Spectral determination of quantum yields of psoralen photodestruction in water and alcohol environments

N.E. Kovalskaya, N.A. Kuznetsova,* and I.V. Sokolova

V.D. Kuznetsov Siberian Physical Technical Institute at the Tomsk State University, Tomsk
** State Scientific Center of Russian Federation NIOPIK, Dolgoprudny, Moscow Region*

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We estimate the quantum yields of photochemical conversion of differently structured psoralens in water and alcohol. In water, the psoralen and angelicin during illumination at 313 nm wavelength are found to photodissociate with quantum yields of 0.01 ± 0.002 and 0.025 ± 0.005, respectively. In alcohol, the photochemical stability of psoralen and angelicin increases abruptly. Even in water solution, 5-methoxy psoralen and 8-methoxy psoralen are stable to ultraviolet illumination. We studied the psoralen properties in water solutions and suggested main pathways of psoralen photochemical destruction.

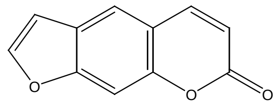
Introduction

Psoralens (or furocoumarins) are a group of compounds possessing sensitizing properties, explaining their use in photochemiotherapy of many skin diseases.[1]

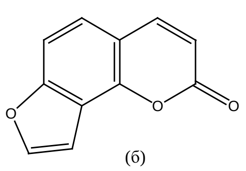
Most papers in the field of psoralen photochemistry deal with the study of psoralen photochemical reactions with biologic substrates,[2,3] as well as identification of photochemical products formed from exposed water and alcohol solutions.[4–7] Survey of literature shows that the quantitative data on the efficiency of photochemical psoralen destruction in solutions are absent. We studied some aspects of the psoralen photolysis mechanism and determined quantum yields of psoralen photodissociation in water, a universal natural dissolvent, as well as in the alcohol.

1. Goals and experimental methods of the study

We have studied psoralen, angelicin, and 5- and 8-methoxy substituted psoralen. The structural formulas of compounds are presented below: (*a*) psoralen, (*b*) angecilin, (*c*) 5-methoxy psoralen, and (*d*) 8-methoxy psoralen.



(a)



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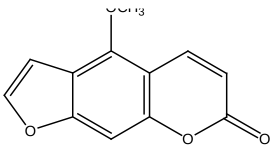

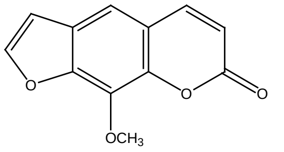

The hexadecylmethylammonium bromide (Sigma) and sodium dodecyl sulfate (Roanal, Hungary) were used without any extra refinement. As solvents we utilized the distilled water and ethanol containing 5% of water.

1.1. Illumination

The psoralen solutions (with concentration (2–7) × 10^{-5} M) were illuminated in quartz cells with 1-cm thick optical layer. The mercury-quartz high-pressure lamp SVD-120A was the source of radiation. The line of the mercury spectrum at wavelength of 313 nm was separated using ZhS-3 and UFS-2 pigmented glass filters. The light flux ($0.38 \cdot 10^{-16}$ quantum/s · cm^2) was determined by the method of Kalvert and Pitts[8] using 0.006-mole solution potassium ferrioxalate.

Photolysis in water was performed at a constant oxygen concentration, by bubbling continuously the air. Because of the solvent volatility, the quantum yields of psoralen destruction in ethanol are estimated in diffusion regime. The solutions were deoxygenated by bubbling the helium for 20 min before and during its illumination.

The electron absorption spectra were recorded using a HP-8453 spectrophotometer.

1.2. Determination of the quantum yields of photochemical destruction

The psoralen consumption was controlled spectrophotometrically by monitoring absorption reduction at maximum of the long-wave bands. The magnitudes of absorption maxima and the corresponding molar extinction coefficients for the initial substances (ε) and photolysis products (ε_{eff}), used in the calculations, are presented in Table 1.

Table 1. Spectral characteristics of psoralens in water

Compound	$\lambda_{\max}$, nm	ε, cm^{-1} · mol^{-1} · l	ε_{eff}, cm^{-1} · mol^{-1} · l
Psoralen	295	13900	6700
Angelicin	301	8800	4200
8-methoxy psoralen	303	11200	4800
5-methoxy psoralen	315	9200	5200

The number of absorbed photons of a monochromatic radiation was determined from the measured quantum intensity of radiative flux incident on the cell with solution and from known absorption by solution in this spectral range.

