Chapter One
Introduction

1.1 Introduction:

Non-steroidal Anti-Inflammatory Drug: ((NSAID)):

Are drugs with analgesic effect and antipyretic in normal doses, and have anti-inflammatory effects in high doses.Can be defined as a group of drugs that are three and pharmaceutical Daub important, namely:

- Anti-inflammation.
- Pain relievers.
- Antipyretics or high body temperature.

Well-known examples of them: Aspirin. The work of this kind of drugs to inhibit the action of the enzyme cyclooxygenase which is the enzyme responsible for the production of Prostaglandins and Thromboxane A2.

NSAIDs non-narcotic : -One of the most prominent members of this group of drugs:

- Aspirin.
- Ibuprofen.
- Naproxen.

But paracetamol is not considered a member of this group.Beginning in 1829 when Alsalesan isolated from the bark

of the white willow, which was Kkhavd uses heat in folk medicine, has become NSAIDs.

(1.1.1) The mechanism of action :

Operate most NSAIDs non-selective inhibitors of the enzyme cyclo-oxygenase

Vtthbt Aloazosemen Alsichaeloaxginaz (1 -) -1 and Alsichaeloaxgen Sox (02 -) COX-2 .And stimulate the formation of enzymes Alsichaeloaxginaz Albroositaglandinat and Iirumboxan of arachidonic acid, which is derived from the membrane by cellular enzyme Alvesvoulibaz. One of the functions of prostaglandins works Kdzeiat Mersalh in the inflammation process.The broad mechanism of action of NSAID.

(1.1.2) Examples :

Can be classified as NSAIDs, according to their chemical structure. We find that members of the group of NSAIDs have similar properties and carry. There are slight differences between NSAIDs in efficacy when used in doses equal. Is also linked to the differences between the vehicles system taking doses half-life is vital and Route of administration and drug tolerance.

From these examples:

(a) Salicylates :

- Acetyl salicylic acid.
- Amokcyprin.
- Beanoralat.
- Colin magnesium salicylate.
- Devlonizal.
- Athenzamad.
- Veisselamin.
- Methyl salicylate.
- Magnesium salicylate.
- Salsell salicylate.
- Salsell amide.

(b)Acetic acid derivatives :

- Diclofenac.
- Osimithasin.
- Brumvinak.
- Atodelac.
- Ketorolac.
- Andomithazen.
- Neboumyton.
- Ooxamithazen.
- Brogloumithazen.
- Sulindac.
- Tolmetin.

(c) Propionic acid derivatives (Albroovinat) :

- Ibuprofen.
- Olmenobrovin.
- Carprofen.
- Dicksyebobrovin.
- Dickskitobrovin.
- Fenbufen.
- Fenoprofen.
- Flurbiprofen.
- Aabobroxam.
- Indoprofen.
- Ketoprofen.
- For Oxobrovin.
- Naproxen.
- Oxhexamat.
- Piroxicam.
- Droxickam.
- Meloxicam.
- Tonoxickam.
- Ocassaprosen.
- Berbrovin.
- Sobrovin.

(d)N acids - Ariel Ontraneljk (Mefenamic acids) :

- Mefenamic acid.

- Vlovinamik Acid.
- Makulovinamek Acid.
- Nulfinamek Acid.

1.2 Mefenamic acid about:

(1.2.1)General Notices:

(a)DEFINITION:

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 C15H15NO2

(b)Description:

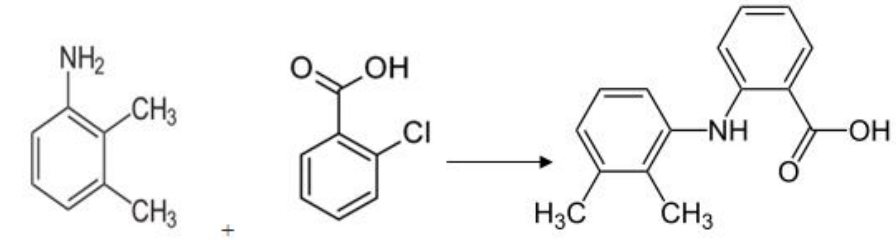
Occurs as white to light yellow powder. It is odorless and tasteless at first, but leaves a slightly bitter aftertaste.It issparingly soluble in diethyl ether, slightly soluble in methanol (95) and in chloroform, and practically in soluble in water.It dissolres in sodium hyroxidets.

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

(c)Synthesis :

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

2-chlorobenzoic acid and 2, 3-dimethylaniline.



