The Simultaneous Determination of Ibuprofen and Paracetamol in Pharmaceutical Formulations by High-performance Liquid Chromatography with Ultraviolet Detection

By :
Amall Jamil
5th Stage

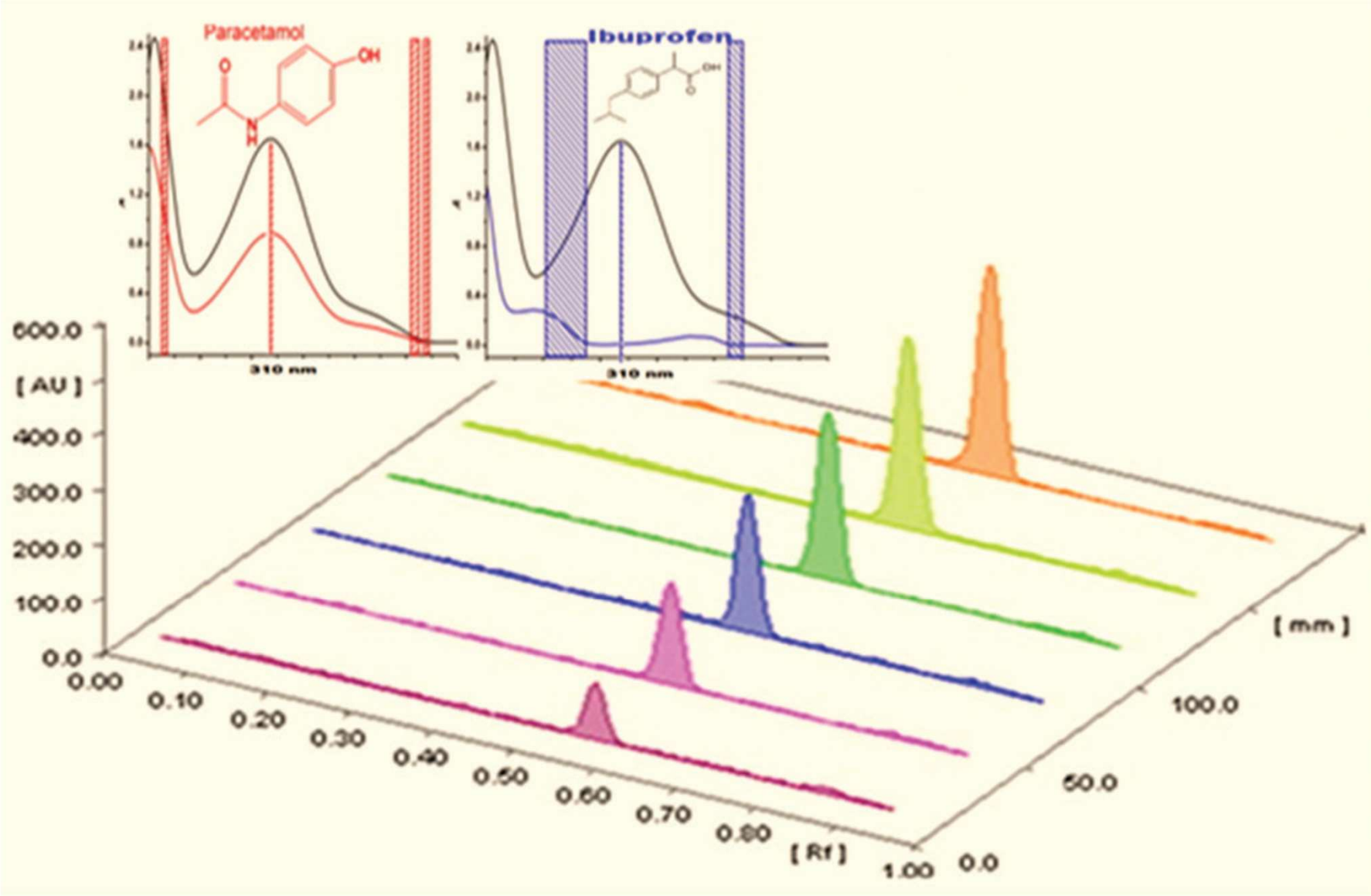
HIGHLIGHTS

- *A new method of estimating ibuprofen and paracetamol in pharmaceutical formulations.*
- *Use of high-performance liquid chromatography- ultraviolet technology for LC100 in the estimation of ibuprofen and paracetamol in pharmaceutical formulations.*
- *Study the stress degradation for ibuprofen and paracetamol in pharmaceutical formulations in the neutral, acid, and base media.*
- *Studying the relative stability of ibuprofen and paracetamol in pharmaceutical formulations during the experimental estimation process.*
- *Perform different applications for the purpose of validating the chromatographic method in the estimation of the Ibuprofen and paracetamol in pharmaceutical formulations.*

