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Review on Analytical Method Validation for Trithioparamethoxy Phenylpropene & Chlorpheniramine Maleate in Pharmaceutical Dosage Form

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Abstract:- Analytical method validation is a crucial step in ensuring the reliability and accuracy of analytical procedures employed for the determination of active pharmaceutical ingredients (APIs) in pharmaceutical dosage forms. This study focuses on the validation of analytical methods for the quantification of trithioparamethoxy phenylpropene and chlorpheniramine maleate in pharmaceutical dosage forms. The methods were developed using high-performance liquid chromatography (HPLC) or using ultra performance liquid chromatography (UPLC) with appropriate detection techniques. Parameters such as specificity, linearity, precision, accuracy, robustness, ruggedness, range, stability, LOD, LOQ and system suitability were evaluated according to International Conference on Harmonization (ICH) guidelines. The validated methods demonstrated excellent specificity, linearity over a wide concentration range, precise and accurate results, robustness against variations in method parameters, and suitable system suitability. The validated methods are suitable for routine quality control analysis of pharmaceutical formulations containing trithioparamethoxy phenylpropene and chlorpheniramine maleate, ensuring the reliability and consistency of drug products.

Keywords:- *Analytical Method Validation; Chlorpheniramine Maleate; Antiallergic Agent; Trithioparamethoxy Phenylpropene; Hepatoprotective Agent.*

I. INTRODUCTION

As a member of the antihistamine drug class, chlorpheniramine maleate is an antiallergic substance. When the body comes into contact with allergens such as pollen, dust, pet dander, etc., the body produces histamines. Skin rashes, itching, sneezing, blocked noses, runny noses, and watery eyes are the results of this. To reduce these symptoms, chlorpheniramine maleate inhibits the action of histamine. With the molecular formula $C_{16}H_{19}ClN_2$, chlorpheniramine maleate (CPM) is chemically 2-[pChloro-α-[2-(dimethylamino) ethyl]benzyl] pyridine maleate. It is a white, crystalline, odorless powder with a bitter taste that dissolves easily in water, alcohol, and chloroform, and dissolves somewhat in ether and benzene. It is an effective first-generation H-1 receptor antagonist and a member of the alkyl amines class.[2,15]

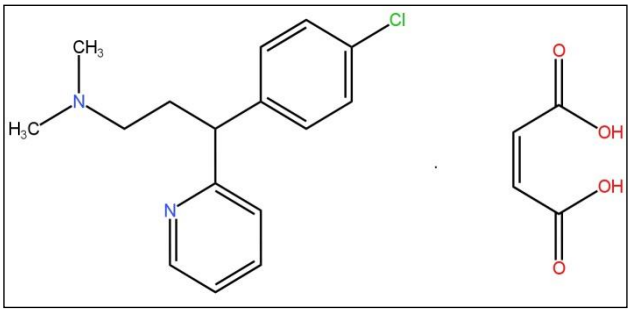

Fig. 1. Chlorpheneramine maleate

Among the medications classified as hepatoprotective agents is trithioparamethoxy phenylpropene. Alcohol, fatty acids, and other hepatotoxic substances are prevented from harming the liver by trithioparamethoxy phenylpropene.[3] Blood cholesterol is lowered by trithioparamethoxy phenylpropene, which results in smoother blood flow. For the purpose of easing constipation and dry mouth brought on by tranquilizer use, trithioparamethoxy phenylpropene is also prescribed.[6,7]

Franco Indian Remedies, based in Mumbai, India, manufactures and distributes Hepasulfol AA tablets, a fixed dose combination medication. This tablet contains trithioparamethoxy phenylpropene (12.5 mg) along with 3 mg of chlorpheniramine maleate.[4,5] To quantify chlorpheniramine maleate alone in pharmaceutical samples, a few analytical techniques are suggested, such as UV spectrophotometry, chemometry, fluorescence spectrophotometry, and HPLC. Any approach that isn't suggested to measure trithioparamethoxy phenylpropene on its own.[18,9]

