. The electrodes based on Udenafil-TmCIPB ion pair showed the best Nernstian slope and response range, their linear dynamic ranges being $1.0 \times 10^{-2} \sim 1.0 \times 10^{-5.85}$ M ($r^2 =$ 0.9984) and the Nernstian slopes 58.0 mV/decade (at 20 ± 0.2°C). The composition of this solid contact electrode based on Udenafil-TmCIPB ionophore was Udenafil-TmCIPB ion pair 0.050 : PVC 0.190 : NPOE 0.350 : KTpCIPB 0.001. However, it appeared that remaining two electrodes compared to the electrode based on Udenafil-TmCIPB ionophore had decreased Nernstian slopes and reduced response ranges. The linear dynamic range and Nernstian slope of solid contact electrodes based on Udenafil-TPB ionophore was $1.0 \times 10^{-2} \sim 1.0 \times 10^{-5.04}$ M and 47.0 mV/decade ($r^2 =$ 0.9981) and those of the electrode based on Udenafil-PMA ionophore was $1.0 \times 10^{-2} \sim 1.0 \times 10^{-5.73}$ M and 55.0 mV/decade ($r^2 = 0.9985$). The electrode based on Udenafil-TmCIPB ion pair without any liphophilic additives, such as KTpCIPB, showed decreased nernstian slope and response range, its linear dynamic range was $1.0 \times 10^{-2} \sim 1.0 \times 10^{-4.0}$ M and Nernstian slope showed 48.6 mV/decade (at 20 ± 0.2°C). Solid contact electrodes based on Udenafil-TmCIPB ion pair with plasticizers besides other than NPOE had decreased Nernstian slopes and reduced response ranges. [DBP (−53.0 mV/decade, $1.0 \times 10^{-2} \sim 1.0 \times 10^{-5.0}$ M), DOP (−49.0 mV/decade, $1.0 \times 10^{-2} \sim 1.0 \times 10^{-5.0}$ M), DOA (−42.0 mV/decade, $1.0 \times 10^{-2} \sim 1.0 \times 10^{-5.3}$ M), TEHP (−32.0 mV/decade, $1.0 \times 10^{-2} \sim 1.0 \times 10^{-5.8}$ M), DOS (−46.7 mV/decade, $1.0 \times 10^{-2} \sim 1.0 \times 10^{-5.4}$ M)].

Potentiometric selectivity $-\log K^{\text{pot}}_{\text{Udenafil, M}}$ of Udenafil-PMA, Udenafil-TPB, Udenafil-TmCIPB based solid contact electrode was measured by the separate solution method [19]. The obtained results are represented in Fig. 2. We were able to observe a reasonable selectivity towards udenafil in the presence of many nitrogenous compounds such as amines, amino acids, and some inorganic cations. The results showed no serious interference ta a number of pharmaceutical excipients, diluents and active ingredients commonly used in the drug formulations (e.g. glucose, lactose, maltose, and mannitol) in concentration 10–100 times higher than udenafil. The selectivity studies of the *o*-NPOE-plasticized Udenafil-TmCIPB solid contact electrodes containing excluder KTpCIPB in its chemical composition showed better results over the Udenafil-TPB or Udenafil-PMA-based electrodes under the same conditions of operation. The plasticized PVC membrane solid contact electrodes behave differently from liquid membrane sensors. Effectively, the ion exchange sites are hardly mobile. Therefore the coefficient $-\log K^{\text{pot}}_{\text{Udenafil, M}}$ of such system is given by the equation:

$$-\log K^{\text{pot}}_{\text{Udenafil, M}} = \log U_{\text{udenafil}} + \log K_{\text{udenafil}} - \log U_{\text{M}} - \log K_{\text{M}},$$

where $U_{\text{udenafil}}$ and $U_{\text{M}}$ are the mobilities of udenafil and the interfering species in the membrane phase, and $K_{\text{udenafil}}$ and $K_{\text{M}}$ are the molar distribution coefficients of udenafil and the interfering ions between the aque-

