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Photodegradation of sulphadimethoxine in water by medium pressure UV lamp

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ABSTRACT

The photodegradation rate of sulphadimethoxine (SMT) in water was studied under polychromatic UV light, in a bench scale apparatus. SMT photolysis was carried out at pH levels of 2.5, 6.5 and 10 to study the impact of acid base properties on the degradation of SMT. The highest SMT photolysis fluence based rate was found at pH = 2.5 ($k = 7.22 \times 10^{-4}\,cm^2/mJ$) and the lowest rate at pH = 10 ($k = 4.72 \times 10^{-4}\,cm^2/mJ$), thus the reaction rate decreases with an increase in pH between pH values of 2.5–10. Results indicated that direct photolysis is not satisfactory for degradation of SMT by polychromatic UV lamp as a fluence of approximately 7,000 mJ/cm^2 is needed to break down 99% of SMT at pH 6.5. The photodegradation products of SMT were studied at various pH values. Photodegradation of SMT results in dissimilar relative amounts of intermediates formed at different pH values which may exert a photon demand and impact on SMT photodegradation rate.

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INTRODUCTION

Sulphonamides, a group of synthetic antimicrobial agents, are commonly used in food-producing animals as growth promoters and as therapeutic and prophylactic drugs for a variety of bacterial and protozoan infections (Crosby 1991). Sulphadimethoxine (SMT), a sulphonamide antibiotic, is known for its broad activity against multiple bacterial infections and in many animal species with coccidial infections. As the majority of antibiotics administered are excreted unchanged, and given that land application of animal waste as a supplement to fertiliser is a common practice, there is a growing concern about the potential impact of antibiotic residues on the environment (Sarmah et al. 2006). As such, the low cost of SMT and the wide use on regular basis in the livestock industry can potentially contribute to an environmental load.

Sulphonamides are water soluble, polar and weakly absorbed to mineral soil colloids with sorption influenced by pH (Thiele-Bruhn et al. 2004). Once an antibiotic enters surface waters it may undergo abiotic degradation through processes such as photodegradation or biotic degradation through microorganisms. SMT is quite stable in water, with a reported half-life for degradation greater than 21 days (Boxall et al. 2004). Moreover, SMT was found to be very persistent in sediments as only 20% degraded after 180 days (Samuelsen et al. 1994). Traces of SMT in the streams of USA probably reflect inputs of sewage and agricultural sources (Kolpin et al. 2002). Batt et al. (2006) found SMT at concentrations from 0.046 to 0.068 µg/L in the local groundwater of Idaho, USA, which confirms contamination from animal waste. On the other hand, Miao et al. (2004) did not find any traces of SMT in effluents from eight waste-water treatment plants (WWTPs) in Canada. Antibiotics can also reach soil via liquid manure application. Wang et al. (2006) found SMT in liquid manure and evaluated conditions for improved biodegradation. Consequently, SMT can actually find its way into the receiving environment; and the question regarding their fate as parent compound or metabolites remains.

Studies showed that SMT exerted some growth inhibitory activity on green algae which is fundamental to the whole ecosystem; however a weaker toxic effect results if metabolised in animals to N-acetyl sulpha (AcSa) (Eguchi *et al.* 2004). Sulphonamides are also used for the management of infectious diseases in humans. The primary metabolite AcSa is lost in the urine; however, a small fraction is metabolised to sulphonamide hydroxylamine which exerts an immunosuppressive effect and may risk certain subpopulations in humans (Sisson *et al.* 1997). The metabolites (N acetylation and 6-hydroxylation) have also been found in SMT biotransformation from *in vitro* experiments on laying hens (Furusawa 2001). In another study, a photo-catalytic process with near-UV light and titanium dioxide used to simulate environmental photo-transformation also showed the formation of 6-hydroxy sulphadimethoxine (among other metabolites) (Calza *et al.* 2004). These studies show the importance of identifying the transformation pathways and toxicity of the sulphonamides residues and metabolites.

