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Determination of Promethazine Hydrochloride via Area under Curve

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ABSTRACT

Promethazine hydrochloride was determined by developing a simple, sensitive, and economical spectrophotometric method. The method was based on calculating the area under the curve of the zero-order spectrum and obeyed the Beer-Lambert law over a range of concentrations (5-45 µg/mL). The Rec% in the method was 101.413-99.13043. In the area under the peak method, the recovery percentage (Rec%) ranged from 98.85714% to 102.0916%, while the relative standard deviation percentage (RSD%) ranged from 0.3288% to 0.7443%. In the accuracy and consistency test of the method, the Rec% value ranged from 99.7942% to 100.838%, while the RSD% value ranged from 0.3288% to 0.7443% for the drug. In the application of the method, the Rec% value ranged from 99.1725% to 101.983%, while the RSD% ranged from 0.584265% to 0.900128%. In the standard addition method, the Rec% value was between 99.06859-102.4576%, while the RSD% ranged between 0.1941-0.7412% and the limits of detection were 0.0478, while the limits of quantification were 0.0628 for Promethazine hydrochloride. The method was successfully applied to estimate the drug in its pure form and in pharmaceutical preparations.

1. Introduction

Considered a neuroprotective antidepressant, hydrochloride bromide belongs to the class of antihistamines in the phenytoin class of drugs (1). It is frequently used for its sedative, antihistamine, anti-inflammatory, anticholinergic, and analgesic effects. Hydrochloride bromide can also be used in humans for the treatment of urticaria, asthma, and other respiratory conditions.

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Therefore, it is important to note that its use in traditional and synthetic formulations (2) is important. This drug modifies allergic rhinitis (hives), urticaria, and anaphylaxis. (3). Bromhexine hydrochloride is a potent anti-inflammatory, anti-rheumatic drug. It also treats eczema and pruritus in children and adolescents (4). Central nervous system disorders, including urticaria, gastrointestinal disorders, and central nervous system disorders, which include nausea, vomiting, drowsiness, blurred vision, and dizziness. (5). Take the medicine within 30 minutes of ingestion. For additional relief, consult a doctor or pharmacist. It can also be used as a preservative (6). Bromide hydrochloride dissolves in water, Molecular formula: $C_{17}H_{20}N_2S$, HCl, M.Wt 320.9 g/mol, UV max: 294 – 297 nm. A white or faintly yellowish, as shown in Figure 1 (7,8)

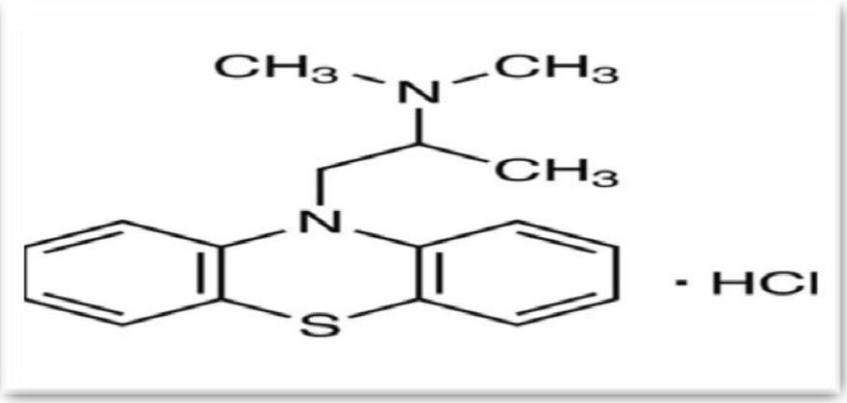

Figure 1. Structural formula of the drug promethazine hydrochloride.

