Title
THE LIFE OF PHARMACEUTICALS THROUGH THE BODY, TREATMENT, AND THE ENVIRONMENT

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Publication Date
2026-06-15

THE LIFE OF PHARMACEUTICALS THROUGH THE BODY, TREATMENT, AND THE ENVIRONMENT

By

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A capstone project submitted for Graduation with University Honors

May 13, 2026

University Honors

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Abstract

There are many pollutants in our water, pharmaceuticals being one of the main contributors to the pollution. This literature review quantifies some of the pharmaceuticals (Acetaminophen, Naproxen, and Diclofenac) that are introduced into our water, tracks their excretions through the body, their degradation by wastewater treatment, and determines if they persist in the environment. This was done by looking at various research papers and compiling information related to excretion rates, degradation rates, and more to develop into sankey diagrams tracking the fate of these pharmaceuticals. This research found that of the three drugs investigated, only Naproxen persisted in the environment after a year.

Keywords

Acetaminophen, Naproxen, Diclofenac, Degradation, Wastewater, Environment

Acknowledgements

Firstly, I would like to sincerely thank my faculty mentor Amanda Rupiper for mentoring me throughout the entire Honors capstone process. She was wonderful to work with and was also interested in the topic that I was interested in. Amanda Rupiper was constantly pushing me in the right direction and invested so much time into me, even with her already busy schedule. She pushed me out of my comfort zone and allowed my access to success in this project. She was an amazing faculty mentor and I cannot thank her enough for investing so much time and effort in my success.

I want to thank my family for supporting me throughout more than just the research process. My family has always asked for updates about my research and argued with me about any doubts I had about myself. My family was genuinely a shining light that, in conjunction with Amanda Rupiper, pushed me to complete this project. I hope that this project will be able to surpass their expectations and make it feel like any worry they had about me was not founded. I would also like to thank my friends for giving me suggestions about my work and listening to me rant about my research.

Finally, I would like to thank the Honors Department for accepting me and allowing me this opportunity to perform detailed research. This capstone project was definitely a highlight in my undergraduate student life at UCR and this was a substantial experience for me that I will always remember.

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Introduction

Hundreds of millions of pounds of pharmaceuticals are disposed of annually, making their way into our waterways. They are dumped into the trash, down drains, or even through our waste. Some of the most popular of these pharmaceuticals are Acetaminophen (APAP), Naproxen, and Diclofenac (Kane 2024 18). Currently there are trace amounts of these drugs in the water (as seen in Table 1.) however, if nothing is done to fix the problem, these drugs begin to accumulate in the water and will begin to affect us. In this literature review, the degradation values, the excretion values, the movement, and the overall lifespan of Acetaminophen, Naproxen, and Diclofenac were looked into.

Table 1. Max Dosage is the maximum amount of a drug that can be taken before negative effects begin to occur. Concentrations found is the amount of the drug that has been found in the U.S. The partition coefficient is the ratio of the drug's preference to stay in water or organic material, with higher partition coefficient being more of a preference to stay in organic material. Percent Excretion is the percentage of the drug that is excreted from the human body after the body uses all it can. Removal efficiency (η) is the percentage of the drug that is degraded in wastewater treatment facilities. Best removal η is the highest removal η with known techniques while worst removal η is the lowest η with known techniques. Avg. removal η is the average between these two values.

	Max Daily Dosage	Concentrations Found	Partition Coefficient	% Excretion	Avg. Removal η	Best Removal η	Worst Removal η
APAP	7.5-10g[12]	150 mcg/L[29]	6.237[25]	2[1]	84.6[23]	-	-
Naproxen	1000	6 mcg/L[10]	1.729[21]	95[7]	58[20]	100[20]	16[20]

	mg/day[7]						
Diclofenac	Min. Effective Dosage[3]	ng-mcg/L[24]	13.4[26]	65[4]	46.5[20]	89[20]	4[20]

For example, there is up to 10 μg L^{-1} of Acetaminophen in US natural waters which is below the daily recommended dose of 4g, but we do not fully understand how chronic low level exposures will impact our health (Wu et al 2012, Nichols et al 2019).

