QUALITY CONTROL ANALYSIS OF ACTIVE PARMACEUTICAL INGRADIENTS"

An Industrial Training Report submitted
for the partial fulfillment of the Degree of Master of Science
By

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RAJKOT (GUJARAT) – 360005

2019-2020

C E R T I F I C A T E

This is to certify that this training report on **ENDOC Life Care Pvt. Ltd.** was successfully carried out by Miss **Gadhethariya priya h.** towards the partial fulfillment of requirements for the degree of Master of Science in Microbiology of SHREE M. & N. VIRANI SCIENCE COLLEGE (AUTONOMOUS) Rajkot. It is an authentic record of her own work, carried out by her under the guidance of (Name of Supervisor) for a period of **2.5 month** during the academic year of **2020-2021**. The content of this report, in full or in parts, has not been submitted for the award of any other degree or certificate in this or any other University.

Name & Signature of the Head of the Department

Name & Signature of the supervisor

D E C L A R A T I O N

I hereby declare that the work incorporated in the present training report **"QUALITY CONTROL ANALYSIS OF ACTIVE PHARMACEUTICAL INGRDIENTS"** is my own work and is original. This work has not been submitted to any University for the award of any Degree or a Diploma.

Acknowledgement

The satisfaction and euphoria that accompany the successful completion of any task would be incomplete without the mentioning if the people whose constant guidance and encouragement made it possible, which are the result of studying blend of both research and knowledge.

We express our earnest gratitude to our head of department, **Dr.S.D. sorathiya** and Industrial Training guide, **Mr. Dharmesh pithadiya department of Quality control** for their constant support, encouragement and guidance. We are grateful for their cooperation and their valuable suggestions.

Finally, we express our gratitude to all other member who are involved either directly or indirectly in the completion of this training.

Sincerely,
Gadhethariya priya

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LIST OF FIGURE

LIST OF ABBREVATIONS

INITIAL/SIGN/UNIT	FULL FORM
%	PERCENTAGE
µg	MICROGRAM
L.O.D	LOSS OF DRYING
API	ACTIVE PARMACEUTICAL INGRADIENTS
TLC	THIN LAYER CHROMATOGRAPHY
HPLC	HIGH-PERFORMANCE LIQUID CHROMATOGRAPHY
IR	INFRARED

List of table

Abstract

Quality is not an accident, it is the outcome of intelligent efforts. The quality of pharmaceutical products is essential to assure the maximum level of patient's satisfaction. The most important criteria for the qualities of any pharmaceutical in dosage form are its safety, potency, efficacy, stability, patient acceptability and regulatory compliance. Pharmacopoeias are referred as drug standards. They provide standards, specifications and test methods that are expected to be used in the pharmaceutical industry to ensure the quality of pharmaceuticals. Furthermore, regulatory bodies are continually developing their requirements to ensure the safety, quality and efficacy for pharmaceutical development and manufacturing with respect to time. The main standard for the quality of any pharmaceutical is the intrinsic and extrinsic elements which contribute directly or indirectly to the quality parameters of pharmaceutical. Quality should be incorporated into a drug product during product and process design. The crucial objective of this book is to provide various quality control tests for pharmaceuticals, according to pharmacopoeial standards and specifications.

CHAPTER –1:
GENERAL INTRODUCTION

Name of company : - ENDOC Life care Pvt. Ltd.

Name of the product :- ornidazol ,

fluconazole

tizanidine hydrochloride

Section where I worked :- QC DEPARTMENT

Important of QC in **Pharmaceuticals** :-

- The pharmaceutical environment today is changing quickly due to globalization, increased competition, cost constraints, demands for efficiency, development of international regulation, supply chain complexity, and product/process complexity.
- In this fast-changing environment, the people and companies that learn to adapt will prosper. To manufacture & deliver consistently zero defect products to the patients.
- The quality, efficacy and safety attributes of products must be ensured so that the consumer health is not compromised

What is an API:

- Active Pharmaceutical ingredients
- Any substance or mixture of substances intended to be used in the manufacture of a drug product and that when used in the production of a drug becomes an active pharmaceutical ingredient of the drug product. Such substances are intended to furnish pharmacological activity or other direct efffect in the diagnosis,cure,mitigation,treatment or prevention of the disease or to efffect the structure and function of the body.