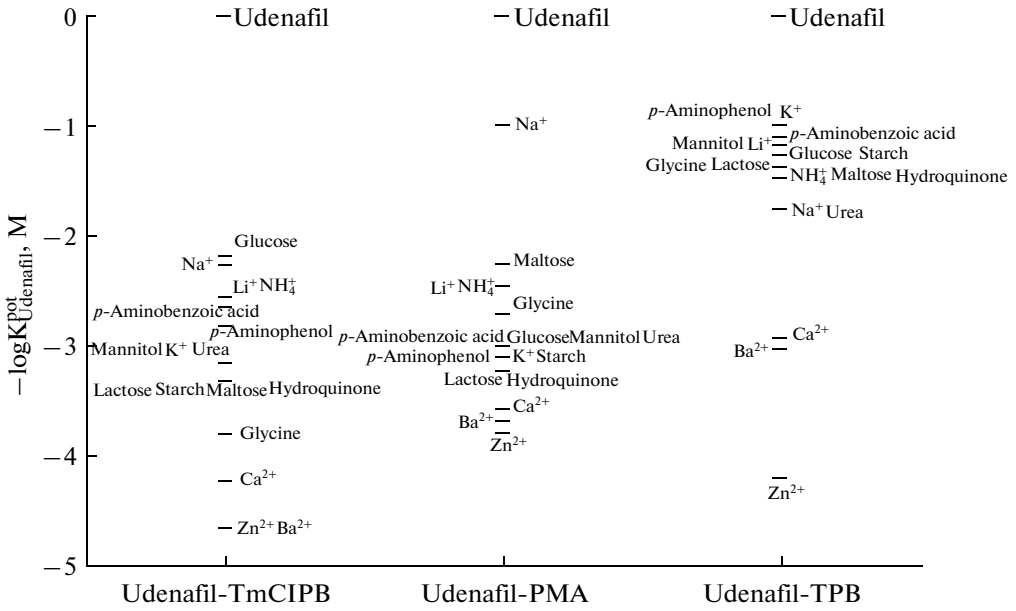


**Fig. 2.** Selectivity coefficients for udenafil of solid contact electrode based on optimised PVC membrane with three ion pair in various interference solutions.

ous phase and the PVC membrane [20]. In the PVC membrane the ions mobilities are restricted. Mobilities are approximately the same for all counter-ions when they are complexed with long chain complexing agents [21]. Thus, the selectivity was related to the partition coefficients of udenafil and the interfering ion between the membrane and the aqueous phase. Eventually, the mobilities of various ions and purtition coefficients were related with the mature of the plasticizer in PVC phase of solid contact electrodes. In Fig. 3, when six solid contact electrodes with different plasticizers based on Udenafil-TmCIPB ion pair were compared, there was not any tendency in the dynamic range as dielectric constant increased. However, as dielectric constant increased, so was the Nertstian slope. The solid contact electrodes based on Udenafil-TmCIPB which used NPOE plasticizer (dielectric constant of about 24) showed the best Nernstian slope, and those using another plasticizer as DBP (6.4), DOP (5.1), DOS (4.6), DOA (about 4.0), TEHP (about 4.0) had lower Nernstian slope and narrower dynamic range. According to the increase in the dielectric constant of plasticizers, the Nernstian slope of solid contact electrode increases. The tendency of this type of electrodes is that the dielectric constant of plasticizer and liphophilicity of KTpCIPB in PVC layer reduces the membrane resistance by reducing the activation barrier at the PVC outer surface—sample solution interface and increases the mobility of udenafil between the PVC outer surface and the sample solution. So, solid contact electrodes based on Udenafil-TmCIPB plasticized with *o*-NPOE containing KTpClPB showed better recovery precision, response time and less standard deviation than solid contact electrodes with other plasticizers or with no KTpCIPB at all.

For the solid contact electrode based on Udenafil-TmCIPB ionophore, the stability of emf measurements was assessed in the $1.0 \times 10^{-3}$ M pH 4.5 acetate buffered udenafil standard solution. Within first 600 s, the measured emf value decreased rapidly, and after 600 s, it increased. However, before 1800 s, it stabilized, the change of the emf being under 1 mV. So, before using the electrode, we had to condition all electrodes in distilled water or $1.0 \times 10^{-3}$ M pH 4.5 acetate buffered udenafil standard solution at least 30 min. As shown in table, response time of the electrodes obtained by injection of 10 mL of $1.0 \times 10^{-2}$ M udenafil solution into pH 4.5 acetate buffered $1.0 \times 10^{-3}$ M udenafil standard solution was less than 20 s. The reproducibility of emf measurements with the electrode was checked by alternating measurements (1 min each) on two pH 4.5 acetate-buffered udenafil standard solutions of $1.0 \times 10^{-2}$ M and $1.0 \times 10^{-3}$ M, respectively (25 ± 1°C). The standard deviation in the measured emf differences was ±0.5 mV ($n = 5$) for the $1.0 \times 10^{-2}$ M and ±1.1 mV for the $1 \times 10^{-3}$ M udenafil standard solution. In the pH range of pH 4.3~7.0, the potential was stable regardless of the hydrogen ion concentration (Fig. 4), compared to the electrodes based on a different ion pair such as [Udenafil-PMA, Udenafil-TPB], the Electrode based on Udenafil-TmClPB had the best result in stabilization time, response time and reproducibility. As expected from the selectivity data given, above, there is no interference from containing in electrolytes of artificial serum, physiologically relevant various ions. In artificial serum, the Nernstian slope of these electrodes

