Green Atomic Absorption Spectroscopic Methods for the Determination of Rabeprazole Sodium and Fluvastatin Sodium in Pure and Pharmaceutical Dosage Forms

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Authors' contributions

Article Information

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ABSTRACT

Aims: Novel green analytical methods have been proposed for the assay of Rabeprazole sodium and Fluvastatin sodium in their pure and formulated dosage forms.
Study Design: The methods determine each drug through the estimation of its sodium content, using Flame Atomic Absorption Spectroscopy at wavelength 589 nm.
Place and Duration of Study: Central laboratory at Faculty of Pharmacy, Damanhour University. Time duration January-March, 2020.
Methodology: Methods are developed and optimized for maximum sensitivity, selectivity and degree of greenness. Linearity is achieved in the range of 8.29- 66.33 ppm of Rabeprazole sodium (equivalent to 0.5- 4 ppm Na) and 14.13- 141.32 ppm of Fluvastatin sodium (equivalent to 0.75 -7.5 ppm Na). The proposed assays are fully validated regarding ICH guidelines.

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Results: Atomic spectroscopic assays are compared to reported spectrophotometric ones for each drug separately using Student t-test and F-variance ratio.
Conclusion: Satisfactory values indicate good agreement and the insignificant difference between both methods. The obtained percentages of recovery (99-101%) indicate no interference from excipients in formulation matrices.

1. INTRODUCTION

Green Analytical Chemistry is defined briefly as the application of chemical methodologies and procedures to reduce the use of hazardous reagents, solvents and chemicals. This concept has been targeted and achieved in our study with validated accuracy, precision and sensitivity of the proposed assay techniques, Atomic Absorption Spectroscopy (AAS) [1].

AAS is a potent analytical technique that targets elemental analysis in trace amounts. Assay methods based on such technique are of high sensitivity and possess highly selective resonance radiation absorption. They achieve the minimum detection limits at the widest dynamic range and eradication of any spectral interferences. Furthermore, AAS is nominated as eco-friendly and green; owing to the use of distilled water throughout the process, without the incorporation of any hazardous reagents or complex reactions. AAS has been widely applied for estimation of residual active pharmaceutical ingredients in specimens of cleaning validation [2], environmental measurements [3,4], direct as well as the indirect assay of compounds of pharmaceutical interest [5,6].

Rabeprazole sodium (RAB), an official drug in USP 2021 [7], is a proton pump inhibitor that suppresses gastric acid secretion through inhibition of hydrogen/potassium adenosine triphosphatase (H+ /K+ ATPase) enzyme system. It is indicated in GERD, dyspepsia, aspiration syndromes and peptic ulcers. RAB is chemically known as 2-[[[4-(3-Methoxypropoxy) -3-methyl -2-pyridinyl] methyl] sulfinyl] -1H-benzimidazole sodium (Fig. 1) [8]. Literature review shows several analytical techniques for RAB determination by spectrophotometry [9-10], HPLC [11,12], UPLC [13], HPTLC [14], LC-MS/MS [15], and capillary electrophoresis [16].

Fluvastatin sodium (FLU) is officially listed in USP 2007, chemically named as (6-Heptenoic acid, 7-[3-(4- fluorophenyl)-1-(1-methylethyl)-1H-indol-2-yl]-3,5- dihydroxy-monosodium salt, [R*, S*-(E)]- (±)-) (Fig. 1). It is one of the first generation agents of synthetic statins, used to treat hyperlipidemia through inhibition of hydroxyl methyl glutaryl coenzyme A (HMG-CoA) reductase, which is considered a rate limiting step of cholesterol biosynthesis. It is used to lower cholesterol levels, lipoproteins and reduces the risk of cardiovascular diseases [17]. Different analytical approaches were reported for FLU determination including spectrophotometric method [17-19], HPLC [20,21], HPTLC [22] and capillary electrophoresis [23].

All of the previously mentioned and reported techniques either for the assay of RAB or FLU require complex reactions as derivatization, coloring or oxidation reactions, simultaneous equation methods or by chemometrics besides using hazardous and sophisticated reagents. As far as we can tell, no atomic absorption spectroscopic method has been developed for the determination of any of the two drugs.

The proposed work presents green and reliable flame atomic absorption spectroscopic methods for the assay of RAB and FLU in bulk and their pharmaceutical dosage forms through the estimation of their sodium content. The methods are validated regarding ICH elements [24].

2. MATERIALS AND METHODS

2.1 Instrumentation

Thermo Atomic Absorption Flame Spectrophotometer, (UK) computed with solar data station. Sodium was measured at wavelength of 589 nm, band pass of 0.5 nm, relative noise of 1.0 nm, lamp current of 10 mA, and integration time of 5 sec.

