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Research Article

SIMULTANEOUS DETERMINATION OF PARACETAMOL AND TAPENTADOL IN TABLETS BY RATIO SPECTRA DERIVATIVE SPECTROPHOTOMETRY

Shah Esha Bhavin [1]*, Gajjar Anuradha [2]

[1] Babaria Institute of Pharmacy, BITS Edu Campus, Vadodara, Gujarat, India & Ramanbhai Patel College of Pharmacy, Charotar University of Science and Technology, Changa, Gujarat. India.

[2] L.M. College of Pharmacy, Ahmedabad, Gujarat, India

*Corresponding Author Email: eshahshah.bip@bitseducampus.ac.in

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ABSTRACT

The application of the ratio spectra derivative spectrophotometry to the simultaneous determination of Paracetamol (PCM) and Tapentadol (TAP) in combined pharmaceutical tablets is presented. The spectrophotometric procedure is based on the use of the first derivative of the ratio spectra obtained by dividing the absorption spectrum of the binary mixtures by a standard spectrum of one of the compounds. The first derivative amplitudes were measured at 220 and 232 nm for the assay of TAP and PCM, respectively. Calibration graphs were established for 1-5 µg mL^{-1} for TAP and 6.5-32.5 µg mL^{-1} for PCM in binary mixture. The detection limits for TAP and PCM were found 0.098 and 0.595 µg mL^{-1}, respectively, while the quantification limits were 0.298 µg mL^{-1} for TAP and 1.805 µg/ml for PCM. The relative standard deviations were found to be less than 2%, indicating reasonable repeatability of both methods. The proposed methods were hence validated as per ICH guidelines and successfully applied to the determination of these drugs in commercial tablets.

KEYWORDS: Ratio spectra derivative spectrophotometry, Paracetamol, Tapentadol Bulk and tablets, ICH guidelines

INTRODUCTION

Multicomponent analysis is a challenging and an intriguing research domain in the pharmaceutical sector. The pivotal issue faced by the analysts with spectrophotometric analysis of multi component mixtures is the simultaneous determination of two or more active compounds in the same mixture, without prior separation. An elaborate literature review highlights several methods like Classical derivative spectrophotometry, Vierordt's method, Orthogonal function method, Fourier functions method etc. for resolving complex analytical mixtures with overlapping spectra [1]. But unfortunately, there are times when the treatment of the normal absorbance data is unable to compete with the level of interference especially when the spectra are strongly overlapping, stressing the need for special data treatment. In the present-day scenario, the treatment of absorbance ratio spectra has been the base pillar of some analytical procedures so as to produce signals for the mixture depending only on a single analyte, the Examples of which include Ratio-derivative spectrum method, Derivative ratio spectra-zero-crossing method (DRSZ) and Double divisor ratio spectra derivative method (DDRD) [2].

It is specifically noted that the fundamental concept behind the adoption of ratio spectra derivative spectrophotometry, lies in measuring the analytical signals at wavelengths corresponding to either maximums or minimums for both drugs in first derivative spectra of ratio spectra obtained by using either spectrum as divisor. Spectrophotometric method termed Ratio-derivative spectrophotometry, for the simultaneous determination of two compounds in binary mixtures is proposed in the literature [3]. Their method is based on the derivative of the ratio spectra for a binary mixture. The absorption spectrum of the mixture is divided by the absorption spectrum of a standard solution of one of the compounds and the first derivative of the ratio spectrum is obtained [4]. The concentration of active compounds are then determined from the calibration graphs obtained by measuring the amplitudes at points corresponding to the minimum or maximum wavelengths.

This spectroscopic method is based on dividing the spectrum for a mixture into the standard spectra for each of the analytes and driving the quotient to obtain a spectrum that is independent of the analyte concentration used as a divisor. The use of standardized spectra as a divisor shall minimize the experimental errors and background noise [5].

Advantages of ratio spectra derivative method

- Simple measurements on separate peaks, higher values of the analytical signals and negating the need to work only at zero-crossing points (sometimes co-existing compounds have no maximum or minimum at these wavelengths), is an enormous advantage of this method.
- The ratio spectra derivative method provides many wavelength maxima and minima, which provides a chance for the detection of these components in the presence of other active compounds and excipients that would otherwise interfere with the assay.
- Adoption of this method is useful in analysis of multicomponent complex mixtures.

