

A Simple and Sensitive UV Spectrophotometric Method for the Determination of Ibandronate Sodium in Pharmaceutical Formulations and Bulk Drugs

ABSTRACT:

Aims: A simple and cost effective spectrophotometric method is developed for the determination of Ibandronate sodium in pure form and in pharmaceutical formulations

Place and Duration of Study: Department of Pharmacognosy and Ethnopharmacology Division, CSIR-National Botanical Research Institute and Integral University up to 5 month,

Methodology: The drug was highly soluble in sodium hydroxide so it was selected as the solvent system for the drug. This ensured adequate drug solubility and maximum assay sensitivity. The linearity range for Ibandronate sodium at its wavelength of detection of 215nm was obtained as 25–200µg/ml. The linear regression equation obtained by least square regression method, were $Y = 0.0011X + 0.034$, where Y is the absorbance and X is the concentration (in µg/ml) of pure drug solution.

Results: The absorbance was found to increase linearly with increasing concentration of Ibandronate sodium, which is corroborated by the calculated correlation coefficient value of 0.9999. The limit of detection and limit of quantification was found to be 8.6900 µg/ ml & 26.333µg /ml respectively.

Conclusion: The validity of the described procedure was assessed. Statistical analysis of the result shows high accuracy and good precision. The proposed method was successfully applied to the determination of Ibandronate sodium in pharmaceutical formulations without any interference from common excipients.

Keywords: Ibandronate sodium, Absorbance, Validation, Detection Limit

1. Introduction:

Ibandronatesodium is a nitrogen-containing bisphosphonate. Chemically is 3-(N-methyl-N-pentyl) amino-1-hydroxypropane-1, 1-diphosphonic acid, monosodium salt, monohydrate with the molecular formula $C_{9}H_{22}NO_7P_2Na.H_2O$ and a molecular weight of 359.23. It inhibits osteoclast-mediated bone resorption[1]. Ibandronate is effective for the treatment of hypercalcemia of malignancy [2], metastatic bone disease [3], postmenopausal osteoporosis, corticosteroid-induced osteoporosis, and Paget's disease. The action of ibandronate on bone tissue is

based on its affinity for hydroxyapatite, which is part of the mineral matrix of bone [2]. In postmenopausal women, it reduces the elevated rate of bone turnover leading to, on average, a net gain in bone mass [4-5]. Literature survey reveals only one HPLC method for the estimation of Ibandronate and its related substances. The aim of the study is to develop a simple, sensitive, accurate and precise method for determination of ibnadronatesodium in pharmaceutical formulations and bulk drugs using UV spectrophotometer [6] (Fig .1).

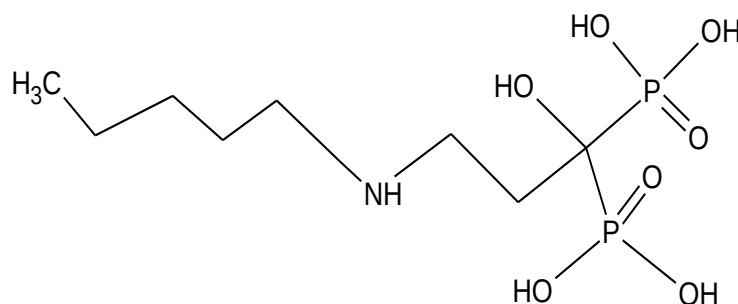


Fig.1. Ibandronate sodium

2. MATERIAL AND METHODS:

2.1 Instruments & Reagents

All solvents and reagents used in this work were purchased from Fisher Scientific, Mumbai. Ibandronate sodium pure drug (Batch No. E/999/11002) is a gift sample of MacLeod's pharmaceuticals Pvt Ltd, Baddi. Shimadzu UV- Visible Spectrophotometer (UV-1700) with a matched pair of 10 mm quartz cells were used for experimental purpose. Shimadzu AUX-220 balance was used for weighing the samples

2.2 Preparation of 0.1N NaOH 0.4 gm of NaOH was accurately weighed in a 100ml volumetric flask, dissolved in 10 ml of double distilled water & final volume was made to 100ml.

2.3 Scanning and determination of maximum wavelength (λ_{max}) In order to ascertain the wavelength of maximum absorption (λ_{max}) of the drug, qualitative solution of the drug was prepared in NaOH and scanned using UV spectrophotometer within the wavelength region of 200-400 nm against NaOH as blank. The absorption curve showed characteristic absorption maxima at 215 nm for Ibandronae Sodium (Fig. 2).

