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# Spectrophotometric and Potentiometric Methods for the Determination of Alfuzosin Hydrochloride and Doxazosin Mesylate in Drug Substances and Drug products

**Mona M. Abdel-Moety[1]*, Nagiba Y.M. Hassan[2], Samar G. Abdel-Hamid[1], Abdel-Aziz A. Abdel-Aleem[2]**

**[1] National Organization for Drug Control and Research, (NODCAR), P.O.Box 29 Cairo, Egypt**
**[2]Chemistry Department, Faculty of Pharmacy, Cairo University, Cairo, Egypt**

***Corres. author: monaabdelmoety@yahoo.com**
**Phone number: 01004762438**

**Abstract:** Two simple, accurate and precise spectrophotometric and potentiometric methods were developed for the determination of alfuzosin hydrochloride (ALF) and doxazosin mesylate (DOX) either in drug substances or in drug products. The spectrophotometric method is based on the extraction of drugs into chloroform as ion pairs with bromocresol green (BCG) or into dichloromethane with phenol red (PR).
Under the optimum conditions, Beer's law was obeyed with good correlation coefficients (r= 0.9995- 0.9997) in the concentration range 1-17 and 2-17 µg $mL^{-1}$ ALF or 1-19 and 2-21 µg $mL^{-1}$ DOX using BCG and PR, respectively.
The potentiometric method involves the direct titration of ALF and DOX with N-bromosuccinimide (NBS) or N-bromophthalimide (NBP) in acidic medium and the end point is determined potentiometrically using platinum electrode. ALF and DOX can be determined quantitatively in the concentration range of 0.425- 1.700 and 0.547- 2.188 mg with recovery values of 99.68- 99.92 and 99.97- 100.00% and relative standard derivations (RSD) 0.2 -0.47 and 0.08- 0.10% for ALF and DOX, respectively. The proposed methods were successfully applied for the determination of ALF and DOX in drug substances and drug products with good accuracy and precision. Statistical comparison of the results was performed using Student's t-test and Variance ratio F-test at 95% confidence level. Further, the validity of the proposed methods was confirmed using ICH guidelines.
**Keywords**: Alfuzosin hydrochloride; Doxazosin mesylate; Bromocresol green; Phenol red; Spectrophotometry, Potentiometry, Tablet analysis.

## Introduction

Alfuzosin hydrochloride (ALF) is N-[3-[4-Amino-6,7-dimethoxyquinazolin-2-yl(methyl)amino] propyltetra hydro-2-furamide hydrochloride (Scheme 1) and doxazosin mesylate (DOX) is 1-(4-amino-6,7-dimethoxy-2-quinazolinyl)-4-[(2,3-dihydro-1,4-benzodioxin-2-yl) carbonyl] piperazine monomethane sulfonate (Scheme 1). These drugs are alpha-adrenoreceptors blocker and are used in the symptomatic treatment of urinary obstruction caused by benign prostatic hyperplasia and have been tried in the treatment of hypertension[1]

Several techniques have been published for the determination of ALF including spectrophotometry[2-5], chromatography[6-12], voltammetry[13] and potentiometry [14]. Other techniques have been described for the determination of DOX including spectrophotometry[15-17], chromatography[18-20] and polarography[21].

Spectrophotometric methods are sensitive, simple and inexpensive and have a considerable attention for various applications to a wide range of pharmaceutical compounds. Some sulphonephthalein dyes can be used in determination of ALF [2] and DOX [17] in tablets, but BCG and PR did not include in these previous studies.

For this purpose we studied the formation of ion pairs between the two drugs and BCG or PR dye, and the possibility for their extraction and determination in this way.

N- bromosuccinimide (NBS) and N-bromophthalimide (NBP) have been widely used as an oxidizing agents in many organic and inorganic determination[22]. NBS and NBP are also used for determination of some drugs using chemiluminescence[23,24], titrimetric[25-28] and spectrophotometric[29-31] methods. However, no reports have appeared dealing with the potentiometric method for the determination of ALF or DOX using NBS and NBP so far. Therefore, the aim of the present work is to develop a new reliable method as a continuation of some studies related to potentiometric titration in our laboratory for determination of some drugs[32,33]. The proposed methods are simple, accurate and reproducible indicating their suitability for routine determination of ALF and DOX in bulk and dosage forms.

## Experimental

### Apparatus

A Shimadzu UV-visible 2450 spectrophotometer, double beam (Tokyo, Japan) with two quartz cells of 1-cm optical path length, connected to an IBM compatible computer and HP desk jet printer are used for all absorbance measurements of data. HI 9321 Hanna Microprocessor mV/pH meter with a combined platinum-saturated calomel electrode was used.

### Materials and reagents

All chemicals were of analytical grade and water was always doubly distilled.

Alfuzosin HCl (99.97± 0.90% according to official method by non aqueous titration [34] and Xatral tablets (5 mg ALF/ tablet) were kindly provided from Amriya Company for Pharmaceutical Industries, Alexandria, Egypt. Doxazosin mesylate analyzed and found to be 99.97±0.19 by HPLC method [34] and Doxacor tablets (4 mg DOX/ tablet) were provided from Minapharm Company for Pharmaceutical and Chemical Industries, Cairo, Egypt.

