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DEVELOPMENT AND VALIDATION OF SCPECTROPHOTOMETRIC METHODS FOR THE DETERMINATION OF ALENDRONATE SODIUM IN TABLETS

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ABSTRACT

Two simple and precise visible spectrophotometric methods (A and B) were developed for the estimation of alendronate sodium (ALS) in bulk drug as well as in pharmaceutical dosage forms (tablets). Method A is based on the formation of purple coloured chromogen by the diazotization and coupling reaction of ALS with Bratton – Marshall reagent (N-1-naphthyl)-ethylene diamine dihydrochloride) which has absorption maximum at 555 nm. Method B is based on the condensation reaction of ALS with Ehrlich's reagent (p-dimethylaminobenzaldehyde) to from a yellow chromogen with λ_{max} at 402 nm. Beer's law is obeyed in the concentration range of 100-600 µg/mL and 40-140 µg/mL for methods A and B, respectively. The proposed methods are statistically validated and found to be useful for the routine determination of ALS in tablets.

Key words: Alendronate sodium, Colorimetry, Tablets, Validation

INTRODUCTION

Alendronate sodium (ALS), an amino-bisphosphonate[1] is a potent inhibitor of bone resorption and cartilage destruction. Chemically it is 4-amino-1-hydroxy butylidine-1, 1-biphosphonate. Literature review revealed very few analytical methods including HPLC[3] for simultaneous determination of the bisphosphonate alendronate in human plasma and urine, ion chromatography[3] with indirect UV detection, and spectrophotometric determination[4] of ALS via complex formation with Fe (III) ions in pharamaceutical formulations. In the present work, two simple and sensitive colorimetric methods (A and B) have been developed for the estimation of ALS in bulk drug and pharmaceutical dosage

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forms. In method A, ALS is first diazotized with an aqueous solution of nitrous acid followed by coupling with Bratton-Marshall reagent[5(a)] to from an azo derivative, which absorbs intensely at 555 nm. In method B, ALS is treated with the carbonyl reagent p-dimethylaminobenzaldehyde (Ehrlich's reagent)[5(b)] to from a condensation product which has absorption maximum at 402 nm. Spectrophotometric parameters are established for standardization of the methods including statistical analysis of data.

EXPERIMENTAL

Instrument

All spectral and absorbance measurements were made on Shimadzu UV-VIS spectrophotometer – 1650.

Reagents

(i) Bratton – Marshall reagent (0.5% w/v),

(ii) Sodium nitrite (0.1M),

(iii) Hydrochloric acid (2M),

(iv) Ehrlich's reagent (0.5% w/v).

All reagents used were of analytical grade.

Preparation of standard solution

A 1 mg/mL stock solution of ALS was prepared by dissolving 100 mg of drug in 100 mL of double – distilled water.

Sample preparation

Twenty tablets were weighed and powdered. A quantity equivalent to 25 mg of ALS was weighed accurately, transferred to a beaker, dissolved in double distilled water, filtered through Whatmann filter paper No. 1 into 25 mL volumetric flask and made upto volume with distilled water to get a concentration of 1 mg/mL.

Assay

Method A

Aliquots of ALS ranging from 2.5-15 mL (1.0 mL = 1000 μg) were pipetted out into a series of 25mL volumetric flasks. To each flask, 1 mL of sodium nitrite (0.1 M), 2

mL of hydrochloric acid (2 M) and 2 mL of Bratton – Marshall reagent (0.5% w/v) were added, mixed thoroughly and made upto volume with double distilled water. The absorbance of the purple coloured chromogen was measured at 555 mm against the reagent blank. The purple chromogen was stable for more than 3 hours. The analytical curve was constructed by plotting concentration versus absorbance.

