Determination of photolytic degradation of Sensit tablet (Flupentixol-Melitracen) Combination Product

The thesis entitled **"Determination of photolytic degradation of Sensit tablet (Flupentixol-Melitracen) Combination Product"** submitted to the Department of Pharmacy, East West University in the partial fulfillment of the requirement for the award of the degree of Bachelor of Pharmacy.

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EAST WEST UNIVERSITY

In The Name of Allah (SWT) the Most Mercifull, the Most Beneficient.

Dedication

This Paper Is Dedicated To

My Parents, Brother, Sister

And Friends

Declaration by the Research candidate

I, Md. Famidur Rahman, hereby declare that the dissertation entitled **"Determination of photolytic degradation of Sensit tablet (Flupentixol-Melitracen) Combination Product",** submitted by me to the Department of Pharmacy, East West University, in the partial fulfillment of the requirement for the award of the degree of Bachelor of Pharmacy (Honors) is a genuine & authentic record of original research work carried out by me during 2011-2012 under the supervision and guidance of Dr. Repon kumer saha, Assistant professor, Department of Pharmacy East West University and it has not formed the basis for the award of any other Degree/Diploma/Fellowship or other similar title to any candidate of any University.

Place: Dhaka

Date:

Signature of Candidate

(Md. Famidur Rahman)

ID: 2008-3-70-039

Thesis Certificate

This is certify that the thesis entitled **"Determination of photolytic degradation of Sensit tablet (Flupentixol-Melitracen) Combination Product",** 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 of Bachelor of Pharmacy (B. Pharm) is a genuine & authentic record of original research work carried out by **Md. Famidur Rahman (2008-3-70-039)** during the period 2011-2012 of his research in the Department of Pharmacy at East West University, under the supervision and guidance of me and the thesis has not formed the basis for the award of any other Degree/Diploma/Fellowship or other similar title to any candidate of any University.

Dhaka
Date:

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Supervisor
Assistant Professor
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I, as the Responsible Academic Chairperson, endorse the above statements:

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Acknowledgement

In the name of Allah (swt) the most merciful and most graceful, have successesfully completed my research work. I would like to express my thanks to my research supervisor Dr. Repon kumer saha, Dean, Assistant Professor,Dept. of Pharmacy, EWU, who had been always optimistic and full of enthusiasm and ideas. His intellectual capability and vast knowledge in the research work help me to do such an intellactul and interesting research work. His friendly behave always help me to do my research work with encourage.

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ABSTRACT

Sensit tablet is a combination product of flupentixol and melitracen in which Flupentixol is neuroleptic and melitracen is anti-depressant drug. This formulation is widely used in Bangladesh in severe depression and neuralgia which have high prevalence in Bangladesh perspective. The purpose of this work is to find whether the drugs photosensitive or not. The stability of drugs in the formulation was determined by scrutinizing the potency level by spectrphotometric method and physical parameters of the tablet. Specific amounts of tablet were exposed to different environment including sunlight, florescent light and normal room condition at definite temperature. The sample then was collected at definite time interval and physical parameter and potency was later determined. All the cases, the physical parameters were within range but for potency degraded as downhill. Throughout the process this was ensured adequate drug solubility and maximum assay sensitivity. The linearity ranges for the two drugs were measured accurately with precision. From the study of the project it is concluded that the drugs require light protection to remain stable within the shelf life.

Keywords: Neuroleptic, Anti-depressant, photosensitive, spectrphotometric method, shelf life.

Chapter1:

Introduction

1.1 Flupentixole

Flupentixole is a typical antipsychotic or neuroleptic drug. Flupentixole has the structure illustrated below and the name 2-(4-{3-[2-(trifluoromethyl)-9,9a-dihydro-4a-thioxanthen-9-ylidene]propyl}piperazin-1-yl)ethan-1-ol. The compound lies in the class of thioxanthene group. It is soluble in water and alcohol but insoluble in dichloromethane (DCM).

(Acharjya, S. K. et al, 2010)

The compound was first divulged in the GB patent 925538 to Smith Kline & French Laboratories in 1963 and reported to have e.g. tranquilising and central nervous system depressant activity.It is used to treat schizophrenia thus having antagonistic effect on wide variety of receptor especially dopamine, serotonine receptor. Its antipsychotic effect is due to D_2 and/ or 5-HT_{2A} antagonism whereas its antidepressant effect is owing to preferential D_2/D_3 autoreceptor blockade, resulting in increased postsynaptic activation.

(Flupentixol, 2012)

Flupentixole absorption occurs slowly or incomplete after oral absorption. It is highly bound to plasma protein (>95%).its metabolism occurred in liver and has a half life about 19 to 39 hours. (Yunus, M, 2011)

1.2 Melitracen

Melitracen is a tricyclic class of anti-depressant drug. The structure is illustrated below and has a systemic name 3-(10,10-dimethylanthracen-9(10*H*)-ylidene)-*N*,*N*-dimethylpropan-1-amine. Kefalas revealed the drug in the GB patent 939856 in 1963. The mechanism of melitracen is sorted out and it is said to have suppression on the receptor of nor-adrenaline and serotonine. It also shows attraction to muscarinic and histaminic (H_1) receptor in varying

extents. Onset of action of melitracen takes place instantly. The drug is used in the treatment of Trigeminal Neuralgia and severe depression. (Sheikh, I.A, 2009)

Due to show some side effects, it is co- administered with flupentixole to reduce the side effect in lower doses in combinationally. (Tripathi K.D, 2003)

The combination has niggling serious side effects due to low drug dosage (10 mg, Melitracen and 0.5 mg Flupentixol per tablet). The aim of this work is to scrutinize the effect of light on SENSIT tablet (Flupentixole-Melitracen combination products).

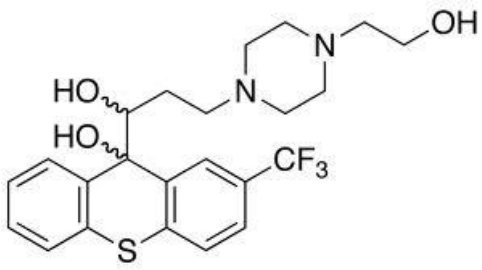


Fig 1.1: Molecular structure of Flupentixol

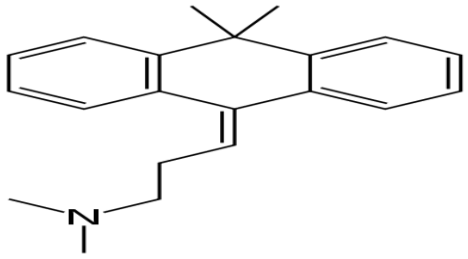


Fig 1.2: Chemical structure of Melitracen

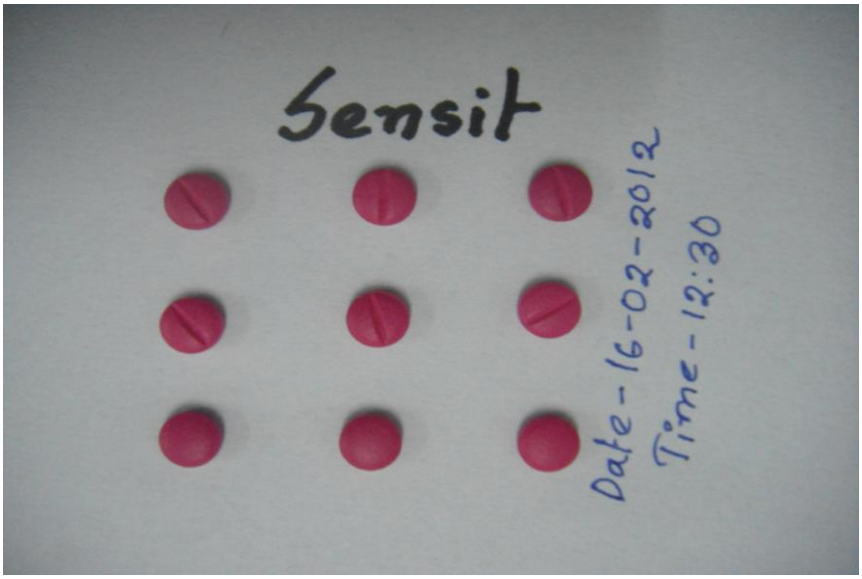


Fig 1.3: Sensit Tablet

Chapter 2:

LITERATURE REVIEW

2.1 Studies on Flupentixole and Melitracen combination product:

Meng. Q et al (2007) determined the a method using LC/ESI-MS/MS, for simultaneous quantitation of flupentixol and melitracen—antidepressant drugs, in human plasma