Acetaminophen is an analgesic, meaning that it is used for pain relief, and can be bought without a prescription. Naproxen and Diclofenac are non-steroidal anti-inflammatory drugs (NSAIDs), which means that they are used to combat inflammation, and can also be bought over the counter. The goal of this paper is to look into the Biodegradation, Toxicity, Excretion, and Mobility of Acetaminophen, Naproxen, and Diclofenac to understand if these drugs are accumulating in our environment and what effects they may have on it.

Acetaminophen

The toxicity of a drug, for the purposes of this paper, can be defined in terms of what too much of the drug does to the human body. The "minimum toxic dose" (which means the dose at which adverse effects first begin) of acetaminophen is 7.5-10g for adults and 150mg/kg for children, as seen in Table 1., and symptoms of overdose can begin occurring as soon as half an hour after ingestion (Farrell 2024). Initial symptoms (30 minutes-24 hours) may include nausea, vomiting, diaphoresis (sweating to an unusual degree), pallor (pale appearance), lethargy (extreme tiredness), and malaise (feeling of discomfort) (Agrawal et al 2025). Later stage (72-96 hours later) symptoms may include liver failure, renal failure, hypoglycemia, and lactic acidosis (lactic acid builds up in the blood stream) (Agrawal et al 2025). However, with concentrations being found in the environment at most being 150 micrograms per liter from Table 1., the water alone won't be enough to cause overdose but if someone took acetaminophen and drank water with that high of concentration, there may be cause for concern or a chronic low exposure of these drugs may have an effect on people (Wu et al 2012). In addition, the concentration of acetaminophen may cause concern for aquatic life as they are smaller than humans which means that a smaller amount of acetaminophen could be lethal for the fish. If the fish begin to die due to the concentration of Acetaminophen, whole ecosystems will begin to change. Fish are a more sensitive species because they are smaller than most other creatures and they adsorb through their skin and gills so they are uptaking from their environment all the time which would indicate when a problem is beginning to occur. This concern is not caused only from Acetaminophen, but Naproxen, Diclofenac, and all the other pollutants being introduced into the water.

The partitioning coefficient (Kow) of Acetaminophen is 6.237 and the partitioning coefficient is the ratio of a pollutant in non-aqueous phase to the aqueous phase at equilibrium (U.S. National Library of Medicine 1990). The partitioning coefficient gives good insight as to how much APAP will stay in the water versus how much will be absorbed by the animals. The 6.237 partitioning coefficient from Table 1 then shows that Acetaminophen will likely prefer to be absorbed by the fish in the water or animals drinking the water than to stay in the water.

Table 1. shows that, in humans, 98% of APAP that comes into the body is metabolized in the liver and the remaining 2% is excreted unchanged in the urine (Agrawal et al 2025). With a

significant number of consumers using APAP, running into the millions, a lot of APAP is being put into the sewage and runs into the wastewater treatment facility (Kane 2024 15.). The wastewater treatment has 84.6% removal efficiency with treatment with Fe_3O_4 nanomaterials (Pirvu et al 2023). The removal efficiency is high in comparison to Naproxen's worst removal efficiency, as it will be talked about in Naproxen's section.

Naproxen

The maximum recommended dosage for Naproxen is not to exceed 1000 mg/day by mouth, as seen in Table 1. (Brutzkus et al 2023). Some of the adverse effects of Naproxen are gastrointestinal (GI) ulcers, increased bleeding risk, stroke, heart failure, and more (Brutzkus et al 2023). These adverse effects and others such as decreased sperm production have been seen in rat experimentation (Aledani et al 2022). They can also be a threat in the future population of humans because while adverse effects are more likely to occur as dosages are increased, they can occur at low dosages and the likelihood of the adverse effects only grows as concentrations in the water grow. The concentration of Naproxen is currently low with concentrations of around 6 micrograms per liter being found in water samples, however, due to the nature of adverse effects the drug can still affect the people who drink the water (Durán-Álvarez et al 2015).

According to Table 1. the surfactant free partitioning coefficient of Naproxen in olive oil-water systems is 1.729 (Nachari & Jabbari, 2021). Surfactant free partitioning means that there is no substance that reduces surface tension, which allows the Naproxen to spread more into the water than going to the oil. The 1.729 partition coefficient means that Naproxen is slightly more likely to prefer to be absorbed by the fish or other animals than to stay in the water, however, of the three drugs researched it is the least likely to be absorbed by animals.

