

Photochemical behavior under UVA radiation of β -cyclodextrin included Parsol[®] 1789 with a chemometric approach

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Abstract

In this work, the photochemical behavior of β -cyclodextrin (β CD) encapsulated Parsol[®] 1789 sunscreen under ultraviolet radiation UVA (320–400 nm) is reported using chemometrics. The photochemical study on the free and β CD included molecule in some solvents was carried out under UVA light and probing by fluorescence and absorption spectroscopies. The chemometric method developed by Lawton and Sylvestre was employed in order to resolve the spectra and the concentration profiles. The results showed that β CD complexation did not increase the Parsol[®] photochemical stability, regardless of the employed solvents. However, it may reduce the effects related to photoallergy/phototoxicity through inclusion of the photo-products. © 1999 Elsevier Science B.V. All rights reserved.

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1. Introduction

The decrease of the ozone layer results in an increase of ultraviolet radiation reaching the Earth's surface [1]. Public health agencies warn about the need of sunscreens to prevent skin cancer. However, it is difficult to find an effective sunscreen that does not cause allergic reactions, which is also resistant to degradation and absorbs in a wide range of ultraviolet region (mainly UVA/UVB).

A cyclodextrin (CD) encapsulated sunscreen is a good candidate for obtaining a satisfactory composition. The α , β and γ CDs are cyclic oligosaccharides formed by, respectively, 6, 7 and 8 glucose units in chair conformation and connected by α 1,4-glycosidic bond. The CD molecules show a rigid structure with relatively

hydrophobic cavity and hydrophilic exterior [2,3]. This feature suggests that they might increase the solubility and bioavailability of the guest, as well as to reduce the intensity of photooxidation and its volatility. Also, it is expected that CDs can delay the beginning of the process of photodegradation. Variation of photochemical parameters, enhancement of photoconversion rates, induction of stereo-, regio-, and enantioselectivity on the product distribution, and protection from undesired photoprocesses have been reported [3–5].

Besides, regarding sunscreen as guest, the inclusion of photoproducts originated from sunscreen decomposition can prevent the contact of allergenic substances with the skin, reducing the possibility of side reactions. An example is Parsol[®] 1789, a sunscreen used for photoprotection in UVA (320–400 nm) spectral region. Toxicological tests have shown that it may cause cutaneous and ocular irritation, phototoxicity and subcutaneous toxicity [6].

This work presents the spectroscopic and

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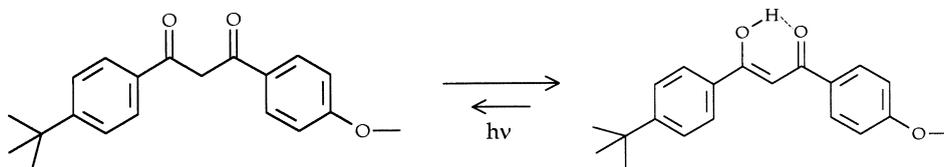


Fig. 1. The keto–enolic equilibrium for Parsol[®] 1789.

photochemical studies of the sunscreen Parsol[®] 1789, included in β CDs. To solve the overlapped spectra and concentration profile of the species, the “Self-Modeling Curve Resolution” (SMCR), developed by Lawton and Sylvestre [7] was used.

2. Experimental

The following reagents were used: β CD heptahydrated (Sigma); Parsol[®] 1789 (Givaudan); ethanol p.a. (Merck); isopropyl myristate (Croda); and deionized water (from Millipore, Milli Q-plus). A Germetec UVA lamp (Cosmetex UVA-Plus) 100 W was used as a light source. Solutions with concentration of $1.00 \times 10^{-5} \text{ mol dm}^{-3}$ of Parsol[®] in ethanol (ET) 50% (v/v) and in isopropyl myristate (IM) and $1.00 \times 10^{-5} : 5.00 \times 10^{-3} \text{ mol dm}^{-3}$ of Parsol[®] : β CD complex in ET were placed in quartz cells of 1 cm path length, at 25°C. UV absorption spectra were recorded on a Hewlett-Packard Spectrophotometer (8452A), with a diode array detector. UV/VIS fluorescence spectra were obtained on a SLM-AMINCO Spectrofluorimeter (SPF-500C), with a Xe lamp (250 W) as excitation source. The solutions were not degassed. Such a procedure was intentionally adopted in order to maintain the experimental conditions as close as to the sunscreen formulation.

