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Research Article

FIRST ORDER DERIVATIVE SPECTROSCOPIC METHOD FOR SIMULTANEOUS ESTIMATION OF MELOXICAM AND PARACETAMOL IN THEIR COMBINED DOSAGE FORM

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ABSTRACT

This study describes the development and validation for the simultaneous estimation of meloxicam and Paracetamol by the first-order derivative spectroscopy method. The quantification was achieved by the first-order derivative spectroscopy method at 277.47 nm and at 269.44nm over the concentration range of 10-40 µg/ml for meloxicam and 3-8 µg/ml for Paracetamol for the estimation of both drugs in a combined tablet formulation. This method does not require any prior separation of components from the sample. Meloxicam (22 µg/ml) and Paracetamol (6 µg/ml) were determined at with a recovery of 99.13 % – 99.42 % and 99.45% – 100.68% respectively. Calibration curves were linear with a correlation coefficient of 0.9981 and 0.9992 for meloxicam and Paracetamol, respectively. The relative standard deviation was found to be < 2.0%. The result shows that the proposed method can be successfully used for simultaneous determination of both the drugs content in the marketed formulations.

Keywords: first order derivative spectroscopy, meloxicam, Paracetamol, ZCP, fluorescence.

INTRODUCTION

Meloxicam (MELO) chemically, 4-Hydroxy-2-methyl-N-(5-methyl-2-thiazolyl)-2H-1,2-benzothiazine-3-carboxamide 1,1-dioxide is analgesic drug with preferential COX-2 inhibitory activity (10) . Anti-inflammatory effects of Meloxicam is due to inhibition of prostaglandin synthetase (cylooxygenase), leading to the inhibition of prostaglandin synthesis (10). As prostaglandins sensitize pain receptors, inhibition of their synthesis may be associated with the analgesic effects of Meloxicam. Paracetamol chemically, N- (4-hydroxyphenyl) acetamide is an analgesic-antipyretic agent. It is effective in treating mild to moderate pain such as headache, neuralgia and pain of musculo-skeletal origin (10). Paracetamol acts predominantly by inhibiting prostaglandin synthesis in the central nervous system (CNS) (9). Paracetamol probably produces antipyresis by acting centrally on the hypothalamic heat-regulating center to produce peripheral vasodilation resulting in increased blood flow through the skin, sweating, and heat loss. The central action probably involves inhibition of prostaglandin synthesis in the hypothalamus (9). A literature survey revealed that methods have been reported for the estimation of MELO in plasma using LC (13, 1-2). Paracetamol has been determined by various Pharmacopeial and nonpharmacopeial methods (3-8). The pharmacopeial methods include potentiometric titraton and LC. Many LC methods have been reported or the estimation of PCM alone in bulk drug and in combination with other drugs (3-8). Recently, MELO has been combined with PCM to obtain anti-inflammatory and analgesic effect. To the best of our knowledge, there is no official

pharmacopeial as well as non official method reported for simultaneous determination of MELO and PCM pharmaceutical formulations or from biological fulids as PCM having absorption property while MELO gives flauroscence so it was difficult to develop such a method that could determine simultaneously MELO and PCM from combine dosage forms .Thus, efforts are made to develop a fast, selective and sensitive analytical method for the estimation of MELO and PCM in their combined dosage form using derivative spectroscopic method.

EXPERIMENTAL

Chemicals

The MELO and PCM pure powders were procured as gratis samples from Swanna Pharmaceuticals (Nadiad, India) and Relax Pharmaceuticals (Vadodara, India) with 99.95 % and 99.94 % purity, respectively. Tablet formulation, Melodol (Aristo Pharmaceutical Ltd.), was obtained commercially with the labeled amounts of 7.5 mg MELO and 325 mg PCM. The HPLC grade Acetonitrile, methanol, and water were purchased from E. Merck (Mumbai, India).

Instruments

Spectorphotometric analysis was performed on Perkin-Elmer lambda 19 (Perkin-Elmer, Norwalk, CT, USA), a computer controlled double-beam UV visible spectrophotometer using 10 mm quartz cell with a slit width of 1 nm and a scan speed of 60 nm/min.

Solutions

A 10 mg of MELO standard and 10 mg of PCM standard was weighed and transferred to a 100 ml volumetric flask and dissolved in 25 ml methanol. The flask was sonicated for 10 minutes and volume was made up to the mark with methanol to give a solution containing 100µg/ml MELO. From the above working standard solution suitable aliquots were taken, standard solution of meloxicam were prepared in the range of 10-40 µg/ml and for standard Paracetamol 3-8 µg/ml.