Approximately 95% of Naproxen is excreted in urine after being metabolized in the liver as reflected in Table 1. (Brutzkus et al 2023). The amount of Naproxen that gets through the body unchanged is quite high compared to the APAP excretion value. A membrane bioreactor has the highest removal efficiency of Naproxen with a 100% removal efficiency while the worst treatment method was a wastewater treatment facility with nothing specialized in removing pharmaceuticals which had a 16% removal efficiency (Mussa et al 2022). Membrane bioreactors are rare however and wastewater treatment facilities without specialization in pharmaceuticals are far more common. The average removal efficiency from the highest and lowest ends up being 58% removal efficiency.

Diclofenac

Diclofenac's dosage must be kept at a minimum effective dosage (Diclofenac dosage varies based on the consumer and is regulated) and the patient must be monitored while taking it in order to avoid the possible adverse effects that occur (Alfaro & Davis, 2023). These included heart failure, stroke, decreased mucin production, and less bicarbonate secretion (Alfaro & Davis, 2023). The possible chronic adverse effects are renal complications, hepatitis, and gastrointestinal damage (Alfaro & Davis, 2023). As the dosage of Diclofenac increases, the risk of these adverse effects increases, however even small chronic dosages have the risk of the adverse effects so the small concentrations in the water can cause these effects. The Diclofenac concentrations range from nanograms to low micrograms per liter around the world (Tüzün & Karapinar, 2022).

The partition coefficient of Diclofenac is 13.4 in an N-octanol/aqueous buffer via Table 1. (U.S. National Library of Medicine, n.d.). This higher partition coefficient would explain why only 65% of a dose is excreted in the urine rather than something like Naproxen which has a 95% excretion (Altman et al 2015). The high partition coefficient also shows that Diclofenac is much more likely to be absorbed by the fish or other animals than it is to stay in the water. However, other variables are involved as well because APAP has a partition coefficient of 6.237 and 2% of the dose gets excreted in urine unchanged.

In wastewater treatment facilities, the best degradation of Diclofenac achieved is 89% with fine screening of the wastewater first and then using microorganisms to treat the wastewater after that (Mussa et al 2022). The worst achieved degradation is 4% with no treatment method used on the wastewater. Even compared to the worst removal efficiency of Naproxen, the worst removal efficiency of Diclofenac is far less than that degradation. Diclofenac needs a treatment method to remove any noticeable amount from the water. Taking into account the best and worst case scenarios, Diclofenac's average removal efficiency then ends up being 46.5%.

Methods

Simplified Explanation

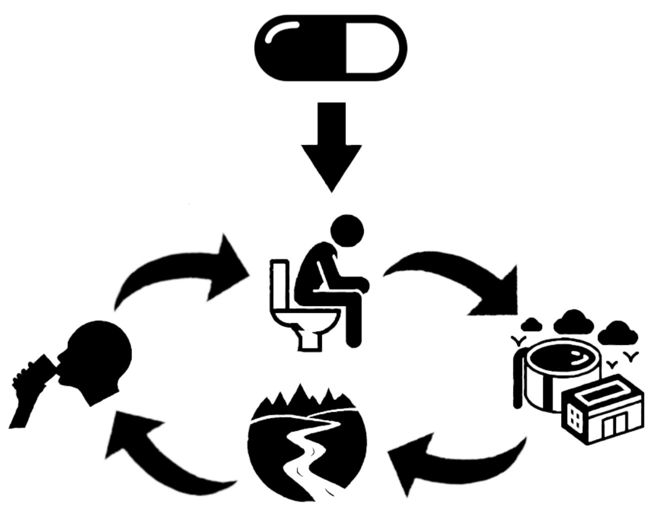

Figure 1. A figure showing the life of pharmaceuticals.

For a simpler overview of what is being looked at for the Sankey diagram, a much simpler flow diagram was created. This flow diagram excludes things such as metabolized, drainage dump, and trash dump but these can be explained relatively easily. First, the flow diagram will be explained. The excretion is when you take a drug, some of it will leave through your body after the body takes in some of it and uses it. The wastewater treatment facility is where wastewater (like the sewage that contains the excreted pharmaceuticals) goes to be treated by various methods and have the waste removed from the water. After the wastewater is treated in the treatment facility, the water then flows back into water sources such as rivers. Metabolism is when the drug breaks down in the body to be used for its effect. When a drug is in the trash dump, that means the drug is put directly into the trash and eventually goes to a trash dump where the drug will leak into the environment through the soil. When a drug is in the drainage dump section, that means the drug is dumped directly down the drain such as if you dump the drug into the toilet or down the sink. Dumping a drug into the drain allows a more concentrated amount of the drug to be put into the wastewater and eventually the environment.

