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Virtual Screening of Fluorescent Heterocyclic Molecules and Advanced Oxidation Degradation of Rhodamine B in Synthetic Solutions

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Abstract: A virtual screening, a process based on computational chemistry that involves the rapid evaluation of a large number of compounds to identify those with the most promising characteristics, is presented. This screening found concordance in the fluorescent heterocyclic compounds with isosteres of similar reactivity, determining that rhodamine B (RhB) meets the necessary criteria for its use. Furthermore, with the values calculated *in silico*, it is considered to be a compound with low adsorption and oral bioavailability, so its degradation was evaluated by advanced oxidation processes (POAs), such as the catalytic process with titanium dioxide (TiO₂), hydrogen peroxide (H₂O₂), and presence or absence of dissolved oxygen (O₂), in which the concentration of RhB and amount of TiO₂ were varied, and the photo-Fenton process with an ultraviolet light emitting diode (UV-LED), zero-valent iron (ZVI) and H₂O₂, in which the amount of ZVI and H₂O₂ were varied. The results indicate that the catalytic process achieves a removal of 95.11% compared to 80.42% in the photo-Fenton process, concluding that the greater the amount of ZVI in the solution, the greater the degradation of RhB and that the residual amount of iron (II) (Fe²⁺) ions in the solution is less than 0.3 mg/L without causing secondary contamination. These results highlight the efficacy and feasibility of POAs for the removal of dyes such as RhB, which offers a promising solution for the remediation of contaminated waters.

Keywords: virtual screening; titanium dioxide; zero-valent iron; rhodamine B



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1. Introduction

The demand for freshwater has increased at a rate of 64 km³/year since 1965 [1] and is projected to reach 5890 km³/year by 2050 [2]. Consequently, the quantity of generated wastewater has also increased (approximately 411 km³/year) [3]. Industrial effluents represent one sewage category, distinguished by diverse contaminants such as macro-contaminants, heavy metals, emerging contaminants, dyes, and others [4].

The textile industry is particularly concerning in environmental matters, not only due to its high-water consumption (around 1,608,800 m³ of water/day) but also because it accounts for approximately 7% of the global consumption of synthetic dyes [5,6]. However, the real problem lies in the poor quality of discharged water, leading to several environmental contamination cases. Indeed, dyeing and finishing processes in textiles represent between 17% and 20% of industrial water contamination [6]. Textile wastewater contains organic contaminants such as dyes, surfactants, and phenols and inorganics such as heavy metals [7]. Dyes, primarily water-soluble organic molecules that impart color, rank among the most environmentally harmful substances, with RhB a notable example. RhB, also known as *N*-[9-(ortho-carboxyphenyl)-6-(diethylamino)-3H-xanthen-3-ylidene] diethylammonium chloride Chemistry Abstract Service (CAS) 81-88-9, is a vibrant red

organic dye extensively utilized in industries such as textiles, paper, plastics, printing, biomedicine, and leather. Its versatile applications include functioning as a coloring agent, photosensitizer, water tracer, and fluorescent marker [8]. RhB is a hydro-soluble cationic dye (50 g/L at 20 °C) with high coloring efficiency and low cost. Consequently, wastewater contains this contaminant at concentrations of approximately 1.0 mg/L [5,8]. Despite its low concentrations, RhB remains noticeable in the environment due to its strong coloring ability. Furthermore, it exhibits high resistance to biological and chemical degradation due to its complex, stable molecular structure with strong bonds and high oxidation resistance, posing health risks to humans and animals ($LC_{50} = 14$ mg/L, $EC_{50} = 24$ mg/L, $NOAEL = 1$ mg/kg/d) [5,9]. Additionally, its toxicity has led to irritation in the respiratory tract, skin, and eyes, and it has even been considered carcinogenic and mutagenic [8,10]. Moreover, by preventing sunlight penetration into deep waters, RhB directly affects photosynthesis and respiration processes [11]. Therefore, there is an escalating need to discover effective methods for removing RhB and other molecules with similar structural or behavioral characteristics.

In this context, computational screening emerges as a valuable and promising tool to identify molecules, evaluate their electronic behavior and affinity compared to reference compounds, assess their toxicity, and determine effective removal processes [5]. While these technological tools are helpful for their results, optimizing contaminant removal processes for real-world applications is necessary.

For the removal of dyes such as RhB, various techniques are employed, including adsorption (utilizing activated carbon, nanomaterials, and biomass), sedimentation, coagulation-flocculation, ozonation, ion exchange, and filtration (filters and membranes) [5,12,13]. However, many of these methods and technologies incur high costs due to energy consumption and produce toxic byproducts or solid waste [13]. Advanced Oxidation Processes (AOPs) present a more efficient alternative for dye removal. AOPs, encompassing methods such as photocatalysis, ozonation, and Fenton reactions, offer significant advantages over conventional techniques [11]. They can degrade a broad spectrum of organic pollutants, including recalcitrant compounds, into less harmful or fully mineralized forms. Furthermore, AOPs can often be applied under mild conditions and potentially achieve higher removal efficiencies without generating secondary pollution [12]. AOPs rely on forming hydroxyl radicals ($OH\cdot$) to oxidize and degrade organic pollutants. Some AOPs utilize photochemical media, such as UV radiation from UV lamps or sunlight. Among the best-known AOPs are homogeneous and heterogeneous photocatalysis, ozonation, and electrochemical oxidation [14]. Nevertheless, they have some disadvantages, such as high costs and the generation of more toxic by-products. Meanwhile, catalytic oxidation using TiO_2 as a catalyst and H_2O_2 as an oxidant offers greater selectivity and efficiency, achieving complete mineralization of the dye. It also allows for easy recovery and recycling of the catalyst, thereby reducing treatment costs [15]. In contrast, the photo-Fenton process is a lower-cost alternative. In this process, ZVI oxidation occurs in the presence of hydroxyl radicals generated by the decomposition of hydrogen peroxide under UV-LED light. The photo-Fenton process uses relatively tiny lamp sizes with a more than 50,000 h lifespan, serving as a constant energy source. Additionally, the efficiency of this process is not affected by atmospheric conditions such as excessive heat, humidity, or fog, unlike solar light [14]. Considering the importance of removing RhB and other similar molecules from wastewater, the present work aimed to develop a preliminary hypothesis-driven computational framework to establish “gold standard” electronic behavior patterns among libraries of rhodamine-like compounds. This framework will enable the identification and characterization of molecules with high structural similarity, thereby facilitating more detailed in situ studies. Moreover, experimental studies were conducted to evaluate the effectiveness of two types of AOPs in degrading RhB from synthetic solutions: catalytic oxidation with TiO_2 (without light) and H_2O_2 and the photo-Fenton process with UV-LED light, H_2O_2 , and ZVI.

2. Materials and Methods

2.1. Virtual Screening

A series of computational filters were applied based on Structure-Activity Relationship (SAR) analysis. This process involved two-dimensional comparisons and an evaluation of the electronic behavior of fluorescent molecules, leading to the identification of the standard base structure, referred to as the initial computational hypothesis.

2.1.1. Compilation of a Molecule Library

A comprehensive review of current research was conducted to compile a list of fluorescent heterocyclic molecules. Based on their chemical structures, these molecules were organized into a library of initial and derivative molecules [16–18].

2.1.2. Search and Reporting of Similar Molecules

The base structure of the most representative molecule was input into the SwissADME platform from the Swiss Institute of Bioinformatics, available at <http://www.swissadme.ch/> (accessed on 28 June 2024). Spectrophotometric methods were then employed to develop a second computational hypothesis [19,20].

2.1.3. Toxicity Analysis of the Computational Hypothesis

The Absorption, Distribution, Metabolism, Excretion, and Toxicity (ADME-Tox) predictive platform, available at <https://preadmet.qsarhub.com/toxicity/> (accessed on 28 June 2024), was used for toxicity analysis. The MOLFILE file extension generated the online structure from the exported initial file. Before starting the simulation, the positive formal charge on the nitrogen atom must be considered. The reported values will indicate whether the standard substance is toxic, mutagenic, poses a medium risk, or is harmless [21,22].

2.1.4. 2D and 3D Description of the Pattern and Its Isostere

Graphical and modeling software for three-dimensional structures were used for comparative analysis. This comparison involved examining the molecules from the second computational hypothesis and their reactivity isosteres in two-dimensional and three-dimensional formats [23–25].

2.2. Experimental Tests

2.2.1. Materials

Rhodamine B powder with a purity of 95 w/w% (HPLC, SIGMA-ALDRICH, Bangalore, India) was used as a contaminant. TiO₂ (AEROXIDE P90, Evonik, Germany, BET surface area: 70–110 m²/g) was employed in the catalytic oxidation process, while 35 w/w% H₂O₂ (EMPROVE, Merck, Darmstadt, Germany) solution served as the oxidizing agent. For the UV-LED 450 W photo-Fenton process, ZVI with a surface area of 200 m²/kg (BASF, Germany) was used as the catalyst.

TiO₂ was utilized due to its chemically inert nature, non-toxicity, chemical and thermal stability, photocatalytic activity, and relative cost-effectiveness compared to zinc oxide (ZnO), silver, and copper [26,27]. Furthermore, TiO₂ can be synthesized in several forms, such as nanoparticles, nanotubes, or mesoporous titanium dioxide and could be doped with other materials such as Fe, N, S, zinc peroxide (ZrO₂), and silica (SiO₂), among others, to enhance its catalytic performance [28].

