Photo-Degradation Of Sarcet® (Cetirizine Dihydrochloride) Under Different Extreme Lighting Condition: An UV Analysis

Submitted By

Shahrin Arby Romana

ID: 2014-1-70-035

Department of Pharmacy

East West University, Dhaka

Research Supervisor: Md. Anisur Rahman, Assistant professor

"A thesis report, submitted to the Department of Pharmacy, East West University, in partial fulfillment of the requirements for the degree of Bachelor of Pharmacy"

IN THE NAME OF ALLAH

THE MOST GRACIOUS AND MOST MERCIFUL

DEDICATION

This Research Project Is Dedicated to My Beloved Parents.

DECLARATION BY THE CANDIDATE

I, Shahrin Arby Romana, hereby declare that the dissertation entitled "Photolytic Degradation of Sarcet® (Cetirizine Dihydrochloride)" under accelerated condition, submitted by me to the Department of Pharmacy, East West University, in the partial fulfilment of the requirement for the degree of Bachelor of Pharmacy with original research work carried out by me under the supervision and guidance of Md. Anisur Rahman, Assistant Professor, Department of Pharmacy, East West University, Dhaka.

.....

Shahrin Arby Romana

ID: 2014-1-70-035

Department of Pharmacy

East West University, Dhaka

CERTIFICATE BY THE SUPERVISOR

This is to certify that the dissertation entitled "Photolytic Degradation of Sarcet® (Cetirizine Dihydrochloride) under accelerated condition" submitted to the department of pharmacy, East West University in partial fulfilment of the requirements for the degree of Bachelor of Pharmacy was carried out by Shahrin Arby Romana (ID: 2014-1-70-035) under our guidance and supervision and that no part of the research has been submitted for any other degree. We further certify that all the sources of information and laboratory facilities availed of in this connection is duly acknowledged.

.....

Md. Anisur Rahman

Assistant Professor

Department of Pharmacy

East West University, Dhaka.

CERTIFICATE BY THE CHAIRPERSON

This is to certify that, the thesis "Photolytic Degradation of Sarcet®" submitted to the Department of Pharmacy, East West University, Rampura, Dhaka for the partial fulfilment of the requirements for the degree of Bachelor of Pharmacy was carried out by Shahrin Arby (ID: 2014-1-70-035).

.....……..

Dr. Chowdhury Faiz Hossain

Professor and Chairperson

Department of Pharmacy

East West University, Dhaka.

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Abstract

A brand of Cetirizine Dihydrochloride, a photosensitive drug, was chosen to test the photolytic degradation under accelerated condition. Tablets were taken from the same batch of Sarcet® and exposed to different lighting conditions- Direct sunlight, 25 watt bulb and 40 watt bulb- for a defined period. A group of tablet was kept in dark as control to compare the result. Physical parameter and potency of the tablets were determined by weight variation test measured according to USP and no significant change was found. Potency test was performed by UV spectroscopy at 230nm wavelength showed gradual decline in potency of the tablet. Percent variation in potency in case of 25 watt bulb, 40 watt bulb and sunlight exposed tablets was 3.77%, 8.35%, 11.14% respectively. So it can be suggested to protect the drug from photolytic decomposition making the packaging opaque which may be an effective way.

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CHAPTER 1

INTRODUCTION

The objective of the research was to determine the potency reduction of Cetirizine which is a photosensitive drug. So, it degrades in the presence of light. To prevent this degradation it should be packaged in opaque packaging so that, light cannot pass through it. But several companies do not make the packaging opaque for Cetirizine. A brand of Cetirizine, Sarcet® of White Horse Pharmaceuticals, was chosen for the research project and was exposed to different lighting conditions for the determination of efficiency of blister packing to prevent its photodegradation.

1.1 **Antihistamines:** (Chm.bris.ac.uk, 2008)

Antihistamines are drugs that block the action of histamine (a compound released in allergic inflammatory reactions) at the H1 receptor sites, responsible for immediate hypersensitivity reactions such as sneezing and itching. Members of this class of drugs may also be used for their side effects, including sedation and antiemesis (prevention of nausea and vomiting).

Histamine Receptors

Histamine receptors are proteins situated in various parts of the body that bind with histamine to produce a specific effect on the organism. There are four known receptors, designated H1 - H4. The receptor that the histamine reacts with is dependent upon where the histamine is released in the body.

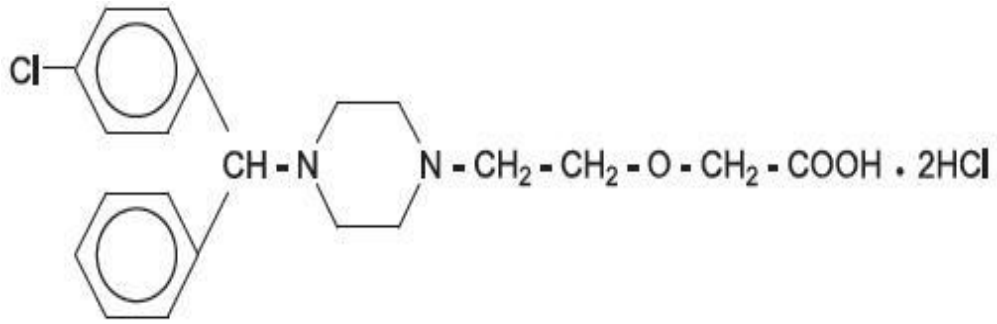
- H1: These are one of the most important receptors for modulating internal clock, and are a main target for many clinical drugs. When histamine reacts with these receptors in your brain (see image, right), it alters your neurochemistry to make you more awake and alert. This is why antihistamines cause drowsiness, as they oppose the reaction of histamine with the H1 receptors. Stimulation of these receptors causes hives (skin rashes), broncho-constriction, motion sickness, separation of the cell-lining of blood vessels, and smooth muscle relaxation.
- H2: These are found on parietal cells located in the stomach lining, and are mainly responsible for regulating the levels of gastric acid. Histamine action at these receptors

stimulates the release of gastric acid, excess of which can result in gastroenteritis. These receptors are also found on heart, uterus and vascular smooth muscle cells.

- H3: These are present throughout the nervous system, though most notably in the central nervous system. They regulate histamine in the body, by inhibiting the further synthesis of histamine.
- H4: Discovered in 2001, these receptors regulate the levels of white blood cell release from bone marrow. They have also been show to direct mast cells. They are located in the thymus, small intestine, spleen, the colon, bone marrow and basophils.

1.2 Structure of Cetirizine Dihydrochloride: (Drugs.com, 2017)

Cetirizine Dihydrochloride is an orally active and selective H1-receptor antagonist. The chemical name is (±) - [2- [4- [(4-chlorophenyl) phenylmethyl] -1- piperazinyl] ethoxy]acetic acid, dihydrochloride. Cetirizine Dihydrochloride is a racemic compound with an empirical formula of $C_{21}H_{25}ClN_2O_3 \cdot 2HCl$. The chemical structure is shown below:



Structure of cetirizine Dihydrochloride

1.2.1 physical properties of cetirizine Dihydrochloride: (Drugs.com, 2017)

- White in color
- Odorless
- Crystalline powder
- Molecular weight: 388.892g/mole

- Melting point 112.5 ºC
- Water solubility 101 mg/l
- Very soluble in water, chloroform, alcohol.

1.3 Mechanism of action of Cetirizine Dihydrochloride: (RIMMER and CHURCH, 1990)

Cetirizine, a human metabolite of hydroxyzine, is an antihistamine; its principal effects are mediated via selective inhibition of peripheral H1 receptors. The antihistaminic activity of Cetirizine has been clearly documented in a variety of animal and human models. In vivo and ex vivo animal models have shown negligible anticholinergic and anti-serotonergic activity. In clinical studies, however, dry mouth was more common with Cetirizine than with placebo. In vitro receptor binding studies have shown no measurable affinity for other than H1 receptors. Autoradiographic studies with radiolabeled Cetirizine in the rat have shown negligible penetration into the brain. Ex vivo experiments in the mouse have shown that systemically administered Cetirizine does not significantly occupy cerebral H1 receptors.

