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Research Article

DEVELOPMENT AND VALIDATION OF STABILITY INDICATING UV SPECTROPHOTOMETRIC METHOD FOR THE ESTIMATION OF SODIUM RISEDRONATE

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ABSTRACT

A simple, sensitive, reproducible and cost effective stability indicating UV spectrophotometric method has been developed for quantitative determination of sodium risedronate. The UV spectrum was scanned between 200 to 400 nm and 262 nm was selected as optimum wavelength for maximum absorption. Beer's law was obeyed in the concentration range of 2-120 µg/ml. Good accuracy (99.49-100.54%), precision (%RSD 0.325) were obtained. The limit of detection and limit of quantification were found to be 0.07 µg/ml & 0.23 µg/ml respectively. Results of the analysis were validated as per ICH guidelines. Forced degradation studies include the effect of acid, alkali, hydrogen peroxide, UV light and thermal were carried out according to the ICH requirements (Q1A(R2) and Q1B) which can be used for the routine and quality control analysis of sodium risedronate in raw material and pharmaceutical formulations.

Keywords: Sodium risedronate, UV Spectrophotometry, Stability indicating, Validation.

INTRODUCTION

During the pharmaceutical development of a new drug, it is necessary to select as soon as possible the formulation with the best stability characteristics. Regulations regarding stability testing for registration application are provided by International Commission for Harmonization (ICH), which emphasizes the stress testing conditions with the aim of assessing the effect of severe conditions on the drug in practice, the effects of pH and temperature changes on drug stability are often used in such studies. The results of such studies are of vital importance in the estimation of a drug product shelf life during early stages of its pharmaceutical development. The results may also serve as guide for better drug design, drug formulation and drug analysis[1].

Sodium risedonate (SR) is chemically designated as (1-hydroxy-1-phosphono-2-pyridin-3-yl-ethyl)phosphonic acid is used for the treatment of Paget's disease of bone (a disease in which the formation of bone is abnormal) and in persons with osteoporosis[2, 3,4] (Fig 1). Bone is continually being formed and dissolved. By slowing down the rate at which bone is dissolved, risedronate increases the amount of bone. Risedronate has a chemically unique component as compared with the other bisphosphonates which is believed to reduce the likelihood of gastro-intestinal side effects. Risedronate is more potent in blocking the dissolution of bone. The FDA approved risedronate for treatment of Paget's disease in 1998 and for the prevention and treatment of osteoporosis in 1999.

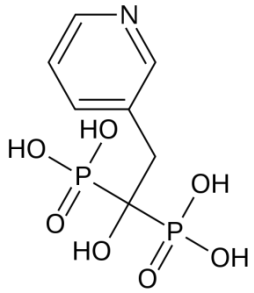

Fig. 1: Chemical structure of sodium risedronate

Sodium risedronate is a white crystalline powder, molecular weight 283.112 g/ mol, soluble in water, insoluble in common organic solvents. It is commercially available as pharmaceutical dosage forms in tablet form. Each risedronate sodium tablet for oral administration contains the equivalent of 5, 30, 35, 75, or 150 mg of anhydrous risedronate sodium in the form of the hemi-pentahydrate with small amounts of monohydrate.

Among the various methods available for the determination of drugs, spectrophotometry continues to be very popular, because of its simplicity, specificity and low cost. In the present study, a simple, sensitive, accurate and reproducible analytical method with better detection range for estimation of sodium risedronate in pure form has been developed and validated. Literature survey reveals that UV Spectrophotometric method for determination of sodium risedronate is reported[5]. The goal of this paper is to propose an alternative, low cost, easy handling method to determinate sodium risedronate by UV-VIS spectrophotometry and in addition to that forced degradation study has been carried out. Also, the complete analytical validation has been performed according to the ICH guideline and available literature [6-8].

Forced degradation studies may help facilitate pharmaceutical development as well in areas such as formulation development, manufacturing, and packaging, in which knowledge of chemical behaviour can be used to improve a drug product. The available regulatory guidance provides useful definitions and general comments about degradation studies[9]. The International Conference on Harmonization (ICH) guidelines[10,11] indicates that stress testing is designed to determine the intrinsic stability of the molecule by establishing degradation pathway in order to identify the likely degradation products and to validate the stability indicating power of the analytical procedure used. ICH guidelines 'stability testing of new drug substances and products' Q1A(R2)[10] and (Q1B)[11] requires that stress testing should be carried out to elucidate the substance. It suggests that the degradation products that are formed under the variety of condition should include the effect of temperature, appropriate oxidation, photolysis and susceptibility to hydrolysis across a wide range of pH value. In the guideline, the study of effect of temperature is suggested to be done in 10 ^{0}C increment above the accelerated temperature (50 ^{0}C, 60 ^{0}C etc.) and that of humidity at a level of 75 % or greater. No exact details are however provided for the study of oxidation, photolysis and hydrolysis at different pH values[12].

