Optimizing Pharmaceutical Wastewater Treatment: A Comprehensive Review and Unique Experimental Insight

Arnav Muthali

Abstract

The increased production and consumption of pharmaceuticals to combat evolving diseases, bacteria, and generally as a treatment (or an aid to) for unsolvable ailments (i.e. psychiatric treatments for Alzheimer's), results in higher concentrations of pharmaceuticals exposed to the environment both from production processes and human waste. Both in the production and in the disposal of pharmaceuticals does an increase of it as waste arises, seen at greatest effect at a local (to the production facility) level but can potentially become a global issue. The paper goes over conventional treatments for pharmaceutical wastewater. These treatments are classed under Advanced Oxidation Processes, Bio-activated methods, and treatments that involve separation methods. These treatments are then evaluated for their qualities, good and bad, when dealing with pharmaceutical wastewater, and then are either chosen or discarded for the final two sections. The final two sections then create an experimental treatment solution post-evaluation of wastewater treatment solutions that are considered stable and beneficial, and then that will be evaluated, with the limitations being discussed and alternative perspectives given.

Introduction

Medicine as we know it has evolved to not only better human ailments but also advance human health, leading to transformations in the medical field. However, what are often overlooked are the impacts medicines, and pharmaceuticals, in particular, can have on the environment. Pharmaceuticals are chemical compounds that are produced to be used as medicinal drugs, and these pharmaceuticals react to the environment when they are disposed of. Recently, there has been an increase in literature regarding the effects of pharmaceuticals on the environment (Deegan et al.; Stumm-Zollinger and Fair). For example, it has been revealed that 3000 different chemical substances are used in medicines, and when those are exposed to the environment they can have toxic effects, and cannot be removed by traditional wastewater treatment methods due to the complexity of the compounds as of 2017 (Renita et al.).

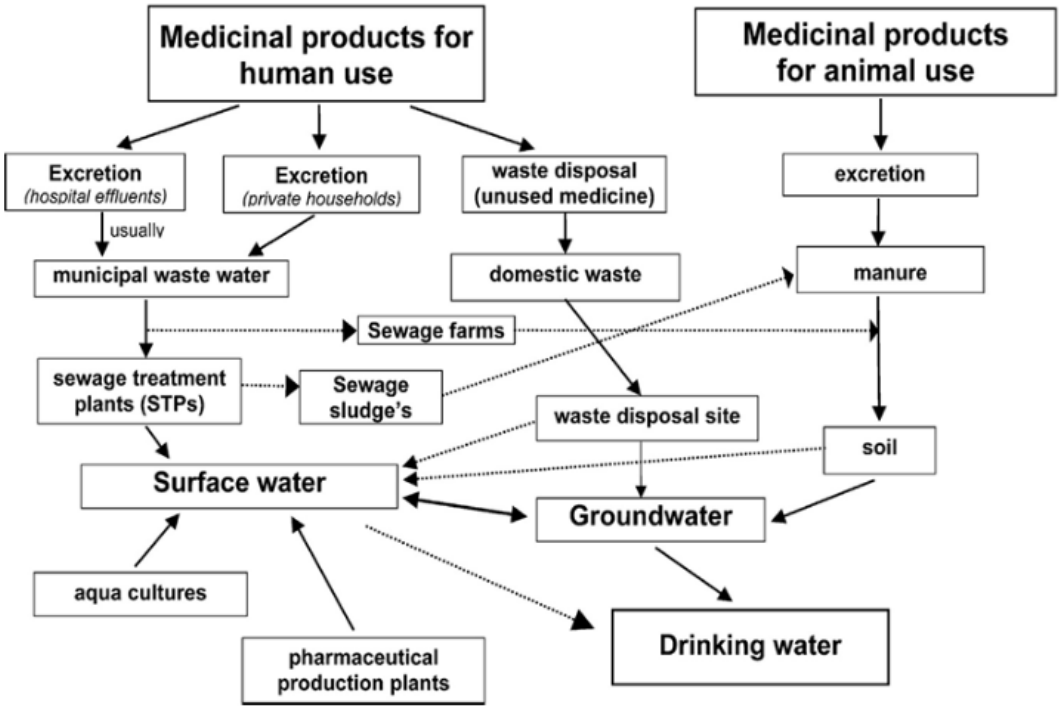

Fig 1. Routes of Pharmaceutical Waste into the Environment, taken from Ganiyu et al.

Figure 1 shows how pharmaceuticals enter the environment (Ganiyu et al.). Regardless of the route of pharmaceuticals into the environment, the presence of pharmaceutical waste in the environment has detrimental effects on environmental and human health.

The waste arises largely from pharmaceutical production plants, wastewater treatment plants (WWTPs), and landfills (Heberer). Due to the avenues of exposure, APIs have become widespread in waterways, and are present in 80% of 139 U.S. streams (Barnes et al.). Despite past literature yielding inconclusive results as to the effects of pharmaceuticals on the environment (Madukasi et al.; Ankley et al.), recent literature as to the effects, for example in aquatic environments, as previous studies have provided more tangible evidence regarding the effects of pharmaceuticals in environments, particularly aquatic ones, due to molecular pathways common between the environment and humans being affected by pharmaceutical waste (Fent et al.).

Pharmaceutical contamination has been shown to damage aquatic ecosystems (Miège et al.). Aquatic life that has been exposed to pharmaceutical waste showed changes in behavior, such as inhibitions of reproductive activity and reduction in activity, subsequently leading to a decrease in feeding (Adeleye et al.; Chopra and Kumar). In a different study, various fish species have exhibited inhibitions of cardiovascular systems and reproductive functions due to ibuprofen throughout their habitat (Corcoran et al.; Adeleye et al.). Prozac, an antidepressant, was found to have behavior changes in freshwater fish, such as territorial aggression, decreases in growth, feeding rate inhibition, and inhibition of predatory activities at low concentrations (Corcoran et al.). These studies show that, even though the effects aren't

lethal, even at low concentrations of pharmaceutical entry into aquatic life behavioral changes like these are prevalent, which can lead to a disruption of ecosystems and long-term potential of environmental devastation.

It's proven that aquatic life and ecosystems are affected by pharmaceutical deposits, but that water is also fed on by other organisms, which are affected as well. Organisms reliant on direct waterways affected by pharmaceutical waste, experience antibiotic resistance to viruses (Fick et al.). Antibiotic-resistant genes (ARG) will proliferate in humans in the event of exposure to high non-lethal concentrations of pharmaceutical wastewater and pharmaceutical compounds (Aydin et al.; Rizzo et al.).

