A Review On Development And Validation Of Phenylephrine Hcl By Various Analytical Method .

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Abstract

A simple , precise , rapid , and economic , accurate ultra- violet spectroscopic method of phenylephrine HCL was developed in in bulk dosage and combined dosage form . this method involves first order derivative spectroscopy using 237nm as crossing points for phenylephrine HCL for spectrophotometric method 0.1 NaOH was used as solvent .another method of UV spectroscopy was developed and validated for the estimation of PHE in a pharmaceutical nasal drop formulation . PHE was estimated at 291nm in 1 mol.cm-3 sodium hydroxide (PH 13.5) . selected linearity ranges for PHE was 12-42 ppm for UV method .The UV method are based upon absorption correction and multicomponent analysis approach .the method was validated according to ICH guidelines .

Key Words - Phenylephrine Hcl , UV Spectroscopy ,Trimethylamine , Multicomponent Analysis.

I. INTRODUCTION

II. SPECTROSCOPY METHOD [1, 2]

It is the branch of science dealing with the study of interaction Between Electromagnetic radiation and matter. It is a most powerful tool available for the study of atomic and molecular structure/s and is used in the analysis of wide range of samples. Optical spectroscopy includes the region on electromagnetic spectrum between 100 Å and 400 μm

Region	Wavelength
Far UV	10_200nm
Near UV	200_400nm
Visible UV	400_750nm
NearInFra red	0.75_2.2
Mid Infrared	2.5_ 50
Far Infrared	50_ 1000

UV visible spectroscopy

UV-Visible spectrophotometry [3]is one of the most frequently employed technique pharmaceutical analysis. It involves measuring the amount of ultraviolet or visible radiation absorbed by a substance in solution. Instrument which measure the ratio, or function of ratio, of the intensity of two beams of light in the U.V-Visible region are called uv visible spectroscopy. **Beer's law**: It states that the intensity of a beam of parallel monochromatic radiation decreases exponentially with the number of absorbing molecules. In other words, absorbance is proportional to the concentration

Lambert's law: It states that the intensity of a beam of parallel monochromatic radiation decreases exponentially as it passes through a medium of homogeneous thickness. A

Beer-Lambert law: When beam of light is passed through a transparent cell containing a solution of an absorbing substance, reduction of the intensity of light may occur.

Mathematically, Beer- Lambert law is expressed as

A=a b c

Where, A=absorbance or optical density

a=absorptivity or extinction coefficient

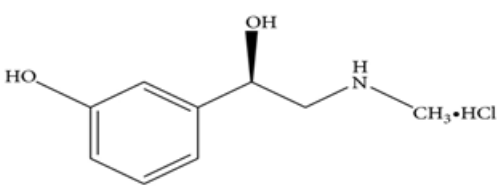
b=path length of radiation through sample (cm)

c=concentration of solute in solutiBoth b and a are constant so a is directly proportional to the concentration c

$$A = A\frac{1\%}{1cm}bc$$

When c is in gm/100 ml, then the constant is called A The principle of uv visibl spectroscopy is base on tha absobtion of ultraviolet light or visible light chemical compounds , which results in the production of distrint spetra . spectroscopy is based on the interaction between light and meter energy stat to another energy state .The beers lambert law state that for given material sample path length , and concentration of the sample are directly proportion to the absorbance of the light .

Introduction of phenylephrine hcl Phenylephrine (PEH) 1-4 is a sympathomimetic amine and an α1-adrenergic receptor agonist used primarily as a decongestant, to increase blood pressure and as an agent to dilate the pupil (mydriatic) [4] .Chemically it is l-(3- Hydroxyphenyl)-N-methyl ethanolamine and exhibits its pharmacological activity by acting on α1 adrenergic receptors present on peripheral smooth muscles .



It is soluble in water. DMSO, alcohol, and methanol . Phenylephrine hydrochloride (PHP), is a white crystalline powder, freely soluble in water, melts at 143°C [1,2] and It belongs to a group of drugs named sympathomimetics [3]. It s timulates alpha receptors in certain areas of the body. It is used locally, as decongestant, for non-specific and allergic conjunctivitis, sinusitis, and nasopharyngitis [4]. Phenylephrine nasal drops are used for treating symptoms such as runny nose, sneezing, itching of the nose, and throat [5]. PHP is normally used to increase the blood pressure unstable patients with hypotension, especially resulting from septic shock [5].

