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Review Article

A REVIEW ON ANALYTICAL TECHNIQUES FOR THE ESTIMATION OF TREPROSTINIL IN PHARMACEUTICAL DOSAGE FORM

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ABSTRACT:
Pharmaceutical drugs play a vital function in human existence by aiding in the treatment of various disorders. As a consequence, developing analytical methods has become the primary activity of analysis. People have been searching for safe and effective ways to cure viral infections since ancient times. Due to the emergence of new fungal infections, the discovery of medications for their treatment is becoming equally important in the contemporary context. These medications should be validated before they are released to the market. High-performance liquid chromatography (HPLC) in conjunction with ultraviolet (UV), photodiode array detectors (PDA), mass spectrophotometer (MS) detectors, and other technologies is one of the quickest, safest, and most precise methods for determining and separating pharmaceutical drugs, impurities, and biological samples. When compared to older liquid chromatography techniques, HPLC is more flexible and takes less time to quantify pharmaceuticals. Treprostinil is a prostacyclin vasodilator used to treat pulmonary arterial hypertension. The current research demonstrated that the HPLC technique, as well as the spectroscopic approach, has been the most commonly examined for analysis. The investigatory review may give thorough facts to researchers functioning in the Treprostinil analytical study.

Key Words: Treprostinil, HPLC, LC-MS, Pharmaceutical analysis.

INTRODUCTION

Pharmaceutical analysis is a branch of practical chemistry that involves a series of process for identification, determination, quantification and purification of a substance, separation of the components of a solution or mixture, or determination of structure of chemical compounds. The substance may be a single compound or a mixture of compounds and it may be in any of the dosage form. The substance used as pharmaceuticals are animals, plants, microorganisms, minerals and various synthetic products [1,2]. The main goal of the pharmaceutical industry is to provide drug products with sufficient quality, efficacy and safety. The development of a new drug product and its production consist of many pharmaceutical processes, including analytical testing. The analytical data generated support further decisions on how development should be pursued or provide information on whether a drug product should be released[3]. Analytical methods are among the most critical processes in drug product development and production. They play a key role in supporting other development and production processes throughout all stages of a drug product's life cycle. It is essential that an analytical method be precise, accurate and reliable, making it suitable for its intended purpose [4,5].

In most situations, the separation of analytes present in a sample is the main operating principle of an analytical procedure. Liquid chromatography methods, such as HPLC or UPLC, are most typically used, generally in reversed-phase mode with UV absorbance detection. The goals of analysis vary based on the quantity, significance, and relationship of analytes that must be identified. The most often used analytical procedures are those for assaying an active pharmaceutical ingredient (API) or determining its associated compounds and degradation products (6). An analytical technique for determining stressed condition-maintained products must be capable of detecting their rise during the product's shelf life, and the assay method must be capable of

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detecting any reduction in the drug substance's content during the product's shelf life. Such approaches are used to indicate stability [7-9].

Continuous subcutaneous infusion of treprostinil, a stable, long-acting prostacyclin analogue, is possible. One A major multicentre randomized controlled research has shown that subcutaneous Treprostinil improves exercise capacity, clinical state, functional class, pulmonary hemodynamic, and quality of life in individuals with pulmonary arterial hypertension, a rare illness with a poor prognosis.[10-11] Prostacyclin frequently causes adverse effects, such as headache, jaw pain, facial flush, abdominal cramps, and diarrhoea, which can be managed with dose adjustments based on symptoms. Pain at the infusion site may stop patients from receiving more treatment in 7% to 10% of cases. Individuals with pulmonary arterial hypertension who received intravenous epoprostenol and subcutaneous Treprostinil showed similar long-term survival rates.12

Treprostinil chemically Fig-1 known as 2-{[(1R,2R,3aS,9aS)-2-hydroxy-1-[(3S)-3-hydroxyoctyl]-1H,2H,3H,3aH,4H,9H,9aH-cyclopenta[b]naphthalen-5-yl] oxy} acetic acid, Treprostinil, a stable tricyclic counterpart of prostacyclin, inhibits platelet aggregation and encourages the dilatation of the pulmonary and systemic artery vascular beds.13 Treprostinil was licensed by the FDA in 2002 for the treatment of pulmonary arterial hypertension (PAH) and pulmonary hypertension linked to interstitial lung disease. It helps patients with these conditions by reducing their symptoms.[14]

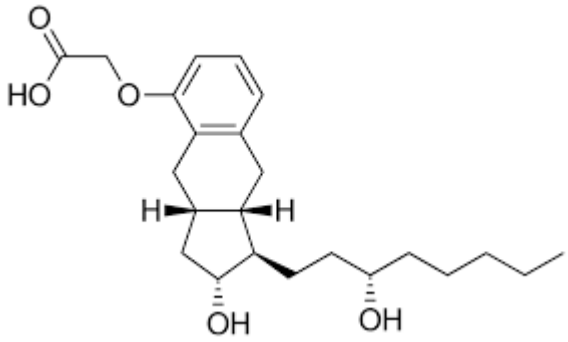

Figure 1: Structure of Treprostinil

Quantitative & Qualitative Analytical Techniques for Treprostinil

Quantitative & Qualitative analysis techniques help to determine precisely the concentration of each variable and type of medication present in the sample.

