Int J Pharm Bio Sci 2012 Oct; 3(4): (P) 171 - 176

Research Article **Analytical Chemistry**

International Journal of Pharma and Bio Sciences **ISSN 0975-6299**

UV- SPECTROPHOTOMETRIC METHOD DEVELOPMENT AND VALIDATION FOR ESTIMATION OF STRONTIUM RANELATE IN BULK

A.S. SWAMI*, S.A. PISHAWIKAR AND H.N. MORE

Department of Pharmaceutical Chemistry, Bharati Vidyapeeth College of Pharmacy, Kolhapur-416012, India

ABSTRACT

Strontium ranelate is used for treatment of osteoporosis. The present work deals with method development for estimation of Strontium ranelate in bulk dosage form by UV spectrophotometry. A new simple, accurate and sensitive method for estimation of Strontium ranelate from bulk dosage form has been developed. The method employs zero order derivative spectroscopy. Estimation of Strontium ranelate was done in zero order derivative mode at 323 nm and obeyed Beer's law in the range of 4-28 µg/ml . The results of analysis were validated statistically as per ICH guidelines and recovery studies showed satisfactory results. Thus the method is accurate and reproducible and can be employed for routine analysis of the drug from bulk dosage forms.

KEYWORDS: **Strontium ranelate, UV spectrophotometry, Method development, Method Validation**

A.S. SWAMI
Department of Pharmaceutical Chemistry, Bharati Vidyapeeth College of Pharmacy, Kolhapur-416012, India
ashwini.swami87@gmail.com

INTRODUCTION

Strontium ranelate (SR) chemically, it is distrontium-5-[bis(2-oxido-2-oxoethyl)amino]-4-cyano-3-(2-oxido-2-oxoethyl)thiophene-2-carboxylate, an antiosteoporetic drug used to treat osteoporosis disease and post-menopausal osteoporosis[1,2,3]. It has a molecular formula of $C_{12}H_6N_2O_8SSr_2$ and a molecular weight of 513.491 g/mol (Fig 1). SR is the first antiosteoporetic drug approved for treatment of osteoporosis as well as postmenopausal osteoporosis. SR, a novel orally active agent consisting of two atoms of stable strontium and the organic moiety ranelic acid, has been developed for the treatment of osteoporosis[4,5].

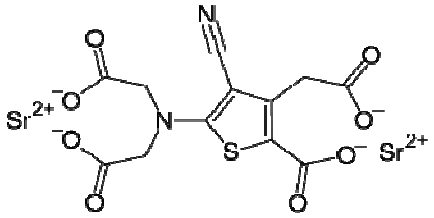

Figure 1
Chemical structure of strontium ranelate

SR is a new antiosteoporotic drug with a dual mode of action, both increasing bone formation and decreasing bone resorption, which rebalances bone turnover in favour of bone formation and increases bone strength. It has been shown to enhance osteoblastic cell replication and increase collagen synthesis while it decreases preosteoclast differentiation and bone-resorbing activity of mature osteoclasts in vitro[1]. The antifracture efficacy of strontium ranelate, 2 g per day orally, in the treatment of postmenopausal osteoporosis has been investigated in a large-scale, international, multicenter, phase 3 programme with more than 7000 patients[6].

Literature survey has revealed a number of analytical methods for determination of SR. SR presents a challenge in analysis due to very limited/no solubility in many solvents such as water, methanol, acetonitrile etc and polar nature of SR with the strontium ions not attached by covalent bonds. Considering these factors, use of buffer solution is necessary. Reversed phase (RP)-HPLC for determination of content uniformity and estimation of SR has been reported[7]. Estimation of SR with potassium dihydrogen ortho phosphate has also been reported[8]. Hence it has attracted us very much to develop an analytical method for determination of strontium ranelate by UV spectrophotometry with potassium dihydrogen ortho phosphate : methanol (3:1) as solvent system and pH adjusted to 3 with ortho phosphoric acid. The present study illustrates a simple, accurate and reproducible procedure and so far, this UV spectrophotometric method has not been reported and it can be utilized for routine quality assurance.

