ISSN: 0975-766X
CODEN: IJPTFI
Available Online through
www.ijptonline.com
Research Article

# DEVELOPMENT OF NEW VISIBLE SPECTROPHOTOMETRIC METHODS FOR THE DETERMINATION OF RANOLAZINE IN PHARMACEUTICAL DOSAGE FORMS

**Ch.V.Suresh[1*], K R S Sambasiva Rao[1], G. Vidya Sagar[2]**

[1]Dept. of Biotechnology, Acharya Nagarjuna university, Nagarjuna Nagar, Guntur, A.P, India
[2]Dept. of Pharmaceutical Analysis, Veerayatan Institute of Pharmacy, Kutch, Gujarat, India.
*Email: sureshchennupati@rediffmail.com*

*Received on 06-12-2011* *Accepted on 18-12-2011*

**Abstract**

Three simple and sensitive Spectrophotometric methods have been developed for the determination of Ranolazine (RNL) in pure and pharmaceutical dosage forms. Method A is based on the formation of colored species by nucleophilic substitution of the drug with 1, 2-Naphthaquinone-4-sulfonate sodium (NQS) in the presence of alkaline medium ($\lambda_{max}$: 454 nm). Method B is based on oxidation of the drug under acidic conditions by oxidizing agents like potassium dichromate and subsequent formation of green colored chromogen ($\lambda_{max}$ : 590 nm). Method C is based on oxidation followed by complex formation with 1, 10-Phenanthroline (PTL) in the presence of ferric chloride to form a colored chromogen ($\lambda_{max}$: 500 nm). These methods have been statistically evaluated and found to be precise and accurate.

**Keywords:** Ranolazine, Spectrophotometry.

## Introduction

Ranolazine (RNL)[1,2] is chemically 1-piperazineacetamide, N-(2,6-dimethyl phenyl)-4-[2-hydroxy-3-(2-methoxyphenoxy) propyl] with selective clinical activity against chronic angina pectoris. A number of methods such as HPLC[3] and LCMS[4] were reported for the estimation of RNL. Literature survey reveals that few visible Spectrophotometric methods have been reported for its quantitative determination in its pure form and pharmaceutical formulations. In the present investigation, three simple and sensitive Spectrophotometric methods have been developed for the determination of RNL. The developed methods involve the formation of colored

complexes based on aromatic amino group present in the drug. In method A, NQS[5] reacts with Ranolazine under alkaline conditions to form an orange colored species. In Method B, oxidizing agents like potassium dichromate oxidizes the drug and converts into colored species. Method C is based on oxidation followed by complex formation with 1, 10-Phenanthroline[6-9] (PTL) in the presence of ferric chloride to form a colored chromogen. Beer's law is obeyed and results of analysis for the three methods have been validated statistically and by recovery studies.

**Materials and Methods**

**Instrument:**

A Systronics Model 2201 UV-VIS spectrophotometer was used for the measurements.

**Reagents:**

All the chemicals used were of analytical grade. NQS (0.1%), Sodium hydroxide (0.5 N), Potassium dichromate (5%w/v), 1, 10-Phenanthroline (0.2%w/v), and Ferric Chloride (0.1%w/v) were prepared.

**Standard drug solution:**

The working standard solution (5 mg/ml) of RNL was prepared by dissolving 500 mg of the drug in 100 ml of methanol. This stock solution was further diluted with sufficient volume of water to get 1000 µg/ml (Methods A & C) and 100 µg/ml (Method B) working standard solution.

**Sample solution:**

Twenty tablets of RNL were weighed and powdered. A quantity of powder equivalent to 500mg was dissolved in 100 ml of methanol. The solution was sonicated for 15min, filtered and made up to the mark with water. This stock solution was further diluted with sufficient volume of water to get 1000 µg/ml of working standard solution for methods A and C and 100 µg/ml of working standard solution for method B.

**Assay Procedures**

**Method A**

Aliquots of standard RNL solution (1000 µg/ml) ranging from 0.4 to 2.0 ml were transferred into a series of 10 ml volumetric flasks. To each flask 2 ml 0f 0.1%w/v NQS and 2 ml of 0.5N NaOH were added and kept aside for 15 min. The final volume was made up to the mark with distilled water. The absorbance of the resulting orange

colored solution was measured at $\lambda_{max}$ of 454 nm against corresponding reagent blank. The amount of RNL was calculated from the corresponding Beer-Lambert's plot.

**Method B**

Aliquots of standard RNL solution (100 µg/ml) ranging from 0.9 to 4.5 ml were transferred into a series of 10 ml volumetric flasks. To each flask 1 ml 0f 5%potassium dichromate and 4 ml of conc. $H_2SO_4$ were added and kept aside for 25 min. The final volume was made up to the mark with distilled water. The absorbance of the resulting green colored solution was measured at $\lambda_{max}$ of 590 nm against corresponding reagent blank. The amount of RNL was calculated from the corresponding Beer-Lambert's plot.