Few studies have been conducted to evaluate the effectiveness of treatment technologies on the removal of antibiotics in water treatment plants (WTPs) and WWTPs. Adams *et al.* (2002) found that oxidation and chlorination was very efficient in the removal of SMT at typical doses in WTP. Other studies showed that oxidation with free chlorine and monochloramine (Chamberlain & Adams 2006), ferrate (VI) (Sharma *et al.* 2006) and ozonation (Huber *et al.* 2005) have great potential in the removal of sulphonamides including SMT. Adams *et al.* (2002) showed little removal of SMT at monochromatic UV ($\lambda = 254$ nm) common in water disinfection. They received 75% removal of 50 μg/L of SMT spiked in deionised water at a UV dose of 3,000 mJ/cm^2, which is 100 times higher than typical UV dose at WTPs mostly due to low absorbance of SMT and high absorbance of natural waters at these wavelengths. With natural sunlight, Boreen *et al.* (2004) found that sulpha drugs are subjected to direct photolysis while Lunestad *et al.* (1995) found that SMT is not readily photodegradable as only 18% degraded after 21 days. Thus, direct photolysis by natural processes and engineered enhanced monochromatic UV were also not promising with regard to SMT degradation. In addition, the SMT photolysis rate exhibited significant pH dependence at pH values between 6.2–9 with decreasing natural light photolysis upon increasing pH values (Boreen *et al.* 2005). Therefore, SMT removal by utilising enhanced UV intensities and photon energies with artificial polychromatic UV sources in a wide range of pH values has not been suggested yet as a treatment process.

The treatment of water contaminated with organic pollutants, applying polychromatic ultraviolet UV light (200–400 nm), has significantly increased in recent years. Numerous chemical contaminants of concern absorb UV at these wavelengths and therefore can undergo efficient direct photolysis. The absorption of high-energy radiation (UV) can cause the destruction of chemical bonds and breakdown of the contaminant. When suggesting an engineered-based treatment for the removal of SMT in water, it is important to further understand the impact of intermediate products on process removal efficiency. The purpose of this study was to determine the photodegradation rate of SMT under polychromatic UV light (medium pressure UV lamp) applicable for engineered treatment processes, in a bench scale apparatus. The specific goals of this study were to (1) study the degradation kinetics of SMT and its by-products at various pH values, (2) determine the extinction coefficient and quantum yields for treating SMT by UV at various pH values and (3) compare degradation kinetics at deionised water to synthetic wastewater effluent. Photodegradation pathways of SMT were proposed based on the identification of several byproducts using HPLC/MS/MS apparatus. This study can also serve as a basis for future studies on combining polychromatic UV with an oxidant for breakdown of SMT by advanced oxidation technologies (AOP).

MATERIALS AND METHODS

Chemicals

SMT standard (99.9% purity) was obtained from Sigma-Aldrich, ULC grade methanol, acetonitrile and water from Bio-Lab Ltd. (Jerusalem, Israel). SMT stock solution was prepared by dissolving the compound in methanol at a concentration of 100 mg/L. Formic acid and ammonia, obtained from Bio-Lab, were used to change the pH of SMT solution. All chemicals were used as obtained and working

solutions were prepared with ULC grade water. Synthetic wastewater recipe was adopted from Seo *et al.* (1997) and represents biologically treated sewage effluent. The stock solution was further diluted with deionised water by a factor of 25 to obtain a UVT of 75% at 254 nm. Characteristics of the diluted synthetic wastewater effluent used in this study are presented in Table 1.

