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RESEARCH ARTICLE

Development of spectrophotometric method for simultaneous estimation of dexketoprofen and dicyclomine

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ABSTRACT

Objectives: The objective of this work was to develop a simple, fast, and reliable ultraviolet (UV) spectrophotometric method for simultaneous estimation of dexketoprofen and dicyclomine in tablet dosage forms. **Materials and Methods:** Dexketoprofen and dicyclomine solutions were prepared separately in the range of 2 µg/mL–10 µg/mL. The solutions were scanned over a range of 200–400 nm. The isoabsorptive point for both drugs was determined. The developed method was evaluated for accuracy, precision, and linearity. In linearity correlation coefficient was found. **Results:** A simple, fast, and reliable UV spectrophotometric method was developed for quantitative estimation of dexketoprofen and dicyclomine. The precision study showed that the percent relative standard deviation was within the range of acceptable limits, and the percent recovery was found to be in the range of 0.3–1.5 (intraday) and 0.23–1.7 (interday). In the accuracy study, the percent recovery was found to be 97 (50%), 96 (100%), and 95 (150%). **Conclusion:** The developed spectrophotometric method in this study was simple, accurate, precise, specific, sensitive, and reproducible and can be directly and easily applied to pharmaceutical dosage forms.

KEY WORDS: Accuracy, Dexketoprofen, Dicyclomine, Linearity, Precision, Pharmaceutical analysis, Simultaneous estimation

INTRODUCTION

Dexketoprofen, also known as (S)-2-(3-benzoylphenyl) propionic acid with the molecular formula $C_{16}H_{14}O_3$ and the molecular weight 254.28 g/mol, is a non-opioid, non-steroidal anti-inflammatory drug that exhibits antipyretic, anti-inflammatory, and analgesic characteristics and is mostly used to reduce inflammation and relieve pain such as pain associated with menstrual periods, dental pain, and pain in the joints and muscles.[1-4] Dicyclomine, also known as 2-(diethylamino)ethyl 1-cyclohexylcyclohexane-1-carboxylate with the chemical formula $C_{19}H_{35}NO_2$ and molecular weight 309.487 g/mol, is an anticholinergic and antispasmodic drug that works by inhibiting cholinergic receptors in the smooth muscle to minimize the effects of acetylcholine. It has a direct calming effect on smooth muscles as well.[5-7] The spasmolytic action of dicyclomine is used to treat a variety of smooth muscle spasms, especially those in the gastrointestinal system. It is beneficial in the treatment of pylorospam, dysmenorrhea, and biliary dysfunction.[8] It is also used in the treatment of irritable bowel syndromes such as spastic colon, irritable colon, and mucous colitis.[9] The combination of dexketoprofen and dicyclomine has a synergistic effect. This combination

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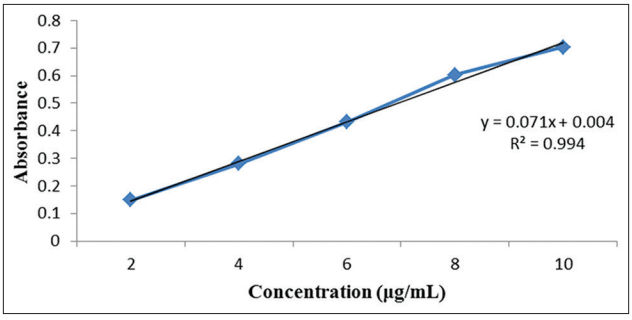

Figure 1: Standard plot of dexketoprofen in phosphate buffer pH 7.4

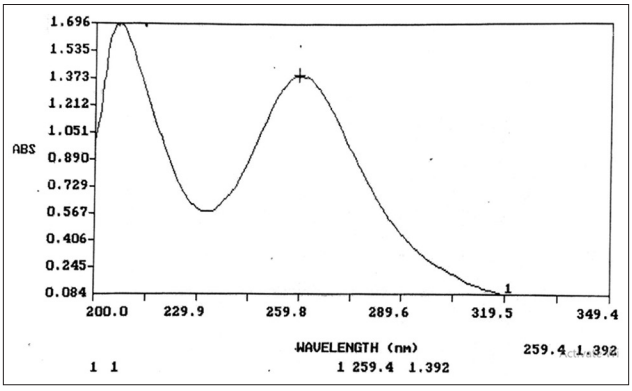

Figure 2: Ultraviolet scan of dexketoprofen

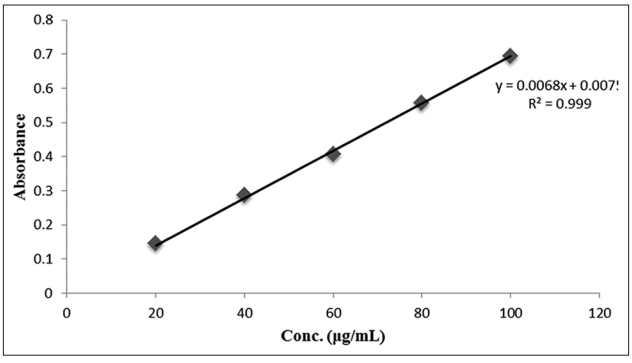

Figure 3: Standard curve of dicyclomine in phosphate buffer pH 6.8

is highly effective in relieving pain associated with inflammation.