**Method C**

Aliquots of working standard solution (1000 µg/ml) of RNL ranging from 0.1-0.5 mL were transferred into a series of 10 mL volumetric flasks. To these, 2mL of ferric chloride and then 1ml of 1, 10-Phenanthroline was added. The volume was equalized with water and kept for boiling for 15 min. The flasks were cooled to room temperature and 2ml of O-phosphoric acid was added to each flask, finally the volume was brought to 10 ml with distilled water. The absorbance was measured at 500nm against reagent blank. The amount of RNL present in the sample solution was computed from its calibration curve.

**Results and Discussion**

The optical characteristics such as Beer's law limits, Sandell's sensitivity, molar extinction coefficient, percent relative standard deviation and percent range of error (0.05 and 0.01 confidence limits) were calculated for all the three methods. The results are summarized in Table 1.The precision and accuracy were performed by analyzing six replicate samples containing known amount of drug and the results were summarized in Table1. The values obtained for the determination of RNL in pharmaceutical formulations (tablets) by the proposed methods are presented in Table 2. Studies reveal that the common excipients and other additives usually present in the tablets did not interfere in the proposed methods.

**Table-1: Optical characteristics, Precision and Accuracy of the proposed methods.**

| Parameter | Method A | Method B | Method C |
|---|---|---|---|
| $\lambda_{max}$ (nm) | 454 | 590 | 500 |
| Beer's law limit(μg/mL) | 40-200 | 9-45 | 10-50 |
| Sandell's sensitivity (μg/cm$^2$/0.001 abs. unit) | 0.0285 | 0.00445 | 0.0048 |
| Molar absorptivity (litre.mole$^{-1}$.cm$^{-1}$) | 1.496 x $10^4$ | 0.959x $10^5$ | 8.764 x $10^4$ |
| Regression equation (Y*) | | | |
| Slope(b) | 0.0029 | 0.0216 | 0.0126 |
| Intercept(a) | 0.0086 | 0.0105 | 0.0098 |
| Correlation coefficient(r) | 0.9992 | 0.9991 | 0.9992 |
| %Relative standard deviation** | 1.060 | 0.901 | 1.050 |
| %Range of error | | | |
| 0.05 significance level | 0.6542 | 0.1372 | 0.3632 |
| 0.01 significance level | 0.9584 | 0.2152 | 0.5694 |

**Y=a+bX, where Y is the Absorbance and X is the Concentration*

*** For Six Replicates*

**Table-2: Estimation of Ranolazine in Pharmaceutical dosage Forms.**

| Formulation | Labeled Amount (mg/tablet) | Amount found* by proposed methods (mg) | | | % recovery** by proposed methods | | |
|---|---|---|---|---|---|---|---|
| | | Method A | Method B | Method C | Method A | Method B | Method C |
| Tablet 1 | 500 | 497.65 | 499.92 | 501.26 | 99.91 | 99.72 | 99.64 |
| Tablet 2 | 1000 | 1001.67 | 1000.27 | 997.45 | 100.59 | 100.79 | 99.85 |

****** Average of six determinations*

********Recovery of amount added to the pharmaceutical formulation (Average of three determinations)*

## Conclusion

The proposed methods are applicable for the assay of RNL and have an advantage of wider range under Beer's law limits. The proposed methods are simple, selective and reproducible and can be used in the routine determination of RNL in pure form and formulations with reasonable precision and accuracy.

## Acknowledgements

The authors are grateful to Department of Biotechnology, Acharya Nagarjuna University, Nagarjuna Nagar and Sri Siddhartha Pharmacy College, Nuzvid, Krishna Dist, Andhra Pradesh for providing the necessary facilities to carry out this research work.

**References**

1. Martindale, The Extra Pharmacopeia, 31st edition, Reynolds, J.E.F., (ED), Royal Pharmaceutical Society, London, U.K,1012 (2002).
2. The Merck Index, 13th edition, Merck Research laboratories, White House station, NJ, 1454 (2001).
3. Ashish Sharma, Dev Prakash, Sachin kumar Singh, International Journal of ChemTech Research, 2 (4), 1945-1948, 2010.
4. Vivek Nalawade, Parag gide, govind nunnaware, mitesh phale, International Journal of Pharmaceutical Sciences, 2 (1), 369-374, 2010.
5. CH.Aswani Kumar, T. Anil Kumar, B.M. Gurupadayya, S.Navya sloka, and M.B.Rahul Reddy, Archives of Applied Science Research, 2(4), 278-287, 2010.
6. Sastry, C.S.P., Sankar, D.G., Reddy, M.N. and Aruna, M., Indian J. Pharm. Sci., 1988, 50, 178.
7. M. Narayana Reddy, D. Gowri Shankar, G. Devala Rao and K. Sridhar, The Eastern Pharmacist, 127, May 1991.
8. M.N. Reddy, D.G. Sankar, V.V. Sekhar, N. Ravindra and G. Devala Rao, Indian Drugs, 28(7), 331, 1991.
9. Raggi, M.A., Cavrini, A.M., Di Pietra and Lacche, D., Pharm. Acta Hel., 1988, 63, 19.
10. G. Vidya Sagar, N.V.S. Gangadhara Rao, and B.S. Sastry, Indian Journal of Pharmaceutical Sciences, 66(3), 356-358, 2004.

**Corresponding Author:**

**Ch.V.Suresh[1*],**

**Email:** *sureshchennupati@rediffmail.com*