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Determination of pKa Value for Ranolazine and Atenolol Using UV Spectroscopy

H. D. Bandhavya[1] and K. C. Chaluvaraju[2*]

[1]Department of Pharmaceutical Chemistry, Visveswararapura Institute of Pharmaceutical Sciences, Bengaluru-560 070, India

[2]Department of Pharmaceutical Chemistry, Government College of Pharmacy, Bengaluru-560 027, India

***Corresponding Author**

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ABSTRACT

To develop innovative drug delivery methods the knowledge of a drug's physicochemical properties, namely its ionization constants is essential. Ranolazine and Atenolol are two key drugs used in clinical practice to treat cardiac arrest and their pKa values are important in developing new formulations these drugs. In the present study pKa values were measured experimentally using UV-spectrophotometry, which is known for providing accurate and reproducible pKa values. In pharmaceutical research, the ionization constant (pKa) is an important physicochemical parameter since it determines the dissolving capacity of active substances and to decide the route of administration. The study found that the pKa values for Ranolazine and Atenolol were approximately 7.6 and 9.3, respectively.

Keywords: UV-spectrophotometry, Ranolazine, Atenolol, pKa value etc.,

INTRODUCTION

The dissociation constant that is pKa, is an important parameter since it governs a substance's ionization profile and aids in the prediction of drug behavior in pharmaceutical formulations. The pKa of a therapeutic molecule is also critical for drug development since it influences its solubility, absorption, distribution, metabolism, and elimination. In formulations, the vehicles are frequently adjusted to a specific pH to achieve a desired level of ionization of the drug for solubility and stability. [1]

Ranolazine is clinically utilized to treat chronic stable angina, and it decreases the number of times the chest pain occurs. Relieving symptoms of angina can increase the ability to exercise and perform strenuous work. Atenolol belongs to a group of adrenergic classes that is beta-blockers. It is recommended as a remedy for high BP and arrhythmia. It is also be used to prevent chest pain triggered by angina pectoris.

Consuming Atenolol for high blood pressure reduces the risk of future heart attacks. Ranolazine, alone can inhibit fatty acid oxidation partially thereby improving threadmill exercise performance; nonetheless, its safety and efficacy is investigated in combination with calcium antagonists or beta-blockers in a significant number of patients with acute chronic angina. Taking Ranolazine twice daily can improve exercise capacity and offer antianginal relief for individuals with acute chronic angina who are taking regular Atenolol doses. There are no long-term side effects after a year or two of medication. [2,3]

Previous studies have reported pKa values for Ranolazine in the range of 7.5–7.7 using potentiometric titration and UV spectroscopy [8], and for Atenolol in the range of 9.2–9.4 using multi wavelength UV analysis and potentiometric methods [9]. However, variations exist in the reported values due to differences in buffer composition, ionic strength, temperature, and instrumentation. Moreover, comparative determination of pKa

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values for both drugs under identical experimental conditions using a single validated method is limited in the literature.

Thereby determining pKa values helps to design combined formulation of Ranolazine and Atenolol to treat angina for long-term. This study addresses that gap by determining the pKa values of Ranolazine and Atenolol under the same buffer system using UV spectrophotometry, with replicate measurements and statistical analysis to ensure reproducibility. Potential experimental error sources are discussed to enhance method transparency.

MATERIALS AND METHODS:

Table No 01: INSTRUMENTAL SPECIFICATIONS:

UV/Visible Spectrophotometer	SHIMADZU 1800
Software	UV Probe Version 2.43
Balance	Sartorius
pH meter	Elico

Chemicals and Reagents:

Methanol (AR Grade)-HIMEDIA

Water - Millipore water

Table No 02: Working standards/ reference standards/ active pharmaceutical ingredients:

Working standard	**Source**	**Potency**
Ranolazine (RAN)	Medelis Health care	99.8%
Atenolol (ATN)	Simson pharma	99.5%

Procedure followed:

About 6-8 aliquots of the buffer solutions were prepared. For preparations of these buffer procedure followed was as per IP 1996. First, 13.60 gm of KH_2PO_4 was taken in 500 ml volumetric flask, dissolve in small amount of distilled water, then make volume up to 500 ml with same. It will give 0.2 M 500 ml KH_2PO_4 and in the similar pattern freshly prepare 100 ml 0.2 M NaOH. Now place 50 ml 0.2 M KH_2PO_4 in 200 ml volumetric flask add sufficient volume of 0.2 M NaOH then make volume 200 ml, so it will give 200 ml specific pH buffer solution. Different volumes of 0.2 M NaOH and 0.2 M HCl were added to the potassium hypo Phosphate solution to obtain different pH buffer solutions. To prepare pH 1 and 2 buffer solution 127 ml and 102.8 ml of 0.2 M HCl and for 5.8, 7, 9, 11 pH 22.6 ml, 27 ml, 32 ml, 68 ml of 0.2 M NaOH were added. The exact pH of the solutions was determined by a pH meter.