1.4 pharmacological properties of Cetirizine Dihydrochloride: (Drugs.com, 2017)

1.4.1 Pharmacokinetics:

a) Absorption

Cetirizine was rapidly absorbed with a time to maximum concentration (Tmax) of approximately 1 hour following oral administration of tablets or syrup in adults. Comparable bioavailability was found between the tablet and syrup dosage forms. When healthy volunteers were administered multiple doses of Cetirizine (10 mg tablets once daily for 10 days), a mean peak plasma concentration (Cmax) of 311 ng/mL was observed. No accumulation was observed. Cetirizine pharmacokinetics were linear for oral doses ranging from 5 to 60 mg. Food had no effect on the extent of Cetirizine exposure (AUC) but Tmax was delayed by 1.7 hours and Cmax was decreased by 23% in the presence of food.

b) Distribution

The mean plasma protein binding of Cetirizine is 93%, independent of concentration in the range of 25–1000 ng/mL, which includes the therapeutic plasma levels observed.

c) Metabolism

A mass balance study in 6 healthy male volunteers indicated that 70% of the administered radioactivity was recovered in the urine and 10% in the feces. Approximately 50% of the radioactivity was identified in the urine as unchanged drug. Most of the rapid increase in peak plasma radioactivity was associated with parent drug, suggesting a low degree of first-pass metabolism. Cetirizine is metabolized to a limited extent by oxidative O-dealkylation to a metabolite with negligible antihistaminic activity. The enzyme or enzymes responsible for this metabolism have not been identified.

d) Elimination

The mean elimination half-life in 146 healthy volunteers across multiple pharmacokinetic studies was 8.3 hours and the apparent total body clearance for Cetirizine was approximately 53 mL/min.

1.4.2 Pharmacodynamics: (Drugs.com, 2017)

Cetirizine Dihydrochloride at doses of 5 and 10 mg strongly inhibited the wheal and flare caused by intradermal injection of histamine in 19 pediatric volunteers (aged 5 to 12 years) and the activity persisted for at least 24 hours. In a 35-day study in children aged 5 to 12, no tolerance to the antihistaminic (suppression of wheal and flare response) effects of Cetirizine Dihydrochloride was found. In 10 infants 7 to 25 months of age who received 4 to 9 days of Cetirizine in an oral solution (0.25 mg/kg bid), there was a 90% inhibition of histamine-induced (10 mg/mL) cutaneous wheal and 87% inhibition of the flare 12 hours after administration of the last dose. The clinical relevance of this suppression of histamine-induced wheal and flare response on skin testing is unknown.

The effects of intradermal injection of various other mediators or histamine releasers were also inhibited by Cetirizine, as was response to a cold challenge in patients with cold-induced urticaria. In mildly asthmatic subjects, Cetirizine Dihydrochloride at 5 to 20 mg blocked bronchoconstriction due to nebulized histamine, with virtually total blockade after a 20-mg dose. In studies conducted for up to 12 hours following cutaneous antigen challenge, the late phase recruitment of eosinophils, neutrophils and basophils, components of the allergic inflammatory response, was inhibited by Cetirizine Dihydrochloride at a dose of 20 mg.

1.5 Dosage form of Cetirizine Dihydrochloride: Tablet, Syrup

1.5.1 Route of Administration: Oral

1.6 Indication of Cetirizine Dihydrochloride: (Drugs.com, 2017)

- Hay fever
- Upper respiratory allergies such as stuffy nose; runny nose; sneezing; itching of the nose and throat; and itchy,
- Watery eyes
- Chronic hives

1.7 Cetirizine Dosage and Administration: (Drugs.com, 2017)

Cetirizine Dihydrochloride Syrup can be taken without regard to food consumption.

- Children 2 to 5 years for Chronic Urticaria

The recommended initial dose of Cetirizine Dihydrochloride syrup in children aged 2 to 5 years is 2.5 mg (½ teaspoon) syrup once daily. The dosage in this age group can be increased to a maximum dose of 5 mg per day given as 1 teaspoonful syrup once a day, or one ½ teaspoonful syrup given every 12 hours.

- Children 6 months to <2 years for Perennial Allergic Rhinitis and Chronic Urticaria

The recommended dose of Cetirizine Dihydrochloride syrup in children 6 months to 23 months of age is 2.5 mg (½ teaspoonful) once daily. The dose in children 12 to 23 months of age can be increased to a maximum dose of 5 mg per day, given as ½ teaspoonful (2.5 mg) every 12 hours.

1.8 Cetirizine side effects: (Drugs.com, 2017)

- fast, pounding, or uneven heartbeat;
- weakness, tremors (uncontrolled shaking), or sleep problems (insomnia);
- severe restless feeling, hyperactivity;
- confusion;
- problems with vision; or
- urinating less than usual or not at all.

Less serious side effects may include:

- dizziness, drowsiness;
- tired feeling;
- dry mouth;
- sore throat, cough;
- nausea, constipation; or
- headache.

1.8.1 Contraindication: (Drugs.com, 2017)

If someone is allergic to any ingredient in cetirizine or to hydroxyzine should contact doctor or health care provider right away if any of these applied.

1.8.2 Precaution: (Drugs.com, 2017)

Some medical conditions may interact with cetirizine. Patient should tell doctor or pharmacist if he/she have any medical conditions, especially if any of the following applied on them:

- The patient is pregnant, planning to become pregnant, or are breast-feeding
- taking any prescription or nonprescription medicine, herbal preparation, or dietary supplement
- allergies to medicines, foods, or other substances
- kidney or liver problems or are receiving dialysis

1.8.3 Drug interaction: (Drugs.com, 2017)

Some medicines may interact with cetirizine. Tell your health care provider if you are taking any other medicines, especially any of the following:

Perampanel or theophylline because they may increase the risk of cetirizine's side effects. This may not be a complete list of all interactions that may occur. Ask your health care provider if cetirizine may interact with other medicines that you take. Check with your health care provider before you start, stop, or change the dose of any medicine.

1.8.4 Cetirizine toxicity: (Drugs.com, 2017)

Toxicity has been reported with Cetirizine Dihydrochloride. In one adult patient who took 150 mg of Cetirizine Dihydrochloride, the patient was somnolent but did not display any other clinical signs or abnormal blood chemistry or hematology results. In an 18 month old pediatric patient who took an overdose of Cetirizine Dihydrochloride (approximately 180 mg), restlessness and irritability were observed initially; this was followed by drowsiness. Should overdose occur, treatment should be symptomatic or supportive, taking into account any concomitantly ingested medications. There is no known specific antidote to Cetirizine Dihydrochloride. Cetirizine Dihydrochloride is not effectively removed by dialysis, and dialysis will be ineffective unless a dialyzable agent has been concomitantly ingested. The acute minimal lethal oral doses were 237 mg/kg in mice (approximately 95 times the maximum recommended daily oral dose in adults on a mg/m2 basis, or approximately 40 times the maximum recommended daily oral dose in infants on a mg/m2 basis) and 562 mg/kg in rats (approximately 460 times the maximum recommended daily oral dose in adults on a mg/m2 basis, or approximately 190 times the maximum recommended daily oral dose in infants on a mg/m2

basis). In rodents, the target of acute toxicity was the central nervous system, and the target of multiple-dose toxicity was the liver.

1.9 Photodegradation: (Mead et al., 2014)

It is the process by which light sensitive drugs or excipient molecules are chemically degraded by light, room light, or sunlight. The variation of degradation depends on the wavelength of light, shorter wavelengths because more damage than longer wavelengths. Before a photodegradation reaction can occur, the energy from light radiation must be absorbed by the molecules.

