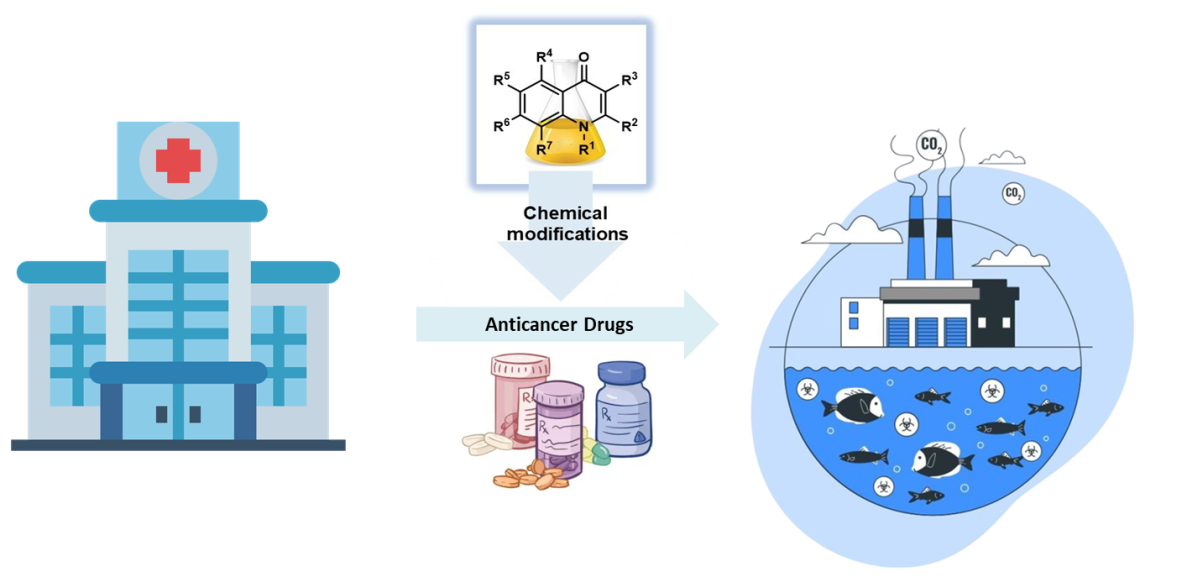
*Review Article*

**Ecological Risks of Anticancer Drugs in Aquatic Ecosystems: Monitoring and Advanced Remediation Strategies**

ABSTRACT

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| --- |
| **Aims:** This study seeks to evaluate the ecological risks associated with anticancer drugs in aquatic environments, emphasizing their environmental behavior, toxicity, and persistence. It examines the presence of specific anticancer compounds and assesses their effects on aquatic organisms utilizing data derived from the EU "Cytothreat" project.  **Study design:** Experimental and observational research integrating laboratory toxicity assessments and environmental sampling to evaluate the ecological risks of anticancer pharmaceuticals.  **Methodology:** Five-fluorouracil (5FU), cisplatin (CDDP), imatinib mesylate (IM), and etoposide (ET) are four commonly used anticancer drugs that work in different ways. They were tested on different indicator species, such as cyanobacteria, algae, higher plants, rotifers, crustaceans, fish, and human and fish-derived cell lines. Toxicity tests looked at short-term, medium-term, and long-term exposure situations. The Polar Organic Chemical Integrative Sampler (POCIS) was used to keep an eye on anticancer drugs in wastewater. It found capecitabine, ifosfamide, and cyclophosphamide, which were steadily absorbed over a 15-day period. We used site-specific sampling rates to figure out the average environmental concentrations.  **Results:** Cisplatin was determined to be the most dangerous substance, with its hazard concentration ranking in the 5th percentile among the drugs tested. Acute toxicity rankings against Daphnia magna showed the following order of strength: alkylating agents > antibiotics > endocrine therapy agents > platinum complexes > antimetabolites. POCIS consistently detected capecitabine at 32 ± 1 ng·L⁻¹ over five days, demonstrating a robust correlation with concentrations measured in grab samples.  **Conclusion:** Anticancer drugs have measurable ecological risks because they are toxic and stay in water systems for a long time. POCIS and standardized ecotoxicological assays are two examples of monitoring tools that can accurately describe environmental exposures. This information can help us understand the need for better wastewater treatment and pharmaceutical stewardship to reduce the impact of these new contaminants. |



Graphical Abstract

*Keywords: Anticancer Drugs, Aquatic Toxicity, Ecological Risks, Wastewater remediation.*