Rationale behind the combined dosage form

Osteoarthritis, also referred as degenerative joint disease, is a type of arthritis that occurs due to wearing of protective tissue at the end of bones and progressively worsens over time resulting in chronic pain. The combination of Tapentadol hydrochloride and Paracetamol was used for the research work, which is a classical combo for pain relief. The use of combination therapy for the management of the pain associated with osteoarthritis has been recommended and adopted worldwide to improve efficacy and provide better relief. The use of two or more analgesics in combination, especially with different mechanisms of action and pharmacokinetics, leads to a synergistic effect and has the potential to overcome the efficacy and safety limitations of the individual agents and provide desired pain relief. The new American Pain Society 2002 guidelines pertaining to osteoarthritis pain management specifically stress the use of Tramadol in combination with Acetaminophen at any time during treatment when NSAIDs alone fail to provide desired pain relief [6-8]. Therefore, Tapentadol, a new generation semi-opioid analgesic with a dual mechanism of action, emerged as a wonder drug [9-12].Tapentadol offers broad efficacy, as demonstrated in a plethora of preclinical analgesia models and has a low side effect profile and rapid onset of action, in addition to being an impressive treatment option for the relief of moderate-to-severe acute pain, acute postoperative pain, osteoarthritis pain and/or low back pain [13, 14]. On the other hand, the conventional classic, Paracetamol, is a widely used OTC (Over-the-counter) analgesic-antipyretic molecule. Hence, in combination with Tapentadol, Paracetamol could be explored also in the management of chronic pain [15-18]. Therefore, this dynamic combination of Tapentadol and Paracetamol is a better alternative in comparison to other drug combinations of similar class such as Tramadol and Paracetamol because efficacy and safety goes hand-in-hand, and fewer side effect profile is a bonus point [19-25].

MATERIALS AND METHODS

Paracetamol: Gratis sample from Alembic Pharmaceuticals Pvt. Ltd, Baroda.
Tapentadol Hydrochloride: Gratis sample from Ami Lifescience Baroda Ltd.
Tablets: Tablet formulation consisting of Tapentadol Hydrochloride 50 mg and Paracetamol 325 mg was purchased from local market.

Chemicals and reagents used: Methanol (AR Grade, Loba Chemie Pvt. Ltd)

Instrumentation: UV/Visible Spectrophotometer: UV 1800, Shimadzu Corporation, Japan**,** Digital analytical balance: Shimadzu Corporation, Japan

Preparation of standard stock solution of PCM and TAP

Methanol (AR grade) for UV spectroscopy was used as solvent for preparation of solutions.

PCM 1st stock solution/working solution (100 µg mL^{-1}): Accurately weighed 100 mg PCM was taken in 100 mL volumetric flask and then diluted with methanol up to the mark. Further 10 mL of this solution was pipetted out in a 100 mL volumetric flask and then diluted with methanol upto the mark. This gave 100 µg mL^{-1} solution.

TAP 1st stock solution/working solution (100 µg mL^{-1}): Accurately weighed 100 mg TAP was taken in 100 mL volumetric flask and then diluted with methanol up to the mark. Further 10 mL of this solution was pipetted out in a 100 mL volumetric flask and then diluted with methanol upto the mark. This gave 100 µg mL^{-1} solution.

Preparation of calibration solutions of PCM and TAP

Calibration solutions were prepared by diluting working solutions of PCM and TAP to get concentrations ranging from 6.5 to 32.5 µg mL^{-1} for PCM and 1-5 µg mL^{-1} for TAP. Aliquots of 0.65, 1.3, 1.95, 2.6 and 3.25 mL from working solutions of PCM were transferred separately to 10 mL volumetric flasks and diluted up to the mark with methanol (using micro pipette) giving solutions corresponding to the concentrations of 6.5, 13, 19.5, 26 and 32.5 µg mL^{-1} respectively. Aliquots of 0.1, 0.2, 0.3, 0.4 and 0.5 mL of working solutions of TAP were transferred separately to 10 mL volumetric flasks and diluted up to the mark with methanol (using micro pipette) giving solutions corresponding to the concentrations of 1, 2, 3, 4 and 5 µg mL^{-1} respectively.

