Determination of photolytic degradation of Frenxit (Flupentixol- Melitracen)

A research paper is submitted to the department of pharmacy, East West University is conformity with the requirements for the degree of Bachelor of pharmacy.

Submitted by

Rajiya Sultana

ID: 2008-1-70-049

Department of Pharmacy

East West University

East West University

The research paper is dedicated

To my

Parents, my brother and Sister-in-law

Acknowledgement

I am thankful to Almighty in blessing in successful completion of the project. I express my heartiest gratitude to my respected teachers and supervisor **Mr. Repon Kumar Saha,** Assistant Professor, Department of pharmacy, East West University; for his continuous supervision, innovative ideas, enthusiastic encouragement, support, persistent assistance and care to accomplish this dissertation.

I am grateful to the chairman of department of pharmacy Dr. Ms. Sufia Islam, Dean prof. Dr. Chowdhury Faiz Hossain and pro-Vice Chancellor Profssor Munir Uddin Ahmed of East West University, for arranging the project.

I am also grateful to **Md. Anisur Rahman**, Lecturer, department of pharmacy, who provided his valuable input perform the project.

I would also like to thank all who willingly consented to participate in the project.

I would also like to express my thanks to the authority of East West University for their heartfelt help in my project work.

Finally, I would like to thank all the rest of pharmacy department for their continuous support throughout my project work.

Certificate

This is to certify that the thesis "Determination of photolytic degradation of Flupentixol-Melitracen combination product" is submitted to the department of pharmacy, East West University, Aftabnagar, Dhaka-1212, In partial fulfillment of the requirements for the degree of bachelor of pharmacy (B.Pharm) was carried out by Rajiya sultana (ID: 2008-1-70-049) under my guidance and supervision and that no part of the thesis has been submitted for any other degree. I further certify that all the sources of information and laboratory facilities availed of this connection is duly acknowledged.

…….

Dr. Repon Kumar Saha,

Assistant Professor,

Department of pharmacy,

East West University

Aftabnagar, Dhaka-1212

This research paper is submitted to the department, East West University in conformity with the requirements for the degree of bachelor of pharmacy (B.Pharm) was carried out by Rajiya Sultana (ID: 2008-1-70-049).

……

Dr. SUFIA ISLAM

Associate professor and Chairperson

Department of Pharmacy

East West University

Abstract

Photodegradation of the product can be easily and precisely describe by measuring the potency of the product. The purpose of the study was to determine the photo degradation of Flupentixol and Melitracen combine tablet. Flupentixol and Melitracen is a combination antipsychotic and antidepressation drug. The photo degradation of flupentixol and Melitracen was determined by the UV spectrophotometer by measuring the absorbance of the compound. Beside the absorbance determination the changes in the physical parameters were also measured for the determination.The sunlight and normal room temperature sample showed a good and impressive result of photodegradation of the compound according to the temperature and duration. Bulb light exposure also showed the degradation but in a same manner.

Flupentixol and melitracen are photosensitive drug and espousing it to the light and radiation may hamper the content uniformity of the tablet of compound.

Keywords: Flupentixol and melitracen, Potency determination, UV spectrophotometer, photodegradation, physical parameters.

List of Tables

List of Tables:

Literature Review of the photo degradation of flupentixol – melitracen was not actually revealed but fewer analytical methods for flupentixol - melitracen, single or along with other drugs and photosensitive drugs from the same class of the test drug where obtained from the review.

In 1997, Bourrain JL et al, conducted a test by diagnosis of photosensitivity to flupentixol by photo prick testing. Which reported the case of a 38-year-old patient with an erythematous

eruption, initially confined to photo-exposed areas and then becoming more generalized, which was attributable to flupentixol, a thioxanthene derivative used for its neuroleptic properties. The compound has the same polycyclic aromatic hydrocarbons as phenothiazines, but without any cross-reaction in our patient. A photoallergic cause for the eruption was verified on clinical, histological and photobiologic grounds. Photopatch tests were negative, but photoprick testing was positive after UV irradiation of the test site. Photo patch test methods using better skin penetration have been already reported for testing drug photosensitivity. Photo prick testing combines better penetration with greater ease of use.(Bourrain JL et al, 1997)

In 2011 Mohd Yunus et al, demonstrated a simple UV spectrophotometric method for determination of flupentixol HCL in bulk and pharmaceutical formulation. In which the authors describe the a simple and cost effective spectrophotometric method for the determination of flupenthixol dihydrochloride in pure form and in pharmaceutical formulations.(Yunus, 2011)

In 2004 Kelly M. Shields, conducted a research where the author provided a chart of Drug-Induced Photosensitivity. among them anti psychotic and anti depressant drugs was at the lead.

(Kelly, 2004)

In 2006 Kimberly S. et al, represented an article where they define the term photo toxicity and photosensitivity. They demonstrated that many drugs may be phototoxic or photosensitive during their use. Drug induced phototoxic or photosensitivity reaction may occur. The author provided a list of such drugs, among them the list of photosensitive anti psychotic and anti depressation drugs are given below:

Generic	**Therapeutic catagory**	**Frequency**
Amitriptyline	Tricyclic antidepressant	Reported
Amoxapine	Tricyclic antidepressant	< 1%
Aripiprazole	Atypical antipsychotic	0.1% to 1%
Clomipramine	Tricyclic antidepressant	Reported
Clozapine	Atypical antipsychotic	Reported

Desipramine	Tricyclic antidepressant	Reported
Doxepin	Tricyclic antidepressant	Reported
Haloperidol	Typical antipsychotic	Reported
Imipramine	Tricyclic antidepressant	Reported
Nortriptyline	Tricyclic antidepressant	Reported
Olanzapine	Atypical antipsychotic	0.1% to 1%
Perphenazine	Phenothiazine antipsychotic	Reported
Protriptyline	Tricyclic antidepressant	Reported
Thiothixene	Thioxanthene antipsychotic	Reported
Trimipramine	Tricyclic antidepressant	Reported

(Kimberly S. et al, 2006)

In 2011 Usmangani K. Chhalotiya et al, published a research article of the "Development of LCMethod for the Simultaneous Determinationof Antidepressant Drug CombinationMelitracen Hydrochlorideand Flupentixol Dihydrochloride in their Combined Dosage Form".Which demonstrated the a simple, specific and stability-indicating reversed-phase high-performance liquid chromatographic method for the simultaneous determination of melitracen hydrochloride and flupentixol dihydrochloride in tablet dosage form.(Usmangani, 2011)

In 2010 Spectrophotometric methods ware developed by Acharjya et al. for simultaneous estimation of combined tablet dosage form of Flupentixol Dihydrochloride and Melitracen Hydrochloride (Acharjya , 2010).

In 2009 I.A.Sheikh et al, Developed a method for the estimation of the melitracen HCl in single dosage form by RP-HPLC method. (Sheikh,2009)

In 2008 Hanne Hjorth Tønnesen published an article of Photoreactivity of drugs, according to that article A drug substance or drug product can be exposed to natural or artificial light during production, storage, administration and use. The great majority of drug substances and pharmaceutical excipients absorb UV and possibly visible radiation. Absorption is a first indication that a compound may participate in a photochemicalprocess i.e. be photoreactive,

which can result in its own decomposition or that of other components of the formulation in vitro. The photoreactivity may also give rise to adverse photosensitivity in patients, like phototoxic and photoallergic reactions. It is, however, possible to take advantage of the photoprocesses initiated by the drug substance in vivo. (Tonnesen, 2008)

In 2010 M. C. Sharma et al developed method of estimation of Novel application and spectrophotometric estimation of Melitracen HCl tablet dosage form using Niacinamide as hydrotropic solubilizing agent. Various organic solvents like methanol, chloroform, alcohol, dimethyl formamide; acetonitrile, hexane, acetone and carbon tetrachloride have been employed for solubilization of poorly water-soluble drugs for spectrophotometric estimations. The primary objective of the present investigation was to employ these hydrotropic solutions to extract the drugs from their dosage forms, precluding the use of costlier organic solvents. Ultraviolet absorption spectrophotometric method for the estimation of poorly water soluble drugs like Melitracen HCl in pharmaceutical formulations has been developed.

By reviewing the article, journals etc my study was design to determine the photodegradation of the drug flupentixol and melitracen. As the drug is the good representative of the photosensitizer and phototoxicdrug as it have both anti psychotic and anti- depressation property. Beside the determination of the photo degradation of the compound my study also includes the deterioration of the physical parameter of the compound.

Chapter One

INTRODUCTION

1.1 Drug Profile:

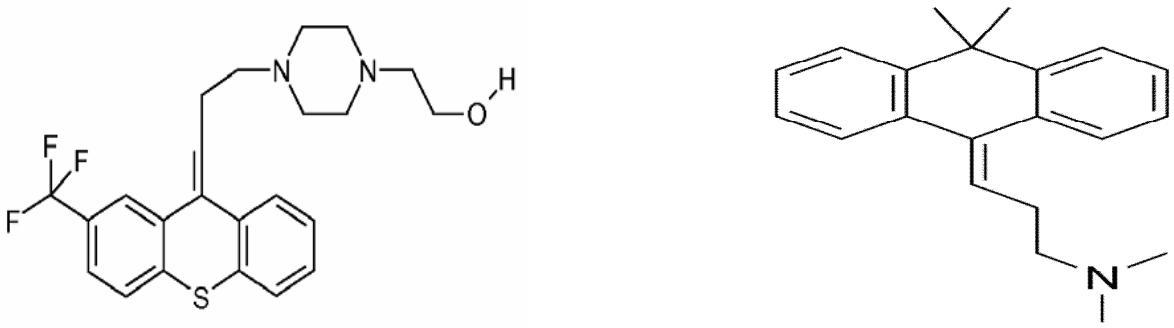
Flupentixol hydrochloride and Melitracen is a combination drug with anxiolytic, antidepressant and activating properties if given in low dose. Flupentixol is a typical antipsychotic compound of thioxanthan class producing neuroleptic activity. Melitracen is tricyclic antidepressant with bipolar thymoleptic along with activating properties.

The IUPAC name of flupentixol is 2-(4-{3-[2-(trifluoromethyl)-9,9a-dihydro-4aH-thioxanthen-9-ylidene]propyl}piperazin-1-yl)ethan-1-ol. and for melitracen it is 3-(10,10-dimethylanthracen-9(10*H*)-ylidene)-*N*,*N*-dimethylpropan-1-amine.

1.1.1 Pharmacology:

The mechanism of action of flupentixol is identifying by blocking postsynaptic dopamine receptors in the brain. They also produce a α-adrenergic blocking effect and thus depress the release of most hypothalamic hormones. Its antipsychotic property is mainly caused by blocking the postsynaptic dopamine receptor in the CNS.

Melitracen is antidepressant agent in the combination and act similar to other tricyclic antidepressant. It was found that melitracen has a quite similar activity as imipramine and amitryptyline. It works by inhibiting the re-uptake of neurotransmeter of the norepinephrine and serotin by neuron, thus reducing the symptoms of depression.



(a) (b)

Figure 1.1: (a) structure of Flupentixol (b) structure of Melitracen

1.1.2 Pharmacokinetics:

The pharmacokinetic of flupentixol and melitracen are given below:

Flupentixol:

Absorption: Readily absorbed from the GI tract, peak plasma concentrations after 3-8 hr (oral); slowly absorbed from the inj site, peak plasma concentrations after 4-7 days (IM). Distribution: crosses the blood-brain barrier and placenta; bound to plasma protein.

Metabolism: Extensively hepatic via sulfoxidation.

Excretion: The elimination half-life ($T_{½\beta}$) is about 35 hours and the mean systemic clearance (Cl_s) is about 0.29 l/min.

Melitracen:

Absorption: rapidly absorbed after oral administration and bind strongly to plasma albumin, 90–95% at therapeutic plasma concentrations.

Distribution: a large volume of distribution, extensive protein binding,

Metabolism: Metabolism of TCAs, especially their hydroxylation, results in the formation of active metabolites, which contribute to both the therapeutic and the adverse effects of these compounds.

Excretion: an elimination half-life averaging about 1 day (up to 3 days for protriptyline).

1.1.3: Indication:

As it is combination drug, the drug act both as anti-psychotic and anti-depressant. The Flupentixol, which is used to treat psychosis disorder. The primary objective is to treat schizophrenia, but they are also effective in other psychotic states, such as manic states with

pshychotic symptoms such as grandiosity or paranoia, hallucinations and delirium. Schizophrenia is a particular type of psychosis- that is mental disorder caused by some inherent dysfunction of the brain. It is characterized by delusion, hallucination (often in form of voice), and thinking or speech disturbances. All currently available antipsychotic drugs that alleviate symptoms of schizophrenia decrease dopaminergic neurotransmission like the flupentixol. The traditional or typical neuroleptic drugs like flupentixol called conventional or first generation anti-psychotic.

Anti-psychotic drugs are classified in two parts according to potency, which are low, high potency class. The anti-psychotic agent flupentixol is a high potency drug.

Melitracen is used as anti-depressant agent. Depression is a serious disorder. The symptoms of depression are intense feelings of sadness, hopelessness, and despair, as well as the inability to experience pleasure in usual activities, changes in sleep patterns and appetite, lose of energy and suicidal thoughts.

1.1.4 Prevalence of psychotic and depression condition in Bangladesh:

The national encyclopedia of Bangladesh published an article about the mental illness in Bangladesh. According to the article the scenario of psychotic and depression of people in Bangladesh is increasing day by day as Bangladesh is a developing country with poor economic condition. The following table collected from the “Powell, G. The future of clinical psychology in Bangladesh, 1995” shows the people of Bangladesh suffering from different types of psychotic and depression during their life time.

Table 1.1: Estimated population suffering from mental or related illness in Bangladesh.

Problem/illness	Population (age group)	Percentage	No. of cases (million)

Major depression	General	3	3.6
Anxiety disorder	---	5	6.0
Obsessions	---	0.5	0.6
Schizophrenia/psychosis	---	1	1.2
Learning disability	---	2.5	3.0
Chronic illness (eg, asthma, diabetes, pain)	---	10	12.0
Head injury/head trauma	---	.25	0.3
Hypertension/sleepnessness	Adults	14	8.4
Addictions (inc smoking)	Adults	10	6.0
Dementia (inc memory impairment)	Over 65 years	5	1.2

According to WHO, the number of mentally ill people in Bangladesh is about 8.4 million ie, 7% of the population of 120 million. During a survey it was found that both in rural and urban people are suffering from different kinds of mental disorder or depression in Bangladesh and it is getting widespread day by day. It was also found that about 30 % of the patient visits to the general practitioners are for psychological problems. A survey that had being conducted to a community in a rural area of Bangladesh, which shows that 15 per thousand people are affected with severe mental disorder and 50 per thousand are suffering from psychoneurotic and psychosomatic disorder. In Bangladesh women's are more affected then men. There are some important mental illness which is addressed in Bangladesh is:

- Psychoses: In this stage it is very difficult for a person to think, feel properly. Some time behavioral disturbances occur.
- Neuroses: Neuroses is primarily characterized by anxiety. Emotional disorder is common in neuroses.
- Personality disorders: Long standing inflexible, maladaptive inner experience and behaviours that impair social or occupational functioning.
- Substance related disorders and Childhood behaviour disorders/problems: A survey on the mental illness of the children of Bangladesh found that mother encountering 11.8% of

boys and 10.7% of girls, and teachers encountered 12.8% of boys and 11.2% of girls to have some mental disorder in the range of the clinic.

Schizophrenia is the only single condition of mental disorder for which is the largest cause of people admission to the mental hospital or clinic in Bangladesh. It is reported that about 1.3 million which is 1% of the population of the Bangladesh is suffering from schizophrenia. In which the anti-psychotic drug are the only treatment.

Mental health problems among the elderly people in Bangladesh are increasing in rapid way. It is one of the major sites in the percentage of mentally ill person in Bangladesh. This is because of the poor family and poor tradition structure.

Along with the psychotic disorder mental depression is also occur in Bangladesh in a higher rate. It was found in a study near a village of Dhaka city that about 2.9% of the people were suffering from depression. It was also found that one third of the patient were prescribed depressive drug.

1.1.5 Introductory discussion of the protocol:

The study of flupentixol-melitracen tablets is to identifying the photolytic degradation of the tablets. It is well known that light or other electromagnetic radiation can change the properties of some drug compounds. According to Reisch and Zappel in 1993, European pharmacopoeia listed 250 drugs to be prescribed in light protected condition. New compounds are also added to the list in the time.

The study was to determine the photostability of the drug, by identifying the compound respond to various light exposures.

The most obvious way to identifying the responds is to measure the potency degradation of the drug, which I have conducted in my research project. The potency loss can explain well enough that a drug is in its active form or not. Beside a small degradation of the potency may also cause adverse effect, photolytic degradation etc. According to De varies et al in 1984, Adverse effects

due to the formation of minor degradation products during storage and administration have been reported.

If a drug is photosensitive then it might produce light induced side- effects after administration to a patient by forming reaction with the endogenous compound of the body.

