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Potentiometric determination of alfuzosin hydrochloride in pharmaceutical preparations and biological fluids using modified carbon paste electrodes

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Abstract

The performance characteristic of sensitive modified carbon paste electrodes (MCPE) was suggested for alfuzosin hydrochloride (ALFHC) determination in its pure, pharmaceutical preparations and biological samples. Various experimental conditions namely materials types that used to prepare the working electrodes (plasticizer), pH, titrant, interfering ions and life time were studied. MCPE gave suitable response to ALFHC over pH range 2.9 – 6.7 for electrode (I) and 2.9-7.7 for electrode (II). ALFHC selectivity relative to different potential interfering species was reported. The MCPEs were used over a period of 3 months with a good reproducibility. The studied sensors were successfully applied to determine ALFHC in its pharmaceutical preparations and biological fluid samples. The obtained results are compared with the official method.

Keywords: Modified carbon paste electrodes, Alfuzosin hydrochloride, Biological samples
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1. Introduction

Alfuzosin hydrochloride (ALFHC, Fig. 1) belongs to α1-adrenoreceptor blocker which used in the treatment of urinary obstruction symptoms caused by benign hyperplasia of prostate and has been tried in the hypertension treatment. It is a quinazoline derivative which reduces the contractions tone of the bladder base, prostate and proximal urethral smooth muscle, performing as a competitive and selective α1-adrenoceptors antagonist with direct vasodilator properties [1, 2]. It is considered as first line therapy for treatment of non-complicated mild to moderate benign prostatic hyperplasia symptoms, as it gives sustained and rapid symptom relief irrespective of prostate size [3-6].

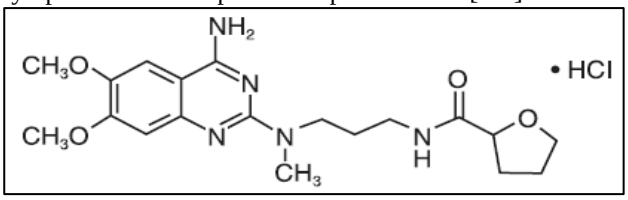

Fig. (1): Structural formula of alfuzosin hydrochloride.

Recent studies reported that alfuzosin hydrochloride is also used for urinary bladder dysfunction in patients who suffered from nephrotuberculosis [7, 8]. Chemically, alfuzosin hydrochloride is known as N-{3-[(4-Amino-6,7-dimethoxyquinazolin-2-yl(methyl)amino]propyl}-tetrahydro-2-furamide hydrochloride [9]. Several determination methods were proposed for alfuzosin hydrochloride in pharmaceutical preparations including RP-HPLC [9-13], HPLC and HPTLC [14, 15], conductometry [16], titrimetry [17], colorimetry [18], spectrophotometry [19-26] and voltammetry [27]. Alfuzosin hydrochloride was also determined in biological samples by HPLC [28], spectrophotometric [25] and voltammetric methods [27, 29]. Most of these mentioned methods are expensive, very complex and/or time-consuming. On the other hand, potentiometric sensors applications in biomedical and pharmaceutical analysis have been advocated [30]. The approach provides simple, rapid, and selective technique for many drugs determination [31–36]. Among these techniques, potentiometric determination method using several carbon paste electrodes was selected for determination of ALFHC which is the aim for this study. Potentiometric detection that based on ion-selective electrodes (ISEs), provides a group of advantages such as simple instrumentation, fast response, ease of procedures and preparation, reasonable selectivity, wide dynamic range and low cost [37]. The aim of this present investigation is to provide simple, selective, cost effective, accurate and fast for the ALFHC determination.

In this work, carbon paste potentiometric sensors were introduced for ALFHC selective determination in pharmaceutical preparations and biological samples. This method is based on the formation of ion-pair between ALFHC and sodium tetraphenyl borate as an electroactive material using tricresylphospate (TCP) as plasticizer in ALFHC matrix. These sensors are useful as indicator electrodes in potentiometric titrations of ALFHC in its pure preparations, tablet and biological fluids (serum and urine) samples.