Method Validation

Linearity and range
The linearity of the proposed method was evaluated by analyzing a series of six different concentrations of PCM (6.5 to 32.5 µg mL^{-1}) and TAP (1 to 5 µg mL^{-1}) and each was repeated three times.
Acceptance criteria: The correlation coefficient value should not be less than 0.995 over the working range.

Accuracy
Accuracy of the method was confirmed by recovery study from formulation at 3 levels of standard addition (80%, 100%, and 120%) of label claim in triplicates.
Acceptance criteria: % Recovery should be within 98-102 % with low SD.

Precision
Inter-day and intra-day precision were measured in terms of % RSD. The experiment was repeated 3 times in a day for intra-day and on 3 different days for inter-day precision.
Acceptance criteria: The average % RSD of intra-day and inter-day measurements for determination of both the drugs should be less than 2.

LOD & LOQ
Calibration curve was repeated for 6 times and the standard deviation (SD) of the intercepts was calculated.

Assay
Twenty tablets were weighed accurately, average weight was determined and then all the 20 tablets were ground to a fine powder. A quantity equivalent to 50 mg of TAP and 325 mg of PCM were transferred to a 100 mL volumetric flask and volume made up with methanol. The contents were ultrasonicated for 10 min and filtered through Whatmann filter paper. From this solution, 2 mL was taken and diluted upto 50 mL with methanol (130:20 µg mL^{-1}). From this solution, 1 mL was taken and further diluted with methanol, to give concentrations of 13 and 2 µg mL^{-1} of PCM and TAP, respectively.
Acceptance criteria: % Assay values should lie with 98-102%.

RESULTS AND DISCUSSION

Optimization of method parameters
Major parameters that affect Ratio Derivative Spectrophotometry are:

1. Selection of divisor concentration
2. Analytical wavelength
3.Δλ
4. Scaling factor

For selection of **divisor concentration**, various concentrations of PCM and TAP were individually tested. PCM 13 µg mL^{-1} and TAP 4 µg mL^{-1} gave the best results in terms of highest correlation coefficient values, being an indication of the quality of fitting of the data to the straight line. Table 1 and 2 depict the Optimized method parameters for ratio derivative spectrophotometry and the optimized conditions while figure 1 and 2 illustrates the Optimized Method Parameters for Ratio Derivative Spectrophotometry. The figures 3 and 4 depict the division stages of this method for TAP and PCM respectively while figures 5 and 6 illustrate the representative Ratio Derivative Spectra of Tapentadol and Paracetamol, respectively.

Table 1: Optimized Method Parameters for Ratio Derivative Spectrophotometry

Compound	Divisor Conc. (Using TAP 4 µg mL^{-1} as a Divisor) (µg mL^{-1})	Analytical Wavelength (nm)	r^2
PCM (6.5,13,19.5,26,32.5 µg mL^{-1})	1	232	0.954
	2	232	0.993
	3	232	0.997
	4	232	**0.998**
	5	232	0.995

Compound	Divisor Conc. (Using PCM 13 µg mL^{-1} as a Divisor) (µg mL^{-1})	Analytical Wavelength (nm)	r^2
TAP (1,2,3,4,5 µg mL^{-1})	6.5	220	0.998
	13	**220**	**0.999**
	19.5	220	0.975
	26	220	0.981
	32.5	220	0.995

Table 2: Optimized Conditions of the Developed method

Sr.No.	Method Parameter	Optimized Value
1.	Wavelength Range (nm)	200-400 nm
2.	Scan speed	Fast
3.	Divisor Concentration for PCM	13 µg mL^{-1} PCM
4.	Divisor Concentration for TAP	4 µg mL^{-1} TAP
5.	Δ λ	8 nm
6.	Scaling factor	1
7.	Analytical wavelength for PCM	232 nm
8.	Analytical wavelength for TAP	220 nm
9.	Solvent	Methanol

