Journal of Advances in Medical and Pharmaceutical Sciences
6(3): 1-7, 2016, Article no.JAMPS.20079
ISSN: 2394-1111

SCIENCEDOMAIN *international*
www.sciencedomain.org

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

Lubna Azmi[1*], Ila Shukla[1], Shyam Sundar Gupta[1], Paramdeep Bagga[2] and Ch. V. Rao[1]

[1]Pharmacognosy and Ethnopharmacology Division, CSIR-National Botanical Research Institute, Lucknow-226 001, Uttar Pradesh, India.
[2]Integral University, Kursi Road, Lucknow, Uttar Pradesh, India.

Authors' contributions

This work was carried out in collaboration among all authors. Author LA designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors IS and SSG managed the analyses of the study. Authors PB and CVR provide guidance for work. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/JAMPS/2016/20079
Editor(s):
(1) Dongdong Wang, Department of Pharmacogonosy, West China College of Pharmacy, Sichuan University, China.
Reviewers:
(1) Anonymous, Cukurova University, Turkey.
(2) Md. Tariq Namad, Military Hospital Meknes, Morocco.
(3) Giulio Mari, Desio Hospital, Italy.
Complete Peer review History: http://sciencedomain.org/review-history/13065

Original Research Article

Received 10th July 2015
Accepted 1st January 2016
Published 25th January 2016

ABSTRACT

Aims: A uncomplicated and outlay efficient spectrophotometric method is developed for the determination of Ibandronate sodium in unadulterated form and in pharmaceutical formulations.
Place and Duration of Study: Department of Pharmacognosy and Ethnopharmacology Division (Pilot plant), CSIR-NBRI, Lucknow, India and Integral University up to 6 month.
Methodology: The drug was highly soluble in sodium hydroxide (NaOH) so it was selected as the solvent system for the drug. This method determines sufficient solubility of drug and assay

**Corresponding author: E-mail: azmilubna@gmail.com;*

sensitivity. The linearity range for Ibandronate sodium at its wavelength of detection of 215 nm was obtained as 25–200 µg/ml. The linear regression equation determined 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 be set up to rise linearly with increasing concentration of Ibandronate sodium, which is obtained by the calculated correlation coefficient value of 0.9999. The limit of detection and limit of quantification was set up to 8.6900 µg/ ml & 26.333 µg /ml respectively.

Conclusion: The validity of the determined procedure was assessed. Statistical analysis of the result shows elevated accuracy and good precision. The proposed method was effectively applied to the fortitude of Ibandronate sodium in pharmaceutical formulations without any interference from ordinary excipients.

Keywords: Ibandronate sodium; absorbance; validation; detection limit.

ABBREVIATIONS

UV: Ultraviolet spectroscopy; HPLC: High pressure liquid chromatography; LOD: Limit of detection; LOQ: Limit of quantitation; SD: Standard deviation; and RSD: Relative standard deviation; MW: Molecular weight; CV: Coefficient of variation.

1. INTRODUCTION

Ibandronate sodium is one of the nitrogen-carrying bisphosphonate. According to IUPAC nomenclature it is 3-(N-methyl-N-pentyl) amino-1-hydroxypropane-1,1-diphosphonic acid, sodium salt, monohydrate with the molecular formula $C_{9}H_{22}NO_{7}P_{2}Na.H_{2}O$ and MW of 359.23. It prevent osteoclast-conciliate bone resorption [1]. It is precious for the cure of hypercalcemia of malignancy [2], Paget's disease, postmenopausal osteoporosis, and corticosteroid-induced osteoporosis metastatic bone disease [3]. The activity of ibandronate on bone tissue is depending on its resemblance for hydroxyapatite, which is fraction of the mineral matrix of bone [2]. In postmenopausal women, it decrease the high rate of bone mass, leading to, a net gain in bone mass [4-5]. For quantification of impurity and assay of ibandronate sodium, there are so many analytical methods have been determined [6-9]. Literature assessment exposed only one HPLC method for the estimation of Ibandronate and its related substances The chromatographic separation was performed on an anion column with a particle size of 7µ (150X4.6) and 0.2% v/v formic acid adjusted to pH 3.2 as mobile phase at flow rate of 1.2 mL/minutes [10]. The aim of our study is to develop a easy responsive accurate and precise method for determination of ibandronate sodium in pharmaceutical formulations and bulk drugs using UV spectrophotometer [11] (Fig. 1).