RAN and ATN in buffer solutions were prepared in which concentration of RAN and ATN were 10 µg/ml, absorbance of each buffer solutions of RAN and ATN were measured with the help of UV-visible spectrometry. The λmax achieved was 272 nm and 225.6 nm for RAN and ATN in water, respectively. Both the solutions were measured separately at 272 nm for RAN and 225.6 nm for ATN in which each buffer was considered as blank each time. The obtained absorbance was plotted in the calibration graphs with pH on the x-axis and absorbance at the y-axis in **Graph:1**. The regression equation obtained was used for the pKa value calculation. The absorbance of RAN and ATN in different pH buffer solutions are listed in **table: 03**. The pKa values of the RAN and ATN were calculated.

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CALCULATION

Now from half of maximum absorption is plotted in graph and the value of pH on X-axis directly gives the value of pKa.

From equation of the chart i.e., y = 0.0618x + 0.0908 the value of y=0.396/2 =0.198 is taken. **Graph: 1**

0.198=0.618x+0.0908

x =0.198-0.0908/0.618

x = 9.3

pKa of ATN was found to be 9.3

Similarly from the half of maximum Absorption plotted in the graph the value of pH on x-axis directly gives value of pKa. So from the equation of the chart i.e., y = 0.0168x + 0.0222. The value of y=0.182/2 =0.091 and pKa for RAN was found to be 7.6.

Statistical Analysis:

All statistical analyses were performed using Microsoft Excel. Data are expressed as mean ± SD. The relative standard deviation (RSD) was calculated to assess reproducibility

RESULT AND DISCUSSION

Table 03 shows the mean ± SD absorbance values for Ranolazine and Atenolol at different pH levels. Low SD values (generally < 0.005) indicate high reproducibility of measurements.

Table No 03: pKa value determination for RAN and ATN:

SL.No.	pH of solution prepared	pH determined by pH meter	ml of HCl /NaOH added	Absorbance (nm)	
				RAN (mean ± SD)	**ATN** (mean±SD)
01.	2	2.4	102.8 ml of HCl	0.073± 0.002	0.140± 0.003
02.	5.8	5.4	22.6 ml of HCl	0.075± 0.002	0.227± 0.003
03.	7	6.3	27 ml of NaOH	0.063± 0.001	0.285± 0.003
04.	9	9.1	32 ml of NaOH	0.182± 0.003	0.333± 0.003
05.	11	11	68 ml of NaOH	0.147± 0.002	0.396± 0.003

The regression equations obtained were:

Ranolazine: $y = 0.0168x + 0.0222$ ($R^2 = 0.973$)

Atenolol: $y = 0.0618x + 0.0908$ ($R^2 = 0.9888$)

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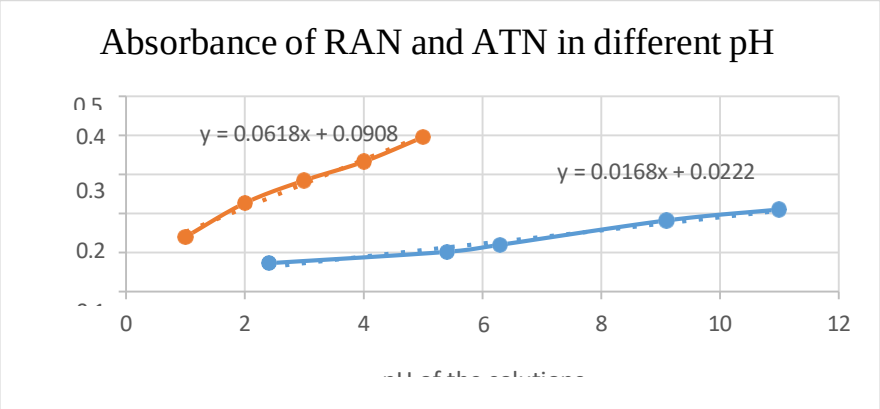

