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Simultaneous Spectrophotometric determination of Paracetamol and Caffeine in Tablet Formulation

Vijaya Vichare*, Preeti Mujgond, Vrushali Tambe and Dhole S.N.

PES Modern College of Pharmacy for Ladies, Borhadewadi, Dehu-Alandi Road, Moshi, Pune-412105,MS,India

Corres.author : mane_vijaya@yahoo.com
Phone No-02025139177

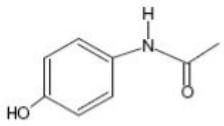
Abstract: Two sensitive, precise, accurate and simple UV spectrophotometric methods have been developed for simultaneous estimation of Paracetamol (PARA) and Caffeine (CAF) in pharmaceutical dosage forms. Method A involved simultaneous equation method. The two wavelengths 243 nm (λ_{max} of Paracetamol) and 273 nm (λ_{max} of Caffeine) were selected for the formation of Simultaneous equations. Whereas method B involved formation of Q-absorbance equation at isobestic point (259.5 nm). Linearity was observed in the concentration range of 2-16 mcg/ml for paracetamol and 2-32 mcg/ml for caffeine by these methods. The proposed methods have been applied successfully to the analysis of cited drugs in pharmaceutical formulations. Recovery study was performed to confirm the accuracy of the methods. The methods were validated as per ICH guidelines.
Keywords: Paracetamol. Caffeine, simultaneous estimation, validation.

INTRODUCTION:

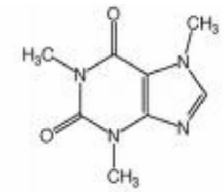
The pharmaceutical formulations with combinations of drugs have shown an increasing trend to counteract the symptoms specific to one drug and formulation, and hence analytical chemist will have to accept the challenge of developing reliable and easy simultaneous estimation methods because it does not require manual individual calculations and gives marginally better results.

Paracetamol (4-acetamidophenol) is one of the most common drugs used in the world. It causes reduction in the amount of prostaglandin, therefore, helps to prevent headache and other pain like migraine headache, muscular aches, neuralgia, backache, joint pain, rheumatic pain, general pain, toothache, teething pain, period pain, and also used for the reduction of fever of bacterial or viral origin. It is suitable for most people, including elderly and young children, because it has very few side effects [1].

Caffeine (1, 3, 7 trimethylxanthine) is mainly used as diuretic, stimulant to the central nervous and to the cardiovascular systems [2]. The use of the mixture of paracetamol and caffeine as an analgesic and antipyretic is well established in pharmaceutical formulation [3]. In order to achieve better curative effect and lower toxicity, it is very important to control the content of paracetamol and caffeine in pharmaceutical tablets [4].



Paracetamol



Caffeine

Literature survey revealed the most recent methods for determination of paracetamol like chromatographic [5-7], electrochemical [8-10] and spectrophotometric [11-13] techniques.
Caffeine is estimated using Spectrophotometry [14], HPLC [15] and FTIR [16]. Various methods like Flow injection–solid phase spectrometry, using C18 silica gel as a sensing support [17], flow-injection spectrophotometric determination in tablets and oral solutions [18], High performance liquid chromatography (HPLC) [19] , Reverse phase High performance liquid chromatography (RP-HPLC) [20], have been described in literature for the determination of paracetamol and caffeine in various biological and pharmaceutical preparations.
However, there are no reports yet for determination of this combination by proposed methods.

MATERIALS AND METHODS

Instrumentation

JASCO V 530 double beam UV-visible spectrophotometer with 1 cm matched quartz cuvettes were used for all absorbance measurements. All weighing were done on single pan balance (Shimadzu).

Reagents and Chemicals:

Paracetamol and caffeine standard samples are kindly provided by Nu-life Pharmaceuticals, Bhosari MIDC, Pune. Multicomponent tablet formulation of Paracetamol (500 mg) and caffeine (32 mg) was considered for analysis. Analytical reagent grade chemicals were used throughout the experiment.

Preparation of standard solutions

Standard stock solutions of both drugs were prepared separately (100 mcg/ml).Standard stock solutions were further diluted with distilled water to obtain concentration ranges of 2 to32 mcg/ml for both drugs.

