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# Validated Spectrophotometric Method Development for Strontium Ranelate from Newly Developed Floating Tablet Formulation

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**Abstract:** ***In Present work, successful development of a simple, sensitive, rapid, accurate and precise spectrophotometric method has been done for the estimation of strontium ranelate in bulk and pharmaceutical dosage forms. The wavelength maxima for strontium ranelate was found to be 323 nm. Beer's law was obeyed in the concentration range of 5-50 µg/ml. The limit of detection (LOD) and limit of quantification (LOQ) were found to be 0.2263 µg/ml and 0.68 µg/ml, respectively. The percentage recovery of the drug for the proposed method ranged from 96.86-104.54% indicating no interference of the tablet excipients. The result of analysis were validated as per ICH guidelines[Q2(R1)].***

**Keywords:** Strontium ranelate, UV spectrophotometry, Percentage recovery, Method development, Method validation

## 1. Introduction

The di-strontium salt of ranelate is a novel orally active agent consisting of two atoms of stable strontiumand the organic moiety ranelic acid, has been developed for the treatment of osteoporosis. The IUPAC name of Sr(Strontium ranelate is distrontium 5-[bis(2-oxido-2-oxoethyl)amino]-4-cyano-3-(2-oxido-2-oxoethyl)thiophene-2-carboxylate **.**

Postmenopausal osteoporosis is a major public health problem which is increasing significantly as the population of theworld is growing along with increased number of aged people. Worldwide, lifetime risk for osteoporotic fractures in women is 30-50%. While in men is 15-30%.Osteoporosis is often called the "silent disease" because bone loss occurs without symptoms. In many cases the first "symptom" is a broken bone. Patients with osteoporosis may not know that they have the disease until their bones become so weak that a sudden strain, bump, or fall causes a hip fracture or a vertebra to collapse. The recommended dose of strontium ranelate for adults is one 2 g sachet, taken once daily at bedtime preferably at least 2 hours after eating.[1-2]

The objective of treatment is to either follow anti-resorptiveor bone forming strategies. Currently available medications, such as bisphosphonates, selective estrogen receptor modulators, and teriparatides, have shown their ability to reduce vertebral and/or nonvertebral fractures. But it remains sub-optimal. There is, therefore, an urgent need of new effective, safe, and user-friendly medications to optimize the treatment of postmenopausal osteoporosis. Among these recent advances strontium ranelate(Sr) has gained importance in the treatment and prevention of osteoporosis.

Strontium ranelateis a new antiosteoporotic treatment 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 pre- osteoclast differentiation and bone-resorbing activity of mature osteoclasts in vitro. Studies performed at preclinical level have shown that strontium ranelate not only increases bone mass at various skeletal sites but also improves mechanical properties of femoral, humeral and vertebral bones. [3-4]According to literature survey, it reveals that, strontium ranelate is not official in any of the pharmacopoeia like IP, BP and USP. Still it is substantially used in the treatment. The number of drugs introduced into the market is increasing every year. These drugs may be either new entities or partial structural modification of the existing one. Very often there is a time lag from the date of introduction of a drug into the market to the date of its inclusion in pharmacopoeias. This happens because of the possible uncertainties in the continuous and wider usage of these drugs, reports of new toxicities (resulting in their withdrawal from the market), development of patient resistance and introduction of better drugs by competitors. Under these conditions, standards and analytical procedures for these drugs may not be available in the pharmacopoeias. It becomes necessary, therefore to develop newer analytical methods for such drugs.[3-7]Major disadvantage associated with strontium ranelate is it's absolute bioavailability. It is only of 20-25% after an oral dose of 2g strontium ranelate. The absorption window is from stomach, hence to increase the residence time in stomach the development of floating tablet formulation has been done. As part of formulation development it is necessary to develop analytical method.[4-5]The objective of the present work was to develop a new, simple, rapid, effective and reproducible UV spectrophotometric analytical method for the determination of strontium ranelate in bulk and tablet dosage form.

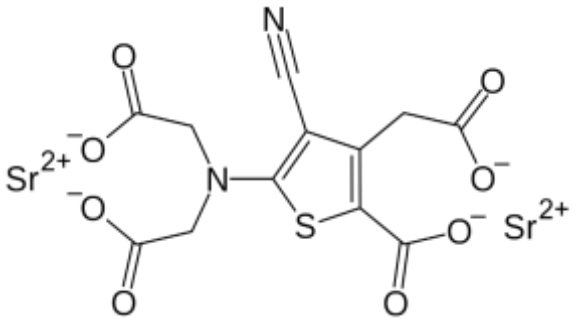

**Figure 1:** Chemical structure of strontium ranelate

## 2. Materials and Method

### 2.1 Instrument

PC basedJasco V&630 UV&Visible double beam spectrophotometer with 1 cm matchedquartz cells and spectral bandwidth of 2 nm.

