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Study on the inclusion complex between β-cyclodextrin and celecoxib by spectrofluorimetry and its analytical application

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Abstract

The supramolecular interaction of celecoxib (chemically 4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl] benzene sulfonamide) and β-cyclodextrin (β-CD) has been studied by spectrofluorimetry. The results showed that β-CD reacted with celecoxib to form an inclusion complex. 1:1 stoichiometry for β-CD-celecoxib complex was established and its association constant at different temperatures was calculated by applying a non-linear regression method to the change in the fluorescence of celecoxib that brought about by the presence of β-CD. The thermodynamic parameters (ΔH°, ΔS° and ΔG°) associated with the inclusion process were also determined. Based on the significant enhancement of the fluorescence intensity of celecoxib produced through complex formation, a simple, rapid and highly sensitive spectrofluorimetric method for the determination of celecoxib in aqueous solution in the presence of β-CD was developed. The measurement of relative fluorescence intensity was carried out at 390 nm with excitation at 270 nm. A linear relationship between the fluorescence intensity and celecoxib concentration was obtained in the range of 0.1–4.0 μg ml^{-1}, with a correlation coefficient of 0.9996. The detection limit was 7.29 ng ml^{-1} and the relative standard deviation was 1.28%. The method was successfully applied to the determination of celecoxib in pharmaceutical preparations.

Keywords: Inclusion complex; Celecoxib; Cyclodextrin; Spectrofluorimetry

1. Introduction

Cyclodextrins (CDs) are water-soluble cyclic oligosaccharides composed of six (α–), seven (β–) and eight (γ–) units of D-(+)-glucopyranose arranged in a truncated cone shape structure. The hydrophobic cavity of CDs can host a large variety of organic and inorganic compounds of suitable size. The formation of an inclusion complex greatly affects the physical chemical properties of the guest molecules, such as solubility, chemical reactivity and the spectroscopic and electrochemical properties, and most of these effects can be utilized in many fields including pharmaceutical industry (to improve the solubility, stability and bioavailability of pharmaceuticals, as a carriers of active substances in biological systems and to retard the release of active substances from the pharmaceutical matrix) and various branches of analytical chemistry [1–3]. From an analytical point of view the formation of inclusion complexes allows, in certain cases, to improve the performance of the methods for the determination of different analytes including pharmaceuticals [4–9].

Celecoxib (celebrex), 4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide (Fig. 1), a non-steroidal anti-inflammatory drug (NSAID), is the first selective inhibitor of cyclooxygenaze-2 (COX-2) approved to treat patients with rheumatism and osteoarthritis. Preliminary data suggested that celecoxib also has analgesic and anti-cancer properties. The drug has similar efficacy as conventional NSAIDs in improving the symptoms of osteoarthritis and

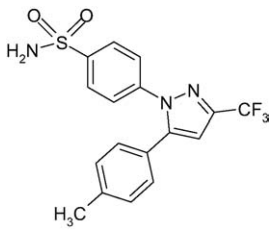

Fig. 1. Structural formula of celecoxib.

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rheumatoid arthritis but celecoxib is associated with a lower incidence of gastrointestinal ulceration and complication [10]. The chemopreventive effect of celecoxib on colon cancer [11] and its clinical effects on blood platelets [12] have been investigated and reported. Furthermore, another study showed that celecoxib can reduce the polyps formation in patients with familial adenomatous polyposis [13] and has led to the approval of celecoxib as adjuvant treatment of familial adenomatous polyposis. Many analytical methods have been described for the determination of celecoxib in pharmaceutical formulation and human plasma. These methods include micellar electrokinetic chromatography (MEKC) [14], spectrophotometry [15], first-derivative spectrophotometry [16], thin-layer chromatography (TLC) [16], adsorptive stripping voltammetry [17], liquid chromatography (LC) [18,19] liquid chromatography–mass spectrometry(LC–MS) [20–22], solid-phase extraction and high-performance liquid chromatography (SPE-HPLC) [23], high-performance liquid chromatography with UV [24–26] and fluorimetric [27] detection.