1. INTRODUCTION

The purpose of these chemicals is to inhibit and destroy cancer cells. These chemicals are among the most toxic that have been produced commercially and have been classified as “dangerous” under the European Commission's Waste Framework Directive (Dannarm et al., 2025; Jureczko & Przystaś, 2024). Their discharge into wastewater has raised concerns about their potential negative impact on aquatic ecosystems (Parker & Miller, 2024). Therefore, efforts have been made to develop effective handling strategies to understand their fate in the environment and evaluate their toxic effects on various organisms (de Souza et al., 2024; Parker & Miller, 2024). These pollutants include new chemicals such as medicines, hormone disruptors, and toxins, as well as tiny biological contaminants like bacteria and viruses that are found in soil, sediments, groundwater, industrial wastewater, city wastewater, aquaculture wastewater, and both freshwater and ocean environments. Anticancer agents, often poorly metabolized, are excreted unchanged through feces and urine into hospitals and domestic wastewater (Sangwan et al., 2025). Therefore, their detection has frequently been reported in contaminated aquatic ecosystems. A high concentration of the agents, however, has been found in the wastewater of the pharmaceutical plants where anticancer drugs are manufactured (Nassour et al., 2021; Nassour et al., 2020; Nassour et al., 2024; Ahmed et al., 2025). Many anticancer agents are persistent or “pseudo-persistent” organic pollutants in wastewater and are often difficult to remove by secondary treatment methods (Hamidon et al., 2024). Tertiary treatment in wastewater treatment plant effluent (STEP) poses a threat to aquatic ecosystems (Xie et al., 2024). The presence of anticancer agents in aquatic environments raises concerns about the ecosystem, as many of these agents bioaccumulate and interact directly or indirectly with the DNA of marine organisms (Sugumaran et al., 2022; Abdul et al., 2025; Abdulrahman et al., 2025).

Many anticancer drugs also don't target specific cells, so they attack both tumors and healthy cells. This can cause mutagenic, teratogenic, cytotoxic, and endocrine-disrupting effects, as shown in Fig. 1. (Fasiku et al., 2025). The bioaccumulation of these agents in aquatic environments could lead to long-term ecological concerns, including disruptions to food chains and biodiversity loss (Tison et al., 2024). Despite the introduction of anticancer agents into aquatic ecosystems, the potential risks associated with these agents have not yet been well characterized. Among 100 approved cancer drugs by the US Food and Drug Administration (FDA), 33 of them have been detected in aquatic ecosystems, 26 of them are classified as cytotoxic agents with various mechanisms of action (alkylating agents, antimetabolites, anticancer antibiotics, etc.), and seven substances have internal targets (Olivier et al., 2021). Concentration and occurrence are discussed and compared with acute and chronic toxicity parameters to create a risk index (Macko et al., 2021). Predictions of bioavailability and environmental sustainability are also provided using quantitative structure-activity relationship (QSAR) models. We provide discussions of uncertainties and make recommendations for future research to better characterize the risks of anticancer agents in aquatic ecosystems (Macko et al., 2021). Moreover, there is a growing need for advanced wastewater treatment technologies, such as advanced oxidation processes (AOPs), membrane filtration, and bioaugmentation, to efficiently remove these persistent pollutants from wastewater before it is released into the environment (“Innovative Approaches to Sustainable Wastewater Treatment,” 2024). Regulatory frameworks and monitoring programs must be implemented to address the environmental risks posed by anticancer agents, ensuring that their production, use, and disposal are managed in an environmentally sustainable manner (A. A.-W. Ali et al., 2018; Thakkar, 2025; R. Ali et al., 2025).



Fig.1. Worldwide Presence and Environmental Hazard of Anticancer Pharmaceuticals in Aquatic Ecosystems (Hughes, Thompson, & Kasprzyk-Hordern, 2021)

Reports have documented the teratogenic effects of some anticancer agents (AD), including 5-FU, capecitabine, cisplatin, doxorubicin, etoposide, and imatinib (Table 1). These anticancer agents seem to interfere with the development of embryos and change cell division rates in onion root cells, indicating that different living things and groups of vertebrates may respond very differently to these drugs. However, exposure to environmentally relevant concentrations of the agents needs to be further investigated to assess the ecological risks that might be posed by those agents in aquatic and terrestrial ecosystems (Khaki & Kumar, 2025; Sdiq et al., 2025).

