*Journal of Toxicological Studies* 2025, 3(2), 3197.
https://doi.org/10.59400/jts3197

Article

# Emerging contaminants in Colombian water sources and their oncological risk: A QSAR modeling approach

**Giovanny Jurado-Gamez[1], Patricia Eugenia Velez-Varela[1], Vanessa Jurado-Davila[2,*]**

[1] Molecular Biology, Environment and Cancer Group, Department of Biology, University of Cauca, Popayán 190003, Colombia
[2] Physikalische Chemie, TUM School of Natural Sciences, Technische Universität München, Lichtenbergstraße 4, 85748 Garching, Germany
*** Corresponding author:** Vanessa Jurado-Davila, vannessa_jd@hotmail.com

**CITATION**

Jurado-Gamez G, Velez-Varela PE, Jurado-Davila V. Emerging contaminants in Colombian water sources and their oncological risk: A QSAR modeling approach. Journal of Toxicological Studies. 2025; 3(2): 3197.
https://doi.org/10.59400/jts3197

**ARTICLE INFO**

Received: 30 April 2025
Revised: 20 June 2025
Accepted: 30 June 2025
Available online: 29 July 2025



**Abstract:** This study investigates the presence and potential oncogenic risks of pharmaceuticals as emerging contaminants in aquatic environments in Colombia. These substances enter ecosystems primarily through human and veterinary use, and are discharged via sewage and wastewater systems. A selection of pharmaceuticals found at high concentrations in effluents across different Colombian regions was identified based on a comprehensive review of indexed scientific literature. To assess their potential health impact, a Quantitative Structure-Activity Relationship (QSAR) approach was applied to predict the toxicological behavior of each compound based on its molecular structure. The findings indicate that while many parent pharmaceuticals show relatively low carcinogenic potential, several degradation products and metabolites exhibit structural features linked to carcinogenicity. Functional groups such as nitrosamines, phenols, and epoxides—known for their genotoxic effects—were identified in some metabolites, suggesting they may damage DNA, induce mutations, and promote cancer development. These results emphasize the importance of considering both parent compounds and their transformation products in environmental health risk assessments. Long-term exposure to such contaminants may represent a significant oncological risk, reinforcing the need for stricter monitoring and predictive toxicology models like QSAR to support environmental and public health policies.

**Keywords:** emerging contaminants; QSAR; water sources; pharmaceutical compounds; diseases

## 1. Introduction

The presence of contaminants in water sources is a focus of research in many parts of the world. The study of different types of contaminants, such as organic and non-organic, their interaction with the environment, and their persistence after effluent treatment processes is of interest to the scientific community. Among the most studied pollutants it is possible to highlight anions [1,2], dyes [3], biostimulators [4], among others. On the other hand, emerging contaminants are chemical substances whose presence in environmental matrices such as water, air, soil, and sediments raise significant concerns due to their potential risks to both human health and ecosystems [5]. Among these, pharmaceuticals, industrial chemicals, and pesticides are of particular concern because they can contain carcinogenic substances or act as endocrine disruptors, which interfere with hormonal regulation and contribute to the development of various diseases, including cancer [6,7]. The widespread occurrence of these substances in the environment has led to growing apprehension about their long-term impacts, as they can bioaccumulate in aquatic organisms, thus increasing exposure risks through the food chain and posing a significant threat to both human and environmental health [8,9]. This environmental

exposure is further complicated by the complex interactions between pollutants and biological systems, which can lead to the accumulation of multiple harmful effects over time. It is increasingly recognized that chronic exposure to certain emerging contaminants can alter metabolic and endocrine processes, contributing to the onset of various cancers and other chronic diseases [10,11]. The need for effective monitoring, risk assessment, and mitigation strategies for these emerging contaminants has never been more urgent, given their potential for both acute and long-term detrimental effects on health.

Moreover, the connection between environmental contaminants and diseases is further underscored by the concept of the "exposome." This term refers to the comprehensive set of environmental exposures an individual experience over their lifetime, from birth onwards, and its impact on health outcomes. According to the World Health Organization (WHO), cancer remains a leading cause of death globally, with approximately 10 million deaths in 2019, ranking second only to cardiovascular diseases [12,13]. Genetic factors are known to contribute to only a small fraction—approximately 10%—of the overall cancer risk, with the remaining 90% being attributed to environmental and lifestyle factors, including exposure to carcinogens such as emerging contaminants [14]. This highlights the growing importance of understanding and quantifying environmental exposures to better assess cancer risks and to design targeted prevention strategies.

In this way, pharmaceutical compounds are a type of emerging contaminant that have been became in an important issue to solve in water remediation. Among the range of PCs existing, to several classes of human and veterinary antibiotics, human prescription and non-prescription drugs, and some sex and steroid hormones as well [15,16]. Therefore, one of the major challenges in addressing pharmaceutical compounds as water pollutants is the fact that they are not typically removed by conventional wastewater treatment methods. This is because these treatment methods are not designed to remove chemicals at low concentrations as well as not their degradation byproducts [17].

To address these concerns, new methodologies are being employed to assess the environmental impact of contaminants more effectively. In particular, computational modeling approaches, such as in silico methods, have become valuable tools in predicting the behavior and potential toxicity of chemicals without the need for expensive or ethically questionable animal testing [18–20]. One widely used tool in this field is the QSAR model, which facilitates the prediction of a compound's biological effects based on its chemical structure. By analyzing these relationships, QSAR modeling can provide critical insights into the potential toxicity of substances, helping to identify harmful chemicals early in the research process while reducing both research costs and the need for animal testing [21,22].

Therefore, the aim of this study is to evaluate the potential cancer risks associated with emerging contaminants found in Colombian water sources by applying in silico predictive models, specifically the QSAR model. This in-silico approach offers the advantage of saving time and resources, reducing the need for costly testing or animal experimentation, and accelerating the identification of potentially hazardous chemical substances. The research aims to establish a quantitative relationship between the chemical structure of these emerging contaminants and their toxicity. By leveraging this computational approach, we aim to predict the toxicity and biological impact of

prevalent chemical substances in the water supply, providing insights into their potential role in diseases development. This study seeks to enhance our understanding of how specific environmental contaminants interact with biological systems, contributing to diseases risks, and to inform future regulatory and public health initiatives aimed at mitigating these risks.

## 2. Methodology

**Figure 1** presents a summary of the main methodological stages of the present study. Each of these topics will be discussed in the following sections.

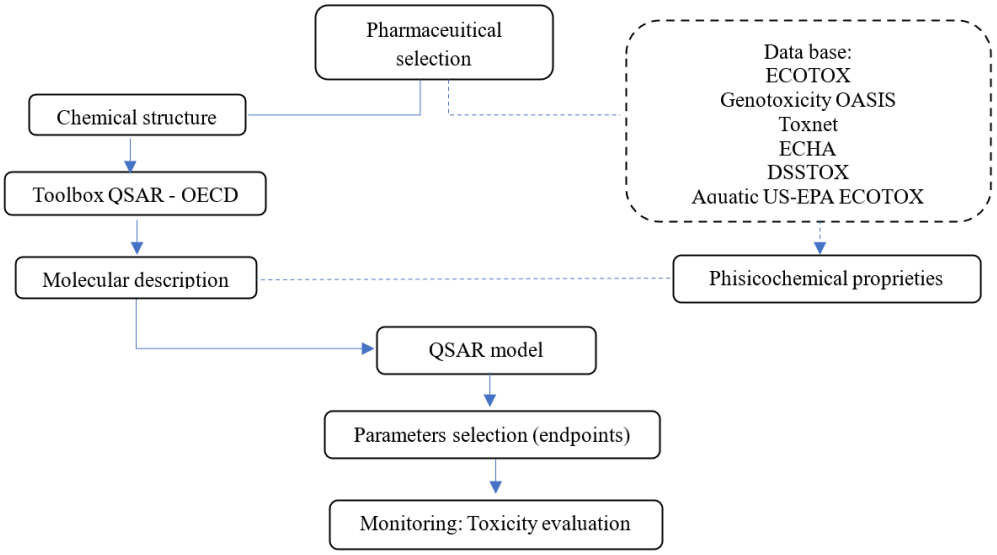


**Figure 1.** Flowchart summary.

The first stage of this study involved a comprehensive literature review aimed at identifying the main pharmaceutical compounds found in water sources across Colombian territory. The information was gathered based on scientific publications from indexed journals, focusing primarily on water matrices in various regions of the country, as well as the detected concentrations of these compounds. The identification and selection of representative sampling sites, according to the data found in the literature, aimed to include diverse water sources in Colombia, such as rivers, streams, and bodies of water in both urban and rural areas. This approach seeks to encompass a wide range of environmental conditions and levels of contamination. After selecting the pharmaceuticals of interest from the bibliographic review, those with the highest concentrations and presence in the water sources. These included Paracetamol, Carbamazepine, Loratadine, Sulfamethoxazole, Trimethoprim, Erythromycin, and Azithromycin. These compounds were evaluated and classified based on their structure, application, concentration, and CAS number. Subsequently, their physicochemical properties were analyzed using the QSAR tool developed by the OECD. After gathering information on the chemical structure of the selected pharmaceutical contaminants, the QSAR-ECOSAR tool was used to predict their carcinogenic and toxicological potential based on their molecular structure.

The in silico QSAR analysis was conducted using the OECD Toolbox (version 4.3.1) in the integrated model (OECD, Paris, France) following the interest for some

researchers working in water treatment [5,19,23]. First, the chemical structures of the drugs and their transformation and degradation products were imported into the QSAR platform. The ECOSAR model, based on the Structure-Activity-Relationship (SAR), was then applied. In ECOSAR, a profile analysis was conducted to classify the chemical structure of the pharmaceuticals and determine the relevant ECOSAR classes for both the contaminants and their degradation products. Subsequently, the model's response parameters were defined based on database information and their predictions. The following parameters of interest were evaluated for each drug: Aquatic toxicity in organisms, Developmental Toxicity/Teratogenicity, Metabolism Simulator, Biodegradability, DNA and Protein Impact, Chromosomal Impact, Carcinogenicity Alerts, Bioaccumulation, Mutagenicity, Toxicity Classification, Skin Irritation/Corrosion, along with the following analyzed databases: ECOTOX, Genotoxicity OASIS, Toxnet, ECHA, DSSTOX, Aquatic US-EPA ECOTOX.

The molecular transformations of the selected pharmaceuticals were evaluated using the QSAR-OECD Toolbox. This model is proposed because, according to Yordanova et al. [24], it is possible to sequentially apply the model to the parent structure (pharmaceutical compound) to assess its toxicological potential and also produce first-level metabolites and their potential toxicological impact. Once the initial metabolites were predicted, the same transformations were applied to produce the next metabolic level, and so on. The product of the probabilities of obtaining the following structures (*m*) and the probability of their metabolism for sequencing molecules (*n*) will yield the likelihood of obtaining the information of the previous metabolite (Equation (1)).

$$\mathrm{FC}(\rightarrow n) = FC(\rightarrow m)FC(m \rightarrow n) = FC(\rightarrow m)\left[1 - \prod\nolimits_{i-1}^{N}(1 - FC_i)\right]\frac{FC_n}{\sum_{i=1}^{N} FC_i} \quad (1)$$

where $FC(\rightarrow n)$ and $FC\ (\rightarrow m)$ are the probabilities for obtaining *n* and *m* metabolites from each pharmaceutical compounds, FC is the pharmaceutical structure, and $FC\ (\rightarrow m)\left[1 - \prod_{i-1}^{N}(1 - ATZ_i)\right]\frac{FC_n}{\sum_{i=1}^{N} FC_i}$ is the probability of *m* being metabolized in *n*.

## 3. Results and discussion

**Table 1** shows the detection of mayor pharmaceutical contaminants in water sources of Colombian Territory. It shows the presence and quantitative load of emerging contaminants in Colombian water, besides, it supports the exposome approach faced by local populations. The literature brings information about water sources include both urban and rural settings, such as Bogotá, Medellín, Tumaco, Antioquia, and the Gulf of Urabá, encompassing both hospital and municipal wastewater, reflecting a broad exposome spectrum relevant to environmental health. Outcomes show that pharmaceuticals such as Paracetamol, Diclofenac, and Azithromycin are persistent across multiple studies, with concentrations reaching up to 293.8 µg/L for Paracetamol in Tumaco and 39.2 µg/L in Bogotá. Besides, Ibuprofen also was reported at significantly high concentrations (32–41 µg/L) in university wastewater, which raises concerns regarding chronic exposure in urban populations. It is important to take into consideration that pharmaceuticals such as the Diclofenac, Azithromycin, and Carbamazepine are suspected to have endocrine-disrupting or

genotoxic properties [25,26]. In this way, to predict the potential impact of the previously detailed molecules (**Table 1**) as possible toxic and carcinogenic agents, the computational tool developed by the Organization for Economic Cooperation and Development (OECD), QSAR, was used. A literature review was conducted (**Table 1**), and the results indicated the presence of several recalcitrant molecules in water sources across different regions of the country. Therefore, the pharmaceuticals that were most persistent and found in higher concentrations were selected: Azithromycin, Carbamazepine, Erythromycin, Loratadine, Trimethoprim, Paracetamol and Sulfamethoxazole. The results of the predictions made by the QSAR model and the discussion of these are presented below.