UV-Vis absorption spectroscopy: Spectroscopy can be defined as the science that studies the interaction of electromagnetic radiation with matter (9). Electromagnetic radiation is a form of energy that travels in a vacuum at a very high speed. It also has multiple forms such as light, radiant heat, X-rays, ultraviolet-visible rays, infrared rays, microwaves, and radio waves (10). The importance of spectroscopic analysis lies in the fact that absorbed radiation is a characteristic of the absorbing material. When a sample is exposed to electromagnetic radiation, an absorption spectrum is produced, representing the amount of radiation absorbed at a specific wavelength by the molecule or atom. Therefore, this method has been used for qualitative and quantitative analysis (11). Despite the limited use of absorption in the ultraviolet-visible region for qualitative analysis, it remains one of the most important methods for quantitative analysis due to its high selectivity, accuracy, and precision, as well as the ease and speed of analytical performance (12). It can also be used to estimate very small concentrations of a substance, ranging between (10-5-

10-6 M) (13). The absorption of radiant energy depends on the number and arrangement of electrons in the absorbing molecules or ions (14). There are a number of transitions (15):

Transitions $\sigma^* \leftarrow \sigma$ that occur at short wavelengths less than 200 nanometers. Transitions $\pi^* \leftarrow n$ that occur at wavelengths of (150-600) nanometers.

Transitions $\pi^* \leftarrow \pi$ that occur in the ultraviolet and visible regions (180-700) nanometers.

Rays below 190 nanometers require a vacuum, free of oxygen and other gases. Therefore, the important ultraviolet region lies between 200 and 380 nanometers, as it provides the energy needed for the (π←π*) transition. (16). As the number of pi bonds in a molecule increases, the energy required for excitation decreases to reach the visible region of the spectrum. Measuring the radiation absorbed by the solution particles is subject to the Beer-Lambert Law. (17). The sensitivity of the spectroscopic method is measured using the molar absorption coefficient and Sandell's index, which can be defined as the number of micrograms of the compound to be measured that are converted into a colored product, giving an absorbance of 0.001 absorption unit when in a cell with a thickness of 1 cm, which is a measure of the sensitivity of the spectral method (18).

Whereas the IR spectrometer is a device that generates a continuous wavelength of light, the light source is a continuous source of visible light. When the prism is applied, the spectrometer is focused on a fixed point. The prism is a device that contains a sample of particles or elements. The spectrometer remains continuous, allowing light to be absorbed by the particles or elements in the sample. This limited range of light can be detected by scanning. Here, absorption spectroscopy is employed. (19).

To produce ultraviolet radiation, a hydrogen or deuterium discharge lamp (HDL) is used. The deuterium arc source (DC) is used to emit or scatter a continuous wave of light at 400 nm, especially in the beam path when using a Tensail lamp (20)

The measurements are designed to detect the scattered radiation emitted by the electrons, which causes a difference in absorption values. This is due to the electrical radiation of deuterium or hydrogen at a constant low angular velocity of ultraviolet radiation. This radiation is formed as a result of the formation of atoms and also ultraviolet radiation, as shown below. The electrical impedance D = 2 --- D2*---D'+D"+hv (21).

Area under curve method: The area under the curve (AUC) spectroscopy method is a straightforward spectroscopic technique suitable for regions where the absorption spectrum peaks are broad or lack a sharp peak. It involves calculating the integral value of the area enclosed between two selected wavelengths that fall within the curve region (22-24). Zero-order spectra obtained from a series of concentrations are used to construct an AUC calibration curve for a single drug or a mixture of drugs, to calculate the area of a peak enclosed between two wavelengths (25-27)

The wavelength range is determined based on observations and repeated measurements to obtain a linear relationship representing the area under the curve versus concentration (28-29).

To calculate the area under the curve for a binary mixture consisting of two components (X and Y), the following information is obtained from the spectra of the two components: (30)

• The area under the curve for component (X) in the wavelength range λ_1-λ_2.

• The area under the curve for component (X) in the wavelength range λ_3-λ_4.

• The area under the curve for component (Y) in the wavelength range λ_1-λ_2.

• The area under the curve for component (Y) in the wavelength range λ_3-λ_4.

The aim of the research: The aim of this research is to find new spectroscopic analytical methods for the quantitative spectroscopic determination of promethazine hydrochloride with high sensitivity, accuracy, and low cost.

