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ANALYTICAL METHODS FOR QUANTITATIVE ESTIMATION OF CETIRIZINE HYDROCHLORIDE: A REVIEW

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ABSTRACT:

Bachground: Cetirizine is a medication used in the treatment of allergic rhinitis and urticaria. It is a second-generation antihistamine. Cetirizine was FDA- approved in the United States as a prescription-only product in 1995, and later in 2007, it got approval as an over-the-counter medication. This activity reviews the indications, action, and contraindications for cetirizine as a valuable agent in treating rhinitis and urticaria. This activity will highlight the mechanism of action, adverse event profile, and other key factors (e.g., off-label uses, dosing, pharmacodynamics, pharmacokinetics, monitoring, relevant interactions) pertinent for members of the interprofessional team in the treatment of patients using cetirizine.

Method: Various analytical techniques for the quantification of cetirizine hydrochloride for bulk, pharmaceutical formulations and biological samples have been reported. Assay methods include UV-spectroscopy, high performance liquid chromatography, high performance thin layer chromatography, capillary electrophoresis, spectrofluorimetric, super critical fluid chromatography.

Results: Literature review reveals that methanol is the most commonly used solvent for the analysis of montelukast sodium by spectroscopic technique. For estimation of cetirizine hydrochloride by high performance liquid chromatography, methanol and acetonitrile are the commonly used organic solvents in the mobile phase and phosphate buffer or trifluoroacetic acid is used to maintain the pH of the mobile phase. Protein precipitation technique is used widely for extraction of the montelukast from biological samples though liquid-liquid extraction and solidphase extraction has also been reported in fewer articles. The electroanalytical 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 cetirizine hydrochloride.

Keywords: Cetirizine Hydrochloride , analytical methods , HPLC

1. INTRODUCTION:

Cetirizine Hydrochloride (CTZ), chemically (±)-[2-[4-[(4-Chlorophenyl) phenylmethyl]-1-piperazinyl] ethoxy] acetic acid –, monosodium salt (Figure 1), is a potent and selective histamine (H(1))-receptor antagonist (1). It is used for the treatment of of allergic rhinitis and urticaria. CTZ was patented in 1983 and come into medical use in 1987 generic name cetirizine was obtained. CTZ was FDA- approved in the United States as a prescription only product in 1995 and later in 2007, it got approval as an over-the-counter medication. CTZ is available as solid oral dosage form as oral tablet , oral chewable tablet , oral disintegrating tablet having strength 5mg to 10mg, 5mgto 10mg and 10mg CTZ is available either individually or in combination with other APIs like paracetamol, phenylephrine hydrochloride, pseudoephedrine, hydroxyzine, ketotifen, montelukast, Ambroxol, diethylcarbamazine etc are available in the market

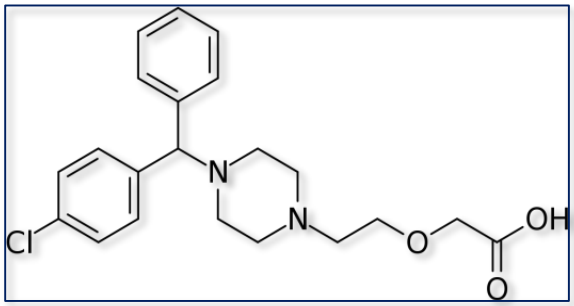

Figure 1 chemical structure of Cetirizine HCl

The molecular weight of CTZ is 388.89 g/mol and it is a white, crystalline powder. The Cetirizine is the active metabolite of the piperazine H1- receptor antagonist hydroxyzine. It is preserve in tight containers, protected from light and moisture and store at room temperature. It is soluble in Water, diethyl sulfoxide, ethanol and methanol while practically insoluble in acetone and methylene chloride. It is a relatively high lipophilicity at physiological pH (LogD=1.5). Having a pka of 2.2, 2.9 and 8.0.The present review of literature is based on the several reported analytical methods for estimation of CTZ in bulk, pharmaceutical formulations as well as biological samples. Methods like spectrophotometry, chromatography including UV, HPLC, RP-HPLC, HPTLC, UPLC and LC-MS, LC-UV, GC-MS. HPLC methods have been extensively used

Sample preparation: As per Indian Pharmacopeia CTZ is required stored from at 20^0 C to 25^0C excursion permitted to 15^0C to 30^0C as per USP. Water and methanol has been usedas diluents for majority of the spectroscopic method of analysis for CTZ. Extraction of the drug from the biological samples includes sample preparation via protein precipitation. Liquid- liquid extraction and solid phase extraction acetonitrile has been reported extensively for the sample preparation of HPLC.