MATERIALS AND METHODS

(i) Instrument

PC based Jasco V-530 UV-Visible double beam spectrophotometer with 1 cm matched quartz cells and spectral bandwidth of 2 nm.

(ii) Reagents and Materials

Working standards of pharmaceutical grade strontium ranelate was obtained as a gift sample from Enaltech Lab Ltd, Mumbai. The other chemicals used were of AR grade and purchased from SD fine chemicals, Mumbai.

(iii) Selection of solvent system

50 mM potassium dihydrogen o-phosphate solution was prepared using double distilled water. SR was dissolved in mobile phase, potassium dihydrogen ortho phosphate buffer

solution :methanol (3:1), (pH-3), and final volume was made up with mobile phase. The absorbances of SR at respective wavelengths were determined.

(iv) Preparation of standard Stock Solution

A standard stock solution of SR (10 mg) was prepared in mobile phase, potassium dihydrogen ortho-phosphate solution: methanol, and made up to 100 ml with mobile phase to get the final concentration of 100 µg/ml.

(v) Selection of wavelength (λmax)

Standard solution was scanned in the range of 200-400 nm, against solvent phase as reference. SR (Fig 2) showed absorbance maxima (λmax) at 323 nm.

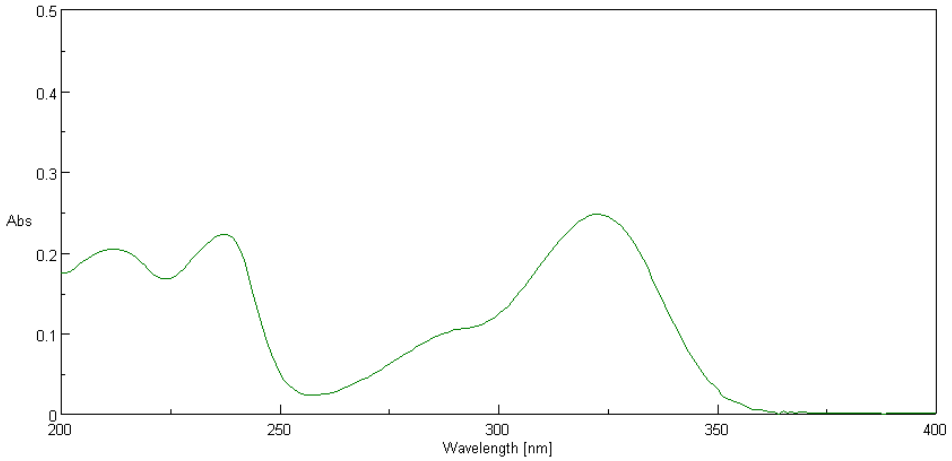

Figure 2
Scanning of strontium ranelate (10 µg/ml) in the range of 200 - 400 nm

(vi) Preparation of calibration standards

From the standard stock solution of SR, different concentrations were prepared respectively in the range of 4-28µg/ml and the absorbance was measured at 323nm (Fig 3). The calibration curve was plotted (Fig 4) and data presented in Table 1.

