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A Novel UV Spectroscopic Method for the Estimation of Frusemide in Tablet Dosage Form Using Buffer Capsule

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ABSTRACT

A novel simple and cost-effective UV spectroscopic method has been developed for the estimation of frusemide in tablet dosage form using Buffer capsule. Frusemide is a diuretic drug which is insoluble in water and has solubility in aqueous alkali hydroxides. Hence the drug can be solubilised in a buffer solution having an alkaline pH. This method indicates that frusemide can be solubilised by altering pH. The method was developed by measuring the absorbance of frusemide in buffer capsule solution (pH-9.2) at 276nm. The developed methods were validated as per ICH guidelines. Linearity of the methods was determined over a concentration range of 5-25 µg/mL. The accuracy of the method was determined by recovery studies. The inter day and intraday precision were carried out and the % RSD is less than 2. The LOD and LOQ values were found to be 1.7525µg/mL & 5.3106 µg/mL respectively. Amount of drug obtained from this method lies within the IP limit. The results showed that the developed methods can be used for the routine analysis of Frusemide in bulk and tablet dosage.

INTRODUCTION

The development and validation of analytical methods is an essential aspect of pharmaceutical quality control. Frusemide is a commonly used diuretic medication that is prescribed for the treatment of hypertension and oedema. Therefore, the accurate and reliable determination of the amount of frusemide in tablet dosage form is crucial for ensuring its safety and efficacy. This study aims to develop and validate a method for the determination of frusemide in tablet dosage form using the absorbance maxima technique. Frusemide is a water insoluble drug which has solubility in aqueous alkali hydroxides. Several spectroscopic methods were developed for the estimation of Frusemide using different organic solvents. Hydrotropic solubilisation was also carried out for the estimation of this drug. The current study mainly aims to develop a cost effective and simple spectroscopic method for the estimation of Frusemide by altering the pH using buffer capsules.

The proposed method involves measuring the absorbance of frusemide at its maximum wavelength using a UV-visible spectrophotometer. The method is simple, accurate, and precise, and it is expected to be a useful tool for routine quality control analysis of frusemide in tablet dosage form. The validation of the method was performed as per the International Council for Harmonisation (ICH) guidelines, which ensures that the method is reliable and can be used to produce accurate and reproducible results.

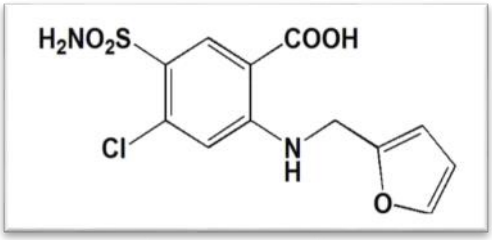

Fig. No. 1: Structure of Frusemide

MATERIALS AND METHODS

Reagents and Chemicals

Frusemide reference standards were brought from Yarrow Chem Products Mumbai. Buffer capsule (pH 9.2) from Merck Specialties Pvt Ltd. Distilled water, Lasix 40 tablets were purchased from a local market.

INSTRUMENTATION

Double beam spectrophotometer Hitachi UH5300, Shimadzu ATX 224 weighing balance, Power sonic 405 were used for the spectrophotometric analysis.

METHOD

Absorbance Maxima Method

The absorbance maxima method is a technique used to determine the wavelength at which a particular substance has its maximum absorbance of light. This method is commonly used in spectroscopy and analytical chemistry to identify and quantify the presence of a particular molecule or compound in a sample.

The basic principle of the absorbance maxima method is based on the fact that every molecule absorbs light at a specific wavelength, which is unique to that molecule. When a sample is exposed to light of different wavelengths, the amount of light absorbed by the sample at each wavelength is measured. The wavelength at which the maximum amount of light is absorbed is known as the absorbance maxima, or the peak absorbance wavelength.

By determining the absorbance maxima of a substance, it is possible to identify the substance and quantify its concentration in a sample. This method is widely used in various fields, including environmental monitoring, pharmaceuticals, and food analysis etc.

EXPERIMENTAL WORK

Preparation of Buffer solution

Buffer solution was prepared by dissolving a buffer capsule of pH 9.2 in 100 mL of distilled water.