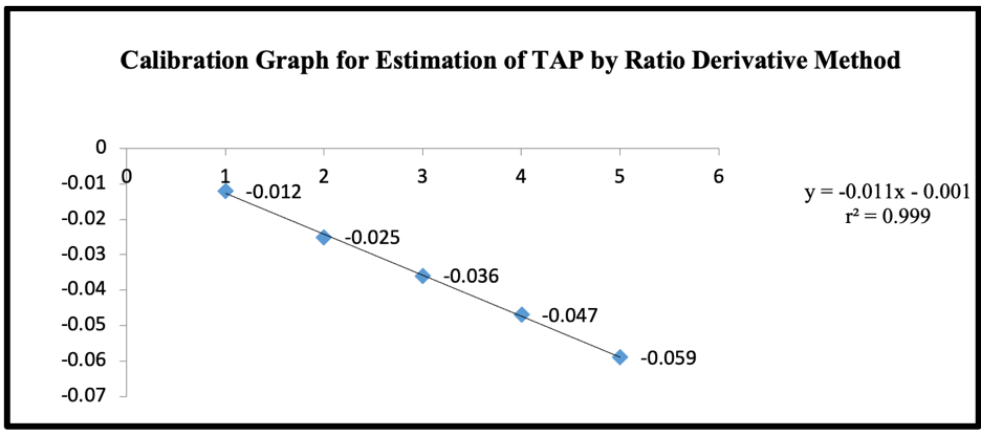

Figure 1: Calibration Graph for Estimation of TAP Using 13 µg mL^{-1} of PCM as Divisor Concentration

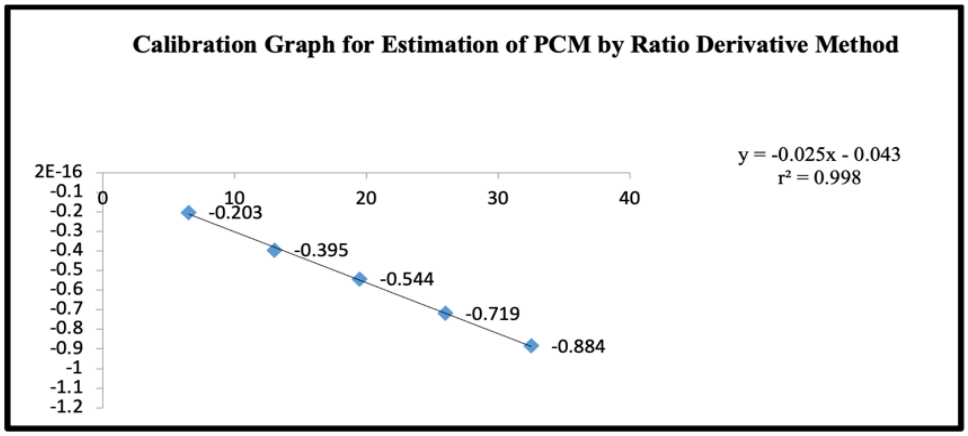

Figure 2: Calibration Graph for Estimation of PCM Using 4 µg mL^{-1} of TAP as Divisor Concentration