Under this method they stated 'the determination of the target compounds was quantified in a positive ion mode and multiple reactions monitoring (MRM). The method involved a repeated liquid–liquid extraction with diethyl ether and analytes were chromatographed on a C-8 chromatographic column by elution with acetonitrile–water–formic acid (36:64:1, v/v/v) and analyzed by tandem mass spectrometry. The method was validated. The correlation coefficients of both analyst were >0.998 for six sets of calibration curves. The recovery was 60.9–75.1% for flupentixol, melitracen and internal standard. The minimum limit of quantitation detection was 26.1 pg/ml and 0.206 ng/ml for flupentixol and melitracen respectively . Intra- and inter-day precision of the assay at three concentrations were 2.15–5.92% with accuracy of 97.6–103.0% for flupentixol and 0.5–6.36% with accuracy of 98.7–101.7% for melitracen. The method was suitable for bioequivalence study of flupentixol and melitracen in healthy human male volunteers'. (Meng Q. et al, 2007: p 785-792)

Li-hong, C., Jin-hong, L. (2010) investigated the therapeutic effect of Flupentixol and Melitracen on patients of dyspepsia with anxiety and depression. Their approach was One hundred twenty eight dyspepsia patients with different degree of anxiety and depression were randomly divided into two groups: group 1 is treatment group, and group 2 is comparison group.For group 2, on the basis of mental leading, patients were dealed with the routine treatment on the principle of idividuality, while for group one, patients were treated by Flupentixol and Melitracen (Deanxit) every morning and midday, 1 pill per time. Comparing with group 2, both the apparent efficiency and the total efficiency of group 1 were prior to the

other (P0.05). The study shows Flupentixol combined with Deanxit is therapeutically effective in treating FD patients with anxiety and depression. (Li-hong C, Jin-hong L, 2010)

Chhalotiya, U K et al (2011) determined a chromatographic method have been developed for the simultaneous estimation of Flupentixol dihydrochloride and Melitracen hydrochloride in combined tablet dosage form. The first method is based on the use of simultaneous equation, the second method is based on the simultaneous equation using AUC of the two drugs, the third method is based on the use of absorbance ratio method and the fourth one is based on first order derivative method. Both the drugs obey the Beer's law in the concentration ranges employed for these methods. The methods were validated by following the analytical performance parameters suggested by the International Conference on Harmonization (ICH). All validation parameters were within the acceptable range. The developed methods were successfully applied to estimate the amount of Flupentixol dihydrochloride and Melitracen hydrochloride in combined tablet dosage forms. (Chhalotiya, U K et al, 2011)

Yunus, M. et al (2011) established a method to quantify the Flupenthixol Dihydrochloride in bulk and pharmaceutical formulations. In their experiment linearity range for flupenthixol dihydrochloride at its wavelength of detection at 230 nm was found. The linear regression equation obtained by least square regression method, were $Y = 0.0639X + 0.0013$, where Y is the absorbance and X is the concentration (in μg/ml) of pure drug solution. The limit of detection and limit of quantification was found to be 0.324μg/ml & 0.982μg/ml. The validity of the described procedure was assessed. The result was effective with good precision. The procedure was successfully applied to the determination of flupenthixol dihydrochloride in pharmaceutical formulations without any interference from common excipients.

(Yunus. M et al, 2011: vol 2)

CHAPTER 3:

MATERIALS & METHODS

3.1 Experimental:

Spectral and absorbance measurements were accomplished on UV visible Spectrophotometer. Electronic balance was used for measuring the weight of samples. Commercially available tablets of flupentixol and Melitracen combined drugs as brand name "SENSIT' manufactured by "ESKAYEF BANGLADESH LTD" were purchased from the local market and estimated.

3.1.2 CHEMICALS AND REAGENTS

Reagents Name	Source (Supplier Name)
Concentrated Sulfuric acid	Germany (Merk)
Distilled Water	SMIC/Chaina
Flupentixol & Melitracen Tablets	SENSIT(Eskayef Bangladesh Ltd)
Standard Tablet	Melixol(Square pharmaceuticals Ltd)

3.1.3 APPARATUS/INSTRUMENTS

Name	Model/Code	Manufacturer/Supplier
UV- Vis spectrophotometer	UV-1800	Shimadzu, Japan
Friabilator	VEGGO	India
Electronic balance	Precisa -FD120A	Switzerland
Vernier caliper	0-150 mm	Shanghai,China
Tablet Hardness tester	Manually operated	India

3.2. Optimization:

3.2.1 Scanning and determination of maximum wavelength (λmax) for drugs:

In order to find out the wavelength of maximum absorption of the drug, qualitative solution of the drug was dissolved in sulfuric acid and scanned using UV spectrophotometer within the wavelength region of 200- 400 nm against 0.1 N H_2SO_4 as blank. The absorption curve in UV-Vis spectrometer gave the absorption maxima at 229 nm for Flupentixol and at 258 nm for melitracen separately run during the analysis. The literature review suggests that the absorption maxima are for flupentixol at 229 nm and for Melitracen at 258 nm.

3.3 Sample collection:

Determination of photolytic degradation of my interested tablets was done by exposing the specific amount of tablets in a variety of specific exposure condition and then collected for carrying out experiments to determine the physical parameters followed by potency measurements. Three types of photo exposure condition were chosen for this purpose which included the following: Sunlight exposure (winter and summer), Exposure to normal room temperature (2 weeks, 1 month, 2 month) and Bulb light exposure (25 watt, 40 watt bulb).

Each of the cases, thirty tablets were exposed to that environments and isolating them by using plastic transparent paper and box to prevent the interference of outside particulates. While undergoing the experiment which lasts for nine hours, after every three hours ten tablets were collected and labeled as “3 Hours”. These processes were done with every three hours until nine hours. The sample were collected and labeled as “6 Hours” and “9 Hours” respectively. Temperature was measured in sunlight exposure by thermometer. In winter the temperature noted was in the range from 98° F to 105° F and in summer the temperatures noted were in the range from 99° F to 108° F and more. But for nine hours sample, exposed temperatures were less than 108° F.

3.4 Determination of physical parameter:

Several physical parameters were checked before in engaging in potency estimation. Hardness tests, friability test, weight variation test, thickness test of the tablets were the notable parameters. All these physical tests were done to see whether any close relationship with photo- degradation or not.

3.4.1 Tablet Hardness:

Hardness tester was used in this purpose of the eruption of the tablets to determine the tensile strength of the tablet and reading was measured in kilogram (kg).

3.4.2 Friability test:

The test is accomplished to evaluate the effect of friction or shocks which results in breaking, capping or chapping of the tablet. The friabilator was used for this purpose. Preweighed sample of tablets (10) was placed in the friabilator, which was then operated for 100 revolutions. Tablets were dusted and reweighed. The tablets should not lose more than 1% of their weigh.

3.4.3 Weight variation test:

Ten tablets were weighed individually and the average was taken and comparing the individual tablet weight to the average one and observed whether the individual tablet were within range or not according to USP.

3.4.4 Tablet thickness: Thickness test was done by using by precise measuring instrument called vernier calliper. The measurement was expressed in length unit in (cm or mm).

Calculation:

Thickness = sliding scale (mm) + vernier scale (mm) × vernier constant

3.5 Preparation of sample solution:

Three Sensit tablets of flupentixol-Melitracen combo drugs were accurately weighed and finely powdered and mixed. The average weight of powder was transferred into 100 ml

volumetric flask. Powder was dissolved into the 100 ml of 0.1N H_2SO_4. The prepared solution was later filtered through a filter paper. 10 ml of filtered solution was diluted to 100 ml by adding 0.1N H_2SO_4 in 100 ml volumetric flask. Then the absorbance of these solutions was measured at 229nm and 258nm for flupentixol and melitracen respectively by the UV-Vis spectrophotometer.

3.6 Preparation of Standard solution & Calibration curve for Melitracen and Flupentixol:

Before the preparation of standard calibration curve for Melitracen and Flupentixol, it was worthwhile to prepare the standard solution. The weight of 5 standard tablets was accurately weighed and finely powdered and mixed. The average weight of powder for 5 tablets was transferred to 100 ml volumetric flask, where it was allowed to dissolve in 100 ml 0.1N H_2SO_4. A succession of dilution (5 times) was carried out with the standard stock solution, thus getting a known amounts of flupentixol (10, 2, 0.4, 0.08, 0.016 μg/mL) and melitracen (200, 40, 8, 1.6, 0.32 μg/mL).the absorbance of MEL and FLU were estimated by respective **λmax** through scanning by UV-Vis spectrophotometer and by fitting these values against concentration in the graph led to the straight-line equation of calibration curve.

CHAPTER 4:

RESULTS & DISCUSSION

4.1 Result & Discussion:

After collections of sample physical parameters were checked in which the weight variation of the entire sample were within the range for ten tablets according to USP which is ± 10 for 130 mg or less dosage form. There was no major divergence in content uniformity in exaggerated condition.

Tables and figures of weight variation for control or normal room, sunlight exposed and under florescent light condition are illustrated below:

Table 4.1: The percentage weight variation of 2 weeks sample.

