PHOTO-DEGRADATION OF ACITRIN® (CETIRIZINE DIHYDROCHLORIDE) UNDER DIFFERENT EXTREME LIGHTING CONDITION : AN UV ANALYSIS

Submitted By:

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

Declaration By The Research Candidate

I, Md. Abu Hanif, hereby declare that the dissertation, entitled "Photo Degradation Of Acitrin® (Cetirizine Dihydrochloride) Under Different Extreme Lighting Condition: An UV Analysis", submitted by me to the Department of Pharmacy, East West University and in the partial fulfillment of the requirement for the award of the degree Bachelor of Pharmacy, under the supervision and guidance of Md. Anisur Rahman, Assistant Professor, Department of Pharmacy, East West University, Dhaka.

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Certificate By The Supervisor

This is to certify that the thesis entitled "Photo Degradation Of Acitrin® (Cetirizine Dihydrochloride) Under Different Extreme Lighting Condition: An UV Analysis", submitted to the Department of Pharmacy, East west University for the partial fulfillment of the requirement for the award of the degree Bachelor of Pharmacy, is a original record and genuine research work carried out by Md. Abu Hanif Edan, ID: 2014-1-70-054 , in 2017 of his research project in the Department of Pharmacy, East West University, under my supervision and guidance. We further certify that all the sources of information and laboratory facilities availed of in this connection is duly acknowledged.

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Endorsement By The Chairperson

This is to certify that the thesis entitled "Photo Degradation Of Acitrin® (Cetirizine Dihydrochloride) Under different Extreme Lighting Condition : An UV Analysis" submitted to the Department of Pharmacy, East west University for the partial fulfillment of the requirement for the award of the degree Bachelor of Pharmacy, is a original record and genuine research work carried out by Md. Abu Hanif Edan, ID: 2014-1-70-054 in 2017.

Dr. Chowdhury Faiz Hossain

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DEDICATION

This research paper is dedicated to my beloved parents, who are my biggest inspirations.

Abstract

The goal of the study was to detect of the photosensitivity of cetirizine dihydrochloride.It was seen if there was any change of cetirizine dihydrochloride under extreme lighting conditions (25 watt,40watt,direct sunlight). In normal lighting condition degradation of cetirizine dihydrochloride was not reported. Under different extreme lighting conditions potency ceased differently with a percent deviation of 4.74% (1.47%), 7.76% (2.88%) and 16.68% (4.01%) for 25 watt,40 watt and direct sunlight..So it can be concluded that Acitrin® contanining cetirizine dihydrochloride is sensitive to extremelight and an opaque packaging is required in combination with coating to provide stability and impede degradation.

Keywords:

Cetirizine Dihydrochloride, Stability, Photosensitivity, Potency, Batch,USP

CHAPTER ONE

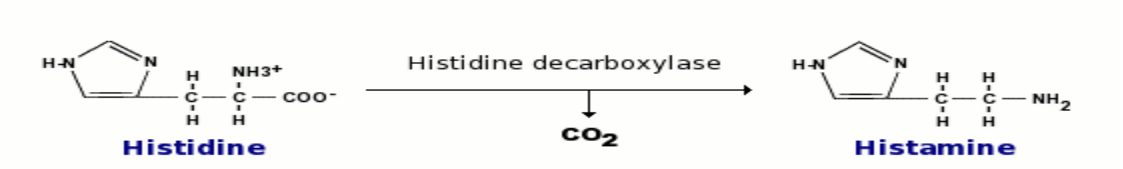
INTRODUCTION

1.1Introduction

Histamine: The biogenic amine histamine is a major a mediator of inflammation, anaphylaxis and gastric acid secretion.It is a small molecule which is derived from amine.(Goodman, Gilman and Brunton, 2008).

Distribution: Histamine is widely distributed in animal kingdom and can be found in many venom, plant and bacteria. Almost all mammalian tissues contain histamine. In cerebrospinal fluid amount of histamine is high meanwhile in plasma and other body fluid it is low in concentration. Concentration of histamine is particularly high in body parts like skin, bronchial mucosa, intestinal mucosa. (Goodman, Gilman and Brunton, 2008).

Synthesis: Histamine is synthesized from the decarboxylation of amino acid histidine by the enzyme L-histidinedecarboxylase. Usually histidine is found in almost every human tissue. Mast cells and basophils synthesize histamine and store them in secretory granules. (Goodman, Gilman and Brunton, 2008).



(vivo.colestate.edu,2017)

Metabolism: Histamine is metabolized by N-methyltransferase to N-methylhistamine and imidazoleacetic acid by nonspecific enzyme diamineoxidase. These metabolites have little or no activity and excreted in urine.(Goodman, Gilman and Brunton, 2008).

1.2Histamine Receptors: Four histamine receptors have been identified, all of which are G protein-coupled receptors. These different receptors are expressed on different cell types and work through different intracellular signalling mechanisms, which explains, at least at a simple level, the diverse effects of histamine in different cells and tissue.

Receptor Type	Major Tissue Locations	Major Biologic Effects
H_1	smooth muscle, endothelial cells	acute allergic responses
H_2	gastric parietal cells	secretion of gastric acid
H_3	central nervous system	modulating neurotransmission
H_4	mast cells, eosinophils, T cells, dentritic cells	regulating immune responses

(vivo.colestate.edu,2017)

Function:

- ✓ This histamine release causes the capillaries to become more permeable to white blood cells, which move into the capillaries and proceed to target and attack foreign bodies in the affected tissue. Sensory neural stimulation associated with the histamine release leads to sneezing; the glandular tissue secretes fluids and nasal congestion occurs due to the vascular engorgement caused by increased vasodilation and capillary permeability.
- ✓ In the stomach, histamine stimulates the parietal cells to produce the gastric acids required for digestion.

- ✓ Non-mast cell histamine is released in the brain where it acts as a neurotransmitter. The histamine neurons are found in the tuberomammaliary nuclei of the posterior hypothalamus. From there, they extend throughout the brain into the cortex and medial forebrain bundle. These neurons increase wakefulness and also prevent sleep.
- ✓ In addition some clinically useful drugs act directly on mast cells to release histamine,thereby explaining some of their untoward effects.(Xie&He,2005)

1.3Pharmacologic effect:

Cardiovascular system

- ✓ Histamine enhances Ca2+ influx into cardiac myocytes, this leads to minor increases in heart inotropism (force of contraction) and in chronotropism

Peripheral nervous endings:

- ✓ Histamine stimulates sensory nerve endings, especially those mediating pain and itching. This effect, mediated by H1 receptors, is responsible for pain and itch after an injury such as insect bite.

Bronchial smooth muscle

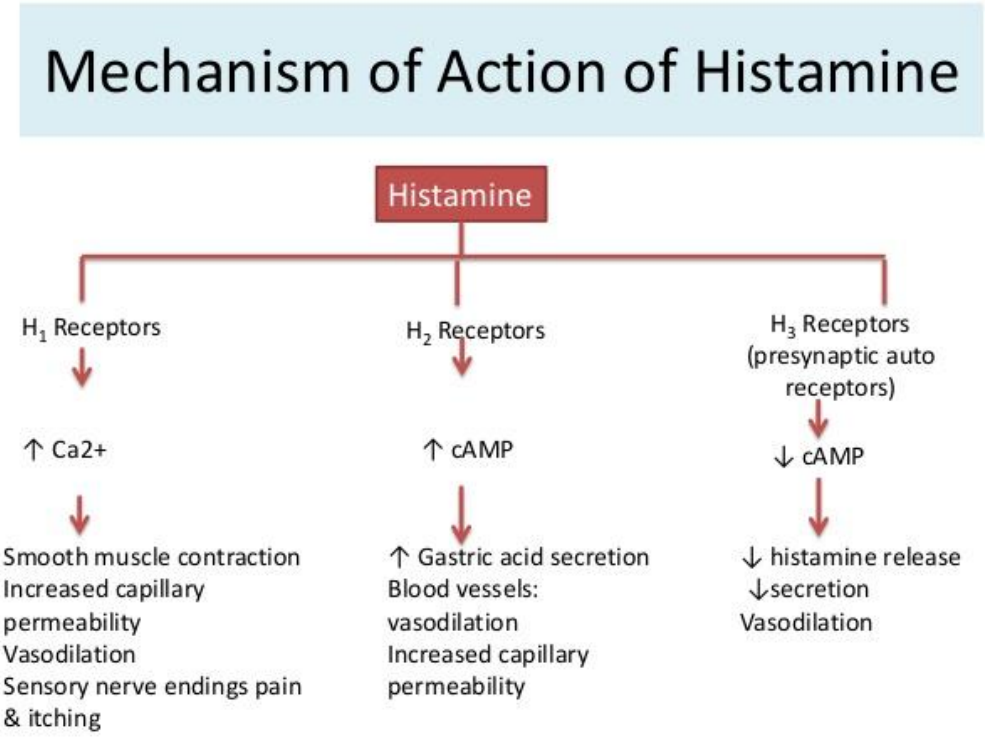
- ✓ Histamine causes contraction of bronchial smooth muscle, thus narrowing the airways. Asthmatic patients may be up to 1,000 times more sensitive to histamine mediated bronchoconstriction than individuals not affect by the disease.

