

**ESTIMATION OF PARACETAMOL, ASPIRIN, IBUPROFEN, CODEINE AND
CAFFEINE IN SOME FORMULATED COMMERCIAL DOSAGE USING UV –
SPECTROSCOPIC METHOD.**Ahmed Mahdi Saeed*¹ and Noor Qasim Ahmed²¹Department of Chemistry, College of Education for Pure Science, University of Diyala, Diyala, Iraq.²Department of Chemistry, College of Science, University of Diyala, Diyala, Iraq.***Corresponding Author: Dr. Ahmed Mahdi Saeed**

Department of Chemistry, College of Education for Pure Science, University of Diyala, Diyala, Iraq.

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ABSTRACT

The estimation of paracetamol (PCM), aspirin (ASP), ibuprofen (IB), codeine (COD) and caffeine (CAF) drugs percentage in standard and some formulated commercial dosage using UV-Spectroscopic method was investigated in this work. The absorption maxima of drugs were found to be at (244.8 nm, 238 nm, 220.6 nm, 278 nm and 272.6 nm) for PCM, ASP, IB, COD and CAF respectively in deionized water: acetonitrile (90:10 v/v) as solvent. These wavelengths were selected for the analysis of drugs as standard and formulated samples. The purposed method obeyed Beer-Lambert's Law in the concentration range of (0.4-40 µg/mL) for PCM, (0.5-100 µg/mL) for ASP, (0.4-40 µg/mL) for IB, (1-100 µg/mL) for COD and (0.2-20 µg/mL) for CAF with R² values of (0.9994, 0.9989, 0.9992, 0.9995 and 0.9979) for PCM, ASP, IB, COD and CAF respectively. Recovery means were found to be (100.05, 102.20, 102.88, 100.17, and 99.95) for PCM, ASP, IB, COD and CAF. 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: Estimation, UV- Spectroscopic, Formulated, Recovery.**INTRODUCTION**

There is no analgesic agent to treat all forms of pain and there is no ideal analgesic factor, but each worker has advantages and disadvantages to distinguish him from the rest of the painkillers.^[1] Each mechanical dwelling has a special function to inhibit pain. For non-steroidal anti-inflammatory drugs (NSAIDs), its mechanism of action is its ability to inhibition the enzyme (COX) responsible for the synthesis of prostaglandins (pain transducers)^[2], PCM, ASP and IB are classified as (NSAIDs) and each of these analgesics has advantages over the other.^[3] PCM used to joint aches, middle ear aches, a painkiller effect on headaches, toothaches, neuralgia, aches stem from cold, flue and lumbago.^[4] ASP used as an analgesic and antipyretic, is also used in low doses as a blood thinner to prevent blood clots.^[5] IB used extensively in the treatment of chronic pain and acute osteoarthritis, related conditions and rheumatoid arthritis.^[6] 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.^[7] CAF which is considered as an alkaloid of the Purina group^[8] used both recreationally and medically. It produces increased wakefulness, focus and better general body coordination.^[9] It is usually in combination with analgesic drugs such as paracetamol to increase the effectiveness of the dwelling.^[10] Numerous

analytical methods were reported for the determination of this drugs in pharmaceuticals such as SP-FT-Raman^[11], HPLC^[12-15], Electromagnetic^[16], GC/MS^[17], Spectrophotometric^[18-21], GC- Ion trap^[22] and Ion Selective Electrode^[23]. 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 METHODS**Materials**

PCM, ASP, IB, COD and CAF 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 µg/mL)

Five portions of 0.01 g of each standard drugs were weighed and dissolved in (H₂O: ACN 90:10 v/v), transferred to a 100 mL five 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 (H₂O: 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 solutions were carried out, the maximum absorbance was found at λ_{\max} (244.8 nm, 238 nm, 220.6 nm, 278 nm and 272.6 nm) for PCM, ASP, IB, COD and CAF respectively as shown in (Fig 1).