Abstract

Context: In this manuscript, high-performance liquid chromatography technology equipped with ultraviolet detector has been developed that it has the sensitivity, accuracy, and high reliability for the simultaneous identification of the ibuprofen (IB) and paracetamol (PA). Methods: Chromatographic separation was achieved on Ion Pac column; Arcus EP-C18 (5 µm, 4.6 mm × 250 mm) by a mobile phase consisted of acetonitrile and water (30:70, v/v)+40 mmol/L phosphate buffer at pH 6.0 with a flow rate of 1.0 mL/min. The detection wavelength was set range at 300–330 nm. The IB and PA were subjected to different forced degradation conditions. In all the conditions, the degradation products were well obtained from the peaks of IB and PA. The method was linear at a concentration range of 5–25 µg/mL (R2 = 0.9987) and 1–5 µg/mL (R2 = 0.9989) for the IB and PA, respectively. Results: The limit of detection (LLOD) was 0.0133 µg/mL and limit of quantitation (LLOQ) was 0.0420 µg/mL for IB and the LLOD was 0.0213 µg/mL and LLOQ was 0.0521 µg/ml for PA, respectively. The precision of the method was satisfactory; the relative standard deviations values did not exceed 1%. The accuracy of the method was proved; the mean recovery was in the range of 99.88%–100% for the IB and in the range 98.99–101.0% for the PA. Conclusion: The developed and validated method was applied successfully for the assay of the IB and PA in combined tablet dosage with good precision and accuracy.

