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Analytical Methods for Quantitative Estimation of Chlorpheniramine Maleate: A Review

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ABSTRACT

Background: Chlorpheniramine Maleate is a first-generation alkylamine antihistamine used in the prevention of the symptoms of allergic conditions such as rhinitis and urticarial. Chlorpheniramine maleate was FDA approved in the United States as a prescription-only product in 1948, and later in 2010, it got approval as an over-the-counter medication.

Design, synthesis of chlorpheniramine maleate has one asymmetric carbon atom, exists as racemic mixture of R and S forms and does not show optical rotation. It is a histamine H1 receptor antagonist used as an antihistamine.

Method: Various analytical techniques for the quantification of chlorpheniramine maleate for bulk, pharmaceutical formulations and biological samples have been reported. Assay methods include UV-spectroscopy, high performance liquid chromatography, high performance thin layer chromatography.

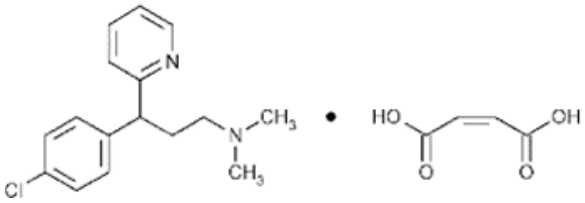
Result: Literature review reveals that methanol is the most commonly used solvent for the analysis of chlorpheniramine maleate by spectroscopic technique. For estimation of chlorpheniramine maleate by high performance liquid chromatography, methanol and acetonitrile are the commonly used organic solvents in the mobile phase and phosphate buffer or triuroacetic acid is used to maintain the pH of the mobile phase. Protein precipitation technique is used widely for extraction of the chlorpheniramine maleate from biological samples though liquid-liquid extraction and solid phase extraction has also been reported in fewer articles. The electro analytical techniques reported for the analysis of the drug have provided methods with lower analysis time.

Conclusion: Amongst all the developed analytical methods, HPLC has been reported extensively for the quantitation for chlorpheniramine maleate.

Keywords: Chlorpheniramine Maleate, analytical methods, HPLC.

1. INTRODUCTION:

Antihistamines are pharmaceutical agents which act by stimulating histamine action in the H1- receptors, thereby antagonizing most of the smooth muscles to alleviate or prevent the symptoms of hay fever and other allergies and put a stop to motion sickness, nausea, vomiting, and dizziness. In addition, since antihistamines may cause drowsiness as a side effect, some of them may be used as an opponent to insomnia. Some antihistamines are used in the handling of nervous and emotional conditions to help control anxiety and to relax patients before surgery.[1] The less sedating behavior of new antihistamines have led to higher doses, which may contribute to asthma therapy by increasing vascular permeability.[2–6] Chlorphenamine, a histamine H1 receptor antagonist has been proven to reverse chloroquine resistance in Plasmodium falciparum[7] and is recommended for runny noses and seasonal allergies. Although cetirizine and levocetirizine are both important second generation antihistamines, their study has revealed that the antihistaminergic activity of the racemate is primarily due to levocetirizine.[8] Chlorpheniramine maleate (CPM), (R/S)-3-(4-chlorophenyl)-N,N-dimethyl-3-(pyridin-2- yl)propan-1-amine maleate 2-chloropyridine (Fig. 1)[9] is a first-generation alkyl amine antihistamine, act by antagonizing H1-receptors. It is commonly used in pharmaceutical preparations for symptomatic relief of the common cold and allergic rhinitis with mild sedative property. [10] It is commonly formulated as tablets, injections and syrups as single component preparations and is one of the popular ingredients in other formulations such as cough remedies and creams. Numerous UV, HPLC and HPTLC based methods have been reported [11-16] and NMR spectroscopy,[17] polarographic method, [18] electrokinetic chromatography, [19] for estimation of these drugs alone as well as in combination with other drugs in pharmaceutical dosage forms. But no method had yet been reported for simultaneous estimation of these two drugs using HPLC in bulk drug and pharmaceutical dosage forms. Therefore, the present work was aimed to new developed synthesis and validate a new HPLC method for estimation of CPM in pharmaceutical dosage forms



The molecular weight of chlorpheniramine maleate is 390.9 g/mol and it is appears as odourless, white crystalline solid or white powder with bitter taste**.** It is freely soluble in water soluble in alcohol and in chloroform, slightly soluble in ether and in benzene.

SAMPLE PREPERATION: CPM is unstable in the presence of light and moisture thus the monograph in the pharmacopoeia indicates special storage condition. As per the Indian Pharmacopoeia CPM is required to be stored protected from light as well as moisture and at a temperature 37°C. US Pharmacopoeia indicates preserve the API in tight containers (12). Thus sample preparation is required to be done in amber glassware. It has been mentioned to use freshly prepared solvents always for the drug (10-11). Methanol has been used as a diluent for majority of the spectrophotometric method of analysis for CPM. Extraction of the drug from the biological sample includes sample preparation via protein precipitation, liquid-liquid extraction and solid phase extraction (44-57). Acetonitrile has been reported extensively for the sample preparation by protein precipitation.

