RESEARCH ARTICLE

Chemometric Exploration of Photostability of Ornidazole in Aqueous Solution with Soft and Hard Modelling Multivariate Curve Resolution Method

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ABSTRACT

The photodegradation study of ornidazole in an aqueous solution was performed by using the multivariate curve resolution-alternative least square technique. The sample solution was exposed to direct sunlight for 42 hours, and the spectroscopic data was obtained at predetermined intervals of wavelengths. MCR-ALS, which is a chemometric technique, was applied to the data set. Initially, soft modeling was used, followed by hard modeling. The results show that ornidazole undergoes photodegradation via a two-step process in an aqueous medium, with three species involved in the degradation process. The initial concentration of pure ornidazole decreases while the concentration of intermediate start increasing and the concentration of intermediate falls with the formation of a new product. Thus, we have got three pure spectra in the MCR-ALS process. The reaction kinetics was performed with the hard modeling technique using kinetic constrain and the rate constant of the reaction was found to be k1 = 0.0955 and k2 = 1.287, respectively.

Keywords: Ornidazole, Photostability, Photodegradation, Chemometrics, Multivariate curve resolution.

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INTRODUCTION

Photostability of drug molecules is a very important aspect when it comes to the formulation of the drug molecule. The photostability of the drug molecule is related mainly to its chemical structure and the presence of some characteristic functional groups. Photochemical reactions can lead to the decomposition of the drug molecule which may result in the formation of some degradation products that may be harmful to the human being. The study of photodegradation reaction is very essential at the time of formulation development and selection of the packaging material for the formulation. These photochemical reactions may change the molecule's and formulation's physical or chemical nature. Drug molecules can undergo decomposition by absorbing photons emitted by sunlight, possibly in the form of UV-vis light or Infrared radiations.[1]

Most of the time, chromatographic methods like HPLC, UPLC, and HPTLC are used for the identification of drug degradation. MCR-ALS is a chemometric approach that can be used to demonstrate the stability of the drug molecule using spectrophotometric data. It helps to understand multiple sources of variability in spectroscopic measurements and can be used to investigate complex chemical reactions by assessing the number of constituents involved in the reaction process, along with their concentration profile. It also allows the determination of rate constants when the investigated process is a kinetic reaction (k).[1,2]

The present work is focused on studying the photo-degradation of ornidazole in an aqueous medium and gaining knowledge of the number of species that the photochemical interaction will form. Ornidazole is used as an antiprotozoal and antimicrobial agent. Chemically it is 1(3-chloro-2-hydroxypropyl)-2-methyl-5-nitro imidazole, and it is a third-generation nitroimidazole.[3] A soft-modeling approach was first applied to get information regarding the concentration profile in the photodegradation process of ornidazole. This data was further used in the hard-modeling approach, which helps to understand the photodegradation kinetics of the Ornidazole degradation.

The theoretical background of multivariate curve resolution and alternative least square technique is already available in the

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previously published literature.[4-13] The MCR-ALS algorithm performs a bilinear decomposition of the experimental data matrix into the product of two-factor matrices having reduced size.

MATERIAL AND METHOD

Preparation of Standard Ornidazole Solution

A stock solution of ornidazole was prepared by dissolving 100 mg of the pure drug in 100 mL of double-distilled water. The stock solution was covered properly with aluminum foil to avoid unnecessary reaction with sunlight or daylight. This stock solution was further diluted to get a concentration of 25 ppm.

Apparatus and Software

A double beam UV-vis spectrophotometer (Jasco; model V-650) having a 10-mm quartz cell was used to record the UV-vis spectra. Data was recorded for an interval of 1 nm wavelength. MCR-ALS was performed by utilizing the MATLAB environment (MathWorks, USA) using the MCR-ALS toolbox developed and designed by Tauler and de Juan. The toolbox can be found by using the link http://www.ub.es/gesq/mcr/mcr.htm on the MCR site.

Photodegradation of ornidazole was performed in the presence of natural sunlight. A 25 µg/mL aqueous solution of ornidazole was transferred in a transparent volumetric flask and the flask was exposed to sunlight on consecutive sunny days from 10:00 a.m. to 4:00 p.m. After 4 o'clock in the afternoon, the same solution was covered with aluminum foil, then stored in a suitable refrigerator to prevent any more degradation of the concerned sample solution. The next day the solution was removed from the refrigerator and kept out at room temperature for some time, then the solution was again exposed to the natural sunlight. The absorbance of the solution kept in sunlight was measured in the wavelength range of 200–400 nm every 1 hour. The experiment was continued for up to 42 hours or until the drug degrades. The resulting absorbance spectra were digitized and recorded in the data matrix at 1.0 nm intervals.

RESULTS AND DISCUSSION

When the aqueous solution of ornidazole was exposed to natural sunlight for 42 hours and UV absorbance measurements were acquired, changes in the spectral profile of ornidazole were observed (Figure 1). The ornidazole spectrum has two absorption maxima at 320 and 230 nm. Upon exposure to light, a decrease in the absorbance is observed for the 320 nm wavelength. Furthermore, for the 230 nm wavelength, an increase in absorbance was seen. These modifications in the spectral region could be caused by the decomposition of ornidazole, forming degradation product (s). The lack of a comprehensive or narrow isosbestic point may reflect that the reaction involves more than one step, that two distinct products are formed, or that an intermediate product is generated, which may be converted to a new product.

