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Method Development and Validation of Antihypertensive Drug by using UV Spectroscopy

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Abstract: *Hypolipidemic drugs are therapeutic agents designed to lower lipid levels, particularly cholesterol and triglycerides, in the blood. These drugs play a crucial role in managing conditions such as hyperlipidemia, cardiovascular diseases, and metabolic disorders. As the global prevalence of such diseases continues to rise, the demand for effective hypolipidemic treatments grows, prompting ongoing research and development in this field. Rosuvastatin, belongs to class of statins. Which are used to treat the high cholesterol and use to prevent the cardiovascular disease. Rosuvastatin chemically is (3R,5S,6E)-7[4-(4-Flurophenyl)-2- (N-Methyl- methanesulfonamido)-6-(Propan-2-ylPyrimidin-5-yl]-3,5-dihydroxyhept-6-enoic acid.[1] Spectroscopy offers a promising alternative due to its rapid, non-destructive nature and minimal sample requirements.*

Keywords: Hypolipidemic drugs

I. INTRODUCTION

Propranolol belongs to a β-blocker. β-blocking drugs impact blood circulation and myocardial performance.
Propranolol is utilized to treat shaking sensations, angina (chest ache), elevated blood pressure (hypertension), heart rhythm disorders, and other coronary and vascular problems. It is also used for treating or avoiding cardiac arrest, and to minimize the duration and intensity of migraine related headaches.
Propranolol is categorized as a β -blocker drug. It is used to treat elevated blood pressure, ventricular fibrillation, thyrotoxicosis, capillary hemangiomas, performance anxiety, and vital shaking sensations, as well as to prevent symptoms of migraines and possible heart problems in people who have angina or have had previous heart attacks.
It can be administered orally (by mouth) or via intravenous injection. Propranolol is used to treat high blood pressure either by itself or in conjunction with other drugs. In addition, it is used to treat hypertrophic subaortic stenosis, a disorder of the heart muscle, pheochromocytoma, a tumor on a tiny gland close to the kidneys, and irregular heartbeats.
Propranolol is also used to enhance survival following a heart attack and to prevent migraine headaches and angina (chest discomfort). Propranolol belongs to a group of drugs known as beta blockers. It improves blood flow and lowers blood pressure by relaxing blood vessels and lowering heart rate.

Drug Profile: -
Name Of Drug:- Propranolol
Drug Classes:- Non-selective beta-adrenergic blocking agent-
IUPAC Name:- RS)-1-(1-methylethylamino)-3-(1-naphthyloxy) propane-2-ol
Molecular Formula:- $C_{16}H_{21}NO_2$
Molecular Mass:- 259.349 $gmol^{-1}$
Melting Point:- 96 °C (205 °F)
Solubility of Drug:- Water, Alcohol, dimethyl formamide, dimethyl sulfoxide.
Physical Form:- Powder

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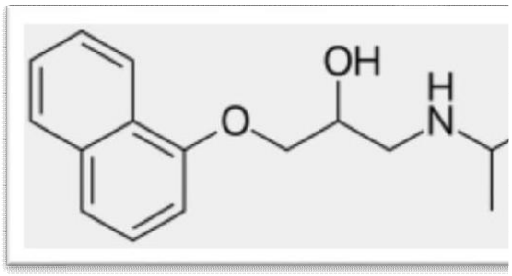
Dosage Forms:- Intravenous solution (1 mg/mL), oral capsule, extended-release(120 mg; 160 mg; 60 mg; 80 mg), oral liquid (4.28 mg/mL), oral solution (20
mg/5 mL; 40 mg/5 mL), oral tablet (10 mg; 20 mg; 40 mg; 60 mg; 80 mg)

Protein Binding:- 90%
Structure: -



Mechanism of Action

Propranolol is a non-selective β-adrenergic receptor antagonist, or beta blocker;that is, it inhibit the action of epinephrine (adrenaline) and norepinephrine (noradrenaline) at both β1- and β2-adrenergic receptors.
It works by relaxing blood vessels and lower heart rate to improve blood flow and reduce arterial pressure.[17]

Action in Heart

Propanalol
↓
Selectively block β1-receptor in heart
↓
Decerease force of contraction and heart rate and cardaic output
↓
Decrease the blood pressure
↓
Action in Kidney :-
↓
Propanolol
↓
Selectively block β1-receptor in kidneys
↓
Selectively block β1-receptor in kidney
↓
Decrease the blood pressure

UV- Spectroscopy:-

UV spectroscopy, often known as ultraviolet spectral analysis, is a technique for measuring how much ultraviolet light a substance absorbs. This approach is widely used in biological and chemical sciences to investigate the characteristics of diverse compounds, particularly those with double bonds composed of conjugated or aromatic rings.