Standards of alfuzosin HCl or doxazosin mesylate, 50 mg/ 100 mL and $1x10^{-3}$ M, were freshly prepared by dissolving pure drug in water and completed to 100 mL with water in a 100-mL volumetric flask. More dilute solutions whenever required were obtained by appropriate dilution with water.

Bromocresol green (BCG) from Aldrich, $1x10^{-3}$ M is freshly prepared in chloroform and phenol red (PR) from Aldrich, $1x10^{-3}$ M is freshly prepared in ethanol-water mixture (10: 90, v/v). N-bromosuccinimide and N- bromophthalimide (Aldrich, $1x10^{-3}$ M), aqueous solutions were prepared fresh daily and standardized by an iodometric method[22].

Chloroform, 1, 2 dichloroethane, and dichloromethane were of HPLC grade and were directly used as supplied. $H_2SO_4$, HCl, $HNO_3$ and $CH_3COOH$ (BDH, UK), 2M aqueous solutions were prepared.

Universal buffer of acidic pH 2-6 (0.04 M) was freshly prepared by adding 2.47 g boric acid, 2.74 ml orthophosphoric acid and 2.31 ml glacial acetic acid into 1000 ml volumetric flask and completed to the mark with water. The pH of the solution was adjusted with 0.2 M NaOH.

## General procedures

### Spectrophotometric method

To 2 ml of ALF or DOX solution (10-210 µg) placed in a separating funnel (50 ml), add 1ml of dye solution ($1x\ 10^{-3}$ M) of BCG or PR, 2 ml of universal buffer (pH 2.2) and completed to 10 mL with water. The reaction mixture was extracted by shaking for 1 min with two 4 mL portions of chloroform or dichloromethane in case of BCG or PR reagent, respectively. The organic layer was collected and completed to 10 mL with the same solvent and then filtered if necessary. The absorbance of the organic phase was measured at 417 and 422 nm for ALF or at 418 and 420 nm for DOX using BCG and PR, respectively, against a reagent blank similarly prepared omitted of drug. All measurements were made at room temperature (25± 2 $^{o}$C). Standard calibration

graphs of drugs were constructed by plotting the absorbance versus concentration and the regression equations were computed and recorded in Table 1.

**Table 1 Analytical data for the reaction of ALF or DOX with BCG and PR**

| Parameters | BCG | | PR | |
|---|---|---|---|---|
| | ALF | DOX | ALF | DOX |
| $\lambda_{max}$ (nm) | 417 | 418 | 422 | 420 |
| Linear range (µg $mL^{-1}$) | 1-17 | 1-19 | 2-17 | 2-21 |
| Molar absorptivity(L $mol^{-1}$ $cm^{-1}$) | $2.09x10^4$ | $2.62x10^4$ | $2.42x10^4$ | $2.35x10^4$ |
| Sandell sensitivity (µg $cm^{-2}$) | 0.019 | 0.021 | 0.018 | 0.023 |
| Slope (b)[a] | 0.058 | 0.053 | 0.053 | 0.039 |
| S.E of slope | 0.001 | 0.001 | 0.001 | 0.001 |
| Intercept (a)[a] | -0.05 | -0.047 | 0.035 | 0.038 |
| S.E of intercept | 0.006 | 0.008 | 0.0006 | 0.006 |
| Correlation coefficient (r) | 0.9997 | 0.9996 | 0.9997 | 0.9995 |
| Accuracy (n=5) | 99.57±0.02 | 99.72±0.06 | 99.55±0.02 | 99.73±0.04 |
| LOD(µg $mL^{-1}$) | 0.18 | 0.18 | 0.25 | 0.31 |
| LOQ(µg $mL^{-1}$) | 0.54 | 0.55 | 0.76 | 0.94 |
| Intraday precision (n= 9)[b] | 0.75 | 0.20 | 0.33 | 0.55 |
| Interday precision (n= 9)[b] | 0.80 | 0.66 | 0.25 | 0.78 |

[a] Regression equation: A =a+ bC, where C is the drug concentration (µg $mL^{-1}$) and A is the absorbance.
[b] Relative standard deviation (RSD %).

### Potentiometric method

Volumes containing 0.425- 1.700 mg of ALF and 0.547- 2.188 mg of DOX, 1 mL 2 M each of $H_2SO_4$ and HCl were added using NBS reagent for ALF and DOX, respectively, where 2 mL of 2M HCl were added for both drugs using NBP reagent and the volume was completed to 50 mL with bidistilled water. The Pt electrode was immersed in the solution and the titration was carried out potentiometrically using NBS or NBP ($1x10^{-3}$ M) solution as titrant from the micro burette (capacity of 5 mL with division of 0.05 mL). The amount of NBS or NBP solution equivalent to the reacted drug amount was calculated.