2, 3-dimethylaniline + 2-chlorobenzoic acid → Mefenamic acid

(1.2.2) What form(s) does Mefenamic Acid come in?

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 .

(1.2.3) What are 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

(1.2.4) Who should NOT take Mefenamic?

Do not take this medication if you:

- Are allergic to mefenamic acid or any ingredients of the medication.
- Are in the third trimester of pregnancy (after 28 weeks of pregnancy)
- Have active stomach bleeding such as gastric or duodenal ulcers.
- Have a history of asthma, itchy skin rash, or allergic reactions after taking ASA (acetylsalicylic acid) or other no steroidal anti-inflammatory drugs (NSAIDs; e.g., ibuprofen, celecoxib, Diclofenac, indomethacin, etc.).
- Have bleeding in the brain.
- Have or recently had an inflammatory condition of the stomach and intestines such ulcerative colitis.
- Have recently had heart bypass surgery.
- Have severe or active kidney disease.

- Have severe or active liver disease.
- Have severe, uncontrolled heart failure.
- Have too much potassium in the body (hyperkalemia).

Mefenamic acid

Clinical data	
Trade names	Ponstel, Ponstan
AHFS/Drugs.com	monograph
MedlinePlus	a681028
Pregnancy cat.	• AU: C • US: C
Legal status	• AU: Pharmacy Only (S2) • UK: POM • US: ℞-only
Routes	Oral
Pharmacokinetic data	
Bioavailability	90%
Protein binding	90%
Metabolism	Hepatic (CYP2C9)
Half-life	2 hours
Excretion	Urine (66%), faeces (20-25%)
Identifiers	
CAS number	61-68-7 ✓
ATC code	M01AG01
PubChem	CID 4044
IUPHAR ligand	2593
DrugBank	DB00784
ChemSpider	3904 ✓
UNII	367589PJ2C ✓
KEGG	D00151 ✓
ChEBI	CHEBI:6717 ✗
ChEMBL	CHEMBL686 ✓
Chemical data	
Formula	$\mathbf{C_{15}H_{15}NO_2}$
Mol. mass	241.285 g/mol

1.3 Warnings and Recommendations and Side Effects:

(1.3.1) Warnings for Mefenamic acid:

a\ Allergy:

Some people who are allergic to NSAIDs also experience allergic reactions to Mefenamic acid. Before you take this drug, inform your doctor.

People who have experienced difficulty breathing after taking NSAIDs should not take Mefenamic acid.

Contact your doctor at once if you experience signs of an allergic reaction, such as skin rash, itching, difficulty breathing or swelling of the face and throat

b\ Anemia:

This medication may cause anemia (low red blood cell).

c\ Asthma:

People with asthma are at increased risk of severe and even fatal allergic reactions when taking this medication .

d\ Bleeding disorder:

Mefenamic acid may increase bruising and bleeding from cuts may take longer to stop.

e\ Blood pressure:

Mefenamic acid may cause an increase in blood pressure, even when there have been no blood pressure problems in the past.

f\ Diarrhea:

If diarrhea occurs, the dosage should be reduced or the medication stopped temporarily.

g\ Fluid retention:

Mefenamic acid can cause fluid retention and may result in swelling or puffiness. In severe cases, this can make symptoms of congestive heart failure worse.

h\ Heart problems:

Mefenamic acid, like other NSAIDs, may increase the risk of serious heart problems such as heart attack, stroke, or blood clots. People who are at risk for heart disease, such as high blood pressure, high cholesterol, diabetes, or heart disease.

i\ Kidney function:

Long term use of Mefenamic acid may lead to a higher risk of reduced kidney function. This is most common for people who already have kidney disease, liver disease, or heart failure; for people who take diuretics (water pills); and seniors.

j\ Stomach problems:

Stomach ulcers, perforation, and bleeding from the stomach have been known to occur during therapy with Mefenamic acid.

k\ Pregnancy:

This medication should not be used during pregnancy unless the benefits outweigh the risks. If you become pregnant while taking this medication, contact your doctor immediately.

The use of Mefenamic acid during the last 3 months of pregnancy may result in harm to the baby or longer labor for the mother. Mefenamic acid should not be used during this time.

l\ Breast-feeding:

This medication passes into breast milk. If you are a breast-feeding mother and are taking Mefenamic acid, it may affect your baby. Talk to your doctor about whether you should continue breast-feeding.

m\ Children:

Mefenamic acid is not recommended for children under the age of 18 years. The safety and effectiveness of using this medication have not been established for children.

n\ Seniors:

Seniors appear to have a higher risk of side effects, such as bleeding and kidney problems. The lowest effective dosage should be used for the shortest period of time possible.