Graphical abstract



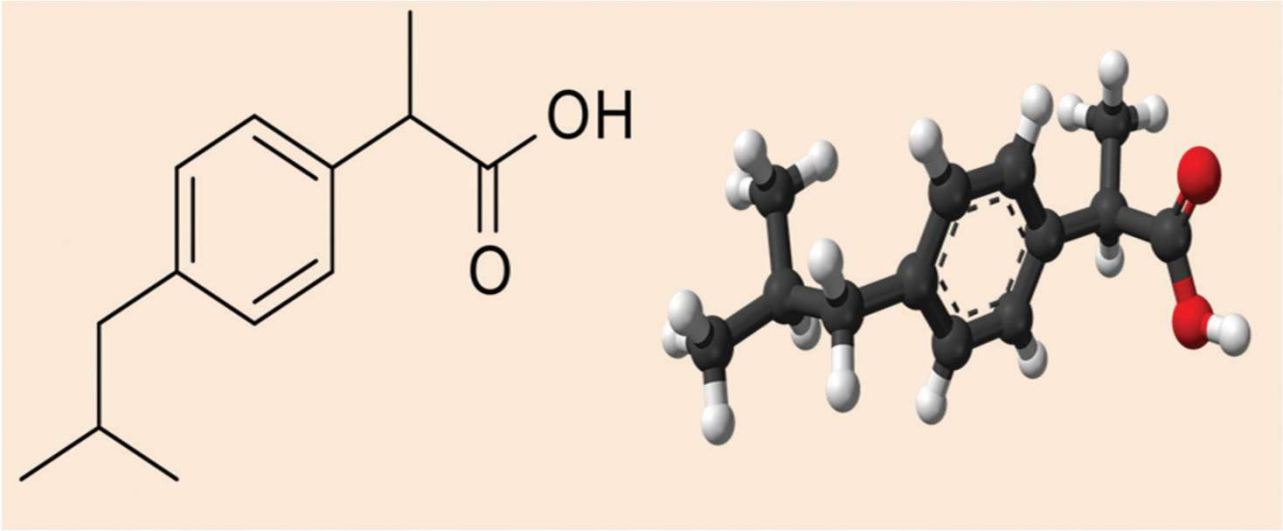


Figure 1: Structure of ibuprofen

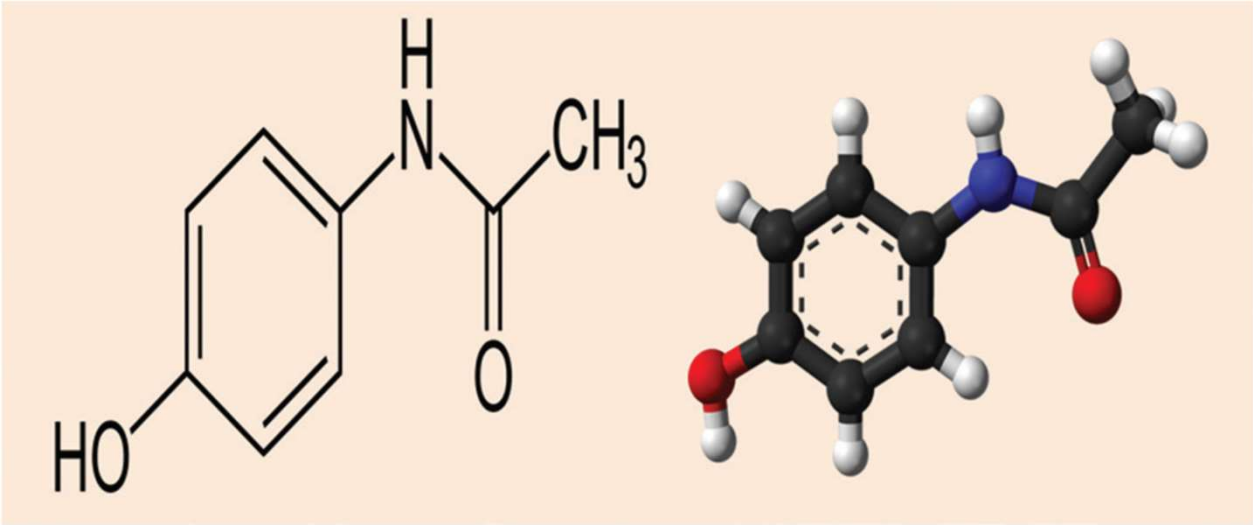


Figure 2: Structure of paracetamol

INTRODUCTION

The study of the simultaneous estimation of the ibuprofen (IB) and paracetamol (PA) requires first to know the physicochemical properties of each of these materials and to know the structural and spectral formulas of each. A number of studies and literature mentioned the precise description of the simultaneous estimation of the IB and PA.

An extensive study was conducted to determine the type and quantity of these substances in pharmaceuticals. The study was done by the chromatographic separation method using the detector of ultraviolet (UV) ray for the purpose of the chemical analysis of pharmaceuticals.[3-5]

The simultaneous determination of the IB and PA requires knowledge of the various physicochemical properties, then the optimal conditions for the separation, and estimation process for pharmaceuticals. The use of the high-performance liquid chromatography (HPLC) method using a UV detector has greatly assisted in the determination of the components of substances in pharmaceuticals in general.[6-8]

The objective of the study

The objective of the study was to develop and verify the reverse phase-HPLC (RP-HPLC) method with a UV detector for simultaneous determination of the IB and PA samples in the raw pharmaceuticals.

Market sample

Ibuprofen-Razifen tablets, batch No. 180512, were labeled to contain 200 mg IB and 500 mg PA per tablet and were manufactured by ElRazy Pharmaceutica NV® for Pharmaceuticals and Medical Appliances; the other drug Megafen® tablets, batch No. 180555, were labeled to contain 200 mg IB and 325 mg PA per tablet, it was manufactured by Rameda Pharma (Limited Tenth®) for Pharmaceuticals and Medical Appliances.

RESULTS OBTAINED

Chromatographic conditions Table 1 shows the values of the basic parameters obtained using the RP chromatography system (RP-HPLC).

Mean centering of ratio spectra method Calibration curve

The standard calibration curves of the proposed method were prepared over concentration ranges of 5–25 µg/mL for the IB and 1.0–5.0 µg/mL for PA. Each solution was prepared in triplicate and 20 µl of each solution was injected into the column. Thecalibration peaks were determined at the wavelength of 260 nm.

The calibration curves of the IB and PA were constructed by the relationship plotting of the peak area versus concentrations.[25]

Laboratory prepared mixtures

The calibration curves prepared in the laboratory contain different percentages of IB and PA. The absorbance spectra

Table 1: Parameters of RP-HPLC method

Column	***Ion Pac column; Arcus EP-C18; 5µm, 4.6×250 mm)***
Mobile phase (v/v)]	***Acetonitrile: water 30:70 + 40 mmol/L phosphate buffer at pH 6.0***
Flow rate	***1.0 mL/min***
Detection wavelength	***At range 300–330 nm***
Column temperature	***Room temperature***
Injection volume	***20 µL***
Run time	***3.30 and 3.53 min***