MATERIALS AND METHODS

Sodium risedronate was obtained as a gift sample. All solvents and other chemicals used were of analytical reagent grade purchased from SDFine Chemicals Ltd, Mumbai. The instrument used for the present study was PC based Jasco V-530 UV-Visible double beam Spectrophotometer with 1 cm matched pair quartz cell and spectral bandwidth of 2 nm. Double distilled water was used throughout the experiment.

Preparation of standard stock solution

10 mg of sodium risedronate working standard was weighed accurately and transferred to a 100 ml volumetric flask. Solution was sonicated and diluted up to the mark with double distilled water.

Preparation of calibration curve for sodium risedronate

By scanning a suitable standard solution in the UV spectrophotometer in the wavelength range of 200-400 nm, the λ_{max} of the drug was determined, shown in Fig 2. Aliquots (0.2, 0.5, 2, 5,8 and 12 ml) from standard solution of sodium risedronate were pipetted out in to a series of five volumetric flasks and the volume was made up to 100 ml with double distilled water.

The absorbance was measured at 262 nm against reagent blank. The calibration curve was constructed by plotting absorbance v/s concentration (µg/ ml) (Fig 3). Correlation coefficient was also estimated.

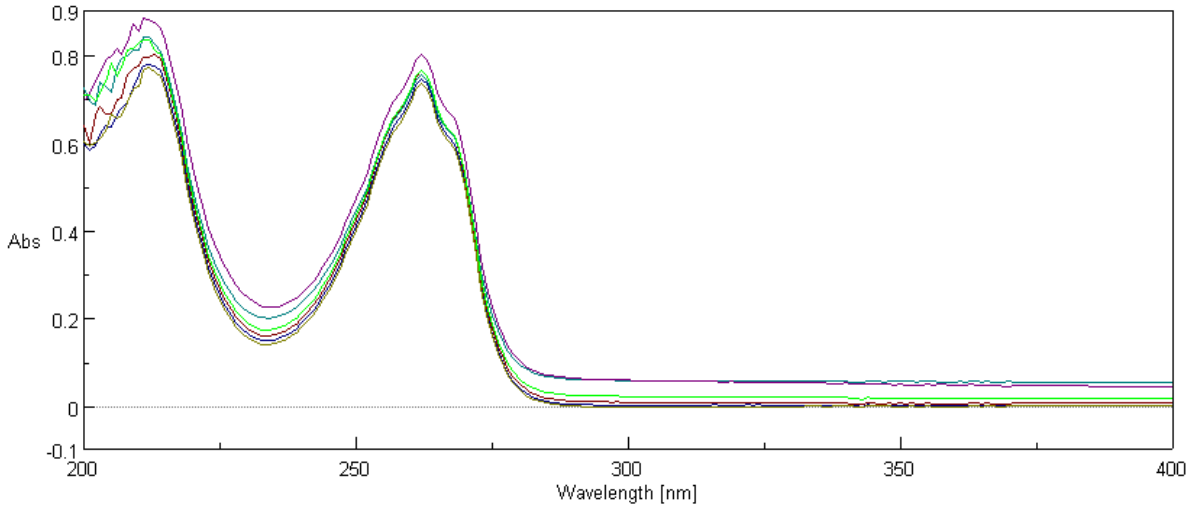

Fig. 2: UV overlay spectra of Sodium Risedronate

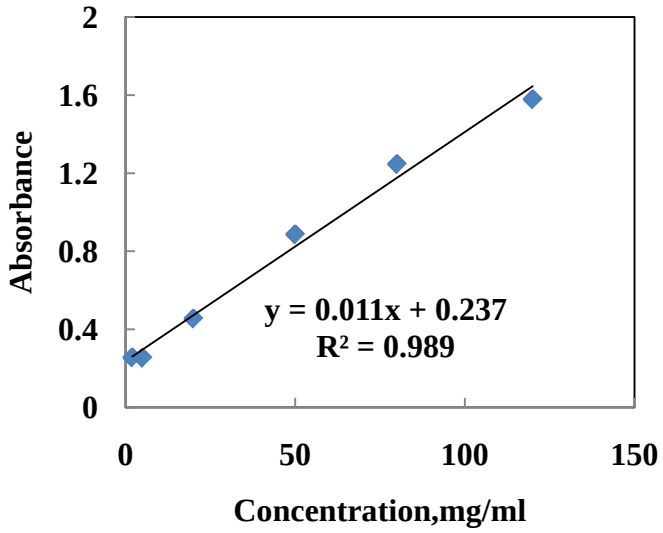

Fig. 3: Calibration curve of Sodium Risedronate at 262 nm

Method validation

The method was validated according to ICH Q2B guidelines[6] to determine the Linearity, sensitivity, precision, and accuracy of the analyte. Linearity of the proposed method was determined by measuring the absorbance of the standard solutions in the concentration range of 2-120 µg/ml and performing least square regression analysis. In addition, the accuracy of the proposed method was checked using standard addition method and recovery studies were carried out at 80%, 100% and 120% of target concentration. The percent analytical recovery was calculated by comparing the concentration resulted with the addition of spiked samples with actual expected theoretical increase in concentration. Precision was measured in terms of repeatability of application and measurement. Repeatability was carried out using six replicates of the same standard concentration (10 µg/ml for standard application). For precision study, three samples from same preparation and three different preparation have been used. Precision studies were carried out by estimating the corresponding responses. The summary of analytical parameters is presented in Table 1. Performing replicate analyses of the standard solutions was used to assess the accuracy and precision of the proposed methods (Table 2 and 3, respectively). LOD and LOQ of the proposed methods were calculated.

Table 1: Optical characteristics of the proposed method

Parameters	Result
Measured wavelength (λmax)	262 nm
Beers law limit (µg/ml)	2-120
Regression equation (y = m x + c)	Y=0.011X +0.237
Slope	0.011
Intercept	0.237
Correlation coefficient (r)	0.989
LOD µg/ml	0.07
LOQ µg/ml	0.23

