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Determination of ibuprofen by high performance liquid chromatography

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Abstract

Ibuprofen in its pure form and in pharmaceutical formulations (tablets and suspension-dose forms) was determined by high-performance liquid chromatography (HPLC). The analysis was performed on a C18 column (3.9 mm × 150 mm, 5 µm) with a mobile phase consisting of methanol-water-phosphoric acid in ratios [75:24.7:0.3] respectively, and a flow rate of 0.8 mL/min. A UV detector with a wavelength of 214 nm was used. The results were linear in the range of 3,125-100,000 µg/mL for ibuprofen. Correlation coefficients were R = 0.999993 The relative standard deviations (n = 6) for the daytime assay and the inter-day assay were 0.152%, 0.382% This method was characterized by high precision and accuracy and is suitable for quality control in the pharmaceutical industries.

Keywords: High performance liquid chromatography; Correlation coefficients; Quality control; High precision

1. Introduction

C13H8O2 ibuprofen is used as an analgesic, anti-inflammatory and antirheumatic agent, and has analgesic and antipyretic properties in addition to non-steroidal anti-inflammatory properties [1–3]; Therefore, it is possible to analyze ibuprofen by known analytical methods such as titration [4, 5] or spectrophotometric methods [6, 7]. Researcher Wu-Hong, Zhang and colleagues [8] studied the possibility of hydrolyzing ibuprofen in a pharmaceutical formulation in capsule form using liquid chromatography. , using a chromatography-CN column and a mobile phase consisting of methanol and phosphate buffer solution at pH = 6.6 and in proportions [60:40], respectively, and a detector operating at a detection wavelength of 223 nm, the linear result was within the studied range from 21.0 to 86.124 µg/mL for ibuprofen, the standard deviation in percentage was less than 31.0%. The researcher(Vp, Gods) and others with him [9] also studied the determination of both ibuprofen and paracetamol in tablet form using the HPLC method using a moving column and phase (4.6 mm x 250 mm and 5 µm) with dimensions C18 chromatography. Methanol - and water in proportions [70:30], respectively, at a flow rate of 1 ml / min, and the result was linear in the range from 2 to 50 µg / ml for ibuprofen and from 5 to 50 µg / ml for paracetamol, and it was concluded that this method is valid for the analysis of such formulations. There are many references [10-20] that have examined the identification of medicinal compounds. All these studies showed that the analysis using this method led to a high accuracy of the analysis as well as its linearity. It also emphasized the accuracy, sensitivity, ease, speed and applicability of this method, which gave it more credibility in the analysis than others.

2. Materials used

Standard materials were used to prepare all standard solutions. Solvents (methanol, water) of high purity (HPLC grade) from Chemlab Company were used, with a purity between 0.100-7.99%, especially for chromatographic analysis. As for the studied samples, they were produced by Syrian pharmaceutical companies (Extraprofen Tablets, Extraprofen

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Suspension) Table No. (1) shows the name of the preparation with the quantities declared for the active ingredients by the manufacturer.

Table 1 the quantities of active substances declared by the manufacturer of the preparations

The name of the preparation	Authorized quantity(mg) / ibuprofen	the manufacture company
Extraprofen Tablets	400	Medipharm Company (Syria)
Extraprofen Suspension	100	Medipharm Company (Syria)

2.1. Devices used

Use the US-made High-Performance Liquid Chromatography (HPLC) from Waters Which consists of a pump model pump HPLC isocratic, 1515 Waters, and a detector that works in the field of visible and ultraviolet rays, model Detector Absorbance λ Dual Waters2487. connected to a computer containing special programs for data processing. Use the USP C18 chromatographic column Waters company production of (3.9 mm x 150 mm, 5 µm) dimensions, L1 per column American. A sensitive electronic balance (S B120 Sartorius) was used, with a measurement accuracy of ± 1.0 mg, to weigh all the studied subjects.

2.2. Mobile phase selection

A mixture of methanol-water-phosphoric acid was used as the mobile phase in proportions [75:7.24:3.0], respectively. The mobile phase was filtered on a filter whose pores did not exceed 45.0 µm, and the gas particles were removed using an ultrasonic device, and this mixture was selected as the mobile phase and the sample solution as well; This is for several reasons, the most important of which are: All the studied compounds dissolve in it, and it does not absorb light at the wavelength at which the analysis is 214 nm, and it has a separation factor of RS >2 for the studied mixture.