The total annual dosages for each of the drugs was 2.8×10^{10} for Acetaminophen (Kane 2024 15.), 3.0×10^{10} for Naproxen (Kane 2024 17.), and 2.9×10^{10} for Diclofenac (Kane 2024 16.). According to Equation 1., the percentage of the types of dosages could be found so that was used to multiply the percentage of the type (e.x. 36.6% was 75mg Diclofenac) with the milligrams of the dosage with the total dosage used and added them all together to get the total milligrams used.

$$(U\% * (T) * DOS) + (U\% * (T) * DOS) + (U\% * (T) * DOS) = TM \text{ (Equation 1)}$$

Equation 1. The math done to get the total milligrams for Diclofenac. Where U% is the percentage of that type of dose used, T is the total number of dosages used, DOS is the milligrams of that dosage, and TM is the total amount of mass.

An excretion percentage of what gets through the body unchanged was found (2% for Acetaminophen, 95% for Naproxen, and 65% for Diclofenac) and multiplied by the total milligrams used (Agrawal et al 2025, Brutzkus et al 2023, Altman et al 2015). A general percentage of the amount of medications that are put in the trash and dumped down the drain were found (26% down the drain and 29% into the trash) and used for all the medications (Han et al 2023). The milligrams that are excreted, the milligrams that are put in the trash, and the milligrams that get dumped into the drain were all added together for the total milligrams that go to wastewater treatment. The degradation of each of the medicines during wastewater treatment were found with some assumptions in place. The beginning assumption was that there is no medication pre-existing in the environment. One other assumption being that the degradation method found is the only type of degradation being used for degradation. This assumption is being made because there are so many different methods to degrade medicines in wastewater, all with varying degrees of success.

For example, Acetaminophen had 84.6% degradation with Fe_3O_4 nanomaterials (Pirvu et al 2023), Naproxen had 58% degradation and Diclofenac had 46.5% on average with microbiological reactors (Mussa et al. 2022). After finding the degradation percentage, the percentage is used to determine the total milligrams that leave the wastewater treatment facilities and go to various bodies of water. The bodies of water that are being represented as all of the water in the United States are the five great lakes (Environmental 2024). The five great lakes were a good representation of all the surface water in the U.S. because they are a majority of the water in the U.S. already (Environmental 2024). Water also constantly flows in and out of the U.S. so it would be difficult to correctly identify the total amount of water in the U.S., however, the lakes can hold a constant amount of water and therefore can be measured. A specific bacterial culture will degrade all of the APAP (Wong, & Wang, 2016). This specific strain of bacteria is Pseudomonas Aeruginosa Strain HJ1012. This strain of bacteria that is commonly found in the environment such as water and soil and is known to cause infection in humans (Centers for Disease Control and Prevention. 2025). Due to its diverse metabolic network and its ability to secrete biosurfactants, Pseudomonas Aeruginosa Strain HJ1012 has the ability to facilitate degradation of various pollutants such as Acetaminophen (Hu, F., et al. 2023).

Naproxen was found to degrade 28% every 35 days. To model this removal, the mass of Naproxen was multiplied by 0.72 iteratively 10 times to represent a full year of degradation (365 divided by 35 is 10.43) (Wojcieszyńska et al 2014). For the following year, the amount that leaves from wastewater was added to the 10th multiplication of 72% and was then multiplied by 72% as well. The entire process was repeated 5 times to represent the degradation of Naproxen over 5 full years, which showed accumulation in the environment.

