Electronic Supplementary Material (ESI) for Environmental Science: Processes & Impacts

Supporting Information
for

Direct Photodegradation of Lamotrigine (an Antiepileptic) in Simulated Sunlight – pH Influenced Rates and Products

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For Environmental Science: Processes and Impacts

11 pages, including 5 figures

Pages S2 through S6 (including Figure SI-1) provide details on chemicals and solutions, analytical methods, chemical actinometry, and data processing.

Pages S7 through S10 include Figures SI-2 through SI-5, which are referred to in the text.

Experimental

Chemicals and Solutions

Ultrapure deionized water (18.2MΩ·cm) was obtained from a Milli-Q reagent water purification system (Millipore, Bedford, MA, USA) fed by distilled water. Lamotrigine (LTG) was purchased from Sigma-Aldrich (≥ 98%) and Enzo Life Sciences (≥ 98%, Farmingdale, NY, USA). Pyridine (ACS reagent ≥ 99.0%), ammonium acetate (NH_4OAc, ≥ 98%), and formic acid (Fluka brand, ~98%) were purchased from Sigma-Aldrich Corp. (St. Louis, MO, USA), and 4-nitroacetophenone (PNAP, 98%) was purchased from Alfa Aesar (Ward Hill, MA, USA). Finally, acetonitrile (MeCN, ACS/HPLC grade), methanol (MeOH, ACS grade), monobasic sodium phosphate monohydrate ($NaH_2PO_4•H_2O$, certified ACS), dibasic sodium phosphate heptahydrate ($Na_2HPO_4•7H_2O$, certified ACS), hydrochloric acid (HCl, 12N, certified ACS plus), and ammonium hydroxide (NaOH, 20-22% as NH_3, Optima brand) were purchased from Thermo Fisher Scientific, Inc. (Waltham, MA, USA).

Phosphate buffer solutions (5 mM PO_4) were prepared by dissolving $NaH_2PO_4•H_2O$ or $Na_2HPO_4•7H_2O$ into deionized water, and adjusting to pH 3.3 (± 0.2) or pH 7.7 (± 0.1) with HCl or NaOH.

Stock solutions of LTG were prepared directly in the phosphate buffer solutions at pH 3.3 (11.4 mg L^{-1}) and pH 7.7 (12.0 mg L^{-1}). The LTG stock solution at pH 5.3 ± 0.4 (11.7 mg L^{-1}) was prepared by mixing the pH 3.3 and pH 7.7 stock solutions (50/50 v/v), and adjusting the solution pH with HCl or NaOH. All LTG stock solutions were stored at 3 °C in 500 mL amber glass bottles until use. A stock solution of PNAP (1,586 mg L^{-1}) was prepared in MeCN and stored at −14 °C in amber glass vials until use.

Analytical Methods

The spectrum of the Suntest CPS+ solar simulator was measured with a Maya 2000 Pro spectrometer (Ocean Optics, Inc., Dunedin, FL, USA) using a 400 μm solarization-resistant optical fiber (P400-2-SR) and no cosine corrector. Solution pH was measured with an accumet Excel XL60 pH meter (Thermo Fisher Scientific, Inc.).

Absorption spectra were measured with an Agilent 8453 UV-visible spectrophotometer using a 1 cm quartz cuvette, 0.5 s integration time, 1 nm interval, and Agilent UV-visible ChemStation software. To eliminate non-representative solvent effects, all absorption spectra were measured in deionized water except PNAP (0.1% MeCN in deionized water).

LTG was quantified using an Agilent 1200 series HPLC system equipped with a UV-diode array detector (HPLC-UV; Agilent Technologies, Inc., Santa Clara, CA, USA). The chromatographic method used a Kinetex PFP column (100 × 3.1 mm i.d., 2.6 μm particle size, Phenomenex, Torrance, CA), maintained at 40 °C, a constant flow rate of 500 μL min^{-1}, and the following binary gradient: 10% (A) deionized water with 5 mM ammonium acetate and 0.1% v/v formic acid, and 90% (B) acetonitrile, for 4 min; increased to 65% B over 5.5 minutes; stepped to 100% B and held for 4 minutes to flush the column; and equilibrated at 10% B for 4.5 minutes. The injection volume of each sample was 10 μL, and the samples were quantified at 260 nm using a seven-point external calibration curve (method detection limit < 0.1 mg L^{-1}).

