قال تعالى:

بسم الله الرحمن الرحيم

﴿ وَأَخْرِجْنِي مُخْرَجَ صِدْقٍ وَاجْعَل لِّي مِن لَّدُنكَ سُلْطَانًا نَّصِيرًا ﴾

صدق الله العظيم

سورة الاسراء الآية

(80)

Dedication

To the candle of my Life my mother

To my father whome encourage me to complete this work.

To my colleagues and friends

I dedicate this work

Acknowledgements

First I thank Allah for grating me the strength to do this study.

I would like to express my immense graduate and appreciation to my wonderful supervisor ***Ustaza. Amira Anwar*** *for her help, suggestions and close supervision throughout the study.*

Finally all my thanks go to everyone who supported and helped me to accomplish this study.

Abstract

This research is aimed to study the in-use stability of paracetamol, two sample where taken one local and the other was imported. Four bottles (from the same batch) from each sample were taken and undergo the same condition, any drug in-use could be effected by . The samples undergone the same condition any drug in-use undergo such as 40°C temperature humidity 75% and 30°C temperature humidity 65% . Then the drug was analyzed for month (0time,15days, 30days). The contents of paracetamol were measured by HPLC and the result was too close during the time of study. IR spectroscopy was used to know the effect of condition of the functional group. Another device can be used such as UV\VIS spectroscopy, NMR spectroscopy and MASS spectroscopy. The changes were minor because the stability of product was high.

المستخلص :

يهدف هذا البحث لدراسة أستقرارية شراب البندول أثناء فترة الاستخدام ، أخذت عينتين للتحليل ؛ محلية ومستوردة واستخدمت أربعة زجاجات من نفس الدفعة ومن كل عينة تحت نفس الظروف. وعرضت العينات المراد تحليلها للظروف (درجة حرارة 40 درجة مئوية ، درجة حرارة 30 درجة مئوية ، ضوء شمس مباشر ، درجة حرارة 8 درجة مئوية) ثم حلل الدواء للظروف أعلاه لمدة شهر (قبل تعريضه للظروف ، بعد أسبوعين ، بعد شهر). ثم قيست تراكيز محتويات شراب البندول بجهاز HPLC ، ومن النتائج وجد أن التراكيز متقاربة خلال فترة الدراسة. استخدم جهاز IR لمعرفة تأثير الظروف على الزمر الوظيفية الموجودة بالمركب. ويمكن استخدام أجهزة أخرى للتحليل مثل جهاز VIS/UV ، NMR ، MASS Spectroscopy.

ومن دراستنا للبحث وجد أن التغيرات في التراكيز بسيطة لأن استقرارية المركب عالية جداً.

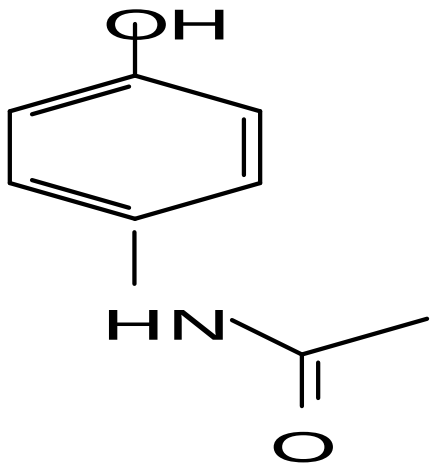
Table of Contents

List of Figures

List of Tables

Chapter one

1.1 Introduction:



paracetamol is a common analgesic and antipyretic drug that is used for the relief of fever, headaches and other minor aches and pains. Their determination in pharmaceuticals is of paramount importance, since an overdose of paracetamol can cause fulminating hepatic necrosis and other toxic effects. Many analytical methodologies have been proposed for the determination of paracetamol. The aim of the present study is to evaluate the utility of different techniques for quantification of paracetamol content in pharmaceutical formulations and biological samples [1].

1.2 Functional group:

-Amide group.

-Hydroxyl group.

-Carbonyl group.

-Benzene ring**.**

1.3 Physical properties of paracetamol:

- whitecrystalline substance melts at 170℃.

- Dissolve in alcohols well as in boiling water but is weak decay with cold water.

- The densityof paracetamol in the solid state is 1.293g\cm^3.

- Has molar mass amount of 151.165 g\mol.

- Its weakly acidic such as phenol, and the pHvalue of the aqueous solution ranging from 5.5 to 6.5[2].

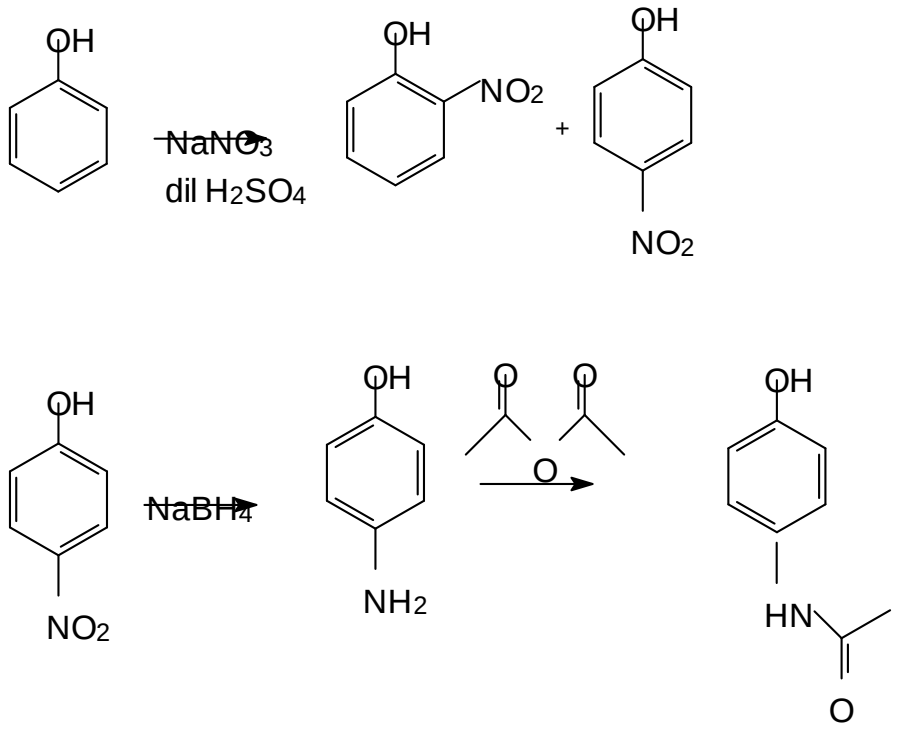
1.4chemical properties:

Paracetamol consists of a benzene ring core, substituted by one hydroxyl group and the nitrogen atom of an amide group in the *para* (1,4)pattern.[2]The amide group is acetamide(ethanamide). It is an extensively conjugated system as the lone pair on the hydroxyl oxygen, the benzene pi cloud, the nitrogen lone pair, the p orbital on the carbonyl carbon, and the lone pair on the carbonyl oxygen are all conjugated. The presence of two activating groups also make the benzene ring highly reactive toward electrophilic aromatic substitution. As the substituentsare *ortho, para*-directing and *para* with respect to each other, all positions on the ring are more or less equally activated. The conjugation also greatly reduces the basicity of the oxygens and the nitrogen, while making the hydroxyl acidic throughDelocalisation of charge developed on the phenoxide anion

1.5Synthesis:

1.5.1 Original method:

The original method for production involves the nitration of phenol with sodium nitrate gives a mixture of two isomers, from which the wanted 4-nitrophenol(bp 279 °C) can easily be separated by steam distillation. In this electrophilic substitutionreaction, phenol's oxygen is strongly activating, thus the reaction requires only mild to an amine, giving 4-aminophenol. Finally, the amine is acetylated with acetic anhydride.[3] Industrially direct hydrogenation is used, but in the laboratory scale sodium borohydride serves.[4][5]



1.6Note for guidance on in-use stability testing of human medicinal product:

The continued integrity of products in multidose containers after the first opening is an important quality issue. While this principle is acknowledged in the Ph. Eur. and EU. Guidelines, no specific guidance is available on defining test design and conduct of studies to be

undertaken to define in-use shelf life in a uniform fashion. Therefore, this document attempts to define a framework for selection of batches, test design, test storage conditions. Test parameters, test procedures etc., taking into consideration the broad range of product concerned. Nevertheless should this Note for guidance also be read in connection with notes for guidance on development pharmaceutics(CPMP/QWP/155/96), stability testing of existing active substances and related finished products(CPMP/QWP/556/96) and stability testing of new drug substances and product (CPMP/ICH/2736/99). Registration dossier for amulti-dose product should include either the in-use stability data on which the in-use shelf life is based or a justification why no in-use shelf life is established this justification can also be based on experimental results

1.6.1objective:

The purpose of in-use stability testing establish-where applicable- a period of time during which a multidose product can be used whilst retaining quality within an accepted specification once the container is opened.

1.6.2 scope:

This guideline refers to medicinal product in multidose containers which-by nature of their physical form and chemical composition-due to repeated opening and closing,may pose a risk to its content with regard to microbiological contamination, proliferation and/or physic-chemical degradation once the closure system Paula, Peter Atkins, Julio de

(2009). *Elements of physical chemistry* (5th ed.). Oxford: Oxford U.P. p. 459has been breached.

1.6.3Selection of batches:

A minimum of two batches, least pilot scale batches, should be subjected to the test. At least one of the batches should be chosen towards the end of it shelf life. If such results are not available, one batch should be tested at the final point of the submitted stability studies.The batch number, date of manufacture and size of each batch should be stated. The container and closure of the product and, if present, the medicinal device should be equivalent to that proposed for marketing.If the product is to be supplied in more than one container size or in different strengths, the in-use stability test should be applied to the product which presents the greatest susceptibility to change. The choice of the tested product should be justified.

1.6.4Test design:

As far as possible the test should be designed to simulate the use of the product in practice taking into consideration the filling volume of the container and any dilution/reconstitution before use. At intervalscomparable to those which occur in practice appropriate quantities should be removedby the withdrawal methods normally use and described in the product literature. Sampling should take place under normal environmental conditions of use.The appropriate physical, chemical and microbial properties of the product susceptible to change during storage should be determined over the period of the proposed in-use shelf life. If possible, testing should be performed at intermediate

time points and at the end of the proposed in-use shelf life on the final remaining amount of the product in the container.

1.6.5Test storage conditions:

The product should be stored under the conditions as recommended in the product literature (SPC and PIL) throughout the in-use stability test period.Any other storage conditions should be justified.

1.6.6Test parameters:

The appropriate physical, chemical and microbial properties of the product susceptible to change during use should be monitored. the tests used must be appropriate to individual dosage forms, however examples of parameter types which may need to be studied are given below:

Physical: colour, clarity,closure integrity, particular matter, particle size. Chemical:active substance assay(s), antimicrobial preservative and antioxidant content(s), degradation product level(s), pH.

Microbial: total viable count, sterility.

1.6.7Analytical procedures:

The analytical procedure used in the study should be described and fully validated. Stability indicating assays should be employed.

1.6.8Presentation of the results:

The results should be summarized and tabulated.If relevant, the results should be presented graphically.

1.6.9Evaluation:

Conclusions reached based on the data provided should be stated.In the case of anomalous results these should be explained.Where applicable and justified an in-use shelf life specification should be given.In-use stability data should be used to determine whether or not a declaration of an in-use shelf life and additional storage conditions are necessary.

1.6.10Labelling of the primary container:

The in-use shelf life should be stated on the label. in addition(if space allows) there should be a space for the user to write the date of opining or the "use-buy" date.

1.6.11Spc, leafet and labelling of the secondary container:

The in-use shelf life and in-use storage recommendations -if applicable – should be included in SPC, leaflet and outer carton text[6].

1.7High-performance liquid chromatography:

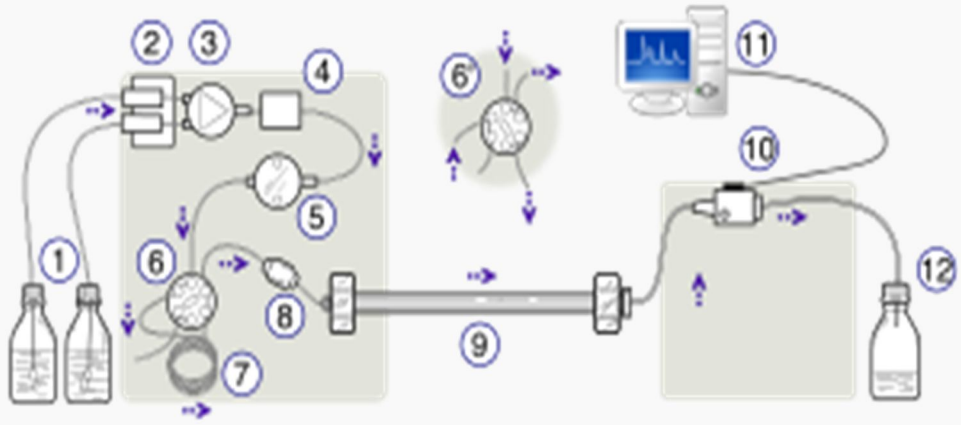
High-performance liquid chromatography

Fig 1.1: HPLC

An HPLC. From left to right: A pumping device generating a gradient of two different solvents- a steel-enforced column and a detector for measuring the absorbance.

