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Studying the Assay and the effect of temperature and Sun light on the stability of Mefanamic acid Tablets

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Abstract: In the present work, the assay and the effect of temperature and sun light on the stability of Mefanamic acid tablets were studied. The result showed that the percentage of the active substance and stability of this medication affected by temperature and direct sunlight when exposed to it for a period of time. Infra-Red obtained showed that Experimental and theoretical vibration band assignments were performed considering the presence of Centro-symmetric dimmers, bands assigned to N–H bending out of plane are observed at 626 and 575 cm^{-1} for polymorphs I and II, respectively. The best conditions for the drug storage, was at room temperature and away from sunlight and moisture. Because the highest percentage of active ingredient on the same day and in the production room temperature was 100.7% and when saved for a day in the refrigerator was 100.7% but when exposed to direct sunlight for a day it decreased to 99.7%. After a week of production at room temperature, the percentage of the active substance was 98.7%, and 96.8% when hold it in the refrigerator and it was 76.4% at direct sunlight. The percentage of the active ingredient after two weeks from the date of production at room temperature was 95.8% and when stored in the refrigerator was 91.9% and 61.9% at direct sunlight.

Keywords: Mefenamic acid, a non-steroidal, polymorphism, anti-inflammatory.

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1. Introduction:

Mefenamic acid is a non-steroidal anti-inflammatory drug used to treat pain, including menstrual pain. It is typically prescribed for oral administration.

Occurs as white to light yellow powder. It is odorless and tasteless at first, but leaves a slightly bitter aftertaste.It issparingly soluble in diethyl ether, slightly soluble in methanol (95) and in chloroform, and practically in soluble in water.It dissolres in sodium hyroxidets. MEFENAMIC ACID Tablets (250mg) contain MEFENAMIC ACID .The tables comply with stated under tables and with the following requirements.:95 to 105.0% of stated amount *Content of Mefenamic acid $C_{15}H_{15}NO_2$. Each yellow and blue capsule, with "250" marked on it contains 250 mg of Mefenamic acid. No medicinal ingredients: stearic acid, croscarmellose sodium, sodium lauryl sulfate, colloidal silicon dioxide, microcrystalline cellulose, gelatin, FD&C Yellow No. 10, FD&C Yellow No. 6, FD&C Blue No. 1, and titanium dioxide .

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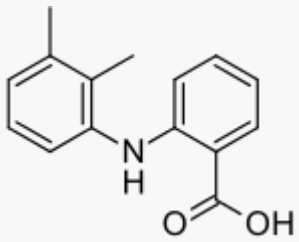
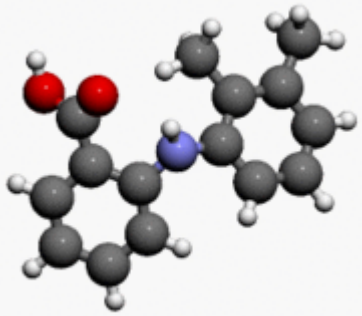
Mefenamic acid





Systematic (IUPAC) name	
2-(2,3-dimethylphenyl)amino benzoic acid	
Clinical data	
Trade names	
AHFS/Drugs.com	monograph
Medline Plus	a681028
Pregnancy cat.	C (AU) C (US)
Legal status	Pharmacy Only (S2) (AU) POM(UK) ℞-only (US)
Routes	Oral
Pharmacokinetic data	

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Bioavailability	90%
Protein binding	90%
Metabolism	Hepatic (CYP2C9)
Half-life	2 hours
Excretion	Urine (66%), faces (20-25%)
Identifiers	
CAS number	61-68-7 ✓
ATC code	M01AG01
PubChem	CID 4044
IUPHAR ligand	2593
DrugBank	DB00784
Chemical data	
Formula	$C_{15}H_{15}NO_2$
Mol. mass	241.285 g/mol
Melting point	225 C