**Table 1.** Detection of major pharmaceutical contaminants in water sources of the Colombian territory.

| Reference | Pharmaceutical | Concentration | Water source |
|---|---|---|---|
| Pemberthy et al. [25] | Diclofenac | 0.12 to 1.54 μg/L | Golfo de Urabá, Colombia |
| Serna-Galviz et al. [26] | Paracetamol | 293.8 μg/L | Waste water from hospital, Tumaco-Colombia. |
| | Diclofenac | 0.04 μg/L | |
| | Carbamazepine | 1.9 μg/L | |
| | Loratadine | 0.0015 μg/L | |
| | Sulfametoxasol | 8.1 μg/L | |
| | Trimetropim | 0.001 μg/L | |
| | Azitromicine | 0.36 μg/L | |
| | Eritromicine | 0.36 μg/L | |
| Lancheros et al. [27] | Ibuprofen | 32 and 41 μg/L | Waste water from University of Atlantico's campus, Barranquilla, Colombia. |
| Botero-Coy et al. [28] | Paracetamol | 39.2 μg/L for Bogotá | Waste water urban from Bogotá and Medellín |
| | Paracetamol | 9.2 μg/L for Antioquia | |
| | Azitromicine | 6.32 μg/L for Bogotá | |
| | Azitromicine | 5.84 μg/L for Antioquia | |

The first stage of this study aimed at defining the molecules of interest. These molecules were selected based on their characteristics as pharmaceutical compounds and their common usage within Colombian populations.

**Azithromycin:** According to QSAR correlating the effects of different pharmaceutical compounds of interest with their molecular structures, the results indicated that for Azithromycin, the mathematical model predicted the possible degradation of the drug into 23 secondary metabolites, each with different properties and impacts (**Figure 2**). Based on information obtained from the tool developed by OECD and the US-EPA (United States Environmental Protection Agency), which groups chemical substances prior to manufacturing based on shared chemical and toxicological properties in chemical categories, azithromycin was flagged as a concern due to its aliphatic amine structural part, as well as in its metabolites. One metabolite was flagged for acute toxicity due to the presence of the aldehyde functional group. The OECD-HPV (High Production Volume Chemicals) classification, which evaluates high-production chemicals to understand environmental and health risks, reported the classification of azithromycin and its metabolites as tertiary amines. In

the general mechanism results, azithromycin as a drug was found to have recalcitrant biodegradation. Additionally, the results indicated that, according to the Biowin 4 method, a computational model to estimate the likelihood that chemical compounds will be biodegraded by microorganisms under aerobic or anaerobic conditions in the early stages of their environmental exposure, some metabolites degrade over weeks to months. The predictive model also indicated that, according to Cramer's toxicological hazard classification, which classifies substances based on their toxicological potency through the evaluation of various criteria such as the presence of specific functional groups, water solubility, lipophilicity, chemical stability, etc., the drug and metabolites were flagged as high hazard (Class III). Furthermore, when evaluating aquatic acute toxicity using the OASIS method, a platform that provides algorithms and databases for predicting protein interactions based on sequence and structure, the results indicated that the presence of ester groups in the drug and metabolites posed a risk of acute toxicity. For specific parameters, the OASIS method indicated the presence of ester groups in the drug and metabolites, as well as the presence of aldehyde groups, suggesting the potential for damage to sensitive aquatic organisms over a short period, as reported in some studs [27,28].

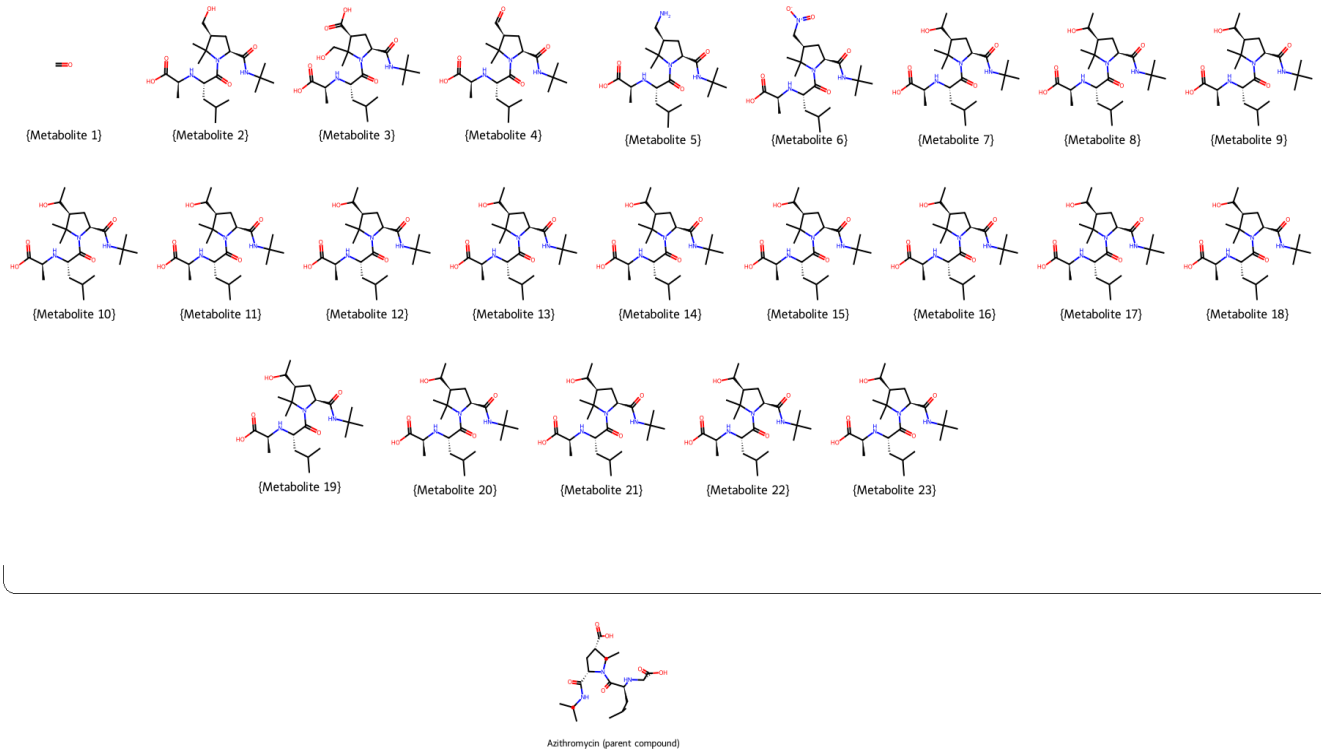


**Figure 2.** Azithromycin structure and its possible degradation metabolites.

Additionally, the tool highlighted the presence of an aliphatic amine functional group and an ester functional group in the evaluation of aquatic toxicity using the ECOSAR method. Regarding in vivo mutagenicity, ISS monitoring for micronucleus presence indicated DNA damage due to exposure to mutagenic agents, and azithromycin along with metabolites exhibited potential mutagenic alerts according to the mathematical model. This suggests that histaminergic receptors may be involved in the mutagenicity process in living organisms. If there is evidence that activation of

these receptors by a substance or mutagenic agent is related to the ability to induce mutations in the DNA of a living organism, then the presence of histamine receptors can be associated with in vivo mutagenicity. On the other hand, ISS did not declare any carcinogenicity alert (genotoxic or non-genotoxic) for azithromycin. This information is crucial for assessing the risk associated with the use or exposure to these substances. The results also determined that the computational tool did not flag protein binding for chromosomal aberration by OASIS for either the drug or metabolites, nor did it predict the potential of a substance to interact with proteins involved in DNA repair and chromosomal stability, leading to chromosomal aberrations such as breaks or structural changes in chromosomes, and the development of genetic diseases or cancer. According to the results obtained, azithromycin's toxicity and that of its metabolites, evaluated through repeated dose systemic exposure studies (HESS), which assess the effects of continuous exposure to chemicals in living organisms like rats or mice over several weeks or months, revealed the capacity of these molecules to cause liver damage, known as hepatotoxicity, supporting results reported in the literature [29].

**Table A1** in Appendix presents QSAR toxicity data for azithromycin. Acute aquatic toxicity studies on *Daphnia magna* showed that a concentration of 148 mg/L caused adverse effects in 50% of the organisms, including mortality and behavioral alterations [30]. The Lowest Observed Effect Concentration (LOEC) was 0.49 mg/L within 24 h, indicating sensitivity to low concentrations, while the No Observed Effect Concentration (NOEC) was 0.048 mg/L over 72 h, suggesting tolerance at this level [31]. Terrestrial toxicity studies against *Cryptosporidium parvum* reported a No Observed Effect Level (NOEL) of 15 mg/L after 48 h, demonstrating no adverse effects on terrestrial organisms at this concentration [32]. In vivo acute oral toxicity testing in rats found an LD50 of 2000 mg/kg, indicating moderate acute toxicity [database Acute Oral Toxicity DB]. Regarding the pharmacokinetic data using ADME models showed that 34% of intravenously administered azithromycin is absorbed in the human intestine [33]. The volume of distribution at steady state (VDss) was 1.52 log(L/kg), suggesting moderate tissue distribution beyond plasma [34]. Additionally, the half-life of azithromycin was approximately 69 h, reflecting a slow elimination rate and informing dosing intervals to maintain therapeutic levels [34].

**Carbamazepine:** According to the QSAR tool, carbamazepine metabolizes into 10 different compounds (**Figure 3**). The US-EPA identifies the phenol group in carbamazepine's chemical structure as responsible for its acute toxicity, since phenol is known to irritate skin, eyes, and the respiratory tract, and can damage internal organs if exposure is excessive or prolonged [35]. This raises concerns regarding the presence of carbamazepine or its metabolites in the environment or pharmaceutical products, as these compounds could pose toxic risks to public health. Further findings indicate that carbamazepine contains ammonium and primary amine groups, which according to OECD HPV guidelines, may influence the drug's degradation or transformation in environmental settings. This is particularly relevant because such transformations can potentially impact aquatic ecosystems and human health negatively. Importantly, carbamazepine itself exhibits low biodegradability, meaning it does not readily break down in the environment, which suggests a risk of prolonged exposure and accumulation. However, its metabolites have higher biodegradability, breaking down

within days to weeks.

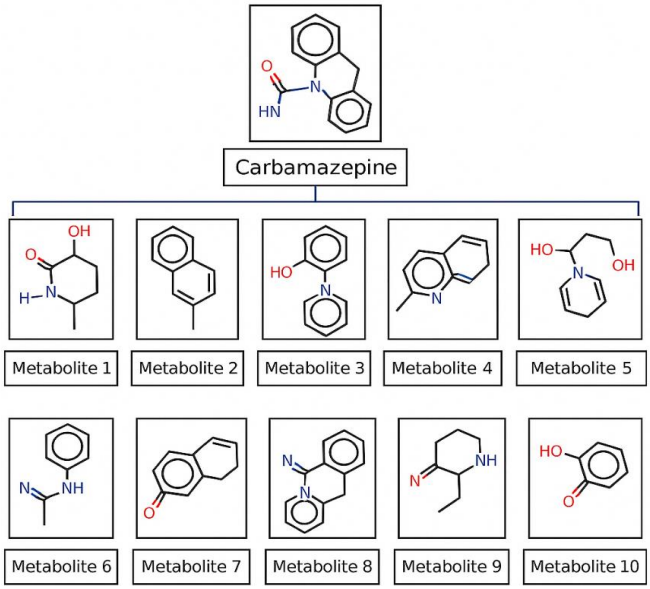


**Figure 3.** Carbamazepine structure and its possible degradation metabolites.

In toxicological classification, carbamazepine falls into Cramer Class III, indicating a high toxic hazard and significant potential risk to human health. Despite this, neither carbamazepine nor its metabolites showed alerts for in-vivo mutagenicity, suggesting no strong evidence of genetic mutations under test conditions. The oncological classification model identified the presence of aromatic amines and phenol functional groups in some metabolites, which are structural elements linked to carcinogenic potential. Although the ISS has not issued a carcinogenicity alert for carbamazepine itself, a structural alert was found in one metabolite containing an alpha, beta-unsaturated carbonyl group, which may exhibit carcinogenic properties. The carcinogenicity risk is thought to arise mainly from these compounds' ability to interact with biomolecules such as DNA and proteins through oxidation reactions and adduct formation, potentially leading to cancer. Finally, toxicity assessments using the HESS tool revealed that carbamazepine and its metabolites can induce hepatotoxicity, meaning they have the capacity to cause liver damage [36]. This highlights the importance of monitoring the presence and effects of carbamazepine and its derivatives in both environmental and clinical contexts.

