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DEVELOPMENT SPECTROPHOTOMETRIC METHOD FOR SIMULTANEOUS ESTIMATION OF IBUPROFEN AND CAFFEINE IN PURE AND TABLET DOSAGE FORMS

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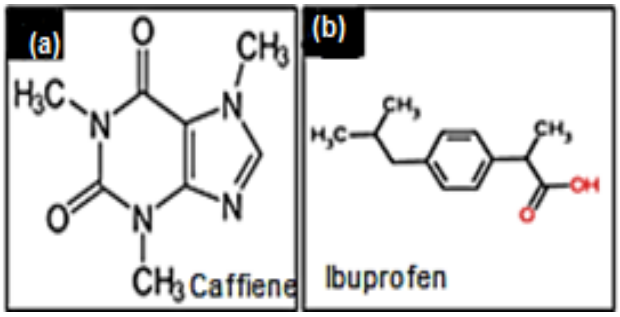
ABSTRACT
This research involved the development of spectrophotometric method for determination of Ibuprofen (IB), Caffeine (CAF)) in mixture of standard and manufactured tablets without any separation method between the two drugs in the mixture. The process was conducted using deionized water: acetonitrile mixture (90:10 v/v) as solvent. The maximum absorbance of drugs in mixture was found to be at (223 nm and 272 nm) for IB, CAF respectively. These wavelengths were selected for the analysis of drugs as mixtures standard and manufactured samples. The method was linear in the range of (0.3- 30 µg/mL) for (IB, CAF), with an R^2 of (0.9994, 0.9992) for IB and CAF respectively in the mixture. Recovery means were found to be (100.72, 100.90) for IB and CAF respectively. The method was applied for the estimation of the active gradient of the drugs in different samples of manufactured dosage. The accuracy of method was validated by mean percentage recovery, which was found to be in the acceptable range.

KEYWORDS: Determination, Spectrophotometric, Manufactured, Recovery.

INTRODUCTION
Prepare medicines Non-steroidal anti-inflammatory drug is one of the most common analgesics around the world with a total production of about 50,000 tons (annually). This is evidence of the importance of this article to date. These drugs are used on a scale, it is widely used as a painkiller to relieve inflammation, joint pain, osteoporosis, and antipyretic. Analgesic and anti-inflammatory, IB is classified as (NSAIDs). Although the pharmaceutical industry has contributed to saving humanity from scourges epidemics and pathological pests, but they became an obsession that afflicts this humanity because of the side effects and complications cure due to cumulative action. The liver, which is the main organ of the metabolism of drugs, is at the same time counted the main place of drug diseases.[1-3]

Ibuprofen ((*RS*)-2-(4-(2-methylpropyl)phenyl) propanoic acid), crystal structure data are significant to characterize and interpret the particularities of chiral compounds. Pure enantiomers form crystals in chiral space groups, (IB) as a rep of non steroidal anti-inflammatory drugs were executed.[4,5]

Caffeine (1,3,7-trimethyxanthine), is in the family of alkaloid methyl xanthine, caffeine is partially soluble in water due to its mild polarity, caffeine is a natural central nervous system stimulant, having the impacts of reducing drowsiness and recovering preparedness. Since it is widely consumed by humans, caffeine is considered the most often used psychoactive substance in the world.[6,7]



Numerous analytical methods were reported for the determination of these drugs in pharmaceuticals such as HPLC[8,9], Spectrophotometric[10-13], Gas Chromatography–mass Spectrometry[14], Thermodynamics[15], UPLC.[16] The aim of this work is to use the ease and accurate spectrophotometric method for the determine these drugs content in tablet samples from different pharmaceutical companies available in Iraqi pharmaceutical market, to give information about these products, which may or may not comply with the

requirements of the standard method or other official methods.

MATERIALS AND METHOD

Materials

IB and CAF were purchased from Samara Drug Industries (SDI), Iraq. Different Tablets were used as marketed formulation as in Table 5. Acetonitrile HPLC grade (BDH) and freshly prepared deionized water was used throughout the experiment

Apparatus

UV- VIS spectrophotometer (Jasco V-650 Japan) is applied to record the spectra of drugs, Sartorius balance (Germany), sonic bath (Korea), shaking water bath (Taiwan) and furnace (Germany) were used through this study.

Preparation of stock solutions of drugs (100 mg/L)

A 0.01 g of each standard drugs was weighed and dissolved in (H_2O: ACN 90:10 v/v), transferred to a 100 mL volumetric flask, then completed to the mark with the same solvent. More diluted solutions were prepared by simple dilution of stock solution of drugs.

Procedure for the drugs assay in pharmaceuticals tablets

Ten tablets from each drug formulated sample were accurately weighed and mashed to a powder, finely powdered and an accurately weighed quantity of the powdered tablet equivalent to 0.1 g was dissolved in (H_2O: ACN 90:10 v/v) transferred to a 100 mL volumetric flask and completed to the mark with the same solvent. Known volume containing the appropriate amount of each one drug corresponding to the range of the calibration curve was further transferred in 25 mL flask and analyzed at the same λ_{max} applied for standard measurements. The equation of straight line was applied to calculate drugs concentration.