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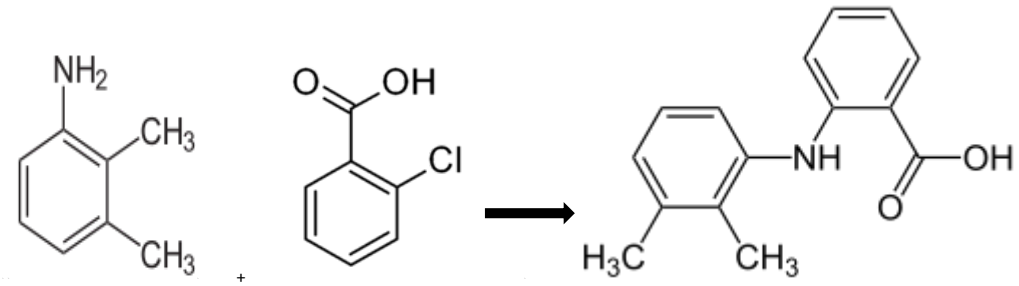
- **Synthesis :**

Analogous to Mefenamic **acid** this compound may be synthesized from-

2-chlorobenzoic acid and 2, 3-dimethylaniline.



Mefenamic acid

2, 3-dimethylaniline **2-chlorobenzoic acid**

Action and used:

Cyclo-oxygenase inhibitor; analgesic; anti-inflammatory.

Mechanism of action of the drug:-

Mefenamic acid is a group of non-steroidal anti-inflammatory drugs, which reduces the release of prostaglandin, which causes inflammation, pain and swelling, and is used to relieve pain, fever and inflammation caused by rheumatoid arthritis. The work of these painkillers work by blocking the enzyme Alsichaelo Oxeginaz which contributes to the production of prostaglandin. But these drugs affect the lining of the stomach and intestinal lining .

The diseases addressed by this drug:

Rheumatoid arthritis-Stylized disease.-Osteoporosis -Muscle aches and pains teeth -Headache -

Analgesic after operations -Menstrual pain and uterine -Metrorrhagia -Sports Injuries.

The aim of research:

Identify the active ingredient in tablets, hydrolysis the tablets, Calculate the Assay and Study the effect of temperature and sunlight on medication.

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2. Experimental:

2.1. Materials and Tools:

2.1.1. Materials (All chemicals used were analytical grade type):

Absolute ethanol, 2, 3-Dimethylaniline, Ammonia (18M), 1, 4-Dioxan, Toluene, Dichloromethane, Methanol, Phenol red solution, Sodium hydroxide solution (0.1M), Distilled water, GM-Mefenamic tables.

2.1.2. Tool and Apparatus:-

Sensitive balance, Water bath (Ultra sonic405), Infrared Absorption spectrum (FTAR-460 plus), TLC254plate, Ultraviolet light, Burette 50 ml, Conical flask 250ml, Disintegration Tester.

2.2. The method:

2.2.1. PRACTICAL TESTS

2.2.1.1. IDENTIFICATION:

A quantity of the powdered tablets containing 0.25g of Mefenamic acid was extracted with two 30ml quantities of ether, the combined was washed with water ,evaporated to dryness on a water bath and the residue was dried at 105^0C. A sufficient quantity was dissolved in the minimum volume of absolute ethanol and evaporated to dryness on the water bath .The infrared absorption spectrum, was concordant with the reference spectrum of Mefenamic acid (RS 210nm).

2.2.1.2. Test of 2, 3-Dimethylaniline:

The method for thin-layer chromatography was carried out , using a TLC silica gel planet and mixture of 1 volume of 18M ammonia ,25 volumes of 1,4-dioxan and 90 volumes of toluene as the mobile phase . Apply separately to the plate 40ml of each of the following solutions .for solution (1) the powdered tablets containing 0.25g of Mefenamic acid was shaken with a quantity of with amixture of 7.5ml of dichloromethane and 2.5ml of methanol for 10 minutes. Centrifuge and use the supernatant liquid. Solution (2) contains 0.00025% w/v of 2,3-dimethyl-aniline in a mixture of 3volumes of dichloromethane and 1volume of methanol. After the plate was removed, it was dried and the chromatogram was obtained with solution (100ppm).