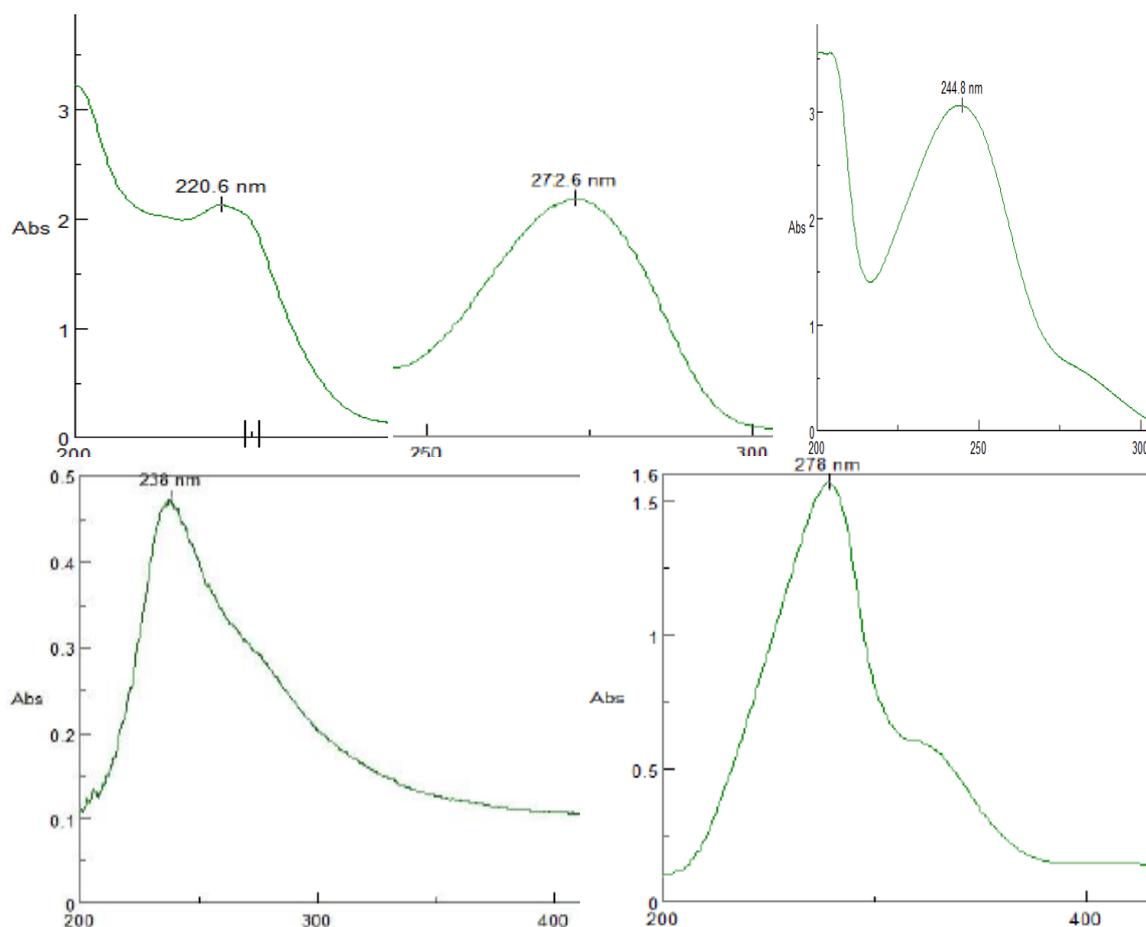


Fig: 1: UV – Spectrum of drugs.

Preparation of calibration curves

The stock solution of drugs were appropriately diluted with (H₂O: ACN 90:10 v/v) to obtain concentration range of (0.4-40, 0.5-100, 0.4-40, 1-100 and 0.2-20 µg/mL) for PCM, ASP, IB, COD and CAF respectively and measured at λ_{\max} of each drugs. The calibration curves (Fig 2) 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 were linear with an R^2 of (0.9994, 0.9989, 0.9992, 0.9995 and 0.9979) for PCM, ASP, IB, COD and CAF respectively, indicating that there is a strong correlation between the variation of concentration and response. Linearity was determined by the regression analysis.