**Table 1: Summary of Anticancer Drugs, Mechanisms of Action, and Teratogenic Effects**

|  |  |  |  |
| --- | --- | --- | --- |
| **Drug** | **Mechanism of Action** | **Teratogenic Effects** | **Environmental Persistence** |
| 5-FU | Inhibits thymidylate synthase, disrupts RNA | Embryonic development inhibition, mitotic index modification | High |
| Capecitabine | Prodrug of 5-FU, inhibits DNA synthesis | Similar to 5-FU | Moderate |
| Cisplatin | DNA crosslinking, induces apoptosis | Embryonic toxicity, mitotic disruption | High |
| Doxorubicin | Topoisomerase II inhibitor, DNA intercalation | Cardiotoxicity, developmental defects | Moderate |
| Etoposide | Topoisomerase II inhibitor | Embryonic lethality, chromosomal aberrations | High |
| Imatinib | Tyrosine kinase inhibitor (BCR-ABL, c-KIT) | Skeletal abnormalities, developmental delays | Low |

To measure the average concentration of a specific chemical agent in the air, we need to adopt an efficient and applicable method that ensures real-time estimation of this agent while considering environmental factors such as temperature, pH, water flow, and the presence of other chemicals or particulate matter that might negatively affect our estimations and their variability based on the placement of sampling devices. Moreover, calibrating a lab's equipment requires a significant amount of spiked water, resulting in substantial waste. Meanwhile, an alternative approach, such as in situ calibration, ensures waste reduction and provides more accurate and direct sampling rate values, which reflect real-world conditions (González-Burciaga et al., 2025; A. Mahmood et al., 2021; Omer et al., 2025; Wei et al., 2017a).

Grab sampling and passive sampling are two ways to test for drugs in water. “Grab sampling is used a lot. However, detecting small amounts of anticancer drugs in water is challenging and necessitates a large volume of water for testing, which complicates the overall testing process (Law et al., 2025). Solid-phase extraction (SPE), a commonly used technique in grab sampling, is time-consuming and labor-intensive, and it has a significant drawback in that it provides only a snapshot of contaminant levels at the time of sampling (Kumar et al., 2022; A. A. Mahmood et al., 2025). Meanwhile, passive sampling has several advantages over traditional sampling methods, including lower costs and greater rapidity. Passive samplers can collect and concentrate pollutants, storing substances for an extended period. We can then calculate the average amount of the substance over a specific time interval (Abdulatif & Ali, 2024; Attiah et al., 2023; Ehalt Macedo et al., 2025).

Our current understanding of the occurrence, toxicity, concentration range, and environmental persistence of anticancer drugs detected in hospital wastewater is limited and requires an efficient wastewater treatment plant (WWTP) for tributaries and effluents, as well as surface water, river sediments, groundwater, and drinking water. In this review, we tried to present the impact of anticancer drugs on aquatic organisms and ecosystems and demonstrate currently used biotechnology and physicochemistry for anticancer drug removal from the environment, which is very challenging and requires further investigation (Ahmed et al., 2018; Inaudi et al., n.d.; Maolood & Mhmood, 2021).

**2. Cytotoxic Substance**

**2.1. Alkylating Drugs**

Alkylating agents are one of the oldest anticancer chemotherapies used (Gallenzi et al., 2025; A. Mahmood et al., 2025). Alkyl carbon groups in the structure of these agents can often bind to various biological molecules, particularly the aromatic nitrogen and exocyclic oxygen of DNA bases, altering their structure in a way that potentially disrupts cellular functions, especially in rapidly dividing cancer cells. Additionally, they pose risks of secondary malignancies due to their mutagenic potential and the formation of DNA adducts, which can lead to several downstream cytotoxic phenomena. These include reduced DNA synthesis by hindering the progression of replication forks, the formation of cross-links that prevent DNA cleavage for synthesis or transcription, as well as chromosomal aberrations and genetic mutations in cells (Al-Jumaili et al., 2025; ).

Among the alkylating drugs, cyclophosphamide (CP) and ifosfamide (IF) are the most extensively investigated among all identified anticancer agents (Rajput & Singh, 2025). Researchers estimated the concentrations of CP in clinic wastewater effluents to range from 0.2 ng/L to 22.1 g/L, with a discovery rate ranging from 8% to 100% (D. Li et al., 2021a; A. A. Mahmood et al., 2021). The reported concentrations of IF varied from 0.2 ng/L to 86.2 ng/L, exhibiting a detection rate ranging from 30% to 69.3% (Wang et al., 2022). The effluents of WWTPs contained 300 ng/L of CP, with detection recurrence rates ranging from 20% to 100%. The concentration of IF within the examined effluents of WWTPs was 2.9 µg/L to 12.5%. The persistence of these drugs in wastewater necessitates the use of advanced treatment technologies to mitigate their environmental impact (Rajput & Singh, 2025; Sundararaman et al., 2022).

