

Salicylic Acid Boosts the TiO₂ and ZnO-Mediated Photodegradation of Paracetamol

Matheus Ruffo Peres^a , Bruna Pastrello^a , Júlio Ricardo Sambrano^b , Nelson Henrique Morgon^c ,
Aguinaldo Robinson de Souza^a , Valdecir Farias Ximenes^{**} 

^aUniversidade Estadual de São Paulo, Faculdade de Ciências, Departamento de Química, 17033-360, Bauru, SP, Brasil.

^bUniversidade Estadual de São Paulo, Faculdade de Ciências, Departamento de Matemática, 17033-360, Bauru, SP, Brasil.

^cUniversidade de Campinas, Instituto de Química, Departamento de Físico-Química, 13083-861, Campinas, SP, Brasil.

Received: May 01, 2021; Accepted: June 16, 2021.

Titanium dioxide (TiO₂) and zinc oxide (ZnO) are among the most used catalysts in photodegradation. Paracetamol and salicylic acid are widely used as pharmaceutical drugs. We found that paracetamol is less susceptible to photodegradation compared to salicylic acid. From a chemical perspective, this was not expected since paracetamol is more vulnerable to chemical oxidation. Aiming the comprehension of this phenomenon, studies were performed comparing the efficiency of photodegradation of paracetamol versus salicylic acid and acetophenone versus 4-aminoacetophenone. The presence of amino/amide group decreased the efficiency of degradation significantly. It was also found that salicylic acid improved the degradation of paracetamol when both compounds were present in the reaction medium. The lower efficiency of photodegradation of the amino-based compounds seems to be related to the deactivation of the excited states of the TiO₂ and ZnO. Theoretical calculations at the TD-PBE0/6-311++G(3df,2p) high level were performed and corroborated our proposal.

Keywords: Photodegradation, Titanium Dioxide, Zinc Oxide, Paracetamol, Salicylic Acid.

1. Introduction

Photodegradation catalyzed by nanostructured semiconductors is an efficient and inexpensive methodology widely used to degrade chemicals and pharmaceuticals in aqueous medium¹⁻³. As such, this procedure has been extensively studied for wastewater treatment, aiming at the elimination of organic contaminants that cannot be removed from the environment via conventional wastewater treatment plants^{4,6}. The decomposition is provoked by intensive oxidation via reactive oxygen species (ROS) produced by the interaction of the photoexcited semiconductor with water. Among the ROS produced in the process, hydroxyl radical (HO•) has been argued as the most effective one, being responsible by hydrogen abstraction and/or direct electrophilic attack on aromatic moieties, which are usually present in the pollutants and pharmaceuticals⁷⁻¹³. After that, a cascade of oxidative reactions takes place leading to partial or total mineralization of the chemicals. The generation of HO• occurs by electron transfer from water or hydroxyl anion to the photogenerated hole (h⁺) in the semiconductor surface and the energy comes from radiation in the UV-Vis range, depending on the bandgap of the material¹⁴⁻¹⁶. In this concern, nanostructured titanium dioxide (TiO₂) and zinc oxide (ZnO), pure or doped, are among the most used catalysts in photodegradation studies^{1,6,16-18}. According, the literature

brings more than 65.000 papers in the last 5 years using the entries TiO₂ or ZnO and photodegradation (Web of Science).

Once HO• is one of the most powerful oxidants¹⁹, it can be supposed that any aromatic-based chemical is potentially susceptible to degradation when submitted to the aforementioned process. Also, it could be expected that as easily oxidizable is a chemical as efficient should be its degradation. However, this does not seem the case. Here, using the same experimental condition, we found that paracetamol was less susceptible to photodegradation compared to salicylic acid. Following the above rationalization, this behavior should not be expected since paracetamol is more susceptible to chemical oxidation than salicylic acid. The same behavior was observed by comparing acetophenone with 4-aminoacetophenone. From these findings, an explanation was proposed based on the deactivation of excited states of the semiconductors.

2. Materials and Methods

2.1. Chemicals

Salicylic acid, paracetamol, acetophenone, 4-aminoacetophenone, 2,2-diphenyl-1-picrylhydrazyl radical (DPPH), hydrogen peroxide (H₂O₂), titanium (IV) oxide (TiO₂, brookite, nanopowder 50-100 nm), titanium (IV) oxide (TiO₂, Aeroxide® P25, nanopowder 21 nm), zinc oxide (ZnO, wurtzite, nanopowder < 50 nm) and iron(II, III)

*email: valdecir.ximenes@unesp.br

oxide (Fe_3O_4 , nanopowder, 50-100 nm) were purchased from Sigma-Aldrich Chemical Co. (St. Louis, MO, USA). Stock solutions of the studied compounds (10 mmol L^{-1}) were prepared in ethyl alcohol.

2.2. Photodegradation studies

The reactions were performed on a magnetically stirred suspension (25 mL) containing the studied compounds ($100 \mu\text{mol L}^{-1}$) and the nanostructured metal oxides (10 mg) in ultrapure Milli-Q® water. The irradiations were performed using UVA or UVC lamps (model T5, potency 12 W, base G5, China). The temperature was controlled using a water circulation bath (25°C), and irradiation was carried out over the reactor. Aliquots of the suspension (1.5 mL) were removed at 30 min intervals and centrifuged at 4000 rpm for 10 min before UV-Vis spectrophotometry (Perkin Elmer Lambda 35 UV-visible spectrophotometer (Shelton, CT, USA) and/or high-performance liquid chromatography (HPLC) analysis (HPLC, Jasco, Tokyo, Japan). The concentrations of the studied compounds were evaluated by light absorption at wavelengths of maximum absorbance or peak area in the HPLC analysis, which were carried out under isocratic conditions on a Luna® C18 reversed-phase column (Phenomenex, $250 \times 4.6 \text{ mm}$, $5 \mu\text{m}$). The mobile phase was constituted by solvent (A) 0.1% aqueous formic acid and solvent (B) 0.1% formic acid in methanol. For salicylic acid, the mobile phase composition was 30:70 (A: B) and paracetamol 15:85 (A: B). The flow rate was 1 mL min^{-1} . The UV-Vis detector was set at 254 nm.

