



## A New, Simple and Economical Spectrophotometric Method for the Estimation of Alendronate Sodium in Pharmaceutical Formulation

<sup>1</sup>Asad Gulzar, <sup>1</sup>Sajid Mahmood\*, <sup>2</sup>Zaheer Ahmad, <sup>1</sup>Muhammad Aslam, <sup>1</sup>Aysha Akbar, <sup>1</sup>Abbar Hussain, <sup>3</sup>Naresh Kumar

<sup>1</sup>Division of Science and Technology, University of Education, Township Campus, College Road, Lahore, Pakistan.

<sup>2</sup>Department of Chemistry, University of Wah, Wah Cantt, Pakistan.

<sup>3</sup>Underground Coal Gasification Project Thar, Islamkot, Pakistan.

\*Corresponding author's E-mail: [sajid\\_iccs@yahoo.com](mailto:sajid_iccs@yahoo.com)

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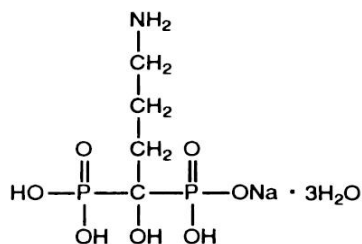
### ABSTRACT

A new, simple, precise and accurate U.V-Spectrophotometric method was developed and validated for the analysis of alendronate sodium in raw material and tablets. The method employed copper sulphate and nitric acid as (1:1) diluent solution and used to derivatize a drug. This derivatized product was measured at 234 nm. The linear regression analysis data for the calibration plot showed good linear relationship with ( $R^2 = 0.9926$ ) in the concentration range 10-120 ppm with correlation coefficient  $r = 0.999$ . Recovery studies for alendronate sodium were found to be  $99.9 \pm 0.964\%$ . It was also found that the excipients in the commercial tablets did not interfere with the method. The results of the tablet analysis were validated with respect to accuracy, precision and recovery studies which were found to be satisfactory. LOD and LOQ for alendronate sodium were found to be 4.242 and 12.857 ppm respectively. The method has successfully applied in the analysis of marketed formulation.

**Keywords:** Alendronate sodium, U.V spectroscopy, Copper sulphate and Nitric acid as (1:1) diluent solution.

### INTRODUCTION

Alendronate sodium (Figure 1) is a nitrogen containing bisphosphonate which binds bone surfaces and inhibits bone resorption by osteoclasts. It belongs to the bisphosphonate group and is used for the treatment of Paget's disease of bone and osteoporosis. It diminishes bone resorption and thus reduces bone turnover<sup>1</sup>.



**Figure 1:** Chemical structure of Alendronate sodium

Alendronate sodium has low bioavailability, less than 1%, and this is due to its poor lipophilicity, which refers to the ability of a chemical compound to dissolve in fats, oils, lipids, and non-polar solvents such as hexane or toluene. Poor lipophilicity of alendronate sodium prevents transcellular transport, in which the transport of molecules is done through the cells of an epithelial cell layer, across the epithelial barriers<sup>2</sup>.

Among the different strategies to overcome the difficulty of low bioavailability of alendronate sodium or of other drugs, the microencapsulation is one of the most important<sup>3</sup>.

The adverse effects related to alendronate sodium may include nausea, vomiting, abdominal pain, heartburn,

difficulty, swallowing, flu-like symptoms such as fever, muscle aches, and fatigue, back, chest, bone, and joint pain, skin blistering or discoloration, which may be delayed, dizziness or headache, and skin rash. Possible allergic reaction may occur if inhaled, ingested or in contact with skin. Overdose of alendronate sodium may lead to hypocalcemia (muscle or nerve twitches, numbness or tingling of fingers and toes, and mood or mental changes) and hypophosphatemia (shortness of breath and muscle weakness).

The acute and chronic effects that may occur are the irritation in eyes, skin, gastrointestinal or respiratory tract and possible hyper sensitization respectively<sup>4</sup>.

Literature survey shows that few analysis methods like HPLC/ESI-MS for the quantitative determination of alendronate<sup>5</sup>, osteoporosis clinical studies<sup>6</sup>, quantifying of alendronate sodium in human plasma by HPLC<sup>7</sup> (USP-2010) and pi-acceptors for UV-spectrometry<sup>8</sup> are reported.

Since these methods were based on HPLC/ESI-MS, pi-acceptors for UV-Spectrometry only and there was no method has been developed by using copper sulphate and nitric acid (1:1) as diluent solution in UV-Spectrophotometrically and also this procedure was economical and more precise for the determination of alendronate sodium in tablet dosage form at 234 nm, so here an attempt has been made to develop a new UV-Spectrophotometric method for the estimation of alendronate sodium in pharmaceutical formulation with simplicity, accuracy and economy.

The aim of the present work is to develop and validate an economical, accurate, precise and reproducible UV-

Spectrophotometric method for the determination of alendronate sodium as in solid dosage form.