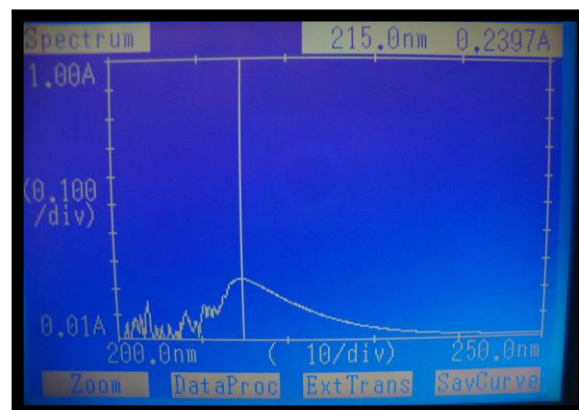


Fig.2. UV curve of Ibandronate sodium in 0.1 N NaOH solution

2.4 Preparation of Standard Stock Solutions Standard stock solution (primary) was prepared by dissolving 10 mg of Ibandronate sodium in 10 ml of NaOH to get concentration of 1mg/ml (1000 μ g/ml) and was stored at 25 $^{\circ}$ C during the study.

2.5 Preparation of calibration standard solutions The calibration standard solutions were prepared daily by diluting primary stock solution with NaOH to get calibration standard solutions of 25, 50,100,150,200 μ g/ml of ibandronate sodium to construct Beer's law plot for pure drug, the absorbance was measured at λ_{max} 215 nm, against NaOH as blank.

2.6 Procedure for formulations Twenty tablets of Ibandronate sodium were accurately weighed, finely powdered and mixed. A portion of the powder equivalent to 10mg of ibandronate sodium was transferred into a 10 ml volumetric flask and small volume of NaOH was added. The content of the flask was sonicated for 15 min and diluted to final volume of 10ml with NaOH (1000 μ g/ml). This solution was centrifuged for 15 min at 5000 rpm to separate out the insoluble excipients. Appropriate solutions were prepared by taking suitable aliquots of the clear supernatant and diluting them with NaOH to give final concentration (150 μ g/ml). The absorbance of these solutions was measured at 215 nm. The amount of ibandonate sodium per tablet was calculated using the calibration curve

93 **3. RESULT AND DISCUSSION:**



94 **3.1 Validation**

95 Validation is one of the most important steps in method development for analytical
96 determinations. The main validation parameters such as linearity and range,
97 accuracy and precision, limit of detection (LOD), limit of quantitation (LOQ),
98 recovery and ruggedness were evaluated in developed method.

99 **3.2 Linearity and Range:**

100 Under the experimental conditions, the calibration graphs of the absorbance versus
101 concentration were found to be linear over the range of 25-200µg/ ml for proposed
102 method. The statistical analysis of data obtained for the estimation of ibandronate
103 sodium in pure solution indicated high level of accuracy for the proposed methods
104 as evidenced by the low values of standard deviation and coefficient of variation.
105 The linear regression equation obtained was $Y = 0.0011X + 0.034$, where Y is the
106 absorbance and X is the concentration (in µg/ml) of pure drug solution. Linearity of
107 the regression equation and negligible scatter of points for the two drugs by the
108 proposed methods were demonstrated from the highly significant ($p > 0.05$)
109 correlation coefficient value. The reported slope values without intercept on the
110 ordinate at 95% confidence limits, suggested that the calibration lines of Ibandonate
111 sodium solutions in NaOH did not deviate from the origin as the above-obtained
112 values fall within the confidence limits (Table.1 &2, Fig.3).

113 **Table. 1** Linearity table of Ibandronate sodium in Working Standard

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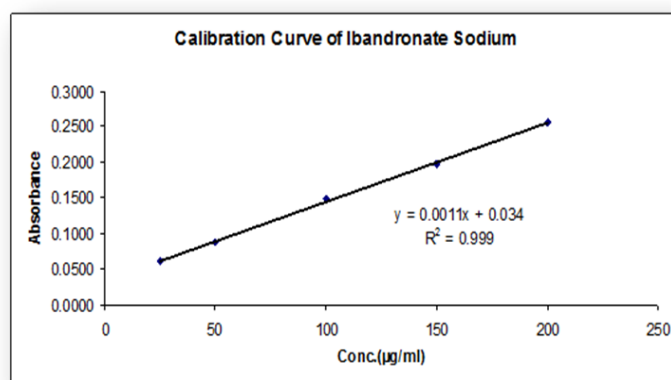
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Conc. (µg/ml)	Mean Absorbance*	Std. Error	%CV
25	0.0606±0.0012	0.0007	1.9278
50	0.0886±0.0017	0.0010	1.8972
100	0.1493±0.0015	0.0009	1.0145
150	0.1985±0.0019	0.0011	0.9617
200	0.2555±0.0013	0.0007	0.4893

125 *Average of three determinations with standard deviations

126 CV – Coefficient of variation

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129 **Fig.3.** Linearity curve of ibandronate sodium

