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ELECTROCHEMICAL DETERMINATION OF ALENDRONATE SODIUM IN A PHARMACEUTICAL FORMULATION

Abdulaziz N. Amro*1

^{1*}Department of Chemistry, Faculty of Science, Taibah University, Al Madinah Al Munawwarah, Kingdom of Saudi Arabia.

ABSTRACT

Voltammetric determination has been applied for Alendronate Sodium (ALN) assay in a pharmaceutical formulation. Britton - Robinson Buffer (BRB) solutions of pH (2.1-11.6) were studied as supporting electrolyte, BRB solution of pH 10.52 with Glassy Carbon GC working electrode exhibited the optimum conditions for ALN assay. Cyclic voltammetry (CV), square wave voltammetry (SWV) and differential pulse voltammetry (DPV) techniques have been applied in this study. CV indicated that ALN is electroactive compound with anodic current peak at 1.5V. DPV showed the best Limit of Detection (LOD) and limit of quantification LOQ of 0.176 and 0.216mg.mL⁻¹ respectively. All studied voltammetric techniques illustrated high accuracy and precession with linear range 0.25-1.25mg.mL⁻¹. SWV recovery is 96.57% and 98.28% for 0.35mg.mL⁻¹ and 0.70mg.mL⁻¹ of commercially available ALN (Osteve[®]70mg) tablets respectively. In addition, DPV inter and intraday results precession values are better than other used voltammetric techniques with 1.84 and 2.08% RSD respectively.

KEYWORDS

Alendronate Sodium, Cyclic voltammetry, Square wave voltammetry and Differential pulse voltammetry.

Author for Correspondence:

Abdulaziz N. Amro, Department of Chemistry, Faculty of Science, Taibah University, Al Madinah Al Munawwarah, Kingdom of Saudi Arabia.

Email: abdulazizamro@yahoo.com

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INTRODUCTION

Standard analytical methods of pharmaceutical different medium compounds in are chromatographic spectroscopic methods¹. or Voltammetric determinations have several advantages over other analytical methods such as simple analysis requirements, short time of sample preparation and analysis, high sensitivity and low and running cost², furthermore instruments voltammetry is considered a green analytical method compared to chromatographic methods.

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Several research works applied voltammetric methods for quantitation of pharmaceutical compounds using commercially available electrodes or modified electrodes²⁻⁵. Voltammetric methods showed reliable results with comparable accuracy and precision values^{2, 5}.

Alendronate monosodium trihydrate salt (ALN), 4amino-l-hydroxybutane- 1, l-bisphosphonic acid (Figure No.1) classified as bisphosphonate drug. ALN is used as a treatment of several bone diseases such as osteoporesis, Paget's disease and hypocalcemia⁶.

Several studies have been done on ALN quantification using chromatographic and spectroscopic methods. Ion chromatography has been applied using conductivity detectors⁷ and refractive index⁸ detectors. High-performance liquid chromatographies (HPLC)⁹, LCMS¹⁰ and LCMS/MS¹¹ have been also applied for ALN quantification. Ptacek et al. studied ALN as 9florenylmethyl derivative by high-performance liquid chromatography¹². El-Yazbi et al. studied how Hantzsch pre-column derivatization Affect HPLC determination of ALN¹³. Al Deeb et al. Applied and compared spectroscopic and HPLC methods for the determination of alendronate in tablets and urine samples¹⁴. Kuljanin et al. worked on spectrophotometric determination of ALN in pharmaceutical formulations after complexation with Fe (III) ions¹⁵. Reed *et al.* applied Inductively Coupled Plasma Spectroscopy (ICP) for ALN in determination in tablets¹⁶.

Jia *et al.* modified detector using Copper (II)– mediated silver nanoclusters as a fluorescent platform for ALN detrmination¹⁷. In this work ALN is quantified in a pharmaceutical formulation and final product tablets using different voltammetric techniques, voltammetric analysis parameters are optimized to have the best analysis conditions.

EXPERIMENTAL

Materials and reagents

The standard pharmaceutical formulation of Alendronate Sodium was obtained from Jordanian Pharmaceutical Manufacturing Company (JPM) (Jordan). A commercial Alendronate Sodium Available online: www.uptodateresearchpublication.com Osteve [®]70mg tablets manufactured by SPIMACO (Saudi Arabia), were bought from local market. Britton–Robinson universal buffer solutions (BRB) pH (2.1-11.6) have been used as supporting electrolytes, all buffer solutions were prepared by mixing certain amount of all required components (phosphoric acid, acetic acid and boric acid) and adjusting to required pH with sodium hydroxide (0.2 M).

Standard solutions

(BRB) solutions of pH (2.1-11.6) were used to prepare stock standard solutions, furthermore BRB solutions were used for the dilution of stock solutions to prepare the standard working solutions. Standard stock solutions of 2.0mg/mL ALN were prepared.

Preparation of sample solutions

The Osteve [®]70mg tablets were weighed then grounded using mortar and pestle, and then a certain amount of powder was dissolved in the BRB solution pH 10.52 using water bath sonicator. Next, undissolved substance was removed by simple filtration. BRB solution pH 10.52 was used to wash filter paper which used in the filtration; then it was used to complete solution volume.

Apparatus

All voltammetric methods measurements were carried out using potentiostat (Metrohm Autolab) PGSTAT 204 (Netherlands). Three electrodes system was used in this study, i.e., A Glassy Carbon (GC) or Platinum (Pt) working electrode, Ag/AgCl (3M KCl) reference electrode and a platinum (Pt) sheet counter electrode.