**Table A2** in Appendix presents the results from QSAR tool-based toxicological studies on carbamazepine. According to a study in Chemosphere listed in the ECOTOX database, carbamazepine bioaccumulation was examined in *Raphidocelis subcapitata*. The Biological Accumulation Factor (BAF) over 24 h was 3.34 log(L/kg), indicating a significant ability of this species to accumulate carbamazepine in its tissues during short-term exposure. This accumulation can have implications for the aquatic food chain and overall environmental and human health [37]. Conversely, in *Ruditapes philippinarum*, bioaccumulation was assessed over 28 days, showing a Biological Concentration Factor (BCF) of −0.046 log(L/kg). This negative value suggests that the species either does not accumulate carbamazepine significantly or may eliminate it faster than it accumulates, indicating limited bioaccumulation

potential in this organism [38]. Aquatic toxicity studies on *Daphnia pulex*, from the ECOTOX database, evaluated a "Complete Life Cycle" test over 14 days with carbamazepine concentrations ranging from 0.0001 to 0.2 mg/L. This allowed assessment of effects on growth, reproduction, egg hatching, and offspring survival, providing comprehensive insights into sublethal effects on this key freshwater species [39]. Additionally, *Hyalella azteca* showed an EC10 (effective concentration causing effects in 10% of the population) of 2.4 mg/L during a 10-day exposure, meaning low levels could still affect a portion of this aquatic organism. The EC25 for the same species was 6.1 mg/L, and the LC25 (lethal concentration causing death in 25%) was 2.3 mg/L, showing that mortality occurs at concentrations relatively close to those causing sublethal effects [40].

For *Xenopus laevis*, the EC16 was greater than 100 mg/L over 96 h, indicating higher tolerance compared to other species studied [41]. The EC20 for *Ceriodaphnia dubia* was 0.163 mg/L over 14 days, revealing moderate sensitivity in this organism [42]. The green algae *Chlorella pyrenoidosa* showed an EC50 (median effective concentration) of 10.1 mg/L, reflecting its relative tolerance [43]. *Oryzias latipes* had an LC50 of 35.4 mg/L over 48 h, indicating a higher lethal threshold than other aquatic species [44]. A particularly sensitive species, *Stenonema* sp., showed adverse effects at a very low LOEC (Lowest Observed Effect Concentration) of 0.002 mg/L over 9 days, demonstrating that even trace levels of carbamazepine may cause ecological harm. In terrestrial toxicity studies, the fungus *Glomus intraradices* had an EC10 of 0.0033 mg/L over 28 days, confirming that carbamazepine can affect soil organisms at low concentrations [45]. Regarding human pharmacokinetics, carbamazepine's half-life was estimated at 1.87 days, indicating the time required for the body to eliminate half the drug through urine, feces, or respiration. An in vitro assay using *Salmonella typhimurium* showed no mutagenic effects under test conditions, suggesting low genotoxicity [46]. However, carbamazepine demonstrated positive photoinduced toxicity, including photoallergy and photosensitivity, implying potential adverse skin reactions upon exposure to sunlight or UV radiation [47].

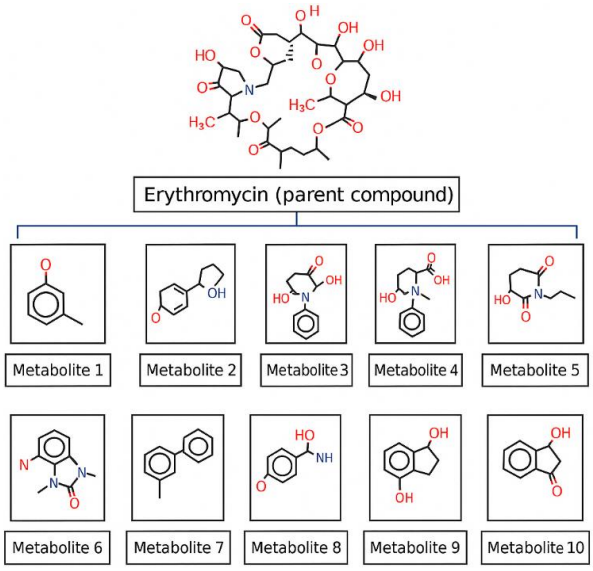


**Figure 4.** Erythromycin structure and its possible degradation metabolites.

**Erythromycin:** According to the QSAR tool findings, erythromycin decomposes into 10 distinct metabolites (**Figure 4**). The US-EPA classifies erythromycin as a toxicity alert due to the presence of aliphatic amine functional groups in both the parent compound and its metabolites. Additionally, the OECD HPV highlights the presence of tertiary amines in erythromycin and its metabolites as a key concern, since these groups can potentially form nitrosamines—chemical compounds known for their carcinogenic properties. Nitrosamines have been demonstrated to induce cancer in laboratory animals and have been linked to increased cancer risk in some human epidemiological studies [48].

Based on its molecular structure and the applied mathematical model, erythromycin and its metabolites exhibit recalcitrant biodegradation, meaning they are resistant to decomposition in the environment. This resistance can lead to environmental persistence, causing erythromycin to accumulate in soil, water, and other media over time. Such persistence poses risks to aquatic and terrestrial ecosystems and human health if these compounds enter food chains or contaminate drinking water sources. The biodegradation process, typically driven by microbial activity, may be slowed or inhibited depending on environmental conditions, compound concentrations, and the availability of appropriate microorganisms to facilitate decomposition. Furthermore, the detection of esters in erythromycin and aldehydes in one of its metabolites, as noted in Acute Toxicity-OASIS studies, suggests the formation of byproducts during decomposition or metabolism. These functional groups can influence the compound's biological and toxicological activity. Esters and aldehydes are known to interact with biological systems in various ways, potentially affecting toxicity and adverse effects.

In the context of Acute Toxicity-ECOSAR, the presence of aliphatic amines, esters, ketones, and alcohols in erythromycin and its metabolites further supports the possibility of byproduct formation during metabolism or degradation. The combined effects of these substances could negatively impact human health and the environment, especially with acute or chronic exposure to high concentrations. Regarding mutagenicity, the H-receptor result in the ISS in vivo model suggests that erythromycin and its metabolites might interact with histamine receptors in living organisms. While this interaction could have implications for genetic mutations, further studies are needed to clarify the relationship between histamine receptor binding and in vivo mutagenicity within the ISS evaluation framework. No carcinogenicity alerts were identified by the QSAR tool through ISS assessments, indicating no current evidence of carcinogenic risk. Similarly, the OASIS model did not detect any signals of chromosomal protein linkage disruption, suggesting that erythromycin and its metabolites likely do not pose significant risks of chromosomal damage based on available data. However, the primary oncological classification, which considers microbial metabolism, identified aldehydes in both erythromycin and its metabolites. This indicates that microbial metabolism may transform erythromycin into potentially carcinogenic metabolites containing aldehyde groups. Finally, the HESS model indicates that repeated, prolonged doses of erythromycin may induce hepatotoxicity—liver damage, inflammation, or dysfunction. This toxic effect was observed not only for erythromycin but also for its metabolites, underscoring potential risks associated with long-term exposure to this drug [49].

**Table A3** in Appendix presents the toxicological results for erythromycin as obtained through the QSAR model, providing valuable data on its aquatic and terrestrial toxicity as well as pharmacokinetic properties. The aquatic toxicity information for Paramecium caudatum shows an LC50 value of erythromycin between 10 and 24 mg/L for a 48-h exposure period. This means that at these concentrations, erythromycin is lethal to 50% of this species' population during the specified timeframe. Such data, sourced from the ECOTOX database, are crucial for assessing the impact of erythromycin on freshwater ecosystems and aquatic biodiversity [50]. Additionally, for Raphidocelis subcapitata, the ECOTOX database reports an Effective Concentration 10 (EC10) of 0.036 mg/L over a 72-h exposure. This indicates that this low concentration causes observable adverse effects in 10% of the population, highlighting the compound's toxicity even at minimal environmental levels [51]. For Litopenaeus vannamei, a shrimp species, the Lowest Observed Effect Concentration (LOEC) was recorded as higher than 50 mg/L over 48 h. This suggests that concentrations above this threshold lead to observable negative effects in this species, providing insight into safety margins for this organism in aquatic environments [52]. Regarding the green alga Chlorella vulgaris, the No Observed Effect Concentration (NOEC) was 12.5 mg/L during a 72-h exposure. This implies that erythromycin at this level does not produce significant adverse effects on this species, suggesting a higher tolerance relative to other species [53]. In terrestrial environments, data from the ECOTOX database on Triticum aestivum (wheat) reveal a Lowest Observed Effect Level (LOEL) for erythromycin at 1.5 mg/L in soil or growth medium over a one-week exposure. This concentration is sufficient to cause the lowest detectable adverse effect in wheat, indicating potential phytotoxicity at this level [54]. Correspondingly, the No Observed Effect Level (NOEL) for wheat was identified as 0.5 mg/L under the same exposure conditions, showing no adverse effects below this concentration [54]. A study examining the non-lethal resistance level (NR-LETH) for protozoa species exposed to erythromycin for 24 h reported a concentration of 0.05%, indicating that this level does not produce lethal effects on protozoa populations in terrestrial media, reinforcing its relative safety at low concentrations for some microorganisms [54].

The pharmacokinetic parameters obtained from the ADME database provide additional important insights. The PAMPA assay, which models passive absorption through membranes, recorded a low erythromycin absorption rate of 0.0002 cm/s, indicating very slow absorption [55]. The plasma protein binding percentage (PBexp) was approximately 83%, meaning that most erythromycin in circulation binds to plasma proteins, influencing its distribution, metabolism, and pharmacological activity. These binding characteristics are essential for understanding drug efficacy and toxicity [55]. Regarding elimination, the half-life of erythromycin reflects the time required for its concentration in the human body to reduce by half after equilibrium between administration and elimination is reached. This parameter is vital to understand drug persistence and dosing frequency [55]. Carcinogenicity testing using rodent models showed no evidence of erythromycin inducing cancer. The rodent carcinogenicity test, which involves prolonged exposure to detect malignant tumor formation, produced negative results for erythromycin, indicating a lack of carcinogenic potential under the tested conditions [56]. Furthermore, chromosomal aberration tests conducted in vitro demonstrated that erythromycin did not cause

chromosomal damage or disturbances in the tested cells or tissues. This suggests erythromycin lacks genotoxic effects in this assay system [56].

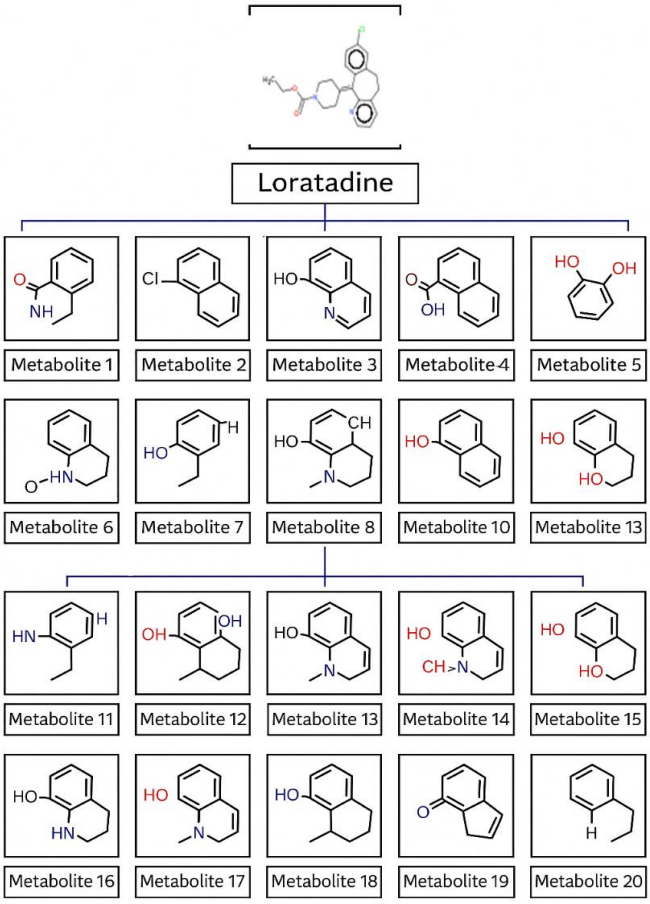


**Figure 5.** Loratadine structure and its possible degradation metabolites.

**Loratadine:** According to the mathematical model, loratadine breaks down into 20 distinct metabolites. Within the framework of the US-EPA, loratadine is classified as a neutral organic compound (**Figure 5**). This designation highlights its potential role as an environmental contaminant, a concern that extends to its metabolites as well. Being neutral means loratadine carries no net electrical charge, which can influence its environmental behavior, such as persistence, mobility, and toxicity. These factors are important when assessing how long the compound remains active in ecosystems and how it moves through soil and water [57]. The presence of the phenol functional group, especially in loratadine's metabolites, is significant in the context of acute toxicity according to US-EPA guidelines. Phenol groups are known for their toxic effects, including potential irritation and harm to living organisms, which could contribute to the overall toxicity profile of these substances.