2.2.2. Catalytic Oxidation Process of Rhodamine B with TiO₂ and H₂O₂

For the catalytic process, the initial concentration values of RhB were based on previous studies. According to Lin et al. [29] and Xu et al. [30] the optimal initial concentration was 20 mg/L. Consequently, an RhB solution of 25 mg/L was used, which was then doubled to 50 mg/L to observe the effects on contaminant degradation.

Different masses of TiO₂ (0.4 g and 0.8 g) were added to these solutions, along with 20 mL of H₂O₂. The initial pH of the solution ranged from 3.78 to 3.95 across the different

experiments, which was considered optimal for achieving a higher degradation percentage of RhB. For instance, Lin et al. [29] indicate the highest degradation percentages are achieved at acidic pH values, below the pKa of RhB (3.7), around 3. At these pH values, the carboxyl group of RhB deprotonates, allowing the generation of OH[•] radicals. These radicals enhance the adsorption of RhB on TiO₂ and increase the oxidation capacity under these conditions. The solutions were stirred at 1100 rpm for 60 min.

Two types of gases (air and nitrogen) were used to compare the results of aeration with those of a non-aerated system to determine the impact of aeration on the degradation efficiency of RhB. For this, 0.4 standard cubic feet per hour (scfh) of air or nitrogen was used during 60 min of agitation, and aliquots of 1.5 mL were sampled at the beginning and the end of each experiment. Finally, the samples were centrifuged for 2 min at 10,000 rpm to separate the TiO₂ particles from the solution and analyze the supernatant.

2.2.3. Kinetics of the Catalytic Reaction

The experiment that resulted in the highest degradation of RhB and the lowest catalyst consumption, using an initial RhB concentration of 25 mg/L and 0.8 g of TiO₂, prompted a kinetic analysis. This analysis employed one of the most widely utilized models in heterogeneous catalytic reactions: the Langmuir–Hinshelwood (L-H) non-linear model, as described by Asenjo et al. [31] in Equation (1).

$$-\frac{dC}{dt} = \frac{k_r K_e C}{1 + K_e C} \quad (1)$$

where C represents the concentration of RhB degraded (mg/L) over time (t, min), k_r denotes the kinetic rate constant of the reaction (mg/L min), and K_e stands for the adsorption equilibrium constant on the catalyst surface (L/mg).

However, the terms $k_r K_e$ can be combined into an apparent rate constant k_{app} (min^{−1}) [31]. Additionally, for first-order reactions like RhB, or zero-order responses, when the degradation concentrations are shallow, it is assumed that $K_e C$ tends to zero, resulting in Equation (2):

$$-\frac{dC}{dt} = k_{app} C^n \quad (2)$$

To directly evaluate the RhB degradation and determine the reaction order (n), the integrated form of Equation (2) was employed, as shown in Equation (3).

$$C = \left[C_0^{1-n} - (1-n)k_{app}t \right]^{1/(1-n)} \quad (3)$$

where C_0 represents the initial concentration of RhB (mg/L).

To minimize errors in concentration data when compared to experimental data, the exponential equation depicted in Equation (4) was used.

$$C = C_0 \exp(-k_{app}t) \quad (4)$$

2.2.4. Photo-Fenton Treatment of Rhodamine B with UV-LED Light

The efficacy of this treatment was assessed through five distinct experiments using 25 mg/L of RhB, the concentration that achieved the highest degradation efficiency during the catalytic process. Additionally, varying masses of ZVI (0.0038 g and 0.0076 g) and volumes of H₂O₂ (0.02–0.04 mL) were used, with H₂O₂ addition times spanning 1 to 3 h. The pH was kept within the range of 4.61 to 4.70, with samples collected at 30-min intervals over 6 h. The experiments underwent UV-LED irradiation while being agitated at 100 rpm.

2.3. Analytical Analysis

2.3.1. Quantification of Rhodamine B

Initially, a scan was conducted using a 25 mg/L RhB solution between 400 and 800 nm, revealing the highest peak at 555 nm. Subsequently, a calibration curve was constructed using solutions ranging from 5 mg/L to 30 mg/L. This resulted in the equation $C = 17.7619A - 0.634$, with an R^2 value of 0.998, where C represents the concentration of the contaminant and A represents the absorbance obtained. The concentration of RhB was analyzed using a Varian Cary 50 UV-Vis spectrophotometer manufactured by Agilent Technologies, based in California, USA.

2.3.2. Residual Amount of Fe^{2+} Quantification

A semi-quantitative analysis measured the residual Fe^{2+} remaining in the water after photo-Fenton treatment. This residual can cause secondary contamination, not harmful to humans at concentrations below 0.3 mg/L [32]. The analysis utilized the 5–26 REF 931226 Visocolor ECO Iron 2 colorimetric test, assessing values ranging from 0.04 to 1.00 mg/L.

2.4. Statistical Analysis

Data from kinetics Langmuir–Hinshelwood non-linear models considered descriptive statistical means, standard deviation, error, and linear regressions using Microsoft Excel Solver version 2016. For this purpose, in catalytic oxidation tests of RhB, the coefficient of determination (R^2), the chi-square (χ^2), and the sum of squared errors (SSE) were calculated in Equations (5)–(7), respectively:

$$R^2 = 1 - \frac{\sum (V_{e,exp} - V_{e,cal})^2}{\sum (V_{e,exp} - V_{e,mean})^2} \quad (5)$$

$$\chi^2 = \sum \frac{(V_{e,exp} - V_{e,cal})^2}{V_{e,cal}} \quad (6)$$

$$SSE = \sum (V_{e,exp} - V_{e,cal})^2 \quad (7)$$

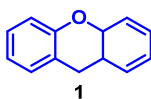
where $V_{e,exp}$ are the experimental value of parameters (C_f/C_o), $V_{e,cal}$ are the calculated parameters using the Solver tool, and $V_{e,mean}$ is the mean of $V_{e,exp}$ value [33].

3. Results and Discussion

3.1. Virtual Screening

Based on the most referenced heterocyclic molecules, molecule **1**, traditionally known as xanthene, was selected as the initial computational hypothesis. This decision was due to its core nucleus, which features a significant electronic cloud within its heterocyclic structure [25].

The two-dimensional structure of molecule **1**, xanthene or 4a,9a-dihidro-9H-xanteno, its molecular formula, exact mass, and elemental composition are shown in Figure 1. These data are essential for defining the core nucleus of the molecules that will be included in the molecule library. This common fragment generates a resonance effect, which leads to the fluorescence of the heterocycle due to the extension of its electronic cloud [34].



1

Chemical Formula: $C_{13}H_{12}O$

Exact Mass: 184.0888

Molecular Weight: 184.2380

Elemental Analysis: C, 84.75; H, 6.57; O, 8.68

Figure 1. Initial computational hypothesis—2D structure of xanthene.

3.2. Molecule Library

To construct the molecule library utilizing molecule **1**, a literature review to identify its most representative derivatives was conducted. These derivatives possess intrinsic heterocyclic characteristics and incorporate the nucleus of the initial computational hypothesis into their structure.

Seventeen derivative molecules (**2–18**) are reported and detailed in an orderly manner with their IUPAC nomenclature in Table 1, while their semi-developed formula is presented in Figure 2. These molecules primarily exhibit cyclic/aromatic substitutions and contain non-metallic heteroatoms such as sulfur, bromine, chlorine, and iodine.

Table 1. Molecule library based on the initial computational hypothesis.

Molecule Number	IUPAC Nomenclature
2	2-(6-hydroxy-3-oxo-3H-xanthen-9-yl)benzoic acid
3	2-(2,4,5,7-tetrabromo-6-hydroxy-3-oxo-3H-xanthen-9-yl)benzoic acid
4	2-(4,5-dibromo-6-hydroxy-2,7-dinitro-3-oxo-3H-xanthen-9-yl)benzoic acid
5	2',4',5',7'-tetrabromo-4,5,6,7-tetrachloro-6'-hydroxy-3H-spiro[isobenzofuran-1,9'-xanthene]-3,3'(9a'H)-dione
6	6'-hydroxy-2',4',5',7'-tetraiodo-3H-spiro[isobenzofuran-1,9'-xanthene]-3,3'(9a'H)-dione
7	2,3,4,5-tetrachloro-6-(6-hydroxy-2,4,5,7-tetraiodo-3-oxo-9, 9a-dihydro-3H-xanthen-9-yl)benzoic acid
8	(2,7-dibromo-9-(2-carboxyphenyl)-6-hydroxy-3-oxo-9,9a-dihydro-3H-xanthen-4-yl) (hydroxy) mercury
9	(2',7'-dibromo-6'-hydroxy-3,3'-dioxo-3',9a'-dihydro-3H-spiro[isobenzofuran-1,9'-xanthen]-4'-yl)(hydroxy)mercury
10	6-amino-9-phenyl-3H-xanthen-3-iminium
11	(E)-N-(9-(2-(ethoxycarbonyl)phenyl)-6-(ethylamino)-2,7-dimethyl-3H-xanthen-3-ylidene)ethanaminium
12	N-(9-(2-carboxyphenyl)-6-(diethylamino)-3H-xanthen-3-ylidene)-N-ethylethanaminium
13	6-amino-9-(2-(methoxycarbonyl)phenyl)-3H-xanthen-3-iminium
14	N-(9-(2-carboxy-4-(prop-2-yn-1-ylcarbamoyl)phenyl)-6-(dimethylamino)-3H-xanthen-3-ylidene)-N-methylmethanaminium
15	N-(9-(2-carboxy-5-isothiocyanatophenyl)-6-(dimethylamino)-3H-xanthen-3-ylidene)-N-methylmethanaminium
16	N-(6-(diethylamino)-9-(2,4-disulfophenyl)-3H-xanthen-3-ylidene)-N-ethylethanaminium
17	5-chlorosulfonyl-2-(3-oxa-23-aza-9-azoniaheptacyclo [17.7.1.15, 9.02, 17.04, 15.023, 27.013, 28] octacosa-1(27), 2(17), 4, 9(28), 13, 15, 18-heptaen-16-yl) benzenesulfonate
18	4-(6-amino-3-imino-4,5-disulfo-3H-xanthen-9-yl) isophthalic acid