Spectrophotometric Conditions

Using memory channels, the first-order derivative spectra were overlapped. The zero crossing point (ZCP) values of MELO at which the PCM showed derivative response were recorded. The wavelength 277.47 nm was selected for the quantification of MELO (where the derivative response for PCM was zero). Similarly 269.44 nm was selected for the quantification of PCM (where the derivative response for MELO was zero). Characteristic wavelengths (ZCP) for MELO and PCM were confirmed by varying the concentration of both drugs.

RESULTS AND DISCUSSION

The overlain derivative spectrum (first order) of MELO AND PCM at different concentrations revealed that at 277.47 nm different concentration of PCM possess zero D_1 absorbance whereas MELO possess significant D_1 absorbance. In a similar manner, at 269.44 nm different concentrations of MELO possess zero D_1 absorbance whereas PCM possess significant D_1 absorbance. Considering above facts, wavelength 277.47 nm and 269.44 nm were selected for the estimation of MELO and PCM respectively

Method Validation

Accuracy

Accuracy is the closeness of the test results obtained by the method to the true value.

To study the accuracy 20 tablets were weighed and powdered and analysis of the same was carried out. Recovery studies were carried out by addition of standard drug to the sample at 3 different concentration levels taking into consideration percentage purity of added bulk drug samples. The result of the recovery study was found to be 99.13 % – 99.42 % for Meloxicam and for Paracetamol 99.45 % – 100.68 %.

Precision

The precision of an analytical method is the degree of agreement among individual test results when the method is applied repeatedly to multiple samplings of homogenous samples.It provides an indication of random error results and was expressed as coefficient of variation (CV)

Repeatability

Standard solutions of MELO (10, 16, 22, 28, 34 and 40 µg/ml) were prepared and first derivative spectrums were recorded. Absorbance was measured at 277.47 nm taking the methanol as the blank. The absorbance of the same concentration solution was measured five times and RSD was calculated. In the similar manner solutions of PCM (3, 4, 5, 6, 7 and 8 µg/ml.) were prepared and first

derivative spectrums were recorded. Absorbance was measured at 269.44 nm taking the methanol as the blank. The procedure was repeated for five times.

Intra and inter day precision

Variation of results within the same day (intra day), variation of results between days (inter day) were analyzed. The result of the Intra day and Interday precision were shown in and

Reproducibility

The absorbance readings were measured at different laboratory using another spectrophotometer by another analyst and the values obtained were evaluated using t- test to verify their reproducibility. Instrument 1 was Perkin Elmer and Instrument 2 was Chemito UV -2600

Linearity and Range

The linearity of analytical method is its ability to elicit test results that are directly proportional to the concentration of analyte in sample within a given range. The range of analytical method is the interval between the upper and lower levels of analyte that have been demonstrated to be determined within a suitable level of precision, accuracy and linearity.

Specificity and selectivity

Specificity is a procedure to detect quantitatively the analyte in presence of component that may be expected to be present in the sample matrix. While selectivity is the procedure to detect qualitatively the analyte in presence of components that may be expected to be present in the sample matrix. Commonly used excipients in capsule preparation were spiked in a pre weighed quantity of drugs and then absorbance was measured and calculations done to determine the quantity of the drugs.

Ruggedness

The solutions were prepared and then analyzed with change in the analytical conditions like different laboratory, different analyst, and different instrument.

Limit of Detection

Limit of Detection for the Meloxicam and Paracetamol was found to be 0.073922 µg/ml and 0.07831 µg/ml respectively.

Limit of Quantitation

Limit of Detection for the Meloxicam and Paracetamol was found to be 0.224007 µg/ml and 0.237304 µg/ml respectively.

Assay determination of meloxicam and Paracetamol form formulation

Twenty tablets were weighed and finely powered. Powder equivalent to 325 mg MELO and 7.5 mg PCM was accurately weighed and transferred to volumetric flask of 100ml capacity. 50 ml of methanol was transferred to this volumetric flask and sonicated for 15 min. The flask was shaken and volume was made up to the mark with methanol. The above solution was filtered through whatman filter paper (0.45µ). From this solution 1 ml was transferred to volumetric flask of 10 ml capacity. Volume was made up to the mark to give a solution containing 325 µg/ml MELO and 7.5 µg/ml PCM (solution A).From the solution A, 0.92 ml was transferred to volumetric flask of 50 ml capacity and in same flask 10.95 ml of 100 µg/ml std solution of Meloxicam was added. Volume was made up to the mark to give a solution containing 6 µg/ml PCM and 22 µg/ml MELO .This solution was used for the estimation of MELO and PCM. The results obtained for meloxicam and Paracetamol were compared with the corresponding labeled amounts that are presented in table 3.