2.3. The method of work

2.3.1. Applicable chromatographic conditions:

During the analysis, the following chromatographic conditions were applied:

The used column is C18 or what is known as the L1 column, its dimensions are (5µm, 150mm×9.3mm). The temperature used is room temperature.

- The detector used is the ultraviolet detector, and the detection wavelength is 214 nm = λ.
- The total analysis time is 7 minutes.
- The volume of the injection cell is 20 microliters.
- The used mobile phase is a mixture of methanol - water - phosphoric acid in proportions of [75: 7.24: 3.0], respectively, as the value of the acidity of the solution was within limits 2.8.
- The rate of mobile phase flow rate is 8.0 ml/min.

2.3.2. Determine the purity of the standard active ingredients used

The purity of the used standard active substances was confirmed by calibrating them according to the methods used in each of the British and American Pharmacopoeia [21, 22]. This was done by titration method. The purity ibuprofen was 100.02%.

2.3.3. Preparation of standard series solutions

To prepare standard series solutions, you must accurately weigh 100.0 mg standardized ibuprofen. It was dissolved in an appropriate amount of the mobile phase, then the solution was quantitatively transferred to a 100 ml volumetric flask and the volume was completed in the mobile phase until the mark, then the solution was filtered through a filter with a pore diameter of 0.45µm. The resulting solution represents the parent solution. The standard series solutions were prepared from the parent solution by making the appropriate extension in the mobile phase. Table No. (2) shows the concentrations of the prepared standard series solutions.

Table 2 concentrations of standard series solutions

Standard solutions	Concentration of the active substance(µg/ml) / ibuprofen
Standard solution (1)	100.000
Standard solution (2)	75.000
Standard solution (3)	50.000
Standard solution (4)	25.000
Standard solution (5)	12.500
Standard solution (6)	6.250
Standard solution (7)	3.125

2.3.4. Preparation of sample solutions

The studied samples' solutions were prepared from the preparations referred to in Table (1). according to the following:

Preparation of tablet sample solutions:

To prepare a test sample solution for Extraprofen Tablets, a minimum weight is required About twenty tablets, and the average weight of one tablet was determined, then it was ground the tablets were all finely ground and the equivalent of the average weight of one tablet was taken. The weight was dissolved in an appropriate amount of the mobile phase using the ultrasonic device Then transfer the solution quantitatively to a volumetric flask of 100 ml capacity, and complete the volume with the mobile phase. up to the mark, then filter the solution through a filter with a pore diameter of 0.45 µm. Then all the previous solutions were quantitatively diluted until the concentrations of the active substances were obtained default (according to the manufacturer), as shown in Table (3).

Preparation of suspension sample solutions:

To prepare the test sample solution for Extraprofen Suspension, 6.15 mL of Suspension (equivalent to 200 mg paracetamol and 123 mg ibuprofen) It was placed in a volumetric flask of 100 mL capacity and the volume was supplemented with the mobile phase up to the mark.

Table 3 Concentrations of active substances in the analyzes prepared samples (according to the manufacturer).

The name of the preparation	Concentration of active substances in the analysis samples (µg/ml)
Extraprofen, tablets	20.000
Extraprofen, suspension	12.30

3. Results and discussion

The analysis method was chosen using liquid chromatography High performance than others, as it does not need a long time Within 7 minutes, equivalent to 6 ml of the mobile phase, the active substances are dissolved in one go and possible Repeating the analyzes many times with high accuracy, and there is no need to extract one component from another Components as well as the low economic cost of the analyzes compared to some analytical methods other. Confirm the linearity of the analysis within the measurement range of the standard series solutions contained in Table (2), these solutions were analyzed, and then chromatography was drawn for them as shown In Figure (1).

