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Simultaneous spectrophotometric determination of Celecoxib and Diacerein in bulk and capsule by absorption correction method and chemometric methods

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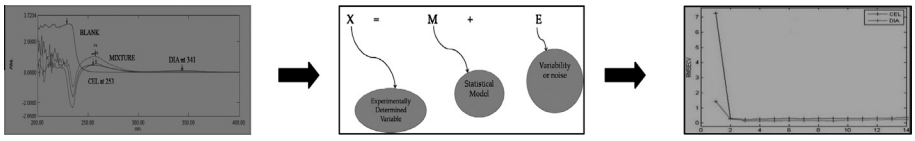
HIGHLIGHTS

- Development and validation of chemometric methods for simultaneous estimation of DIA and CEL.
- Development and validation of absorption correction method for simultaneous estimation of DIA and CEL.
- Statistical comparison of developed methods using ANOVA.

GRAPHICAL ABSTRACT



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ABSTRACT

Two methods, absorption correction and multivariate spectrophotometric methods were developed for simultaneous estimation of Celecoxib (CEL) and Diacerein (DIA) in combined dosage form. Absorption correction method involves direct estimation of DIA at wavelength 341 nm in which CEL has zero absorbance and shows no interference. For estimation of CEL, corrected absorbance was calculated at 253 nm due to the interference of DIA at this wavelength. Linearity was observed in the range of 6–22 μg mL^{-1} for CEL and 3–11 μg mL^{-1} for DIA. The method was validated as per ICH guidelines. Chemometric methods including classical least square (CLS), inverse least square (ILS), principal component regression (PCR) and partial least square (PLS) were studied for simultaneous determination of CEL and DIA in capsule using spectrophotometry. A set of 25 standard mixtures containing both drugs were prepared in range of 5–25 μg mL^{-1} for CEL and 3–15 μg mL^{-1} for DIA. Analytical figure of merit (FOM), such as sensitivity, selectivity, analytical sensitivity, limit of detection and limit of quantitation were determined for chemometric methods. The proposed methods were applied for determination of two components from combined dosage form.

Introduction

Celecoxib (CEL) is a selective COX-2 inhibitor. CEL is chemically, *p*-[5-*p*-Tolyl-3-(trifluoromethyl) pyrazol-1-yl] (Fig. 1A) [1]. Diacerein (DIA) is an interleukin-1 inhibitor (Fig. 1B). DIA is chemically, 9, 10-dihydro-4, 5-dihydroxy-9, 10-dioxo-2-anthranoic acid diacetate [2]. The marketed formulations OSTEGARD® 100 mg (Zydus healthcare, Ahmedabad) containing 100 mg of Celecoxib and 50 mg of Diacerein per capsule and OSTEGARD® 200 mg (Zydus healthcare, Ahmedabad) containing 200 mg of Celecoxib and 100 mg of Diacerein per capsule are available. The formulations are used in the treatment of osteoarthritis [3].

Based on literature review it was found that number of methods are available for estimation of CEL and DIA individually as well as in combination with other drugs. Spectrophotometric [4], HPLC

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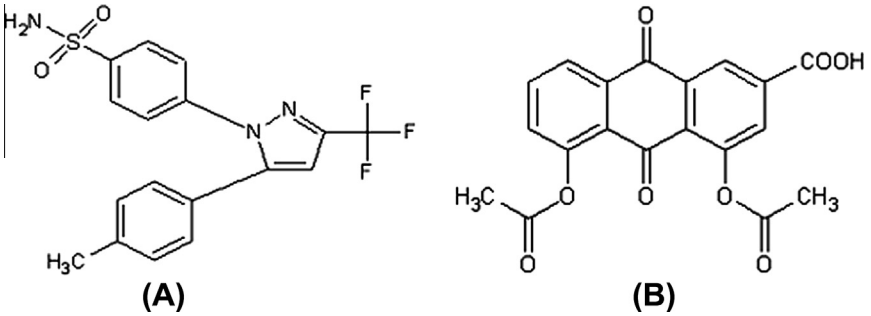

Fig. 1. Structure of (A) CEL, (B) DIA.

