DEGRADATION OF NIRMATRELVIR IN WATER BY UV-C/H_2O_2 AND UV-C/$S_2O_8^{2-}$ PROCESSES

Lidija Furač*, Lucija Švegović, Matija Cvetnić, Viktorija Martinjak, Kristina Bule Možar, Martina Miloloža, Marinko Markić, Dajana Kučić Grgić, Tomislav Bolanča, Šime Ukić

University of Zagreb Faculty of Chemical Engineering and Technology, Trg Marka Marulića 19,10000 Zagreb, Croatia

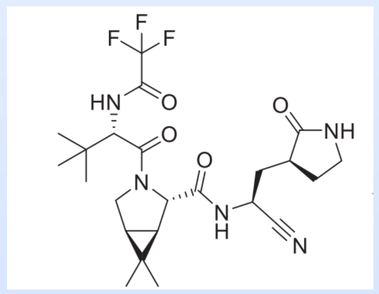
lfurac@fkit.unizg.hr

INTRODUCTION

Antiviral substances aimed to treat severe acute respiratory syndrome coronavirus (SARS-CoV-2) are mostly new environmental pollutants whose occurrence in the environment is continuously increasing. They present a serious ecological and health risk that includes the safety of drinking water, antiviral resistance and destabilization of sensitive microbial communities. Unfortunately, there is very few information about their fate and behavior in the environment as well as the approaches for their efficient removal from the environment.

In this study, degradation of the SARS-CoV-2 antiviral substance nirmatrelvir (NTV) by two advanced oxidation processes (AOP) : UV-C/H_2O_2 and UV-C/$S_2O_8^{2-}$, was investigated. The influence of two process parameters: the pH value of the solution and the concentration of the oxidant (OX, H_2O_2 or $S_2O_8^{2-}$) on the process efficiency was studied. Degradation kinetics was evaluated and the optimal degradation conditions determined.

EXPERIMENTAL



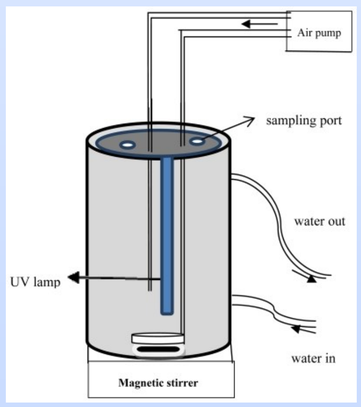
Nirmatrelvir
Molecular formula: $C_{23}H_{32}F_3N_5O_4$
Molar mass: 499.5 g/mol,
CAS number: 2628280-40-8

UV reactor

V (reactor) = 100 mL
V(solution NTV) = 80 mL
c_0 (NTV) = 0.1 mmol/ dm^3 [mM]

UVP, Ultra Violet Products, PenRay Lamp, 11SC-1, Analytik Jena, USA

UVP, Ultra Violet Products, Pen-Ray, Upland, CA, USA, *v* = 50 Hz, *U* = 230 V, *I* = 0,21 A



Full factorial plan

Plan development, statistical analysis and analysis of variance (ANOVA) were carried out using the software packages *Design Expert* 10.0, StatEase, USA and *STATISTICA* 12.7, StatSoft Inc., USA. The optimal values of the process parameters predicted by the *Response Surface Methodology* (RSM model) were calculated using the Mathematica 10.0 software package, Wolfram Research, USA.

HPLC analysis

The kinetics of nirmatrelvir degradation was monitored by HPLC analysis

Instrument : HPLC Perkin Elmer Flexar FX20, detector Dionex PDA-100 (USB)
Flow : 1 mL/min
Mobile phase: 30 % CH_3OH /70 % MQ Water
Analysis duration: 10 min
System pressure: 312 bar
Column temperature: 30°C
Retention time: 5,1 min
Wavelenght: 215 nm
Injection volume: 30 µL
Column: XTERRA RP 18 3.5µm ,4.6 x 1mm

RESULTS

UV-C/H_2O_2

Table 1. Full factorial design of the experiment with two independent variables expressed in coded and real values and calculated first-order NTV conversion values **UV-C/H_2O_2**

