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# Forced degradation studies of cetirizine hydrochloride, phenylephrine hydrochloride, paracetamol by RP-HPLC

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**Abstract**
Stability of drug and formulations are important parameter to be considered for the several regulatory guidelines as per the ICH guidelines stability of drug and formulations are tested by using stress degradation studies. In this research article the forced degradation studies of Cetirizine Hydrochloride, Phenylephrine Hydrochloride, and Paracetamol had been studied under various stress conditions of pH, Temperature, Light and Oxidizing agents by using RP-HPLC.

**Keywords:** cetirizine hydrochloride, phenylephrine hydrochloride, paracetamol, RP-HPLC

## Introduction

The combination of Cetirizine hydrochloride, Phenylephrine hydrochloride and Paracetamol treatment in anti-allergic, as a nasal decongestant to relieve stuffy nose or nasal congestion & antipyretic. Cetirizine hydrochloride, Phenylephrine hydrochloride and Paracetamol are a potential combination for us. Further investigations to assess the potential effect on the evaluation of drug resistance, disease transmission, and safety of Cetirizine hydrochloride, Phenylephrine hydrochloride and Paracetamol are warranted. Cetirizine hydrochloride is a second generation antihistamine drugs and HPLC methods have been reported for analysis of cetirizine individually and in combination with several other drugs [1-3].

Phenylephrine hydrochloride is an ingredient used in prescription and drug products s used to relieve nasal discomfort caused by colds, allergies, and hay fever. It is also used to relieve sinus congestion and pressure. Phenylephrine will relieve symptoms but will not treat the cause of the symptoms or speed recovery. Analytical Technique to determine Phenylephrine in pharmaceuticals has been generally used GC and HPLC method individually and in combination with other drugs. Paracetamol is acetanilide derivative having analgesic, antipyretic and weak anti-inflammatory action. [4-5]

The analytical research is carried out on cetirizine hydrochloride i.e. high-performance Liquid chromatographic determination of cetirizine in human plasma, urine, serum and Phenylephrine hydrochloride high-performance liquid chromatographic determination of Phenylephrine hydrochloride in tablet, multi componants formulations and analysis paracetamol in tablets by HPLC. These three drugs analytical methods are already reported in the market individually and combination of several other drugs.

We study RP-High Performance Liquid Chromatographic method for the analysis of Cetirizine hydrochloride, Phenylephrine hydrochloride and Paracetamol drugs that is a ternary combination which is simple sensitive and new method and not yet reported in the market. [6]

## Material and Methods

### Material

The required chemicals were purchased from local market of Nanded and are of HPLC grade.

### Methods

**Selection of Analytical Wavelength:** From the standard stock solution further dilutions were done using methanol and scanned over the range of 200-400 nm and the spectra were overlain (Figure 1)

**Selection of mobile phase [7]:** The solutions of Cetirizine hydrochloride, Phenylephrine hydrochloride, Paracetamol working standards were injected into the HPLC system and run in different solvent systems. Different mobile phases containing methanol, water and acetonitrile, buffer in different proportions were tried and finally Phosphate buffer pH4.0 and Acetonitrile in the ratio of (85:15) was selected as an appropriate mobile phase which gave good resolution and acceptable peak parameters for Cetirizine hydrochloride, Phenylephrine hydrochloride, Paracetamol.

**Preparation of mobile phase:** Phosphate buffer pH4.0 and Acetonitrile in the ratio of (85:15) was prepared, filtered through 0.2 µm membrane filter and sonicated on ultra-sonic bath.

### Preparation of standard stock solution

**Cetirizine hydrochloride standard stock solution: (50 µg/ml) [8, 9]:** 5 mg cetirizine hydrochloride weighed accurately and transferred in to 100 ml volumetric flask. Drug was dissolve in 50 ml Acetonitrile with shaking 10 min and then volume was made up mark so as to get the concentration 50 µg/ml. stock solution was filter through 0.2 µm membrane filter paper, for the preparation work standard, suitable aliquots of stock solution were pipetted out and volume were made up to the mark with mobile phase.