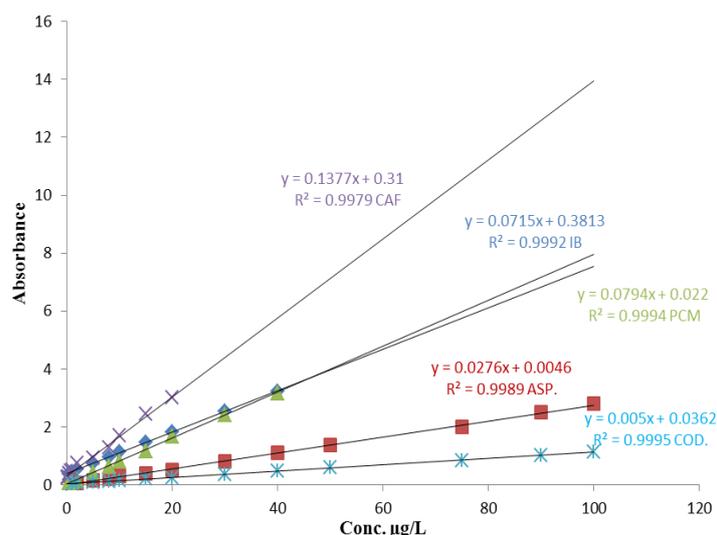


Fig. 2: Drugs calibration curves

Table 1: Calibration curve statistical calculations

Statistical factors	Value				
	Paracetamol	Aspirin	Ibuprofen	Codeine	Caffeine
Linear equation	$y = 0.0794[X] + 0.022$	$y = 0.0276[X] + 0.0046$	$y = 0.0715[X] + 0.381$	$y = 0.005[X] + 0.0362$	$y = 0.1377[X] + 0.31$
Slope (m)	0.0794	0.0276	0.0715	0.005	0.1377
Intercept	0.022	0.0046	0.3813	0.0362	0.31
Correlation coefficient "R ² "	0.9994	0.9989	0.9992	0.9995	0.9979
Percentage linearity (R ² %)	99.94	99.89	99.92	99.95	99.79
Correlation coefficient (r)	0.9996	0.9994	0.9995	0.9997	0.9989
Intercept standard error	0.0104	0.0122	0.0103	0.0042	0.0293
Intercept standard deviation	0.0360	0.0458	0.0358	0.0152	0.1058
"R.S.D."	0.2888	0.2664	0.2877	0.2763	0.2769
"LOD" µg/mL	0.4	0.5	0.4	1	0.2
"LOQ" µg/mL	1.32	1.65	1.32	3.30	0.66
Linearity range µg/mL	0.4-40	0.5-100	0.4-40	1-100	0.2-20
Molar Absorptivity L. mol. ⁻¹ . Cm ⁻¹	1.198×10^4	5.070×10^3	1.656×10^4	3.364×10^3	2.919×10^4
Calculated (t) values $t_{cal.} = \frac{t/r/\sqrt{n-2}}{\sqrt{1-r^2}}$	129.03 >> 2.179	104.28 >> 2.145	111.69 >> 2.179	148.02 >> 2.160	68.97 >> 2.179

Accuracy and precision of proposed method

PCM, ASP, IB, COD and CAF was determined at three different selected concentrations (3, 5, 10 µg /mL). The obtained results were tabulated in (Table 2), which

indicated that the proposed method for the determination of five drugs using this method was 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				
3	3.05	101.66	Mean = 102.88 S.D. = 1.2722	1.66	0.15
5	5.21	104.20		4.20	0.13
10	10.28	102.80		2.80	0.12
Aspirin µg/mL		% Recovery		% Error	R.S.D n = 3
Taken	Found				
3	3.12	104.00	Mean = 102.20 S.D. = 2.9461	4.00	0.20
5	5.19	103.80		3.80	0.14
10	9.88	98.80		1.20	0.11
Paracetamol µg/mL		% Recovery		% Error	R.S.D n = 3
Taken	Found				

