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A Validated Titrimetric Method for the Quantitative Estimation of Fexofenadine Hydrochloride in Pure form and in their Pharmaceutical Preparations with Pyridinium Fluoro Chromate(PFC) as Reagent

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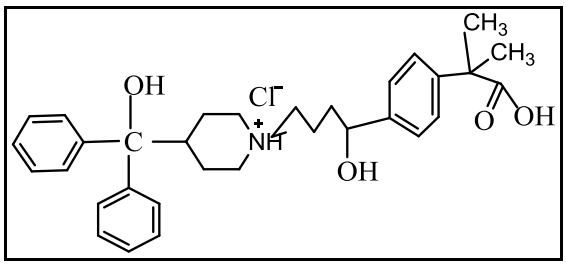
Abstract : Fexofenadine hydrochloride (FFH) is an antihistamine drug of second generation. It is an novel antiallergic drug and is well efficient in treating allergic diseases. In the present work simple, convenient, accurate, precise and cost effective visual titrimetric method have been developed for the quantitative estimation of Fexofenadine hydrochloride (FFH) i.e. an antihistamine drug in pure form and in its dosage forms with pyridiniumfluoro chromate (PFC) reagent. The principle of this method involves the oxidation of –OH(hydroxyl) of the Fexofenadine hydrochloride (FFH) by a known excess of potassium iodate in sulphuric acid medium followed by iodometric titration in presence of reagent pyridiniumfluoro chromate (PFC). The value of percentage error, coefficient of variation (CV) and standard deviation (SD) have been calculated for accuracy and precision of result.

Key Words : Antihistamine drugs, Fexofenadine hydrochloride drugs, Pharmaceuticals, Pyridiniumfluoro chromate (PFC),titration.

Introduction:

Fexofenadine hydrochloride (FFH) is an antihistamine drug of second generation. Its molecular formula is $C_{32}H_{39}NO_4$.HCl and is known as (±)-4-[1-hydroxy-4-[4-(hydroxydiphenylmethyl)-1-piperidinyl]-butyl]-α,α-dimethyl benzene acetic acid hydrochloride[1].The chemical structure of Fexofenadine hydrochloride (FFH) is as follows:



Fexofenadine hydrochloride (FFH) is official in United States Pharmacoepia[2] and in Indian Pharmacoepia[3]pharmacopeia. Fexofenadine hydrochloride (FFH) is used to relieve the allergic conditions which includes seasonal allergic rhinitis and urticaria[4,5] having symptoms such as sneezing, runny nose, itchy throat, or itchy, watery eyes. This FFH is also used to treat hives and skin itching. This is also important drug for the treatment of asthma[6] and atopic dermatitis[7].Thus, today Fexofenadine (FFH) is an novel antiallergic drug

and is well efficient in treating allergic diseases[8].For the estimation of this drug no any visual titration method have been employed by any researcher's for its determination other than Raghu *et al.*[9].They have employed Bromate-bromide mixture in acid medium as oxidising agent for the determination of Fexofenadine(FFH) in pharmaceutical preparation and in its pure form.Potentiometric titration has been introduced by Rajan V. *et al.*[10] for the quantitative determination of Fexofenadine from bulk drug and pharmaceutical formulations by using perchloric acid as titrant.Resercher's Maher *et al*.[11] introduced chromatographic technique for the determination of Fexofendine (FFH) and its impurities present in pharmaceutical tablets whereas, Breir *et al.*[12] described a HPLC method in his research for dissolution tests of Fexofenadine (FFH) in Capsules and coated tablets. Zafar *et al.*[13] developed a dissolution and RP-HPLC method for the determination of Fexofenadine in tablet formulation.Liquid chromatographic method for the determination of Fexofenadine in tablets and to analyse its uniformity of contents have been employed by Shraraf *et al*.[14]

It has been observed that although the majority of researcher's had determined Fexofenadine hydrochloride (FFH) drugs by applying various physical and analytical techniques by using different oxidants, but is noteworthy that no any work/research has yet been done about the determination of antihistamine drug by using Pyridiniumfluoro chromate (PFC) as an oxidant by applying volumetric titration.

The main objective of this research paper is to develop a simple, rapid, cost effectiveness, non sophisticated, accurate and precise technique i.e. visual titration(Volumetric titration) by using mild and versatile oxidant like Pyridinium fluoro chromate (PFC) for the quantative estimation of the fexofendine hydrochloride drug in pure form and in their pharmaceutical preparations for the routine quality analysis of pharma industries.