EXPERIMENT	Variables				Conversion NTV UV-C/H_2O_2	
	Variable 2, x_2		Variable 1, x_1			
	Cod	pH	Cod	c(OX) [mM]	k_{obs} [s^{-1}]	R_{LR}^2
1	-1	4	-1	1,00	0,0052	0,9961
2	-0,5	5,5	-0,5	5,75	0,0078	0,9851
3	0	7	0	10,50	0,0086	0,9847
4	0,5	8,5	0,5	15,25	0,0048	0,9698
5	1	10	1	20,00	0,0046	0,9839
6	-1	4	-1	1,00	0,0039	0,9509
7	-0,5	5,5	-0,5	5,75	0,0090	0,9942
8	0	7	0	10,50	0,0031	0,9939
9	0,5	8,5	0,5	15,25	0,0039	0,9787
10	1	10	1	20,00	0,0033	0,9960
11	-1	4	-1	1,00	0,0062	0,9614
12	-0,5	5,5	-0,5	5,75	0,0089	0,9863
13	0	7	0	10,50	0,0034	0,9809
14	0,5	8,5	0,5	15,25	0,0035	0,9635
15	1	10	1	20,00	0,0024	0,9984
16	-1	4	-1	1,00	0,0048	0,9574
17	-0,5	5,5	-0,5	5,75	0,0090	0,9892
18	0	7	0	10,50	0,0029	0,9700
19	0,5	8,5	0,5	15,25	0,0046	0,9869
20	1	10	1	20,00	0,0017	0,9738
21	-1	4	-1	1,00	0,0142	0,9957
22	-0,5	5,5	-0,5	5,75	0,0051	0,9766
23	0	7	0	10,50	0,0056	0,9903
24	0,5	8,5	0,5	15,25	0,0039	0,9818
25	1	10	1	20,00	0,0019	0,9622

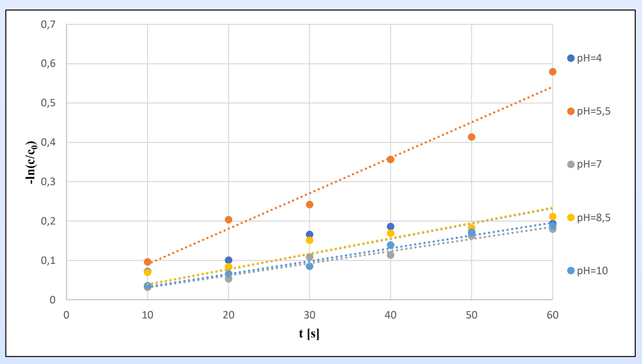


Figure 1. Determination of the first-order constants for the degradation of NTV in a treatment time of 60 with the UV-C/H_2O_2 process at *c*(NTV):*c*(H_2O_2)= 1:57.5, c_0 (NTV) = 0.1 mM

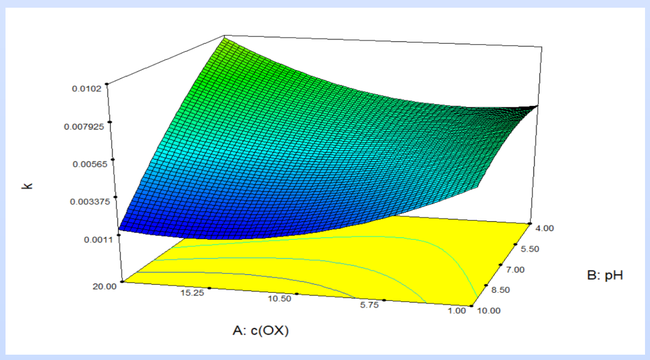


Figure 2. 3D diagram of the influence of pH value and H_2O_2 concentration on the rate of decomposition of the model pollutant NTV.