Two important factors should be considered in relation to the potential of a drug to be degraded following absorption of electromagnetic radiation. First, the absorption spectrum is normally described by the maximum absorption wavelength and the molar absorptivity at that wavelength; however, the spectrum of a drug molecule is usually broad, and any overlap of the absorption spectrum with the output of the photon source impinging upon it has the potential to lead to photochemical change. Second, the decomposition may be initiated by another component of the formulation that has absorption characteristics that overlap with the incident radiation while the therapeutic component does not. In this case, the process is called photosensitization and the absorbing component, or photosensitizer, may transfer the absorbed energy completely and not be altered in the process (although it is more likely that it will undergo some degradation).

A catalogue of the most common reaction types shows that, following light absorption, a drug might experience:

- Addition
- Cyclization
- N-Dealkylation
- Decarbonylation
- Decarboxylation
- Dehalogenation

- Dimerization
- Oxidation
- Reduction
- Isomerization
- Rearrangement
- Hydrolysis

CHAPTER 2

LITERATURE REVIEW

A literature review was done to provide a thorough introduction on the photolytic degradation of Cetirizine Dihydrochloride which presents all the analyses and findings of the previous studies. It was observed that studies done on Cetirizine Dihydrochloride were similar to the current research work. The findings of the current research can then be compared and contrasted with previous findings and used as takeoff point for further research. A gist of some studies is given below:

In the year of 2005, a prospective method capillary electrophoresis (CE) was developed for the chiral analysis of a drug cetirizine (CET). Various separation mechanisms were applied and several parameters affecting the separation were studied, including the type and concentration of chiral selector, coselector, and carrier ion, and pH of buffer. The proposed method was successfully applied to the enantioselective assay of CET in pharmaceutical formulations using fexofenadine (FEX) as an internal standard. (Mikuš, Valášková and Havránek, 2005)

Then at 2007, Capillary electrophoresis (CE) and high-performance liquid chromatography (HPLC), were used for analysis of cetirizine dihydrochloride in small sample volumes of human plasma were compared. The CE and HPLC assays were developed and validated by analyzing a series of plasma samples containing cetirizine dihydrochloride in different concentrations using these two methods. The extraction procedure is simple and no complicated purification steps or derivatization are required. Both methods were selective, robust and specific, allowing reliable quantification of cetirizine dihydrochloride. (Kowalski and Plenis, 2007)

Then in the next year at 2008, a rapid reversed-phase HPLC method was used for the determination of antihistaminic-decongestant pharmaceutical dosage forms containing binary mixtures of pseudoephedrine Dihydrochloride (PSE) with fexofenadine Dihydrochloride (FEX) or cetirizine dihydrochloride (CET). The chromatographic separation of PSE, FEX and CET was achieved on a Zorbax column using UV detection at 218 and 222 nm. The optimized mobile

phase was consisted of TEA solution (0.5%, pH 4.5)–methanol–acetonitrile (50:20:30, v/v/v). The proposed method was found to be specific, accurate. (Karakuş, Küçükgüzel and Küçükgüzel, 2008)

A research was accomplished for simultaneous estimation of Ambroxol Dihydrochloride and Cetirizine Dihydrochloride in tablets. Ambroxol Dihydrochloride (λmax 243) and Cetirizine Dihydrochloride (λmax 229) were examined under UV spectrophotometer. Results of recovery studies given as percentage of label claim ± relative standard deviation were found to be 99.88 ± 0.3811 and 100.36 ± 2.0480 for Ambroxol Dihydrochloride and Cetirizine Dihydrochloride respectively. (Bhatia, Ganbavale and Nivrutti, 2008)

Another research was done for the analysis and chiral discrimination of cetirizine. The first method was based on the enantioseparation of cetirizine on silica gel TLC plates using different chiral selectors as mobile phase additives. The second method was a validated high performance liquid chromatography (HPLC), based on stereoselective separation of cetirizine and quantitative determination of its eutomer (R)-levocetirizine on a monolithic C18 column using hydroxypropyl-β-cyclodextrin as a chiral mobile phase additive. The third method used a 1H-NMR technique to characterize cetirizine and (R)-levocetirizine. These methods are selective for determination of cetirizine in drug substance and drug product in quality control laboratory. (Elham A. Taha, Salama and Wang, 2009)

After that in 2010, the objective of this study was to determine Cetirizine dihydrochloride in tablets and compounded capsules by a comparative study between capillary electrophoresis (CE) method and high performance liquid chromatography (HPLC). The proposed method was compared with the high performance liquid chromatographic (HPLC) method previously validated for this drug and the result given as statistical analysis showed no significant difference between the techniques. (Bajerski et al., 2010)

In the same year a prospective method was developed for the determination of reaction between active drug substances and excipients in the drug formulation. The drug substance cetirizine was chosen as the model substance as it is already marketed. Among the marketed products are oral solutions and oral drops containing excipients like sorbitol and glycerol. It was found that the carboxylic acid cetirizine readily reacts with sorbitol and glycerol to form monoesters at a temperature as low as 40 °C. The studies of the reaction revealed that the esters were unstable and they degraded especially at higher temperatures. (Yu et al., 2010)

In this analysis a method was developed to manage the post burn each with antihistamines and emollients but the treatment was ineffective in a large percentage of patients. For this method gabapentin, cetirizine and their combination was used in relieving itch. Twenty patients were randomly recruited and administered the respective drug(s) in doses. VAS scores were evaluated over next 28 days (days 3, 7, 14, 21 and 28), and no emollients were prescribed for the study period. The initial mean VAS score reduced 95% in gabapentin group compared to 52% for the cetirizine group, which was highly significant ($p < 0.01$). There was a 94% reduction in mean VAS score in the combination group which was comparable to the relief observed with gabapentin alone ($p > 0.05$). So, from this study the result was gabapentin is significantly better than cetirizine as monotherapy in relieving post-burn itch and it also has a faster action. (Ahuja et al., 2011)

For this study a method was developed to demonstrate the efficacy and safety of bilastine 20mg compared to cetirizine Dihydrochloride 10mg and placebo in patients with perennial allergic rhinitis (PAR). In this study, patients with symptomatic PAR ($n = 650$) received bilastine 20 mg, cetirizine 10 mg, or placebo once daily for 4 weeks. The primary efficacy outcome was the mean area under the curve (AUC) of reflective total 6-symptom scores (rT6SS) from baseline visit to day 28 (D28). Secondary outcome measures included mean AUC of instantaneous total 6-symptom scores (iT6SS), and mean AUCs of reflective and instantaneous total 4-nasal symptom scores (T4NSS) and total 2-ocular symptom scores (T2OSS) from baseline to D28. The result

was no significant differences in efficacy outcomes were found between active treatments and placebo. (Sastre et al., 2011)

For this research work high performance liquid chromatography (HPLC) method was developed for the determination of cetirizine Dihydrochloride (CTZ) in tablets using CLC-ODS reverse phase column (4.6 × 250 mm, 5 µm). Salicylic acid was used as internal standard. A mixture of methanol and water of 70:30 with pH 4 was used as mobile phase. The eluents were detected at 231 nm. The result given as CTZ was found to be stable at accelerated condition of temperature and relative humidity after storage of six months. (Khan et al., 2011)

A randomised, placebo controlled study was conducted to determine the pharmacokinetics and efficacy in reducing dermatitis in horses with insect bite. Cetirizine given orally at 0.4 mg/kg twice daily for 3 weeks. The influence of protection blankets and stabling were also investigated. The findings indicated that cetirizine was of no apparent benefit in treating IBH at the dose rate tested. The use of blankets and stabling were shown to have favourable influence on the dermatitis. (Olsén et al., 2011)

This study was done to determine the effects of cetirizine on bone modeling processes during orthodontic tooth movement. 3 groups of Wistar rats were used: control group (n = 16), appliance-only group (n = 16) and cetirizine group (n = 16). Each animal of the last 2 groups was fitted with a superelastic closed-coil spring appliance and treated daily with saline solution or cetirizine. Tooth movement was measured weekly from day 0 to day 42. The result was, Cetirizine influences bone modeling, mainly by inhibiting bone resorption. (Meh et al., 2011)