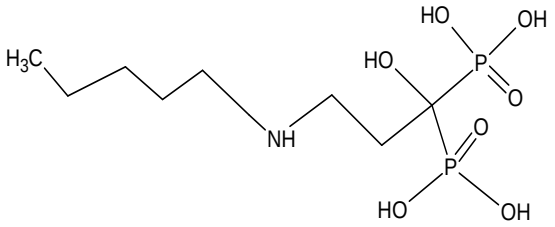

Fig. 1. Ibandronate sodium

2. MATERIALS AND METHODS

2.1 Instruments and Reagents

Ibandronate sodium drug (Batch No. E/999/11002) was obtained from MacLeod's pharmaceuticals Pvt Ltd, Baddi. Shimadzu UV Visible Spectro- photometer (UV-1700) with a synchronized pair of 10 mm quartz cells were used for experimental reason.

2.2 Preparation of 0.1N NaOH

0.4 gm of NaOH was accurately weighed in 100 ml volumetric flask and it was dissolved in 10 ml of double distilled water & final volume was made to 100 ml.

2.3 Determination of Maximum Wavelength (λmax)

In order to ascertain the wavelength of utmost absorption (λ_{max}) of the drug, solution of the drug

was prepared in NaOH and solution was scanned within the wavelength region of 200-400 nm against NaOH as blank using UV spectrophotometer. At 215 nm ibandronate sodium maximum absorption in absorption curve (Fig. 2).

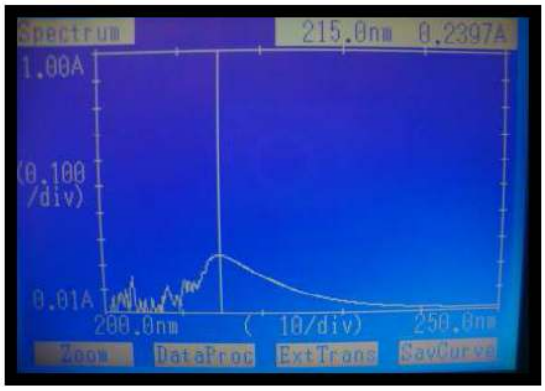

Fig. 2. UV curve of Ibandronate sodium in 0.1 N NaOH solution

2.4 Preparation of Primary Stock Solutions

Normal stock solution (primary) was geared up by dissolving 10 mg of Ibandronate sodium in 10 ml of NaOH, to get end point concentration of 1 mg/ml (1000 µg/ml) and stock solution was stored at 25℃ during the study.

2.5 Preparation of Calibration Standard Solutions

Standard solution was prepared daily by diluting primary stock solution with NaOH. To get calibration standard solutions of 25, 50,100,150,200 µg/ml of ibandronate sodium to construct Beer's law plot for pure drug, the absorbance was calculated at λ max 215 nm, against NaOH which was considered as blank.

2.6 Process for Formulations

20 tablets of Ibandronate sodium were precisely weighed powdered and finally assorted A part of the powder equivalent to 10 mg 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 up to final volume of 10 ml by means of NaOH (1000 µg/ml). Sample was centrifuged for 15 min at 5000 rpm to break up out the insoluble excipients. Solutions were prepared by taking suitable aliquots of the clear supernatant and diluting them with NaOH to give final concentration (150 µg/ml). The absorbance of these solutions was measured at 215 nm. The amount of ibandonate sodium per tablet was calculated using the calibration curve.

3. RESULTS AND DISCUSSION

3.1 Validation

Validation is one of the noteworthy step for analytical determination of any drug. There are a number of most significant validation parameters such as linearity and range, accuracy and precision, LOD, LOQ, recovery and ruggedness were assessed in developed method.

3.2 Linearity and Range

Under the appropriate experimental conditions, the calibration graphs of the absorbance against concentration were found to be linear over the range of 25-200 µg / ml for projected method. The arithmetical analysis of data obtained for the determination of ibandronate sodium in pure solution summit to high echelon of accuracy for the optional methods as corroboration via the minute principles of deviation coefficient of variation and standard. Linear regression equation was: Y = 0.0011X + 0.034, Y is the absorbance and X is the concentration (in µg/ml) of unadulterated drug solution. Linearity of the regression equation and trifling were determined from the exceptionally significant ($p > 0.05$) correlation coefficient value. Without intercept determined slope values at 95% confidence limits, optional that the calibration lines of Ibandonate sodium solutions in NaOH did not diverge from the source as the above-obtained values fall inside the confidence limits (Tables 1 and 2, Fig. 3).