Acronym	HPLC
Classification	Chromatography
Analytes	Organicgmolecules biomolecules ions polymers

Fig 1.2:A modern self-contained HPLC.



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

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

HPLC has been used for manufacturing (e.g. during the production process of pharmaceutical and biological products), 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 medical (e.g. detecting vitamin D levels in blood serum) purposes [7].

Chromatography can be described as a mass transfer process involving adsorption. HPLC relies on pumps to pass a pressurized liquid and a sample mixture through a column filled with adsorbent, leading to the separation of the sample components. The active component of the column, the adsorbent, is typically a granular material made of solid particles (e.g. silica, polymers, etc.), 2–50 micrometers in size. The components of the sample mixture are separated from each other due to their different degrees of interaction with the absorbent particles. The pressurized liquid is typically a mixture of solvents (e.g. water, acetonitrile and/or methanol) and is referred to as a "mobile phase". Its composition and temperature play a major role in the separation process by influencing the interactions taking place between sample components and adsorbent. These interactions are physical in nature, such as hydrophobic (dispersive), dipole–dipole and ionic, most often a combination.

HPLC is distinguished from traditional ("low pressure") liquid chromatography because operational pressures are significantly higher (50–350 bar), while ordinary liquid chromatography typically relies on the force of gravity to pass the mobile phase through the column. Due to the small sample amount separated in analytical HPLC, typical column dimensions are 2.1–4.6 mm diameter, and 30–250 mm length. Also HPLC columns are made with smaller sorbent particles (2–50 micrometer

in average particle size). This gives HPLC superior resolving power (the ability to distinguish between compounds) when separating mixtures, which makes it a popular chromatographic technique.The schematic of an HPLC instrument typically includes a sampler, pumps, and a detector. The sampler brings the sample mixture into the mobile phase stream which carries it into the column. The pumps deliver the desired flow and composition of the mobile phase through the column. The detector generates a signal proportional to the amount of sample component emerging from the column, hence allowing for quantitative analysis of the sample components. A digital microprocessor and user software control the HPLC instrument and provide data analysis. Some models of mechanical pumps in a HPLC instrument can mix multiple solvents together in ratios changing in time, generating a composition gradient in the mobile phase. Various detectors are in common use, such as UV/Vis,photodiode array (PDA) or based on mass spectrometry. Most HPLC instruments also have a column oven that allows for adjusting the temperature at which the separation is performed.

1.8Infrared spectroscopy:

Fig 1.3 Infrared

Infrared spectroscopy (IR spectroscopy or Vibrational 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. It covers a range of techniques, mostly based on absorption spectroscopy. As with all spectroscopic techniques, it

can be used to identify and study chemicals. For a given sample which may be solid, liquid, or gaseous, the method or technique of infrared spectroscopy uses an instrument called an infrared spectrometer (or spectrophotometer) to produce an infrared spectrum. A basic IR spectrum is essentially a graph of infrared light absorbance (ortransmittance) on the vertical axis vs. frequency or wavelength on the horizontal axis. Typical units of frequency used in IR spectra are reciprocalcentimeters (sometimes calledwave numbers), with the symbol cm^{-1}. Units of IR wavelength are commonly given in micrometers (formerly called "microns"), symbol μm, which are related to wave numbers in areciprocal way. A common laboratory instrument that uses this technique is a Fourier transform infrared (FTIR) spectrometer. Two-dimensional IR is also possible as discussedbelow.

The infrared portion of the electromagnetic spectrum is usually divided into three regions; the near-, mid- and far- infrared, named for their relation to the visible spectrum. The higher-energy near-IR, approximately 14000–4000 cm^{-1} (0.8–2.5 μm wavelength) can excite overtone or harmonic vibrations. The mid-infrared, approximately 4000–400 cm^{-1}(2.5–25 μm) may be used to study the fundamental vibrations and associated rotational-vibrational structure. The far-infrared, approximately 400–10 cm^{-1} (25–1000 μm), lying adjacent to the microwave region, has low energy and may be used for rotational spectroscopy. The names and classifications of these subregions are conventions, and are only loosely based on the relative molecular or electromagnetic properties[8].

Chapter two

2.1 Sample:

A- Local product (Light orange colored liquid).

B- Imported product (Light Pink colored liquid).

2.1.1 Sample conditions:

1= At 8 ^{o}C temperature .

2= At 40 ^{o}C temperature .

3= At 30 ^{o}C temperature .

4= Sunlight .

2.2 Instrument:

- pH meter

-HPLC

-IR

2.3 method of HPLC :

Analytical specification and test methods for finished product:

2.3.1Procedure:

-weight an amount equivalent to the weight in one bottle.

-measure the pH reading of the resulting solution and record it in the laboratory notebook.

2.3.2Weight per ml:

Weight the empty 25 ml of dried specific gravity bottle.tare.add solution up to the mark.

Weight the filled specific gravity bottle.D=wt/ml

D=weight (g)/volum (ml) =g/ml.

2.3.3Assay:

Between 95.0% to 105.0% of stated dose.

2.3.4Standard preparation:

Take 0.125gms paracetamol in 250 ml volumetric flask.Dissolve and make the volume with mobile phase.

2.3.5 Sample preparation:

Take weight quantity of 5.00 ml of sample in 250 ml volumetric flask.Sonicate for 10 min with mobile phase. Filter through

2.4 Method of IR:

One drop of sample was placed in kbr dish then pressed by another dish until it become a flat surface between the disk, the cell was placed in the IR device.

2.5Calculation:

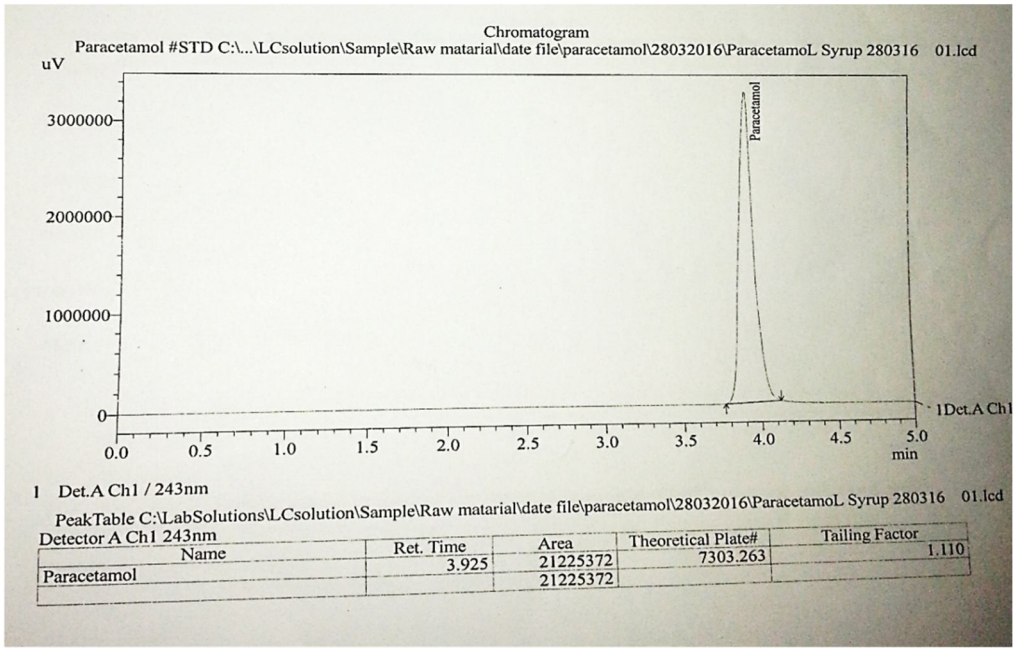
Peak area of sample× weight of standard× 250×5× weight per ml×potency/peak area of standard×250×weight of sample×0.1250 = % of stated dose[9].

HPLC Spectrum:

0 time

STD of Paracetamol:

Fig 2.1



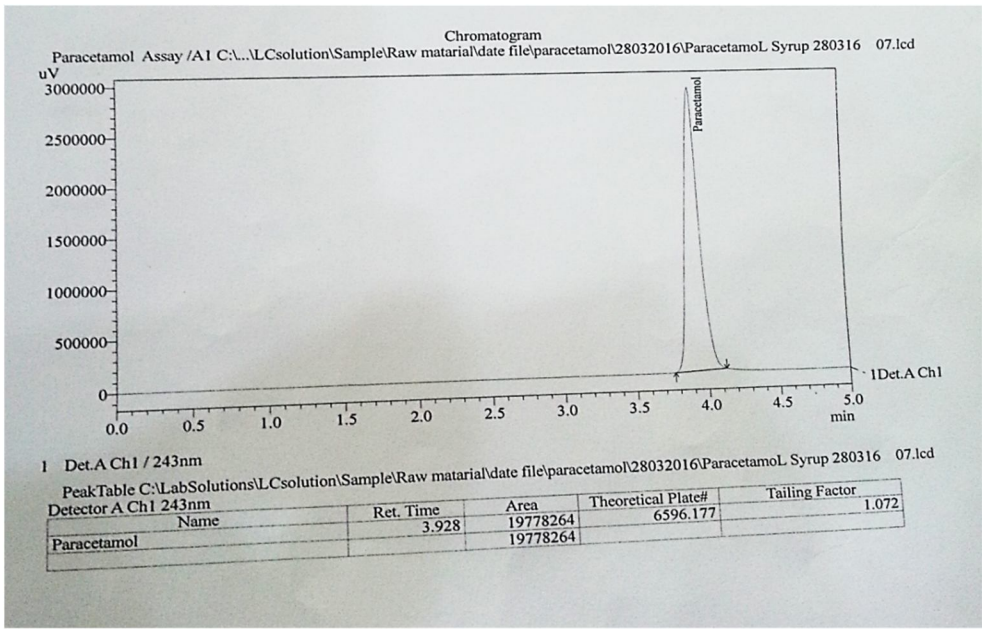
1 Det.A Ch1 / 243nm

PeakTable C:\LabSolutions\LCsolution\Sample\Raw matarial\date file\paracetamol\28032016\ParacetamoL Syrup 280316 01.lcd

Detector A Ch1 243nm

Name	Ret. Time	Area	Theoretical Plate#	Tailing Factor
Paracetamol	3.925	21225372	7303.263	1.110
		21225372		

Fig 2.2: A_1



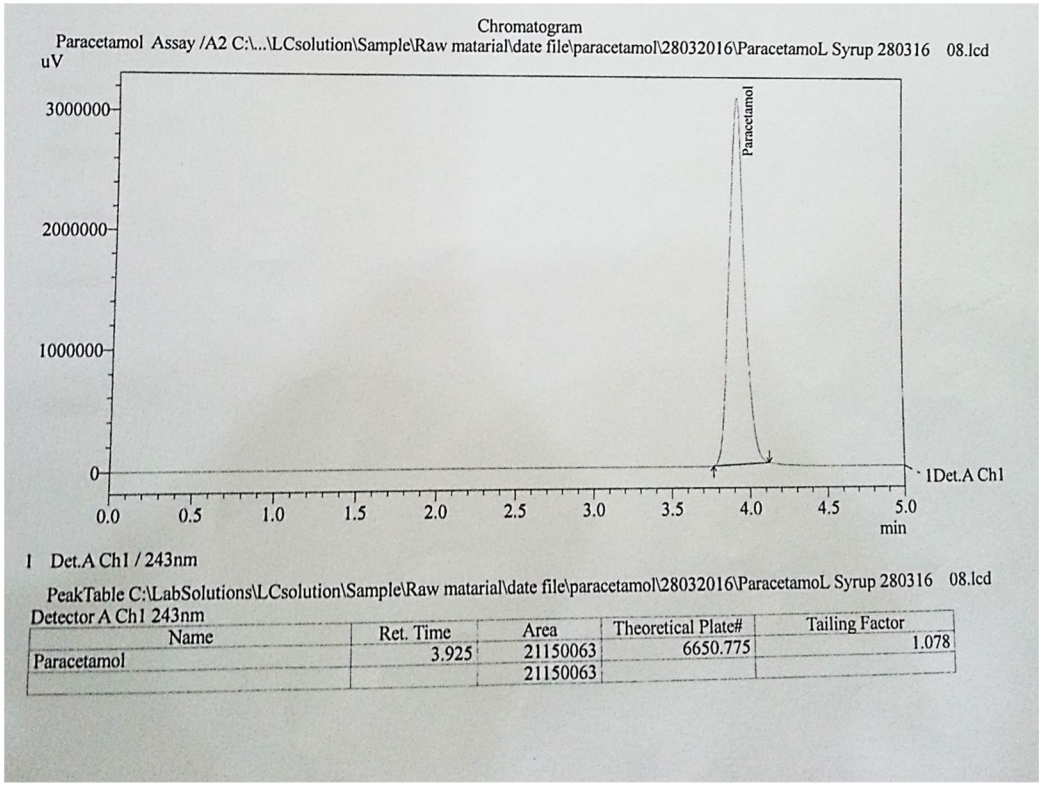
1 Det.A Ch1 / 243nm

PeakTable C:\LabSolutions\LCsolution\Sample\Raw matarial\date file\paracetamol\28032016\ParacetamoL Syrup 280316 07.lcd