Method B

Aliquots of ALS ranging from 1.0 – 3.5 mL (1.0 mL = 1000 μg) were transferred into a series of 25 mL volumetric flasks. To each flask, 3 mL of Ehrlich's reagent (0.5% w/v) was added and shaken well and made upto volume with double distilled water. The absorbance of the yellow chromogen was measured at 402 nm against the reagent blank. The yellow chromogen was stable fore more than 3 hours. The analytical curve was constructed by plotting concentration versus absorbance.

Sample analysis

Pharmaceutical formulation of ALS was successfully analysed by the proposed methods.

Appropriate aliquots were subjected to the above methods and the amount of ALS was determined from the calibration curves. The results of sample analysis are furnished in Table 2.

RESULTS AND DISCUSSION

The optical characteristics such as absorption maxima, Beer's law limits, molar absorptivity and Sandell's sensitivity are furnished in Table 1.

Table 1. Optical characteristics and precision of the proposed methods A and B

Parameter	Method A	Method B
λ_{max} (nm)	555 nm	402 nm
Beer's law limits (μg/mL)	100-600	40-140
Molar absorptivity (L mol^{-1} cm^{-1})	2.408 x 10^3	2.373 x 10^3
Sandell's sensitivity (μg/cm^2/0.001 absorbance unit)	0.05057	0.01395

Cont…

Parameter	Method A	Method B
Regression equation (*y)		
Slope (b)	0.00341	0.00708
Intercept (a)	-0.6366	0.00513
Correlation co-efficient (r)	1.000	1.000
% RSD	0.4839	0.4934
Standard error (SE)	0.0197	0.0201

*y = a + bc where c is the concentration of ALS in μg/mL

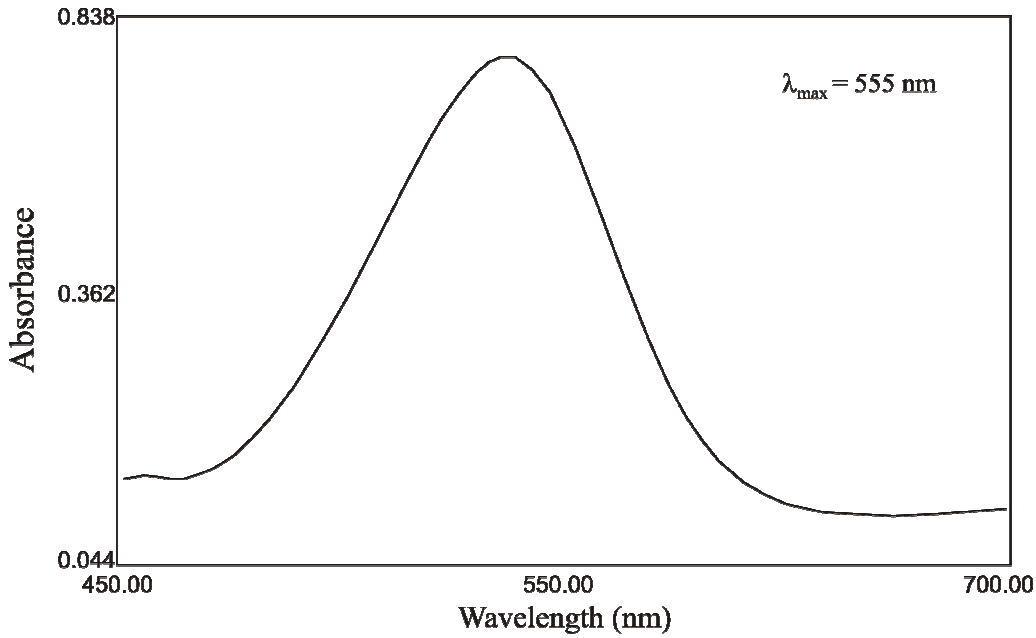

Fig. 1: λ_{max} of purple chromogen by method A

The regression characteristics like slope (b), intercept (a), correlation co-efficient (R), percent relative standard deviation (% RSD) and standard error (SE) were calculated and the results are summarized in Table 1. The results of sample analysis showed that the drug determined by the proposed methods was in good agreement with the label claim proving the accuracy of the proposed methods.