VALIDATION Validation is concerned with assuring that a measurement process produces valid measurements. Results from method validation can be used to judge the quality, reliability and consistency analytical results. It is an integral part of any good analytical practice. A measurement process producing valid measurements for an intended application is fit for purpose.Method validation is the process used to confirm that the analytical procedure employed for a specific test is suitable for its intended use. Results from method validation can be used to judge the quality, reliability and consistency of analytical results; it is an integral part of any good analytical practice.(6 , 7) Analytical methods need to be validated or revalidated,

Types of Analytical Procedures to be validated The objective of the analytical procedure should be clearly understood since this will govern the validation characteristics which need to be evaluated. Typical validation characteristics which should be considered are listed below:

- Accuracy
- Precision
- Intermediate Precision
- Specificity
- Detection Limit
- Quantitation Limit
- Linearity
- Range

Drug profile

Phenylephrine hydrochloride

IUPAC name	(R)-1-hydroxyphenyl)2methylaminoehano hydrochloride.
Solubility	Soluble in methanol , distilled Water and Alcohol
Uses	Nasal Decongestant
Formula	C9H14ClNO2
Molecular weight	203.66
Melting point	143 – 145 degree celcius
Odour	Odourless
Nature	White microcrystalline powder

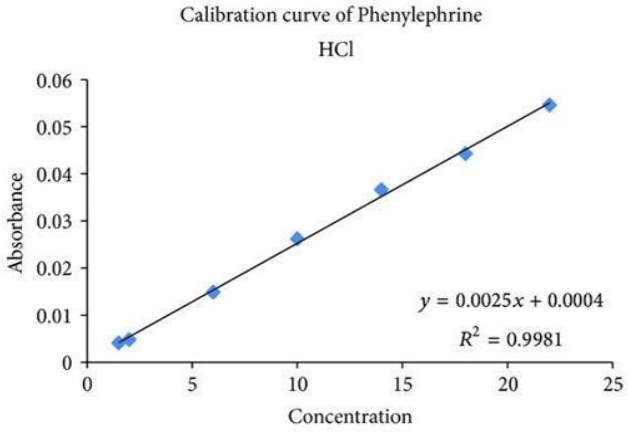
ApparatusA Shimadzu UV-Visible 1700 Pharma Spectro double beam spectrophotometer with a wavelength accuracy (±0.3 nm), 1 cm matched quartz cells, and UV probe 2.34 software was used. Calibrated analytical balance Shimadzu BP211D (Sartorius Gottingen AG, Germany) was used for weighing purpose. All statistical calculations were carried out using Microsoft Excel 2007 analytical tool.(8**)**

MATERIALS AND METHOD; Phenylephrine hydrochloride as a gift sample from Amrut Drug Research Lab Pvt. Ltd. , Tarapur. Phenylephrine hydrochloride IP (10 mg). Distilled water was used to prepare all solutions. Spectroscopic analysis was carried out using a double-beam Shimadzu UV-Visible spectrophotometer. simple mobile phase composition of mixture of buffer (water +0.2 %v/v Triethylamine , PH 7.5 by dilute H3PO4) .(9)

DETERMINATION OF λmax The tablet solution were suitably diluted with diluent and subjected for determination of λmax in the range of 200-400 nm.

Preparation of standard solution 10mg Phe transfer into 10 Flask diluted with methanol .working solution phe having 100 ug/ml con by withdrawing solution and volume was made unto10 ml volumetric Flask using Same diluent.

(10) Take A quantity of powder equivalent to 50mg was weighed and was dissolved in 20 ml of 0.1N NaoH Sonicated for 2 minutes. Then it was diluted up to the mark with water in 100 ml standard measuring flask. The solution was filtered using Whatman filter paper 42. From this 1ml of the solution was again diluted to 100ml with distilled water. Absorbance was recorded.11, 12)

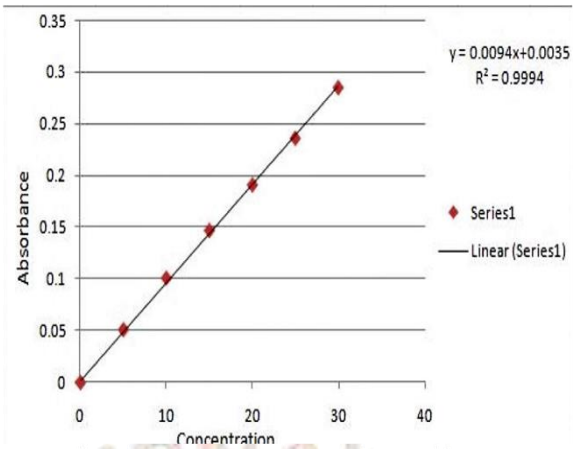


Method validation Specificity: Resolution of the analyte peak from the nearest peak: Solution of each of the analyte was injected separately and their retention time is noted. The standard working solution containing a mixture of the component being analyze is also injected and each of analyte peaks is check for its resolution from the nearest(13).