2. ANALYATICAL METHODS

2.1 UV SPECTROPHOTOMETRY:

In the literature, different UV –Spectrophotometric method have been explored for the quantitative estimation of CPM in combination with drug, including simultaneous equation method, Q-absorbance Ratio method and derivative method. Water is commonly used as a solvent for CPM in the spectrophotometric method have reported method for estimation of CPM alone while other have reported simultaneous estimation with other API. Table 1 list

The spectrophotometric method for analysis of CPM.

Table 1: Reported spectroscopic method for determination of chlorpheniramine maleate Individually or in combination with other drugs from the Pharmaceutical Dosage Form.

Sr. No	API	Combined Drug	Solvent	Method	λ max	Reference
1	Chlorpheniramine maleate	Paracetamol Phenylephrine HCL	0.1 N NaOH	Spectrophotometric method	222.4 nm	1
2	Chlorpheniramine maleate	Dextromethorphen HBr	Methanol	UV-Spectrophotometric method	262.6 nm	2
3	Chlorpheniramine maleate	-	Distilled H2O sulfuric acid (0.25 mol/L)	UV-Spectrophotometric method	265 nm	3
4	Chlorpheniramine maleate	Diethylcarbamazine citrate	Distilled H2O	UV-Spectrophotometric method	261 nm	4
5	Chlorpheniramine maleate	Phenylephrine HCl, phenylpropanolamine HCl	Distilled water	UV-Spectrophotometric method	269.5 nm	5

6	Chlorpheniramine maleate	-	HCL, acetate buffer, phosphate buffer, distilled water	UV-Spectrophotometric method	261 nm	6
7	Chlorpheniramine maleate	Phenylephrine HCL, Caffeine, Paracetamol	Methanol, ethanol, 0.1N HCL	UV - Spectrophotometric method	263 nm	7
8	Chlorpheniramine maleate	Diphenylamine hydrochloride	Potassium Permanganate.	UV-Spectrophotometric method	250 nm	8
9	Chlorpheniramine maleate	Phenol Propanolamine Hydrochloride	Distilled Water	UV-S Spectrophotometric method	261.6 nm/257	9
10	Chlorpheniramine maleate	-	Distilled Water	UV-Spectrophotometric method	257 nm	10
11	Chlorpheniramine maleate	Tincture Ipecac	Acetic Acid,	UV-Spectrophotometric method	254 nm	11
12	Chlorpheniramine maleate	Caffeine	Distilled Water	Spectrophotometric method	261 nm	12
13	Chlorpheniramine maleate	Phenylephrine HCl, Caffeine	Methanol Ethanol HCL	UV-Spectrophotometric method	263 nm	13
14	Chlorpheniramine maleate	Methscopolamine nitrate	Methanol Lcgrade Distilled Water	Multiwavelength Spectrophotometric method	265 nm	14
15	Chlorpheniramine maleate	Phenylephrine Hydrochloride	-	UV-Spectrophotometric method	262 nm	15
16	Chlorpheniramine maleate	Phenylephrine Hydrochloride	0.1 N NaOH equimolar solution in methanol	UV-Spectrophotometric method	271.6 & 250.2 nm	16

2.2 HPLC METHOD:

Among the chromatography method employed for the analysis of pharmaceuticals, high performance liquid chromatography is the most widely used technique. Several assay procedures and analysis related substance mentioned in the pharmacopeias comprise the HPLC technique. More than 15 HPLC method for the estimation of chlorpheniramine maleate have been summarized in table and several methods for estimation of the drug in biological samples have been summarized in table 2.