2. Practical part

2.1. Chemical materials and Instrumentals

The standard substance of the drug was used in preparing the solution on which the study experiment was conducted. A dual-beam SHIMADZU UV-1650 device (Japan) was used in analyzing the drug. Measurements were carried out in the wavelength range of 200-400 nm using quartz cells and an ultrasonic water bath.

2.2. Promethazine Hydrochloride standard solution (1000 ppm)

The classical solution was prepared by dissolving 0.1 grams of the wonderful substance in a 100 ml volumetric flask with aqueous distillate, then making up the volume with the same solvent. The 100 μg. The ml-1 trademark of the classical solution was prepared by taking a 10 mL volume and adjusting it to a 100 mL flask. The complete distilled volume is unlimited.

2.3. Area Under Curve Procedure and Construction of Calibration Curve

Different volumes ranging from 0.5 to 4.5 mL of the standard solution of the drug, with a concentration of 100 µg/mL, were transferred into a series of 10 mL volumetric bottles. All bottles were then diluted with distilled water to the mark. The absorption spectrum was recorded over a wavelength range of 200 to 400 nm against the chelating solution. A drug calibration curve was then prepared by plotting the peak area value versus the concentration. The limit of detection (LOD) and the limit of quantification (LOQ) are common parameters used to evaluate the sensitivity of analytical methods. This study calculated the limit of detection (LOD) and limit of quantification (LOQ) for highly sensitive analytical methods. We then compared the obtained results with the lower limit of quantification (LOQ), as defined by US Food and Drug Administration guidelines. The calibration curve and standard deviation are essential components in evaluating the sensitivity of a method. An analytical technique uses LOD (limit of detection) and LOQ (limit of quantification) as metrics to describe the minimum concentration of an analyte that it can accurately detect and quantify. We refer to the limit of quantification (LOQ) as the minimum concentration that can be accurately measured, and the limit of detection (LOD) as the minimum concentration that can be detected. One widely used method to determine LOD/LOQ

Limit of Detection (LOD). The limit of detection can be calculated using the following equation, as per ICH guidelines.

$$LOD = 3.3 \times (N / S)$$

Where N is the standard deviation of the peak areas of the drug and S is the slope of the corresponding calibration curve.

Limit of Quantification (LOQ). The limit of quantification can be calculated using the following equation as per ICH guidelines.

$$LOQ = 10 \times (N / S)$$

Where N is the standard deviation of the peak areas of the drug and S is the slope of the corresponding calibration Curve.

2.4. Accuracy and precision

The accuracy and consistency of the proposed method for the drug were calculated by performing five repetitions of the measurement process at different drug concentrations within the calibration curve range. The Rec % value and RSD% % value were used to express the accuracy and consistency of the results, respectively.

2.5. Application of method

The easy method of light has now been applied. Five bars of measurement process were carried out. Different concentrations of promethazine hydrochloride were selected to fall within the concentration range of the regeneration curves. The concentrations are 1, 2, 3 μg.mg^{-1} for the drug

2.6. Analysis of the drug form of Promethazine Hydrochloride by the multi-standard additions method

The multiple standard addition method was applied to the pharmaceutical preparation of promethazine hydrochloride. Ten tablets of the pharmaceutical preparation containing 10 mg of the active ingredient were weighed. Ten tablets, each weighing 0.200 g, were taken, for a total weight of 2.00 g. They were dissolved in a 100 mL volumetric flask using water as the solvent, yielding a concentration of 200 μg/mL. Equal volumes of 1 mL of the drug were transferred into seven 10 mL volumetric bottles, and then increasing volumes of 0-3.5 mL of the drug standard solution with a concentration of 100 μg/mL were added to them. The solution was diluted with water to the mark, and the absorbance was measured against the solution**.**

3. Results and discussion

3.1. Area under the curve method

The drug was estimated spectroscopically by calculating the area under the curve. The recorded spectrum of both drugs showed that this technique can successfully estimate the drug. The absorption spectrum of promethazine hydrochloride was scanned in the region between 200-400 nm for a range of concentrations ranging from 0.1-6 μg.ml^{-1} of the drug, and these values were plotted against the concentration. The Beer-Lambert law was applied to a range of concentrations, from 5 to 45 μg/mL of the drug, to calculate the area under the curve for the region between 280 and 315 nm. The Rec % was between 99.13043% and 101.413% of the drug, as shown in Figures 2 and 3.