Given the negative impacts of pharmaceutical contamination of waterways, treatment methods to break down or remove pharmaceuticals are required. Common methods involving the breaking down of pharmaceutical compounds are Advanced Oxidation Processes (AOPs) and Bio-activated methods. AOPs generate radicals that break down APIs while Bio-activated methods use bacteria and other microorganisms for the same purpose. Treatments to separate pharmaceuticals use tightly packed filters to separate the pharmaceutical compounds from the target water source.

In this paper, I will provide further details of the types of treatment solutions mentioned above, and I will provide the effectiveness and the drawbacks of each method. The final goal is to design a method that incorporates and improves upon the conventional treatments that have been used in treating APIs.

Section 2- Types of Waste Treatment Solutions

In order for wastewater treatments to be successful in the removal of APIs, the treatment must be economical, non-toxic, and have versatile scalability. Current methods are effective, sometimes across a wide range of pharmaceutical compounds, but they fail in the application, either due to issues with versatility, purification effectiveness, or the production of toxic byproducts. In the following subsections, I will explain the working principles and highlight the effectiveness and limitations of radical-based, bio-, and separation-based treatments.

Radical-Involved Treatments

Advanced oxidation processes are oxidation reactions that make use of radicals, specifically the hydroxyl radical, to oxidize and aid in the breakdown process of biochemical molecules (Wang and Xu). Hydroxyl radicals (·OH), differ from hydroxide ions (OH^-) primarily in their electron configuration. Hydroxide ions possess an overall charge of -1 to satisfy the octet rule, whereas ·OH is characterized by an unpaired electron on the oxygen atom. This characteristic makes radicals extremely reactive, which makes them an excellent species for pharmaceutical wastewater treatments. Figure 2 below (adapted from Krishnan et al.) gives a general overview of radicals' effects on Pharmaceutical and Personal Care Prodcuts (PPCPs) and pharmaceutical compounds.

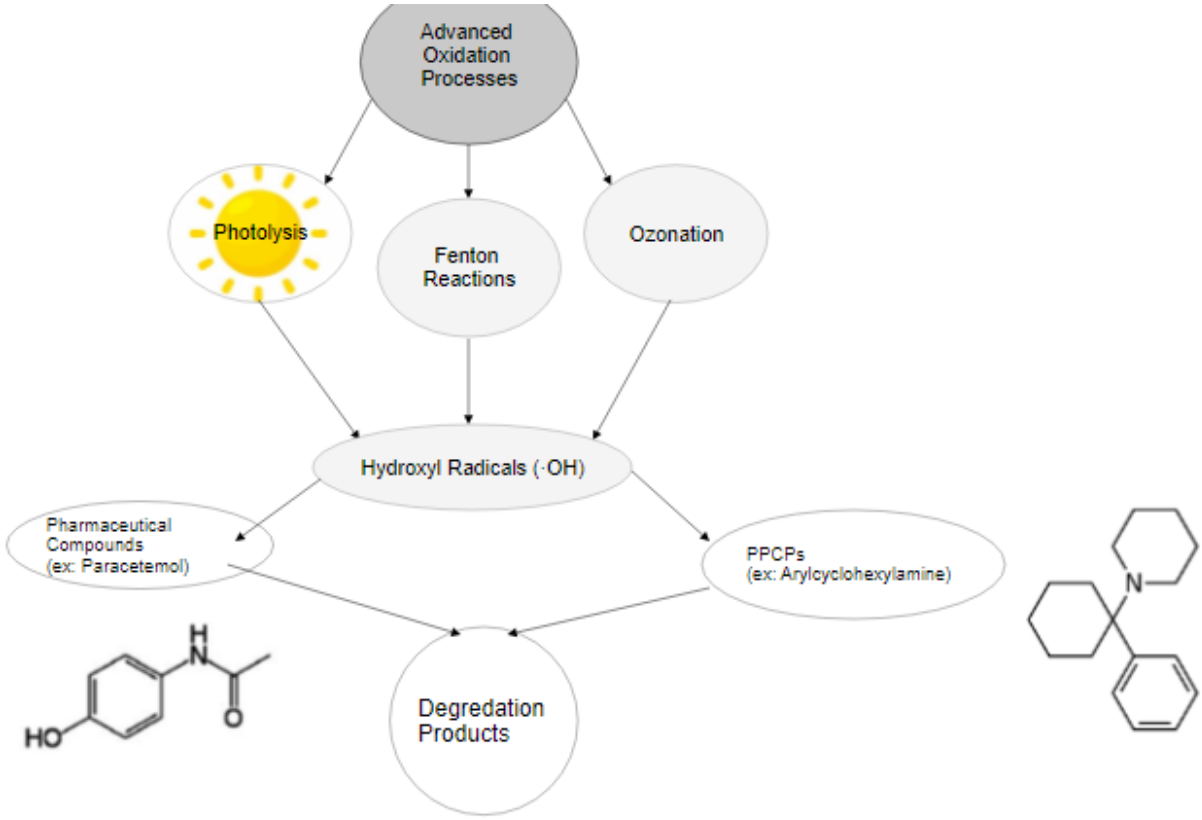

Figure 2: Process flow of pharmaceuticals and PPCPs through AOPs, adapted from Krishnan et al

There are two types of photolysis, direct and indirect. Direct photolysis involves the degradation of a compound through direct absorption of UV light (either direct sunlight or a UV lamp), while indirect photolysis occurs when the compound reacts with another substance that has absorbed light, leading to degradation. Direct photolysis, which is particularly effective for APIs, is the preferred approach (Legrini et al.). It's demonstrated by a successful experiment using an ultraviolet lamp to break down 2-chloropyridine, a pharmaceutical effluent component, in just 20 minutes (Stapleton et al.). A general direct photolysis treatment starts with an entrance of influent through a reactor with a UV lamp, and being pumped into a biological aerating filter (BAF), then through a filter and into a water tank (Jing and Cao).

