The Photodegradation of Zoloft®

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Abstract

Recent studies have identified the presence pharmaceuticals in surface and ground water. The accumulation of these drugs has shown to have hazardous effects on the environment. The ability of Zoloft to photodecompose was analyzed through the use of direct and indirect photolysis of Sertraline Hydrochloride, the major constituent of the antidepressant Zoloft. The photolysis was conducted in deionized water and East Gemini Lake water in an Ace Photochemical Reactor. It was evident that Sertraline undergoes direct photolysis at pH 9 as well as the East Gemini Lake surface water. The mechanism that causes the decomposition was investigated through the introduction of 1,4-Diazabicyclo[2.2.2]octane (DABCO) and isopropanol, to measure the role of singlet oxygen and hydroxyl radical in indirect photolysis in the East Gemini Lake water.

Introduction

Pharmaceuticals and personal care products (PPCPs) are constantly being released into the environment through human activities. Previous studies have identified PPCPs in surface and ground water which with accumulation is extremely hazardous to the ecosystem, especially aquatic organisms. It has also been determined that pharmaceuticals are not completely removed from waste water through treatment processes, thus what is thought to be clean, treated, water may actually still contain small amounts of harmful chemicals.

There are several loss processes that play an important role in the environmental impact of the accumulation of these compounds. Two of the processes that are likely to degrade pharmaceutical compounds in surface water are direct and indirect photolysis. Direct photolysis is the direct absorption of light by a compound resulting in a reaction which transforms the parent compound into one or more new products. Indirect photolysis does not directly absorb light but rather is mediated by reactive organic materials (ROM) which interact with light to form singlet oxygen and hydroxyl radicals.

The potential impact of the antidepressant, Zoloft®, on the environment through analysis of photodecomposition rates of the active ingredient of Zoloft®, Sertraline hydrochloride,

was investigated. Sertraline has one active metabolite N-desmethylsertraline and is a selective serotonin reuptake inhibitor (SSRI). The mechanism in which sertraline decomposes was determined through the addition of radical scavengers added in excess, 1,4-Diazabicyclo[2.2.2]octane (DABCO) and isopropanol. DABCO prevents indirect photolysis via decomposition from singlet oxygen by trapping the singlet oxygen radicals. Isopropanol prevents hydroxyl radicals from contributing to the decomposition of sertraline in indirect photolysis.

Experimental

Preparation of Solutions

Sertraline hydrochloride solutions were prepared at 100 μM concentration with E-pure deionized water. Sertraline sample solutions were prepared with 20 mL pH 3 formate buffer, pH 6 ammonium acetate buffer, or pH 9 ethanolamine buffer and, 1 mL sertraline 10 mM stock solution and diluted with E-pure deionized water to 100 mL volume. Natural water samples were collected from East Gemini Lake (EGL), Saint John's University, Minnesota. EGL water samples were vacum filtered with 0.45 μm filters and stored at 6°C before use. EGL sertraline solutions were prepared as above with EGL water replacing the deionzed E-pure water.

Sertraline-isopropanol solutions were prepared at a 0.085 M isopropanol final concentration with 1 mL of the 10mM stock solution and diluted to volume with EGL water. The DABCO solutions were prepared the same as above with a final DABCO concentration of 10^{-3} M.

Sample collection

Solutions were photolyzed with an Ace Photochemical reactor with an ultraviolet light source; a medium pressure, quartz, mercury vapor 450 ultraviolet lamp. Duplicate solutions were photolyzed in quartz test tubes along with a control (dark) for each of the solutions which were covered with tin foil to prevent UV light exposure. The temperature was held constant through continuous flow of cold water around the system, along with the minimization of breakdown due to increased temperature throughout the

photolysis process. Samples of 700 µL were taken at various time intervals to be analyzed by Surveyor Liquid Chromatography and Mass Spectroscopy.

Analysis

Surveyor liquid chromatography with ultraviolet detection was used for analysis along with a ThermoFinnigan LCQ Advantage with a photodiode array detector (PDA) and mass spectroscopy. A C_{18} reversed-phase column with a mobile phase of 90% HPLC grade acetonitrile and 10% ethanolamine buffer solution, flow rate of 0.5 mL min^{-1} was used. 10µL injection volumes were used.