[5–9] and spectro-flourimetry [10,11] methods have been used for estimation of CEL and spectrophotometric [12–17], HPLC [18–23] and HPTLC [24–27] methods have been used for estimation of DIA. So far, UV-spectrophotometric [28] and HPLC [29] methods have been reported for estimation of CEL and DIA in combination.

UV/VIS spectroscopy is an instrumental technique of choice for the mentioned purpose in industrial laboratories due to its simplicity and ease of operation. Absorption correction method (ACM) is a simple spectrophotometric method which involves simultaneous estimation of both the drugs at their own λ_{max}. ACM is the modification of simultaneous estimation method. Here, quantitative determination of one drug is carried out by A (1%, 1 cm) and quantitation of other drug is carried out by subtracting absorbance of the other drug using absorption factor.

In recent years, multivariate calibrations such as classical least square (CLS), inverse least square (ILS), Principle component regression (PCR) and Partial lest square (PLS) have been employed extensively in quantitative spectral analysis to get selective information from the unselective data. These methods are widely accepted, as it gives the best results in terms of complex mixture resolution. These methods can be applied for the simultaneous spectrophotometric estimation of drugs in pharmaceutical formulation containing two or more drug compounds. CLS and ILS are some of the simplest methods having multivariate least square procedure based directly on Beer's law. PCR and PLS are factor analysis methods which are used to establish a relationship between matrices of the chemical data [30].

The reported spectrophotometric method for simultaneous estimation of these drugs, have used methanol as solvent for Diacerein [2] whereas the pharmacopoeia suggest use of more vigorous solvent such as DMSO, as DIA is practically insoluble in methanol. Another reported HPLC method utilizes acetonitrile in its mobile phase which raises the cost of analysis for simultaneous estimation of DIA and CEL [29]. Hence, there was a need to develop simple and cost-effective method for simultaneous estimation of these drugs in their combined dosage form. The present manuscript discusses about resolution of CEL and DIA using absorption correction method and its extension to chemometrics in order to improve its reliability and sensitivity.

Experimental

Instruments

A double beam UV-spectrophotometer, UV-1800 (Shimadzu, Japan) equipped with 1 cm quartz cells and 2 nm fixed slit width connected to a computer loaded with Shimadzu UVPC software was used. An analytical balance (CP 124S, Sartorius, Germany) was used to weigh accurately the standard and test samples. The additional PLS-tool box software (EIGENVECTOR) and MATLAB 7.8 were used for chemometric methods. The zero order spectra was recorded over 200–400 nm wavelength with one data point per nanometer for absorption correction and chemometric methods.

Chemicals

Standards for Celecoxib and Diacerein were obtained as gift samples from Zydus healthcare, Ahmedabad. Di-methyl sulphoxide (DMSO) and methanol of analytical grade purity were purchased from Finar chemicals, Vadodara. Double distilled water (In house) was used throughout study.

Standard stock solution of drugs

Standard stock solutions of CEL and DIA (1000 μg mL^{-1}) were prepared individually by dissolving 100 mg in 100 mL in DMSO.

The working standard solutions of CEL and DIA (100 μg mL^{-1}) were prepared individually by further dilution of standard stock solution with methanol:water (50:50).

ACM method

The solutions were prepared by diluting the suitable aliquots of working standard solution with methanol: water (50:50) to reach a concentration range 6–22 μg mL^{-1} for CEL and 3–11 μg mL^{-1} for DIA.

Chemometric methods

The working standard solutions were prepared by diluting suitable aliquots of working stock solution with methanol: water (50:50) to obtain a concentration range 5–25 μg mL^{-1} for CEL and 3–15 μg mL^{-1} for DIA.

Methods

Absorption correction method

UV absorbance spectra of CEL and DIA were recorded between 200 and 400 nm. CEL showed maximum absorbance at 253 nm and DIA showed maximum absorbance at 257 nm and 341 nm. At 341 nm CEL did not show any absorbance. Hence, DIA can be directly estimated by measuring absorbance at 341 nm. Absorbance of CEL can be determined by use of absorbance factor.

ACM method validation

Linearity and range

Aliquots of working stock solutions of CEL and DIA were diluted with methanol: water (50:50, v/v) to get final concentrations in range of 6–22 μg mL^{-1} for CEL and 3–11 μg mL^{-1} for DIA. The study was performed five times and average absorbance was calculated for respective wavelengths. The calibration curves were