Photolysis has a low efficiency in breaking down APIs. For example, indirect photolysis accounted for 38% of the degradation of sulfamethoxazole, while direct accounted for 48% (Ryan et al.). Given the higher degradation efficiency of direct photolysis, this is more useful for the proposed solution than indirect photolysis. The solution needs a treatment that is nontoxic, which both provides, and high efficiency which doesn't provide. However, since direct photolysis is 10% better than indirect photolysis, this makes direct photolysis more favorable for the proposed solution. To combat the low efficiency of direct photolysis, photolysis needs to be catalyzed/paired with a complementary reaction such as the Fenton reaction. Photolysis when coupled with Fe (III) and H_2O_2 or TiO_2 can be more efficient than the treatment on its own, as it's shown to remove over 98% of pharmaceuticals including estrogens (Benotti et al.; Feng et al.).

Fenton reaction mechanisms involve, in the presence of excess iron, the following reactions:

$$Fe^{2+} + H_2O_2 \rightarrow Fe^{3+} + OH^- + HO\bullet$$

$$Fe^{3+} + H_2O_2 \rightarrow HOO\bullet + Fe^{2+} + H^+$$

$$2H_2O_2 \rightarrow HOO\bullet + HO\bullet + H_2O$$

Here, excess H_2O_2 following the reaction is decomposed into diatomic oxygen and water, which is later converted into hydroxyl radicals to break down APIs (Kremer). Superoxide molecules (O_2^-), which are formed via partial reduction of molecular oxygen (O_2), can recycle Fe^{3+} back to Fe^{2+} at the reaction's end by donating its electron to Fe^{3+} in the following reaction:

$$Fe^{3+} + O_2^- \rightarrow Fe^{2+} + O_2$$

This makes Fenton reactions reusable. Fenton involves the preparation of $Fe(ClO_4)_2$ (see Figures 3 and 4 below) under molecular nitrogen (N_2) (Kremer).

Wastewater purification by Fenton reactions is aided by UV. The photoreduction of Fe (III) to Fe (II) is aided by UV, which is helpful for water treatment due to the non-toxic nature of iron. Complete oxidation does not require UV, enabling the procedure to work without sunlight as well, but it does help enhance Fenton reactions (Leónidas A. Pérez-Estrada et al.). This works on a larger scale since the conditions can be done without a complicated setup while working at normal pressure and room temperature (Kavitha and Palanivelu). The downside is that there is a need for an aqueous solution system with a pH requirement between 2-4 to make hydroxide radicals. There is also a need to regulate and control the concentrations of hydrogen peroxide & ferrous ions, as well as facilitate the disposal of the iron sludge (Shemer et al.). Fenton can be used partially to make a non-toxic biodegradable intermediate and then treated with another biological step for complete oxidation (Muñoz et al.).

Ozonation works as a treatment due to its strong disinfection and sterilization properties (Araña et al.). The hydroxide radicals and the ozone (O_3) molecules that help in a chemical attack increase the oxidation capacity of the wastewater (Ternes et al.); thus making ozonation a staple for wastewater treatment. A general ozone wastewater treatment starts with the entrance of wastewater to an ozone contact column where it is met with ozone. Following the reaction the water is transported to a tank, and then the effluent is filtered out following a biofilter, while the ozone is released into the atmosphere (Lin).

Even if the initial treatment isn't as effective on a larger scale, ozonation can be paired with complementary treatments to make up for the lack of effectiveness (Cokgor et al.). However, while aromatic compounds, amino groups, and other compounds containing a double carbon bond (C=C) are susceptible, amides are resistant (Nakada et al.). A study of ozonation attacks on amoxicillin showed that the phenolic ring was broken down, causing the formation of hydroxyl derivative intermediates. Still, there was no evidence of the sulfur being oxidized (Andreozzi et al.). The main limitation of ozonation is that the target compounds are often not fully oxidized but transformed, making it a possibility for further harmful products. This results in an additional treatment, such as sand filtration, to be used as an additional treatment to deal with the harmful products. Due to ozone causing the reduction of the microbial count, odor, color, and foam, this causes multiple reactive oxidation products to be generated, meaning ozonation as a whole is expensive, as the detoxifying treatments following are additional costs (Larsen et al.). Overall, while ozonation is effective as a treatment, it is not what we want for an experimental solution to wastewater treatment, due to the need to be paired with other treatments in

order to be effective (which means higher costs), the incapability to attack amides, and the toxic byproducts that are a result of the treatment.

Bio-Activated Treatments

Activated sludge is a form of treatment where excretion and waste products are related to the target effluent. The downside to this treatment is the inability to be on-site, leading to multitudes of wastewater effluent being shipped to activated sludge plants, causing operational issues such as color, foaming, and bulking in secondary clarifiers, which separate the suspended solids from the wastewater (Oz et al.). This also requires high energy consumption and the bulk tons of sludge produced for this purpose (Sreekanth et al.). Efficiency is also inhibited by temperature or pH changes, dissolved oxygen (DO), organic load, microbial community, and toxic or recalcitrant substances (LaPara et al.; Suman Raj and Anjaneyulu). Figure 3 provides an overview of how activated sludge treatment works. Wastewater is fed through a grid, as solids are removed and the sludge is added to the water to rid it of organic compounds, and following filtration and disinfection, the effluent is released (Pandey and Singh).

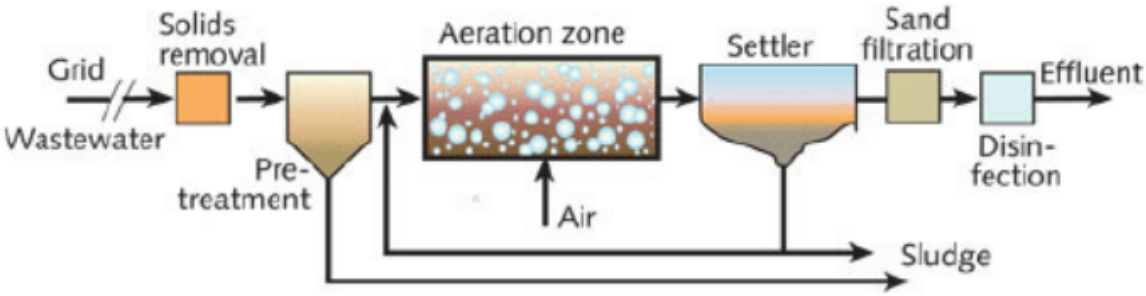

Fig. 3 A simplification of Activated Sludge Procedures taken from Pandey and Singh

This was seen in a wastewater treatment plant in India, called Patancheru Enviro Tech Ltd (PETL), where activated sludge was used on pharmaceutical-water samples (Fick et al.). Overall, activated sludge is neither sanitary when the water source is for sustenance, nor is it good enough to remove APIs and other pharmaceutical constituents in water (Deegan et al.). Moreover, the treatment cannot work in the open, requiring the use of transportation of the target water source to WWTPs (Oz et al.). Moreover, the pharmaceutical compounds that are not broken down in the WWTPs are released back into the environment via the plants, as seen with PETL which shows that the facility is not the only environmental source for poorly treated effluents containing high levels of APIs (Fick et al.). All this makes activated sludge and other bio-activated methods a poor option for the experimental solution to pharmaceutical wastewater treatment.