- All drugs are made up of two core components; the API, which is the central ingredient and the excipients,the substance other than the drug that helps deliver the medication to your system.Excipients are chemically inactive substance, such as lactose or mineral oil. For instance,if you have a headache,acetaminophen is the active ingredient, while the liquid in the gel- capsule or a hulk of a pill is the excipients.

Test perform in QC department:-

Physicochemical method:- Physical appearance

Solubility test

Ph test

LOC test

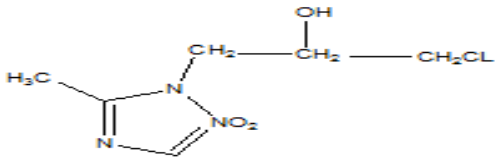
Melting point

Sulfated ash

Testing services for identity and purity :- HPLC & IR

CHAPTER –2:
DRUG PROFILE/MATERIALS

❖ **Name of drug:-** Ornidazole

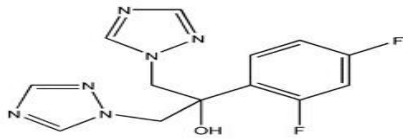


- **Use of the drug**:-

  These are widely used for the treatment of protozoan infections Or it's prevent infection after surgery.

  It's Antiprotozoal or antibiotic kind of drug

- **Name of drug:-** Fluconazole

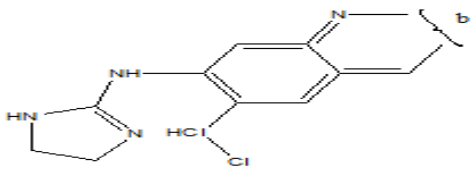


- **Use of the drug:-**

  it's antifugal drug

  These are widely use for treatment of fungal and yeast infection, or to cure urinary tract infection.

- **Name of drug:-** Tizanidine Hydrochloride



- **Use of the drug**:-

  it's a Muscle Relaxant Drug

  By blocking nerve impulses that sent to brain

CHAPTER –3:
INSTRUMENTATION & METHODS

INTSTRUMENTION

Sr.no	Name of instruments	Company name
1	Weight balance	OHAUS
2	Melting point apparatus	GALLENKAMP
3	Hot air oven	KRUSHNA
4	Karl- fisher	LABTRONICS
5	PH meter	LABINDIA
6	Muffle furnace	BIONIC
7	HPLC	AGILENT-1200
8	UV spectrophotometer	SHIMADZU
9	FTIR	PERKIN ELMER SPECTRUM 100
10	UV cabinet	

TABLE NO:3.1 LIST OF INSTRUMENT

(1) Melting Point Apparatus

A melting point apparatus is a scientific instrument used to determine the melting point of a substance. Some types of melting point apparatus include the Thiele tube, Fisher-Johns apparatus, Gallenkamp (Electronic) melting point apparatus and automatic melting point apparatus. While the outward designs of apparatus can vary greatly most apparatus use a sample loaded into a sealed capillary that is then placed in the apparatus. The sample is then heated, either by a heating block or an oil bath and as the temperature increases the sample is observed to determine when the phase change from solid to liquid occurs. The operator or the machine records the temperature range starting with the initial phase change temperature and ending with the completed phase change temperature.

The temperature range that is determined can then be averaged to gain the melting point of the sample being examined. Apparatus usually have a control panel that allows the starting and final temperatures, as well as the temperature gradient (in units per minute) to be programmed. Some machines have several channels which permit more than one sample to be tested at a time. The control panel might have buttons which allow the start and end of the melting point range to be recorded.

