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Short communication

Application of a self-modeling curve resolution method for studying the photodegradation kinetics of nitrendipine and felodipine

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Abstract

Dihydropyridine (DHP) derivatives, as calcium channel blockers with cardiovascular activity, are highly photosensitive and converted in the presence of light to compounds that are inactive. In this work, a self-modeling curve resolution method was applied to study the photodegradation kinetics of nitrendipine and felodipine by spectrophotometric method. The methanolic solutions of drugs were separately exposed to UV and daylight, respectively. A fully soft-modeling multivariate curve resolution method based on the combination of iterative target transformation and Kubista methods were used to analyze the recorded absorbance data, extracting the concentration profiles and pure spectra of the drugs and their photodegradation products. By fitting the concentration profiles of the studied DHP drugs to different kinetic equations, it was found that at the beginning of lighting, the reaction is zero-order and in the case of nitrendipine it changes to a first-order kinetic when the concentration of products exceeded than that of the initial compounds.

Keywords: Photodegradation; Multivariate curve resolution; Nitrendipine; Felodipine

1. Introduction

Nitrendipine, 4-(3-nitrophenyl)-1,4-dihydro-2,6-dimethylpyridine-3,5-dicarboxylate and felodipine, 4-(2,3-dichlorophenyl)-1,4-dihydro-2,6-dimethylpyridine-3,5-dicarboxylate (see Fig. 1), are calcium channel antagonists of dihydropyridine (DHP) class used in the treatment of hypertension [1–3]. DHP derivatives are highly photosensitive and converted in the presence of light to compounds that are inactive, and the most of the methods used for these studies were different chromatographic methods [4–12]. Of course chromatographic methods are difficult to operate and use relatively expensive instruments. In addition, further degradation of drugs may occur during the chromatographic analysis.

In the other hand, spectrophotometric methods are in general simple, sensitive and very suitable for studying chemical reactions in solutions. The spectral overlapping, as the major problem in almost all of the spectrochemical methods, can be overcome utilizing different chemometric methods [13]. For example, spectral curve deconvolution or multivariate curve resolution (MCR) methods are chemometrics techniques concerning with the extraction of the pure spectra and concentration profiles of the components in a chemical reaction preceded in an evolutionary process [14–16]. There are some literature reports on the use of different MCR methods for studying the forced degradation kinetics of drugs and other biologically important compounds [17,18].

In our research group, we have some interests on DHP derivatives and many papers have been published from this group regarding this type of molecules in different subjects [19–24]. We employed a constrained self-modeling MCR method for monitoring the photodegradation kinetics of nifedipine, the prototype of DHP drugs [25]. Since the photodegradation kinetic of DHP-based drugs is complex and it is preceded in zero- and first-order manners, application of hard-modeling methods is not straightforward. Thus, we extend our previously self-modeling method for studying the photodegradation monitoring

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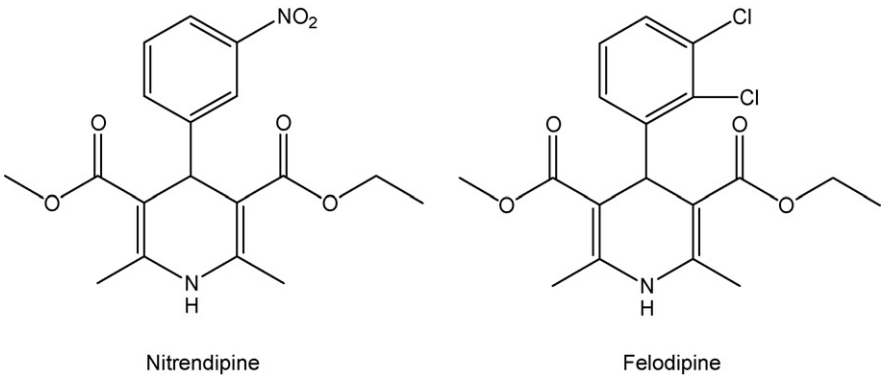

Fig. 1. Chemical structures of nitrendipine and felodipine.

of two other DHP derivatives, i.e., nitrendipine and felodipine.