Detector A Ch1 243nm

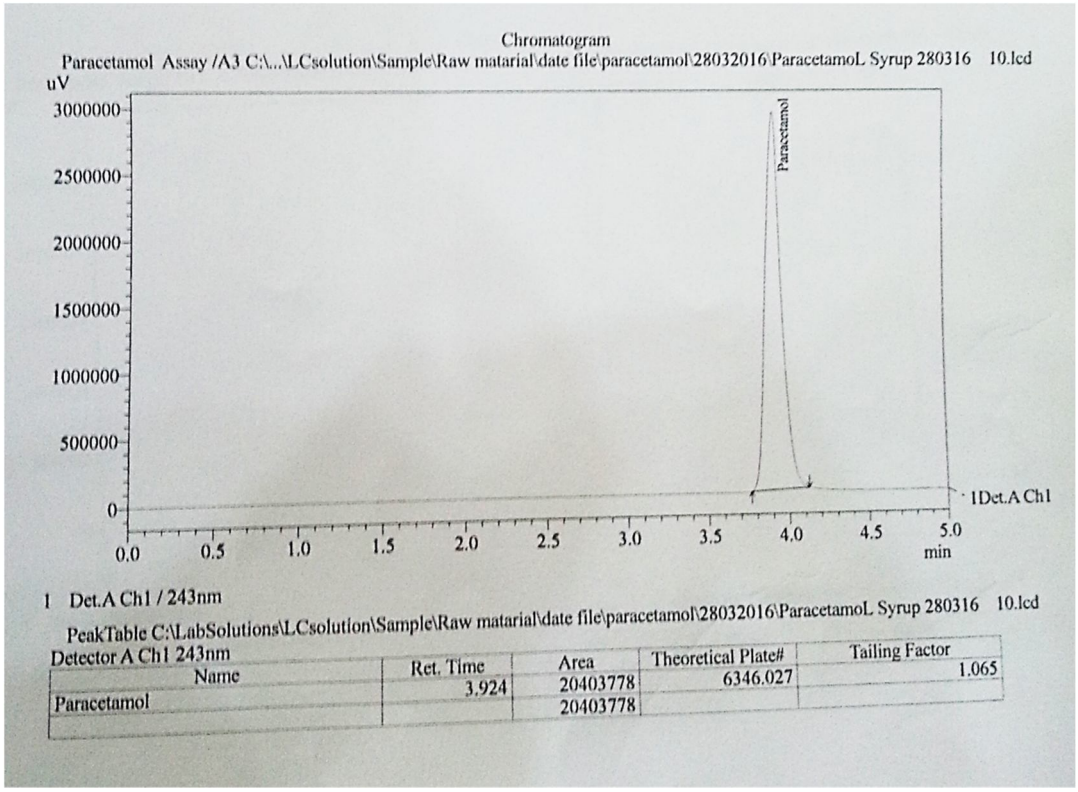
Name	Ret. Time	Area	Theoretical Plate#	Tailing Factor
Paracetamol	3.928	19778264	6596.177	1.072
		19778264		

Fig 2.3 : A_2



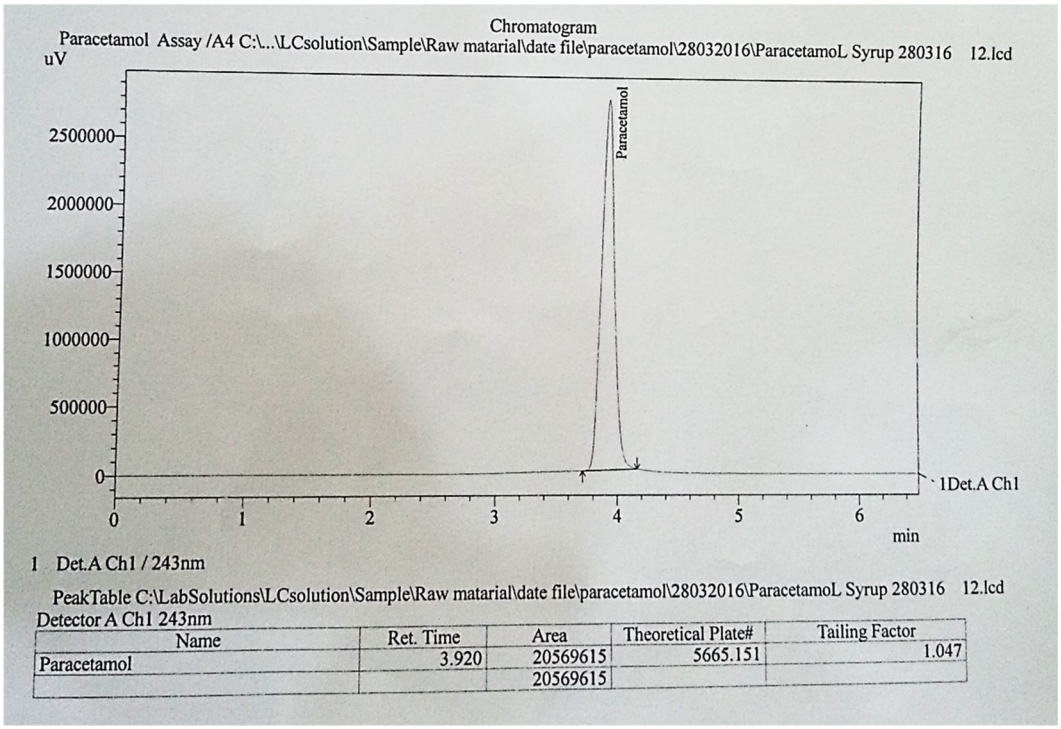
Name	Ret. Time	Area	Theoretical Plate#	Tailing Factor
Paracetamol	3.925	21150063	6650.775	1.078
		21150063		

Fig 2.4 : A_3



Name	Ret. Time	Area	Theoretical Plate#	Tailing Factor
Paracetamol	3.924	20403778	6346.027	1.065
		20403778		

Fig 2.5: A_4



1 Det.A Ch1 / 243nm

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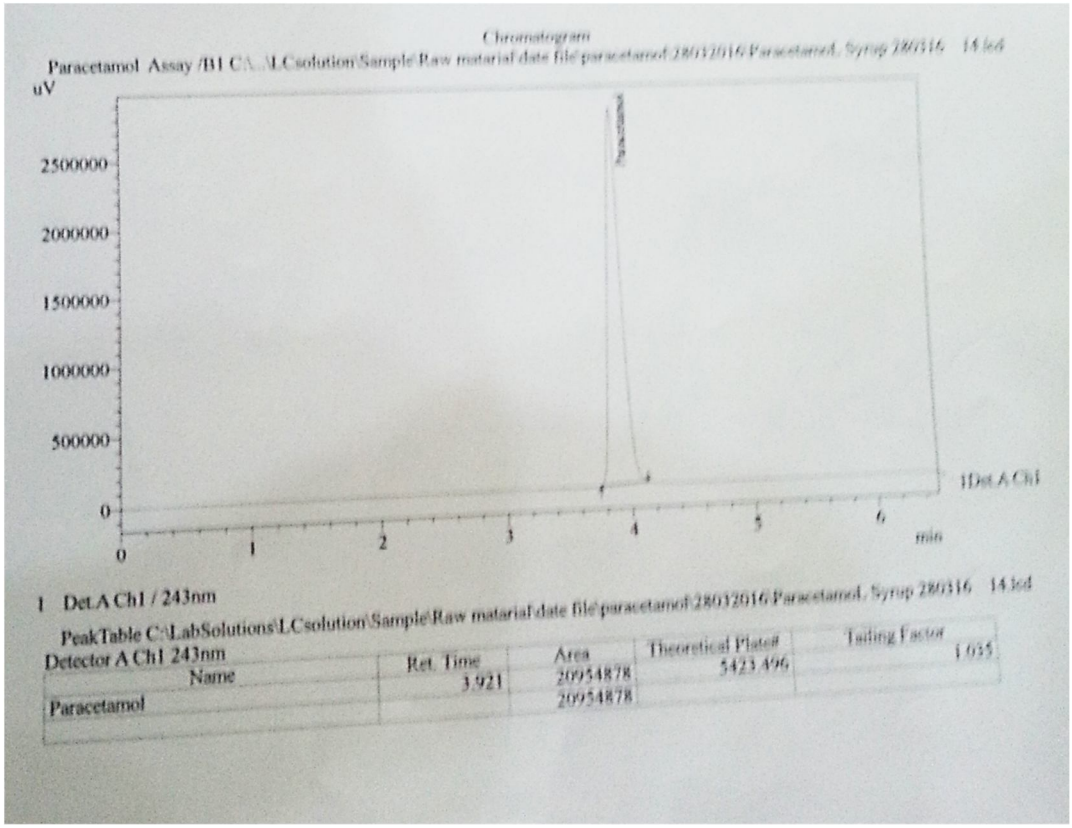
Detector A Ch1 243nm

Name	Ret. Time	Area	Theoretical Plate#	Tailing Factor
Paracetamol	3.920	20569615	5665.151	1.047
		20569615		

Fig 2.6: B_1



1 Det.A Ch1 / 243nm

PeakTable C:\LabSolutions\LCsolution\Sample\Raw matarial\date file\paracetamol\28032016\Paracetamol, Syrup 280316 14.lcd

Detector A Ch1 243nm

Name	Ret. Time	Area	Theoretical Plate#	Tailing Factor
Paracetamol	3.921	20954878	5423.496	1.035
		20954878		