Two simple methods were developed for simultaneous estimation of Phenylephrine Dihydrochloride and Cetirizine Dihydrochloride. First method, employs formation and solving of simultaneous equation using 237.5 nm and 232.0 nm as the λmax of Phenylephrine Dihydrochloride and Cetirizine Dihydrochloride respectively in distilled water. Second method is first order derivative spectroscopy, wavelengths selected for quantitation were 232.0 nm for

Phenylephrine Dihydrochloride and 242.5 nm for Cetirizine Dihydrochloride. The result was without resolving mixtures of Cetirizine Dihydrochloride and Phenylephrine Dihydrochloride, simultaneous estimation has been successfully achieved by spectrophotometry. (Wankhede, Lad and Chitlange, 2012)

The purpose of the research work was the development and optimization of a Gum tragacanth–acrylic acid based hydrogel for in situ release of cetirizine dihydrochloride under different pH conditions such as 2.0, 7.0 and 9.2 at 37 °C. Various process variables like solvent, temperature, pH, treatment time, concentration of monomer and cross-linker were screened using a fractional factorial design approach. These significant parameters (solvent, pH and monomer) are further optimized using center composite design. The result showed that initial diffusion coefficient has a greater value than the later diffusion coefficient indicating a higher drug release rate during the early stage. (Kaith, Jindal and Bhatti, 2012)

In this study, the efficacy of intranasal Botulinum Toxin-A (BTX-A) to cetirizine in the treatment of allergic rhinitis (AR) was compared. Fifty AR patients at the age of 26.2 ± 9.1 years (64% females), were recruited to the trial according to the Allergic Rhinitis and its Impact on Asthma (ARIA) criteria. Participants randomly received either intranasal injection of BTX-A (75IU Dysport®) or cetirizine (10mg/day). The result was nasal injection of BTX-A shows the same therapeutic effects as cetirizine in the management of AR. (Hashemi et al., 2013)

This study evaluates the thermal degradation of two drug samples (cetirizine and simvastatin) by differential scanning calorimetery (DSC) and simultaneous differential thermal analysis (DTA) techniques. The results of TG analysis revealed that the main thermal degradation for the cetirizine occurs during two temperature ranges of 165–227 and 247–402 °C and the main thermal degradation for the simvastatin occurs during two endothermic behaviors in the temperature ranges of 238–308 and 308–414 °C. (Sovizi and Hosseini, 2013)

A high performance thin layer chromatography (HPTLC)-densitometric method was developed for separation and determination of cetirizine (CET) and montelukast (MON) in pharmaceutical dosage forms. UV detection was performed at 230 nm. Quantitative analysis was performed by absorbance densitometry using peak area. It was observed that the proposed HPTLC method could be used for efficient analysis and monitoring of the CET and MON in combined tablet dosage forms. (Haghighi et al., 2013)

In the same year, an enantioselective method was developed to analyze hydroxyzine and cetirizine. A dispersive liquid–liquid microextraction (DLLME) procedure was optimized to extract these analytes from liquid culture medium. The study shown to be stereoselective with predominant formation of (S)-cetirizine. (Fortes et al., 2013)

A high performance liquid chromatographic (HPLC) method was developed for simultaneous determination of ketotifen fumarate and cetirizine dihydrochloride in solid dosage forms. Chromatographic separation was achieved on Grace Smart C18 column (250 × 4.6 mm, 5 μm) using an isocratic mobile phase that consisted of acetonitrile and 10 mM disodium hydrogen phosphate buffer (pH 6.5) in a ratio of 45:55 % v/v at a flow rate of 1 mL/min. Detection was carried out at 230 nm. Salbutamol sulphate was used as an internal standard. In conclusion, the developed method is specific and stability-indicating as no interfering peaks of degradants and excipients were observed. (Kabra, Nargund and Murthy, 2014)

The purpose of this method was to develop the invitro interaction of cetirizine and non-steroidal anti-inflammatory drugs (NSAIDs) by A high-throughput HPLC method. This method was validated in the presence of NSAIDs and was further used to study the interactions of cetirizine in the presence of NSAIDs at four different pH levels. Purospher Star, C18 column (5 μm, 25 cm × 0.46 cm) with a mobile phase of methanol/water (90:10 v/v, pH adjusted to 3.5) at a flow rate of 1.0 mL/min and a wavelength of 240 nm was used. Complexes were characterized using infrared (IR) and nuclear magnetic resonance (NMR) techniques. (Shamshad, Arayne and Sultana, 2014)

In the same year, a novel technique of laccase enzyme as a catalyst under the influence of ultrasound irradiation used for the degradation of Cetirizine dihydrochloride. Effect of various process parameters such as enzyme loading, temperature, power, duty cycle, frequency and speed of agitation has been studied along with identification of the degradation intermediates. The result was, maximum degradation obtained in ultrasound assisted enzymatic degradation and also reduces the time of degradation as compared to conventional enzymatic degradation technique. (Sutar and Rathod, 2014)

This prospective study explained the fetal safety of cetirizine. Pregnant women who were counselled by the 'Motherisk Program' regarding cetirizine exposure were enrolled in a cohort study and compared with pregnant women counselled for non-teratogenic exposures. A meta-analysis of cohort studies was also conducted that examined the pregnancy outcomes of women exposed to hydroxyzine or cetirizine during pregnancy. In the cohort study, there were no significant differences in the rates of major malformations between the cetirizine exposed and comparison group. In the meta-analysis, cetirizine was not associated with increased teratogenic risk. (Etwel et al., 2014)

In the year of 2015, A high-performance liquid chromatography–diode array detection (HPLC–DAD) procedure was used for the analysis of phenylephrine Dihydrochloride (PHE), paracetamol (PAR), caffeine anhydrous (CAF), cetirizine Dihydrochloride (CET), nimesulide (NIM) in pharmaceutical mixture. The result was effective chromatographic separation of PHE, PAR, CAF, CET and NIM was achieved using a Kinetex-C18 (4.6 mm, 150 mm, 5 mm) column with gradient elution of the mobile phase composed of 10 mM phosphate buffer (pH 3.3) and acetonitrile. (Dewani et al., 2015)

In this study, liquid chromatography coupled with high-resolution mass spectrometry (LC/HRMS) was applied to capture the characteristic features of the impurity profile for three

brands of marketplace Cetirizine tablets, using full scan data-dependent MS/MS scan mode (FS-ddMS2). In conclusion, 16 differential impurities were finally found, their structures were speculated by HRMS2 data. (Zhou, 2016)

This research was done to investigate the effect of cetirizine on P-gp function and expression in vitro and in situ. The in-vitro rhodamin-123 (Rho123) efflux assay in Caco-2 cells was used to study the effect of cetirizine on P-gp function. Western blot analysis was used for surveying the effect of cetirizine on expression of P-gp in Caco-2 cells. Rat in situ single-pass intestinal permeability technique was used to calculate the intestinal permeability of a known P-gp substrate (digoxin) in the presence of cetirizine. Therefore, it is concluded that cetirizine is a P-gp inhibitor and this should be considered in co administration of cetrizine with other P-gp substrate drugs. (Abbasi et al., 2016)

This study explained that the UV/S2OView the MathML source system was applied for degradation of cetirizine dihydrochloride (CTZ) from aqueous waste and toxicity was analyzed. More than 95% CTZ was degraded within 90 min of UV irradiation. The studied process enhanced the biodegradability, BOD5/COD ratio from 0.15 to 1.94 of the aqueous wastewater. The sulfate radical generated from the photochemical decomposition of S2OView the MathML source showed that this system is a kinetically favorable process in removing cetirizine Dihydrochloride from aqueous waste along with reduction of toxicity. (Gadipelly, Rathod and Marathe, 2016)

Another prospective study was done in the same year with a simple capillary electrophoresis (CE) method for chiral separation and quantitation of zwitterionic cetirizine (CTZ), as the main metabolite of hydroxyzine (HZ), and HZ has been developed. In addition, the effect of zwitterionic property of CTZ on enantioseparation was investigated. Maltodextrin, as a chiral selector was used and several parameters affecting the separation such as pH of BGE, were studied. Results showed that, compared to HZ, pH of BGE was an effective parameter in enantioseparation of CTZ due to the zwitterionic property of CTZ. (Nojavan and Fakhari, 2016)