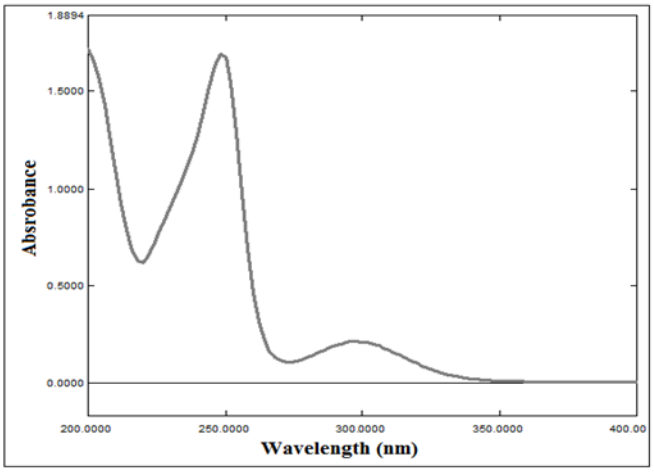

Figure 2. Spectrum of promethazine hydrochloride

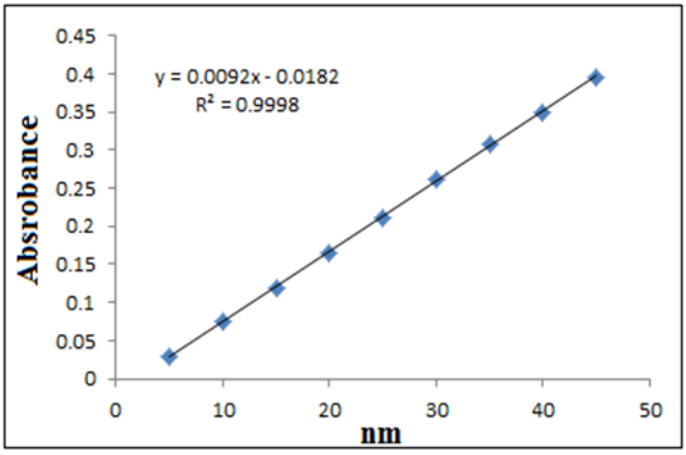

Figure 3. Calibration curve

3.2. Calibration Curve of the method: Area Under the peak

The Beer-Lambert law was followed for a range of concentrations from 5-45 µg.ml^{-1} in the area under the curve method, and the Rec% in the method was 98.85714-102.0916%, while the RSD % value in the method was 0.3288-0.7443 %. The limits of detection were 0.0478, while the limits of quantification were 0.0628 for Promethazine hydrochloride, as shown in Figures 4 and 5.