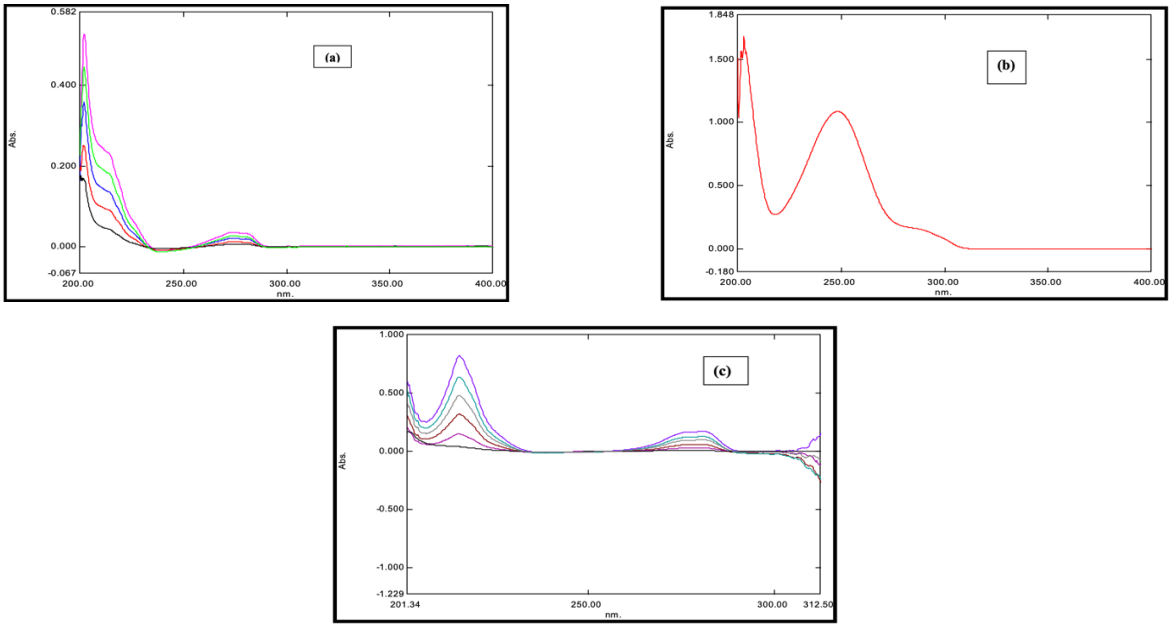

Figure 3: Spectra of TAP (a) divided by spectra of 13 µg mL^{-1} PCM (b)Derivative Ratio spectra (c)

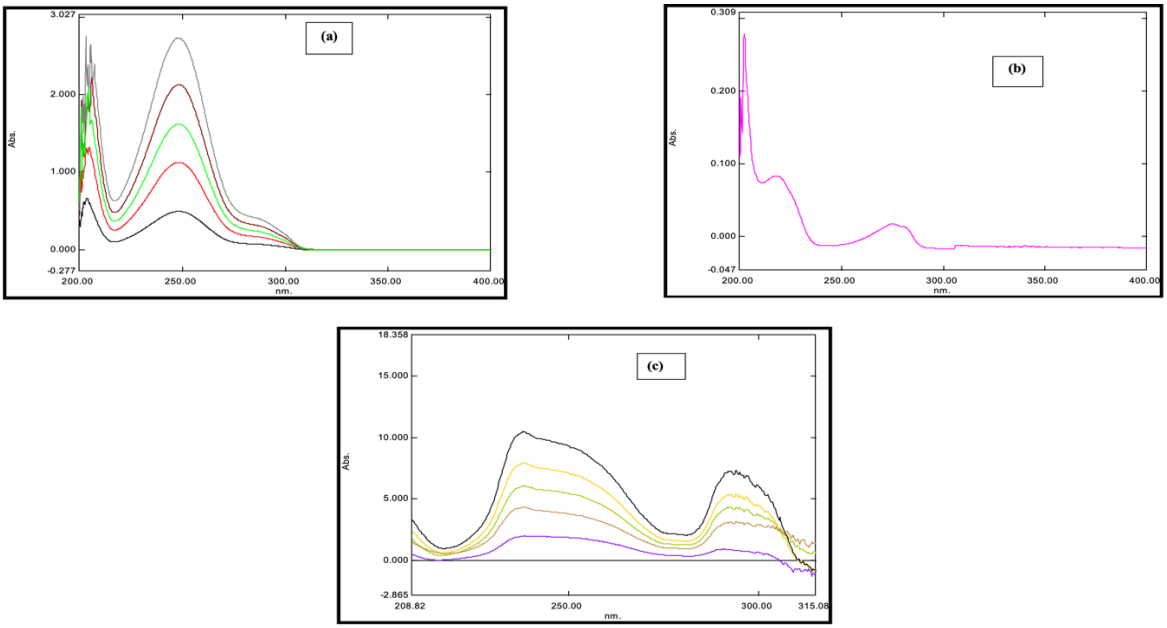

Figure 4: Spectra of PCM (a) divided by spectra of 4 µg mL^{-1} TAP (b) Derivative Ratio spectra (c)

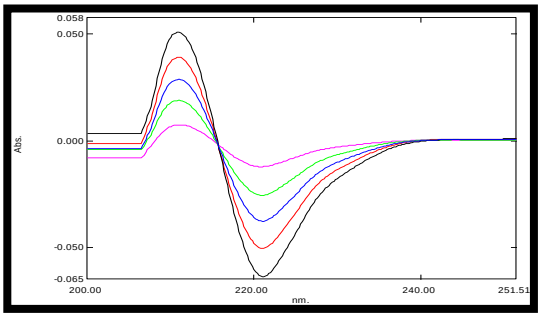

Figure 5: Ratio Derivative Spectra of TAP (1, 2, 3, 4, and 5 µg mL^{-1})