### 2.2 Reagents and Materials

A new floating drug delivery system in the form of floating tablet was developed for strontium ranelate. The tablet contained 500mg strontium ranelate as active pharmaceutical ingredient along with sodium bicarbonate, citric acid as gas generating agent and water soluble polymer (suitable grade of HPMC) as hydrophilic matrix. Using different combinations of ingredients different batches were prepared and analyzed. The developed optimized formulation (F-1) of floating tablet formulation of strontium ranelate was used for quantative analysis. 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. Water used in analysis was double distilled obtained using glass distillation apparatus.

### 2.3 Selection of solvent system

SR was dissolved in solvent phase prepared by using0.1N HCL: methanol in 80:20 proportion and final volume was made with same.

### 2.4 Preparation of standard Stock Solution

A standard stock solution of SR (10 mg) was prepared in solvent phase, 0.1N HCL: methanol, and made up to 100 ml with same to get the final concentration of 100 µg/ml.

### 2.5 Selection of wavelength (λmax)

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

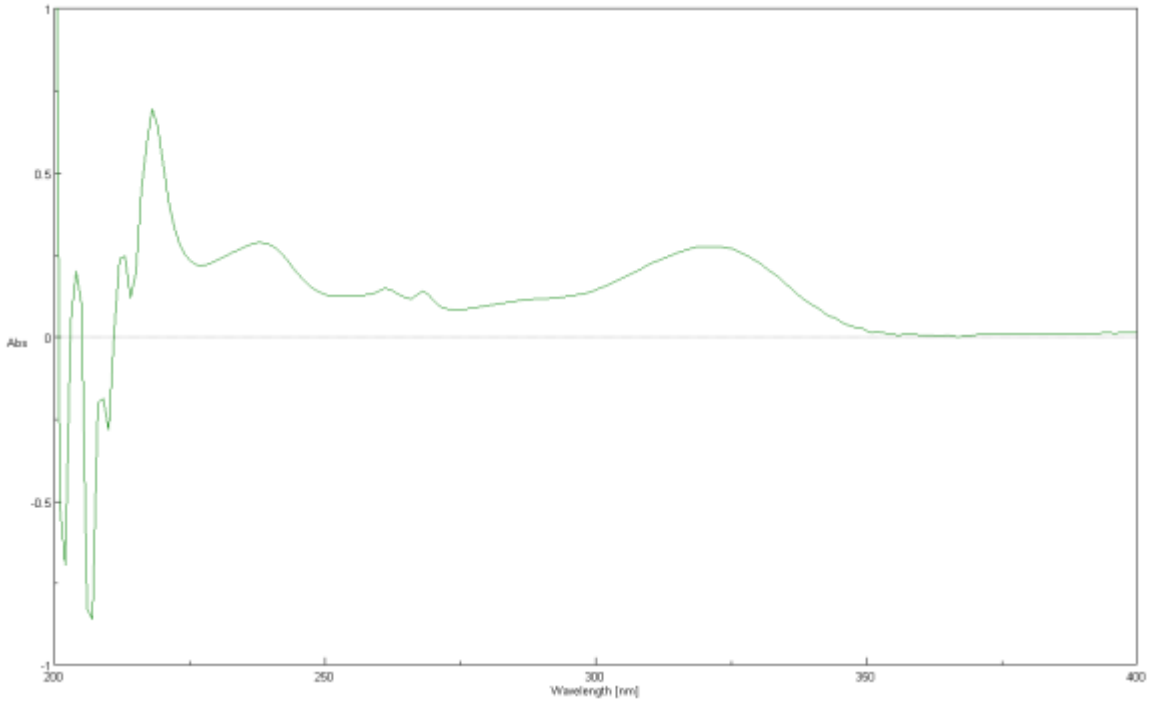


**Figure 2:** Scanning of Strontium Ranelate (10 µg/ml) solution in 200 & 400 nm.

### 2.6 Preparation of calibration curve

From the standard stock solution of SR, different concentrations were prepared respectively in the range of 5-50µg/ml and the absorbance was measured at 323nm. The calibration curve was plotted and data is presented in Table 1.

