# TRANSFORMATION OF SULFADIMETHOXINE AND TRIMETHOPRIM IN VUV RADIATED AQUEOUS SOLUTIONS

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**Abstract**
The combination of trimethoprim and sulfonamides (e.g., sulfadimethoxine) is often used as a growth promoter and antibiotic in animal husbandry. In this work, the efficiency of the low pressure mercury vapour (LPM) lamp, emits at 254 and 185 nm (UV/VUV$_{185\ nm}$ lamp) and Xe-excimer lamp, emits at 172 nm (VUV$_{172\ nm}$) photons were compared in the transformation of sulfadimethoxine (SDM) and trimethoprim (TRIM). Both light sources were effective on the transformation of both components. Although the VUV photon flux of the excimer lamp was significantly higher than of LPM lamp, there was no significant difference between the transformation rates of organic substances. The reason was most probably the extreme inhomogeneity of 172 nm radiated solution. VUV$_{185\ nm}$ photolysis increased the initial rate of transformation comparing to that determined in UV (254 nm) radiated solution mainly in the case of TRIM, and just slightly for SDM, probably because the direct UV photolysis is also effective for SDM transformation, opposite to the TRIM. The VUV$_{172\ nm}$ photolysis was found to be more effective in mineralization, for both compounds than UV/VUV$_{185\ nm}$ photolysis. Dissolved O$_2$ has significant effect only in the case of the UV/VUV$_{185\ nm}$ photolysis of TRIM.

**Introduction**
In recent decades, environmental protection has placed increasing emphasis on preventing the release of persistent, biologically active pollutants into the environment, in particular antibiotics, the inappropriate or excessive use of which poses a serious risk to public health. Human medicine are excreted from the urine and faces and discharged into wastewater, where conventional wastewater treatment plants are often unable to remove these biologically active organic contaminants [1]. Even though, the drug residues are present in very low concentrations in wastewater. Due to the limitations of conventional biological water treatment process, antibiotics can return to drinking water bases, so the drug loading of living organisms through water become continuous. Consequently, it is particularly important to investigate and develop additive water treatment processes, which are able to effectively remove the active pharmaceutical ingredients, and their residues from pre-treated wastewater.

In this study UV/VUV$_{185\ nm}$ and VUV$_{172\ nm}$ photolysis of SDM and TRIM were investigated and compared. The combination of SDM with TRIM is widely used for the treatment of infections in animal husbandry.

Trimethoprim is a widely used antibiotic drug since 1960's. It is commonly used with various sulfonamides together to treat urinary tract infections and it is effective to treat ear infections and diarrhea. Due to its extensive use, and hard biodegradability, it was detected in various waters e.g. rivers [2] or domestic wastewater [3].

Sulfadimethoxine is a long lasting sulfonamide antibiotic, which is used as a veterinary drug to treat urinary tract, enteric, or soft tissue infections. Due to the excessive use of sulfonamides (e.g. sulfadimethoxine), sulfadimethoxine was detected in many cases in various waters such as wastewater, ground water, or surface waters [4-6].
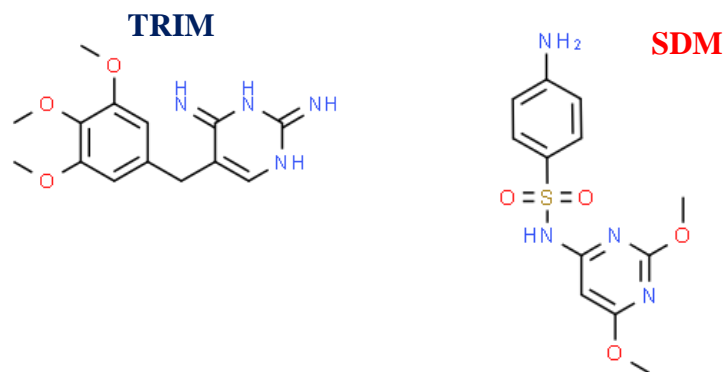
**Fig. 1.** Chemical structures of TRIM and SDM