The QSAR tool's biodegradation analysis shows that loratadine and its metabolites undergo primary biodegradation over a timescale of weeks. This finding means that while these compounds do degrade, the process is not immediate but neither is it extremely slow. Metabolites follow a similar biodegradation timeline, lasting from several days to weeks. This intermediate degradation rate indicates that loratadine and its metabolites can persist in the environment for extended periods,

which may have ecological implications. When assessing the chemical's risk based on molecular structure, the QSAR tool classifies loratadine and its metabolites as high hazard (Class III). This classification suggests these compounds pose a considerable risk to human health due to possible acute toxic effects, potential for causing chronic health issues, or reproductive toxicity. These risks highlight the need for careful monitoring and regulation of loratadine in environmental and pharmaceutical contexts.

Carcinogenicity assessments using the ISS model revealed positive alerts for the presence of alkyl carbamate and thiocarbamate groups in loratadine and its metabolites. Thiocarbamates, in particular, are chemical groups linked to tumor formation and carcinogenic potential in living organisms. This finding indicates that exposure to these metabolites could pose a cancer risk, necessitating further investigation and caution. Finally, the HESS model, which evaluates toxicity under repeated dosing conditions, indicates that loratadine may cause hepatotoxicity when administered over extended periods. Hepatotoxicity refers to liver damage, inflammation, or dysfunction resulting from exposure to certain chemicals or drugs. This adverse effect can significantly impact liver health and overall metabolism, reinforcing the importance of understanding long-term exposure risks to loratadine [57].

**Table A4** in Appendix summarizes the toxicological data obtained for loratadine through the QSAR tool, with an emphasis on its aquatic toxicity, pharmacokinetics, and potential carcinogenic risks. Regarding aquatic toxicity, data extracted from the ECOTOX database reveal that loratadine exhibits toxic effects on the species Danio rerio (zebrafish) within a concentration range of 0.0383 to 3.83 mg/L during a 24-h exposure period. This concentration range indicates that loratadine can negatively impact this aquatic species even at relatively low levels in the environment, highlighting the importance of monitoring its presence in water bodies [58]. Moreover, a study focusing on a longer exposure of 5 days showed that exposure to a loratadine concentration of 12.4 mg/L resulted in approximately 25% mortality in Danio rerio. This demonstrates the increased toxicity risk when aquatic organisms are subjected to sustained exposure at higher concentrations [58].

The Lowest Observed Effect Level (LOEL) was determined to be 0.0383 mg/L for loratadine in Danio rerio over 5 days, which is the minimum concentration where adverse effects begin to manifest. Correspondingly, the No Observed Effect Level (NOEL) was also found at 0.0383 mg/L, suggesting that below this concentration no harmful effects were detected in the fish during the same exposure period. These two values help define safety thresholds for loratadine contamination in aquatic ecosystems [58]. From a pharmacokinetic perspective, the QSAR model estimates that loratadine binds strongly to human serum proteins, with a plasma protein binding (PBexp) value of 97%. This high degree of protein binding affects the drug's distribution, metabolism, and clearance in the human body and is a key factor in its pharmacological behavior [59]. Regarding elimination, estimates show that loratadine's half-life in humans is approximately 0.35 days (8.4 h), indicating a relatively rapid clearance from the body. This pharmacokinetic property influences dosing schedules and potential accumulation risks during prolonged use [59].

In terms of carcinogenic potential, analysis of loratadine's metabolites reveals the presence of several functional groups known for their toxic, mutagenic, or

carcinogenic properties, including aldehydes, phenols, aliphatic amines, carbamates, and thiocarbamates. Of particular concern is the potential formation of nitrosamines from secondary and tertiary amines present in loratadine and its metabolites. Nitrosamines are widely recognized as potent carcinogens, capable of inducing genetic mutations and promoting cancer development in exposed organisms. This highlights the need for careful evaluation of the long-term health risks associated with loratadine exposure, especially in environmental and pharmacological contexts [60].

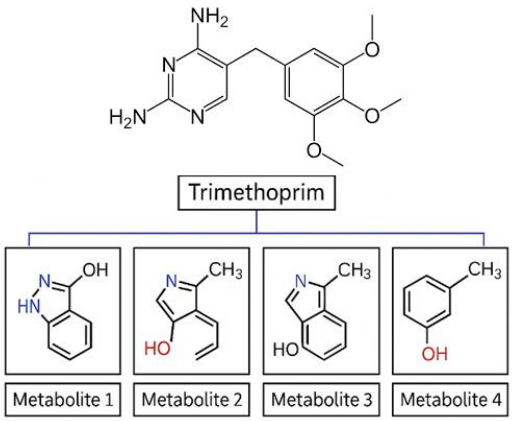


**Figure 6.** Trimethoprim structure and its possible degradation metabolites.

**Trimethoprim:** According to QSAR tool results, trimethoprim decomposes into four distinct metabolites. The OECD HPV classification identifies aliphatic acids in both trimethoprim and its metabolites (**Figure 6**), relevant for assessing health and environmental risks. Trimethoprim exhibits slow biodegradation, indicating resistance to breakdown in the environment through biological processes [61]. This suggests that trimethoprim either metabolizes into simpler products or is eliminated within a certain time frame, information useful for assessing its safety in humans and environmental impact. Risk assessment via QSAR classifies trimethoprim as high hazard (Class III), indicating potential significant adverse effects including acute toxicity, chronic effects, or reproductive toxicity. The primary oncological classification model detected aromatic amines in trimethoprim and aldehydes, aromatic amines, and phenols in its metabolites, suggesting possible carcinogenic risks [62]. Mutagenic groups such as aromatic amines, hydroxylamines, and derived esters were found in trimethoprim and its metabolites, associated with genetic mutation potential. ISS carcinogenicity evaluation confirmed these groups, indicating possible cancer risk. ECOSAR aquatic toxicity modeling identified anilines and aldehydes in trimethoprim and metabolites, indicating potential harm to aquatic organisms. Additionally, repeated-dose HESS studies suggest prolonged trimethoprim use may cause liver damage, inflammation, or dysfunction in rats, highlighting concerns for long-term exposure [62].

**Table A5** in Appendix summarizes the toxicity and environmental behavior of trimethoprim, based on QSAR modeling and empirical data extracted from various databases. Terrestrial bioaccumulation was assessed by determining the Biological Accumulation Factor (BAF) in the plant species *Brassica rapa*, with a recorded value of 38.3 mg/L after an 80-day exposure period. This value indicates that trimethoprim

can accumulate in plant tissues at concentrations approximately 38 times higher than those found in the surrounding soil or growth medium, suggesting significant bioaccumulation potential and raising concerns about transfer into terrestrial food webs [63]. Regarding aquatic toxicity, the ECOTOX database provides data indicating that trimethoprim concentrations ranging from 0.3 to 30 mg/L produce toxic effects in *Moina macrocopa,* a freshwater cladoceran. This species is often used as an indicator for aquatic ecosystem health due to its sensitivity to contaminants. The toxicity range highlights the potential risk posed by trimethoprim residues in freshwater environments where this concentration window may be present. Similarly, terrestrial toxicity data from the ECOTOX database report an effective concentration of 0.233 mg/L in soil that causes adverse effects on *Brassica rapa* over an 80-day exposure, indicating potential risks to plant health and growth in environments contaminated with this antibiotic [63]. Additional terrestrial toxicity metrics for other plants include an EC10 value greater than 10 mg/L for *Daucus carota* (carrot) over a 7-day exposure, implying that concentrations below this threshold do not significantly affect 10% of the population. Likewise, *Lactuca sativa* (lettuce) demonstrated an EC25 greater than 10 mg/L, suggesting no significant adverse effects in 25% of exposed organisms at this concentration. For *Cichorium endivia* (endive), the EC50 was measured at 86 mg/L, reflecting the concentration at which half of the tested population experienced toxic effects [47]. These values help establish toxicity benchmarks for various terrestrial plant species potentially exposed to trimethoprim residues.

In terms of acute toxicity, data extracted from the ChemIDplus database indicate an LD50 of 5300 mg/kg for rats, measured over 24 h. This relatively high LD50 suggests that trimethoprim has low acute toxicity in mammals, requiring a substantial dose to induce mortality in half of the tested population. From a pharmacokinetic perspective relevant to human exposure, ADME (Absorption, Distribution, Metabolism, and Excretion) data reveal that trimethoprim is efficiently absorbed in the human intestine, with an absorption percentage estimated at 98%. This high absorption rate underscores the drug's bioavailability when administered orally. The permeability coefficient, measuring the rate at which trimethoprim crosses intestinal epithelial cells in vitro, was found to be $1 \times 10^{-5}$ cm/s, reflecting moderate membrane transport capability under experimental conditions. In contrast, passive membrane permeability evaluated by the Parallel Artificial Membrane Permeability Assay (PAMPA) was comparatively low at 0.0003 cm/s, indicating limited passive diffusion through biological membranes, possibly due to the drug's physicochemical properties [64]. These comprehensive data from QSAR models and experimental studies highlight trimethoprim's potential for bioaccumulation in terrestrial plants, variable toxicity thresholds across aquatic and terrestrial species, relatively low acute mammalian toxicity, and efficient human absorption. This information is critical for assessing the environmental risks posed by trimethoprim residues in ecosystems as well as understanding its pharmacological behavior in humans, contributing to informed decisions on its safe use and environmental management.

**Paracetamol:** The QSAR tool results identified that Paracetamol breaks down into a metabolite (**Figure 7**). The results showed that the US-EPA issues an alert regarding the acute toxicity of paracetamol due to the presence of the phenol functional group. Although paracetamol does not contain phenol in its composition, phenolic

compounds, such as phenol, may be produced as byproducts during its synthesis or metabolism. This situation is concerning due to its potential impact on human health and the environment. For the OECD HPV, the presence of aliphatic acids in the paracetamol drug could be relevant for assessing its safety and potential risks to human health and the environment [23]. It was found that paracetamol does not biodegrade rapidly, indicating that this compound does not easily break down in the environment through biological processes such as biodegradation. The QSAR tool indicates that paracetamol has a primary biodegradation period of days, and metabolite ranges from days to weeks. Primary biodegradation refers to the initial decomposition process of a substance into simpler compounds due to the action of microorganisms. The fact that paracetamol and its metabolites undergo primary biodegradation implies that this process is not immediate, though it is not extremely slow either. When evaluating the risk level associated with a chemical substance based on its molecular structure, the QSAR tool alerts a low toxicological risk classification (Class I) according to Cramer for paracetamol, implying that this compound has a lower potential to cause significant adverse effects on human health. This suggests that, overall, paracetamol is less toxic or has a reduced capacity to generate acute, chronic, or reproductive adverse effects.

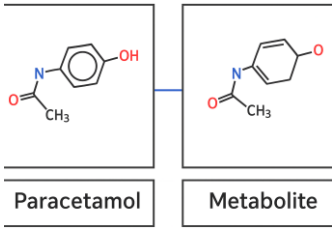


**Figure 7.** Paracetamol structure and its possible degradation metabolite.

**Table A6** in Appendix summarizes QSAR findings regarding the toxicity and pharmacokinetics of paracetamol. Aquatic toxicity data from the ECOTOX database indicate that paracetamol has an LC50 value of 1510 mg/L for *Danio rerio* (zebrafish), representing the concentration required to cause adverse effects in this species [65]. More sensitive species such as *Daphnia magna* showed an EC50 of 3.2 mg/L after 24 h of exposure, and an EC50 of 39.7 mg/L after 48 h, demonstrating the importance of exposure time on toxicity outcomes [65,66]. Lower EC50 values correspond to higher toxicity; thus, *Daphnia magna* is more sensitive to paracetamol than zebrafish. For green algae *Selenastrum capricornutum*, an IC25 (inhibitory concentration affecting 25% of the population) above 0.032 mg/L was reported after 72 h, indicating relatively low toxicity but sensitivity to paracetamol [66]. The protozoan *Paramecium tetraurelia* exhibits an IC50 of 0.0801 mg/L after just 2 h of exposure, signifying a relatively high sensitivity to paracetamol [66]. Regarding *Tetrahymena pyriformis*, an IGC50 of 999 mg/L over 48 h was reported, suggesting lower toxicity for this species [67]. Terrestrial toxicity data show a toxicity range of 300–1000 mg/kg for *Rattus norvegicus* during a 6-hour exposure period. Acute toxicity studies from the ZEBET database report an IC50 of 410 mg/L, representing the concentration needed to inhibit biological activity in 50% of exposed cells or organisms during acute exposure [68]. Further, the Acute Oral Toxicity Database lists an LD50 of 1940 mg/kg for rats, indicating the dose at which half of the test population would be expected to die within

24 h after oral administration [69].