Spectrofluorimetry has been widely used in the determination of pharmaceutical compounds [4–9] because it is highly sensitive, selective, easily operated and economic. The enhancement of the fluorescence emission of celecoxib due to its complexation with β-CD might be very useful from an analytical point of view. To the best of our knowledge, the use of β-CD as the sensitizing agent for the determination of celecoxib in the aqueous solution has not been reported. Therefore, in the present study, the host-guest complexation of celecoxib with β-CD was investigated by using fluorescence spectroscopy. The stochiometry and association constant of the β-CD -celecoxib complex were studied and its thermodynamic parameters were obtained. Based on the inclusion reaction, a sensitive spectrofluorimetric method for the determination of celecoxib was developed and compared with the results obtained in the absence of β-CD. The proposed method was applied to the determination of celecoxib in capsules.

2. Experimental

2.1. Apparatus

1. Fluorescence spectra and intensity measurements were made on a Shimadzu RF-540 spectrofluorimeter equipped with a 150 W xenon lamp.

2. All measurements were performed at 25 ± 0.1 °C by the use of a thermostated cell holder and a thermostatically controlled water bath.

3. A Metrohm model 654 pH meter was used for pH measurements. A micropipette (Eppendorf, 3130 Germany) was used for transfer of the acid or base solution throughout the pH study stage.

4. A balance (Libror AEL-200, shimadzu) was used for weighting the solid materials.

2.2. Reagents

1. Pure celecoxib was obtained from Ipca Laboratories Limited (India).

2. α- and β-cyclodextrin (α- and β-CD) were purchased from Merck, and hydroxypropyl-β-cyclodextrin (HP-β-CD) was obtained from Acros organics (Geel, Belgium). β-CD was recrystallized once from boiling water.

3. A 100 μg ml^{-1} stock standard solution of celecoxib was prepared by dissolving 10.0 mg of drug in a methanol (Merck) and diluting to the mark in a 100 ml volumetric flask with methanol. Dilute standard solutions were prepared daily in water just before use.

4. All reagents were of analytical reagent grade and all solutions were prepared in triply distilled water. The materials and vessels used for trace analysis were precleaned by soaking in sulfochromic acid mixture (saturated $K_2Cr_2O_7$ in concentrated H_2SO_4) for at least 1 h and subsequently rinsed four times with triply distilled water before use.

2.3. Procedures

2.3.1. Determination of celecoxib

A 1.0 ml portion of 10 μg ml^{-1} celecoxib standard solution was transferred into a 5 ml volumetric flask and 3.0 ml of 1.5×10^{-2} mol l^{-1} β-CD solution was added. After dilution to mark with water, the mixture was shaked and equilibrated at room temperature for 5 min, then using 1.0 cm quartz cell, the relative fluorescence intensity of the solution was measured at 390 nm with excitation at 270 nm against a reagent blank prepared with the same reagent concentrations, but no celecoxib. Both excitation and emission slit widths were set at 5 nm. The fluorescence spectra were recorded at scan rate of 254 nm min^{-1}.

2.3.2. Influence of pH

The change in steady state fluorescence intensity of both celecoxib and celecoxib-β-CD complex solutions as a function of pH were studied by following procedure. To a stirred sodium hydroxide solution of celecoxib or celecoxib-β-CD, small increments of HCl solution (0.1–2 mol l^{-1}) were added. For each pH point an aliquot of solution was extracted and fluorescence spectrum was read. The initial concentration of celecoxib and β-CD in the reaction vessel were 5.42×10^{-6} and 0.01 mol l^{-1}, respectively. The ionic strength of solution was maintained at 0.1 mol l^{-1} using NaCl.

2.3.3. Influence of β-CD concentration

The effect of β-CD concentration on the fluorescence intensity of celecoxib was studied. The celecoxib concentration was held constant in 5.42×10^{-6} mol l^{-1}, while the β-CD concentration was varied from 0 to 0.01 mol l^{-1}. Individual samples were prepared according to the following procedure. A 1.0 ml aliquot of 2.62×10^{-5} mol l^{-1} celecoxib solution (prepared by dilution of stock solution with water just before use) was transferred into a 5 ml volumetric flask and