Fig 2.7: B_2

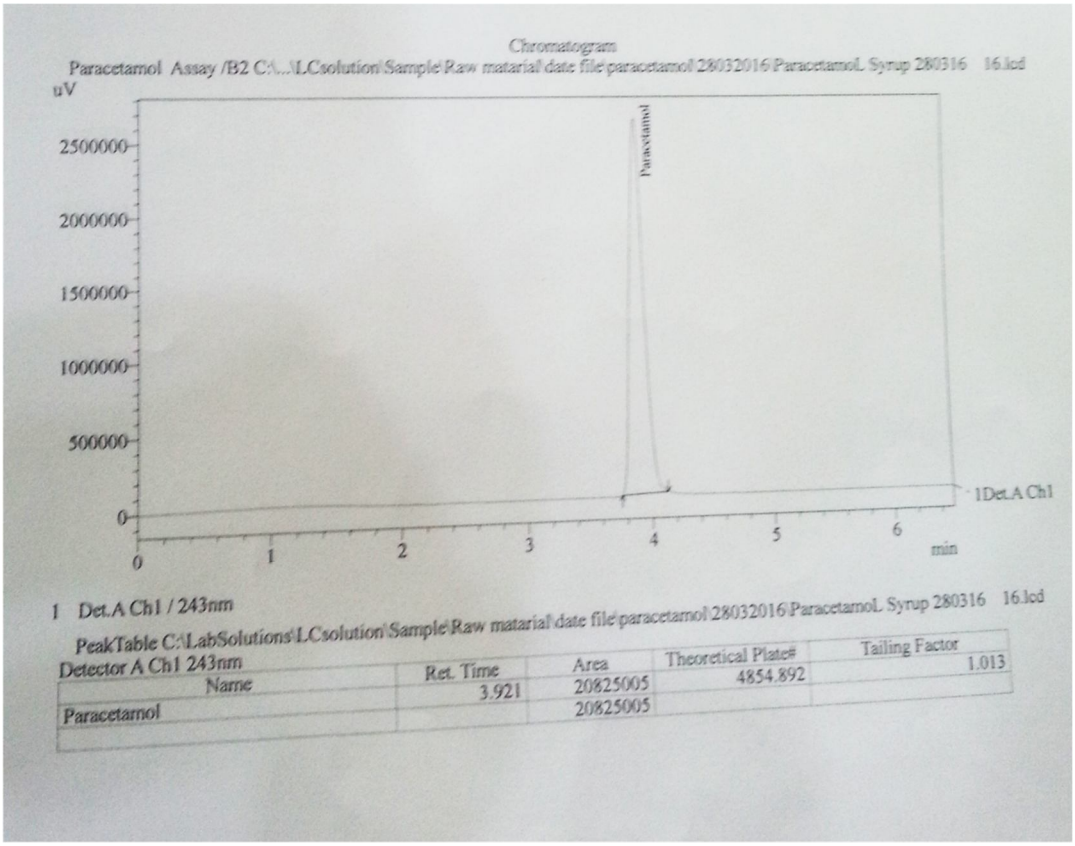


Fig 2.8: B_3

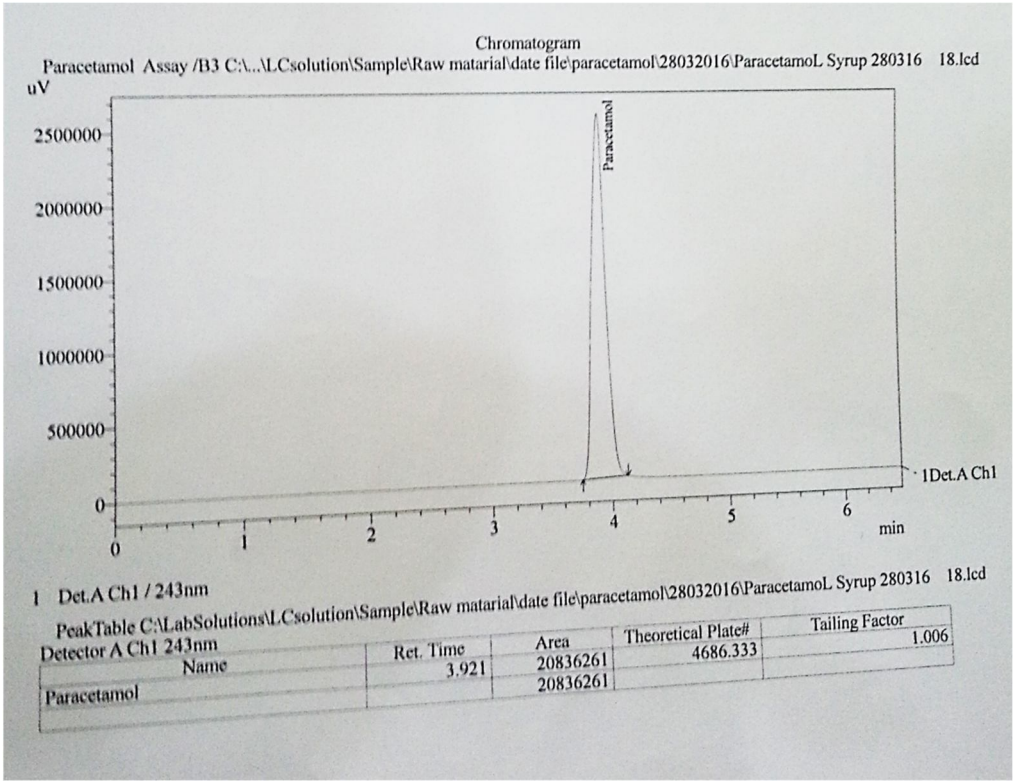
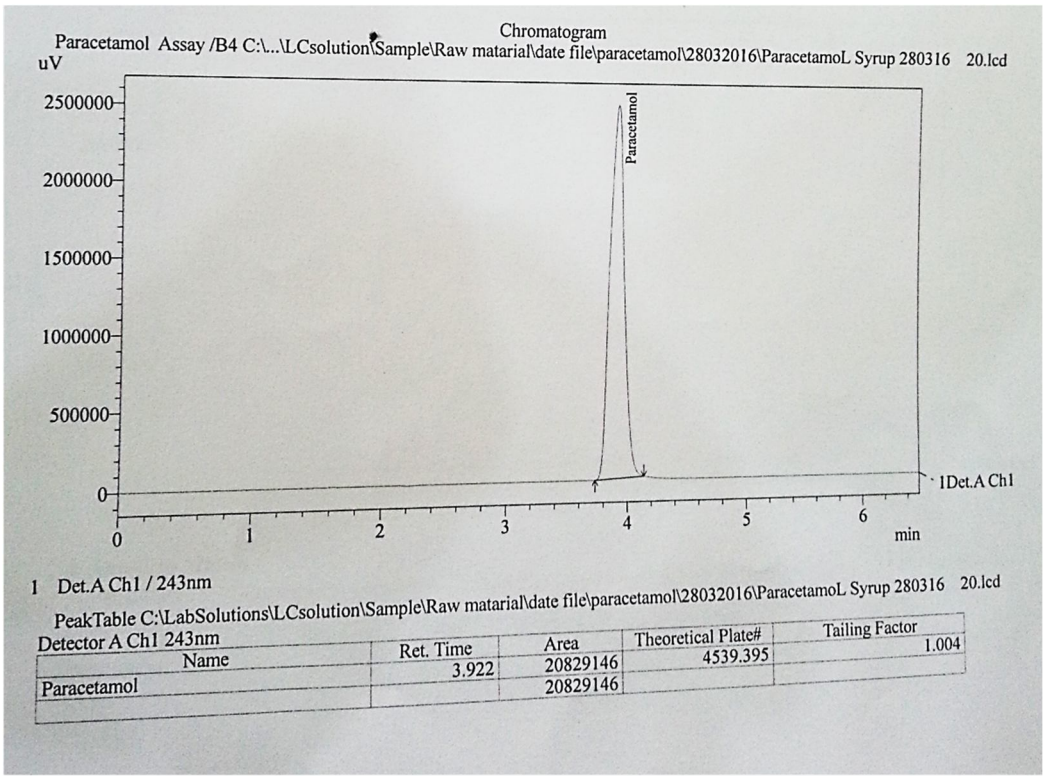


Fig 2.9: B_4



1 Det.A Ch1 / 243nm

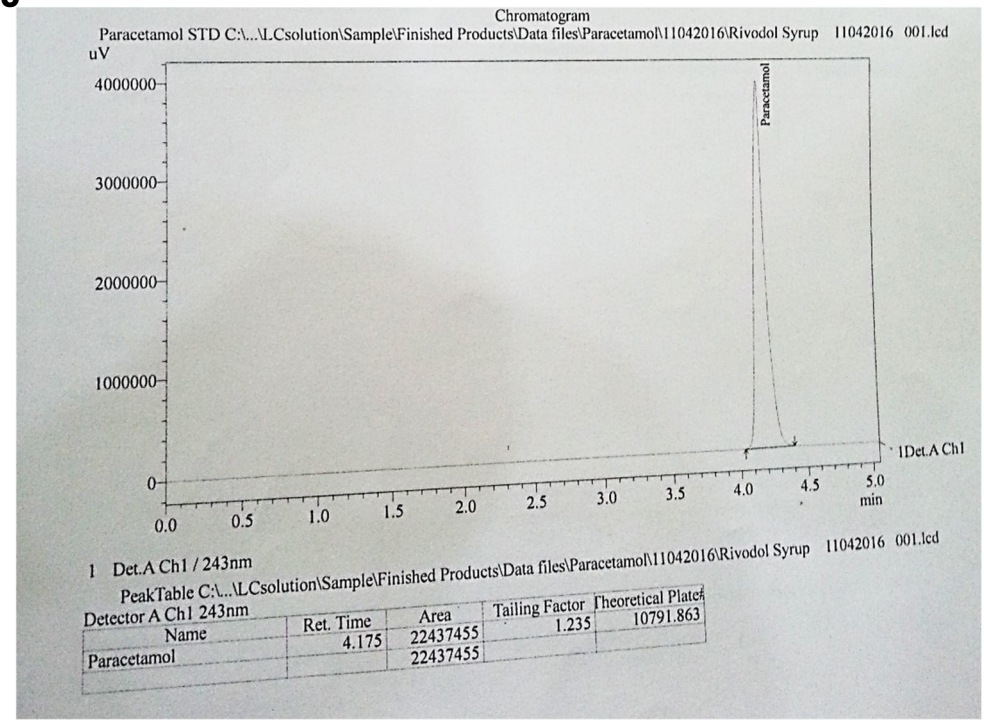
PeakTable C:\LabSolutions\LCsolution\Sample\Raw matarial\date file\paracetamol\28032016\ParacetamoL Syrup 280316 20.lcd

Detector A Ch1 243nm

Name	Ret. Time	Area	Theoretical Plate#	Tailing Factor
Paracetamol	3.922	20829146	4539.395	1.004
		20829146		

After 15 days :

Fig 2.10 : STD



1 Det.A Ch1 / 243nm

PeakTable C:\...\LCsolution\Sample\Finished Products\Data files\Paracetamol\11042016\Rivodol Syrup 11042016 001.lcd

Detector A Ch1 243nm

Name	Ret. Time	Area	Tailing Factor	Theoretical Plate#
Paracetamol	4.175	22437455	1.235	10791.863
		22437455		