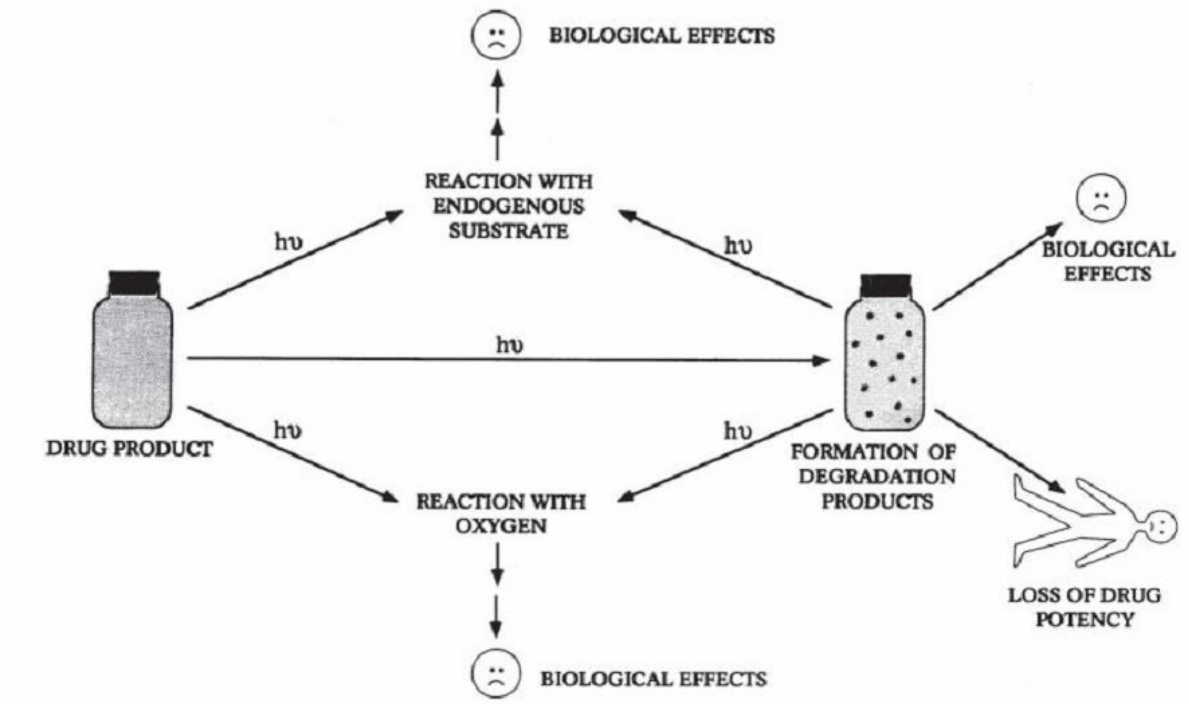


Figure 1.2: Possible consequences of drug photostability (Taylor and francis, 1996)

The purpose of the present study is to determine the photolytic degradation of the proposed tablets by measuring the loss of potency by UV- spectrophometry. Beside the potency observation physical parameters were also determine to observed change of the physical characteristic like thickness, weight variation, hardness etc of the tablets.

Literature Review of the photo degradation of flupentixol – melitracen was not actually reveal but fewer analytical methods for flupentixol - melitracen, single or along with other drugs and photosensitive drugs from the same class of the test drug where obtained from the review.

1.1.6 The aim of the study:

The aim of the study was to determine the photo degradation of the drug by measuring its potency after exposure to different light or radiation.

1.1.7 Instrument used in the project:

The UV spectrophotometry is one of the most valuable pharmaceutical analysis techniques, which is used for the determination of the potency of the tablets. The spectrophotometer deals with the spectra of the compound and is measured by the absorption of the electromagnetic radiation in a narrow wavelength which is denoted by "λ "by the substance of the tablets

The IR or infrared spectroscopy was also use to identify the functional group of the samples. Infrared spectroscopy (IR spectroscopy) is the spectroscopy that deals with the infrared region of the electromagnetic spectrum that is light with a longer wavelength and lower frequency than visible light.

Beside the spectrophotometer hardness tester, fraibilator machine, electronic balance was also used of the determination of the physical parameter of the exposed and the control tablets.

Concentrated Sulfuric acid was used as the reagent from MERK, Germany as a solvent for the crushed samples.

Chapter Two

Method and Material

2.1 Materials:

2.1.1 Sample collection and quantity:

500 tablet of Flupentixol-Melitracin (Frenxit product of Beximco pharmaceutical, Bangladesh) of same batch was bought from a local pharmacy shop of Dhaka. Among them 100 tablet was kept for the control test and remaining 400 tablet where subjected to various photo exposure or sample test. Each tablet containing flupentixol hydrochloride BP equivalent to 0.5 mg flupentixol and melitracen hydrochloride INN equivalent to 10 mg melitracen.

Figure 2.1: Packaged Sample tablets

2.1.2 Raw Materials:

Table 2.1: Raw Materials used in the experiment including source

Materials Name	Source (Supplier Name)
Frenxit tablets	Beximco Pharmaceuticals LTD

2.1.3 Reagents:

Table 2.2: Reagents used in the experiment including source

Reagents Name	Source (Supplier Name)
Concentrated Sulfuric acid	MERK, Germany
Distilled Water	Laboratory(East West University)

2.1.4 Equipments & Instruments:

Table 2.3: Equipments & Instruments used in the experiment including source

Serial No.	Equipments Name
01	Tablet Hardness tester
02	Friabilitor
03	Electronic balance
04	Vernier caliper
05	UV spectophotometer

Table 2.4: List of apparatus/ glassware's used throughout this project

Serial No	Name
01	Several Plastic Containers
02	Mortar & Pastels
03	Test tubes
04	Volumetric Flasks (50 ml & 100 ml
05	Pipette
06	Pipette pumper
07	Tharmometer
08	Forceps
09	Fanel
10	Beakers
11	Spatula
12	Glass rod
13	Filter papers
14	Aluminum foil

2.5 Methods:

2.5.1 Preparation of the solvent: The solvent was prepared by diluting 5ml of concentrated H_2SO_4 in a 1000ml volumetric flask with distilled water.

2.5.2 Scanning and determination of the maximum wavelength (λ_{max}) : In order to measure the maximum wavelength of the drug, a qualitative solution of the drug was made in 0.1N H_2SO_4 and was scanned by using a UV- spectrophotometer within the region of 200-400 nm, were 0.1 N H_2SO_4 was used as blank.

An absorption curve was obtained showing the characteristic maximum absorption. It was found that the λ_{max} flupentixol was 229nm and λ_{max} for melitracen was 258 nm.

2.5.3 Preparation of calibration standard curve and equation derivation:

The standard curve was prepared to compare the test result with it to determine the degradation of the drug. For standard curve preparation the average weight of 10 tablets were taken and all the 10 tablets was crashed by using mortar and pestle.

The average weight of the 10 tablets which was previously measured was weight from the crashed powder tablets. After measuring the powder drugs by the help of a balance, it was left to dissolve in 100ml of 0.1N H_2SO_4 solvent.

Series of dilution was carried out with the standard stock solution by pipetting 2 ml of the stock solution in test tube (1) and adding 8 ml of solvent to it. Then again pipetting 2 ml solution from test tube (1) to test tube (2) and adding 8 ml solvent to it. This was continued for more 3 times. Thus producing a known concentration ranging from 0.2. 0.04, 0.008, 0.0016 for melitracen and 0.01, 0.002, 0.0004, 0.00008 for flupentixol . Then the solutions where scanned ranging from 400-200 nm wavelength against the blank, and we got 229nm wavelength for flupentixol and 258nm wavelength for melitracen.

After identifying the wavelength of flupentixiol and melitracen, absorbance of the above solutions was taken for both 229nm for flupentixol and 258nm for melitracen. The observed value was plotted against concentration and a linear regression equation was obtained.

2.5.4 Sample collection:

The UV and partially the visible range of solar radiation have some major influence on the photolytic degradation of flupentixol and melitracen. To determine the photostability of the drug the tablets were subjected to various types of photo exposure, which are:

- Sunlight exposure(winter and summer)
- Exposure to normal room temperature (2 weeks, 1month,2 month)
- Bulp light exposure (25 watt, 40 watt)

2.5.4.1 Sunlight exposure: The sunlight exposed sample was collected by dividing the collection process in two segments, one in winter season and another in summer. In winter season, 30 tablets were kept on a solid surface and was place to the roof for the sun exposure. A thermometer was also kept aside the solid surface containing the tablets which submerge in glass of water. After 3 hour 10 tablets was collected exposed in a temperature of 99°F.Then, again 3 hour later 10 tablets was collected and the exposed temperature was 108°F.Finally, the remaining 10 tablets were collected exposed for total 9 hour falling the temperature from 108-100°F.

In the summer the sample was collected in similar strategy as the winter sample. But the temperature of the sunlight was much higher than the winter sunlight, which was 100°F, 108°F, and 108-106°F accordingly for 3 hour, 6 hour, and 9 hour exposed samples.

2.5.4.2 Exposure to normal room temperature:

The exposure of the tablets was done in normal room temperature. The tablets were kept in the normal room temperature in 3 plastic transparent box 20 tablets in each of the box. The box was labeled as 2 week, 1 month, and 2 month.

2.5.4.3 Bulb light exposure (25 watt, 40 watt): The photostability of the drug can be altered by the effect of some artificial light.

Two power ranges of bulb, 25 watt and 40 watt were used as the artificial light source. Thirty tablets were kept on a solid surface and were placed under 25 watt containing lamp. A

thermometer was kept behind the tablets submerge in a glass of water to measure the temperature. After three hour 10 tablet were collected

After the sample collection analysis of the sample was conducted by measuring some physical parameters and UV visible spectroscopy to determine the potency of the drug.

2.5.5 Sample analysis:

After the collection of the sample it was time to proceed to the analysis step. At first the average weight of the three sample tablets were taken by the electronic balance. Then the tablets were crashed to fine powder by the help of mortar and pestle. The average weight that was previously accounted was then weighted from the crashed powdered sample and was allowed to dissolve into 100ml of 0.1N H_2SO_4 in a 100 ml volumetric flask. The solution of the volumetric flask was then filtered thought a filter paper.10 ml of the filtrate was pipetted to a 100ml volumetric flask and 0.1 N H_2SO_4 was then added to the filtrate.

After all that, the sample solution was prepared for the potency test using UV-vis spectroscopy. For that, each of the tests was run against a blank, and for the test the test solution was poured into the quartz cell. The quartz cell was then placed into the holder situated inside the machine. Using a specified software technology the absorbance of the sample solution was established in the computer.

2.5.6 Physical parameters determination:

For determination of the physical parameters of the tablets, some set of test was carried out. The parameters are:

- Weight variation test
- Thickness
- Friability test
- Hardness test

2.5.6.1 Hardness Test of Tablets:

Tablet hardness is usually expressed as the load required crushing a tablet placed on its edge. Hardness is thus sometimes termed the tablet crushing strength. The suitability of a tablet in regard to mechanical stability during packaging and shipment can usually be predicted on the basis of hardness. Tablet hardness, in turn, influences tablet density and porosity. It may affect tablet friability and disintegration time. It usually affects drug dissolution and release and it may affect bioavailability.

Procedure:

1. The slide scale of the hardness tester was made zero
2. One tablet was placed vertically between two jaws.
3. Force was applied with a screw thread and spring until the tablet fractured.
4. Reading in Kg was taken from the sliding scale.

2.5.6.2 Friability Test of Tablets:

Friction and shock are the forces that most often cause tablets to chip, cap or break. The friability test is closely related to tablet hardness and is designed to evaluate the ability of the tablet to withstand abrasion in packaging, handling and shipping. The value is expressed as a percentage. A maximum weight loss of not more than 1% of the weight of the tablets being tested during the friability test is considered generally acceptable and any broken or smashed tablets are not picked up. Normally, when capping occurs, friability values are not calculated. A thick tablet may have less tendency to cap whereas thin tablets of large diameter often show extensive capping, thus indicating that tablets with greater thickness have reduced internal stress.

Procedure:

1. 10 tablets were weighted. It was considered as an initial reading
2. The tablet were placed in the section 1 of the drum of the friability tester and rotated 100 times.

3. The tablets were re-weighted. It was considered as a final reading.
4. The percent loss was calculated.
5. According to the U.S.P the tablets should not lose more than 1% of their total weight

Calculation%:

Percent of friability = (M1 – M2) / M1 ×100%

Where, M1 = weight of the tablets before the rotation

M2 = weight of the tablets after the rotation

$$\%\,\text{Loss} = \left(\frac{\text{Initial weight} - \text{Final weight}}{\text{Initial weight}} \right) \times 100$$

Figure 2.2: Tablet friability test apparatus.

2.5.6.3 Weight Variation Test of Tablets:

Weight variation test is most significant because it has a relationship with content uniformity of a solid dosage forms. A small weight variation does not ensure good content uniformity between

dosage units; a large weight variation precludes good content uniformity. Any of the following factors, can produce excessive tablet variations:

1. Poor granulation flow properties, resulting in uneven die fill.
2. A wide variation in granulation particle size, which result in a variation in die fill density as a function of particle size and particle size distribution at different points in the production run,

Differences in lower punch length, which result in different size die cavities

Procedure:

1. 10 tablets were taken and weighed all the tablets
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 2.5 :According to the USP the percentage difference range

Average weight	**Percentage difference**
130 mg or less	± 10
More than 130 to 324 mg	±7.5
More than 324 mg	±5

Calculation:

$$\text{Weight variation} = \frac{\text{Tablet weight- Average Weight}}{\text{Average Weight}} \times 100$$

2.5.6.4 Thickness test:

The thickness test was carried out to measure the thickness of the sample tablet. To determine if there is any deviation of the tablet due to the exposure of the light. It was done by using a Vernier caliper.

Procedure:

1. First placing the tablet between the two jaws of the vernier caliper.
2. Then, the main scale reading was taken.
3. The vernier scale was taken also.
4. The two reading was added together by multiplying with the vernier constant.

Figure 2.3: Vernier caliper

Calculation:

Main scale reading + (vernier scale reading *vernier constant)

Chapter Three

RESULTS & DISCUSSION

3.1 Result :

The result include the potency determination and estimating some physical parameters of the test samples.

3.1.1 Physical parameter estimation:

3.1.1.1 The control tablets:

The physical parameter estimation of the control tablet are being done for comparing it with the sample tablets.

Table 3.1: percentage weight variation of control

Tablet no.	Initial Weight, I(gm)	Average wight A(gm)	% Weight Variation
1	0.0754	0.7391/10=0.07391	-2.24
2	0.0733		0.5
3	0.0729		1.11
4	0.0753		-2.11
5	0.0737		0.01
6	0.0753		-2.11
7	0.0717		2.8
8	0.0749		-0.64
9	0.0723		1.95
10	0.0743		-0.79

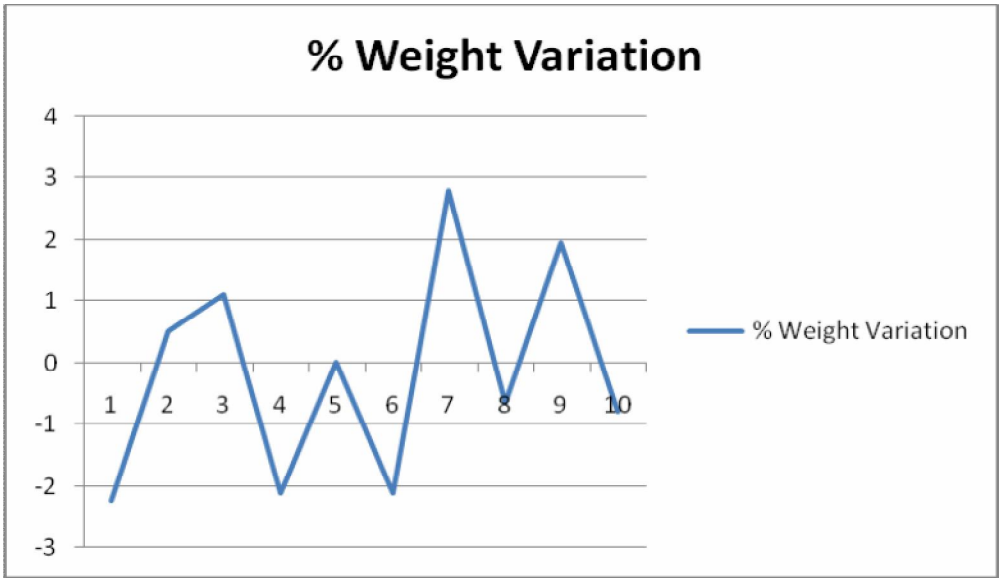


Figure 3.1: Graph of % weight variation of control tablets.