**2.2. Antimetabolites**

They disrupt the growth and division of cells by slowing down the process of DNA replication, which is crucial for rapidly growing cancer cells, especially during a specific stage of the cell cycle. Some examples include methotrexate, fludarabine, cytarabine, 5-fluorouracil, tegafur, gemcitabine, and capecitabine (Lee et al., 2024).

The most commonly detected antimetabolites in hospital wastewater in low concentrations are MTX, 5-FU, and CAP (Sengar et al., 2025a). Their detection rates were between 23.1% and 100% for MTX, between 50% and 100% for 5-FU, and 6.7% to 60% for CAP. The highest concentration (124 µg/L) of 5-FU was found in the wastewater of a hospital in Austria. MTX and CAP detected concentrations in Spain were 4.8 µg/L and 1.75 µg/L, respectively. In 2018, MTX appeared to be the most frequently detected molecule, with a concentration ranging from less than 1.8 to 53 nanograms per liter of wastewater. Spanish wastewater revealed CAP as the most commonly detected antimetabolite (75%) with a high concentration (158 ng/L). However, the study found that GEM, with a concentration of 88.4 nanograms per liter of wastewater, was the least frequently detected antimetabolite (8.3%). 5-FU concentration in the Gaoping River in Taiwan was about 160 ng/L. The detected concentration of TEG was 56 ng/L, and the detection rate was 25% in the Yodo River area in Japan. A substance, called CYT, was also detected at a concentration of 13 nanograms per liter and a 100% frequency rate in the Guadalquivir River in Spain (Lee et al., 2024; D. Li et al., 2021b; A. Mahmood et al., 2025). The general detection of antimetabolites in aquatic environments underscores their environmental persistence and the need for improved wastewater treatment strategies (Verlicchi et al., 2012).

**2.3. Alkaloids from Plants**

They are plant-derived chemical agents known for their potential anticancer properties (Hoang et al., 2024). They fall into four groups: vinca alkaloids, epipodophyllotoxin lignans, taxane diterpenoids, and camptothecin quinoline derivatives. Primarily, they can inhibit DNA replication and protein synthesis in cancer cells, inducing apoptosis (Hoang et al., 2024; Verlicchi et al., 2012). Their natural origin often makes them less toxic to normal cells compared to synthetic drugs, but they can still cause significant side effects due to their potent mechanisms of action (Hussain et al., 2025).

The most frequently reported alkaloids in wastewater are vincristine, vinorelbine, etoposide, paclitaxel, and docetaxel (Sengar et al., 2025b). Some hospitals found the highest concentration of ETO, 714 nanograms per liter, with a detection rate of 66.7% in their wastewater. Meanwhile,  VINC, PAC, and DOC concentrations in some hospital wastewaters were 49 ng/L, 100 ng/L, and 97.7 ng/L, respectively, according to a study (Asselin-Labat et al., 2025; Sernita et al., 2025). DOC, ETO, and VINC have been detected in the sewage at concentrations of 175.1 ng/L, 83 ng/L, and 22.9 ng/L. VINO levels were 170 ng/L and 4 ng/L in both wastewater and surface water, respectively. The presence of these plant-derived alkaloids in water systems illustrates the value of monitoring natural compounds alongside synthetic drugs in environmental risk assessments (Asselin-Labat et al., 2025).

**2.4. Platinum Complexes**

Platinum-based agents (cisplatin, carboplatin, and oxaliplatin) disrupt the interactions between DNA strands and between DNA and proteins in cancer cells. A study conducted in Iran found that the detection rate of platinum complexes in hospital wastewater is 100% at a concentration of 762 µg/L. However, the potential for platinum accumulation in aquatic organisms raises concerns about long-term ecological effects (Y. Li et al., 2025; Zitvogel et al., 2008a).

**2.5. Protein Kinase Inhibitors**

Protein kinase inhibitors block the signaling pathways of proteins within cells (D. Li et al., 2021c). The most commonly used protein kinase inhibitors are Erlotinib (ERL) and Irinotecan (IRI) (Franquet-Griell et al., 2017; Zitvogel et al., 2008b).