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2.2.1.3. Test of related substances:

the method for thin-layer chromatography was Carried out, using a TLC Silica gel GF254 plate and a mixture of 1volume of glacial acetic acid , 25 volumes of 1,4-dioxan and 90 volumes of toluene as mobile phase was Applied separately to the plate 20ml of each of the following solution : For solution (1) the supernatant liquid obtained in the test for 2,3-dimethylaniline was used .For solution(2): 1volume of solution (1) was diluted to 500 ml with a mixture of 3 ml of dichloromethane and 1 ml of methanol . After removal of the plate it was allowed to dry in air. Exposed to iodine vapors for 5minutes and it was examined under ultraviolet light (254nm). Any secondary spot in the chromatogram obtained with solution (1) was not more intense than the chromatogram obtained with solution (2)(0.2%). any spot was Disregard with an RF value of 0.004 or less.

2.2.1.4.Test for ASSAY:

20 tablets of the powder were Weighted and Dissolved, a quantity of the powdered tablets containing 0.5g of Mefenamic acid in about 80ml of warm absolute ethanol previously neutralized to phenol red solution (1ml)alternating between heating and ultrasound to a dissolution .was Cooled ,and neutralized with absolute ethanol to produce 100ml. mixed well and titrated with 0.1M sodium hydroxide by using phenol red solution as indicator .each 1ml of 0.1Msodium hydroxide is equivalent to 24.13mg of C15 H 15NO 2 ..

Assay of Mefenamic acid in GM- Mefenamic tables (250mg) was calculated in the same day of production. The Experiment was repeated when the sample was saved in the refrigerator and again when saved in direct sunlight on the same day, and then after a week of keeping the sample at room temperature and stored in the refrigerator and save them in direct sunlight. The same procedure was carried again after two weeks of keeping the sample at room temperature and stored in the refrigerator and save them in direct sunlight.

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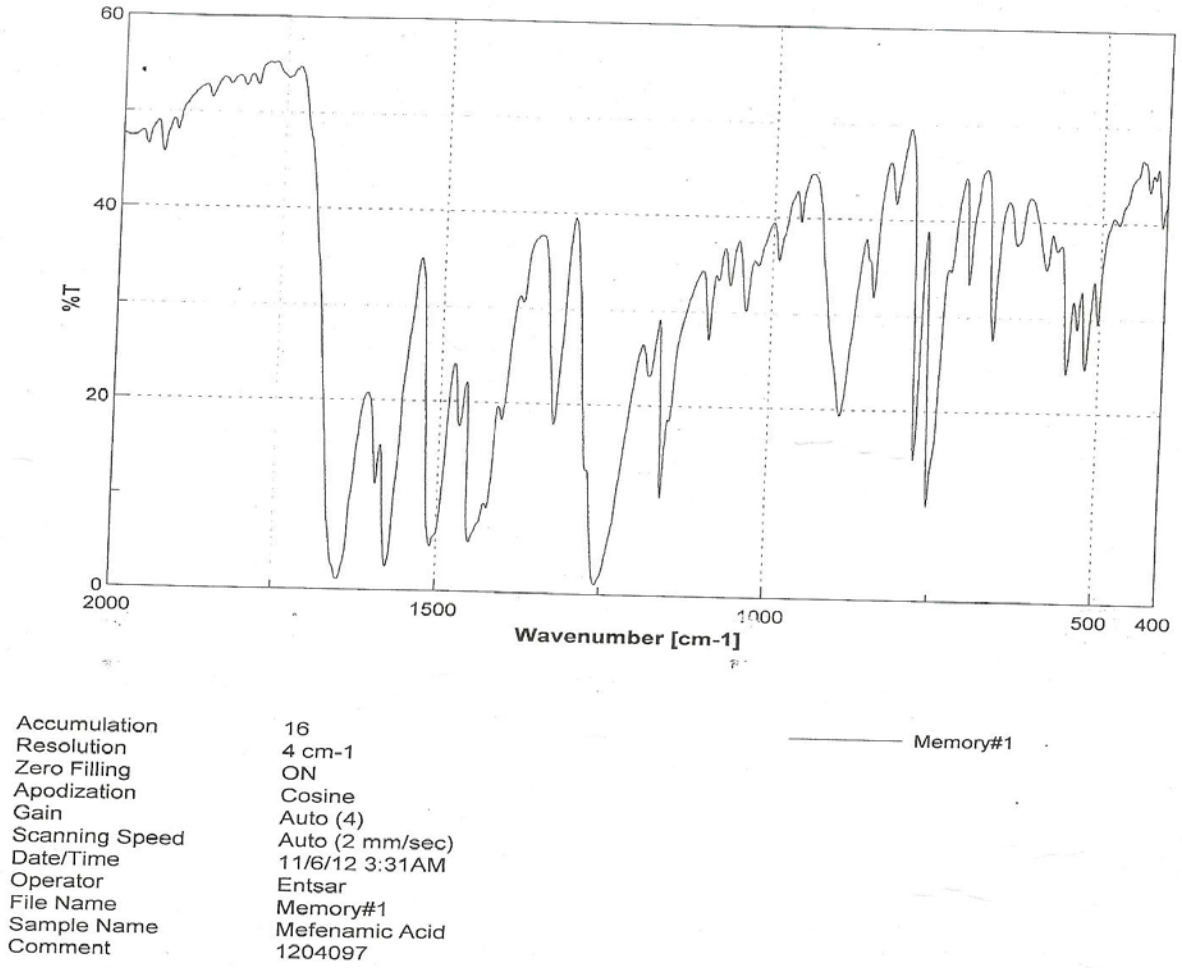
2.5. Discussion of the results:

(i) Identification:



Mefanamic acid (2-[(2, 3-(dimethylphenyl) amino] benzoic acid), known as forms I and II. Polymorph it was obtained by recrystallization in ethanol, to promote the solid phase transition. Experimental and theoretical vibration band assignments were performed considering the presence of Centro-symmetric dimmers. Besides band shifts in the 3345–3310 cm^{-1} range, important vibration modes to distinguish the polymorphs are related to out-of-phase and in-phase N–H bending at 1577 (IR) cm^{-1} and 1568 (IR) cm^{-1} for forms I and II, respectively. In IR spectra, bands assigned to N–H bending out of plane are observed at 626 and 575 cm^{-1} for polymorphs I and II, respectively.

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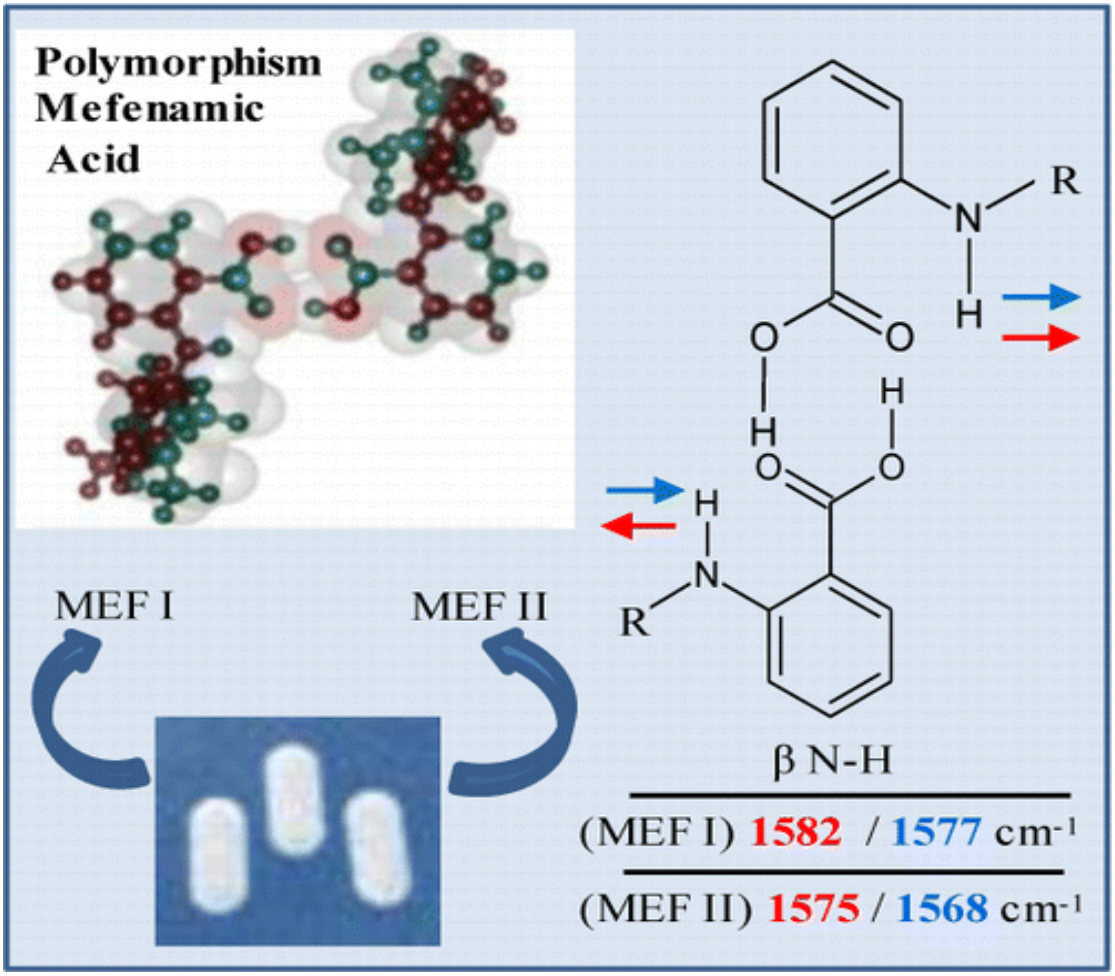