Table 3.2: Thickness reading of the control drugs

Tablet no.	Main scale reading(cm), M	Verniear scale reading(cm), V	Thickness of the tablets (cm),i.e.(M+V) cm
1	0.3	0.005	0.305
2	0.3	0.005	0.305
3	0.3	0.005	0.305
4	0.3	0.005	0.305
5	0.3	0.005	0.305
6	0.3	0.005	0.305
7	0.3	0.005	0.305
8	0.3	0.005	0.305
9	0.3	0.005	0.305
10	0.3	0.005	0.305

Table 3.3: Data of the hardness test in kg of the controls

Tablet no.	Hardness(kg)	Hardness Averege(kg)
1	3.5	3.1
2	3.1	
3	3	
4	2.9	
5	2.9	
6	3.2	
7	3	
8	3.1	
9	3.2	

Table 3.4: Friability data of control tablets

Initial weight	Weight after rotation	Friability
0.7371	0.737	0.01%

3.1.1.2 The normal room condition:

Table 3.5 : The percentage weight variation of 2 week sample

Tablet no.	Initial Weight, (gm)	Average weight (gm)	% Weight Variation
1	0.0761	0.745/10=0.0745	2.14
2	0.0746		0.13
3	0.0762		2.28
4	0.0729		-2.14
5	0.0744		-0.13
6	0.076		2.01
7	0.0742		-0.4
8	0.0733		-1.61
9	0.0743		-0.26
10	0.0724		-2.81

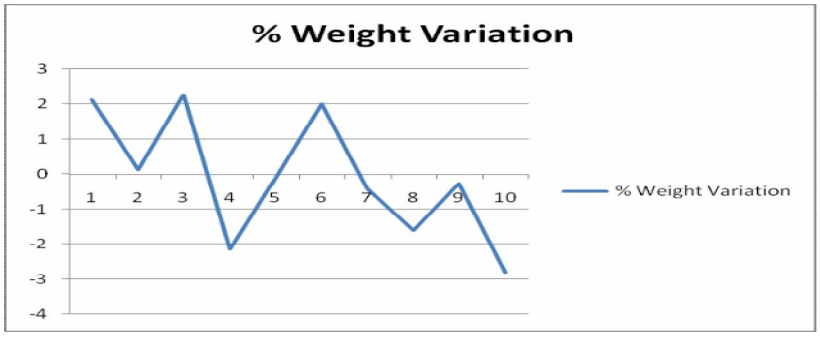


Figure 3.2: graph of % weight variation of 2 week samples.

Table 3.6: Percentage weight variation data of 1 month samples

Tablet no.	Initial Weight, (gm)	Average weight (gm)	% Weight Variation
1	0.0762	0.7379/10=0.07379	0.03
2	0.0709		-3.91
3	0.0744		0.8
4	0.0727		-0.01
5	0.0727		-0.01
6	0.0753		2.04
7	0.0746		1.09
8	0.0731		-0.9
9	0.0736		-0.2
10	0.0744		0.8

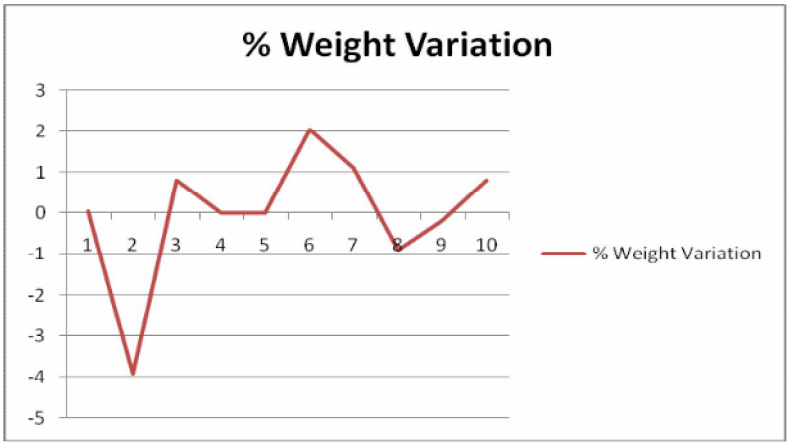


Figure 3.3: Graph of percentage weight variation of 1 month samples

Table 3.7: percentage weight variation of 2 month samples

Tablet no.	Initial Weight, (gm)	Average weight (gm)	% Weight Variation
1	0.0711	0.7478/10=0.07478	-4.92
2	0.0749		0.16
3	0.0778		4.03
4	0.0736		-1.5
5	0.0765		2.3
6	0.0748		0.02
7	0.0764		2.16
8	0.0734		-1.84
9	0.0726		-2.91
10	0.0767		2.56

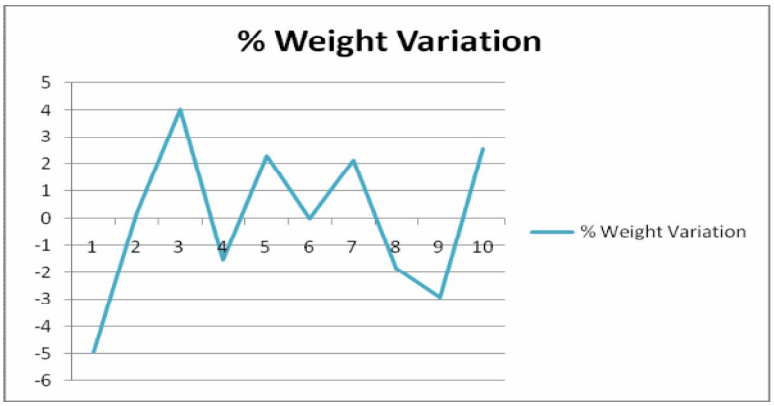


Figure 3.4: Graph of the percentage weight variation of 2 month samples.

Table 3.8 : Thickness reading of the 2 week sample tablets.

Tablet no.	Main scale reading(cm), M	Verniear scale reading(cm), V	Thickness of the tablets (cm),i.e.(M+V) cm
1	0.31	0.01	0.32
2	0.3	0.005	0.305
3	0.3	0.005	0.305
4	0.31	0.01	0.32
5	0.31	0.01	0.32
6	0.3	0.005	0.305
7	0.3	0.005	0.305

8	0.3	0.005	0.305
9	0.31	0.01	0.32
10	0.29	0.09	0.38

Table 3.9: Thickness reading of the 1 month sample tablets

Tablet no.	Main scale reading(cm), M	Verniear scale reading(cm), V	Thickness of the tablets (cm),i.e.(M+V) cm
1	0.3	0.004	0.304
2	0.31	0.015	0.325
3	0.32	0.015	0.335
4	0.32	0.015	0.335
5	0.31	0.015	0.325
6	0.31	0.004	0.314
7	0.3	0.004	0.304
8	0.3	0.004	0.304
9	0.3	0.004	0.304
10	0.3	0.004	0.304

Table 3.10: Thickness reading of the 2 month sample tablets

Tablet no.	Main scale reading(cm), M	Verniear scale reading(cm), V	Thickness of the tablets (cm),i.e.(M+V) cm
1	0.3	0.004	0.304
2	0.29	0.07	0.36
3	0.29	0.07	0.36
4	0.3	0.004	0.304
5	0.29	0.07	0.36
6	0.31	0.01	0.041
7	0.3	0.004	0.304
8	0.3	0.004	0.304
9	0.3	0.004	0.304
10	0.31	0.004	0.314

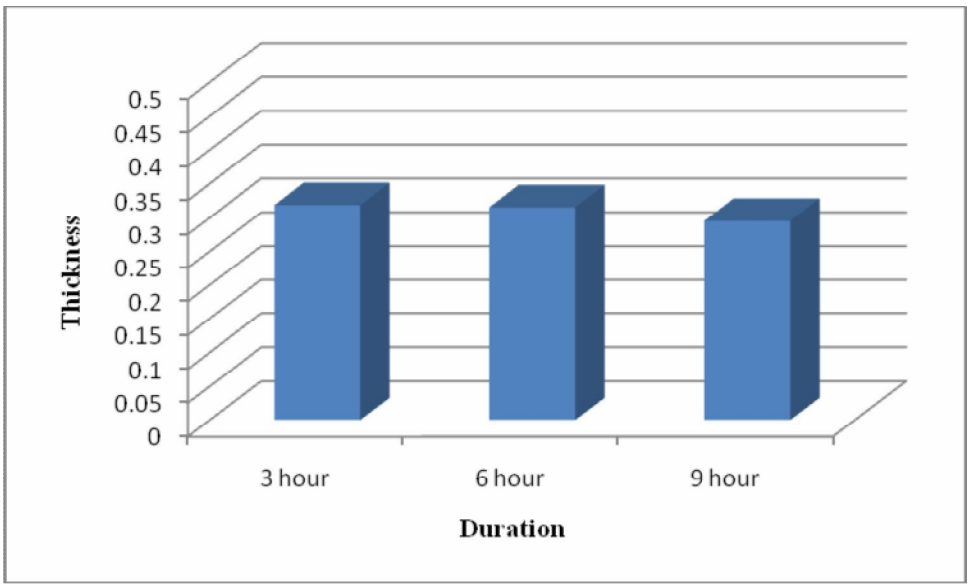


Figure 3.5 : Graphical representation of the mean thickness value among the three sample of normal room temperture

Table 3.11: Data of the hardness test in kg of 2 week samples

Tablet no.	Hardness(kg)	Hardness Averege(kg)
1	3.1	3.134
2	3.1	3.134
3	3.2	3.134

Table 3.12: Data of the hardness test in kg of 1 month samples

Tablet no.	Hardness(kg)	Hardness Averege(kg)
1	2.6	2.767
2	2.8	2.767
3	2.9	2.767

Table 3.13: Data of the hardness test in kg of 2 month samples

Tablet no.	Hardness(kg)	Hardness Averege(kg)
1	2.5	2.634
2	2.6	2.634
3	2.8	2.634

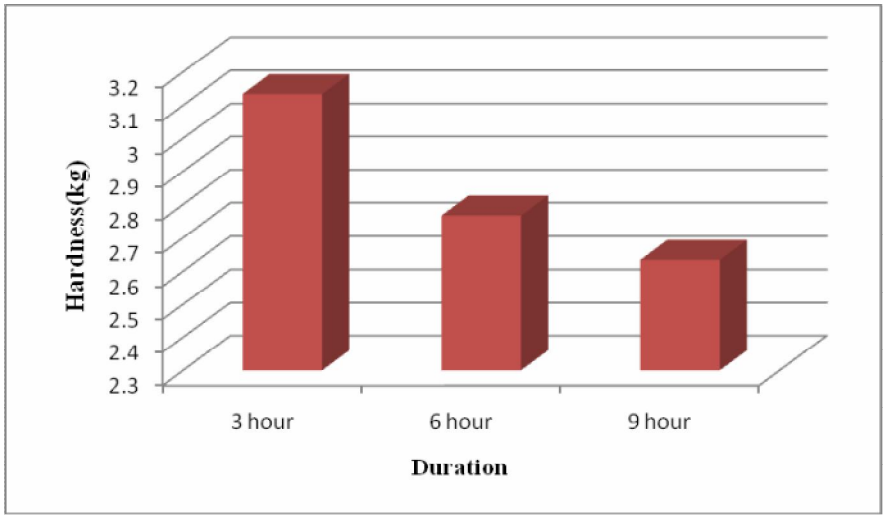


Figure 3.6: Graphical representation of the mean Hardness value of the normal room condition samples

Table 3.14: Friability data of 2 week sample tablets

Initial weight	Weight after rotation	Friability
0.7464	0.7457	0.09%

Table 3.15: Friability data of 1 month sample tablets

Initial weight	Weight after rotation	Friability
0.7451	0.7448	0.04%

Table 3.16: Friability test data of 1 month sample tablet

Initial weight	Weight after rotation	Friability
0.7451	0.7448	0.04%

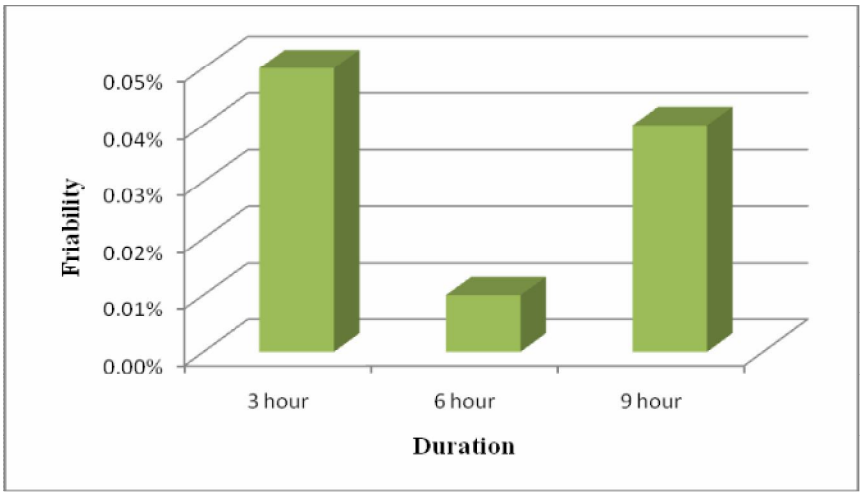


Figure 3.7: Graphical representation of the friabilty percentage

3.1.1.3 Sunlight exposed samples:

3.1.1.3.4 Summer sunlight:

Table 3.17: The percentage weight variation of 3hour exposed tablet sample in summer season

Tablet no.	Initial Weight, (gm)	Average weight (gm)	% Weight Variation
1	0.0719	0.7387/10=0.07387	-0.02
2	0.0719		-0.02
3	0.076		0.02
4	0.0744		0.71
5	0.0722		-0.02
6	0.0741		0.31
7	0.0725		-1.85
8	0.0726		-1.71
9	0.0743		0.582
10	0.0788		6.67

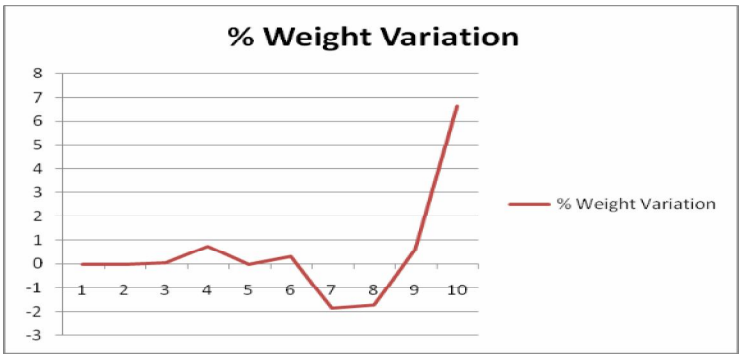


Figure 3.8: Graph of the percentage weight variation of 3 hour exposed in the summer season

Table 3.18: The percentage weight variation of 6 hour exposed tablet sample in summer season

Tablet no.	Initial Weight, (gm)	Average weight (gm)	% Weight Variation
1	0.0734	0.7413/10=0.07413	-0.98
2	0.0739		-0.31
3	0.0764		3.06
4	0.0754		1.71
5	0.0738		-0.44
6	0.0734		-0.9
7	0.0767		3.46
8	0.0756		1.98
9	0.0706		-4.76
10	0.0721		-2.73

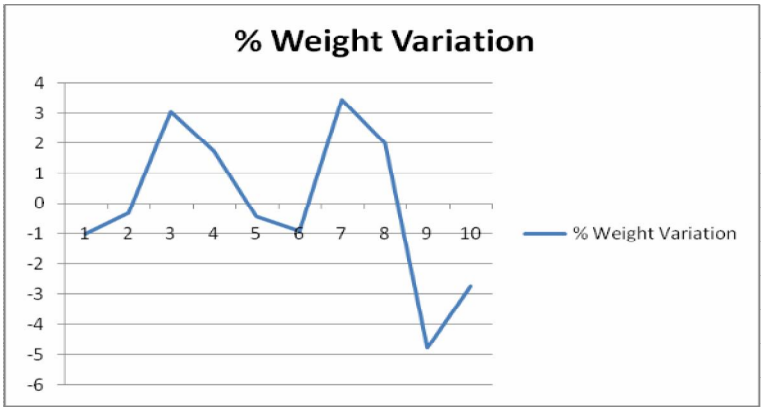


Figure 3.9 : Graph of the percentage weight variation of 6 hour exposed tablet samples in summer season

Table 3.19: The percentage weight variation of 9 hour exposed tablet sample in summer season

Tablet no.	Initial Weight, (gm)	Average weight (gm)	% Weight Variation
1	0.074	0.7357/10=0.07357	0.5
2	0.0747		1.5
3	0.071		-3.49
4	0.0727		-1.18
5	0.074		0.5
6	0.0721		-1.99
7	0.0748		1.67
8	0.0736		0.04
9	0.0741		0.7
10	0.0747		1.5

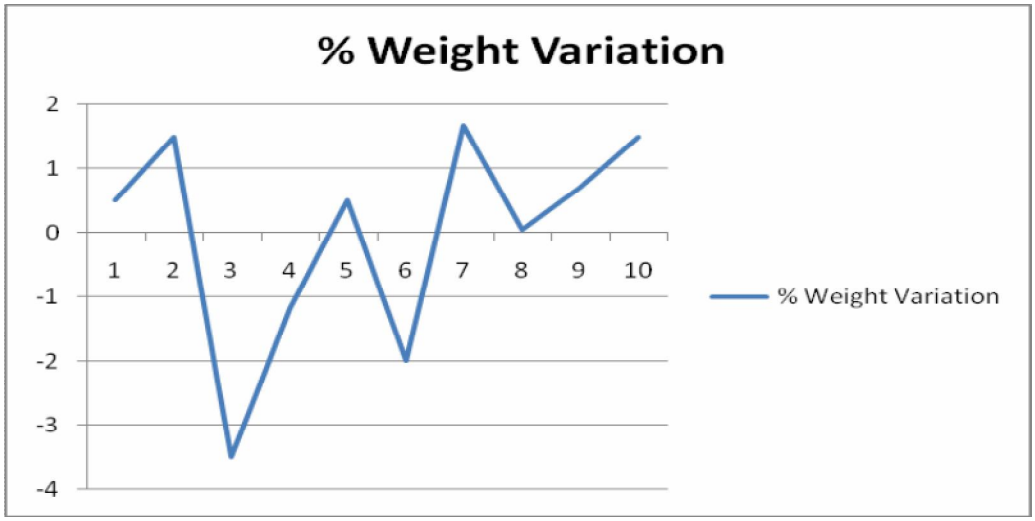


Figure 3.10 : Graph of the percentage weight variation of 9 hour exposed tablet samples in summer season