Graph 1: Calibration data of RAN and ATN for pKa value by Spectroscopy

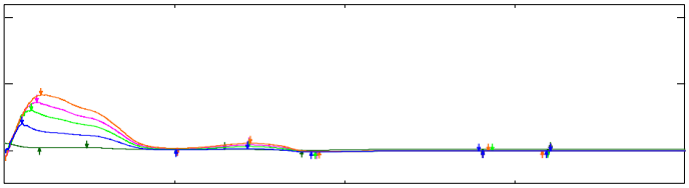

Fig 1: Calibration curves for RAN

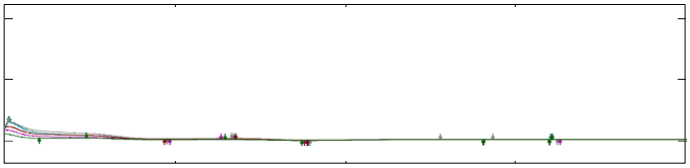

Fig 2: Calibration curves for ATN

In this work pKa value for RAN and ATN was determined using potassium dihydrogen phosphate with various pH. Different concentration of NaOH and HCl were used to get different pH solutions. The pH was altered and absorbance was taken. The pKa value was calculated by using regression equation obtained by plotting absorbance and pH of the solutions. The pKa value for RAN and ATN was found to be 7.6 and 9.3 respectively.

Experimental Error Sources

Potential sources of experimental error include:

- Minor fluctuations in buffer pH due to environmental CO_2 absorption.

- Variability in pipette volume delivery during buffer preparation.

- Slight instrument baseline drift during long measurement runs.

- Temperature changes affecting dissociation equilibria.

Despite these possible influences, the low RSD values and high R^2 from regression analysis indicate that the method is precise and reproducible.

CONCLUSION

UV- spectrophotometry technique is very useful for determination of pKa value because it is less time consuming and gives reproducible result than other techniques. This work concludes pKa value for RAN and ATN can be precisely determined using UV- Spectrometer. The obtained results shows that the pka values obtained are near

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to the values mentioned in various literatures. [8,9] . The pKa values was determined to be 7.6 and 9.3 for RAN and ATN respectively.

ACKNOLEDGEMENTS

None.

Conflict Of Interest

The authors declare that they have no conflicts of interest.

REFERENCE

1. Babić S, Horvat AJ, Pavlović DM, Kaštelan-Macan M. Determination of pKa values of active pharmaceutical ingredients. TrAC Trends in Analytical Chemistry. 2007 Dec1;26(11):1043-61.
2. Allen RI, Box KJ, Comer JE, Peake C, Tam KY. Multiwavelength spectrophotometric determination of acid dissociation constants of ionizable drugs. Journal of pharmaceutical and biomedical analysis. 1998 Aug 1;17(4-5):699-712.
3. Chaitman BR, Pepine CJ, Parker JO, Skopal J, Chumakova G, Kuch J, Wang W, Skettino SL, Wolff AA, Combination Assessment of Ranolazine In Stable Angina (CARISA) Investigators, Combination Assessment of Ranolazine In Stable Angina (CARISA) Investigators. Effects of Ranolazine with Atenolol, amlodipine, or diltiazem on exercise tolerance and angina frequency in patients with severe chronic angina: a randomized controlled trial. Jama. 2004 Jan 21; 291(3): 309-16.
4. Sendón, J.L., Lee, S., Cheng, M.L., Ben-Yehuda, O. and CARISA study investigators), 2012. Effects of Ranolazine on exercise tolerance and angina frequency in patients with severe chronic angina receiving maximally-tolerated background therapy: analysis from the Combination Assessment of Ranolazine In Stable Angina (CARISA) randomized trial. European journal of preventive cardiology; 19(5): 952-959.
5. Völgyi G, Ruiz R, Box K, Comer J, Bosch E, Takács-Novák K. Potentiometric and spectrophotometric pKa determination of water-insoluble compounds: validation study in a new cosolvent system. Analytica chimica acta. 2007 Feb 5;583(2):418-28.
6. Pandey MM, Jaipal A, Kumar A, Malik R, Charde SY. Determination of pKa of felodipine using UV–Visible spectroscopy. Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy. 2013 Nov 1;115:887-90.
7. Silva FV, Resende S, Araújo AN, Prior JA. Determination of pKa (s) of nilutamide through UV-visible spectroscopy. Microchemical Journal. 2018 May 1;138:303-8.
8. Peters CH, Sokolov S, Rajamani S, Ruben PC. Effects of the antianginal drug, ranolazine, on the brain sodium channel Na(V)1.2 and its modulation by extracellular protons. Br J Pharmacol. 2013 Jun;169(3):704-16. doi: 10.1111/bph.12150. PMID: 23472826; PMCID: PMC3682716.
9. Carl A. Gruetter, Atenolol, xPharm: The Comprehensive Pharmacology Reference,Elsevier;2007:Pages 1-6:ISBN 9780080552323, https://doi.org/10.1016/B978-008055232-3.61259-0.