Figure :-3.1 Melting Point Apparatus

(2) HPLC - High-performance Liquid Chromatography

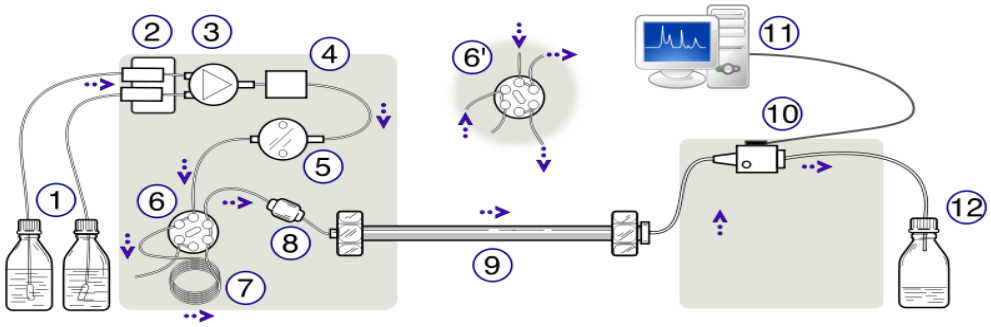
High-performance liquid chromatography (formerly referred to as high-pressure liquid chromatography), HPLC is a technique in analytic chemistry used to separate the components in a mixture, to identify each component and to quantify each component.

It relies on pumps to pass a pressurized liquid solvent containing the sample mixture through a column filled with a solid adsorbent material.

Each component in the sample interacts slightly differently with the adsorbent material, causing different flow rates for the different components and leading to the separation of the components as they flow out the column.

FIGURE :3.2 HPLC

HPLC has been used for medical (e.g. detecting vitamin D levels in blood serum), legal (e.g. detecting performance enhancement drugs in urine), research (e.g. separating the components of a complex biological sample, or of similar synthetic chemicals from each other), and manufacturing (e.g. during the production process of pharmaceutical and biological products) purposes.



1. Solvent reservoirs
2. Solvent degasser
3. Gradient valve
4. Mixing vessel for delivery of the mobile phase
5. High-pressure pump

6. Switching valve in "inject position"
7. Switching valve in "load position"
8. Sample injection loop
9. Pre-column (guard column)
10. Analytical column
11. Detector (i.e. IR,UV) & Data acquisition
12. Waste or fraction collector.

(3) UV Cabinet

How UV Inspection UV Cabinet works? The front of the box is closed with a roller shutter, which can be slid to the left or to the right as required for inserting or marking objects. A glass filter in the viewing window protects the eyes against reflected short-wave UV light.

Great care has been taken to ensure the correct distances between UV lamp, object and the observer's eye in the interest of good illumination and untroubled viewing. Hardly any TLC laboratory can be without the use of UV light for inspecting chromatograms.

Figure :-3.3 UV cabinet

(4) FTIR (Fourier Transform Infrared Spectrometer)

FTIR is a sensitive technique particularly for identifying functional group of organic chemicals and also characterize some inorganics.

FTIR relies on the fact that the most molecules absorb light in infra red region of the electromagnetic spectrum. This absorption corresponds specifically to the bond present in the molecule .

The frequency range is measured as wave numbers typically over the range 4000-600 cm^{-1} .

The background emission spectrum of the IR source is first recorded, followed by the emission spectrum of the IR source with the sample in place . the ration of the sample spectrum to the background spectrum is directly related to the sample's absorption spectrum .