Results

Acetaminophen is fully degraded from a bacterial culture after it goes through the wastewater treatment facility. The Sankey Diagram shows that the Acetaminophen is able to get to the river. As stated earlier, the excretion value of Acetaminophen is only 2%, however, with the large amount of dosages used yearly ($2.8*10^{10}$) there is a significant amount of acetaminophen that goes into wastewater. Wastewater treatment facilities that use nanomaterials also have an 84.6% removal efficiency. While these values mean there is a low amount of acetaminophen that gets to the rivers, it is still a significant amount due to the sheer bulk amount coming through the facility. According to two separate sources (Wong, & Wang. 2016 and Chopra, & Kumar. 2020) all of the acetaminophen will decay in the rivers within a year. *Biodegradation and kinetic analysis of acetaminophen* - by Chopra and Kumar, gave a degradation of 1200mg/L every 10 days which can be used to see how much of Acetaminophen would decay within a year . Combining this degradation value with the volume of the five great lakes, an estimation of how much acetaminophen would be degraded per year by bacterial strains was created (Environmental Protection Agency. 2024). The estimation of 2.62×10^{20} mg/yr was created and showed that any Acetaminophen created over the year would be degraded because the APAP value that got through wastewater had the found degradation estimation subtracted from it and the APAP value became negative, essentially 0.

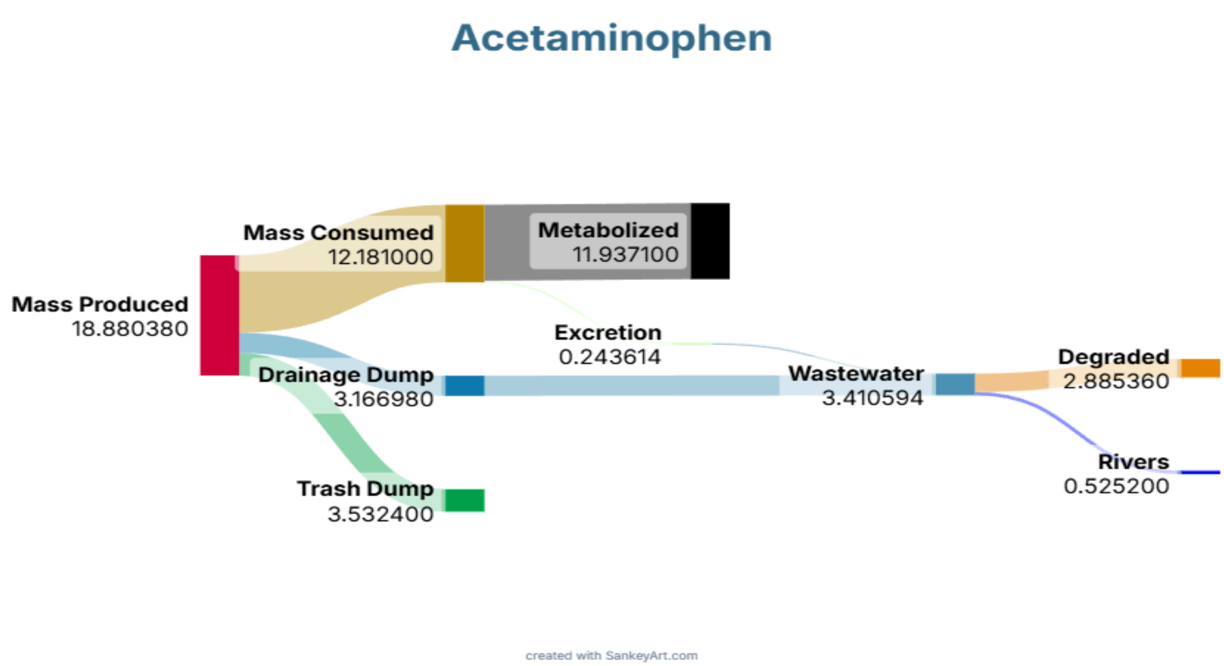

Figure 2. Sankey Diagram showing the flow of Acetaminophen through humans and the environment. The sankey diagram's numbers are all in Kg x 10^6.

A sankey diagram and future prediction were established based on the average value of the amount of filtration (58%) for Naproxen in wastewater treatment facilities (Mussa et al. 2022). After Naproxen leaves the wastewater treatment facility, it was found that Naproxen is biodegraded by stenotrophomonas maltophilia KB2 with a degradation efficiency of 28% in 35 days in the environment (Wojcieszyńska et al. 2014). This very low degradation efficiency when the drug gets into the environment, allows the drug to begin to accumulate in the environment as seen in Figure 3. Stenotrophomonas maltophilia KB2 is an uncommon bacteria that is often found on the roots of plants and the roots of plants are typically connected to underground water sources or water sources directly (Mukherjee & Roy 2016). This displays that the degradation from this bacteria does occur naturally. Stenotrophomonas maltophilia KB2 has great genomic and metabolic diversity which enables it to biodegrade various pollutants such as Naproxen.