3	2.96	98.66	Mean = 100.05 S.D. = 1.3260	1.34	0.17
5	5.01	100.2		0.20	0.08
10	10.13	101.3		1.30	0.12
Caffeine µg/mL		% Recovery		% Error	R.S.D n = 3
Taken	Found				
3	2.99	99.66	Mean = 99.95 S.D. = 0.2730	0.34	0.10
5	5.00	100.0		0	0.01
10	10.02	100.2		0.2	0.09
Codeine µg/mL		% Recovery		% Error	R.S.D n = 3
Taken	Found				
3	3.01	100.33	Mean = 100.17 S.D. = 0.5173	0.33	0.06
5	5.03	100.6		0.60	0.10
10	9.96	99.60		0.40	0.11

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	100.05	100.26 ^[24]
2	Aspirin	102.20	98.42 ^[25]
3	Ibuprofen	102.88	99.70 ^[26]
4	Codeine	100.17	100.2 ^[27]
5	Caffeine	99.95	98.66 ^[28]

Quantitative assessment of drugs in tablets

Twelve types of pharmaceutical formulations of drugs have been analyzed as described under recommended procedure, a good accuracy and precision were obtained. COD and CAF were added to commercial formulated sample as shown in Table 4. Obtained results were confirmed the reality and the applicability of the proposed method for the determination of PCM, ASP, IB, COD and CAF in pharmaceutical formulations. The

results indicate that the recovery percentages for applying methods are with an acceptable range of (99.95-102.88) 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 – 102.53 %, which confirmed the validity of the method for analysis the drugs in pharmaceutical formulations.

Table 4: Estimated quantity of drugs in different tablets sample

Ibuprofen	Label Claim	Mean amount	% Mean amount	R.S.D
Company	mg/ tab.	found mg/tab.	found	n = 3
Ajanta	400	397.04	99.26	0.113
Julphar	400	398.92	99.73	0.116
Aspirin	Label Claim	Mean amount	% Mean amount	R.S.D
Company	mg/ tab.	found mg/tab.	found	n = 3
SDI	100	102.53	102.53	0.108
Wockhardt	300	298.52	99.53	0.118
Bayer	81	81.24	100.3	0.105
Paracetamol	Label Claim	Mean amount	% Mean amount	R.S.D
Company	mg/ tab.	found mg/tab.	found	n = 3
Troge	500	498.85	99.77	0.116
SDI	500	494.50	98.90	0.120
Meheco	500	500.50	100.10	0.117
Caffeine	Label Claim	Mean amount	% Mean amount	R.S.D
Sample	mg/ tab.	found mg/tab.	found	n = 3
Panadol extra	65	64.61	99.40	0.105
Algesic SDI	50	50.56	101.12	0.101
Codeine	Label Claim	Mean amount	% Mean amount	R.S.D
Sample	mg/ tab.	found mg/tab.	found	n = 3

Algesic SDI	10	10.15	101.5	0.098
Co-codamol	8	7.98	99.75	0.076

CONCLUSIONS

A simple, rapid, accurate, precise, and economical UV spectrophotometric method for the quantitative determination of PCM, ASP, IB, COD and CAF in bulk and pharmaceutical formulations. The method was linear with an R^2 value of (0.9994, 0.9989, 0.9992, 0.9995 and 0.9979) for PCM, ASP, IB, COD and CAF respectively. Results of this study were compared with the official method and are very close and good. The accuracy of method was validated by mean percentage recovery which was found to be in the acceptable range.