The literature indicates that the molecule ((2-carboxyphenyl)thio)(ethyl) mercury **9a**, commonly known as thiomersal or thimerosal, shown in Figure 3, exhibits properties very similar to those of molecule **9**. Thiomersal has the same electrostatic function as molecule **9** and serves as its isostere but lacks the nucleus of the computational hypothesis.

Furthermore, a library of parallel molecules was compiled, including 11 derivatives of Alexa Fluor® (Figure 4). Due to their limited applications as dyes, these substances were not included in the main molecule library used in the virtual screening process [35]. The comparison focused solely on their structure and biological applications. However, it is noteworthy that these molecules have similar applications to RhB, primarily employed for biological purposes such as cell viability assays, conjugation, and amplification of signals from primary and secondary antibodies [36]. All molecules feature the nucleus of the initial computational hypothesis except for Alexa Fluor® 647, which exhibits fluorescent characteristics derived from the number of conjugated bonds in the bridge linking the two monomeric units.

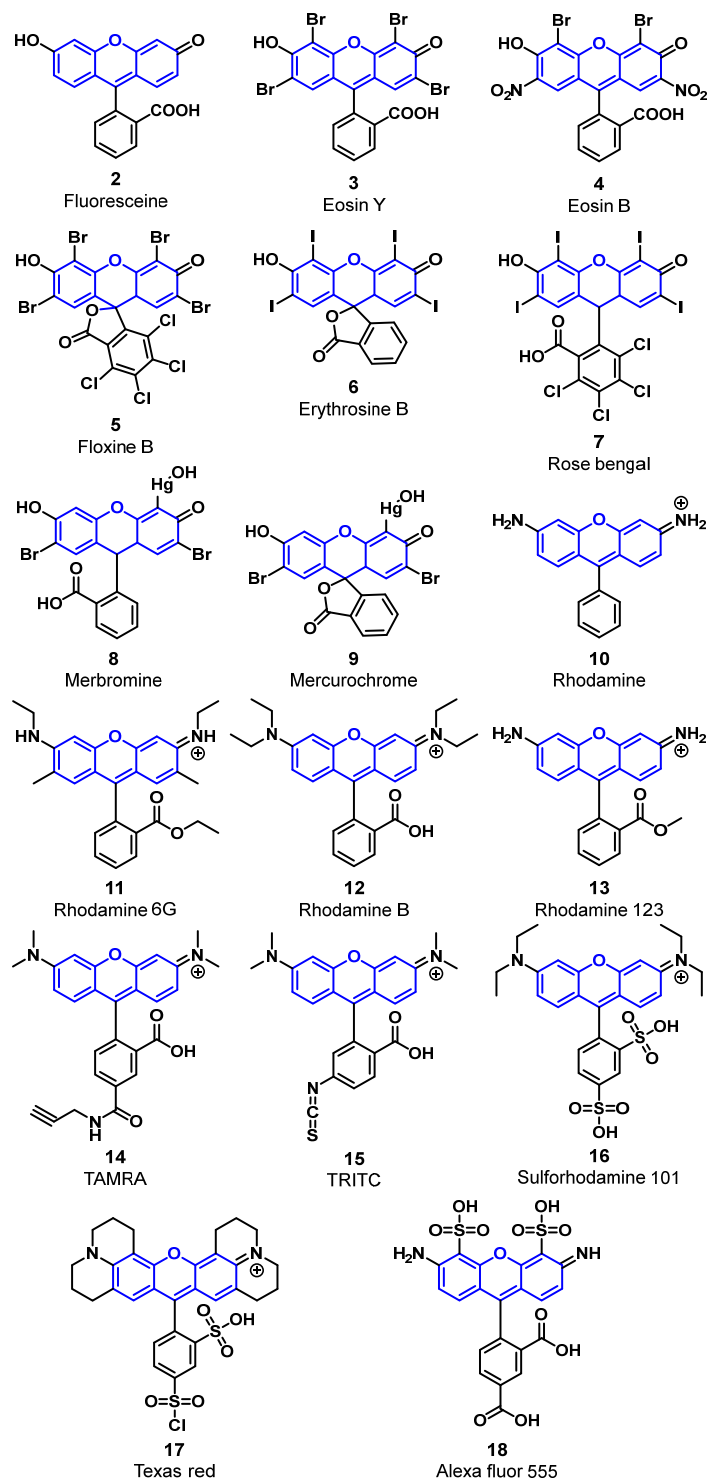


Figure 2. Library of fluorescent heterocyclic molecules 2–18. In blue, the common core for heterocyclic compounds.

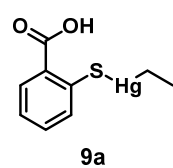


Figure 3. Isostere of molecule 9.

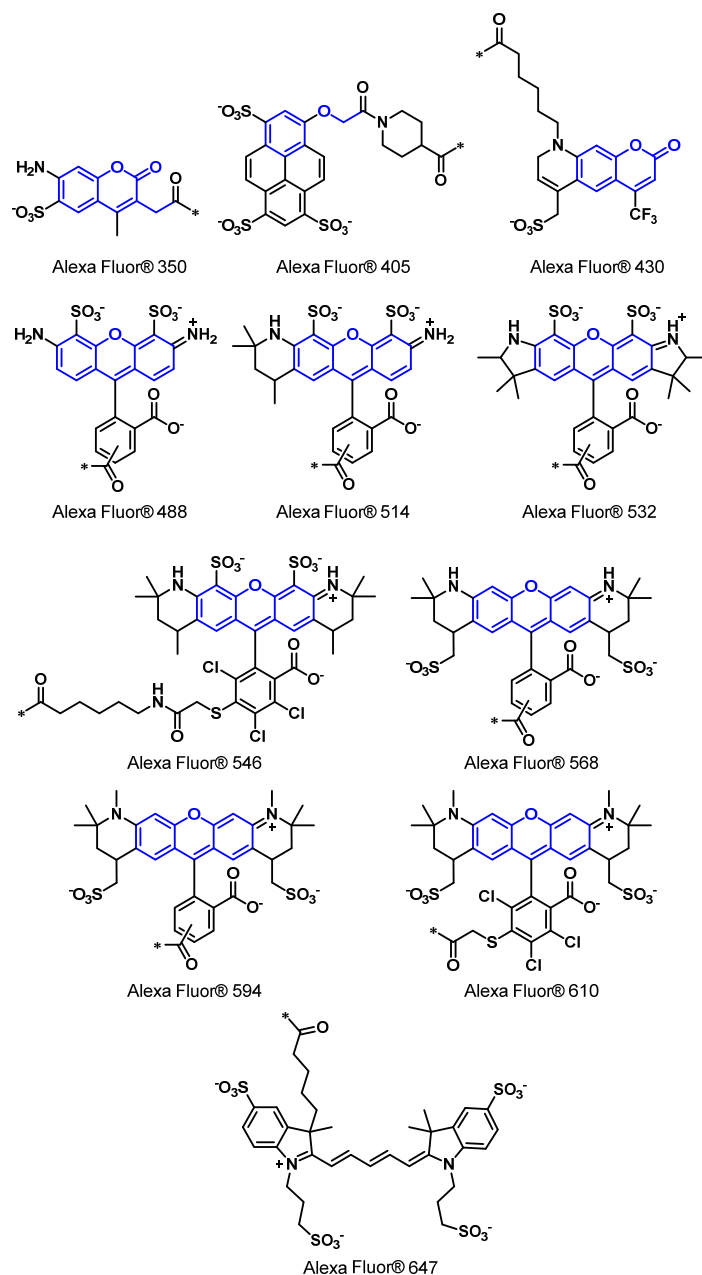
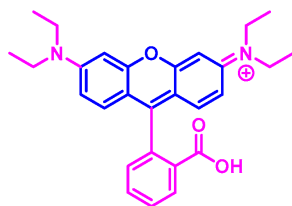


Figure 4. Molecules for biotechnological purposes Alexa Fluor®; In blue, the common core for heterocyclic compounds.