Fig 2.11 : A_1

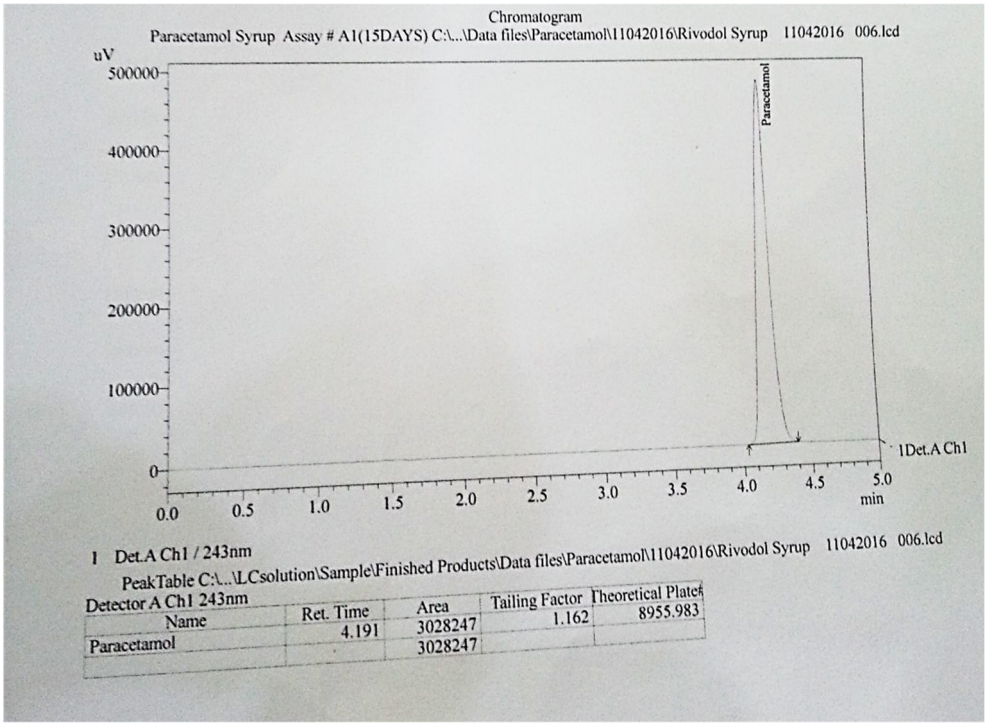


Fig 2.12 : A_2

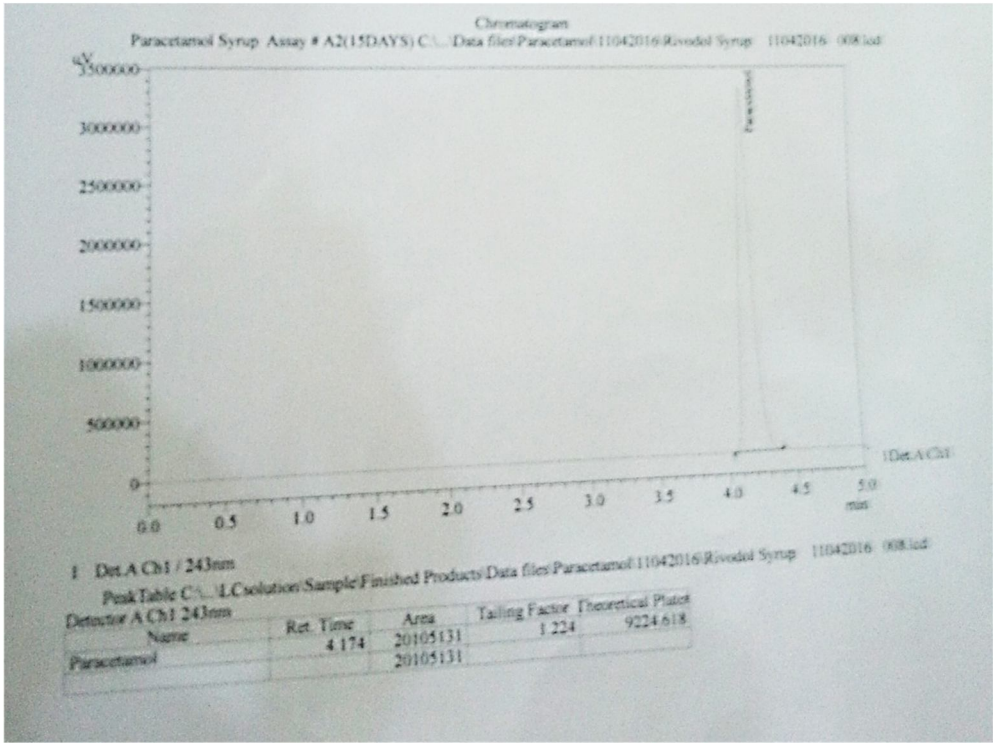


Fig 2.13 : A_3

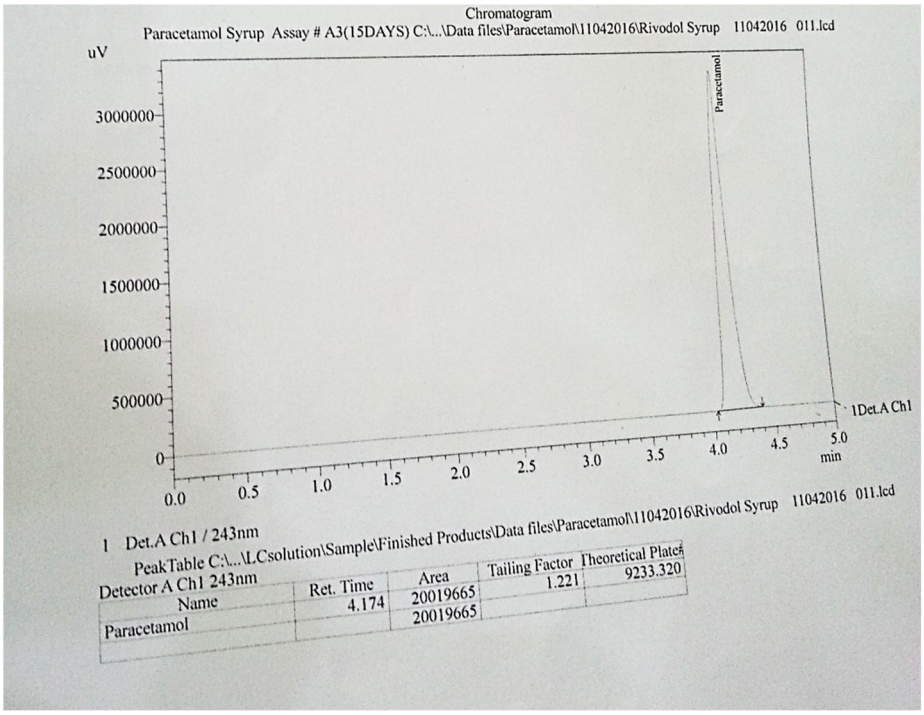


Fig 2.14 : A_4

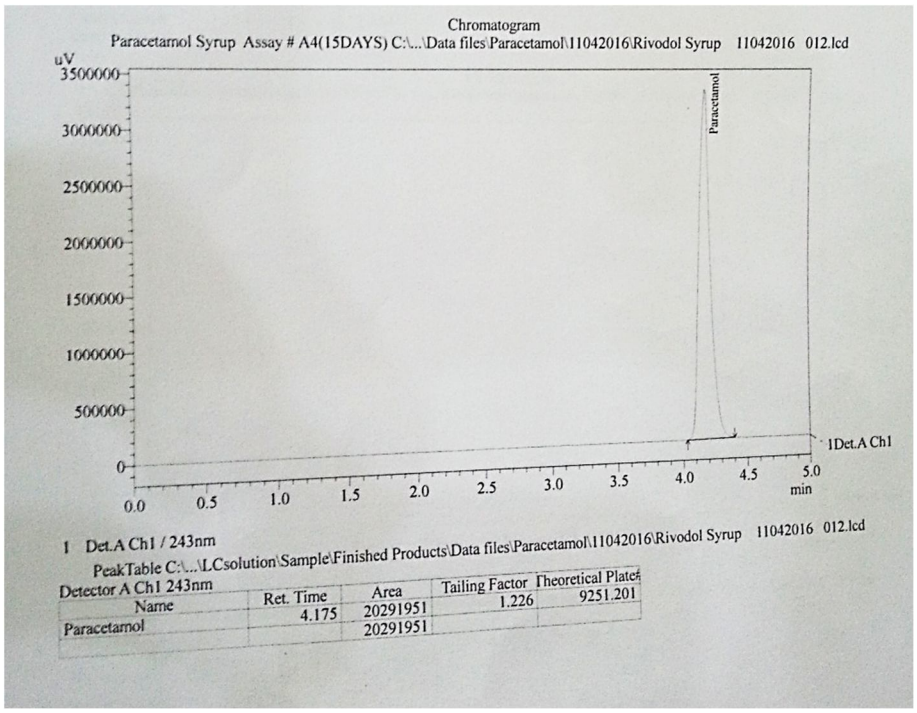


Fig 2.15 : B_1

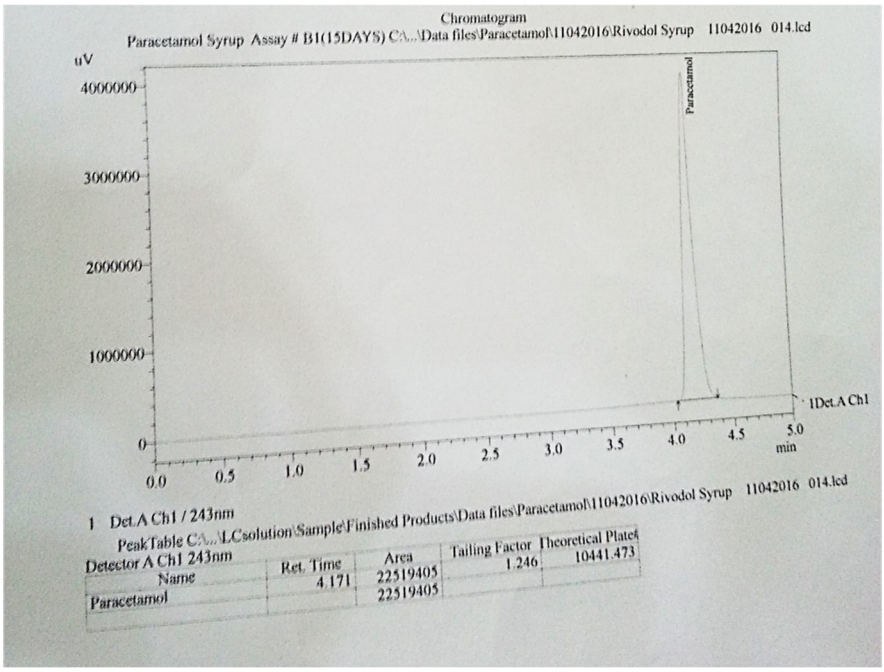


Fig 2.16 : B_2

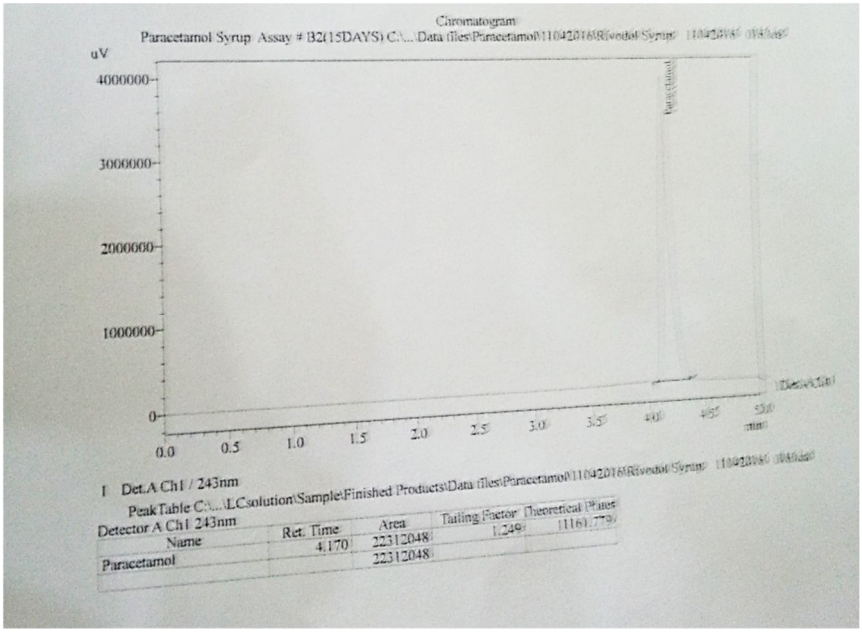


Fig 2.17 : B_3

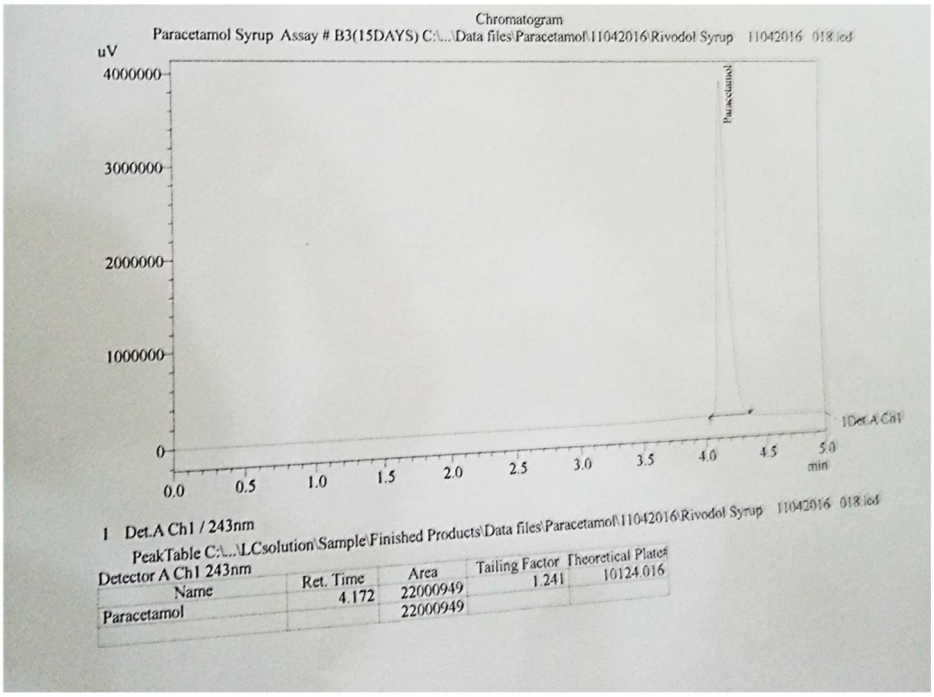
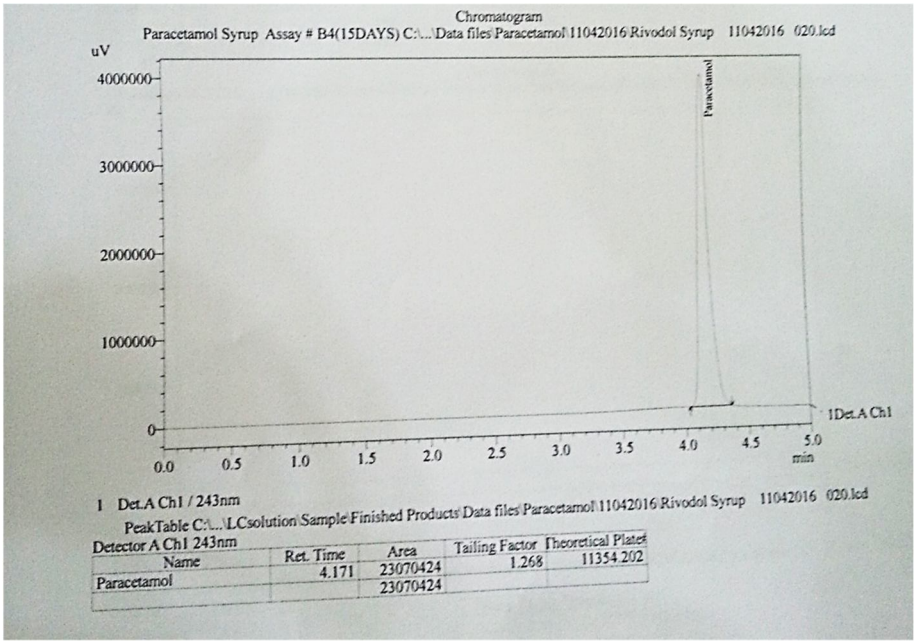
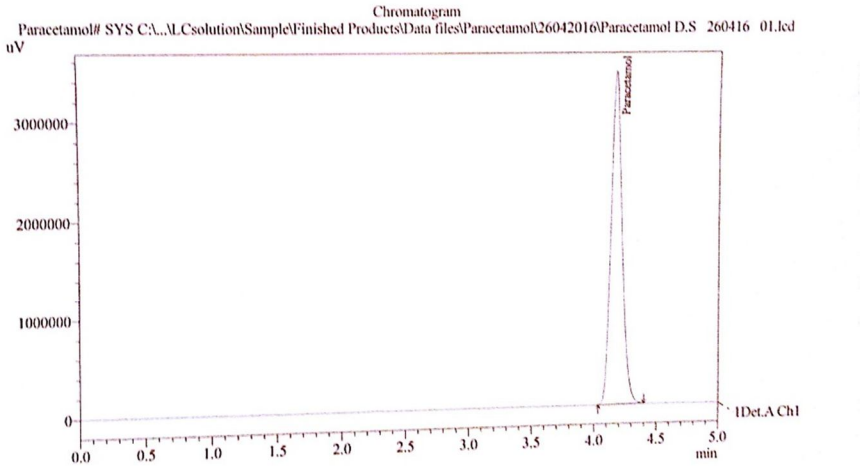