RESULTS AND DISCUSSION

Determination wavelength of maximum absorbance

The UV-VIS spectra of drugs mixture solution was carried out, the maximum absorbance of drugs in mixture was found to be at (223 nm and 272 nm) for IB, CAF respectively, as shown in Fig. 1.

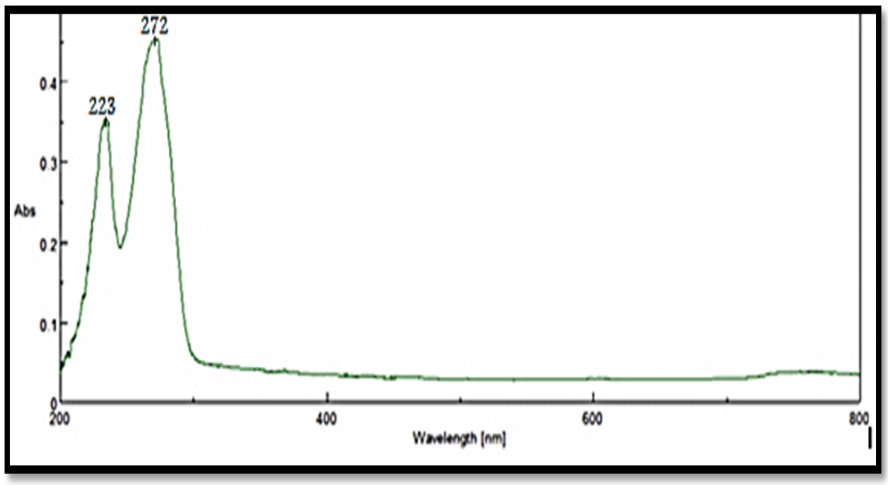


Fig. 1: UV – Spectrum of Ibuprofen and Caffeine mixture.

Preparation of calibration curves

The stock solutions of drugs were appropriately diluted with (H_2O: ACN 90:10 v/v). The two similar drug concentrations were mixed together to obtain IB and CAF mixture, have concentration range of (0.3-30 µg/mL) for the two drugs. A series of solutions for each drug was prepared within its range of concentrations (0.5-30) and (0.5-20) for IB and CAF respectively. Absorbance of all solutions were measured at λ_{max} of each drugs. The calibration curves Fig.3, were obtained by plotting absorbance versus known concentrations. The results in Table 1 showed that the values of t_{cal} are larger than t_{tab} values. The method is linear with an R^2 (0.9994, 0.9992) for IB and CAF in mixture respectively, and (0.9992, 0.9993) for IB and CAF alone respectively, indicating that there is a strong correlation between the variation of concentration and response. Linearity was determined by the regression analysis.

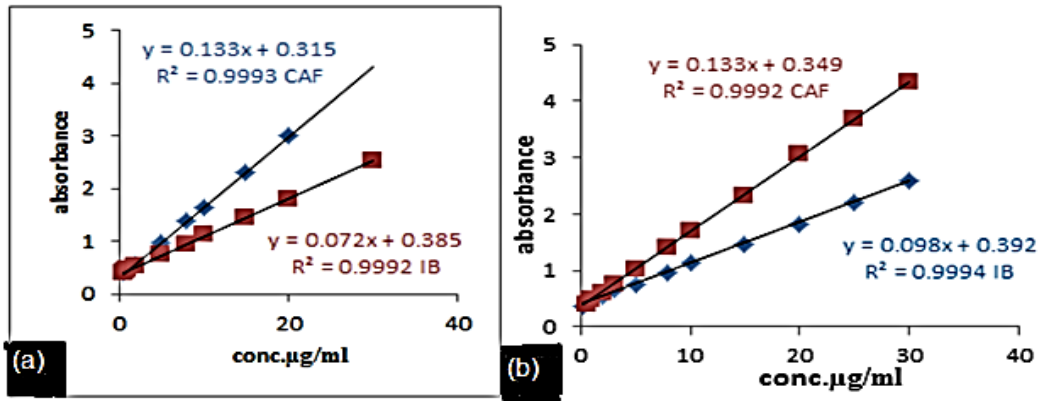


Fig. 3: (a) Calibration curves of IB alone and CAF and (b) for IB and CAF in mixture.

Table 1: Calibration curves statistical calculation for Ibuprofen and Caffeine.

Statistical factors	Value			
	Ibuprofen		Caffeine	
	Drug in mix.	Drug only	Drug in mix.	Drug only
Linear equation	y=0.098 [X]+0.392	y=0.072 [X]+0.385	y=0.133 [X]+0.349	y=0.133 [X]+0.315
Slope (m)	0.098	0.072	0.133	0.133
Intercept	0.392	0.385	0.349	0.315
Correlation coefficient "R^2"	0.9994	0.9992	0.9992	0.9993
Percentage linearity (R^2%)	99.94	99.92	99.92	99.93
Correlation coefficient (r)	0.9996	0.9995	0.9995	0.9996
Intercept standard error	0.00836	0.00821	0.01059	0.00866
Intercept standard deviation	0.028976	0.02596	0.03669	0.02598
"R.S.D."	1.72	2.47	3.27	2.09
"LOD" µg/mL	0.06	0.04	0.02	0.01
"LOQ" µg/mL	0.2	0.13	0.06	0.03
Linearity range µg/mL	0.3 – 30	0.5 – 30	0.3 – 30	0.5 – 20
Molar Absorptivity L. $mol.^{-1}$. Cm^{-1}	$2.979*10^4$	$1.748*10^4$	$1.6679*10^4$	$2.9216*10^4$
Calculated (t) values $t_{cal.} = \frac{/r/\sqrt{n-2}}{\sqrt{1-r^2}}$	129.07>>>2.18	99.96>>>2.23	111.76>>>2.18	99.96>>>2.26