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II. LITERATURE REVIEW

Sr. No.	Author name	Journal name	Title name	Summary
1.	Rajendra Patil,et.al.,2014[8]	Research &Reviews: Journal of Pharmaceutical Analysis	Review on Analytical Method Development and validation	To provide reliable information for regulatory submissions, analytical method development needs to be validated. These techniques are necessary to test for quality control release, stability sample testing, reference material testing, and to provide data to support specifications, among other uses. a crucial step in the drug discovery process that involves an analytical approach and the establishment of evidence that offers a high level of assurance. This is to guarantee the medication's quality and safety. This review provides insights into different approaches to evaluating a drug's stability and different validation metrics according to different regulatory bodies.
2.	P. Ravisankar, et.al., 2014[10]	Indian Journal of Research in Pharmacy and Biotechnology	A review on analytical method development	Official test procedures are the ultimate product of analytical method development. Drug products' identity, purity, safety, efficacy, and performance are guaranteed by means of these techniques in quality control labs. An increased focus on analytical methods in manufacturing is being made by regulatory bodies. Applicant must demonstrate control over the entire drug development process using validated analytical methods in order for regulatory bodies to approve the drug.
3.	Chauhan A, et.al., 2015[11]	Journal of Analytical & Bioanalytical Techniques	Analytical Method Development and Validation: A Concise Review	Development and validation of analytical methods are ongoing, interdependent tasks related to the departments of research and development, quality control, and quality assurance. In risk assessment and management, analytical techniques are essential for equivalency. It supports the stability of outcomes and the development of acceptance criteria unique to a product. Validation should show that the analytical method is appropriate for the intended use. An effective tool for characterizing and validating a method is experiment design.
4.	Santosh Kumar Bhardwaj, et.al., 2015[12]	International Journal of Analytical and Bioanalytical Chemistry	A review: HPLC method development and validation	The development and validation of HPLC methods are crucial for novel drug discovery, drug manufacturing, and other human and animal study applications. To test a specified property of the drug substance or drug product against predetermined acceptance criteria, an analytical procedure is developed. This review provides details on the different phases of the HPLC method's development and validation. The ICH Guidelines for HPLC method validation address every aspect of performance characteristics related to validation, including robustness, system suitability testing, range and limit of detection, linearity, specificity, accuracy, precision, and limit of quantification.

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5.	Maria Ashfaq, et.al., 2018[13]	Pakistan Journal of Pharmaceutical Sciences	Spectrophotometric method development and validation for determination of chlorpheniramine maleate in bulk and controlled release tablets	Acetate buffer (pH 4.5), phosphate buffer (pH 6.8), distil water (pH 7.0), and 0.1N HCl (pH 1.2) were among the solvent systems used to measure drug absorption. With a λmax of 261 nm and an R2 value of 0.9998, high drug absorption was seen in the 0.1N HCl medium. More than 99% of the drugs were recovered at three different levels of assessment, which was used to evaluate the accuracy of the method. The developed technique demonstrated high accuracy and precision as evidenced by the computed % RSD value <1 for both intraday and interday analysis. Because it exhibits no discernible variation even with small changes, the developed method is robust. The determined LOD and LOQ values were 2.2µg/mL and 6.6µg/mL, respectively. Because the examined method demonstrated its sensitivity, accuracy, and precision, it couldbe effectively applied to calculate the CPM content of pharmaceutical and bulk matrix tablets.
6.	Shivani Sharma, et.al., 2018[14]	International Journal of Applied Pharmaceutics	A Review On Analytical Method Development And Validation	This review article's primary goal was to examine the evolution and validation of the process used for the drug, from the formulation stage to the completion of the commercial batch. The pharmaceutical sector follows good manufacturing practice (GMP) rules, and validation policies are defined to explain how to execute validation and what kinds of validation are required. Validation is crucial to the efficient operation of pharmaceutical companies. Validation was done everywhere, from the raw material to the final, stable state. Validation characteristics are presented in terms of accuracy, specificity, precision, ruggedness, robustness, limit of detection (LOD), limit of quantitation (LOQ), and system appropriateness testing with the example of particular drugs.The routine and stability analysis make use of all validation parameters.
7.	Prasanthi Chengalva, et.al., 2019[15]	International Journal of Applied Pharmaceutics	Stability Indicating Ultra Performance Liquid Chromatographic Method for Simultaneous Determination of Phenylephrine Hydrochloride, Chlorpheniramine Maleate, Paracetamol, Guaiphenesin and Bromhexine Hydrochloride in Bulk and Pharmaceutical Formulation	Using a Hibar C18 (100 mm x 2.1 mm, 1.6 µm) column with a detection wavelength of 220 nm, the medicines were separated in the chromatographic column. With acetonitrile added at a 70:30% v/v ratio and pumped at a flow rate of 0.3 ml/min, the mobile phase consisted of sodium phosphate monobasic monohydrate buffer (pH was adjusted to 3.5 using orthophosphoric acid). Researchers used acid, base, peroxide, light, and heat to forcefully degrade pharmaceuticals. n three minutes, the five medications were all eluted. The duration of retention for phenylephrine, paracetamol, guaiphenesin, bromhexine, 1.199 min, 1.600 min, 1.979 min, and 2.525 min were determined, in that order. For each medicine, the correlation coefficient (r2) was found to be 0.999. It was shown that the recovery percentages ranged from 98.06% to 100.28%. Drugs were found to have RSD values of less than 2%. The developed method's sensitivity was determined by analyzing the results of quantitation and detection limit. In accordance with the International Conference on Harmonization's (ICH) requirements, all of the