3. Method

The method chosen to solve the overlapped spectra and concentration profiles was the SMCR [7], which can be applied to overlapped curves represented by Eq. (1). An example that shows this kind of curve is an absorption spectrum for a chemical substance A, that follows the Beer’s Law:

$$a_{ki} = c_A(k)b_A(\lambda_i), \quad (1)$$

where a_{ki} is the absorbance for sample k at wavelength

λ_i , $c_A(k)$ is the concentration of substance A, in sample k (mol dm^{-3}), $b_A(\lambda_i)$ is the molar absorption coefficient of substance A at wavelength λ_i ($\text{dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$) and the optical path is 1 cm.

For a mixture of substances A and D, which absorbs in the same spectral region, the absorption spectrum from the absorbance of both substances can be written as:

$$R_{ki} = c_A(k)b_A(\lambda_i) + c_D(k)b_D(\lambda_i)$$

or

$$\mathbf{R} = \mathbf{C} \cdot \mathbf{B}^t, \quad (2)$$

where \mathbf{R} is the matrix of absorption spectra, \mathbf{C} is the matrix of the concentrations of A and D, and \mathbf{B} is the matrix of the molar absorption coefficients for both substances.

The SMCR method [7] has the following assumptions: (A1) the curves must be non-negative; (A2) the curves in the data set must be a linear combination of two linearly independent curves (it means that the mixtures must have only two substances); (A3) the ratio c_{AK}/c_{DK} must be non-constant; (A4) there are two wavelengths λ_1 and λ_2 such that:

$$b_A(\lambda_1) = 0 \text{ and } b_D(\lambda_1) > 0,$$

$$b_A(\lambda_2) > 0 \text{ and } b_D(\lambda_2) = 0.$$

The spectra matrix has its dimension reduced by linear transformation to an orthogonal basis set. The vectors for the new basis can be found by the mathematical procedure of Singular Value Decomposition (SVD). Using the earlier assumptions and the normalization of the spectra by area under its curve, it is possible to solve the overlapped spectra. After the normalized pure spectra was obtained, the concentration profiles can be found by Eq. (3):

$$\mathbf{R} = \mathbf{C} \cdot \mathbf{B}^t \quad \therefore \quad \mathbf{R} \cdot \mathbf{B} = \mathbf{C} \cdot \mathbf{B}^t \cdot \mathbf{B}$$

$$\mathbf{C} = \mathbf{R} \cdot \mathbf{B} \cdot (\mathbf{B}^t \cdot \mathbf{B})^{-1}. \quad (3)$$

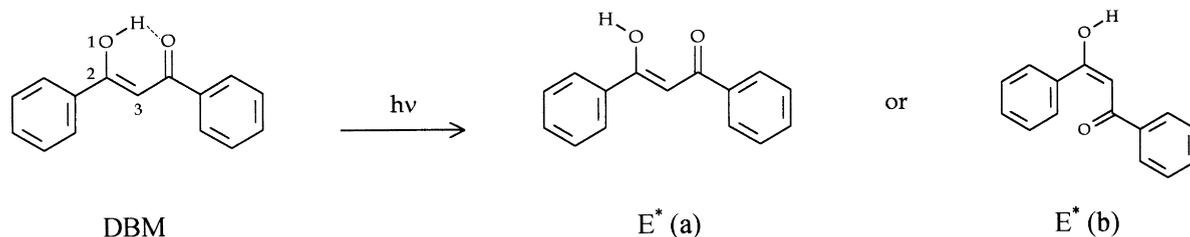


Fig. 2. Formation of transient enol (E^*) for dibenzoylmethane molecule (DBM) [9].