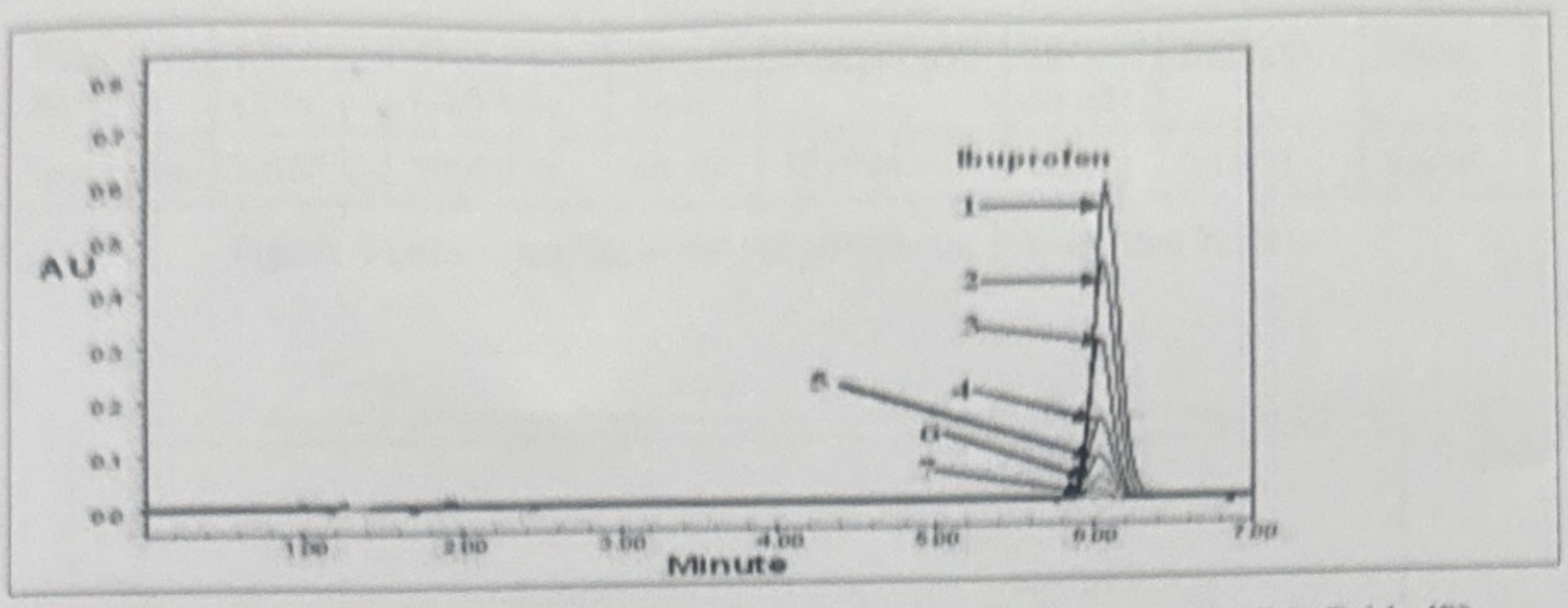


Figure 1 Chromatography of standard series solutions from No. 1 to No. 7 in Table (2).

From the chromatography of the previous standard series solutions, the standard curve is drawn the concentrations of standard series solutions against the area of their peaks as shown in Figure (2) It represents the standard curves for ibuprofen, which contain the correlation coefficient, the linear relationship that represents the graph line, and a table showing the amount of the standard active substance as prepared compared to its amount calculated graphically, and the percentage deviation.