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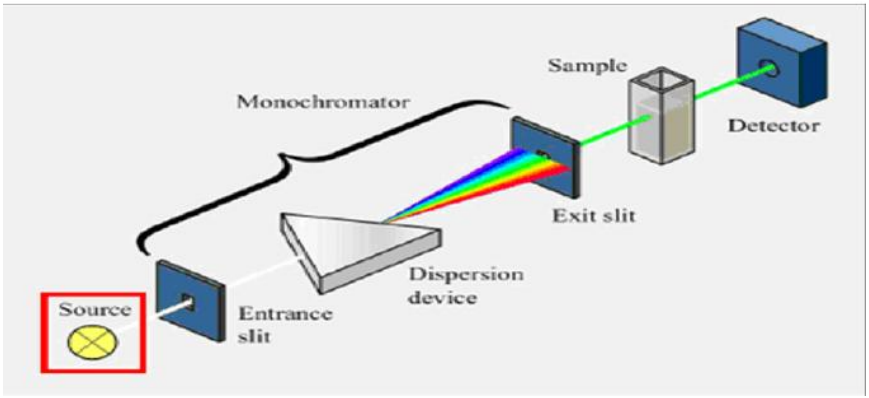

Principle:-

UV Light Absorption: At stipulated wavelengths, molecules absorb UV light and undergo electronic changes. The energy absorbed can move electrons from the ground state to the excited state.

Beer–Lambert Law: The equation for calculating absorbance (A), concentration (c), route length (l), and molar absorptivity (ε) is as follows: $A=\varepsilon clA = \varepsilon clA=\varepsilon cl$.

This rule enables the measurement of chemicals in a sample

Wavelength region: UV spectroscopy often studies the wavelength region of 200 to 400 nm, which is where many organic molecules absorb light.[5][17]

Feature: -

A cost-effective, straightforward, adaptable, and benign analytical approach, UV-vis spectroscopy may be used with a wide range of organic molecules and certain inorganic species. UV-vis spectrophotometers detect the absorption or transmission of light through a material as a function of wavelength.

UV/visible spectroscopy is heavily utilized in research than in detection. The trace metal content of an alloy, such manganese in steel, can be detected by first treating the sample to bring the metal into solution as an ion.

UV-Visible spectrophotometry is a commonly utilized method for precise measurement of analytes in analytical research, government regulatory research facilities, and QA/QC. The approach's fundamental concepts, such Beer's Law, are learned in schools. Mid-range to upper end UV-visible The majority of research testing facilities, including those at institutions and firms, employ spectrophotometers.

In order to quantify the ion in a form, it is then complexed or made to react; manganese is the manganate (VII) ion, for example. Since the mass of the metal in the sample and the concentration of the solution may be ascertained by knowing the chromophore's absorption coefficient, the absorbance is the most useful piece of information when the color spectrum is registered.

Measurements concerning the ultraviolet/visible area (UV-Vis) ranged in intensity from roughly 200 nm to 800 nm. Transitions between the electrical energy levels of a molecule occur when it absorbs ultraviolet or visible light. Characterization may be done using the spectral and electrical characteristics of many resources, including liquids, films, powders, and homogeneous solids.[5]

Advantages

- The method is non-destructive so that the sample can be reused.
- The technique is fairly simple and can be used easily. No prior training is necessary.
- Measurement can be done in a short span of time, helping easy integration into experiments.
- Data analysis is simple and requires less processing.
- Instrumentation is relatively inexpensive and can be procured easily by laboratories.[17]