Pharmacokinetic data from the EDETOX and ADME databases show that dermal absorption of paracetamol is about 3.7% of the applied dose, indicating limited skin penetration under typical conditions [59]. Oral absorption in humans is relatively high, with approximately 85% of ingested paracetamol absorbed through the intestinal lining [64]. The permeability coefficient (Kp) for paracetamol's membrane absorption is 0.0016 cm/h, suggesting a modest rate of permeation across biological membranes [64]. Plasma protein binding (PBexp) experiments indicate that roughly 8% of paracetamol binds to plasma proteins, leaving 92% freely available to distribute throughout the body [59]. These findings present a comprehensive toxicological and pharmacokinetic profile of paracetamol, illustrating its varying toxicity across species and exposure times, alongside its absorption and distribution characteristics in humans. This information is essential for evaluating environmental risks and human health implications associated with paracetamol exposure.

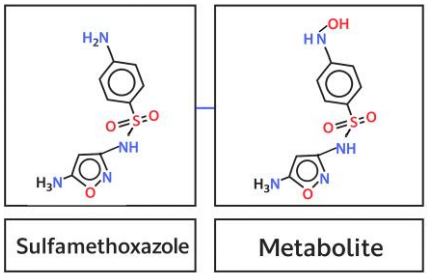


**Figure 8.** Sulfamethoxazole structure and its possible degradation metabolite.

**Sulfamethoxazole:** The QSAR tool analysis revealed that sulfamethoxazole decomposes into one metabolite (**Figure 8**). The US-EPA has issued an acute toxicity alert for sulfamethoxazole due to the presence of the aniline functional group, indicating potential toxic risks to human health and the environment. According to the OECD HPV framework, the presence of aliphatic acids in both sulfamethoxazole and its metabolite is relevant for safety assessments, as these groups may influence potential risks. Both the parent compound and its metabolite exhibit slow biodegradation rates, suggesting environmental persistence and potential bioaccumulation, which raises concerns about long-term exposure and ecosystem impact [70]. Primary biodegradation for sulfamethoxazole and its metabolite is estimated to occur over days to weeks, indicating a moderate rate of initial breakdown by microbial activity. The QSAR tool classifies both compounds in Cramer Class III, reflecting a high toxicological risk due to possible acute toxicity, chronic effects, or reproductive toxicity. The primary oncological classification identified aromatic amines in sulfamethoxazole, compounds often linked to increased carcinogenic risk. In vivo mutagenicity tests (ISS) detected positive signals for N-Aromatic Amines, hydroxylamine, and ester derivatives in sulfamethoxazole and its metabolite, implying a potential to induce genetic mutations in living cells. The carcinogenicity evaluation via ISS also revealed positive associations with benzyl esters, methylation, and hydroxylamine, suggesting these chemical features may contribute to carcinogenesis through DNA methylation or the formation of reactive metabolites that damage DNA. The QSAR and ISS data indicate that sulfamethoxazole and its metabolite possess

chemical groups associated with mutagenic and carcinogenic potential, emphasizing the need for careful risk assessment regarding human health and environmental safety [71].

**Table A7** in Appendix presents toxicity data for sulfamethoxazole across various environmental compartments and species. Terrestrial bioaccumulation studies using the Bioaccumulation Factor (BAF) found that sulfamethoxazole accumulates in *Brassica rapa* tissues at a concentration approximately 80.5 times higher than in the surrounding environment, based on an 80-day exposure [63]. Aquatic toxicity results indicate that sulfamethoxazole concentrations between 0.988 and 127 mg/L cause toxic effects in *Poeciliopsis lucida*. Additionally, an EC10 value of 0.153 mg/L was reported for *Lemna gibba* after 7 days, showing that this concentration caused effects in 10% of the exposed plants without significant adverse outcomes [63]. For *Caenorhabditis elegans*, the EC15 was $1 \times 10^{-5}$ mg/L (15% effect over 72 h), and the EC20 was $1 \times 10^{-5}$ mg/L (20% effect over 96 h), highlighting high sensitivity to sulfamethoxazole [72]. The Lowest Observed Effect Concentration (LOEC) for *Raphidocelis subcapitata* was 1.5 mg/L, indicating the minimum concentration at which measurable adverse effects occur. Terrestrial toxicity data include an EC10 of 0.0021 mg/L for *Daucus carota* (carrot), showing no significant adverse effects at this low concentration [47]. The EC25 for *Lactuca sativa* (lettuce) was reported as >10 mg/L over 5 days, suggesting relatively low toxicity at concentrations up to 10 mg/L [72]. Furthermore, an EC50 of 0.0407 mg/L was observed for *Glomus intraradices* after 21 days, indicating a moderate toxicity level in this soil fungus [47]. In acute toxicity studies, the LD50 for rats was found to be 6200 mg/kg, meaning that this oral dose would cause death in approximately 50% of exposed rats within 24 h under test conditions [69].

Despite chemical diversity, common structural motifs such as amines, phenols, aldehydes, and carbamates were frequently associated with hepatotoxicity and potential genotoxicity. These findings align with known mechanisms of oncogenesis, such as DNA alkylation, oxidative stress, and endocrine disruption. This study confirms that QSAR-based modeling is a valuable tool for preliminary toxicological screening, enabling prioritization of emerging contaminants within environmental health assessments. However, predictive limitations underscore the need for complementary experimental validation, including long-term in vivo and mechanistic studies, to support regulatory action and public health protection. It is important to take into consideration that QSAR models rely on statistical correlations between chemical structures and known biological activities. However, their predictive accuracy is highly dependent on the quality, diversity, and size of the training datasets. The study highlights the potential oncological risks of metabolites, but without in vitro or in vivo validation, these remain theoretical risks. As highlight the QSAR models cannot confirm metabolic activation pathways, only predict potential structural liabilities. To establish real oncological risk, complementary methods such as long-term bioassays, genotoxicity assays, and omics-based profiling are needed.

## 4. Conclusion

The systematic analysis of various drugs and their metabolites using QSAR modeling tools has revealed crucial information about their potential carcinogenic

risks. The application of QSAR allowed for the identification of chemical structures and functional groups that may be associated with adverse health effects, including carcinogenicity. The results obtained suggest that while azithromycin presents a low cancer risk, certain metabolites, particularly its metabolites, show signs of carcinogenicity. This finding is associated with the presence of alkylcarboxylic acids, which may induce direct DNA damage or promote tumor growth through non-genotoxic mechanisms. These results highlight the need for a detailed analysis of metabolites, which could have significant implications for public health. The evaluation of carbamazepine showed that several of its metabolites contain potentially dangerous functional groups, such as phenols and epoxides, capable of causing DNA damage and promoting carcinogenesis. Although not all metabolites indicated mutagenic or carcinogenic effects in in vivo studies, bioaccumulation in aquatic organisms and hepatotoxicity in repeated exposure studies are concerns that need to be addressed. Mathematical models used did not detect a significant carcinogenicity risk for erythromycin, although its resistance to biodegradation and the possible formation of nitrosamines are risk factors that should be considered. This case highlights how the environmental persistence of certain compounds can increase the risk of prolonged exposure in humans and ecosystems. The analysis of loratadine and its metabolites indicates that some of the functional groups present could induce genetic mutations, suggesting a potential oncological risk associated with prolonged exposures. Nitrosamines formed from amines represent an additional concern in terms of carcinogenicity. Trimethoprim also revealed a high carcinogenicity risk, particularly with metabolites containing chemical groups associated with mutations. The toxicity observed in aquatic organisms highlights the need for careful management of this compound in the environmental context. Although paracetamol has been classified as non-carcinogenic in traditional studies, the ability of some of its metabolites to induce cellular transformation raises concerns about its long-term safety.

The results were interesting, however, it is important to take into consideration that, even if eco toxicity is a valid tool to predict the impact of pollutants on the environment, the accuracy of QSAR predictions depends on the quality and diversity of the training data used to develop the model. To obtain more precise results, it is recommended to use experimental toxicity data and well-validated QSAR models specific.

**Author contributions:** Conceptualization, GJG; methodology, GJG and VJD; investigation, GJG; writing—original draft, GJG and VJD; writing—review and editing, VJD; project administration, PEVV. All authors have read and agreed to the published version of the manuscript.

**Institutional review board statement:** Not applicable.

**Informed consent statement:** Not applicable.

**Conflict of interest:** The authors declare no conflict of interest.

## References


1. Jurado-Davila V, Toffoli de Oliveira J, Féris LA. Analytical Perspective and Modeling of Breakthrough Curves for a Fixed-Bed Column of Modified Dolomite by Calcination and Ultrasound for Phosphate Immobilization: Experimental Design, Bayesian Statistics, and Data Prediction. Industrial & Engineering Chemistry Research. 2023; 63(1): 551–565. doi: 10.1021/acs.iecr.3c03477
2. Lu W, Zhang C, Su P, et al. Research progress of modified natural zeolites for removal of typical anions in water. Environmental Science: Water Research & Technology. 2022; 8(10): 2170–2189. doi: 10.1039/d2ew00478j
3. Jurado Dávila I, Rosset M, Perez Lopez O, et al. Removal of reactive red 120 in aqueous solution using mg-hydrotalcites as adsorbents solids: kinetics and isotherms. Revista Internacional de Contaminación Ambiental. 2020; 36(2). doi: 10.20937/rica.53539
4. Dávila IVJ, Hübner JVM, Nunes KGP, et al. Caffeine Removal by Adsorption: Kinetics, Equilibrium Thermodynamic and Regeneration Studies. The Journal of Solid Waste Technology and Management. 2021; 47(1): 95–103. doi: 10.5276/jswtm/2021.95
5. Jurado-Davila V, Dall Agnol G, Reggiane de Carvalho Costa L, et al. Degradation and mineralization of atrazine by ozonation: A toxicological prediction by QSAR toolbox. Environmental Nanotechnology, Monitoring & Management. 2024; 22: 101002. doi: 10.1016/j.enmm.2024.101002
6. Chaturvedi P, Shukla P, Giri BS, et al. Prevalence and hazardous impact of pharmaceutical and personal care products and antibiotics in environment: A review on emerging contaminants. Environmental Research. 2021; 194: 110664. doi: 10.1016/j.envres.2020.110664
7. Omolaoye TS, Skosana BT, Ferguson LM, et al. Implications of Exposure to Air Pollution on Male Reproduction: The Role of Oxidative Stress. Antioxidants. 2024; 13(1): 64. doi: 10.3390/antiox13010064
8. Al Aukidy M, Verlicchi P, Jelic A, et al. Monitoring release of pharmaceutical compounds: Occurrence and environmental risk assessment of two WWTP effluents and their receiving bodies in the Po Valley, Italy. Science of The Total Environment. 2012; 438: 15–25. doi: 10.1016/j.scitotenv.2012.08.061
9. Khan S, Naushad Mu, Govarthanan M, et al. Emerging contaminants of high concern for the environment: Current trends and future research. Environmental Research. 2022; 207: 112609. doi: 10.1016/j.envres.2021.112609
10. Martínez-Oviedo A, Monterrubio-Martínez E, Tuxpan-Vargas J. Assessing the water contaminants in San Luis Potosi and its effects on its inhabitants: An interdisciplinary study on environmental contamination and public health. Journal of Hazardous Materials. 2024; 464: 132828. doi: 10.1016/j.jhazmat.2023.132828
11. Zhang R, Zhu S, Zhang Z, et al. Long-term variations of air pollutants and public exposure in China during 2000–2020. Science of The Total Environment. 2024; 930: 172606. doi: 10.1016/j.scitotenv.2024.172606
12. Sung H, Ferlay J, Siegel RL, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA: A Cancer Journal for Clinicians. 2021; 71(3): 209–249. doi: 10.3322/caac.21660
13. Bray F, Laversanne M, Weiderpass E, et al. The ever-increasing importance of cancer as a leading cause of premature death worldwide. Cancer. 2021; 127(16): 3029–3030. doi: 10.1002/cncr.33587
14. Chang CQ, Yesupriya A, Rowell JL, et al. A systematic review of cancer GWAS and candidate gene meta-analyses reveals limited overlap but similar effect sizes. European Journal of Human Genetics. 2013; 22(3): 402–408. doi: 10.1038/ejhg.2013.161
15. Puyang C, Han J, Guo H. Degradation of emerging contaminants in water by a novel non-thermal plasma/periodate advanced oxidation process: Performance and mechanisms. Chemical Engineering Journal. 2024; 483: 149194. doi: 10.1016/j.cej.2024.149194
16. Jurado-Davila V, Oshiro GP, Estumano DC, et al. Immobilization of Marbofloxacin for Water Treatment by Adsorption in Batch Scale and Fixed-Bed Column: Applying of Monte Carlo Bayesian Modeling. Industrial & Engineering Chemistry Research. 2024; 63(22): 9976–9987. doi: 10.1021/acs.iecr.4c01103
17. Jurado-Davila V, Reolon LS, Nunes KGP, et al. Classical and Bayesian Computational Statistics Applied to Acetylsalicylic Acid Mitigation in Aqueous Solutions: Study of Batch Scale, Kinetic Modeling, and Fixed-Bed Column Adsorption. Industrial & Engineering Chemistry Research. 2024; 63(22): 9943–9954. doi: 10.1021/acs.iecr.4c00050
18. Singh AK, Bilal M, Iqbal HMN, et al. In silico analytical toolset for predictive degradation and toxicity of hazardous