**Phenylephrine hydrochloride standard stock solution: (100 µg/ml):** 10 mg Phenylephrine hydrochloride weighed accurately and transferred in to 100 ml volumetric flask. Drug was dissolve in 50 ml Acetonitrile with shaking 10 min and then volume was made up mark so as to get the concentration 100 µg/ml. stock solution was filter through 0.2 µm membrane filter paper, for the preparation work standard, suitable aliquots of stock solution were pipette out and volume were made up to the mark with mobile phase.

**Paracetamol standard stock solution: (1000 µg/ml):** 500 mg Paracetamol weighed accurately and transferred in to 100 ml volumetric flask. Drug was dissolve in 50 ml Acetonitrile 10 min and then volume was made up mark so as to get the concentration 1000 µg/ml. stock solution was filter through 0.2 µm membrane filter paper, for the preparation work standard, suitable aliquots of stock solution were pipette out and volume were made up to the mark with mobile phase.

A mixed standard solution was prepared from these stock solutions by transferring 10 mL of each of the stock solution to a 100 mL volumetric fl ask and diluting with acetonitrile to get a solution of 10, 500 and 5 µg/ml of PHE, PAR and CET respectively.

**Optimized chromatographic conditions**

Column: Kinetex-C18 (4.6, 150 mm, 5 mm)
Mobile phase: Phosphate buffer pH4.0 and Acetonitrile (85:15)
Flow rate: 1.5 ml/min
Detection Wavelength: 220 nm
Sample injector: 20 µl loop
Temperature: Ambient

**Forced Degradation Study [10]**

Cetirizine hydrochloride, Phenylephrine hydrochloride and Paracetamol were subjected to variety of stress conditions to affect degradation up to about 5-20%. The drugs were stressed under a variety of stress conditions like acid, alkali, effect by oxidation, light and dry heat. The stressed samples were subjected to chromatographic separation to resolve the drug from any potential degradation products.

Stress degradation of analytes was performed. For study 10mg of Cetirizine hydrochloride, Phenylephrine hydrochloride and Paracetamol were accurately weighed, transferred to separate 10ml volumetric flask, dissolved in the mobile phase and dilute to volume with the same solvent mixture to furnish stock solutions containing 1000µg/ml of Cetirizine hydrochloride, Phenylephrine hydrochloride and Paracetamol 1ml of above solution transferred in 10ml of volumetric flask and the volume was made with diluents. The concentration of both drugs is 100µg/ml.

All of above samples were stressed with acid, base, and peroxide stress solutions and kept aside for required time. After completion of stress, acid/alkali solutions were neutralized and volume made up with mobile phase up to the marks. These solutions were used for acid, alkali, oxidation and photolytic degradation. For thermal degradation oven heated drugs were used to make equivalent concentration.

**Acid/ alkali hydrolysis:** For acid/ alkali hydrolysis, 2ml of 0.1N HCL and 0.1N NaOH was added to the solutions. These solutions were kept aside for 1hr at 60ºC. Resultant solutions were injected in to system after neutralization and chromatogram were recorded to access stability.

**Oxidation Degradation:** For oxidation degradation 3ml of 2% hydrogen peroxide (H2O2) was added and kept aside for 24 hr at 60ºC and injected in system and chromatogram were recorded.

**Photo Degradation:** For photo degradation solutions were exposed to near UV light for 24hr and resultant solutions were injected in chromatographic system and compared with standard drug solution.

**Thermal Degradation:** Cetirizine hydrochloride, Phenylephrine hydrochloride and Paracetamol were transfer into petri plate separately and kept in a hot air oven at 70ºc for 12hrs. from the above stressed sample, 10 mg was weighed accurately and transferred to 10 ml volumetric flask separately and volume was made up to the mark with the mobile phase to get the concentration 1000µg/ml of both drug solution.5 ml of above solution transferred in 10 ml volumetric flask and the volume was made with diluents.

**Result and Discussion**

**Selection of wavelength**

The wavelength selected for the analysis was 220 nm for Cetirizine hydrochloride, Phenylephrine hydrochloride and Paracetamol showed considerable absorbance.