Table 3.20 : Thickness reading of the 3 hour sample tablet in summer season

Tablet no.	Main scale reading(cm), M	Verniear scale reading(cm), V	Thickness of the tablets (cm),i.e.(M+V) cm
1	0.3	0.005	0.305
2	0.31	0.01	0.32
3	0.29	0.005	0.295
4	0.29	0.06	0.35
5	0.3	0.005	0.305
6	0.3	0.005	0.305
7	0.31	0.01	0.32
8	0.31	0.01	0.32
9	0.3	0.005	0.305
10	0.3	0.005	0.305

Table 3.21 : Thickness reading of the 6 hour sample tablet in summer season

Tablet no.	Main scale reading(cm), M	Verniear scale reading(cm), V	Thickness of the tablets (cm),i.e.(M+V) cm
1	0.3	0.005	0.305
2	0.3	0.01	0.31
3	0.3	0.08	0.38
4	0.3	0.005	0.305
5	0.3	0.08	0.38
6	0.3	0.005	0.305
7	0.31	0.01	0.32
8	0.3	0.005	0.305
9	0.29	0.07	0.36
10	0.3	0.005	0.305

Table 3.22 : Thickness reading of the 9 hour sample tablet in summer season

Tablet no.	Main scale reading(cm), M	Verniear scale reading(cm), V	Thickness of the tablets (cm),i.e.(M+V) cm
1	0.3	0.005	0.305
2	0.31	0.005	0.315
3	0.3	0.09	0.39
4	0.3	0.09	0.39
5	0.29	0.09	0.38
6	0.3	0.005	0.305
7	0.3	0.005	0.305
8	0.29	0.09	0.38
9	0.29	0.07	0.36
10	0.3	0.005	0.305

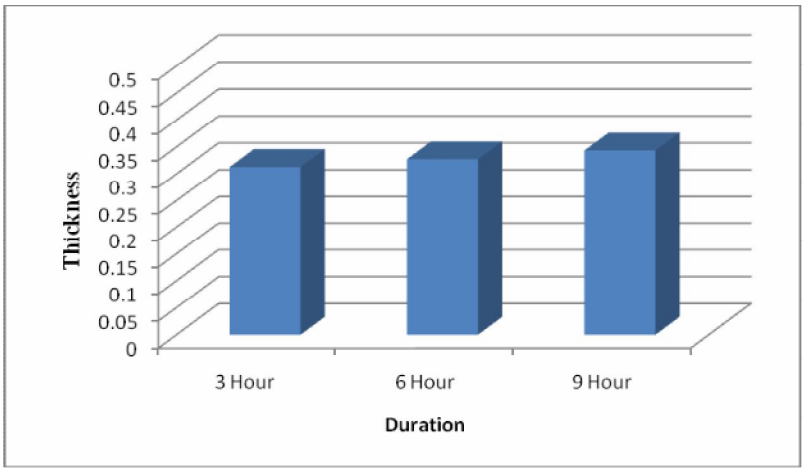


Figure 3.11 : Graphical representation of the mean thickness value among the three sample of sunlight exposure in summer.

Table 3.23: Data of the hardness test of the 3 hour exposed tablets in the sunlight exposure in summer.

Tablet no.	Hardness(kg)	Hardness Averege(kg)
1	2.5	2.766
2	2.7	2.766
3	3.1	2.766

Table 3.24: Data of the hardness test of the 6 hour exposed tablets in the sunlight exposure in summer.

Tablet no.	Hardness(kg)	Hardness Averege(kg)
1	2.5	2.766
2	2.7	2.766
3	3.1	2.766

Table 3.25: Data of the hardness test of the 9 hour exposed tablets in the sunlight exposure in summer.

Tablet no.	Hardness(kg)	Hardness Averege(kg)
1	2.8	2.933
2	2.9	2.933
3	3.1	2.933

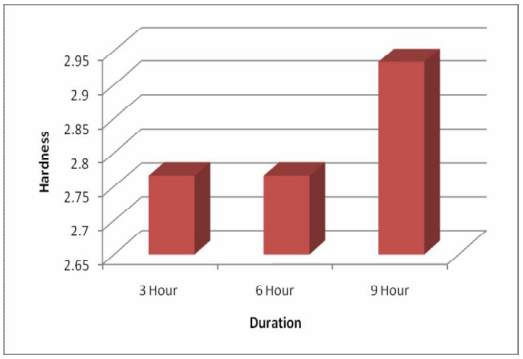


Figure 3.12 : Graphical representation of the mean hardness value of the sunlight exposure samples in summer.

Table 3.26: data for the friability test of the 3 hour exposed tablets in summer season

Initial weight	Weight after rotation	Friability
0.7367	0.736	0.09%

Table 3.27: data for the friability test of the 6 hour exposed tablets in summer season

Initial weight	Weight after rotation	Friability
0.7416	0.7413	0.04%

Table 3.28: data for the friability test of the 6 hour exposed tablets in summer season

Initial weight	Weight after rotation	Friability
0.7357	0.7354	0.04%

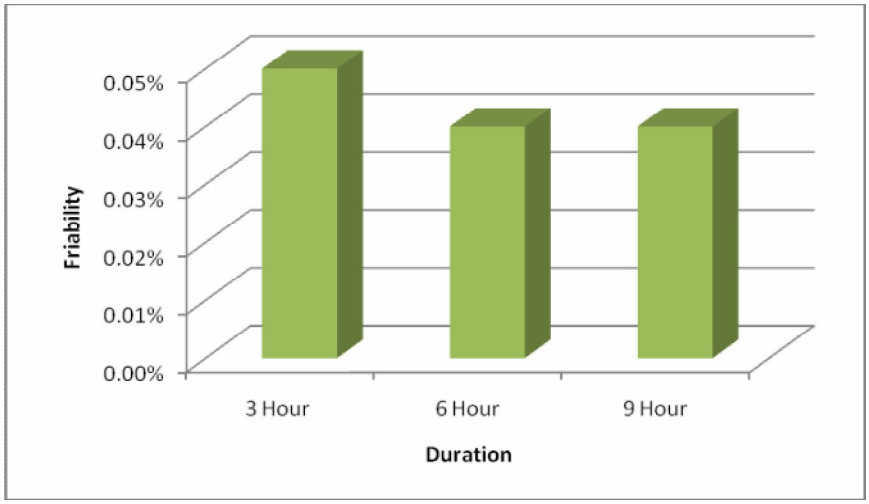


Figure 3.13: Graphical representation of the friabilty percentage

3.1.1.3.4 Winter sunlight:

Table 3.29: The percentage weight variation of 3 hour exposed tablet sample in winter season

Tablet no.	Initial Weight, (gm)	Average weight (gm)	% Weight Variation
1	0.0764	0.7419/10=0.07419	2.97
2	0.0752		1.36
3	0.0733		-1.19
4	0.0717		-3.35
5	0.0724		-2.41
6	0.0725		-2.27
7	0.0706		-0.04
8	0.0752		1.36
9	0.0769		3.65
10	0.0777		4.73

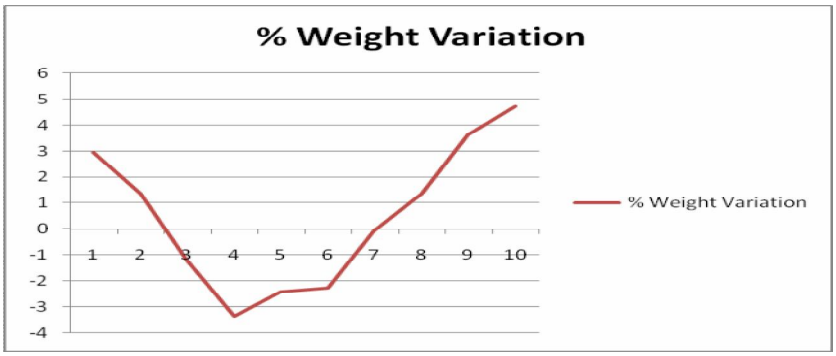


Figure 3.14 : Graph of the percentage weight variation of 3 hour exposed tablet samples in winter season

Table 3.30: The percentage weight variation of 6 hour exposed tablet sample in winter season

Tablet no.	Initial Weight, (gm)	Average weight (gm)	% Weight Variation
1	0.0697	0.7439/10=0.07439	-6.99
2	0.0763		2.56
3	0.075		0.82
4	0.0763		2.56
5	0.0778		4.58
6	0.0734		-1.33
7	0.0732		-1.59
8	0.0746		0.28
9	0.0748		0.55
10	0.0728		-2.13

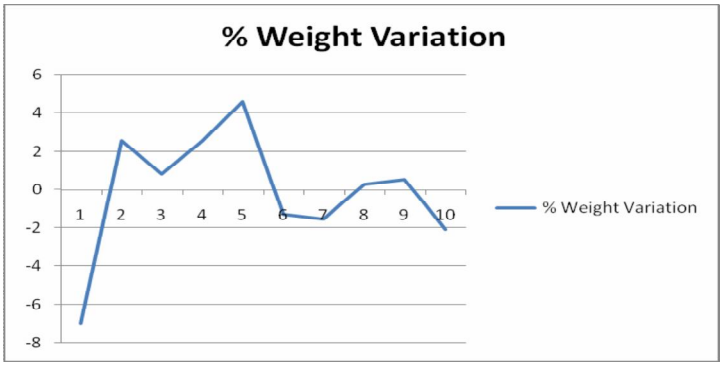


Figure 3.15: Graph of the percentage weight variation of 6 hour exposed tablet samples in winter season

Table 3.31: The percentage weight variation of 9 hour exposed tablet sample in winter season

Tablet no.	Initial Weight, (gm)	Average weight (gm)	% Weight Variation
1	0.0749	0.7446/10=0.07446	0.5
2	0.0726		-2.49
3	0.0737		-1
4	0.0751		0.85
5	0.0731		-1.82
6	0.0742		-0.34
7	0.0732		-1.6
8	0.075		0.72
9	0.0775		4.08
10	0.0753		1.12

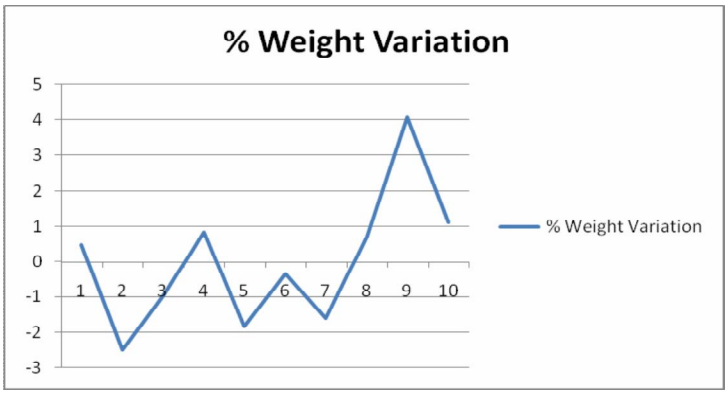


Figure 3.16 : Graph of the percentage weight variation of 6 hour exposed tablet samples in winter season

Table 3.32: Thickness reading of the 3 hour sample tablet in winter season

Tablet no.	Main scale reading(cm), M	Verniear scale reading(cm), V	Thickness of the tablets (cm),i.e.(M+V) cm
1	0.3	0.005	0.305
2	0.3	0.005	0.305
3	0.3	0.005	0.305
4	0.31	0.005	0.315
5	0.3	0.005	0.305
6	0.31	0.005	0.315
7	0.32	0.01	0.33
8	0.31	0.01	0.32
9	0.3	0.005	0.305
10	0.3	0.005	0.305

Table 3.33: Thickness reading of the 6 hour sample tablet in winter season

Tablet no.	Main scale reading(cm), M	Verniear scale reading(cm), V	Thickness of the tablets (cm),i.e.(M+V) cm
1	0.3	0.005	0.305
2	0.3	0.005	0.305
3	0.3	0.005	0.305
4	0.31	0.005	0.315
5	0.3	0.005	0.305
6	0.31	0.005	0.315
7	0.32	0.01	0.33
8	0.31	0.01	0.32
9	0.3	0.005	0.305
10	0.3	0.005	0.305

Table 3.34: Thickness reading of the 9 hour sample tablet in winter season

Tablet no.	Main scale reading(cm), M	Verniear scale reading(cm), V	Thickness of the tablets (cm),i.e.(M+V) cm
1	0.3	0.005	0.305
2	0.3	0.005	0.305
3	0.3	0.005	0.305
4	0.3	0.005	0.305
5	0.3	0.005	0.305
6	0.3	0.005	0.305
7	0.29	0.01	0.3
8	0.31	0.01	0.32
9	0.3	0.005	0.305
10	0.3	0.005	0.305

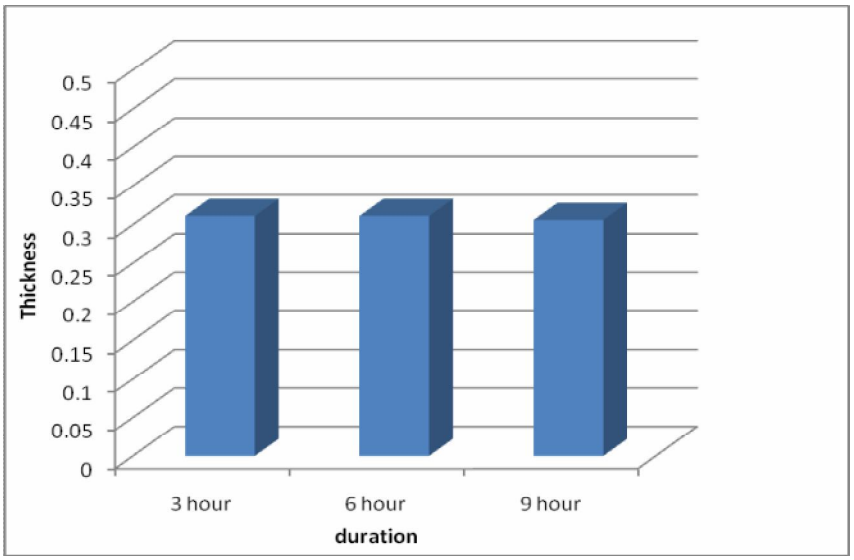


Figure 3.17 :Graphical representation of the mean thickness value among the three sample of sunlight exposure in winter.

Table 3.35: Data of the hardness test of the 3 hour exposed tablets in the winter season.

Tablet no.	Hardness(kg)	Hardness Averege(kg)
1	2.5	3.26
2	3.3	3.26
3	4	3.26

Table 3.36: Data of the hardness test of the 3 hour exposed tablets in the winter season.

Tablet no.	Hardness(kg)	Hardness Averege(kg)
1	3	3.63
2	4.1	3.63
3	3.8	3.63

Table 3.37: Data of the hardness test of the 9 hour exposed tablets in the winter season.

Tablet no.	Hardness(kg)	Hardness Averege(kg)
1	3.8	3.9
2	4	3.9
3	3.9	3.9

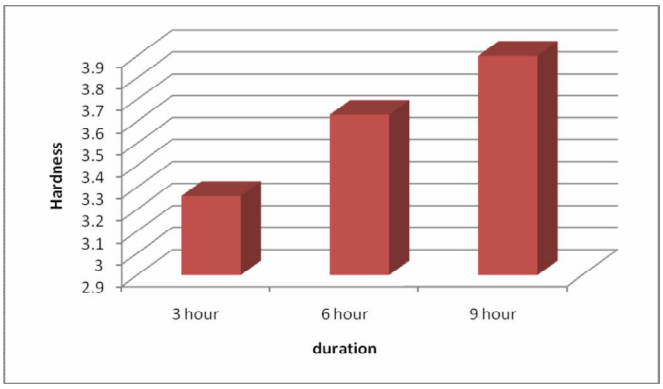


Figure 3.18 : Graphical representation of the mean hardness value of the sunlight exposure samples in summer.