pollutants in water sources. Chemosphere. 2022; 292: 133250. doi: 10.1016/j.chemosphere.2021.133250
19. Jurado-Davila V, Nunes KGP, Oshiro GP, et al. Marbofloxacin mitigation by simultaneous process of adsorption and advanced oxidative process: An approach to the degradation mechanism and evaluation of the eco-toxicological impact using the QSAR tool. Journal of Environmental Chemical Engineering. 2023; 11(6): 111423. doi: 10.1016/j.jece.2023.111423
20. Li F, Sun G, Fan T, et al. Ecotoxicological QSAR modelling of the acute toxicity of fused and non-fused polycyclic aromatic hydrocarbons (FNFPAHs) against two aquatic organisms: Consensus modelling and comparison with ECOSAR. Aquatic Toxicology. 2023; 255: 106393. doi: 10.1016/j.aquatox.2022.106393
21. Russom CL, Bradbury SP, Broderius SJ, et al. Predicting modes of toxic action from chemical structure: Acute toxicity in the fathead minnow (Pimephales promelas). Environmental Toxicology and Chemistry. 1997; 16(5): 948–967. doi: 10.1002/etc.5620160514
22. Sun P, Zhao W. Strategies to Control Human Health Risks Arising from Antibiotics in the Environment: Molecular Modification of QNs for Enhanced Plant–Microbial Synergistic Degradation. International Journal of Environmental Research and Public Health. 2021; 18(20): 10610. doi: 10.3390/ijerph182010610
23. Jurado-Davila V, Silva Silveira F, Reggiane de Carvalho Costa L, et al. Paracetamol and Atenolol mitigation by Fenton and adsorption in-simultaneous process – Adsorbent regeneration and QSAR eco-toxicity prediction. Environmental Nanotechnology, Monitoring & Management. 2024; 22: 100972. doi: 10.1016/j.enmm.2024.100972
24. Yordanova D, Kuseva C, Tankova K, et al. Using metabolic information for categorization and read-across in the OECD QSAR Toolbox. Computational Toxicology. 2019; 12: 100102. doi: 10.1016/j.comtox.2019.100102
25. Pemberthy M D, Padilla Y, Echeverri A, et al. Monitoring pharmaceuticals and personal care products in water and fish from the Gulf of Urabá, Colombia. Heliyon. 2020; 6(6): e04215. doi: 10.1016/j.heliyon.2020.e04215
26. Serna-Galvis EA, Silva-Agredo J, Botero-Coy AM, et al. Effective elimination of fifteen relevant pharmaceuticals in hospital wastewater from Colombia by combination of a biological system with a sonochemical process. Science of The Total Environment. 2019; 670: 623–632. doi: 10.1016/j.scitotenv.2019.03.153
27. Lancheros JC, Madera-Parra CA, Caselles-Osorio A, et al. Ibuprofen and Naproxen removal from domestic wastewater using a Horizontal Subsurface Flow Constructed Wetland coupled to Ozonation. Ecological Engineering. 2019; 135: 89–97. doi: 10.1016/j.ecoleng.2019.05.007
28. Botero-Coy AM, Martínez-Pachón D, Boix C, et al. 'An investigation into the occurrence and removal of pharmaceuticals in Colombian wastewater.' Science of The Total Environment. 2018; 642: 842–853. doi: 10.1016/j.scitotenv.2018.06.088
29. Klopčič I, Markovič T, Mlinarič-Raščan I, et al. Endocrine disrupting activities and immunomodulatory effects in lymphoblastoid cell lines of diclofenac, 4-hydroxydiclofenac and paracetamol. Toxicology Letters. 2018; 294: 95–104. doi: 10.1016/j.toxlet.2018.05.022
30. Puri M, Gandhi K, Kumar MS. Degradation of endocrine-disrupting chemicals using various sulfate radical activation methods: kinetics and mechanism. Journal of Chemical Technology & Biotechnology. 2023; 98(10): 2401–2414. doi: 10.1002/jctb.7461
31. Han Y, Hu LX, Liu T, et al. Discovering transformation products of pharmaceuticals in domestic wastewaters and receiving rivers by using non-target screening and machine learning approaches. Science of The Total Environment. 2024; 948: 174715. doi: 10.1016/j.scitotenv.2024.174715
32. Styszko K, Bolesta W, Worek J, et al. Tracking nonregulated micropollutants in sewage sludge: Antimicrobials, OH-PAHs, and microplastics — Environmental risks, fertilizer implications and energy considerations. Energy Reports. 2025; 13: 4756–4768. doi: 10.1016/j.egyr.2025.04.013
33. Guardiano MG, Carena L, Pazzi M, et al. Simultaneous heterogeneous photo-Fenton degradation of azithromycin and clarithromycin in wastewater treatment plant effluent. Journal of Water Process Engineering. 2025; 69: 106870. doi: 10.1016/j.jwpe.2024.106870
34. Fotouh A, Abdel-Maguid DS, Abdelhaseib M, et al. Pathological and pharmacovigilance monitoring as toxicological imputations of azithromycin and its residues in broilers. Veterinary World; 2024.
35. Yang W, Huang X, Wu Q, et al. Acute toxicity of polychlorinated diphenyl ethers (PCDEs) in three model aquatic organisms (Scenedesmus obliquus, Daphnia magna, and Danio rerio) of different trophic levels. Science of The Total Environment. 2022; 805: 150366. doi: 10.1016/j.scitotenv.2021.150366
36. Anthony A, Meloni BPM Reynoldson JA, et al. Assessment of drugs against Cryptosporidium parvum using a simple in vitro screening method. FEMS microbiology letters. 1999; 178(2): 227–233. doi: 10.1016/S0378-1097(99)00361-4

37. Shiba K, Shindo N, Sakai O. Pharmacokinetics of Azithromycin in Patients. New Acrolides, Azalides, and Streptogramins in Clinical Practice; 1995.
38. Luke DR, Foulds G, Cohen SF, et al. Safety, toleration, and pharmacokinetics of intravenous azithromycin. Antimicrobial Agents and Chemotherapy. 1996; 40(11): 2577–2581. doi: 10.1128/aac.40.11.2577
39. Li J, Ma M, Wang Z. In vitro profiling of endocrine disrupting effects of phenols. Toxicology in Vitro. 2010; 24(1): 201–207. doi: 10.1016/j.tiv.2009.09.008
40. Bai Z, Jia K, Chen G, et al. Carbamazepine induces hepatotoxicity in zebrafish by inhibition of the Wnt/β-catenin signaling pathway. Environmental Pollution. 2021; 276: 116688. doi: 10.1016/j.envpol.2021.116688
41. Vernouillet G, Eullaffroy P, Lajeunesse A, et al. Toxic effects and bioaccumulation of carbamazepine evaluated by biomarkers measured in organisms of different trophic levels. Chemosphere. 2010; 80(9): 1062–1068. doi: 10.1016/j.chemosphere.2010.05.010
42. Almeida Â, Freitas R, Calisto V, et al. Chronic toxicity of the antiepileptic carbamazepine on the clam Ruditapes philippinarum. Comparative Biochemistry and Physiology Part C: Toxicology & Pharmacology. 2015; 172–173: 26–35. doi: 10.1016/j.cbpc.2015.04.004
43. Dussault ÈB, Balakrishnan VK, Sverko E, et al. Toxicity of human pharmaceuticals and personal care products to benthic invertebrates. Environmental Toxicology and Chemistry. 2008; 27(2): 425–432. doi: 10.1897/07-354r.1
44. Richards SM, Cole SE. A toxicity and hazard assessment of fourteen pharmaceuticals to Xenopus laevis larvae. Ecotoxicology. 2006; 15(8): 647–656. doi: 10.1007/s10646-006-0102-4
45. Lamichhane K, Garcia SN, Huggett DB, et al. Chronic Effects of Carbamazepine on Life-History Strategies of Ceriodaphnia dubia in Three Successive Generations. Archives of Environmental Contamination and Toxicology. 2012; 64(3): 427–438. doi: 10.1007/s00244-012-9845-5
46. Kim Y, Choi K, Jung J, et al. Aquatic toxicity of acetaminophen, carbamazepine, cimetidine, diltiazem and six major sulfonamides, and their potential ecological risks in Korea. Environment International. 2007; 33(3): 370–375. doi: 10.1016/j.envint.2006.11.017
47. Hillis DG. Effects of selected pharmaceuticals on arbuscular mycorrhizal fungi. University of Guelph; 2008.
48. Onoue S, Tsuda Y. Analytical Studies on the Prediction of Photosensitive/Phototoxic Potential of Pharmaceutical Substances. Pharmaceutical Research. 2006; 23(1): 156–164. doi: 10.1007/s11095-005-8497-9
49. Song B, Zhou Y, Jin H, et al. Selective and sensitive determination of erythromycin in honey and dairy products by molecularly imprinted polymers based electrochemical sensor. Microchemical Journal. 2014; 116: 183–190. doi: 10.1016/j.microc.2014.05.010
50. Tang L, Feng H, Luan X, et al. Occurrence, distribution, and behaviors of erythromycin A, production byproducts, transformation products, and resistance genes in a full-scale erythromycin A production wastewater treatment system. Water Research. 2023; 245: 120640. doi: 10.1016/j.watres.2023.120640
51. El-Bassat R, Touliabah H, Harisa G. Toxicity of four pharmaceuticals from different classes to isolated plankton species. African Journal of Aquatic Science. 2012; 37(1): 71–80. doi: 10.2989/16085914.2012.666376
52. Ardila C, Bedoya-García J, González-Arroyave D. Antimicrobial resistance in patients with endodontic infections: A systematic scoping review of observational studies. Australian Endodontic Journal. 2022; 49(2): 386–395. doi: 10.1111/aej.12680
53. Williamson DH, Maroudas NG, Wilkie D. Induction of the cytoplasmic petite mutation in Saccharomyces cerevisiae by the antibacterial antibiotics erythromycin and chloramphenicol. Molecular and General Genetics MGG. 1971; 111(3): 209–223. doi: 10.1007/bf00433106
54. Richter MF, Drown BS, Riley AP, et al. Predictive compound accumulation rules yield a broad-spectrum antibiotic. Nature. 2017; 545(7654): 299–304. doi: 10.1038/nature22308
55. Welling PG, Craig WA, Welling PG, et al. Pharmacokinetics of Intravenous Erythromycin. Journal of Pharmaceutical Sciences. 1978; 67(8): 1057–1059. doi: 10.1002/jps.2600670809
56. Madia F, Kirkland D, Morita T, et al. EURL ECVAM Genotoxicity and Carcinogenicity Database of Substances Eliciting Negative Results in the Ames Test: Construction of the Database. Mutation Research/Genetic Toxicology and Environmental Mutagenesis. 2020; 854–855: 503199. doi: 10.1016/j.mrgentox.2020.503199
57. Jabber EJ, Sarhat ER, Wadee SA, et al. Histological and biochemical evaluation of the effect of desloratadine drug in hepatic tissues. Journal of Hunan University Natural Sciences. 2021; 48(9).