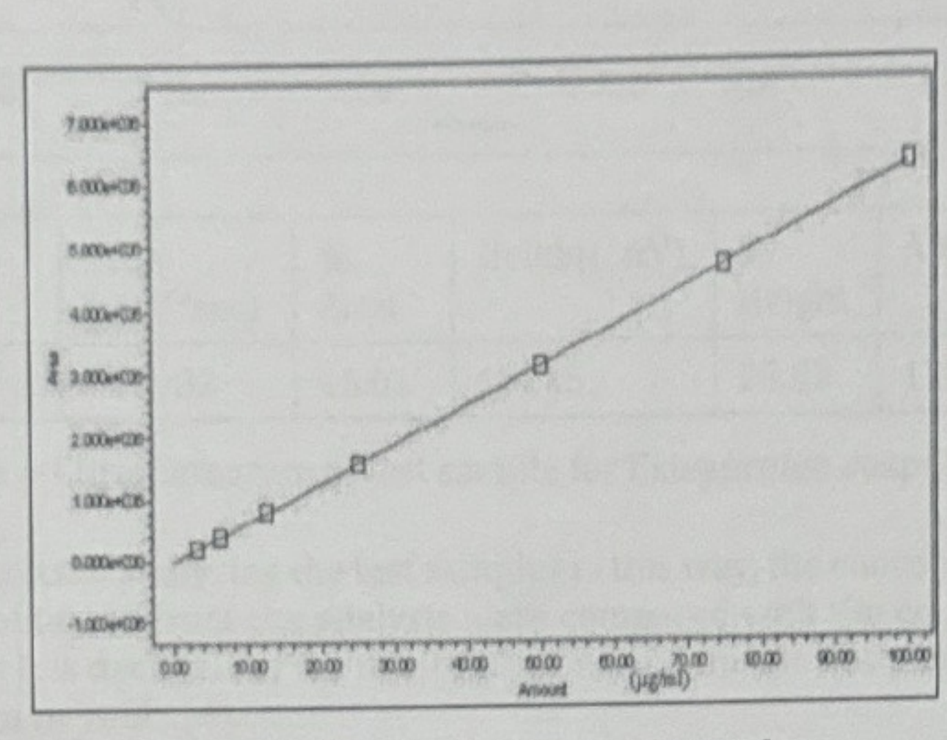
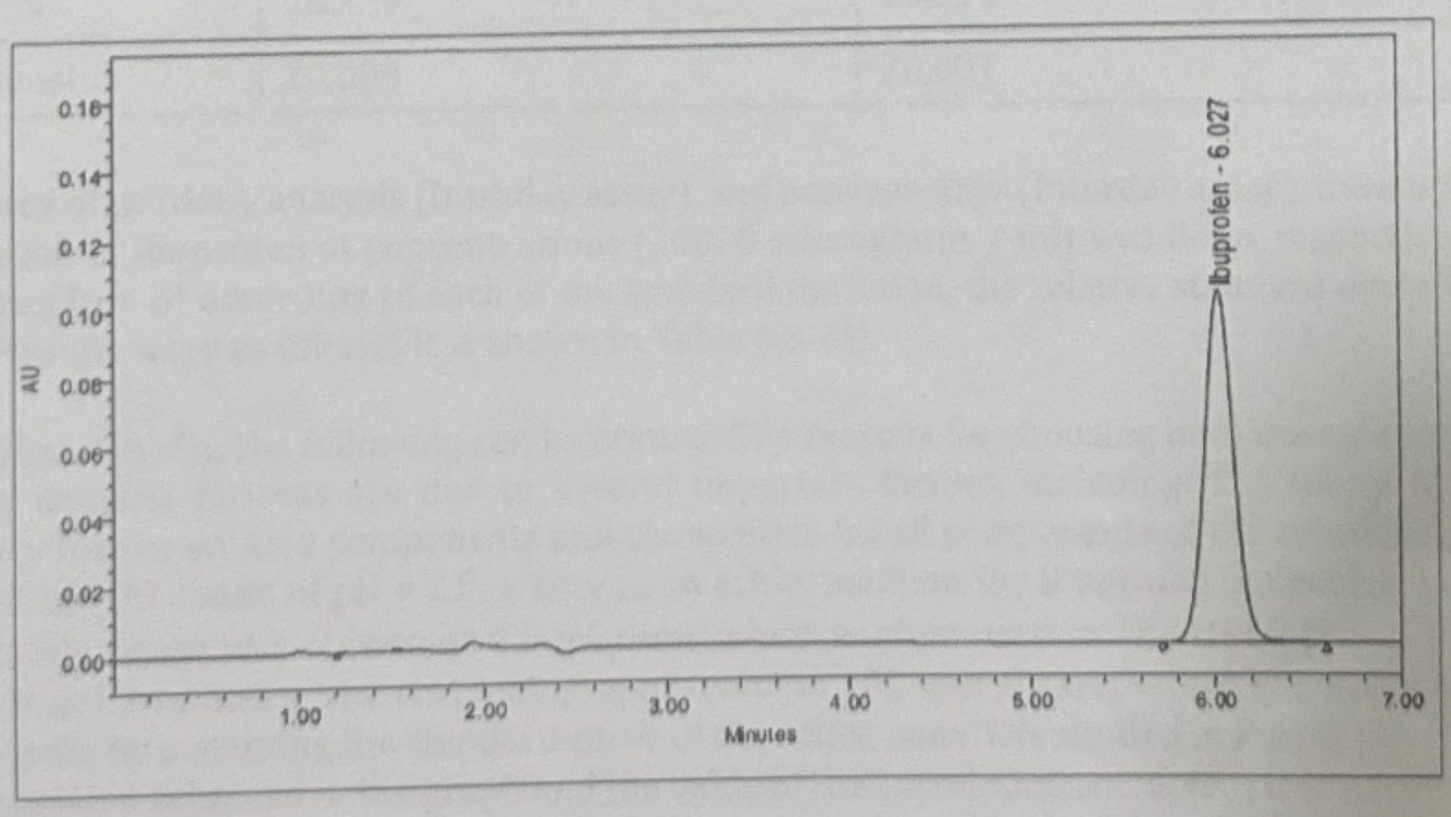