Intestinal smooth muscle

- ✓ Histamine activation of H1 receptors produces constrictiction of intestinal smooth muscle, which results in increased bowel peristalsis and diarrhea.

(Tiligada et al.,2010)

1.4 Mechanism of action of histamine:



(Charles F.Code,1982)

1.5Adverse effect of histamine release:

- ✓ Sedation
- ✓ Dizziness
- ✓ Tinnitus
- ✓ Fatigue
- ✓ Blurred vision
- ✓ Diplopia
- ✓ Insomnia

(Goodman, Gilman and Brunton, 2008)

1.6Antihistanine:

It is a histamine antagonist that blocks different histaminic receptors.It is used for ailing allergy,gastric acid secretion and many other symptoms.
(Goodman, Gilman and Brunton, 2008)

Antihistamines are medicines often used to relieve symptoms of allergies, such ashay fever,hives,conjunctivitis,and reactions to insect bite or stings.They're also sometimes used to motion sickness, and as a short-term treatment for insomnia.(Nhs.uk,2017)

1.7Antihistamine classification: Antihistamines can be classified into 4 groups.

- ✓ H1 receptor antagonist
- ✓ H2 receptor antagonist
- ✓ H3 receptor antagonist
- ✓ H4 receptor antagonist

(Goodman, Gilman and Brunton, 2008)

H1 receptor antagonist: H_1 antihistamines act as inverse agonists that combine with and stabilize the inactive conformation of the H_1receptor, shifting the equilibrium toward the inactive state. H_1 antihistamines down-regulate allergic inflammation through the H_1 receptor, either directly or indirectly through nuclear factor-κB, an ubiquitous transcription factor, through which they down-regulate antigen presentation, expression of proinflammatory cytokines and cell adhesion molecules, and chemotaxis. In addition, through their effects on calcium ion channel activity, H_1 antihistamines decrease mediator release; however, this effect is only seen at high H_1-antihistamine concentrations.

- ✓ **First generation H1 receptor antagonist**
  - Chlorpheniramine
  - Diphenhydramine
  - Promethazine
  - Hydroxyzine
  - Brompheniramine
  - Triprolidine
  - Doxepin
  - Methdilazine
  - Clemastine
  - Azatadine

- ✓ **Second generation H1 receptor antagonist**
  - Loratidine
  - Cetirizine
  - Levocetirizine
  - Desloratidine
  - Rupatadine
  - Terfenadine

(Simon & Simons,2008)

1.8 Pharmacological action of antihistamine:

Smooth muscle: It blocks the constriction of smooth muscles especially of the respiratory smooth muscle.It inhibits the vasoconstrictor effect of histamine.

Capillary permeability:H1 antagonists strongly block the capillary permeability and formation of wheal and edema caused by histamine.

Anaphylaxis and Allergy: In case of hypersensitivity autacoids like histamine is released.In human H1 antagonists effectively suppress edema and itching.Hypotension is less well antagonized.They are well used in anaphylaxis and allergy.

Central nervous system: They depress the central nervous system and bring out drowsiness.This is more evident with the first generation of H1 antagonists.So why the second generation of antihistamine emerged. (Goodman, Gilman and Brunton, 2008)

1.9 Therapeutic Uses of antihistamine:

- ✓ Allergic rhinitis and common cold
- ✓ Allergic dermatitis,urticarial,itching
- ✓ Wasp bite
- ✓ Mild blood transfusion reaction
- ✓ Allergic conjunctivitis
- ✓ Motion sickness
- ✓ Morning sickness
- ✓ Vertigo
- ✓ Chronic Urticaria
- ✓ Drug indeced parkinsonism

(Motala,2009)

1.10 Absorption,Distribution,Metabolsim and Excretion:

H1 antagonists are well absorbed after oral administration and often reaches peak plasma concentration within two hours.Protein binding ranges from 78-99 percent.Most of the H1 antagonists are metabolized by the hepatic microsomal mixed function oxygenase system.

Plasma concentration is relatively low after single oral doses which indicates considerable first pass extraction by the liver.Values for half life plasma are variable.Thehalf lives of active metabolites may differ from those of the parent compound.Astemizole has a half life of 1.1 days where as its active metabolite N-desmethylastemizole has a half life of 9.5 days.Thehalf lives of some H1 antagonists may be shorter in children and prolonged in geriatrics especially the patients with hepatic dysfunction or patients receiving ketoconazole,erythromycin.

Cetirizine the active carboxylic acid metabolite of hydroxyzine is not metabolized to a great extent in vivo.60% of the dose is excreted unchanged in urine within first 24 hours.Plasma concentration is relatively high and volume of distribution is smaller than any other H1 antagonists.Thehalf life of cetirizine may be prolonged in patients with renal insufficiency.(Simons and Simons,1994)

1.11 Adverse effect of antihistamine:

Cardiac toxicity:In the 1980s two H1 antagonists astemizole and terfenadine prolonged QT interval and caused polymorphic ventricular arrhythmia.Albeit cardiac toxicity is not a class effect and does not occur through H1 receptor some 1^{st} generation generation antihistamines may be associated with prolonged QT and cardiac arrhythmia when these drugs are taken in overdoses.The 2^{nd} generation antihistamines has not been reported with any of the above problems. (Church et al.,2010)

- **Infants:**Using1^{st} generation antihistamines are potentially dangerous in case of infants.Albeit reports of fatal intoxication are are not common and acciedental homicides of infants have been reported.Sometimes over the counter cold medications can be fetal for childrens and can lead them to death due to toxicity. (Church et al.,2010)

- **Geriatrics:**The elderly patients are too much prone to the adverse effect of 1st generation antihistamins.25% of patients older than 65 years have some cognitive impairment and histamine neurtotansmission is disrupted in individulas with neurogenerativediseases.Administration of 1st generation antihistamines to this population are associated with increased of inattention,disorganizedspeech,altered consciousness and impaired function. (Church et al.,2010)

- **Pregnancy:**The 1st generation antihistamines are categorized as B according to FDA.They are prescribed in pregnancy due to no evidence of teratogenicity.The main concern with these antihistamines is when they are used in large doses just before parturition they cause contraction due to oxytosin like effect.Moreover if it is taken in large dose just before delivery the neonate may exhibit withdrawl symptom including tremulousness and irritability. (Church et al.,2010)

1.12Dose and Administration of Antihistamine:

For azatadine

- **For oral dosage form (tablets):**
  - Adults—1 to 2 milligrams (mg) every eight to twelve hours as needed.
  - Children 12 years of age and older—0.5 mg to 1 mg two times a day as needed.
  - Children 4 to 12 years of age—Use and dose must be determined by your doctor.
  - Children and infants up to 4 years of age—Use is not recommended .

For Cetirizine

- **For oral dosage forms (syrup and tablets**):
  - Adults—5 to 10 milligrams (mg) once a day.
  - Children 6 years of age and older—5 to 10 mg once a day.
  - Children 4 to 6 years of age—2.5 mg once a day, up to a maximum of 5 mg once a day or 2.5 mg twice a day.
  - Children and infants up to 4 years of age—Use is not recommended .

For cyproheptadine

- **For oral dosage forms (tablets or liquid):**
  - Adults and children 14 years of age and older—4 milligrams (mg) every eight hours. The doctor may increase the dose if needed.
  - Children 6 to 14 years of age—4 mg every eight to twelve hours as needed
  - Children 4 to 6 years of age—2 mg every eight to twelve hours as needed
  - Children and infants up to 4 years of age—Use is not recommended .

For desloratadine

- **For oral dosage form (tablets):**
  - Adults and children 12 years of age and older—5 milligrams (mg) once a day.
  - Children 4 to 12 years of age—Use and dose must be determined by your doctor.
  - Children and infants up to 4 years of age—Use is not recommended .

  - Childrens and infants upro 4 years of age—Use is not recommended .