(1.3.2) Side effects of Mefenamic acid:

- Abdominal pain
- Constipation
- Decreased or loss of appetite
- Diarrhea
- Dizziness
- Drowsiness
- Gas
- Headache
- Heartburn
- Lightheadedness
- Nausea
- Nervousness
- Trouble sleeping
- Vomiting

.(1.3.3) Recommendations for this medicine:

- Store this medication at room temperature.
- Protect it from light and moisture
- Keep it out of the reach of children.

- Mefenamic acid is best taken with or after food.
- The recommended adult dose (for people more than 14 years old) is 500 mg for the first dose followed by 250 mg every six hours as needed.
- Usually not to exceed one week of treatment
- In the case of menstrual cramps, treatment is usually not necessary for longer than two or three days.

Chapter Tow
The Practical Part

2.1 The Aim:

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

2.2 Material and Tools:

-- Materials:

- 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

2.3 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..

2.4 The Methods:

PRACTICAL TESTS

(i) IDENTIFICATION:

Extracted a quantity of the powder tablets containing 0.25g of Mefenamic acid with two 30ml quantities of ether. Was washed the combined with water , steamed to dryness on a water bath and dry the residue at 105.dissolve a sufficient quantity in the minimum volume of absolute ethanol and steamed to dryness on the water bath .The infrared absorption spectrum, Appendix II A, is concordant with the reference spectrum of Mefenamic acid (RS 210nm).

(ii) Test 2, 3-Dimethylaniline:

Carried out the method for thin-layer chromatography ,Appendix III, was used 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 . Applyed separately to the plate 40ml of each of the following solutions .for solution (1)shaked a quantity of the powdered tablets containing 0.25g of Mefenamic acid with amixture of 7.5ml of dichloromethane and 2.5ml of methanol for 10 minutes. Centrifuge and was used 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 removal of the plate, dryed it in the chromatogram obtained with solution (100ppm).

(iii)Test related substances:

Carry out the method for thin-layer chromatography ,Appendix III A , was used 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 . Apply separately to the plate 20ul of each of the following solution : For solution (1) was used the supernatant liquid obtained in the test for 2,3-dimethylaniline .For solution(2):dilute 1volume of solution (1)to 500 ml with amixture of 3 ml of dichloromethane and 1 ml of methanol . After removal of the plate .allow into dry in air. Expose to iodine vapours for 5minutes and examine under

ultraviolet light (254nm). Any secondary spot in the chromatogram obtained with solution (1) is not more intense than the spotting the chromatogram obtained with solution (2)(0.2%).Disregard any spot with an RF value of 0.004 or less

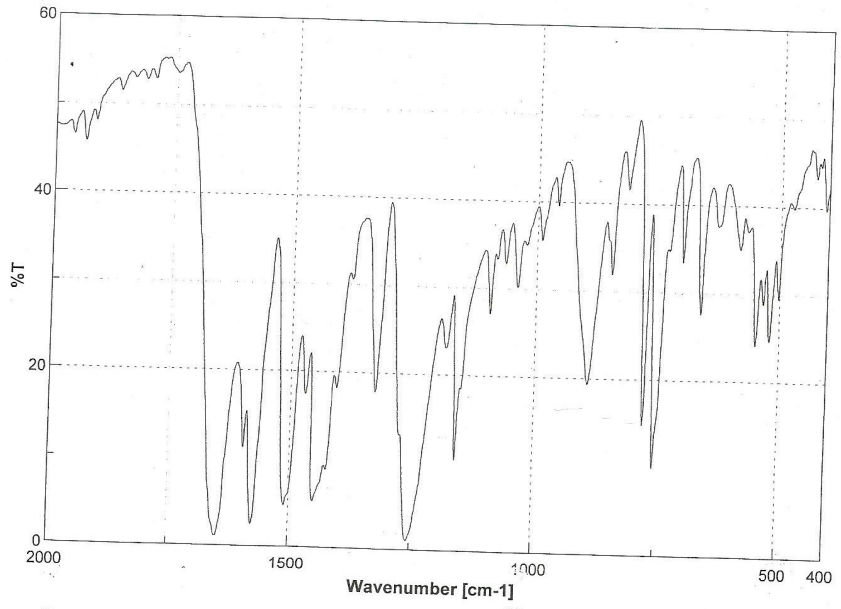
(vi)Test for ASSAY:

Weigh and powder 20 tablets .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 .Cool ,add sufficient of the neutralized absolute ethanol to produce 100ml. was mixed and titrated with 0.1M sodium hydroxide Vs was used phenol red solution as indicator .each 1ml of 0.1Msodium hydroxide Vs is equivalent to 24.13mg of C15 H 15NO 2 ..