REFERENCES

- Raffa, R. B. Pharmacology of oral combination analgesics: rational therapy for pain. *Journal of Clinical Pharmacy and Therapeutics*, 2001; 26(4): 257-264.
- Madni, A. U., Ahmad, M., Akhtar, N. and Usman, M. New simultaneous High Performance Liquid Chromatographic method for determination of NSAIDs and opioid analgesics in advanced drug delivery systems and human plasma. *World Academy of Science, Engineering and Technology*, 2009; 3(7): 158-163.
- Van Dyke, T., Litkowski, L. J., Kiersch, T. A., Zarringhalam, N. M., Zheng, H. and Newman, K. Combination oxycodone 5 mg/ibuprofen 400 mg for the treatment of postoperative pain: a double-blind, placebo-and active-controlled parallel-group study. *Clinical Therapeutics*, 2004; 26(12): 2003-2014.
- Tunca, A. K. Quantitative Analysis of Paracetamol, Acetyl cysteine and Guaifenesin in Commercial Cold Medicines by UV-Vis Spectroscopy. *Sop Transactions On Analytical Chemistry*, 2014; 1(1): 40-47.
- Pawar, P. Y., Ankita, R., Lokhande, B. R. and Bankar, A. A. Simultaneous estimation of atorvastatin calcium and aspirin in pure and capsule dosage form by using UV spectrophotometric method. *Der. Pharma Chemica*, 2013; 5(3): 98-103.
- Grisales, J. O., Arancibia, J. A. and Olivieri, A. C. Determination of enantiomeric composition of ibuprofen in pharmaceutical formulations by partial least-squares regression of strongly overlapped chromatographic profiles. *Journal of Chromatography B*, 2012; 910: 78-83.
- Švorc, L., Sochr, J., Svítková, J., Rievaj, M. and Bustin, D. Rapid and sensitive electrochemical determination of codeine in pharmaceutical formulations and human urine using a boron-doped diamond film electrode. *Electrochimica Acta*, 2013; 87: 503-510.
- Andrews K., Schweitzer A., Zhao C., Holden J.M., Roseland J.M., Brandt M., Dwyer J., Picciano M., Saldanha L., Fisher K., Yetley E., Betz J. and Douglass L., The caffeine content of dietary supplements commonly purchased in the U.S.: Analysis of 53 products having caffeine containing ingredients, *Analytical and Bio analytical Chemistry*, 2007; 389(1): 231-239.
- Patil, P. N. Caffeine in various samples and their analysis with HPLC-A review. *International Journal of Pharmaceutical Sciences Review and Resear*, 2012; 16(2): 76-83.
- Delvadiya, K., Kimbahune, R., Kabra, P., Sunil, K. and Patel, P. Spectrophotometric simultaneous analysis of paracetamol, propyphenazone and caffeine in tablet dosage forms. *Der. PharmaChemica*, 2011; 3(3): 170-74.
- Armenta, S., Garrigues, S. and de la Guardia, M. Solid-phase FT-Raman determination of caffeine in energy drinks. *Analytica Chimica Acta*, 2005; 547(2): 197-203.
- Franeta, J. T., Agbaba, D., Eric, S., Pavkov, S., Aleksic, M. and Vladimirov, S. (2002). HPLC assay of acetylsalicylic acid, paracetamol, caffeine in tablets. *Farmaco*, 57 (9): 709-713.
- Gandhimathi, M., Ravi, T. K., Abraham, A. and Thomas, R. Simultaneous determination of aspirin and isosorbide 5-mononitrate in formulation by reversed phase high pressure liquid chromatography. *Journal of pharmaceutical and biomedical analysis*, 2003; 32(6): 1145-1148.
- Nogueira, T. and do Lago, C. L. Determination of caffeine in coffee products by dynamic complexation with 3, 4-dimethoxycinnamate and separation by CZE. *Electrophoresis*, 2007; 28(19): 3570-3574.
- Ramjith, U. S., Sunith, D. K. and Sameer, P. A. HPLC study of aspirin and aspirin derivatives. *International Journal Of Research In Pharmacy And Chemistry*, 2013; 3(1): 1-5.
- Yang, X., Feng, J., Chen, Z., Liao, R. and Li, X. Determination of six analgesics by CE with an improved electromagnetic induction detector. *Chromatographia*, 2012; 75(1-2): 71-76.
- Hu, Z., Zou, Q., Tian, J., Sun, L. and Zhang, Z. Simultaneous determination of codeine, ephedrine, guaifenesin and chlorpheniramine in beagle dog plasma using high performance liquid chromatography coupled with tandem mass spectrometric detection: application to a bioequivalence study. *Journal of Chromatography B*, 2011; 879(32): 3937-3942.
- Saeed, A. M., Spectrophotometric Determination of Paracetamol in Some Manufactured Tablets in Iraqi markets. *Int. J. Pharm. Sci. Rev. Res.*, 2017; 42(2): 53-57.
- Shahlaei, M., Andisheh, H., Derakhshandeh, K., Havadi, K. S. and Azami, M. A novel method for simultaneous determination of codeine and acetaminophen in plasma by combination of UV-Vis spectroscopy and artificial neural network. *Journal*