UV-C/$S_2O_8^{2-}$

Table 2. Full factorial design of the experiment with two independent variables expressed in coded and real values and calculated first-order NTV conversion values **UV-C/$S_2O_8^{2-}$**

EXPERIMENT	Variables				Conversion NTV UV-C/$S_2O_8^{2-}$	
	Variable 2, x_2		Variable 1, x_1			
	Cod	pH	Cod	c(OX) [mM]	k_{obs} [s^{-1}]	R_{LR}^2
1	-1	4	-1	1,00	0,0053	0,9735
2	-0,5	5,5	-0,5	5,75	0,0060	0,9928
3	0	7	0	10,50	0,0101	0,9928
4	0,5	8,5	0,5	15,25	0,0121	0,9811
5	1	10	1	20,00	0,0113	0,9922
6	-1	4	-1	1,00	0,0041	0,9610
7	-0,5	5,5	-0,5	5,75	0,0068	0,9897
8	0	7	0	10,50	0,0049	0,9421
9	0,5	8,5	0,5	15,25	0,0182	0,9497
10	1	10	1	20,00	0,0123	0,9820
11	-1	4	-1	1,00	0,0037	0,9911
12	-0,5	5,5	-0,5	5,75	0,0036	0,9773
13	0	7	0	10,50	0,0084	0,9907
14	0,5	8,5	0,5	15,25	0,0214	0,9916
15	1	10	1	20,00	0,0120	0,9944
16	-1	4	-1	1,00	0,0052	0,9973
17	-0,5	5,5	-0,5	5,75	0,0023	0,9972
18	0	7	0	10,50	0,0111	0,9916
19	0,5	8,5	0,5	15,25	0,0124	0,9843
20	1	10	1	20,00	0,0120	0,9755
21	-1	4	-1	1,00	0,0041	0,9757
22	-0,5	5,5	-0,5	5,75	0,0037	0,9901
23	0	7	0	10,50	0,0139	0,9501
24	0,5	8,5	0,5	15,25	0,0228	0,9490
25	1	10	1	20,00	0,0107	0,9888

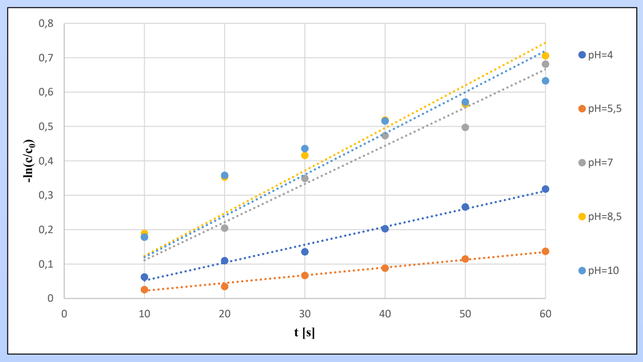


Figure 3. Determination of the first-order constants for the degradation of NTV in a treatment time of 60 with the UV-C/$S_2O_8^{2-}$ process at *c*(NTV):*c*(H_2O_2)= 1:57.5, c_0 (NTV) = 0.1 mM

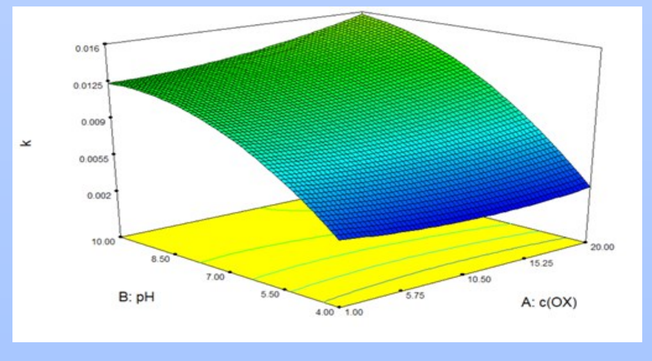


Figure 4. 3D diagram of the influence of pH value and $S_2O_8^{2-}$ concentration on the rate of decomposition of the model pollutant NTV.

CONCLUSION

The optimum treatment conditions were deduced by the response surface modeling. In both cases, degradation kinetics is dependent on both pollutant/oxidant ratio and pH.

The degradation of NTV by both investigated photooxidative processes obeyed first - order kinetics.

The highest degradation rate constant for the UV/ H_2O_2 process is achieved at the maximum concentration of H_2O_2 at pH = 4 which can be attributed to the greater sensitivity of the protonated form of NTV to attack by HO· radicals.

The highest degradation rate constant for the UV/ $S_2O_8^{2-}$ process is achieved at the maximum concentration of $S_2O_8^{2-}$ at pH = 10. In an alkaline medium, HO· radicals are generated that decompose NTV in combination with SO_4^{-}· radicals.

ACKNOWLEDGMENT

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