ANALYTICAL METHOD:

1.SPECTROPHOTOMETRY: In the literature, different UV-Spectrophotometric methods have been explored for the quantitative estimation of CTZ in commonly used as solvent for CTZ in combination with other drugs, including simultaneous equation method. Water is commonly used as solvent for CTZ in spectrophotometric method have reported method for estimation of CTZ alone while other have reported simultaneous estimation with other API. Table 1.1 is the spectrophotometric methods for analysis of CTZ.

Table 1: Reported spectrophotometric methods for determination of cetirizine hydrochloride individually or in combination with other drugs from the pharmaceutical dosage forms.

Sr.No.	API	Combined Drug	Solvent	Method	λ_{max}	Reference
1	Cetirizine Hydrochloride	-	1.Methanol 2.Water and 0.1NaOH Solution	Spectrophotometric Method	1)238nm 2)230nm	1
2	Cetirizine dihydrochloride	-	Distilled Water	UV-Spectrophotometric Method	225nm to 235nm	2
3	Cetirizine Hydrochloride	Phenylephrine hydrochloride	Distilled Water	UV-Spectrophotometric Method	237.5nm to232.0nm	3
4	Cetirizine	Phenyl Propanolamine and Nimesulide	Monolithic column Mobile phase composed of 0.1M Phosphate buffer and Methanol (40:60v/v)	Spectrophotometric method	215nm	6
5	Cetirizine	Montelukast	Stock standard solution where diluted to50 ml with methanol	Spectrophotometric method	217nm and 335nm	7
6	Cetirizine Hydrochloride	AmbroxolHCl	Water	Spectrophotometric and HPLC Method	244nm , 230nm	8
7	Cetirizine	NSAIDs Drugs	Mobile phase of Methanol/ Water (90:10v/v, pH 3.5)	Spectrophotometric method (In-vitro)	240nm	9
8	Cetirizine HCl	Phenylephrine HCl	Distilled water	UV-Spectrophotometric method	232nm	10
9	Cetirizine HCl	Phenylephrine HCl	Distilled water	Spectrophotometric method	230.2nm	11
10	Cetirizine	-	Methanol	Spectrophotometric method (UV – Spectrophomeric assay)	229nm	12

11	Cetirizine HCl	Phenyl PropanolamineHCl	Mobile phase consist of Water : Methanol : Triethylamine (20:80:0.5v/v/v)	RP- HPLC Method	254nm	13
12	Cetirizine HCl	Salbutamol sulphate, AmbroxolHCl	Phosphate buffer of pH 6.2	Spectroscopic method	1)276nm 2)244nm 3)230nm	16
13	Cetirizine	Montelukast	Methanol	Spectrophotometric method	217nm , 335nm	17
14	Cetirizine dihydrochloride	-	Methanol	Spectrophotometric method	424.5nm	18

CHROMATOGRAPHY:

1 HPLC METHOD: Among the chromatographic methods employed for the analysis of pharmaceuticals, high performance liquid chromatography is the most widely used technique. Several assay procedures and analysis related substances mentioned in the pharmacopeias comprise the HPLC technique. HPLC methods for the estimation of cetirizine HCl have been summarized in the table 2 and several methods for estimation of the drug in biological samples have been summarized in table 3.

Table 2: Reported HPLC methods for determination of cetirizine hydrochloride individually or in combination with other drugs from the pharmaceutical dosage forms.

Sr. no	API	Combined Drug	Solvent	Method	λ_{max}	Reference
1	Cetirizine	Paracetamol, Phenylephrine HCl, Caffeine, Nimesulide in tablet	C18 column with gradient elution of mobile phase composed of 10mm phosphate buffer (pH 3.3) and Acetonitrile	RP-HPLC Method	280nm	20
2	Cetirizine HCl	Phenylephrine hydrochloride	C18 column with simple mobile phase composition of mixture of buffer (Water + 0.2%v/v Triethylamine , pH 7.5 by dil.H_3PO_4) and acetonitrile (63 : 37 v/v)	New HPLC - UV	232nm	21
3	Cetirizine HCl	Diethyl carbamazine	C18 column , aided by a mobile phase mixture of Methanol : pH 6 Phosphate buffer in a ratio of 80:20 % v/v	RP-HPLC Method	231nm	22
4	Cetirizine in human plasma	-	C18 column mobile phase used is 35:65v/v of Acetonitrile to 0.3% triethylamine (TEA) buffer fixed at pH 3 by Phosphoric acid	HPLC	237nm	23
5	Cetirizine HCl	Diethyl carbamazine citrate	C18 column mobile phase containing Acetonitrile and mixed phosphate buffer (KH_2PO_4 and K_2HPO_4 , adjusted to pH 3.0 with 10% ortho-phosphoric acid) in ratio of 60:40%v/v	RP-HPLC	230nm	24

