International Journal of Scientific Research and Engineering Development-– Volume 8 Issue 5, Sep-Oct 2025

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REVIEW RTICLE OPEN ACCESS

A Review on Analytical Method Development and Validation of Nadolol and Bendroflumethiazide by UPLC

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Abstract:

Nadolol is a beta-blocker that affects the heart and circulation, helping to lower blood pressure by reducing heart rate and workload. Bendroflumethiazide is a thiazide diuretic that helps prevent the body from absorbing too much salt, which can cause fluid retention. The combination of these two medications works synergistically to lower blood pressure and reduce the risk of heart-related complications. Nadolol and Bendroflumethiazide combination is used to treat high blood pressure (hypertension). High blood pressure adds to the workload of the heart and arteries. If it continues for a long time, the heart and arteries may not function properly. This can damage the blood vessels of the brain, heart, and kidneys, resulting in a stroke, heart failure, or kidney failure. High blood pressure may also increase the risk of heart attacks. These problems may be less likely to occur if blood pressure is controlled.

Keywords — Bendroflumethiazide**,** Nadolol, UV-Spectrophotometer, RP-HPLC, LC-MS**.**

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I. INTRODUCTION

Nadolol is a beta-blocker. Beta-blockers affect the heart and circulation (blood flow through arteries and veins). Bendroflumethiazide and nadolol is a combination medicine used to treat high blood pressure (hypertension). Bendroflumethiazide and nadolol may also be used for purposes not listed in this medication guide. Bendroflumethiazide and nadolol may cause serious side effects. Call your doctor at once if you have: fast, slow, or uneven heartbeat; numbness or cold feeling in your hands and feet; a light-headed feeling, like you might pass out; little or no urination. Nadolol is popular synthetic beta blocker drug for controlling hypertension and reduce the chest pain especially for second line prolonged users. It can significantly control the blood pressure with very minute effect on cardiac[1]. The improved performance of Nadolol

was achieved by adding small portion of diuretic. Few other authors are also studied Safety and their effects of the Beta-Blocker, Nadolol, in Mild Asthma condition[15].

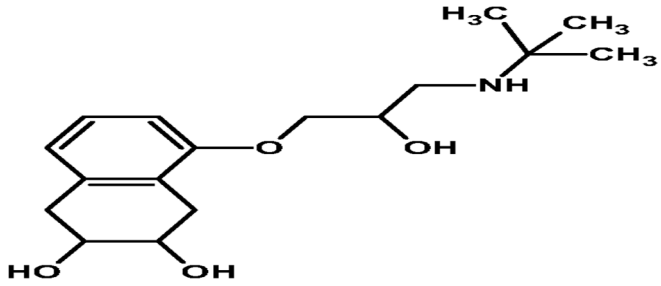

Fig.No.1: Structure of Nadolol

Bendroflumethiazide is a sulphonamide containing category of thiazide have several synonyms one of which is 3-benzyl-3,4-dihydro-6-(trifluoromethyl)-2H-1,2,4-benzothiadiazine-7-sulfonamide1,1-dioxide. It is a diuretic agent and antihypertensive drug with lower risk of cardiovascular effects[2].

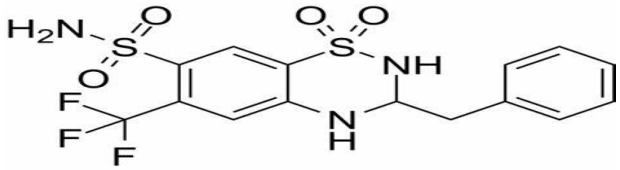

Fig.No.2: Structure of Bendroflumethiazide

UPLC INSTRUMENTATION

High-Performance Liquid Chromatography (HPLC) has proved to at least one of the foremost and predominant technology used in the analytical laboratory for the analysis of medicine word wide throughout the past 30-plus years UPLC can be regarded as a new invention for liquid chromatography[3].

UPLC refers to Ultra Performance Liquid Chromatography. It is a method of separating a mixture of components into individual components through a porous medium under the influence of the solvent. UPLC is a derivative of HPLC whose underlying principle is that as column packing particle size decreases, efficiency and thus resolution increases. If we decrease particle size less than 2µm, the efficiency shows a significant gain and it does not diminish at increased linear velocities or flow rate according to the common Van- Demeter equation.