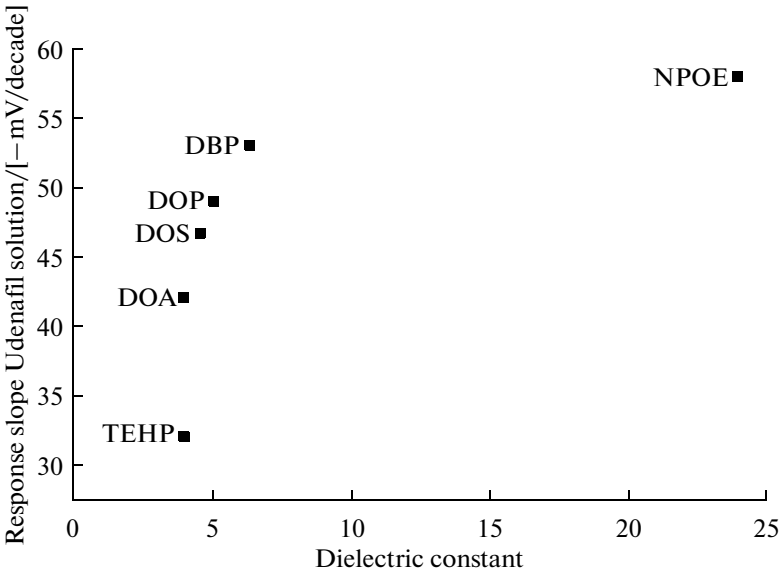


**Fig. 3.** Variation of response slope of udenafil solid contact electrode with various plasticizers in pH 4.5 acetate buffered udenafil solution.

showed 60.3 mV/decade (20 ± 0.5°C) but the dynamic range of these electrodes showed minor decrease to $1.0 \times 10^{-2}$~$1.0 \times 10^{-5.78}$ M ($r^2 = 0.998$). Measured results in artificial serum are almost the same as those measured in acetate-buffered and Tris-buffered udenafil solutions decrease in the Nernstian slope is considered to be the interference effect of inorganic ions such as $Ca^{2+}$. Thus, the slope does not seem to be affected by abundant interfering ions existing in human blood.

***

The solid contact electrodes for udenafil have been fabricated from PVC cocktail solutions with ion selective Udenafil-TmCIPB, Udenafil-PMA and Udenafil-TPB ion pairs. In these electrodes, solid contact electrodes with Udenafil-TmCIPB ionophore have shown wide detection range, the best response slope, selectivity, reproducibility of e.m.f., long-term stability, and response time (< 20 s). The slope of EMF

Response characteristics of poly(aniline) solid contact electrodes based on different ion pair

| Ion pair | Detection Limit, (M) | Stabilization Time, (min) | Response Time, (s) | Reproducibility in $10^{-2}$ M udenafil solution, (mV) | Reproducibility in $10^{-3}$ M udenafil solution, (mV) | Stability range in pH sample solution |
|---|---|---|---|---|---|---|
| Udenafil-TPB | $1 \times 10^{-2}$~$1 \times 10^{-5.04}$ | 30 | 20 | ±0.5 | ±1.1 | 4.3~7.0 |
| Udenafil-PMA | $1 \times 10^{-2}$~$1 \times 10^{-5.73}$ | 45 | 60 | ±1.2 | ±1.5 | 5.0~8.0 |
| Udenafil-TmClPB | $1 \times 10^{-2}$~$1 \times 10^{-5.85}$ | 45 | 60 | ±1.3 | ±1.8 | 4.0~6.0 |