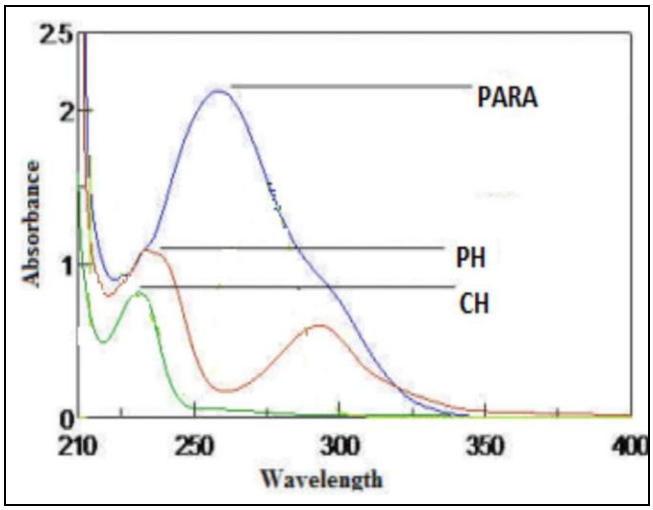


**Fig 1:** Overlain spectra of Cetirizine Hydrochloride, Phenylephrine Hydrochloride and Paracetamol

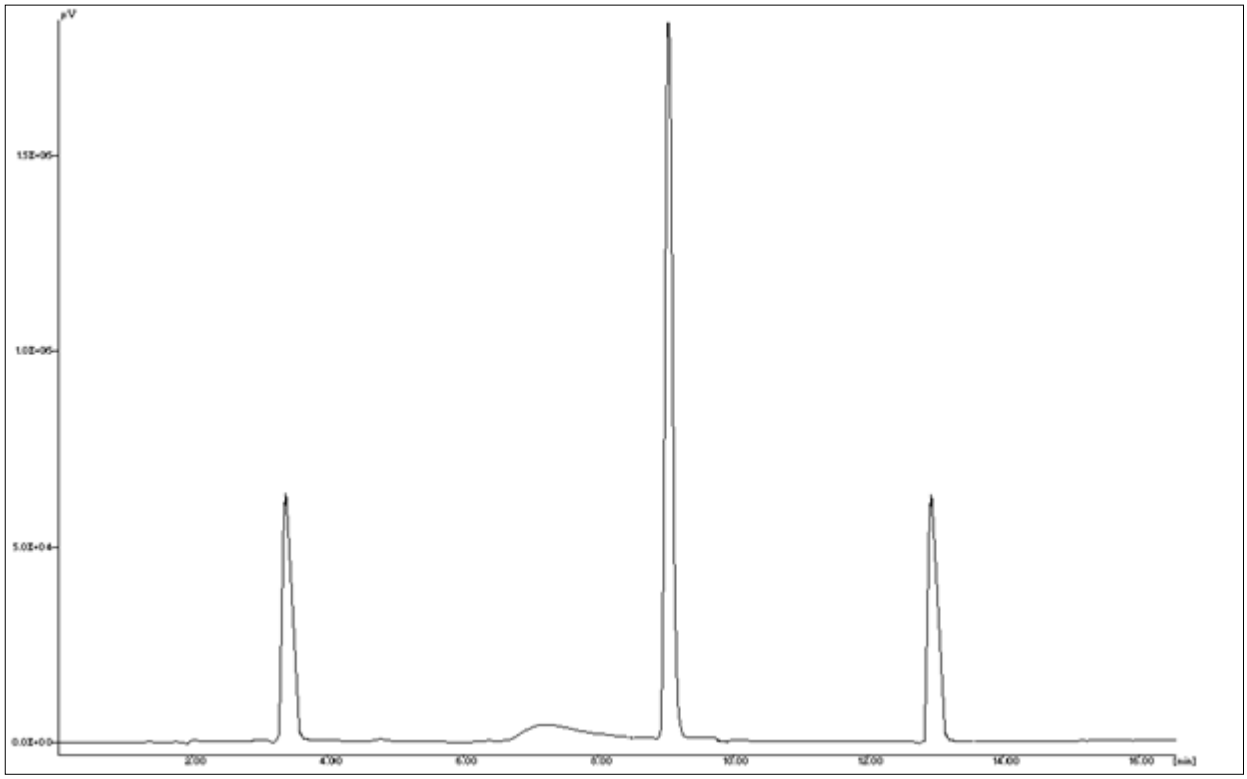

**Fig 2:** Chromatogram of working standard mixture of Phenylephrine, Paracetamol and Cetirizine Hydrochloride.

**Forced Degradation study**

**Acid /Alkali hydrolysis**

For Acid/Alkali hydrolysis, 2ml of 0.1M Hydrochloric acid (HCL) / 2ml of 0.1N Sodium hydroxide (NaOH) were added to solutions. These solutions were kept aside for 1hr at $60^0$C. Resultant solutions were injected in to system after neutralization and chromatograms were recorded to access stability.

**Thermal degradation**

Cetirizine hydrochloride, Phenylephrine hydrochloride and Paracetamol were transferred to petri plate separately and kept in a hot air oven at 70˚C for 12hrs. From the above stressed sample, 10mg was weighed accurately and transferred to 10ml volumetric flask separately and volume was made up to the mark with the methanol to get the concentration of 1000µg/ml of both drug solution. 5ml of above solution transferred in 10 ml volumetric flask and volume was made with diluents.

**Table 1:** Summary of degradation data for Cetirizine hydrochloride.

| Stress Condition | Retention Time | Area of Peak | Degradation (%) | API after degradation % |
|---|---|---|---|---|
| Std. Drug | 4.152 | 2563824 | - | - |
| Acidic (0.1N HCL) | 4.048 | 2189745 | 83.25 | 16.75 |
| Alkaline (0.1 N NaOH) | 4.176 | 1562897 | 64.38 | 35.62 |
| Oxidation (3% H2O2) | 3.987 | 1971038 | 77.28 | 22.72 |
| Photolytic (UV) | 3.879 | 2345687 | 96.87 | 3.13 |
| Thermal | 4.123 | 2483764 | 99.05 | 0.95 |

**Table 2:** Summary of degradation data for Phenylephrine hydrochloride

| Stress Condition | Retention Time | Area of Peak | Degradation (%) | API after degradation % |