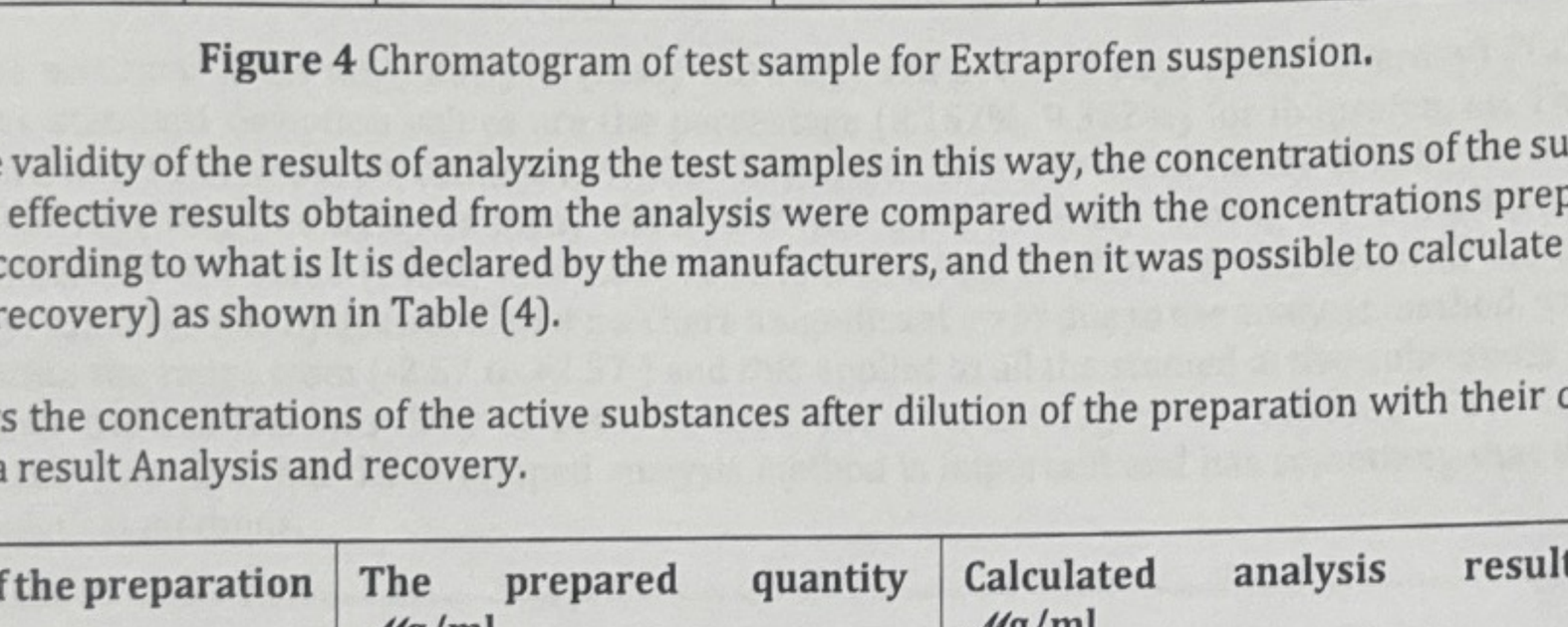
Figure 2 Standard curve for ibuprofen

To ensure the validity of the method, it was tested on different samples of the studied preparations which are present in Table (3) of Syrian-made pharmaceutical preparations (tablets + suspension), and after conducting analyzes for them, and The chromatograms shown in Figure (3) with a table showing some of the calculated amounts of these chromatograms such as: name of the apex, retention time, and area of the apex and its percentage, its height and its percentage, and the concentration (amount) to calculate the concentration.