Results

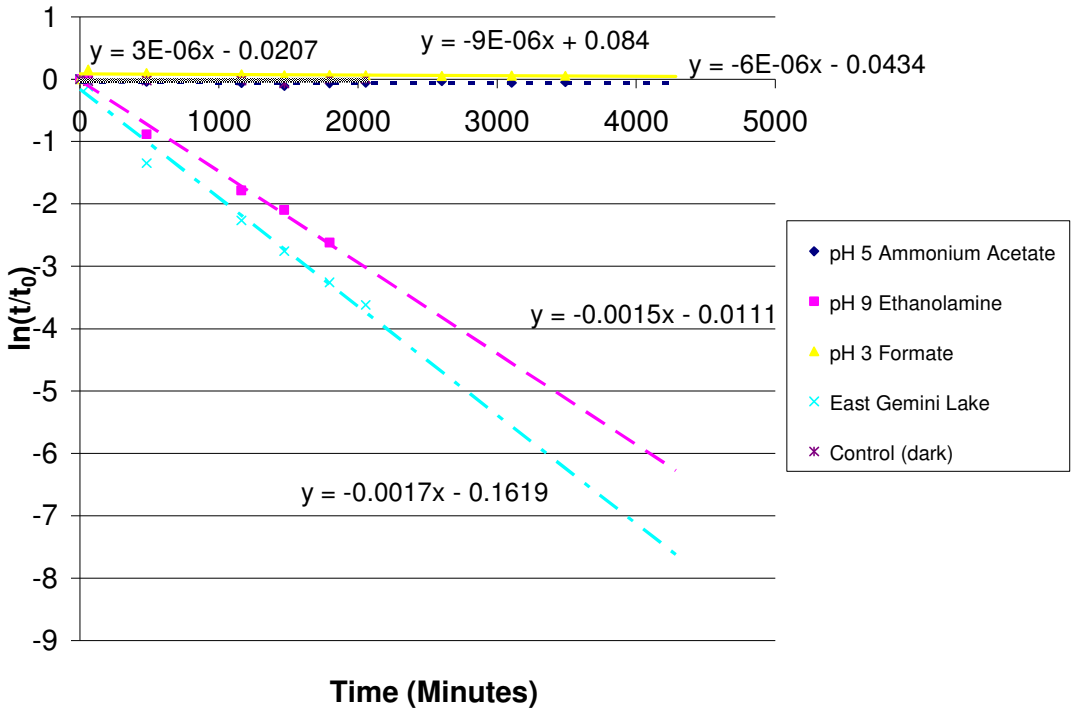

Figure 1. Direct photolysis of sertraline hydrocholoride solutions.