2.2 Materials and Reagents

RAB was kindly supplied from SIGMA Pharmaceutical Industries and FLU was provided by Novartis Pharma.

A

B
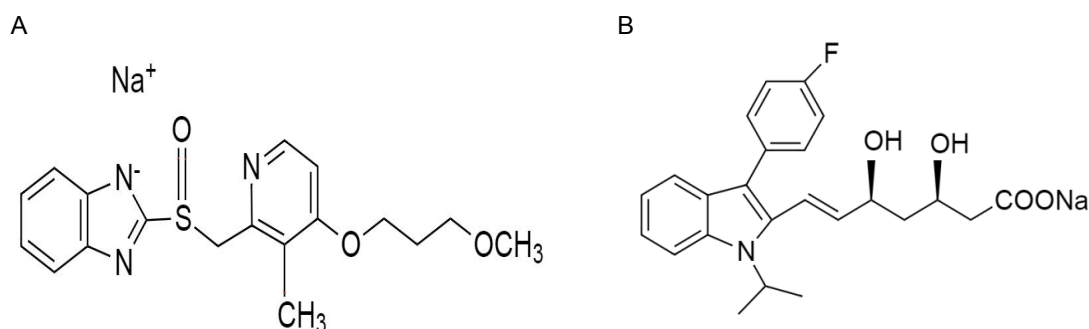
Fig.1. Chemical structures of RAB (A) and FLU (B)

All reagents used throughout the procedure were of analytical grade. Methanol of HPLC grade (Sigma Aldrich, Germany). Hydrochloric acid and Nitric acid (El-Nasr chemical industry company, Egypt). In-house double distilled and deionized water was used.

Lescol xl ® and Pariet ® 20 mg manufactured by Novartis pharma and Janssen, respectively, were purchased from local pharmacy.

2.3 Preparation of Standard Stock Solutions

All glassware was carefully washed with distilled water, methanol and finally with acidified water. In 100-mL volumetric flasks, 50 mg of each of RAB and FLU were accurately weighed and dissolved individually in 25 mL methanol, then the volume was completed to the mark with double distilled water to prepare 0.5 mg/mL stock solution of each drug. Further dilution was made with distilled water.

2.4 Procedure

2.4.1 Construction of the calibration graphs

Into two series of 10-mL volumetric flasks, measured aliquots of RAB and FLU were transferred individually to the flasks. Each solution was diluted to the mark with distilled water to give a concentration range of 8.29-66.33 µg/mL of RAB equivalent to 0.5- 4.0 ppm Na and 14.13- 141.32 µg/mL of FLU equivalent to 0.75 -7.50 ppm Na. Each prepared solution was injected in triplicate. Blank was subtracted from all values. Then, the measured absorbances were plotted against the given sodium concentrations (related to their corresponding drugs concentrations) to obtain the calibration curves for both compounds.

2.5 Preparation of Pharmaceutical Formulations

A number of 10 tablets of each of Lescol xl ® and Pariet ® were accurately weighted. Quantity equivalent to 25 mg of each drug was finally powdered and transferred separately into two 50-mL volumetric flasks, 15 mL of methanol was added to each flask for drugs' extraction. The two volumetric flasks were then sonicated for 20 min and the volume was completed to the mark with distilled water. Finally, the two solutions were filtered by Whattman membrane filter into another two 50-mL volumetric flasks to give final concentration of 0.5 mg/mL for each sample solution. Working sample solutions were prepared by further dilution with distilled water.

3. RESULTS AND DISCUSSION

3.1 Method Optimization

Sodium concentrations (contents) were quantified in both drugs by atomic absorption spectrometry under the following operation conditions: wavelength 589 nm, lamp current 10 mA, band pass 0.5 nm, relative noise 1.0 nm and integration time 5 seconds.

The present study offers simple, eco-friendly and low cost techniques used for the determination of RAB and FLU in their pure form and pharmaceutical preparations. Least consumption of reagents; minimal amount of methanol was used to extract the drugs. Double-distilled water was used throughout the procedure. All glassware was washed with acidified water to prevent any interference from any other elements present in tap water. Thus, sodium concentration can be accurately determined by atomic absorption technique. To investigate the stability

of the two drugs in our method, 1 mL 0.1 M conc HNO_3 was added to both drugs' solutions individually, insignificant difference in absorbance measurement was observed.

3.2 Methods Validation

The presented approach was validated in terms of linearity and range, accuracy, precision, limits of detection and limits of quantification according to the ICH guidelines [24].