### Analysis of tablets

An accurately weighed amount of the finely powdered tablets (Xatral and Doxacor) equivalent to 50 mg of drug was transferred to a 100 mL conical flask. ALF or DOX was extracted with four 20 mL portions of water. The combined extracts were filtered into 100-mL volumetric flask and then diluted to volume with water. This solution contains 500 µg/mL of drug; $1x10^{-3}$ M of drug was also prepared. Dilute solution was prepared if necessary and analyses the resulting solution as described under general procedures.

## Results and Discussion

### Ion-pair methods using BCG and PR

ALF or DOX is protonated in acidic buffer, formed yellow or orange colored ion- pair complexes with the acidic sulphonephthalein dyes BCG or PR, respectively, and these complexes were quantitatively extracted into chloroform or dichloromethane, respectively. The absorption spectra of these complexes were measured at 417 and 418 nm with BCG or 422 and 420 nm with PR for ALF and DOX, respectively (Figs. 1 & 2). The different parameters affecting the color development were extensively studied to give the maximum sensitivity, adherence to Beer's law, and stability.

The effect of the pH of buffer solution in the range 2- 6 on the absorbance reading of the drug-dye ion pair was examined. The results showed that the most efficient extraction of the ion pair with chloroform or dichloromethane was obtained at a pH of 2.2 (2 mL in the total volume of 10 mL) using BCG or PR dye, where maximum absorbance and high stability were achieved (Fig.3). The shape of the absorption spectra and the position of the absorption maxima of the ion pairs formed did not vary with pH; these results indicate that only one type of complex is formed.

The color intensity of the ion-pair complexes increased with increasing concentration of either the dye or the drug. Up to 200 µg ALF or DOX was converted quantitatively in the presence of 1 mL of $10^{-3}$ M dye in the final aqueous solution (10 mL), at which the absorbance of the ion pair reaches a maximum.

The effect of the extracting solvent used both on extraction efficiency and color intensity was examined. Chloroform, dichloromethane and, 1,2-dichloroethane proved useful solvents; chloroform and dichloromethane were selected using BCG and PR, respectively, because of their slightly higher efficiency and considerably lower extraction ability of the reagent blank. Two extractions each with shaking for one min. were necessary for the quantitative estimation of the complex.

The optimum reaction time was determined at ambient temperature (25± 2$^{o}$C). It was found that the color appeared immediately upon mixing and the developing colors were stable for at least 24 h.

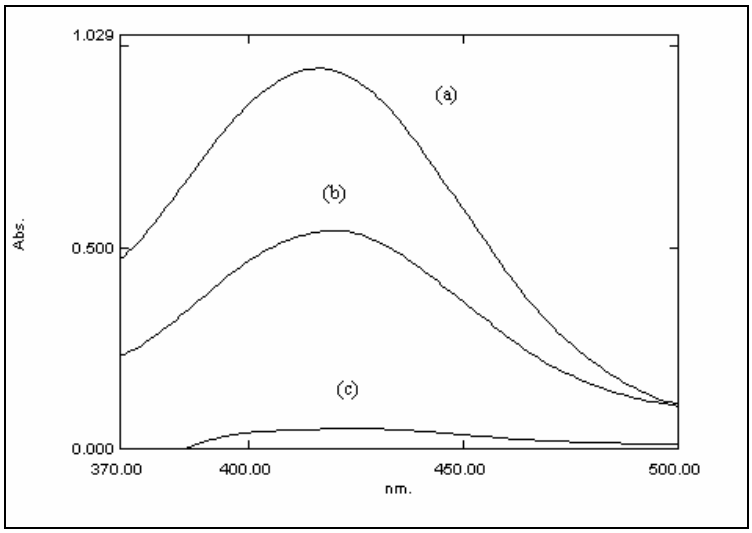



**Fig.1. Absorption spectra of (a) ALF -BCG and (b) DOX -BCG ion pair complexes against reagent blank and (C) reagent blank against solvent.**

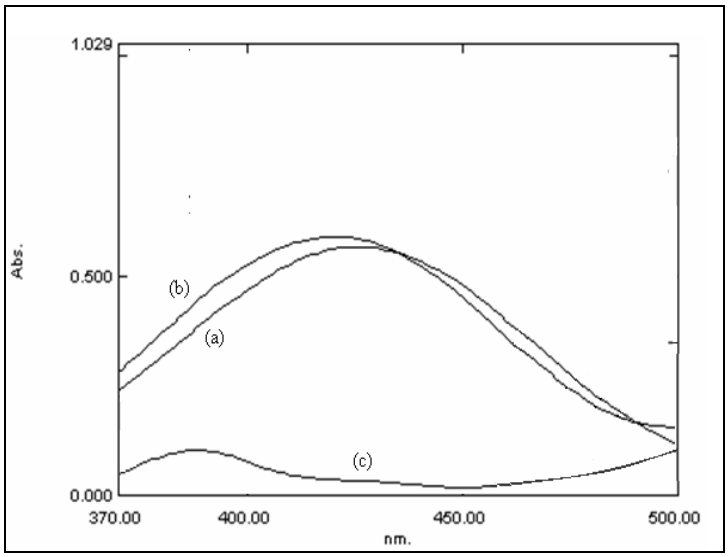



**Fig.2. Absorption spectra of (a) ALF - PR and (b) DOX - PR ion-pair complexes against reagent blank and (c) reagent blank against solvent.**