Photolysis experimental set up

Photolysis was carried out using a 0.45 kW polychromatic (200–300 nm) medium-pressure (MP) (Ace-Hanovia Lamp Cat. No. 7830-61, from Ace Glass Inc.) Hg vapour lamp housed in a quasi-collimated beam apparatus. A 150 mL sample was spiked with SMT to achieve a starting concentration of 3.2 μM (1 μg/mL) and irradiated with gentle stirring in a 90×50 mm crystallisation dish ($56.8\ cm^2$ surface area, solution depth approximately 2.8 cm) open to the atmosphere. Samples of 0.5 mL were withdrawn at appropriate intervals for chromatography analysis, determination and quantification of SMT and byproducts. Exposure times necessary to achieve UV fluences from 0 to approximately 6,000 mJ/cm^2 were determined from the average irradiance between 200–300 nm. The average irradiance was calculated using the solution spectral absorbance, the spectral incident irradiance obtained from a calibrated spectroradiometer (RPS900 wideband, International Light, Co., Newburyport, MA) placed in the same position as the centre of the crystallisation dish, the reflection at the sample surface and the measured petri-factor for the dish (Bolton & Linden 2003). A UV spectrophotometer, Cary Bio100 (Varian, Inc., Palo Alto, CA), with 1 nm step size was used to measure the aqueous solution absorbance and the molar absorption spectra for SMT at different pH values. The average irradiance value for the MP lamp (integration between 200–300 nm) for 3.2 μM spiked at pH 6.5 was 1.59 mW/cm^2. The emission spectra of the UV lamp is shown in Figure 1.

HPLC gradient conditions

The HPLC mobile phase consists of water (eluent A) and acetonitrile (eluent B), adjusted to pH 3.3 by the addition of formic acid. The elution started with 65% of eluent A, followed by a 2-min linear gradient to 15% of eluent A, 2-min isocratic elution and a 1-min linear gradient to 65% of eluent A, which was maintained for 10 min to equilibrate the column.

Byproducts analysis

The SMT and its byproducts were separated, detected and quantified by HPLC-MS/MS Agilent, model 1100 – Finnigan LCQ (ACE- RP C18 column 2.5 $\times$ 250 mm), consisting of a binary pump, a micro vacuum degasser, a diode array detector and a thermostatic column compartment.

The column temperature was 28°C, the flow rate was 0.5 mL/min and the volume injected was 100 μL. The absorption of the SMT and its obtained fractions were recorded at 215, 260 and 280 nm. The mass spectrometer was used in positive electro-spray ionisation (ESI) mode and the probe temperature was set to 220°C. The flow from the HPLC was passed through a split connector with 60 μl/min of effluent introduced into the MS interface. Ions in the range 85–400 m/z were registered in the conventional scanning mode. The sheath gas flow was 93 (arbitrary units), auxiliary flow was 26 (arbitrary units) and capillary temperature was set at 200°C. The spray voltage was set to 4.5 kV. Instrument control, data acquisition and evaluation were performed with Xcalibur software. MS/MS tune file was created for SMT standard in continuous flow mode, and the optimum capillary voltages, lens settings, collision energies and the product ions of the highest intensities were determined (Table 2). MS/MS was also applied on the byproducts (full scan), for better identification and understanding of the photo-degradation process.

Table 1 | Diluted synthetic wastewater effluent quality

pH	TOC mg/L C	Alk mg/L	COD	TDS	Ca^{2+}	Cl^-	NO_3^-	PO_4^{3-}	Fe^{2+}	HCO_3^-	SO_4^{2-}
6.4	1.25	5	26	215	0.4	1.9	<1	1.2	0.035	6.1	<5

Figure 1 | Extinction coefficient of SMT spiked in deionised water at pH from 2.5, 6.5, 10 and for SMT spiked in synthetic effluent and emission spectrum of the MP lamp.

RESULTS AND DISCUSSION

Extinction coefficient of SMT

The impact of photolysis of SMT with an MP lamp was carried out at pH 2.5, 6.5 and 10 to study the impact of acid base properties on degradation of SMT and possibly suggest conditions for enhanced removal. The acid base speciation of SMT is presented in the following chemical Equation:

Deprotonation of SMT occurs either at the NH group or at the NH_2 of the aniline. The isoelectric point (pI) is at 4.5; which means that below pI SMT carries a positive charge and above it SMT carries a negative charge. At pH 10 the molecule is negatively charged (c) and a decrease in pH to 6.5 results in an increase in the percentage of the neutral form (b), and at pH of 2.5, which is close to the pKa of the aniline group (2.13), the protonated form (a) of the SMT is the dominant species. Therefore, the degradation rate of SMT and the intermediates can be pH dependent as well.

