Available online www.jocpr.com

Journal of Chemical and Pharmaceutical Research, 2012, 4(12):5191-5194

Research Article

ISSN : 0975-7384
CODEN(USA) : JCPRC5

A Sensitive method for the spectrophotometric determination of anti osteoporotic drug

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ABSTRACT

A new simple spectrophotometric method for the assay of Strontium Ranelate (SRN) has been described. SRN effects a reduction of 1,2 or 3 oxygen atoms, from tungstate or molybdate in Folin Cio Calteu reagent (phosphomolybdo tungstate), there by producing one or more of several reduced species which have a characteristic blue colour.The λ_{max} was at 740nm and obeyed Beer's law in the range of 8-40(µg ml^{-1})and recoveries from formulations are 99.40±0.38to100.65±1.13 respectively. The proposed method is selective, simple and accurate. The results obtained are reproducible and statistically validated. The proposed method can be successfully applied to the determination of SRN in pharmaceutical formulations.

Key words: Spectrophotometric, Strontium Ranelate, Folin Cio Calteu Reagent(F.C)

INTRODUCTION

Strontium Ranelate(SRN) is chemically known as Distrontium 5 - [bis (2-oxido-2 oxoethyl) amino]-4-cyano-3-(2-oxido-2-oxoethyl) thiophene-2-carboxylate (**Fig.1**). It is official in[1-7].The active functional groups present in SRN are Carboxyl and its strontium salt, tertiary amine, substituted thiopene. SRN is the only anti osteoporotic agent which both increases bone formation and reduces bone resorption, resulting in a rebalance of bone turnover in favor of bone formation.Strontium ranelate stimulates the calcium sensing receptors and leads to the differentiation of pre-osteoblast to osteoblast which increases the bone formation. Strontium ranelate also stimulates osteoblasts to secrete osteoprotegerin in inhibiting osteoclasts formed from pre-osteoclasts in relation to the RANKL system, which leads to the decrease of bone resorption.Strontium ranelate is un usual in that the cation (strontium) is responsible for the pharmacological effect, whereas in most modern medications it is the base (anion) that is the active ingredient. In early scientific pharmacology, cations such as arsenic, bismuth, mercury and lithium were frequently used but recently anions have been much more in vogue. A very few physio-chemical methods appeared in the literature for the determination of SRN in pharmaceutical formulations (less) and more for the plasma samples. The methods so far reported includes HPLC[8-9],AAS[10] spectrophotometric[11-12].The analytically important functional groups of SRN were not properly exploited designing suitable spectrophotometric methods for the determination of the selected drug and no method was reported in the literature to determine the amount of the selected drug using the F.C[13-19] reagent.Therefore in the present paper, we describe one simple visible spectrophotometric method based on reaction of the selected drug with F.C reagent.

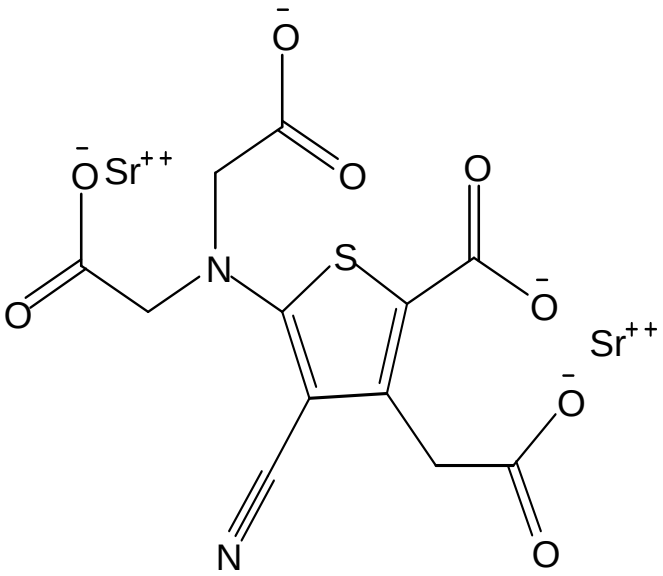

Fig.1: Chemical structure of Strontium Ranelate

EXPERIMENTAL SECTION

A UV – 1601, and SHIMADZU digital spectrophotometer with 1cm matched quartz cells were used for the spectral and absorbance measurements. SYSTRONICS digital pH meter361 was used for pH measurements. All the chemicals and reagents used were analytical grade and the solutions were prepared freshly.FC reagent (Loba, 2N) Folin Ciocalteu reagent used as it is. Na_2CO_3 solution (Loba, 10%, $9.43x10^{-1}$M) Prepared by dissolving 10 gm of the substance in 100 ml of distilled water.

Preparation of standard drug solution: A 1mg/mL stock solution of RIT was prepared by dissolving 100 mg of the drug in aldehyde free 100 mL Methanol.This stock solution was further diluted with appropriate solvent to get the working standard solutions (50-250 µg/mL).

Procedure:
Aliquots of standard SRN solution (1-5 ml, 200 µg/ml) were transferred into a series of 25 ml calibrated test tubes and the volume was adjusted to 3.0 ml with distilled water. To each of test tubes, 5.0 ml of sodium carbonate and 1.5 ml of F.C reagent were added and kept aside for 15 min. The volume was brought to the mark with distilled water. The absorbance was measured at 740 nm(**Fig.2**) against a reagent blank prepared under identical conditions. Amount of the drug in a sample was deduced from the Beer-Lambert's plot (**Fig.3**)

Pharmaceutical formulation solution:
The tablet powder (Shreya,Glen mark)equivalent to 100 mg of SRL was taken and triturated with (3x25 ml) portions of chloroform. The combined chloroform extract was made upto 100 ml with the same solvent to get mg/ml stock solution. From one portion of chloroform extract (25 ml), $CHCl_3$ was gently evaporated. The residue was dissolved in minimum amount of 0.1N HCl and diluted to 100 ml of distilled water and subsequently brought the volume to 50 ml with the same solvent to get 500µg/ml. It was further diluted stepwise with the same solvent as described under standard solution preparation to obtain 100µg/ml for the proposed method.