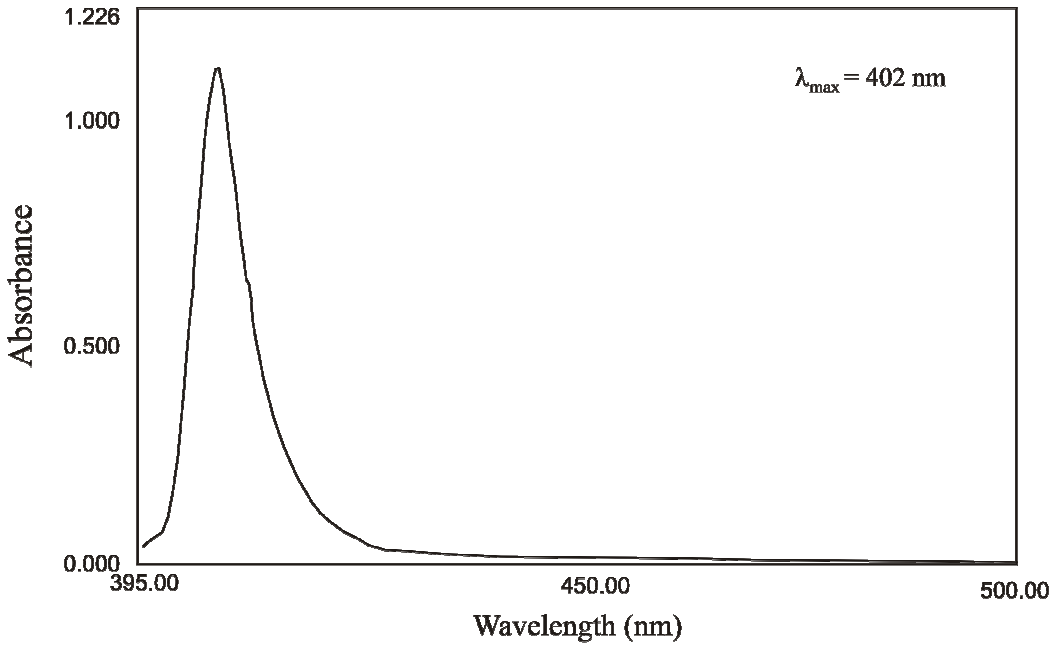

Fig. 2: λ_{max} of yellow chromogen by method B

Table 2. Assay and recovery of ALS in dosage forms

Method	Labelled amount (mg)	Amount obtained (mg)*	Percentage recovery**
A	10	10.04	99.98%
B	10	9.97	100.1%

*Average of six determinations

**Average of three determinations

To study the accuracy and reproducibility of the proposed methods, recovery experiments were carried out by adding a known amount of drug to prenalysed sample and the percentage recovery was calculated. The results are furnished in Table 2. The results indicate that there is no interference of other ingredients present in the formulations. Thus, the proposed methods are simple, sensitive, economical, accurate, reproducible and are useful for the routine determination of alendronate sodium in bulk drug and its pharmaceutical dosage forms.

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REFERENCES

1. P. P. Lehenkari and P. Heikkila, Mol. Pharmacol, **62**, 1255 (2002).
2. W. F. Klinee and B. K. Matuszewski, J. Chromatogr. Biomed. Appl., **121(2)**, 183-193 (1992).
3. E. W. Tsai, S. D. Chamberlin, R. J. Forsyth and C. Bell, J. Pharm. Biomed. Anal., **12(8)**, 983-991 (1994).
4. J. Kuljanin, I. Janckovic, J. Nedeljkevic and V. Marinkovic, J. Pharm. Biomed. Anal., **28(6)**, 1215-1220 (2002).
5. A. H. Beckett and J. B. Stenlake, Practical Pharmaceutical Chemistry, Vol. II, 4th edition, Atholone Press, U. K. (a) p. 301, (b) p. 303.

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