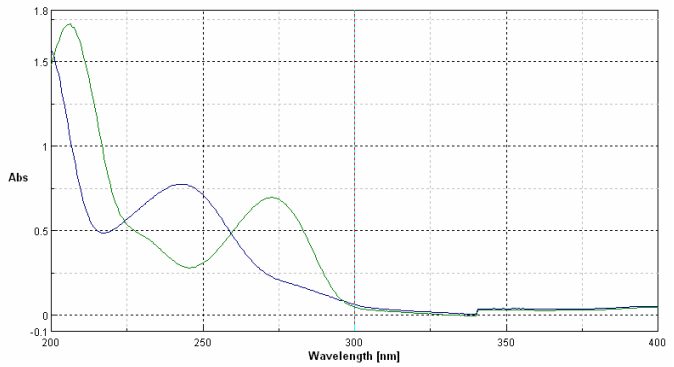
Analysis of tablet formulations

20 tablets were weighed and ground to fine powder. An accurately weighed powder equivalent to 500 mg of Paracetamol and 32 mg of caffeine was transferred to a 100 ml of volumetric flask containing 10 ml methanol and 50 ml of distilled water and ultrasonicated for about 15 min. The volume was made up to the mark with distilled water. The solution was filtered through Whatman filter paper no. 41. Appropriate aliquots were subjected to Method A and Method B. The amounts of PARA and CAF were determined.

Method A: Simultaneous Determination

The standard solutions of PARA and CAF (10 mcg/ml) were scanned seperately in the range of 200 to 400 nm against distilled water as blank and wavelengths of maximum absorbance were determined. The absorbances of all dilutions were recorded at selected wavelengths λ_1 (243 for PARA) and λ_2 (273 for CAF) and calibration curves were plotted. The overlay spectrum of these drugs is shown in Fig. 1. Absorptivity coefficients of two drugs were determined at both wavelengths and two simultaneous equations were formed.

Fig-1 Overlay spectra of PARA and CAF.



243nm (λmax for PARA), 273 nm (λmax of Caffeine) and 259.5 nm (isobestic point)
The concentrations of drugs were determined using following equations.

$Cx = (A_2 . ay1 - A_1 . ay2) / (ax2.ay1 - ax1.ay2)$

$Cy = (A_1 . ax2 - A_2 . ax1) / (ax2.ay1 - ax1.ay2)$

Where
Cx = Concentration of Paracetamol in gms/lit
Cy = Concentration of caffeine in gms/lit
A_2 =Absorbance at 273nm
A_1 =Absorbance at 243nm
ax1= absorptivity of PARA at 243 nm (68)
ay1= absorptivity of CAF at 243 nm (15)
ax2= absorptivity of PARA at 273 nm (15)
ay2= absorptivity of CAF at 273 nm (51)

Method B

Absorption Ratio Method (Q Method)

The solutions of PARA and CAF (10 mcg/ml) were scanned in the range of 200 to 400 nm against distilled water as blank. For Q method, 259.5 nm (isobestic point) and 273 nm (λmax of Caffeine) were selected as wavelengths of measurements. Concentrations of PARA and CAF were determined using following equations.

$Cx = (Qm-Qy).\ A_1 / (Qx-Qy).\ a_{x1}$
$Cy = (Qm-Qx).\ A_1 / (Qy-Qx).\ a_{y1}$
Where
$Qm = A_2 / A_1$
$Qx = a_{x2} / a_{x1}$
$Qy = a_{y2} / a_{y1}$

$A_{2=}$ Absorbance of Mixture at 273nm
$A_{1=}$ Absorbance of Mixture at 259.5 nm
ax1= absorptivity of PARA at 259.5 nm (39)
ay1= absorptivity of CAF at 259.5 nm (38)
ax2= absorptivity of PARA at 273 nm (15)
ay2= absorptivity of CAF at 273 nm (51)

Table 1: Calibration data for PARA and CAF for both the methods

Sr. No.	Parameters	PARA			CAF		
		At 243nm	At 273nm	At 259.5	At 243nm	At 273nm	At 259.5
1	Linearity range (mcg/ml)	2-16	2-32	2-32	2-32	2-32	2-32
2	Slope	0.068	0.015	0.039	0.015	0.051	0.038
3	Correlation Coefficient (R^2)	0.998	0.998	0.997	0.997	0.998	0.990

