Simultaneous Spectrophotometric Determination of Aspirin and Codeine.

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ABSTRACT

A novel, accurate, and simple UV – spectrophotometric method for simultaneous determination of Aspirin (ASP) and Codeine (COD) in mixture of standard and tablets formulation was investigated in this work without any separation method between the drugs. The absorption maxima of drugs in mixture were found to be at (238 nm and 278 nm) for ASP and COD respectively, in deionized water: acetonitrile mixture (H_2O: ACN 90:10 v/v) as solvent. These wavelengths were selected for the analysis of drugs as mixture standard and formulated samples. The purposed method is linear in the concentration range of (0.3 – 30 µg/mL) for ASP and COD in the mixture, with R^2 values of (0.9992, 0.9991) for ASP and COD respectively. Recovery means were found to be (100.13, 99.81) for ASP and COD respectively. The method was applied for the estimation of the active gradient of the drugs in different samples of formulated dosage. The accuracy of method was validated by mean percentage recovery which was found to be in the acceptable range.
Keywords: Novel, Simultaneous, Formulated, Recovery.

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INTRODUCTION

Aspirin and codeine are classified from Mild analgesics, which appear good coughing to relieve and remove pain simple to medium intensity such as arthritis, minor injuries, headaches and postpartum pain, and the reason of the effect of these drugs is its direct impact on the central nervous system and peripheral [1] ,There is no analgesic agent to treat all forms of pain and there is no ideal analgesic factor. Hence, clinical outcomes might be improved under certain conditions with the use of a combination of analgesics, rather than reliance on a single agent. A combination is most effective when the individual agents act through different analgesic mechanisms and act synergistically. By activating multiple pain-inhibitory pathways, combination analgesics can provide more effective pain relief for a broader spectrum of pain, and might also reduce adverse drug reactions. This overview highlights the therapeutic potential of combining analgesic medications with different mechanisms of action, particularly aspirin with an opioid [2, 3]. COD is an opioid analgesic and has been one of the most powerful analgesics. This drug was used to treat acute pain and for progressive severe chronic illnesses [4]. ASP classified as nonsteroidal anti-inflammatory drug (NSAID) analgesics, is often used as an analgesic, antipyretic, anti-inflammatory and also has an antiplatelet effect by inhibiting the production of thromboxane, which under normal circumstances binds platelet molecule together to create a patch over damage of the walls within blood vessels [5,6]. Numerous analytical methods were reported for the determination of this drugs in pharmaceuticals such as HPLC [7-10], Electromagnetic [11], Spectrophotometric [12-15], Ion selective electrode [16], Thermo gravimetric analysis (TGA) [17], Voltammetry [18]. Aim of this work is to use the ease and accurate spectrophotometric method for the determine the 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

ASP and COD were supplied from Samara Drug Industries (SDI), Iraq. Different Tablets were used as marketed formulation, Table 4. Acetonitrile HPLC grade (BDH) and freshly prepared deionized water was used throughout the experiment

Apparatus

UV - VIS spectrophotometer (Jasco V-650 Japan), Sartorius balance (Germany), sonic bath (Korea), shaking water bath (Taiwan) and furnace (Germany) were used through this study .

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

A 0.01 g of each standard drugs were weighed and dissolved in (H_2O: ACN 90:10 v/v), transferred to a 100 mL two 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 crushed to a powder. Amount equivalent to 0.1 g was weighed, 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 and it's weight.

RESULTS AND DISCUSSION

Determination wavelength of maximum absorbance

The UV-VIS spectra of drugs mixture solution was carried out, the maximum absorbance was found at λ_{max} (238 nm and 278 nm) for ASP and COD respectively as shown in Fig. 1.
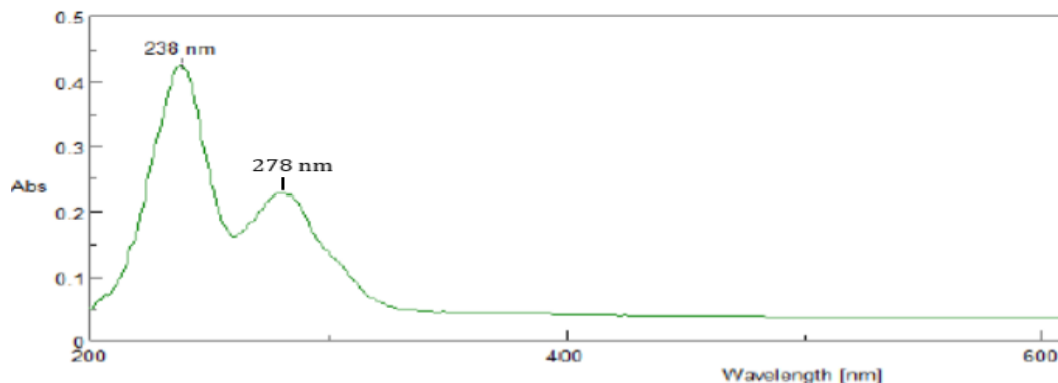