This study purposed the effectiveness of 4 allergic rhinitis (AR) drugs (loratadine, cetirizine, montelukast, and desloratidine) in reducing functional problems in patients, as indicated by rhinoconjunctivitis. After a multistep screening and elimination process, a total of 13 randomized controlled trials contributed to this network meta-analysis on 4 different medications. In conclusion, a comparison of these 4 interventions clearly showed that cetirizine is the most optimal medication for AR treatment. (MM et al., 2016)

In 2017, a successful study explained that Cetirizine 10mg effectively relieves subjects' worst seasonal allergic rhinitis (SAR) symptom(s). A posthoc analysis of data from randomized controlled trials (RCTs) was conducted to evaluate the efficacy of oral cetirizine 10mg. Subjects (aged >_12 years), rated severity for 5 or 6 symptoms, daily in 2-week RCTs of cetirizine 10mg or placebo for SAR symptom relief. Of these symptoms, those with the highest baseline score were predefined as the individual's worst symptom(s) in the posthoc analysis. (Harshini et al., 2017)

CHAPTER 3

MATERIALS & METHODS

3.1 MATERIALS

3.1.1 Sample Collection

For the purpose of experimentation to observe the photolytic degradation of Cetirizine Dihydrochloride, 500 tablets of Sarcet® (Cetirizine Dihydrochloride 10mg) were collected from the local drug store in Dhaka as a sample. All the tablets were from the same batch (167610). Among them 200 tablets were kept light protected for control tests and the remaining 300 tablets were subjected to various lighting conditions over certain periods of time for conducting experiments to determine their potency.

3.1.2 Samples

Table 3.1: Samples used in the experiment including source (The White Horse Pharmaceuticals, 2012)

Sample Name	Source (Supplier Name)	Batch No.
Sarcet® Tablets	The White Horse Pharmaceuticals	167610

Figure 3.1: Sarcet®10 mg tablet

3.1.3 Reagents

Reagents Name	**Source (Supplier Name)**
Concentrated H_2SO_4 (98% / 36.8N)	Analar, United Kingdom
Distilled Water	Laboratory (East West University)

Table 3.2: Reagents used in the experiment including source

3.1.4 Equipments& Instruments

Table 3.3: Lists of equipments used for the experiment

Serial No.	**Equipment**	**Source (supplier name)**	**Origin**
1	UV-Spectrophotometer	Shimadzu UV1800	Japan
2	Distill Water Plant	Bibby Scientific W4000	United Kingdom
3	Electronic Balance	Shimadzu AY220	Japan

3.1.5 Images of Instruments

Some of the important instruments those were used in different tests during research work.

Figure 3.2: Shimadzu UV-1800 Double Beam Spectrophotometer and Electronic Balance [Left to right]

3.1.6 Apparatus

Some technical equipment or machinery needed for a particular activity or research work. Apparatus may refer to machine, equipment and critical apparatus. Some apparatus are listed in the following table those were widely used throughout the experiments and research work.

Table 3.4: List of Apparatus used throughout this project

Serial No.	Apparatus
1	Funnel
2	Spatula
3	Beakers
4	Forceps
5	Test tubes

6	Glass Rod
7	Table Lamp
8	Pipette (5 ml)
9	Filter Papers
10	Masking Tap
11	Thermometer
12	Pipette pumper
13	Plastic Dropper
14	Test tube Holder
15	Mortar & Pestles
16	Plastic Containers
17	Aluminum foil paper
18	Electric Bulb (25 Watt & 40 Watt)
19	Volumetric Flasks (50 ml, 250ml & 1000 ml)

3.2 METHOD

3.2.1 Preparation of the solvent (0.1N H_2SO_4)

1. Lab solvent (H_2SO_4), stock solution with 98% (v/v) of strength was collected.

2. Then the concentration of the lab solvent stock solution was determined in normality where the specific gravity of solvent is 1.84.

Determination of the Concentration of the Lab Solvent (H_2SO_4) in Normality (N):

100 ml of the lab solvent stock solution contains = 98ml of H_2SO_4

100 ml of lab solvent stock solution contains = (98 x 1.84)gm of H_2SO_4

= 180.32gm of H_2SO_4

1000 ml of stock solution contains = (180.32 x 1000)/100 gm of H_2SO_4

= 1803.2gm of H_2SO_4

1000 ml of stock solution contain 49gm of H2SO4 = 1N of H_2SO_4

1000 ml of stock contain 1803.2gm of H2SO4 = (1803.2/49)N ofH_2SO_4

= 36.8N ofH_2SO_4

3. After the determination of the concentration of the lab solvent stock solution in Normality (N), the amount of lab solvent (36.8N H_2SO_4) stock solution required to make 1000ml of 0.1N HCL solvent was calculated as below.

Determination of the amount of 36.8N H_2SO_4 required to make 1000ml of 0.1N H_2SO_4 by using the $V_1S_1 = V_2S_2$

Where

S_1 = Conc. of lab solvent (H_2SO_4) stock solution = 36.8N

S_2 = Final concentration of the solvent (H_2SO_4) = 0.1N

V_1 = Volume of the lab solvent (H_2SO_4) stock solution =?

V_2 = Final volume of the solvent (H_2SO_4) = 1000ml

So that,

$V_1 = (V_2S_2) / S_1$

⇨ V_1 = (1000ml x 0.1 N) / 36.8N

⇨ V_1 = 2.717ml (~ 2.72 ml of lab solvent H_2SO_4 stock solution)

4. Then 2.72ml of 36.8N H_2SO_4 was transferred from the lab solvent stock solution to a 1000ml volumetric flask which was then filled with water up to mark to make 1000ml of 0.1N H_2SO_4.

3.2.2 Determination of λ_{max} & Preparation of the Standard Curve of Cetirizine Dihydrochloride.

1. Standards of Cetirizine Dihydrochloridewas collected from a pharmaceutical company. The potency of standard compounds was 99.5%.
2. The specific λ_{max} for Cetirizine Dihydrochloride, at which the absorbance would be measured, was determined to be 230 nm from the UV spectrometer by using the standard. Five serial concentrations of the standards of Cetirizine Dihydrochloride were prepared for the purpose of creating a standard curve.

Preparation of the stock solution for Cetirizine Dihydrochloride using the standard :

10 mg of the standard compound, that is Cetirizine Dihydrochloride was weighed and dissolved in 250ml of 0.1N H_2SO_4 (which is the solvent) in a 250ml volumetric flask.

Thus the concentration was calculated to be:

Concentration of 1st dilution = Amount of substance added / volume = (10 / 250) mg/ml = 0.04 mg/ml

Preparation of five serial concentrations of solution for Cetirizine Dihydrochloride:

- ⇨ Cetirizine Dihydrochloridehad the concentration of its stock solution is 0.04 mg/ml.
- ⇨ Five serial concentrations that were prepared for Cetirizine Dihydrochloridewere as follows 0.005 mg/ml, 0.006 mg/ml, 0.007 mg/ml, 0.008 mg/ml and 0.009 mg/ml for a final volume of 10 ml.

- The amount of the solution that were required from the stock solution to prepare the above concentrations were calculated using $S_1V_1=S_2V_2$ formula, where S_1= initial strength or concentration, S_2= final strength or concentration, V_1= initial volume and V_2= final volume.
- Thus the following concentrations were prepared as such for Cetirizine Dihydrochloride as per the calculations provided below.

Table 3.5: Concentrations for preparation of Standard Curve of Cetirizine Dihydrochloride

Sample Name	Sample no.	Concentration(mg/ml)
Cetirizine Dihydrochloride	1	0.005
	2	0.006
	3	0.007
	4	0.008
	5	0.009

- $V_1= S_2V_2 / S_1$ = (0.005 x 10) / 0.04 = 1.25 ml of stock solution required to make 0.005 mg/ml concentration of the final solution of 10 ml (1.25 ml of stock solution + 8.75 ml of 0.1N H_2SO_4) of Cetirizine Dihydrochloride.