For diphenhydramine

- **For oral dosage forms (capsules, tablets, or liquid):**
  - Adults and teenagers—25 to 50 milligrams (mg) every four to six hours as needed.
  - Children 6 to 12 years of age—12.5 to 25 mg every four to six hours.
  - Children 4 to 6 years of age—6.25 to 12.5 mg every four to six hours.

- **For injection dosage form:**
  - Adults—10 to 50 milligrams (mg) injected into a muscle or into a vein.
  - Children 4 years of age and older—1.25 mg per kg (0.6 mg per pound) of body weight injected into a muscle four times a day.
  - Children and infants up to 4 years of age—Use is not recommended .

For fexofenadine

- **For oral dosage form (capsules):**
  - Adults and teenagers—60 milligrams (mg) two times a day as needed or 180 mg once a day.
  - Children 6 to 11 years of age—30 mg twice a day as needed.
  - Children 4 to 6 years of age—Use and dose must be determined by your doctor.
  - Children and infants up to 4 years of age—Use is not recommended .

For loratadine

- **For oral dosage forms (tablets or liquid):**
  - Adults and children 6 years of age and older—10 milligrams (mg) once a day.
  - Children 4 to 5 years of age—5 mg once a day.
  - Children and infants up to 4 years of age—Use is not recommended .

(Mayoclinic.org,2017)

1.13Missed Dose

If you miss a dose of this medicine, take it as soon as possible. However, if it is almost time for your next dose, skip the missed dose and go back to your regular dosing schedule. Do not double doses. (Mayoclinic.org,2017)

1.14Storage

Keep out of the reach of children.

Store the medicine in a closed container at room temperature, away from heat, moisture, and direct light. Keep from freezing. (Mayoclinic.org,2017)

1.15 Proper Use

For patients taking this medicine by mouth:

- Antihistamines can be taken with food or a glass of water or milk to lessen stomach irritation if necessary.
- If it is taken in extended-release tablet form of this medicine,the tablets should be swallowed whole.
- For patients taking dimenhydrinate or diphenhydramine for motion sickness:
- The medicine should be taken at least 30 minutes or, even better, 1 to 2 hours before you begin to travel.

For patients using the suppository form of this medicine:

- To insert suppository:Removal of the foil wrapper and then moisten of the suppository with cold water is required. Patient should lie down on his side and use his finger to push the suppository well up into the rectum. If the suppository is too soft to insert, the suppository should be chilled in the refrigerator for 30 minutes or run cold water over it before removing the foil wrapper.

For patients using the injection form of this medicine:

- If injection is given,it should be ensured to understand exactly how to give it.
- Antihistamines are used to relieve or prevent the symptoms of your medical problem.They should be taken only as directed.(Mayoclinic.org,2017)

1.16Dosing

The dose medicines in this class will be different for different patients.Thedoctors order or the directions on the label should be followed.The following information includes only the average doses of these medicines

The amount of medicine that is taken depends on the strength of the medicine.Also, the number of doses taken on each day, the time allowed between doses, and the length of time you take the medicine depend on the medical problem for which you are using the medicine.(Mayoclinic.org,2017)

Cetirizine hydrochloride: Cetirizine, a piperazine derivative and carboxylated metabolite of hydroxyzine, is a potent histamine H_1-receptor antagonist with antiallergic properties. It has special affinity for peripheral histamine H_1-receptors and, at the standard dose of 10mg daily.It lacks the CNS depressant effects of standard antihistamines(Campoli-Richards,Buckley& Fitton.,2012)

1.17Physical properties:

- **Color**: White
- **State**:Crystalline powder
- **Melting Point**: 110-115^0 celsius
- **Solubility**:Soluble in water

(pubchem.ncbi.nlm.nih.gov,2017)

1.18Chemical properties:

- **Molecular Formula**:$C_{21}H_{25}CIN_2O_3$
- **Molecular Weight**:388.892 g/mol
- **Chemical Name**: CETIRIZINE HYDROCHLORIDE; 2-(2-(4-((4-chlorophenyl)(phenyl)methyl)piperazin-1-yl)ethoxy)acetic acid hydrochloride; 83881-52-1; 798544-25-9; MLS002222268;Cetirizine diHCl

(pubchem.ncbi.nlm.nih.gov,2017)

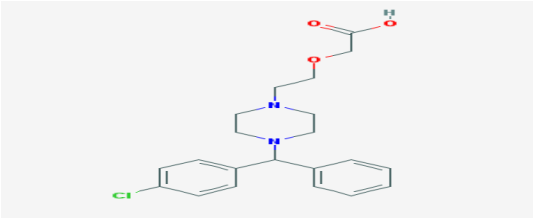
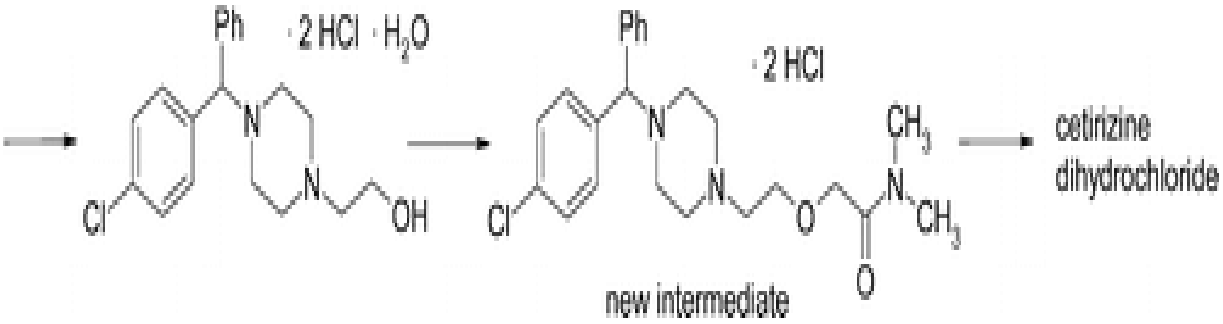


Figure: Chemical Structure of Cetirizine (pubchem.ncbi.nlm.nih.gov,2017)

1.19Synthesis of cetirizine:



(Pflum et al.,2002)

1.20Mechanism of action: Cetirizine competes with histamine for binding at H_1-receptor sites on the effector cell surface, resulting in suppression of histaminic edema, flare, and pruritus. The low incidence of sedation can be attributed to reduced penetration of cetirizine into the CNS as a result of the less lipophilic carboxyl group on the ethylamine side chain.(Drugbank.ca,2017)

1.21Indication:

- Allergy
- Hay fever
- Urticaria
- Perennial and seasonal allergic and vasomotor rhinitis
- Symptoms of cold

- Angioedema
- Anaphylactic reaction
- Pruritus
- Allergic Conjunctivitis

(Referance.medscape.com,2017)

1.22Dosage form and strength:

- Tablet (5/10mg)
- Tablet oral disintegrating (10mg)
- Tablet chewable (5/10mg)
- Syrup (5mg/5ml)
- Solution (5mg/5ml)

(ACI limited)

1.23Dosage and administration: Adults and children aged 6 years and over
Acitrin® Tablet10 mg once daily or 5 mg twice daily.
Acitrin® Syrup: 2teaspoonfuls once daily or 1 teaspoonful twice daily. In patients with decreased renal function (creatinine clearance 11-31 mL/min), patients on hemodialysis (creatinine clearance less than 7 mL/min) and in hepatically impaired patients, a dose of 1/2 tablet or 1 teaspoonful once daily is recommended. Children aged 2 to 6 years
Acitrin® Tablet: 5 mg once daily or 2.5 mg twice daily
Acitrin® Syrup: 1 teaspoonful once daily or 1/2 teaspoonful twice daily.
(ACI limited)

1.24Dosing Modifications

Renal impairment

- GFR >50 mL/min: Dose adjustment is not necessary

- GFR ≤ 50 mL/min: 1 tablet of 5mg per day by mouth
- Peritoneal dialysis: 1 tablet of mg per ay by mouth
- Intermittent hemodialysis: 1tablet of mg per day by mouth.It may also be administerd 3 times weekly

Hepatic impairment

- Dose adjustment not provided by manufacturer's label

(Referance.medscape.com,2017)

1.25 Pharmacokinetic properties of cetirizine:

Absorption

Peak plasma concentration: 114 ng/mL

Peak serum time: 1 hr

Duration: >24 hr(suppression of skin wheal and flare reactions)

Distribution

Protein bound: 93%

Volume of distribution: 0.56 L/kg

Metabolism

Metabolism: Liver; low first pass

Limited extent by oxidative O-dealkylation to inactive metabolite

Elimination

Half-life: 7.9hr

Excretion: Urine (70%); feces (10%)

(Referance.medscape.com,2017)

1.26 Side effects:

- Tiredness
- Dizziness
- Headache
- Dry Mouth
- Abdominal pain
- Diarrhoea (in children)
- Throat/Nose irritation (in children)

(ACI limited)

Contraindication: Cetirizine Dihydrochloride is contraindicated in those patients with a known hypersensitivity to it or any of its ingredients or hydroxyzine.