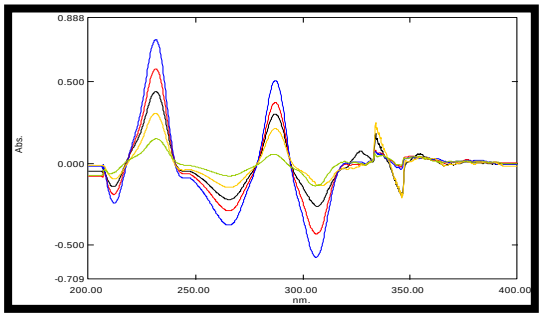

Figure 6: Ratio Derivative Spectra of PCM (6.5, 13, 19.5, 26, and 32.5 µg mL^{-1})

Method Validation

The developed method was validated according to ICH guidelines. Following table 3 crisply summarizes the validation results.

Table 3: Summary of Validation Parameters

Parameter	Drug	
	TAP	**PCM**
Analytical Wavelength	220	232
Beer's Range	1-5 µg mL^{-1}	6.5-32.5 µg mL^{-1}
Slope	y = -0.011x - 0.001	y = -0.025x - 0.043
Intercept	-0.001	-0.043
Correlation Coefficient (r^2)	0.999	0.998
Intraday precision (%RSD)	1.4593	0.353
Interday precision (%RSD)	1.814	0.6508
LOD (µg mL^{-1})	0.098	0.595
LOQ (µg mL^{-1})	0.298	1.805

CONCLUSION

A simple, specific, accurate and precise UV spectrophotometric method was developed for simultaneous estimation of Paracetamol and Tapentadol. The developed method was validated according to ICH guidelines. The value of %RSD for intra-day and inter-day precision was found to be less than 2. This value confirms that method is precise. % Recovery within 98-102 % for this method shows that the method is accurate and free from the interference of excipients used in formulation. The method can be successfully applied for the simultaneous estimation of PCM and TAP in the combined dosage form without any prior separation of individual drugs.

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REFERENCES

1. French CS, Church AB. Carnegie Inst. of Washington Year Book 54 (1954) 162; 56 (1956) 281. AT Giese and CS French. Appl. Spectroscopy. 1955; 9:78.
2. Salinas F, Nevado JB, Mansilla AE. A new spectrophotometric method for quantitative multicomponent analysis resolution of mixtures of salicylic and salicyluric acids. Talanta 1990 Mar 1; 37(3):347-51.
3. Moffat AC, Osselton MD, Widdop B, Watts J. Clarke's analysis of drugs and poisons. London: Pharmaceutical press; 2011.
4. A.H Bekett JBS Practical Pharmaceutical Chemistry, CBS Publishers & Distributors.
5. Nevado JB, Cabanillas CG, Salinas F. Spectrophotometric resolution of ternary mixtures of salicylaldehyde, 3-hydroxybenzaldehyde and 4-hydroxybenzaldehyde by the derivative ratio spectrum-zero crossing method. Talanta 1992 May 1; 39(5):547-53.
6. Chou R, Qaseem A, Snow V, Casey D, Cross Jr JT, Shekelle P, Owens DK. Diagnosis and treatment of low back pain: a joint clinical practice guideline from the American College of Physicians and the American Pain Society. Annals of Internal Medicine. 2007 Oct 2; 147(7):478-91.
7. Parojčić J, Karljiković-Rajić K, Durić Z, Jovanović M, Ibrić S. Development of the second-order derivative UV spectrophotometric method for direct determination of paracetamol in urine intended for biopharmaceutical characterization of drug products. Biopharmaceutics & Drug Disposition 2003 Oct; 24(7):309-14.
8. Shihana F, Dissanayake D, Dargan P, Dawson A. A modified low-cost colorimetric method for Paracetamol (Acetaminophen) Measurement in Plasma. Clinical Toxicology 2010; 48(1):42-6.
9. Vilchez J, Blanc R, Avidad R, Navalón A. Spectrofluorimetric determination of Paracetamol in pharmaceuticals and biological fluids. Journal of Pharmaceutical and Biomedical Analysis 1995; 13(9):1119-25.
10. Vyas A, Aggarwal N, Nagori B, Patel J, Jobanputra C, Viramgama D. Simultaneous estimation of Nabumetone and Paracetamol by vierodt's method in combined tablet dosage form. Int Jour of Chemtech Research 2010; 2(1):543-7.
11. Murtaza G, Khan SA, Shabbir A, Mahmood A, Bin Asad M, Farzana K, *et al*. Development of a UV-Spectrophotometric method for the simultaneous determination of Aspirin and Paracetamol in tablets. Scientific Research and Essays 2011; 6(2):417-21.