The IRI detection rate in Spanish hospital wastewater was  71.4% at a concentration of 3.4 µg/L (D. Li et al., 2021c; Zitvogel et al., 2008b). It was reported that when the concentration of ERL and IRI is less than 10 nanograms per liter of wastewater, it can be removed by wastewater treatment plants (D. Li et al., 2021c). The low concentrations of these inhibitors in treated wastewater suggest that current treatment approaches are somewhat practical, but further optimization of the methods used is required to ensure their complete removal (Eggen et al., 2014).

**2.6. Immunosuppressants**

Chemical agents known as immunosuppressant drugs suppress the immune system. They have several clinical applications, such as the treatment of some allergic reactions, the prevention of organ and tissue transplant rejection, and the treatment of some specific types of cancer to inhibit the autoimmune complications of cancer therapies and their direct anticancer activities, such as cell proliferation and blood vessel regeneration (Franquet-Griell et al., 2017; D. Li et al., 2021c). Azathioprine (AZA) and mycophenolic acid (MPA) are immunosuppressants and anticancer agents. The azathioprine (AZA) detection rate was 4.8%. In the Besos River, the detection rate of mycophenolic acid (MPA) reached 100% at a concentration of 656 ng/L (D. Li et al., 2021c; Zitvogel et al., 2008b). The presence of immunosuppressants in water systems poses a risk to aquatic life, as these compounds might disturb the immune systems of marine organisms (Zimmermann et al., 2017).

**2.7. Endocrine Therapy Agents**

Megestrol is considered one of the most common pollutants (1.3 micrograms/liter) in Spanish hospital wastewater (Zitvogel et al., 2008b). Researchers also detected tamoxifen (TMX) in 36.5% to 100% of the waste samples, with concentrations ranging from 4 to 170 nanograms per liter (D. Li et al., 2021c; Zitvogel et al., 2008b). In 2013, Isidori and his colleagues did a study. Tauxe-Wuersch and Alencastro conducted another study in 2016. In 2010, Yin and his team conducted a similar survey. TMX and bicalutamide (BLT) appear not to be removed entirely in effluents from wastewater treatment plants. Their concentrations ranged from 740 nanograms per liter to 1.03 micrograms per liter (D. Li et al., 2021c; Zitvogel et al., 2008b). The water's surface contained 212 ng/L and 254 ng/L of TMX and BLT (D. Li et al., 2021c; Zitvogel et al., 2008b). When cancer drugs that don't dissolve in water are administered, they may adhere to particles in the water or sink to the bottom (D. Li et al., 2021c; Zitvogel et al., 2008b). They could also be taken out of the water and put in the sludge. TMX was detected in solid particles in high amounts, at 658 micrograms per kilogram, and was also found in the muddy parts of the Yodo River Basin at levels of 250 nanograms per kilogram (D. Li et al., 2021c). TMX was found in wastewater 4 to 100% of the time and in surface waters 19 to 100% of the time. Spain's underground water contained TMX at levels as high as 223 nanograms per liter (D. Li et al., 2021c; Zitvogel et al., 2008b). These agents are particularly concerning because they have the potential to act as endocrine disruptors in aquatic ecosystems (Jobling et al., 1998). Various environmental compartments monitor and remediate the persistence of endocrine therapy agents (Richardson & Kimura, 2016).

**3. Bioavailability and environmental persistence of anticancer drugs**

In this research, a model was used to estimate the log Kow (octanol-water partition coefficient), bioconcentration factor (BCF), and half-lives (t1/2) in air, water, soil, and sediments for certain anticancer drugs to evaluate their effect on the environment. This was done using the United States Environmental Protection Agency's (EPA) EPI Suite version 4.11, a program designed for estimating environmental impact (Araújo et al., 2019; Booker et al., 2014; Castellano-Hinojosa et al., 2023; Cristóvão et al., 2021; D. Li et al., 2021c; Mišík et al., 2019; Zitvogel et al., 2008b). The use of predictive models, such as EPI Suite, is critical for understanding the environmental fate of pharmaceuticals, especially when experimental data are limited (Williams et al., 2021).