3.3. Report of Similar Molecules

Molecule 12 (RhB) represents fluorescent heterocyclic molecules, which can be considered a bidentate ligand due to the presence of nitrogen atoms at its ends. It also contains a fragment derived from benzoic acid, providing solubility despite having several aromatic rings [37]. Thus, the second computational hypothesis is presented as a reference molecule, summarizing the behavior of the molecule library. As a fluorescent heterocyclic molecule with a broad spectrum, it finds versatile applications, particularly in the textile industry (Figure 5) [30]. However, as the introduction mentions, this violet-colored substance is commonly employed in liquid environments to measure variables such as leaks, flow direction, and transportation [8]. Due to its extended electronic cloud, it exhibits fluorescence and can be detected using fluorometers, with a maximum absorption at 564 nm and a maximum emission at 589 nm. Ethanol serves as its mobile phase [34].

**12**

Rhodamine B

Chemical Formula: $C_{28}H_{31}N_2O_3^+$

Exact Mass: 443.2329

Elemental Analysis: C, 75.82; H, 7.04; N, 6.32; O, 10.82

Figure 5. Second computational hypothesis—molecule **12**. In blue, the common core for heterocyclic compounds, and in magenta, all the possible substituents of the computational hypothesis.

Absorption, Distribution, Metabolism, Excretion, and Toxicity (ADME-Tox) Response

RhB is known for its high toxicity, so understanding its action (both toxicokinetics and toxicodynamics) will allow for a better comprehension of its behavior upon entering a living organism. Through analysis of the second computational hypothesis and the simulation of its ADME-Tox properties, it was determined that, initially, its ADME behavior reflects significant reactivity, as shown in Table 2. As it is an *in silico* test and application of a mathematical model imposed by a virtual screening, a contraction of all generated is suggested, explaining only what is most representative and outside the standard range. The identification of the method corresponds to the organism with which its activity is contrasted and the most common proteins in the aerobic and anaerobic respiratory chain. This is consistent with theory, as it is a molecule that exhibits an extended electronic cloud. Only in the Ames test does it present a significant mutagenic value, while all other values are medium or negative, suggesting that it is primarily harmless [19].

Table 2. ADME behavior.

ID	Response
Algae_at *	0.01200
Ames_test *	Mutagen
Carcino_Mouse *	Negative
Carcino_Rat *	Negative
Daphnia_at *	0.02888
hERG_inhibition **	Medium_risk
medaka_at *	0.00199
minnow_at *	0.01048
TA100_10RLI **	Negative
TA100_NA **	Negative
TA1535_10RLI **	Negative
TA1535_NA **	Negative

Notes: * *In silico* prediction in living organisms. ** Tests involving proteins, enzymes, antigens, and specific antibodies in the respiratory or metabolic chain.

Additionally, Table 3 presents the ADME-Tox properties, including lipophilicity, molar volumes of the most electronegative heavy atoms, penetration through the blood-brain and gastrointestinal barriers, and interaction with various respiratory chain enzymes. Across all parameters, the values are relatively low, indicating that physiologically, they exhibit low reactivity with active biological molecules; this is evident when the *in silico* results are generated within ranges such as Lipinski's rule of 5 [38]. Their potential activity as inhibitors is justified by the presence of oxygen and nitrogen atoms, which, as heavy and electronegative atoms, could engage in Van der Waals interactions or hydrogen bonding [19].

Table 3. ADME-Tox properties.

ID	Response
AlogP98_value	3477.100
AMolRef	135.27950 **
BBB	0.03079
Buffer_solubility_mg_L	1.59686
CaCO ₂	54.44300
CYP_2C19_inhibition	Non
CYP_2C9_inhibition	Non
CYP_2D6_inhibition	Inhibitor
CYP_2D6_substrate	Non
CYP_3A4_inhibition	Inhibitor
CYP_3A4_substrate	Substrate
HIA	97.53539
MDCK	0.04403
Pgp_inhibition	Inhibitor
Plasma_Protein_Binding	77.61136
Pure_water_solubility_(mg/L)	578.57100
Skin Permeability	−2.96547
Solvation Free Energy	−23.23000 **

Notes: ** Values outside the range for appropriate absorption and oral bioavailability in the body.

3.4. 2D and 3D Description

To provide a comprehensive understanding of the computational hypothesis formulation sequence, its 1D, 2D, and 3D representations are typically compared to illustrate the spatial dimensions involved in the process.

The one-dimensional structure is depicted using Simplified Molecular Input Line Entry Specification (SMILES), as shown in Figure 6a. The two-dimensional representation, obtained through chemical modeling software, displays RhB in a planar molecular visualization, as depicted in Figure 6b. Finally, spatial optimization was performed in three-dimensional modeling software, yielding a calculated energy of 412.49 kJ/mol in Figure 6c. Each atom has its coordinates (*x*, *y*, *z*), hybridization, and molecular geometry in this representation. This was achieved by optimizing RhB using the MMFF94 force field, ensuring that the final three-dimensional structure has the appropriate spatial arrangement concerning its substituents, considering the attractions and repulsions inherent to the fluorescent heterocyclic molecule.

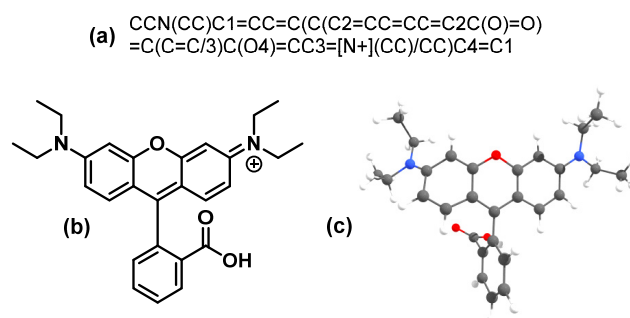


Figure 6. Second computational hypothesis—molecule 12; (a) SMILES code; (b) 2D structure; (c) 3D structure for molecule 12.

RhB was entered into the SwissADME platform using its SMILES code in the similarity section, specifically comparing it with commercial substances (with lower or similar prices to each other), electrostatic volume, and the ZINC library (<https://zinc.docking.org/> accessed on 28 June 2024), which contains approximately 750 million commercial substance and their analogs. This initiated an automated screening process to search for commercial substances with equivalent electronic properties, evaluated through SAR [39].

Three molecules were obtained (Figure 7) with equivalence within a maximum 15% significant difference range. The first molecule was (S)-1-(5-cyclopropyl-1,3,4-thiadiazol-2-yl)-3-(4-(1-methyl-1H-pyrrol-2-yl)butan-2-yl)urea (molecule 19). The second molecule was 4-benzyl-N-(3-methyl-1,2,4-thiadiazol-5-yl)piperidine-1-carboxamide (molecule 20). The third molecule, labeled as molecule 21, was 1-isopropyl-3-(5-(2-phenylpropan-2-yl)-1,3,4-thiadiazol-2-yl)urea. The results of the second computational hypothesis and the three derivatives obtained from the last screening are similar: molecule 19, with 87.3%; molecule 20, with 86.1%; and molecule 21, with 85.6%. All of them were compared electronically, overlapping with the virtual ZINC library; RhB (CAS) 81-88-9 has a price of USD 88.88/g for fluorescence assays. In contrast, molecules 19 (ZINC000089895787), 20 (ZINC000055255281), and 21 (ZINC000078544960) [40], available from commercial suppliers such as Emanine, Ambiter, and eMolecules, have prices ranging from USD 50 to 80/g of fluorescence reagent.

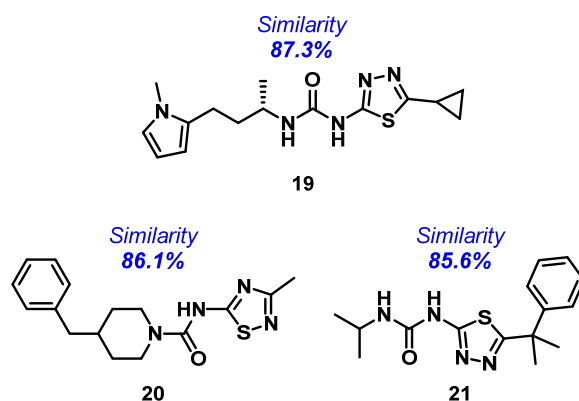


Figure 7. Commercial substances electronically equivalent to RhB.

3.5. Experimental Tests

3.5.1. Catalytic Oxidation Process of Rhodamine B with TiO_2 and H_2O_2

Figure 8 shows the results of RhB degradation percentage obtained from experiments using the catalytic oxidation process. It is evident from Figure 8a that higher initial concentrations of RhB result in lower degradation efficiency due to a decrease in $\text{OH}^\cdot$ radicals generation. Additionally, a lower amount of catalyst leads to a reduced degradation percentage because of the rapid saturation of active sites on the TiO_2 surface. This finding is consistent with studies conducted by El-Dossoki et al. [41], who worked with RhB concentrations ranging from 4 to 9 mg/L and TiO_2 concentrations ranging from 0.1 to 0.6 g/L, achieving the highest degradation percentage (93.80%) at 6 mg/L with 0.4 g/L of TiO_2 . Furthermore, the presence of air increases RhB degradation, as shown in Figure 8b, reaching a percentage of 95.11% compared to 78.60% achieved with N_2 . This is because air promotes the generation of $\text{OH}^\cdot$, $\text{O}^\cdot$, and $\text{H}^\cdot$ radicals, which can oxidize organic contaminants [42].