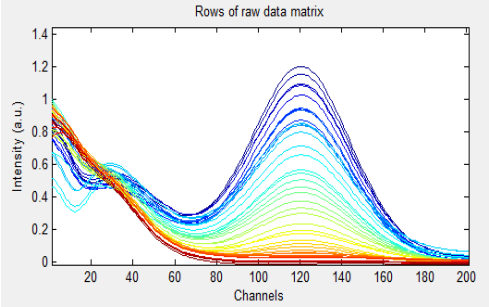

Figure 1: Overline UV spectra of ornidazole for an interval of 42 hours

The experimental data was first subjected to principal component analysis (PCA) to determine the exact independent absorbing species number formed in the photodegradation process of ornidazole. Assessment of singular data (also called Eigenvalues) can provide a preliminary insight into estimating the number of chemical components. This was further confirmed with the Pure variable section. In this step, a 10% noise level was allowed and two different spectral profiles were present in the given spectral data. We can go for Evolving factor analysis for further confirmation about values or components.

Analysis of SVD data shows that there are three unique values that are significantly greater than the others, implying that about three chemical species might be present. This conclusion was backed up by the EFA. Figure 2 shows that the forward, as well as backward EFA graphs and overall EFA (Figure 3 a) reveal a gap of a considerable amount between the initial three Eigen data results. Also, the remainder confirms the existence of three components or chemical species in the ornidazole photodegradation mechanism.

ALS optimization was performed and the results also confirmed three species with good agreements of percentage variance explained by the model and the maximum R^2 square value. The standard deviation of residuals against experimental data was 0.0055, the Percent lack of fit was 0.44% (< 1% anticipated), and the model demonstrated variability is significantly larger than 99.98%. The rectified concentration profiles and pure spectra (ST) of ornidazole photodegradation by MCR-ALS reveal that when subjected to direct sun, the corresponding concentration of the ornidazole preliminary reactant or starting element reduces as an intermediate product is formed. The fraction of the transitional product progressively declined as the exposure expanded, accompanied by the formation of new chemical species, which is the finished product of the reaction. Thus, the soft modeling approach gave an idea about the concentration profile and showed that the photodegradation of ornidazole follows a two-step reaction. The rate of reaction and kinetic profile obtained for the three-component system were obtained by the hard modeling approach used in the MCR-ALS.

Figure 3(b) shows that the concentration of the first species, which was pure ornidazole, decreases as time increases. The concentration profile of the 2nd species, which is an

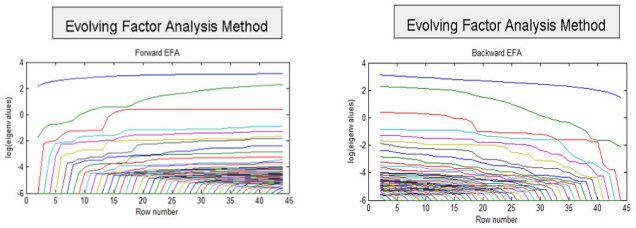

Figure 2: Forward and backward EFA

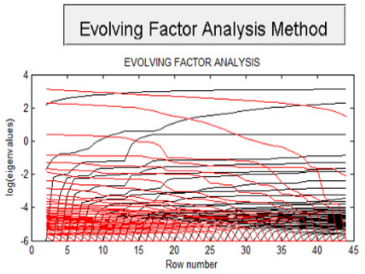

Figure 3:(a) Results of overall EFA

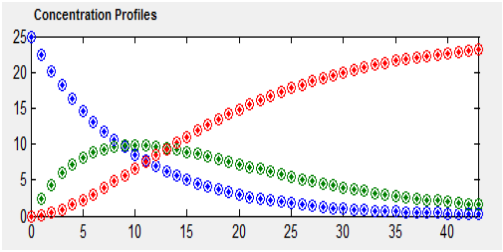

Figure 3: (b) Kinetic of the photodegradation reaction of ornidazole

intermediate, show that the initial concentration of this species increases but after a certain time, it again starts decreasing and falls to zero at the end.

The concentration profile of the third species shows that the initial concentration of this species is zero which goes on a gradual increase as time proceeds and finally, all the starting material is converted into the third species, which is a new degradation product of ornidazole. The rate of reactions K1 and K2 are calculated and were found to be 0.0955 and 0.128, respectively.

CONCLUSION

The versatility of multivariate curve resolution approaches for hard and soft model prediction in the exploration of a drug degradation reaction under the influence of sunlight was demonstrated in this research. The use of MCR-ALS and Hard Soft -MCR techniques provided precise representations of ornidazole's photocatalytic degradation kinetics. The MCR-ALS study revealed that the reaction system has three chemical components: one is ornidazole, and the other two are photo-degraded products. The reaction was noted to be first order. The reaction rate constants were found to be 0.0955 and 0.128 for step 1 and step 2, respectively.

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