4-nitroacetophenone (PNAP) was also quantified using the Agilent HPLC-UV system. The chromatographic method used an XSelect CSH C_{18} XP column (75 × 4.6 mm i.d.; 2.5 μm particle size; Waters Corporation, Taunton, MA, USA), maintained at 40 °C, and the following binary gradient: (A) 60% deionized water, and (B) 40% acetonitrile, at the beginning; increased to 90% B over 5 minutes at 600 μL min^{-1}; stepped to 100% B and held for 1.5 minutes at 750 μL min^{-1} to flush the column; and equilibrated at 40% B for 4 minutes at 600 μL min^{-1}. The injection volume of each sample was 10 μL, and the samples were quantified at 270 nm using a seven-point external calibration curve (method detection limit < 0.1 mg L^{-1}).

Photoproducts were analyzed by an Agilent G3250AA MSD TOF system interfaced with an Agilent 1100 Series HPLC. The mass spectrometer was operated in ESI^+ mode under the following parameters: 325 °C temperature; 4000V capillary voltage; 190V fragmentor voltage; 45V skimmer voltage; 300 Vpp Oct 1 RF; 45 psig nebulizer pressure; and 10 L min^{-1} drying gas (nitrogen) flow. The injection volume of each sample was 10 or 50 μL. The chromatographic method was the same method used to quantify LTG. Agilent MassHunter Workstation Qualitative Analysis software was used for data processing.

Chemical Actinometry

Aqueous solutions of 4-nitroacetophenone (PNAP, 1.586 mg L^{-1}) were prepared in deionized water with a pyridine concentration of 0.05%. The use and preparation of the actinometer solutions followed procedures described in the literature, except that the spectral irradiance of the solar simulator was corrected using the solar simulator's measured spectrum and the calibration factor (*F*) determined pursuant to Equation I.

$$F = \frac{k_{dA}}{\phi_A \times \sum I_{0\lambda}\, \varepsilon_{\lambda A}} \qquad \text{(I)}$$

where: k_{dA} is the observed first order rate constant for PNAP direct photodegradation (t^{-1}); Φ_A is the reaction quantum yield of the PNAP actinometer solution (mol einstein^{-1}); $I_{0\lambda}$ is the measured irradiance of the solar simulator at each incident wavelength λ (einstein L^{-1} t^{-1}); and $\varepsilon_{\lambda A}$ is PNAP's molar absorptivity at each incident wavelength λ (L mol^{-1} cm^{-1}).

The calibration factor is intended to correct the intensity of the solar simulator's measured irradiance, assuming that the spectral distribution remains fixed. The quantum yield of the PNAP actinometer solution is linear as a function of pyridine concentration (Φ_{PNAP} = 0.0169 [pyridine] up to 0.2 M pyridine in 10 μM PNAP) [1, 2].

The reaction quantum yields of the buffered aqueous solutions of LTG at pH 3.3, 5.3 and 7.7 were determined using Equation II:

$$\phi_C = \phi_A \times \frac{k_{dC}}{k_{dA}} \times \frac{\sum I_{0\lambda}\varepsilon_{\lambda A}}{\sum I_{0\lambda}\varepsilon_{\lambda C}\, S_\lambda} \qquad \text{(II)}$$

$$S_\lambda = \frac{(1 - 10^{-\alpha_\lambda l})}{2.303\, \alpha_\lambda l} \qquad \text{(III)}$$

where: Φ_C is LTG's reaction quantum yield (mol einstein^{-1}) at the relevant pH; k_{dC} is the first order rate constant for LTG direct photodegradation at the relevant pH (t^{-1}); $I_{0\lambda}$ is the corrected irradiance of the solar simulator at each incident wavelength λ

(einstein L^{-1} t^{-1}); $\varepsilon_{\lambda C}$ is LTG's molar absorptivity at each incident wavelength λ and the relevant pH (L mol^{-1} cm^{-1}); S_λ is the light screening factor determined under Equation III; α_λ is the measured attenuation coefficient for the LTG solution at each incident wavelength and the relevant pH; and all other terms are as defined above.