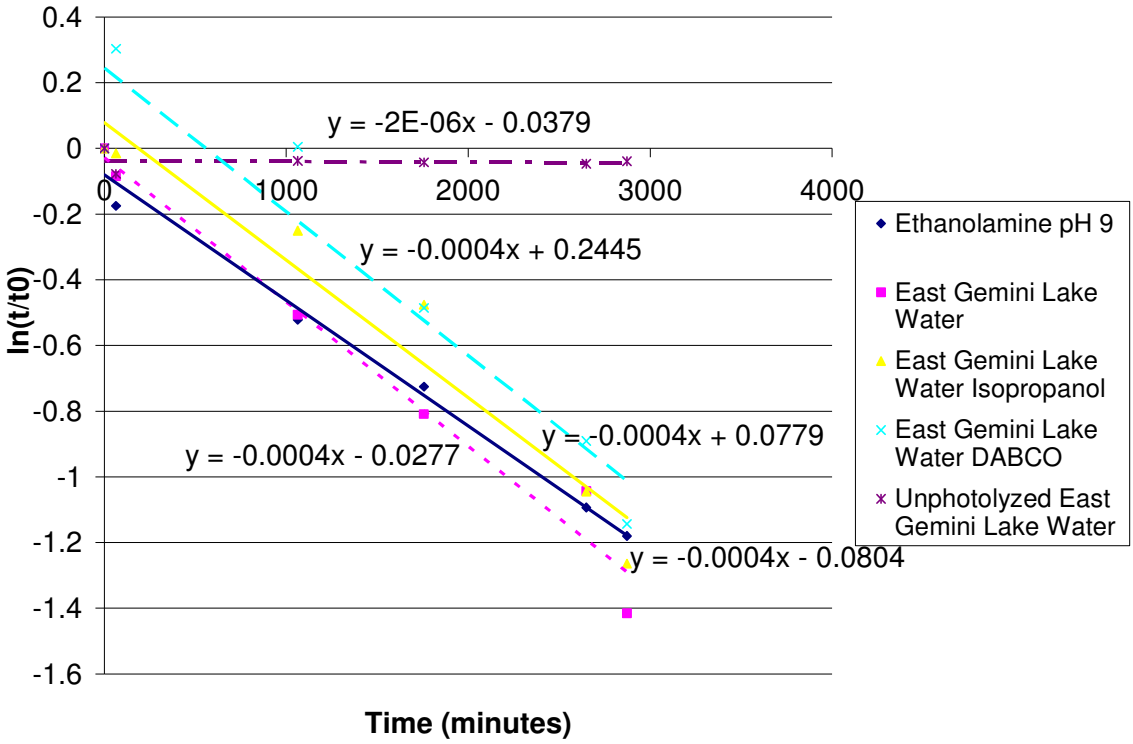

Figure 2. Indirect photolysis of sertraline hydrochloride solutions.

Sertraline Solution	**Half Life**
Ethanolamine	385 Hours (16 days)
Photolyzed Ethanolamine	29 Hours
East Gemini Lake (EGL)	385 Hours (16 days)
Photolyzed East Gemini Lake	29 Hours
Formate	578 hours (24 days)
Ammonium Acetate	1540 hours (64 days)

Table 1. Half lives of photolyzed and control (dark) sertraline solutions.

Discussion

It was found that sertraline decomposes when exposed to ultraviolet light in the ethanolamine pH 9 solution as well as the East Gemini lake water solution, as seen in Figure 1. East Gemini Lake water was slightly basic with a pH of about 8.75. Neither the formate pH 3 buffer solution nor the ammonium acetate pH 5 buffer solution

displayed any degradation in the samples in comparison to basic solutions and the control dark pH 9 solution. The slopes of the curves in the above figures are related to the half lives of the sertraline in each of the solutions. As seen in Table 1, the half life of the ethanolamine and the EGL solutions were 29 hours when photolyzed and 16 days for the unphotolyzed, control. The formate and ammonium acetate solutions had much longer half lives of about 24 days and 64 days respectively. There was also evidence of breakdown products in the ethanolamine and East Gemini lake solutions but they were unidentifiable due to the high concentration of acetonitrile and ethanolamine from the mobile phase in comparison to the trace amounts of the breakdown products.

The mechanism in which the sertraline photodecomposed was determined through the addition of radical scavengers: DABCO and isopropanol added to separate sertraline solutions in excess. Sertraline solutions of EGL-DABCO, EGL-isopropanol, EGL, and ethanolamine buffer were photolyzed and analyzed as seen in Figure 2. It was evident that all of the sertraline solutions that were exposed to ultraviolet light decomposed, whereas the control dark solutions did not. Since the DABCO and isopropanol trap the singlet oxygen and hydroxyl radicals respectively and all of the solutions had the same half life of about 29 hours, indirect photolysis was eliminated as a decomposition mechanism.

It was found that sertraline had a half life about 29 hours suggesting that there is little chance of accumulation of Setraline in the environment. However, since the presence of breakdown products of Sertraline were observed but were unidentifiable, it is uncertain if these products will accumulate or not and if so, have potential hazardous effect on the environment.

Conclusion

Through the use of an Ace photochemical reactor and liquid chromatography, it was determined that sertraline hydrochloride photodecomposes via direct photolysis. The presence of indirect photolysis occurring as part of the decomposition process was eliminated given that the half life of the sertraline lake water solution was the same as the

half lives with either the DABCO or isopropanol, all at about 29 hours. The likelihood of the accumulation of sertraline in surface water is low due to its short half life, but this may differ when sertraline is exposed to sunlight rather than ultraviolet light in the laboratory setting. Future research would consist of determining the breakdown products and photodecomposition of sertraline via direct sunlight.

References

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