**Experimental**

For the VUV$_{172\,nm}$ radiation Xe$_2$* excimer lamp (Radium Xeradex$^{TM}$, 130 mm long, 46 mm diameter, 20 W) was used, which was centred in a high purity silica quartz envelope (53 mm diameter), able to transmits the 172 nm light. The aqueous solution was circulated continuously (375 mL min$^{-1}$) between the reactor and the reservoir. Double walled, water cooled reactor was used, the temperature was set to 25 ± 0.5 °C. Samples were taken from the reservoir. The volume of the treated solution was 500 mL, the thickness of radiated water layer was 5 mm.
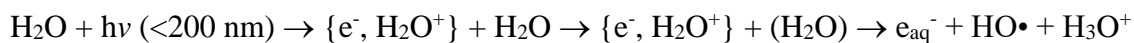
The low-pressure mercury vapour (LPM) lamp (UV/VUV$_{185\,nm}$ lamp GCL307T5VH/CELL, 227 mm arc length, produced by LightTech) was used for the UV/VUV (254 nm/185 nm) photolysis. The UV/VUV$_{185\,nm}$ lamp's envelope was made of synthetic quartz to be able to transmit the VUV$_{185\,nm}$ photons. Another LP lamp (UV lamp, GCL307T5L/CELL, 227 mm arc length, produced by LightTech) was used for UV photolysis. The parameters of the UV and UV/VUV$_{185\,nm}$ lamps were the same, but the envelope of UV lamp was made from commercial quartz, which absorbs the 185 nm light, but transmits the 254 nm UV light.

In the case of UV (254 nm), VUV$_{172\,nm}$ and UV/VUV$_{185\,nm}$ photolysis, O$_2$ or N$_2$ gas was bubbled continuously trough the solution. Gas bubbling was started at least 20 min before the measurement. SDM (Sigma-Aldrich, ≥98%) and TRIM (Sigma-Aldrich, ≥98.5%) solutions with initial $1.0 \times 10^{-4}$ mol L$^{-1}$ concentration were made in ultrapure MILLI-Q water (MILLIPORE Milli-Q Direct 8/16).

Separation of the aromatic components in the treated solutions was performed by Agilent 1100 type HPLC, equipped with diode array detector (DAD). For the analysis of sulfadimethoxine and its degradation products, Lichrospher 100, RP-18; 5 μm coloumn was used at 30 °C, the flow rate of eluent was 1.0 mL min$^{-1}$, and 20 μL sample was injected. The wavelength of the detection was 269 nm. For the analysis of trimethoprin and its degradation products, Kinetex 2.6u XB-C18 100A (Phenomenex) coloumn was used at 30 °C, the flow rate of eluent was 0.75 mL min$^{-1}$, and 20 μL sample was injected. The wavelength of the detection was 285 nm.

**Results and discussion**

In the case of the VUV photolysis, the 172 nm and 185 nm VUV light is absorbed by water to form reactive species, such as hydrogen radical (H•), hydroxyl radical (HO•) and with lower yield hydrated electron (e$_{aq}^-$) [2].

$$H_2O + h\nu \ (<190 \ nm) \rightarrow H\bullet + HO\bullet \qquad\qquad \Phi(HO\bullet) = 0.33$$

$$H_2O + h\nu \ (<200 \ nm) \rightarrow \{e^-, H_2O^+\} + H_2O \rightarrow \{e^-, H_2O^+\} + (H_2O) \rightarrow e_{aq}^- + HO\bullet + H_3O^+$$
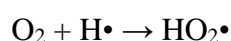
$$\Phi(e_{aq}^-) = 0.045 - 0.05$$

There is a significant difference between the aqueous systems, radiated with 185 nm and 172 nm light. The molar absorbance of water at 172 nm, highly exceed (10.0 M$^{-1}$cm$^{-1}$) its molar absorbance at 185 nm (0.032 M$^{-1}$cm$^{-1}$). Consequently the 185 nm VUV photons are absorbed within 11 mm, while the 172 nm VUV photons are absorbed within 0.04 mm thin water layer. The VUV photon flux was determined with methanol actinometry, and was found to be 32 times higher (1.04×10$^{-5}$ mol$_{photon}$ s$^{-1}$) for the excimer lamp than for the LPM lamp (3.23×10$^{-7}$ mol$_{photon}$ s$^{-1}$). The UV photon flux was 3.70×10$^{-6}$ mol$_{photon}$ s$^{-1}$.

Table 1. shows the initial transformation rates and apparent quantum yields of TRIM and of SDM transformation, determined in UV, UV/VUV$_{185 nm}$ and VUV$_{172 nm}$ radiated solutions at 1.0×10$^{-4}$ M initial concentration. The UV photolysis was effective for transformation of SDM; its transformation rate was almost the same than in UV/VUV$_{185 nm}$ radiated solution. The TRIM practically does not transform in UV radiated solution. It can be explained by the significant difference between the molar absorbance of these compounds at 254 nm: TRIM: $\varepsilon_{254 nm}$=4477.5 M$^{-1}$ s$^{-1}$ and SDM: $\varepsilon_{254 nm}$=16050 M$^{-1}$ s$^{-1}$. The transformation rate determined not only by the molar absorbance but also the quantum yield of the transformation, which is relatively high of SDM. The presence of 185 nm photons, which have a photon flux one magnitude higher than that of 254 nm light, dramatically increased the transformation rate of TRIM, but only slightly increased that of SDM, probably due to the contribution of the direct UV photolysis.
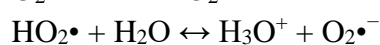
**Table 1:** The initial transformation rates of sulfadimethoxine (SDM) and trimethoprim (TRIM) at 1.0×10$^{-4}$ M initial concentration