Separation-Based Treatments

Separation-based treatments involve the use of highly packed filters to separate organic molecules and compounds from water. Adsorption is a separation-based treatment where organic pollutants (even at the trace level) bind to the adsorbent surface. This is becoming a widely used method for sterilizing (Renita et al.). Meanwhile, membrane treatments act as filters under the influence of water. Figure 4 below shows a general process flow of separation treatments being used, where separation is being used to treat wastewater (Loganathan et al.).

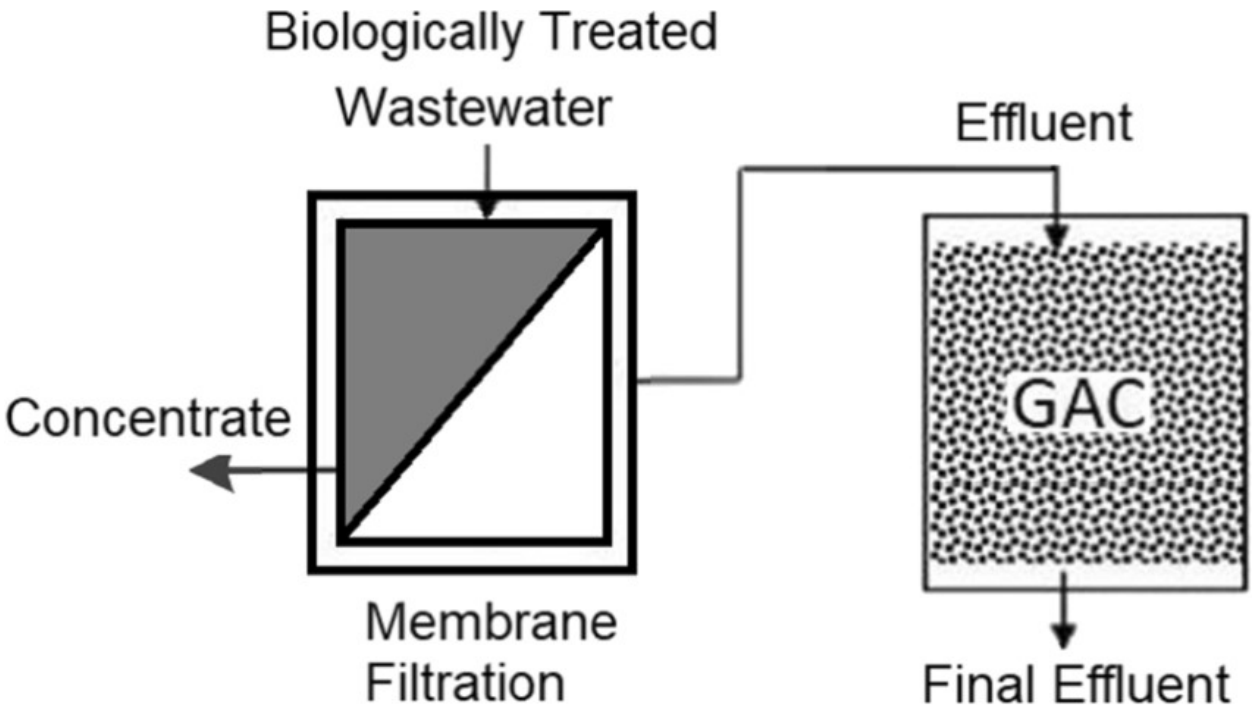

Fig. 4: Membrane Filtration generalized to treat wastewater, taken from Loganathan et al.

A general schematic of adsorption treatment involves waste being fed into the column, where waste is treated. Following that, the water exits the process (Bogush et al.). A form of adsorption treatment is called activated carbon, which involves a carbon that has been processed to have low-volume pores for greater Tadsorption of pharmaceuticals (Renita et al.). There are two main types of activated carbon classifications, granular activated carbon (GAC), which excels at continual contact and pollution treater, whereas powdered activated carbon (PAC) while having less contact time, is cheaper and still effective (Renita et al.). GACs and PACs target different pharmaceutical compounds, for example, GACs excel at filtering pharmaceutical compounds and endocrine-disrupting substances (EDS) (Yu et al.). Overall, adsorption is an effective removal agent and has the ability to be reusable, but the cons of this process are the high costs and oftentimes the need for specialized adsorptive materials.

Membrane treatments are done under the driving force of water, components within the water are driven through a membrane filter and, as a result, the permselective membrane leaves behind the components while the water goes through (Guo et al.). A general membrane treatment solution

has the wastewater being pumped through a filter, and the purified water exits the process while another round of wastewater is cycled back again through the process (Singh).

There are four broad types of membrane filtration: microfiltration (MF), ultrafiltration (UF), nanofiltration (NF), and reverse osmosis (RO); these different kinds of membranes differ in filter-pore size (Rosman et al.) NF/RO membranes are efficient in rejecting pharmaceutical particles and substances in the micro size due to the smaller pore structure (Rosman et al.). MF and UF methods are ineffective for smaller particles but are comparable with a larger concentration of pharmaceuticals in the target area (Gerrity et al.).

Section 3- Next Steps in R&D

I am seeking an efficient and cost-effective solution that can offer a more generalized approach to API treatment, to reduce the resource utilization and mitigate the expense associated with the prolonged practice of transporting wastewater via trucks between the site and WWTPs. Past research done on measuring the effectiveness of pharmaceutical wastewater treatments, as covered above, has been done in isolation, instead of coupling these treatment technologies together. Moreover, it is imperative that this solution minimizes the generation of biohazardous sludge, which further contributes to waste management concerns. In the following subsections, I will describe the more common wastewater treatment solutions and their implementation for pharmaceutical wastewater. Here, I will propose further research to test coupling these processes to develop a more effective pharmaceutical wastewater treatment procedure.