4. Results and discussion

4.1. Photochemical study

Parsol[®] is a β -dicarbonyl compound that has a keto-enolic equilibrium, where the enol with an intramolecular hydrogen bond is preferential [8–10] (Fig. 1).

Under UV radiation, the ketonization takes place, resulting in a proton transfer, which involves the enol forms without intramolecular hydrogen bond. In the following step, there is the formation of a transient nonchelated enol (E^*) [9]. Fig. 2 shows the formation of E^* for dibenzoylmethane compound (DBM). We believe that Parsol[®], a DBM derivative, has the same behavior. We observe that the formation of E^* via rotation around the double bond 2-3 is energetically less favored than the rotation around the single bond 1-2. In contrast, in the excited state, the order of the double bond is decreased which facilitates the rotation and E^* (a) is closer to the *cis*-enol form and E^* (b) to the keto form [9].

E^* may interact with solvent molecules (S), giving the exciplex [$E^* \cdots S$]^{*}. In this step the keto compound (K) is formed, through a proton transfer [9] (Fig. 3(a)). In protonic solvents, such as ethanol, the equilibrium

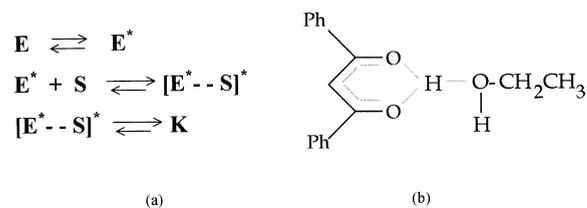


Fig. 3. (a) Photoactive ketonization processes and (b) complex between enol with “U” conformation and solvent, for dibenzoylmethane compound [7].

for the enol molecules is shifted to the “U” conformation, which may form a complex (E_U) with solvent molecules (Fig. 3(b)). The ketonization is reduced, as a result of the higher energy barrier between the E_U and the keto [9]. The keto–enolic equilibrium may be altered by inclusion in CD, modifying the proton transfer [3,11,12]. Similarly, in Parsol[®], it is expected that β CD encapsulation will lead to the enol with an intramolecular hydrogen bond.

The photochemical study of Parsol[®] and its β CD complex, under UVA, was evaluated by absorption and fluorescence spectroscopies in different time intervals. For absorption spectroscopy, the samples were prepared in ethanol (ET) 50% (v/v) and in pure isopropyl myristate (IM) and had been exposed for 345 min. It was not possible to evaluate the Parsol[®] : β CD in IM, owing to its low solubility. In fluorescence spectroscopy, the two samples had been monitored up to 3240 min in ET.

The absorption spectra of Parsol[®] in both the solvents possesses a wide band near 370 nm with a shoulder near 380 nm and a weak band near 270 nm. A small *red shift* of the wide band is observed when the solvent polarity is increased (IM to ET), indicating that this band is the result of a $\pi-\pi^*$ transition. No shift is observed for the other bands, but it is known that the shoulder and the weak band correspond, respectively, to the $n-\pi^*$ and $\pi-\pi^*$ transitions of the keto and the wide band to the enol [8,10].

During the ketonization, the intensity of enol band decreases while that of the weak keto band increases. After this process, the keto and enol bands decrease, indicating the beginning of photolysis. The enol concentration almost vanishes under the Parsol[®] ketonization in IM, as the formation of a complex with hydrogen bond does not exist and in this solvent Parsol[®] does not have an esteric effect as in ET. The