A thorough review of the literature revealed that several high-performance liquid chromatographic, ultraviolet (UV), and stability-indicating techniques for dexketoprofen and dicyclomine hydrochloride, either alone or in combination with other medications, have been published. To the best of our knowledge, no spectrophotometric method for the combination of these two drugs has been described. The aim of this study was to develop a fast, novel, accurate, simple, repeatable, sensitive, and cost-effective spectrophotometric method for the determination of dexketoprofen and dicyclomine hydrochloride in the tablet dosage form. The proposed method was developed and validated in accordance with the International Conference on Harmonization (ICH) guidelines.

Table 1: Major infrared band assignments of dexketoprofen

Band position (cm^{-1})	Assignment
3200–2500	0-H stretching
3024	C-H stretching of aromatic groups
2978, 2937	C-H stretching of CH3 group (asymmetric)
2879	C-H stretching of CH3 group (symmetrical)
1708	C=0 stretching of the acid
1654	C=0 stretching of the ketone
1593, 1448	C-C stretching of the aromatic ring
1370	C-H deformation of aromatic rings
650–880	C-H deformation of aromatic rings

MATERIALS AND METHODS

Materials

All the chemicals used were of analytical grade. Dexketoprofen was supplied as a gift sample by Emcure Pharma, India, and dicyclomine hydrochloride was received as a gift sample from Crystal Pharmaceuticals, Ambala, India.

Method development

Dexketoprofen and dicyclomine solutions were prepared separately in the range of 2 µg/mL–10 µg/mL. The solutions were scanned over a range of 200–400 nm. The isoabsorptive point for both drugs was determined. The developed method was evaluated for accuracy, precision, and linearity. In linearity correlation coefficient was found.

Method validation

The developed method was validated as per ICH guidelines. The validation parameters were linearity, accuracy, precision, ruggedness, assay, limit of detection (LOD), and limit of quantification (LOQ).

Linearity

The linearity of calibration curves in pure solution was checked over the ranges of 2–10 µg/mL for dexketoprofen and dicyclomine. The samples were scanned through a UV-visible spectrophotometer using methanol as a blank. It was found that the selected drug shows linearity between the ranges of 2 µg/mL and 10 µg/mL. The absorbance values of these solutions were measured at 200–400 nm. The slope, intercept, and correlation coefficient of standard curves were calculated.

Table 2: Absorbance for the standard plot of dicyclomine at 276 nm

S. No.	Concentration (µg/mL)	Absorbance				Standard deviation
		1	2	3	Average	
1.	20	0.145	0.145	0.147	0.146	0.001
2.	40	0.284	0.286	0.289	0.286	0.003
3.	60	0.402	0.402	0.414	0.406	0.007
4.	80	0.547	0.551	0.576	0.558	0.016
5.	100	0.694	0.689	0.699	0.694	0.005

Table 3: Precision of dexketoprofen and dicyclomine showing intraday and interday absorbance

Concentration (µg/mL)	Standard absorbance	Intraday absorbance (*n*=3)	Interday absorbance (*n*=3)
2 µg/mL	0.064	0.062	0.063
		0.064	0.064
		0.063	0.061
6 µg/mL	0.502	0.499	0.501
		0.501	0.498
		0.500	0.502
10 µg/mL	0.846	0.841	0.843
		0.845	0.845
		0.840	0.844

Table 4: Precision sample containing dexketoprofen and dicyclomine showing SD and RSD

Concentration (µg/mL)	SD		%RSD	
	Intraday	Interday	Intraday	Interday
2 µg/mL	±0.001	±0.0012	1.5	1.7
6 µg/mL	±0.002	±0.0016	0.3	0.31
10 µg/mL	±0.004	±0.002	0.47	0.23

SD: Standard deviation, RSD: Relative standard deviation

Precision

Three replicate measurements of three distinct concentrations were used to calculate the system precision. To evaluate the method's precision, interday (3 days) and intraday (3 times) sample measurements were done, with percent relative standard deviation (%RSD) calculated for replicate samples (n = 3) using concentrations of 50% (50 g/mL), 100% (100 g/mL), and 150% (150 g/mL). On the day of analysis, both interday and intraday results were calibrated using a standard curve that was prepared concurrently.