Fig 2.18 : B_4



After 30 days :

Fig 2.19 : STD



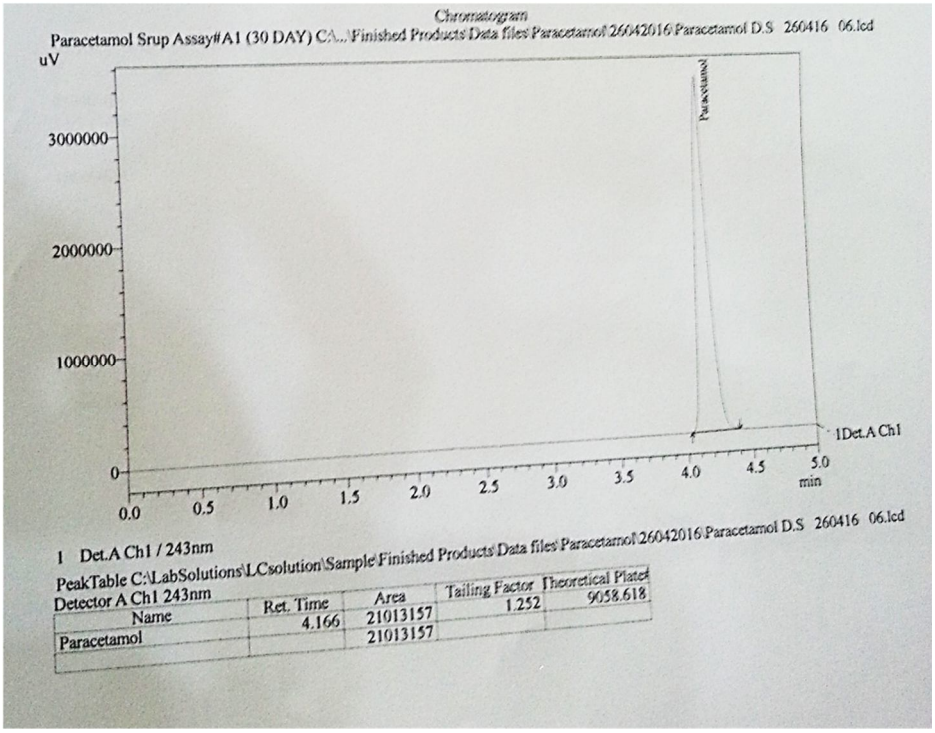
1 Det.A Ch1 / 243nm

PeakTable C:\LabSolutions\LCsolution\Sample\Finished Products\Data files\Paracetamol\26042016\Paracetamol D.S 260416 01.lcd

Detector A Ch1 243nm

Name	Ret. Time	Area	Tailing Factor	Theoretical Plates
Paracetamol	4.167	21311335	1.253	9050.483
		21311335		

Fig 2. 20 : A_1



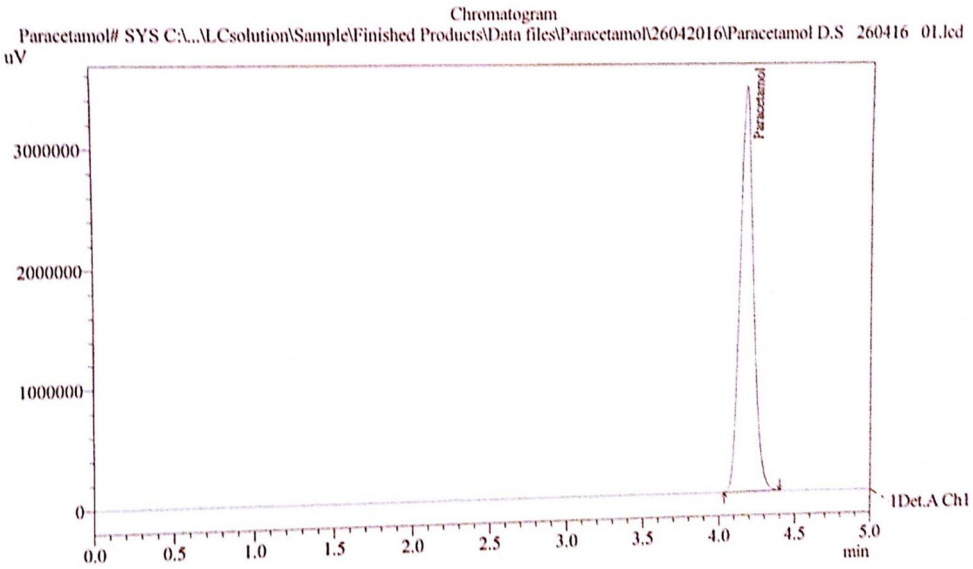
1 Det.A Ch1 / 243nm

PeakTable C:\LabSolutions\LCsolution\Sample\Finished Products\Data files\Paracetamol\26042016\Paracetamol D.S 260416 06.lcd

Detector A Ch1 243nm

Name	Ret. Time	Area	Tailing Factor	Theoretical Plates
Paracetamol	4.166	21013157	1.252	9058.618
		21013157		

Fig 2.21 : A_2



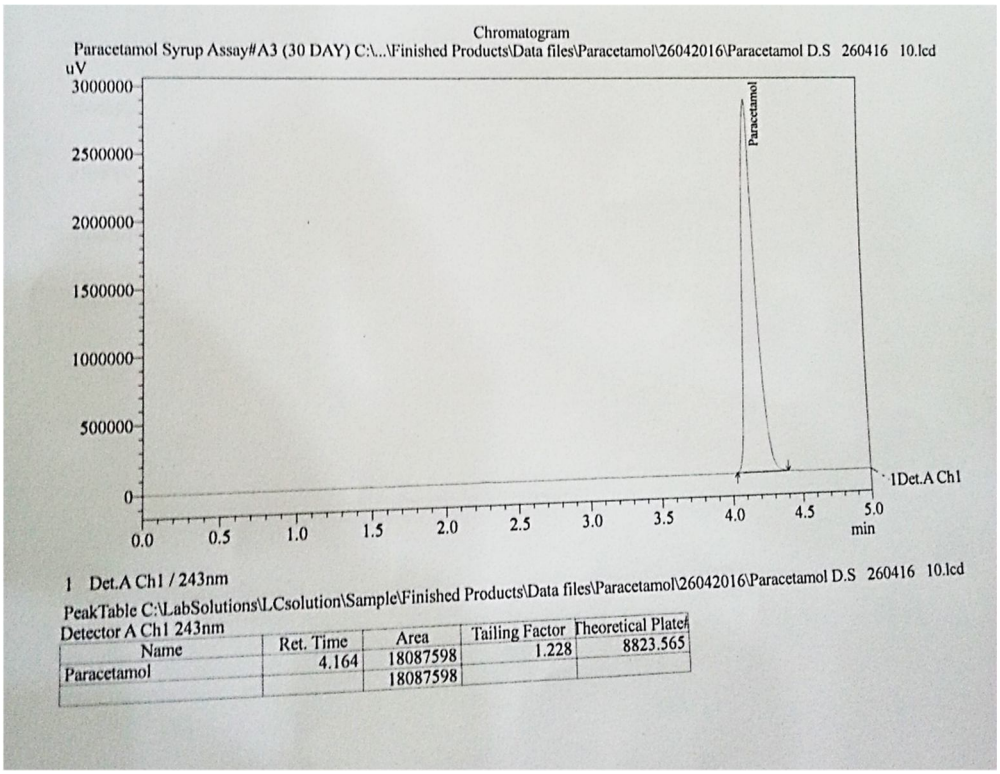
1 Det.A Ch1 / 243nm

PeakTable C:\LabSolutions\LCsolution\Sample\Finished Products\Data files\Paracetamol\26042016\Paracetamol D.S 260416 01.lcd

Detector A Ch1 243nm

Name	Ret. Time	Area	Tailing Factor	Theoretical Plate
Paracetamol	4.167	21311335	1.253	9050.483
		21311335		

Fig 2.22 : A_3



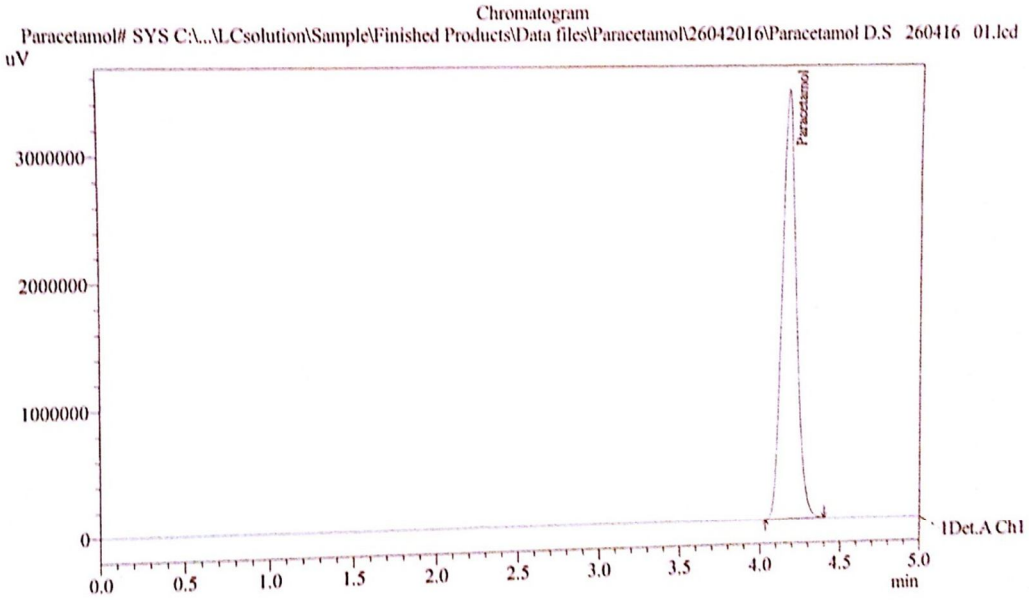
1 Det.A Ch1 / 243nm

PeakTable C:\LabSolutions\LCsolution\Sample\Finished Products\Data files\Paracetamol\26042016\Paracetamol D.S 260416 10.lcd

Detector A Ch1 243nm

Name	Ret. Time	Area	Tailing Factor	Theoretical Plate
Paracetamol	4.164	18087598	1.228	8823.565
		18087598		

Fig 2.23 : A_4



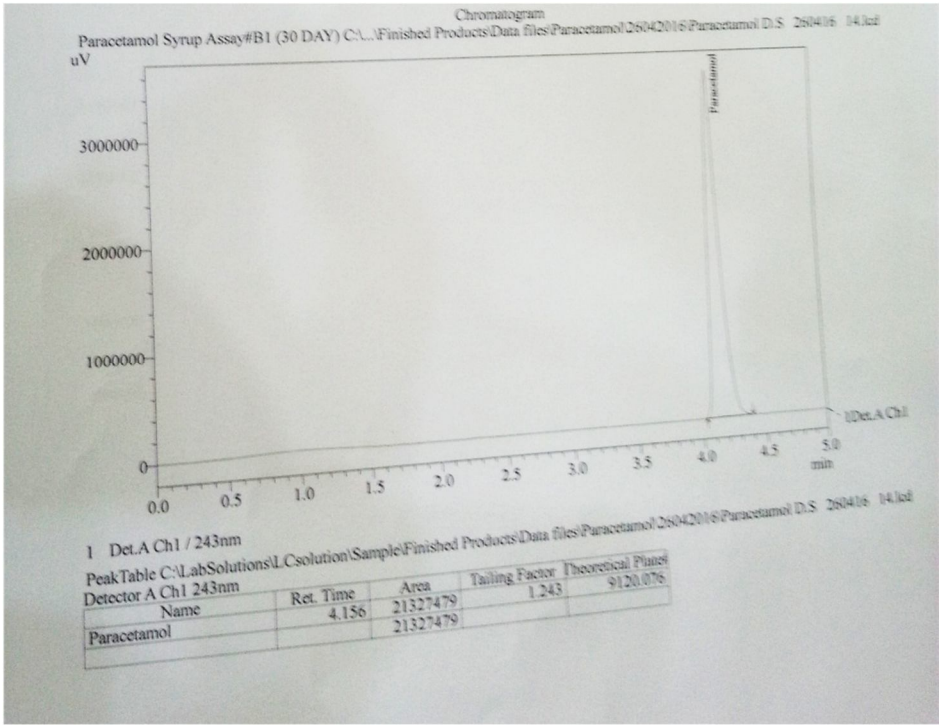
1 Det.A Ch1 / 243nm

PeakTable C:\LabSolutions\LCsolution\Sample\Finished Products\Data files\Paracetamol\26042016\Paracetamol D.S 260416 01.lcd