RESULTS AND DISCUSSION

Voltammetric Method development and optimization

Cyclic voltammetry technique has been used to study the electro activity of ALN and the proper working electrode for ALN assay. Both Pt and GC electrodes have been studied in this work, cyclic voltammograms indicated that GC electrode is the proper working electrode since Pt electrode didn't show current signal for ALN using different BRB solutions with different pH values.

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BRB solutions of pH values range (2.1-11.6) have been studied for supporting electrolytes optimization. Figure No.2 shows a comparison of anodic peak current values between ALN and blank supporting electrolytes at potential 1.5V. ALN with BRB solution of pH 10.52 supporting electrolyte showed the highest difference of anodic peak current value between analyte and supporting electrolyte.

CV study of ALN shows irreversible voltammograms (Figure No.3) with anodic peak current at 1.5V. ALN (0.25-1.20)mg.mL⁻¹ have been analyzed using CV, SWV and DPV (Figures No.3, 4 and 5), all techniques showed high correlation coefficients R^2 values (Table No.1), SWV illustrate the highest R^2 value of 0.9999. The slopes of SWV and CV standard calibration curves indicated that both are close to each other and more sensitive than DPV. Peak currents of all applied techniques have been recorded at potential 1.5V since this potential showed the best correlation between concentration and anodic current. Linear range of all applied voltammetric techniques is 0.0.25- 1.25mg.mL⁻¹. Limit of detection (LOD) and Limit of Quantification (LOQ) of all techniques are close to each other, SWV and DPV exhibited better LOD and LOQ than CV as shown n Table No.1.

Precision

Intraday repeatability and inter day reproducibility have been studied for all applied voltammetric techniques of this work (Table No.2). 1.00mg.mL⁻¹ of standard ALN in BRB solution pH 10.52 has been used in this work for all studied voltammetric techniques. Relative standard deviations (RSD) of triplicate of same day for intraday study and RSD of three consecutive days have been calculated for inter day study. All studied voltammetric techniques showed good precision values but DPV showed the lowest RSD of 1.84 and 2.08% of intraday and inter day respectively.

Accuracy

Commercial preparation of ALN Osteve [®]70mg tablets has been used to study the accuracy of voltammetric techniques in ALN analysis. Two concentrations have been prepared and studied 0.35 and 0.70mg.mL⁻¹. Each concentration has been done triplicate (Table No.3). Recovery values indicated that accuracy of all techniques fall in the desired range, SWV exhibited the best recovery for both studied concentrations as shown in Table No.3. Recovery values of SWV indicated that it has the highest accuracy compared to other voltammetric techniques.

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S.No	Method	LR	\mathbb{R}^2	LOD (mg.mL ⁻¹)	LOQ (mg.mL ⁻¹)
1	CV	y = 99.807x + 105.32	0.9939	0.221	0.246
2	DPV	y = 10.352x + 11.882	0.9992	0.176	0.216
3	SWV	y = 97.519x + 86.924	0.9999	0.185	0.225

 Table No.1: Linearity of ALN (0.25-1.20mg.mL⁻¹, BRB solution pH 10.52)

LR: Linear regression, R²: correlation coefficient, LOD: Limit of detection, LOQ: Limit of Quantification

		ALIA (1.00 mg.ml), DKD Solutio	n pri 10.52)
S.No	Method	Intraday RSD%	Inter day RSD%
1	CV	2.78	4.73
2	DPV	1.84	2.08
3	SWV	2.32	3.66

 Table No.2: Precision of ALN (1.00mg.mL⁻¹, BRB solution pH 10.52)

Intraday (repeatability) RSD: relative standard deviation of triplicate determinations on the same day, Inter day (reproducibility) RSD: relative standard deviation of three consecutive days.

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S.No	Method	Method 0.350mg.mL ⁻¹		0.700mg.mL ⁻¹			
		Found ±SD	0.367±0.005	0.717±0.033			
1	CV	Recovery%	104.85	102.42			
	Cv	RSD%	1.52	4.77			
		Found ±SD	0.361±0.006	0.746±0.008			
2		Recovery%	103.14	106.53			
	DPV	RSD%	1.82	1.06			
		Found ±SD	0.338±0.004	0.688±0.025			
3	SWV	Recovery%	96.57	98.28			
	5 VV V	RSD%	1.02	3.61			

Table No.3: Accuracy and Precision of Commercial preparation of ALN Osteve ®70mg GC electrode (B.R. Buffer pH 10.52)

SD: Standard deviation of triplicate determinations, **RSD:** relative standard deviation, **Recovery**= found/added*100.





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Figure No.3: CV study of ALN (0.25 – 1.2mg.ml⁻¹) using GC as working electrode and BRB pH 10.52 as supporting electrolyte, scan rate 0.1V.S⁻¹, each concentration has done in triplicate



Figure No.4: SWV study of ALN (0.25 – 1.2mg.ml⁻¹) using GC as working electrode and BRB solution pH 10.52 as supporting electrolyte, each concentration has done in triplicate

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Figure No.5: DPV study of ALN (0.25 – 1.2mg.ml⁻¹) using GC as working electrode and BRB solution pH 10.52 as supporting electrolyte, each concentration has done in triplicate

CONCLUSION

Voltammetric determinations indicated that Alendronate sodium is electroactive compound. Parameters affecting voltammetric assay of ALN have been optimized. Basic medium supporting electrolytes should be used for ALN analysis with GC as working electrode. DPV exhibited the best LOD and LOQ, but SWV shows the best accuracy and precision when commercially available ALN (Osteve [®]70mg) tablets have been studied. According to the statistical results of voltammetric analysis of ALN in pharmaceutical formulation, voltammetric determination showed а good repeatability and reproducibility values.

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CONFLICT OF INTEREST

We declare that we have no conflict of interest.

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