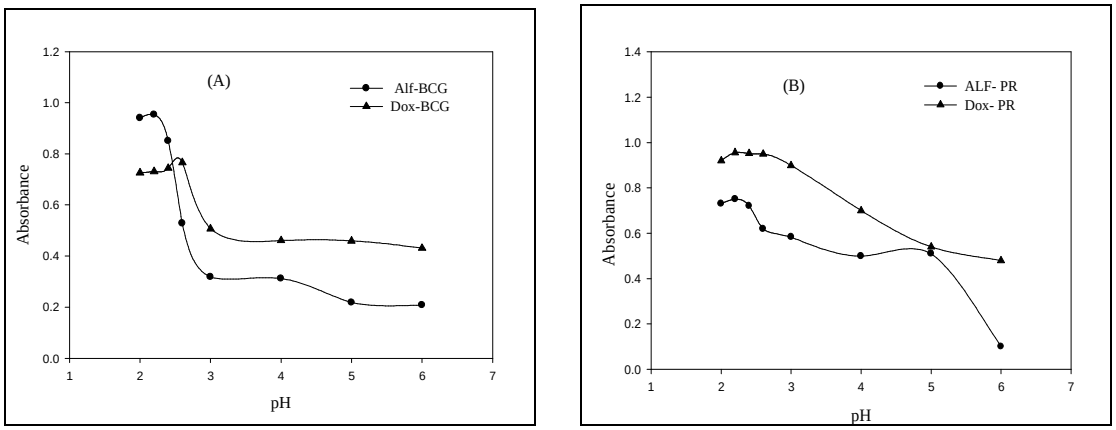



**Fig.3. Effect of pH on Alfuzosin HCl (10 µg/ml) and Doxazosin mesylate (13 µg/ml) with BCG (A), and Phenol red (PR) (B).**

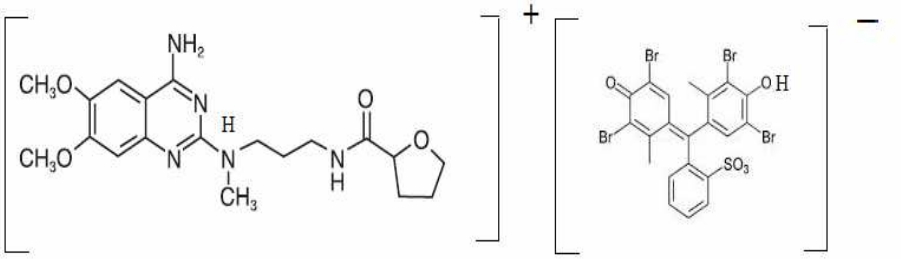
**Stoichiometry of the complexes**

The continuous variations method[35] was applied to determine the stoichiometry of the reaction between the cited drugs and BCG or PR. The method showed molar ratio of 1:1 under the described conditions (Figs. 4 & 5).

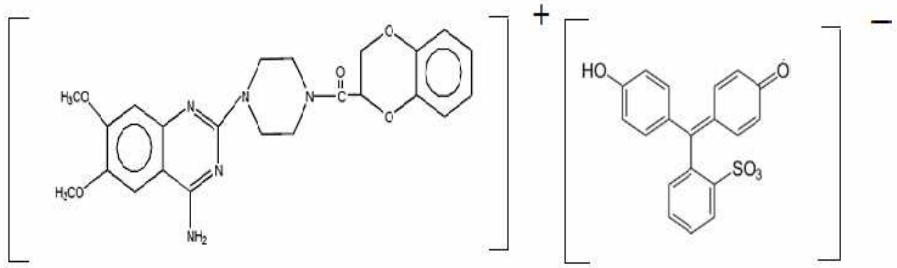
This finding is in conformity with the presence of one basic center of tertiary amino group which is protonated in acid medium, while sulphonic acid group is present in the two dyes that is the only group undergoing dissociation in the pH range 1-5. The color of BCG or PR is due to the opening of lactoid ring and subsequent formation of quinoid group. It is supposed that the two tautomers are present in equilibrium, but due to the strong acidic nature of the sulphonic group, the quinoid body must predominate[36]. Finally, the protonated drugs form ion pairs with BCG or PR anion which are quantitatively extracted into chloroform or dichloromethane, respectively.

The proposed ion-pair complexes are shown in Scheme 1.