RP-HPLC: Reverse phase high-performance liquid chromatography

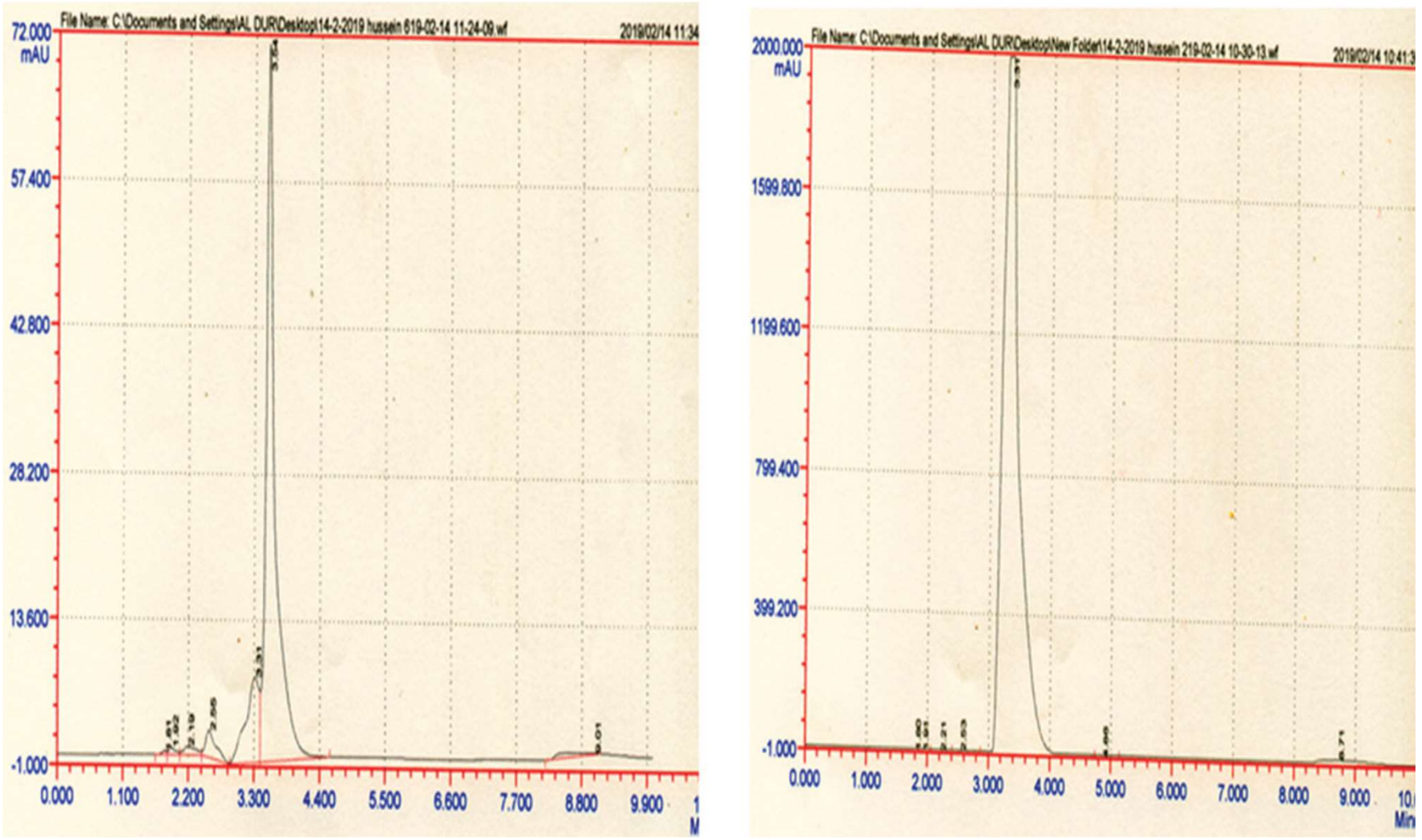
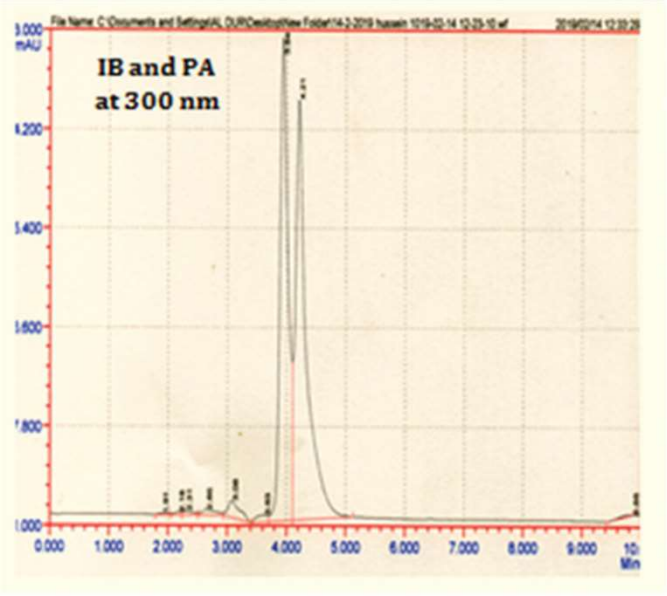
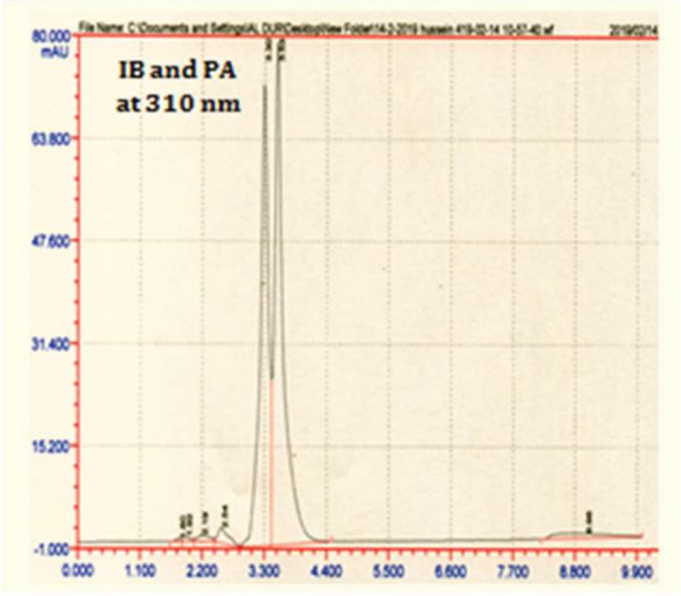
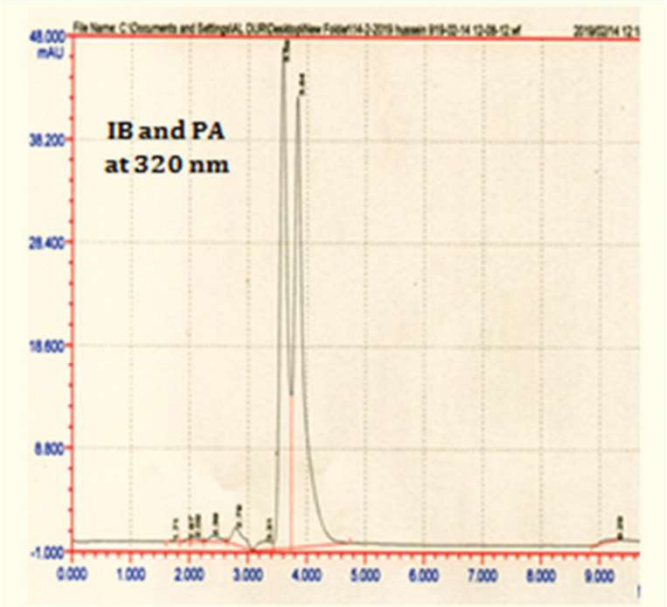