Quantum yields of photochemical destruction were calculated by the following formula:

$$\varphi = \frac{\Delta D N_A V}{l(\varepsilon - \varepsilon_{\text{eff}})(1 - T) I S t},$$

where ΔD is the variation of optical density at the maximum of a long-wave absorption band ($\lambda_{\max}$) for the layer with the thickness l, cm, for the illumination period t, s; N_A is the Avogadro number; V is the volume of illuminated solution, l; ε is molar extinction coefficient of the initial psoralen at maximum of its long-wave absorption band ($\lambda_{\max}$); ε_{eff} is the effective molar absorption coefficient of photochemical products at maximum of the long-wave absorption band of the initial psoralen ($\lambda_{\max}$); T is the transmission of illuminated solution at the wavelength of exciting radiation; I is the radiative flux, in quanta/($\text{s} \cdot \text{cm}^2$); and S is the illuminated area, cm^2.

The quantum yields were determined with the error ~15%.

2. Discussion of the results

The studies have shown that all the compounds considered here are readily soluble in alcohol environments, but in water these compounds, especially methoxy substituted ones, are insufficiently soluble. In this regard, we have studied the psoralen states in water solution. In the case study of angelicin and 8-methoxy psoralen we have found that introduction of these detergent species (bromide hexadecyltrimethylammonium or sodium dodecylsulfate) in water solution does not cause change of electron absorption spectra. This fact, as well as obedience to the Lambert–Beer law (the obedience to the Lambert–Beer law in the range of concentrations $5 \cdot 10^{-6} - 5 \cdot 10^{-5}$ M is demonstrated by data presented in Fig. 1) indicates that, despite low solubility in water, the psoralens in water solution are in the monomer state.

It was found that when the solutes studied are illuminated both by spectrally wide ultraviolet and filtered (with λ_v = 313 nm) light, spectral changes are observed, indicating consumption of the species studied. As an example, Figure 2 shows spectral changes observed during illumination of angelicin in water in the presence of oxygen of air. To discuss the photochemical conversions responsible for these spectral changes we will turn to available literature data.

It is well known[9] that psoralens exposed to light enter the photocyclic addition reactions both with other molecules and with each other. In the latter case, photodimers form. However, the scarcity of psoralens and the absence of aggregation in solution has led us to a conclusion that the bimolecular processes leading to the formation of dimers have low efficiency under conditions of the experiment discussed.

The literature data also point out to oxidation of 4′5′ double band of furane cycle and hydroxy aldehyde formation.[10] However, the deoxygenation of solution by helium flow was found to have no effect on photolysis process, in contrast to the photooxidation mechanism.

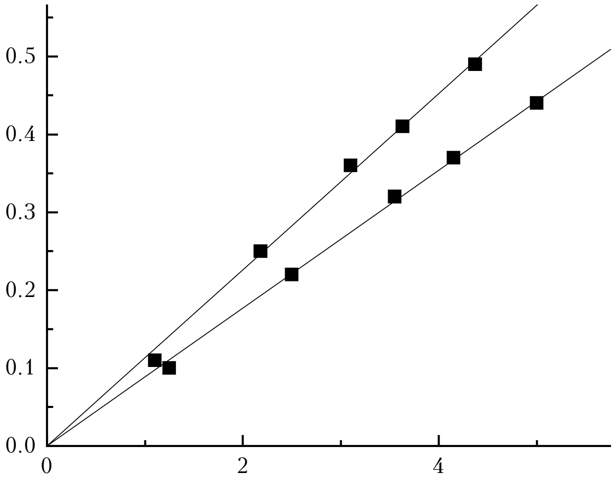

Fig. 1. Dependence of the optical density D on concentration c of the substance in water solution: 8-methoxy psoralen (*1*) and angelicin (*2*).

Fig. 2. Absorption spectra of angelicin ($c = 4 \cdot 10^{-5}$ mol/l) in water solution. Each curve corresponds to photolysis determined every 1 min in case of illumination by fully ultraviolet radiation from mercury lamp during 15 min.

In our opinion, most probable photochemical destruction mechanism is photosolvolysis, proposed in Ref. 10 for psoralen in water and alcohol environments.