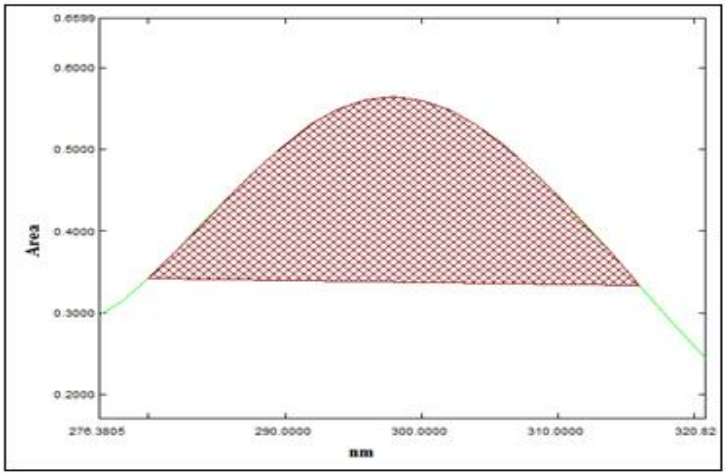

Figure 4. Area under the top of the property

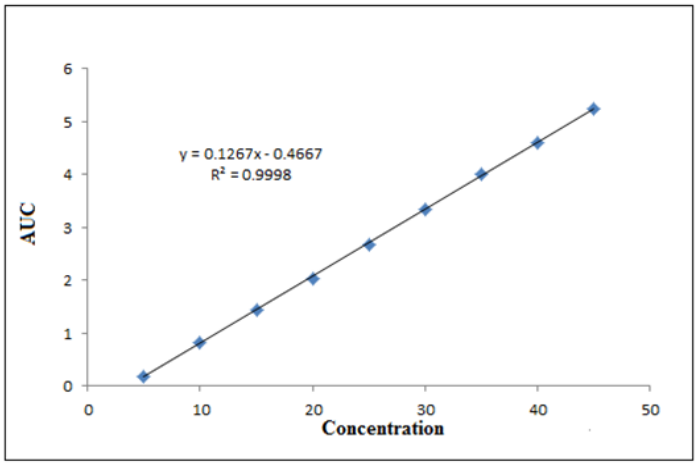

Figure 5. Subapical area of promethazine hydrochloride

3.3. Accuracy and precision

The accuracy and consistency of the method were tested by performing five repetitions of the measurement process at a concentration of 15.25 µg/mL of the drug, which falls within the calibration curve range. The Rec% value ranged from 99.7942 to 100.838%, while the RSD% value ranged from 0.3288 to 0.7443% for the drug. These values indicate that the method has good accuracy and consistency, as shown in Table 1.

Table 1. Accuracy and precision in the method of administration of promethazine hydrochloride

Drug	concentration		Rec%	RSD%
	Taken(µg.ml^{-1})	Found(µg.ml^{-1})		
proH	15	15.1258	100.8386	0.3288
	35	34.8528	99.7942	0.7443

3.4. Application of method

The method was successfully applied to a drug, with concentrations within the calibration curve range of 10, 20, and 30 µg.ml^{-1} selected. The Rec% value ranged from 99.1725 to 101.983%, and the RSD% value ranged from 0.584265 to 0.900128 µg.ml^{-1} for the drug, as shown in Table 2.

Table 2. Application of the method to promethazine hydrochloride

Drug	concentration		Rec%	R.S.D%
	Taken(µg.ml^{-1})	Found(µg.ml^{-1})		
ProH	10	10.1983	101.983	0.900128
	20	19.8345	99.1725	0.720842
	30	30.4773	101.591	0.584265

3.5. Analysis of the drug form of Promethazine Hydrochloride by the multi-standard addition's method

The multiple standard addition method was applied to promethazine hydrochloride, yielding results that demonstrated the method's efficiency and success. The Rec% for the drug ranged from 99.06859 to 102.4576%, while the RSD% for the drug ranged from 0.1941 to 0.7412%, as shown in Table 3 and Figure 5.

Table 3. Multiple Standard Additions

A	concentration	Found(µg.ml^{-1})	Rec%
-0.5			
0	0.5151	-0.0203	#DIV/0!
0.5	1.0628	0.496743	99.34863
1	1.5993	1.00321	100.321
1.5	2.1646	1.536864	102.4576
2	2.6588	2.003398	100.1699
2.5	3.1932	2.507883	100.3153
3	3.6849	2.972057	99.06857