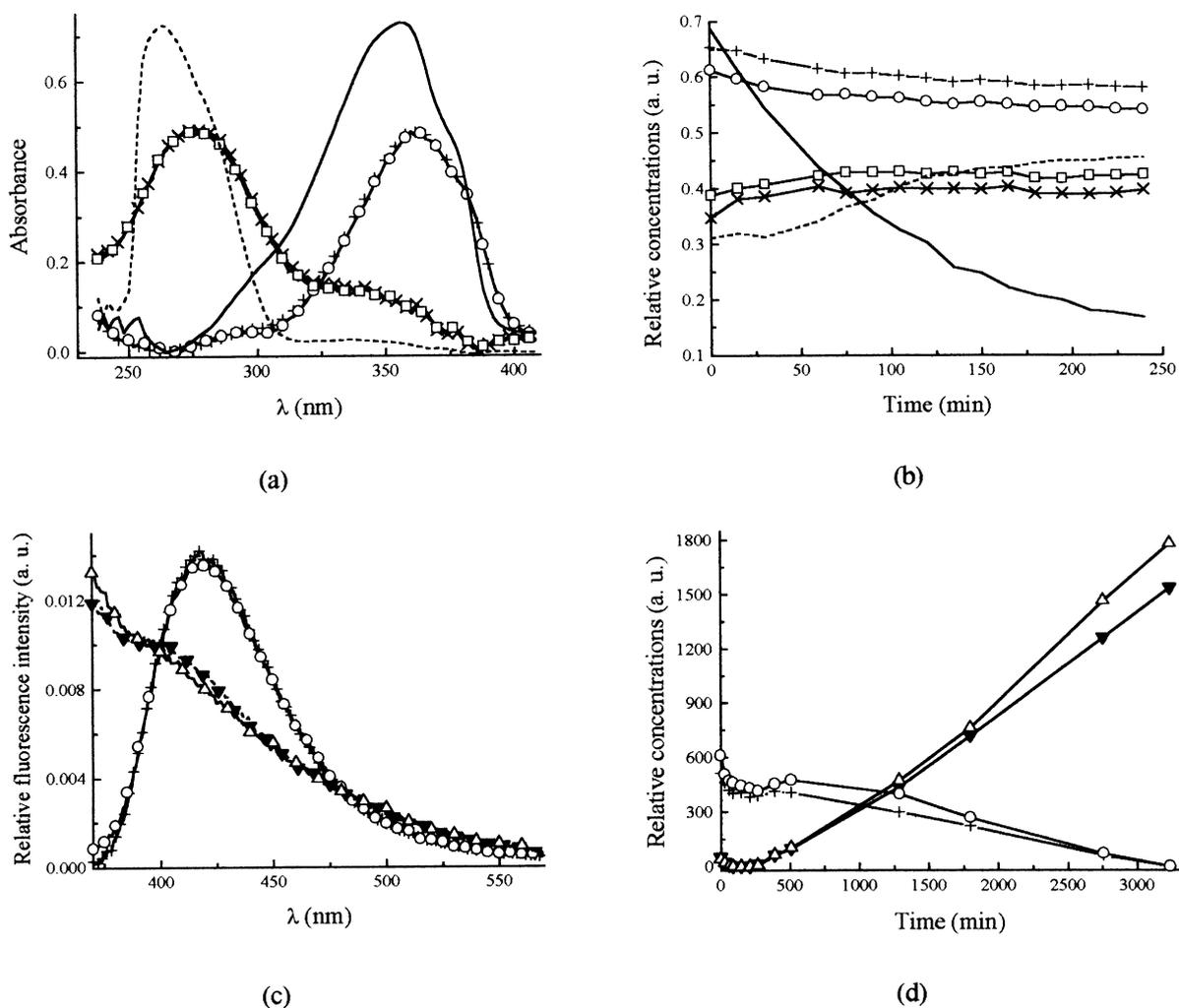


Fig. 4. (a) Resolved absorption spectra with unity concentration, (b) relative concentrations, (c) resolved emission spectra normalized by area and (d) relative concentrations. Enolic form of Parsol in ethanol 50% (v/v) (- - -) and in isopropyl myristate (—) and of Parsol : β CD complex in ethanol 50% (v/v) (-O-); ketonic form of Parsol in ethanol 50% (v/v) (- \times -) and in isopropyl myristate (- -) and of Parsol : β CD complex in ethanol 50% (v/v) (- \square -); products of Parsol photolysis in ethanol 50% (v/v) (- \blacktriangledown -) and of Parsol : β CD photolysis in ethanol 50% (v/v) (- Δ -).

products are in low concentrations, being detected only by fluorescence spectroscopy.