Tablet no.	Initial Weight, I(gm)	Average weight A(gm)	% Weight Variation
1	0.0872	0.08638	-0.94
2	0.0859		0.56
3	0.086		0.44
4	0.0849		1.74
5	0.0886		-2.51
6	0.0864		-0.02
7	0.085		1.62
8	0.0867		-0.37
9	0.0874		-1.17
10	0.0857		0.79

Table 4.2: The percentage weight variation of 1 month sample.

Tablet no.	Initial Weight, I(gm)	Average weight A(gm)	% Weight Variation
1	0.0877	0.08706	-0.73
2	0.0864		0.76
3	0.0877		-0.73
4	0.0877		-0.73
5	0.0876		-0.62
6	0.0871		-0.05
7	0.0858		1.47
8	0.0867		0.42
9	0.0874		-0.39
10	0.0865		0.65

Table 4.3: The percentage weight variation of 2 months sample.

Tablet no.	Initial Weight, I(gm)	Average weight A(gm)	% Weight Variation
1	0.0864	0.0863	-0.12
2	0.0849		1.65
3	0.0867		-0.46
4	0.0859		0.47
5	0.0879		-1.82
6	0.0855		0.94
7	0.0853		1.17
8	0.0861		0.23
9	0.0873		-1.15
10	0.088		-1.93

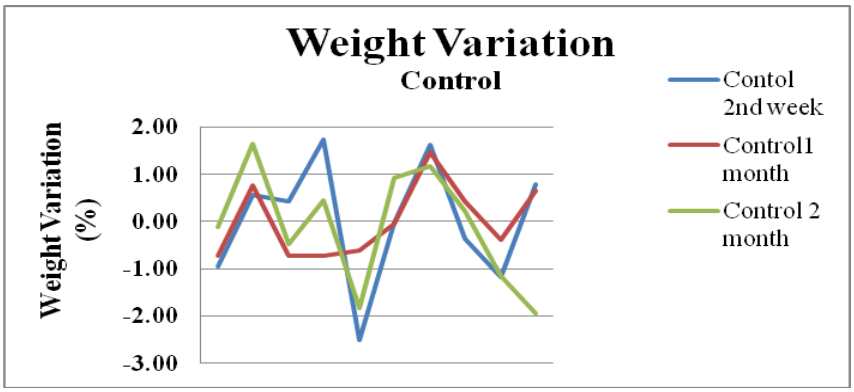


Fig 4.1 : Graph of percentage weight variation of control samples

Table 4.4: The percentage weight variation of 25 watt 3 Hours sample.

Tablet no.	Initial Weight, I(gm)	Average weight A(gm)	% Weight Variation
1	0.0861	0.08729	1.38
2	0.086		1.50
3	0.0865		0.91
4	0.0878		-0.58
5	0.0877		-0.47
6	0.0881		-0.92
7	0.0882		-1.03
8	0.0891		-2.03
9	0.0868		0.56
10	0.0866		0.80

Table 4.5: The percentage weight variation of 25 watt 6 Hours sample

Tablet no.	Initial Weight, I(gm)	Average weight A(gm)	% Weight Variation
1	0.0873	0.08609	-1.39
2	0.085		1.28
3	0.0863		-0.24
4	0.0872		-1.27
5	0.0887		-2.94
6	0.0872		-1.27
7	0.0844		2.00
8	0.0857		0.46
9	0.0866		-0.59
10	0.0874		-1.50

Table 4.6: The percentage weight variation of 25 watt 9 Hours sample

Tablet no.	Initial Weight, I(gm)	Average weight A(gm)	% Weight Variation
1	0.0872	0.08708	-0.14
2	0.087		0.09
3	0.0871		-0.02
4	0.0858		1.49
5	0.088		-1.05
6	0.0864		0.79
7	0.0856		1.73
8	0.0884		-1.49
9	0.088		-1.05
10	0.0873		-0.25

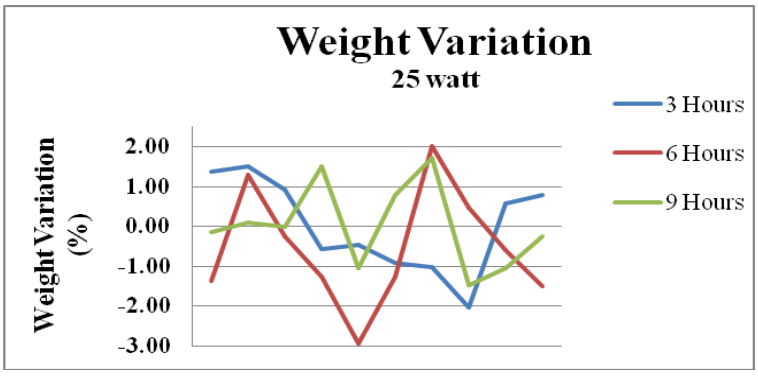


Fig 4.2: Percentage weight variation of Florescent light(25 watt) sample.

Table 4.7: The percentage weight variation of 40 watt 3 Hours sample.

Tablet no.	Initial Weight, I(gm)	Average weight A(gm)	% Weight Variation
1	0.0865	0.08617	-0.38
2	0.0865		-0.38
3	0.0867		-0.61
4	0.0838		2.83
5	0.0871		-1.07
6	0.0875		-1.52
7	0.0858		0.43
8	0.0864		-0.27
9	0.0861		0.08
10	0.0848		1.62

Table 4.8: The percentage weight variation of 40 watt 6 Hours sample.

Tablet no.	Initial Weight, I(gm)	Average weight A(gm)	% Weight Variation
1	0.0856	0.08709	1.74
2	0.087		0.10
3	0.0873		-0.24
4	0.0872		-0.13
5	0.0876		-0.58
6	0.0872		-0.13
7	0.0865		0.68
8	0.0879		-0.92
9	0.0864		0.80
10	0.0868		0.33

Table 4.9: The percentage weight variation of 40 watt 9 Hours sample.

Tablet no.	Initial Weight, I(gm)	Average weight A(gm)	% Weight Variation
1	0.0861	0.0871	1.16
2	0.0862		1.04
3	0.0869		0.23
4	0.0873		-0.23
5	0.0877		-0.68
6	0.088		-1.02
7	0.0878		-0.80
8	0.0864		0.81
9	0.0856		1.75
10	0.0885		-1.58

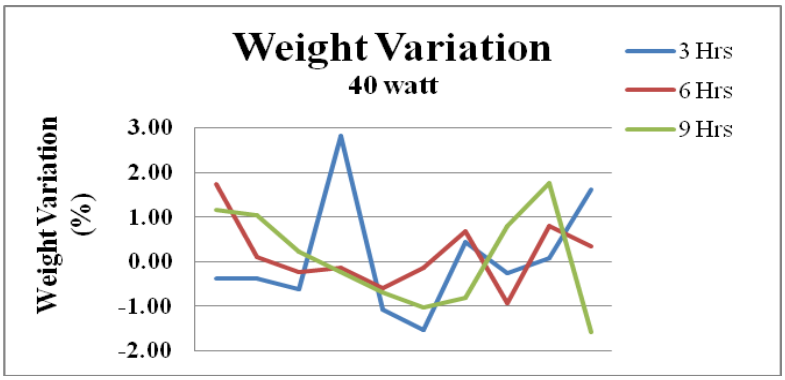


Fig 4.3: Percentage weight variation of Florescent light(40 watt) sample.

Table 4.10: The percentage weight variation of sunlight summer 3 Hours sample

Tablet no.	Initial Weight, I(gm)	Average weight A(gm)	% Weight Variation
1	0.088	0.08637	-1.85
2	0.0854		1.14
3	0.0849		1.73
4	0.0859		0.55
5	0.0879		-1.74
6	0.0875		-1.29
7	0.0867		-0.38
8	0.0861		0.31
9	0.0864		-0.03
10	0.0875		-1.29

Table 4.11: The percentage weight variation of sunlight summer 6 Hours sample

Tablet no.	Initial Weight, I(gm)	Average weight A(gm)	% Weight Variation
1	0.0864	0.08742	1.18
2	0.0869		0.60
3	0.0879		-0.55
4	0.0867		0.83
5	0.0876		-0.21
6	0.0879		-0.55
7	0.0868		0.71
8	0.0849		2.97
9	0.0854		2.37
10	0.088		-0.66

Table 4.12: The percentage weight variation of sunlight summer 9 Hours sample

Tablet no.	Initial Weight, I(gm)	Average weight A(gm)	% Weight Variation
1	0.0862	0.08723	1.19
2	0.0869		0.38
3	0.0864		0.96
4	0.0845		3.23
5	0.0877		-0.54
6	0.0878		-0.65
7	0.089		-1.99
8	0.0877		-0.54
9	0.0867		0.61
10	0.0879		-0.76

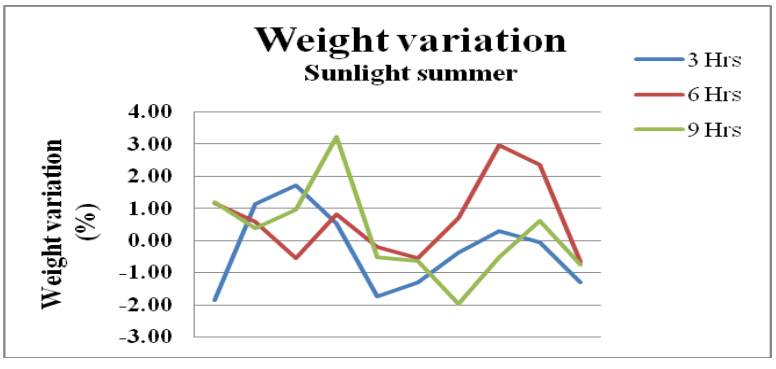


Fig 4.4: Percentage weight variation of Sunlight summer sample.