Accuracy and precision of proposed method

IB and CAF were determined at three different selected concentrations (2, 5, 8 µg/mL). The obtained results were tabulated in Table 2, which indicated that the proposed method for the determination of drugs is quite satisfactory in reality with respect to the procedure and parameters calculated.

Table 2: Accuracy and precision of proposed method.

Ibuprofen µg/mL		% Recovery		% Error	R.S.D n = 3
Taken	Found				
2	2.01	100.50	Mean = 100.72 S.D. = 1.77	0.50	0.53
5	4.97	99.40		0.60	1.03
8	8.18	102.25		2.25	1.12
Caffeine µg/mL		% Recovery		% Error	R.S.D n = 3
Taken	Found				
2	2.06	103.00	Mean = 100.90 S.D. = 2.42	3.00	0.19
5	5.01	100.2		0.20	0.61
8	7.96	99.50		0.50	1.09

T-test carried out as shown in Table 3, indicated that there was no significant difference between the developed method and the official one at 95% confidence interval as the calculated t-value is less than tabulated one.

Table 3: Comparison between the new method and official methods.

Sample No.	Drug Sample	% Recovery	
		New Method	Official Method
1	Ibuprofen	102.88	99.70 [17]
2	Caffeine	99.95	98.66[18]

Quantitative assessment of drugs in tablets and in standard mixture

We attended three mixtures of standard drugs at different concentrations as shown in Table 4**.**

Table 4: **Analysis of standard mixture of drugs.**

Mix. No.	St. drug µg/mL		Mean amount found µg/mL		% Mean amount found		R.S.D n = 3	
	IB	CAF	IB	CAF	IB	CAF	IB	CAF
1	12	8	12.06	7.94	100.50	99.25	0.115	0.102
2	9	11	8.99	10.86	99.88	98.73	0.126	0.123
3	7	7	6.97	7.07	99.57	101.00	0.118	0.114

Foure types of pharmaceutical formulations of drugs have been analyzed as described under recommended procedure, a good accuracy and precision were obtained as shown in Table 5.

Table 5: **Analysis of pharmaceutical formulation.**

Sample company	Label Claim mg/ tab.		Mean amount found mg/ tab.		% Mean amount found		R.S.D n = 3	
	IB	CAF	IB	CAF	IB	CAF	IB	CAF
Ibuprofen-Ajanta	400	65	395.12	64.68	98.78	99.50	0.203	0.152
Ibuprofen-Julphar	400	50	391.92	49.45	97.98	98.90	0.135	0.116
Algesic-SDI	8	50	8.03	49.34	100.38	98.67	0.121	0.315
Extra Panadol-POZO	10	65	9.87	64.36	98.70	99.01	0.143	0.261

Obtained results were confirmed the reality and the applicability of the proposed method for the determination of IB and CAF in pharmaceutical manufactured and in standard mixture. The results indicate that the recovery percentages for applying method (98.73-101.00) for standard drugs sample and the quantity of drugs in tablets was accepted within the normal percentage according to official method. Recovery percentages for drugs in manufactured tablets were found to range from 97.98– 100.38%, which confirmed the validity of the method for analysis the drugs in pharmaceutical formulations. The results in Table 6, revealed that the difference of drugs absorbance in mixtures and in drugs solutions alone for three selected concentrations were in acceptable range (0.77 – 1.74), that mean the results obtain are with good accuracy.

Table 6: Absorbance of selected concentration of drugs in mixture and alone.

Drugs	Conc. µg/mL	Abs. in mixture	Drug abs.	Difference	% diff.	Mean
IB	10	1.1512	1.1421	0.0091	0.79	Mean = 0.77 S.D. =0.33
	15	1.4655	1.4584	0.0071	0.48	
	20	1.8331	1.8142	0.0189	1.04	
CAF	10	1.6897	1.6435	0.0462	2.81	Mean = 1.74 S.D. =1.24
	15	2.3302	2.3133	0.0169	0.73	
	20	3.0568	3.0064	0.0504	1.68	

CONCLUSIONS

The most striking feature of this novel method is its simplicity, rapidity and economy, UV spectrophotometric method for the quantitative determination of (IB, CAF) in standard and pharmaceutical manufactured mixture samples simultaneously without any separation method. The new method can be employed for routine analysis in quality control drugs analysis. The described methods give accurate and precise results for the determination of (IB, CAF) in another mixture in marketed formulation with recovery percentages range of 97.98– 100.38%.

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