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Analytical Method for Estimation of Fexofenadine in Formulation-A Review

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Abstract:
An effective second-generation anti-inflammatory specific histamine H1 receptor inhibitor Fexofenadine interacts with peripheral H1 histamine receptors in the GI tract, blood vessels, and bronchial smooth muscle in a highly selective and reversible method. By preventing calcium ion inflow across the mast cell/basophil plasma membrane or by preventing intracellular calcium ion release within the cells, this chemical prevents the release of mediator from mast cell. Additionally, leukotrienes, prostaglandins, or an anti-platelet activating factor effect may be produced by fexofenadine in order to block the late-phase allergic reaction. In general, this medication prevents endogenous histamine from acting, which temporarily relieves histamine-related symptoms and produces benefits including reduced vascular permeability, decreased pruritus, and localised smooth muscle relaxation. Analytical methods play an important role in describing the physicochemical properties of drugs. In this review, various analytical methods for estimating fexofenadine, including spectrophotometric and chromatographic, have been fully reviewed and discussed..

Keywords: fexofenadine, Analytical method, sample matrix, pharmacological activity.

INTRODUCTION

Fexofenadine, (±)-4-[1-Hydroxy-4-[4-(hydroxyl diphenylmethyl)-1-piperidinyl]butyl]-alpha, alpha dimethyl benzene acetic acid a terfenadine functional metabolite, is a selective histamine receptor agonist H1 receptor antagonists, such as loratadine and cetirizine, are clinically effective first-line treatments for chronic

idiopathic urticaria and seasonal allergic rhinitis. Angioedema, allergic rhinitis, and chronic urticaria are now all treated with this second-generation antihistamine.

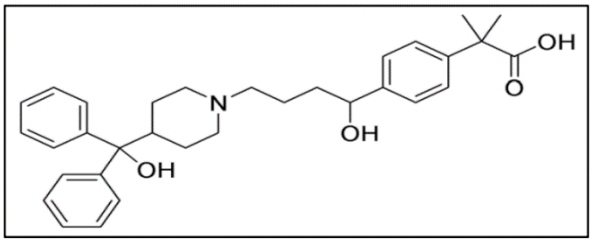

Figure 1.chemical structure of fexofenadine

Insufficient reason to compare fexofenadine to clinically obvious acute liver injury or to blood enzyme increases during medication. Fexofenadine is a piperidine-based anti-histamine compound . In addition to being an allergen, it functions as an H1-receptor antagonist. A tertiary amine that belongs to the family of piperidines. It has characteristics similar to isobutyric acid in terms of functionality [1].

Mechanism of Action:

Allergy and hypersensitivity responses are mediated by the H1 histamine receptor. Histamine and other inflammatory mediators are released by mast cells and basophils as a result of degranulating in response to allergen contact. Histamine interacts to and stimulates H1 receptors, causing basophils and mast cells to produce cytokines that are pro-inflammatory such interleukins. The subsequent implications of these histamine binds include many allergy symptoms such as pruritus, rhinorrhea, and watery eyes. Fexofenadine is considered to be a "inverse stimulator" of the H1 receptor since it interacts to and stabilises the inactive form of the receptor, which quits the receptor from stimulating and the downstream effects that proceed. It is highly specific and affine for H1 receptors, Neither does it appear to have sedative, antidopaminergic, antiserotonergic, anticholinergic, or antiadrenergic properties. Since fexofenadine cannot cross the barrier between the blood and the brain, it is unlikely to have a significant negative impact on the central nervous system [2].

Pharmacodynamics:

Fexofenadine limits the effects of histamine, an endogenous substance that is mainly responsible of causing allergic symptomatology, which reduces allergy symptoms. Fexofenadine can be taken once or twice daily because to its relatively lengthy half-life (approximately 24 hours), rapid absorption, and early onset of action (one to three hours). Fruit juice cannot be intoxicated with fexofenadine since it may affect how well it absorbs the medication [3].

Absorption:

Since it is administered orally, fexofenadine is readily absorbed and has a 33% absolute bioavailability. After oral administration, the T max lasts for about 1– 3 hours. . The stable state AU Css (0– 12 h) and Cmax the results of taking 60 mg twice daily are 1367 ng/mL.h and 299 ng/mL, respectively. Fexofenadine AUC is decreased by >20% fruit juices (such as apple, orange, and grapefruit) since they interfere with the OATP transporters; for this reason, According to the prescription advice, fexofenadine should only be used with water.

Similar to this, taking fexofenadine simultaneously with a substantial amount of fat seems to reduce AUC and Cmax by >20% [4].

Volume of Distribution:

The volume of distribution is approximately 5.4-5.8 L/kg. Fexofenadine has an intermediate oral clearance of 50.6 L/h and an approximate renal clearance of 4.32 L/h.