2.3. Degradation with $\text{H}_2\text{O}_2/h\nu$

Hydrogen peroxide (10 mmol L^{-1}) was incubated with the studied compounds ($100 \mu\text{mol L}^{-1}$) and submitted to UVC irradiation. Samples (1.5 mL) were removed at 30 min intervals and centrifuged at 4000 rpm for 10 min before UV-Vis analysis as described above.

2.4. DPPH scavenging assay

The ethanolic solution of DPPH ($100 \mu\text{mol L}^{-1}$) was incubated with increasing amounts of the studied compounds for 30 min in the dark. The scavenging activity was evaluated spectrophotometrically at 517 nm using the absorbance of unreacted DPPH radical as control and was calculated as follow: % Scavenging = $(A - B)/A \times 100$. A: absorbance of DPPH in the absence of the studied compounds; B: absorbance of DPPH in the presence of the studied compounds. From the analytical curve (% scavenging versus concentration of the studied compound), the effective concentration to reduced 50% of DPPH (EC50) was obtained²⁰.

2.5. Theoretical Studies

The calculations and structure optimization for ground states were performed at the density functional theory (DFT) levels at the PBE0 exchange and correlation functional along with the 6-311++G(2d,p) basis sets. Third-order Grimme's empirical dispersion correction (GD3) in combination with the Becke-Johnson dumping (BJ) and the continuum solvation model SMD (for implicit water solvent) were included in all calculations. Harmonic vibrational frequencies were calculated for ground states to ensure is

a stationary point (minimum or transition state). Normal mode analysis of the stationary point of the initial and final molecular structures provides only real frequencies. Single point energies were obtained at the PBE0/6-311++G(3df,2p). Singlet excitation energies from Time-Dependent Density Functional Theory (TD-PBE0/6-311++G(3df,2p)) were calculated for the first 15 excited electronic states at ground state molecular geometries (vertical process). All calculations were carried out using the Gaussian 16 program²¹. The electronic energies and optimized molecular geometries of all molecular systems are depicted in Supplementary Material (Tables S1 to S8).

The reactants and products were calculated at the ground state, considering the multiplicity duplet for the oxygen atoms on paracetamol and salicylic acid. The reaction energy barrier, ΔE , was obtained considering the difference between the energies of the reactants: the paracetamol (E1) and the salicylic acid radical (E2), and the energies of the products: the salicylic acid (E3) and paracetamol radical (E4) according to Equation 1.

$$\Delta E = (E1 + E2) - (E3 + E4) \quad (1)$$

The paracetamol molecule was considered as charge and multiplicity equal to zero and 1 (singlet) respectively, and the charge on the salicylic acid was set as equal to -1 due to the ionized nature of this molecule in the pH used in the experimental setup; the multiplicity of this molecule was equal to 1 (singlet). Both calculations were done in the ground state.

3. Results and Discussion

Considering that the anodic peak potential of salicylic acid ($E_{pa} = 0.94 \text{ V}$)²² is higher than the paracetamol ($E_{pa} = 0.77 \text{ V}$)²³, it should be expected, the last one as more susceptible, or at least, similar to salicylic acid when submitted to photodegradation. In fact, as well-established, the oxidability increase as the E_{pa} value decreases²³. However, an unexpected behavior was observed when these compounds were submitted to TiO_2 -mediated photodegradation. The results depicted in Figure 1 show that salicylic acid was degraded at least three-fold faster compared to paracetamol. For both drugs, the degradation profile suggests mineralization, as can be concluded by the UV-Vis spectra, which decreased without the appearance of new bands. The same conclusion can be reached by analyzing the solutions by liquid chromatography, where new peaks of intermediates were detected in the first measurements and degraded in the final process (Figure S1). In agreement, mineralization of salicylic acid and paracetamol has been described, and their mechanism of mineralization is initiated by the attack of photogenerated $\text{HO}\cdot$ on the target compounds^{24,25}.

Looking for an explanation for these findings, several experiments were performed by changing the variables in the photodegradation process. The first one was the light source. The theoretical concept was that by acting as a light filter, the dissolved drug could decrease the light penetration in the solution and, consequently, the photoexcitation in the TiO_2 surface. UVC has its emission below 280 nm and UVA in the range of 320-400 nm. Paracetamol has an absorption