**(A).**



**(B).**



**Scheme 1.** ALF-BCG complex (A) and DOX – PR complex (B)

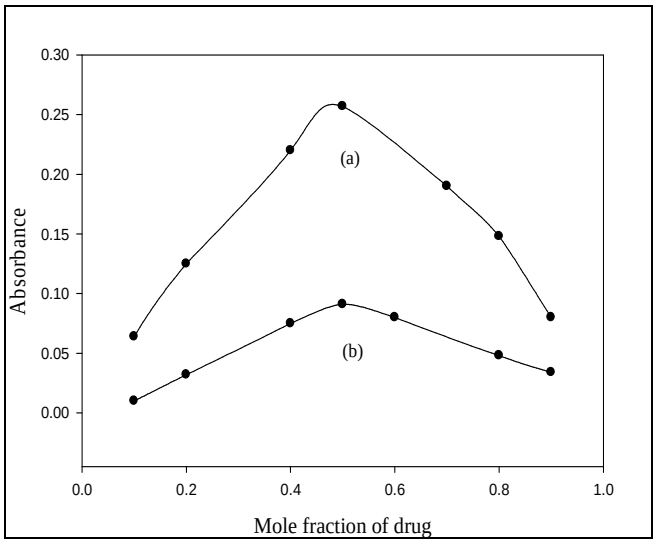



**Fig.4. Continuous variation plots for Alfuzosin HCl with (a) BCG and (b) Phenol red (Total molar concentration= $10^{-4}$ M).**

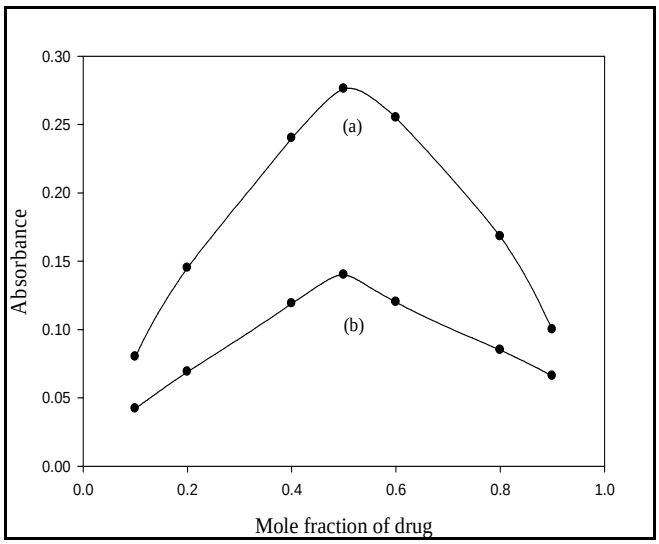



**Fig.5. Continuous variation plots for Doxazosin mesylate with (a) BCG and (b) Phenol red (Total molar concentration= $10^{-4}$ M).**

## Analytical data

Under the experimental conditions described above, Beer's law was verified and was found to be satisfactory in the concentration range 1- 17 and 2- 17 µg $mL^{-1}$ or 1- 19 and 2- 21 µg $mL^{-1}$ DOX using BCG and PR, respectively. The molar absorptivities, Sandell sensitivities and the regression equations were included in Table 1. The correlation coefficients were between 0.9995- 0.9997, indicate good linearity of the present method.

According to the International Conference on Harmonization (ICH) Recommendation[37], the limits of detection (LOD) and quantification (LOQ) can be determined and included in Table 1.

To measure the degree of method repeatability (intraday precision), three of different concentrations of ALF or DOX were prepared and analyzed each five times within the same day and in five successive days (interday precision). The results obtained in Table 1, show that no significant difference for the assay, which tested within day (repeatability) and between-day (reproducibility). The relative standard deviation (RSD) was less than 1% which indicates high degree of precision of the proposed method.

The accuracy of the spectrophotometric method was calculated by repeating the method five times for three different concentrations of pure samples. The mean recovery percentages were calculated and tabulated in Table 1. The excellent recoveries and the low relative standard deviations obtained, suggest the good accuracy of the proposed method.

## Potentiometric method

The potentiometric titration of ALF or DOX showed a well-defined inflection on the titration curve, precisely indicating the end point. The potentiometric determination was less subjective and more precise than the use of visual indicators[25-27,38]. Therefore this method was chosen for the analyses. NBS and NBP have reported to be the most oxidizing and brominating agents in acidic medium[25,38]. These reagents have been utilized extensively in the determination of a fast number of compounds, especially those of pharmaceutical interest[25-27,38]. The reaction conditions were studied extensively and the molar ratio was calculated and the reaction mechanism was also included.

The conditions optimized are the choice of medium for a quantitative reaction to proceed towards completion and the amount of reagent added.

The effect of acids such as $H_2SO_4$, HCl, $HNO_3$ and $CH_3COOH$ on the quantitative reaction of ALF and DOX with NBS and NBP was studied at a suitable ratio [drug]: [reagent] of 1: 1. The data indicates that reproducible and stoichiometric results are obtained when using $H_2SO_4$ or HCl for ALF in case of NBS or NBP, respectively,

and HCl for DOX in case of the two reagents. The results obtained show sharp inflections lying in the immediate vicinity of the expected end points using 1.0 mL of both 2 M $H_2SO_4$ and 2 M HCl using NBS for ALF and DOX, respectively, whereas 2 mL of 2 M HCl can be used for both drugs using NBP. The concentrations of these reported acids are maintained constant during the current investigations. $H_2SO_4$ or HCl acts a $H^+$ donor and works as supporting electrolyte to keep the ionic strength constant during the titration process. The dilution of acidic drug solution to 50 mL with distilled water gave the best results. Then the dilution of drug solution to 50 mL will be used for all experiment processes.