The resultant absorption from the bond natural vibration frequencies indicates the presence of various chemical bounds and function group present in the sample

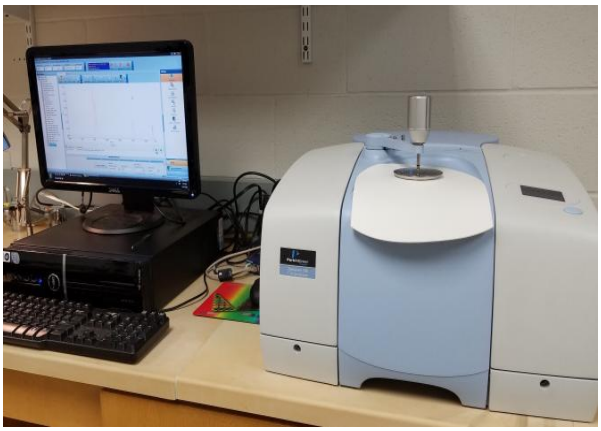


Figure :-3.4 FTIR

METHODS-STANDARD OPERATING

1) LOD TEST

this test is a widely used test method to determine the moisture content of a sample, although occasionally it may refer to the loss of any volatile matter from the sample.

PROCEDURE :-

Weight accurately a dry empty crucible

Take the sample and weight crucible + sample accurately (take record)

Heat the sample in muffle furnace or in oven at temp. 105˚+/-5˚c for 2 hours

after drying is completed Allow the sample to cool in desiccators.

Weight it and calculate the LOD .

Repeat that until the 2 result are not came same

Calculation :-

Wt of crucible =w

Wt of crucible +sample =w1

Wt of sample=m

After drying Wt of crucible +sample =w2

Loss of drying%=(W1-W2)×100/M

2) Sulfated ash test

The test is usually used for determining the content of inorganic impurities in an organic substance.

OR

to determine sulfate related impurities in an organic substance.

PROCEDURE:-

Weight accurately a dry empty crucible

↓

Take the sample and weight crucible + sample accurately (take record)

↓

Heat the sample in muffle furnace or in oven at temp. 105˚+/-5˚c for 2 hours

↓

after drying is completed Allow the sample to cool in desiccators.

↓

Add 1 ml sulfuric acid

↓

Heat on hot plate until white fumes not involve

↓

Ignite at 800˚ black particle disappear

↓

Cool and add few drop of H_2SO_4 acid and heat

↓

Allow to cool & weight

↓

Calculate the % of sulfated ash

Calculate :-

% of ash= weight of ash ×100/ weight of sample

3) Melting point test

A melting point apparatus is a scientific instrument used to determine the melting point of a substance.

PROCEDURE :- First take capillary tube which is seal at one end

↓

Fill the capillary tube with the sample (4-5 mm in powder form)

↓

Tap sealed end of capillary on porous plate gently

↓

Insert this capillary tube in to a slot behind the viewfinder of a melting point apparatus

↓

Turn on the apparatus and adjust the setting to an appropriate heating rate (the rate of heating is often experimental)

↓

Note the result

4) HPLC ASSAY

this is done by comparing the chromatogram with the reference peak.

Discrepancies between the expected and experimental chromatograms may indicate sources of impurity within the lot.

AIM :-To identify and check the impurity of the drug in HPLC

Analyte :-flucanozole usp

chromatographic conditions :-

Wavelength – 260 nm

Column – L1(4.6-mm×15-cm)3.5µm

Flow rate – 0.5ml/min

Temp. of column - 40˚

Injection volume –20µl

Process :-

sample preparation :- 30 mg of fluconazole dilute with mobaile phase.

mobile phase – mixture of water and acetonitrile

standard – USP fluconazole RS,

USP fluconazole related compound A RS

USP fluconazole related compound B RS

USP fluconazole related compound C RS

Run the assay

Compare result to the standard

Analyte :- ornidazole

chromatographic conditions :-

Wavelength – 315 nm

Column – c18(4.6-mm×125-cm)5µm

Flow rate – 1.0 ml/min

Temp. of column - 40˚

Injection volume –10µl

Process :-

sample preparation :- 30 mg of fluconazole dilute with mobaile phase.

mobile phase – buffer:acetonitrite

buffer : dissolve 1.0 ml T.E.A 500 ml of distilled water adjust to ph 3.15 with orthophoshoic acid .