Table 4.13: The percentage weight variation of sunlight winter 3 Hours sample.

Tablet no.	Initial Weight, I(gm)	Average weight A(gm)	% Weight Variation
1	0.0883	0.08735	-1.08
2	0.0874		-0.06
3	0.086		1.57
4	0.0869		0.52
5	0.0875		-0.17
6	0.0875		-0.17
7	0.0886		-1.41
8	0.0857		1.93
9	0.0881		-0.85
10	0.086		1.57

Table 4.14: The percentage weight variation of sunlight winter 6 Hours sample

Tablet no.	Initial Weight, I(gm)	Average weight A(gm)	% Weight Variation
1	0.0868	0.08638	-0.48
2	0.0869		-0.60
3	0.0864		-0.02
4	0.0872		-0.94
5	0.0879		-1.73
6	0.0864		-0.02
7	0.0845		2.22
8	0.0855		1.03
9	0.0867		-0.37
10	0.0879		-1.73

Table 4.15: The percentage weight variation of sunlight winter 9 Hours sample

Tablet no.	Initial Weight, I(gm)	Average weight A(gm)	% Weight Variation
1	0.0889	0.08705	-2.08
2	0.0869		0.17
3	0.0857		1.58
4	0.0868		0.29
5	0.0881		-1.19
6	0.0869		0.17
7	0.0849		2.53
8	0.0852		2.17
9	0.0879		-0.97
10	0.0883		-1.42

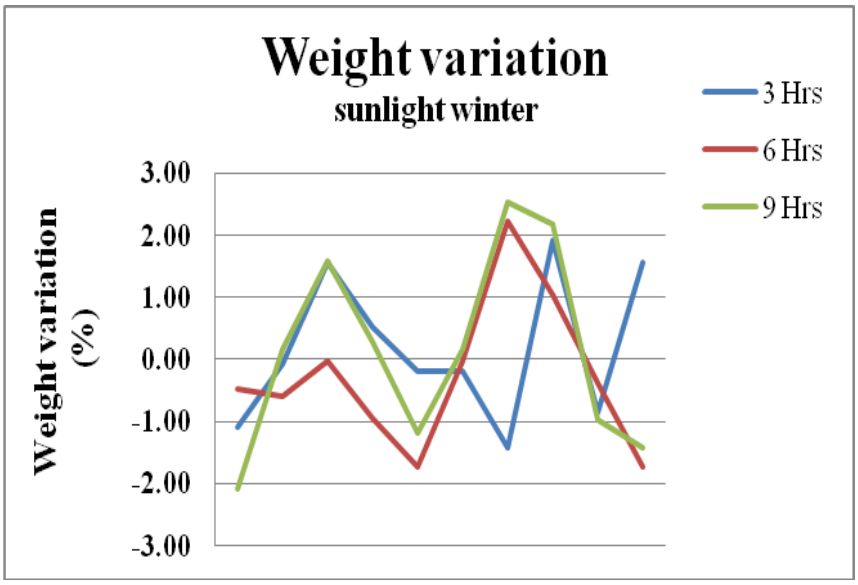
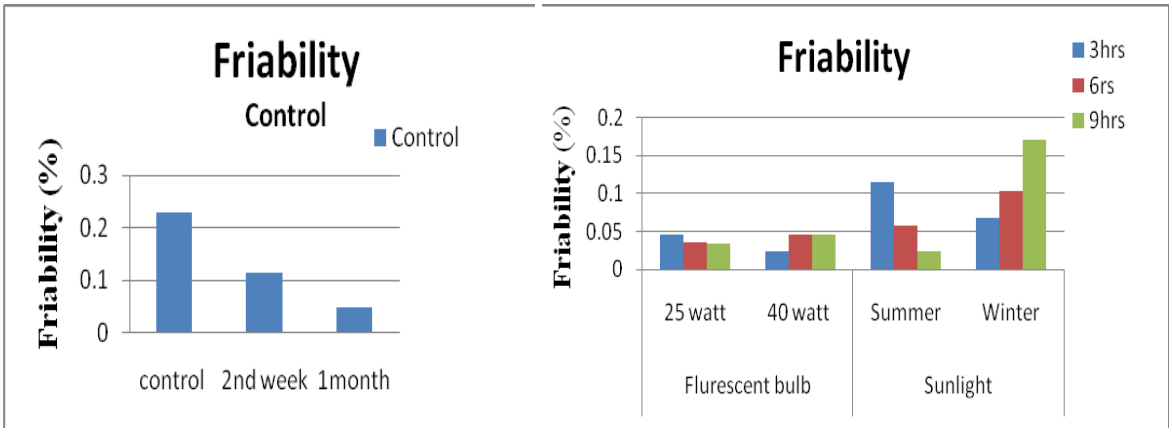


Fig 4.5: Percentage weight variation of Sunlight winter sample.

There is hardly any effect on the friability of the tablets on exposure of the light and radiation. the parameters falls within the range for all the sample, for friability it was not more than 1%. Friability of tablets for control, under florescent light and sunlight exposure is given in table:

Table 4.16: Data for the friability test of all sample.

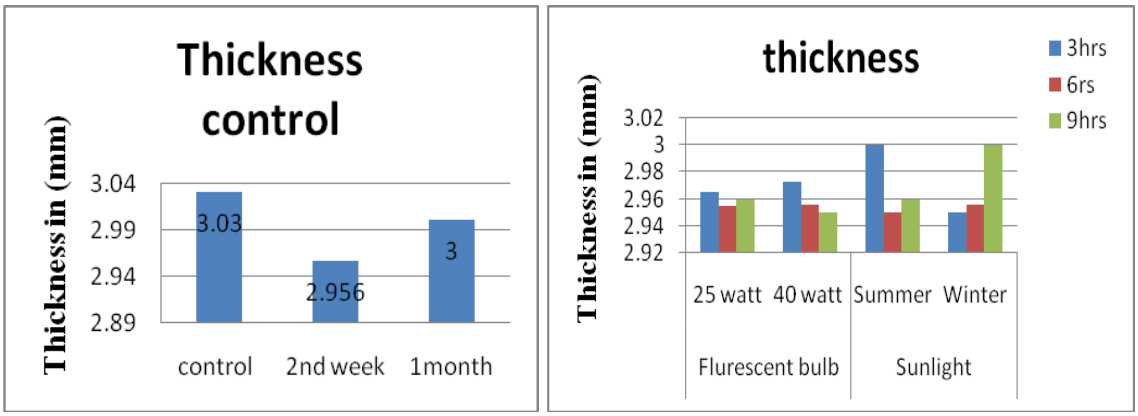
	Sample	Initial weight (gm)	Weight after Rotation (gm)	Friability (%)
Control	1st days	0.8638	0.8618	0.23
	2nd week	0.8706	0.8696	0.115
	1 month	0.8609	0.8604	0.05
Bulb(25watt)	3hrs	0.8729	0.8725	0.046
	6hrs	0.8609	0.8606	0.035
	9hrs	0.8708	0.8705	0.034
Bulb(40watt)	3hrs	0.8617	0.8615	0.023
	6hrs	0.8709	0.8705	0.046
	9hrs	0.8710	0.8706	0.046
Sunlight(summer)	3hrs	0.8637	0.8627	0.116
	6hrs	0.8742	0.8737	0.057
	9hrs	0.8723	0.8721	0.023
Sunlight (winter)	3hrs	0.8735	0.8729	0.068
	6hrs	0.8638	0.8629	0.104
	9hrs	0.8705	0.869	0.172



(a) (b)

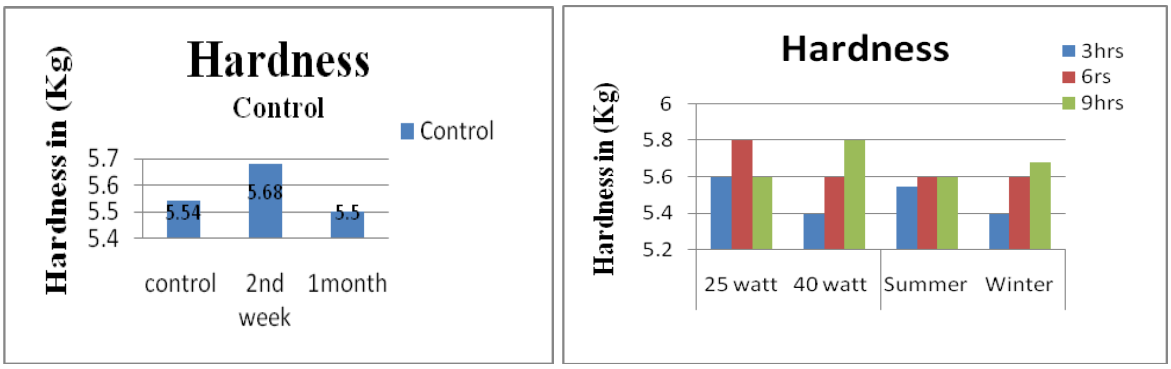
Fig 4.6: Bar diagram of Friability for (a).control and (b). under light condition.