Table 3.38: data for the friability test of the 3 hour exposed tablets in winter season

Initial weight	Weight after rotation	Friability
0.7419	0.7406	0.17%

Table 3.39: data for the friability test of the 6 hour exposed tablets in winter season

Initial weight	Weight after rotation	Friability
0.7405	0.7394	0.14%

Table 3.40: data for the friability test of the 9 hour exposed tablets in winter season

Initial weight	Weight after rotation	Friability
0.7421	0.742	0.01%

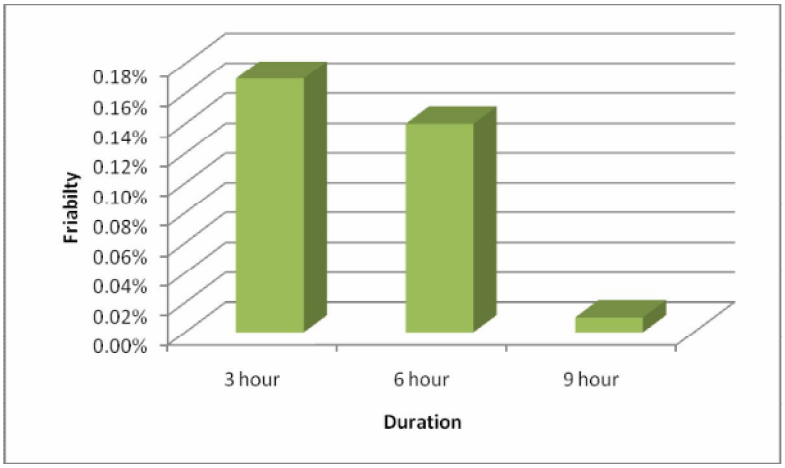


Figure 3.19 : Graphical representation of the friabilty percentage

3.1.1.4 Electrical light exposure:

The electrical light exposure also showed the degradation of the compounds comparing to the control tablets but not as the same manner as the normal room temperature and the sunlight exposure. The result and discussion of the bulb light exposure samples are given below:

3.1.1.4.1 25 Watt:

Table 3.41: The percentage weight variation of 3 hour exposed tablet sample

Tablet no.	Initial Weight, (gm)	Average weight (gm)	% Weight Variation
1	0.0729	0.7412/10=0.07412	-1.6
2	0.0733		-1.1
3	0.0752		1.4
4	0.0759		2.4
5	0.0732		-1.2
6	0.0755		1.8
7	0.0724		-2.3
8	0.0747		0.7
9	0.0751		1.3
10	0.073		-1.5

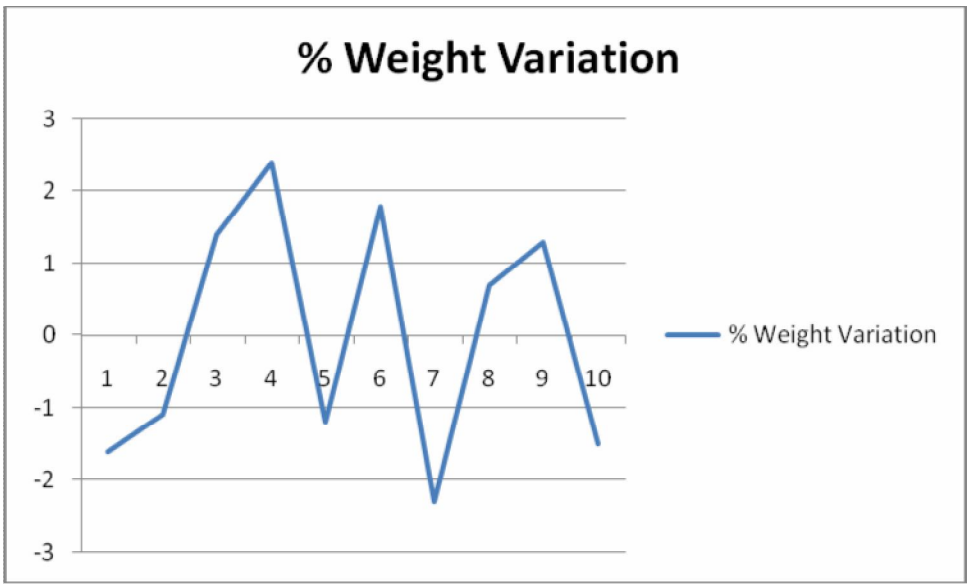


Figure3.20 : Graph of the percentage weight variation of 3 hour exposed samples.

Table 3.42: The percentage weight variation of 6 hour exposed tablet sample

Tablet no.	Initial Weight, (gm)	Average weight (gm)	% Weight Variation
1	0.0729	0.7371/10= 0.07371	-1.09
2	0.0733		-0.55
3	0.0735		-0.28
4	0.0753		2.15
5	0.073		-0.9
6	0.0736		-0.14
7	0.0734		-0.4
8	0.0753		2.1
9	0.0711		-3.5
10	0.0757		2.69

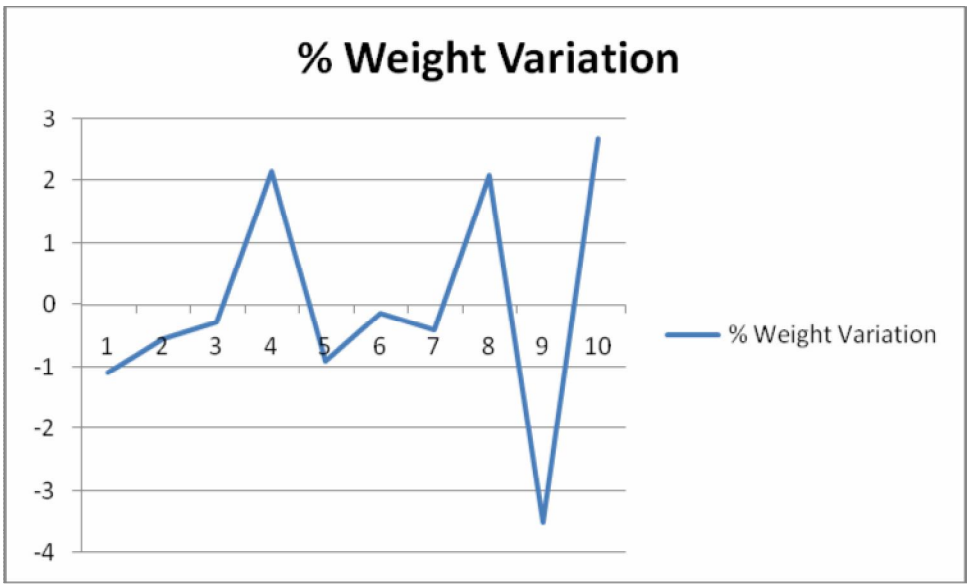


Figure 3.21: Graph of the percentage weight variation of 6 hour exposed samples.

Table 3.43: The percentage weight variation of 9 hour exposed tablet sample

Tablet no.	Initial Weight, (gm)	Average weight (gm)	% Weight Variation
1	0.0752	0.7489/10=0.07489	0.4
2	0.0761		1.6
3	0.0729		-2.65
4	0.0747		-0.2
5	0.0756		0.9
6	0.0747		-0.2
7	0.0757		1.08
8	0.0736		-1.7
9	0.0744		-0.6
10	0.076		1.48

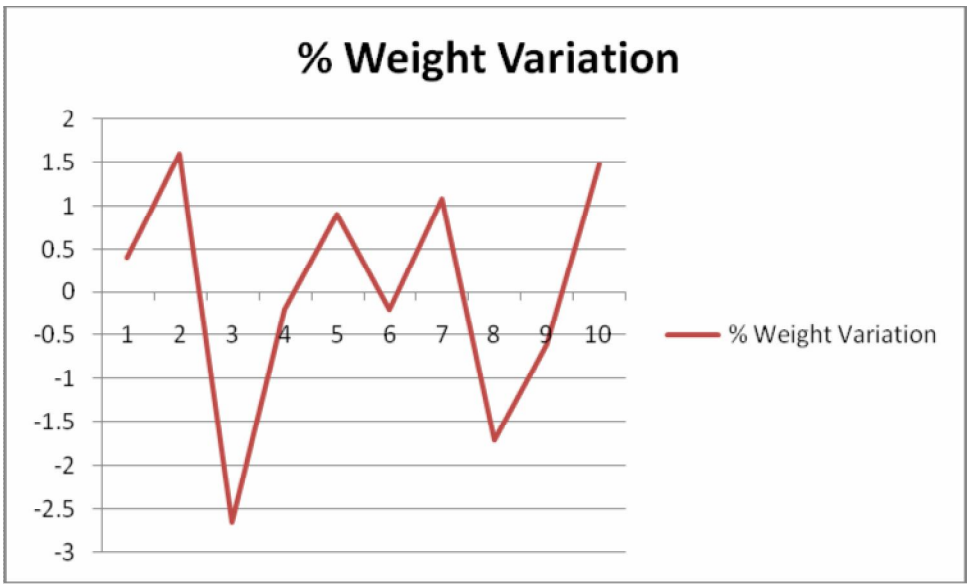


Figure 3.22 : Graph of the percentage weight variation of 9 hour exposed samples.

Table 3.44: Thickness reading of the 3 hour exposed sample tablet

Tablet no.	Main scale reading(cm), M	Verniear scale reading(cm), V	Thickness of the tablets (cm),i.e.(M+V) cm
1	0.3	0.005	0.305
2	0.3	0.005	0.305
3	0.3	0.005	0.305
4	0.3	0.005	0.305
5	0.29	0.07	0.36
6	0.3	0.005	0.305
7	0.3	0.005	0.305
8	0.3	0.005	0.305
9	0.31	0.005	0.305
10	0.31	0.01	0.32

Table 3.45 : Thickness reading of the 6 hour exposed sample tablet

Tablet no.	Main scale reading(cm), M	Verniear scale reading(cm), V	Thickness of the tablets (cm),i.e.(M+V) cm
1	0.3	0.005	0.305
2	0.3	0.005	0.305
3	0.3	0.005	0.305
4	0.3	0.005	0.305
5	0.29	0.07	0.36
6	0.3	0.005	0.305
7	0.3	0.005	0.305
8	0.3	0.005	0.305
9	0.31	0.005	0.305
10	0.31	0.01	0.32

Table 3.46: Thickness reading of the 9 hour exposed sample tablet

Tablet no.	Main scale reading(cm), M	Verniear scale reading(cm), V	Thickness of the tablets (cm),i.e.(M+V) cm
1	0.3	0.005	0.305
2	0.3	0.005	0.305
3	0.3	0.005	0.305
4	0.3	0.005	0.305
5	0.29	0.07	0.36
6	0.3	0.005	0.305
7	0.3	0.005	0.305
8	0.3	0.005	0.305
9	0.31	0.005	0.305
10	0.31	0.01	0.32

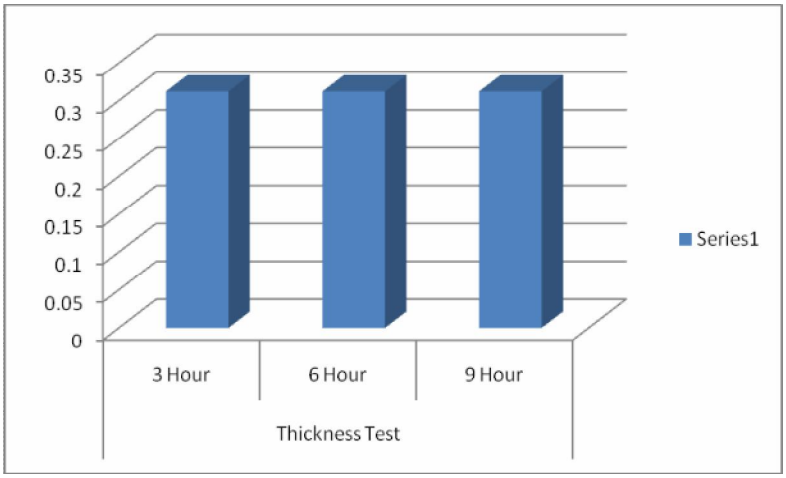


Figure 3.23 : Graphical representation of the mean thickness value among the three sample of 25 Watt bulb exposure.

Table 3.47: Data of the hardness test of the 3 hour exposed tablets.

Tablet no.	Hardness(kg)	Hardness Averege(kg)
1	2.9	2.66
2	2.5	2.66
3	2.6	2.66

Table 3.48: Data of the hardness test of the 6 hour exposed tablets.

Tablet no.	Hardness(kg)	Hardness Averege(kg)
1	2.9	2.8
2	2.5	2.8
3	3.1	2.8

Table 3.49: Data of the hardness test of the 9 hour exposed tablets.

Tablet no.	Hardness(kg)	Hardness Averege(kg)
1	2.9	3.0667
2	3.1	3.0667
3	3.2	3.0667

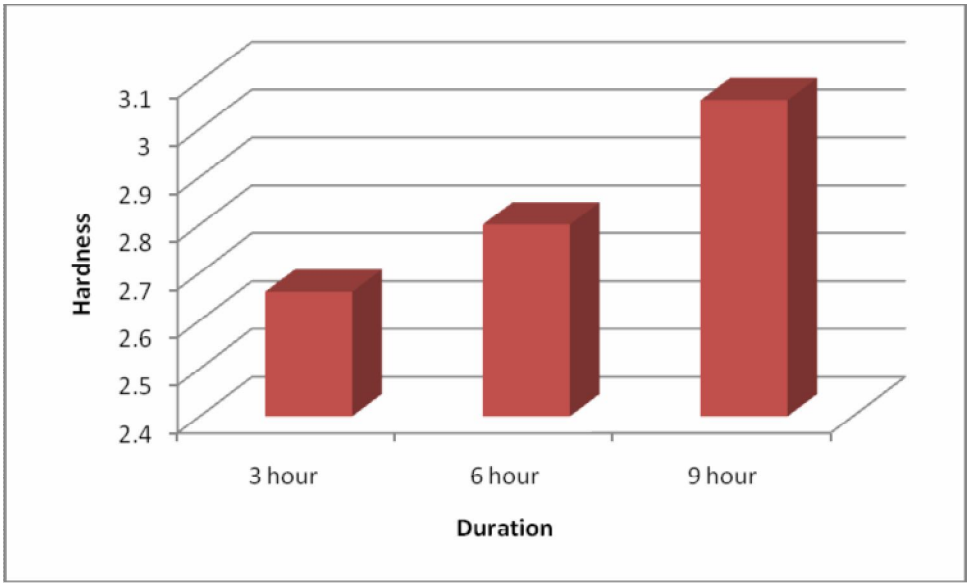


Figure 3.24: Graphical representation of the mean hardness value of the 25 watt exposed tablets

The friability was within the range.

Table 3.50: data for the friability test of the 3 hour exposed tablets

Initial weight	Weight after rotation	Friability
0.7411	0.741	0.01%

Table 3.51 : data for the friability test of the 6 hour exposed tablets

Initial weight	Weight after rotation	Friability
0.7338	0.7335	0.04%

Table 3.52: data for the friability test of the 9 hour exposed tablets.

Initial weight	Weight after rotation	Friability
0.7482	0.7481	0.01%

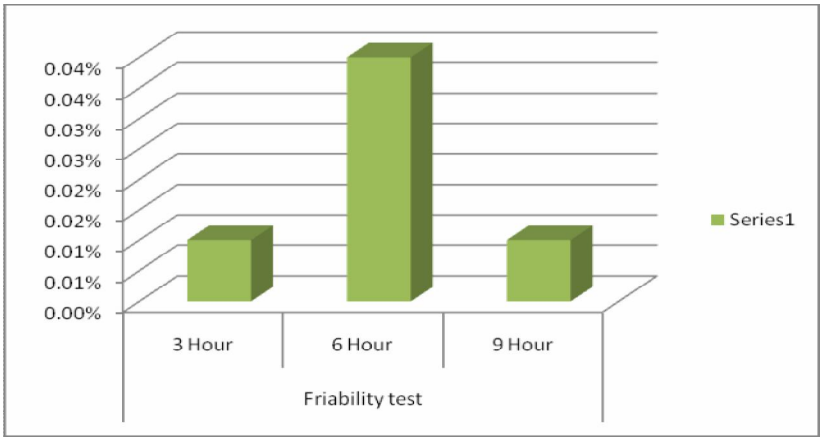


Figure 3.25 : Graphical representation of the friabilty percentage

3.1.1.4.2 40 watt exposed samples:

Table 3.53: The percentage weight variation of 3 hour exposed tablet sample

Tablet no.	Initial Weight, (gm)	Average weight (gm)	% Weight Variation
1	0.0796	0.7340/10=0.0734	8.4
2	0.0714		-27
3	0.0762		3.81
4	0.0627		-14.57
5	0.0714		-2.7
6	0.077		4.9
7	0.0745		-1.6
8	0.075		2.17
9	0.0718		-2.17
10	0.0744		1.36

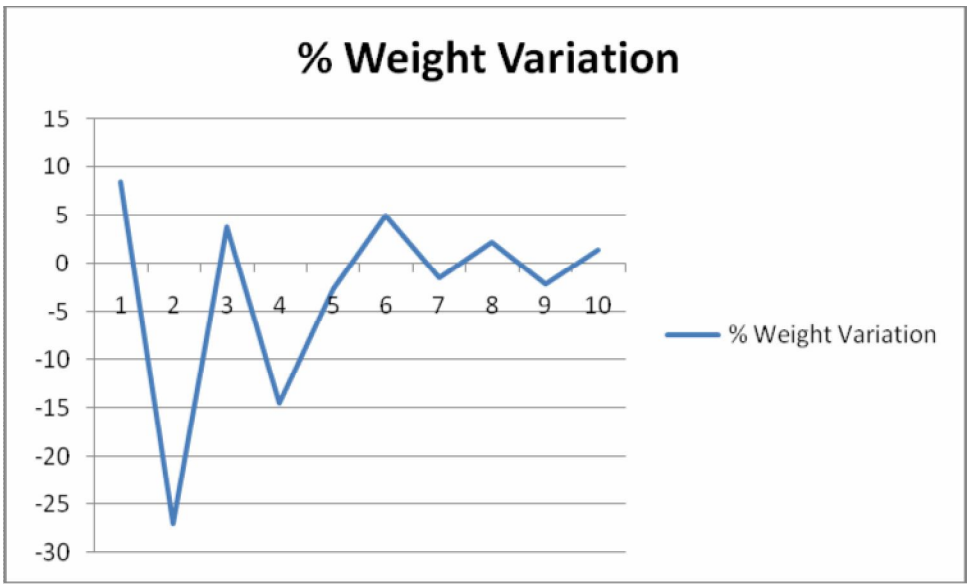


Figure 3.26: Graph of the percentage weight variation of 3 hour exposed samples.