Fig: 1: UV – Spectrum of aspirin and codeine mixture

Preparation of calibration curves

The stock solution of drugs were appropriately diluted with (H_2O: ACN 90:10 v/v). The two similar drug concentrations is mixed together to obtain ASP and COD mixture have concentration range of (0.3-30 µg/mL) for each one of the two drugs. A series of concentrates for each drug was prepared within its range of concentrations (0.5-30 µg/mL) and (1-30 µg/mL) for ASP and COD. Absorbance of all solution was measured at λ_{max} of each drugs. The calibration curves Fig. 2 and 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 methods are linear with R^2 of (0.9992 , 0.9991) for ASP and COD in mixture respectively, and (0.9991,0.9993)) for ASP and COD alone respectively, indicating that there is a strong correlation between the variation of concentration and response. Linearity was determined by the regression analysis.
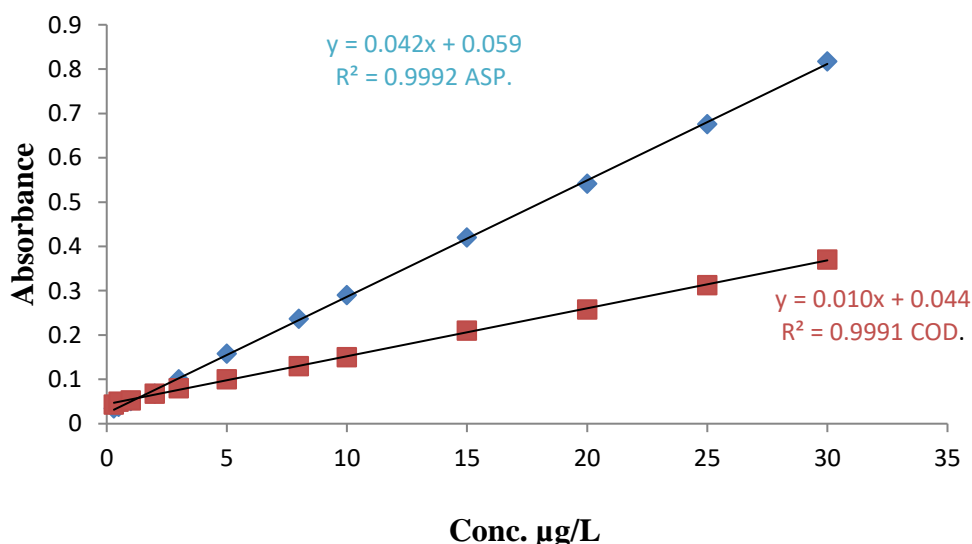

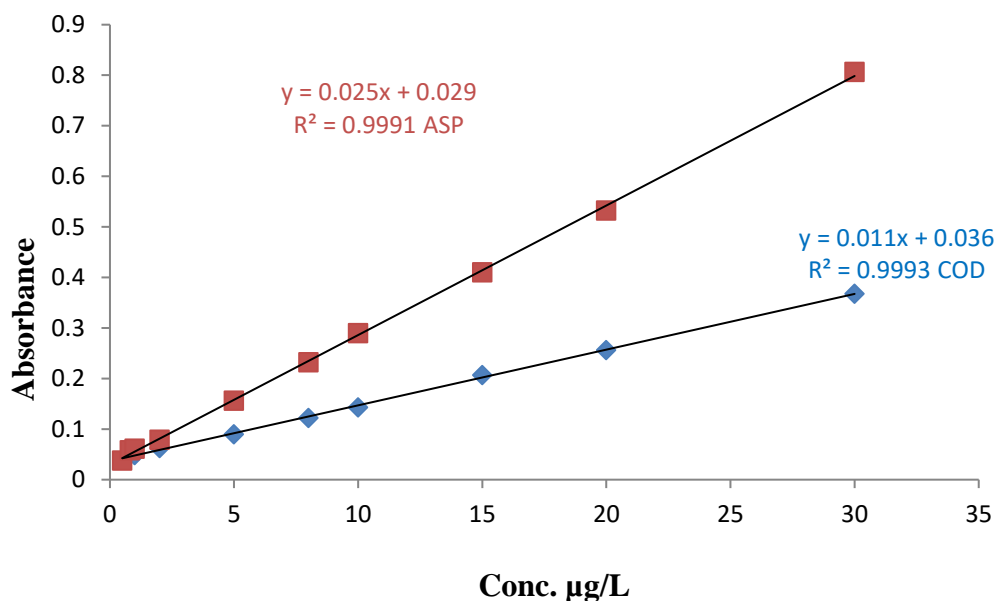**Fig: 2: Calibration curves of ASP and COD in mixture**