| | | UV O$_2$ | UV N$_2$ | UV/VUV O$_2$ | UV/VUV N$_2$ | VUV O$_2$ | VUV N$_2$ |
|---|---|---|---|---|---|---|---|
| **SDM** | $r_0$ (×10$^{-7}$ M s$^{-1}$) | 1.35 | | 1.70 | 1.46 | 1.39 | 1.21 |
| | $\Phi$ | 0.036 | | 0.11 | 0.03 | 0.013 | 0.012 |
| **TRIM** | $r_0$ (×10$^{-7}$ M s$^{-1}$) | 0.07 | 0.004 | 0.93 | 0.46 | 1.39 | 1.39 |
| | $\Phi$ | 0.002 | - | 0.27 | 0.14 | 0.013 | 0.013 |

In the case of VUV photolysis, dissolved O$_2$ reacts with H•. By this way, H• transforms to less reactive HO$_2$/O$_2$•$^-$:

$$O_2 + H\bullet \rightarrow HO_2\bullet \qquad\qquad k = 2.1 \times 10^{10} \text{ M}^{-1} \text{ s}^{-1}$$
$$HO_2\bullet + H_2O \leftrightarrow H_3O^+ + O_2\bullet^- \qquad\qquad pK_a = 4.8$$

At the same time, through the formation of organic peroxyl (ROO•) radicals, O$_2$ opens up a new ways to transform organic substances, and generally increases the transformation rate. The transformation rate increases just slightly for SDM in the presence of O$_2$ (Fig 2 and Table 1). Probably the negative effect (elimination of H•) and the positive effect (formation of peroxyl radical) compensates each other's in this case. In contrast, dissolved O$_2$ doubled the transformation rate of TRIM in the case of UV/VUV$_{185 nm}$ photolysis, while in the case of VUV$_{172 nm}$ photolysis, O$_2$ has no effect (Fig 2 and Table 1). It has to be mention that, in 172 nm radiated aqueous solutions of organic substances, due to the extremely high HO• concentration close to the wall of the lamp, an O$_2$-depletion layer forms. Thus, the positive effect of O$_2$ via peroxyl radical formation is less pronounced, and the relative negative effect (due to the H• elimination) can be amplified.
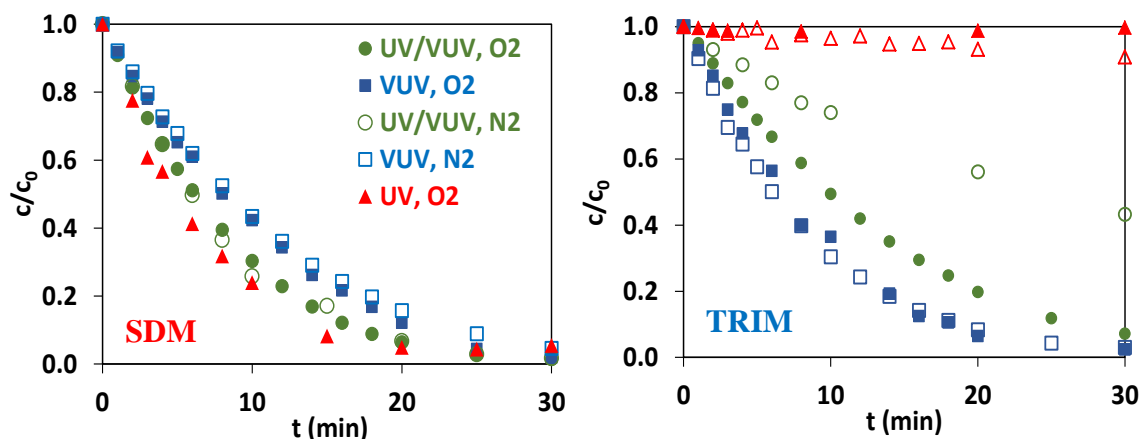
**Fig 2.** Relative concentration of SDM (a) and TRIM (b) versus time of irradiation in the case UV, UV/VUV$_{185\,nm}$ and VUV$_{172\,nm}$ photolysis

