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Simultaneous Spectrophotometric Estimation of Dextropropoxyphene Hydrochloride and Acetaminophen in Capsule Dosage Forms

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A simple and economical dual wavelength spectrophotometric method has been developed for the simultaneous estimation of dextropropoxyphene hydrochloride and acetaminophen in combined dosage forms. The method was based on property of additivity of absorbances. The two wavelengths on acetaminophen curve were found out where it showed same absorbance, which were 216.6 and 262.9 nm. At 262.9 nm, acetaminophen showed some absorbance while dextropropoxyphene hydrochloride showed zero absorbance. Both the drugs gave absorbance at 216.6 nm. The method involved solving of an equation based on measurement of absorbances at two wavelengths 216.6 and 262.9 nm. The proposed method was found to be simple, economical, accurate and reproducible for the routine analysis of both drugs in capsule dosage forms.

Combination of dextropropoxyphene hydrochloride (DXP) and acetaminophen (PCM) provides synergistic analgesic effect. This combination is widely used in treatment of moderate to sever pain[1-3]. A survey of literature revealed that gas chromatography, HPLC and HPTLC methods have been reported for the simultaneous estimation of both drugs in combined dosage forms[4-9]. However, these methods are found to be comparatively expensive and time consuming. A spectrophotometric method has not been reported for the simultaneous estimation of DXP and PCM in combined dosage forms. In the present investigation an attempt has been made to develop a simple, economical, accurate and reproducible spectrophotometric method for the simultaneous estimation of DXP and PCM in combined dosage forms. The method was based on dual wavelength data processing program (dual wavelength spectrophotometry or DW spectrophotometry). The proposed method was successfully applied for simultaneous determination of DXP and PCM in combined dosage forms that are available in market.

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MATERIALS AND METHODS

A double beam Shimadzu 160A UV/Vis spectrophotometer with two matched quartz cells of 1 cm light path was employed. Dextropropoxyphene hydrochloride (Cadila Pharmaceuticals Ltd., Ahmedabad) and acetaminophen (Saga Laboratories, Ahmedabad), hydrochloric acid (AR Grade, S. D. Fine Chem. Pvt. Ltd., Mumbai) and distilled water were used.

Preparation of standard and sample solutions:

DXP powder (10 mg) was accurately weighed and transferred to a 100 ml volumetric flask. It was dissolved and diluted to 100 ml with 0.1 N hydrochloric acid solution to obtain a final concentration of 100 µg/ml. PCM powder (10 mg) was accurately weighed and transferred to another 100 ml volumetric flask. It was dissolved and diluted to 100 ml with 0.1 N hydrochloric acid solution to obtain a final concentration of 100 µg/ml.

Twenty capsules were emptied and the powder equivalent to 50 mg of DXP was accurately weighed and transferred to a 250 ml volumetric flask. Hydrochloric acid (0.1 N, 200 ml) was added to it and sonicated for 20 min. The

solution was filtered through Whatman filter paper No. 41 and the volume was adjusted up to the mark with 0.1 N hydrochloric acid. This solution is expected to contain 200 µg/ml DXP and 1.23 mg/ml PCM. This solution (3 ml) was taken in to a 100 ml volumetric flask and the volume was adjusted up to mark with 0.1 N hydrochloric acid to get a final concentration of DXP (6 µg/ml) and PCM (36.92 µg/ml).

Selection of wavelength for estimation of DXP and PCM:

Absorbance spectrum of pure PCM was scanned in the spectrum basic mode. Using the cursor function, the absorbance corresponding to 216.6 nm (wavelength λ_1, the wavelength of minimum absorbance for PCM) was noted from spectrum. Then the cursor function was moved along with peak curve until the absorbance equal to that of absorbance at 216.6 nm was found. The wavelength obtained corresponding to this absorbance value was 262.9 nm (λ_2). The absorbance of various dilutions of PCM in 0.1 N hydrochloric acid was measured at 216.6 nm. Absorbance spectrum of pure DXP was also scanned in the spectrum basic mode. DXP showed some absorbance value at 216.6 nm (λ_1) while it does not show any absorbance value at 262.9 nm. The absorbance value at 262.9 nm is due to PCM only in the combined mixture of both drugs. Wavelength λ_2 (262.9 nm) was selected for the measurement of PCM.

Calibration curve for DXP and PCM:

Appropriate aliquots from the stock solutions of DXP and PCM were used to prepare three different sets of dilutions, Series A, B and C as follows. Series A consisted of different concentrations of DXP (3-9 µg/ml). Aliquot of the stock solution of DXP (100 µg/ml) was pipetted out into a series of 10 ml volumetric flask and diluted with 0.1 N hydrochloric acid to get final concentration in range of 3-9 µg/ml. Series B consisted of varying concentrations of PCM (15-45 µg/ml). Appropriate volume of the stock solution of PCM (100 µg/ml) was transferred into a series of 10 ml volumetric flask and the volume was adjusted to the mark with 0.1 N hydrochloric acid solution. Series C comprised of mixture of DXP and PCM having varying concentrations of DXP (3-9 µg/ml) and PCM (15-45 µg/ml). The solutions were prepared by pipetting out 0.3, 0.4, 0.5, 0.6, 0.7, 0.8, 0.9 ml of the stock solution of DXP (100 µg/ml) and 1.5, 2, 2.5, 3, 3.5, 4, 4.5 ml of the stock solution of PCM (100 µg/ml), respectively into a series of 10 ml volumetric flasks and the volume was adjusted up to the mark with 0.1 N hydrochloric acid solution.