Biological Half-Life:

Half-life of terminal elimination corresponds to 11-15 hours.

Route of Elimination:

Due to fexofenadine's slow metabolism, about 80% of an ingested dose is removed in the faeces, and 11% is excreted in the urine, possibly substantially unaltered. The biliary and renal systems are the two main organs responsible for fexofenadine elimination.

Drug Indication:

An ingested dose is removed from the body by about 80%. Fexofenadine is prescribed in the United States assist with relieving patients' allergic rhinitis indications under the age of two and chronic idiopathic urticaria in patients under the age of six. Fexofenadine has the same indications in Canada, although it can only be used by patients who are under 12 years old. For the treatment of annual allergic reactions to substances in young patients under the age of twelve, fexofenadine and pseudoephedrine are also offered [5].

Drug Effects during Lactation:

Maternal usage of fexofenadine would not be anticipated to have any due to the absence of sedation and low milk levels, it has adverse impacts on breastfed newborns. Fexofenadine may interfere with lactation, especially when combined with a sympathomimetic drug like pseudoephedrine.

Drug Warnings:

Patients 12 years of age and older with allergic rhinitis who received oral fexofenadine hydrochloride doses of 60 mg twice a day or a placebo reported drowsiness or weariness in 1.3% of cases compared to 0.9% of those obtaining a placebo in randomized clinical studies. In these studies, patients receiving 180 mg of fexofenadine hydrochloride once a day (as conventional pills) or a placebo reported headache in 10.6 or 7.5% of cases, respectively. Season hay fever patients aged 6 to 11 who were given 30 mg of fexofenadine hydrochloride twice daily. or a placebo reported experiencing headaches in 7.6 or 6.6% of cases, respectively, with patients reporting discomfort in 2.4 or 0.4% of cases .

Analytical methods for estimation of fexofenadine:

❖ H. M. Nimje et.al [6] in 2011 has published an article " Stability Indicating RP HPLC Method for estimation of Fexofenadine Hydrochloride in Pharmaceutical formulation" . This article states that acetonitrile and methanol systems give better results than water and other solvent systems. The drug was more absorbed

in methanol and acetonitrile when mixed than in water, however it was insufficient to produce a nice peak with suitable retention duration. The mobile phase was added to with phosphate buffer in an effort of improving peak symmetry, which resulted in incredible chromatography overall, complete baseline resolution, and suitable peak symmetry. And it was chosen for stability and validation studies.

❖ P. Ravisankar, G. Devlala Rao et.al [7] has published an article " A review article on Analytical method development" his review highlights requirements to formulate a new analytical technique and the validation of the intended method to meet the regulatory requirement, and it states that Agility in approach techniques is necessary to generate multiple medication formulations with varied physical shape and strength.

❖ S. Chandran, R.S.P. Singh et.al [8] published a paper on " Comparison of various international guidelines for analytical method validation" . The essential elements of the cycle for creating and validating analytical methods are discussed. Furthermore, it makes an effort to contrast and summarizes the suggestions made by different departments for the approval of the analytical techniques used to examine drug substances both in their purest form and in pharmaceutical products.

❖ T. Radhakrishna, G. Om Reddy et.al [9] has developed and " validated a simple reversed phase liquid chromatographic (RPLC) method for the determination of fexofenadine hydrochloride and its related compounds A and B" . They utilized a C8 (Eclipse XDB) to prevent costly chiral columns and extended analysis durations, use a column as the stationary phase. For related substances A and B, the showedexamine was linear across a range of 0.7-18.7 g/ml, and for the assay of fexofenadine, it was linear over a range of 60-750 g/ml. For the prescribed drug and similar compounds, the RSD (n=3) was 0.5% and 3.4%, correspondingly. The assay's intermediate precision was 0.79% (n = 9) while the related impurities' intermediate precision was 5.16% (n = 9).

❖ Pedro Araujo et.al [10] has published an article about " Key aspects of analytical method validation and linearity evaluation", states that on fast change and many regulatory agencies' efforts to increase the performance-related performance coherence There are constant variations in the terms, estimations, and analysis of various indicators used often in method validation. Operators ought to utilize caution while using the above outlined essential elements of method validation and keep in mind that improper application can have extensive repercussions above the simple rejection of a submitted report or the waste of money, time, and resources. The use and acceptance of inaccurate language can have negative effects on the accuracy of the results, the efficiency of the lab, and the reputation of the institution

❖ Neera Chikanbanjar, Ureena Jyakhwa Gyani et.al [11] has published a review article on " Analytical method validation about the process of confirming the analytical testing strategy utilized for a particular test which is reasonable for its expected use is referred to the method validation" . Conclusions obtained from the technique validation procedure are used to make decisions about the analysis's consistent results. This assures a high-quality, consistent product. A welldeveloped technique is considered as the essential step in a dependable testing procedure.