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II. LITERATURE REVIEW

1. ALI A EL-Emam Et al:- proposed method for determination of propranolol hydrochloride in pure as well dosage forms by using double beam spectrophotometer. The chemical used was Ceric ammonium sulphate This method is stemming from oxidative coupling reaction with 3-methylbenzothiazone-2-one Then calibration graph was plot.Thus we can say purposed method is precise accurate and economical which can be applied to the marketed preparations.
2. Namdev G Shinde Et al:- The propranolol and roswastatin was determined simultaneously Maximum absorbance of was propranolol hydrochloride was calculated they achieved simultaneous equation (Vierodt method).Method were validated for linearity accuracy precision LOD LOQ as per ICH.
3. Lalit Kumar Et al:- By using uv visible spectrophotometer they determined saturated solubility of propranolol hcl .the conclusion of this study was propranolol has ph dependent solubility.
4. Ehsan.D.Habeeb Et al :- Propranolol hydrochloride was determined with spectrophotometric method using 2,4-dinitrophenyl hydrazine by oxidative coupling and coupling with pph in an alkaline medium.
5.Dr.Prashant Et al:- The uv visible spectrometric method was established for simultaneous estimation of solubility of propranolol hydrochloride and amiodarone hydrochloride.the solvents used were methanol and DMSO (Dimethyl sulphoxide).

III. AIM AND OBJECTIVE

Aim: - For determination of safety, efficacy, Side effect, compatibility of drug.

Objective

- Identify the mechanism of action of propranolol.
- Describe the possible adverse effects of propranolol.
- Review the appropriate monitoring for patients taking propranolol.
- Summarize interprofessional team strategies for improving care coordination and communication to advance Propranolol and improve outcomes.

Plan of Work

Literature review
Collect Necessary Solvent and reagent (e.g. Ethanol, water, buffer solution,etc.)
Method of Development

- Selection of wavelength
- Preparation of solution
- Calibration curve
- Linearity
- Accuracy
- Precision
- Specificity
- Robustness

Determination of maximum wavelength by uv spectroscopy
Data Analysis
Documentation

Material and Method:-

Chemicals and Reagents:-

Propranolol hydrochloride, and distilled water will be provided later by P. Wadhwani College of Pharmacy. UV visible spectrophotometer (UV-1800 Shimadzu) was used; data will process using UV probe (version 2.6) software. Experiment will be done later at P. Wadhwani college of Pharmacy, Yavatmal in 2025.[2][6]

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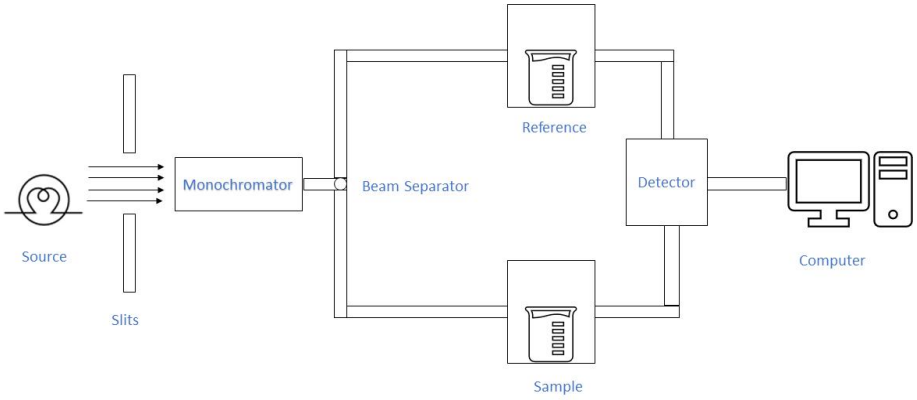
Instrumentation:-

The proposed work was carried out on a Shimadzu UV-visible spectrophotometer (model UV-1800 series), which possesses a double beam double detector configuration with a 1cm quartz matched cell. All weighing was done on electronic balance (MAB 220 Wesner) (sensitivity - 0.1mg).[2][6]



UV-Visible Spectroscopy Instrumentation

Radiation source

Hydrogen-discharge lamp is the most commonly used source of radiation in the U.V region (200-400 nm) whereas a deuterium-discharge lamp is used when more intensity (3-5 times) is desired. A **tungsten-filament lamp** is used when absorption in the Visible region (400-800 nm) is to be determined.