Precision: Precision of the analytical method is ascertained by carrying out the analysis as per the procedure and as per normal weight taken for analysis. Repeat the analysis six times. Calculate the % assay, mean assay, % Deviation and %RSD.(14)

Replicate	**5**	**10**	**15**	**20**	**25**
Replicate1	0.235	0.481	**0.699**	**0.946**	**1.167**
Replicate2	0.238	0.478	**0.698**	**0.941**	**1.168**
Replicate3	0.239	0.475	**0.696**	**0.943**	**1.171**
Replicate4	0.232	0.477	**0.696**	**0.945**	**1.170**
Replicate5	0.232	0.482	**0.98**	**0.942**	**1.169**

L**inearity** : and % relative standard deviationstudy, from the standard stock solutions of 100µg/ml for PHE, different dilutions were prepared for each drug having concentration as shown in Table.with methanol. Then these solutions were scanned over the range of 400-200nmand absorbance's were measured at the respective analytical wavelength 216 nm for PHE respectively for all the five replicates. The calibration curves were plotted between the mean value of the observed absorbance and respective concentration. From the calibration curve given , it was found the drug follows Beer's – Lamberts law within the range of 5-35 µg/ml for drug.(15).



PrecisionThe precision of an analytical procedure expresses the closeness of agreement (degree scatter) between a Series of measurements obtained from multiple sampling of the same homogeneous sample under the prescribed Conditions (16).Precision of the method was studied by intraday and interday variations in the test method of PE. Method repeatability (intra-day precision) was evaluated bassaying six samples, prepared as Described under sample preparation. Inter day precision was performed by assaying six samples Day described in the sample preparation. (17)

Intreday precision

Drug	Concentration	Mean% assay +_assay	%RSD
PHE	20	99.60+_1.036	1.04

Interday precision

Drug	Concentration	Mean% assay+_assay	Mean% assay+_assay
PHE	20	100.76 ± 1.263	1.25

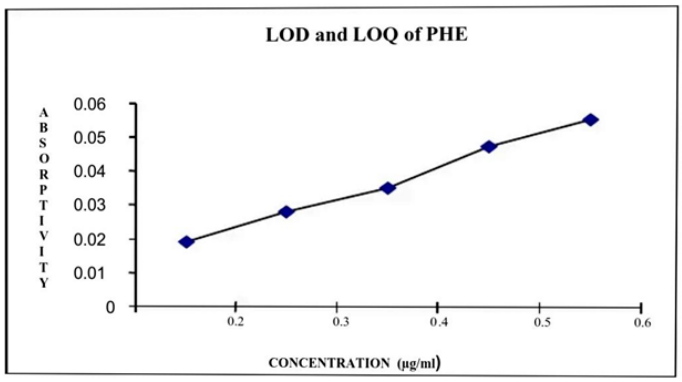
ACCURACY;: Accuracy was assessed by the determination of the recovery of the method by addition of standard drug to the prequantified sample preparation at 3 different concentration levels 80, 100, and 120%, taking into considerations percentage purity of added bulk drug samples. Each concentration was analyzed 3 times, and average recoveries were measured.(20)

Drug	Level	Amount taken	Amount added	Amount recovery	Percent recovered+-SD
PHE	80%	28.8	12.8	28.82	100.06+_0.76
PHE	100%	32	16	31.85	99.53+_1.066
PHE	120%	35.2	19.2	35.04	99.54+_0.625

Extraction Recovery ;Recovery results was found to be satisfactory as these was consistent, precise and reproducible are summarized in Table

Analyte	Qc sample µg mL	Extraction Recovery(%)	RSD(%)
PHE	40	99.97	1.89
PHE	100	97.34	0.24
PHE	200	99.82	0.36

Limit of Detection (LOD): limit of detection and quantitation, lower concentration range solutions of 0.2, 0.3, 0.4, 0.5 and0.6 µg/ml were prepared and the absorbance were determined and LOD and LOQ, (21)were calculated by use of the equation LOD = 3.3 Q/ S and LOQ = 10 Q/ S, where Q is the standard deviation and S is the slope of the calibration curve (**Table**



	Absorbance of PHE at **concentration (µg/ml)**				
Replicate no.	0.2	0.3	0.4	0.5	0.6
Replicate1	0.018	0.028	0.036	0.047	0.055
Replicate2	0.017	0.029	0.035	0.048	0.055
Replicate3	0.018	0.030	0.034	0.045	0.056
Replicate4	0.019	0.026	0.036	0.046	0.055
Replicate5	0.021	0.029	0.033	0.048	0.052
S. D.	0.0014	0.0018	0.003	0.0014	0.017

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