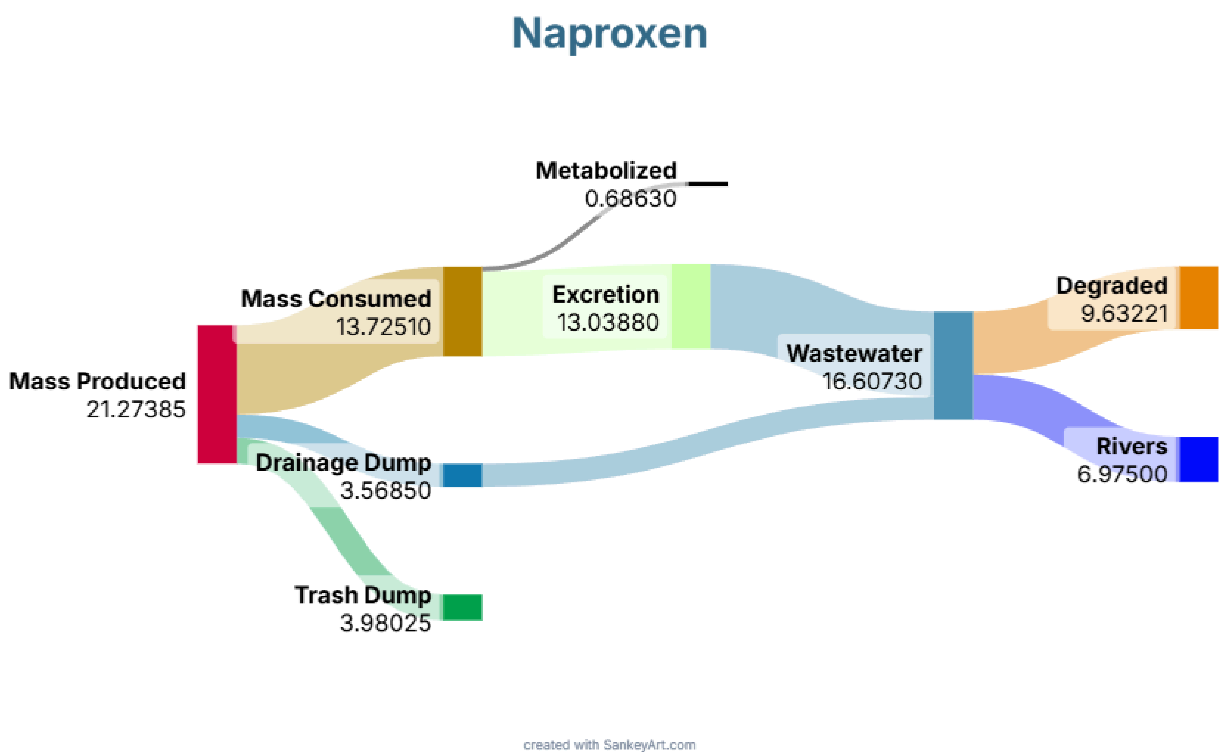

Figure 3. Sankey diagram showing the flow of Naproxen through humans and the environment. The Sankey diagram's numbers are all in Kilograms x 10^6.

The estimated value of Naproxen in the environment after a year of degradation is 2.61139×10^5 kilograms. The estimated value of Naproxen in the environment after five years is 2.71296×10^5 kilograms. Naproxen based on the found values is then suspected to accumulate in the environment at a steady pace if nothing is to be done to address this issue. These scenarios are based on the assumption that there is no Naproxen in the environment already and the assumption that the values are a constant change. This assumption then may underestimate the amount that is already in the environment or, due to human need fluctuating in actuality, may be overestimating the amount that is being added to the environment.