(ii) Test 2, 3-Dimethylaniline and Test Related substances :

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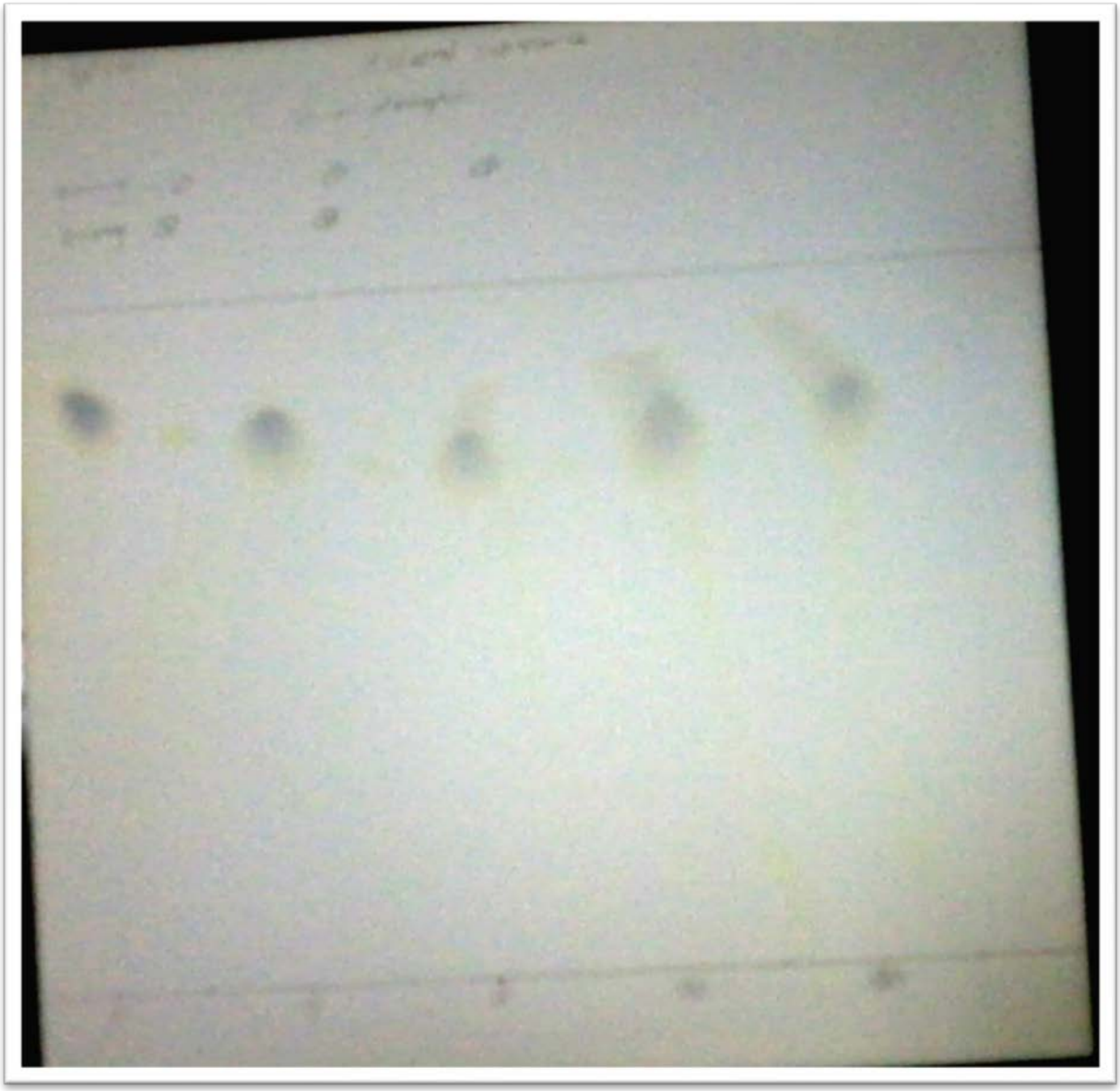