|---|---|---|---|---|
| Std. Drug | 5.752 | 1082574 | - | - |
| Acidic (0.1N HCL) | 4.578 | 758648 | 83.45 | 16.55 |
| Alkaline (0.1 N NaOH) | 4.950 | 710587 | 65.48 | 34.52 |
| Oxidation (3% H2O2) | 4.986 | 744825 | 72.84 | 27.16 |
| Photolytic (uv) | 5.188 | 954876 | 88.67 | 11.33 |
| Thermal | 5.846 | 895204 | 85.48 | 14.52 |

**Table 3:** Summary of degradation data for Paracetamol

| Stress Condition | Retention Time | Area of Peak | Degradation (%) | API after degradation % |
|---|---|---|---|---|
| Std. Drug | 5.755 | 1048527 | - | - |
| Acidic (0.1N HCL) | 4.943 | 753845 | 83.54 | 16.46 |
| Alkaline (0.1 N NaOH) | 4.975 | 706548 | 67.24 | 32.76 |
| Oxidation (3% H2O2) | 4.986 | 744214 | 72.54 | 27.46 |
| Photolytic (uv) | 5.644 | 954245 | 88.64 | 11.36 |
| Thermal | 5.624 | 899458 | 82.95 | 17.05 |

**Conclusion**

Forced Degradation Studies of RP-HPLC method was found to be linear, accurate, precise, specific and robust according to acceptance criteria. The results show that the Forced Degradation Studies HPLC method presented here can be considered suitable for the analytical determination of Paracetamol, Cetirizine hydrochloride and Phenylephrine hydrochloride in bulk and tablet dosage form. This method has effectively resolved all the drugs and their degradation

products. The good % recovery in tablet forms suggests that the excipients present in the dosage forms have no interference in the determination. The %RSD was also less than 2% showing high degree of precision of the proposed method. The method was successfully applied to the available marketed formulation without any interference due to the excipients and can have an application in the industry.

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