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SIMULTANEOUS SPECTROPHOTOMETRIC DETERMINATION OF PARACETAMOL AND CODEINE

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ABSTRACT

A novel, accurate, and simple UV – spectrophotometric method for simultaneous determination of paracetamol (PCM) and codeine (COD) in mixture of standard and tablets formulation was verification in this work without any separation method between the two drugs. The maximum absorbance of drugs in mixture was found to be at (243 nm and 278 nm) for PCM and COD respectively, in deionized water: acetonitrile mixture (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 PCM and COD in the mixture respectively, with R^2 values of (0.9993, 0.9995) for PCM and COD. Recovery means were found to be (99.04, 100.53) for PCM 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.

INTRODUCTION

Paracetamol 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 paracetamol 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] PCM classified as nonsteroidal anti-inflammatory drug (NSAID) analgesics, is often used as an analgesic, joint aches, middle ear aches, a painkiller effect on headaches, toothaches, neuralgia, aches stem from cold, flue and lumbago.[5] Numerous analytical methods were reported for the determination of this drugs in pharmaceuticals such as SP-FT-Raman[6], HPLC[7-10], Electromagnetic[11], Spectrophotometric[12-15], Ion selective electrode[16], Thermogravimetric analysis (TGA)[17] and 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

PCM 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 solutions was carried out, the maximum absorbance was found at λ_{max} (243 nm and 278 nm) for PCM and COD respectively as shown in Fig. 1.

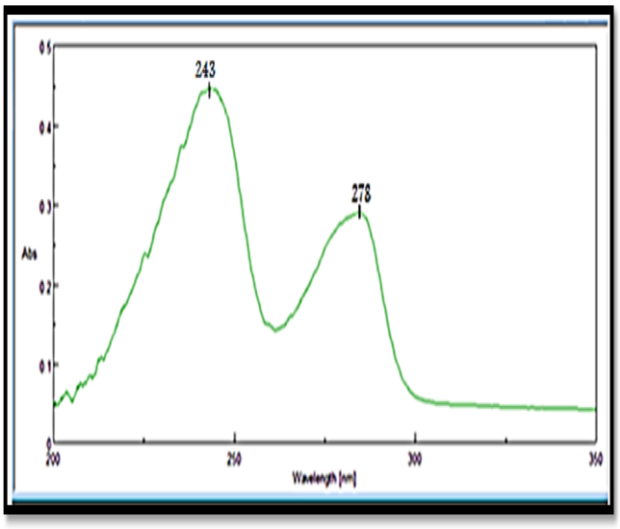

Fig. 1: UV – Spectrum of Paracetamol and codeine mixture.

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 was mixed together to obtain PCM and COD 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 µg/mL) and (1-30 µg/mL) for PCM and COD. Absorbance of all solutions was measured at λ_{max} of each drug. 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 method is linear with an R^2 of (0.9993 , 0.9995) for PCM and COD in mixture respectively, and (0.9992,0.9996)) for PCM 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.

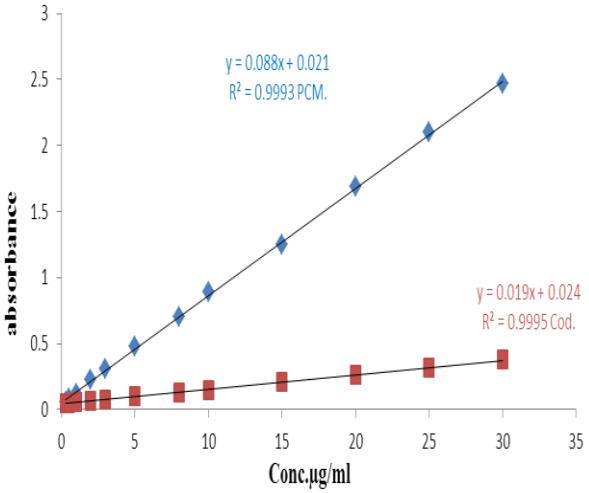

Fig. 2: Calibration curves of PCM and COD in mixture.