For the quantitative determination of drug, the effect of NBS or NBP concentration examined, and 1x $10^{-3}$ M is chosen as an optimum concentration to achieve a constant and highly stable potential reading within 1-2 min of mixing. Concentration less than this led to unstable reading and more time was needed to obtain constant potential values.

Raising the temperature does not accelerate the oxidation process and tends to cause inaccurate results and creates difficulty in detecting the end point because of decomposition of NBS and NBP at higher temperature, thus room temperature (25± 2 $^0$ C) is the most suitable .

**Molar ratio**

As shown in Figs. 6 &7, it is confirmed that 1.0 mole of NBS or NBP was required for complete bromination of each 1.0 mole of ALF or DOX.

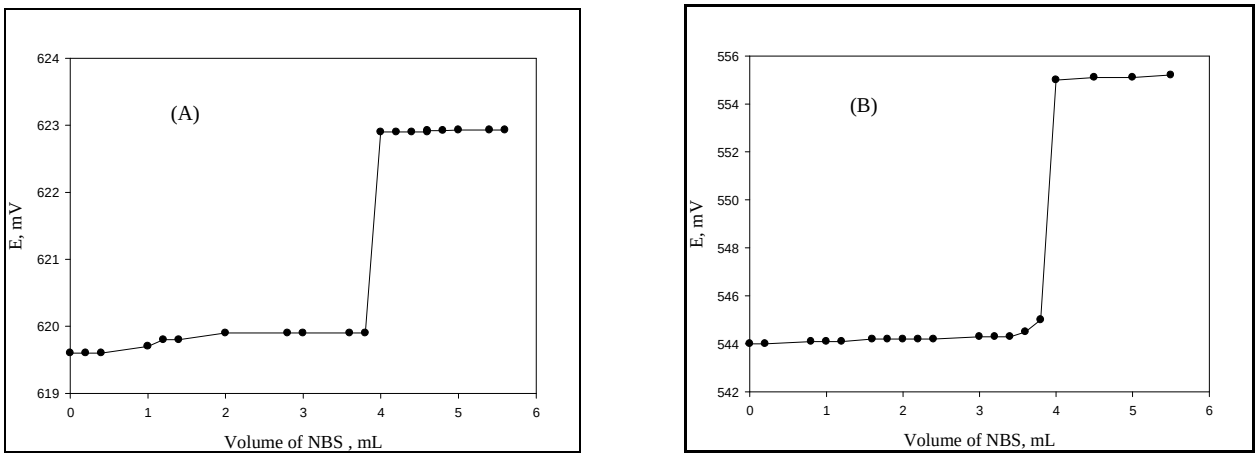



**Fig. 6. Potentiometric titration curves for: (A) ALF (4.0 mL of $10^{-3}$ M) and (B) DOX (4.0 mL of $10^{-3}$ M), with NBS ($10^{-3}$) using pt- electrode.**

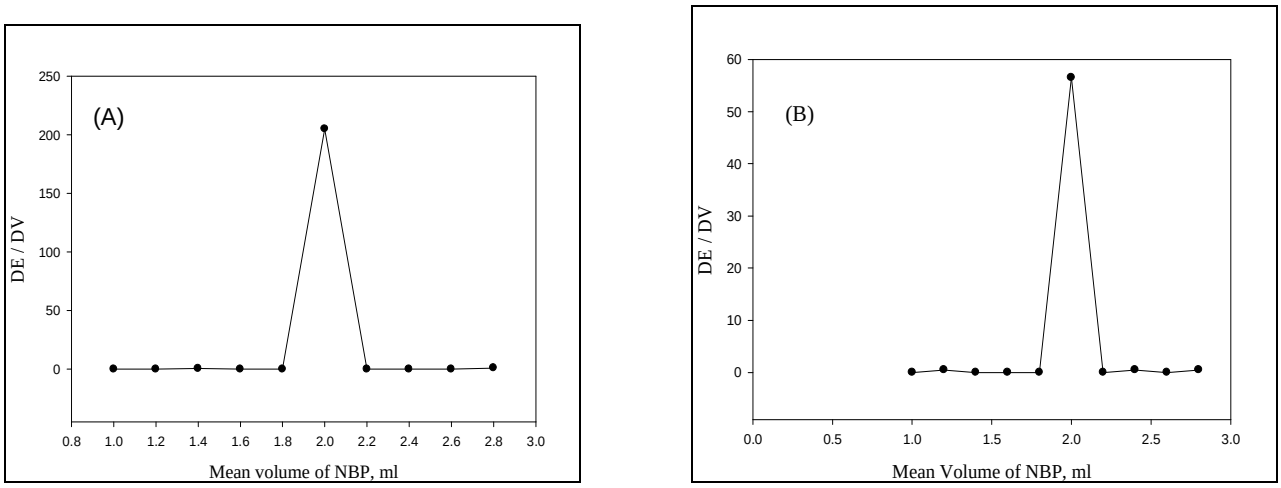



**Fig. 7. Differential curves of potentiometric titration of (A) ALF (2 mL of $10^{-3}$M) and (B) DOX (2 mL of $10^{-3}$M) with NBP ($10^{-3}$ M), using pt- electrode.**