Stability studies of sodium risedronate

Stability studies were performed by forced degradation study of sodium risedronate and it includes the study of effect of acid, alkali, hydrogen peroxide, UV light and thermal. For acidic hydrolysis 1.0 N HCl, for alkaline hydrolysis 1.0 N NaOH and for oxidation study 3% H_2O_2 were used. For carrying out photolysis study the drug was treated with UV light for 24 hours and thermal stress was applied by heating the drug at 60^0C for 30 minutes.

RESULTS AND DISCUSSION

The development of a simple, economic, rapid, sensitive, and accurate analytical method for the routine quantitative determination of samples will reduce unnecessary tedious sample preparations and the cost of materials and labor. The absorption spectrum of sodium risedronate in double distilled water is shown in Fig 2. The λ_{max} of the drug for analysis was determined (262 nm) by taking scans of the drug sample solutions in the entire UV region (200 to 400 nm). Calibration curve data was constructed in the range of the expected concentrations of 2 to 120 µg/ml. Beer's law was obeyed over this concentration range. The regression equation was found to be Y=0.011X+0.237 (Fig 3). The correlation coefficient (r) of the standard curve was found to be 0.989. The LOD and LOQ were found to be 0.07 µg/ml and 0.23 µg/ml respectively (Table 1). To study the accuracy of the proposed method, recovery experiments were carried out. The mean recovery was found to be 99.49-100.54 (Table 2). The method was found to be precise since % RSD value was found to be 0.325 (Table 3). The obtained results demonstrate the validity and accuracy of the proposed method for the determination of sodium risedronate.

Table 2: Result of recovery studies

Level of % Recovery	% Mean recovery	S.D	% RSD
80	100.54	0.5372	0.5368
100	99.70	0.2992	0.2987
120	99.49	0.5138	0.5124

Table 3: Precision Study at concentration 50 □g/ml

Sample	% Assay	% Deviation from mean assay value
1	100.49	-0.491
2	100.42	-0.418
3	100.69	-0.691
4	101.13	-1.127
5	100.33	-0.327
6	100.22	-0.218
Mean	100.54	
±SD	0.327	
%RSD	0.325	

The stability studies indicate that appreciable changes were observed by treating the drug with acid hydrolysis, oxidation, UV light for 24 hours and thermal stress. However, the drug was stable in UV condition. The results are shown in Table 4.

Table 4: Result of forced degradation study of sodium risedronate

S. No.	Conditions applied	Conc. taken(µg/ml)	Conc. Found (µg/ml)	Observation
1	Acidic Hydrolysis 1 N HCl	100	112	Degraded
2	Alkaline Hydrolysis 1 N NaOH	100	74	Degraded
3	3% H_2O_2 (Oxidation)	100	Change in λ_{max}	Degraded
4	UV-Treatment 24 hour at 365 nm	100	94	Stable
5	Thermal Stress (60^0 C, 2 hrs)	100	Change in λ_{max}	Degraded

CONCLUSION

These results reveal that the developed method was simple, economic, rapid, accurate and precise and consequently, can be applied to the determination of sodium risdronate. Based on forced degradation studies according to the ICH requirements, this method can be used for the routine and quality control analysis of sodium risedronate in raw material.

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