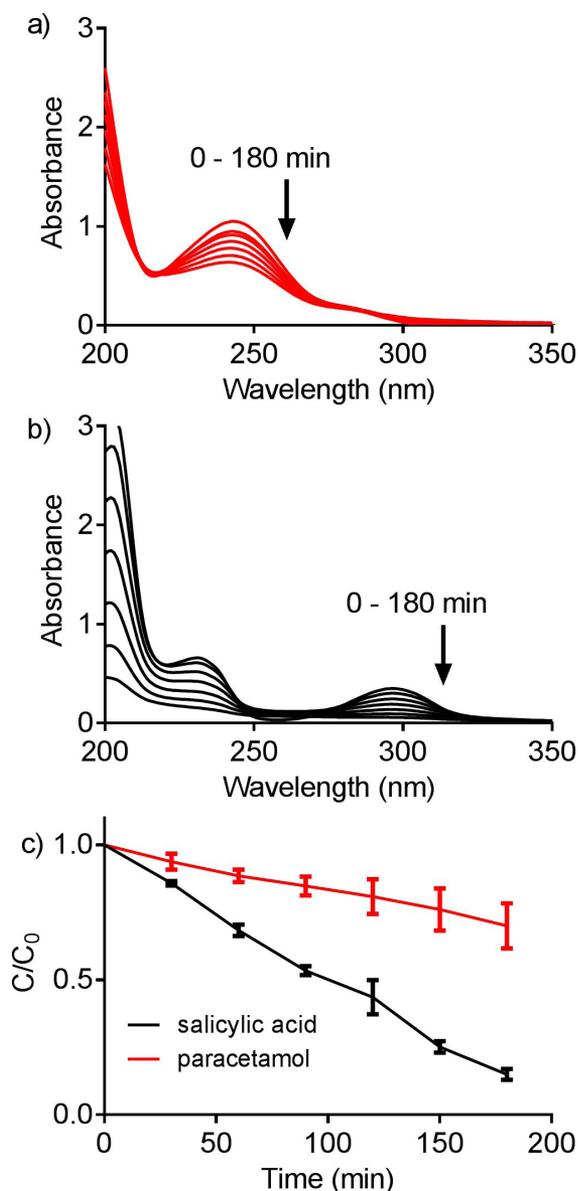


Figure 1. UVC-promoted degradation of (a) paracetamol (100 μmol L⁻¹) and (b) salicylic acid (100 μmol L⁻¹) catalyzed by TiO₂ (10 mg) in the aqueous medium (25 mL) at 25°C. The results (c) are expressed as means and SD of three experiments.

band centered at 240 nm, while salicylic acid absorbs at 295 nm (Figure 1). Therefore, if present and relevant, the light filter effect elicited by salicylic acid and paracetamol must be different for both light sources, and it could explain the results. However, irrespective of the light source (UVA or UVC), salicylic acid degradation was always higher than paracetamol (Figure S2). These results suggest the light filter effect was not responsible for the findings described here.

Another parameter studied was the constitution of the nanostructured material. In this case, TiO₂ P25, which was used throughout the study, was substituted by TiO₂ brookite (nanopowder, 50-100 nm), ZnO wurtzite (nanopowder, < 50 nm), and Fe₃O₄ (nanopowder, 50-100 nm). The results in Table 1 show that, independently of the catalyst, the lower

Table 1. Photodegradation of salicylic acid and paracetamol.

Catalyst	Degradation (μmol L ⁻¹) ^a	
	Salicylic acid	Paracetamol
TiO ₂ (P25)	81.2 ± 6.8	49.6 ± 4.6
	4.4 ± 1.5 ^b	2.5 ± 1.4 ^b
ZnO (wurtzite)	24.9 ± 2.1	12.5 ± 1.3
	0.9 ^b	0.1 ^b
TiO ₂ (brookite)	84.9 ± 2.0	29.7 ± 7.9
Fe ₃ O ₄	30.4 ± 1.0	15.2 ± 2.1

^a Degradation of the pharmaceuticals after 5 hours of UVC irradiation;

^b Without irradiation. The results are the means and SD of three experiments.

efficiency of degradation of paracetamol was always observed. In short, the higher efficiency of degradation of salicylic acid does not rely on the specific chemical, morphological, or crystalline features of the semiconductors. Experiments with TiO₂ and ZnO were also performed in the absence of light. How it can be seen, the consumptions were significantly lower, and the difference between salicylic acid and paracetamol was subtle (Table 1). These results suggest that a putative higher adsorption capacity for salicylic acid cannot be the main factor contributing to its higher degradation efficiency.

The next step was to investigate whether the difference in the efficiency of degradation could be related to the intrinsic chemical reactivity of salicylic acid and paracetamol. It is worth noting that the reactivity of aromatic compounds with HO•, a powerful oxidant, and electrophilic species, increases in the presence of hydroxyl substituents, i.e., electron-donor groups, which are present in salicylic acid and paracetamol. On the other hand, electron-withdrawing groups decrease reactivity^{19,26,27}. In our study, the carboxylate group in salicylic acid is a strong electron-withdrawing group, and the amide in paracetamol, a moderated one. In short, from these well-established chemical features, it could be supposed that paracetamol should be more susceptible to oxidation mediated by HO•, or at least, similar to salicylic acid. This conclusion is also consistent with the lower Epa value (0.77 V) of paracetamol compared to salicylic acid (0.93 V). Indeed, the oxidizability of phenolic compounds increases as their anodic peak potential decreases^{22,23,28}. To evaluate this chemical feature, the reactivity of the studied compounds was tested regarding their efficacy as reducing agents in the DPPH scavenging assay. DPPH is a stable free radical, and its reduction is related to the oxidability of the studied compounds²⁰. The results depicted in Figure 2a confirmed our expectation since 91 μM of paracetamol scavenged 50% of DPPH (EC₅₀), while salicylic acid at 300 μM did not reach the 50% reduction. In short, these results are consistent with the higher oxidability of paracetamol compared to salicylic acid. Therefore, the results obtained by photodegradation are not compatible with the expected oxidability of salicylic acid and paracetamol.

The photodegradation of chemicals and pharmaceuticals mediated by nanostructured metal oxide semiconductors relies on the generation of HO• through water oxidation at the material surface⁷⁻¹³. Aiming to compare the reactivity of salicylic acid and paracetamol with HO• in the absence of the semiconductors, the degradation of the compounds was evaluated using H₂O₂/hv as a source of HO•. This approach is based on the homolytic cleavage of the peroxide bond of

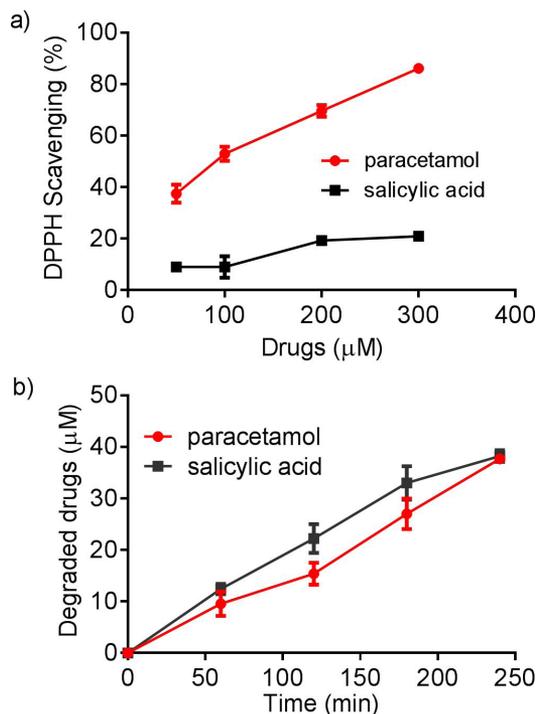


Figure 2. Oxidability of the salicylic acid and paracetamol evaluated by (a) DPPH scavenging and (b) reactivity with HO• generated by H₂O₂/hv in the absence of nanostructured semiconductors. The results (c) are expressed as means and SD of three experiments.