172 nm VUV photolysis enhanced the transformation comparing to the UV/VUV$_{185\,nm}$ photolysis in the case of TRIM, but in the case of SDM, the transformation was faster in UV/VUV$_{185\,nm}$ radiated solution. Results can be explained by the relative high contribution of the direct UV photolysis to the transformation of SDM in UV/VUV$_{185\,nm}$ radiated solution. There is no significant difference between the rate constants of these compounds with HO• ($k_{HO•+TRIM}=8.13\times10^9$ M s$^{-1}$ [7] and $k_{HO•+SDM}=8.13\times10^9$ M s$^{-1}$ [8]). The apparent quantum yield suggests that, the recombination of H• and HO• radicals in the photoreactive zone (0.04 mm) in the 172 nm irradiated solution is preferable to their reaction with organic matter, probably due to the extremely high concentration of these radicals and the lack of dissolved $O_2$. Both effects are negligible in 185 nm radiated solutions.
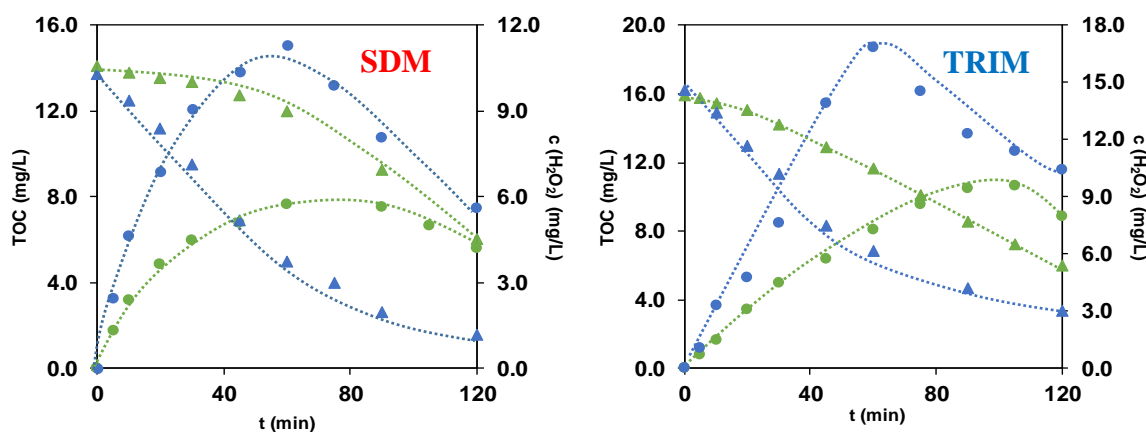


**Fig 3.** The concentration of TOC and $H_2O_2$ versus time of irradiation in the case of UV/VUV$_{185\,nm}$ (green) and VUV$_{172\,nm}$ (blue) photolysis of SDM (a) and TRIM (b)

In the case of UV/VUV$_{185\,nm}$ photolysis the decrease of TOC content starts with an induction period, which is much more pronounced for SDM (Fig. 3a). During this time in VUV$_{172\,nm}$ radiated solution the TOC decreases intensively. In both cases the VUV$_{172\,nm}$ photolysis was more effective for mineralization. The maximum value of $H_2O_2$ concentration is also higher in the case of the excimer lamp, than in the case of LP light, which proves a more intensive mineralization of the organic substances.

## Conclusion

The UV, UV/VUV$_{185nm}$, and VUV$_{185nm}$ photolysis are effective for the elimination of 5-FLU from aqueous solutions, the highest transformation rate was measured in the case of UV/VUV$_{185nm}$ photolysis. Dissolved O$_2$ has no significant effect on the transformation rate even in the case of VUV$_{172nm}$ photolysis. The highest mineralization rate was observed in the case of VUV$_{172nm}$ photolysis. Although the photon flux of 172 nm light is much higher than of 185 nm light, the transformation is slower, partly because of the contribution of 254 nm in the case of UV/VUV$_{185nm}$ photolysis, and partly because of the extreme inhomogeneity of 172 nm radiated aqueous solution.

## Acknowledgements

## References

[1] Zhang, R, Sun, P, Boyer, T.H., Zhao, L., Huang, C.H., Environ Sci Technol, 2015, 49 (5) 3056-3066

[2] Gałwa-Widera, M, Eds: Narasimha M., Prasad V., Vithanage M, Kapley A, Plant-based technologies for removal of pharmaceuticals and personal care products, Butterworth-Heinemann, 2019, 297-319

[3] Karthikeyan, K.G., Meyer, M.T., Sci Total Environ, 2006, 361(1–3), 196–207

[4] Wang, Z., Zhang, X.H., Huang, Y., Wang, H., China Environ. Pollut. 2015. 204, 223–232.

[5] García-Galán, M. J., Díaz-Cruz, S., Barcelo, D., Environ. Intern., 2011. 37 (2), 462–473.

[6] Pailler, J. Y., Krein, A., Pfister, L., Hoffmann, L., Guignard, C., Sci. Total Environ. 2009. 407, 4736–4743.

[7] Wojnárovits, L., Tóth T., Takács, E.; Crit Rev Environ Sci Technol, 2018, 48 (6) 575-613

[8] Boreen A.L., Arnold W.A., McNeill K., Environ Sci Technol, 2005, 15, 39 (10) 3630-3638