Diclofenac, like Acetaminophen, was found to be fully degraded by a bacterial culture after it leaves the wastewater treatment facility. Diclofenac has a 65% excretion value, as stated earlier, and Diclofenac also has an average removal efficiency of 46.5% in wastewater treatment facilities. The significant amount of use from humans, a 65% excretion rate, and a low 46.5% removal efficiency means a lot of Diclofenac is making its way into the rivers. This does not mean that the Diclofenac is necessarily staying in the waters though, with two separate sources showing that all Diclofenac that makes it into the rivers will degrade within a year. The sources that showed Diclofenac produced will degrade within a year are Enrichment of bacterial strains- by Bessa, Moreira, Tiritan, & Castro and Removal of pharmaceuticals- by Wong, & Wang. Enrichment of bacterial strains- gave a degradation rate from bacterial strains of 35% of 10mg/L in 30 days, simplified becomes 0.117 mg/(L*day) (Bessa et al. 2017).

Using the five great lakes volume referenced earlier when talking about Acetaminophen, a degradation rate of 2.55 x 10^{17} mg/yr is found as seen in Table 2., which when subtracted from the amount that gets through wastewater gives a negative value or essentially zero. Removal of Pharmaceuticals- gave a specific bacterial culture that degrades all of the Diclofenac. The bacterial culture's name is Phanerochaete sordida YK-624. Phanerochaete sordida YK-624 is a white rot fungus and has been found to secrete enzymes that are capable of degrading various pollutants such as Diclofenac (Yin et al 2025). White rot fungi are known to typically grow on trees and digest the tree, causing it to rot. The tree's roots are connected to an underground water source which may enable it to connect to water sources as well.

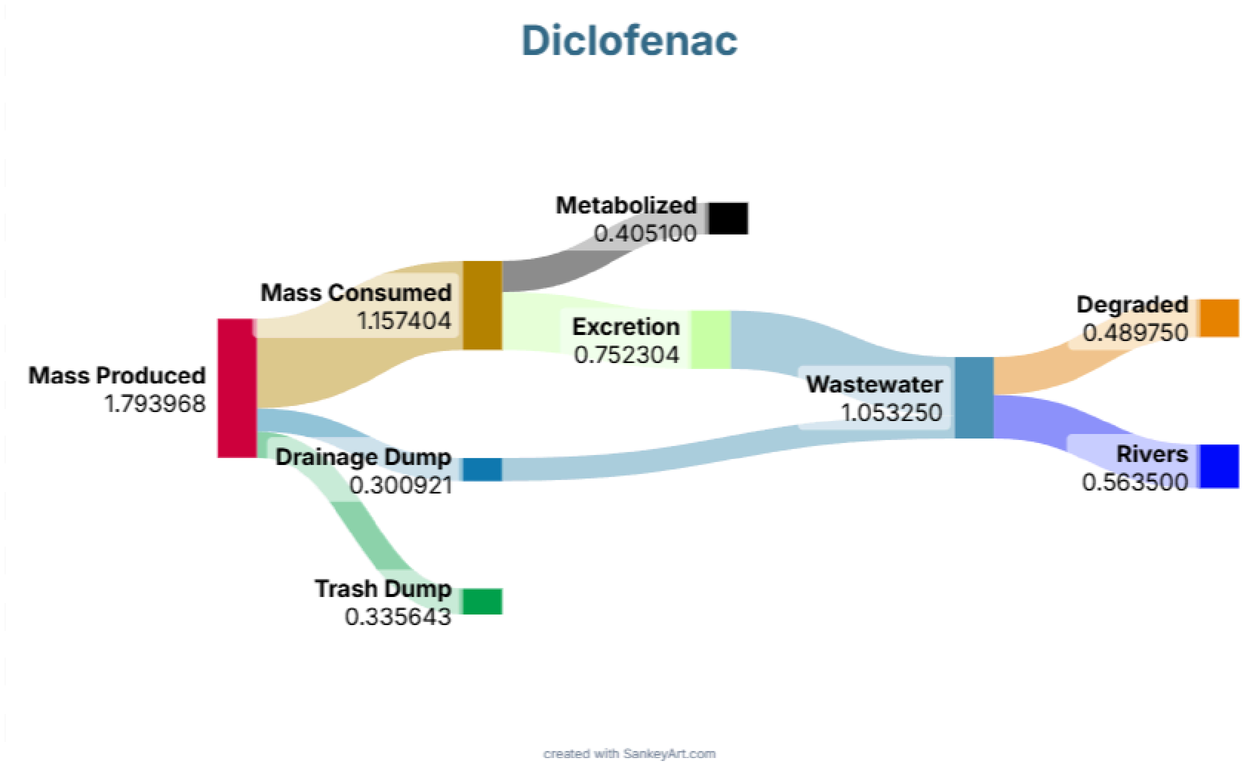

Figure 4. Sankey diagram showing the flow of Diclofenac through humans and the environment. The Sankey diagram's numbers are all in Kilograms x 10^6.