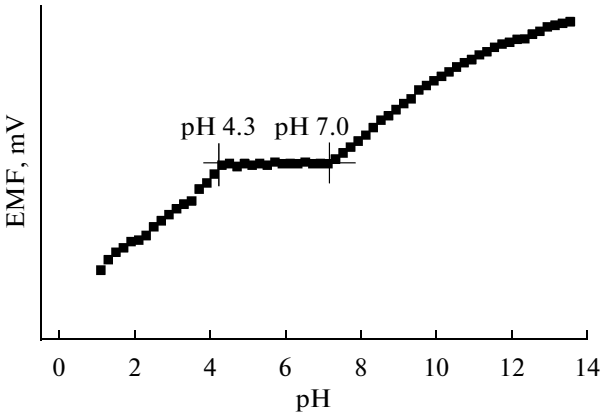


**Fig. 4.** The stabilization range of udenafil solid contact electrodes in Tris-buffered solution.

response for Udenafil-TmCIPB based solid contact electrodes with NPOE plasticizer was 58.0 mV/decade and the linear dynamic ranges were $1.0 \times 10^{-2}$~$1.0 \times 10^{-5.85}$ M ($r^2 = 0.998$). When electrodes with 6 different plasticizers based on Udenafil-TmCIPB were compared, the response slope increased with the dielectric constant of PVC plasticizer. When it was applied directly to artificial serum, same satisfactory results were obtained, [nernstian slope : 60.3 mV/decade, dynamic range $1.0 \times 10^{-2}$~$1.0 \times 10^{-5.78}$ M ($r^2$ = 0.9978)].

## REFERENCES


1. Oh, T.Y., Kang, K.K., Ahn, B.O., Yoo, M., and Kim, W.B., *Arch. Pharm. Res.*, 2000, vol. 223, no. 5, p. 471.
2. Kukreja, R.C., Ockaili, R., Salloum, F., Yin, C., Hawkins, J., Das, A., and Xi, L., *Mol. Cell Cardiol.*, 2004, vol. 36, no. 2, p. 165.
3. Fineman, J.R., Chang, R., and Soifer, S.J., *Am. J. Physiol.*, 1991, vol. 261, no. 5, H1563.
4. Halcox, J.P., Nour, K.R., and Zalos, G., *J. Am. College Cardiol.*, 2002, vol. 40, no. 7, p. 1232.
5. Halcox, J.P., *Life Sci.,* 2006, vol. 78, p. 1211.
6. Cooper, J.D.H., Muirhead, D.C., Taylor, J.E., and Baker, P.R., *J. Chromatogr.*, 1997, vol. 701, p. 87.
7. Liu, Y.M., Yang, H.C., and Miao, J.R., *Yaowu–Fenxi–Zazhi*, 2000, vol. 20, p. 161.
8. Dinesh, N.D., Nagaraja, P., Gowda, N.M., and Kanappa, K.S., *Talanta*, 2002, vol. 57, p. 757.
9. Amin, A.S. and El-Beshbeshy, A., *Microchim. Acta,* 2001, vol. 137, p. 63.
10. Budnikov, G.K., *Zhurn. Anal. Khim.*, 2000, vol. 55, no. 11, p. 1125 [*J. Anal. Chem.* (Engl. Transl.), vol. 55, no. 11, p. 1014].
11. Stefan, R.I., Bailulesu, G.E., and Aboul-Enein, H.Y., *Crit. Rev. Anal. Chem.*, 1997, vol. 21, p. 307.
12. Blackbum, G. and Janata, J., *J. Electrochem. Soc.*, 1982, vol. 129, p. 2580.
13. Han, W.S., Park, M.Y., Cho, D.H., Hong, T.K., Lee, D.H., Park, J.M., and Chung, K.C., *Anal. Sci.,* 2001, vol. 17, p. 727.
14. Han, W.S., Yoo, S.J., Kim, S.H., Hong, T.K., and Chung, K.C*., Anal. Sci.*, 2003, vol. 19, p. 357.
15. Han, W.S., Kim, J.K., Shim, Y.S., Park, J.H., Park, C.K., Hong, K.H., and Hong, T.K., *J. Korean Soc. Environ. Anal.*, 2007, vol. 10, no. 4, p. 209.
16. Yuan, R., Chai, Y.Q., Shen, G.L., and Yu, R.Q., *Talanta*, 1993, vol. 40, p. 1255.
17. Cagodan, A., Gao, Z., Lewenstam, A., and Ivaska, A., *Anal. Chem.*, 1992, vol. 64, p. 2496.
18. Efstanthiou, C.E., Diamandis, E.P., and Hadjiioannow, T.P., *Anal. Chim. Acts*, 1981, vol. 127, p. 173.
19. Ma, .S. and Hassan, S.S.M., *Organic Analysis Using Ion Selective Electrodes*, London: Academic, 1982.
20. Othmana, A.M., Rizk, N.M.H., and El-Shahawi, M.S., *Anal. Chim. Acta*, 2004, vol. 515, p. 303.
21. Eiseman, G., *Anal. Chem.*, 1968, vol. 40, p. 310.