UPLC brings Dramatic enhancement in sensitivity, resolution, and speed of analysis that can be calculated. Its instrumentation that operates at high pressure than that used in HPLC and this system uses fine particles (less than 2.5µm) and mobile phases at high linear velocities decreases the length of the column, reduces solvent consumption, and saves time. • To maintain retention and capacity similar to HPLC, UPLC must use porous particles that can withstand high pressure; though being highly efficient, this sub-2 µm (non-porous) particles suffer from poor loading capacity and retention due to low surface area This technology takes full advantage of chromatographic principles to run separations using columns packed with smaller particles and higher flow rates for increased speed, with superior resolution and sensitivity.

The basic principle of UPLC and HPLC is the same and depends upon mode of separation, i.e. adsorption, partition, exclusion, and ion-exchange depending on the type of chromatographic sorbent[4].

The UPLC is predicated on the principle of the use of a stationary phase consisting of particles less than 2µm (while HPLC columns are typically filled with particles of 3-5 µm). The underlying principle of UPLC is predicated on the Van Demeter relationship that explains the correlation between flow rate and plate height.

The Van Demeter equation shows that the flow range with the smaller particles is much greater in comparison with larger particles for permanent results. H = Height Equivalent to Theoretical Plate (HETP)[14].

$$H=A+B/V+CV$$

Were,

H = Height Equivalent to Theoretical Plate (HETP).

A = Eddy's Diffusion.

B = Diffusion coefficient.

C = Resistance to mass transfer coefficient.

V = Linear velocity

INSTRUMENTATION

The basic Instrumentation of UPLC

1. Sample Injection
2. UPLC Columns
3. Detectors

Sample Injection:

In UPLC, a sample introduction is essential. Conventional injection valves, either automated or manual, are not designed and hardened to work at extreme pressure[5]. To protect the column from extreme pressure fluctuation, the injection method should be comparatively pulsed free and the swept volume of the device also must be minimal to reduce potential band spreading. A fast injection cycle time is needed to fully capitalize on the speed afforded by UPLC, which in turn requires a high sample capacity. Low volume injections with minimal carryover are also required to increase sensitivity. There are also direct injection approaches for biological samples.

UPLC Columns:

The UPLC columns are made up of small particles having a size of less than 2µm. The particles are bonded in the matrix as the bonded stationary phase is needed for providing each retention and selectivity. Four bonded stationary phase columns manufactured by ACQUITY are available in the market, which can be used by the UPLC technique[6].

BEH C18 and C8 columns – These are a straight alkyl chain, most preferred UPLC columns as they can be used over a wide pH range. The tri functional ligands produce low pH stability, which is combined with high pH stability of 1.7µm BEH particles to produce the widest usable pH operating range.

BEH Shield R18 Columns: They supply selectivity to UPLC as it complements C18and C8 columns.

BEH Phenyl Columns: They have tri-functional C6 alkyl ethyl between the phenyl- ring and the silyl functionality.

BEH Amide Columns: The combination of the tri-functionally bonded amide phase with BEH small particles provides an exceptional column lifetime. They facilitate the use of a wide range of phase pH i.e., from pH scale 2 to 11.

Detectors:

The system is often organized with a TUV, ELS, PDA, and FLR detectors or a mixture of them.

TUV (Tuneable Ultra-Violet) detector: It is a 2 channel, absorbance detector. The detector is controlled by Empower or Mass Lynx software for each LC/MS and LC applications.

PDA (Photo Diode Array) detector: It is an optical detector that absorbs UV-Visible light that operates between 190-500nm[7].

ELS (Evaporative Light Scattering) detector: The detector is controlled by Empower or Mass Lynx software, which incorporates a flow type nebulizer that's optimized for UPLC system performance.

FLR (Fluorescence) detector: It is a multi-channel, multi-wavelength detector, which has an excitation wavelength that ranges from 200 to 890 nm, an emission wavelength that ranges from 210- 900 nm, offers 3D scanning capability for easier method development[13].