To begin with the process of creating an experimental method, it is first important to mention how multiple methods complement each other and form a workable, near-standard method that is effective at dealing with pharmaceutical wastewater. An example of this is combined photolysis and Fenton reactions, which have two versions. Direct photolysis plus Fenton reactions involve the use of either sunlight or UV lamp-light, and either one is a viable option. How this experiment works is that, either in the open or in a large reaction vessel, the target water source can have hydrogen peroxide (H_2O_2) plus ferrous salt added, and later can be exposed to sunlight. This can also involve the addition of a UV lamp-light, in case the sunlight procedure either takes too long or is too weak on its own. The process works through the activation of the peroxide by UV light and coupled with the breakdown of the ferrous salt, both reactions begin to form radicals, which aid in the breakdown process.

An example of the efficiency of Photo-Fenton (PFP) reactions is in an experiment to break down the analgesic drug Dipyrone (DIPY), which quickly hydrolyzes to 4-methylaminoantipyrine (4-MAA), where Photo-Fenton reactions on 4-MAA had a 96.4% removal, which lasted around 45 minutes after an 83.2% removal rate after 2.5 minutes (Giri and Golder). The setup involved a large 1.0 L reaction vessel in which 400. mL of DIPY (later hydrolyzed to 4-MAA) was added, afterward Fe^{2+} ions were added & following 5 minutes of magnetic stirring, the H_2O_2 was added. For the PFP experiment, the reaction vessel was put under a UV lamp to activate the peroxide and enhance the formation of radicals (Giri and

Golder). The conclusion of this experiment was that the technology and processes used for pharmaceutical wastewater treatment and mineralization are promising (Giri and Golder).

This is a start, utilizing radicals from other AOP treatments to combine with photolysis, which unfortunately does not break down everything (Ryan et al.). Prior research has shown that AOPs are non-selective, and are versatile at treating a variety of wastewater (pharmaceutical, activated sludge, etc.). However, a limitation of AOPs is that perform only at low acidic pH, and when isolated from each other, they have a low effectiveness percentage. Including a separation process following AOP treatment could address this limitation. Given that the main goal of this experimental solution is for it to be implemented on-site instead of resources being diverted to factories, adding more strain to an already complicated process. A downside to photo-Fenton procedures is that they perform only at low acidic pH, but this can be combated by using chelating agents to raise the reaction pH of the photo-Fenton radicals to be produced at neutral (Clarizia et al.). Beforehand, the use of photo-fenton would have been ineffective for pharmaceutical wastewater treatment, but with chelating agents such as ethylenediaminetetraacetic acid (EDTA), the reaction can proceed at a neutral pH.

Moving on to incorporating separation treatments, there is potential in it. Membrane technology already has made an impact in converting wastewater back into reusable water (Obotey Ezugbe and Rathilal). Moreover, membrane separation can make use of effluent feeding repeatedly through the membranes. However, the problem is with fouling and subsequent cleaning and maintenance of membranes. The most effective and relevant methods for pharmaceutical wastewater treatment are certain physical cleanings, such as pneumatic cleaning (involving air) or ultra-sonic cleaning, which dislodges the particles at the molecular level from the membrane (Maartens et al.). Biochemical cleaning is also useful, involving enzymes and enzymatic mixtures to stir up and dislodge the particles, but in the case of permanent fouling, chemical cleaning, using various chemical agents, is best used; chemical cleaning can be combined with physical methods as well, seeing enhancements of flux recovery up to 95% (Popović et al.; Maskooki et al.).

Given the past research discussed, I've proposed the following solution to pharmaceutical wastewater treatment:

1. Transfer the water that needs to be treated to transparent reaction vessels via pipes.
2. Add the required concentration of hydrogen peroxide to the vessels, along with ferrous ions as catalysts for the radical production phase.
3. Add chelator agents to the vessels to enable the reaction to occur at a neutral pH instead of an acidic pH as is typical of photo-Fenton reactions.
4. Expose the vessels to sunlight and stir the contents of the vessels with a magnetic stirring rod so that the contents generate hydroxyl radicals for the breakdown of the pharmaceutical compounds in the water.
5. Monitor the mixture via chromatography to see if the reaction has proceeded to completion. Once it has, filter out the water using ultrafiltration membranes or activated carbon membranes.
6. Filter out this water with more membrane filters until it arrives at a small tank for observation purposes.

7. Examine the concentration of this final tank to see if it's as close to purity as possible. If so put it through one more filter and observe the purity again. If not, put it back into the reaction vessels for further examination and treatment.

In our experiments, we can change the source of hydroxyl radical production by instead having a 10 to 100 W UV lamp (on average) shining directly downwards into the vessel. The lamp will be more useful than sunlight in a lab setting, as it takes around 20-45 minutes (according to past literature) to break down an API.

The ferrous sludge is a semi-solid that contains ferrous compounds/ions, water, contaminants, pH adjusting agents, and other biological compounds that were initially in the vessels. The superoxide molecules for the Fenton reactions will be an aid in repurposing the ferrous sludge for Fe^{2+} catalysts. The sludge will be difficult to deal with post-repurposing, as it serves no purpose despite its nontoxicity due to the iron. Overall, this is the proposed solution, based on past research, to pharmaceutical wastewater.

Limitations to this solution could possibly be the addition of the chelating agent and maintaining the other pieces of equipment used. While the chelating agent is beneficial, the addition of another chemical to the process (and subsequently the sludge) may have an impact on cleanup. The maintenance of the equipment and potential concerns about reusability will cause a backup in the process. Other limitations that have to be addressed are in applicability and practicality. To begin with, the requirement of sunlight, as this renewable source of energy is limited depending on seasons and time, and this affects efficiency. Another limitation is the purity of the treated water, as the goal is to make this water safe for drinking, but after going through a chemical-heavy process, that's not fully guaranteed. A final limitation is the cost, as such a proposed experiment will be expensive as an on-site solution. The criterias for success are mainly in attaining purity in an efficient process over a certain period of time.