Drug was found to be freely soluble in copper sulphate and nitric acid as (1:1) diluent solution which was chosen for proceeding study.

Physiochemical parameters such as appearance, size, weight variation, average weight, uniformity of content, disintegration time, chemical assay and validation parameters such as linearity, accuracy, precision, robustness, ruggedness, limit of detection and limit of quantitation were performed.

## MATERIALS AND METHODS

All spectrophotometric measurements were carried out using a single beam ultraviolet spectrophotometer (Cecil CE 2041, 2000 series) with 1 cm thickness of cell.

A high precision analytical balance (JS-110, Japan) was used to weigh the sample and standard (Alendronate Sodium) material. A disintegration test apparatus (Model DG-D-202) was used for investigating the disintegration time of sample tablet.

The alendronate sodium reference standard (99.2%) pure was obtained from Cadila Pharma India. An alendronate sodium tablet (Aldrobone tablet label claim 10 mg) was collected from Obsons pharmaceutical Lahore.

Other chemicals, copper sulphate and nitric acid were of analytical grade and were used for derivitization of drug.

## Preparation of Standard solution for Calibration Curve

66 mg of alendronate sodium RS equivalent to 10 mg of alendronate which is the reference standard was dissolved in 60 mL solution of copper sulphate and nitric acid diluent solution (1:1) by means of a reciprocating shaker (ultrasonic bath) for 10 minutes and then made the volume up to 100 mL with diluent solution.

Took 5 mL from the above standard solution and diluted it by adding copper sulphate and nitric acid diluent solution and made the volume up to 100 mL.

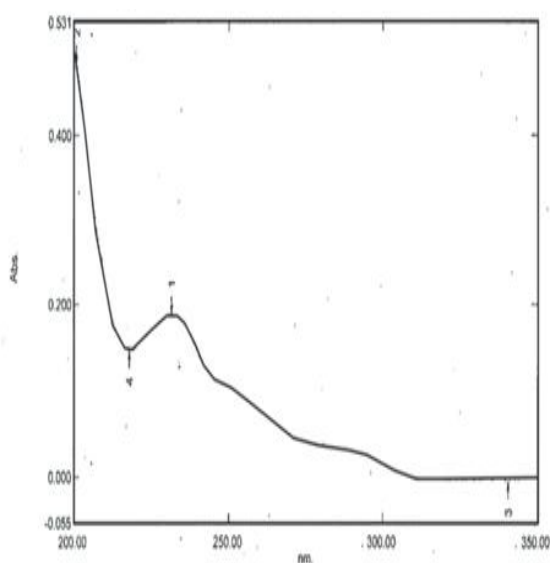
## Determination of Chemical Assay

Twenty tablets weighed, each tablet contains 10 mg of alendronate sodium was weighed, finally powdered and an amount of powder sample equivalent to 10 mg of alendronate was taken in 100 mL volumetric flask and dissolved in 3×30 of copper sulphate and nitric acid as (1:1) diluent solution by means of reciprocating shaker (ultrasonic bath) for 5-10 minutes and extracted by sonication to ensure complete solubility of the drug. The excipients were separated by filtration, finally combined the filtrate of the extract and from the above solution 5 mL were taken and make up to 100 mL with the diluent solution for the analysis. The absorbance of the diluted standard and sample solution was found by means of a spectrophotometer (single beam) at 234 nm. The result of analysis of alendronate sodium from tablet dosage formulation is shown in Table 1. A typical UV-spectrum obtained from a standard and sample is shown in Figure 2 and 3.

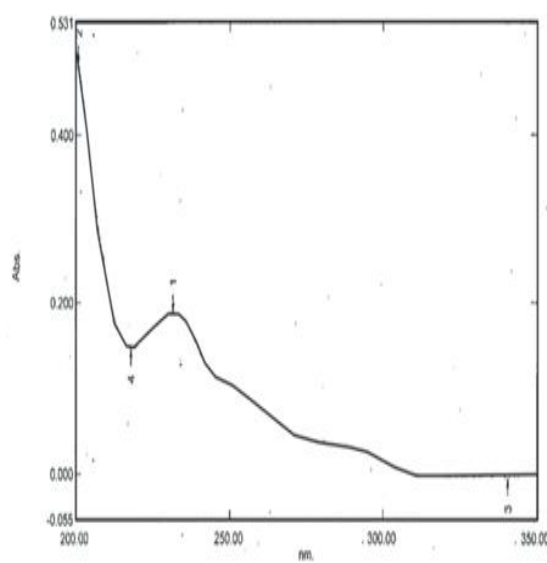
**Table 1:** Percentage Recovery for Alendronate Sodium.