H₂O₂^{29,30}. Figure 2b shows that using H₂O₂/hv as a source of HO•, both salicylic acid and paracetamol were efficiently degraded, and no significant difference was observed. From these results, it can be concluded that the lower efficacy in the photodegradation of paracetamol in the presence of nanostructured materials cannot be explained by its oxidability and/or reactivity with HO•. Therefore, the putative explanation must rely on the process of photoexcitation.

Aiming to comprehend the unexpected behavior of paracetamol, i.e., the lower reactivity compared to salicylic acid by photodegradation, additional experiments were performed with both pharmaceuticals in the same solution. In other words, in this experimental approach, the compounds should compete by the photogenerated HO•. The results were totally unexpected since an inversion in the reactivity of the pharmaceuticals was observed. As depicted in Figure 3a, the presence of salicylic acid increased the efficiency of paracetamol degradation. On the other hand, the degradation of salicylic acid itself was reduced by the presence of paracetamol (Figure 3b). It is worthy of note that to avoid bias due to spectra superposition, the consumption of salicylic acid and paracetamol were measured by liquid chromatography (Figure S3).

The increased reactivity of paracetamol in the presence of salicylic acid suggested an interaction between these molecules during photodegradation. To understand this interaction, additional experiments were performed increasing the concentration of salicylic acid (0–200 µmol L⁻¹) and

keeping constant paracetamol (100 µmol L⁻¹). Figure 3c confirmed our expectation since the efficiency of paracetamol degradation was dependent on salicylic acid concentration.

The results depicted in Figure 3 suggest that salicylic acid boosted the degradation of paracetamol. This effect of salicylic acid was not only observed using TiO₂. The same behavior was obtained using ZnO. In this case, after 8 h, the degradation of paracetamol was 33.4 µmol L⁻¹ in the absence and 47.1 µmol L⁻¹ in the presence of salicylic acid. On the other hand, the degradation of salicylic acid decreased from 50.4 µmol L⁻¹ in the absence to 21.1 µmol L⁻¹ in the presence of paracetamol (Figure S4). In short, the boosting effect of salicylic acid on paracetamol degradation is not dependent on the semiconductor. To clarify these findings, the paracetamol's oxidation was also performed using H₂O₂/UVC as a source of HO• in the presence and absence of salicylic acid. The results depicted in Figure S5 confirmed the expectation since the addition of salicylic acid in the reaction medium also promoted increased oxidation of paracetamol.

Aiming an explanation for the experimental findings, the following points are summarized:

- i) The lower reactivity of paracetamol was not related to its chemical properties, i.e., general oxidability and specific reactivity with HO•;
- ii) Considering that the phenomenon was observed in different nanostructured oxides (TiO₂, ZnO, and Fe₃O₄) and that the adsorptions of salicylic acid and paracetamol were not significantly different; surface phenomena does not explain the findings;
- iii) Salicylic acid boosted the degradation of paracetamol, and its consumption was decreased. It is essential to emphasize that, alone, salicylic acid was more susceptible to degradation.

From these findings, it can be proposed that the lower efficacy in paracetamol degradation might be related to a decreased photoexcitation efficiency when this drug was present in the medium. A putative explanation is the quenching of the excited state of the semiconductors by paracetamol. Pursuing this proposal, the energetic feasibility of energy transfer from 1st electronic excited state TiO₂, ZnO, and Fe₃O₄ to paracetamol and salicylic acid were calculated and compared. How it can be seen, the energy transfer from the excited TiO₂ to paracetamol would be an exothermic process (-16.94 kJ/mol) (Equation 2). Oppositely, the energy transfer to salicylic acid would be unfavorable (14.24 kJ/mol) (Equation 3). In short, paracetamol interaction with excited TiO₂ could promote its deactivation and, consequently, decrease photodegradation efficiency. The same tendency was obtained for ZnO and Fe₃O₄. In these cases, both salicylic acid and paracetamol would lead to exothermic photophysical processes, but the interactions with paracetamol were still more favorable. Eqs 2–13 show the energetic profile for the interactions among the studied compounds and the excited state of the semiconductors. In these equations, PCT (paracetamol), SAA (salicylic acid), ACP (acetophenone), and AACP (4-aminoacetophenone).