Preparation of Standard stock solution

Weighed accurately 25 mg of frusemide and transfer it into a 25 mL volumetric flask with buffer solution. 1 mL of the resulting stock solution were diluted to 10 mL with buffer solution to obtain a 100 µg/mL solution. From this solution, a series of dilutions were prepared in the range of 5-25 µg/mL. The λ_{max} of Frusemide was found to be 276nm.

Preparation of Tablet Formulation

Weighed accurately twenty tablets of Lasix and their average weight was calculated. The tablets were triturated into a fine powder, and an equivalent weight of 25 mg of frusemide were transferred to a 25 mL volumetric flask and dissolved in buffer solution. After sonication for 15 minutes, the volume was made up to the mark with the diluent. The tablet solution was filtered through Whatman filter paper to obtain the 1000 µg/mL stock solution. A 10 µg/mL solution was prepared and absorbance was measured at 276nm.

METHOD VALIDATION

Validating a method is an essential component of drug development and quality control. To ensure the accuracy and consistency of results, it is crucial to establish the reliability and validity of a method developed for frusemide analysis. The validation process involves a series of experiments and tests to evaluate the specificity, accuracy, precision, linearity, robustness, and sensitivity of the method. Method validation is critical in ensuring that the developed method is suitable for its intended use, whether it is for routine analysis, product release, or stability testing.

Accuracy:

In method validation, accuracy refers to the ability of a method to provide results that are reliable and reproducible over a given range of sample concentrations. The accuracy of the method is evaluated by calculating the recovery of the results, which should fall within acceptable limits.

Recovery study were carried out by addition of standard drug solution to pre analysed sample solution at 3 different concentration level (80%, 100%,120%) within the range of linearity of the drug.

Precision:

Precision is important in ensuring that the analytical results are reliable and reproducible. A highly precise method ensures that the analytical results are consistent and can be used for making informed decision. Precisions were considered as two levels.

1. Repeatability of the method was studied using six determination of test concentration (10 µg/mL).

2. Intermediate precision of the method was studied by using the same test concentration which was prepared and analysed at the same time of different days.

Linearity:

Linearity of frusemide was determined by analysing five independent levels of solutions. Frusemide has a linearity range from 5-25 µg/mL.

Limit of Detection:

Detection limit is expressed as; **LOD=3.3*σ/S**

Where; **σ**- The standard deviation of the response

S- Slope of the calibration curve

Limit of Quantification:

The Quantification limit is expressed as; **LOQ=10*σ/S**

Where; **σ**-The standard deviation of the response

S-Slope of the calibration curve

RESULTS AND DISCUSSION

A simple UV spectroscopic method has been developed for the estimation of Frusemide in tablet dosage form. The drug concentrations were found to be linear in the range of 5-25 µg/mL and the correlation coefficient value of 0.9998 indicates that developed method was linear. The % RSD was found to 1.0402 and 0.7938 for intra-day and inter-day precision. The % RSD is less than 2 which indicates that the developed method is precise. The accuracy of the method was assessed by recovery studies at three different levels i.e., 80%, 100%, 120%. The values of standard deviation were satisfactory and the recovery studies were close to 100%. The % RSD value is ≤ 2 indicates the accuracy of the method. The LOD and LOQ values were found to be 1.7525µg/mL & 5.3106 µg/mL respectively. The amount of drug present in the tablet lies between the IP limit.