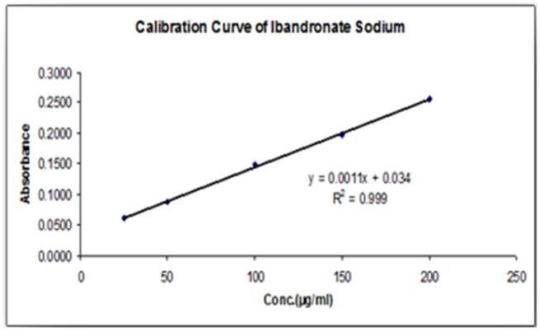

Fig. 3. Linearity curve of ibandronate sodium

Table 1. Linearity table of Ibandronate sodium in working standard

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

**Average of three determinations with standard deviations; CV – Coefficient of variation*

Table 2. Regression analysis of data for the inference of Ibandronate sodium from standard solution

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	1.0445×10^{-3}, 1.1744×10^{-3}
95% confidence interval of Intercept	2.6001×10^{-2}, 4.1974×10^{-2}

3.3 Accuracy

To make a decision the accuracy of the proposed method, recovery studies was approved out by adding different amounts (80%, 100%, and 120%) of samples of Ibandronate sodium within the linearity range were in use and supplementary to the pre-analyzed formulation of concentration 50 µg/ml and percentage recovery values were calculated (Table 3).

3.4 Precision

The precision of the projected method was determined by actual fortitude of six replicates of fixed attentiveness of the drug within the Beer's range and verdict out the absorbance by the anticipated method. From this absorbance, mean, standard deviation and % RSD was calculated (Table 4).

3.5 Recognition & Quantitation Limit

The detection limit of an individual analytical procedure is the buck amount of analyte in a sample which can be detected but not unavoidably quantitated as an accurate value. The quantitation limit of an particular analytical course of action is the buck quantity of analyte in a sample which can be quantitatively determined with apposite precision and accuracy. The LOD and LOQ were intended by using the relation 3.3σ/S and 10 σ /S correspondingly, where σ is the standard error of estimate and S is the slope. Intended values of limit of detection (LOD) and quantitation (LOQ) for Ibandronate sodium were found to be 8.6900 and 26.333 µg/ml respectively.

3.6 Analysis of Pharmaceuticals Formulation

The optimized spectrophotometric method was functional to the through determination of Ibandronate sodium in tablet using calibration curve method without some sample extraction or filtration. The drug content per tablet (on an average weight basis) was calculated from the absorbance value (Table 5).

After satisfactory method development of ibandronate sodium with UV spectroscopy at 215 nm between concentration range 25 to 200 µg/ml (R^2 value= 0.999) it was subjected to method of validation according to ICH guideline [12]. All the parameters of method of validation were demonstrated that adequate validation characteristic. Linearity of the regression equation were determined from the exceptionally significant ($p > 0.05$) correlation coefficient value and slope values were determined 95% confidence limits. Result of accuracy and precision studies was found to be according the criteria that relative standard deviation of replicate injection is not more than 2.0%. Lowest LOD value and wider liner range is most sensitive method to validation which was found in range.

Table 3. Accuracy readings

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

% recovery = (Amount recovered/amount introduced) X 100

Table 4. Precision readings

Concentration	Absorbance	Statistical analysis
100	0.1496	Mean= 0.1511
100	0.1527	
100	0.1536	SD=0.0019
100	0.521	
100	0.1488	% RSD=1.2828

Table 5. Analysis of pharmaceuticals formulation

	Labelled	Amount	% drug	% RSD
Formulation	Amount (mg)	Recovered*	Recovered	
Tablet	150 mg	149.861±0.07954	99.901	0.5308

UV spectrophotometric method

4. CONCLUSION

Bisphosphonates significantly decrease the risk of fractures in men and women with osteoporosis. The confirmation is based on high-quality phase III randomized embarrassed trials (RCTs) with fracture as an endpoint [13,14]. The most widespread adverse effect is gastrointestinal upset with the oral formulations, the frequency of which decreases with flashing treatment such as once weekly or monthly regimens. Intravenous (IV) supervision of nitrogen-containing bisphosphonates may induce an acute phase reaction which manifests as fever, myalgia and arthralgia, although these side effects usually determine within a few days of onset [15-16]. In this study a simple, quick and dependable UV spectrophotometric method was developed and validated for the strength of mind of Ibandronate sodium in bulk drug & pharmaceutical formulations. This method was applied straight to the analysis of pharmaceutical dosage forms without the required for separation such as extraction steps prior to the drug analysis. As this projected method has the lowest LOD value and wider linear range is more sensitive method. From the results obtained, we accomplished that the suggested method showed high sensitivity, accuracy and precision. Moreover, According to this HPLC method development with UV detector with high sensitivity accuracy and precision will easily performed in future. This method is simple and economic and it can be employed for the regular

quality control of Ibandronate sodium in pharmaceutical formulations.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