Sr.no	API	Combined Drug	Solvent	Method	λ max	Reference
1	Chlorphenira mine maleate	Ibuprofen Phenylephrine hydrochloride	Methanol :Phosphate buffer :acetonitrile (20:30:50)	HPLC	220 nm	1
2	Chlorphenira mine maleate	Phenylephrine Hydrocholoride	Acetonitrile & Phosphate buffer (55:45 v/v)	HPLC	255 nm	2
3	Chlorphenira mine maleate	Paracetamol Pseudoephiedtine Bromhexine	Triethylamine- phosphatic acid buffer & MeOH (35:65)	HPLC	215 nm	3
4	Chlorphenira mine maleate	Caffeine acetaminophene	Acetonitrile ion pair solution and tetrahydrofuran (13:14:87 v/v)	HPLC	215 nm	4
5	Chlorphenira mine maleate	acetaminophene phenylephrine dextromethorphan	Methanol	RP_HPLC	227 nm	5
6	Chlorphenira mine maleate	Distilled Water	RP HPLC	HPLC	270 nm	6
7	Chlorphenira mine maleate	Phosphate buffer (pH 6.22) acetonitrile (22:78 v/v)	HPLC	HPLC	265 nm	7
8	Chlorphenira mine maleate	Phenylephrine hydrochloride	Methanol/Phosphate buffer (50 ml 0.2 m Monobasic Potassium Phosphate	HPLC	269.0 nm	8
9	Chlorphenira mine maleate	-	Acetonitrile methanol, tetrahydrofuran, hexasulphonic acid sodium	HPLC	235 nm	9
10	Chlorphenira mine maleate	Paracetamol Caffeine	Methanol 0.05 m dibasic phosphate buffer (pH 4.0) in ration 30:70 v/v	HPLC	215 nm	10
11	Chlorphenira mine maleate	Dexamethasone	methanol chloroform 0.1 N HCl	HPLC	254 nm	11
12	Chlorphenira mine maleate	Ascorbic acid Acetaminophen Caffeine	Double distilled Water	HPLC	215 nm	12
13	Chlorphenira mine maleate	Codeine Phosphate	Mix of acetonitrile & methanol & 1% phosphoric acid in the ration 78:10:12	HPLC	254 nm	13
14	Chlorphenira mine	Caffeine Paracetamol	Acetic Acid glacial bi- n-butyl amine	HPLC	255 nm	14

	maleate	glyceryl guaiacolate				
15	Chlorphenira mine maleate	Aminophylline	H2SO4 : Methanol (60:40 v/v)	HPLC	264 nm	15
16	Chlorphenira mine maleate	Oxolamine citrate Phenylephrine hydrochloride	0.02 m phosphate buffer (pH:4) acetonitrile (85:15v/v)	HPLC	356 nm	16
17	Chlorphenira mine maleate	Paracetamol, ambroxol, guaifenesin phenylephrine hydrochloride	0.01m Sodium per chloride Monohydrate Acetonitrile	HPLC	228 nm	17
18	Chlorphenira mine maleate	Paracetamol, guaiphenesin, phenylephrine HCl, bromohexane HCl	Buffer 10 ml KH2 PO4 & 3.7 mm ion pair reagent. Mix of methanol & acetonitrile (3.2)	HPLC	220 nm	18

HPTLC Method:

Sr.no	API	Combined Drug	Solvent	Method	λ max	Reference
1	Chlorphenira mine maleate	Tartrazinc	Methanol & water (1:1)	HPTLC	217 nm	1
2	Chlorphenira mine maleate	-	Distilled Water	HPTLC	277 nm	2
3	Chlorphenira mine maleate	Ambroxol hydrocholoride Phenylephrine hydrochloride, paracetamol guaiphenesin	-	HPTLC	277 nm	3
4	Chlorphenira mine maleate	Paracetamol, caffeine, phenylephrine	Methanol: N-butanol: Toluene: Acetic acid [8:6:4:4:0,2 V/V)	HPTLC	212 nm	4

3. Review of HPLC method for estimation of Chlorpheniramine maleate in Biological Sample.

Sr. No	Matrix	Internals Standard	Mobile Phase	Flow rate	Column	λ max	Reference
1	Human plasma	Graphene oxide /Fe3O4 polythionine	H2So4 (98%) thionine acetate (85%) HCl (37% w/w)	-	C 18	262 nm	1
2	Biological	-	30:70(v/v) ethanol : H2O mixture 0.1% w/v.	0.8 ml	C 18	190-1100 nm	2

3	Biological Matrix	-	Methanol Potassium dihydrogen Phosphate buffer (60:40 v/v)	08 ml	C 18	230 nm	3
4	Plasma Saliva Urine	-	20% acetonitrile in 0.0075 ml phosphate buffer	2 ml/min	C 18	254 nm	4
5	Human Plasma	Paracetamol Amantadine Hydrocholoride caffeine	Methanol : water [0.5% formic acid 20:80 v/v	-	C 18	250 nm	5

4. Conclusion:

This review is aimed at focusing on the thorough Literature survey of the various analytical techniques Reported for the assay of chlorpheniramine maleate from Different sample matrices. The literature review supports the fact that for estimation of chlorpheniramine maleate from biological samples where the Concentration of the drug is in very small amount, the Choice of detector becomes crucial. Reported methods Show that only fluorescence detector (up to nanogram Level) and mass spectrometer (up to picogram level) are Effective for detection of the drug in the biological Matrix. PDA detector has been reported for estimation of the drug in bulk and pharmaceutical dosage form only.

The conventional UV spectroscopy has been used for assay of the drug individually or in combination with other API from bulk or a dosage form where the Concentration of the analyte is higher in comparison to the biological sample. The presence of multiple drugs in a formulation causes a crucial challenge to the Analyst during the selection of spectrophotometric Methods of analysis. The review has summarised the Simultaneous estimation methods developed for the Assay of chlorpheniramine maleate in presence of multiple Drugs in a formulation.

5. Conflict of interest:

The authors declare that there is no conflict of Interes

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