Consequently, the experiment with the lowest RhB concentration (25 mg/L) and the highest amount of TiO_2 (0.8 g) were used for the kinetic analysis of the reaction using equations 3 of the L-H power rate equation and 4 of the L-H non-linear model, leading to the curves depicted in Figure 9.

The parameters of the kinetic equations obtained from the L-H model are presented in Table 4. It is observed that all experiments yield k_{app} values less than 1, indicating that the catalytic reaction corresponds to a first-order reaction. Interestingly, experiments conducted under bubbling conditions with air or N_2 exhibit “n” values closer to 1. Furthermore, it was observed that the experiment in which N_2 was bubbled showed lower values in SSE and χ^2 , indicating that the experimental data more closely matched the data obtained in both L-H models [33].

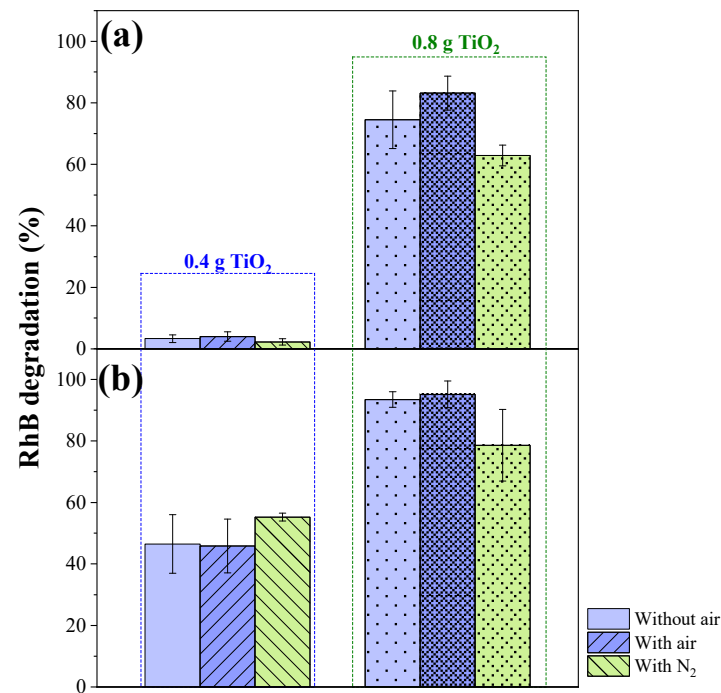


Figure 8. Degradation percentages of Rhodamine B with catalytic oxidation process. (a) RhB initial concentration = 50 mg/L, and (b) RhB initial concentration = 25 mg/L.

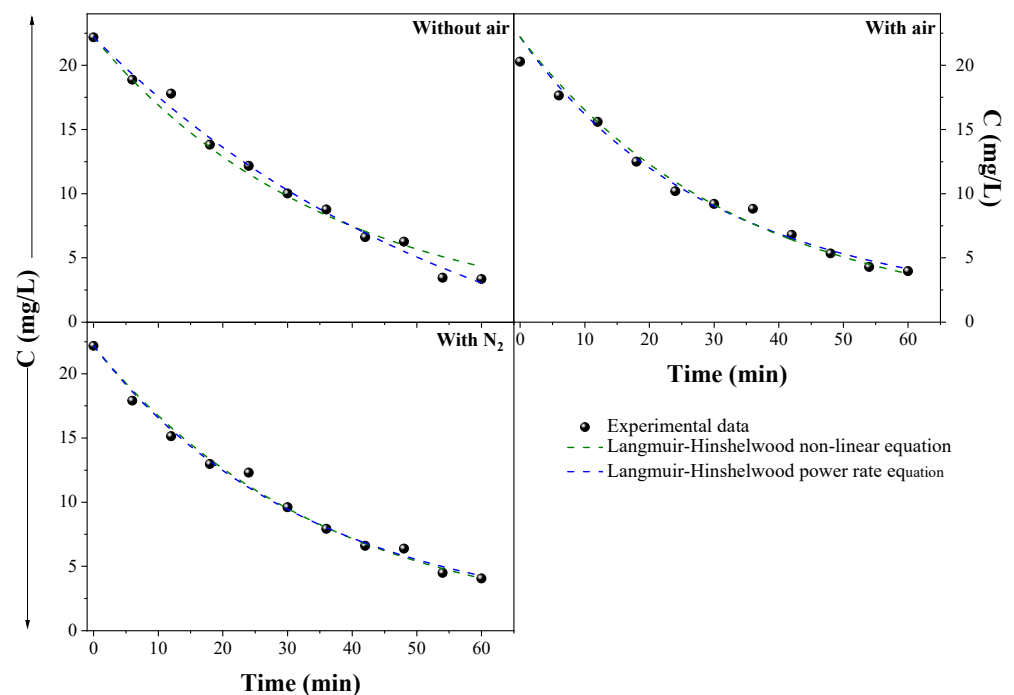


Figure 9. Linearization of the L-H mathematical model for the experiment results with 25 mg/L of RhB and 0.8 g of TiO₂.

Previous studies conducted by Xu and Ma [30] confirm that the degradation percentage increases in the presence of a catalyst such as TiO₂ and is further enhanced by adding air to the catalytic process. The authors evaluated the degradation of RhB using ultrasound while modifying certain conditions, such as the presence of a catalyst, air, and agitation, among others. They achieved a degradation of 90.63% in the process that included an initial RhB concentration of 20 mg/L, 500 mg/L of TiO₂, agitation, and air. In comparison, this study

demonstrates better degradation results, around 95%, without using ultrasound, which enhances adsorption efficiency by generating cavitation bubbles in the water.

Table 4. Results of the kinetic equations obtained from the L-H model.

Test		Without Air	With Air	With N ₂
Langmuir-Hinshelwood power rate equation	k _{app}	0.084 ± 0.022	0.019 ± 0.009	0.022 ± 0.007
	n	0.566 ± 0.103	1.172 ± 0.182	1.091 ± 0.122
	R ²	0.991	0.977	0.991
	χ ²	0.347	0.708	0.312
	SSE	3.1257	6.372	2.807
Langmuir-Hinshelwood non-linear model	k _{app}	0.027 ± 0.001	0.029 ± 0.001	0.0282 ± 0.001
	R ²	0.981	0.977	0.991
	χ ²	0.781	0.696	0.296
	SSE	7.806	6.965	2.960

To evaluate the catalytic efficiency, the degradation rates of RhB were determined, yielding the following values: 0.604 mg/L·min for the process without bubbling, 0.619 mg/L·min for the process with air, and 0.544 mg/L·min for the process with N₂. These results align with the previously observed degradation percentage trends, suggesting that the highest degradation efficiency is achieved in the presence of air and H₂O₂, which facilitates the generation of OH· radicals. This exceeds the degradation rate values reported by Ye et al. [43], who found that at dye concentrations higher than 10 mg/L, the degradation rate decreases. Similarly, at a pH greater than 3, the degradation rate is also below 0.400 mg/L min. These findings indicate that the presence of air and the amount of H₂O₂ are critical factors in the measurement of this parameter.

Alternatives for Saturated TiO₂

The regeneration of saturated TiO₂ is pivotal for maintaining operational efficiency, reducing costs, minimizing environmental impact, and promoting sustainability in catalytic processes. Consequently, the most appropriate methods for TiO₂ regeneration have been investigated. According to previous studies, during the catalytic degradation of RhB, the catalyst surface becomes saturated and poisoned due to intermediate adsorption processes, resulting in decreased activity, stability, and efficiency. El Dossoki et al. [41] indicate that after three cycles, the degradation efficiency of TiO₂ decreases by 6.8%. Therefore, it is necessary to deactivate and regenerate the catalyst under optimal conditions as suggested by Yang et al. [44]: pH 10.5 to 11 with ultrasound treatment for 50 min, achieving an 84% regeneration rate, or by mercury lamp illumination at 700 W for 6 h, achieving a 45% regeneration rate.

In addition to its primary use as a photocatalyst, regenerated TiO₂ can be repurposed as a semiconductor material in solar cells [45] as a self-cleaning coating due to its photocatalytic properties that enable the degradation of organic substances under UV light, and in hydrogen production through photocatalytic reactions that decompose water into its ions, among other applications [46].

3.5.2. Photo-Fenton Treatment of Rhodamine B with UV-LED Light

The results of the photo-Fenton treatment of RhB under UV-LED light are presented in Figure 10. It is observed that increasing the total amount of H₂O₂ does not enhance the catalytic action of ZVI because, with a higher amount of oxidant, the OH· radicals not only attack the organic matter but also the oxidant itself [30], thereby reducing the degradation percentage of RhB. In contrast, increasing the amount of catalyst enhances the degradation efficiency by approximately 8%, attributable to the higher generation of OH· radicals due to the reaction of ZVI with H₂O₂. These findings are consistent with the study by Chang et al. [42], who investigated the influence of catalyst amount on the degradation percentage of azo and anthraquinone dyes. Their study demonstrated that increasing the ZVI concentration from 30 g/L to 70 g/L resulted in a 3% increase in degradation percentage, although the exposure time was reduced from 21 min to 9 min.