Figure 1 illustrates the extinction coefficient of SMT at various pH values and SMT in effluent. Below 230 nm the highest extinction coefficient is for water spiked with SMT at pH 2.5, and a peak appears at around 270 nm and is highest for water at pH 10. The overlap between extinction coefficient and lamp emission at each wavelength quantifies the light absorbance of a compound.

Reaction kinetics

Photo-degradation of 3.2 μM SMT in aqueous solution by the polychromatic MP lamp as a function of time is

(1)

illustrated in Figure 2. In all cases, linear reaction kinetics occurs between $\ln([SMT]_t/[SMT]_0)$ and exposure time, where $[SMT]_0$ is initial SMT concentration and $[SMT]_t$ is SMT concentration at time t. The data were fitted using a linear regression approach resulting in pseudo-first order reaction kinetics which reflects the difference in photo degradation between samples. The slope of the lines in Figure 2 give the time-based rate constant, however, the fluence-based rate constant (cm^2/mW) was also obtained

Table 2 | MS/MS parameters for SMT

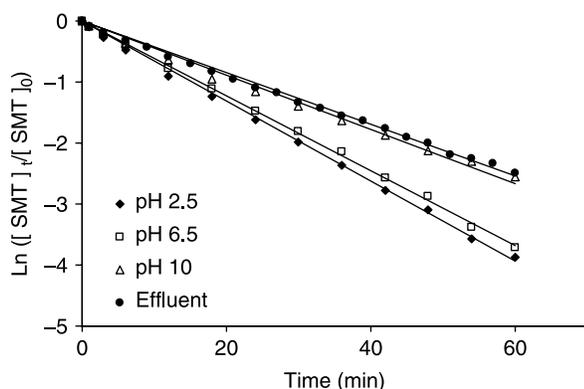| Precursor ion (M + H) +	Fragment ion 1	Fragment ion 2	Fragment ion 3	Collision energy, %
311.3	156.5	245.1	218.0	27

Figure 2 | Photodegradation of SMT with MP lamp at different pH values.

and tabulated in Table 3. The highest SMT photolysis rate in water was found at pH = 2.5 and the lowest rate at pH = 10, thus, as previously suspected, pH is an important factor affecting photolysis rate. Studies showed that SMT photolysis rate exhibited significant pH dependence with decreasing natural light photolysis upon increasing pH values between pH 6.2–9 (Boreen *et al.* 2005), which is in agreement with the current observation. In addition, the water quality also has an impact on degradation rate as observed by lower degradation rate of SMT in synthetic effluent at pH of 6.4. Boreen *et al.* (2005) found enhanced degradation of sulpha drugs in natural waters compared to DI water, suggesting indirect photolysis processes are also important; however, the extent of degradation via natural organic matter (NOM) will depend on the organic matter composition. In the current study the direct photolysis of SMT is influenced by the background absorbance of effluent at wavelengths below 250 nm where SMT also absorbs with no observed enhanced degradation with NOM by indirect photolysis processes.

Table 3 | Quantum yield, time and fluence based rate constant for waters at different pH and for effluent

Water type	Quantum yield[*]	Time based reaction rate[†], 1/s	Fluence based reaction rate[†] cm²/mJ
pH 2.5	0.02359	0.00107 ± 0.00012	7.22×10^{-4}
pH 6.5	0.01977	0.00102 ± 0.00005	6.42×10^{-4}
pH 10	0.01256	0.00070 ± 0.00002	4.72×10^{-4}
Effluent	0.01718	0.00070 ± 0.00002	5.55×10^{-4}

[*]Integrated between 200–300 nm.
[†]Correlation coefficients above 0.99.