The procedure to account for light screening is described in the literature [2, 3]. In deionized water, when no light screening occurs, the value of S_λ is 1 [4]. The pathlength (l) of the quartz glass culture tubes (12 mm o.d. × 100 mm) was assumed to be 1.0 cm in accordance with published literature values [2].

Figure SI-1 sets forth the specific light absorption rates determined with Equation IV for LTG and PNAP solutions in quartz glass culture tubes irradiated by the solar simulator.

$$k_{a\lambda x} = 2.303\, I_{0\lambda}\, \varepsilon_{\lambda x}\, l\, S_\lambda \qquad \text{(IV)}$$

where: $k_{a\lambda x}$ is LTG's (x = C) or the actinometer's (x = A) specific light absorption rate at each incident wavelength λ and the relevant pH (einstein mol^{-1} t^{-1}); and all other terms are as defined above.

When converting between specific light absorption rates in quartz glass culture tubes and in a flat water body, a factor of 2.2 is used, in accordance with published literature values, to account for the increased irradiance in cylindrical tubes exposed to scattered light on all sides [1, 2].

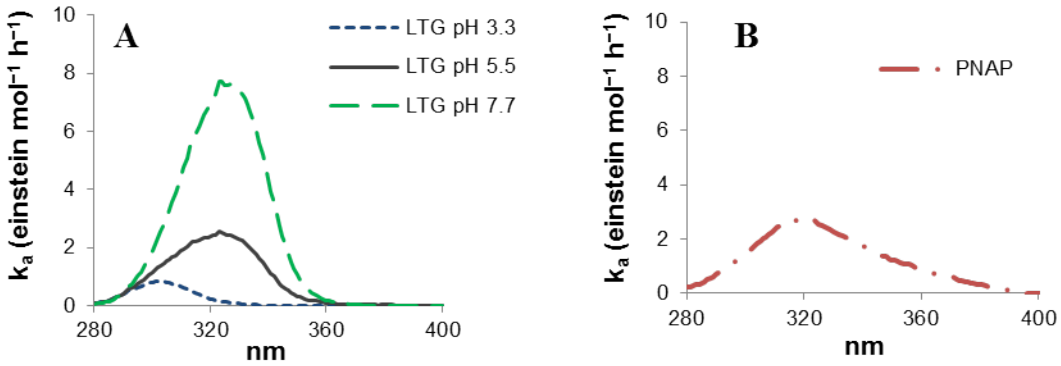

FIGURE SI-1. Specific absorption rates of lamotrigine (LTG) and 4-nitroacetophenone (PNAP). Estimated specific absorption rates of (A) (LTG in buffered aqueous solutions at pH 3.3, 5.3 and 7.7, and (B) PNAP, in quartz glass culture tubes irradiated by the solar simulator.

Data Processing

All least squares linear regression analyses, sample means and confidence intervals were calculated using Microsoft Office Excel 2007 for Windows (Microsoft, Inc., Redmond, WA, USA).