Furthermore, using a UV LED lamp operating within the range of 500 to 700 nm allows for the photochemical regeneration of Fe^{2+} ions to act as catalysts, thereby improving the degradation of RhB. It also promotes the use of lower amounts of ZVI and H_2O_2 , which aligns with the study conducted by Souza et al. [47].

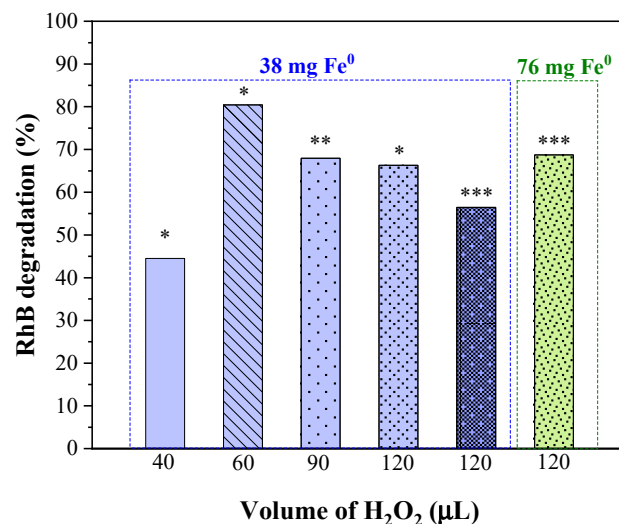


Figure 10. Percentage of Rhodamine B degradation with UV-LED photo-Fenton treatment. * = 20 μL H_2O_2 /h, ** = 30 μL H_2O_2 /h, *** = 40 μL H_2O_2 /h.

Table 5 shows the concentration of Fe^{2+} present in the solution at the end of the UV-LED photo-Fenton treatment. It is observed that this concentration is less than 0.3 mg/L, indicating that, according to Das and Nandi [32], the Fe^{2+} concentration does not affect human health or interfere with the taste, turbidity, or color characteristics of the water.

Table 5. Concentration and percentage of dissolved Fe^{2+} at the end of the experiments with the UV-LED photo-Fenton treatment.

Experiment	Dissolved Fe^{2+} (mg/L)	Dissolved Fe^{2+} (%)
1	0.25	0.33
2	0.15	0.20
3	0.20	0.26
4	0.10	0.13
5	0.07	0.09
6	0.20	0.13

3.5.3. Comparison of RhB Degradation with Previous Studies

Table 6 offers a comprehensive overview of the degradation processes for several azo dyes and other heterocyclic compounds, such as Rh 6G and Brilliant Blue, highlighting their optimal operating conditions and degradation efficiency.

Photocatalytic processes utilizing TiO_2 exhibit higher degradation rates compared to photo-Fenton processes, particularly in acidic media that favor the generation of hydroxyl radicals $\text{OH}^\cdot$ and the adsorption of contaminants. For TiO_2 -based catalytic processes of RhB, the optimal pH range is between 3 and 4, as demonstrated in our study. In this study, the pH was within the optimal range, achieving the highest degradation percentage of 95.11%. Additionally, in this case, UV light was not used for the process with TiO_2 , but H_2O_2 was used as an oxidant along with an air flow to achieve optimal conditions for degradation. Conversely, the optimal pH for the photo-Fenton process is around 3 because the acidic environment ensures the coexistence of Fe^{2+} and Fe^{3+} , which are fundamental for the Fenton reaction [48]. This finding aligns with the studies presented by Chang et al. [42], where the highest degradation rate of RhB was observed.

Catalytic processes depend on the generation of hydroxyl radicals $\text{OH}^\cdot$, which are highly reactive and responsible for the degradation of contaminants. In the case of the photo-Fenton process, the exposure times are typically longer (greater than 120 min) because the generation of these radicals depends primarily on adequate concentrations of H_2O_2 and iron. Furthermore, the decomposition of H_2O_2 under UV light requires time, and the consumption of $\text{OH}^\cdot$ radicals in secondary reactions reduces the degradation efficiency. Lower dye concentrations allow for higher degradation rates since most of the active sites on the catalyst remain available, leading to high efficiency in $\text{OH}^\cdot$ generation [49]. This phenomenon is evidenced in the study by El Dossoki et al. [41], which observed a lower initial concentration of contaminant but suboptimal operating parameters for achieving higher degradation rates. Additionally, in other studies, the introduction of ultrasound or agitation can significantly reduce treatment time by inducing cavitation effects, thereby enhancing degradation efficiency in the photocatalytic processes [30].

Table 6. Comparison of RhB Degradation with Previous Studies.

Type of Process	Operating Parameters	Light	Results	Reference
Photocatalytic	Initial pH: 5 RhB: 6 mg/L TiO_2 : 0.3 g/L	UV lamp λ_{max} : 280 nm E_{photon} : 4.43–12.4 eV	93.80% degradation of RhB after 75 min	[41]
Photocatalytic	Initial pH: 2 RhB: 2.4 g/L TiO_2 : 1.6 g/L	UV irradiation 15 W	75.06% degradation of RhB after 15 min	[50]
Ultrasound-assisted TiO_2 photocatalysis	Initial pH: 7 RhB: 20 mg/L TiO_2 : 500 mg/L Ultrasonic vibration frequency: 40 kHz	No light	90.63% degradation of RhB after 20 min	[30]
Cavitation process	Initial pH: 3 RhB: 10 mg/L H_2O_2 : 0.6% Ultrasonic vibration frequency: 20 kHz	No light	84.06% degradation of RhB after 100 min	[43]
Photocatalytic	Initial pH: 3 Rh 6G: 5 μM Raschig rings supported TiO_2 : 10	UV lamp λ : 365 nm	77.50% degradation of Rh-6G after 90 min	[51]
Photocatalytic	Initial pH: 5.5 Rh 6G: 3.76×10^{-5} mol/L TiO_2 (77 nm): 0.6 g/L	Solar irradiation 150 W/m ²	71.70% degradation of Rh-6G after 100 min	[52]
Photocatalytic	Initial pH: 2.5 Rh 6G: 10 mg/L TiO_2 : 3.0 g/L	Solar irradiation	72% degradation of Rh-6G after 180 min	[53]
Catalytic process	Initial pH: 3.78–3.95 RhB: 25 mg/L TiO_2 : 0.8 g H_2O_2 : 20 mL 1100 rpm Air flow rate: 0.4 scfh	No light	95.11% degradation of RhB after 60 min	This study
Degradation with ZVI and air	Initial pH: 3 Dye (Reactive Blue): 100 mg/L ZVI: 50 g/L Air flow rate: 5 L/min	No light	87.00% degradation of Reactive Blue after 9 min	[42]
Photo-Fenton/ Fe_2O_3	H_2O_2 : 1 mL Fe_2O_3 : 12%	Sunlight simulator lamp $\lambda > 420$ nm	81.00% degradation of RhB after 150 min	[54]
Photo-Fenton /ZVI	Initial pH: 4.61–4.70 RhB: 25 mg/L ZVI: 38 mg H_2O_2 : 20 $\mu\text{L}/\text{h}$	UV Led 450 W	80.42% degradation of RhB for 180 min	This study

Regarding Rh 6G and Brilliant Blue, whose degradation processes were conducted under operational conditions similar to those used with RhB, such as acidic pH, treatment times, and catalysts like TiO₂ and ZVI, lower degradation percentages were reported. These lower degradations are attributed to the differences in their functional groups compared to RhB, which can affect or hinder the interaction with the photocatalyst [51].

4. Conclusions

Based on the 15% significance range, molecules **19–21** can potentially replace Rhodamine B due to their electronic equivalence in fluorescence assays; considering the price difference, molecules **18–20** could be a more cost-effective alternative for multiple assays. However, *in silico* calculations indicate that most values fall outside the optimal range for effective absorption and oral bioavailability, suggesting a level of toxicity that may be either activated or mitigated depending on the substance's intrinsic excitability. Therefore, while the substance shows potential for use in advanced oxidation treatments, its bioavailability and toxicity profile must be carefully managed to ensure safety and efficacy. The catalytic oxidation process with TiO₂ proves effective for degrading RhB in water, with optimal results achieved using 0.8 g of TiO₂, 20 mL of 35% *w/w* H₂O₂, and an airflow of 0.4 scfh for a 25 mg/L concentration of RhB, resulting in approximately 95.11% degradation. These results underscore the effectiveness of the catalytic oxidation process and the importance of adjusting the amounts of catalyst and oxidizing agents to maximize degradation efficiency. The photo-Fenton process for the same initial concentration of RhB yielded a lower degradation percentage of 80.42% over a longer treatment time, attributed to using a low amount of ZVI and UV-LED light. These insights advance understanding of advanced oxidation processes and suggest promising avenues for more efficient and cost-effective water treatment processes.