Peak name	RT (min)	Area (𝒰V*sec)	% Area	Height(𝒰V)	% Height	Amount	Units
Ibuprofen	6.027	1095074	60.33	101944	38.73	20.007	ug/ml

Figure 3 Chromatogram of the test sample for Extraprofen Tablets



Peak name	RT (min)	Area (𝒰V*sec)	% Area	Height(𝒰V)	% Height	Amount	Units
Ibuprofen	6.040	742082	45.01	69225	25.52	12.302	ug/ml

Figure 4 Chromatogram of test sample for Extraprofen suspension.

To find out the validity of the results of analyzing the test samples in this way, the concentrations of the substances were calculated the effective results obtained from the analysis were compared with the concentrations prepared from the preparation according to what is It is declared by the manufacturers, and then it was possible to calculate their achieved percentages (recovery) as shown in Table (4).

Table 4 shows the concentrations of the active substances after dilution of the preparation with their concentrations calculated as a result Analysis and recovery.

The name of the preparation	**The prepared quantity 𝒰g/ml**	**Calculated analysis result 𝒰g/ml**	**Recovery**
Extraprofen tablets	16.250	16.254	100.02
Extraprofen suspension	20.000	20.001	100.01

To study the accuracy of the daily analysis (Intraday assay), and between days (Interday assay), the statistical treatment of a prepared solution of ibuprofen at concentrations (25000 micrograms / ml) was done, respectively, by repeating the analysis six times (n = 6) according to each of the standard deviation, the relative standard deviation, and the test value (t-test). The results were as follows It is shown in Table No. (5).

Observing the previous results, the following can be argued: The reasons for choosing both the solution and the mobile phase used in this analysis process are due to several important factors, including: Possibility of obtaining good separation efficiency for the studied components and cheap price for all components of the solutions. The pH value of the solution was within the limits of pH = 2.8, where in an acidic medium the ibuprofen molecules will not ionize the flow rate of the mobile phase was chosen as 0.8 mL/min, which is often used in The HPLC [23-27], where the total analysis time was about 7 minutes. The chromatographic column 18C was chosen, which showed good separation of the sample components by observing the standard curve of the active materials studied in Figure (2), we find that there is a linearity that has been achieved in the graph and the value of the correlation coefficient is R > 0.9999

Table 5 shows some statistical values resulting from repeated analysis of a solution prepared from ibuprofen

Measurement number	**Concentration of active substances in the analysis samples µg/ml**	
	Ibuprofen 25.000µg/ml	
	Interday assay	Intraday assay
1	24.903	24.961
2	25.084	25.063
3	24.892	25.024
4	25.086	24.973
5	25.067	24.985
6	24.923	25.016
average	24.993	25.004
standard deviation	0.096	0.038
Relative standard deviation% RSD%	0.382	0.152
T-test	0.179	0.258

It is noted from Table (4) that the recovery values (percentage achieved) are all calculated During the analysis of the studied samples were within the constitutionally permitted range that fall what Between 90% to 110% of the declared quantity [23], which indicates the correctness of the method.

By studying the accuracy of the daily analysis (assay intraday) and between days (assay interday) (Table 5) We find that the relative standard deviation values are the percentage (0.152%, 0.382%) for ibuprofen, i.e. The value of the relative standard deviation in the percentage is %RSD <2%, which indicates the accuracy of analysis, and this leads to the possibility of repeating the analysis many times and with good accuracy. During the comparison between the scheduled significant t-test value (t-test) (t = 2.57) at 95% confidence level, n = 6, and between the experimentally calculated t-test values (Table 5) it is noted that no There a significant error due to the analysis method, as the calculated t values fall within the range from (-2.57 to +2.57) and this applies to all the studied active substances in the analysis samples Whether the analysis was daily or between days, and thus the degree of confidence 95% can be adopted. Through this study, we find that the developed analysis method is important and has something that distinguishes it from Other analytical methods.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

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