Figure 4: Standard calibration curve for ibuprofen IB alone and paracetamol alone


IB and PA
at 300 nm


IB and PA
at 310 nm


IB and PA
at 320 nm

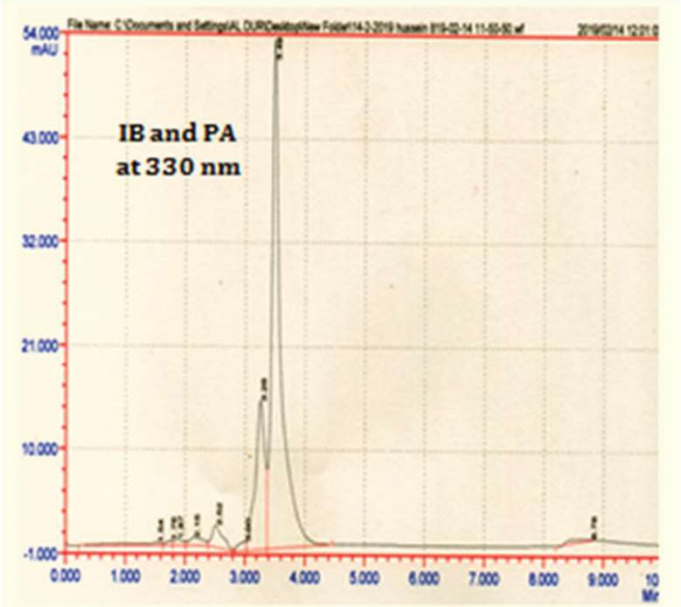

IB and PA
at 330 nm

Table 3: Parameters of the system suitability

Parameters	*Value of the parameters*	*Recommended limits*
Retention time for IB	**3.3 (%RSD 0.499)**	**RSD≤1**
Peak area for IB	*74543.6 (%RSD 0.432)*	*RSD≤1*
USP plate count for I	*2071*	*~2000–2500*
USP tailing factor for IB	*0.68*	*≤ 2-2.5*
Resolution for IB	*0.23 min*	*≥2*
Retention time for PA	*3.532 (%RSD 0.362)*	*RSD≤1*
Peak area for PA	*87337.5 (%RSD 0.300)*	*RSD≤1*
USP plate count for PA	*2056*	*~2000–2500*
USP tailing factor for PA	*5.33*	*≤ 2-2.5*
Resolution for PA	*0.23 min*	*≥2*

IB: Ibuprofen, PA: Paracetamol, RSD: Relative standard deviation

The linearity range and sensitivity[35,36]