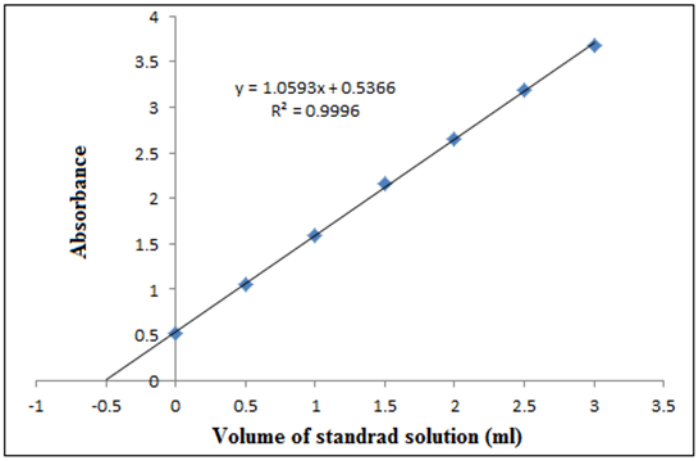

Figure 6. Multiple standard additions.

4. Conclusion

The results of this study demonstrate that the dual pair-length method represents a simple and effective spectrophotometric method for quantifying promethazine hydrochloride in pharmaceutical preparations. The method was characterized by accuracy and reliability, with good linearity and acceptable recovery values, in addition to low detection and quantification limits, confirming its suitability for routine quantitative analysis. This method is also characterized by its rapid performance, low cost, and the absence of the need for solvents or complex equipment, such as that required for chromatographic methods. Accordingly, this method can be considered a practical, environmentally friendly alternative for pharmaceutical quality control, with the potential for widespread application in pharmaceutical analytical laboratories.

References:

[1] Abdulrahman, L. K., Al-Abachi, A. M., & Al-Qaissy, M. H. (2005). Spectrophotmetric Micro determination of promrthazine hydrochloride in pharmaceutical. Baghdad Science Journal, 2(3), 18.

[2] AL-Ayash, A., & Jasim, F. (2008). Spectrophotometric micro determination of drug promethazine hydrochloride in some pharmaceutical by chelating with Rhodium. Baghdad Science Journal, 5(4), 17.

[3] Al-kahdimy, A. S. (2016). Flame emission and molecular absorption spectrophotometric determination of promethazine hydrochloride via potassium dichromate as oxidant reagent. World J Pharm Sci, 4(3), 323-329.

[4] Al-Sabha, T. A. N., Ahmad, N. R., & Ibrahim, M. I. (2006). Spectrophotometric determination of promethazine hydrochloride via oxidative coupling reaction with sulphanilic acid. University of Sharjah J. of Pure Applied Sci, 3(1), 1-12.

[5] Al-Saidi, K. H., & Hammza, R. A. (2014). Spectrophotometric determination of promethazine hydrochloride and paracetamol in pharmaceutical tablets. Al-Nahrain Journal of Science, 17(1), 14-23.

[6] Al-Ward, H. S. (2005). Spectrophotometric Micro Determination of Promrthazinc Hydrochloride in Pharmaceutical Preparations Via Oxidative Coupling Reaction with Sulphanilamide and in the Presence of Ferric Chloride. Baghdad Science Journal, 2(1), 25.

[7] Remington, J. P. (2006). Remington: the science and practice of pharmacy (Vol. 1). Lippincott Williams & Wilkins.

[8] Pharmacopoeia B, Commission BP (2009). Thestationery office. London, UK. 2009;1(123,128).

[9] Skoog, D. A., West, D. M., Holler, F. J., & Crouch, S. R. (1996). Fundamentals of analytical chemistry (Vol. 33, pp. 53-55). Fort Worth: Saunders College Pub.

[10] Skoog, DA, Holler FJ, Crouch SR. (2017). Principles of instrumental analysis.7th, Cengage learning; Jan 27;304

[11] Fejfer, M., Matłoka, A., & Siepak, J. (2021). Spectrophotometric determination of PEG in waterlogged archaeological wood and impregnation solutions. Studies in Conservation, 66(3), 182-189.

[12] Abdullah, M. M., Al-Samarrai, E. T. A., Al-Mashhadani, M. H., Alhuwaymil, Z., Alshareef, S. A., & Bouaziz, M. (2024). Determination of candesartan and amlodipine using ion pair and cloud point methods. Results in Chemistry, 9, 101630.