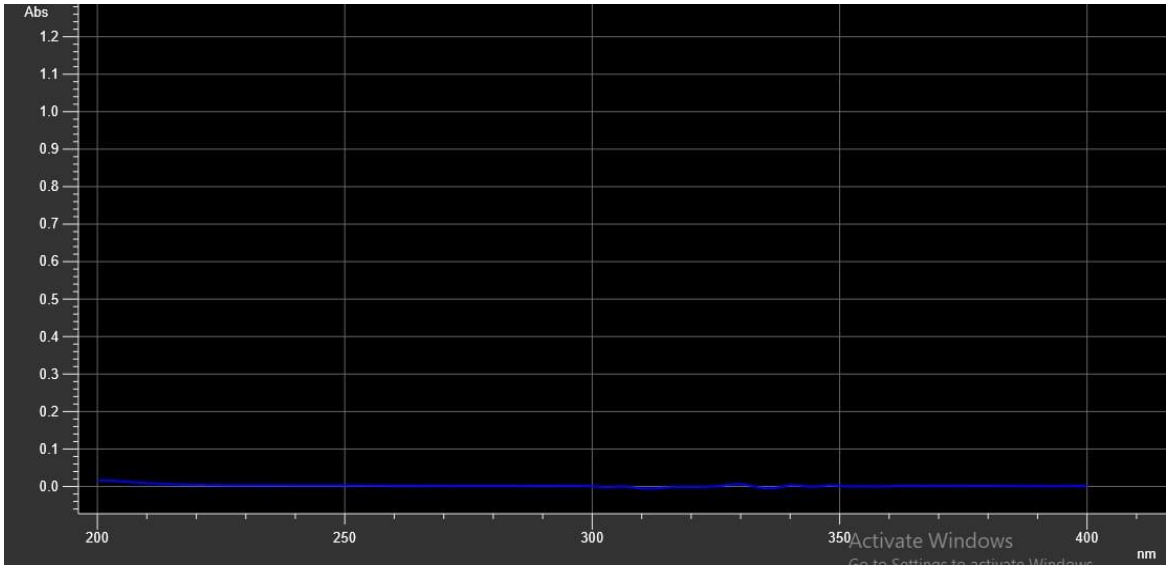

Fig. No. 2: Zero order spectrum of Blank Buffer Solution

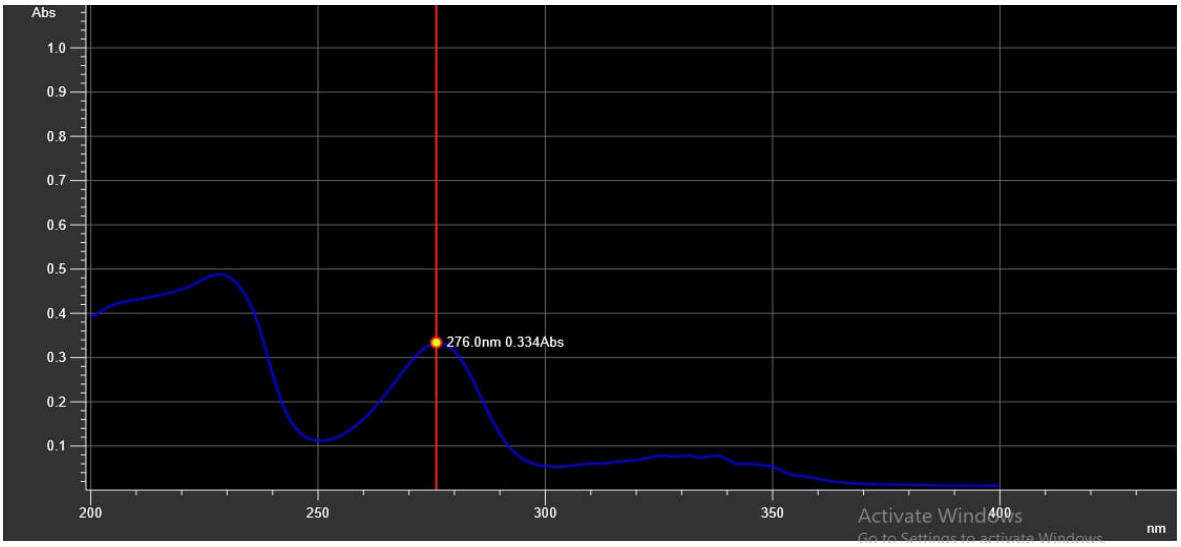

Fig. No. 3: Zero order spectrum of Frusemide

Table No. 1: Absorption Data of Frusemide

Sl No.	Concentration µg/mL	Absorbance
1	5	0.335
2	10	0.617
3	15	0.929
4	20	1.228
5	25	1.557