Some data show that the optical density at maximum of long-wave absorption band of psoralens does not fall to zero even under quite long exposures, instead saturating to some constant level (such as $D \sim 0.25$ for psoralens). We have chosen this level of optical density ourselves as the absorption of photolysis products and used to calculate their effective extinction ε_{eff} (concentration of photochemical products was assumed equal to the initial psoralen concentration). The ε_{eff} value was used to determine the change of concentration of the initial substrate from the formula:

$$\Delta c = \Delta D / [l(\varepsilon - \varepsilon_{\text{eff}})].$$

As an example, Figure 3 presents variations of the angelicin concentration in water during illumination.

Linearization of this dependence in coordinates $\ln(c_0/c_t)$ versus t_{ill} (Fig. 4) indicates that this reaction is of the first order.

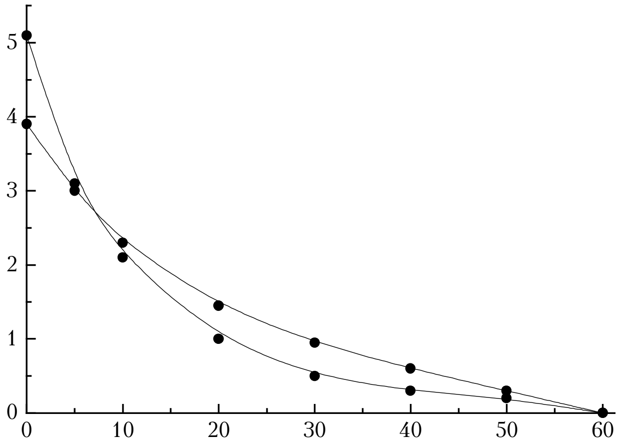

Fig. 3. Dependence of concentration c on the illumination time t_{ill} for psoralen (*1*) and angelicin (*2*) in water solution bubbled by oxygen of air. $\lambda_v = 313$ nm.

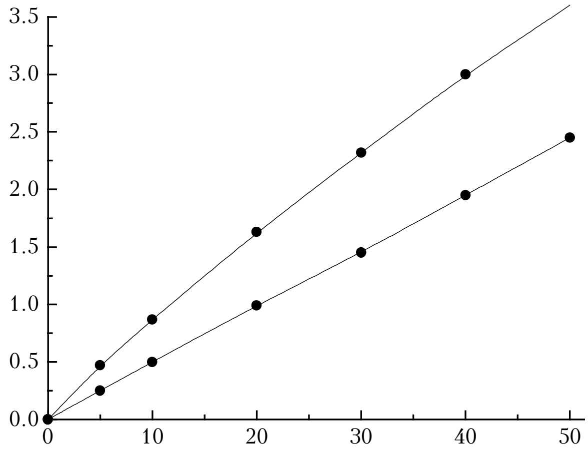

Fig. 4. Dependence of $\ln(c_0/c_t)$ on illumination time t_{ill} for psoralen (*1*) and angelicin (*2*) in water solution bubbled by oxygen of air. Wavelength of exciting radiation is 313 nm; c_0 is the initial concentration of substrate, and c_t is the substrate concentration at the time t.

Quantum yields of photochemical conversions, calculated from the initial linear parts of the curves are summarized in Table 2.

From Table 2 it is seen that psoralen and angelicin in water and air-saturated solutions are destructed much more efficiently than methoxy substituted psoralens. Such a behavior is consistent with photosolvolysis, according to which the initial stage is the nucleophilic attack of solvent molecule on 4′ and 5′ carbon atoms of psoralen in the excited state.[10] In this case, the methyl groups exert steric effect to counteract solvent addition (especially in the case of 5-methoxy psoralen), and, in addition, they seem to reduce the reactivity of substrate, due to increase of electron density at the reaction center.

Table 2. Quantum yields of psoralen photochemical destruction (φ) in water and alcohol

Compound	Psoralen	Angelicin	8-methoxy psoralen	5-methoxy psoralen
Water	0.01 ± 0.002	0.025 ± 0.0005	~ 0.001	≤ 0.0003
Ethanol	0.002 ± 0.0005	≤ 0.00035	~ 0.0008	~ 0.0006

From Table 2 it also follows that in passage to alcohol, the photochemical stability of psoralen and angelicin considerably increases. The increase of the rate of dark nucleophilic substitution in water, possessing high solvation ability, is known from the literature.[11] Seemingly, an analogous mechanism of solvent effect also exists in the case of photosolvolysis of psoralens.

Even in water solution, the methoxy psoralens are highly stable, suffering conversions with quantum yields close to the lowest determinable ones, explaining the failure to obtain reliable data on the solvent effect on the efficiency of the photochemical methoxypsoralen destruction.

Acknowledgments

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