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References

1. Sulaiman, S.O.; Najm, A.B.A.; Kamel, A.H.; Al-Ansari, N. Evaluate the Optimal Future Demand of Water Consumption in Al-Anbar Province in the West of Iraq. *Int. J. Sustain. Dev. Plan.* **2021**, *16*, 457–462. [\[CrossRef\]](#)
2. Philip, L.; Pradeep, T.; Murty Bhallamudi, S. *Technological Solutions for Water Sustainability: Challenges and Prospects. Towards a Water-Secure India*, 1st ed.; IWA: London, UK, 2023.
3. Qadir, M. Potential of Municipal Wastewater for Resource Recovery and Reuse. In *Water and Climate Change*; Elsevier: Amsterdam, The Netherlands, 2022; pp. 263–271.
4. Palani, G.; Arputhalatha, A.; Kannan, K.; Lakkaboyana, S.K.; Hanafiah, M.M.; Kumar, V.; Marella, R.K. Current Trends in the Application of Nanomaterials for the Removal of Pollutants from Industrial Wastewater Treatment—A Review. *Molecules* **2021**, *26*, 2799. [\[CrossRef\]](#) [\[PubMed\]](#)
5. Oladoye, P.O.; Kadhom, M.; Khan, I.; Hama Aziz, K.H.; Alli, Y.A. Advancements in Adsorption and Photodegradation Technologies for Rhodamine B Dye Wastewater Treatment: Fundamentals, Applications, and Future Directions. *Green Chem. Eng.* **2023**. [\[CrossRef\]](#)
6. Kumar, N.; Pandey, A.; Rosy; Sharma, Y.C. A Review on Sustainable Mesoporous Activated Carbon as Adsorbent for Efficient Removal of Hazardous Dyes from Industrial Wastewater. *J. Water Process Eng.* **2023**, *54*, 104054. [\[CrossRef\]](#)
7. Deng, D.; Lamssali, M.; Aryal, N.; Ofori-Boadu, A.; Jha, M.K.; Samuel, R.E. Textiles Wastewater Treatment Technology: A Review. *Water Environ. Res.* **2020**, *92*, 1805–1810. [\[CrossRef\]](#) [\[PubMed\]](#)

8. Yusuf, T.L.; Orimolade, B.O.; Masekela, D.; Mamba, B.; Mabuba, N. The Application of Photoelectrocatalysis in the Degradation of Rhodamine B in Aqueous Solutions: A Review. *RSC Adv.* **2022**, *12*, 26176–26191. [CrossRef] [PubMed]
9. Pepling, M.; Howard, P.; Durkin, P. Use and Assessment of Marker Dyes Used with Herbicides. 1997; p. 11. Available online: https://www.fs.usda.gov/foresthealth/pesticide/pdfs/091602_markerdyes.pdf (accessed on 15 July 2024).
10. Sharma, J.; Sharma, S.; Bhatt, U.; Soni, V. Toxic Effects of Rhodamine B on Antioxidant System and Photosynthesis of Hydrilla Verticillata. *J. Hazard. Mater. Lett.* **2022**, *3*, 100069. [CrossRef]
11. Al-Buriah, A.K.; Al-Gheethi, A.A.; Senthil Kumar, P.; Radin Mohamed, R.M.S.; Yusof, H.; Alshalif, A.F.; Khalifa, N.A. Elimination of Rhodamine B from Textile Wastewater Using Nanoparticle Photocatalysts: A Review for Sustainable Approaches. *Chemosphere* **2022**, *287*, 132162. [CrossRef] [PubMed]
12. Amalina, F.; Abd Razak, A.S.; Krishnan, S.; Zularisam, A.W.; Nasrullah, M. A Review of Eco-Sustainable Techniques for the Removal of Rhodamine B Dye Utilizing Biomass Residue Adsorbents. *Phys. Chem. Earth Parts A/B/C* **2022**, *128*, 103267. [CrossRef]
13. Yang, J.; Han, Y.; Sun, Z.; Zhao, X.; Chen, F.; Wu, T.; Jiang, Y. PEG/Sodium Tripolyphosphate-Modified Chitosan/Activated Carbon Membrane for Rhodamine B Removal. *ACS Omega* **2021**, *6*, 15885–15891. [CrossRef]
14. Rodríguez-Peña, M.; Natividad, R.; Barrera-Díaz, C.E.; Balderas Hernández, P.; Alanis Ramírez, C.I.; Roa-Morales, G. Current Perspective of Advanced Electrochemical Oxidation Processes in Wastewater Treatment and Life Cycle Analysis. *Int. J. Electrochem. Sci.* **2024**, *19*, 100589. [CrossRef]
15. Cuti Merma, R.L.; Oblitas Huallpa, M.E. *Efecto de Concentraciones TiO₂ Sobre La Degradación Fotocatalítica de Cianuro En Aguas Residuales de Minería Aurífera*; Universidad César Vallejo: Trujillo, Peru, 2022.
16. Santana-Romo, F.; Lagos, C.F.; Duarte, Y.; Castillo, F.; Moglie, Y.; Maestro, M.A.; Charbe, N.; Zacconi, F.C. Innovative Three-Step Microwave-Promoted Synthesis of N-Propargyltetrahydroquinoline and 1,2,3-Triazole Derivatives as a Potential Factor Xa (FXa) Inhibitors: Drug Design, Synthesis, and Biological Evaluation. *Molecules* **2020**, *25*, 491. [CrossRef] [PubMed]
17. Santana Romo, F.M.; Morales Ortiz, M.J.; Carreño Otero, A.L.; Vizuete Fiallos, G.E.; Peñaherrera Veintimilla, J.L. Descripción Físico-Química Teórica y Computacional de Los Complejos Enzima-Ligando de La Proteína Bromelina Reportada Mediante Difracción de Rayos X. *Rev. Investig. Talent.* **2024**, *11*, 1–14. [CrossRef]
18. Durán, R.; Barrales-Martínez, C.; Santana-Romo, F.; Rodríguez, D.F.; Zacconi, F.C.; Herrera, B. Substitution Effects in Aryl Halides and Amides into the Reaction Mechanism of Ullmann-Type Coupling Reactions. *Molecules* **2024**, *29*, 1770. [CrossRef] [PubMed]
19. Daina, A.; Michielin, O.; Zoete, V. SwissADME: A Free Web Tool to Evaluate Pharmacokinetics, Drug-Likeness and Medicinal Chemistry Friendliness of Small Molecules. *Sci. Rep.* **2017**, *7*, 42717. [CrossRef] [PubMed]
20. Santana-Romo, F.; Peñaherrera, J.L.; Sanchez, J.S.; Carreño-Otero, A.L. Chemical-Computational Comparison of Organometallic Complexes in Oxygen Carriers and Their Incidence on Blood Color. *Investig. Desarro.* **2023**, *18*. [CrossRef]
21. Daina, A.; Zoete, V. A BOILED-Egg To Predict Gastrointestinal Absorption and Brain Penetration of Small Molecules. *ChemMed-Chem* **2016**, *11*, 1117–1121. [CrossRef] [PubMed]
22. Daina, A.; Michielin, O.; Zoete, V. ILOGP: A Simple, Robust, and Efficient Description of *n*-Octanol/Water Partition Coefficient for Drug Design Using the GB/SA Approach. *J. Chem. Inf. Model.* **2014**, *54*, 3284–3301. [CrossRef] [PubMed]
23. Lorenzo, F.; Ocampo, R.; Rodríguez, D.F.; Santana-Romo, F.; Galdamez, A.; Zacconi, F.C.; Burrow, R.A.; Mandolesi, S.; D'Accorso, N. Solvent-Free Efficient Synthesis of New 4-Thiazolidinones with a Fructose Scaffold through a Microwave-Assisted Cascade Multicomponent Reaction. *Synthesis* **2024**, *56*, 1429–1437. [CrossRef]
24. Santana-Romo, F.; Núñez-Villacís, L.; Cadena-Carrera, S.; Garcés-Moncayo, M.D. Aplicación de Herramientas Informáticas En El Análisis Químico-Biológico de Compuestos Anticancerígenos y Simulación Del Efecto Dual En El Modelo de Coagulación Tipo Cascada. *Rev. Ibér. Sist. Tecnol. Inf.* **2023**, 103–119.
25. Santana-Romo, F.; Zacconi, F.C. Cribado Virtual y Análisis de Complejos Enzima-Ligando Para El Factor Xa (FXa) En La Cascada de La Coagulación Humana. *Bionatura* **2023**, *27*, 1–20. [CrossRef]
26. Siwińska-Ciesielczyk, K.; Świgoń, D.; Rychtowski, P.; Moszyński, D.; Zgoła-Grześkowiak, A.; Jesionowski, T. The Performance of Multicomponent Oxide Systems Based on TiO₂, ZrO₂ and SiO₂ in the Photocatalytic Degradation of Rhodamine B: Mechanism and Kinetic Studies. *Colloids Surf. A Physicochem. Eng. Asp.* **2020**, *586*, 124272. [CrossRef]
27. Dehghani, M.T.; Delnavaz, M. UV-Light-Responsive Ag/TiO₂/PVA Nanocomposite for Photocatalytic Degradation of Cr, Ni, Zn, and Cu Heavy Metal Ions. *Sci. Rep.* **2024**, *14*, 5195. [CrossRef]
28. Bejaoui, B.; Bouchmila, I.; Nefzi, K.; Slimen, I.B.; Koumbad, S.; Martin, P.; Joly, N.; M'hamdi, N. *Nanostructured Titanium Dioxide (NS-TiO₂)*; IntechOpen: London, UK, 2024. [CrossRef]
29. Lin, Z.; Dong, C.; Mu, W.; Han, X. Degradation of Rhodamine B in the Photocatalytic Reactor Containing TiO₂ Nanotube Arrays Coupled with Nanobubbles. *Adv. Sens. Energy Mater.* **2023**, *2*, 100054. [CrossRef]
30. Xu, D.; Ma, H. Degradation of Rhodamine B in Water by Ultrasound-Assisted TiO₂ Photocatalysis. *J. Clean. Prod.* **2021**, *313*, 127758. [CrossRef]
31. Asenjo, N.G.; Santamaría, R.; Blanco, C.; Granda, M.; Álvarez, P.; Menéndez, R. Correct Use of the Langmuir–Hinshelwood Equation for Proving the Absence of a Synergy Effect in the Photocatalytic Degradation of Phenol on a Suspended Mixture of Titania and Activated Carbon. *Carbon N. Y.* **2013**, *55*, 62–69. [CrossRef]
32. Das, D.; Nandi, B.K. Removal of Fe (II) Ions from Drinking Water Using Electrocoagulation (EC) Process: Parametric Optimization and Kinetic Study. *J. Environ. Chem. Eng.* **2019**, *7*, 103116. [CrossRef]