ACKNOWLEDGEMENTS

Lubna azmi and Shyam sundar gupta are gratefully acknowledges the receipt of JRF and SRF from Department of science and technology and Director of NBRI for providing necessary facilities for the work. The Authors also thankful to M/S MacLeod's pharmaceutical privet Limited, Baddi for providing the gift sample of Ibandronate sodium.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Muller R, Hannan M, Smith SY, Bauss F. Intermittent ibandronate preserves bone quality and bone strength in the lumbar spine after 16 months of treatment in the ovariectomizedcynomolgusmonkey. J of Bone Min Rese. 2004;19:1787-1796.
2. Pecherstorfer M, Herrmann Z, Body JJ, Manegold C. Randomized phase II trial comparing different doses of the bisphosphonate ibandronate in the treatment of hypercalcemia of malignancy. J of Clinical Oncology. 1996;14:268-276.
3. Coleman RE, Purohit OP, Black C, Vinholes JJ. Double-blind, randomised, placebo-controlled study of oral ibandronate in patients with metastatic bone disease. Annals of Oncol. 1999;10: 311-316
4. Rogers MJ. New insights into the molecular mechanisms of action of bisphosphonates. Current Pharmaceutical Design. 2003;9:2643-2686
5. Anonymous, Genentech USA, INC.A Member of roche group DNAway. Genentech; 2011.
6. Lovdahl MJ, Pietrzyk DJ. Anion-exchange separation and determination of bisphosphonates and related analytes by post-column indirect fluorescence detection. J. Chromatogr A. 2000;868: 141–142.
7. My H, Xq Z, Bc W. Determination of ibandronate by high performance ion exchange chromatography. Se Pu. 2000;18:254–255.
8. Rodriguez JAB, Desimone MF, Iglesias SL, Giorgieri SL, Diaz LE. Validation of a capillary electrophoresis method for the analysis of ibandronate related impurities. J Pharm Biomed Anal. 2007;44:305–308.
9. Jiang Y, Xie Z. Determination of Ibandronate and its degradation products by ion- pair RP LC with evaporative light-scattering detection. Chromatogr. 2005;62:257–261.
10. Acharya S, Srinivasulu C, Shintre S, Hemant R. A validated Hplc method for determination of Ibandronate sodium residue In cleaning validation by Ri detector. Analytic Chemistry. 2011;10:1-7.
11. Anonymous, ICH, Q2 (R1). Validation of analytical procedures: Text and Methodology International conference on Harmonization, Geneva. 2005;1-13.
12. ICH Q2 (R1) Validation of Analytical Procedure: Text Methodology, US Food and Drug Administration, November; 2005.
13. Black DM, Cummings SR, Karpf DB, Cauley JA, Thompson DE, Nevitt MC, Bauer DC, Genant HK, Haskell WL, Marcus R, Ott SM, Torner JC, Quandt SA, Reiss TF, Ensrud KE. Randomised trial of effect of alendronate on risk of fracture in women with existing vertebral fractures. Fracture Intervention Trial Research Group. Lancet. 1996;348:1535–1541.
14. Black DM, Schwartz AV, Ensrud KE, Cauley JA, Levis S, Quandt SA, Satterfield S, Wallace RB, Bauer DC, Palermo L, Wehren LE, Lombardi A, Santora AC, Cummings SR. Effects of continuing or stopping alendronate after 5 years of treatment: The Fracture Intervention Trial Long-term Extension (FLEX): a randomized trial. JAMA. 2006;296: 2927–2938.
15. Black DM, Delmas PD, Eastell R, Reid IR, Boonen S, Cauley JA, Cosman F, Lakatos P, Leung PC, Man Z, Mautalen C, Mesenbrink P, Hu H, Caminis J, Tong K, Rosario-Jansen T, Krasnow J, Hue TF, Sellmeyer D, Eriksen EF, Cummings SR. Once-yearly zoledronic acid for treatment

of postmenopausal osteoporosis. N Engl J Med. 2007;356:1809–1822.

16. Chesnut CH III, Skag A, Christiansen C, Recker R, Stakkestad JA, Hoiseth A, Felsenberg D, Huss H, Gilbride J, Schimmer RC, Delmas PD. Effects of oral ibandronate administered daily or intermittently on fracture risk in postmenopausal osteoporosis. J Bone Miner Res. 2004;19:1241–1249.

Peer-review history:
The peer review history for this paper can be accessed here:
http://sciencedomain.org/review-history/13065