- $V_1= S_2V_2 / S_1$ = (0.006 x 10) / 0.04 = 1.5 ml of stock solution required to make 0.006 mg/ml concentration of the final solution of 10 ml (1.5 ml of stock solution + 8.5 ml of 0.1N H_2SO_4) of Cetirizine Dihydrochloride.

- ⇨ $V_1 = S_2V_2 / S_1$ = (0.007 x 10) / 0.04 = 1.75 ml of stock solution required to make 0.007 mg/ml concentration of the final solution of 10 ml (1.75 ml of stock solution + 8.25 ml of 0.1N H_2SO_4) of Cetirizine Dihydrochloride.

- ⇨ $V_1 = S_2V_2 / S_1$ = (0.008 x 10) / 0.04 = 2 ml of stock solution required to make 0.008 mg/ml concentration of the final solution of 10 ml (2 ml of stock solution + 8 ml of 0.1N H_2SO_4) of Cetirizine Dihydrochloride.

- ⇨ $V_1 = S_2V_2 / S_1$ = (0.009 x 10) / 0.04 = 2.25ml of stock solution required to make 0.009 mg/ml concentration of the final solution of 10 ml (2.25 ml of stock solution + 7.75 ml of 0.1N H_2SO_4) of Cetirizine Dihydrochloride.

3. Then the absorbance value was measured using a UV spectrophotometer against those five serial concentrations for Cetirizine Dihydrochloride.
4. A standard curve was plotted for Cetirizine Dihydrochloride.
5. From this standard curve a straight line equation was obtained which was in the form of y = mx+c, where the components of the equations are described as provided below:

m = gradient value, y = absorbance values, x = concentrations and c = y-intercept.

3.2.3 Sampling, Analysis by UV-Spectrophotometry & Determination of Potency of the pharmaceutical drugs (Cetirizine Dihydrochloride) under various lighting condition:

To determine the photo-stability of the drug (Cetirizine Dihydrochloride) in their packaging, the tablets were subjected to various types of light exposure, which were as follows:

- ⇨ Electric Bulb exposure (25 watt & 40 watt)
- ⇨ Direct Sunlight exposure

- **Under electronic bulb exposure (25W & 40W)**

1) 15 tablets were exposed to electric bulb lighting conditions for 5 hours at a stretch and 15 tablets were used as control.
2) After every 5 hours, 15 tablets were collected and wrapped up with foil paper to prevent any further exposure to the lighting condition and the temperature was noted using a thermometer.
3) The foil papers should be labeled to identify the intervals.
4) The tablets were then used for potency determination to see the effect of the exposure of bulb's lighting condition to drug ingredients.
5) For potency determination, laboratory analysis was done by using UV spectroscopy technique:

   a. First, 5 tablets from those sampled tablets were taken.
   b. Then the total weight of those 5 tablets was noted using an analytical balance and the average weight was calculated using the formula :

$$\text{Average weight (in grams)} = \frac{\text{Total weight of the tablets}}{\text{Total no. of tablets}}$$

   c. Then the 5 tablets were crushed by using mortar and pestle. Approximately the weight of 1 tablet of crushed tablet powder was taken and dissolved it in 250 ml of the solvent (0.1N H_2SO_4) for 3 times to prepare 3 samples.

d. After that 2 ml of that filtered solution was taken and dissolved in 8 ml of solvent.

e. From then 10ml of each sample was collected and kept into 3 different test-tube and wrapped it by foil paper.

f. From test-tube the solution was poured into a cuvette and was inserted into the UV spectrophotometer to observe the absorbance value.

Table 3.6: Electric Bulb (25W & 40W) Exposed Sample List

No. of samples	Collected sample	Withdrawal intervals(hrs)	Temperature (ºC)	
			25w	40w
15(Control)	15	0	26	28
15	15	5	32	35

6) Then the absorbance value was plotted into the standard curve to obtain the total amount of the drug that is present in one tablet.

7) 15 tablets were used as control and has not been exposed any of the lighting conditions.

N.B: Same procedure (steps 1 to 7) were used to determine the potency of the tablets under both exposure of 25W and 40W lighting condition for two different days for 5 hours each.

- **Under Sunlight condition**

1) 15 tablets were kept in a Glass box and exposed to sunlight condition for 7.5 hours at a stretch.

2) After 5 hours, 15 tablets were collected and wrapped up with foil paper to prevent any further exposure to the lighting condition and the temperature was noted using a thermometer.

3) The foil papers should be labeled to identify the intervals.

4) The tablets were then used for potency determination to see the effect of the exposure of sunlight condition to drug ingredients.

5) For potency determination, laboratory analysis was done by using UV spectroscopy technique:

    a. First, 5 tablets from those sampled tablets were taken.

    b. Then the total weight of those 5 tablets was noted using an analytical balance and the average weight was calculated using the formula:

$$\text{Average weight (in grams)} = \frac{\text{Total weight of the tablets}}{\text{Total no. of tablets}}$$

    c. Then the 5 tablets were crushed by using mortar and pestle.

    d. Approximately the weight of 1 tablet of crushed tablet powder was taken and dissolved it in 250 ml of the solvent (0.1N H_2SO_4) for 3 times to prepare 3 samples.

    e. After that 10 ml solution was filtered and 5 ml of that filtered solution was taken and dissolved in 50ml of the solvent.

    f. From then 10ml of each sample was collected and kept into 3 different test-tube and wrapped it by foil paper.

    g. From test-tube the solution was poured into a cuvette and was inserted into the UV spectrophotometer to observe the absorbance value.

Table 3.7: Sunlight Exposed Sample List

No. of Samples	Collected Sample	Withdrawal Intervals (hr)	Temperature (ºC)
15(control)	15	0	27
15	15	5	36

6. Then the absorbance value was plotted into the standard curve to obtain the total amount of the drug that is present in one tablet.

7. 10 tablets were used as control and has not been exposed any of the lighting conditions.

3.2.4 Determination of Physical parameter:

Weight Variation Test

Procedure

1. 10 tablets were taken and weighed.
2. The average was taken and it was considered as the standard weight of an individual tablet.
3. All the tablets were weighed individually and observed whether the individual tablets are within the range or not.

N.B: The variation from the average weight in the weights not more than two tablets must not differ more than the percentage listed below:

Table 3.8: Accepted percentage list for the weight variation test of tablets

Weight of tablet	Percentage difference
130 mg or less	±10%
More than 130 to 324 mg	±7.5%
More than 324 mg	±5%

Calculation

Following equation was used to determine % Weight Variation of tablets

% Weight Variation = (A~I/A) ×100 %

Where,

I = Initial Weight of Tablet, in gram/grams (gm)

A = Average weight of Tablet, in gram/grams (gm)

CHAPTER 4

RESULTS

4.1 Standard curve preparation

The standard was collected from The White Horse Pharmaceuticals and tried to make a standard curve. For different concentration of Cetirizine different absorption were recorded. Five serial concentrations of the standards of Cetirizine were prepared for the purpose of creating a standard curve. The results are as follows:

Table 4.1: Concentration & Absorbance for Standard Curve of Cetirizine

concentration	Absorbance
0.005	0.166
0.006	0.209
0.007	0.247
0.008	0.261
0.009	0.323

By plotting the absorbance against the concentration of cetirizine a straight line was found. From this an equation was derived where:

$$Y=39.341x-0.0263$$

$$R^2=0.9863$$

This equation was used to determine the concentration of cetirizine from different samples absorbance that was found in several lighting conditions.