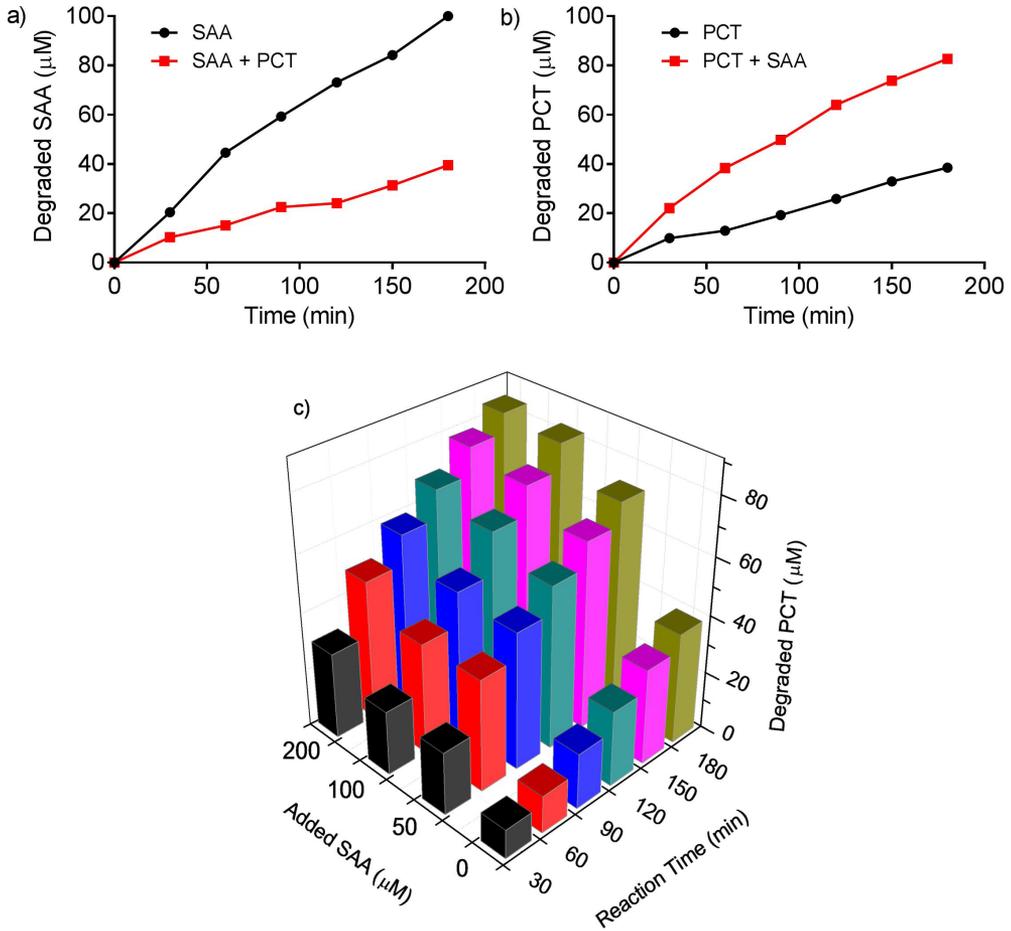
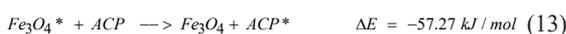
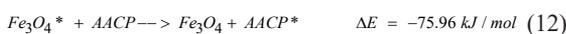
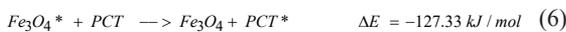


Figure 3. Simultaneous TiO₂-mediated photodegradation of salicylic acid (SAA) and paracetamol (PCT). (a) Photodegradation of SAA in the absence (black line) and presence (red line) of PCT. (b) Photodegradation of PCT in the absence (black line) and presence of SAA (red line). (c) Photodegradation of PCT in the presence of an increasing concentration of SAA. Reactions catalyzed by TiO₂ (10 mg) in the aqueous medium (25 mL) at 25°C.



This proposal could also explain the boosting effect of salicylic acid on paracetamol degradation. By competing with paracetamol, salicylic acid would decrease the deactivation of excited semiconductors by paracetamol. Indeed, as we have demonstrated, the effect of salicylic acid on paracetamol degradation was concentration-dependent (Figure 3c), which is consistent with the interaction between these molecules.

As we also demonstrated, the increased degradation of paracetamol was also accompanied by a decrease in salicylic acid degradation. Hence, an energetically feasible reaction must take place between these species. This proposal was theoretically evaluated by the simulation of the reaction between salicylic acid free radical, a presumed initial species generated during photodegradation, with paracetamol. The computer simulation was performed at the DFT level of theory using the B3LYP hybrid functional and the 6-311+G(3df,2p) basis set. The computational model of the reactants consisted of paracetamol plus salicylic acid molecules calculated at the same time with charge and multiplicity equal to zero and two (duplet), respectively. The same methodology was used for the optimization of the products. The duplet was assigned due to the unpaired electron located at the oxygen

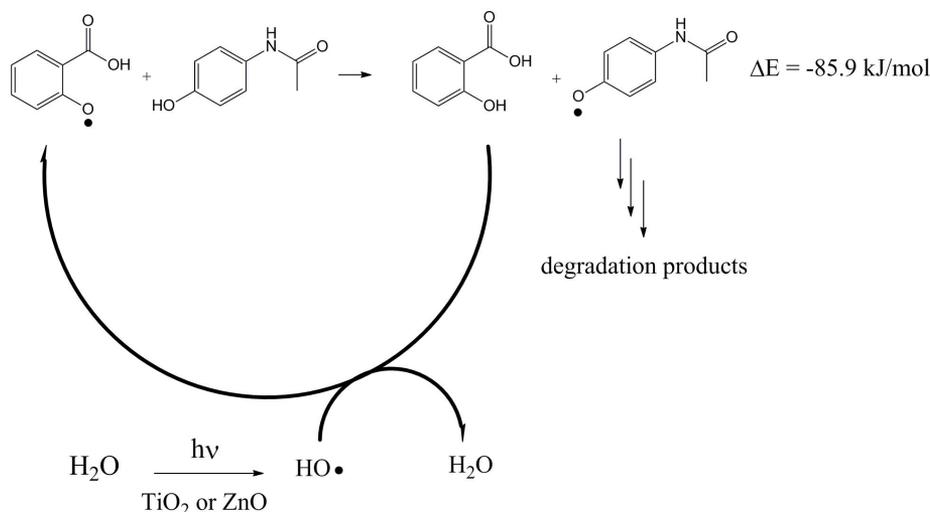


Figure 4. Proposal for the booster effect of salicylic acid on TiO₂ or ZnO-catalysed photodegradation of paracetamol. The energies were: salicylic acid radical + paracetamol (-1011.33559685 Hartree); salicylic acid + paracetamol radical = -1011.36832184 Hartree). $\Delta E = -0.032725$ Hartree (-1.426728x10⁻²² kJ; -85.94 kJ/mol).