Calculated Assay of Mefenamic acid in GM- Mefenamic tables (250mg) in the same day of production.. Repeated the Experience When you save the sample in the refrigerator and again when saved in direct sunlight on the same day. After a week of keeping the sample at room temperature and stored in the refrigerator and save them in direct sunlight. After two weeks of keeping the sample at room temperature and stored in the refrigerator and save them in direct sunlight

2.5 Discussion of the results:

(i) IDENTIFICATION:



Accumulation	16
Resolution	4 cm-1
Zero Filling	ON
Apodization	Cosine
Gain	Auto (4)
Scanning Speed	Auto (2 mm/sec)
Date/Time	11/6/12 3:31AM
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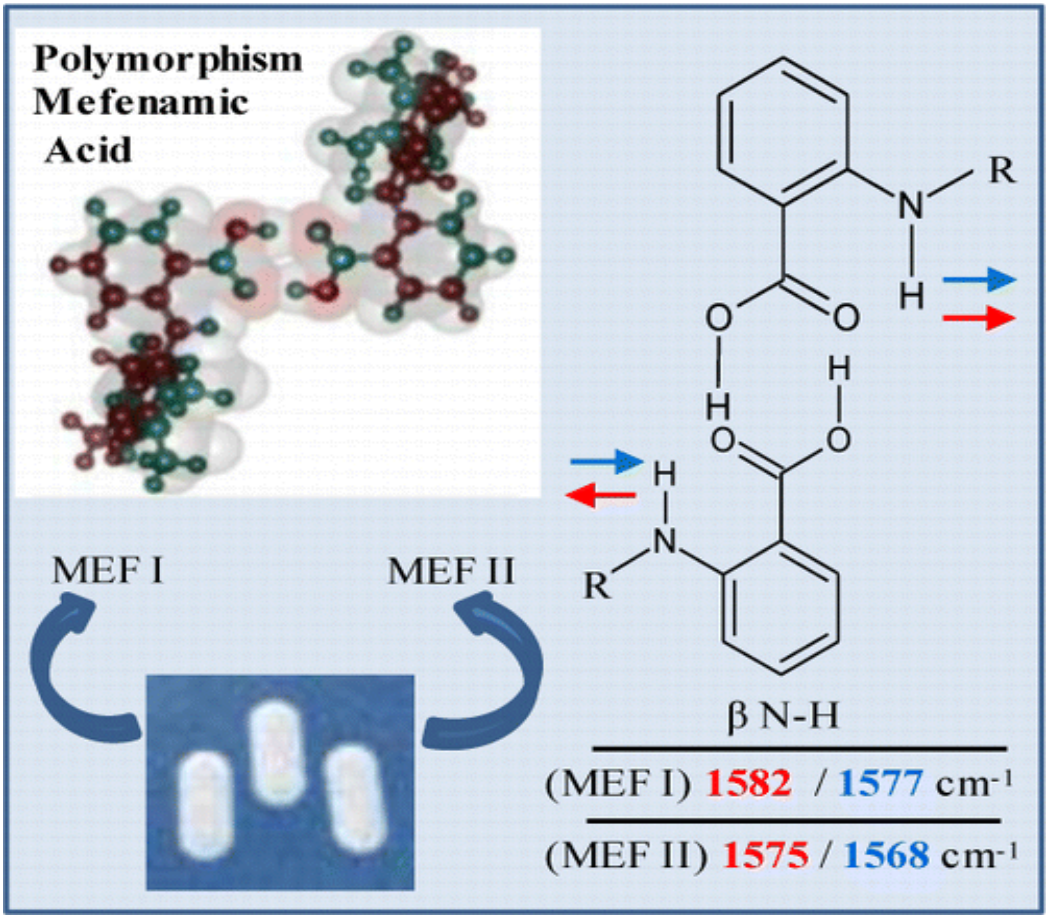
File Name	Memory#1
Sample Name	Mefenamic Acid
Comment	1204097