- of Reports in Pharmaceutical Sciences, 2014; 3(2): 141-158.
20. Feng, X., Zhang, Q., Cong, P. and Zhu, Z. Determination of the paracetamol degradation process with online UV spectroscopic and multivariate curve resolution-alternating least squares methods: comparative validation by HPLC. *Analytical Methods*, 2013; 5(19): 5286-5293.
 21. Kokot, Z. and Burda, K. Simultaneous determination of salicylic acid and acetylsalicylic acid in aspirin delayed-release tablet formulations by second-derivative UV spectrophotometry. *Journal of pharmaceutical and biomedical analysis*, 1998; 18(4): 871-875.
 22. Verenitch, S. S., Lowe, C. J. and Mazumder, A. Determination of acidic drugs and caffeine in municipal wastewaters and receiving waters by gas chromatography-ion trap tandem mass spectrometry. *Journal of Chromatography A*, 2006; 1116(1): 193-203.
 23. Sanghavi, B. J. and Srivastava, A. K. Simultaneous voltammetric determination of acetaminophen, aspirin and caffeine using an in situ surfactant-modified multiwalled carbon nanotube paste electrode. *Electro chimica Acta*, 2010; 55(28): 8638-8648.
 24. Chandra, R. A. J. U., Verma, D. A. L. E. E. P., Sharma, K. D., Kumar, S. U. J. E. E. T., Alam, M. N. and Singh, S. A. N. J. A. Y. Comparative quantitative determination of Paracetamol by RP-HPLC and UV-Spectrophotometry from its formulated tablets. *International Journal of Pharmacy and Pharmaceutical Sciences*, 5(3): 863-865.
 25. Pawar, P. Y., Ankita, R., Lokhande, B. R. and Bankar, A. A. Simultaneous estimation of atorvastatin calcium and aspirin in pure and capsule dosage form by using UV spectrophotometric method. *Der. Pharma Chemica*, 2013; 5(3): 98-103.
 26. Gondalia, R., Mashru, R. and Savaliya, P. Development and validation of spectrophotometric methods for simultaneous estimation of ibuprofen and paracetamol in soft gelatin capsule by simultaneous equation method. *International Journal of Chem Tech Research*, 2010; 2(4): 1881-1885.
 27. Dinç, E., Baleanu, D. and Onur, F. Simultaneous spectrophotometric analysis of codeine phosphate, acetylsalicylic acid and caffeine in tablets by inverse least-squares and principal component regression techniques. *Analytical letters*, 2002; 35(3): 545-558.
 28. Vichare, V., Mujgond, P., Tambe, V. and Dhole, S. N. Simultaneous spectrophotometric determination of paracetamol and caffeine in tablet formulation. *International Journal of PharmTech Research*, 2010; 2(4): 2512-2516.