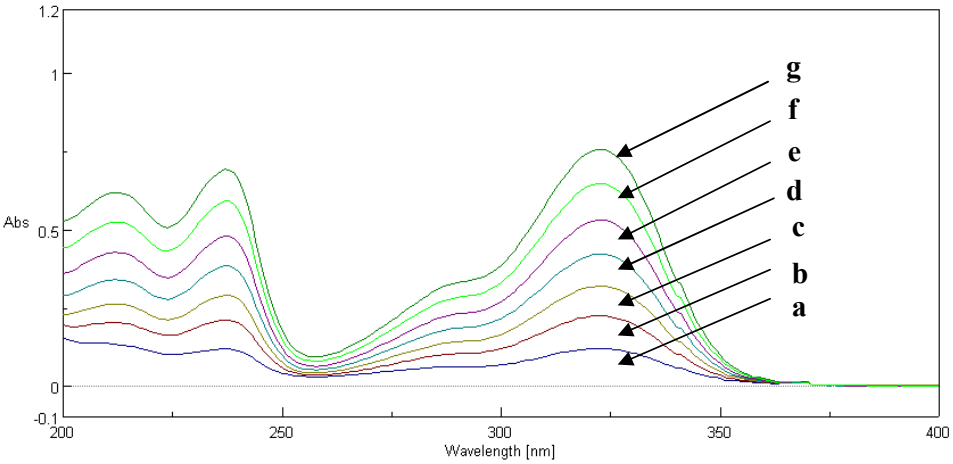

Figure 3
Overlay spectra of linearity (4-28 µg/ml) of strontium ranelate
a = 4 µg/ml, b = 8 µg/ml, c = 12 µg/ml, d = 16 µg/ml,
e = 20 µg/ml, f = 24 µg/ml, g = 28 µg/ml.

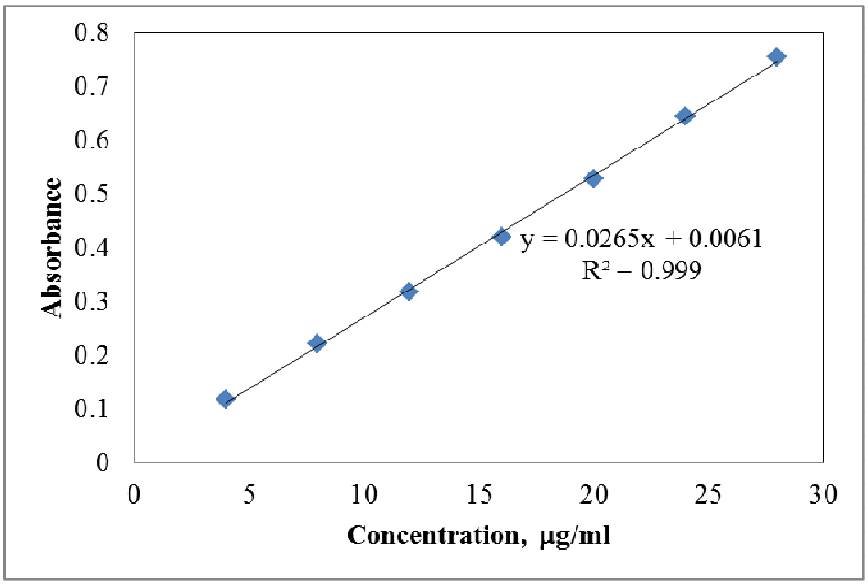

Figure 4
Calibration curve of strontium ranelate (SR) at 323 nm (4-28 µg/ml)

(vii) Validation parameters

(a) Linearity:

Linear correlation was obtained between absorbance and concentration of SR in the range of 4 – 28 µg/ml. Data of regression analysis was summarized in Table 2.

Table 1
Optical characteristics of the proposed method

Parameters	Result
Measured wavelength	323 nm
Beer's law limit (µg/ml)	4-28
Regression equation (y = mx + c)	y= 0.026 x + 0.006
Intercept (c)	0.006
Slope (m)	0.026
Correlation coefficient (R^2)	0.999
LOD (µg/ml)	0.013
LOQ(µg/ml)	0.043

y = mx+c: where y = absorbance at respective λmax, x = concentration of the analyte
LOD – limit of detection, LOQ – limit of quantification.

Table 2
Calibration curve data for strontium ranelate

Sr. No.	Concentration (µg/ml)	Absorbance at 323 nm
1	4	0.1179
2	8	0.2230
3	12	0.3177
4	16	0.4198
5	20	0.5279
6	24	0.6451
7	28	0.7540

(b) Accuracy

The recovery experiments were carried out by the standard addition method. The recoveries obtained were found to be in the range of 99.83 ± 0.62% to 100.35 ± 0.68% for SR. The high percentage recovery and low % RSD values were indicated that method is accurate (Table 3).