Table 3.54: The percentage weight variation of 3 hour exposed tablet sample

Tablet no.	Initial Weight, (gm)	Average weight (gm)	% Weight Variation
1	0.0752	0.7432/10=0.07432	1.18
2	0.0726		-2.3
3	0.0751		1.04
4	0.0734		-1.23
5	0.0742		-0.1
6	0.0751		1.04
7	0.0758		1.99
8	0.0745		0.24
9	0.074		-0.4
10	0.0733		-1.37

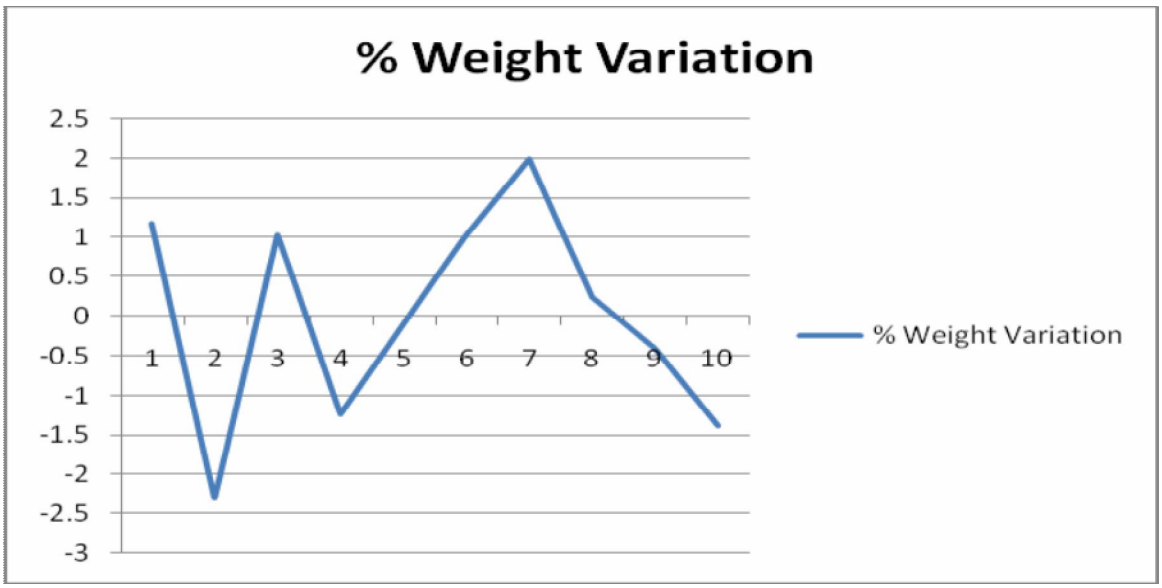


Figure 3.27*:* Graph of the percentage weight variation of 6 hour exposed samples.

Table 3.55 : The percentage weight variation of 9 hour exposed tablet sample

Tablet no.	Initial Weight, (gm)	Average weight (gm)	% Weight Variation
1	0.0719	0.7437/10=0.07437	-3.32
2	0.0716		-3.72
3	0.0751		0.98
4	0.0728		-2.1
5	0.077		3.53
6	0.0773		3.93
7	0.0737		-0.9
8	0.073		-1.8
9	0.0748		0.5
10	0.0765		2.86

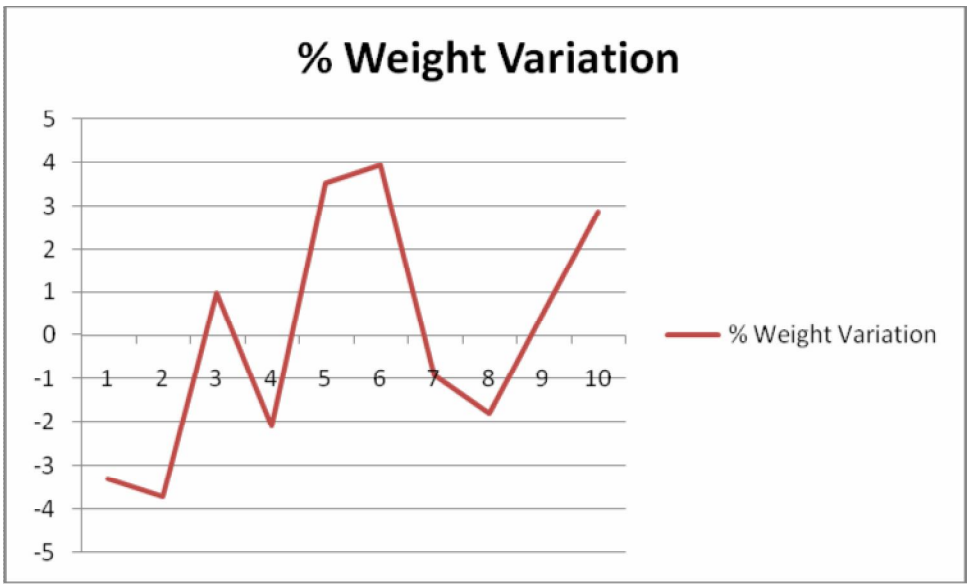


Figure 3.28: Graph of the percentage weight variation of 9 hour exposed samples.

Table 3.56: Thickness reading of the 3 hour exposed sample tablet

Tablet no.	Main scale reading(cm), M	Verniear scale reading(cm), V	Thickness of the tablets (cm),i.e.(M+V) cm
1	0.3	0.005	0.305
2	0.3	0.005	0.305
3	0.3	0.005	0.305
4	0.3	0.005	0.305
5	0.29	0.0048	0.2948
6	0.29	0.0048	0.2948
7	0.3	0.0049	0.3049
8	0.31	0.005	0.315
9	0.28	0.0047	0.2847
10	0.3	0.005	0.305

Table 3.57: Thickness reading of the 6 hour exposed sample tablet

Tablet no.	Main scale reading(cm), M	Verniear scale reading(cm), V	Thickness of the tablets (cm),i.e.(M+V) cm
1	0.29	0.09	0.38
2	0.3	0.005	0.305
3	0.3	0.005	0.305
4	0.3	0.005	0.305
5	0.3	0.005	0.305
6	0.3	0.005	0.305
7	0.3	0.005	0.305
8	0.3	0.005	0.305
9	0.3	0.005	0.305
10	0.3	0.005	0.305

Table 3.58 : Thickness reading of the 9 hour exposed sample tablet

Tablet no.	Main scale reading(cm), M	Verniear scale reading(cm), V	Thickness of the tablets (cm),i.e.(M+V) cm
1	0.29	0.3	0.305
2	0.3	0.005	0.305
3	0.3	0.005	0.305
4	0.3	0.005	0.305
5	0.3	0.005	0.305
6	0.3	0.005	0.305
7	0.3	0.005	0.305
8	0.3	0.005	0.305
9	0.3	0.005	0.305
10	0.3	0.005	0.305

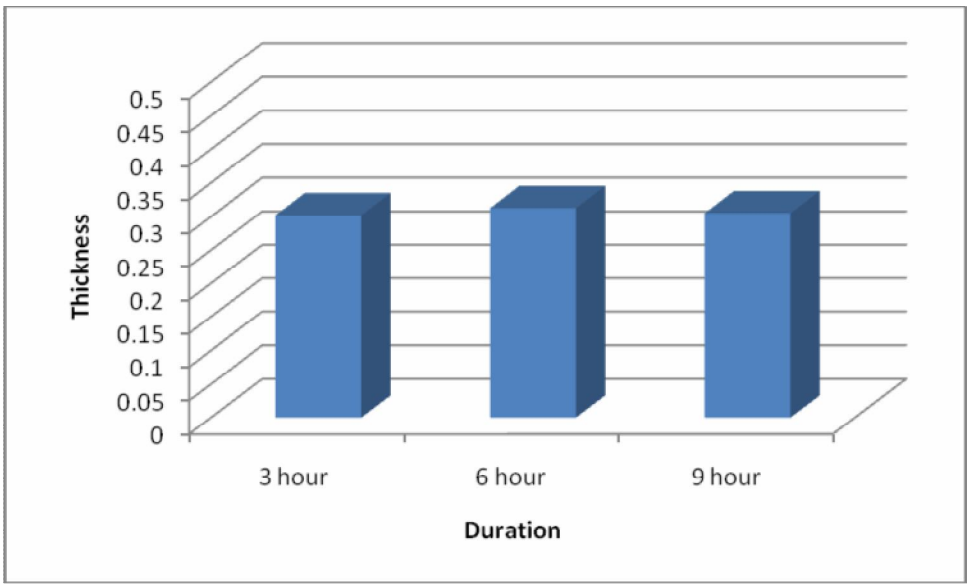


Figure 3.29 : Graphical representation of the mean thickness value among the three sample of 40 Watt bulb exposure.

Table 3.59 : Data of the hardness test of the 3 hour exposed tablets

Tablet no.	Hardness(kg)	Hardness Averege(kg)
1	3.5	3.38
2	3.6	3.38
3	3.6	3.38
4	3.1	3.38
5	3.1	3.38

Table 3.60: Data of the hardness test of the 6 hour exposed tablets

Tablet no.	Hardness(kg)	Hardness Averege(kg)
1	3.1	2.98
2	2.9	2.98
3	2.9	2.98
4	2.9	2.98
5	3.1	2.98

Table 3.61: Data of the hardness test of the 9 hour exposed tablets

Tablet no.	Hardness(kg)	Hardness Averege(kg)
1	2.9	3.1
2	3.1	3.1
3	3.2	3.1
4	3.3	3.1
5	3	3.1

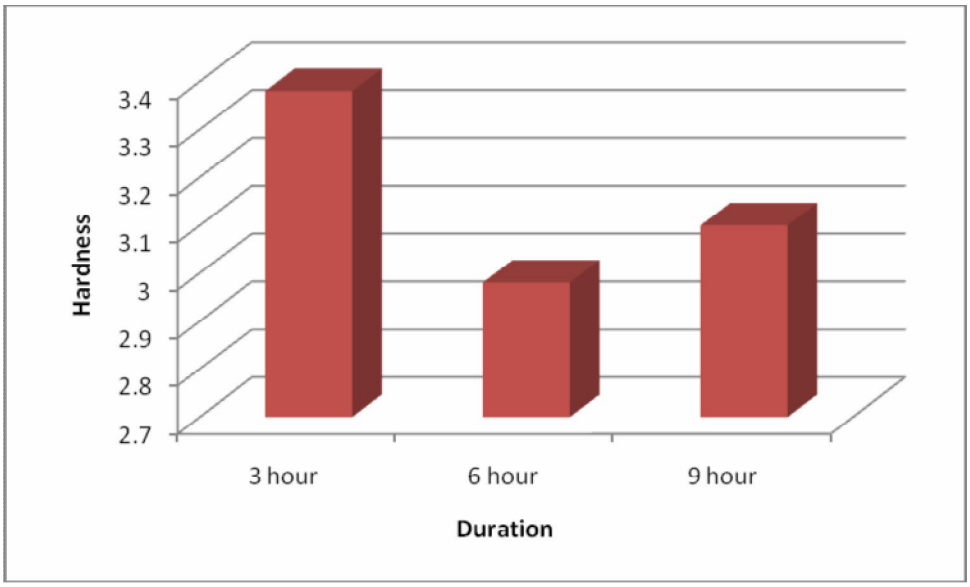


Figure 3.30 *:* Graphical representation of the mean hardness value of the 25 watt exposed tablets

The friabity data was between the range not more than 1%.

Table 3.62 : data for the friability test of the 3 hour exposed tablets

Initial weight	Weight after rotation	Friability
0.7367	0.736	0.09%

Table 3.63: data for the friability test of the 6 hour exposed tablets

Initial weight	Weight after rotation	Friability
0.7409	0.7406	0.04%

Table 3.64: data for the friability test of the 9 hour exposed tablets

Initial weight	Weight after rotation	Friability
0.7396	0.7394	0.02%

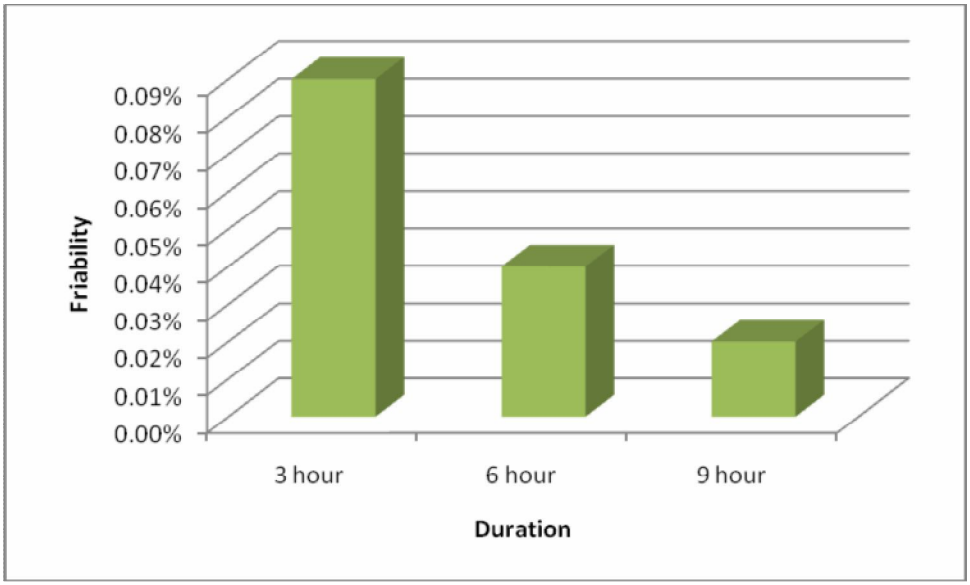


Figure 3.31 : Graphical representation of the friabilty percentage

3.1.2 Potency test:

The potency determination did reveal that there is a occurance of photodegradation of the drug. The liniear regression equation was derived from the calibration curve which was y = 90.16x and R^2=1 for flupentixol and for melitracen it was y=4.077x : R^2 = 0.999,Where y is the absorbance and x is the concentration.The equation shows that a liniear line has being obtained.

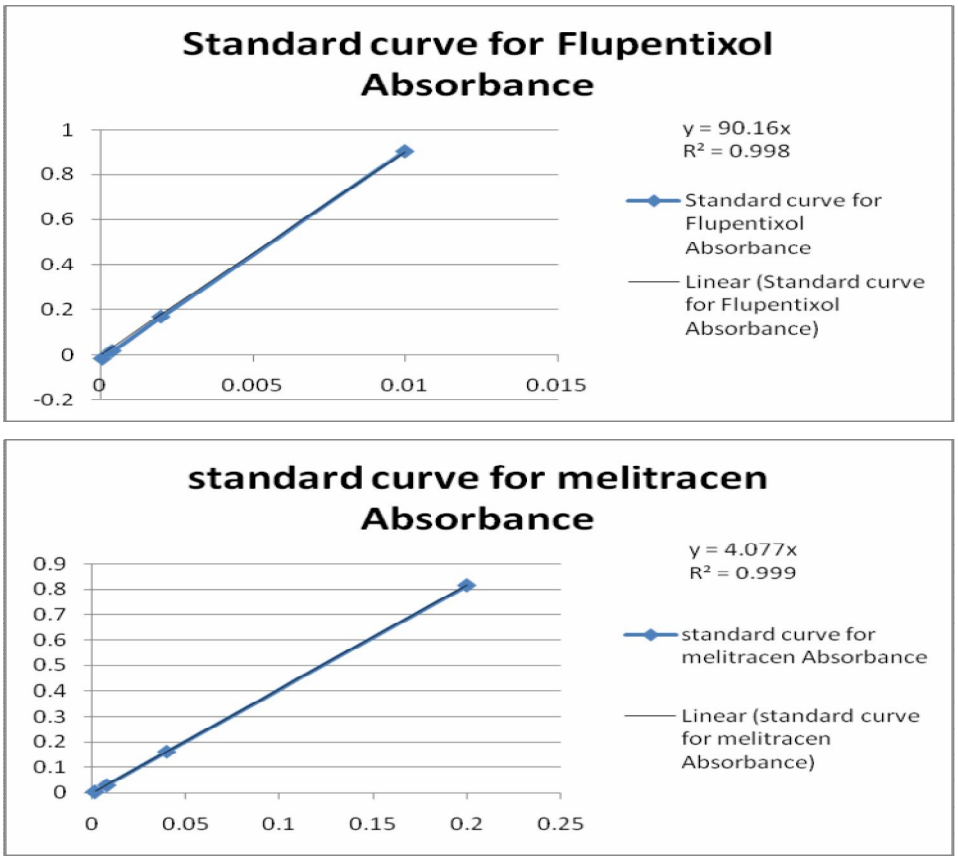


Figure 3.32: Standard curve and equation derivation of flupentixol and Melitracen

3.1.2.1 Control:

Table 3.65: Absorbance and concentration data of the control tablets of flupentixol

UV analysis for flupentixol		
Condition	Concentration (mg)	Absorbance in 229nm
Blank	0	0
control	0.00673	0.606

Table 3.66: Absorbance and concentration data of the control for Melitracen

UV analysis for Melitracen		
Condition	Concentration(mg)	Absorbance in 258nm
Blank	0	0
control	0.12435	0.507

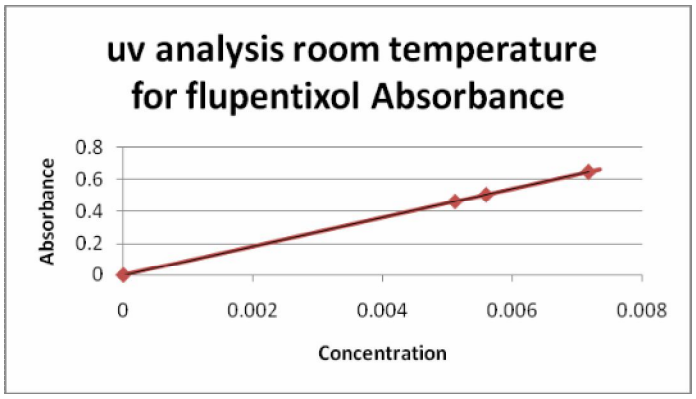
3.1.2.2 Normal room temperature:

Table 3.67: The absorbance and concentration data for Flupentixol of normal room condition samples.