6	Cetirizine HCl	Paaracetamol, phenylpropanolamine HCl	C18 column with isocratic condition and mobile phase containing Methanol: 0.01 M disodium hydrogen phosphate dehydrate buffer (pH 7, adjusted with ortho-phosphoric acid) 60:40	RP-HPLC	217nm	25
7	Cetirizine HCl	Phenylephrine hydrochloride and nimesulide	C18 column Mobile phase Acetonitrile: Water (pH 3) 60:40	HPLC	229nm	26
8	Cetirizine dihydrochloride	-	C18 column and a mixture of 50mm KH_2PO_4 and acetonitrile (60:40v/v , pH 3.5)	HPLC	-	27
9	Cetirizine	Pseudoephedrine	C18 column mobile phase was consisted of TEA solution (0.5 % pH 4.5)- Methanol – Acetonitrile (50:20:30 v/v/v)	RP-HPLC	218nm and 222 nm	28
10	Cetirizine HCl	Phenylpropanolamine HCl	C18 column mobile phase Water : methanol: triethylamine (20:80:0.5 v/v/v) pH 3.5	RP-HPLC	254nm	29
11	Cetirizine	-	C18 column mobile phase 0.067 M Phosphate buffer pH 3.40 / Acetonitrile (1:1 v/v)	HPLC	227nm	30
12	Cetirizine HCl	Ambroxol HCl	C18 column acetonitrile, methanol and water (10:20:70)	HPLC	230nm	31
13	Cetirizine HCl	Phenylephrine hydrochloride	C18 column mobile phase Acetonitrile: 10mm Sodium phosphate dibasic anhydrous buffer solution (40:60% v/v , pH 6.2)	RP-HPLC	220nm	32
14	Cetirizine HCl	-	Methanol: Water (70:30) pH 4	HPLC	231nm	33
15	Cetirizine HCl	Phenylephrine hydrochloride	C18 column Mobile phase methanol: acetonitrile: disodium hydrogen phosphate(80:3:17 v/v/v)	HPLC	272nm	34
16	Cetirizine HCl	Phenylephrine hydrochloride	C18 column Mobile phase buffer (0.1 M ammonium	RP-HPLC	225nm	35

			dihydrogen phosphate pH 5.2+-0.05) : Acetonitrile (50:50%v/v)			
17	Cetirizine dichloride	-	C18 column mobile phase of KH_2PO_4 (0.01mol/l) – Acetonitrile 65:35v/	HPLC	230nm	36
18	Cetirizine	Verapamil / Diltiazem and Amlodipine	Methanol , Acetonitrile and water (65: 5: 30) and pH at 2.8	RP-HPLC	230nm	37
19	Cetirizine	AmbroxolHCl	C18 column Mobile phase Methanol – Acetonitrile – Water (40:40:20 v/v/v)	RP-HPLC	229nm	38
20	Cetirizine HCl	Hyoscine butyl bromide	C18 column at room temp Mobile phase acetonitrile: water (1:1 v/v)	RP-HPLC	205nm	39
21	Cetirizine dihydrochloride	-	C18 column used with Mobile phase Acetonitrile / 0.01M Ammonium dihydrogen phosphate (32:68v/v) containing with 0.1 % w/v Tetra butyl ammonium hydrogen sulphate pH 3 with phosphoric acid	Spectrophotometric method and HPLC Method	230nm	19
22	Cetirizine	Azelastine (in aqueous humor)	Isocratic elution on C8 column with mobile phase made up Acetonitrile: 0.3% Triethylamine of pH 5(60:40v/v)	Reverse Phase HPLC – UV approach	216 nm	15
23	Cetirizine	Ketotifen	C18 column using an isocratic mobile phase Acetonitrile and 10mm Disodium hydrogen phosphate buffer (pH 6.5) in ratio of 45:55%v/v	LC-UV Method	230 nm	14
24	Cetirizine	Ketotifen	C18 column Mobile phase of a acetonitrile and 10mM disodium hydrogen phosphate buffer(pH6.5) in ratio of 45:55%v/v	LC-UV Method	230 nm	5

25	Cetirizine Hydrochloride	Phenylephrine hydrochloride	C18 column Mobile Phase composition of a mixture of buffer (Water + 0.2%v/v triethylamine, pH 7.5 by dilute H_3PO_4 and Acetonitrile (63:37v/v)	UV method	232 nm	4

Table 3. Review of HPLC method for estimation of cetirizine HCl in biological sample:

Sr.No	Matrix	Internal Standard	Mobile Phase	Flow Rate	Column	Detector	Ref.
1	Human Serum	Pyridoxine	HeptoneSulphonic acid salt Buffer and Acetonitrile	1.0 ml/min	C18	230nm	40
2	Human Serum	Diazepam	13mM Phosphoric acid Solution and Acetonitrile (61:39 v/v)adjusted to pH2.8 with 5M MaoH	-	C18	230nm	41
3	Human Plasma and Urine	Nebivolol	Acetonitrile Phosphate Buffer (pH3.5,20mM) (20:80v/v)	0.5 mL/min	C8 Micro bore column and C18 column	230 nm	42
4	Human Serum	Rosuvastation	Methanol Water (70:30) at pH2.8 +- 0.05	_	C18 Column	230nm	43
5.	Human Plasma	-	65% methanol and 35% water(contained 0.1% formic acid , 10mm ammonium formate)	0.2 ml/min	C18 Column	230nm	44

HPTLC: High performance thin layer chromatography technique has been widely accepted for drug analysis. It provides the advantages of ease case of handling, short analysis time and flexibility to study a wide variety of compounds. About five HPTLC methods have been reported for quantitative analysis of cetirizine HCl (Table 4). Mobile phase consisting of a combination of three or more solvents have been reported for cetirizine HCl estimation. The detector involves in all the methods is UV detector.

Table 4 :Reported HPTLC methods for determination of cetirizine hydrochloride individually or in combination with other drugs from the Pharmaceutical Dosage Forms.

Sr. no	API	Combined Drug	Solvent	Method	λ_{max}	Reference
1	Cetirizine HCl	Phenylephrine hydrochloride	Toluene: ethyl acetate : methanol : ammonia (5:2:3:0.4v/v/v/v)	HPTLC	254nm	45
2	Cetrizine dihydrochloride	-	Methanol :distilled water (9.95:0.05v/v)	HPTLC	257nm	46
3	Cetirizine	Montelukast	Ethyl acetate: methanol: ammonia solution (25%) (14:3:2v/v/v)	HPTLC	230nm	47
4	Cetirizine	Pseudoephedrine	Ethylacetate:Methanol: ammonia(7:15:1 v/v/v)	HPTLC	240nm	48
5	Cetirizine HCl	Phenylephrine hydrochloride	Toluene: methanol: ammonia (8:2:1v/v/v)	HPTLC	224nm	49

CONCLUSION:

This review is aimed at focusing on the through literature survey of the various analytical techniques reported for the assay of Cetirizine HCl from different sample matrixes. The literature review supports the fact that for estimation of cetirizine HCl from biological samples where the concentration of the drug is very small amount, the choice of detector become very crucial. Reported method show that only fluorescence detector and mass spectrometer and effective detection of drug in 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 the 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 the comparison to the biological sample. The presence of multiple drugs in a formulation causes a crucial challenge to the analyte during the selection of spectrophotometric methods of analysis. The review has summarized the simultaneous estimation methods developed for the assay of cetirizine HCl in presence of multiple drugs in a formulation.

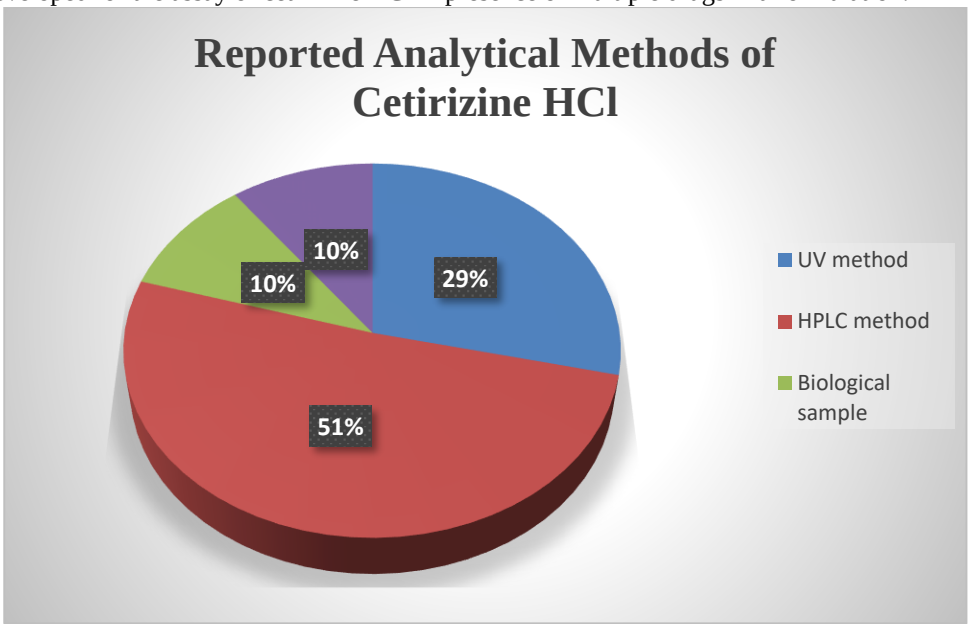

Figure 2: Reported analytical methods of cetirizine HCl

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