Run the assay

Compare result to the standard

5) IR ASSAY

Infrared spectroscopy is a method for determination and identification of pharmaceutical compounds and functional groups within molecules.

Drug-excipients interaction play a vital role in the release of drug from formulation.

FTIR (Fourier transform infrared spectroscopy) has been used to study the physical and chemical interaction between drug and excipient.

PROCEDURE :-

Place sample in FTIR Spectrometer(As small as 10 microns can be evaluated)

The spectrometer directs beams of IR at the sample and measures how much of the beam and at which frequencies the sample absorbs the infrared light .

The reference database houses thousands of spectra , so sample can be identified.

The molecular identities can be determine through this process.

6) THIN LAYER CHROMATOGHRPHY

Thin- layer chromatography is a “solid- liquid adsorption” chromatography. In this method stationary phase is a solid adsorbent substance

In this method , the mobile phase travels upward through the stationary phase.

Every drug has their diff rent flow rates thus separation of analytes is achieved.

RF value is use for identification of API

PROCEDURE:-

Prepare solvent system according to the test sample

Load the sample with the help of capillary on TLC paper and allow to dry

Put that TLC paper in solvent system

When maximum level of solvent is reached the plat are remove and Allow to air dry

And observe TLC paper on UV cabinet and calculate Rf value

7) PH TSTING

test performed to determine the acidity of drug using potentiometer

PROCESS:-

Turn on PH meter , clean your electrode , prepare your buffers for the calibrating PH meter and set the PH

Rinse your electrode with distilled water

Place electrode in the appropriate buffer for respected sample , press the measure button and leave the electrode in sample for approx 1-2 minutes

Once the reading has stabilize , press the measure button

And that was the PH of the sample

CHAPTER –:4 RESULTS

Name of drug :- Tizanidine Hydrochloride

Testing Item	Standard	Result
Appearance	off white or light yellow powder	Complies
Solubility	Soluble in water and methanol	Complies
Melting Point	285˚c to 290˚c	288.2˚c
PH	3.5 to 5.0	4.3
Loss Of Drying	Not more than 0.5 %	0.02%

TABLE NO:-4.1 RESULT TIZANIDINE HYDROCHLORIDE

Name of drug :- Ornidazole

Testing item	Standard	Result
appearance	white or white yellowish crystalline powder	Complies
Solubility	Soluble in Chloroform	Complies
Melting point	85°C to 90°C	89.4°C
pH	4.3 to 5.2	4.7
loss of drying	Not more than 0.5%	0.03%
Sulphated Ash	NMT 0.1%	0.05%

TABLE NO:-4.2 RESULT ORNIDAZOLE

Name of drug :- Fluconazole

Testing item	Standard	Result
Appearance	white crystalline powder	Complies
Solubility	Soluble in methanol ,alcohol acetone and slightly soluble in water	Complies
Melting point	138˚c to 140˚c	138.8˚c
PH	4.5 to 5.3	4.9
loss of drying	Note more than 0.5 %	0.04%

TABLE NO:-4.3 RESULT FIUCONAZOLE

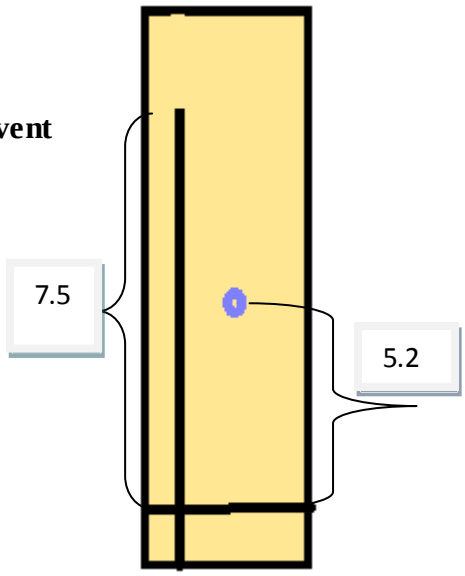
TLC Result

- **ORNIDAZOL**

Solvent system:- Chloroform : aceton (8:2)