2. Experimental

2.1. Reagents and materials

Alfuzosin hydrochloride (ALFHC) was kindly provided, as a gift, from Eva Company for

Pharmaceutical Industry, Giza, Egypt. A pharmaceutical preparation Prostetrol (Each tablet contains 10 mg of alfuzosin) was supplied also from Eva Company. *o*-Nitrophenyloctylether (o-NPOE) was supplied from Fluka (Switzerland), while dioctylphthalate (DOP) and dibutylphthalate (DBP) were supplied from BDH. Tricresylphosphate (TCP) and graphite powder (synthetic 1–2 μm) were supplied from Aldrich (USA). Sodium tetraphenylborate (NaTPB), ammonium reineckate (RN; $NH_4(Cr(NH_3)_2(SCN)_4).H_2O$), phosphotungstic acid (PTA) and acetone were purchased from Fluka (Switzerland). Phosphomolybdic acid (PMA; $H_3[PMo_{12}O_{40}$) was purchased from Aldrich (USA). Lactose, glucose, sucrose, starch, sucrose, chloride salts of potassium, iron, calcium, sodium, chromium, copper and aluminium were used as interfering materials and they were purchased from El-Nasr Company, Egypt. All solutions were prepared using bi-distilled water.

2.2. Apparatus

Laboratory potential measurements were performed using HANNA pH meter model 211 (Romania). Silver-silver chloride double -junction reference electrode (Metrohm 6.0222.100) in conjugation with different drug ion selective electrodes was used. Digital burette was used for the measurement of the drug under investigation. Automatic pipettes Socorex Swiss (50–200 μL and 200–1000 μL) were used to measure the very small volumes whereas glass micropipettes were used to measure the large volumes. Prior to analysis, all glass wares used were washed carefully with distilled water and dried in the oven before use.

2.3. Pharmaceutical preparations

ALFHC was prepared by dissolving the appropriate amount from drug (prostetrol tablets) in a definite volume of bi-distilled water to get the required concentration. Other solutions were prepared by serial dilution from stock solution.

2.4. Preparation of carbon paste electrodes

Carbon paste electrodes were prepared by mixing carbon powder (250 mg) and plasticizer (0.1 ml of DOP, TCP, DBP or o-NPOE) with different amounts (5 –20 mg) of IPs (ALF-TPB) in MCPE. This mixture was carried in the mortar until this mixture achieved homogenization. The obtained paste was then packed firmly into the hole of the electrode body [38]. The surface of the resulting carbon paste electrode was polished using a filter paper to obtain shiny fresh working surface and rinsed carefully with double distilled water [39].

2.5. Potentiometric titration of drug in pure solution

NaTPB solution (10^{-2} mol/L) was prepared by dissolving an accurately weighed amount of it in de-ionized water and completed to the desired volume with water. The resulting solution was standardized. A fresh solution of ALFHC (10^{-2} mol/L) was prepared by dissolving the accurately weighed amount of the drug in 100 mL deionized water. NaTPB was used as titrant in the potentiometric titration of the drug under investigation. The titration process was monitored potentiometrically using the different fabricated electrodes where the potential readings were plotted against the volume added of the titrant to estimate the equivalence points. The first derivatives of the titration curves were treated with origin plotting program.

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2.6. Potentiometric titration of drug in pharmaceutical samples

Aliquots of ALFHC solutions were transferred to 10 mL beaker. The content of ALFHC was determined via potentiometric titration with standard NaTPB solutions using the different CPEs as working electrodes.

2.7. Potentiometric titration of drug in serum and urine samples

Phosphate buffer was added to urine or serum samples dropwise until a pH=4.0 is obtained. 5 mL of the pH-adjusted urine or serum was transferred into four small separating funnels, and then to each was added 5 mL of different concentration standard drug solutions, followed by the addition of 20 mL toluene for urine and 20 mL diethyl ether for serum samples, respectively. After shaking each funnel for 5 min, the aqueous layer was transferred to a centrifuge tube. Centrifuged for 2 min at 1500 rpm, then transferred to a 50 mL volumetric flask and the solution diluted with de-ionized water to the appropriate volume. The procedure described above was applied.