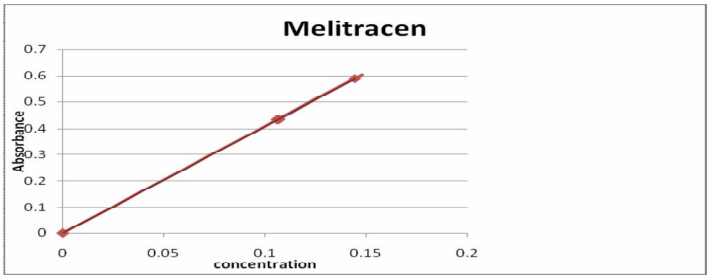
	UV analysis room temperature for flupentixol	
Condition	Concentration (mg)	Absorbance in 229nm
Blank	0	0
2 week	0.00718	0.648
1 month	0.0056	0.505
2 month	0.00512	0.462

Table 3.68 : The absorbance and concentration data for Melitracen of normal room condition samples.

Condition	UV analysis room temperature for Melitracen	
	Concentration (mg)	Absorbance in 258nm
Blank	0	0
2 week	0.1445	0.589
1 month	0.107	0.434
2 month	0.106	0.433

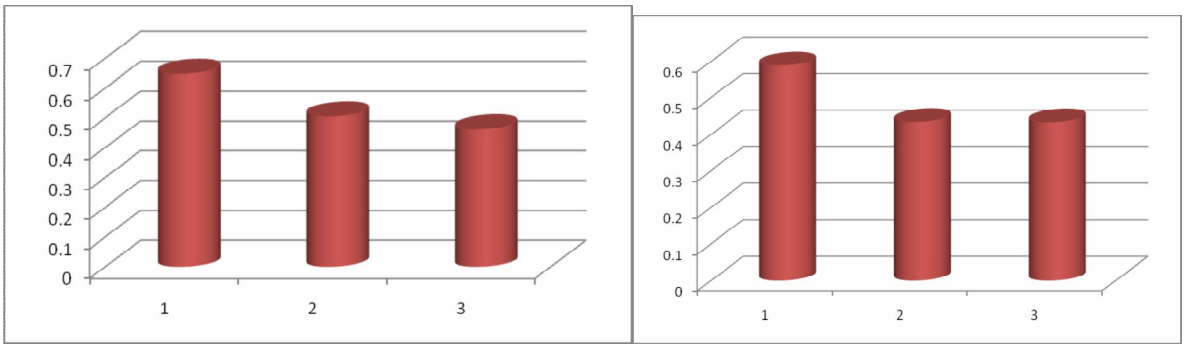


(a)



(b)

Figure 3.33 : UV analysis for flupentixol and melitracen absorbance Vs concentration graph.(a) Flupentixol (b) Melitracen



(a) (b)

Figure 3.34: Bar diagram of the absorbance of the three conditions 1 denote the 2 week sample, 2 denote the 1 month sample and 3 denote the 2 month sample.(a) is for flupentixol and (b) is for Melitracen.

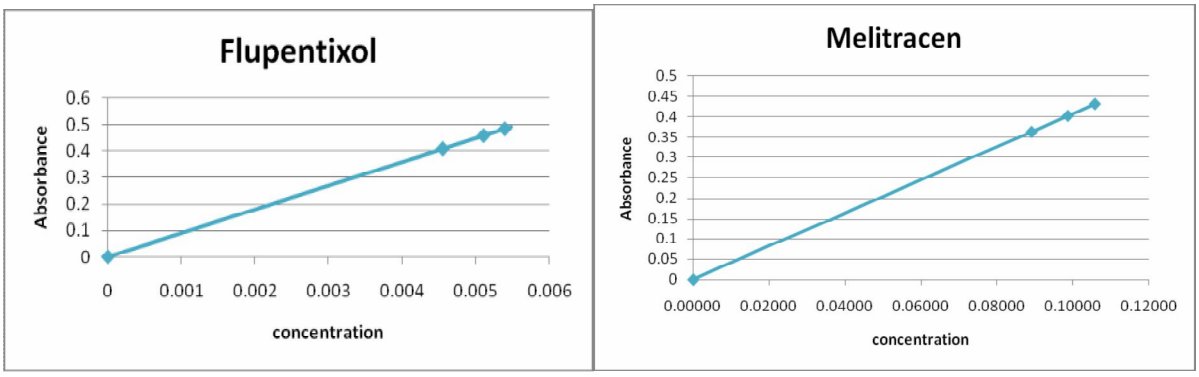
3.1.2.3 Sunlight exposure:

Table 3.69: The absorbance and concentration data for Flupentixol of sunlight exposure in summer samples

UV analysis for flupentixol		
condition	Concentration (mg)	Absorbance in 229nm
Blank	0	0
3 hour	0.0054	0.486
6 hour	0.00454	0.41
9 hour	0.00510	0.46

Table 3.70: The absorbance and concentration data for Melitracen of sunlight exposure in summer samples.

UV analysis for melitracen		
Condition	Concentration (mg)	Absorbance in 258nm
Blank	0.00000	0
3 hour	0.0986	0.402
6 hour	0.0890	0.363
9 hour	0.1057	0.431



(a) (b)

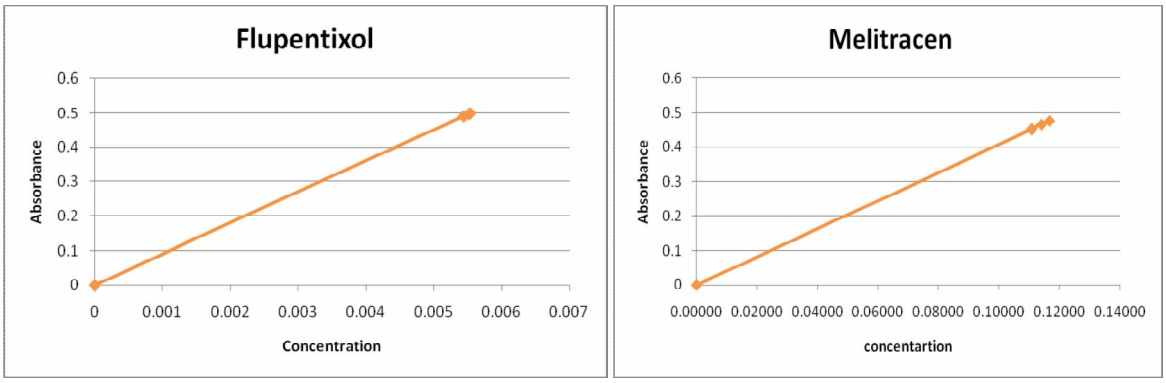
Figure 3.35 : UV spectrophotometry for flupentixol and melitracen absorbance Vs concentration graph.(a)Flupentixol (b) Melitracen of summer sunlight.

Table 3.71: The absorbance and concentration data for Flupentixol of sunlight exposure in Winter samples

UV analysis for flupentixol		
condition	Concentration (mg)	Absorbance in 229nm
Blank	0	0
3 hour	0.00552	0.497
6 hour	0.00543	0.49
9 hour	0.00553	0.499

Table 3.72: The absorbance and concentration data for melitracen of sunlight exposure in winter samples

UV analysis for melitracen		
Duration	Concentration (mg)	Absorbance in 258 nm
Blank	0.00000	0
3 hour	0.11675	0.476
6 hour	0.11405	0.465
9 hour	0.11087	0.452



(a) (b)

Figure 3.36 : UV spectrophotometry analysis for flupentixol and melitracen absorbance Vs concentration graph.(a) flupentixol (b) Melitracen of winter sunlight.

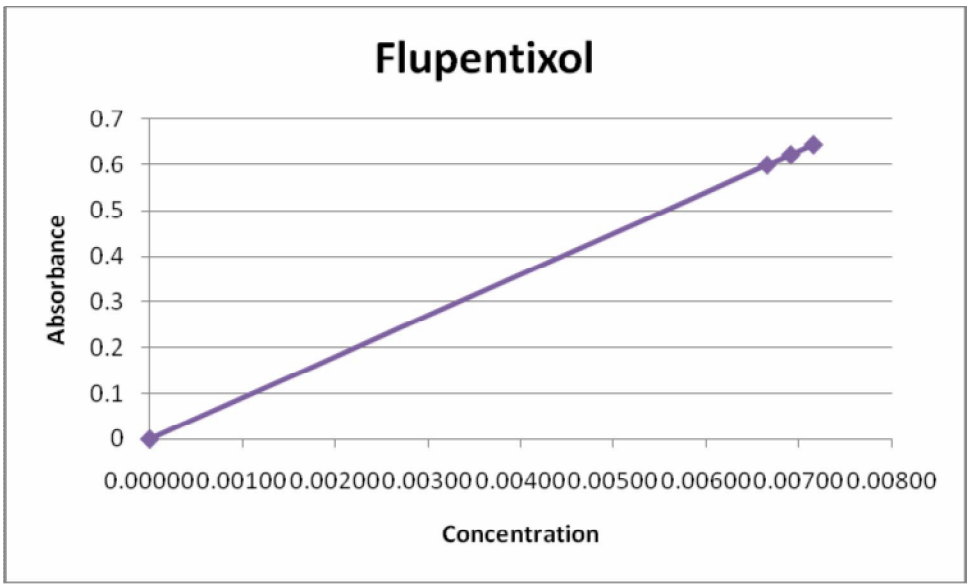
3.1.2.4 Electrical light exposure:

Table 3.73 : The absorbance and concentration data for Flupentixol of 25 watt bulb exposure.

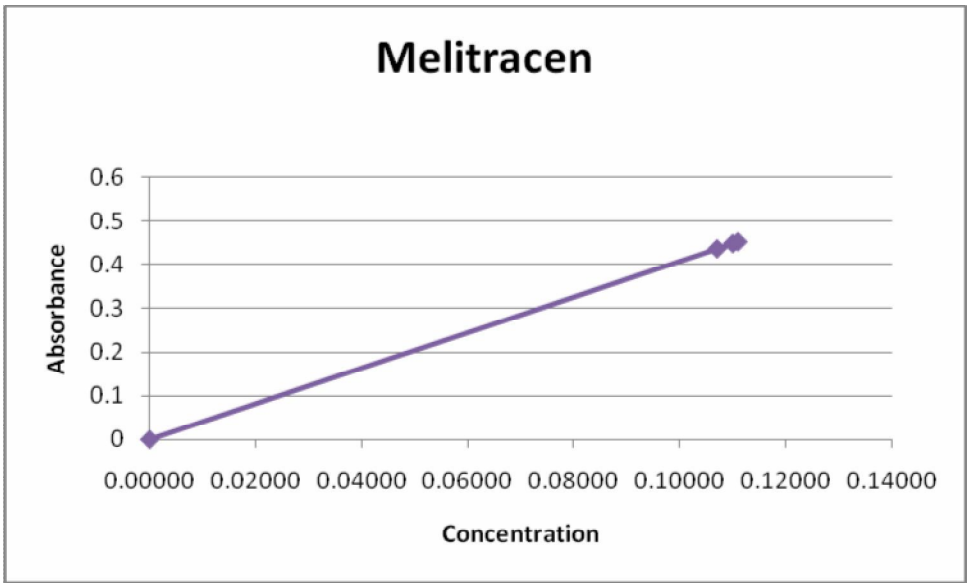
Uv analysis for flupentixol		
condition	Concentration (mg)	Absorbance in 229nm
Blank	0.00000	0
3 hour	0.00665	0.6
6 hour	0.00715	0.645
9 hour	0.00691	0.623

Table 3.74: The absorbance and concentration data for Flupentixol of 25 watt bulb exposure.

Uv analysis of 40 watt sample for melitracen		
Duration	Concentration (mg)	Absorbance in 258nm
Blank	0.00000	0
3 hour	0.10988	0.448
6 hour	0.11087	0.452
9 hour	0.10694	0.436



(a)



(b)

Figure 3.37 : UV spectrophotometry analysis for flupentixol and melitracen absorbance Vs concentration graph. (a) flupentixol (b) Melitracen

Table 3.75 : The absorbance and concentration data for Flupentixol of 40 watt bulb exposure

UV analysis of 40 watt for flupentixol		
condition	Concentration (mg)	Absorbance in 229nm
Blank	0	0
3 hour	0.0051	0.46
6 hour	0.00515	0.465
9 hour	0.00568	0.513

Table 3.76: The absorbance and concentration data for Melitracen of 40 watt bulb exposure

Uv analysis of 40 watt for melitracen		
condition	Concentration (mg)	Absorbance in 258nm
Blank	0	0
3 hour	0.051	0.21
6 hour	0.063	0.259
9 hour	0.07	0.285

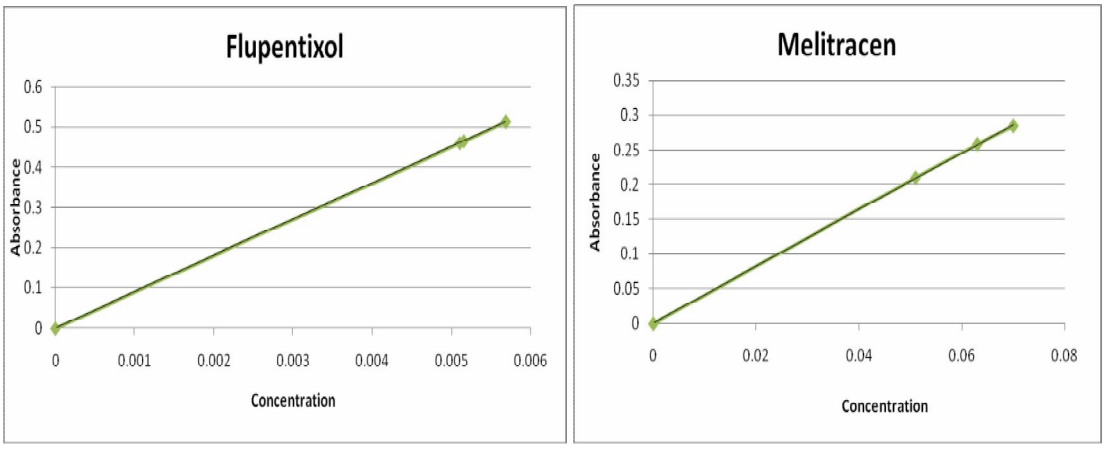


Figure 3.38: UV spectrophotometry analysis for flupentixol and melitracen absorbance Vs concentration graph. (a) flupentixol (b) Melitracen

3.2 Discussion:

3.2.1 The normal room temperature:

3.2.1.1 Physical parameter:

The Table is showing the percentage weight variation of the 2 week ,1 month and 2 month samples.The percentage weight variation of all the sample tablets are with in the range, which is ± 10 for 130 mg or less dosage form according to the united state pharmacopeia. There was no major deviation of the content uniformity by the exposure of the light or radiation. But the weight of the tablet fluctuate than the control tablet that been used. Figure 3.2, 3.3 and 3.4 is just representing the graph of the statistical data of the weight variation of each sample.

The thickness variation among the three sample of the normal room condition.It is showing that there are no major effect of the photo exposure on the thickness of the tablets.All the sample having quite a similar thickness range . but there were a slight deviation of the thickness of 2 month sample.

The mean value of the thickness of each sample. And showing that according to the duration of the exposure the mean thickness value falls. But it was more than the control value.

There have being a little effect on the hardness and the friability of the tablets due to the exposure of the light and radiation compare with the control data.But both of the parameters where at the range. For friability it was not more than 1% according to the USP. For 2 week sample the friability test percentage was 0.09%, for 1 month samples it was 0.04% and for 2 month samples it was also 0.04% and the control value was 0.01% .Where the 2 week tablet have the highest value than the others and the value was same as the control which was 3.1.But it is clearly defining that the hardness of 1 month sample and 2 month sample were degrade according to the duration of exposure having the value 2.7 and 2.6 respectively.

3.2.1.2Potency:

The potency determination of the samples was conducted for the normal room temperature; the potency did losses with the time being kept. The potency did degrade in a good and impressive way eventually with the duration of the exposure time. For 2 week samples the absorbance reading by the UV spectroscopy was 0.648 for flupentixol and 0.589 for melitracen, and for the 1 month samples the absorbance of flupentixol was 0.505 and 0.434 for melitracen , showing the degradation of the potency then the 2 week sample. It was more clear when the degradation drop more than the 1 month in the 2 month sample where the absorbance was recorded 0.462 for flupentixol and 0.433 for melitracen.

It was stated in the “photostability of drugs and drug formulation” by taylor and francis that The most obvious result of drug photodecomposition is a loss of potency of the product. In the final consequence this can result in a drug product which is therapeutically inactive.