The estimated log Kow for the anticancer drugs varied significantly and could be grouped into three categories. Group I included highly water-soluble substances, with log Kow values ranging from −1.0 to 0.97. This group consisted of 5-FU, EPIR, AZA, TEG, ETO, CAP, CP, and IF. These drugs are less likely to accumulate in biological systems due to their high hydrophilicity, but their persistence in aquatic environments can still pose risks to marine organisms (Kümmerer, 2009). The second group, including DAU, DOX, DOC, ERL, IRI, ANA, and BLT, has moderate water solubility. These compounds do not strongly adhere to organic matter in sediments, sludge, or tissues, with log Kow values ranging from 1.89 to 2.83. Their moderate hydrophobicity makes them less likely to bioaccumulate. However, they may be in water systems and contribute to long-term environmental exposure (Fent et al., 2006).

The third group includes the agents that have high log Kow values, such as VINC, VINO, IM, LET, and TMX, which are characterized by having high lipophilic and strong tendencies for bioaccumulation and accumulation in organic matter, especially in aquatic and terrestrial ecosystems, raising anxieties about their long-term ecological and human health consequences (Arnot & Gobas, 2006). The half-life of each agent, however, should be considered in different media. A longer half-life of any agent in water, soil, and ecosystems appears to have more severe impacts than those with a shorter half-life (Zimmermann et al., 2017). Therefore, understanding these properties is essential for developing an effective strategy to mitigate the environmental risks associated with anticancer agents. Advanced treatment technologies, such as advanced oxidation processes and membrane filtration, appear to be necessary to reduce the risk of wastewater contamination and their release into natural water bodies (Jobling et al., 1998).

**Table 2. Calculated physicochemical properties of anticancer drugs based on EPIWEB 4.1 ordered by log Kow (highest to lowest). Log Kow: octanol–water partition coefficient; BCF: bioconcentration factor (D. Li et al., 2021c; Zitvogel et al., 2008b).**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Drugs** | **log Kow** | **BCF** | **Water Solubility at 25 °C (mg/L)** | **Half life(Hours)** | | | | |
| **Air         Water        Soil    Sediment**  **(x 103)    (x103)       (x103)** | | | | **Biodegradation** |
| Tamoxifen | 6.31 | 1230 | 1.90×10-1 | 1.35 | 1.44 | 2.88 | 13.0 | 3.37 |
| Vinorelbine | 4.84 | 772.5 | 7.82×10-3 | 3.40 | 0.90 | 1.80 | 8.10 | 3.50 |
| Mycophenolic acid | 4.22 | 22.07 | 0.50 | 0.81 | 0.90 | 1.80 | 8.10 | 2.69 × 10-4 |
| Cyproterone | 4.18 | 2.42 | 0.65 | 2.06 | 0.36 | 0.72 | 3.24 | 1.81 × 10-3 |
| Megestrol | 4.00 | 2.31 | 1.46 | 3.96 × 10 | 0.36 | 0.72 | 3.24 | 1.20 × 10-3 |
| Chlorambucil | 3.82 | 0.5 | 1.02 × 103 | 4.88 | 0.90 | 1.80 | 8.10 | 4.41 × 10-2 |
| Letrozole | 3.39 | 18.2 | 1.03 × 102 | 6.13 | 0.90 | 1.80 | 8.10 | 4.58 × 10-3 |
| Paclitaxel | 3.31 | 1.59 | 4.85×10-3 | 3.08 | 0.36 | 0.72 | 3.24 | 9.14 × 10-4 |
| Vincristine | 3.11 | 52.1 | 0.12 | 1.14 | 1.44 | 2.88 | 13.0 | 1.03 |
| Imatinib mesylate | 3.01 | 45.2 | 2.10 | 0.42 | 4.32 | 8.64 | 38.9 | 4.13 × 10-13 |
| Docetaxel | 2.83 | 19.1 | 0.03 | 1.80 | 1.44 | 2.88 | 13.0 | 4.30 × 10-3 |
| Erlotinib | 2.79 | 15.4 | 1.40 × 10 | 1.77 | 1.44 | 2.88 | 13.0 | 1.37 × 10-3 |
| Anastrozole | 2.37 | 24.3 | 6.89 × 10 | 0.40 | 4.32 | 8.64 | 3.89 | 1.40 × 10-3 |
| Irinotecan | 2.33 | 1.21 | 8.01 × 102 | 0.23 | 4.32 | 8.64 | 3.89 | 7.57 × 10-3 |
| Bicalutamide | 2.30 | 18.2 | 1.36 × 102 | 0.84 | 1.44 | 2.88 | 13.0 | 1.37 × 10-3 |
| Daunorubicin | 2.19 | 1.92 | 3.92 × 102 | 0.39 | 4.32 | 8.64 | 38.9 | 2.88 × 10-4 |
| Doxorubicin | 1.85 | 1.27 | 9.28 × 10 | 0.38 | 4.32 | 8.64 | 38.9 | 6.91 × 10-4 |
| Cyclophosphamide | 0.97 | 0.50 | 5.94 × 103 | 3.65 | 0.90 | 1.80 | 8.10 | 2.98 |
| Tamoxifen | 0.97 | 1.55 | 3.78 × 103 | 0.67 | 4.32 | 8.64 | 38.9 | 0.14 |
| Capecitabine | 0.56 | 0.96 | 1.82 × 103 | 0.83 | 1.44 | 2.88 | 13.0 | 1.21 |
| Etoposide | 0.04 | 0.97 | 5.87 × 10 | 0.31 | 4.32 | 8.64 | 38.9 | 6.22 × 10-4 |
| Tegafur | −0.02 | 0.50 | 3.64 × 102 | 0.37 | 0.36 | 0.72 | 3.24 | 0.5 |
| Azathioprine | −0.09 | 0.95 | 2.72 × 102 | 1.27 | 0.90 | 1.80 | 8.10 | 0.41 |
| Epirubicin | −0.23 | 0.50 | 2.71 | 0.43 | 4.32 | 8.64 | 38.9 | 3.22 × 10-10 |
| 5-fluorouracil | −0.81 | 0.50 | 2.59 × 104 | 1.38 × 10-2 | 1.44 | 2.88 | 13.0 | 1.05 × 102 |
| Methotrexate | −1.28 | 0.98 | 2.60 × 103 | 8.58 | 4.32 | 8.64 | 3.8 | 7.94 |
| Goserelin | −1.33 | 0.50 | 1.12× 10-2 | 1.02 × 10 | 1.44 | 2.88 | 13.0 | 2.50 × 10 |
| Gemcitabine | −2.01 | 0.89 | 5.14 × 104 | 6.99 × 10 | 0.90 | 1.80 | 8.10 | 5.90 × 10 |
| Cytarabine | −2.46 | 0.50 | 1.76 × 105 | 0.45 | 1.44 | 3.88 | 13.0 | 9.38 |
| Bleomycin | −10.0 | 0.89 | 7.71 × 103 | 3.54 | 4.32 | 8.64 | 38.0 | 4.32 × 10 |
| Capecitabine | 0.56 | 0.96 | 1.82 × 103 | 0.83 | 1.44 | 2.88 | 13.0 | 1.21 |