Precautions: It could be exercised when driving a car or operating potentially dangerous machinery. Concurrent use of Cetirizine with alcohol or other CNS depressants should be avoided 2 because additional reductions in alertness and additional impairment of CNS performance may occur.

1.27 Drug Interactions: No clinically significant drug interactions have been found with theophylline at a low dose, azithromycin, pseudoephedrine, ketoconazole, or erythromycin.

1.28 Instrumentation:

Ultraviolet Spectrophotometer : In a UV spectrophotometer the radiation of specific wavelength is passed through the sample of interest. A detector is placed that detects the light that absorbed at a specific wavelength and measures the extent of absorption. (Soderberg, 2016)

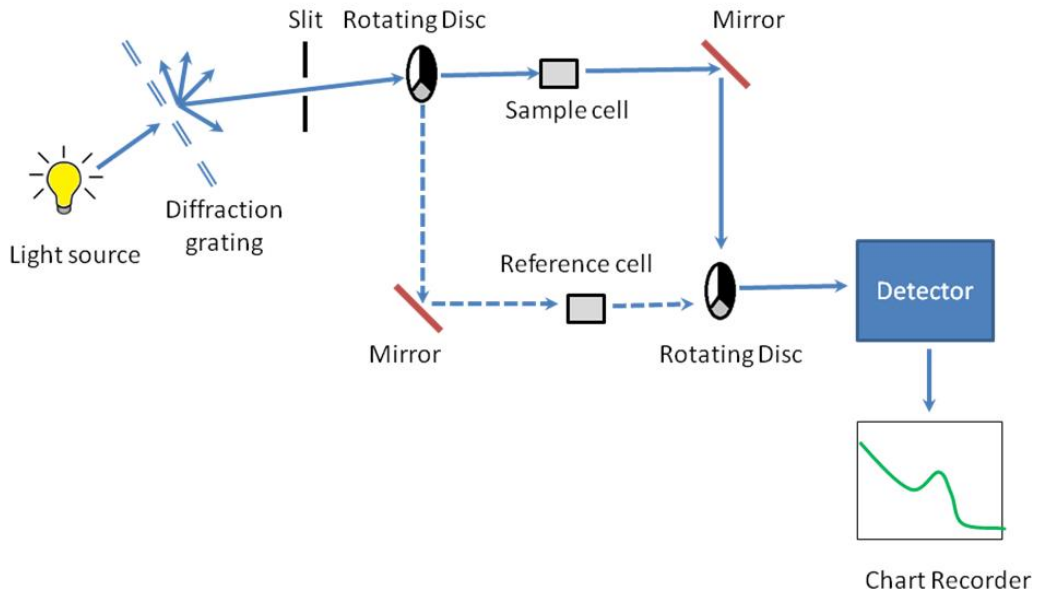


Figure 1.5: Schematic diagram for UV spectroscopy (Soderberg, 2016)

In this experiment the ultraviolet absorption of drug samples were measured by using a double beam T90+ UV/VIS spectrometer that is controlled by a computer having a specific software named 'UVWIN spectrophotometer', version 5.2.0 over a 10 mm path length. Quartz cuvettes were used as the sample holder.

CHAPTER TWO

LITERATURE REVIEW

2.1. Literature Review

Photosensitive drugs degrade under the exposure of normal or extreme light condition. In Bangladesh, there are different cetirizine Hydrochloride drugs available and they are marketed as different brands. From available brands one brand that is **"Acitrin®"** was chosen for determining its photosensitivity. These products are available in blister packaging system in most case in the market of Bangladesh. To find whether this drug is photosensitive or not, we operate a research program to establish a data about photolytic degradation of cetirizine Hydrochloride and for this-

A **"literature review "** was done to evaluate the previous works that were done on the cetirizine Hydrocloride. It was observed that the studies done on the Cetirizine hydrochloride were not similar to this research project.But those studies helped to find the information's that help in the research work and also helped to compare this research work with other research projects. jeast of some studies are given below :

A study described that antihistamine dose was waxed for the treatment of urticarial refractory patients.Efficacy and safety of doubling the dose of cetirizine was compared with olpotadine despite the treatment with standard cetirizine.Cetirizine was administered to 51 patients with a dose of 10mg once daily in one group and 20mg once daily to that 51 patients again.Skindex-16 was used to evaluate the severity of wheal and itching.Results showed that the the group in which dose was increased showed significant improvement in wheal and itching.

(Okubo et al,2011)

A research was done to review cetirizine hydrochloride for the treatment of allergy and it showed that it blocks the peripheral H1 receptors.Negligible anticholinergic and antiserotonergic effect was seen in in vivo and ex vivo animal model.Radiolabelled rat with cetirizine showed negligible penetration into brain.It is used in asthma treatment due to its anti-inflammatory property.Cetirizien does not interact with other drug and it has no teratogenicity or cardiac side effect.It is rapidly absorbed and as well as eliminated via kidney.Several clinical trials prove that it is prolific in the treatment of urticarial and allergic respiratory diseases.(Portnoy& Dinakar,2005)

A prospective study was performed to evaluate H1 receptor occupancy after oral administration of cetirizine to examine dose dependency by PET(positron emission tomography).Cetirizine was administered to 15 male patients with a dose of 10mg or 20mg while radiolabelled with ^{11}C-Doxepin.It was compared with placebo one.Binding potential and H1RO values were calculated.It was inferred from there of orally administered cetirizine was dose dependent.(Tashiro et al,2009)

A research was accomplished for the simultaneous determination of ambroxylhydrochloride,cetirizinehydrochloride,methylpareben,propylparaben in liquid pharmaceutical solution.stability using reversed phase ultra performance liquid chromatography. The optimized mobile phase consists of a mixture of 0.01 M phosphate buffer and 0.1 % triethylamine as a solvent-A and acetonitrile as a solvent-B and was detected in a wavelength of 237nm.This method helped to separate all the compounds.Stability indicating capability was established by forced degradation experiments and seperation of known and unknown degradation products. This validated method is applied for simultaneous estimation of AMB, CTZ, MP and PP in commercially available syrup samples.(Trivedi,Patel& Jadhav,2011)

A research was done for the enantioselective synthesis of cetirizine hydrochloride using highly stereospecific chiral oxazaborolidine reduction of 4-chlorobenzene to establish benzhydryl stereo center.Chromiumtricarbonyl also served as a stereocenter to allow stereospecific displacement of hydroxyl by amino at the benzylicstereocenter.(Corey & Helal,1996)

A study evaluates the ocular drying effect of 2 systemic antihistamines loratidine and cetirizine hydrochloride in individuals with normal ocular health when they were exposed to a controlled adverse environment.A dose of 10mg daily for 4 days of loratidine or cetirizine was given to 18

individuals in a controlled adverse environment.Keratitis,conjunctival staining and tear film break up time werexamined.Dosing for 4 days augmented the pointed values of the parameters.It was concluded from there that loratidine and cetirizine are associated with the signs and symptoms of ocular dryness including increased corneal and conjunctival staining decreased TFUBT and increased ocular discomfort.(Ousler BS et al.,2004)

A study narrated a HPLC method for quantative determination of cetirizine hydrochloride using hyoscine butyl bromide. The chromatographic system consisted of Shimadzu LC-10 AT VP pump, SPD-10 AV VP with UV/visible detector and a CBM-102 Bus Module integrator. The samples were introduced through an injector valve with a 10 µl sample loop. Acetonitrile-water (1:1 v/v) was used as mobile phase, with flow rate 2 ml/minutes. pH was adjusted to 2.9 with phosphoric acid.UV detection was performed at 205 nm. The results obtained showed a good agreement with the declared content. Recovery values for cetirizine hydrochloride were 99.19 - 100.82 %.The result showed that the method was rapid,sensitive and reliable and may be used in the quantitative determination of cetirizine hydrochloride.(Arayne,Sultana& Siddiqui,2005)