There was no spectacular effect shown on tablet's thickness and hardness due to exposure of light in varying condition. Also there was no wide changes in result between control and other under light sample. They fall in within the range proximity to control experiment.



(a) (b)

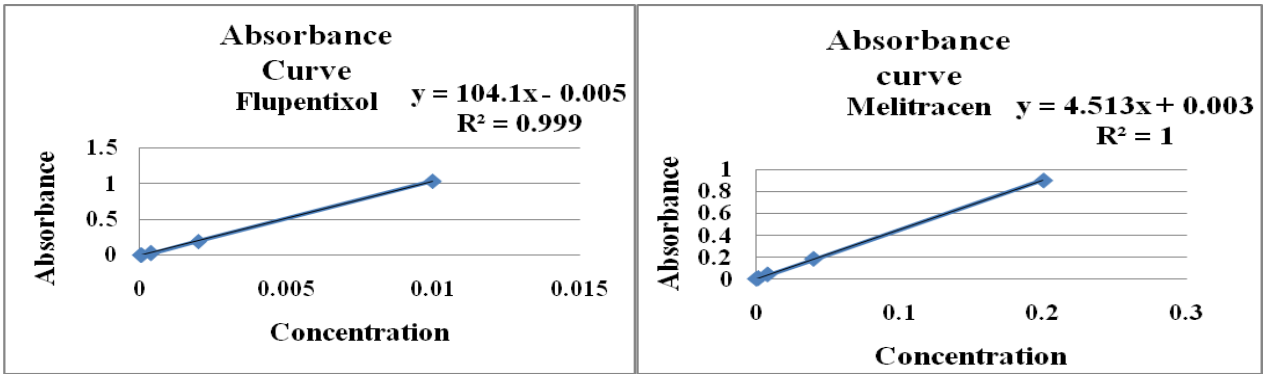
Fig 4.7: Bar diagram of Thickness for (a).control and (b). under light condition.



(a) (b)

Fig 4.8: Bar diagram of Hardness for (a). control and (b). under light condition.

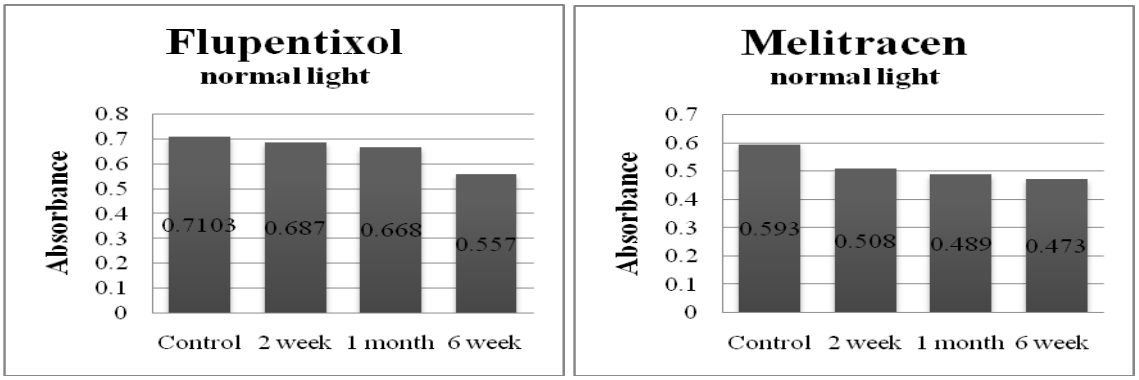
There was significant result shown about potency in various exaggerated environment. In normal or control sample the linearty of the curve was conspicuous. Both the Flupentixol and Melitracen gave linear curve of a wave length at 229nm and 258nm respectively. The linear regression equation obtained was Y =104.1x - 0.005, for flupentixol and Y = 4.513x + 0.003, for melitracen. In which Y is the absorbance and X is the concentration (in µg/ml) of pure drug solution.



(a) (b)

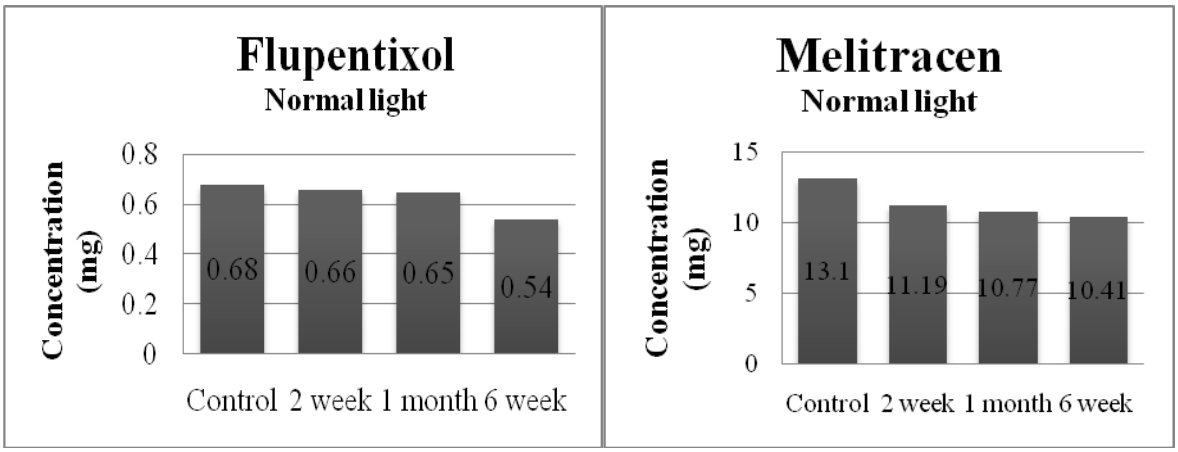
Fig 4.9: Graphical representation of linearity curve of (a). flupentixol and (b). Melitracen for control/ Standard sample.

The potency of control changes with time during experiment. The absorbance of first control tablet was 0.7103 and 0.593 for flupentixol and melitracen respectively. With time the potency of tablet decreases gradually. They can be illustrated as potency in milligram below



(a) (b)

Figure 4.10: Bar diagram of the absorbance of the Control or normal light sample. (a). flupentixol and (b). Melitracen.

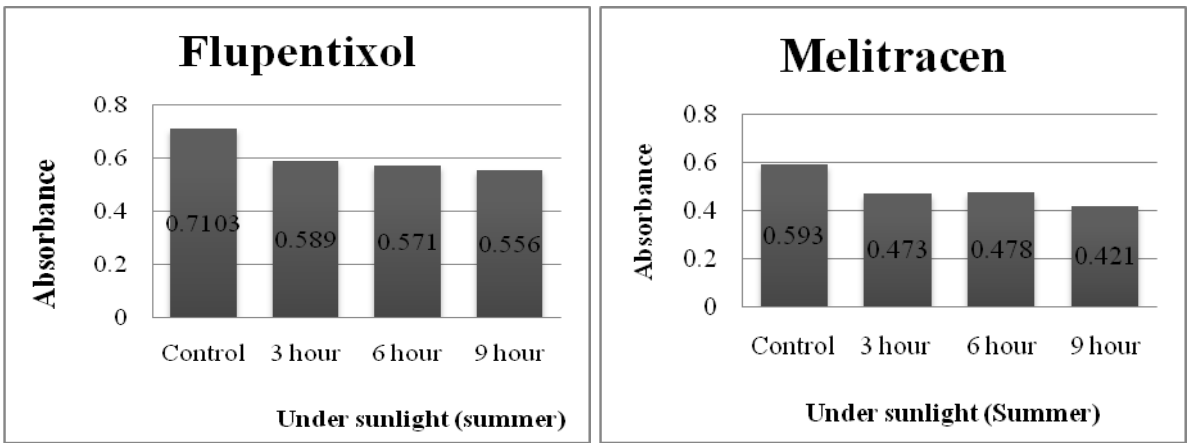


(a) (b)

Figure 4.11: Bar diagram in concentration of normal light sample. (a). flupentixol and (b). Melitracen.