The half-lives of some anticancer agents in water range from 15 to 180 days (Table 1). , BLE, DAU, DOX, VINC, VINO, ETO, PAC, DOC, ERL, IRI, TMX, and ANA appear to have long half-lives in water, which makes them more harmful pollutants (D. Li et al., 2021c; Zitvogel et al., 2008b). Meanwhile, the degradation rates of 5-FU and CAP are higher and can persist in water for only 15 days. (Table 1). We expect the half-life of IF, AZA, and LET in water to be 37.5 days. After being exposed to water, UV-C light, and simulated sunlight for 90 minutes in a dark lake at 20°C, CP was found to resist for 80 days (D. Li et al., 2021c; Zitvogel et al., 2008b). Despite a high pH (8.08), 251 mmol/L alkalinity, 1.6 mg/L dissolved organic carbon, 0.7 mg N/L nitrate, 2.0 µg N/L nitrite, and less than 0.1 mg/L, the water treatment was not found to be effective to prevent surface water contamination with CP (D. Li et al., 2021c; Zitvogel et al., 2008b).

Due to insufficient information regarding the persistence, bioaccumulation rates, and impacts of most anticancer agents on the food chain, estimating the consequences of their presence in the environment, particularly in aquatic ecosystems, would be challenging. However, the estimated log Kow levels for TMX, BLT, ANA, LET, and MEG indicate their expected bioaccumulation, especially in aquatic animals. Researchers have only explored the half-lives of a few anticancer agents, such as ANA, LET, and TMX, in lab settings. Adult Cunner fish received oral administration of 750 mg/kg of ANA and LET for 16 days, resulting in plasma concentrations of 0.066 mg/g and 0.54 mg/g, respectively (D. Li et al., 2021c; Zitvogel et al., 2008b). Exposing Rerio fish to 10.0 µg/L of TMX for 21 days, the bioaccumulation of the agent in the D's muscle, liver, and gonad was found to be 85,600 times higher than in the water; this indicates a high potency of its bioaccumulation. Therefore, further research is required to address the bioaccumulation and fate of anticancer agents in the ecosystem, particularly in aquatic animals and food chains (D. Li et al., 2021c; Zitvogel et al., 2008b).