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				validation parameters were discovered to be within acceptable bounds.
8.	T. Sravanthi, et.al., 2020[16]	Asian Journal of Chemistry	Validated Stability Indicating HPLC Method for Simultaneous Quantification of Trithioparamethoxy Phenylpropene and Chlorpheniramine Maleate in Tablet Forms	The concurrent evaluation of trithioparamethoxy phenylpropene in combination with chlorpheniramine maleate has led to the development of a unique easy stability indicating high performance liquid chromatography method employing a Luna C8 column with UV detection at 224 nm. A flow rate of 1.5 mL/min was utilized to supply the mobile phase, which consisted of 0.02 N phosphate buffer (pH 5.5) and acetonitrile (55:45 v/v). For trithioparamethoxy phenylpropene (6.25–18.75 µg/mL) and chlorpheniramine maleate (1.5–4.5 µg/mL), the procedure was linear. 1.57 µg/mL for trithioparamethoxy phenylpropene and 0.969 µg/mL for chlorpheniramine maleate were the limits of quantification. Trithioparamethoxy phenylpropene (100.083-100.287%) and chlorpheniramine maleate (99.827-100.277%) were the computed recoveries. Chlorpheniramine maleate and trithioparamethoxy phenylpropene were subjected to thermal, oxidative, and acid hydrolysis as forms of imposed stress. Drug degradation was seen at the applied circumstances.
9.	P.Sreenivasa Prasanna, et.al., 2021[17]	International Journal of Health Care and Biological Sciences	Development and Validation of New Analytical Method for the Simultaneous Estimation of Levodropropizine and Chlorpheniramine in Pharmaceutical Dosage Form	Levodropropizine and chlorpheniramine dose forms were simultaneously estimated using a straightforward, accurate, and precise procedure. Through Ascentis C18 150 x 4.6 mm, 5m, the chromatogram was passed. The 40:60 ratio of acetonitrile in the mobile phase, which contained Buffer Kh2po4, was pushed across the column at a flow rate of 1.0 ml/min. Kh2po4 served as the buffer in this procedure. 30°C was the constant temperature. 260 nm was chosen as the ideal wavelength. The percentage RSD of levodropropizine and chlorpheniramine was determined to be 0.7 and 0.7, respectively. The retention times of levodropropizine and chlorpheniramine were found to be 2.276min and 2.848. (%)Levodropropizine recovery was found to be 100.73%, whereas Chlorpheniramine recovery was found to be 99.03%. The regression equations for levofloxacin and chlorpheniramine yielded LOD and LOQ values of 0.14, 0.02, and 0.43, 0.06, respectively. The suggested approach was straightforward and cost-effective, suitable for routine quality control testing in industries, as both retention times and run times were reduced.
10.	Mahmoud A. Mohamed, 2022[18]	Journal of AOAC International	Stability-Indicating New RP-UPLC Method for Simultaneous Determination of a Quaternary Mixture of Paracetamol, Pseudoephedrine, Chlorpheniramine, and Sodium Benzoate	An Acquity UPLC HSS T3 C18 column (2.1 mm x 100 mm), 1.8 mm particle size with pore size 100 A^, is used to carry out the specified procedure. The mobile phase is a combination of purified water, methanol, and trifluoroacetic acid (72.5:27.5:1.5, v/v) flowed at a rate of 0.3 mL/min. 1.15 minutes is the column void volume. UPLC detection is calibrated with a photodiode array detector at 205 nm. With a correlation coefficient > 0.9992, calibration curves are