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(VI)Test for ASSAY:

Titration of NaOH (0.1M):

	On the day of production/ml	After a week of day production/ml	After two weeks on production/ml
At refrigerator temperature	10.5	10.1	09.6
At room temperature	10.5	10.3	10.0
In direct sunlight	10.4	08.0	06,5

-Each 1ml NaOH (0.1M) =24.13mg of Mefenamic acid.

** On the day of production:

-Titrate volume=10.5 ml

- Concentration of the Blank solution=0.1 mole/l.

- The concentration of sodium hydroxide solution is measured=0.1003 mole/l.

- Constant (F) = the concentration of sodium hydroxide solution is measured

Concentration of the Blank solution

$$= \frac{0.1003}{0.1} = 1.003$$

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-Weight of 20 tablets=6.9090 gram..

- Weight of one tablet= $\frac{6.9090}{6}$ = 0.34545gram.

-ASSAY= $\frac{\text{(Titrate volume - Concentration of the Blank solution)*24.13 *100 *F}}{\text{Weight}}$

= $\frac{(10.5-0.1)*24.13*100*1.003}{250}$ = 100.7%

ASSAY	On the day of production	After a week of day production	After two weeks on production
At refrigerator temperature	100.7%	96.8%	91,9%
At room temperature	100.7%	98.7%	95,8%
In direct sunlight	99.7%	76.4%	61.9%

(VII) Disintegration Tester:

Disintegration time =7:3 min:sec .

The number of windings of the device =29-32 rpm.

In the present work analysis of Mefenamic (the active ingredient) tablets 250 mg was studied, At different conditions of temperature and the sun's rays, by using IR spectroscopy, and calculated the percentage of the active substance to conduct calibrations and the percentage of the active substance under the influence of these circumstances. On the same day and in the production room temperature the percentage of active ingredient was 100.7% and when saved for a day in the refrigerator it was 100.7% but when exposed to direct sunlight for a day it decreased to 99.7%.

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After a week of production at room temperature the percentage of the active substance was 98.7%, and when it hold in the refrigerator it was 96.8% and at direct sunlight 76.4%.

After two weeks from the date of production at room temperature the percentage of the active ingredient was 95.8% and when stored in the refrigerator it was 91.9% and at direct sunlight 61.9%.

One can concluded that the percentage of the active substance and stability of this medication Affected by temperature, the best conditions for the storage was at room temperature away from sunlight and moisture.