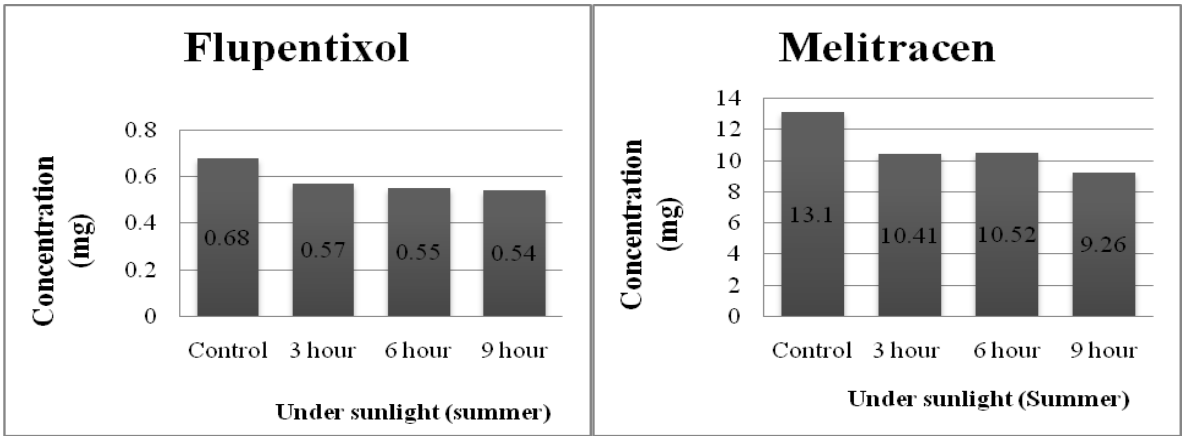
The absorbance in sunlight and under florescent bulb exposure gently down with the more expose time. It was shown that the absorbance of three to nine hours samlple was downhill.

From the control it was implied that it has photosensitive effect in the exposure to light. The absorbance bar diagram for sunlight and florescent bulb is given below:



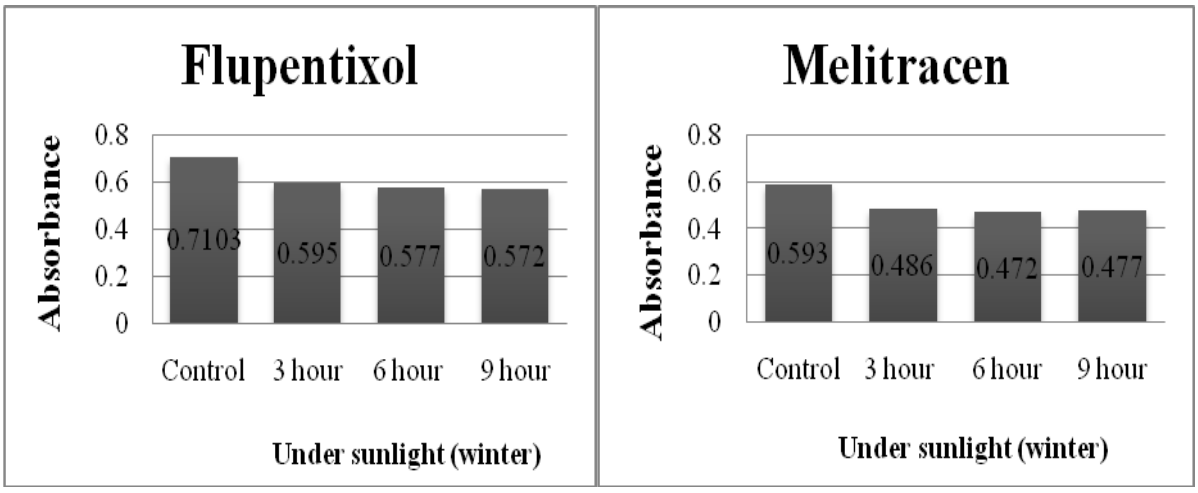
(a) (b)

Figure 4.12: Bar diagram of the absorbance of the sun light (summer) sample. (a). flupentixol and (b). Melitracen.



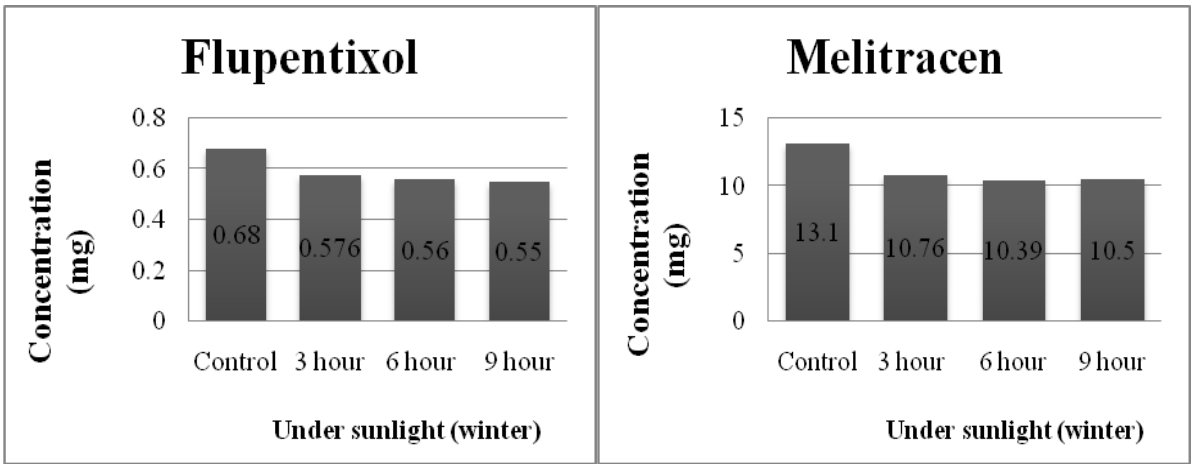
(a) (b)

Figure 4.13: Bar diagram in concentration of the sun light (summer) sample. (a). flupentixol and (b). Melitracen.



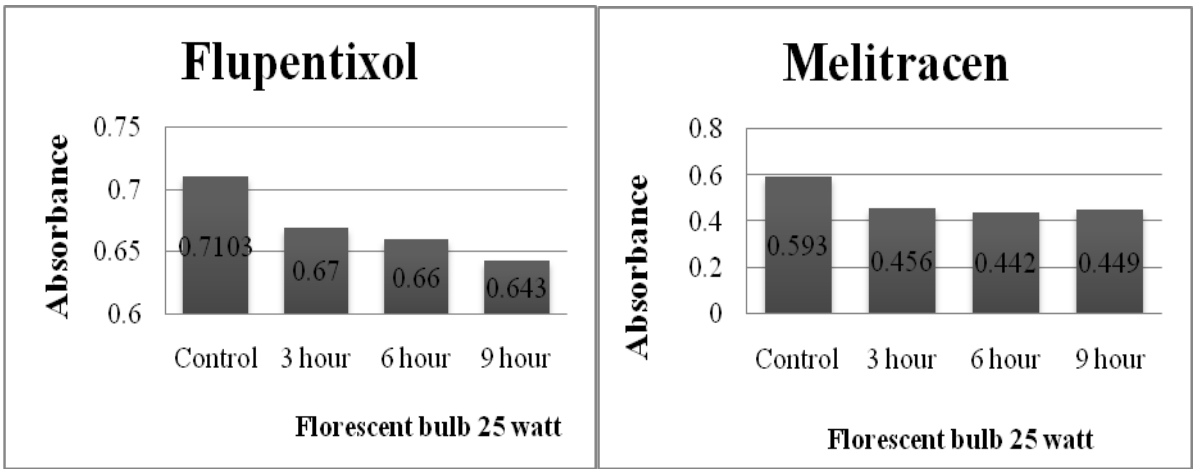
(a) (b)

Figure 4.14: Bar diagram of the absorbance of the sun light (winter) sample. (a). flupentixol and (b). Melitracen.