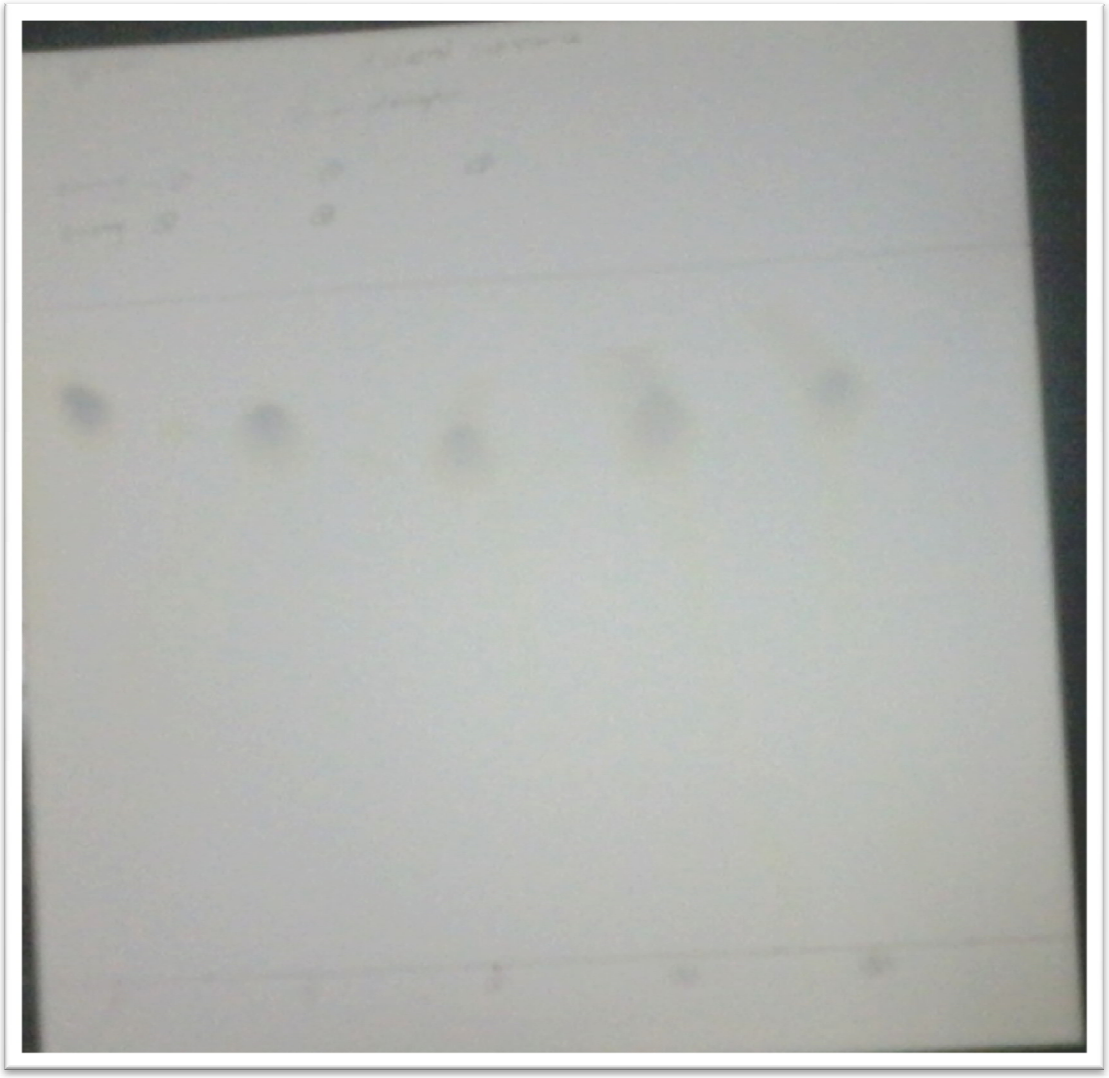
Memory#1

Mefenamic acid known as forms I and II. Polymorph I was obtained by recrystallization in ethanol, , to promote the solid phase transition. Experimental and theoretical vibration band assignments were performed considering the presence of centrosymmetric 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 1582 (Raman)/1577 (IR) cm–1 and 1575 (Raman)/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.



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



(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 1mlNaOH (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)

$$= \frac{\text{The concentration of sodium hydroxide solution is measured}}{\text{Concentration of the Blank solution}}$$

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

-Weight of 20 tablets=6.9090 gram..

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

-ASSAY= (Titrate volume - Concentration of the Blank solution) * 24.13 *100 *F

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%

Disintegration Tester:

Disintegration time =7:3 min:sec .