Materials and Methods

Reagents and Solutions

Pyridinium Fluorochromate (0.03 N): Solution of PFC was prepared by dissolving 0.497 gm of PFC in 150 ml glacial acetic acid **(MERCK)** and made up the volume with distilled water in 250 ml volumetric flask. The prepared solution was standardised iodometrically with standard Sodium thio sulphate solution using starch as an indicator.

Sodium thio sulphate (0.01 N): Stock solution of sodium thio sulphate(0.01N) wasprepared by dissolving 3.16 gm of sodium thio sulphate (Unhydrous) AR grade of **HI MEDIA** in distilled water of 1000 ml volumetric flask and made up to the mark with distilled water. The stock solution prepared in this way was standardised by using 0.01 N potassium dichromate **(Moly Chem)** solution iodometrically by using starch as an indicator.

Potassium Dichromate (0.01 N): Stock solution of $K_2Cr_2O_7$ was prepared by dissolving 0.245 gm of $K_2Cr_2O_7$ **(A.R Grade of Moly Chem)** in distilled water of 500 ml volumetric flask.

Potassium Iodide(10%): 10% W/V aqueous solution was prepared in distilled water. The Potassium iodide used for an experiment is of AR grade of RANKEM.

Starch Solution (1%):1% of W/V aqueous solution of starch **(LOBA Chemie)** was prepared in boiling distilled water. The paste formed this way was filtered and kept to cool for some minutes. Always fresh starch solution has been prepared for accurate results.

Preparation of Sample Solution :

Taken 100 mg pure compound(in form of powder) of Fexofenadine hydrochloride (FFH) supplied on request, as gift sample by Sanofi India Ltd, Ankleshwar, Distt-Bharuch in 100 ml volumetric flask and thereafter dissolved this compound in 60ml of solvent mixture containing Acetic acid (CH_3COOH) OF **MERCK** and distilled water (H_2O) in the ratio of 1:2 .i.e 20ml:40ml of acetic acid: distilled water and shaken the solution of volumetric flask thoroughly for 20 minute for dissolving the compound properly and after getting homogenous solution the flask was made upto the mark with the same mixture of solvent containing acetic acid and distilled water in the ratio of 1:2.

Preparation of tablet Solution :

The 20 Allegra-120 mg tablets (Manufactured by Sanofi India Ltd, Ankleshwar, Distt-Bharuch, India) has been obtained from local commercial source and these tablets were crushed to fine power. The powder equivalent to 100 mg of sample was taken in 100 ml calibrated flask and dissolved in the same process as described above for the pure solution of FFH.

Method:

Aliquots of drug samples containing 1 to 5 mg were taken in 100 ml stoppered conical flask (Iodine flask) and to this 5 ml of 0.03 N PFC reagent (Prepared in 60% acetic acid) was added to it. Again 10 ml of 5N sulphuric acid was added to same reaction mixture of said flask. There after reaction mixture was shaken thoroughly, in order to mix the contents of flask properly and kept to stand the whole solution of flask for required reaction time at room temperature (25-30^{o}C) so that reaction between the contents of flask may be completed. After the completion of reaction 5 ml of 10% KI was added to same reaction mixture and whole reaction mixture was shaken properly and again allowed to stand for one minute. The unconsumed PFC was determined by iodometric titration by using starch as an indicator. Similarly blank experiment was also performed using all the regents under identical condition except the drug sample. The amount of PFC consumed for the given drug sample was calculated by the difference in the titre values of sodium thio sulphate solution for blank and actual experiment. The recovery of the drug sample was calculated with the amount of PFC consumed for the sample. Later on for accuracy and precision percentage error, coefficient of variation and standard deviation of each drug sample were calculated. Finally Standard Drug Addition method was also performed to evaluate the authenticity of the method.

Formula used for calculation:

The expression used to determine the amount of drug present in the measured aliquot for each experiment is as follows:

$$\text{Weight (mg) of sample} = \frac{M \text{ X } N(B - S)}{n}$$

Where,
M = Molecular weight of the sample.
N = Normality of sodium thiosulphate solution.
B = Volume of sodium thiosulphate solution for blank.
S = Volume of sodium thiosulphate solution for sample.
n = Stoichiometry of the reaction.