In the emission spectra only the enol band can be observed, as it is unaffected by Raman scattering for the excitation wavelength used. In free and complexed Parsol[®], this band decreases during the ketonization. During the photolysis, a new band appears overlapping the enol band, indicating photoproducts of Parsol[®]. Before irradiation, the enol band of complexed Parsol[®] is more intense than that of free compound, indicating a protection by inclusion in

β CD, as this increasing may be because of the decreased fluorescence quenching, to the chromophores protection against quenchers or to the chromophores exposition to a less polar environment [3]. It is supposed that the complex Parsol[®] : β CD stoichiometry is 1 : 2, owing to the involved geometries of these molecules. However, this encapsulation might be partial, not occurring the enol/carbonyl protection, as a result of the formation of E_U complex in ethanol [9], hindering the approximation of the two β CD. In contrast, if the encapsulation was complete, the

formation of E* via rotation around the double bond 2-3 should not be possible. Consequently, the ketonization would not occur and the enol would be exposed to photolysis.

The overlapped spectra and the kinetic behavior of the free and complexed Parsol[®] and also the photoproducts were investigated using chemometrics. The solvent effect was subtracted from all absorption spectra prior to analysis.

The absorption spectra were resolved using the SMCR method and the keto-enolic concentrations were obtained by Eq. (3). Fig. 4(a) shows the resolved spectra with unity concentration of free and complexed Parsol[®] in ET. Note that they are very similar. The relative concentrations obtained for both species in the solvents used are shown in Fig. 4(b). As expected, the kinetics for the free and complexed species in ET are similar, as the encapsulation does not affect the ketonization. The results obtained for Parsol[®] in IM confirms the fact that the ketonization occurs easily.

For the fluorescence spectra, the A4 assumption (SMCR) cannot be accepted, as it is valid for only one wavelength. However, in this case, where there is no photoproduct in the beginning of irradiation and the enolic concentration is almost zero in the end, it is possible to apply the method to solve the concentration profiles (C). The next step is to use the Eq. (4) to resolve the spectra (B):

$$\mathbf{B}^t = (\mathbf{C}^t \cdot \mathbf{C})^{-1} \cdot \mathbf{C}^t \cdot \mathbf{S} \quad (4)$$

Considering that the fluorescence intensity is not simply related to the concentration as in absorption [3], the resolved concentration profiles have an included factor, which might be assumed to be constant in the whole sampled interval, related to β CD.

Fig. 4(c),(d) show the resolved fluorescence spectra and concentrations, respectively. Apparently, the fluorescence spectra of the species are unchanged in the presence of β CD. An important alteration does not also exist between the variation of free and complexed enol concentrations. However, a significant increase of this variation exists for the encapsulated products, after 2000 min. It is believed that after this period the photoproducts have smaller dimensions, being totally included by β CD.

5. Conclusions

The results obtained by SMCR has shown that the photochemical processes occur similarly in free and β CD complexed Parsol[®]. However, the significant increase of included products concentrations (after 2000 min) indicates that they are totally encapsulated by β CD, owing to its smallest dimensions. As the photoproducts are well-known allergenic substances, their inclusion in β CD can avoid the contact on skin, reducing the possibility of toxic reactions. Therefore, this work allowed to conclude, with chemometrics help, that Parsol[®] encapsulation in β CD did not affect its photochemical stability, regardless of the employed solvents, but the complexation may reduce the effects related to photoallergy/phototoxicity through inclusion of the photoproducts.

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