It will be clearer from table which denotes the absorbance and concentration of the flupentixol and melitracen in the sample tablet.

The absorbance vs concentration curve where the line is linear.It clearly shows that, due to the duration of the exposure the change of the absorbance is according to the duration of exposure.

The 2 week have long column, then the 1 month sample and then the 2 month sample.

3.2.2 Sunlight exposure :

3.2.2.1 Physical parameter:

The weight variation did not really express the degradation due to the exposure of light or radiation. The percentage variation was in between the USP range.

The thickness was also not deviate and was with in the range for all three samples. But few tablet having a littile change in there thickness due to the exposure comparing it with the control tablets.. Figure and the tables showing that the changes of the thickness comparing it with the

control the 3 hr exposed samples having the lowest mean value than the 6 hour and 9 hour samples.

The hardness and the friability did had some variation. The friability did not exceed 1 % for all the three samples. But the average hardness value is low comparing to the control tablets. It was 2.7 kg for both 3 hour and 6 hour exposed tablet and 2.9 kg for 9 hour exposed tablets. But the hardness of 9 hour exposed drug was grater than the 3 and 6 hour samples.

Winter exposure:

The friability was good and impressive as it was not above 1 %. Below the data table and the bar diagram of the data can explain it more easily.

Comparing to the summer sample the winter samples degraded less, the reason was identified as the temperature of the winter season was less comparing to the summer season. The table listed above giving the percentage weight variation of the samples and it was not clearly proving the degradation. The weight of the tablet did not impressively explain the degradation as for most cases the weight was same as the control.

The mean value of the hardness test of the sample of three duration exposure to the sunlight was 3.26 for 3 hour exposed tablet,3.63for 6 hour exposed tablets and for 9 hour it was 3.9 hour. In figure 3.22 the bar diagram is shown between the mean values of the hardness test. It is showing that the mean hardness value is increased in the 9 hour exposed tablet, comparing to the others.

According to the article “Moisture, Hardness, Disintegration and Dissolution Interrelationships in Compressed Tablets Prepared by the Wet Granulation Process” by Z. T. Chowhan , after equilibration under high humidities, a decrease in tablet hardness occurred which depended linearly on tablet hardnesses at the time of compression. After overnight exposure to ambient room conditions, the softened tablets increased in hardness and this increase greatly exceeded the initial hardnesses. The magnitude of hardness increase was independent of the hardnesses at the time of compression. (chowhan, 1979)

3.2.2.2 Potency:

The test analysis was carried out like the normal room temperature samples. And the result was quite similar to the normal room temperature. There was no major deviation in the physical parameters of the tablets but photo degradation was occurring as the potency was measured by the absorbance of the two compounds. It was less than the control tablets, which proving the degradation of the potency due to the photolytic exposure.

The degradation was bit higher in the summer season as the temperature increases. The winter sample was degrading less than the summer samples as the temperature was not that much as the summer season. For the three hour exposed tablets in winter the temperature was 99° F but in summer the temperature was 100°, and for the 6 hr exposed samples the temperature in winter was 108°F and in summer it was more than 108°F. But for the 9 hr sample the temperature was dropping as the sun was starting to set.

It was estimate that the degradation was dropping according to the temperature of the environment of the sample.

The potency analysis has being conducted and tables showing the photo degradation of the drug components. It showing that the 6 hour exposed sample degrade the most as the temperature of the 6 hour exposed tablets was high than others. And the 9 hour sample degrade more comparing to the 3 hour but not more than the 6 hour because the temperature was falling and so the degradation was less.

.The degradation was clear to explain that the temperature did have an effect on the degradation rate of the tablets. The winter sample had degraded less than the summer samples as the temperature was low at the winter season. The absorbance value for the 3 hour exposed tablets was 0.497, for 6 hour exposed tablets it was 0.49 and for 9 hour exposed tablet it was 0.499 for flupentixol and 0.476, 0.465 and 0.452 accordingly for melitracen. The values that were obtained were less than the control value and proving the degradation of the samples due to the exposure of the sunlight.

3.2.3 Electrical light exposure:

3.2.3.1 Physical parameters:

In figure 3.30 the mean hardness value of the 9 hour exposed sample has the highest mean value among the three samples. It may be the reason of the humidity of the exposure environment an according to Z. T. Chowhan in 1979, After overnight exposure to ambient room conditions, the softened tablets increased in hardness and this increase greatly exceeded the initial hardnesses.

The friability was within the range.

3.2.3.2: Potency test:

25 watt bulb exposure:

As all the above mention weight variation the sample of the bulb light exposure also did not clearly explain the degradation. No such changes were noticed in the weight variation test. The thickness of the samples also did not change in a major way but very few deviations were noticed. The potency analysis of the 25 watt bulb exposure was quite different from the above mentioned categories. For the 25 watt bulb light exposure the absorbance of the 6 hour exposed sample had the highest absorbance value than the others which is 0.645 for Flupentixol and 0.452 for Melitracen.

40 watt exposed samples:

As like the 25 watt bulb light the 40 watt bulb light also produced a different data comparing with the normal room temperature and sunlight exposure excluding the weight variation test. The hardness seems to be increasing more than the control tablets. The thickness mean value also changes increasingly.

The UV spectrophotometer analysis of the potency of the 40 watt samples was totally different from the other sample as the value was opposite. The 9 hour exposed samples had the highest value of the absorbance comparing to the 3 and 6 hour sample.

3.2.4 IR determination of the flupentixol and melitracen:

Infrared spectroscopy (IR spectroscopy) is the spectroscopy that deals with the infrared region of the electromagnetic spectrum that is light with a longer wavelength and lower frequency than visible light. Figure 3.43 is representing the IR spectrum of the control drug and figure 3.44 is showing the IR spectrum of the sample of 4 week in normal room temperature condition. From the spectrum of figure 3.44 the red circle is denoting the deviation of the structural compound of the control drug.

The deviation was occurred on the wavenumber of 3566.38 (cm^{-1}) which was not present on the control spectrum. The wave number is denoting that a new compound might be interrupting the original structure. The unusual wavenumber of 3566.38 (cm^{-1}) denoting that an alcohol or phenol group may be present on the sample that was not present in the original compound.

Beside the wavenumber of 3566.38 (cm^{-1}) other two unusual peak was obtained from the IR determination which are 808.17(cm^{-1}) and 534.28 (cm^{-1}) , by which it shows that alkene and aromatic hydrocarbon like C-H bend (trisubstituted) and C-H bend (para) respectively may be present. From the 534.28 (cm^{-1}) ,wavenumber it can be expressed that alkyl halides like C-Br stretch, C-I stretch etc may be present on the sample.

Moreover, three minor deviations on the spectrum also was appeared on the 4 week spectrum which was on the wavenumber on 3838.34 (cm^{-1}), 38320.98 (cm^{-1}) and on 3408.22 (cm^{-1}).

The wavenumber thus explaining that O-H stretch motion compound may be present as alcohol or as carboxylic acid group.

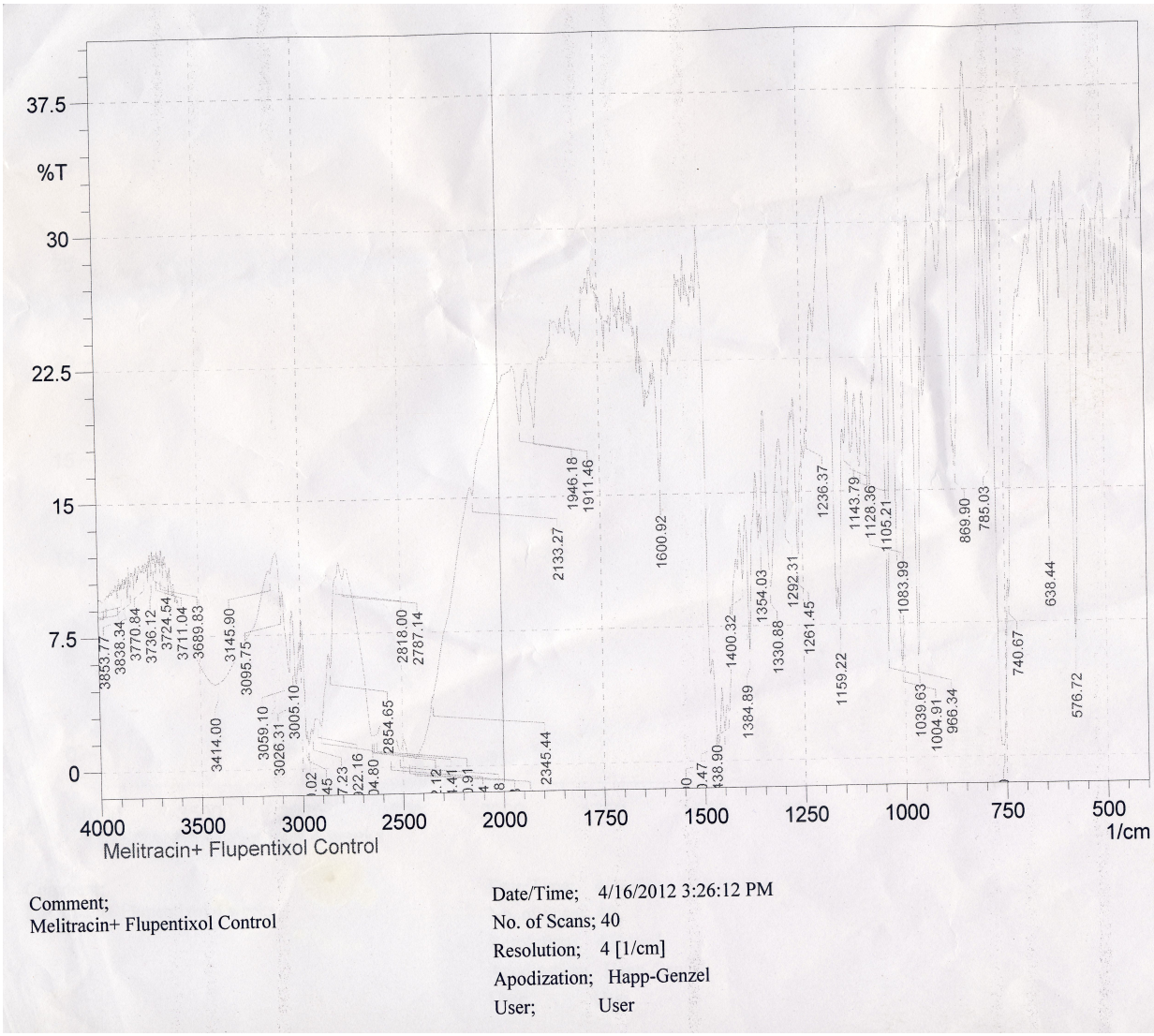


Figure 3.43: IR spectrum of Flupentixol + Melitracen of control compound.

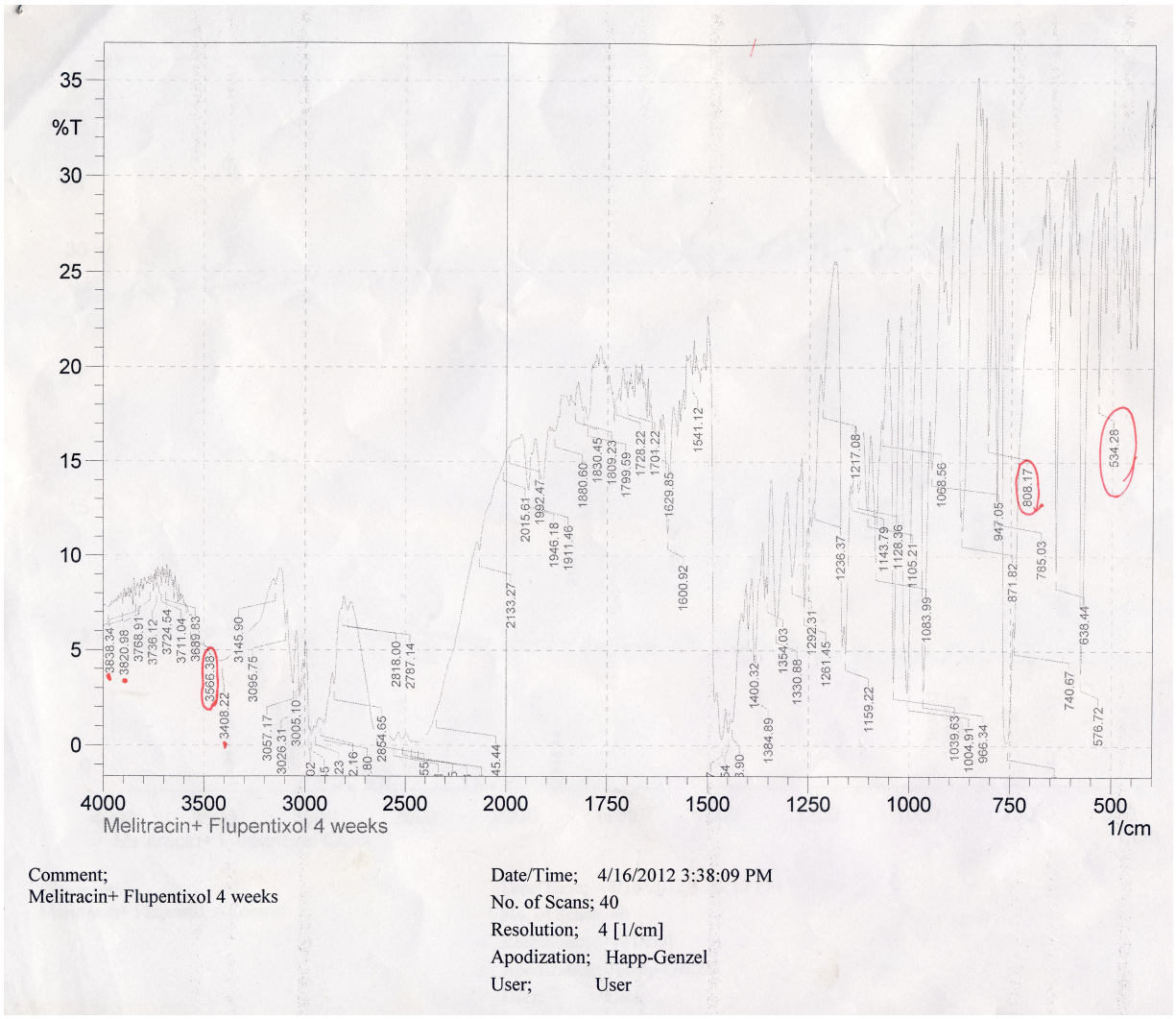


Figure 3.44 : IR spectrum of Flupentixol + Melitracen of 4 week in normal room condition.

Chapter 04

Conclusion

Conclusion

A photo stability assay for pharmaceutical products should provide information related to the practical use of the product, i.e. the light-exposure conditions the product will experience under its normal applications. Well-designed photo stability studies ensure the quality of the product throughout the shelf-life and guarantee its safety, efficacy and acceptability to the patient. In this study, the potency determination was done by the use of UV spectrophotometer and Flupentixol and melitracen did degrade by the photolytic effect. It prove that the drug is not photo stable and should have some protection in the final dosage form to save it from degradation.

Chapter 5

Reference

Reference

Kimberly S. (2006), Drug-Induced Photosensitivity. Volume 41, Number 2, pp 196–206

2006 Wolters Kluwer Health, Inc..

Chowhan, (1979), Moisture, Hardness, Disintegration and Dissolution Interrelationships in Compressed Tablets Prepared by the Wet Granulation Process. Vol. 5, No. 1 , Pages 41-62 (doi:10.3109/03639047909055661) .

Tonnesen, (1996)The Photostability of Drugs and Drug Formulations. Published in the Taylor & Francis e-Library, 2003, pp.1-6

Banglapedia, national encyclopedia of Bangladesh. Mental illness in Bangladesh.Retrieved from

http://www.banglapedia.org/httpdocs/HT/M_0218.HTM.

Bourrain . (1997). Diagnosis of photosensitivity to flupenthixol by photoprick testing. 13(4):159-61.

Tønnesen.(2008). Photoreactivity of drugs. The Norwegian Academy of Science and Letters, 2008

Yunus,(2011). a simple UV spectrophotometric method for the determination of flupenthixol dihydrochloride in bulk and pharmaceutical formulations. IJPSR, 2011; Vol. 2(8): 2152-2155.

Quintero, and miranda, .(2000). Mechanisms of photosensitization induced by drugs: A general survey. Ars Pharmaceutica, 41:1; 27-46, 2000.

Sharma.(2010). Novel application and spectrophotometric estimation of Melitracen HCl tablet dosage form using Niacinamide as hydrotropic solubilizing agent. J. Chem. Pharm. Res., 2010, 2(2): 416-420.

Kelly.(2004). Drug-Induced Photosensitivity. Volume 20

Acharjya S.K et al.(2010). Spectrophotometric methods for simultaneous estimation of Flupentixol Dihydrochloride and Melitracen Hydrochloride in combined tablet dosage form. J. Chem. Pharm. Res., 2010, 2(3):158-171.

Infrared Spectroscopy. (2007). IR Absorptions for Representative Functional Groups. Retrieved From: http://www.chemistry.ccsu.edu/glagovich/teaching/316/ir/table.html

Goodman and Gillman.(2006). *The pharmacological basis of therapeutics*. Drugs therapy of depression and anxiety disorders. Edition 11. pp: 429-454.