Conclusion

Past research suggests that the solution can be feasible, but further testing is required. Having gone through the previously established treatment methods for APIs, the proposed experimental solution seeks to combine the positives of all treatment methods mentioned, while cutting back on their drawbacks. Due to the rising consumption and production of pharmaceuticals, the byproducts and only partially degraded compounds that end up as waste in aquatic environments, changing ecosystems and their inhabitants' behaviors. Established wastewater treatments employ the use of radicals, bacteria in bio-activated treatments, or utilize separation-based treatments. Given the effectiveness of these treatments on their own, further research is required to see how coupling different types of methods are feasible

Works Cited:

Adeleye, Adeyemi S., et al. “Abundance, Fate, and Effects of Pharmaceuticals and Personal Care Products in Aquatic Environments.” *Journal of Hazardous Materials*, vol. 424, Feb. 2022, p. 127284. *DOI.org (Crossref)*, https://doi.org/10.1016/j.jhazmat.2021.127284.

Andreozzi, Roberto, et al. “Antibiotic Removal from Wastewaters: The Ozonation of Amoxicillin.” *Journal of Hazardous Materials*, vol. 122, no. 3, July 2005, pp. 243–50. *DOI.org (Crossref)*, https://doi.org/10.1016/j.jhazmat.2005.03.004.

Ankley, Gerald T., et al. “Repeating History: Pharmaceuticals in the Environment.” *Environmental Science & Technology*, vol. 41, no. 24, Dec. 2007, pp. 8211–17. *DOI.org (Crossref)*, https://doi.org/10.1021/es072658j.

Araña, J., et al. “TiO2-Photocatalysis as a Tertiary Treatment of Naturally Treated Wastewater.” *Catalysis Today*, vol. 76, no. 2, Nov. 2002, pp. 279–89. *ScienceDirect*, https://doi.org/10.1016/S0920-5861(02)00226-2.

Aydin, Sevcan, et al. “Development of Antibiotic Resistance Genes in Microbial Communities during Long-Term Operation of Anaerobic Reactors in the Treatment of Pharmaceutical Wastewater.” *Water Research*, vol. 83, Oct. 2015, pp. 337–44. *DOI.org (Crossref)*, https://doi.org/10.1016/j.watres.2015.07.007.

Barnes, Kimberlee K., et al. “A National Reconnaissance of Pharmaceuticals and Other Organic Wastewater Contaminants in the United States — I) Groundwater.” *Science of The Total Environment*, vol. 402, no. 2–3, Sept. 2008, pp. 192–200. *DOI.org (Crossref)*, https://doi.org/10.1016/j.scitotenv.2008.04.028.

Benotti, Mark J., et al. “Evaluation of a Photocatalytic Reactor Membrane Pilot System for the Removal of Pharmaceuticals and Endocrine Disrupting Compounds from Water.” *Water Research*, vol. 43, no. 6, Apr. 2009, pp. 1513–22. *ScienceDirect*, https://doi.org/10.1016/j.watres.2008.12.049.

Bogush, A. A., et al. “Removal of Arsenic, Nitrate, Persistent Organic Pollutants and Pathogenic Microbes from Water Using Redox-Reactive Minerals.” *Redox-Reactive Minerals: Properties, Reactions and Applications in Clean Technologies*, by K.A. Hudson-Edwards, edited by I.A.M. Ahmed, 1st ed., Mineralogical Society of Great Britain & Ireland, 2007, pp. 405–42. *DOI.org (Crossref)*, https://doi.org/10.1180/EMU-notes.17.12.

---. “Removal of Arsenic, Nitrate, Persistent Organic Pollutants and Pathogenic Microbes from Water Using Redox-Reactive Minerals.” *Redox-Reactive Minerals: Properties, Reactions and Applications in Clean Technologies*, by K.A. Hudson-Edwards, edited by I.A.M. Ahmed, 1st ed., Mineralogical Society of Great Britain & Ireland, 2007, pp. 405–42. *DOI.org (Crossref)*, https://doi.org/10.1180/EMU-notes.17.12.

Chopra, Sunil, and Dharmender Kumar. “Pharmaceuticals and Personal Care Products (PPCPs) as Emerging Environmental Pollutants: Toxicity and Risk Assessment.” *Advances in Animal Biotechnology and Its Applications*, edited by Suresh Kumar Gahlawat et al., Springer, 2018, pp. 337–53. *Springer Link*, https://doi.org/10.1007/978-981-10-4702-2_19.

Clarizia, L., et al. “Homogeneous Photo-Fenton Processes at near Neutral pH: A Review.” *Applied Catalysis B: Environmental*, vol. 209, July 2017, pp. 358–71. *DOI.org (Crossref)*, https://doi.org/10.1016/j.apcatb.2017.03.011.

Cokgor, Emine Ubay, et al. “Biological Treatability of Raw and Ozonated Penicillin Formulation Effluent.” *Journal of Hazardous Materials*, vol. 116, no. 1, Dec. 2004, pp. 159–66. *ScienceDirect*, https://doi.org/10.1016/j.jhazmat.2004.08.011.

Corcoran, Jenna, et al. “Pharmaceuticals in the Aquatic Environment: A Critical Review of the Evidence for Health Effects in Fish.” *Critical Reviews in Toxicology*, vol. 40, no. 4, Apr. 2010, pp. 287–304. *DOI.org (Crossref)*, https://doi.org/10.3109/10408440903373590.

Deegan, A. M., et al. “Treatment Options for Wastewater Effluents from Pharmaceutical Companies.” *International Journal of Environmental Science & Technology*, vol. 8, no. 3, June 2011, pp. 649–66. *DOI.org (Crossref)*, https://doi.org/10.1007/BF03326250.

Feng, Xianghua, et al. “Degradation of Estrone in Aqueous Solution by Photo-Fenton System.” *Science of The Total Environment*, vol. 345, no. 1, June 2005, pp. 229–37. *ScienceDirect*, https://doi.org/10.1016/j.scitotenv.2004.11.008.

Fent, K., et al. “Ecotoxicology of Human Pharmaceuticals.” *Aquatic Toxicology*, vol. 76, no. 2, Feb. 2006, pp. 122–59. *DOI.org (Crossref)*, https://doi.org/10.1016/j.aquatox.2005.09.009.

Fick, Jerker, et al. “Contamination of Surface, Ground, and Drinking Water from Pharmaceutical Production.” *Environmental Toxicology and Chemistry*, vol. 28, no. 12, Dec. 2009, pp. 2522–27. *DOI.org (Crossref)*, https://doi.org/10.1897/09-073.1.