**** Picture shows the device Water bath (Ultra sonic405):**

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**** Picture shows the device Disintegration Tester:**

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**** Picture shows the device Infrared Absorption spectrum (FTAR-460 plus)**

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**** Picture shows the device Ultraviolet light:**

Picture shows the end point of the calibration and the starting point: *

Before

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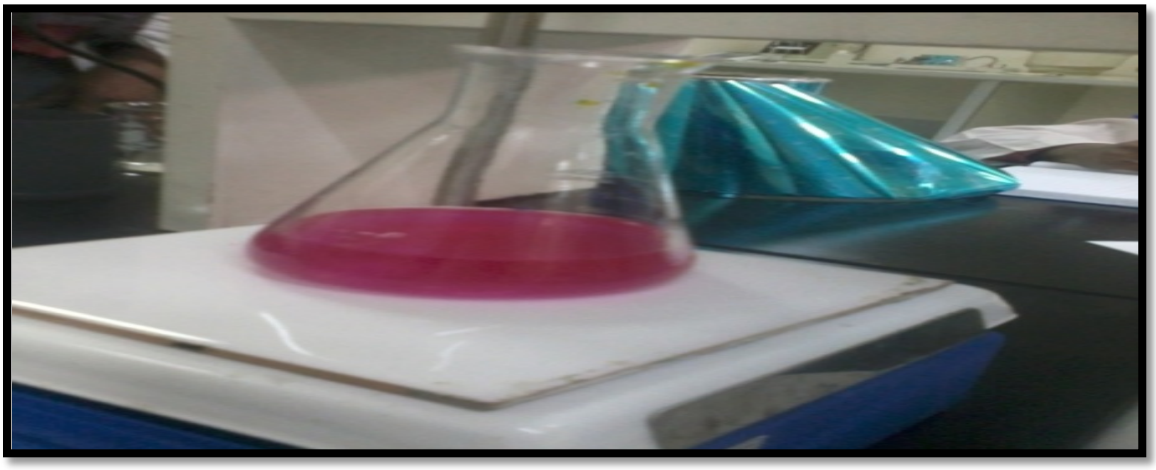
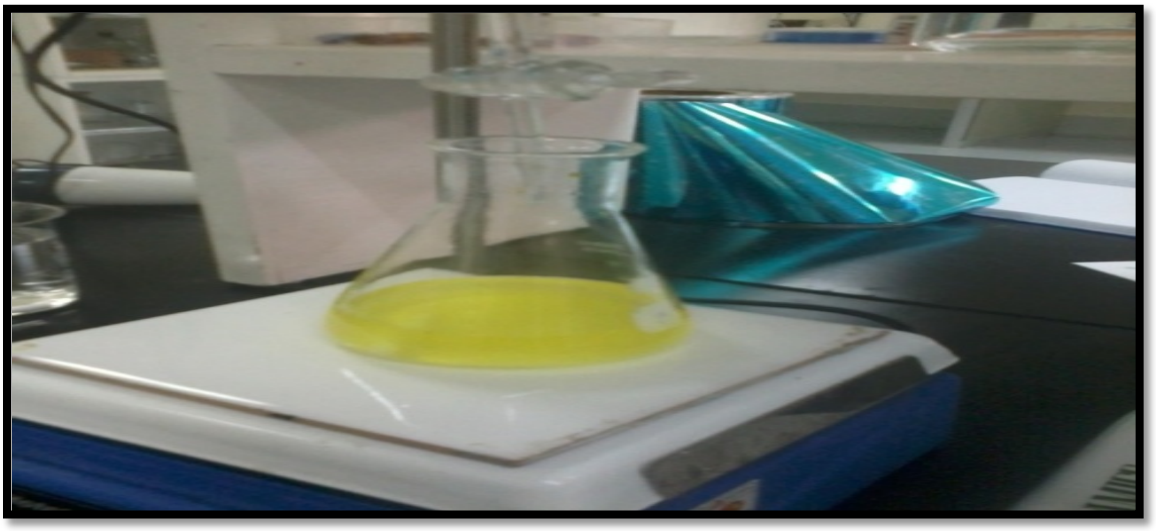


After



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