Table 2: Assay results for the determination of PARA and CAF in its tablets by the proposed methods

Drug	Label Claim (mcg/ml)	Amount Found (mcg/ml)	% label Claim	S. D.	Amount Found (mcg/ml)	% label Claim	S. D.
		Method A			Method B		
PARA	500	487.3	97.46	± 0.44	470.3mg	95.46%	± 0.33
CAF	32	31.70	99.02	± 0.38	31.57mg	98.66%	± 0.78

n=6

Table 3: Result of Recovery studies by the proposed methods

Amount added (µg/ml)	Amount recovered (Method A)	% Recovery (Method A) ±S.D.	Amount recovered (Method B)	% Recovery (Method B) ±S.D.
PARA				
2.0 µg/ml	1.95	97.5±0.64	1.95	97.5 ± 0.42
5.0 µg/ml	4.91	98.2±0.87	4.91	98.2 ± 0.55
8.0 µg/ml	7.88	98.5±0.37	7.88	98.5 ± 0.49
CAF				
2.0 µg/ml	1.96	98.00±0.51	1.96	98.0 ± 0.41
5.0 µg/ml	4.95	99.00±0.44	4.95	99.0 ± 0.74
8.0 µg/ml	7.92	99.00±0.39	7.92	99.0 ± 0.60

n=6

Table 4: Intra and Interday Precision

Conc. (µg/ml)	Intraday Precision		Interday Precision		Intraday Precision		Interday Precision	
	Method A		Method A		Method B		Method B	
	S.D.	%R.S.D.	S.D.	%R.S.D.	S.D.	%R.S.D.	S.D.	%R.S.D.
PARA	0.40	0.41	0.75	0.78	1.14	1.15	1.17	1.18
CAF	0.94	0.96	0.45	0.48	1.72	1.75	1.14	1.15

n=6

RESULTS AND DISCUSSION

The proposed methods for simultaneous estimation of PARA and CAF in combined dosage form were found to be accurate, simple and rapid which can be well understood from validation data.

The % R.S.D. was found to be less than 2, which indicates the validity of method. Linearity was observed by linear regression equation method for PARA and CAF in different concentration range. The Correlation coefficient of these drugs was found to be close to 1.00, indicating good linearity. The assay results obtained by proposed methods are in fair agreement, hence it can be used for routine analysis of two drugs in combined dosage forms. There was no interference from tablet excipients was observed in these methods. It can be easily and conveniently adopted for routine quality control analysis. Both methods are accurate, simple, rapid, precise, reliable, sensitive, reproducible and economic and are validated as per ICH guidelines.

CONCLUSION

A simple UV spectrophotometric method was developed for the simultaneous determination of Paracetamol and caffeine in bulk and tablet formulation without any interference from the excipients. To the best of our knowledge, the present study is the first report for the purpose. The present methods succeeded in adopting a simple sample preparation that achieved satisfactory extraction recovery and facilitated its application in coformulated formulation.

The results of our study indicate that the proposed UV spectroscopic methods are simple, rapid, precise and accurate. Statistical analysis proves that, these methods are repeatable and selective for the analysis of PARA and CAF. It can therefore be concluded that use of these methods can save much time and money and it can be used in small laboratories with accuracy.

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REFERENCES:

[01] Rodenas V, Garcia MS, Sanchez-pedreno C, Albero MI. Simultaneous determination of propacetamol and paracetamol by derivative spectrophotometry Talanta, 2000, 52, 517-523

[02] Zen JM, Ting YS, Shih Y., Voltammetric determination of caffeine in beverages using a chemically modified electrode, Analyst,1998,123, 1145-1147.

[03] Erdal D., A comparative study of the ratio spectra derivative spectrophotometry, Vierordt's method and high-performance liquid chromatography applied to the simultaneous analysis of caffeine and paracetamol in tablets, J. Pharmaceut. Biomed, 1999, 21, 723-730.

[04] Safavi A, Tohidi M. Simultaneous kinetic determination of levodopa and carbidopa by H-point standard addition method. J. Pharmaceut. Biomed, 2007, 44(1), 313-318.