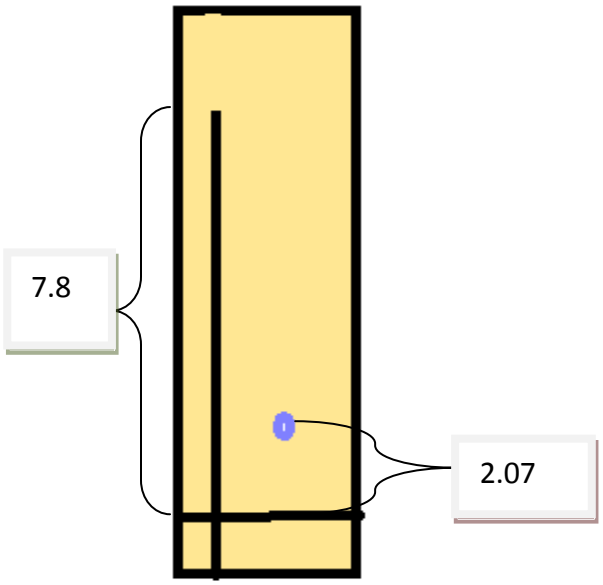
- **Rf = distance by analyte from origin/distance move by solvent front form origin So,..**
- **Rf=5.29/7.5**