Under the optimum experimental conditions, a linear relationship was established by plotting the peaks areas for drug against the drug concentration (µg/mL). The concentration range was found to be 5–25 µg/mL for IB and 1–5 µg/ml for PA. The linear regression analysis of the data gave from the following equations

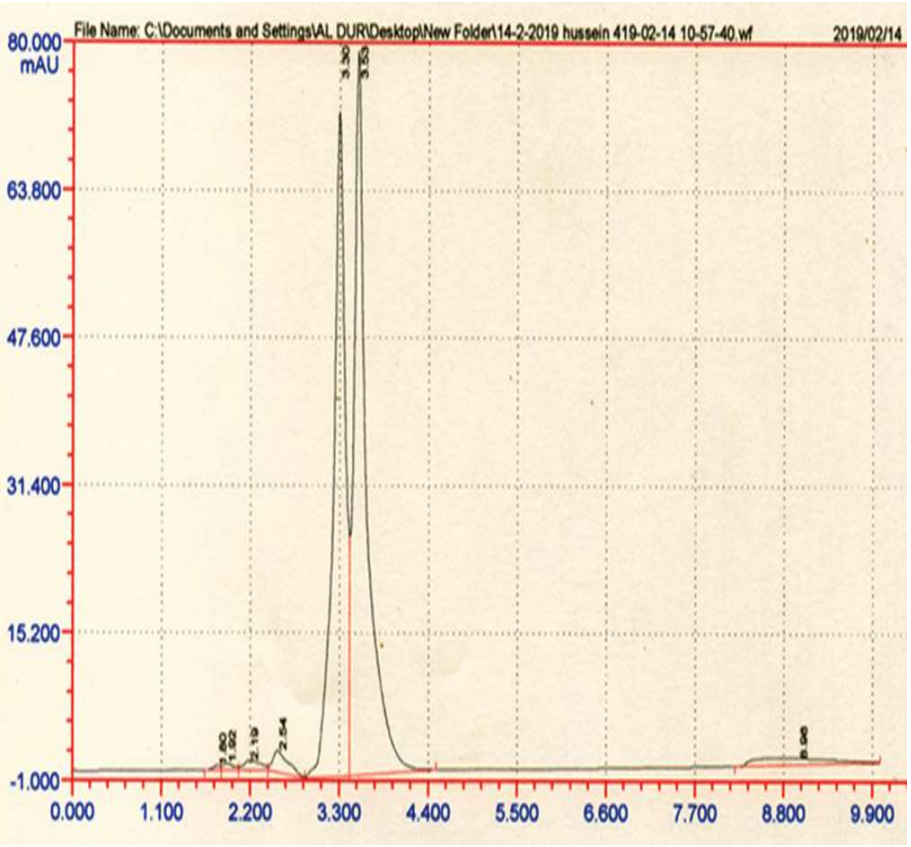


Figure 5: Standard calibration curve for Ibuprofen and paracetamo

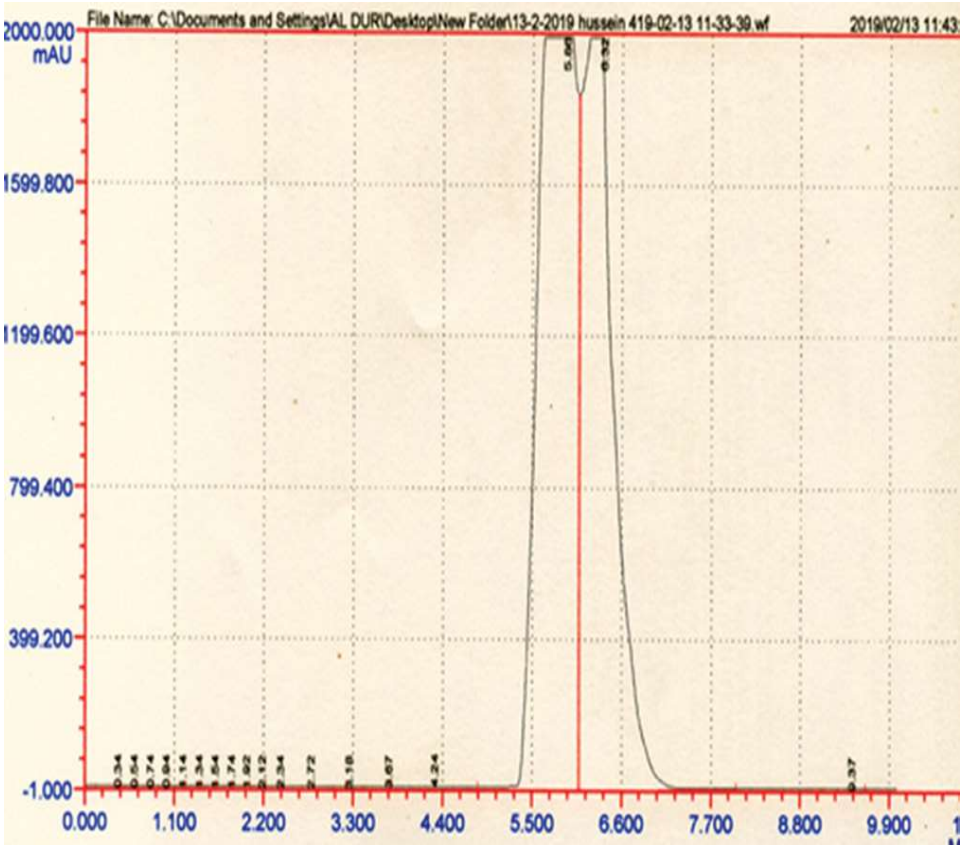


Figure 6: Chromatogram of acid degradation

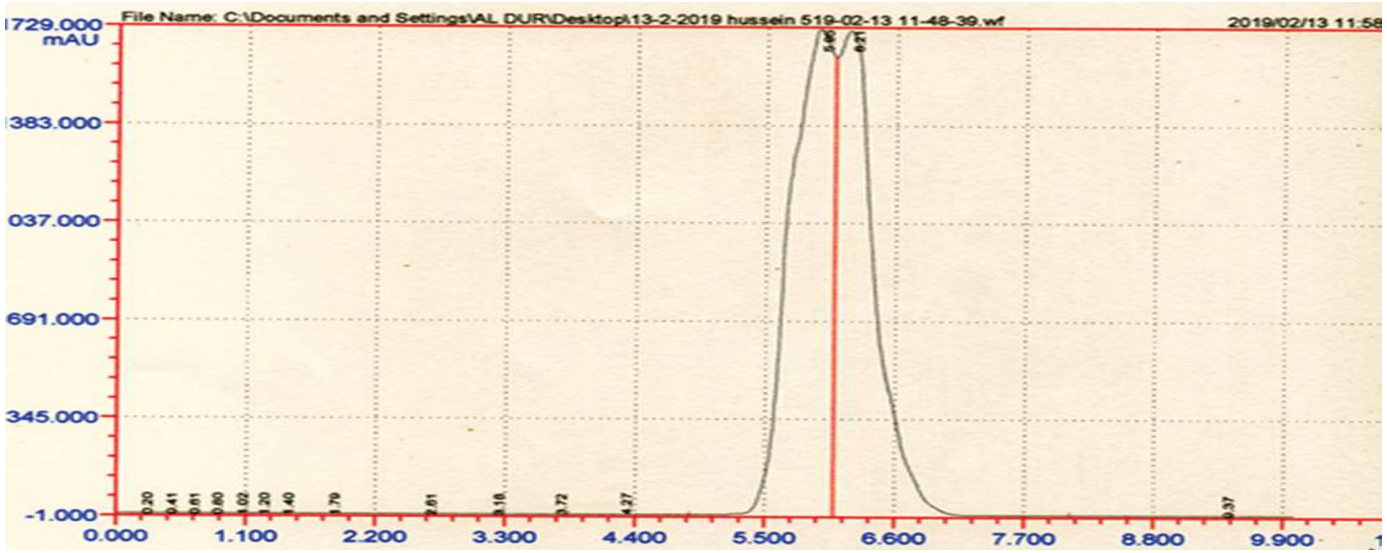


Figure 7: Chromatogram of base degradation

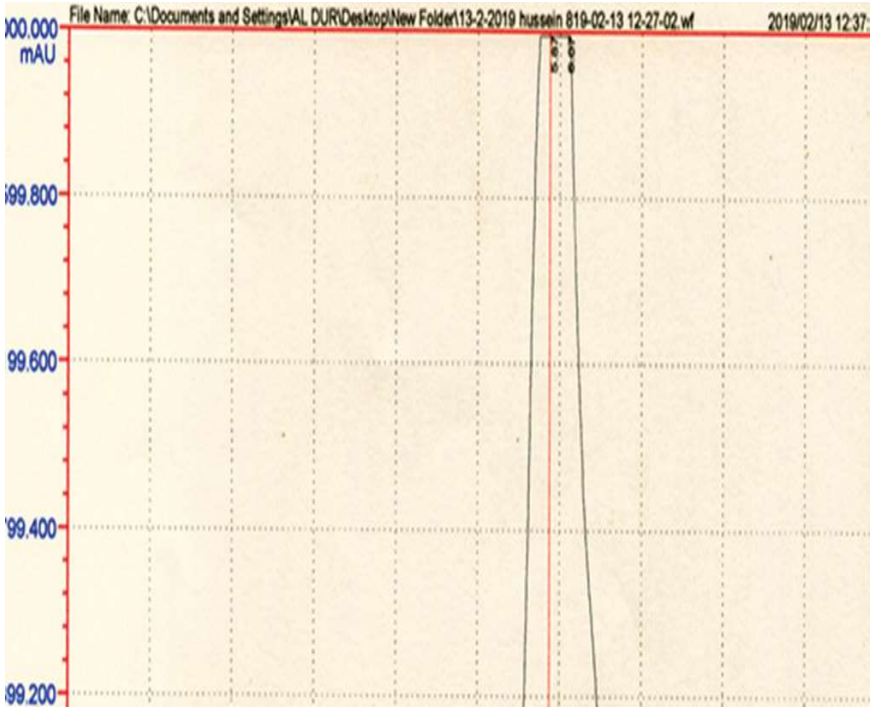


Figure 8: Chromatogram of oxidative degradation

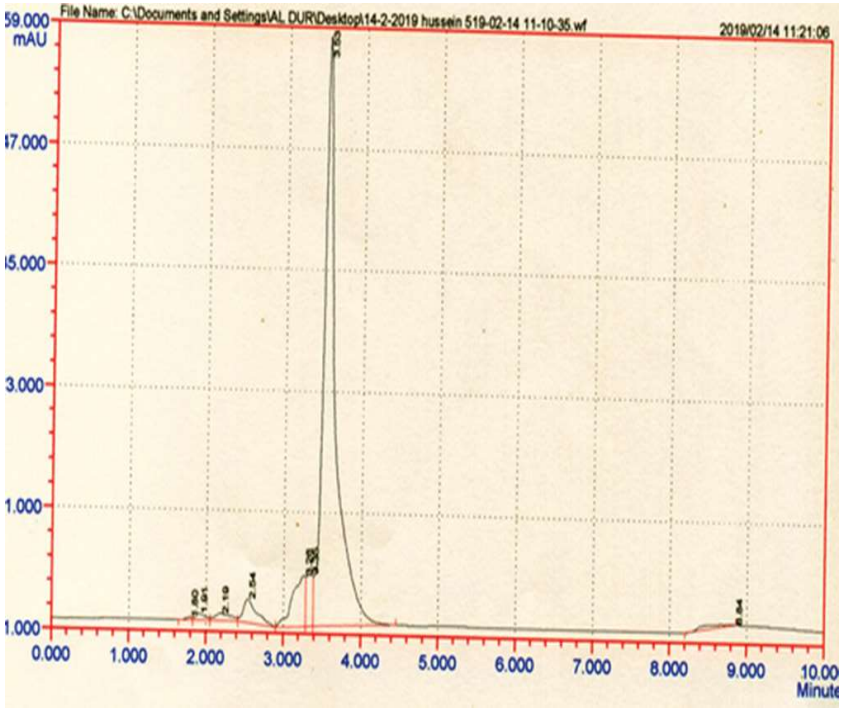


Figure 9: Chromatogram of thermal degradation degradation

Table 9: Assay of IB and PA in commercial tablets

Analyte	*Labeled claim (mg)*	*Found (mg)*	*Mean (mg)*	*%Recovery*	*%RSD*