Table 3
Result of recovery studies

Level of % Recovery	% Mean recovery	±SD	% RSD
80	100.35	0.6782	0.6758
100	99.87	0.7198	0.7207
120	99.83	0.6238	0.6249

(c) Precision

The % RSD values of SR were found to be 0.19. The RSD values found below 2% indicated that the proposed method is in good precision (Table 4).

Table 4
Precision study at concentration 10 µg/ml

Sample	% Assay	% Deviation from mean assay value
1	99.46	0.538
2	99.61	0.384
3	99.53	0.461
4	99.69	0.307
5	99.19	0.807
6	99.30	0.692
Mean	99.46	
±SD	0.189	
%RSD	0.190	

(d) LOD & LOQ

LOD & LOQ of SR was found to be 0.013 µg/ml and 0.043 µg/ml respectively. These data show that microgram quantity of both drugs can be accurately determined.

RESULTS AND DISCUSSION

Literature review indicated that various methods have been reported for the analysis of SR by UV[8] and RP-HPLC[7]. But no analytical method was reported for the estimation of SR using the solvent system [potassium dihydrogen ortho-phosphate solution: methanol (3:1)] by UV spectroscopy. The absorption maxima of SR was found at 323 nm. With this wavelength absorbance of SR was noted. The results showed an excellent correlation between absorbance and concentration of the drug. Validation parameters like accuracy, precision and linearity found low %RSD values which indicates that the method is precise. The percentage recovery of SR was found to be in the range of 99.83 ± 0.62% and 100.35 ± 0.68%. The main advantage of the proposed method is its suitability for routine determination of SR.

CONCLUSION

Simple UV spectrophotometric method was developed for the determination of SR in bulk. The present method succeeded in adopting a non-complicated sample preparation and achieved satisfactory percentage recovery and therefore it can be concluded that use of this method can save time and money. The proposed method is accurate and precise for the determination of SR. Hence, it can be employed for routine analysis in Quality Control Laboratories.

ACKNOWLEDGEMENT

One of the authors (Swami Ashwini) is thankful to Enaltech Lab Ltd, Mumbai, India, for providing the gift sample of strontium ranelate. The authors are thankful to the Principal, Bharati Vidyapeeth College of Pharmacy, Kolhapur for providing all necessary Laboratory facilities needed in the completion of the proposed Project Work.

.REFERENCES

1. Tandon V.R., Sharma S., Mahajan A., Parihar A., Singh K, Strontium Ranelate. Drug Review (JK Science), 8(2):114-115, (2006).
2. Durie B.G.,Katz M., Crowley J., Osteonecrosis of the jaw and bisphosphonates. N. Engl. J. Med. 353(1):99-102, (2005).
3. Sharma S., Tandon V.R., Mahajan A., Therapeutic strategies for postmenopausal osteoporesis: Present and future. Obs and Gynae Today, 9(11):758-762, (2004).
4. Dimai H.P., Strontium ranelate: a novel concept for the treatment of osteoporesis. Wien Klin Wochenschr, 117(21-22):728-738, (2005).
5. Marie P.J., Strontium ranelate: A physiological approach for optimizing bone formation and resorption, Bone, 38:S10-S14, (2006).
6. Ortolani S., Vai S., Strontium ranelate: an increased bone quality leading to vertebral antifracture efficacy at all stages. Bone, 38(2): 19-22, (2006).
7. Mythili K., Gayatri S., Teja K.R., Chitra K,, Uma C, Maheswara R, Development and validation of RP-HPLC method for the Estimation of strontium ranelate in sachet. Int. J. Pharma and Bio Sciences 2(2): 258-263, (2011).
8. Mythili K, Gayatri S, Mukesh Kumar E, Adi Reddy T, Chitra K, Uma C, Maheswara R, Development and Validation of UV Spectrophotometric Method for the Estimation of Strontium Ranelate in Sachet Formulation, Research Journal of Pharmaceutical Technology, 4(9):1468-1470, (2011).