The absorbance of the solutions of series A and C were measured at 216.6 nm (λ_1) and 262.9 nm (λ_2) while absorbance of the solutions of series B was measured at 262.9 nm (λ_2). The difference in absorbances between 216.6 nm and 262.9 nm is due to DXP and this difference in absorbances was plotted against DXP concentration (µg/ml). The absorbance at 262.9 nm is due to PCM only and was plotted against PCM concentration (µg/ml).

Analysis of combined capsule dosage form:

The absorbance of final sample solution was measured against hydrochloric acid (0.1 N) as blank at 216.6 and 262.9 nm. The amount of DXP and PCM was computed using respective equation of straight line.

RESULTS AND DISCUSSION

The utility of dual wavelength data processing program is its ability to calculate unknown concentration of a component of interest in a mixture containing an interfering component. For elimination of the effects of an interfering component, two specific wavelengths are chosen: (i) first wavelength λ_1 at which minimum absorbance of interfering component and some absorbance of pure component of interest was observed. (ii) Second wavelength λ_2 was the wavelength at which the absorbance of the interfering component was equal to the absorbance of the interfering component at λ_1[10-11].

In the proposed procedure the absorbance of DXP alone in a mixture of DXP and PCM was determined using dual wave-

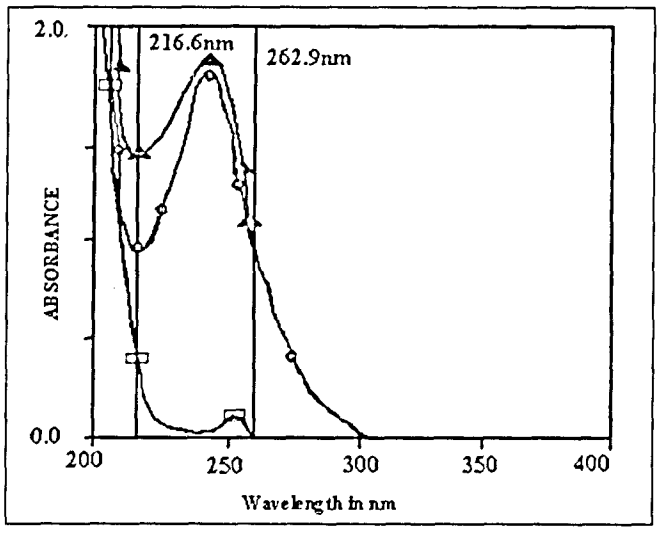

Fig. 1: Overlain spectra of the drugs.

Overlain spectra of mixed standards (-▲-), PCM (-○-) and DXP (-□-).

TABLE 1: DETERMINATION OF DXP ALONE AND DXP IN PRESENCE OF PCM BY THE PROPOSED DW SPECTROPHOTOMETRY.

Series A				Series C			
Composition of mixture (μg/ml)		Absorbance at 216.6 nm ± S.D. (n=5)	% C.V.	Composition of mixture (μg/ml)		Absorbance at 216.6 nm -Absorbance at 262.9 nm ± S. D. (n=5)	% C.V.
DXP	PCM			DXP	PCM		
3	0	0.11±0.003	2.62	3	15	0.112±0.004	3.13
4	0	0.148±0.005	3.42	4	20	0.147±0.004	2.60
5	0	0.178±0.006	3.43	5	25	0.179±0.004	2.28
6	0	0.211±0.003	2.85	6	30	0.210±0.003	1.50
7	0	0.242±0.003	2.43	7	35	0.242±0.003	1.28
8	0	0.278±0.005	1.87	8	40	0.280±0.008	2.93
9	0	0.312±0.006	2.07	9	45	0.311±0.007	2.30

length data processing program. To remove the interference of PCM to the absorbance at 216.6 nm (λ_1), the wavelength of minimum absorbance for PCM, another wavelength 262.9 nm (λ_2) was found out at which the absorbance of DXP was zero. This was confirmed by measuring the absorbance of various dilutions of PCM in 0.1 N hydrochloric acid solution at 216.6 nm and 262.9 nm, respectively. The absorbances at these two wavelengths were found to be equal. These two selected wavelengths were employed to determine the concentration of DXP from the mixture of DXP and PCM. The difference in absorbance at these two wavelengths ($A_{216.6}$-$A_{262.9}$) cancels out the contribution of absorbance of PCM in measurement of DXP at 216.6 nm and the difference in absorbance is proportional to the concentration of DXP in the mixture. It was found that this difference in absorbance values was linear in the range of 3-9 μg/ml of DXP with correlation coefficient 0.9997 (Table 1).