The direct photochemical kinetics of SMT can be described by Equations (2) and (3), adapted from Sharpless & Linden (2003).

$$-\frac{d[SMT]}{dt} = \left(\sum \kappa s(\lambda)\right)\phi[SMT] \Rightarrow -\frac{\ln\frac{[SMT]_t}{[SMT]_0}}{t} = \sum \kappa s(\lambda)\cdot\phi \quad (2)$$

$$\kappa s(\lambda) = \frac{E_p^0(\lambda)\varepsilon(\lambda)[1 - 10^{-a(\lambda)z}]}{a(\lambda)z} \quad (3)$$

where $ks(\lambda)$ is the specific rate of light absorption by SMT ($E\,mol^{-1}\,s^{-1}$), Φ is the quantum yield (QY) for removal (mol E − 1), $E^0p(\lambda)$ is the incident photon irradiance ($10^{-3}\,Ecm^{-2}\,s^{-1}$), $\epsilon(\lambda)$ is the molar extinction coefficient of SMT ($M^{-1}\,cm^{-1}$), $a(\lambda)$ is the solution absorbance (cm^{-1}), and z is the depth of solution. The summation in Equation (2) was taken over the wavelength range 200–300 nm and the quantum yield (Φ) of SMT at different pH values can be further calculated by Equation 2.

The key parameters to evaluate the rate of a photochemical reaction are both QY and the overlap between the emission spectra of the UV lamp and extinction coefficient. The QY value decreases with a decrease in pH which correlates to decrease in time based rate constant (Table 3). Since most of the UV lamp output occurs at the range of 240–450 nm, the increase in extinction coefficient at pH 2.5 below 240 nm is possibly not the cause for the high degradation rate at pH 2.5 compared to other pH values. In addition, the rate of SMT degradation at pH 2.5 is higher than the other waters at pH 6.5 and 10, clearly not due to light absorption as the extinction coefficient between 240–280 nm is highest for pH 10 water. The differences in QY at different pH values correlate to the differences in reaction rate at different pH values, thus even though at pH 2.5 the light absorption between 240–280 is lower the higher QY may be the factor impacting degradation. SMT degradation rate varied over the range of pH values studied possibly due to (a) speciation between the cationic, neutral and anionic forms and (b) "photon demand" of the intermediates formed upon photolysis which absorb photons and thus less photons reach the parent compound. The absorbance spectra of the intermediates formed upon photolysis at various pH values and the quantum yield of the by-products formed may provide an explanation. The intermediates obtained at the different pH

values after UV degradation of 60 minutes will be further evaluated to test this hypothesis. The removal rate of another sulphonamide antibiotic, sulphamethoxazole (SMX), in the same polychromatic apparatus at pH 6.5 resulted in a reaction rate of 0.00591 (1/s). The QY for SMX in this study was 0.121 which is similar to a value of 0.09 obtained by Boreen *et al.* (2004) under natural sunlight at pH 6.9.