CONCLUSION

The present results provide clear evidence that the proposed method can be successfully used for simultaneous estimation of both the drugs from marketed formulations.

ACKNOWLEDGMENTS

We are grateful to Swanna Pharmaceuticals (Nadiad, India) and Relax Pharmaceuticals Ltd (Baroda, India) for the gratis samples of pure MELO and PCM, respectively.

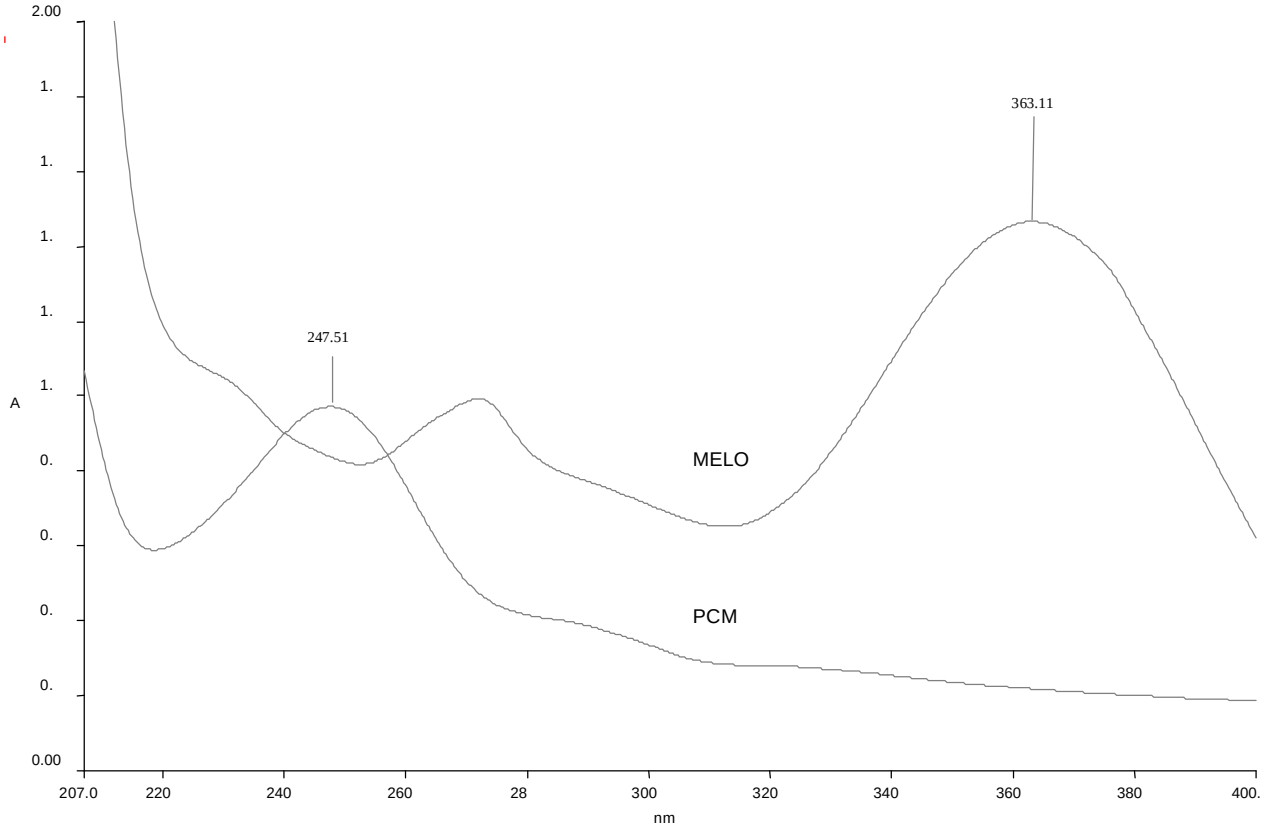

Fig. 1: Overlain spectrum of MELO (22 ppm) and PCM (7 ppm) in methanol

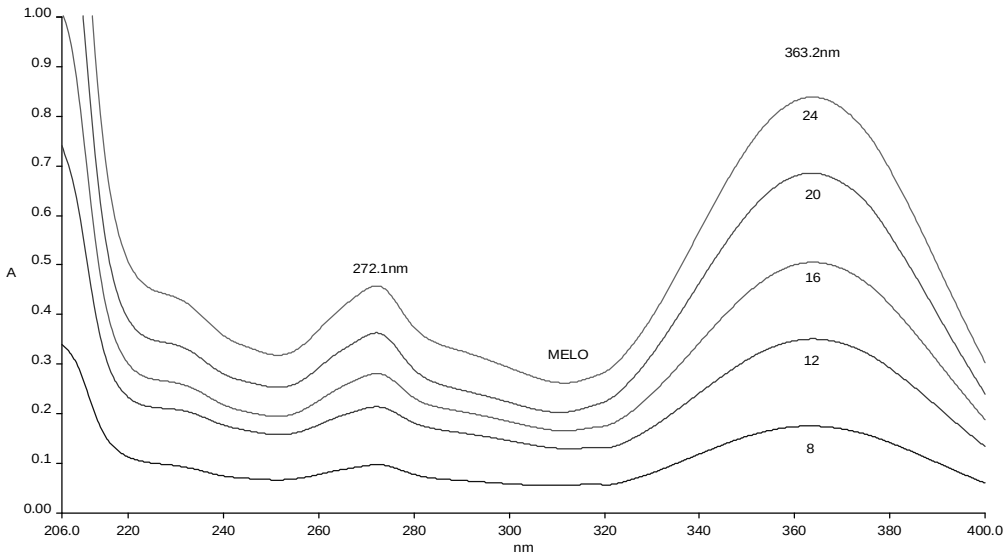

Fig. 2: Overlay spectrum of MELO in methanol

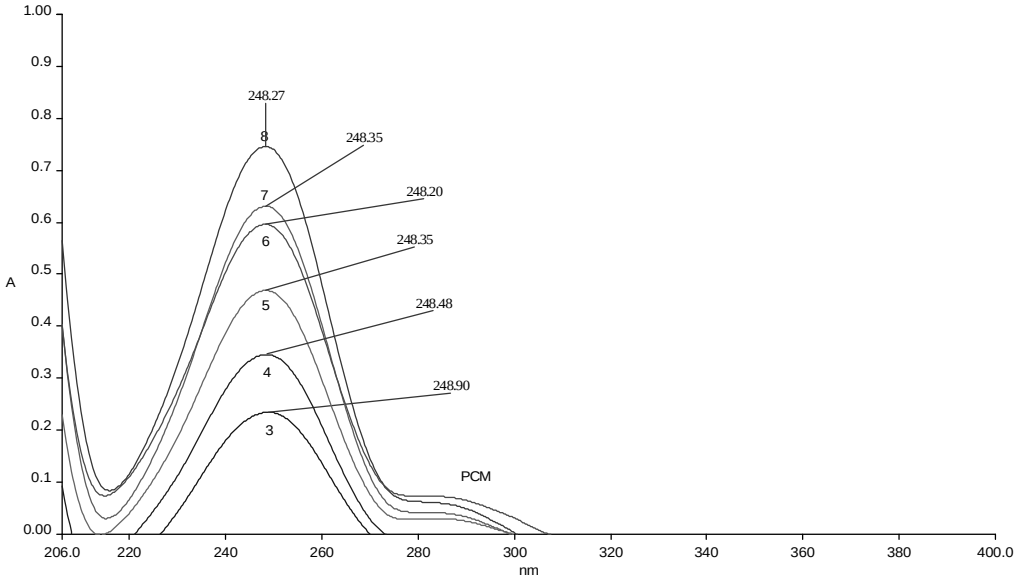

Fig. 3: Overlay spectrum of PCM in methanol

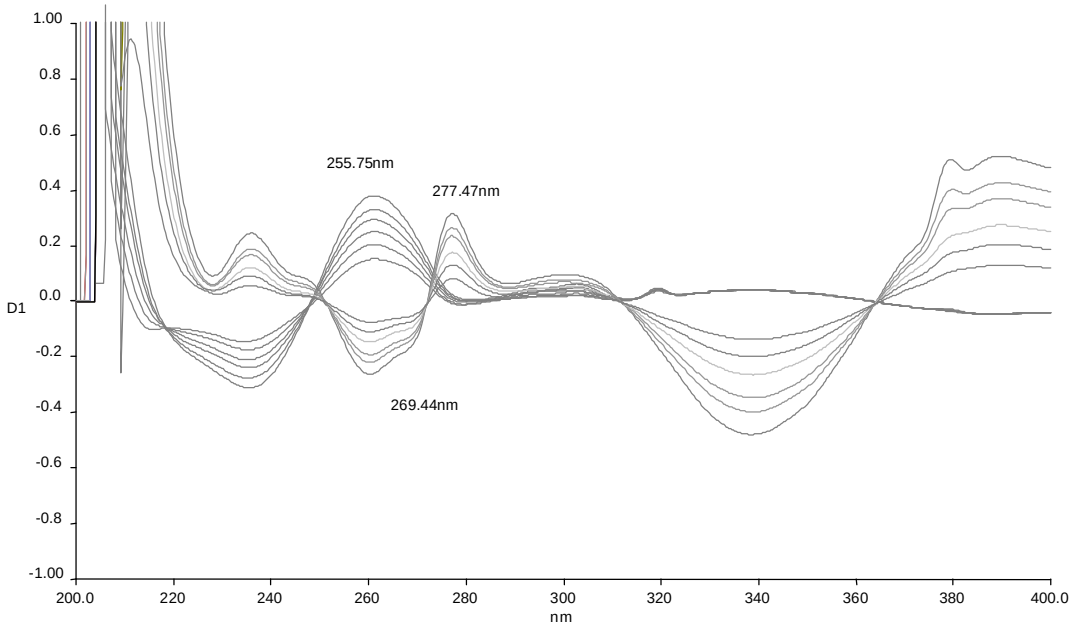