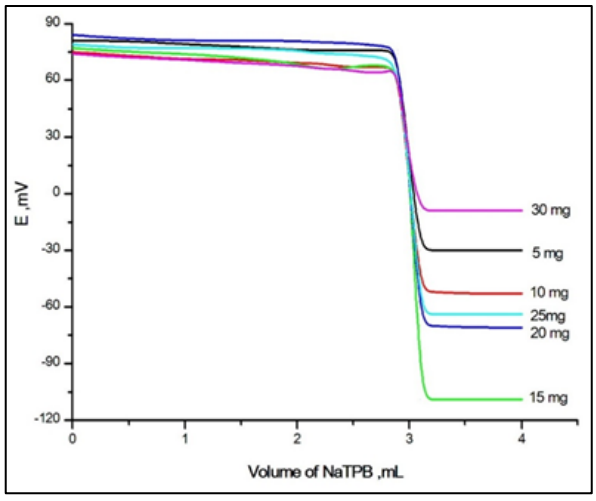
3. Results and discussion

3.1. Elemental analysis

It is known from the previous reports [40] that the isolated solid ion-pair has a white color and is characterized using elemental analysis which indicates the formation of 1:1 [ALFHC]: [TPB] ion pair with calculated %C=74.7, %H=6.7, %N=9.9 and found %C=75.2, %H=6.6 and %N=10.1 .

3.2. Effect of the ion-pairs content

Since the electrode performance affected by the ion pairs content, so the amount of the electro-active material in the electrode matrix was studied that should be sufficient to chemical equilibrium at the electrode/solution interface that is responsible for the electrode potential by achieving reasonable ionic exchange (selective extraction of the target ion). If such material was present in excess, over saturation occurred in the membrane network, hindering the ionic exchange process and leading to unsatisfactory performance.



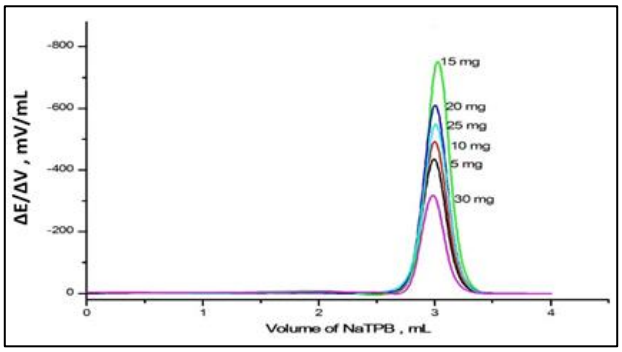


Fig (2): Effect of ALF-TPB content on the performance of CPEs in the potentiometric titration of 3mL of 10^{-2} mol/L ALFHC with 10^{-2} mol/L NaTPB.

3.3. Effect of the plasticizer type

The CPE sensitivity and selectivity can be affected by the plasticizer polarity. Using these electrodes as indicator electrodes to monitor the potentiometric titration based on IP formation, the potential break magnitude and the inflexion point sharpness of the titration curve is predetermined by the plasticizer polarity as a result of higher extractability of the IP into the plasticizer [31–34]. The influence of the plasticizer on the CPE performances has been studied as the electrode plasticized with o-NPOE, DBP, DOP, and TCP. It is clear from Fig. 3 that, TCP and DBP show the highest total potential change (173 ±1.15 and 156±0.57 mV, respectively).

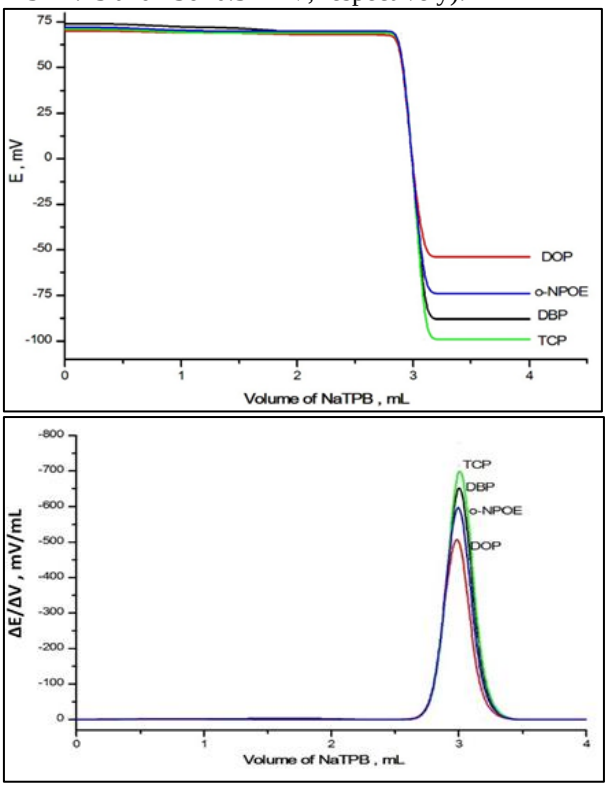


Fig. (3): The effect of plasticizer type on the MCPE performance in the potentiometric titration of 3 mL of 10^{-2} mol L^{-1} ALFHC with 10^{-2} mol L^{-1} NaTPB