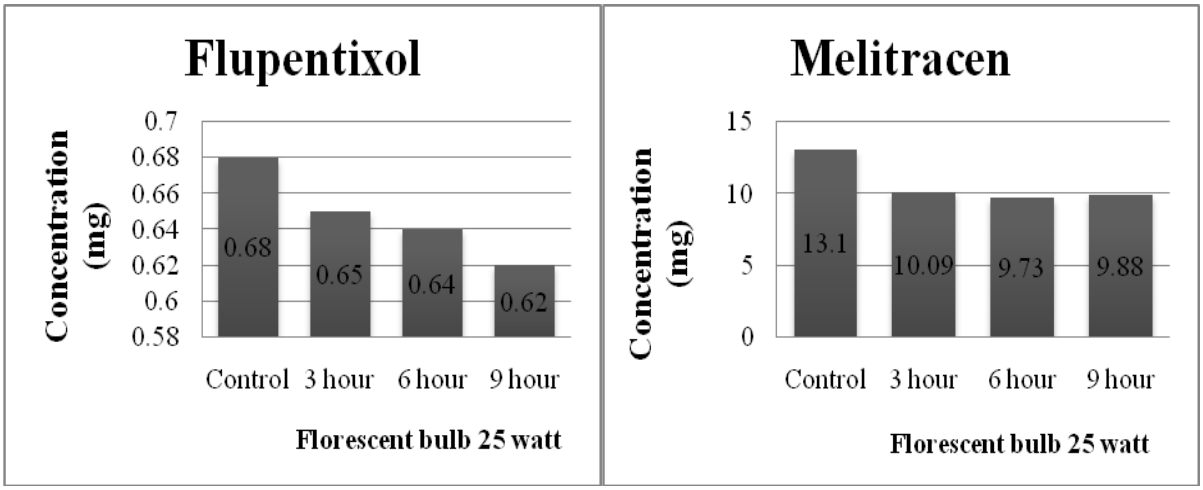
(a) (b)

Figure 4.15: Bar diagram in concentration of the sun light (winter) sample. (a). flupentixol and (b). Melitracen.



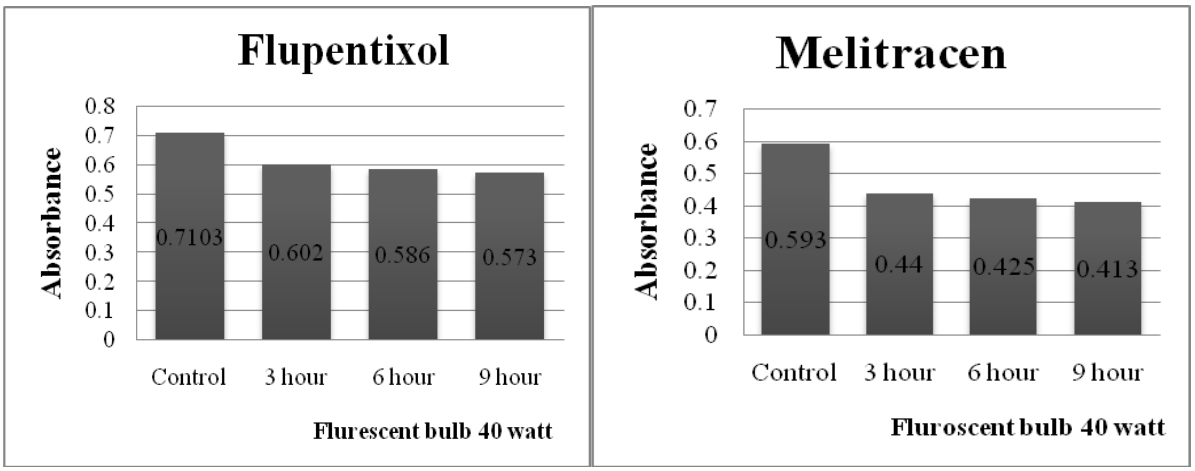
(a) (b)

Figure 4.16: Bar diagram of the absorbance of the florescent light (25 watt) sample. (a). flupentixol and (b). Melitracen.



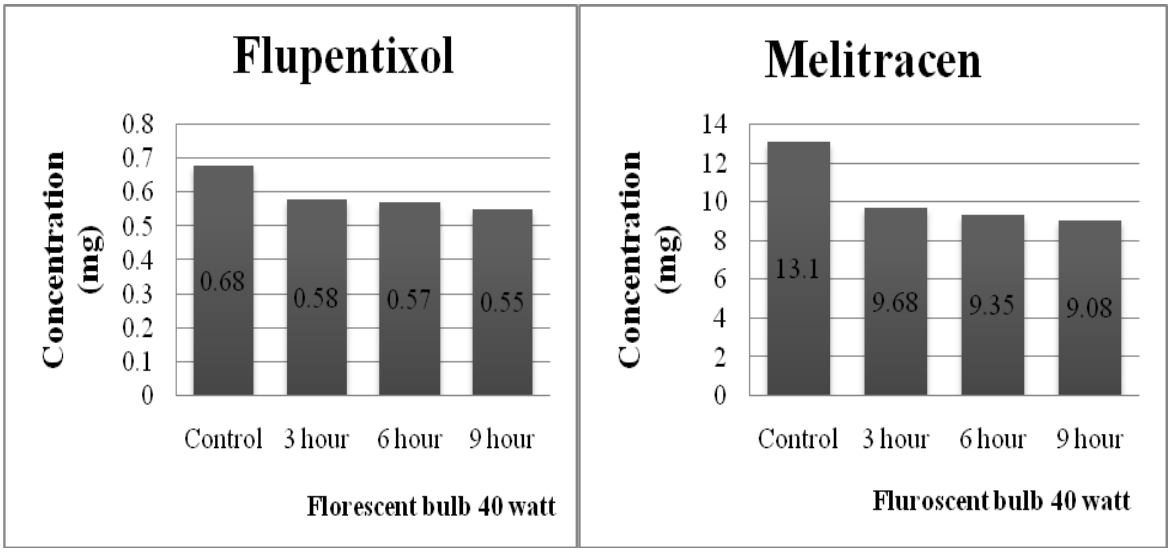
(a) (b)

Figure 4.17: Bar diagram in concentration of the florescent light (25 watt) sample. (a). flupentixol and (b). Melitracen.



(a) (b)

Figure 4.18: Bar diagram of the absorbance of the florescent light (40 watt) sample. (a). flupentixol and (b). Melitracen.



(a) (b)

Figure 4.19: Bar diagram in concentration of the florescent light (40 watt) sample. (a). flupentixol and (b). Melitracen.

Spectral analysis:

From the diagram it is shown the absorbance changes with time. From the experiment it suggests that the combo drugs have photosensitivity. Thus, we interested to find in which group's decay was responsible for altering in absorbance. Scanning of sample tablet through

IR spectroscopy gave spectroscopic data which gave characteristics bands. Characteristics bands at 3000-3100 cm^{-1} and 1400-1600 cm^{-1} were due to aromatic ring skeleton vibration. Bands near 3200-3650 cm^{-1} signifies the presence of –OH group. For strong bands near 1000-1400 cm^{-1} indicates C-F present in any of the compound. For bands near 2850-3000 cm^{-1} signifies the presence of C-H bond stretching. Tertiary amine may present due to the band near 1200-1350 cm^{-1}.