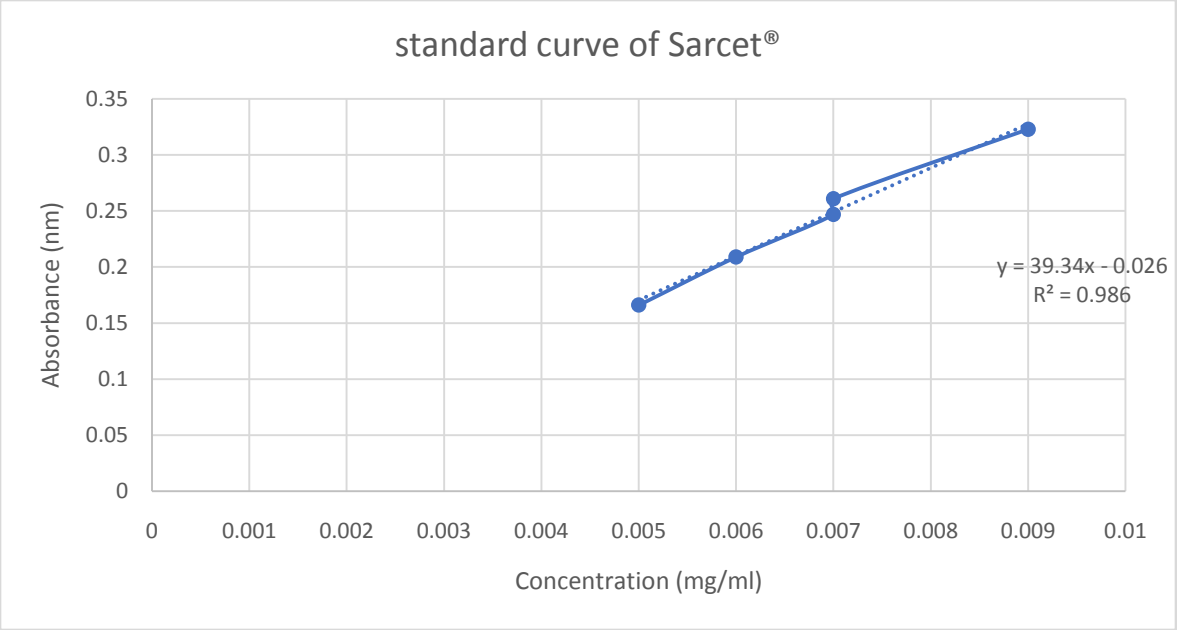


Figure 4.1: Plot showing straight line for absorbance with respect to concentration for Cetirizine

4.2 Physical parameter Test

4.2.1 Weight variation test

Table 4.2: Results of weight variation test for Cetirizine®

Table No.	Initial weight of tablet (g), I	Average weight of tablet (g), A	% weight variation (A-I)/I×100
1	0.1075	0.1096	2.018
2	0.1096		0.063
3	0.1091		0.522
4	0.1128		-2.77
5	0.1134		-3.289
6	0.1079		1.640
7	0.1094		0.246
8	0.1088		0.799
9	0.1086		0.985
10	0.1096		0.063

4.3 Result from Potency Determination by UV- spectroscopy

4.3.1Result of samples that were exposed under 25W bulb

In experimental day, a tablet strip containing 15 tablets was taken and 5 tablets were collected for the test and observed 3 different absorbance of cetirizine for three samples (A, B, C) exposed under the lamp (25W bulb); each for 5 hours' time interval and it was observed that the concentration of cetirizine was declined in each time interval.

Table 4.3: Concentration & Absorbance for Cetirizine (Sarcet®)

Test type	Initial potency %	Potency after 5 hours %	Potency decrease	Mean potency decrease of each formulation	Standard deviation +/- of each formulation	Mean potency decrease	Standard deviation +/- (%)
Sample1A	**100.02**	**95.4**	**4.62**	**4.01**	**0.547**	**3.77**	**0.281**
Sample2A	**99.62**	**96.05**	**3.55**				
Sample3A	**98.88**	**96**	**3.88**				
Sample1B	**98.7**	**95.2**	**3.5**	**3.46**	**0.740**		
Sample2B	**98.92**	**96.21**	**2.71**				
Sample3B	**99**	**94.81**	**4.19**				
Sample1C	**99.32**	**94.21**	**5.11**	**3.84**	**1.109**		
Sample2C	**98.33**	**95.3**	**3.03**				
Sample3C	**99.21**	**95.81**	**3.4**				

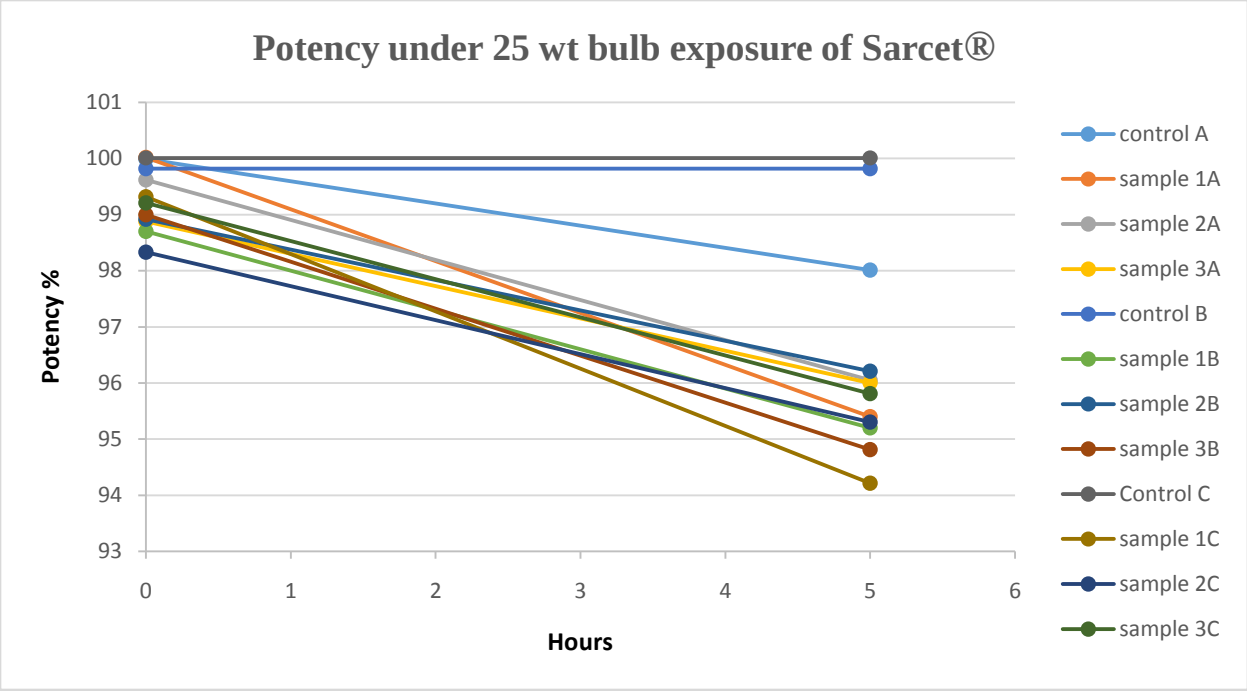


Figure 4.2: Difference in concentration after 5 hours time interval for cetirizine

4.3.2 Result of samples that were exposed under 40W bulb

In experimental day, a tablet strip containing 15 tablets was taken and 5 tablets were collected for the test and observed 3 different absorbance of cetirizine for three samples exposed under the lamp (40W bulb); each for 5 hours' time interval and it was observed that the concentration of cetirizine was declined in each time interval.