**4. Discussion**

In our study, we found that 17 out of 33 anticancer drugs are polluting water systems and harming aquatic organisms. The toxicity of these drugs was assessed using Daphnia magna, a commonly used indicator species in ecotoxicological studies (Table 2). The results revealed that some anticancer drugs, such as cisplatin (CDDP), tamoxifen (TAM), and doxorubicin (DOX), caused severe toxic effects even at low concentrations. The most poisonous drugs were platinum complexes, followed by endocrine therapy agents, antibiotics, antimetabolites, and alkylating agents. This hierarchy of toxicity underscores the varying mechanisms of action and environmental persistence of these compounds.

The presence of anticancer drugs in aquatic environments is particularly concerning due to their potential for bioaccumulation and biomagnification. Similar to the effects of heavy metals on antioxidants and physiological parameters in humans (Ajeel et al., 2021), the bioaccumulation of anticancer drugs in aquatic organisms could lead to oxidative stress, disruption of physiological functions, and long-term ecological consequences. For example, drugs like tamoxifen (TMX) and letrozole (LET) have been shown to accumulate in fish tissues, raising concerns about their potential to disrupt aquatic food chains and biodiversity. The persistence of these drugs in water, soil, and sediments further exacerbates their environmental impact, as they can remain active for extended periods, exerting toxic effects on non-target organisms.

The findings of this study also highlight the limitations of current wastewater treatment methods in removing anticancer drugs. While treatment partially removes some drugs, others, like cyclophosphamide (CP) and ifosfamide (IF) continue to persist in effluents and surface waters. This highlights the need for advanced treatment technologies to mitigate the environmental impact of these persistent pollutants. Emerging technologies, such as nanotechnology and biosensors, offer promising avenues for detecting and removing anticancer drugs from wastewater (Majeed & Qaddoori, 2022). For instance, superparamagnetic iron oxide nanoclusters are utilized for the targeted imaging of liver tumors, which illustrates the potential of nanotechnology for precise and efficient applications in medical diagnostics (Ahmed Mahmood et al., 2019; Wei et al., 2017b). Similar approaches could be adapted for environmental monitoring, where nanotechnology-based solutions could be used to detect and remove anticancer drugs from wastewater with high specificity and efficacy.

Moreover, the variability in biological responses to anticancer drugs among different organisms and vertebrate groups suggests that the ecological risks of these compounds may be underestimated. For instance, crustaceans like Daphnia magna are highly sensitive to low concentrations of 5-fluorouracil (5-FU), cisplatin (CDDP), and imatinib mesylate (IM), indicating that even trace amounts of these drugs could have significant ecological consequences. This variability in sensitivity indicates that there must be further research to evaluate the effects of exposure to these drugs at environmentally relevant concentrations.

The environmental persistence and toxicity of anticancer drugs pose significant risks to aquatic ecosystems. While the immediate toxic effects of these compounds may not be evident, their long-term ecological impacts, including bioaccumulation and potential disruptions to food chains, warrant serious attention. Advanced treatment technologies, such as nanotechnology and biosensors, could play a crucial role in addressing this issue by improving the detection and removal of these persistent pollutants from wastewater. Nanotechnology can be applied for targeted medical imaging (Wei et al., 2017b), and similar principles could be extended to environmental applications, such as the selective removal of anticancer drugs from wastewater. Additionally, regulatory frameworks and monitoring programs need to be strengthened to ensure that the production, use, and disposal of anticancer drugs are managed in an environmentally sustainable manner.

**5. Conclusion**

This study found that cancer drugs can enter the water system in cities. They can enter rivers, sediment, groundwater, and drinking water from hospitals and wastewater treatment plants. Although anticancer drugs break down at different rates, they still stay in the environment for a long time in soil, water, and sediments. Combined, the current research suggests that the toxic effects of cytostatics in water are unlikely to occur immediately or within a short period. However, they could happen if the chemicals are not adequately removed from hospital wastewater. Moreover, they show that some types of animals (like crustaceans) are susceptible to harmful effects when exposed to low levels of 5FU, CDD,P and IM traits or characteristics from one generation to the next.

Ethical approval

This study did not include human participants or animal subjects, thus formal ethical approval was unnecessary. All procedures were executed in compliance with institutional and international standards for environmental research.

**Disclaimer (Artificial intelligence)**

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.) and text-to-image generators have been used during the writing or editing of this manuscript.

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