A research was done on the development of simultaneous estimation of Phenylephrine hydrochloride and Cetirizine hydrochloride. First method, employs formation and solving of simultaneous equation using 237.5 nm and 232.0 nm as the λmax of Phenylephrine hydrochloride and Cetirizine hydrochloride respectively in distilled water. Second method is first order derivative spectroscopy, wavelengths selected for quantitation were 232.0 nm for Phenylephrine hydrochloride and 242.5 nm for Cetirizine hydrochloride. The result was without resolving mixtures of Cetirizine hydrochloride and Phenylephrine hydrochloride, simultaneous estimation has been successfully achieved by spectrophotometry.This method is rapid,economic, and accurate for routine simultaneous estimation and was successfully applied to carry out

dissolution study of commercial tablet formulation by using USP II dissolution test apparatus.(Wankhede,Lad& Chitlange,2012)

In a research done in 2011,cettirizine hydrochloride was formulated with various concentrations of super disintegrants like croscarmellose sodium (CCS), crospovidone (CP), sodium starch glycolate (SSG) for preparing mouth fast dissolving tablets.These tablets would not require any water and easily disintegrates or dissoves in the mouth cavity.Tablet was prepared by direct compression and hardness,friability ,wetting time,disintegrationtime,percent drug release was tested.FT-IR studies disclosed that there was no interaction between cetirizine hrdrochloride and excipients and stability testing was also passed by this formulation.The result also indicated that that formulation prepared with 5% croscarmellose sodium was found to be optimized which provides maximum drug release (99%) and minimum disintegration time (less than 20sec).(Patro et al.,2011)

A research was done to improve encapsulation efficiency of cetirizine HCL microspheres as a model for water soluble drugs and control the release using response surface methodology.Different excipients were used and all available formulations were evaluated and morphologically characterized by scanning electron microscopy(SEM).After oral administration on healthy volunteers a double blind,randomized tests were done to compare the bioavilability of the control and optimized product.The result showed that the optimized cetirizine HCL microspheres exhibited a slow and controlled release over 12 hour and a improved bioavailability compared to the marketed tablets.(El-Say et al.,2014).

A dissolution test developed for a combination dose of cetirizine HCL for immediate release and pseudophedrine hydrochloride for extended release.CetirizineHCl is given in outer layer barred with a semipermeable membrane of cellulose acetate and PEG meanwhile pseudophedrineHClremains in inner core.For dissolution a USP apparatus 2 with a rotation of 50 rpm was used and deaerated water was used as dissolution medium.Reversed phase HPLC was

used for quantification.The culmination was cetirizine HCl dissolved rapidly and pseudophedrineHCl was independent of dissolution conditions.(Likar,Mansour& Harwood,2005)

A clinical trial was done to evaluate the efficacy of cetirizine HCl in the treatment of allergic pruritus on cats.CetirizineHCl was administered orally at a dose of 5mg to 32 cats in every 24 hrs with allergic disease.The outcome showed that the antipruritic effect was reproducible and sustainable.Upon cetirizine administration no significant association between age,disease severity or cutaneous reaction pattern.No adverse side effect was also reported.(Griffin et al.,2012)

A research was accomplished to see the effect of cetirizine HCl in the expression of neurokinin 1(NK-1R) receptor and induced cytokine production by substance P in dermal fibrobalsts.Expression of NK1R receptor by cetirizine was detected by flow cytometry and western blotting.Cytokine and interferon gamma production was measured by ELISA.The culmination showed that cetirizine inhibited the expression of NK-1R receptor and had no effect on the production of IFN gamma.These results suggest that cetirizine may be used in the treatment of substance P induced skin inflammation.(Liu JY et al.,2008)

The research was done to examine the fetal safety of cetirizine. Here a comparative study was done with pregnant women who were counselled for non-teratogenic exposure and who were counselled by the ‘Motherisk Program’ regarding cetirizine exposure in a cohort study.The pregnancy outcomes of women when exposed to cetirizine HCl or hydroxyzine was also examined in a meta analysis.The cohort study did not show major malformation between exposed and non-exposed group.Even in the meta-analysis, cetirizine was not associated with increased teratogenicrisk.Overall cetirizine is not associated with the risk of fetal outcomes.(Etwel et al.,2014)

The research was accomplished for chiral separation and quantitation of zwitterionic cetirizine (CTZ) by using a simple capillary electrophoresis (CE), as the main metabolite of hydroxyzine (HZ), and HZ has been developed.Additively influence on enantioseperation by the zwitterionic property of CTZ was investigated. Maltodextrin, served as a chiral selector.pH of BGE, concentration of chiral selector and applied voltage these parameters that would affect separation were studied. Results says that pH of BGE is a more effective parameter than in enantioseperation than hydroxyzine.(Nojavan& Fakhari,2011)

The research was done to compare the efficiency of intranasal Botulinum Toxin-A (BTX-A) to cetirizine in the treatment of allergic rhinitis (AR). Fifty ellergic rhinitis patients were recruited to the trial according to the Allergic Rhinitis and its Impact on Asthma (ARIA) criteria. Participants were randomly given 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 allergic rhinitis.(Hashemi et al.,2013)

This research was done to see the influence of cyclodextrin on the release fromt he formulation of cetirizine and the masking the tasting capacity of it.Using a three cell chewing apparatus in vitro release profiles of cetirizine from compressed chewing gums containing α-, β- and γ-cyclodextrine were investigated.Release experiments from all compressed chewing gum formulations gave similar release patterns, but with variations in the total amount released. The result was, chewing gum formulated with cetirizine alone, demonstrated a release of 75% after 8 min of chewing. The presence of CDs resulted in increased cetirizine release.(Stojanov& Larsen,2011)

In the year of 2012 this study was done to examine 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.TheDTa analysis of simvastatin indicates that it melts before it decomposes.The result also indicates that the more is the heating rate the more is the decomposition temperature.(Sovizi& Hosseini,2012)

A reseach was accomplished to determine the pharmacokinetics and efficacy in reducing dermatitis in horses with insect bite by a double blinded placebo controlled field study.Cetirizine was administered orally twice daily for 3 weeks at a dose of 0.4 mg/kg. The harvest indicated that cetirizine did not provide any apparent benefit in treating insect bite hypersensitivity at the dose rate tested. The use of blankets and stabling were shown to have favourable influence on the dermatitis.(Olsen et al.,2011)

This study was done for a high-performance liquid chromatography–diode array detection (HPLC–DAD) for the analysis of phenylephrine hydrochloride (PHE), paracetamol (PAR), caffeine anhydrous (CAF), cetirizine Dihydrochloride (CET), nimesulide (NIM) in pharmaceutical mixture.Effective chromatographic separation was obtained using a Kinetex-C18 column and a mobile phase of 10mM phosphate buffer and acetonitrile.It was a 3 step elution process.The proposed HPLC method was validated with respect to linearity,ranges,precision.This HPLC method was applied in tablet dosage forms in which analytes were successfully quantified. (Dewani et al.,2015)

The intent of this study is to demonstrate the efficacy and safety of bilastine 20mg compared to cetirizine hydrochloride 10mg and placebo in patients with perennial allergic rhinitis (PAR). In this study, patients with symptomatic perennial allergic rhinitis received bilastine 20 mg,

cetirizine 10 mg, or placebo once daily for 4 weeks.No significant differences in efficacy outcomes were found between active treatments and placebo.(Mullol et al.,2011)

This study was done to see the reaction between active drug substance and excipients in drug formulation process.Cetirizine was chosen as the active drug substance to evaluate the reaction with a substance having carboxylic acid moiety. The study 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)

This reseach was done for the determination of cetirizine and montelukast analysis in combined tablet dosage form.A high performance thin layer chromatography was used for this.Ethylacetate,methanol and ammonia solution were used as mobile phase.UV detection was performed at 230nm.It was observed that the HPTLc method could be used for efficient analysis and monitoring of cetirizine and montlukast in combined tablet dosage form.(Haghighi et al.,2013)

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)

The goal of this research was to perform oral challenge tests with cetirizine and hydroxyzine if it led to the same cutaneous reactions. In this study, a 44-year-old man was given the diagnosis of drug eruption from cetirizine and hydroxyzine, which suggests that there were cross-reactions among cetirizine, hydroxyzine, and ethylenediamin.(Lew et al ,2004)

This study was done to evaluate cetirizine-induced anaphylaxis which was a rare adverse drug reaction.In this study, a 30-year-old female patient was prescribed oral cetirizine 10 mg at night for the treatment of chronic idiopathic urticaria. Within 15 min of oral ingestion of cetirizine 10 mg, the patient experienced severe pruritis and urticarial eruption all over the body.Inconclusion,it was confirmed that even though the safety of cetirizine has been widely established, there is an extremely rare chance of it causing anaphylaxis. Cetirizine may be used in the treatment of anaphylaxis.(Afonso et al ,2009)