Ganiyu, Soliu O., Eric D. Van Hullebusch, et al. “Coupling of Membrane Filtration and Advanced Oxidation Processes for Removal of Pharmaceutical Residues: A Critical Review.” *Separation and Purification Technology*, vol. 156, Dec. 2015, pp. 891–914. *DOI.org (Crossref)*, https://doi.org/10.1016/j.seppur.2015.09.059.

Ganiyu, Soliu O., Eric D. van Hullebusch, et al. “Coupling of Membrane Filtration and Advanced Oxidation Processes for Removal of Pharmaceutical Residues: A Critical Review.” *Separation and Purification Technology*, vol. 156, Dec. 2015, pp. 891–914. *ScienceDirect*, https://doi.org/10.1016/j.seppur.2015.09.059.

Gerrity, Daniel, et al. “Pharmaceuticals and Endocrine Disrupting Compounds in Drinking Water.” *Biophysico-Chemical Processes of Anthropogenic Organic Compounds in Environmental Systems*, Jan. 2011, pp. 233–50, https://doi.org/10.1002/9780470944479.ch10.

Giri, Ardhendu Sekhar, and Animes Kumar Golder. “Fenton, Photo-Fenton, H_2O_2 Photolysis, and TiO_2 Photocatalysis for Dipyrone Oxidation: Drug Removal, Mineralization, Biodegradability,

and Degradation Mechanism." *Industrial & Engineering Chemistry Research*, vol. 53, no. 4, Jan. 2014, pp. 1351–58. *DOI.org (Crossref)*, https://doi.org/10.1021/ie402279q.

Guo, Y., et al. "A Review on Advanced Treatment of Pharmaceutical Wastewater." *IOP Conference Series: Earth and Environmental Science*, vol. 63, May 2017, p. 012025. *DOI.org (Crossref)*, https://doi.org/10.1088/1755-1315/63/1/012025.

Heberer, Thomas. "Occurrence, Fate, and Removal of Pharmaceutical Residues in the Aquatic Environment: A Review of Recent Research Data." *Toxicology Letters*, vol. 131, no. 1–2, May 2002, pp. 5–17. *DOI.org (Crossref)*, https://doi.org/10.1016/S0378-4274(02)00041-3.

Jing, Zhaoqian, and Shiwei Cao. "Combined Application of UV Photolysis and Ozonation with Biological Aerating Filter in Tertiary Wastewater Treatment." *International Journal of Photoenergy*, vol. 2012, 2012, pp. 1–6. *DOI.org (Crossref)*, https://doi.org/10.1155/2012/140605.

Kavitha, V., and K. Palanivelu. "The Role of Ferrous Ion in Fenton and Photo-Fenton Processes for the Degradation of Phenol." *Chemosphere*, vol. 55, no. 9, June 2004, pp. 1235–43. *ScienceDirect*, https://doi.org/10.1016/j.chemosphere.2003.12.022.

Kremer, Mordechai L. "Mechanism of the Fenton Reaction. Evidence for a New Intermediate." *Physical Chemistry Chemical Physics*, vol. 1, no. 15, 1999, pp. 3595–605. *DOI.org (Crossref)*, https://doi.org/10.1039/a903915e.

Krishnan, Radhakrishnan Yedhu, et al. "Removal of Emerging Micropollutants Originating from Pharmaceuticals and Personal Care Products (PPCPs) in Water and Wastewater by Advanced Oxidation Processes: A Review." *Environmental Technology & Innovation*, vol. 23, Aug. 2021, p. 101757. *ScienceDirect*, https://doi.org/10.1016/j.eti.2021.101757.

LaPara, Timothy M., et al. "Stability of the Bacterial Communities Supported by a Seven-Stage Biological Process Treating Pharmaceutical Wastewater as Revealed by PCR-DGGE." *Water*

Research, vol. 36, no. 3, Feb. 2002, pp. 638–46. *ScienceDirect*, https://doi.org/10.1016/S0043-1354(01)00277-9.

Larsen, Tove A., et al. "How to Avoid Pharmaceuticals in the Aquatic Environment." *Journal of Biotechnology*, vol. 113, no. 1–3, Sept. 2004, pp. 295–304. *DOI.org (Crossref)*, https://doi.org/10.1016/j.jbiotec.2004.03.033.

Legrini, O., et al. "Photochemical Processes for Water Treatment." *ACS Publications*, American Chemical Society, 1 May 2002, https://doi.org/10.1021/cr00018a003. world.

Leónidas A. Pérez-Estrada, †, et al. "Photo-Fenton Degradation of Diclofenac: Identification of Main Intermediates and Degradation Pathway." *ACS Publications*, American Chemical Society, 21 Sept. 2005, https://doi.org/10.1021/es050794n. world.

Lin, Yen-Hui. "Molecular Weight Distribution of Organic Matter by Ozonation and Biofiltration." *Water Science and Technology : A Journal of the International Association on Water Pollution Research*, vol. 66, Oct. 2012, pp. 2604–12. *ResearchGate*, https://doi.org/10.2166/wst.2012.484.

Loganathan, Paripurnanda, et al. "Submerged Membrane/Adsorption Hybrid Process in Water Reclamation and Concentrate Management—a Mini Review." *Environmental Science and Pollution Research*, vol. 30, no. 15, Sept. 2022, pp. 42738–52. *DOI.org (Crossref)*, https://doi.org/10.1007/s11356-022-23229-9.

Maartens, A., et al. "An Enzymatic Approach to the Cleaning of Ultrafiltration Membranes Fouled in Abattoir Effluent." *Journal of Membrane Science*, vol. 119, no. 1, Oct. 1996, pp. 9–16. *DOI.org (Crossref)*, https://doi.org/10.1016/0376-7388(96)00015-4.

Madukasi, E. I., et al. "Potentials of Phototrophic Bacteria in Treating Pharmaceutical Wastewater." *International Journal of Environmental Science & Technology*, vol. 7, no. 1, Dec. 2010, pp. 165–74. *DOI.org (Crossref)*, https://doi.org/10.1007/BF03326128.

Maskooki, Abdolmajid, et al. “Cleaning of Spiralwound Ultrafiltration Membranes Using Ultrasound and Alkaline Solution of EDTA.” *Desalination*, vol. 264, no. 1–2, Dec. 2010, pp. 63–69. *DOI.org (Crossref)*, https://doi.org/10.1016/j.desal.2010.07.005.