TABLE 2: DETERMINATION OF PCM ALONE AND PCM IN PRESENCE OF DXP BY THE PROPOSED DW SPECTROPHOTOMETRY.

Series B				Series C			
Composition of mixture (μg/ml)		Absorbance at 262.9 nm ± S.D. (n=5)	% C.V.	Composition of mixture (μg/ml)		Absorbance at 262.9 nm ± S. D. (n=5)	% C.V.
DXP	PCM			DXP	PCM		
0	15	0.443±0.009	2.07	3	15	0.442±0.007	1.64
0	20	0.585±0.008	1.41	4	20	0.585±0.008	1.36
0	25	0.734±0.006	1.88	5	25	0.730±0.010	1.47
0	30	0.859±0.003	1.99	6	30	0.856±0.022	2.6
0	35	1.021±0.003	1.96	7	35	1.016±0.013	1.36
0	40	1.157±0.005	1.61	8	40	1.152±0.022	1.98
0	45	1.271±0.006	1.22	9	45	1.281±0.022	1.73

TABLE 3: REGRESSION ANALYSIS DATA OF THE CALIBRATION CURVE OBTAINED USING SERIES A, B AND C.

Series	Composition of the sample solution		Regression equation of the curve	Coefficient of correlation
	DXP (μg/ml)	PCM (μg/ml)		
Series A	3-9	0	Y=0.0322x±0.0191	0.9940
Series B	0	15-45	Y=0.0282x±0.0204	0.9940
Series C	3-9	15-45	*Y=0.0331x±0.0131	0.9997
			**Y=0.0281x±0.0222	0.9997

Y is absorbance and x is concentration in μg/ml. *Regression equation for DXP, **Regression equation for PCM

Further, the absorbance value at 262.9 nm is only due to PCM, as DXP gives no absorbance value at this wavelength. It gave linear range of 15-45 μg/ml of PCM with correlation coefficient of 0.9997 (Table 2). These results confirm the suitability of the proposed method to determine the DXP and PCM simultaneously.

Regression analysis for series A and C shows no difference in the equations of straight line and thus indicates that there is no interference of PCM in determination of DXP (Table 3). Regression analysis for series B and C shows no difference in the equations of straight line indicates that there is no interference of DXP on measurement of PCM (Table 3). The optical characteristics of the series C such as Beer's law limit, Sandell's sensitivity, molar extinction coefficient of proposed method for determinations of both DXP and PCM were incorporated in Table 4.

For recovery study, known amounts of pure drug was added to the previously analyzed pharmaceutical preparations and the mixtures were analyzed by proposed method and the percent recovery was calculated which was found to be 99.6-102.4 for DXP and 99.9-101.3 for PCM. The method was applied for the analysis of three marketed formulations containing PCM 400 mg and DXP 65 mg per capsule. The results of analysis of capsule formulations are shown in Table 5. All of them meet pharmacopieal requirement of DXP and PCM.

The proposed method is based on dual wavelength data processing and only requires measurement of absorbance at selected wavelengths. The values of percent relative standard deviations were 1.59 for DXP determination and 0.86 for PCM determination showing reproducibility of the method. Interference studies revealed that the common

TABLE 4: OPTICAL CHARACTERISTICS OF THE PROPOSED METHOD.

Parameters	DXP estimation at 216.6 nm.	PCM estimation at 262.9 nm.
Wavelength for measurement	216.6 nm	262.9 nm
Beer's Law limit	3-9 μg/ml	15-45 μg/ml
Molar absoptivity (lit/mole/cm)	1.42×10^{4}	4.48×10^{3}
Sandell's sensitivity (μg/ml/cm²/0.001 abs. unit)	2.68×10^{-2}	3.43×10^{-2}
Regression equation (Y)		
Slope (b)	0.0331	0.0281
Intercept (a)	0.0131	0.0222
Correlation coefficient (r)	0.9997	0.9997
Relative standard deviation (%) (n=5)	1.59	0.86
% Recovery (n=5)	99.55-102.40%	99.88-101.33%

TABLE 5: ANALYSIS OF PHARMACEUTICAL FORMULATIONS.

Formulation	DXP % Found ±S. D. (n=3)	Acetaminophen % Found ±S. D. (n=3)
Capsule-1	96.8±1.37	95.6±0.38
Capsule-2	98.8±0.48	97.2±0.27
Capsule-3	98.5±0.25	95.0±0.54

Capsule 1 is Proxyvon, Wockhardt Pharmaceuticals Ltd., Mumbai, capsule 2 is Walagesic from Wallace Pharmaceuticals Ltd., Mumbai and Capsule 3 is Parvon from Jagsonpal Pharmaceuticals, New Delhi. SD is the standard deviation

excipients and other additives usually present in the dosage forms did not interfere in the proposed method for estimations of both drugs. The proposed method was found to be simple, rapid, economical, accurate and precise. It is particularly useful for routine in-process quality control and simultaneous quantification of DXP and PCM in combined capsule dosage forms.

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