**Reaction mechanism**

The reaction of NBS and NBP with both ALF and DOX may take place via the attack on the respective $NH_2$ group of the two drugs, where $NH_2$ group are reported to react with brominating agent to form NH- Br [22]. The actual brominating species here is the bromium ion ($Br^+$) produced by hydrolytic fission [25]. Also the N-Br bond in NBS or NBP is very polar owing to the fact that the nitrogen atom is attached to either two C=O groups. In the bromination reaction there is no possibility of any of the bromine escaping during the titrations. NBS or NBP reacts readily and quantitatively with aqueous solutions of ALF and DOX, being it self reduced to succinimide or phthalimide, respectively.

**Potentiometric titration of drugs**

The titration curves of drugs show one well-defined S-shaped stoichoimetric end point using a pt-electrode. The titration data is given in Fig. 6 as representative curves for NBS, which represent the plot of E vs. volume (mL) of titrant for the determination of drug. The first differential curves which represent the plot of $\Delta E/\Delta V$ vs. mean volume of titrant, are characterized by sharp inflections lying in the immediate vicinity of the expected end points (Fig.7 as example for NBP) these sharp inflections permit the accurate of the end point. The results in Figs. 6&7 indicate that the two reagents (NBS and NBP) are equal for accurate and sensitive methods for the determination of the two drugs. The results indicate that 1.0 mL of 1x $10^{-3}$ M NBS or NBP is equivalent to 0.426 mg of ALF and 0.548 mg of DOX.

The results of the drug determination presented in Table 2 showed that good recoveries and low relative standard deviations were obtained. In order to establish whether the proposed method exhibits any fixed or proportional bias, a simple linear regression of observed drug concentration against the theoretical values was calculated [39]. The calculated t-values in the range of 0.06- 0.44 which are lower than the tabulated values at 95% confidence level and four degrees of freedom (2.776). This there are no systematic differences between the determined and the true concentration over a wide range of 0.425- 1.700 and 0.547- 2.188 mg for ALF and DOX, respectively.

**Table 2 The potentiometric determination of ALF and DOX in pure solutions using NBS and NBP (1 x$10^{-3}$ M)**

| Taken (mg) | NBS | | NBP | |
|---|---|---|---|---|
| | Found (mg)[a] | Recovery (%) | Found (mg)[a] | Recovery (%) |
| **Alfuzosin HCl (ALF)** | | | | |
| 0.425 | 0.424 | 99.76 | 0.423 | 99.52 |
| 0.637 | 0.637 | 100.00 | 0.638 | 100.10 |
| 0.850 | 0.850 | 100.00 | 0.851 | 100.10 |
| 1.062 | 1.054 | 99.24 | 1.060 | 99.81 |
| 1.275 | 1.260 | 98.82 | 1.274 | 99.92 |
| 1.487 | 1.487 | 100.00 | 1.488 | 100.00 |
| 1.700 | 1.700 | 100.00 | 1.700 | 100.00 |
| Mean (%) | | 99.68 | | 99.92 |
| RSD (%) | | 0.47 | | 0.20 |
| **Doxazosin mesylate (DOX)** | | | | |
| 0.547 | 0.548 | 100.10 | 0.548 | 100.10 |
| 0.820 | 0.821 | 100.10 | 0.821 | 100.10 |
| 1.094 | 1.094 | 100.10 | 1.093 | 99.90 |
| 1.367 | 1,366 | 99.92 | 1.366 | 99.92 |
| 1.641 | 1.640 | 99.93 | 1.641 | 100.00 |
| 1.995 | 1.995 | 100.00 | 1.993 | 99.890 |
| 2.188 | 2.187 | 99.95 | 2.186 | 99.90 |
| Mean (%) | | 100.00 | | 99.97 |
| RSD (%) | | 0.08 | | 0.10 |

[a] **Average of three determinations.**

**Methods validation**

**Specificity**

The Specificity of the methods was investigated by observing any interference encountered from the tablet excipients such as: talc, lactose, glucose, sucrose, starch and magnesium stearate. These excipients did not interfere with the proposed methods. This fact indicates good selectivity of the methods for determination of ALF and DOX both in raw materials and in tablets.

**Robustness and Ruggedness**

The robustness of the spectrophotometric method is demonstrated by the constancy of the absorption intensity with the deliberated minor change in the experimental parameters such as the change in the volume of reagent (± 0.2 mL) and pH solution (± 0.1). These minor changes that may take place during the experimental operation did not affect the absorption intensity of the reaction product.

The ruggedness of the proposed methods was evaluated by applying the developed procedure to assay of drug using the same instrument by two different analysts under the same optimized conditions at different days. Since there were no significant differences between the results obtained by the two analysts, the proposed methods may be considered rugged.