[13] Bennett, P. N., & Brown, M. J. (2007). Clinical Pharmacology E-Book: With studetconsult Access. Elsevier health sciences.

[14] Sawyer, D. T., Heineman, W. R., Beebe, J. M., & Reilley, C. N. (1984). Chemistry experiments for instrumental methods.

[15] Abraham, J., & Mathew, F. (2014). Taste masking of peadiatric formulation: a review on technologies, recent trends and regulatory aspects. Int J Pharm Pharm Sci, 6(1), 12-19.

[16] Prichard, L., & Barwick, V. (2003). Preparation of calibration curves: A guide to best practice. LGC Group, Ltd. TR LGC/VAM/2003/032, Teddington, Middlesex, UK.

[17] Sawyer D T., Heineman W R., Beebe J M. (1984) Chemistry experiments for instrumental method.3th, John Wiley and Sons. New York, 330.

[18] Skoog D A, D.M. West (1980). Principles of Instruments Analysis. 2th, Saunders, Philadelphia, chapter.6; 412.

[19] Christian, G. D. (1994) Analytical Chemistry,5th, John Wiley and Sons, Inc., New York, 327-332.

[20] Kellner, R., Mermet J.M., Otto M., Widmer H. M. (1998). Analytical Chemistry. Wiley-VCH Verlag Gmbh,New York,1st. 533.

[21] Galen W and wing E. (1981) Instrumental Methods of Chemical Analysis,4th, Kosido Co., Ltd. Tokyo Japan; 503.

[22] Yin, J., & Tian, L. (2014). Joint confidence region estimation for area under ROC curve and Youden index. Statistics in medicine, 33(6), 985-1000.

[23] Jung, Y., Song, K. H., eun Cho, J., Kim, H. S., Kim, N. H., Kim, T. S., ... & Oh, M. D. (2014). Area under the concentration–time curve to minimum inhibitory concentration ratio as a predictor of vancomycin treatment outcome in methicillin-resistant Staphylococcus aureus bacteraemia. International journal of antimicrobial agents, 43(2), 179-183.

[24] Holmes, N. E., Turnidge, J. D., Munckhof, W. J., Robinson, J. O., Korman, T. M., O'Sullivan, M. V., ... & Johnson, P. D. (2013). Vancomycin AUC/MIC ratio and 30-day mortality in patients with Staphylococcus aureus bacteremia. Antimicrobial agents and chemotherapy, 57(4), 1654-1663.

[25] Sakaguchi, K., Hirota, Y., Hashimoto, N., Ogawa, W., Sato, T., Okada, S., ... & Nakajima, H. (2012). A minimally invasive system for glucose area under the curve measurement using interstitial fluid extraction technology: evaluation of the accuracy and usefulness with oral glucose tolerance tests in subjects with and without diabetes. Diabetes technology & therapeutics, 14(6), 485-491.

[26] Duan, F., Simeone, S., Wu, R., Grady, J., Mandoiu, I., & Srivastava, P. K. (2012). Area under the curve as a tool to measure kinetics of tumor growth in experimental animals. Journal of immunological methods, 382(1-2), 224-228.

[27] Raveendra K S, Rajendra W A and Bhagawantrao K R. (2016). AUC, UV spectrophotometric method for the determination of cefpodoxime proxetil and pharmaceuticals.; 5(6) 1848-59.

[28] Hand D J and Christoforos A (2013). When is the area under the receiver operating characteristic curve an appropriate measure of classifier performance. Patt Reco Lett; 34(5): 492-5.

[29] Jadhav S and Kharat R. (2015) Pirjade Mujawar Farhat and Tamboli Ashpak ; Zero Order and Area Under Curve Spectrophotometric Methods For Determination of Omeprazole Capsules in Pharmaceutical Formulation . Int J of Adva in ScieRese; 1(2): 102 - 7.

[30] Rajan R V. (2014). Simultaneous UV-Spectrophotometric Estimation of Amoxicillin and Carbocisteine by Area Under Curve Method in Combined Dosage Form. Der Pharma Lett; 6(5): 1-7