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			in (Cold–Flu) Syrup Dosage Form	generated in the linearity ranges of 25–500 mg/mL for paracetamol, 10–50 mg/mL for pseudoephedrine, 0.5–5 mg/mL for chlorpheniramine, and 3–30 mg/mL for sodium benzoate. The tested mean recovery of the developed method demonstrates good recovery results in the range of 99–101%; investigations on forced degradation and selectivity are conducted in accordance with the International Council for Harmonisation Guidelines and no interference is detected due to degradation peaks
11.	Sonali U. Navale, et.al., 2024[19]	International Journal of Pharmaceutical Sciences	Comprehensive Review on Analytical Methods for Determination of Chlorpheniramine Maleate in Pharmaceutical Dosage Form and Bulk	The previously mentioned article provides a comprehensive analysis of several approaches for the examination of antihistamine medications. An analytical method's validation process was carried out. The U.S. Food and Drug Administration has authorized chlorpheniramine as a safe and efficient antihistamine for allergies. The review includes the most recent analytical techniques, such as chromatographic techniques (RP-HPLC, HPTLC, LC), and a variety of spectroscopy techniques. Numerous analytical parameters, including stationary phase, flow rate, wavelength, mobile phase, and ratio of mobile phase, are studied in different papers. A comparison between several methodologies and observations with varied base attributes is done using the data from the literature.
12.	Aleti Raja Reddy and Samatha Ch, 2022[20]	World Journal of Pharmacy and Pharmaceutical Sciences	A Review on method development and validation of Methotrexate by different analytical methods	The first line of treatment for many rheumatic and non-rheumatic illnesses is methotrexate (MTX). At the moment, rheumatoid arthritis (RA) is treated with it as an anchor disease, modifying anti-rheumatic medication. This review covers the pharmacokinetic, pharmacodynamic, and mechanism of action of methotrexate. It also covers pharmaceutical analytical techniques, such as Spectrophotometry, Reverse Phase HPLC, Bio-Analytical Techniques, and High Performance Liquid Chromatography, with the bulk and pharmaceutical dosage forms used for determination and validation.
13.	Addagiri Venkatesh, et.al., 2022[21]	World Journal of Pharmacy and Pharmaceutical Sciences	A Review on method development and validation of Atenolol by Spectrophotometric and HPLC techniques	This review aims to compile and clarify the widely dispersed information on published research on potentially inevitable and systematic analytical techniques that can quantify atenolol. β1 receptor antagonists like atenolol are selective. The medication, a beta blocker, is mostly used to treat cardiovascular disorders including hypertension. Since HPLC is a widely available testing method in pharmaceutical laboratories, it should be the backup method for absolute determination of atenolol, according to the reviewed literature. Many criteria influence the choice of analytical procedures, including cost, instrument accessibility, technical competence, speed, convenience, specificity, accuracy, precision, sensitivity, and selectivity.

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III. CONCLUSION

According to this reviewthe analytical method validation conducted for Trithioparamethoxy Phenylpropene and Chlorpheniramine Maleate in pharmaceutical dosage form demonstrates the reliability, accuracy, and robustness of the proposed analytical methods. Through a systematic validation process encompassing specificity, linearity, precision, accuracy, robustness, ruggedness, range, stability, LOD, LOQ and system suitability methods have been shown to meet the regulatory requirements and are suitable for routine analysis in pharmaceutical laboratories. The validated methods offer precise and accurate quantification of the active ingredients, ensuring the quality and safety of the pharmaceutical formulation. Further research could focus on exploring additional validation parameters or optimizing the methods for enhanced efficiency. Overall, the validated analytical methods provide a solid foundation for ensuring the quality and efficacy of Trithioparamethoxy Phenylpropene and Chlorpheniramine Maleate pharmaceutical products.