In this study, an investigation was done to determine the effect of cetirizine, on experimental viral myocarditis induced by encephalomyocarditis (EMC) virus. Cetirizine was administered orally at a dose of 1 or 10 mg/kg per day for the survival study, and 1 mg/kg for the histologic and gene expression studies, beginning on the day of viral inoculation. Finally it was suggested that cetirizine exerts its beneficial effects on viral myocarditis by suppressing expression of pro-inflammatory cytokines, genes related to cardiac remodeling in the hearts of mice.(Matsumori,Yamamoto& Shimada,2010)

This study was done to check if levocetirizne was less soporific than cetirizine.From the time being of January 1,2008 to June 30,2008 a total of 471 patients were prescribed levocetirizine and a retrospective chart was made from there.A subset of patients who were switched from cetirizine to levocetirizine due to sedation was identified.Among these 50 patients 38 patients were found to tolerate levocetirizne.The outcome from chart review was like this that levocetirizine is less sedating than cetirizine in majority of time.(Tzanetos,Buchholz& Fahrenholz,2009)

In the year of 1993 a research was done on the elimination of cetirizine in six patients with primary biliary cirrhosis. The duration of action of cetirizine was prolonged, as evidenced by significant suppression of the histamine-induced wheal and flare for 48 and 72 hours, respectively. After a single dose.In this study it was concluded that Cetirizine elimination was impaired in patients with hepatic dysfunction.(Simmons et al.,1993)

This research was done for the isolation and characterization of cetirizine degradation product formed within a PEG containing formulation and to recondite into the oxidation mechanism.Cetirizine in a PEG containing matrix was forced to degradation condition in a pH range of 3-10 and product was analyzed by HPLC.Moreover pure cetirizine was oxidized by hydrogen peroxide and sodium percarbonate.The findings were verified by spiking of cetirizine degradation sample with cetirizine N-oxide reference standard.Degradation of cetirizine was inferred due to reaction between drug and peroxide intermediate.The mechanism of oxidation was also proposed.(Dyakonov et al.,2010)

This research was accomplished to examine the binding mechanism of cetirizine hydrochloride in serum albumin and bovine protein by spectrofluorimetry,FTIR,UV-Vis absorption and circular dichroism.The drug looked for the fluorescence intensity of the protein.Thermodynamic parameters allowed to measure the nature of the binding force between drug and protein. Through the circular dichroism measurements a change in the secondary structure of protein was observed.The common blood plasma ions K^{+}, Cu^{2+}, Ni^{2+}, Mn^{2+} and Co^{2+} influenced the binding of the drug to the protein. These studies, along with other spectroscopic results, disclosed that the drug was bound to the hydrophobic pocket located in sub domain IIA of site I.(Hegde et al.,2011)

CHAPTER THREE

MATERIALS & METHODS

3.1 Materials

3.1.1 Sample Collection

For the purpose of experimentation to observe the photolytic degradation of Cetirizine Dihydrochloride as well as to assess the coating efficiency, 500 tablets of Acitrin® (CetrizineDihydrochloride 10mg) were collected from the local drug store in Dhaka as a sample. All the tablets were from the same batch (AR045). 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 experiments to determine their potency.

3.1.2 Sample

Table 3.1: Samples Used in the Experiment Including Source (ACI, 2012)

Sample name	Source(Supplier Name)	Batch no
Acitrin 10mg tablets	ACI Limited	AR045

3.1.3 Reagents

Table 3.2: Reagents used in the experiment including source

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

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 H2SO4)

1. Lab solvent (H2SO4), 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 (H2SO4) in Normality (N):

100 ml of the lab solvent stock solution contains = 98ml of H2SO4

100 ml of lab solvent stock solution contains = (98 x 1.84)gm of H2SO4

= 180.32gm of H2SO4

1000 ml of stock solution contains = (180.32 x 1000)/100 gm of H2SO4

= 1803.2gm of H2SO4

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

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

= 36.8N of H2SO4

3. After the determination of the concentration of the lab solvent stock solution in Normality (N), the amount of lab solvent (36.8N H2SO4) 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 Dihydrochloride was collected from a pharmaceutical company. The potency of standard compounds was 99.1%.
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 H2SO4 (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 Dihydrochloride had the concentration of its stock solution is 0.04 mg/ml.
- Five serial concentrations that were prepared for Cetirizine Dihydrochloride were 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	.005
	2	.006
	3	.007
	4	.008
	5	.009

- V1= S2V2 / S1 = (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 H2SO4) of Cetirizine Dihydrochloride.

- V1= S2V2 / S1 = (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 H2SO4) of Cetirizine Dihydrochloride.

- V1= S2V2 / S1 = (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 H2SO4) of Cetirizine Dihydrochloride.

- V1= S2V2 / S1 = (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 H2SO4) of Cetirizine Dihydrochloride.

- ⇨ V1= S2V2 / S1 = (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 H2SO4) 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:

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

- ➢ **Under incandescent bulb exposure (25W & 40W)**

1) 10 tablets were exposed to electric bulb lighting conditions for 5 hours at a stretch and 10 tablets were used as control.

2) After every 5 hours, 10 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, 3 tablets from those sampled tablets were taken.
   b. Then the total weight of those 3 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 3 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: Incandescent Bulb (25W & 40W) Exposed Sample List

No. of samples	Collected sample	Withdrawal intervals(hrs)	Temperature (ºC)	
			25w	40w
10(Control)	10	0	26	28
10	10	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) 10 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) 10 tablets were kept in a Glass box and exposed to sunlight condition for 5 hours at a stretch.
2) After 5 hours, 10 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, 3 tablets from those sampled tablets were taken.

    b. Then the total weight of those 3 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 3 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 H2SO4) for 3 times to prepare 3 samples.

    e. After that 10 ml solution was filtered and 2 ml of that filtered solution was taken and dissolved in 10ml 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)
10(control)	10	0	27
10	10	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.

CHAPTER FOUR

RESULTS

4.1Standard curve preparation

The standard was collected from ACI Pharmaceuticals Ltd. and tried to make a standard curve. For different concentration of acitrin different absorption were recorded. Nine serial concentrations of the standards of acitrin were prepared for the purpose of creating a standard curve.

The results are as follows:

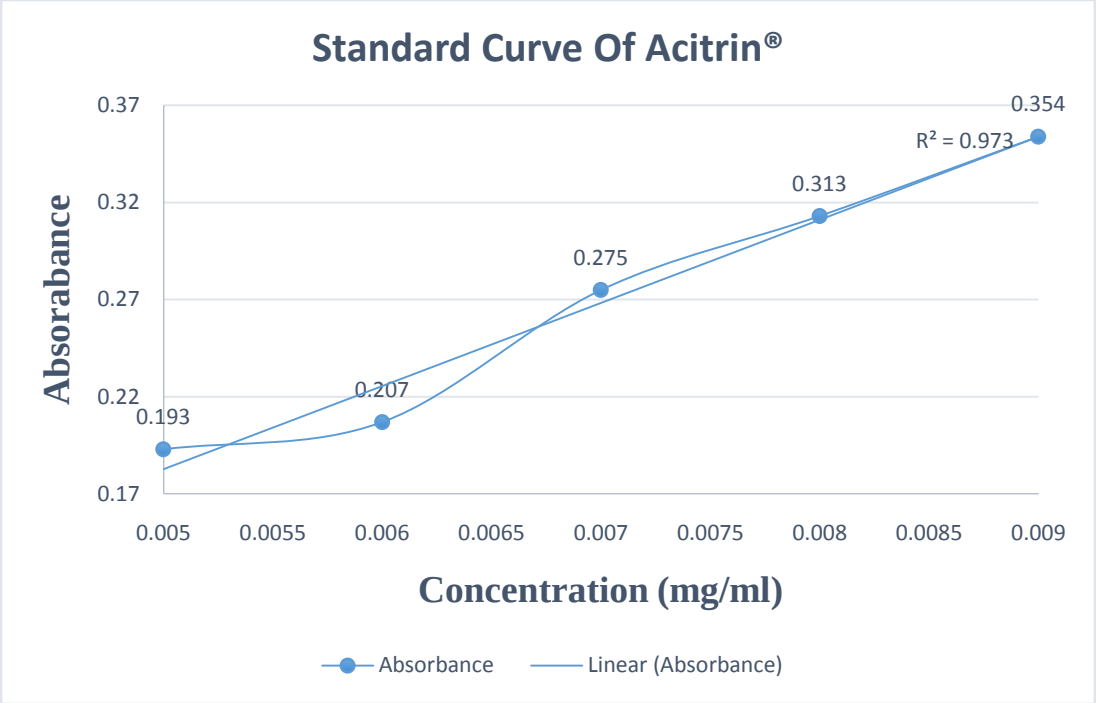
Table 4.1 : Concentration & Absorbance for standarad curve of Cetirizine Dihydrochloride