3.4. Effect of pH

The electrode response for ALFHC solution was tested at different pH values (pH 1–11). The pH value was adjusted by adding very small volumes of HCl and/or NaOH solution (0.1–1 mol L^{-1} of each) to ALFHC solution, and the potential of the electrodes was plotted against the pH of solution. The results obtained showed that the electrodes response was pH independent in the pH range of 2.9 – 6.7 for electrode (I) and 2.9-7.7 for electrode (II). The decrease in mV readings at pH < 3 may be due to hydronium ion interference. At higher pH values (pH > 9.0), free-base precipitates in the test solution and consequently, the concentration of unprotonated species gradually increased. As a result, lower e.m.f. readings were recorded as shown in Figure 4.

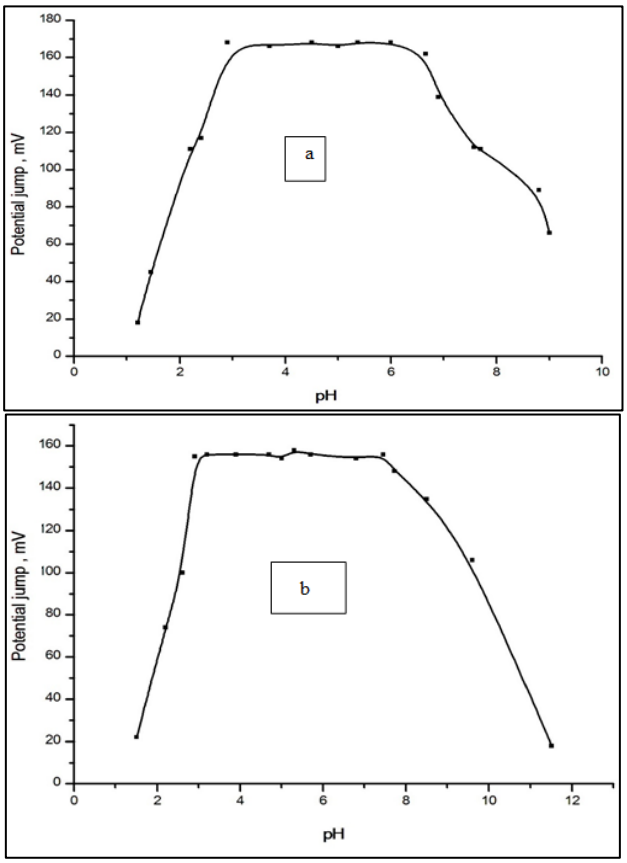


Fig (4): Effect of pH of the test solution on the performance characteristics of (a) electrode (I) and (b) electrode (II).

3.5. Selectivity

Selectivity is an important characteristic, which defines the nature of the device and the range to which it may be successfully employed. The selectivity of the ion selective electrodes under consideration were also, investigated with respect to some cations and many nitrogenous compounds. The selectivity of the proposed ion selective electrodes was determined against a number of different cations and many nitrogenous compounds. The data given for the tested species clearly indicated that, the proposed electrodes were fairly selective to alfuzosin over different tested cations and nitrogenous compounds. So, the studied common cations and nitrogenous compounds would not significantly disturb the determination of ALFHC.

6. Life time

The fabricated CPE performance tested by titrating ALFHC with NaTPB on different intervals ranged from one day to 110 days and the measurement of the total

potential change, potential break at the end point and end point are recorded daily. The change in the potential break at the end point reached to 29% after 110 days for electrode (I) and 22% after 91 days for electrode (II). So that, the two electrodes can be used for over the period of three months. This shows that the fabricated sensors have good mechanical durability.

3.7. Analytical applications

The optimized sensors were successfully used for the ALFHC potentiometric determination by using the potentiometric titration method and the obtained results were summarized in Table (1). ALFHC drug determination in pharmaceutical preparation (Prostetrol) was performed on the prepared sample by direct potentiometry with conventionally prepared electrodes. The averages of the concentrations obtained for each sample and the corresponding standard deviations were shown in Table (1). In order to estimate the quality of the results, recovery values were also determined and were presented in the same table. Statistical evaluation of the results of analysis of ALFHC in pharmaceutical preparation by the proposed electrodes and the official method [41] showed that there was no significant difference between the official and reported method (Table 1). Therefore, the studied sensor can be used successfully for the routine analysis of the ALFHC drug in quality control laboratories.