❖ Hadir M Maher, Ileana V Olah1 et.al [12] has published research article " Development of validated stability-indicating chromatographic method for the determination of fexofenadine hydrochloride and its related impurities in pharmaceutical tablets" . The active medication fexofenadine and its four associated contaminants were separated using the Hypersil BDS C18 column in the current study. To increase the fexofenadine peak's sharpness and symmetry, To the mobile phase, 1-octane sulphonic acid was added. Separations did occur at lower methanol concentrations, but they had severe tailing and longer retention durations. Peak intersecting and loss of sharpness were caused by an increase in the overall amount of methanol. Then, at a flow rate of 1.5 ml/min, the mobile phase is added, which is made up of buffer (0.05 M sodium phosphate buffer containing 0.1 gm% 1-octane sulphonic acid and 1% (v/v) triethylamine adjusted to pH 2.7) and methanol in a ratio of 60:40 (v/v). At 10.716 min, fexofenadine was isolated. Impurity B meta isomer of fexofenadine took 11.987 minutes, impurity A keto fexofenadine took 14.013 minutes, and impurity C methyl ester of fexofenadine took 16.530 minutes. (Impurity D methyl ester and keto fexofenadine) 21.230 min. According to ICH criteria, the new approach was thoroughly verified.

❖ Tadakazu Tokumura, Takuro Kurita et.al [13] has published research article " Validated Assay Method for Fexofenadine Hydrochloride in Powder Preparations of Allegra 60 mg Tablets to Develop a New Method for Grinding Tablets on Dispensing in Japan" The medication fexofenadine was dissolved using acetonitrile-water-perchloric acid (60%)-sodium perchlorate monohydrate (V/V/V/W) as the mobile phase. The typical retention time for fexofenadine could be 6.6 minutes. Here, a method is devised for fexofenadine measurement in powder formulations generated from Allegra 60 mg pills. The findings demonstrated the accuracy and sufficient lower limit of quantification of this method for determining the concentration of fexofenadine in powder formulations.

The use of this method will significantly improve Japan's "grinding tablets on dispensing" practice in preventing medication loss.

❖ M. Saeed Arayne , Shehnaz Amir Haider et.al [14] has published research article " RP-HPLC method for the quantitative determination of fexofenadine hydrochloride in coated tablets and human serum" . Very few procedures in quality control are provided for the presence of fexofenadine in pharmaceutical formulations, urine, serum, and dosage forms. HPLC is the technology that is most frequently used in pharmaceuticals, clinical labs, and R&D institutions. This study's goal was to create a procedure that would be quicker, more focused, linear, accurate, and sensitive (analysis time: 3.78– 4.15 min). It is a preferable option for fexofenadine in human serum estimation due to its low limit of quantification (LOQ) and limit of detection (LOD) values. As an outcome, the suggested RP-HPLC technique is precise, linear, durable, reliable, simple to use, and rapid to identify fexofenadine in dosage forms. Because of this, the RP-HPLC technique is suitable for quality control and routine testing of raw materials, different dosage forms, different formulations, and human serum.

❖ Sherejad Sanam, S.M. Abdur Rahman et.al [15] has published " A Validated RP-HPLC Method and Force Degradation Studies of Fexofenadine Hydrochloride in Pharmaceutical Dosage Form" . Several RP-HPLC techniques were developed, employing gradient techniques with extended run times. It was shown that using more than 40% of acetonitrile produced high-resolution separation of the drug products. Methanol developed a perfect peak and resolution when utilised in excess of 50%. However, in this situation, the organic phase methanol can take the lead in retention time after 15 minutes. Thus, acetonitrile at its optimal concentration of 50% was employed to identify the medication. Methanol and water were initially combined in various ratios. It causes degradation agents to begin to elute in the dead volume. As a result, the resolution improved and the concentration of methanol was reduced. When choosing a buffer, pH was a key consideration for items to dissolve. Also, a pH value of 9.8 must be maintained because a higher pH can harm the column.

❖ K. Raghubabu , K. Sanadhyarani et.al [16] " Assay of fexofenadine hydrochloride in pharmaceutical preparation by visible Spectrophotometry ". A drug combines with an aromatic aldehyde, such vanillin, in the presence of sulfuric acid in a non-aqueous media to produce a colourful condensation product with a maximum absorbance of 590 nm. Beer's law was followed at concentrations between 50 and 300 g/mL. Due to their efficiency, affordability, and environmental safety, the suggested methods for fexofenadine determination have numerous advantages over other analytical techniques. In comparison to HPLC and HPTLC techniques, the device is simple and affordable. All analytical reagents are reasonably priced and available in any analytical laboratory. For the routine assay of fexofenadine formulations, this method can be expanded.