Best/Worst Case Scenarios

The worst case scenario for Acetaminophen's removal efficiency is 52% when the wastewater is treated with ultraviolet-C by itself. When the ultraviolet-C is combined with activated sludge (activated sludge is a mixture of microorganisms such as bacteria), the degradation efficiency boosts all the way to 99% representing the best case scenario (Bingjie et al 2018). These scenarios aren't used because something closer to the average value was preferred to be used.

Naproxen's best case scenario for degradation in a wastewater treatment facility is when it can be fully removed through a combination of a membrane batch reactor with ultraviolet or chlorination (Mussa et al. 2022). Its worst case scenario is when there is basic filtration in the wastewater treatment plant and it only filtrates 16% of the Naproxen out of the water.

Diclofenac's best case scenario removal method in a wastewater treatment facility is with a primary treatment method of Screens and Grit Removal + Sedimentation, a secondary treatment method of Conventional Activated Sludge + Sedimentation, and a disinfection method of Ultraviolet Radiation (Mussa et al. 2022). This removal method results in a removal efficiency of 89%. The worst case scenario removal method for Diclofenac is when a basic filtration method was actually used on the water (Mussa et al. 2022). This results in a 4% removal efficiency of Diclofenac which is likely too low to have any significant effect at all on the amount of Diclofenac that gets to the rivers.

Limitations/Next Steps

Additional steps to this literature review could be someone adding their personal research done to demonstrate their own found numbers and perform a similar example of the movement of pharmaceuticals through the body. If something like this were done to completion, it would be standardized values rather than an estimate from values found all over. For example, if someone were to do research on the excretion values for the drugs, they would perform different wastewater treatment methods on the excretion, and find out how much of the pharmaceutical is biodegraded over time.

This would be a large undertaking so a smaller way to improve upon this literature review would be to add more forms of degradation into the research. The main form of degradation used in this literature review was biodegradation but, as stated earlier, there are many forms of degradation including, but not limited to, environmental degradation and thermal degradation.

This would show that the pharmaceuticals probably degrade more than what was shown in this literature review because there are typically different methods and efficiencies of degradation for each drug.

An assumption for the sake of simplicity in the sankey diagrams and the math for the sankey diagrams was that there were no pharmaceuticals already in the environment. If someone were to find an estimate of the amount of their investigated pharmaceuticals in the environment already, it would be more of a real world following of the approximate amount of pharmaceuticals accumulating, degrading, and even the amount being consumed by wildlife. This mathematical model would be a good prediction of the movement of pharmaceuticals if done correctly and it may even allow for wastewater treatment checkpoints to be made at locations of significant contamination that treat the water.

Another way of expanding upon the research done here, is by looking into different types of pharmaceuticals. The drugs looked in this paper were an analgesic and two different NSAIDS. I attempted to study drugs similar in classification to look for if there were similarities in their degradation or treatment of the drugs. There are multiple hundreds of classifications of drugs that could be used in a study like this. If new drugs were to be looked into however, researching drugs in the top 500 list would likely be more fruitful than an obscure drug that is only used for rare diseases. If an obscure drug is researched with this type of research in mind, there is likely to be little to no research on the drug.

Conclusion

In conclusion, this literature review has shown that of the three drugs chosen to be researched, Naproxen alone will accumulate in the environment. The other two drugs, Acetaminophen and Diclofenac, will be degraded by bacteria that are naturally found in the environment. Whether it be a specific bacterial culture or bacterial strains in general, these two drugs will be completely biodegraded. Naproxen is also degraded by a bacterial strain, however, that bacteria's degradation efficiency is low with it only being able to degrade 28% in 35 days, allowing more Naproxen to come into the environment before the bacteria in the environment can degrade it all. The degradation of these drugs is only from bacterial degradation, the degradation values do not include environmental degradation (degradation from environmental factors such as UV radiation, moisture, etc), thermal degradation, or others. The assumption there was no drugs in the water to begin with was made for the Sankey Diagram along with the assumption that the amount being used was a constant, not fluctuating depending on human use.

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