The studied electrodes have been successfully used for the potentiometric determination of ALFHC in bulk drug solutions and in its pharmaceutical preparations. Three replicate determinations at different concentration levels were carried out to test the precision of methods. Results obtained were compared with the official method Table (2). The data reported in Table (2) indicated that results obtained by the two reported methods are in good agreement; however, the proposed method is more selective, rapid, simple and less time consuming. In addition, the proposed methods were used for determination of the studied drug in pharmaceutical preparations Table (2).

Table (1): Potentiometric determination of ALFHC in its pure samples using MCPE electrodes.

Electrode	Taken ($mg\ mL^{-1}$)	MCPE			Official method [41]		
		Found ($mg\ mL^{-1}$)	Recovery (%) ±SD	RSD %	Found ($mg\ mL^{-1}$)	Recovery (%) ±SD	RSD %
I	0.426	0.425	99.77±0.006	1.41	0.43	100.9±0.0048	1.12
	0.043	0.042	97.67±0.0004	0.95	0.043	100.0±0.0005	1.16
	0.0086	0.009	104.7±0.0002	2.22	0.0084	97.67±0.0001	1.19
		0.423	99.30±0.006	1.42			
		0.042	97.67±0.0004	0.95			
II		0.0087	101.2±0.0001	1.15			
F-test		Potentiometric titration:1.31-3.26					
t-test		Potentiometric titration:0.008-0.196					

At (n =5) and 95% confidence limit: tabulated F value = 5.05 and tabulated t value = 2.571.

Table (2): Potentiometric determination of ALFHC in its pharmaceutical preparation (prostetrol) using MCPE electrodes.

Electrode	Taken ($mg\ mL^{-1}$)	MCPE			Official method [41]		
		Found ($mg\ mL^{-1}$)	Recovery (%) ±SD	RSD %	Found ($mg\ mL^{-1}$)	Recovery (%) ±SD	RSD %
I	0.426	0.424	99.53±0.005	1.12	0.43	100.9±0.0048	1.
	0.043	0.044	102.3±0.0006	1.36	0.043	100.0±0.0005	12
	0.0086	0.0085	98.84±0.0004	4.71	0.0084	97.67±0.0001	1.
		0.423	99.30±0.007	1.65			16
		0.042	97.76±0.002	4.76			1.
II		0.0083	96.51±0.0003	3.61			19
F-test		Potentiometric titration:1.09-3.27					
t-test		Potentiometric titration:0.003-0.196					

3.8. Application to urine and human serum

The studied electrodes applicability was investigated for the ALFHC determination in biological fluid of human urine and serum samples. Drug-free human serum and urine samples obtained from different healthy volunteers. The recoveries from urine and serum were determined by spiking drug-free urine and serum with definite amounts of ALFHC. The results of urine and plasma detection were showed in Tables (3). The recovery %, SD and RSD% were calculated, which indicated that the validated method could be adopted for the determination of the drug under investigation in biological fluids.

Table (3): Determination of ALFHC in spiked human serum and urine samples using MCPE electrodes.

Sample	Sample no.	Electrode type	[ALFHC] Spiked, mg mL^{-1}	Found, mg mL^{-1}	Recovery %	SD	RSD %
Serum sample	1	Electrode I	0.150	0.147	98.0	0.0026	1.77
	2	Electrode II	0.150	0.148	98.6	0.0035	2.36
Urine sample	1	Electrode I	0.150	0.144	96.0	0.0042	2.92
	2	Electrode II	0.150	0.146	97.3	0.0033	2.26

4. Conclusion

The potentiometric procedure proposed here has some significant advantages: the electrodes proved to be simple, successful, providing a rapid, and low cost potentiometric method for the determination of ALFHC in pure solutions and in pharmaceutical preparations; it ensures a good accuracy for the ALFHC assay due to the possibility to control the ion activity continuously and also a fast assay of ALFHC tablets, urine and serum samples. The accuracy of this method was indicated by excellent recovery and low standard deviation.

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