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REFERENCES

[1]. Satinder A., and Henrika R, HPLC Method Development for Pharmaceuticals. 1st ed. Published by Elsevier Academic Press, ed 1, 2007; 10.
[2]. Araujo P. Key aspects of analytical method validation and linearity evaluation. J Chromatogr B, 2009; 877:2224-34.
[3]. Mukesh Maithani, Richa Raturi, Vertika Gautam, Dharmendra Kumar, Amrendra Kumar Chaudhary, Anand Gaurav and Ranjit Singh, Development And Validation Of A Rp-Hplc Method For The Determination Of Chlorpheniramine Maleate And Phenylephrine In Pharmaceutical Dosage Form, Pharmacie Globale (IJCP) 2010, 5 (05).
[4]. Geetha G, Raju KN, Kumar BV, Raja MG, Analytical method validation: an updated review, Int J Pharm Biol Sci 2012;1:64-1.
[5]. Nayudu ST, Suresh PV, Bio-analytical method validation–a review, Int J Pharm Chem Res 2017; 3:283-93. Sci 2013; 3:8.
[6]. Lavanya G, Sunil M, Eswarudu MM, Eswaraiah MC, Harisudha K, Spandana BN, et al. Analytical method validation: an updated review, Int J Pharm Sci Res 2013;4:1280.
[7]. Pathuri R, Muthukumaran M, Krishnamoorthy B, Nishat A, A review on analytical method development and validation of the pharmaceutical technology, Current Pharm Res 2013 :855-70.
[8]. Patil R, Deshmukh T, Patil V, Khandelwal K. Review on analytical method development and validation, Res Rev J Pharm Anal 2014;3:1-10.
[9]. Larisa Alagić-Džambić, Midhat Vehabović, Edina Čekić, Mirsad Džambić, Development and Validation of a HPLC Method for Chlorphenamine Maleate Related Substances in Multicomponents Syrups and Tablets, International Journal of Pharmacy Teaching & Practices 2014, Vol.5, Issue 3, 997-1001.
[10]. P. Ravisankar, S. Gowthami, G. Devlala Rao, A review on analytical method development, Indian Journal of Research in Pharmacy and Biotechnology, 2(3), 2014,1189-1191.
[11]. Chauhan A, Mittu B, Chauhan P, Analytical method development and validation: a concise review, J Anal Bioanal Tech 2015;6:1.
[12]. Bhardwaj SK, Dwivedi K, Agarwal DD, A review: HPLC method development and validation, Int J Anal Bioanal Chem 2015;5:76-1.
[13]. Maria Ashfaq, Ali Akber Sial , Rabia Bushra, Atta-ur-Rehman, Mirza Tasawur Baig, Ambreen Huma and Maryam Ahmed, Spectrophotometric method development and validation for determination of chlorpheniramine maleate in bulk and controlled release tablets, Pak. J. Pharm. Sci., Vol.31, No.1, January 2018, pp.353-358.
[14]. Shivani Sharma, Swapnil Goyal, Kalindi Chauhan, A Review On Analytical Method Development And Validation, International Journal of Applied Pharmaceutics, Vol 10, Issue 6, 2018, 8-15.
[15]. Prasanthi Chengalva, Madhavi Kuchana, Stability Indicating Ultra Performance Liquid Chromatographic Method For Simultaneous Determination Of Phenylephrine Hydrochloride, Chlorpheniramine Maleate, Paracetamol, Guaiphenesin And Bromhexine Hydrochloride In Bulk And Pharmaceutical Formulation, International Journal Of Applied Pharmaceutics, Vol 11, Issue 5, 2019, 284-292.
[16]. T. Sravanthi and N. Madhavi, Validated Stability Indicating HPLC Method for Simultaneous Quantification of Trithioparamethoxy Phenylpropene and Chlorpheniramine Maleate in Tablet Forms, Asian Journal of Chemistry; Vol. 32, No. 6 (2020), 1291.
[17]. Vepa Vishnu Vardhan Reddy, P.Sreenivasa Prasanna, K.Thejomoorthy, Development and validation of new analytical method for the simultaneous estimation of levodropropizine and chlorpheniramine in pharmaceutical dosage form. Int Jou Hea Bio Sci, 2(2),2021,33-42.
[18]. Mahmoud A. Mohamed, Stability-Indicating New RP-UPLC Method for Simultaneous Determination of a Quaternary Mixture of Paracetamol, Pseudoephedrine, Chlorpheniramine, and Sodium Benzoate in (Cold–Flu) Syrup Dosage Form, Journal of AOAC INTERNATIONAL, 105(3), 2022, 703–716.

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[19]. Sonali U. Navale, Chetana A. Padekar, Sonali S. Ghuge, Monali S. Ghuge, Gayatri S. Gaikwad, Comprehensive Review On Analytical Methods For Determination Of Chlorpheniramine Maleate In Pharmaceutical Dosage Form And Bulk, Int. J. of Pharm. Sci., 2024, Vol 2, Issue 2, 224-232.
[20]. Aleti Raja Reddy and Samatha Ch, A Review on method development and validation of Methotrexate by different analytical methods, World Journal of Pharmacy and Pharmaceutical Sciences, Vol 11, Issue 4, 2022.
[21]. Addagiri Venkatesh, Aleti Raja Reddy and Dr. T. Ramarao, A Review on method development and validation of Atenolol by Spectrophotometric and HPLC techniques, World Journal of Pharmacy and Pharmaceutical Sciences, Volume 11, Issue 3, 593-607 06 Feb. 2022.