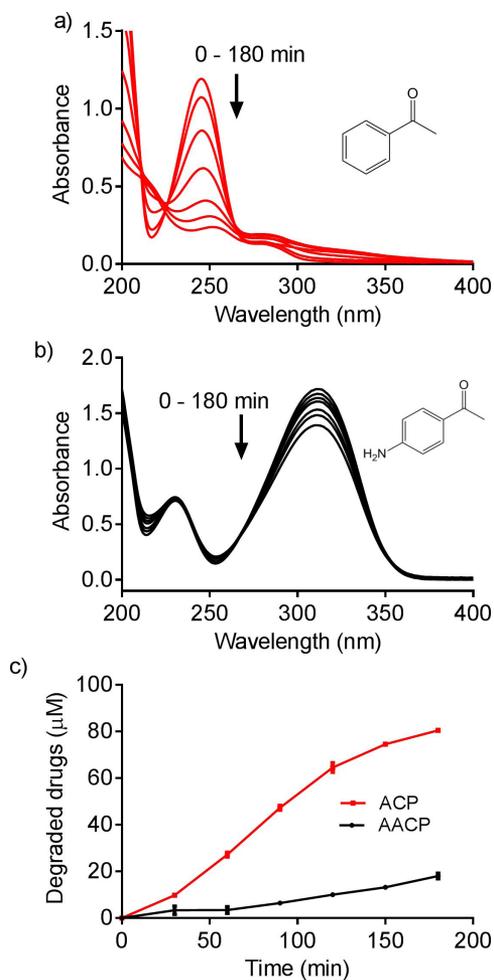


Figure 5. UVC-promoted degradation of (a) acetophenone (ACP, 100 μmol L⁻¹) and (b) 4-aminoacetophenone (AACP, 100 μmol L⁻¹) catalyzed by ZnO (10 mg) in aqueous medium (25 mL) at 25°C. The results (c) are expressed as means and standard deviations of three experiments.

atom of salicylic acid under the reactant side and in the oxygen atom of the paracetamol on the product side. How it can be observed, the reaction is energetically possible and could explain the boosting effect of salicylic acid (Figure 4).

The previous results raised the possibility that the amino/amide groups could be responsible for the low reactivity of paracetamol compared to salicylic acid. Thus, seeking additional evidence, comparative studies were performed with the compounds acetophenone versus 4-aminoacetophenone. Acetophenone is a pollutant, and studies about its photodegradation have been reported^{11,31,32}. On the other hand, 4-aminoacetophenone was never studied in this context, but the presence of the amino group makes this compound more susceptible to oxidation and electrophilic attack^{19,26}. Therefore, it should be expected 4-aminoacetophenone as more reactive, or at least similar to benzophenone. Indeed, the presence of the amino group in aromatic compounds increased, at least two-order of magnitude, the reaction rate constant with HO• in chemical studies³³. However, here, in the presence of nanostructured oxides, the results were the opposite. How it can be seen, the presence of the amino group provoked a decrease in the efficiency of degradation for both ZnO (Figure 5) and TiO₂ (Figure S6). Corroborant with thermodynamic calculations for paracetamol versus salicylic acid (Equations 8-13), 4-aminoacetophenone would be more efficient in deactivating the excited states of the semiconductors than acetophenone.

4. Conclusions

As far as we know, this is the first demonstration of a reaction between two drugs during the photodegradation process mediated by nanostructured semiconductor oxides. It was demonstrated that salicylic acid could increase the degradation of paracetamol and, consequently, be partially recycled. It was also shown that the presence of the amino/amide group in the studied molecules was responsible for the lower susceptibility to degradation, as

demonstrated to paracetamol and 4-aminoacetophenone. The computational studies indicated that the deactivation of the excited state of the semiconductors by paracetamol and 4-aminoacetophenone could explain the lower reactivity of these molecules. In conclusion, this study opens new concepts regarding the chemical features of molecules subjected to photodegradation. These findings can be considered in photodegradation studies and their application to eliminate pharmaceuticals and chemicals of wastewaters.

5. Acknowledgments

This study was financed by the National Council for Scientific and Technological Development (CNPq, grant numbers #303485/2019-1, #152519/2019-0, #305541/2017-0, #302769/2018-8 and #152519/2019-0); National Institute of Science and Technology (INCT-BioNat, grant number #465637/2014-0); State of Sao Paulo Research Foundation (FAPESP, grant numbers #2016/20549-5 and 2019/18445-5). This study was financed in part by the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior - Brasil (CAPES) - Finance Code 001.