2. Experimental

2.1. Reagents and chemicals

Pure powders of drugs (nitrendipine and felodipine) were prepared from Sigma Chemical Co. The 100 μg/mL stock solution of each drug was prepared by dissolving appropriate amounts of drugs in methanol (Merck) under sodium lamp and used to prepare daily solutions.

2.2. Apparatus

The UV–vis absorbance spectra were recorded by a Shimadzu spectrophotometer (Tokyo, Japan) equipped with a 10.0 mm quartz cell and a water-thermostated cell holder. A home-made dark woody cabinet equipped with UV lamps of 254 nm wavelengths was used.

2.3. Procedure

The radiation tests were employed utilizing a 254-nm UV lamp for nitrendipine and natural sunlight for felodipine. In the case of nitrendipine, to protect samples from extraneous light, irradiation was conducted in a dark room with controlled temperature. The UV–vis absorbance spectra of the methanolic solution of nitrendipine, exposed to the UV lamp, were recorded between 220 and 400 nm in 24-h intervals for 15 days. The digitized absorbance data (in 1.0 nm intervals) were collected in a data matrix with a dimension of (182 × 15).

In the case of felodipine, the photodegradation was monitored in sequential sunny days in the time duration of 10 a.m. till 4 p.m. At the end of each day, the resulting solution was protected by aluminum foil and stored in the refrigerator to prevent further degradation and then in the new day, its temperature was raised to room temperature and then subjected to sunlight. The absorbance spectra of the irradiated solutions were recorded between 230 and 400 nm in 2 h intervals for 4 days. Since in each day the drug was exposed to sunlight for 6 h, the total lighting time was 24 h and 14 absorbance spectra were collected through-

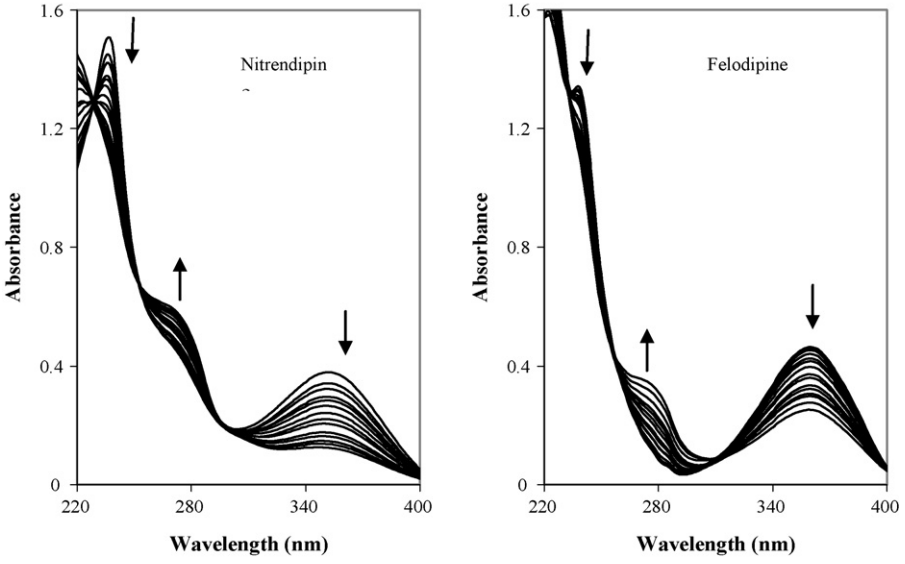

Fig. 2. Absorbance spectra of nitrendipine (6.90×10^{-5} M methanolic solutions, exposure to 254 nm UV lamp) and felodipine (6.50×10^{-5} M methanolic solution exposure to natural sunlight).