  =0.70



- **Fluconazol**

- **Solvent system:- chloroform:methanol:ammoniahydroxide(80:20:1)**



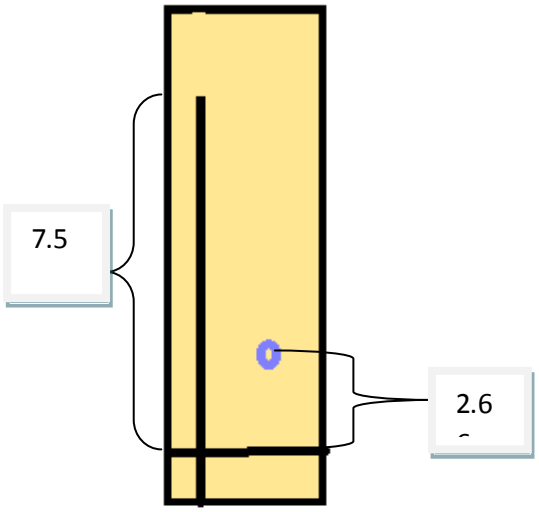
- **Rf= 2.07/7.8**

  = 0.26

Tizanidine hydrocloride

- **Solvent system:- Toluene:acetone:ammonia(40:20:1)**
- **Rf =2.66/7.5**

  =0.32



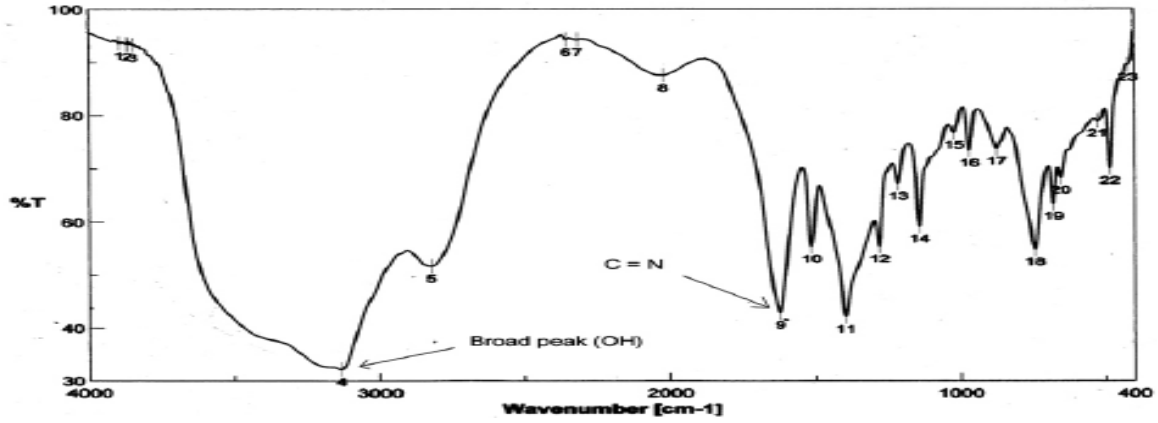


FIGURE :- 4.1 FTIR SPECTRUM OF FLUCONAZOL

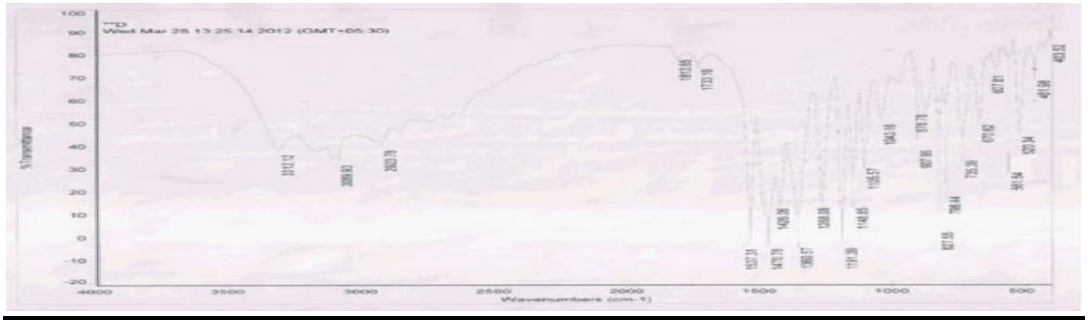


FIGURE :- 4.2 FTIR SPECTRUM OF ORNIDAZOLE

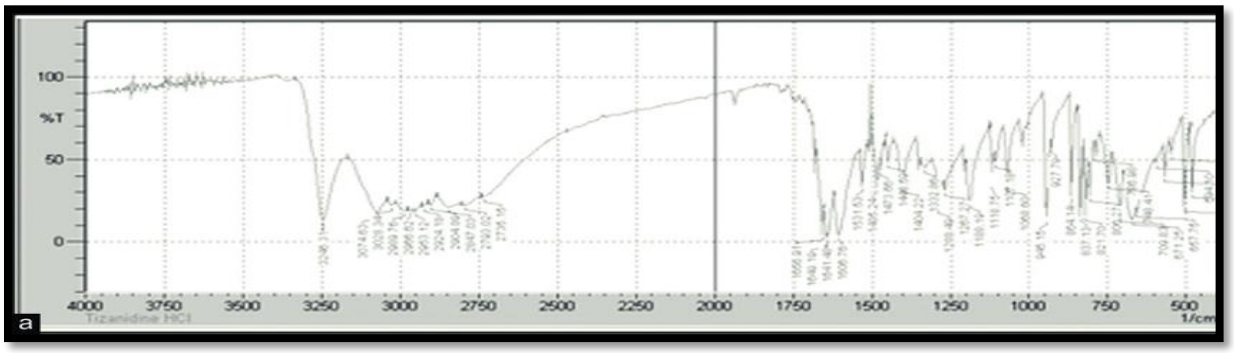


FIGURE :- 4.3 FTIR SPECTRUM OF TIZANIDINE HYDROCHLORIDE

CONCLUSION

- After visiting ENDOC Life Care Pvt. Ltd. I found that it is one of the drugs and pharmaceutical formulations.
- The internal working environment of the firm is very conclusive and healthy. The employees are very friendly and co-operative and the overall impression of the firm is brilliant.
- From my training period I have observed that it has a satisfactory growth and has been successful in building its own image. The firm has observed the market from close angle and has adapted to the changing environment.
- From the present zeal to work and bright ideas, the future of the firm looks bright and is sure to come out with good results.

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