12. Pawar V, Pishawikar S, More H. Spectrophotometric estimation of Aceclofenac and Paracetamol from tablet dosage form. Curr Pharm Res 2010; 1(1):25-9.
13. A DT, Hoang VD. Simultaneous determination of paracetamol and codeine phosphate in combined tablets by first-order derivative and ratio spectra first-order derivative UV spectrophotometry. Asian Journal of Research in Chemistry 2009; 2(2):143-7.
14. Chitlange SS, Soni R, Wankhede SB, Kulkarni AA. Spectrophotometric methods for simultaneous estimation of Dexibuprofen and Paracetamol. Asian J Research Chem 2009; 2(1):30-3.
15. Sharma MC, Sharma S. Determination and validation of UV spectrophotometric method for estimation of Paracetamol and Diclofenac Sodium in tablet dosage forms using hydrotropic solubilizing agents. International Journal of Pharm Tech Research 2011; 3(1):244-7.
16. Sawant R, Bhangale L, Joshi R, Lanke P. Validated spectrophotometric methods for simultaneous estimation of Paracetamol, Domperidone and Tramadol HCl in pure and tablet dosage form. Journal of Chemical Metrology 2010; 4(1):21.
17. Joshi RS, Pawar NS, Katiyar SS, Zope DB, Shinde AT. Development and validation of UV spectrophotometric methods for simultaneous estimation of Paracetamol and Ibuprofen in pure and tablet dosage form. Der Pharmacia Sinica 2011; 2(3):164-71.
18. Toral MI, Richter P, Araya E, Fuentes S. Determination of Mefenamic Acid and Paracetamol by first derivative spectrophotometry. Analytical Letters 1996; 29(15):2679-89.
19. Sawant R, Joshi R, Kawade D, Sarode V. Development and validation of spectrophotometric methods for simultaneous estimation of Paracetamol and Meloxicam in pure and tablet dosage form. Der Pharmacia Lettre 2010; 2:471-8.
20. Erk N, Özkan Y, Banoğlu E, Özkan S, Şentürk Z. Simultaneous determination of Paracetamol and Methocarbamol in tablets by ratio spectra derivative spectrophotometry and LC. Journal of Pharmaceutical and Biomedical Analysis 2001; 24(3):469-75.
21. Chandratrey A, Sharm R. Simulatanous spectrophotometric estimation and validation of three components tablet formulation containing Paracetamol, Nimesulide and Tizanidine. Indian J Chem Technol 2010;17(1): 229-232
22. Anumolu PD, Haripriya A, Sirisha N, Venkat Raju Y, Sunitha G, Rao V. Original research article stability indicating spectrofluorimetric quantification of Tapentadol HCl and application to in-vitro dissolution studies. J App Pharm 2013;5(3):794-804
23. Khokhar V, Shah RM. Simultaneous estimation of paracetamol and tapentadol in combined dosage form by derivative method. International Journal of Pharmaceutical Sciences and Research 2013 May 1; 4(5):1777.
24. Shah R, Magdum C, Patil SK, Chougule DK, Naikwade N. Validated spectroscopic method for estimation of aceclofenac from tablet formulation. Research J Pharm and Tech 2008; 1(4):430-2.
25. Narade S, Patil S, Surve S, Shete D, Pore Y. Simultaneous UV spectrophotometric method for the determination of diacerein and aceclofenac in tablets. Journal of Pharmaceutical Sciences and Research 2010; 2:137-42.

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