Miège, C., et al. “Fate of Pharmaceuticals and Personal Care Products in Wastewater Treatment Plants – Conception of a Database and First Results.” *Environmental Pollution*, vol. 157, no. 5, May 2009, pp. 1721–26. *DOI.org (Crossref)*, https://doi.org/10.1016/j.envpol.2008.11.045.

Muñoz, Ivan, et al. “Life Cycle Assessment of a Coupled Solar Photocatalytic–Biological Process for Wastewater Treatment.” *Water Research*, vol. 40, no. 19, Nov. 2006, pp. 3533–40. *DOI.org (Crossref)*, https://doi.org/10.1016/j.watres.2006.08.001.

Nakada, Norihide, et al. “Removal of Selected Pharmaceuticals and Personal Care Products (PPCPs) and Endocrine-Disrupting Chemicals (EDCs) during Sand Filtration and Ozonation at a Municipal Sewage Treatment Plant.” *Water Research*, vol. 41, no. 19, Nov. 2007, pp. 4373–82. *ScienceDirect*, https://doi.org/10.1016/j.watres.2007.06.038.

Obotey Ezugbe, Elorm, and Sudesh Rathilal. “Membrane Technologies in Wastewater Treatment: A Review.” *Membranes*, vol. 10, no. 5, Apr. 2020, p. 89. *DOI.org (Crossref)*, https://doi.org/10.3390/membranes10050089.

Oz, Nilgun Ayman, et al. “Effect of Wastewater Composition on Methanogenic Activity in an Anaerobic Reactor.” *Journal of Environmental Science and Health, Part A*, vol. 39, no. 11–12, Dec. 2004, pp. 2941–53. *Taylor and Francis+NEJM*, https://doi.org/10.1081/LESA-200034284.

Pandey, Aditi, and Ravi Singh. “Industrial Waste Water Treatment by Membrane Bioreactor System.” *Elixir Chemical Engineering*, vol. 70, Apr. 2014, pp. 23772–77.

Popović, Svetlana, et al. “Application of an Ultrasound Field in Chemical Cleaning of Ceramic Tubular Membrane Fouled with Whey Proteins.” *Journal of Food Engineering*, vol. 101, no. 3, Dec. 2010, pp. 296–302. *DOI.org (Crossref)*, https://doi.org/10.1016/j.jfoodeng.2010.07.012.

Renita, A. Annam, et al. “A Review on Analytical Methods and Treatment Techniques of Pharmaceutical Wastewater.” *DESALINATION AND WATER TREATMENT*, vol. 87, 2017, pp. 160–78. *DOI.org (Crossref)*, https://doi.org/10.5004/dwt.2017.21311.

Rizzo, L., et al. “Urban Wastewater Treatment Plants as Hotspots for Antibiotic Resistant Bacteria and Genes Spread into the Environment: A Review.” *Science of The Total Environment*, vol. 447, Mar. 2013, pp. 345–60. *DOI.org (Crossref)*, https://doi.org/10.1016/j.scitotenv.2013.01.032.

Rosman, Nurafiqah, et al. “Hybrid Membrane Filtration-Advanced Oxidation Processes for Removal of Pharmaceutical Residue.” *Journal of Colloid and Interface Science*, vol. 532, Dec. 2018, pp. 236–60. *DOI.org (Crossref)*, https://doi.org/10.1016/j.jcis.2018.07.118.

Ryan, Christopher C., et al. “Direct and Indirect Photolysis of Sulfamethoxazole and Trimethoprim in Wastewater Treatment Plant Effluent.” *Water Research*, vol. 45, no. 3, Jan. 2011, pp. 1280–86. *DOI.org (Crossref)*, https://doi.org/10.1016/j.watres.2010.10.005.

Shemer, Hilla, et al. “Degradation of the Pharmaceutical Metronidazole via UV, Fenton and Photo-Fenton Processes.” *Chemosphere*, vol. 63, no. 2, Apr. 2006, pp. 269–76. *ScienceDirect*, https://doi.org/10.1016/j.chemosphere.2005.07.029.

Singh, Rajindar. “Chapter 3 - Hybrid Membrane Systems – Applications and Case Studies.” *Membrane Technology and Engineering for Water Purification (Second Edition)*, edited by Rajindar Singh, Butterworth-Heinemann, 2015, pp. 179–281. *ScienceDirect*, https://doi.org/10.1016/B978-0-444-63362-0.00003-3.

Sreekanth, D., et al. “Thermophilic Treatment of Bulk Drug Pharmaceutical Industrial Wastewaters by Using Hybrid up Flow Anaerobic Sludge Blanket Reactor.” *Bioresource Technology*, vol. 100, no. 9, May 2009, pp. 2534–39. *DOI.org (Crossref)*, https://doi.org/10.1016/j.biortech.2008.11.028.

Stapleton, D. R., et al. “Photolytic Destruction of Halogenated Pyridines in Wastewaters.” *Process Safety and Environmental Protection*, vol. 84, no. 4, July 2006, pp. 313–16. *ScienceDirect*, https://doi.org/10.1205/psep.05164.

Stumm-Zollinger, Elisabeth, and Gordon M. Fair. “Biodegradation of Steroid Hormones.” *Journal (Water Pollution Control Federation)*, vol. 37, no. 11, 1965, pp. 1506–10.

Suman Raj, D. Samuel, and Y. Anjaneyulu. “Evaluation of Biokinetic Parameters for Pharmaceutical Wastewaters Using Aerobic Oxidation Integrated with Chemical Treatment.” *Process Biochemistry*, vol. 40, no. 1, Jan. 2005, pp. 165–75. *DOI.org (Crossref)*, https://doi.org/10.1016/j.procbio.2003.11.056.

Ternes, Thomas A., et al. “Ozonation: A Tool for Removal of Pharmaceuticals, Contrast Media and Musk Fragrances from Wastewater?” *Water Research*, vol. 37, no. 8, Apr. 2003, pp. 1976–82. *ScienceDirect*, https://doi.org/10.1016/S0043-1354(02)00570-5.

Wang, Jian Long, and Le Jin Xu. “Advanced Oxidation Processes for Wastewater Treatment: Formation of Hydroxyl Radical and Application.” *Critical Reviews in Environmental Science and Technology*, vol. 42, no. 3, Feb. 2012, pp. 251–325. *DOI.org (Crossref)*, https://doi.org/10.1080/10643389.2010.507698.

Yu, Zirui, et al. *Adsorption of Selected Pharmaceuticals and Endocrine Disrupting Substances by GAC at Low Concentration Levels*.