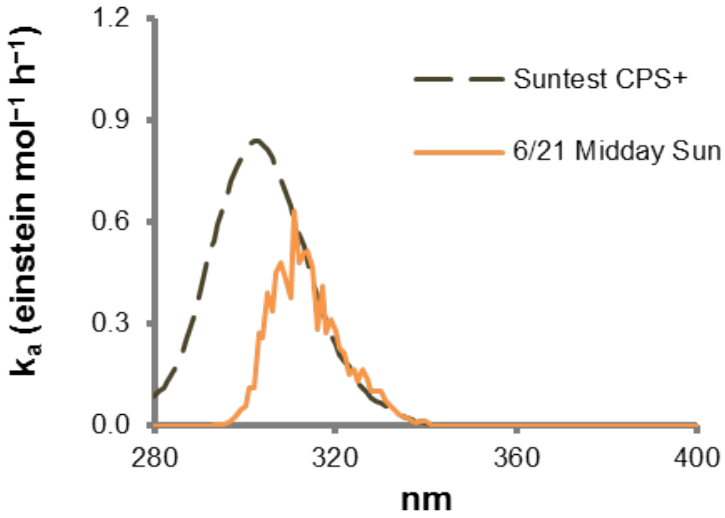

Figure SI-2 Specific absorption rate of lamotrigine (LTG) in quartz glass culture tubes irradiated by the Suntest CPS+ solar simulator or midday, midsummer sun in Denver, CO, USA (estimated for June 21, 2013 at 1:00 p.m. MDT (SMARTS v 2.9.5)).

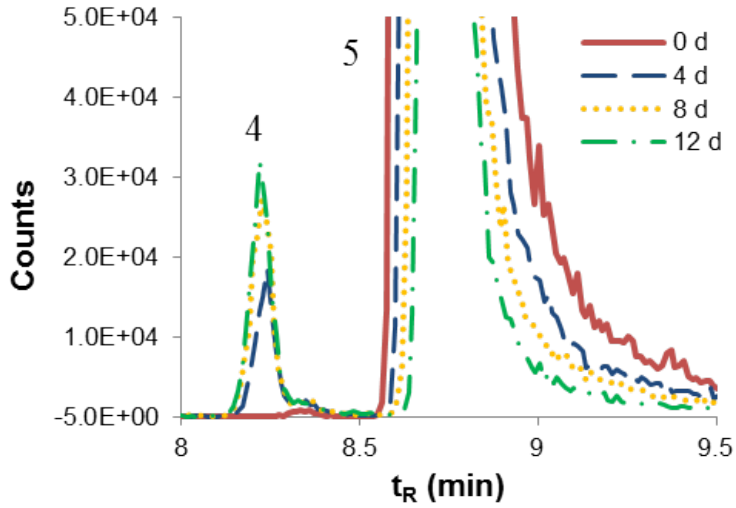

Figure SI-3 Extracted ion chromatograms (m/z 256.01513) of phosphate-buffered aqueous solution of lamotrigine (LTG, 11.7 mg L^{-1}; pH 5.3 ± 0.4) after 0 d (0 h), 4 d (96.2 h), 8 d (190.0 h), and 12 d (290.6 h) of continuous irradiation in the Suntest CPS+ solar simulator. LTG is evidenced by peak 5, and its photoisomer is represented by peak 4.