❖ Ute Hofmann, Martin F. Fromm et.al [17] has published " Determination of fexofenadine in human plasma and urine by liquid chromatography– mass spectrometry" The use of HPLC-electrospray mass spectrometry with MDL 026042 as an internal reference has enabled the development of a systematic method for the detection of fexofenadine in human plasma and urine. For the purpose to remove C solid-phase, filtration were used. For HPLC, the mobile phases were (A) acetonitrile and (B) 12 mM ammonium acetate in water. Using a linear gradient from 40% B to 60% B in 10 minutes, chromatographic separation was accomplished on a LUNA CN column (10 cm32.0 mm I.D., particle size 3 mm). The mass spectrometer was operated in the selected ion monitoring mode with the relevant MH ions— m/z 502.3 for fexofenadine and m/z 530.3 for the internal standard. The maximal quantification limits for this approach were 0.5 ng/ml in plasma and 1.0 ng in 50 ml of urine. Pharmacokinetic studies successfully used the provided technique to determine the presence of fexofenadine in human plasma and urine.

❖ Leonardo Santos Ribeiro Pintoa, Fernanda de Lima Moreiraa et.al [18] has published " Direct chiral LC-MS/MS analysis of fexofenadine enantiomers in plasma and urine with application in a maternal-fetal pharmacokinetic study" . The mechanism of action of fexofenadine enantiomers in the plasma and urine of pregnant women are presented in this study for the first time using LC-MS/MS methods. The chiral CD-Ph column was successfully utilised for evaporating the fexofenadine enantiomers using only 100% methanol as the mobile phase, although the process was not reproducible. Then, using the chiral CD-Ph column in polar

organic elimination mode, different conditions were tested. Although they were tested, organic modifiers (ethanol and acetonitrile), flow rates (0.3– 1 mL/min), column temperatures (10– 27 ° C), and acid or basic additives (glacial acetic acid or diethylamine) did not successfully dissolve the fexofenadine enantiomers. Different ratios of methanol and ammonium acetate buffer were tested (3.8-4.5) at different doses (5-20 mM) and pH levels. When utilised with a mobile phase that included methanol and ammonium acetate (7 mM, pH 4.25, 97:3, v/v), the chiral Chirobiotic V column (250 4.6 mm, 5 m particles) yielded the best results, with peak adsorption of fexofenadine enantiomers occurring at about 24 min and Internal Standard at around 20 min. The methods indicated linearity for each fexofenadine enantiomer at values of 0.025-100 ng/mL plasma and 0.02-10 g/mL urine. The pharmacokinetics of fexofenadine enantiomers in the plasma and urine of parturient women (n = 8) that administered a single oral dosage of racemic fexofenadine at a dose of 60 mg were investigated using these methods.

❖ Suparna S. Tandulwadkar, Ajinkya R. Nikam, et.al [19] has published research article " Method Development and Validation for the Simultaneous Determination of Fexofenadine Hydrochloride in Drug Formulation Using Normal Phase High-Performance Thin-Layer Chromatography" . The HPTLC method is less expensive, faster, and requires less time. The ratio of the mobile phase was optimised to contain toluene, ethyl acetate, methanol, and ammonia (30%) (2.5: 7: 2.5: 1, v/v/v/v), while the amount of fexofenadine was 0.40. A radiant peak form with partial separation was produced. As a consequence, the mobile phase was changed to the previously discussed mixture of ethyl acetate, methanol, and ammonia (30%) (7:1.5:0.5 v/v/v). Fexofenadine Rf of 0.20 indicated considerable separation, however the peak had broad tailing. The mobile phase was composed of toluene, ethyl acetate, methanol, and ammonia (30%) in a ratio of 0.5:7:2:0.5 v/v/v/v. The drugs were separated using HPTLC in the absorbance mode at 220 nm, and then tested using densitometry. Rf values of 0.210.01 indicated that the drugs were satisfactorily resolved. For fexofenadine, the limits of quantitation were 100 ng spot-1 and 50 ng spot-1, respectively.

CONCLUSION:

In the review, fexofenadine is identified in various matrices using a variety of analytical techniques, including spectrophotometric and chromatographic approaches. There are numerous methods for detecting fexofenadine, but the most commonly used ones include chromatographic and spectroscopic methods. The significant disadvantage of the spectrophotometric approach is that it does not reveal the relative composition. Because of its speedy analysis, the majority of analytes believed that the HPLC method was the best option for fexofenadine determination. The choice of analytical techniques for fexofenadine, however, is determined by the nature of the sample matrix and the goal of the analysis.

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