[05] Emre, D., Ozaltin, N., Ibuprofen determination of paracetamol, caffeine and propyphenazone in ternary mixtures by micellar electrokinetic capillary chromatography. J. Of chromatography B: Analytical Technologies in the Biomedical and Life Sciences 2007, 847 (2), 126-132.

[06] Gopinath, R. Rajan, S., Meyyanathan, S.N., Krishnaveni, N., Suresh, B., A RP-HPLC method for simultaneous estimation of paracetamol and aceclofenac in tablets. Indian J. of pharmaceutical sciences, 2007, 69 (1), 137-140.

[07] Senthamil Selvan, P., Gopinath, R., Saravanan, V.S., Gopal, N., Sarvana Kumar, A., periyasamy, K., Simultaneous estimation of paracetamol and aceclofenac in combined dosage forms by RPHPLC method. Asian J. of chemistry, 2007, 19 (2), 1004-1010.

[08] Suntornsuk, L., Pipitharome, O., and Wilairat, P., J. pharm. Biomed. Anal, 2003, 33(3), 441.

[09]. Ni, Y., Wang, Y., Kokot, S., Differential pulse stripping voltammetric determination of paracetamol and Phenobarbital in pharmaceuticals assisted by chemometrices. Analytical Letters 2004, 37, 3219-3235.

[10] Azhagvuel, S., Sekar, R., Method development and validation for the simultaneous determination of cetrizine dihydrochloride, paracetamol, and phenylpropanolamine hydrochloride in tablets by capillary zone electrophoresis. J. of Pharmaceutical and Biomedical Analysis, 2007, 43 (3), 873-878.

[11] Burakham, R., Duangthong, S., Patimapornlert, L. Lenghor, N., Kasiwad, S., Srivichai, L.Lapanantnoppakhun, S., Jakmunee, J., Grudpan, K., Flow-injection and sequential-injection determinations of paracetamol in pharmaceutical preparations using nitrosation reaction. Analytical Sciences. 2004, 20 (5), 837-840.

[12] De Los A. Oliva, M., Olsina, R.A., Masi, A.N., Selective spectrofluorimetric method for paracetamol

determination through coumarinic compound formation. Talanta 2005, 66 (1), 229-235.
[13] Lavorante, A.F., Pires, C.K, Reis, B.F., Multicommuted flow system employing pinch solenoid valves and micro-pumps. Spectrophotometric determination of paracetamol in pharmaceutical formulations. J. of Pharmaceutical and Biomedical analysis, 2006, 42 (4), 423-429.
[14] Abebe Belay, Kassahun Ture, Mesfin Redi and Araya Asfaw Measurement of caffeine in coffee beans with UV/vis spectrometer ,Food Chemistry , Vol-108, Issue-1 , 2008, Pages 310-315
[15] Rasiah S.Ramakrishana, M. Jeganathan M. Dias, S. Palamakumbura, High performance liquid chromatography as an analytical tool for the determination of sulfate in coconut and caffeine in tea, Can. J. Chem. 1987, 65, 101-102.
[16] M.M. Paradkar, J. Irudayaraj, A Rapid FTIR Spectroscopic Method for Estimation of Caffeine in Soft Drinks and Total Methylxanthines in Tea and Coffee, Journal of Food Science, 2002, 67, 7, 2507–2511,
[17] Baralles PO, Weigand RP, Dias AM. Simultaneous Determination of Paracetamol and Caffeine by Flow Injection-Solid Phase Spectrometry Using C18 Silica Gel as a Sensing Support, Anal. Sci. 2002, 18, 1241-1246.
[18] Knochen M, Giglio J, Boaventure FR. Flow-injection spectrophotometric determination of paracetamol in tablets and oral solutions, J. Pharmaceut. Biomed. Analysis 2003, 33, 191-197.
[19] Altun ML. HPLC method for the analysis of paracetamol, caffeine and dipyrone, Turk. J. Chem. 2002, 26, 521-528.
[20] Prodan M, Gere-Paszti E, Farkes O, Forgacs E. Validation and simultaneous determination of paracetamol and caffeine in pharmaceutical formulations by RP-HPLC, Chem. Anal. 2003, 48, 901.

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