High performance liquid chromatography:

HPLC gives a constant quantitative accuracy and precision for the determination of active pharmaceutical compounds and associated substances employing a range of colonnade, solvents, and detectors in the same phase and may be accomplished on fully automated equipment using HPLC System. HPLC has good replicability and may be applied to a wide range of various chemical forms by carefully selecting the HPLC column chemistry. Chiral molecules are also possible to be isolated by HPLC into their respective enantiomers. HPLC is the most effective method for meeting the majority of the quantitative analytical needs for a variety of drugs. Today, HPLC, particularly reversed HPLC, is widely used. It is primarily a fluid chromatographic method for isolating and quantifying complicated mixtures of resolved elements.[15]

Kimavath Pushpa Bai etall., developed method Separation was accomplished on a Phenomenex Luna C18 column (250 X 4.6mm, 5µm) using the mobile phase, which consisted of Methanol: 0.1% Ortho phosphoric acid in a ratio of 20:80 V/V. Validation was done using the isocratic mode with straightforward mobile phase preparation. The mobile stage was pumped at a rate of 1.0 mL/min, and a UV detector set to 223 nm was used for detection. Treprostinil had a retention time of 3.06 minutes. Treprostinil has a linearity range of 10–60 µg/ml and a correlation coefficient of 0.9995. Treprostinil's LOD and LOQ were determined to be 0.691µg/ml and 2.093µg/ml, respectively. For regular analysis that demonstrates strong reproducibility, precision, and accuracy of Treprostinil in pharmaceutical dosage forms, this approach can be used, In the same line Narasimha Raju Alluri Implemented the QbD Approach to the Analytical Method Development and Validation for the Estimation of the Treprostinil Injection by rphplc quantitative estimation of treprostinil, assessing its stability under various forced degradation conditions. Using the optimized method, successful separation of treprostinil was achieved with an Agilent HPLC system with a photodiode array detector and an Express C18 column (5 µm particle size, L × I.D. = 15 cm × 4.6 mm), maintained at 31.4 °C. The mobile phase, a buffer (0.01N KH2PO4) and diluent in a ratio of 36.35:63.35 (v/v), was used at a flow rate of 1.04 mL/min. Detection was performed at 276.0 nm, with treprostinil eluting at 2.579 min within a run time of 6.0 min, Tummala Mani Ratnam etall.., developed a novel, precise, simple, accurate, and sensitive, stability indicating liquid chromatographic method for the estimation of the Treprostinil in bulk and pharmaceutical dosage form. The separation was achieved by using isocratic elution of the mobile phase containing a mixture of Methanol, Acetonitrile and water in the ratio

of 35:35:30% v/v with a flow rate 0.9 ml/min. Chromatographic separation was achieved on a Phenomenex C18 (250mm×4.6mm, 5µm) and chromatographic retention time was stable at 3.064 min, Various HPLC methods and its characteristics available in literature has shown in table 1.

Author	Drug	Stationary phase	Mobile phase	Application	Wave length
Kimavath Pushpa Bai et all..,	Treprostinil	Phenomenex Luna C18 column (250 X 4.6mm, 5µm)	Methanol: 0.1% Ortho phosphoric acid in the ratio of (20:80 V/V)	In API	223nm
Narasimha Raju Alluri	Treprostinil	Express C_{18} column (5 µm particle size, *L* × I.D. = 15 cm × 4.6 mm),	buffer (0.01N KH_2PO_4) and diluent in a ratio of 36.35:63.35 (v/v),	In dosage form	276nm
Tummala Maniratnam	Treprostinil	C18 Phenomenex Luna(250X4.6mm;5µ)	Methanol, Acetonitrile and water in the ratio of 35:35:30%	Bulk Assay	223nm

LC -MS Techniques

LC/MS is a popular approach for liquid chromatographs that is constantly changing. The recommended chromatographic tool is LC/MS. Liquid spectrometry chromatographic mass (LC-MS/MS) is a mass spectrometry fluid chromatography technology (HPLC). Analytical chemistry combines the capacity to physically isolate liquid chromatography (or HPLC) with mass spectrometry for mass analysis. LC-MS/MS is widely utilised in quality and quantity analysis in laboratory research for medicinal components, medical goods, and biological samples. It has been utilised repeatedly in drug development at several levels, including metabolic stability screening, metabolite detection, live drug screening, impurity discovery, peptide mapping, and glycoprotein mapping. LC-MS has been effectively used in a variety of applications, including therapeutic medicinal monitoring (TDM), clinical and forensic toxicology, and doping control. This advancement in LC-MS was initially and continues to be inspired by the demand for more powerful analytical and bio-analytical methods that are sensitive and selective in correctly and precisely distinguishing target analytes from high complexity mixtures. With the advancement of two-dimensional hyphenated (2D) apparatus, the use of liquid (LC) and mass spectrometric (MS) chromatography has become a powerful approach[19]. Table 2 shows LC-MS & UPLC-MS Characteristics methods available in literature.

Table 2: Performance attributes of LC-MS methods[20]

Author	Drug	Column	Mobile phase	Application
Gina M Gallucci et all..,	Treprostinil	LC-MS Phenomenex Kinetex C18 (2.6 µm particle size, 50 mm	gradient condition with aqueous formic acid and pure acetonitrile.	For Quantitative determination In mouse

CONCLUSION:

In this study, the current review covered several analytical approaches used to evaluate Treprostinil Numerous tests have been performed, including bio-analytical, HPLC, LC-MS for evaluation of Treprostinil in bulk from pharmaceutical formulations and also biological fluids. Treprostinil in bulk and in combination with other medications from pharmaceutical formulations and biological fluids was evaluated using LC-MS. A few chromatography techniques, such as Stability-indicating HPLC are also included. A summary of the methods is available in Table1 & 2.

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