130 **Table.2.** Regression Analysis of Data for the Estimation of Ibandronate Sodium from

131 Standard Solution

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Statistical Parameters	Ibandronate Sodium
Regression equation	$Y=0.0011X+0.034$
Correlation coefficient	0.999
Molar absorptivity, $L\ mol^{-1}cm^{-1}$	5.9542×10^2
Standard error of slope	2.0405×10^{-5}
Standard error of intercept ordinate	2.5095×10^{-3}
Standard error of estimate	2.9216×10^{-3}
95% confidence interval of slope	$1.0445 \times 10^{-3}, 1.1744 \times 10^{-3}$
95% confidence interval of Intercept	$2.6001 \times 10^{-2}, 4.1974 \times 10^{-2}$

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134 3.3 Accuracy

135 To determine the accuracy of the proposed method, recovery studies were carried

136 out by adding different amounts (80%, 100%, and 120%) of bulk samples of

137 Ibandronate sodium within the linearity range were taken and added to the pre-
 138 analyzed formulation of concentration 50µg/ml.From that percentage recovery
 139 values were calculated (Table. 3)

140 **Table.3.** Accuracy Readings

Sample ID	Concentration (µg/ml)		% Recovery	Statistical analysis
	Pure drug	Formulation		
S1:80%	40	50	101.3	Mean=100.63 SD=1.53 %RSD=1.52
S2:80%	40	50	102.6	
S3:80%	40	50	98.5	
S4:80%	40	50	99.2	
S5:80%	40	50	100.7	
S6:80%	40	50	101.5	
S7:100%	50	50	98.6	Mean=99.62 SD=0.84 %RSD=0.85
S8:100%	50	50	99.7	
S9:100%	50	50	99.2	
S10:100%	50	50	101.1	
S11:100%	50	50	99.3	
S12:100%	50	50	99.8	
S13:120%	60	50	98.2	Mean=99.23 SD=1.01 %RSD=1.02
S14:120%	60	50	98.9	
S15:120%	60	50	98.4	
S16:120%	60	50	99.1	
S17:120%	60	50	99.9	
S18:120%	60	50	100.9	

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142 % Recovery = (amount recovered/amount introduced) X 100

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144 **3.4 Precision:**

145 The precision of the proposed method was ascertained by actual determination of
146 six replicates of fixed concentration of the drug within the Beer's range and finding
147 out the absorbance by the proposed method. From this absorbance, mean,
148 standard deviation and % RSD was calculated (Table 4).

149 **Table. 4.** Precision readings

150	Concentration	Absorbance	Statistical Analysis
151	100	0.1496	Mean= 0.1511
152	100	0.1527	
153	100	0.1536	SD=0.0019
154	100	0.521	
155	100	0.1488	% RSD=1.2828
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158 **3.5 Detection & Quantitation limit:**

159 The detection limit of an individual analytical procedure is the lowest amount of
160 analyte in a sample which can be detected but not necessarily quantitated as an
161 exact value. The quantitation limit of an individual analytical procedure is the lowest
162 amount of analyte in a sample which can be quantitatively determined with suitable
163 precision and accuracy. The LOD and LOQ were calculated by using the relation
164 $3.3\sigma/S$ and $10\sigma/S$ respectively, where σ is the standard error of estimate and S is
165 the slope. Calculated values of limit of detection (LOD) and quantitation (LOQ) for
166 Ibandronate sodium were found to be 8.6900 and 26.333 $\mu\text{g/ml}$ respectively.

167 **3.6 Analysis of pharmaceuticals formulations:**

168 The optimized spectrophotometric method was applied to the direct determination of
169 Ibandronate sodium in tablet using calibration curve method without any sample
170 extraction or filtration. From the absorbance value, the drug content per tablet (on
171 an average weight basis) was calculated (Table 5).

Table. 5. Analysis of pharmaceuticals formulation

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UV Spectrophotometric Method				
	Labelled	Amount	% Drug	%RSD
Formulation	Amount (mg)	Recovered*	Recovered	
Tablet	150mg	149.861±0.07954	99.901	0.5308

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4.CONCLUSION:

In this study a simple, fast and reliable UV spectrophotometric method was developed and validated for the determination of Ibandronate sodium in bulk drug & pharmaceutical formulations. This method was applied directly to the analysis of pharmaceutical dosage forms without the need for separation such as extraction steps prior to the drug analysis. As this proposed method has the lowest LOD value and wider linear range is more sensitive method. From the results obtained, we concluded that the suggested method showed high sensitivity, accuracy and precision. Moreover, this method is simple and inexpensive and it can be employed for the routine quality control of Ibandronate sodium in pharmaceutical formulations.

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