**Application of the proposed methods for the determination of Alfuzosin HCl and Doxazosin mesylate in their drug products**

The proposed methods were applied for the determination of ALF ad DOX in Xatral and Doxacor tablets, respectively. The results of the assay of drugs in tablets with BCG, PR, NBS and NBP reagents were compared with the official methods as: non-aqueous titration for ALF and HPLC for DOX [34], statistical comparison of the results was performed with regard to accuracy and precision using the Student's t- and F-tests at 95% confidence level. From the results in Table 3, it is clear that there is no significant difference between the proposed and BP methods with regard to accuracy and precision.

Recovery tests were determined by adding standard drug to the pre-analyzed mixture of drug tablets. Assays were performed at three levels of standard drug and one level of sample preparation in the level of 50, 100, and 150 % (Table 4). Spiked Xatral or Doxacor tablets assay was used to determine accuracy and precision of the proposed methods for determination of drug, the average recoveries and RSD% values were recorded in Table 4. The results of analysis of the commercial tablets (Table 3) and the recovery study (standard addition method) of drug (Table 4) suggested that there is no interference from any excipients, which are present in tablets. Also, the extraction of drug ion-pair complexes with chloroform or dichloromethane could eliminate any interference caused by common excipients.

**Table 3 Application of the proposed methods for the determination of ALF and DOX in tablets**

| Drug | Tablets | Found±SD (%)[a] | | | | |
|---|---|---|---|---|---|---|
| | | Spectrophotometric method | | Potentiometric method | | BP method |
| | | BCG | PR | NBS | NBP | |
| ALF | Xatral tablets | 99.95±0.26 | 99.86±0.21 | 99.93±0.23 | 99.94±0.24 | 99.99±0.14[(c)] |
| | t- test[b] | 0.30 | 1.15 | 0.50 | 0.40 | |
| | F-test[b] | 3.45 | 2.25 | 2.70 | 2.94 | |
| DOX | Doxacor tablets | 100.00±0.17 | 99.93=0.18 | 99.95=0.20 | 99.95=0.19 | 99.97=0.16[(d)] |
| | t- test[b] | 0.29 | 0.23 | 0.17 | 0.18 | |
| | F-test[b] | 1.13 | 1.27 | 1.56 | 1.41 | |

[a] Mean and standard deviation for five determinations.
[b] Theoretical values of t- and F-tests = 2.306 and 6.39, respectively, at p= 0.05.
[c] Non- aquous titration method [34].
[d] HPLC method [34].

**Table 4 Standard addition method for the determination of ALF and DOX in tablets**

| Drug | Tablets | Spectrophotometric method | | | |
|---|---|---|---|---|---|
| | | Taken | Added | BCG | PR |
| | | ($\mu g\ mL^{-1}$) | | Recovery (%)[a] | Recovery (%)[a] |
| ALF | Xatral tablets | 6 | 3 | 99.90 | 99.80 |
| | | 6 | 6 | 99.72 | 100.10 |
| | | 6 | 9 | 100.23 | 99.69 |
| | Mean | | | 99.95 | 99.86 |
| | RSD(%) | | | 0.26 | 0.21 |
| DOX | Doxacor tablets | 6 | 3 | 99.90 | 99.90 |
| | | 6 | 6 | 100.20 | 99.81 |
| | | 6 | 9 | 99.92 | 100.10 |
| | Mean | | | 100.00 | 99.93 |
| | RSD (%) | | | 0.17 | 0.15 |
| | | **Potentiometric method** | | | |
| ALF | Xatral tablets | (mg/ 50 mL) | | NBS | NBP |
| | | 0.4 | 0.2 | 99.83 | 99.66 |
| | | 0.4 | 0.4 | 99.87 | 99.75 |
| | | 0.4 | 0.6 | 100.10 | 99.90 |
| | Mean (%) | | | 99.93 | 99.77 |
| | RSD (%) | | | 0.15 | 0.12 |
| DOX | Doxacor tablets | 0.4 | 0.2 | 100.10 | 100.00 |
| | | 0.4 | 0.4 | 99.87 | 99.75 |
| | | 0.4 | 0.6 | 99.80 | 99.90 |
| | Mean | | | 99.92 | 99.89 |
| | RSD (%) | | | 0.16 | 0.10 |

[a] Mean of five determinations

## Conclusion

The spectrophotometric method in this work is simple and do not need the elaborate treatment and tedious extraction required in chromatographic methods. NBS and NBP methods for the quantitation of alfuzosin HCl (ALF) and doxazosin mesylate (DOX) are direct methods. The shapes of the potentiometric titration curves of pure drugs and the corresponding pharmaceuticals are nearly the same which proves that the excipients which might be present in the pharmaceutical preparations do not affect the titration curves. The proposed methods are successfully applied for determination of alfuzosin HCl and doxazosin mesylate in their pharmaceutical preparations by applying the standard addition technique, there is no interference by other excipients.

The proposed methods are statistically compared with the official methods, since the calculated t and F values are less than the tabulated ones. The data given above reveals that the proposed methods are accurate and sensitive with good precision and accuracy. With these methods, one can do the analysis of these drugs at low cost without losing accuracy. The proposed methods are quite suitable for routine quality control analysis of pharmaceutical preparations.

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