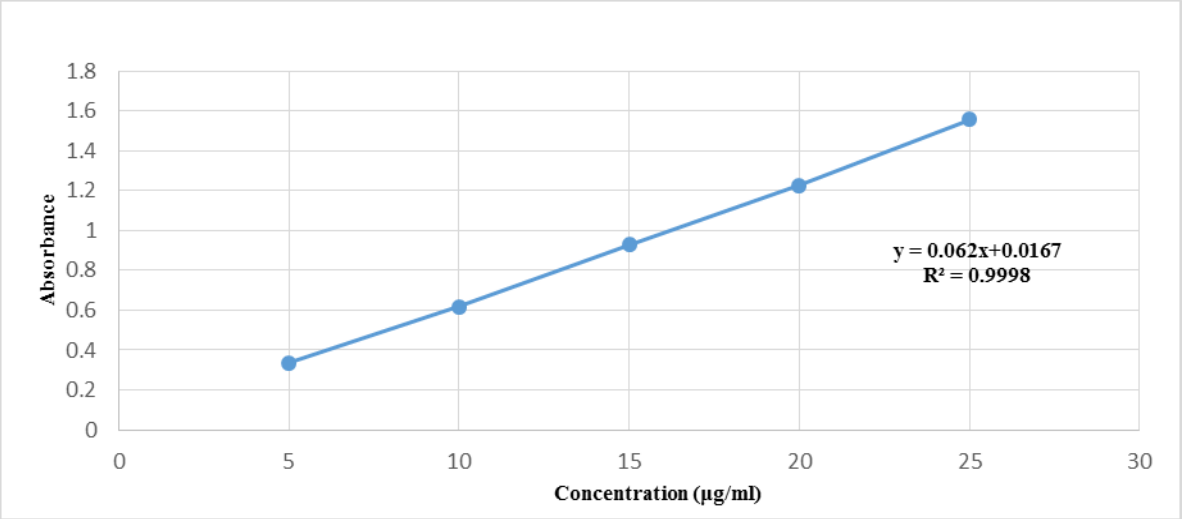

Fig. No. 4: Calibration curve of Frusemide

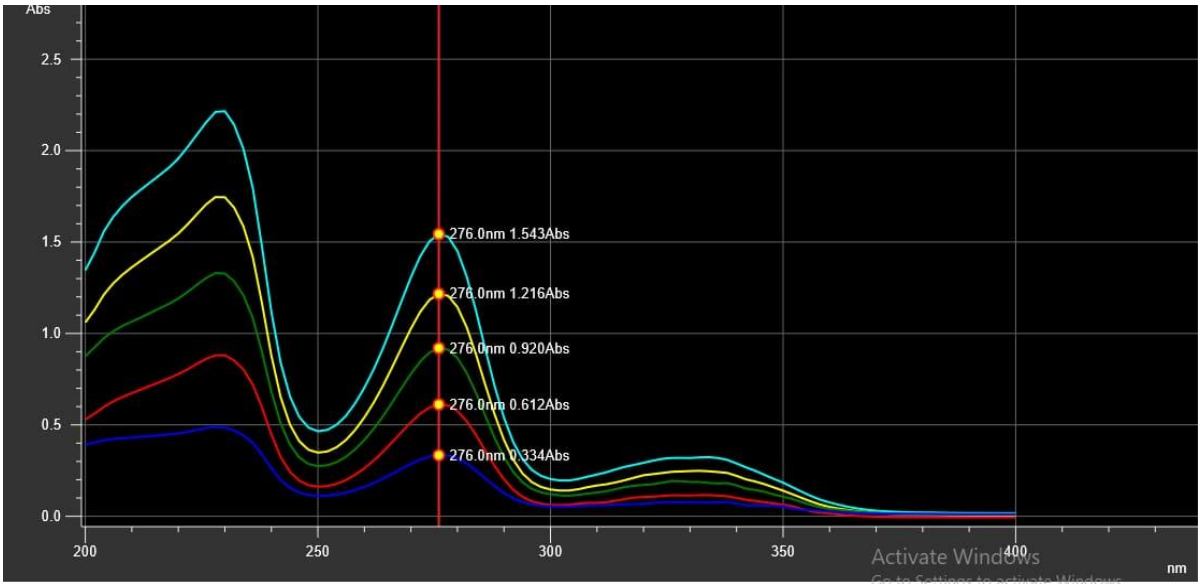

Fig. No. 5: Overlay Spectra of Frusemide

Table No. 2: Parameters from the Calibration curve

Parameter	**Observation**
Calibration curve	Linear
Expression	Y= mx+c
Slope	0.062
Intercept	0.0167
Coefficient(R^2)	0.9998