RESULTS AND DISCUSSION

The optimum conditions for this method were established by varying one parameter at a time and keeping the others fixed and observing the effect produced on the absorbance of the coloured species. The effect of different variables such as nature and strength of alkali, optimum volumes of NaOH and F-C reagent, reaction time were studied and optimized for attainment of maximum color and stability of colored species. Condition under which reaction of drugs with F.C reagent fulfils the essential requirements was investigated. All conditions studied were optimized at room temperature. Beer's law limits, molar extinction coefficient, Sandell's sensitivity and regression characteristics of the method are presented inTable-1. The relative standard deviation and % range of error are also given in Table-1. Results of recovery studies were presented in Table-2.The interference studies in the determination of SRN in

pharmaceutical formulations revealed that the normally existing excipients and additives like hydroxyl propyl cellulose, lactose, carboxy methyl cellulose were found not to interference even when present in excess.

TABLE:1 Optical characteristics, precision, accuracy of the methods proposed in the determination of SRN

S.No	OPTICAL CHARACTERISTICS	F.C
1	λ_{max}(nm)	740
2	Beer's Law limits(µg/ml)	8-40
3	Molarabsorptivity(l $mol^{-1}cm^{-1}$)	$7.76x10^3$
4	Correlation coefficient (r)	0.9999
5	Sandell's sensitivity (µg/cm^2/0.001absorbance unit)	0.0661
6	Regression equation(y=a+bc) (i)slope (b)	0.015
	(ii) Standard deviation on intercept(S_b)	1.73×10^{-4}
	(iii)intercept (a)	0.0001
	(iv) standard deviation (Sa)	4.61×10^{-3}
	(v)Standard error of estimation(S_e)	4.40×10^{-3}
7	Optimum photometric range (µg/ml)	17.37-39.81
8	Relative Standard deviation *	0.462
9	Detection limit	0.486
10	% of range of error(confidence limit) (i)0.05 level	0.761
	(ii)0.01 level	0.241

Table.2 Determination of SRN in pharmaceutical formulations

Pharmaceutical Formulations	Labelled Amount	Recovery		
		F.C	Reference Method	%Recovery by proposed method
SACHET – I	2	1.97±0.26 F=1.33,t=1.38	1.98±0.30	99.40±0.38
GRANULES - II	2	1.99±0.22 F=1.49,t=0.89	1.99±0.18	99.91±0.75
SACHET – III	2	1.99±0.25 F=1.08,t=1.19	1.97±0.26	100.16±0.79
GRANULES - IV	2	1.96±0.18 F=1.12,t=1.72	2.03±0.17	100.65±1.13

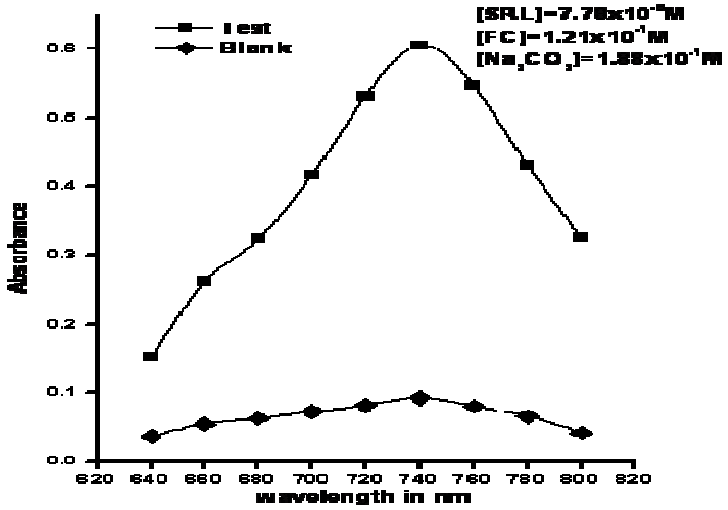

Fig.2.Absorption Spectrum of SRN with F.C.Reagent

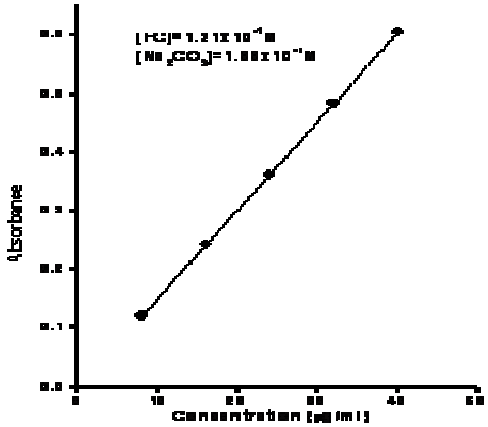

Fig.3.Beer"s plot of SRN with F.C.Reagent

CONCLUSION

The proposed method is superior in one way or other in terms of simplicity, λ_{max}, ϵ_{max} ,stability of coloured species over very few visible spectrophotometric methods reported so far. It can be seen from the results presented above, that the proposed method has good sensitivity and λ_{max}. Stastical analysis of the results(Table.1) shows that the proposed procedure has good precision and accuracy. Results of the analysis of pharmaceutical formulations reveal that the proposed method is suitable for the analysis with virtually no interference of the usual additives. The proposed method is simple, sensitive, and reliable and can be used for routine determination of SRN in bulk samples and pharmaceutical formulations depending upon the needs of the specific situation.

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