For processes that undergo relatively slow photolysis, due to the lack of chromophors or low QY, it is common to combine UV with hydrogen peroxide to produce the powerful OH radicals. N-nitrosodimethylamine (NDMA), which is suitable for direct photolysis (Sharpless & Linden 2003, 2005), had a fluence based rate constant of 2.4×10^{-3} in synthetic water which is an order higher than SMT rate constant in synthetic effluent (although not the same water). Results in the current study show that direct photolysis is not satisfactory for degradation of SMT as a fluence of approximately $1,000\,\text{mJ/cm}^2$ will be required to breakdown
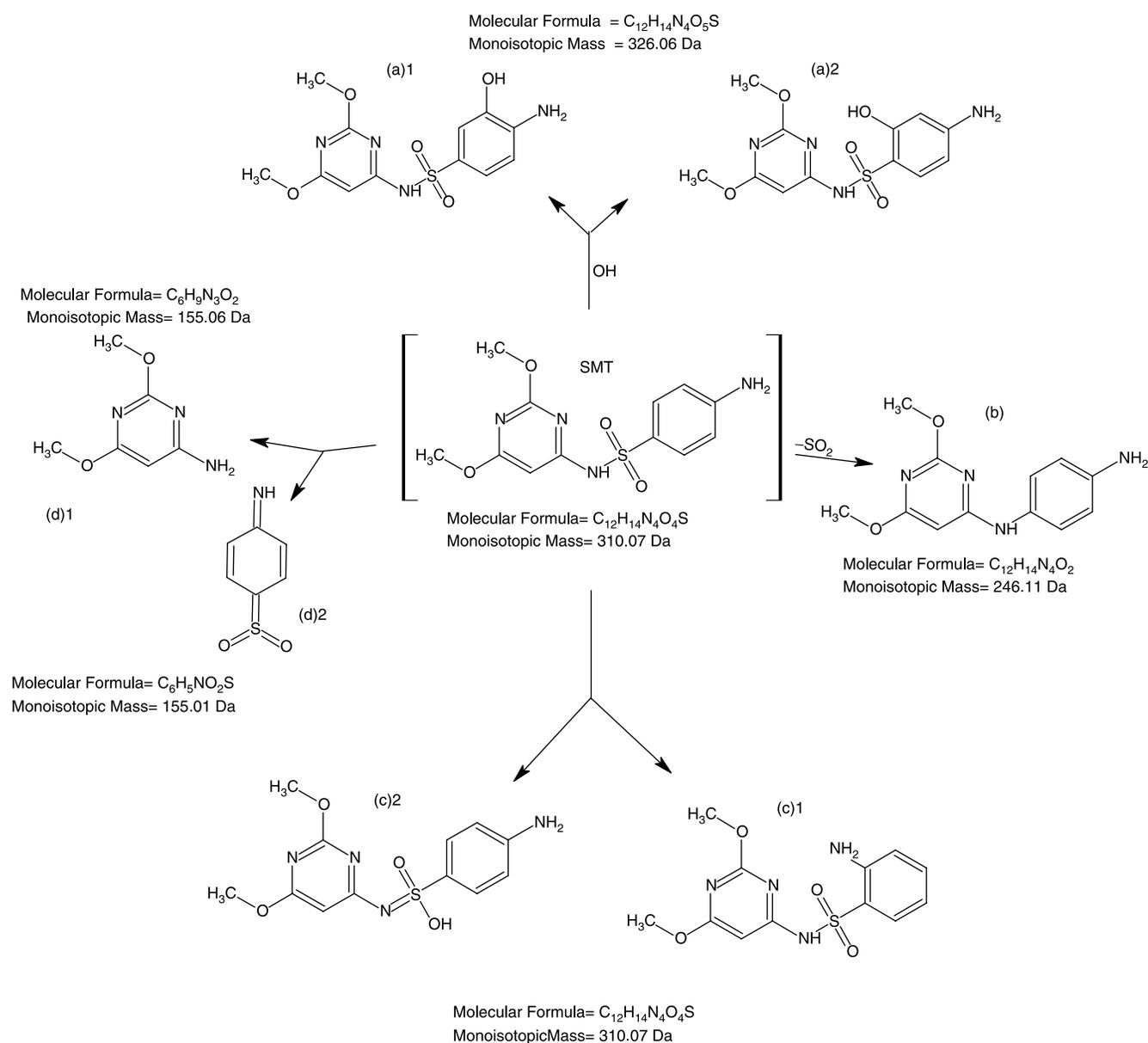

Figure 3 | SMT photoproducts formed at pH = 2.5, 6.5 and 10.

50% of SMT in synthetic effluent and 7,000 mJ/cm^2 will be needed to break down 99% of SMT at pH 6.5. As a comparison, a fluence of approximately 400 mJ/cm^2 will be required to break down 50% of NDMA in synthetic water.