IB in Razifen	*200*	*200*	*400*	*98.0*	*±0.498*
PA in Razifen	*500*	*~490*	*990*	*98.0*	*±0.311*
IB in Rameda pharma	*200*	*~190*	*390*	*96.6*	*±0.441*
PA in rameda Pharma	*325*	*~300*	*625*	*93.3*	*±0.299*

IB: Lbuprofen, PA: Paracetamol, RSD: Relative standard deviation

THE APPLICATIONS OF METHOD

The analytical method of IB and PA in Razifen and Rameda drugs was assessed by examining commercially available tablets (Razifen-tablets® that claiming to contain 200 mg of IB and 500 mg of PA). Table 9 summarizes the application
results that indicate the values of % recovery and RSD%. The proposed method was accurate and precise in IB and PA analysis in dosages forms.

CONCLUSION

This work described HPLC System (LC100 Angstrom advanced) equipped with a UV detector for IB and PA determination in two commercial pharmaceutical drugs. This developed method is considered simple and inexpensive and needs a very small volume of samples as well the ultravioletdetector makes this system very specific because it gives one peak to the IB or the PA and two peaks for both. In this application, there is a need for high sensitivity since the pharmaceutical drugs have a very low concentration.

The method was validated as per the HPLC-UV guidelines and the developed method obeys Beer's law over the concentration range of 5.0–25.0 µg/mL for IB and 1–5 µg/mL for PA. Based on the results, this study divulges with important analytical method used to determine the presence of IB and PA in the dosage forms. The stability and reliability of the results indicate that the HPLC-UV method for drug evaluation is simple, precise, accurate, sensitive, limited, and robust. The proposed method for the routine analysis

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