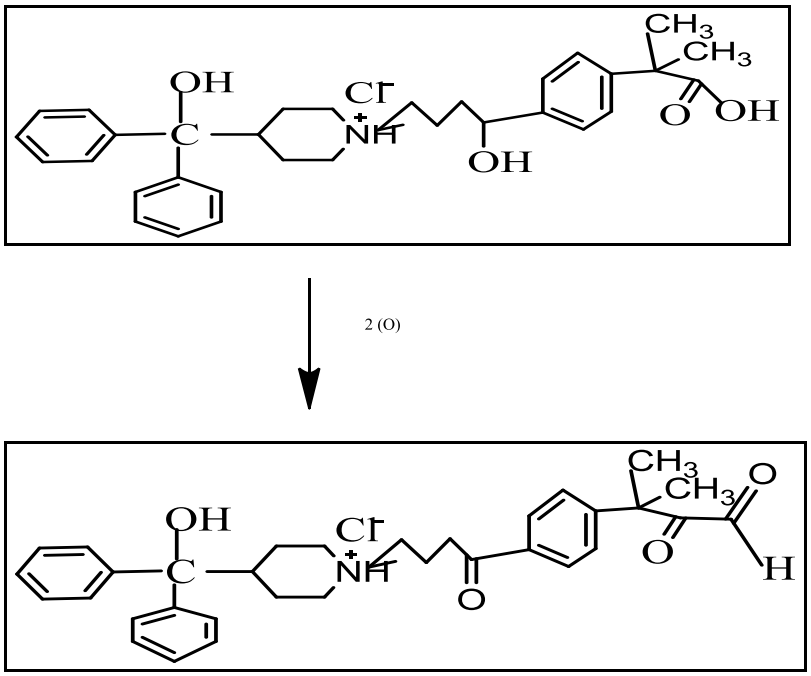
By using above mentioned procedure the estimation of Fexofenadine hydrochloride has been achieved for 1-5 mg of pure sample of FFH and in its pharmaceutical preparation(i.e Allegra) but for convenience, the results as recorded in Table-1 have been shown only for 1,3 and 5 mg of sample size.

Results and Discussion

The results recorded in table-1 were carried out for FFH aliquots of 1 ml to 5ml but for covenience only 1,3 and 5 mg has been shown.This sample sizes always established stoichiometric ratio for FFH: PFC to be 1:2.This stoichiometric ratio is similar for both i.e for pure FFH sample and for pharmaceutical preparations i.e. in Allegra tablet. This stoichiometric ratio 1:2 remains constant for FFH: PFC even under varying reaction conditions i.e in varying reaction time, concentration of the reagent, reaction temperature and reaction medium etc.It has been also observed that 0.03N concentration of PFC and reaction duartion of 10 minute at room temperature is most appropriate condition for the determination of FFH drug.The effect of reaction medium has also been studied and has been observed that in absence of sulphuric acid the reaction proceed very slow and conentration of 5N sulphuric acid gives accurate results.This visual volumetric titration method is simple,rapid, accurate and economically best in comprasion to other method where sophisticated instruments is required.

Possible course of reaction:

The compound fexofenadine exists as raceamte and found in form of zwitterion in aqueous media.The oxidising reagent PFC oxidises the two hydroxyl group of fexofenadine hydrochloride i.e one secondary alcohol to ketonic group and other hydroxyl group of carboxylic acid group to aldehydic group. Due to this only stoichiometric ratio between Drug to reagent(PFC) has been found to be 1:2.On the basis of stoichiometric ratio established between PFC and pharmaceutical drug Fexofenadine hydrochloride (FFH) and after the survey of different literature as mentioned above the proposed reaction may be expressed as:



Scheme:Possibe oxidation reaction

Table-1 Quantative estimation of Fexofenadine hydrochloride (FFH) with 0.03N PFC

S. N	Amount of aliquots taken	Amount Present#	Reaction time	Molecu-larity	Amount obtained by calculation ##	Error	SD	CV
	(ml)	(mg)	(min)		(mg)	(%)	(mg)	(mg)
Analysis of Fexofenadine hydrochloride (FFH) in Pure form								
1	1	0.993	10	2	0.985	− 0.81	0.0026	0.2639
2	3	2.979	10	2	2.958	− 0.70	0.0018	0.0608
3	5	4.965	10	2	4.938	− 0.54	0.0009	0.0182
Analysis of Allegra tablet (Manufactured by Sanofi India Ltd)								
1	1	0.989	10	2	0.982	− 0.71	0.0029	0.2953
2	3	2.955	10	2	2.938	− 0.58	0.0016	0.0545
3	5	4.927	10	2	4.905	− 0.45	0.0011	0.0224

Mean value of three determinations has been done for each case.
Value obtained is the average of nine determination.

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