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

Chapter Three
Discussion

Discussion

Analysis has Mefenamic tablets 250 mg and we got the active ingredient Mefenamic acid, a device using IR spectroscopy, and calculated the percentage of the active substance to conduct calibrations. At different conditions of temperature of the sun's rays has been studied the percentage of the active substance under the influence of these circumstances.

On the same day and in the production room temperature was the highest percentage of active ingredient and 100.7% when saved for a day in the refrigerator was a high percentage of the active substance 100.7% but when exposed to direct sunlight for a day decreased the percentage of the active substance 99.7%.

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

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

Affected by the percentage of the active substance and stability of this medication temperature whenever not offering

medication to temperatures large and long period of time less than its effectiveness, and whenever not offering to direct sunlight and long period of time less than very effective. The best conditions for the save room temperature away from sunlight and moisture.

Chapter Four
Devices and Tools

Picture shows the device Water bath (Ultra sonic405):

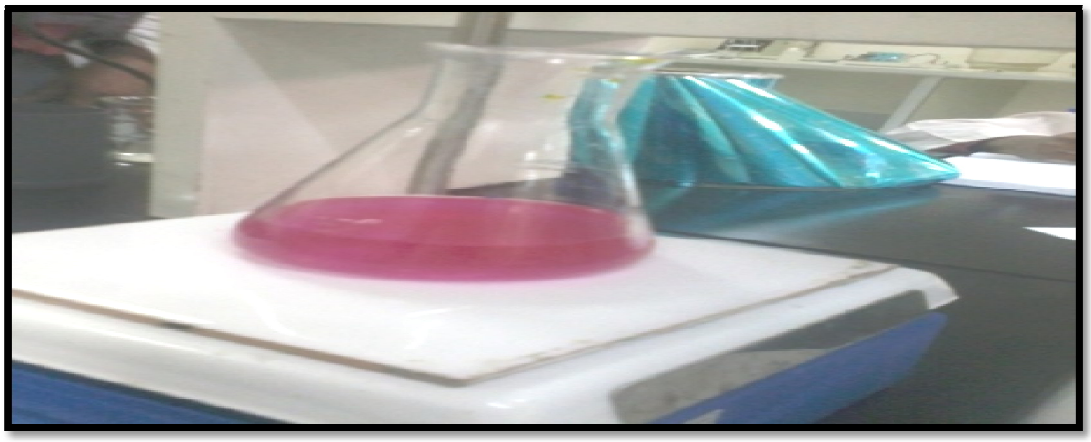
Picture shows the device Disintegration Tester:

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

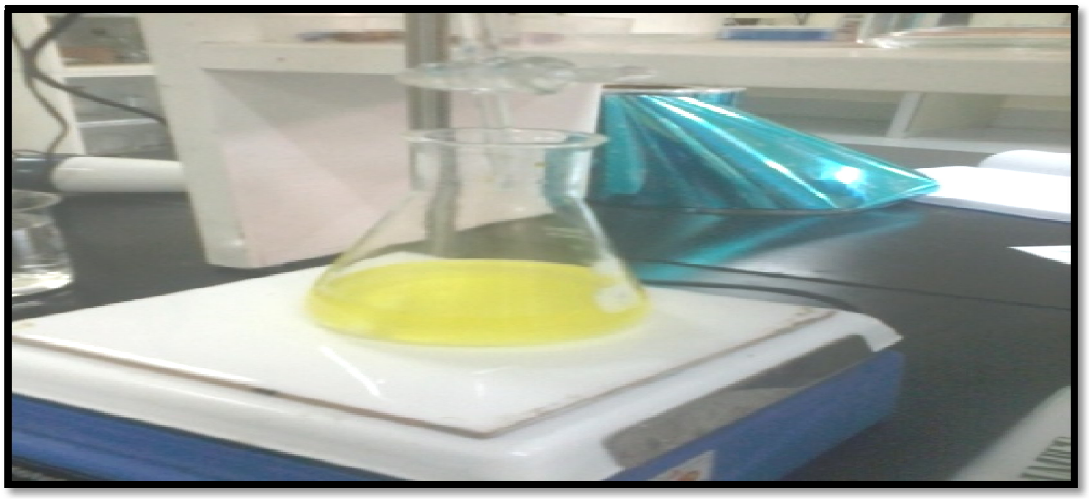
Picture shows the device Ultraviolet light:

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

Before



After



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