33. Nguyen, L.H.; Van, H.T.; Chu, T.H.H.; Nguyen, T.H.V.; Nguyen, T.D.; Hoang, L.P.; Hoang, V.H. Paper Waste Sludge-Derived Hydrochar Modified by Iron (III) Chloride for Enhancement of Ammonium Adsorption: An Adsorption Mechanism Study. *Environ. Technol. Innov.* **2021**, *21*, 101223. [\[CrossRef\]](#)
34. Wu, Y.; Zhao, Y.; Li, X.; Gao, H.; Guo, Z.; Wang, D.; Luan, Y.; Wang, L. Preparation and Characterization of Bilayer Polymer-Dispersed Liquid Crystals Doped with Gd₂O₃ Nanoparticles and Rhodamine B Base Fluorescent Dye. *Molecules* **2024**, *29*, 1126. [\[CrossRef\]](#)
35. Lali, N.; Tsiatsiani, L.; Elfrink, W.; Kokke, B.; Satzer, P.; Dirksen, E.; Eppink, M.; Jungbauer, A. An Inert Tracer: The Binding Site of a Fluorescent Dye on the Antibody and Its Effects on Protein A Chromatography. *J. Chromatogr. A* **2024**, *1728*, 464995. [\[CrossRef\]](#)
36. Jing, Z.; Wu, L.; Pan, Y.; Zhang, L.; Zhang, X.; Shi, D.; Shi, H.; Chen, J.; Ji, Z.; Zhang, J.; et al. Rotavirus Infection Inhibits SLA-I Expression on the Cell Surface by Degrading B2 M via ERAD-Proteasome Pathway. *Vet. Microbiol.* **2024**, *292*, 110036. [\[CrossRef\]](#) [\[PubMed\]](#)
37. Zhao, Y.; Sun, M.; Zhou, F.; Xu, G. Ultratrace Aromatic Anhydride Dopant as Intermediate Island to Promote Charge Transfer of Graphitic Carbon Nitride for Enhancing the Photocatalytic Degradation of Rhodamine B. *Langmuir* **2024**, *40*, 1858–1868. [\[CrossRef\]](#) [\[PubMed\]](#)
38. Lipinski, C.A. Lead and Drug-like Compounds: The Rule of Five Revolution. *Drug Discov. Today Technol.* **2004**, *1*, 337–341. [\[CrossRef\]](#)
39. Irwin, J.J.; Sterling, T.; Mysinger, M.M.; Bolstad, E.S.; Coleman, R.G. ZINC: A Free Tool to Discover Chemistry for Biology. *J. Chem. Inf. Model.* **2012**, *52*, 1757–1768. [\[CrossRef\]](#) [\[PubMed\]](#)
40. Sigma Aldrich. Rhodamine B. Available online: <https://www.sigmaaldrich.com/US/en/search/rhodamine-b?focus=products&page=1&perpage=30&sort=relevance&term=Rhodamine%20B&type=product> (accessed on 26 June 2024).
41. El-Dossoki, F.I.; Atwee, T.M.; Hamada, A.M.; El-Bindary, A.A. Photocatalytic Degradation of Remazol Red B and Rhodamine B Dyes Using TiO₂ Nanomaterial: Estimation of the Effective Operating Parameters. *Desalination Water Treat.* **2021**, *233*, 319–330. [\[CrossRef\]](#)
42. Chang, S.H.; Wang, K.S.; Chao, S.J.; Peng, T.H.; Huang, L.C. Degradation of Azo and Anthraquinone Dyes by a Low-Cost Fe⁰/Air Process. *J. Hazard. Mater.* **2009**, *166*, 1127–1133. [\[CrossRef\]](#) [\[PubMed\]](#)
43. Ye, Y.-F.; Zhu, Y.; Lu, N.; Wang, X.; Su, Z. Treatment of Rhodamine B with Cavitation Technology: Comparison of Hydrodynamic Cavitation with Ultrasonic Cavitation. *RSC Adv.* **2021**, *11*, 5096–5106. [\[CrossRef\]](#) [\[PubMed\]](#)
44. Yang, X.; Sun, H.; Li, G.; An, T.; Choi, W. Fouling of TiO₂ Induced by Natural Organic Matters during Photocatalytic Water Treatment: Mechanisms and Regeneration Strategy. *Appl. Catal. B* **2021**, *294*, 120252. [\[CrossRef\]](#)
45. Zhang, B.; Sun, B.; Liu, F.; Gao, T.; Zhou, G. TiO₂-Based S-Scheme Photocatalysts for Solar Energy Conversion and Environmental Remediation. *Sci. China Mater.* **2024**, *67*, 424–443. [\[CrossRef\]](#)
46. Yang, M.; Liu, G.; Zhao, W.; Meng, F.; Lao, Y.; Liang, Y. Preparation and Properties of TiO₂ Photocatalytic Self-Cleaning Coating Material for Glass. *Int. J. Low-Carbon Technol.* **2023**, *18*, 322–330. [\[CrossRef\]](#)
47. de Souza, Z.S.B.; Silva, M.P.; Fraga, T.J.M.; Motta Sobrinho, M.A. A Comparative Study of Photo-Fenton Process Assisted by Natural Sunlight, UV-A, or Visible LED Light Irradiation for Degradation of Real Textile Wastewater: Factorial Designs, Kinetics, Cost Assessment, and Phytotoxicity Studies. *Environ. Sci. Pollut. Res.* **2021**, *28*, 23912–23928. [\[CrossRef\]](#) [\[PubMed\]](#)
48. Machado, F.; Teixeira, A.C.S.C.; Ruotolo, L.A.M. Critical Review of Fenton and Photo-Fenton Wastewater Treatment Processes over the Last Two Decades. *Int. J. Environ. Sci. Technol.* **2023**, *20*, 13995–14032. [\[CrossRef\]](#)
49. Chen, D.; Lu, R.; Pu, Z.; Zhu, J.; Li, H.-W.; Liu, F.; Hu, S.; Luo, X.; Wu, J.; Zhao, Y.; et al. Ru-Doped 3D Flower-like Bimetallic Phosphide with a Climbing Effect on Overall Water Splitting. *Appl. Catal. B* **2020**, *279*, 119396. [\[CrossRef\]](#)
50. Kumawat, M.Y.S.; Kulkarni, D.A.D.; Scholar, M.-T.; Vidyapeeth, B. Treatment of Textile Wastewater Containing Rhodamine B Using Advance Oxidation Processes. *Int. J. Sci. Dev. Res.* **2017**, *2*, 48–59.
51. Pino, E.; Calderón, C.; Herrera, F.; Cifuentes, G.; Arteaga, G. Photocatalytic Degradation of Aqueous Rhodamine 6G Using Supported TiO₂ Catalysts. A Model for the Removal of Organic Contaminants From Aqueous Samples. *Front. Chem.* **2020**, *8*, 365. [\[CrossRef\]](#) [\[PubMed\]](#)
52. Asiri, A.M.; Al-Amoudi, M.S.; Al-Talhi, T.A.; Al-Talhi, A.D. Photodegradation of Rhodamine 6G and Phenol Red by Nanosized TiO₂ under Solar Irradiation. *J. Saudi Chem. Soc.* **2011**, *15*, 121–128. [\[CrossRef\]](#)
53. Bhaskar, N.S.; Kadam, A.D.; Biwal, J.J.; Diwate, P.M.; Dalbhanjan, R.R.; Mahale, D.D.; Hinge, S.P.; Banerjee, B.S.; Mohod, A.V.; Gogate, P.R. Removal of Rhodamine 6G from Wastewater Using Solar Irradiations in the Presence of Different Additives. *Desalination Water Treat.* **2016**, *57*, 18275–18285. [\[CrossRef\]](#)
54. Van Viet, P.; Van Chuyen, D.; Hien, N.Q.; Duy, N.N.; Thi, C.M. Visible-Light-Induced Photo-Fenton Degradation of Rhodamine B over Fe₂O₃-Diatomite Materials. *J. Sci. Adv. Mater. Devices* **2020**, *5*, 308–315. [\[CrossRef\]](#)

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