58. Panzica-Kelly JM, Zhang CX, Augustine-Rauch KA. Optimization and Performance Assessment of the Chorion-Off [Dechorinated] Zebrafish Developmental Toxicity Assay. Toxicological Sciences. 2015; 146(1): 127–134. doi: 10.1093/toxsci/kfv076
59. Votano JR, Parham M, Hall LM, et al. QSAR Modeling of Human Serum Protein Binding with Several Modeling Techniques Utilizing Structure−Information Representation. Journal of Medicinal Chemistry. 2006; 49(24): 7169–7181. doi: 10.1021/jm051245v
60. Nabizadeh S, Barzegar F, Arabameri M, et al. Chronic daily intake, probabilistic carcinogenic risk assessment and multivariate analysis of volatile N-nitrosamines in chicken sausages. International Journal of Environmental Health Research. 2024; 35(5): 1194–1203. doi: 10.1080/09603123.2024.2383399
61. Wang S, Wang J. Trimethoprim degradation by Fenton and Fe(II)-activated persulfate processes. Chemosphere. 2018; 191: 97–105. doi: 10.1016/j.chemosphere.2017.10.040
62. Otuechere CA, Madarikan G, Simisola T, et al. Virgin coconut oil protects against liver damage in albino rats challenged with the anti-folate combination, trimethoprim-sulfamethoxazole. Journal of Basic and Clinical Physiology and Pharmacology. 2013; 25(2): 249–253. doi: 10.1515/jbcpp-2013-0059
63. Herklotz PA, Gurung P, Vanden Heuvel B, et al. Uptake of human pharmaceuticals by plants grown under hydroponic conditions. Chemosphere. 2010; 78(11): 1416–1421. doi: 10.1016/j.chemosphere.2009.12.048
64. Cao Y, Bairam A, Jee A, et al. Investigating the Mechanism of Trimethoprim-Induced Skin Rash and Liver Injury. Toxicological Sciences. 2021; 180(1): 17–25. doi: 10.1093/toxsci/kfaa182
65. Kühn K. Postoperative sedation and analgesia in children (German). Anesthesia in childhood: Symposium Berlin (German). Springer Berlin Heidelberg; 1985.
66. Kim D, Tan EY, Jin Y, et al. Effects of imatinib mesylate on the pharmacokinetics of paracetamol (acetaminophen) in Korean patients with chronic myelogenous leukaemia. British Journal of Clinical Pharmacology. 2011; 71(2): 199–206. doi: 10.1111/j.1365-2125.2010.03810.x
67. Schultz RK. Physics of tablet compaction: Viscoelastic analysis of pharmaceutical granule deformation behavior. University of Minnesota; 1993.
68. Clemedson C, Barile FA, Chesne CG et al. MEIC evaluation of acute systemic toxicity. Part VII. Prediction of human toxicity by results from testing of the first 30 reference chemicals with 27 further in vitro assays. Alternatives to Laboratory Animals. 2000; 28(suppl 1): 161–200.
69. Kikkawa R, Fujikawa M, Yamamoto T, et al. In vivo hepatotoxicity study of rats in comparison with in vitro hepatotoxicity screening system. The Journal of Toxicological Sciences. 2006; 31(1): 23–34. doi: 10.2131/jts.31.23
70. Jurado-Davila V, L. Oliveira R, Oshiro GP, et al. Removal of Sulfadimethoxine in Aqueous Solution by Adsorption on Mesoporous Carbon/Titania Composites: Batch Scale, Fixed-Bed Column, and Bayesian Modeling. Industrial & Engineering Chemistry Research. 2024; 63(48): 20848–20861. doi: 10.1021/acs.iecr.4c03249
71. Zhang H, Quan H, Song S, et al. Comprehensive assessment of toxicity and environmental risk associated with sulfamethoxazole biodegradation in sulfur-mediated biological wastewater treatment. Water Research. 2023; 246: 120753. doi: 10.1016/j.watres.2023.120753
72. Yu Z, Jiang L, Yin D. Behavior toxicity to Caenorhabditis elegans transferred to the progeny after exposure to sulfamethoxazole at environmentally relevant concentrations. Journal of Environmental Sciences. 2011; 23(2): 294–300.

# Appendix

**Table A1.** Toxicity results from the QSAR computational tool for azithromycin.

| **Toxicity** | | | |
|---|---|---|---|
| **Parameter** | **Measured** | **Value** | **Complementary information** |
| Aquatic toxicity | EC50 | 148 mg/L | Species: *Daphnia magna*<br>Reference: Ecotoxicol. Environ. Saf. 197:7 p.<br>Database: ECOTOX |
| Aquatic toxicity | LOEC | 0.49 mg/L | Species: *Daphnia magna*<br>Reference: Ecotoxicol. Environ. Saf. 197:7 p.<br>Database: ECOTOX |
| Aquatic toxicity | NOEC | 0.048 mg/L | Species: *Daphnia magna*<br>Reference: Ecotoxicol. Environ. Saf. 197:7 p.<br>Database: ECOTOX |
| Aquatic toxicity | NOEL | 15 mg/L | Species: *Cryptosporidium parvum*<br>Reference: FEMS Microbiol. Lett. 178(2): 227-233<br>Database: ECOTOX |
| Aquatic toxicity | LD50 | 2000 mg/kg | Species: *Rat*<br>Reference: ChemIDplus Database, U.S. National Library of Medicine<br>Database: Acute Oral toxicity |
| Absorption | Intestinal/human | 34 % | Reference: Clin Pharmacokinet 1993 25:370-374. Database: ADME |
| Distribution | VDss | 1.52 log(L/kg) | Database: ADME |
| Removal | Half-life | 69 h | Database: ADME |

**Table A2.** Results obtained by the QSAR computational tool for carbamazepine according to its toxicity.

| **Toxicity** | | | |
|---|---|---|---|
| **Parameter** | **Measured** | **Value** | **Complementary information** |
| Aquatic bioaccumulation | BAF | 3.34 log(L/kg) | Species: *Raphidocelis subcapitata*<br>Reference: Chemosphere80(9): 1062-1068<br>Database: ECOTOX |
| Aquatic bioaccumulation | BCF | −0.046 log(L/kg) | Species: *Ruditapes philippinarum*<br>Reference: Comp. Biochem. Physiol. C Toxicol. Pharmacol. 172-173:26-35<br>Database: ECOTOX |
| Aquatic toxicity | EC10 | 2.4 mg/L | Species: *Hyalella azteca*<br>Reference: Environ. Toxicol. Chem. 27(2): 425-432<br>Database: ECOTOX |
| Aquatic toxicity | EC16 | > 100 mg/L | Species: *Xenopus laevis*<br>Reference: Ecotoxicology15(8): 647-656<br>Database: ECOTOX |
| Aquatic toxicity | EC20 | 0.163 mg/L | Species: *Ceriodaphnia dubia*<br>Reference: Arch. Environ. Contam. Toxicol.64(3): 427-438<br>Database: ECOTOX |
| Aquatic toxicity | EC25 | 6.1 mg/L | Species: *Hyalella azteca*<br>Reference: Environ. Toxicol. Chem. 27(2): 425-432<br>Database: ECOTOX |
| Aquatic toxicity | EC50 | 10.1 mg/L | Species: *Chlorella pyrenoidosa*<br>Reference: Environ. Toxicol. Pharmacol. 33(2): 344-352<br>Database: ECOTOX |
| Aquatic toxicity | LC25 | 2.3 mg/L | Species: *Hyalella azteca*<br>References: Environ. Toxicol. Chem. 27(2): 425-432<br>Database: ECOTOX |

**Table A2.** (*Continued*).

| **Toxicity** | | | |
|---|---|---|---|
| **Parameter** | **Measured** | **Value** | **Complementary information** |
| Aquatic toxicity | LC50 | 35.4 mg/L | Species: *Oryzias latipes*<br>Time: 48 h<br>Reference: Environ. Int. 33(3): 370-375<br>Database: ECOTOX |
| Aquatic toxicity | LOEC | 0.002 mg/L | Species: *Stenonema sp.*<br>Reference: Ecotoxicology 23(9): 1701-1712<br>Database: ECOTOX |
| Aquatic toxicity | NOEC | 0.001–0.001 mg/L | Species: *Ruditapes philippinarum*<br>Database: ECOTOX |
| Terrestrial toxicity | - | 0.5-2 mg/kg | Species: *Schoenoplectus tabernaemontani*<br>Reference: Environ. Pollut.181:98-106<br>Database: ECOTOX |
| Terrestrial toxicity | EC10 | 0.0033 mg/L | Species: *Glomus intraradices*<br>Time: 28 d<br>Reference: Chemosphere 73(3): 344-352<br>Database: ECOTOX |
| Acute toxicity | LD50 | 1960 mg/kg | Species: *rat*<br>Time: 24 h<br>Database: Acute Oral toxicity |
| Absorption | Intestinal/human | 100% | Reference: Cao, D., Wang, J., Zhou, R. et al, J Chem Info Model, 2012, 52, 1132-1137<br>Database: ADME |
| Absorption | MDCK | $5 \times 10^{-5}$ cm/s | Database: ADME |
| Absorption | PAMPA | 0.0002 cm/s | Database: ADME |
| Distribution | PBexp(%) | 75% | Reference: Structure, J. Med. Chem. 2006, 49, 7169-7299<br>Database: ADME |
| Removal | Half-life | 1.87 d | Species: *Human*<br>Reference: Environ. Sci. Technol Environ, 48, 723−730.<br>Database: MamTKDB |
| Carcinogenicity | Dosage level | ≥ 600 mg/kg bw/d | Species: *mouse*<br>Reference: Toxicity data on pharmaceuticals (US FDA) |
| Carcinogenicity | NOEL | $\leq 3.2 \times 10^{3}$ mg/kg bw/d | Species: *Hammster*<br>Reference: Toxicity data on pharmaceuticals (US FDA) |
| Genetics toxicity | Genetic mutation | Negative<br>Genetic mutation I | Species: *Salmonella typhimurium*<br>Reference: Mutation Research, 168 (1986) 69-240<br>Database: Genotoxicity OASIS |
| Photoinduced toxicity | Photoalergic | Positive<br>Photosensibility | Reference: J. Dermatol. Sci. 85, 4–11<br>Database: Photosensitivity |
| Repeated dose toxicity | Dosage | ≥ 200 mg/kg bw/d | Species: *rat*<br>Database: Toxicity data on pharmaceuticals (US FDA) |
| Repeated dose toxicity | NOEL | ≤ 100 mg/kg bdwt/d | Species: *canis*<br>Database: Toxicity data on pharmaceuticals (US FDA) |

**Table A3.** Toxicological results obtained by the QSAR computational tool for erythromycin.

| **Toxicity** | | | |
|---|---|---|---|
| **Parameter** | **Measured** | **Value** | **Complementary information** |
| Aquatic toxicity | - | 10–24 mg/L | Species: *Paramecium caudatum*<br>Reference: Afr. J. Aquat. Sci. 37(1): 71-80<br>Database: ECOTOX |
| Aquatic toxicity | EC10 | 0.036 mg/L | Species: *Raphidocelis subcapitata*<br>Reference: Water Res. 47(6): 2050-2064<br>Database: ECOTOX |
| Aquatic toxicity | EC25 | > 1 mg/L | Species: *Lemna gibba*<br>Reference: Environ. Toxicol. Chem. 23(2): 371-382<br>Database: ECOTOX |
| Aquatic toxicity | EC50 | 0.2 mg/L | Species: *Nostoc sp*.<br>Reference: Environ. Toxicol. Chem. 26(4): 601-606<br>Database: ECOTOX |
| Aquatic toxicity | LOEC | > 50 mg/L | Species: *Litopenaeus vannamei*<br>Reference: J. Aquat. Anim. Health 4(4): 262-270<br>Database: ECOTOX |
| Aquatic toxicity | NOEC | 12.5 mg/L | Species: *Chlorella vulgaris*<br>Reference: Chemosphere 57(11): 1733-1738<br>Database: ECOTOX |
| Terrestrial toxicity | ET50 | 120 mg/100 ml diet | Species: *Agria affinis*<br>Reference: J. Insect Physiol. 16(9): 1769-1782<br>Database: ECOTOX |
| Terrestrial toxicity | LOEL | 1.5 mg/L | Species: *Triticum aestivum*<br>Reference: Ecotoxicol. Environ. Saf. 87:70-79<br>Database: ECOTOX |
| Terrestrial toxicity | NOEL | 0.5 mg/L | Species: *Triticum aestivum*<br>Reference: Ecotoxicol. Environ. Saf. 87:70-79<br>Database: ECOTOX |
| Terrestrial toxicity | NR-LETH | 0.05% | Species: *Protozoa*<br>Reference: Appl. Microbiol. 15(5): 1014-1019<br>Database: ECOTOX |
| Absorption | PAMPA | 0.0002 cm/s | Database: ADME |
| Distribution | PBexp(%) | 83% | Reference: Structure, J. Med. Chem. 2006, 49, 7169-7435<br>Database: ADME |
| Distribution | VDss | −0.022 log(L/kg) | Reference: J. Pharm. Sci. 67: 1057-1059.<br>Database: ADME |
| Removal | Half life | 2 h | Reference: J. Pharm. Sci. 67: 1057-1059.<br>Database: ADME |
| Carcinogenicity | Carcinogenicity | Negative Carcinogenicity I (ISSCAN) | Database: EURL ECVAM Genotoxicity and Carcinogenicity Consolidated Database of Ames Negative Chemicals |
| Genetic toxicity | Chromosomal disruption | Negative Mutagenicity I (ECVAM) | Database: EURL ECVAM Genotoxicity and Carcinogenicity Consolidated Database of Ames Negative Chemicals |