Table 4.4: Concentration & Absorbance for Cetirizine (Sarcet®)

Test type	Initial potency %	Potency after 5 hours %	Potency decrease	Mean potency decrease of each formulation	Standard deviation +/- of each formulation	Mean potency decrease	Standard deviation +/- (%)
Sample1A	100.03	91.6	8.43	8.41	1.090	8.35	0.121
Sample2A	99.5	90	9.5				
Sample3A	99.92	92.6	7.32				
Sample1B	99.67	90.9	8.77	8.21	2.33		
Sample2B	100.02	89.8	10.22				
Sample3B	100.05	94.4	5.65				
Sample1C	99.8	90.1	9.7	8.43	1.11		
Sample2C	99.61	92	7.61				
Sample3C	99.5	91.5	8				

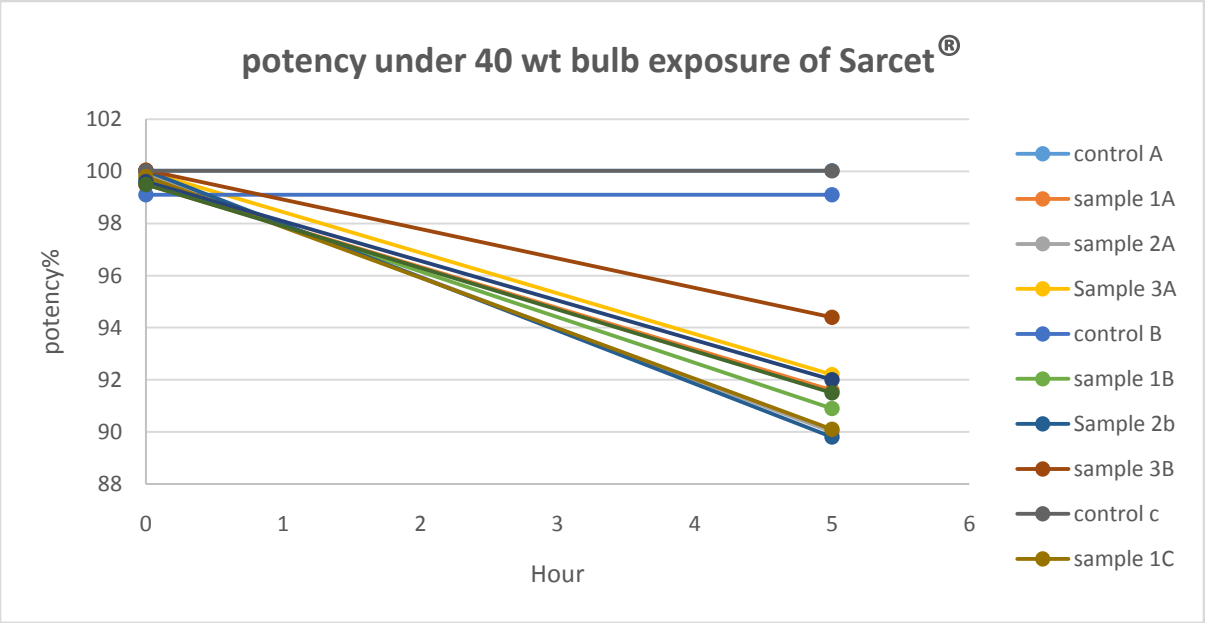


Figure 4.3: Difference in concentration after 5 hours time interval for cetirizine

4.3.3 Result of samples that were exposed under direct sunlight

In experimental day, a tablet strip containing 15 tablets was taken and 5 tablets were collected for the test and observed 3 different absorbance of cetirizine for three samples exposed under the direct sunlight, each for 5 hours' time interval and it was observed that the concentration of cetirizine was declined in each time interval.

Table 4.5: Concentration & Absorbance for Cetirizine (Sarcet®)

Test type	Initial potency %	Potency after 5 hours %	Potency decrease	Mean potency decrease after 5 hours %	Standard deviation +/- of each formulation	Mean potency decrease	Standard deviation +/- (%)
Sample1A	100.02	86.28	13.74	12.49	1.404	11.14	1.213
Sample1B	99.62	86.81	12.81				
Sample1C	98.88	87.9	10.98				
Sample2A	98.7	89.3	9.4	10.79	1.588		
Sample2B	98.92	88.12	10.8				
Sample2C	99	86.43	12.57				
Sample3A	99.32	87.21	12.11	10.14	1.708		
Sample3B	98.33	89.3	9.03				
Sample3C	99.21	89.92	9.29				

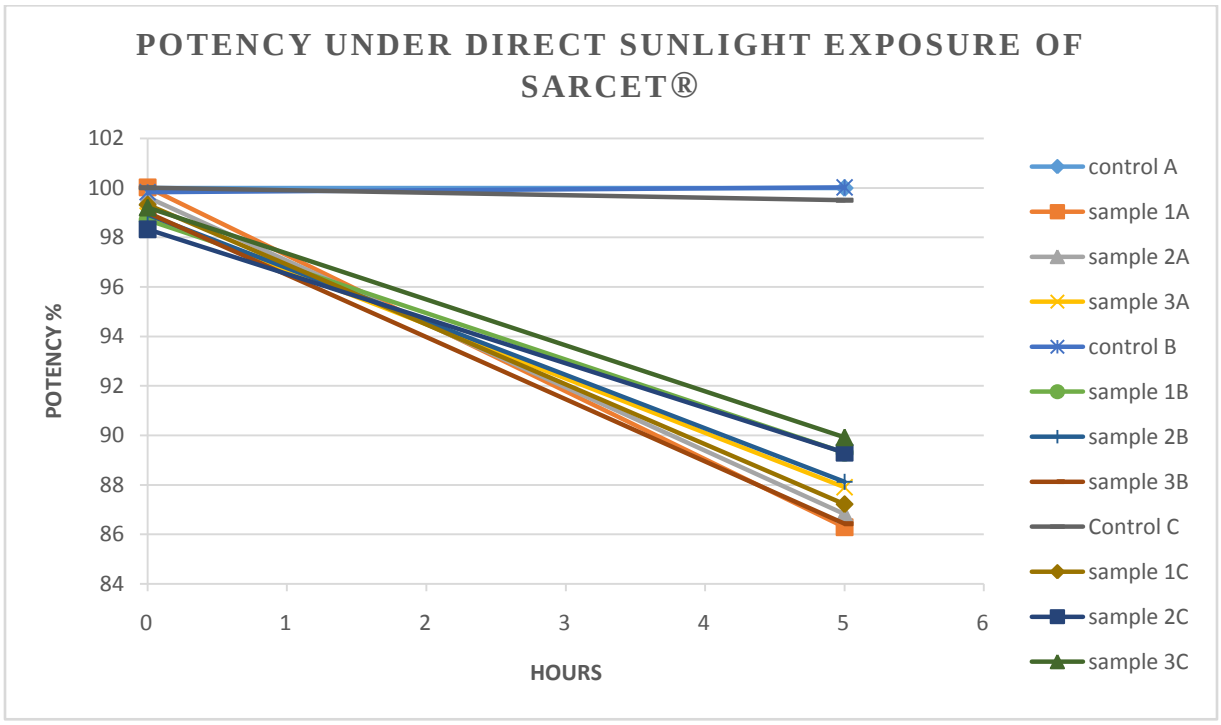


Figure 4.5: Difference in concentration after 5 hours time interval for cetirizine

CHAPTER 5

DISCUSSION

The weight variation of Sarcet® indicated that the solid dosage forms were uniform. According to USP, tablets of specific weight range have a particular limitation of weight variation and Sarcet® meets those specifications. Weight variation test indicates that a tablet is of appropriate size, the content of the formulation is uniform and ultimately it indicates good manufacturing practices (GMP). (Nasrin et al., 2011).

From the above study, it was noticed that significant degradation in potency of Sarcet® (Cetirizine Dihydrochloride) was occurred in all three lighting conditions (25 watt bulb light, 40 watt bulb light & direct sunlight) to which the tablets were exposed. The concentration decreased in percent deviation was 3.77%, 8.35%, 11.14% in 25 watt bulb light, 40 watt bulb light & direct sunlight respectively.

In each lighting condition the tablets were exposed and withdrawn at a specific time interval and measured the potency. Each time of testing the potency of exposed samplesit was compared with the potency of the control which was kept in dark and tested also and was found that controlled samples retained its potency over the period of the study.

CHAPTER 6

CONCLUSION

After analyzing the above experiment, it was figured that when sample tablets (Sarcet®) were kept for incandescent light exposure (25 watt & 40 watt) the concentration of cetirizine was decreased gradually. Same results were found for direct sunlight exposed sample tablets. Therefore, it is mentioned that only transparent blister packaging of tablet containing Cetirizine Dihydrochloride is not sufficient to protect it from photolytic degradation. To prevent this photolytic degradation opaque blister packaging of the tablet can be an effective way.

CHAPTER 7

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