Accuracy

The accuracy was achieved by adding a known amount of pure drug to the previously tested solution containing the pharmaceutical formulation, then analyzing the combination using the suggested method and calculating the recoveries. The standard concentration of the sample was taken at 6 µg/mL, from which the reference standards of the samples were added at levels of 50%, 100%, and 150%. The recovery studies were carried out three times, and the percent recovery and %RSD of the recovery of tablet samples containing dexketoprofen and dicyclomine were calculated.

LOD

The LOD value was calculated from the calibration curve using the equation LOD = 3.3 SD/slope of the corresponding calibration curve.

LOQ

The LOQ value was calculated from the calibration curve using the equation LOQ = 10 SD/slope of the corresponding calibration curve.

Ruggedness

The ruggedness was studied by using different analysts for solutions of the same concentration sample containing dexketoprofen and dicyclomine. SD and %RSD were calculated.

Standard plot of dexketoprofen in pH 7.4 phosphate buffer

100 mg of drug was dissolved in 100 mL of pH 7.4 phosphate buffer; serial dilutions were then prepared to make a final concentration of 2, 4, 6, 8, 10 µg/mL. The absorbances were then measured at the maximum wavelength of 259.4 nm. The standard curve is shown in Figure 1.

The FTIR spectrum of dexketoprofen obtained was compared with the spectrum available in Pharmacopoeia, and both spectra had identical peaks and the same functional groups, which confirmed the identity of the drug [Table 1].

Melting point

The supplied sample of the drug recorded a melting point of 96 ± 1°C (n = 3).

Table 5: Accuracy of sample containing dexketoprofen and dicyclomine showing recovery and RSD

Concentration of sample	Recovery level (%)	Amount of the drug added (µg/mL)	Total amount of the drug added (µg/mL)	Amount of the drug found mean±SD (*n*=3)	% Recovery	%RSD
Dexketoprofen+ dicyclomine (4 µg/mL)	50	2	6	93.11±0.001	97±0.002	0.08
	100	4	8	91.4±0.004	96±0.003	0.12
	150	6	10	90.21±0.003	95±0.004	0.32

SD: Standard deviation, RSD: Relative standard deviation

Table 6: Accuracy of sample containing dexketoprofen and dicyclomine showing mean absorbance

Total amount of the drug added (µg/mL)	Standard absorbance	Calculated absorbance	Mean absorbance
6	0.5	0.499	0.497
		0.497	
		0.496	
8	0.715	0.714	0.713
		0.713	
		0.711	
10	0.844	0.842	0.840
		0.839	
		0.840	

Scanning of drug

Samples of the drug were scanned by double-beam UV spectrophotometer to determine the λ_{max} of dexketoprofen. It was found to be 259.4 nm [Figure 2].

Identification of the dicyclomine

Standard curve of dicyclomine in phosphate buffer pH 6.8

The solution was scanned for maximum absorbance and found a maximum absorbance value of 0.46 at 276 nm. This value lies within the standard range of 0.44–0.51 given in Indian Pharmacopoeia 2014,[10] so the drug was identified as dicyclomine. The results are shown in Table 2, and the standard curve is shown in Figure 3.

RESULTS AND DISCUSSION

Linearity

The linearity of dexketoprofen was determined in the range of 2–10 µg/mL. The correlation coefficient (r^2) for the calibration curve of dexketoprofen was found to be 0.994, which is within the limits of acceptance criteria. The calibration curve was created by plotting absorbance versus concentration, as shown in Figure 1.

Precision

The results of the intraday and interday precision experiments are shown in Tables 3 and 4.

The values of %RSD for intraday and interday precision were found to be <2%. As a result, the method developed for dexketoprofen and dicyclomine was shown to be precise in accordance with ICH guidelines.

Accuracy

The accuracy results are shown in Tables 5 and 6. The percentage recovery was found to be 95–97% and the %RSD was found to be <2%, both of which are well within the limits, indicating that the method was accurate.

CONCLUSION

From the present study, it can be concluded that the optimized and validated ultraviolet spectroscopic method is simple, sensitive, precise, accurate, and reproducible. The developed method has been validated as per ICH guidelines, and it meets all the acceptance criteria given in ICH guidelines [ICH Q2 (R1)]. Hence, it can be used in routine analysis for the simultaneous estimation of tablets containing dexketoprofen and dicyclomine hydrochloride.

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CONFLICT OF INTEREST

Declared None.

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