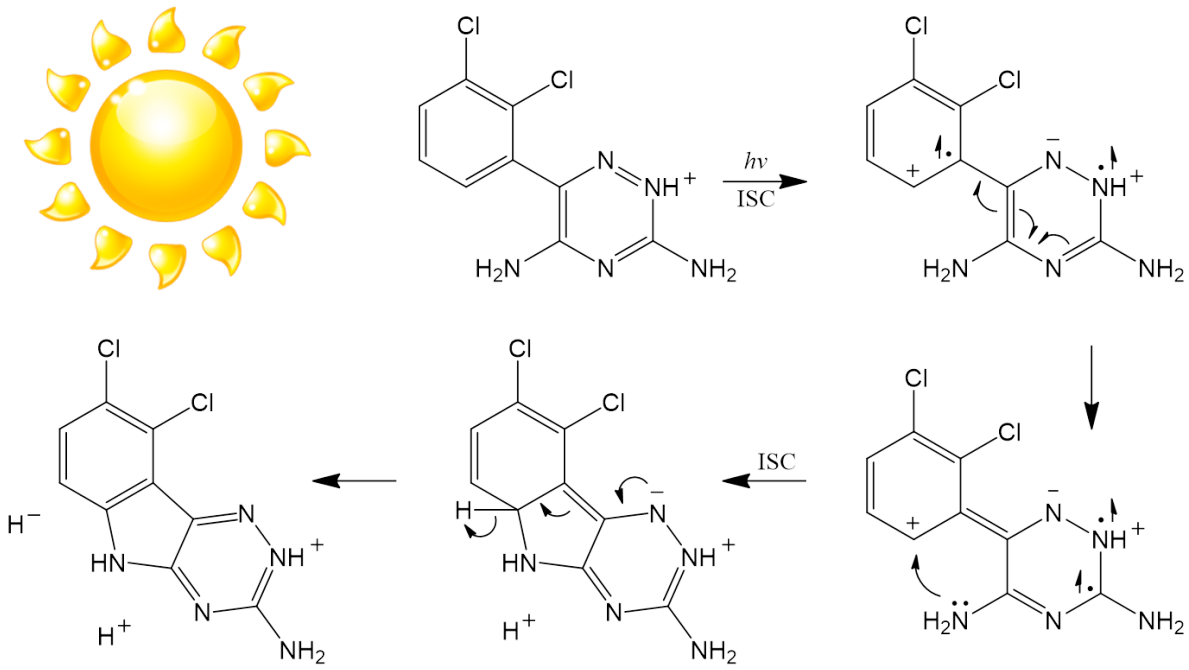

Figure SI-4 Proposed excited triplet state photodegradation pathway from lamotrigine (LTG) to peak 7 (Figure 2; Table 2).

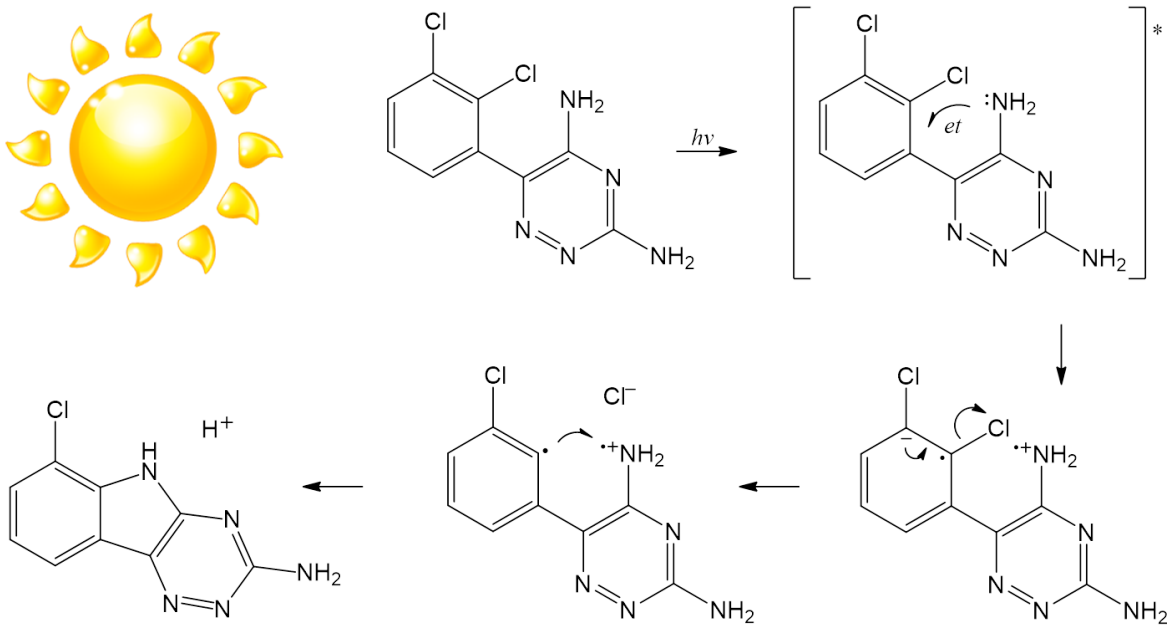

Figure SI-5 Proposed electron transfer (*et*) photodegradation pathway from lamotrigine (LTG) to peak 4 (Figure 2; Table 2).

References

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2. A. Leifer, *The kinetics of environmental aquatic photochemistry: Theory and practice*, American Chemical Society, Washington, DC, 1988.
3. R. G. Zepp, P. F. Schlotzhauer and R. M. Sink, *Environmental Science & Technology*, 1985, **19**, 74-81.
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