6. References

- Basavarajappa PS, Patil SB, Ganganagappa N, Reddy KR, Raghu AV, Reddy CV. Recent progress in metal-doped TiO₂, non-metal doped/codoped TiO₂ and TiO₂ nanostructured hybrids for enhanced photocatalysis. *Int J Hydrogen Energy*. 2020;45(13):7764-78.
- Katal R, Masudy-Panah S, Tanhaei M, Farahani MHDA, Jiangyong H. A review on the synthesis of the various types of anatase TiO₂ facets and their applications for photocatalysis. *Chem Eng J*. 2020;384:123384.
- Hu X, Hu X, Peng Q, Zhou L, Tan X, Jiang L, et al. Mechanisms underlying the photocatalytic degradation pathway of ciprofloxacin with heterogeneous TiO₂. *Chem Eng J*. 2020;380:122366.
- Trawiński J, Skibiński R. Studies on photodegradation process of psychotropic drugs: a review. *Environ Sci Pollut Res Int*. 2017;24(2):1152-99.
- Bartolomeu M, Neves MGPMS, Faustino MAF, Almeida A. Wastewater chemical contaminants: remediation by advanced oxidation processes. *Photochem Photobiol Sci*. 2018;17(11):1573-98.
- Tong A, Braund R, Warren D, Peake B. TiO₂-assisted photodegradation of pharmaceuticals: a review. *Open Chem*. 2012;10(4):989-1027.
- Qu R, Li C, Liu J, Xiao R, Pan X, Zeng X, et al. Hydroxyl radical based photocatalytic degradation of halogenated organic contaminants and paraffin on silica gel. *Environ Sci Technol*. 2018;52(13):7220-9. <http://dx.doi.org/10.1021/acs.est.8b00499>.
- Melchor-Lagar V, Ramos-Ramírez E, Morales-Pérez A-A, Rangel-Vázquez I, Del Angel G. Photocatalytic removal of 4-chlorophenol present in water using ZrO₂/LDH under UV light source. *J Photochem Photobiol Chem*. 2020;389:112251. <http://dx.doi.org/10.1016/j.jphotochem.2019.112251>.
- Jung S-C, Bang H-J, Lee H, Kim H, Ha H-H, Yu YH, et al. Degradation behaviors of naproxen by a hybrid TiO₂ photocatalyst system with process components. *Sci Total Environ*. 2020;708:135216. <http://dx.doi.org/10.1016/j.scitotenv.2019.135216>.
- Romeiro A, Azenha ME, Canle M, Rodrigues VHN, Da Silva JP, Burrows HD. Titanium dioxide nanoparticle photocatalysed degradation of ibuprofen and naproxen in water: competing hydroxyl radical attack and oxidative decarboxylation by semiconductor holes. *ChemistrySelect*. 2018;3(39):10915-24. <http://dx.doi.org/10.1002/slct.201801953>.
- Spazzini FCR, Ximenes TP, Ximenes VF. TiO₂-catalyzed photodegradation of aromatic compounds: relevance of susceptibility to oxidation and electrophilic attack by hydroxyl radical. *J Nanopart Res*. 2018;20(12):326. <http://dx.doi.org/10.1007/s11051-018-4433-x>.
- Rayaroth MP, Aravind UK, Aravindakumar CT. Photocatalytic degradation of lignocaine in aqueous suspension of TiO₂ nanoparticles: mechanism of degradation and mineralization. *J Environ Chem Eng*. 2018;6(3):3556-64. <http://dx.doi.org/10.1016/j.jece.2017.10.050>.
- Gao R, Stark J, Bahnemann DW, Rabani J. Quantum yields of hydroxyl radicals in illuminated TiO₂ nanocrystallite layers. *J Photochem Photobiol Chem*. 2002;148(1-3):387-91. [http://dx.doi.org/10.1016/S1010-6030\(02\)00066-7](http://dx.doi.org/10.1016/S1010-6030(02)00066-7).
- Awfa D, Ateia M, Fujii M, Johnson MS, Yoshimura C. Photodegradation of pharmaceuticals and personal care products in water treatment using carbonaceous-TiO₂ composites: a critical review of recent literature. *Water Res*. 2018;142:26-45. <http://dx.doi.org/10.1016/j.watres.2018.05.036>.
- Grabowska E, Reszeczyńska J, Zaleska A. RETRACTED: mechanism of phenol photodegradation in the presence of pure and modified-TiO₂: a review. *Water Res*. 2012;46(17):5453-71. <http://dx.doi.org/10.1016/j.watres.2012.07.048>.
- He H-Y, Chen P. Recent advances in property enhancement of nano TiO₂ in photodegradation of organic pollutants. *Chem Eng Commun*. 2012;199(12):543-1574. <http://dx.doi.org/10.1080/00986445.2012.684415>.
- Ong CB, Ng LY, Mohammad AW. A review of ZnO nanoparticles as solar photocatalysts: synthesis, mechanisms and applications. *Renew Sustain Energy Rev*. 2018;81:536-51. <http://dx.doi.org/10.1016/j.rser.2017.08.020>.
- Katal R, Farahani MHDA, Masudy-Panah S, Ong SL, Hu J. Polypyrrole- and polyaniline-supported TiO₂ for removal of pollutants from water. *J Environ Eng Sci*. 2019;14(2):67-89. <http://dx.doi.org/10.1680/jenes.18.00003>.
- Cheng M, Zeng G, Huang D, Lai C, Xu P, Zhang C, et al. Hydroxyl radicals based advanced oxidation processes (AOPs) for remediation of soils contaminated with organic compounds: a review. *Chem Eng J*. 2016;284:582-98. <http://dx.doi.org/10.1016/j.cej.2015.09.001>.
- Wolf VG, Bonacorsi C, Raddi MSG, Fonseca LM, Ximenes VF. Octyl gallate, a food additive with potential beneficial properties to treat helicobacter pylori infection. *Food Funct*. 2017;8(7):2500-11. <http://dx.doi.org/10.1039/C7FO00707H>.
- Frisch MJ, Trucks GW, Schlegel HB, Scuseria GE, Robb MA, Cheeseman JR, et al. Wallingford: Gaussian, Inc.; 2016.
- Simić A, Manojlović D, Šegan D, Todorović M. Electrochemical behavior and antioxidant and prooxidant activity of natural phenolics. *Molecules*. 2007;12(10):2327-40. <http://dx.doi.org/10.3390/12102327>.
- Skeika T, de Faria MF, Nagata N, Pessoa CA. Simultaneous voltammetric determination of dypirone and paracetamol with carbon paste electrode and multivariate calibration methodology. *J Braz Chem Soc*. 2008;19(4):762-8. <http://dx.doi.org/10.1590/S0103-50532008000400021>.
- Mills A, Holland CE, Davies RH, Worsley D. Photomineralization of salicylic acid: a kinetic study. *J Photochem Photobiol Chem*. 1994;83(3):257-63. [http://dx.doi.org/10.1016/1010-6030\(94\)03825-2](http://dx.doi.org/10.1016/1010-6030(94)03825-2).
- Rimoldi L, Meroni D, Falletta E, Ferretti AM, Gervasini A, Cappelletti G, et al. The role played by different TiO₂ features on the photocatalytic degradation of paracetamol. *Appl Surf Sci*. 2017;424:198-205. <http://dx.doi.org/10.1016/j.apsusc.2017.03.033>.
- Chen Z, Yu X, Huang X, Zhang S. Prediction of reaction rate constants of hydroxyl radical with organic compounds. *J Chil Chem Soc*. 2014;59(1):2252-9. <http://dx.doi.org/10.4067/S0717-97072014000100003>.