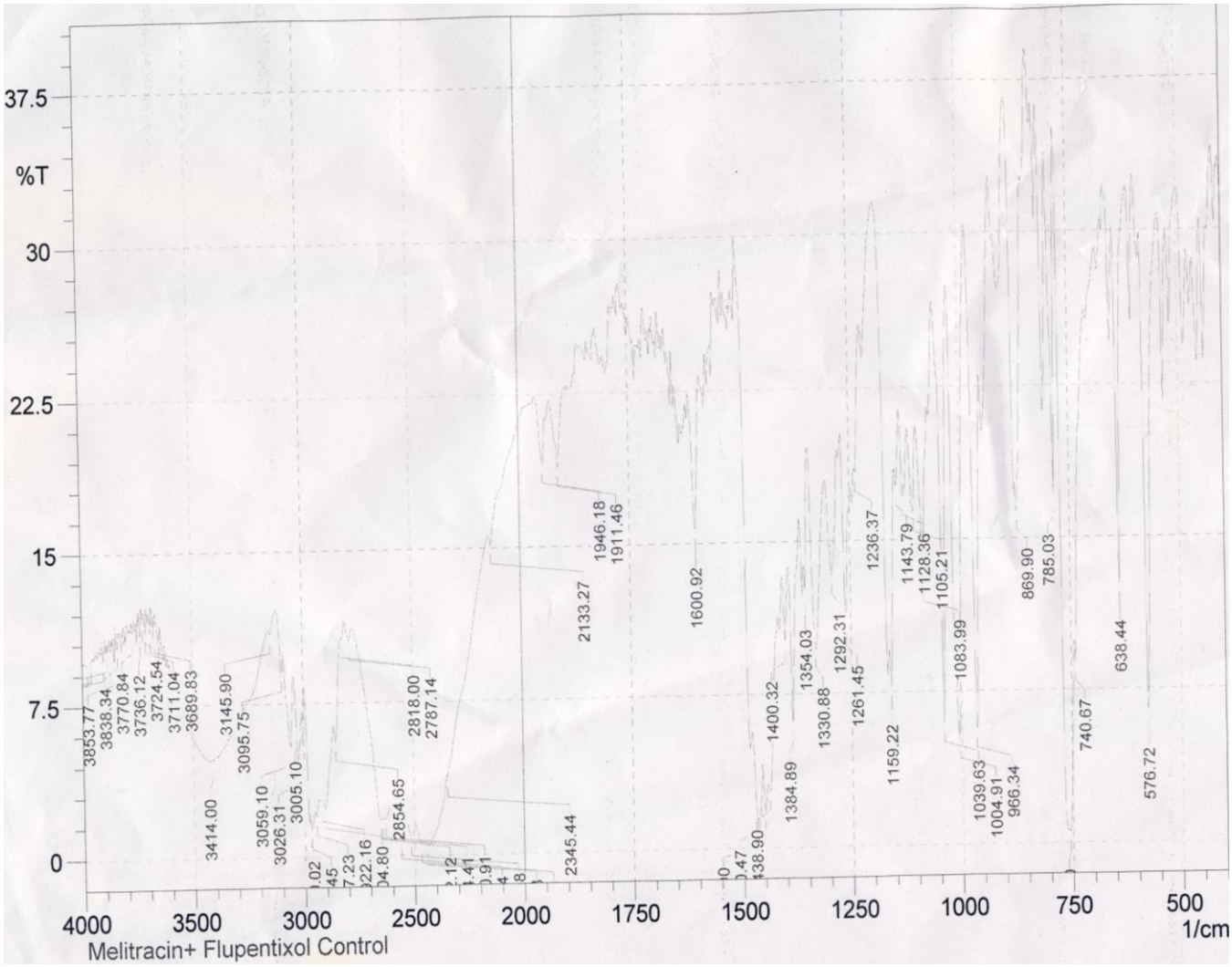


Figure 4.20: IR spectrum of control sample (Flupentixol and Melitracen).

IR spectrum for control tablets after 4 weeks had slightly different spectrum. It showed new band near 3566 cm^{-1}. This new band would be the presence of –OH group due to oxidation of the sample. New band neat 808 cm^{-1} could be the presence of substituted aromatic ring (di substituted).

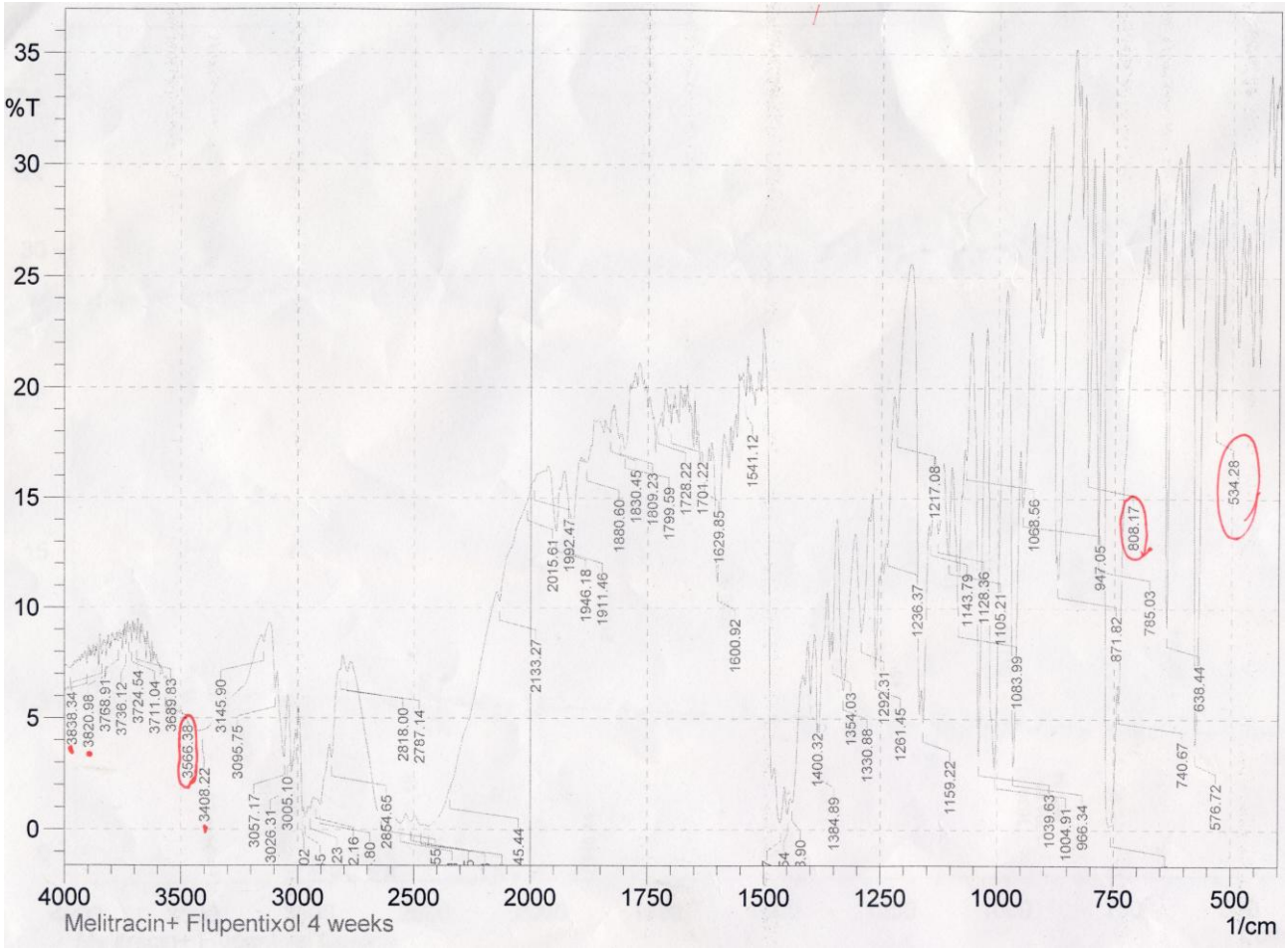


Figure 4.21: IR spectrum of control sample after 4 weeks (Flupentixol and Melitracen).

Chapter 5:

CONCLUSION

Conclusion:

In this project the photodegradation of flupentixol-melitracen are portrayed to show the effect of light on the tablet's physical parameters and potency of the drug itself. The analytical method is done accurately to avoid interference of many parametes. The result obtained is accurate. Moreover the method of analysis is simple, inexpensive to give the various results about potency.

However it shows that the product we use SENSIT is photosensitive require protection from light.

Reference

Acharjya, S. K., Panda, P., Mallick, P., Kumar R.K., Narendra,A., Sravani, A., Y., Shilpa & Annapurna, M. M. (2010) Spectrophotometric methods for simultaneous estimation of Flupentixol Dihydrochloride and Melitracen Hydrochloride in combined tablet dosage form. *Journal of Chemical and Pharmaceutical Research*, 2(3):158-171.

Chhalotiya, U.K., Bhatt, K.K., Shah, D. A., Chauhan, G. R. & Baldanial, S. L. (2011) Development of LC Method for the Simultaneous Determination of Antidepressant Drug Combination Melitracen Hydrochloride and Flupentixol Dihydrochloride in their Combined Dosage Form. *Chromatography Research International*, Volume: 2011.

Flupentixol. (2012) Flupentixol compositions.[online] Available from: http://www.freepatentsonline.com/EP2374450.html. [Accessed 3rd July 2012].

Garcia, L.G., I Forfar-Bares, F Pehourcq, & Jarry, C.(2003) JChromatogr B Analyt Technol. *Biomed Life Sci*, 795(2), 257-64.

Meng, QF. C. J., Chen, Z., San, C., Hou, Y. & Cheng, Y. (2007) Validation of a sensitive LC/MS/MS method for simultaneous quantitation of flupentixol and melitracen in human plasma. *Journal of Pharmaceutical and Biomedical Analysis*; 45:.785–792.

Sheikh, I.A.,Charde, M.S. & Kasture, A.V. (*2009*) Estimation of melitracen HCl in single dosage form by RP-HPLC method. *Journal of Pharmacy Research*, 2(11), 1764-1769.

Sharma, M. C., Sharma, S. & Sharma, A. D. (*2010*) Novel application and spectrophotometric estimation of Melitracen HCl tablet dosage form using Niacinamide as hydrotropic solubilizing agent. *Journal of Chemical and Pharmaceutical Research*, 2(2), 416-420.

Tripathi, KD. (2003) Essentials of Medical Pharmacology, *Jaypee brothers Medical Publishers (P) Ltd*, New Delhi, 5, 395-396.

Walter, S. Bauer, S. & Roots. (1998) Quantification of the antipsychotics flupentixol and haloperidol in human serum by high-performance liquid chromatography with ultraviolet detection. *Journal of Chromatography B: Biomedical Sciences and Applications*, 720, 231-237.

Xiao-hui, W., Li-hong C, Jin-hong L, (2010) the therapeutic effect of flupentixol combined with melitracenon functional dyspepsia in patients with anxiety and depression symptoms. *Journal of Naval General Hospital.* [Accessed 3rd July 2012].

Yunus, M., Siddiqui, H. H., Bagga, P., Ali, M. A. & Singh, K. (2011) A simple UV spectrophotometric method for the determination of flupenthixol dihydrochloride in bulk and pharmaceutical formulations. *International journal of pharmaceutical science and research*, 2(8): 2152-2155.