Fig: 3: Calibration curves of ASP and COD alone

Table 1: Calibration curves statistical calculation

Statistical factors	Value			
	Aspirin		Codeine	
	Drug in mix.	Drug alone	Drug in mix.	Drug alone
Linear equation	y=0.042[X] +0.059	y=0.025[X] +0.029	y=0.010[X] +0.044	y=0.011[X] +0.036
Slope (m)	0.042	0.025	0.010	0.011
Intercept	0.059	0.029	0.044	0.036
Correlation coefficient "R^2"	0.9992	0.9991	0.9991	0.9993
Percentage linearity (R^2%)	99.92	99.91	99.91	99.93
Correlation coefficient (r)	0.99959	0.99954	0.99954	0.99964
Intercept standard error	0.00198	0.00283	0.00115	0.001841
Intercept standard deviation	0.00689	0.00896	0.00399	0.005208
"R.S.D."	2.41	3.36	2.62	3.21
"LOD" µg/mL	0.5414	1.1827	1.3180	1.5624
"LOQ" µg/mL	1.6407	3.584	3.994	4.7345
Linearity range µg/mL	0.3 − 30	0.5 − 30	0.3 − 30	1 − 30
Molar Absorptivity L. mol.$^{-1}$. Cm^{-1}	$4.91*10^3$	$4.84*10^3$	$3.69*10^3$	$3.67*10^3$
Calculated (t) values $t_{cal.} = \dfrac{/r/\sqrt{n-2}}{\sqrt{1-r^2}}$	111.76 >>> 2.18	94.23 >>> 2.23	105.3 >>> 2.18	65.58 >>> 2.31

Accuracy and precision of proposed method

ASP and COD 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 two drugs is quite satisfactory in reality with respect to the procedure and parameters calculated.

Table 2: Accuracy and precision of proposed method.

Aspirin µg/mL		% Recovery		% Error	R.S.D n = 3
Taken	Found				
2	2.01	100.50	Mean = 100.13	0.50	0.101
5	5.00	100,00	S.D. = 0.41	0	0.009
8	7.99	99.88		0.12	0.112
Codeine µg/mL		% Recovery		% Error	R.S.D n = 3
Taken	Found				
2	1.98	99.00	Mean = 99.81	1.00	0.103
5	4.99	99.80	S.D. = 0.03	0.20	0.014
8	8.05	100.63		0.63	0.107

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	Aspirin	100.13	98.42 [19]
2	Codeine	99.81	100.2 [20]

Quantitative assessment of drugs in tablets and in standard mixture

We attended a standard mixture 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	
	ASP	COD	ASP	COD	ASP	COD	ASP	COD
1	12	8	11.89	8.02	99.08	100.25	0.101	0.112
2	9	11	8.98	10.79	99.77	98.09	0.107	0.104
3	7	7	7.03	6.95	100.43	99.28	0.101	0.099

Three types of pharmaceutical formulations of drugs have been analyzed as described under recommended procedure, a good accuracy and precision were obtained. COD was added to commercial formulated sample as shown in Table 5.

Table 5 : Analysis of pharmaceutical formulation

Aspirin company	Label Claim mg/ tab.		Mean amount found mg/ tab.		% Mean amount found		R.S.D n = 3	
	ASP	COD	ASP	COD	ASP	COD	ASP	COD
SDI	100	8	99.36	7.96	99.36	99.50	0.243	0.102
Wockhardt	300	10	297.55	9.89	99.18	98.90	0.335	0.109
Bayer	81	5	80.96	5.01	99.51	100.20	0.104	0.089

Obtained results were confirmed the reality and the applicability of the proposed method for the determination of ASP and COD in pharmaceutical formulations and in standard mixture. The results indicate that the recovery percentages for applying method (98.09-100.43) 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 formulate tablets were found to range from 98.90 – 100.20 %, 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 mixture and in drugs solutions alone for three selected concentrations was in acceptable range (0.91 – 1.98), that mean the results obtain are with a 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
COD	15	0.2101	0.2067	0.0034	1.64	Mean = 0.91 S.D. =0.84
	20	0.2576	0.2564	0.0012	0.47	
	30	0.3701	0.3678	0.0023	0.63	
ASP	15	0.4199	0.4102	0.0097	2.63	Mean = 1.98 S.D. =0.91
	20	0.5414	0.5324	0.009	1.69	
	30	0.8176	0.8067	0.011	1.35	

CONCLUSIONS

The most striking feature of this novel method is its simplicity, rapidity and economy, UV spectrophotometric method for the quantitative determination of ASP and COD in standard and pharmaceutical formulated 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 ASP and COD mixture in marketed formulation with recovery percentages range of 98.90 – 100.20 % for the two drugs.

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