Table No. 3: Analysis of Marketed Formulation

Sl No	Amount Taken (µg/mL)	Absorbance at 276nm	Amount of Drug Found (µg/mL	% Amount Found
1	10	0.621	9.89	98.9
2	10	0.622	9.90	99.0
3	10	0.626	9.97	99.7
4	10	0.627	9.98	99.8
5	10	0.620	9.87	98.7
6	10	0.634	10.10	101

Table No. 4: Statistical Evaluation of Marketed Formulation

% Mean*	S.D.*	% RSD*	± S.E.*
99.51	0.85186	0.8560	0.3477

*Average of 6 determination

Table No. 5: Statistical Evaluation of Recovery Studies

Sl No	Level of recovery	Amount taken (µg/mL)	Amount of Standard added (µg/mL)	Absorbance at 276 nm	Amount recovered	Percentage recovered %
1	80%	10	8	1.087	17.51	97.27
2		10	8	1.096	17.66	98.11
3		10	8	1.097	17.68	98.22
1	100%	10	10	1.214	19.59	97.95
2		10	10	1.218	19.66	98.30
3		10	10	1.215	19.61	98.05
1	120%	10	12	1.326	21.42	97.36
2		10	12	1.328	21.46	97.54
3		10	12	1.331	21.51	97.77

Table No. 6: Statistical evaluation of Recovery Studies

Level of Recovery	% Mean*	S.D.*	%RSD*	±S.E.*
80%	97.86	0.5196	0.5309	0.2999
100%	98.1	0.1802	0.1836	0.1040
120%	97.55	0.20555	0.2107	0.1186

*Average of 3 determination

Analysis of Intraday Precision

Table No. 7: Data of Intraday Precision

Sl No	Amount Taken (µg/mL)	Absorbance at 276nm	Amount of Drug Found (µg/mL)	% Amount Found
1	10	0.621	9.89	98.9
2	10	0.622	9.90	99.0
3	10	0.626	9.97	99.7
4	10	0.627	9.98	99.8
5	10	0.620	9.87	98.7
6	10	0.634	10.10	101

Analysis of Inter-Day Precision

Table No. 8: Data of Inter-Day Precision

Sl No	Amount Taken (µg/mL)	Absorbance at 276nm	Amount of Drug Found (µg/mL)	% Amount Found
1	10	0.620	9.87	98.7
2	10	0.621	9.89	98.9
3	10	0.627	9.98	99.8
4	10	0.633	10.08	100.8
5	10	0.622	9.90	99
6	10	0.627	9.98	99.8

Table No. 9: Statistical Evaluation of Intraday and Inter-Day Precision Studies

Parameter	% Mean*	S.D.*	% RSD*	±S.E.*
Intraday precision	100.033	1.0405	1.0402	0.4247
Inter-day precision	99.5	0.7899	0.7938	0.3224

*Average of 6 determination

Limit of Detection and Limit of Quantification (LOD and LOQ)

Table No. 10: LOD and LOQ

Drug	Wavelength (nm)	LOD ((µg/mL)	LOQ (µg/mL)
Furosemide	276	1.7525	5.3106

CONCLUSIONS

A simple, accurate and cost-effective spectroscopic method was developed for the estimation of frusemide in tablet dosage form. The method was developed by using buffer solution having pH 9.2. Since the drug is insoluble in water there were several methods for the estimation of frusemide. The existing methods mainly use organic solvents and hydrotropic agents. Organic solvents are expensive and toxic in nature. In case of hydrotropic solubilisation techniques, large quantity of hydrotropic agents was required. Hence the developed method is very simple and less expensive and it proves that a buffer capsule can also be used for solubilizing some water insoluble drugs. By altering pH, some insoluble drugs can be solubilized in buffer solution. This buffer solution has no absorbance in the UV region. Hence 276nm is the maximum absorbance of frusemide in buffer solution. The developed method was validated as per ICH guidelines.

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