Brand Name	Label Claim (mg/tab)	Amount Taken for Assay (gm)	Amount of Drug Estimated (mg/tab)	% of Label Claim Estimated $\pm$ S.D*
Alendronate Sodium	10 mg	0.2304	10.05 mg	100.5 %

\* Mean of six determination



**Figure 2:** UV-Spectrum of standard alendronate sodium



**Figure 3:** UV-Spectrum of sample Alendronate sodium

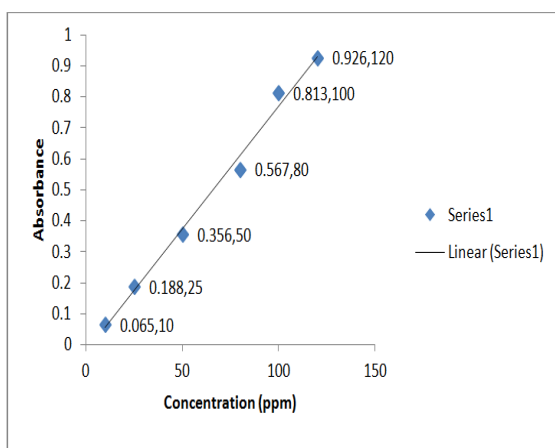


Figure 4: Linearity study for Alendronate Sodium

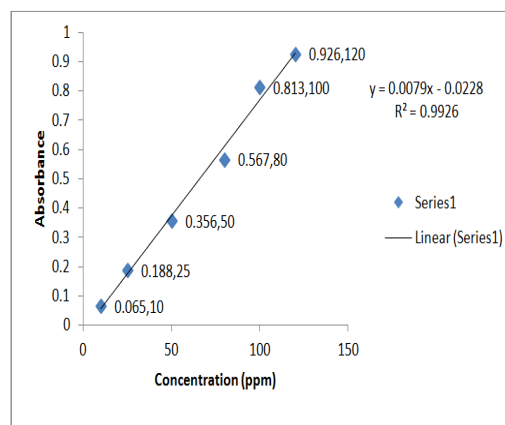


Figure 5: Calibration curve of Alendronate sodium by Ultraviolet Spectroscopy.

### RESULTS AND DISCUSSION

The aim of the present study was to develop and validate the method of alendronate sodium under the suitable spectral conditions. Estimation of alendronate sodium by UV Spectroscopy method was carried out. The standard and sample solution was prepared and the UV- spectrum was recorded. The spectrum of standard and sample solution was presented in Figure 2 and 3. The absorbance of standard and sample solutions was calculated. The assay procedure was repeated according to mean concentration of standard and sample. The percentage of the recovered of individual drug found in formulation was calculated and presented in Table 1. The result of the analysis shows that the amount of the drug was in good agreement with the label claim of the formulation.

#### Method Validation

The given assay was proposed and validated in accordance with ICH guidelines for linearity, accuracy, precision, specificity, ruggedness and robustness (ICH, 1996).

#### Linearity

Table 2: Linearity Study for Alendronate Sodium

S. No	Concentration of Alendronate Sodium (ppm)	Absorbance (234 nm)
1	10	0.065
2	25	0.189
3	50	0.356
4	80	0.567
5	100	0.813
6	120	0.926

Linearity of the drug was found by serially diluted calibration solution ranging from 10-120 ppm as mentioned in Table 2. The standard and sample solutions were taken separately. The calibration data was generated which showed a linear relationship between concentration and absorbance. The value of correlation coefficient and regression coefficient obtained was 0.999

and > 0.992 for the drug which indicated a linear relation exists between concentration and absorbance as is shown in Figure 4 and 5. The regression equation was  $y = 0.007 x - 0.022$ . It is shown in Table 3.

Table 3: Summary of Optical and Regression Parameters

S. No	Parameters	UV-Spectrophotometric Method
1	Linearity Range (ppm)	10-120
2	$\lambda_{max}$	234 nm
3	Beer's Law Limit	10-120
4	Regression Equation	$y = 0.007 x - 0.022$
5	Correlation Coefficient	$r = 0.999$
6	Regression Coefficient	$R^2 = 0.9926$
7	Slope	0.007

#### Accuracy and Precision

Table 4: Summary of Validation Parameters

S. No	Parameters	Validation Results
1	Accuracy (%)	99.9
2	Level of Spiking	9.99
3	Precision (% RSD)	101.2±0.954 and 101.4±0.956
4	LOD (ppm)	4.242 ppm
5	LOQ (ppm)	12.857 ppm

The accuracy of the method was proved by performing recovery study in the commercially available formulations. Values greater than 99% indicated that the proposed method is accurate for the analysis of drug.

The precision of the method was checked in terms of inter-day and intraday, where the methods were repeated on three different days and also repeated on three different time periods in the same day.

The mean % assay for intraday and inter-day was found to be 101.2±0.954 and 101.4±0.956 respectively, which was very close to the proposed assay value (100.5%),

hence the method was found to be precise. Summary of validation parameters are shown in Table 4.

### CONCLUSION

The proposed method for the estimation of alendronate sodium by UV-Spectrophotometer in tablet dosage form is simple, economic, precise, specific and highly accurate, so it can definitely be employed for the routine analysis.

Hence this method of development and validation of alendronate sodium tablet dosage form in UV method is suitable for quality control analysis.

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