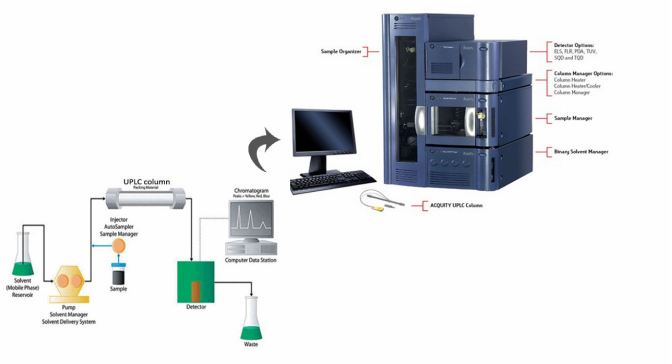

Fig.No.3: UPLC Instrumentation

LITERATURE REVIEW

1. V. Veeramanikandan R. Arun: Development of analytical method and validation of nadolol in pure and pharmaceutical formulations using UV-Spectrophotometry and Spectrofluorimetry. The objective of this research is to describe the wavelength is used for estimation of nadolol is 267 nm by spectrophotometry and 300nm by spectrofluorimetric The % of the drugs recovered 100.37 ± 094% and 99.9 ±0.59% for spectrophotometric and spectrofluorimetric methods. LOD and LOQ of nadolol were found to be 3.531µg/ml and 10.70 µg/ml by Spectrophotometer and 0.45µg/ml and 1.37 µg/ml by spectrofluorimetric[8].
2. Naveen V M K, Veera swami B: was A Particular separation method development and validation of nadolol and

Bendroflumethiazide by using RP-HPLC as Present study describes The chromatographic condition involves isocratic mode using waters symmetry C18 column. The valid method has validated in the linear range of 8-160ng/ml nadolol and 1-20 ng/ml Bendroflumethiazide[9]

3. SVS Sumaltha, D Bharathi, Ramana Taminana: A Particular separation method development and validation of nadolol and Bendroflumethiazide by using RP-HPLC. The objective of this research is to describe the Nadolol and Bendroflumethiazide peaks have been observed at a retention time of 1.757 and 3.208 minutes[10]. The avg correlation coefficient of nadolol and Bendroflumethiazide is 0.999 which indicated good linearity.
4. MR. Mohammod Yakub Pasha, Dr. T. Manilal: Estimation of nadolol and Bendroflumethiazide in API and its dosage form by RP-HPLC. The objective of this research is to describe the Nadolol and Bendroflumethiazide peaks have been observed at a retention time of 1.600 and 3.200 minutes. The avg correlation coefficient of nadolol and Bendroflumethiazide is 0.990which indicated good linearity[11].
5. Bazela Shahwar, Heena Afreen, Asma Begum: Development of stability indicating RP-HPLC method and validation for the estimation of nadolol and Bendroflumethiazide in pure form and marketed pharmaceutical dosage form.. The objective of this research is to describe the LOD & LOQ were found to be 0.08µg/ml and 0.24µg/ml for Nadolol and 0.1 µg/ml,0.3µg/ml for Bendroflumethiazide flow rate 1.0ml/min[12].
6. Neha Deshpande, Parag Kamble, Shravani Kulkarni, Vandana Gawande: Optimized and Validated Stability Indicating RP-HPLC Method for Estimation of Nadolol. The objective of this research is to describe the mobile phase consisted of methanol, acetonitrile, and 0.01 M sodium dihydrogen phosphate buffer pH 7.0 (60:15:25 v/v). The retention time of nadolol was determined to be 4.6 minutes after the spectrophotometric detection was performed at 220 nm. Between 100 and 500 µg/mL, linearity was noted (R2 = 0.999). The recovery rate for drugs was between 98.0 and 99.8%. The substance was found to have LOD and LOQ values of 0.21 and 0.66 µg/mL, respectively[16].
7. Hemant K. Jain, Niraj K. Muley, Neha N. Deshpande: Estimation of Nadolol in Bulk and Tablets by Area under Curve and First Order Derivative Spectrophotometry. The objective of this research is to describe the

first approach used first-order derivative spectrophotometry at a wavelength of 281.6 nm, whereas the second method relied on measuring the area under the curve for the spectrum in the wavelength range of 267.6 to 274.6 nm.

8. V.M.K. Naveen, B. Veeraswami, G. Srinivasa Rao: Bio analytical validation for nadolol and Bendroflumethiazide material - ScienceDirect 2021. The objective of this research is to describe the Under this method I draw the pinnacle zone calibration graphs by using regression concentration range between 8 and 160 ng/ml for Nadolol and 1–20 ng/ml for Bendroflumethiazide materials were maintained. From these results the linear coefficient and correlation coefficient are close similarity was observed and it is 0.999[18].

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