**Table A4.** Toxicological results obtained by the QSAR computational tool for loratadine.

| **Toxicity** | | | |
|---|---|---|---|
| **Parameter** | **Measured** | **Value** | **Complementary information** |
| Aquatic toxicity | - | 0.0383–3.83 mg/L | Species: *Danio rerio*<br>Reference: Reprod. Toxicol. 33(2): 155-164<br>Database: ECOTOX |
| Aquatic toxicity | LC25 | 12.4 mg/L | Species: *Danio rerio*<br>Reference: Reprod. Toxicol. 33(2): 155-164<br>Database: ECOTOX |
| Aquatic toxicity | LOEL | 0.0383 mg/L | Species: *Danio rerio*<br>Reference: Reprod. Toxicol. 33(2): 155-164<br>Database: ECOTOX |
| Aquatic toxicity | NOEL | 0.0383 mg/L | Species: *Danio rerio*<br>Reference: Reprod. Toxicol.33(2): 155-164<br>Database: ECOTOX |
| Aquatic toxicity | NOEL | 0.0383 mg/L | Species: *Danio rerio*<br>Reference: Reprod. Toxicol. 33(2): 155-164<br>Database: ECOTOX |
| Absorption | Intestinal/human | 90% | Reference: J Chem Info Model, 2012, 52, 1132-1137<br>Database: ADME |
| Distribution | PBexp(%) | 97% | Reference: J. Med. Chem. 2006, 49, 7169-7573<br>Database: ADME |
| Removal | Half-life | 0.35 d | Species:*Human*<br>Reference: Sci. Technol Environ, 48, 723−730.<br>Database: MamTKDB |

**Table A5.** Toxicological results obtained by the QSAR computational tool for trimethoprim.

| **Toxicity** | | | |
|---|---|---|---|
| **Parameter** | **Measured** | **Value** | **Complementary information** |
| Terrestrial bioaccumulation | BAF | 38.3 mg/L | Species: *Brassica rapa*<br>Reference: Chemosphere 78(11): 1416-1421<br>Database: ECOTOX |
| Aquatic toxicity | - | 0.3–30 mg/L | Species: *Moina macrocopa*<br>Reference: Ecotoxicology 17(6): 526-538<br>Database: ECOTOX |
| Terrestrial toxicity | - | 0.233 mg/L | Species: *Brassica rapa*<br>Reference: Chemosphere 78(11): 1416-1421<br>Base de datos: ECOTOX |
| Terrestrial toxicity | EC10 | > 10 mg/L | Species: *Daucus carota*<br>Reference: Arch. Environ. Contam. Toxicol. 60(2): 220-232<br>Database: ECOTOX |
| Terrestrial toxicity | EC25 | > 10 mg/L | Species: *Lactuca sativa*<br>Reference: Arch. Environ. Contam. Toxicol. 60(2): 220-232<br>Database: ECOTOX |
| Terrestrial toxicity | EC50 | 86 mg/L | Species: *Cichorium endivia*<br>Reference: Environ. Pollut. 157(5): 1636-1642<br>Database: ECOTOX |
| Terrestrial toxicity | LOEC | > 300 mg/kg | Species: *Oryza sativa*<br>Reference: Environ. Pollut. 157(5): 1636-1642<br>Database: ECOTOX |
| Terrestrial toxicity | NOEC | 0.1 mg/L | Species: *Oryza sativa*<br>Reference: Environ. Pollut. 157(5): 1636-1642<br>Database: ECOTOX |

**Table A5.** (*Continued*).

| **Toxicity** | | | |
|---|---|---|---|
| **Parameter** | **Measured** | **Value** | **Complementary information** |
| Acute toxicity | LD50 | 5300 mg/kg | Species: *rat*<br>Database: Acute Oral toxicity |
| Absorption | Intestinal/human | 98% | Reference: J Chem Info Model, 2012, 52, 1132-1137<br>Database: ADME |
| Distribution | VDss | 0.176 log(L/kg) | Reference: J. Pharm. Biomed. Anal. 1: 293-299.<br>Database: ADME |
| Removal | Half life | 0.4 d | Species: *Human*<br>Reference: Environ. Sci. Technol Environ, 48, 723−730.<br>Database: Half-Life Mammalian Toxicokinetic Database MamTKDB |
| Genetic mutation | Genetic mutation | Positive<br>Genetic mutation I | Species: *Salmonella typhimurium*<br>Reference: CCRIS database,Toxnet databases<br>Database: Bacterial mutagenicity ISSSTY |

**Table A6.** Toxicological results obtained by the QSAR computational tool for paracetamol.

| **Toxicity** | | | |
|---|---|---|---|
| **Parameter** | **Measured** | **Value** | **Complementary information** |
| Aquatic toxicity | - | 1510 mg/L | Species: *Danio rerio*<br>Reference: Proc. Natl. Acad. Sci. U.S.A.107(40): 17315-17320<br>Database: ECOTOX |
| Aquatic toxicity | EC0 | 3.2 mg/L | Species: *Daphnia magna*<br>Reference: Water Res. 23(4): 495-499<br>Database: ECOTOX |
| Aquatic toxicity | EC50 | 39.7 mg/L | Species: *Daphnia magna*<br>Reference: Ecotoxicology 19(4): 662-669<br>Database: ECOTOX |
| Aquatic toxicity | IC25 | > 0.032 mg/L | Species: *Selenastrum capricornutum*<br>Reference: Environ. Toxicol. Chem. 25(8): 2163-2176<br>Database: ECOTOX |
| Aquatic toxicity | IC50 | 0.0801 mg/L | Species: *Paramecium tetraurelia*<br>Reference: Int. J. Biosci. 3(9): 132-141<br>Database: ECOTOX |
| Aquatic toxicity | IGC50 | 999 mg/L | Species: *Tetrahymena pyriformis*<br>Reference: The Science of the Total Environment, 109/110, 581-587.<br>Database: Aquatic OASIS |
| Terrestrial toxicity | - | $300 \times 10^3$ mg/kg | Species: *Rattus norvegicus*<br>Reference: J. Toxicol. Sci. 31(1): 23-34<br>Database: ECOTOX |
| Terrestrial toxicity | EC50 | $> 3 \times 10^3$ mg/L | Species: *Lactuca sativa*<br>Reference: Environ. Sci. Pollut. Res. Int. 23(22): 22530-22541<br>Database: ECOTOX |
| Terrestrial toxicity | LD50 | $1.95 \times 10^3$ mg/kg | Species: *Aedes aegypti*<br>Reference: Drug Metab. Dispos. 13(1): 14-17<br>Database: ECOTOX |
| Terrestrial toxicity | LOEC | 80 mg | Species: *Boiga irregularis*<br>Reference: J. Wildl. Manag. 65(2): 356-365<br>Database: ECOTOX |
| Acute toxicity | IC50 | 410 mg/L | Database: ZEBET |
| Acute toxicity | LD50 | 1940 mg/kg | Species: *Rat*<br>Database: Acute Oral toxicity |

**Table A6.** (*Continued*).

| **Toxicity** | | | |
|---|---|---|---|
| **Parameter** | **Measured** | **Value** | **Complementary information** |
| Absorption | Dermic | 3.7% | Reference: EDETOX<br>Database: ADME |
| Absorption | Intestinal/human | 85% | Reference: Cao, D., Wang, J., Zhou, R. et al, J Chem Info Model, 2012, 52, 1132-1137 |
| Absorption | Kp | 0.0016 cm/h | Reference: EDETOX<br>Database: ADME Database |
| Distribution | PBexp(%) | 8% | Reference: J. Med. Chem. 2006, 49, 7169-7189<br>Database: ADME |
| Removal | Half-life | 0.104 d | Species: *Human*<br>Reference: Environ. Sci. Technol Environ, 48, 723−730.<br>Database: Half-Life Mammalian Toxicokinetic Database MamTKDB |
| Cancerogenity | Cancerogenity | Negative Cancerogenity I (ISSCAN) | Species: *rats*<br>Database: Genotoxicity & Carcinogenicity ECVAM |
| Cancerogenity | Cell transformation | Positive Cell transformation I | Species: *mouse*<br>Reference: OECD 2007<br>Database: Cell Transformation Assay ISSCTA |
| Cancerogenity | TD50 | 495 mg/kg bdwt/d | Species: *Rat*<br>Reference: TR 394; final call in CPDB differs due to additional data<br>Database: Carcinogenic Potency Database (CPDB) |
| Genetic toxocity | Chromosomal distruption | Negative Micronucleus I | Reference: Mutat Res. 1979 Jan; 66 (1):33-43.<br>Database: Genotoxicity OASIS |
| Genetic toxocity | ADN damage and repair | Positive Mutagenicity I (ECVAM) | Reference: EURL ECVAM genotoxicity and carcinogencity<br>Database: Genotoxicity & Carcinogenicity ECVAM |
| Genetic toxocity | In vitro cytogenicity | Positive Chromosomal disruption I | Species: *mammalian cells*<br>Reference: Mutation Research 584 (2005) 1-256<br>Database: Genotoxicity OASIS |

**Table A7.** Toxicological results obtained by the QSAR computational tool for sulfamethoxazole.

| **Ecotoxicity** | | | |
|---|---|---|---|
| **Parameter** | **Measured** | **Value** | **Complementary information** |
| Terrestrial bioaccumulation | BAF | 80.5 mg/L | Species: *Brassica rapa*<br>Reference: Chemosphere78(11): 1416-1421<br>Database: ECOTOX |
| Aquatic toxicity | - | 0.988–127 mg/L | Species: *Poeciliopsis lucida*<br>Reference: Toxicology196:41-55<br>Database: ECOTOX |
| Aquatic toxicity | EC10 | 0.153 mg/L | Species: *Lemna gibba*<br>Reference: Environ. Toxicol. Chem.23(2): 371-382<br>Database: ECOTOX |
| Aquatic toxicity | EC15 | $1 \times 10^{-5}$ mg/L | Species: *Caenorhabditis elegans*<br>Reference: J. Environ. Sci.23(2): 294-300<br>Database: ECOTOX |
| Aquatic toxicity | EC20 | $2 \times 10^{-5}$ mg/L | Species: *Caenorhabditis elegans*<br>Referencia: J. Environ. Sci.23(2): 294-300<br>Database: ECOTOX |
| Aquatic toxicity | LOEC | 1.5 mg/L | Species: *Raphidocelis subcapitata*<br>Referencia: Environ. Pollut.172:23-32<br>Base de datos: ECOTOX |

**Table A7.** (*Continued*).

| **Ecotoxicity** | | | |
|---|---|---|---|
| **Parameter** | **Measured** | **Value** | **Complementary information** |
| Terrestrial toxicity | EC10 | 0.0021 mg/L | Species: *Daucus carota*<br>Referencia: Chemosphere73(3): 344-352<br>Base de datos: ECOTOX |
| Terrestrial toxicity | EC25 | > 10 mg/L | Species: *Lactuca sativa*<br>Reference: Arch. Environ. Contam. Toxicol.60(2): 220-232<br>Database: ECOTOX |
| Terrestrial toxicity | EC50 | 0.0407 mg/L | Species: *Glomus intraradices*<br>Reference: Chemosphere 73(3): 344-352<br>Base de datos: ECOTOX |
| Acute toxicity | LD50 | 6200 mg/kg | Species: *rat*<br>Base de datos: Acute Oral toxicity DB |
| Absorption | Intestinal/human | 100% | Reference: J Chem Info Model, 2012, 52, 1132-1137<br>Database: ADME |
| Distribution | VDss | −0.523 log(L/kg) | Reference: J. Pharm. Biomed. Anal. 1: 293-299.<br>Database: ADME |
| Removal | Half-Life | 0.408 d | Species: *Human*<br>Database: Half-Life Mammalian Toxicokinetic |