Intermediates of SMT photodegradation

Figure 3 presents the photodecomposition of SMT to organic intermediates after the UV irradiation. Four main intermediate compounds have been identified, all exerting retention times shorter then the parent molecule in the HPLC chromatogram. The first intermediate detected, (a) (a1 is more favourite), consisted of 326 mass units and can be attributed to ·OH radical attack on the aromatic ring related to the aniline group (Calza *et al.* 2004), forming a hydroxylated structure. As mentioned earlier, 6-hydroxysulphadimethoxine was found from *in vitro* experiments on laying hens (Furusawa 2001). In humans, a small fraction of SMT is metabolised to sulphonamide hydroxylamine, which exerts an immunosuppressive effect and may risk certain subpopulations in humans (Sisson *et al.* 1997). Intermediate (a) was found at a lesser amount under irradiation at pH 2.5 compared to pH 6.5 and 10, probably due to the fact that the nitrogen of the aniline group is partially positively charged (pKa 2.13). Positively charged nitrogen can not direct the negative charge to the para and ortho position on the aromatic ring (the ortho and/or para substitute product is favourable on the meta product). The second intermediate detected, (b), consisted of 246 mass units and formed through the loss of SO$_2$ (64 mass units). The intermediate formation showed the same pH dependence as intermediate (a). Where the partially positively charged nitrogen on the aniline group resulted in lower amount of intermediate formed at pH 2.5 (by a factor of ten) compared to pH 6.5 and 10. Boreen *et al.* (2005) also observed the loss of SO$_2$ on SMT degradation by natural sunlight, however, a different product was observed compared to this study by MP lamp photolysis.

The third intermediate detected, (c), has the same mass as the SMT parent molecule (310 mass units). This can indicate the occurrence of isomerisation, i.e. displacement of the hydrogen on the para aniline group (c1), or tautomerisation (more favourite), i.e. the formation of S $=$ N double bond. The absorbance spectrum of the intermediate indicates local maxima at wavelength 295 nm, whereas SMT absorbance peak appears at 275 nm. Furthermore, applying MS/MS on this intermediate did not show two of the original fragment ions ("b" and "d"), that require an S-N bond breaking. The above analysis strengthens the assumption regarding the formation of S $=$ N double bond. Intermediate (c) was obtained in much lesser amounts at pH 10 than at pH 6.5 and 2.5, due to the fact that the nitrogen of the sulphonamide group is negatively charged at pH 10 (pKa $\sim$ 6.8) and thus it does not have the same alocalisation as the natural position of the sulphonamide nitrogen. The fourth intermediate (d), holding 155 mass units, follows the fragmentation pathway of the MS/MS apparatus. The intermediate occurs through the cleavage of the S$-$N bond, and is attributed to the species RNH$_2$ (b)1 and RSO$_2$ (b)2.

Consequently, the ratio of intermediates formed by SMT is pH dependent. These results may indicate a possible correlation between the type and quantity of the intermediates formed and SMT degradation rate, through competition on UV photons. Further studies are required to fully understand the byproduct characteristics and its influence on SMT degradation kinetic.

CONCLUSIONS

The highest SMT photolysis rate in water was found at pH $=$ 2.5 ($k = 7.22 \times 10^{-4}$ cm^2/mJ) and the lowest rate at pH $=$ 10 ($k = 4.72 \times 10^{-4}$ cm^2/mJ), thus the reaction rate is pH dependent. Direct photolysis is not satisfactory for degradation of SMT by polychromatic UV lamp as a fluence of approximately 7,000 mJ/cm^2 is needed to breakdown 99% of SMT at pH 6.5. The relative amount of degradation products at various pH values is pH dependent and may exert a photon demand, however, this issue should be further studied. Since SMT undergoes slow direct photolysis it may be beneficial to combine UV with hydrogen peroxide to produce the OH radicals that may enhance SMT degradation rate.

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