Monochromator

It helps to separate the radiations into separate wavelengths that are it only allow to pass a specific wavelength through it. Monochromators are generally made up of prism or grating which is made up of **quartz**. This is so because quartz does not absorb the radiations thus ensuring no loss of intensity and precise results.

Beam separator

As the name suggests, beam separators help to separate the single radiation into two different paths/chambers that is the reference chamber and the sample chamber. The former is called the reference beam and the latter is known as the sample beam

Detectors

Detectors have photocells or photomultiplier tubes that generate a voltage proportional to the radiation energy that strikes them.

Amplifier

The spectrophotometer has a balancing electronic amplifier that subtracts the absorption of the solvent from that of the solution electronically.

Recorder

A recorder automatically records the spectrum as a plot of the wavelengths of absorbed radiations against **absorbance (A) or molar absorptivity (e).**

Selection of Solvent: -

On the basis of solubility of drug in solvent, Water, Alcohol, Dimethylformamide, Dimethyl sulfoxide (DMSO) was selected as the solvent for dissolving Propranolol Hydrochloride.[4][7][8][9]

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Selection of wavelength range for estimation: -

After dissolving propranolol in methanol, aliquots of the initial solution were collected to produce the proper dilutions. A drop of DMSO is added to methanol to make propranolol more readily soluble. The wavelength ranges used for drug estimate were obtained from the 200–400 nm scan of the drug solution.[6]

Preparation of standard stock solutions (1000µg/ml): -

To produce working standard solutions via a concentration of 100µg/ml, 1 ml of propranolol hydrochloride hydrochloride was placed separately from the preparation stock solutions to a 10 ml volumetric flask.[6]

Method Validation

Linearity: -

It's Based on Beer-Lambert Law: The relationship between absorbance (A), concentration (c), path length (l), and molar absorptivity (ε) is described by the equation:

$A=\varepsilon clA = \varepsilon clA=\varepsilon cl$

The linearity of the method was checked in the concentration range of 16-24µg / ml for propranolol. The calibration curves were constructed by plotting the graph of absorbance vs concentration. A linear regression equation was obtained over theconcentration range ($y = mx+c$)

[18] [6]

Precision: -

By repeatedly screening and quantifying the absorbance of propranolol without altering the parameters of the suggested procedures six times (n=6), the method's precision was determined.The reactions were analyzed three times on the same day and three other days over a span of one week for three standard solutions of Propanolol (20, 22, and 24 µg/ml) in order to ascertain the intraday and interday accuracy of the suggested procedures. Both the standard deviation and the percentage of relative standard deviation (% RSD) are used to report outcomes.[18][6]

Formula:-

Relative Standard Deviation Formula = Standard Deviation /Mean x 100

Accuracy: -

Calculating the recovery of propranolol using the conventional addition approach allowed for the determination of the method's reliability. To pre-quantified specimens of propranolol, the known number of standard solutions was added at the 80, 100, and 120% level. The collected numbers were applied to the calibration curve's regression equation to determine the quantity of propranolol.[18][6]

Limit of detection and Limit of quantification: -

The limit of detection and the limit of quantification of the drug was derived by calculating the signal-to-noise ratio (S/N, i.e.,3.3 for LOD and 10 for LOQ) using thefollowing equations designated by International Conference on Harmonization (ICH) guidelines. [18][6]

Formula:- $LOD = 3.3 \times \sigma/S$

$LOQ = 10 \times \sigma/S$

Where, σ = the standard deviation of the response S= slope of the calibration curve

Ruggedness: -

To evaluate the ruggedness, a sample solution was injected six times. Two different analysts conducted two rounds of analysis on the system in question. The percentage RSD value was less than 2, and the test findings were verified to be within reasonable limits.[18][6]

Formula: - Relative Standard Deviation Formula = Standard Deviation /Mean x 10

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Expected Outcome: -

Method will be validated for linearity, accuracy, precision, LOD and LOQ as per ICH.

Thus, we can say purposed method is precise accurate and economical will be applied to marketed preparation

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