Concentration	Absorbance
.005	.193
.006	.207
.007	.275
.008	.313
.009	.354

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

$Y= 42.8x-.0312$
$R^2= 0.9736$

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

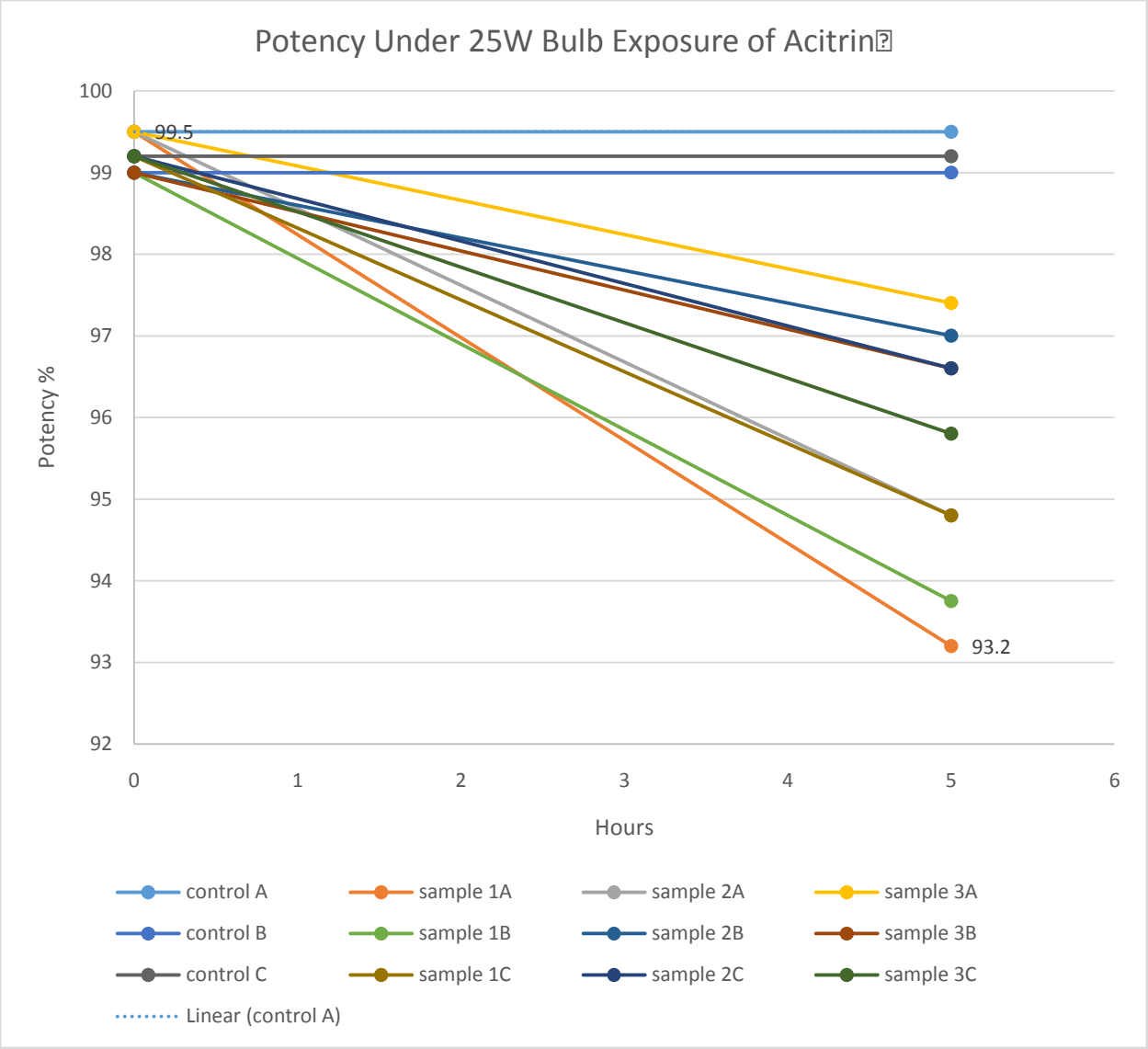


4.2Result of samples that were exposed under 25W bulb:

In experimental day, a tablet strip containing 10 tablets was taken and 3 samples were collected for the test and observed 3 different absorbance of cetirizine dihydrochloride for three samples exposed under the lamp (25W bulb); each for 5 hours' time interval and it was observed that the concentration of cetirizine dihydrochloride was declined in each time interval.

Concentration & Absorbance for Cetirizine Dihydrochloride (Acitrin®)

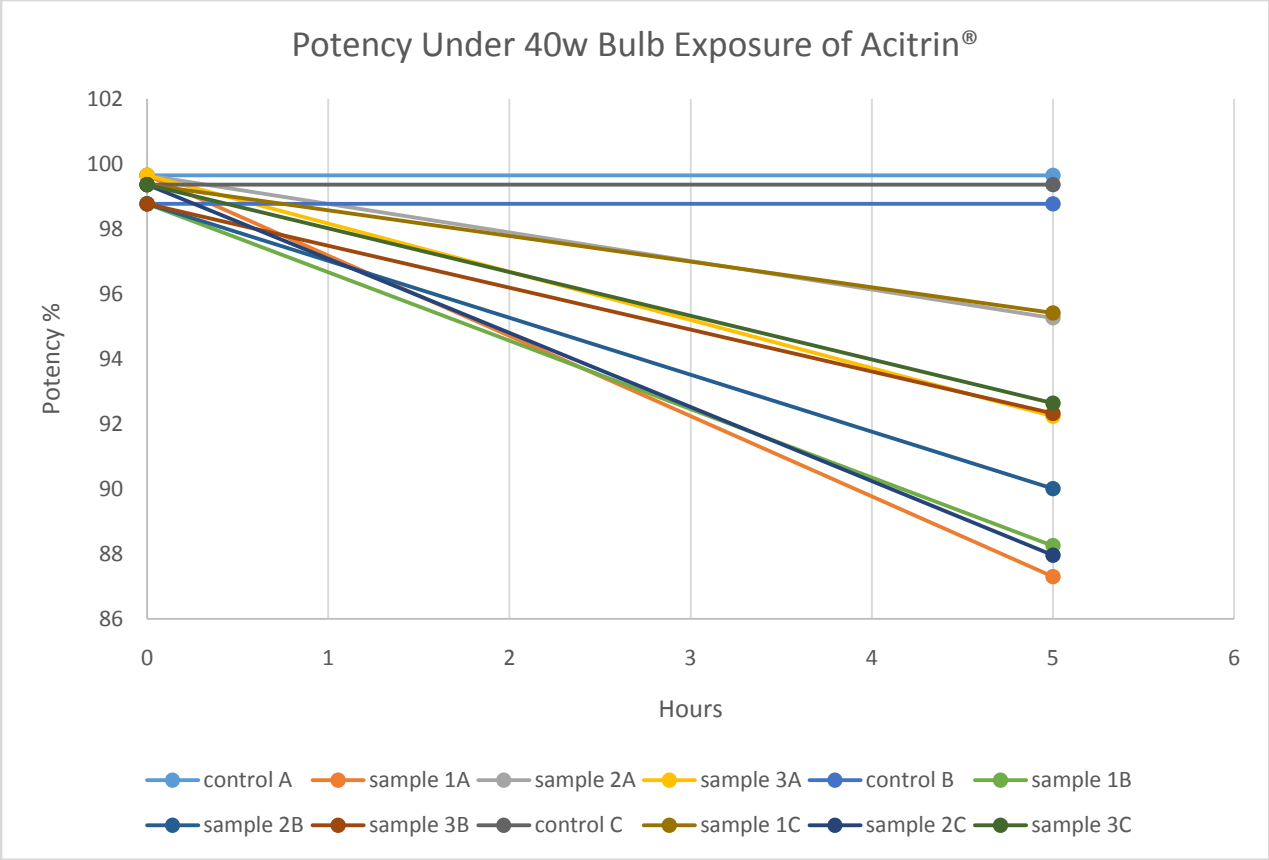
Test Type	Initial potency %	Potency after 5 hours %	Potency Decrease %	Mean Potency decrease of each formulation	Standard deviation+/- of each formulation	Mean potency decrease	Standard Deviation +/-(%)
Sample 1A	99.36	94.10	5.26	4.77	1.66	4.74	1.47
Sample 2A	99.06	96.14	2.92				
Sample 3A	99.36	93.22	6.14				
Sample 1B	99.65	95.56	4.09	4.09	1.46		
Sample 2B	98.48	92.93	5.55				
Sample 3B	99.06	96.44	2.62				
Sample 1C	98.77	91.76	7.01	5.36	1.61		
Sample 2C	98.77	94.97	3.80				
Sample 3C	99.65	94.39	5.26				


Potency Under 25W Bulb Exposure of Acitrin
100
99
98
97
96
95
94
93
92
Potency %
99.5
93.2
0
1
2
3
4
5
6
Hours
control A
sample 1A
sample 2A
sample 3A
control B
sample 1B
sample 2B
sample 3B
control C
sample 1C
sample 2C
sample 3C
Linear (control A)

4.3Result of samples that were exposed under 40W bulb

In experimental day, a tablet strip containing 10 tablets was taken and 3 samples were collected for the test and observed 3 different absorbance of cetirizine dihydrochoride for three samples exposed under the lamp (40W bulb); each for 5 hours' time interval and it was observed that the concentration of cetirizine dihydrochloride was declined in each time interval.