Fig. 4: Overlay first order derivative spectrum of MELO and PCM

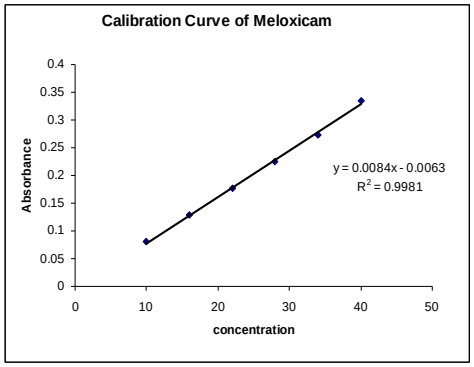

Fig. 5: Calibration curve for Meloxicam at ZCP of Paracetamol at 277.47 nm

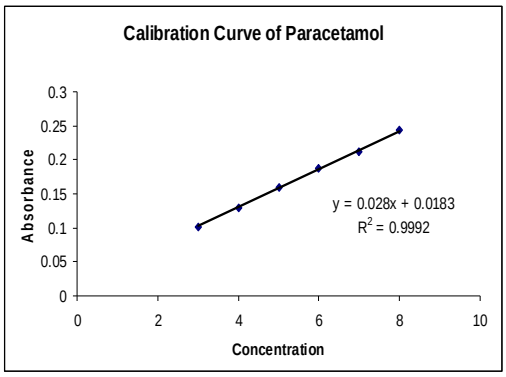

Fig. 6: Calibration curve for Paracetamol at ZCP of Meloxicam at 269.44 nm

Table 1: Regression analysis of the calibration curves for meloxicam and Paracetamol for the proposed derivative spectroscopic method

Parameter	MELO (at 277.47nm)	PCM (at 269.44nm)
Linear Range (µg/ml)	10-40	3-8
Slope	0.0084	0.028
Intercept	0.0063	0.0183
Standard deviation of slope	0.00019	0.000692
Standard deviation of intercept	0.005129	0.003985
Limit of Detection (µg/ml)	0.073922	0.07831
Limit of Quantitation (µg/ml)	0.224007	0.237304

Table 2: Summary of Validation Parameters of Derivative Spectrophotometry

Parameters	MELO	PCM
Recovery%	99.13 -99.42	99.45-100.68
Repeatability (RSD, n=5)	0.0145	0.0172
Precision(CV) Intra-day (n=3) Inter-day (n=3)	 0.14-1.29 0.26-1.22	 0.47-1.86 0.51-2.02
Specificity	99.44 %	100.31 %
Solvent suitability	Suitable for 24 hrs.	Suitable for 24 hrs.

Table 3: Assay Results of Marketed Formulation

Formulation	Actual concentration (µg/ml)		MELO%±SD (n=3)	PCM%±SD (n=3)
	MELO	PCM		
Tablet	22	6	99.44±0.72	100.31±0.45

SD = Standard deviation of three determinations

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