27. Anbar M, Meyerstein D, Neta P. The reactivity of aromatic compounds toward hydroxyl radicals. *J Phys Chem.* 1966;70(8):2660-2. <http://dx.doi.org/10.1021/j100880a034>.
28. Paracatu LC, De Faria CMQG, Zeraik ML, et al. Hydrophobicity and antioxidant activity acting together for the beneficial health properties of nordihydroguaiaretic acid. *Food Funct.* 2015;6(6):1818-31. <http://dx.doi.org/10.1039/C5FO00091B>.
29. de Araujo LG, Oscar Conte L, Violeta Schenone A, Alfano OM, Teixeira ACSC. Degradation of bisphenol A by the UV/H₂O₂ process: a kinetic study. *Environ Sci Pollut Res Int.* 2020;27(7):7299-308. <http://dx.doi.org/10.1007/s11356-019-07361-7>.
30. Zhu H, Jia R, Sun S, Feng G, Wang M, Zhao Q, et al. Elimination of trichloroanisoles by UV/H₂O₂: kinetics, degradation mechanism, water matrix effects and toxicity assessment. *Chemosphere.* 2019;230:258-67. <http://dx.doi.org/10.1016/j.chemosphere.2019.05.052>.
31. Tayade RJ, Bajaj HC, Jasra RV. Photocatalytic removal of organic contaminants from water exploiting tuned bandgap photocatalysts. *Desalination.* 2011;275(1-3):160-5. <http://dx.doi.org/10.1016/j.desal.2011.02.047>.
32. Soltan S, Jafari H, Afshar S, Zabihi O. Enhancement of photocatalytic degradation of furfural and acetophenone in water media using nano-TiO₂-SiO₂ deposited on cementitious materials. *Water Sci Technol.* 2016;74(7):1689-97. <http://dx.doi.org/10.2166/wst.2016.343>.
33. Atkinson R. A structure-activity relationship for the estimation of rate constants for the gas-phase reactions of OH radicals with organic compounds. *Int J Chem Kinet.* 1987;19(9):799-828. <http://dx.doi.org/10.1002/kin.550190903>.

Supplementary material

The following online material is available for this article:

Table S1 - Cartesian Coordinates (in Å) of ACP obtained at [PBE0/6-311++G(2df,p) + GD3BJ] level of theory in water solvent using SMD model.

Table S2 - Cartesian Coordinates (in Å) of AACP obtained at [PBE0/6-311++G(2df,p) + GD3BJ] level of theory in water solvent using SMD model.

Table S3 - Cartesian Coordinates (in Å) of SAA obtained at [PBE0/6-311++G(2df,p) + GD3BJ] level of theory in water solvent using SMD model.

Table S4 - Cartesian Coordinates (in Å) of PCT obtained at [PBE0/6-311++G(2df,p) + GD3BJ] level of theory in water solvent using SMD model.

Table S5 - Cartesian Coordinates (in Å) of TiO₂ obtained at [PBE0/6-311++G(2df,p) + GD3BJ] level of theory in water solvent using SMD model.

Table S6 - Cartesian Coordinates (in Å) of ZnO obtained at [PBE0/6-311++G(2df,p) + GD3BJ] level of theory in water solvent using SMD model.

Table S7 - Cartesian Coordinates (in Å) of Fe₃O₄ (singlet electronic state) obtained at [PBE0/6-311++G(2df,p) + GD3BJ] level of theory in water solvent using SMD model.

Table S8 - Electronic energies (in Hartree) of all molecular systems obtained at [PBE0/6-311++G(2df,2p) + GD3BJ] level of theory in water solvent using SMD model.

Figure S1 - HPLC analysis of the degradation of salicylic acid and paracetamol. UVC-promoted degradation of (a) salicylic acid (100 µmol L⁻¹) and (b) paracetamol (100 µmol L⁻¹) catalyzed by TiO₂ (10 mg) in the aqueous medium (25 mL) at 25°C. See the Material and Methods section for details of the liquid chromatography experimental conditions.

Figure S2 - UVC versus UVA as light sources for degradation of salicylic acid (SAA) and paracetamol (PCT). Paracetamol (100 µmol L⁻¹) and salicylic acid (100 µmol L⁻¹) catalyzed by TiO₂ (10 mg) in the aqueous medium (25 mL) at 25°C.

Figure S3 - HPLC analysis of simultaneous degradation of salicylic acid and paracetamol. (a) Study of the degradation of salicylic acid (alone). (b) Analysis of the degradation of salicylic acid in the presence of paracetamol. (c) Analysis of the degradation of paracetamol (alone). (d) Analysis of the degradation of paracetamol in the presence of salicylic acid. Paracetamol (100 µmol L⁻¹) and salicylic acid (100 µmol L⁻¹) catalyzed by TiO₂ (10 mg) in the aqueous medium (25 mL) at 25°C.

Figure S4 - Simultaneous ZnO-mediated photodegradation of paracetamol (PCT) and salicylic acid (SAA). (a) Photodegradation of PCT in the absence (black line) and presence (red line) of SAA. (b) Photodegradation of SAA in the absence (black line) and presence of PCT (red line). Reactions catalyzed by ZnO (10 mg) in the aqueous medium (25 mL) at 25°C.

Figure S5 - Degradation of paracetamol (PCT) by HO• generated by H₂O₂/hv in the absence of nanostructured semiconductors. The reactions were conducted in the absence and presence of salicylic acid (SAA).

Figure S6 - UVC-promoted degradation of acetophenone (ACP, 100 µmol L⁻¹) and 4-aminoacetophenone (AACP, 100 µmol L⁻¹) catalyzed by TiO₂ (10 mg) in the aqueous medium (25 mL) at 25°C. The results are expressed as means and SD of two experiments.