Detector A Ch1 243nm

Name	Ret. Time	Area	Tailing Factor	Theoretical Plate
Paracetamol	4.167	21311335	1.253	9050.483
		21311335		

Fig 2.24 : B_1



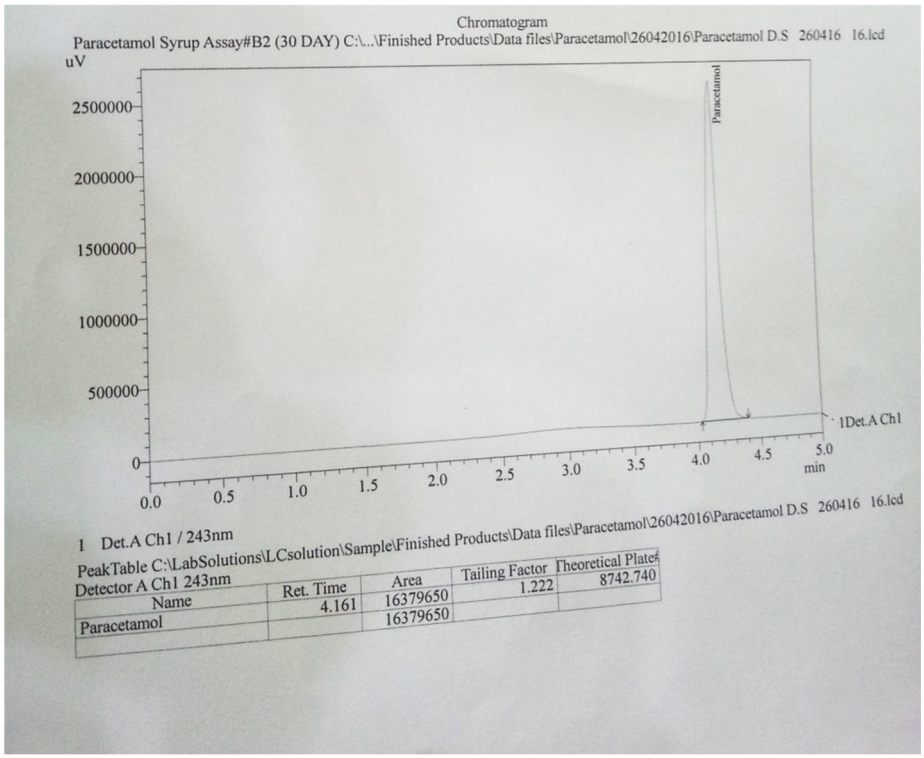
1 Det.A Ch1 / 243nm

PeakTable C:\LabSolutions\LCsolution\Sample\Finished Products\Data files\Paracetamol\26042016\Paracetamol D.S 260416 14.lcd

Detector A Ch1 243nm

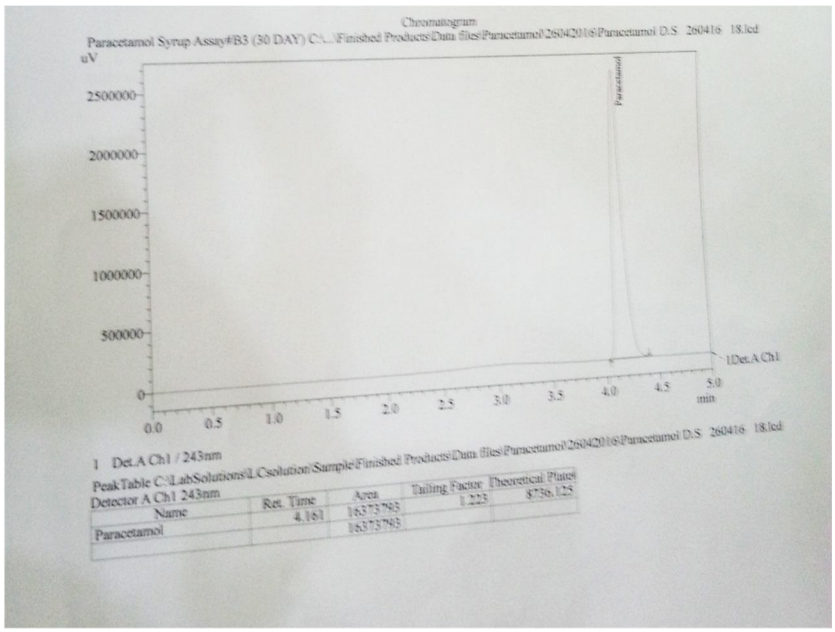
Name	Ret. Time	Area	Tailing Factor	Theoretical Plates
Paracetamol	4.156	21327479	1.243	9120.076
		21327479		

Fig 2.25 : B_2



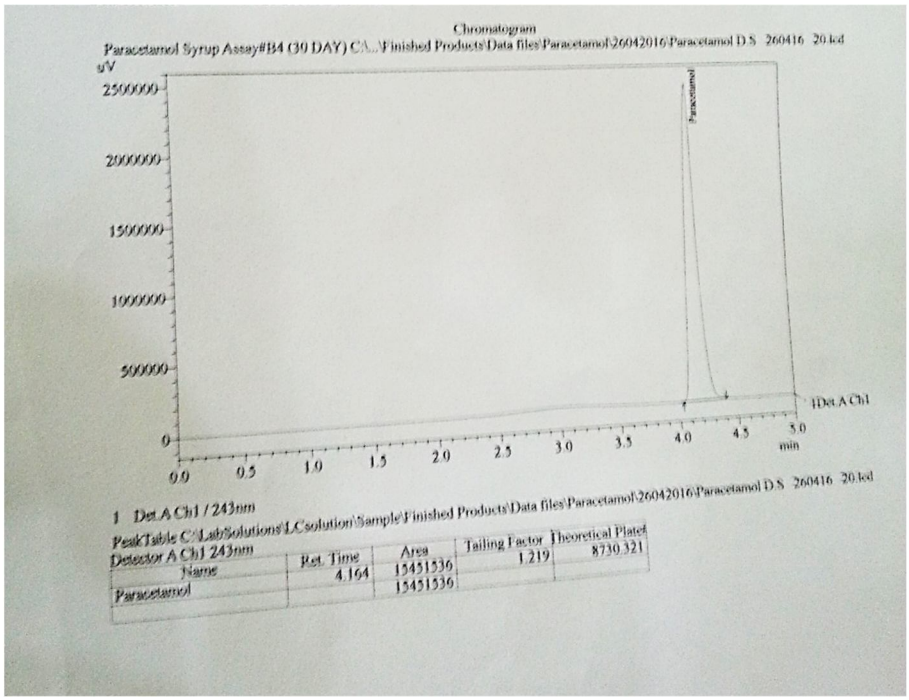
Name	Ret. Time	Area	Tailing Factor	Theoretical Plate
Paracetamol	4.161	16379650	1.222	8742.740
		16379650		

Fig 2.26: B_3



Name	Ret. Time	Area	Tailing Factor	Theoretical Plates
Paracetamol	4.161	16373785	1.225	8736.125
		16373785		

Fig 2.27 : B_4



2.5.1 Assay of paracetamol:

0 time:

$A_{1:}$

(19785550×0.1253×250×5×1.2124×99.9)÷(21138896×250×6.0083×0.125) =94.5٪

$A_{2:}$

(21128241×0.1253×250×5×1.2124×99.9)÷(21138896×250×5.9817×0.125) =101.43

$A_{3:}$

(20374942×0.1253×250×5×1.2124×99.9)÷(21138896×250×5.9885×0.125) =97.7

$A_{4:}$

(20448351×0.1253×250×5×1.2124×99.9)÷(21138896×250×5.9882×0.125) =98.06

$B_{1:}$

(20918115×0.1253×250×5×1.1199×99.9)÷(21138896×250×5.8923×0.120) =98.09

$B_{2:}$

(20792707×0.1253×250×5×1.1199×9.9)÷(21138896×250×5.8749×0.120) =97.7

$B_{3:}$

(20828649×0.1253×250×5×1.1199×99.9)÷(21138896×250×5.8931×0.120) =97.6

$B_{4:}$

(20831689×0.1253×250×5×1.1199×99.9)÷(21138896×250×5.8992×0.120) =97.5

After two weeks:

$A_{1:}$

(19017047×0.1253×250×5×1.2124×99.9)÷(22504576×250×5.8834×0.125) =87.1

$A_{2:}$

(20097232×0.1253×250×5×1.2124×99.9)÷(22504576×250×5.8427×0.125) =92.7

$A_{3:}$

(20035404×0.1253×250×5×1.2124×99.9)÷(22504576×250×5.8599×0.125) =92.2

$A_{4:}$

(20350313×0.1253×250×5×1.2124×99.9)÷(22504576×250×5.8591×0.125) =93.6

$B_{1:}$

(22639205×0.1253×250×5×1.1199×99.9)÷(22504576×250×5.8824×0.120) =99.8

$B_{2:}$

(22382299×0.1253×250×5×1.1199×99.9)÷(22504576×250×5.8558×0.120) =99.2

$B_{3:}$

(22121680×0.1253×250×5×1.1199×99.9)÷(22504576×250×5.8529×0.120) =98.0

$B_{4:}$

(22993105×0.1253×250×5×1.1199×99.9)÷(22504576×250×5.9153×0.120) =100.8

After 30 days:

$A_{1:}$

(20951883×0.1253×250×5×1.2124×99.9)÷(21419561×250×5.9823×0.125) =99.6

$A_{2:}$

(1849048×0.1258×250×5×1.2124×99.9)÷(21419561×250×5.8131×0.125) =90.5

$A_{3:}$

(18072297×0.1258×250×5×1.2124×99.9)÷(21419561×250×5.7219×0.125) =89.8

$A_{4:}$

(19401818×0.1258×250×5×1.2124×99.9)÷(21419561×250×5.6625×0.125) =97.4

$B_{1:}$

(21272509×0.1258×250×5×1.1199×99.9)÷(21419561×250×5.8821×0.120) =99.0

$B_{2:}$

(16380330×0.1258×250×5×1.1199×99.9)÷(21419561×250×5.8131×0.120) =77.1

$B_{3:}$

(16366742×0.1258×250×5×1.1199×99.9)÷(21419561×250×5.7123×0.120) =78.4

$B_{4:}$

(1542375×0.1258×250×5×1.1199×99.9)÷(21419561×250×5.6217×0.120) =75.1

Fig 2.28 : IR spectrum of B1

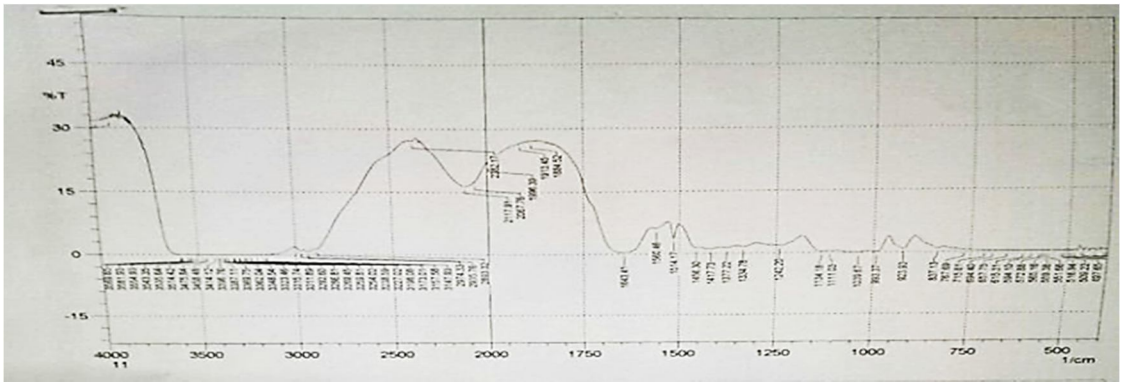


Fig 2.29 IR spectrum of A1

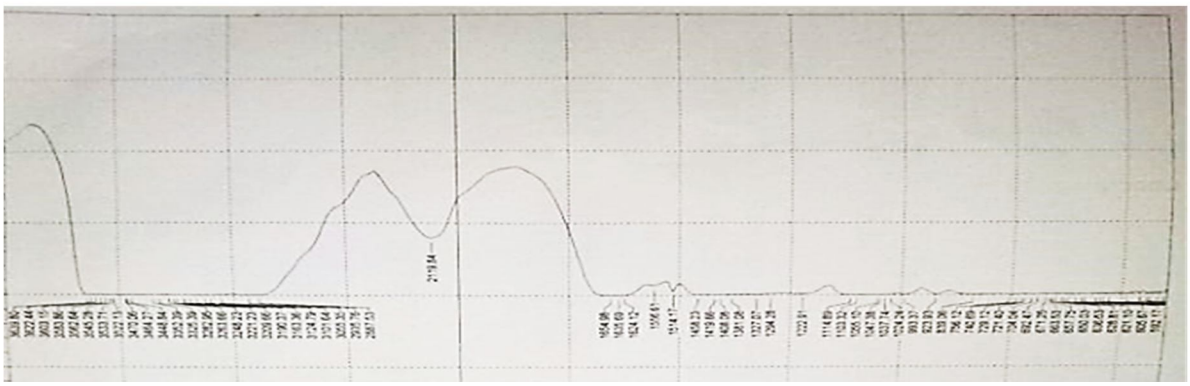


Fig 2.30 IR spectrum of A2

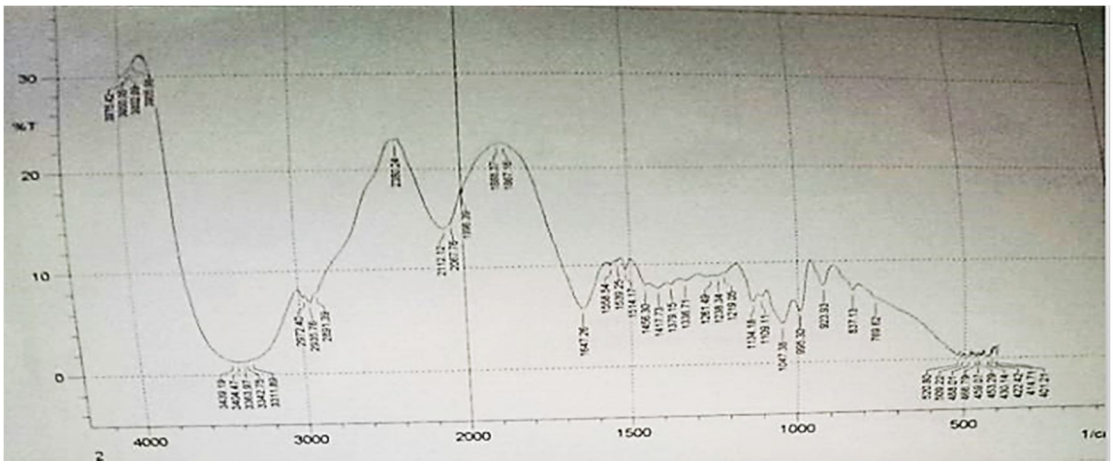


Fig 2.31: IR spectrum of B_2

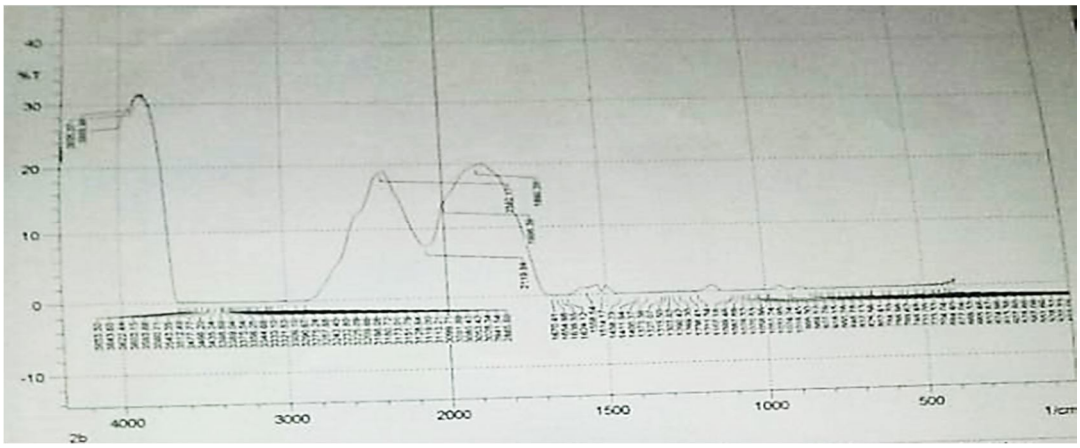


Fig 2.32:IR spectrum of A_3

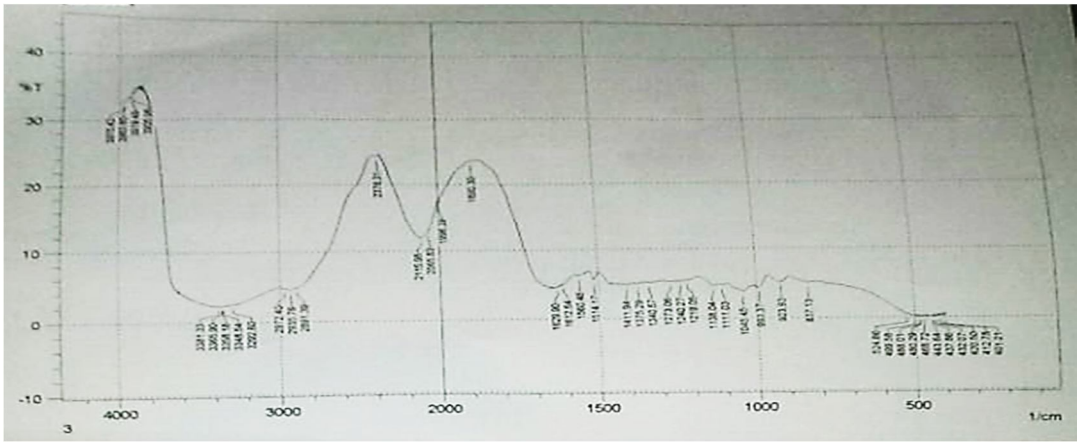


Fig 2.33:IR spectrum of B_3

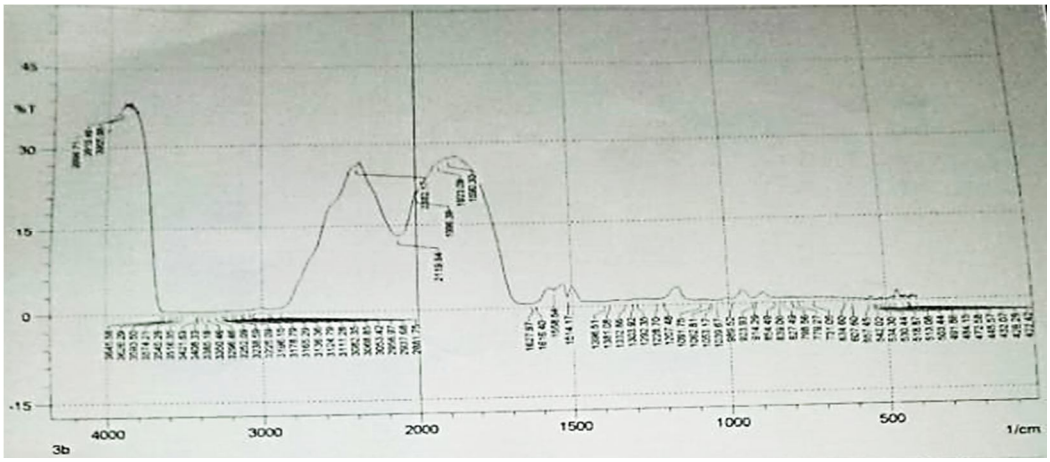


Fig 2.34: IR spectrum of A_4

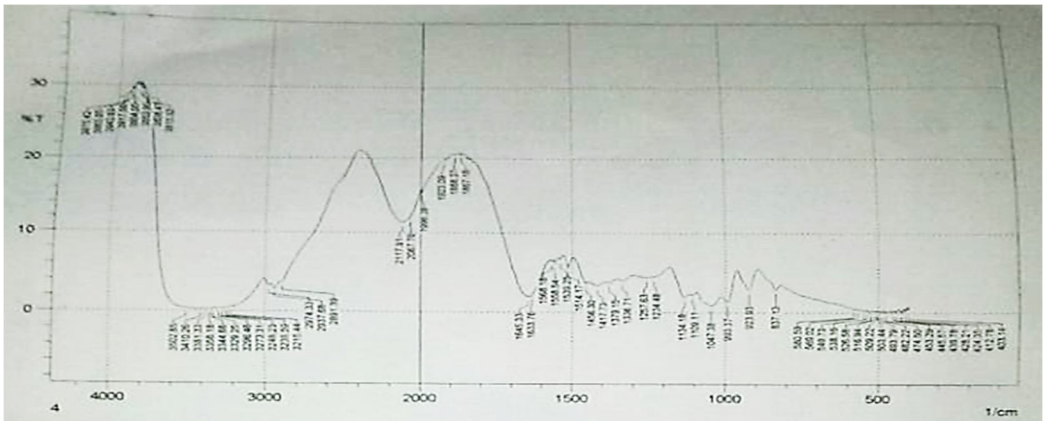


Fig 2.35: IR spectrum of B_4

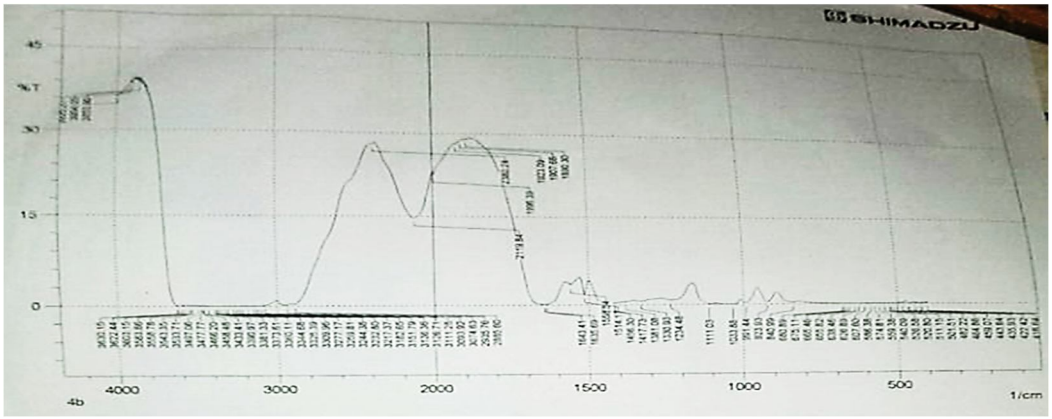


Table 1 : show the peaks of IR spectrum

function / sample	N-H (str) 3560	OH 3300 cm^{-1}	C-H (Arom) 3011	C-H (sp^3) 2700	C=O	Benzene ring	c-o
A_1	3522	3352	2935	2887	1635	1514-1560	1039
B^1	3514	3350	2935	2893	1643	1514-1556	1037
A_2	3439	3342	2935	2891	1647	1514-1556	1047
B_2	3435	3344	2941	2885	1639	1514-1558	1031
A_3	3381	3348	2935	2891	1629	1514-	1045

						1560	
B_3	3516	3350	2937	2881	1627	1514-1558	1039
A_4	3381	3344	2937	2891	1645	15141558	1047
B_4	3381	3344	2935	2885	1643	1514-1558	1033

Table 2: Result of PH:

Sample	pH	Sample	pH
A_1	5.793	B_1	4.640
A_2	5.801	B_2	4.645
A_3	5.782	B_3	4.663
A_4	5.761	B_4	4.639

Chapter three

3.1 Discussion

- At any given condition the differ in assay for the two products in the time of the study are minor (using HPLC), to know the reason for the minor difference and also the structure of the product we analyzed it by IR spectroscopy.

-In IR spectrum Four compound(B-) 1 to 4 imported.Thepeaks at 3514,3435,3516,3381cm^{-1} appear due to NH (str). The peaks at 3350,3344,3350,3344 cm^{-1} appears due to OH (str). The peaks at 2975,2941,2937,2935 cm^{-1} appears due to CH(arom). The peaks at 2893,2885,2881,2885 cm^{-1} appears due to CH (sp^3). The peaks at 1643,1639,1627,1643 cm^{-1} appears due to C=O. the peaks at 1039,1031,1039,1033 cm^{-1} appears due to C-O. And the two peaks at 1514-1560,1514-1558,1514-1558,1514-1558 cm^{-1} appears due to benzene ring (di subs).

-In IR spectrum Four compound(A) 1 to 4 local. The peaks at 3522,3439,3381,3381 cm^{-1} appears due to NH (str). The peaks at 3352,3342,3348,3344 cm^{-1} appears due to OH(str). The peaks at 2935,2935,2935,2935 cm^{-1} appears due to CH(arom). The peaks at 2887,2891,2891,2891 cm^{-1} appears due to CH (sp^3). The peaks at 1635,1647,1629,1645 cm^{-1} appears due to C=O. The peaks at 1037,1047,1045,1047 cm^{-1} appears due to C-O. And the two peaks at 1514-1556,1514-1556,1514-1560,1514-1558 cm^{-1} appears due to benzene ring (di subs).

Finally we see that change of temperature of all compound cannot effect in the functional group absorption. This means the temperature did not effect to this compounds[10].

3.2 Conclusion:

In this research we found that the in use stability of paracetamol is high in any given condition and we determined the assay by HPLC and analyzed it by IR spectroscopy

3.3 Recommendations:

. Another devices can be used such as UV\VIS spectroscopy, NMR and mass spectroscopy is the best one.

. paracetamolcan be used for headache and fever but if it used constantly or overdose it may lead to liver poisoning and drop in both blood sheets and sugar in blood.

. To know the changes that may happen to the drug we recommend to study it at high temperature as 90℃.

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