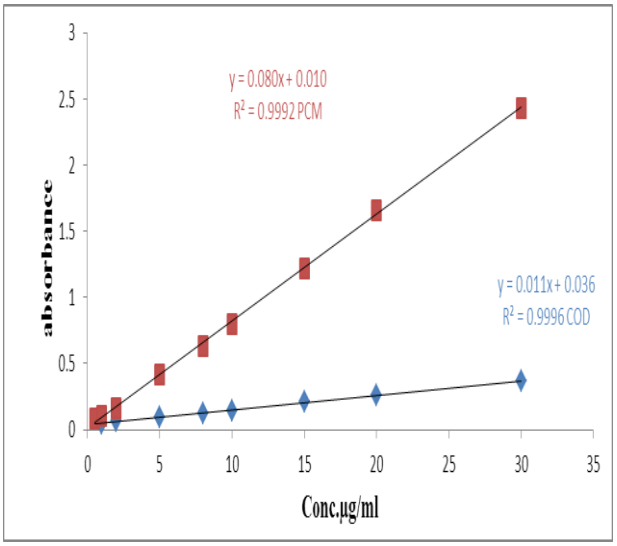

Fig. 3: Calibration curves of PCM and COD alone.

Table. 1: Calibration curves statistical calculations.

Statistical factors	Value			
	Paracetamol		Codeine	
	Drug in mix.	Drug only	Drug in mix.	Drug only
Linear equation	y=0.088 [X]+0.021	y=0.080 [X]+0.010	y=0.019 [X]+0.024	y=0.011[X]+0.036
Slope (m)	0.088	0.080	0.019	0.011
Intercept	0.021	0.010	0.024	0.036
Correlation coefficient "R^2"	0.9993	0.9992	0.9995	0.9996
Percentage linearity (R^2%)	99.93	99.92	99.95	99.96
Correlation coefficient (r)	0.9996	0.9995	0.9997	0.9997
Intercept standard error	0.007237	0.011060	0.00157	0.00184
Intercept standard deviation	0.02507	0.03318	0.005462	0.005208
"R.S.D."	2.901	3.978	3.584	3.21
"LOD" µg/mL	0.03	0.1	0.05	0.08
"LOQ" µg/mL	0.099	0.33	0.165	0.26
Linearity range µg/mL	0.3 – 30	0.5 – 30	0.3 – 30	1 – 30
Molar Absorptivity L. mol.$^{-1}$. Cm^{-1}	$1.2427*10^4$	$1.224*10^4$	$0.3778*10^4$	$0.367*10^4$
Calculated (t) values $t_{cal.} = \frac{/r/\sqrt{n-2}}{\sqrt{1-r^2}}$	119.51 >>> 2.18	93.51 >>> 2.26	141.38 >>> 2.18	122.44 >>> 2.31

Accuracy and precision of proposed method

PCM 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.

Paracetamol mg/L		% Recovery		% Error	R.S.D n = 3
Taken	**Found**				
2	1.95	97.50	Mean = 99.04 S.D. = 2.26	2.50	1.07
5	5.05	101.00		1.00	0.88
8	7.89	98.63		1.37	1.12
Codeine mg/L		**% Recovery**		**% Error**	**R.S.D n = 3**
Taken	**Found**				
2	2.03	101.50	Mean = 100.53 S.D. = 1.19	1.50	1.16
5	5.03	100.6		0.60	0.75
8	7.96	99.50		0.50	0.51

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	Paracetamol	100.5	100.5[19]
2	Codeine	100.17	100.2[20]

Quantitative assessment of drugs in tablets and 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 mg/L		Mean amount found mg/L.		% Mean amount found		R.S.D n = 3	
	PCM	COD	PCM	COD	PCM	COD	PCM	COD
1	12	8	11.87	8.02	98.92	100.3	0.234	0.214
2	9	11	8.91	10.85	99.00	98.67	0.146	0.132
3	7	7	7.05	6.88	100.71	98.29	0.112	0.109

Two 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	
	PCM	COD	PCM	COD	PCM	COD	PCM	COD
Algesic SDI	325	10	321	10.07	98.77	100.70	0.426	0.213
Co-codamol Bristol	500	8	490.25	8.18	98.05	102.25	0.657	0.154

Obtained results were confirmed the reality and the applicability of the proposed method for the determination of PCM and COD in pharmaceutical formulations and in standard mixture. The results indicate that the recovery percentages for applying method (98.29-100.71) 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 98.05 – 102.25 %, 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 (2.17 – 1.71), 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
COD	15	0.2113	0.2067	0.0046	2.23	Mean = 2.17 S.D. =0.96
	20	0.2598	0.2564	0.0034	1.33	
	30	0.3786	0.3678	0.0108	2.94	
PCM	15	1.2488	1.2231	0.0257	2.10	Mean = 1.71 S.D. =0.46
	20	1.6879	1.6631	0.0248	1.49	
	30	2.4657	2.4286	0.0371	1.53	

CONCLUSIONS

The most striking feature of this novel method is its simplicity, rapidity and economy, UV spectrophotometric method for the quantitative determination of PCM 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 PCM and COD mixture in market formulation with recovery percentages range of 98.05 – 102.25 % for the two drugs.

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