3.2.1 Linearity and range

Under the previously mentioned experimental conditions, calibration graphs were attained by plotting the measured A of both drugs (equivalent to Na measured at 589 nm) against their stated concentrations in ppm. Linear relationships were achieved in the range of 8.29- 66.33 µg/mL of RAB equivalent to 0.5- 4 ppm Na and 14.13- 141.32 µg/mL of FLU equivalent to 0.75 -7.5 ppm Na. Statistical data analysis [25] showed satisfactory correlation coefficient values and small values of slope and intercept presented in Table 1.

3.2.2 Limits of detection and quantification

According to the ICH guidelines [24], the following equations were used to measure both; the limits of detection and quantification:

$$LOQ = 10\ \sigma/S$$

$$LOD = 3.3\ \sigma/S$$

Where: σ is the standard deviation of the intercept

S is the slope of the regression line. Table 1 shows LOQ and LOD values for both assays.

3.2.3 Accuracy and precision

Intraday precision was determined by measuring three different concentrations of RAB and FLU covering the linearity range. Each was measured in triplicate within the same day. While, interday precision is measuring the exact concentrations for three successive days. The reported small values of SD and RSD% (<2 shown in Table 2) demonstrate the high precision of the presented methodologies.

Table 1. Regression data for the proposed methods

Parameters	RAB	FLU
Wavelength (nm)	589	589
Linearity range (µg/mL)	8.29 – 66.33	14.13 – 141.32
(Na content in ppm)	0.5 – 4	0.75 – 7.5
Correlation coefficient	0.9988	0.9995
Slope	0.0036	0.0009
Intercept	0.1711	0.2559
LOD (µg/mL)	2.6801	3.8298
(Na content in ppm)	0.1616	0.2032
LOQ (µg/mL)	8.1217	11.6055
(Na content in ppm)	0.4897	0.6158
S_b%	1.9397	1.4815
$S_{y/x}$	0.0035	0.0013

Table 2. Accuracy and precision of the proposed methods

Parameter	Concentration (µg/mL)	Intra-day			Inter-day		
		Mean% recovery ±SD[a]	%RSD[b]	%Er[c]	Mean% recovery ±SD[a]	%RSD[b]	%Er[c]
RAB	16.58	100.12 ± 0.75	0.75	0.12	100.8 ± 1.20	1.19	0.80
	33.16	100.22 ± 1.05	1.05	0.22	99.74 ± 0.79	0.79	-0.26
	49.74	100.09 ± 0.87	0.87	0.09	99.91 ± 0.97	0.97	-0.09
FLU	14.13	99.87 ± 1.17	1.17	-0.13	100.16 ± 1.01	1.00	0.16
	47.11	101.00 ± 0.75	0.74	1.00	99.80 ± 0.62	0.62	-0.20
	94.21	99.91 ± 1.08	1.09	-0.09	100.27 ± 0.72	0.71	0.27

[a] *Mean± standard deviation of three determinations.*
[b] *Percentage relative standard deviation.*
[c] *Percentage relative error*

Table 3. Statistical analysis of the application of the proposed methods on Pariet® and Lescol xl® tablets

Parameter	Pariet® RAB		Lescol xl® FLU	
	Proposed method	Reference method [8]	Proposed method	Reference method [17]
Mean% Recovery ± SD[a]	100.37 ± 1.02	100.81± 0.97	100.58 ± 0.91	100.33 ± 0.81
%RSD[b]	1.02	0.96	0.90	0.80
t-test[*]	0.699		0.429	
F-test[*]	1.105		1.272	

[a] *Mean± standard deviation of five determinations.*
[b] *Percentage relative standard deviation.*
[*] *Theoretical values of t and F at P =.05 are 2.31 and 6.39, respectively.*

3.3 Application to Pharmaceutical Dosage Forms

The suggested assays were applied for the determination of RAB and FLU in Pariet ® and Lescol xl ®, respectively. Satisfactory data outcomes (Table 3) were obtained in terms of mean recovery, SD, and RSD% showing the good accuracy and precision of the technique demonstrating that no excipients or additives have interfered with the results.

The data outcome of the proposed methods was statistically compared (Table 3) using Student's t-test and the variance ratio F-test with reference methods [8,17]. Insignificant differences between them were ascertained.

4. CONCLUSION

A novel, rapid, green and economic analytical method has been developed for the determination of RAB and FLU through quantitation of their sodium ions concentration by flame atomic absorption spectroscopy. The proposed approach shows high accuracy and precision with low values of LOD and LOQ consuming the least amount of reagents. They are directly related to green analytical methodologies that can be incorporated in routine drug analysis in quality control laboratories. Meanwhile, available instrumentation and affordable solvents count as the main privileges for developing countries.

DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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