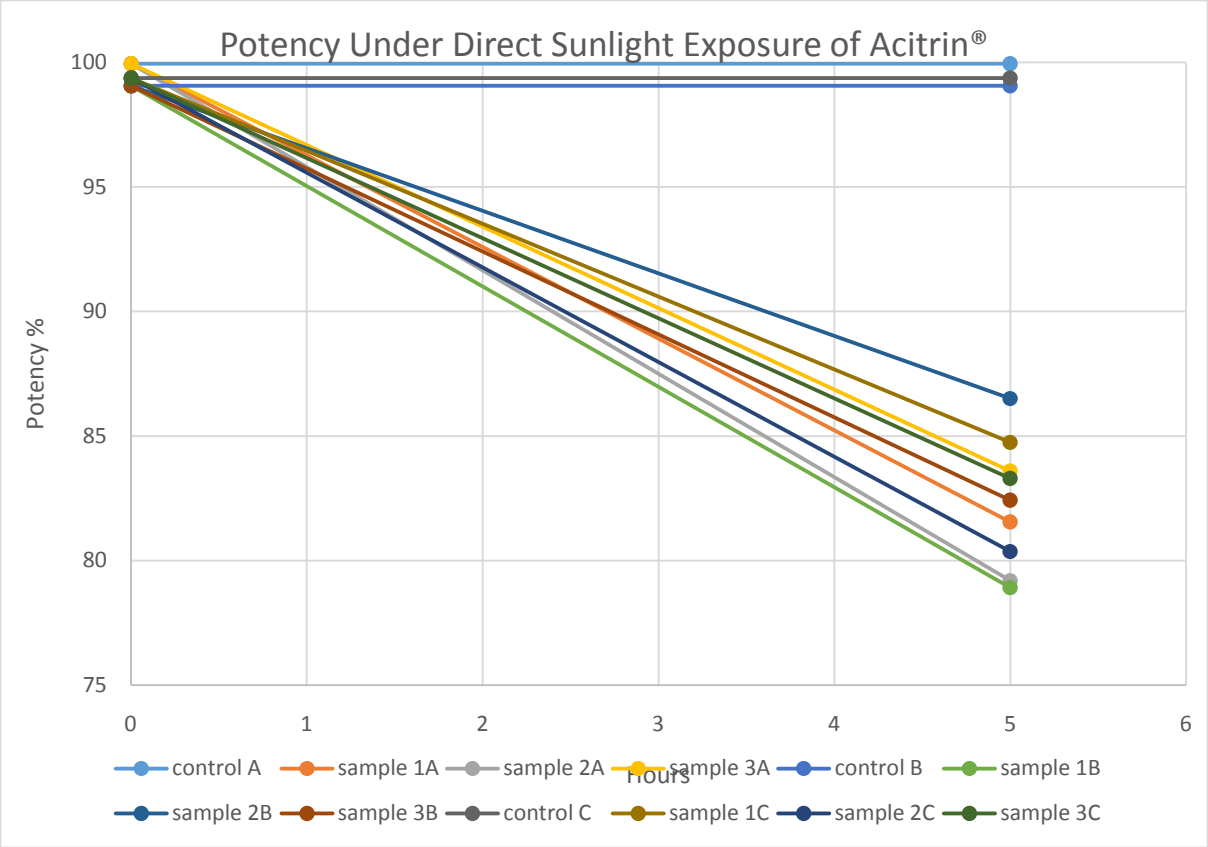
Test Type	Initial potency %	Potency after 5 hours %	Potency Decrease %	Mean Potency decrease of each formulation	Standard deviation+/- of each formulation	Mean potency decrease	Standard Deviation +/-(%)
Sample 1A	99.65	87.30	12.35	7.56	4.46	7.76	2.88
Sample 2A	98.77	95.26	3.51				
Sample 3A	99.06	92.23	6.83				
Sample 1B	99.36	88.25	11.11	8.96	2.36		
Sample 2B	99.36	90.01	9.35				
Sample 3B	98.77	92.34	6.43				
Sample 1C	98.48	95.41	3.07	6.77	4.05		
Sample 2C	99.06	87.96	11.1				
Sample 3C	98.77	92.64	6.13				



4.4 Result of samples that were exposed under direct sunlight

In experimental day, a tablet strip containing 10 tablets was taken and 3 samples were collected for the test and observed 3 different absorbance of cetirizine dihydrochloride for three samples exposed under the direct sunlight, each for 5 hours' time interval and it was observed that the concentration of cetirizine dihydrochloride was declined in each time interval.

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 +/-(%)
Sample 1A	98.48	81.54	16.94	17.71	2.43	16.68	4.01
Sample 2A	99.65	79.20	20.45				
Sample 3A	99.36	83.59	15.77				
Sample 1B	98.77	78.91	19.86	16.06	4.31		
Sample 2B	97.89	86.51	11.38				
Sample 3B	99.36	82.42	16.94				
Sample 1C	99.94	84.75	15.19	16.26	1.38		
Sample 2C	98.19	80.37	17.82				
Sample 3C	99.06	83.29	15.77				


Potency Under Direct Sunlight Exposure of Acitrin®
Potency %
100
95
90
85
80
75
0
1
2
3
4
5
6
Hours
control A
sample 1A
sample 2A
sample 3A
control B
sample 1B
sample 2B
sample 3B
control C
sample 1C
sample 2C
sample 3C

CHAPTER FIVE

DISCUSSION

Discussion

Forced degradation of a drug substance or drug product comprises of conditions which were more severe than normal condition.Stability indicating methods specificity wasshown in these methods and gave an acumen into degradation pathway and helped in lucidification of the structure of the drug products.Chemical nature of a molecule can be established which in turn helps in the development of formulation and packaging.(Blessy.,et al.,2014)

Generally in normal lighting conditions photodegradation of cetirizine dihydrochoride was not reported.We conducted this research to examine the robustness of degradation if the drug samples kept under extreme conditions.Under extreme lighting condition concentration of cetirizine dihydrochloride ceased gradually in every occasion of extreme light exposure.To examine this some of the tablet samples(Acitrin®) were kept under different lighting conditions which comprised of incandescent bulbs of 25watt and 40 watt.After 5 hours the samples were tested and the result showed that the drug degraded under such conditions.Exposing these drug samples to direct sunlight showed the identical result.But the degradation rate of drug samples exposed to sunlight was myriad in contrast with incandescent bulb (25watt and 40watt).So the result showed that the concentration of cetirizine dihydrochloride decreased gradually with a percent deviation of4.74% (1.47%), 7.76% (2.88%) and 16.68% (4.01%)for 25watt 40watt and direct sunlight exposure respectively.

From this research it can be inferred that a moderation in the packaging of the tablet should be introduced because we can notforespell whether the patient will keep the drug sample in proper storage or not..At present all the available brands in the market are packaged in plastic transparent blister pack. So packaging with an opaque substance should be introduced to impede degradation of Acitrin®.

CHAPTER SIX

CONCLUSION

Conclusion

After the experiment the observation showed that a significant change in potency happened due to exposure to different extreme lighting conditions under incandescent bulb of 25watt,40watt and direct sunlight. So from the appearance of the result it can be concluded that Acitrin containing cetirizine dihydrochloride was prone to extreme light and potency decreased with these extremeconditions.It also proved that only coating is not sufficient to protect a drug from degradation. Proper concentration should be imposed in the packaging of the drug sample to eradicate degradation and maintain stability.

CHAPTER SEVEN

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