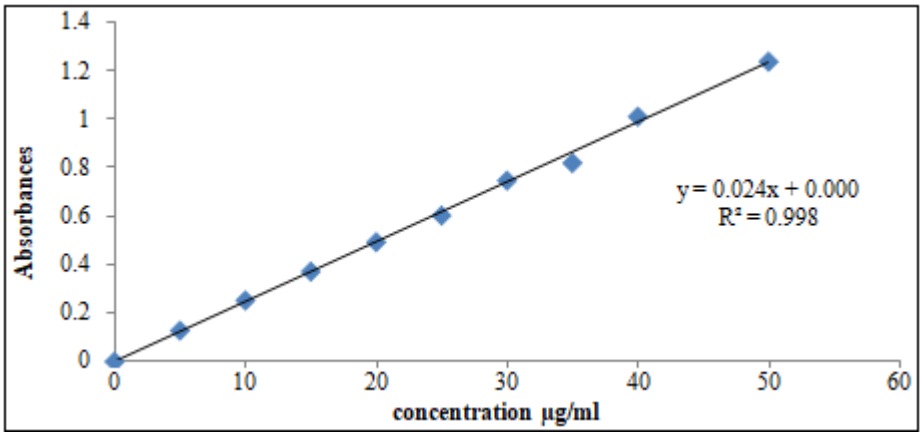


**Figure 3:** Calibration curve of strontium Ranelate (SR) at 323 nm (5-50µg/ml)

**Table 1:** Optical characteristics of the proposed method

| Parameters | Results |
|---|---|
| Measured wavelength | 323 nm |
| Beer's law limit | 5-50 |
| Regression equation (y = mx + c ) | y= 0.024 x + 0.000 |
| Intercept (c) | 0.000 |
| Slope (m) | 0.024 |
| Correlation coefficient ($R^2$) | 0.998 |
| LOD (µg/ml) | 0.2263 |
| LOQ(µg/ml | 0.68 |

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 in µg/ml | Absorbances at 323 nm |
|---|---|---|
| 1 | 5 | 0.1285 |
| 2 | 10 | 0.2529 |
| 3 | 15 | 0.3724 |
| 4 | 20 | 0.4939 |
| 5 | 25 | 0.6040 |
| 6 | 30 | 0.7484 |
| 7 | 35 | 0.821 |
| 8 | 40 | 1.012 |
| 9 | 50 | 1.2394 |

### 2.7 Analysis of Tablet Formulation

The 20 tablets from optimised batch F-1were taken into consideration for the method validation of strontium ranelate in tablet dosage form. From the contents of 20 tablets, an amount equivalent to 10 mg of SR was weighed and dissolved in 80 ml of 0.1 N HCL and 20 ml of methanol in 100 ml volumetric flask. The solution was filtered through Whatmannfilter paper no. 41 and then final volume of the solution was made up to 1000 ml to get stock solution containing 100 µg/ml of SR.

### 2.8 Validation parameters

#### 2.8.1 Linearity

Linear correlation was obtained between absorbance and concentration of SR in the range of 5 – 50 µg/ml. Data of regression analysis was summarized in Table 2.

#### 2.8.2 Accuracy

The recovery experiments were carried out by the standard addition method. The recoveriesobtained were found to be in the range of 96.86% to 104.54 % for SR. The highpercentage recovery and low % RSD values were indicated that method is accurate.

**Table 3:** Result of recovery studies

| Level of % Recovery | % Mean Recovery | SD | % RSD |
|---|---|---|---|
| 80 | 101.9 | 0.2179 | 0.214 |
| 100 | 104.54 | 0.1006 | 0.096 |
| 120 | 96.86 | 0.1154 | 0.119 |

#### 2.8.3 Precision

Assay of method precision (intra-day precision) was evaluated by carrying out three independent assays of test samples of strontium ranelate.

**Table 4:** Results of precision studies:

| Sample | %Assay |
|---|---|
| 1 | 99.375 |
| 2 | 99.33 |
| 3 | 99.33 |
| 4 | 99.375 |
| 5 | 99.45 |
| 6 | 99.375 |
| Mean | 99.372 |
| SD | 0.0439 |
| %RSD | 0.044 |

#### 2.8.4 LOD & LOQ

LOD & LOQ of SR was found to be 0.2263µg/ml and 0.68 µg/ml respectively. These data show that microgram quantity of both drugs can be accurately determined.

## 3. Results and Discussion

**Determination of $\lambda_{max}$:**
In solvent system [0.1N HCL: methanol (3:1)] solution of Strontium ranalate shows the absorption maxima of at323 nm.

**Linearity Range**: It was found that Beer's low is followed in the concentration range of 5-50 µg/ml

**Accuracy, Precision and % recovery**: Accuracy and precision of the developed method was conformed by low values of %RSD. The percentage recovery of SR was found to be in the range of 96.86 ± 0.62% and 104.54 ± 0.68%. The results showed anexcellent correlation between absorbance and concentration of the drug.

Hence present analytical method which is successfully developed can be called simple, sensitive, rapid, accurate and precise. Further it method can be employed for routine analysis in Quality Control Laboratories

## 4. Acknowledgement

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