

Small-Scale Electrochemical Oxidation of Non-Steroidal Anti-Inflammatory Drugs: Conventional Approaches and Conditions

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Abstract – Improper disposal of pharmaceutical wastes, coupled with low pollutant removal efficiency at wastewater treatment plants (WWTPs), has created a disastrous ecological issue. Ecotoxicity reviews have consolidated that low concentrations of pharmaceutical pollutants, specifically non-steroidal anti-inflammatory drugs, impose significant toxicological risks on the aquatic ecosystem. Research solutions have shifted towards electrochemical oxidation for its environmental-friendly, precise, and flexible reduction characteristics over non-electrochemical technologies. However, there isn't significant literature dedicated to finding the conditions for small-scale pretreatment, leaving the environment between the pollutant source and WWTPs at risk. This research explores the optimal conditions to pretreat pharmaceutical wastewater using electrochemical oxidation on a small-scale. A conventional approach, utilizing accessible materials and simple procedures, was selected to ease the implementation of pretreatment outside of WWTPs. Spectrophotometric analysis was performed to identify the concentration changes through absorbance for reagents. Manipulated variables of temperature, pH level, scale, and electrode metal type were analyzed individually per solution and in combination to produce the overall effect. F-Test and Tukey-Kramer post-hoc tests were employed to derive the maximum electrochemical oxidation ability for different variables. Results indicate that at the 95% confidence level, temperatures below 25°C, pH levels below 4, larger scale, and higher reactivity metal plates produce the highest electrochemical oxidation magnitude. Overall analysis comparing the combined optimal conditions with the control group yielded an approximately 50% greater concentration reduction magnitude. Future directions include the implementation of electrochemical oxidation as a pretreatment appliance in the household using our optimal conditions and exploring other manipulative variables to increase the flexibility and efficiency of such devices.

Index Terms – Electrochemical Oxidation, Non-Steroidal Anti-Inflammatory Drugs, Pharmaceutical Pollution, Spectrophotometric Analysis

INTRODUCTION

Intense environmental contamination has raised serious concerns in the scientific community [1]. In the 20th century, research on wastewater pollution focused on priority pollutants [2]. Entering the 21st century, the United States Environmental Protection Agency (US EPA) proposed *Strategic Plan 2000* [3], shifting wastewater research directions toward identifying chemical pollutants holistically. *Strategic Plan 2000* noted an exponential introduction of pharmaceuticals in aquatic ecosystems, cautioning the unknown risks of new biochemical reactions. The proposal emphasized researching advanced treatment methods for pharmaceutical wastewater to alleviate threats to public health and ecological stability [3].

Daughton & Ternes [2], following the goals outlined in *Strategic Plan 2000*, classified common pharmaceuticals as persistent organic pollutants with high polarity characteristics requiring novel removal methods. Halling-Sorensen et al. [4] noted these toxic characteristics create multigenerational exposure and bioaccumulation risks. Consequences of pharmaceutical pollutants include increasing antibiotic resistance reactions and chronic symptoms in aquatic species, even at low concentrations ranging from ng/L to µg/L may degrade the environment [5].

Researchers have since attempted to identify routes of pharmaceuticals entering the environment. Ruhoy & Daughton [6] synthesized the pathways – mainly originate from households – into three main pathways: (1) unmetabolized drug components excreting from the body; (2) removal of medication through bathing; and (3) disposal of leftover pharmaceutical products. In addition to the main contamination routes, Tiwari et al. [7] also noted the importance of considering the exposed environment between the pollutant source and wastewater treatment plants (WWTPs). With pharmaceutical pollutants discovered with ultra-low concentrations and low detection sensitivity at WWTPs, the National Institute of Standards and Technology [8] underscored utilizing pretreatment infrastructure¹ alongside improving WWTPs to mitigate pharmaceutical pollutant threats.

¹ Pretreatment infrastructure, explained by the National Institute of Standards and Technology [8], refers to locations where pharmaceuticals cluster in high concentrations.

According to the US National Research Council (US NRC) [9], the environmental buffer² and infrastructure in all US treatment plants “found no evidence [...that...] provides generally higher dilution and attenuation relative to an engineered system.” US NRC suggested direct potable water technologies to treat emerging biochemical pollutants such as pharmaceuticals instead. Liang et al. [10] agree with the future direction of research, suggesting a physicochemical approach for advanced treatment methods. Research focus has since focused on non-electrochemical and electrochemical techniques at WWTPs, with little regard for small-scale implementation of pretreatment, treating the problem from its source. Detection technologies, as noted by the research and US NRC [9], are currently sufficient for constant monitoring of environmental concentrations.

This research paper intends to close the literature gap in pretreatment by finding the optimal conditions to electrochemically oxidize³ pharmaceutical pollutants conventionally and electrochemically. The conventional approach was selected to ease the implementation through accessible materials and procedures for pretreatment outside of WWTPs – most likely in households. The independent variables of temperature, pH level, electrode type, and scale were analyzed using common non-steroidal anti-inflammatory drugs (NSAIDs)⁴ samples, simulating wastewater conditions in the environment through NSAIDs: a potent drug class. Procedures and conditions were adapted from numerous research from existing literature.

LITERATURE REVIEW

I. Review on Non-Steroidal Anti-Inflammatory Drugs

Ia. Non-Steroidal Anti-Inflammatory Drugs Overview

NSAIDs, a popular over-the-counter prescription drug, pose a higher environmental risk than other drug classes. As the majority population improperly disposes of NSAIDs in the household, it has escalated into the category of serious pollutants. The concentration of NSAIDs in the environment oscillates between seasons, with higher levels detected during the winter. Per Pfluger & Dietrich's [13] environmental survey, samples of NSAID pollution have gradually increased from 10 µg/L to 96 µg/L over a decade. The increasing concentration raised the critical role of conducting an ecotoxicity review and understanding NSAID characteristics to develop modern treatment techniques.

Ib. Characteristics and Effect on Environment

NSAIDs have analgesic, anti-inflammatory, and antipyretic effects [14]. It reduces symptoms such as myocardial reinfarction and stroke by inhibiting the cyclooxygenases: key enzymes catalyzing prostaglandin biosynthesis. Common adverse side effects of NSAIDs

include damage to the gastrointestinal and cardiovascular systems. Similarly, Brodin et al. [15] noted side-effects in humans are reflected amongst aquatic species when exposed to low NSAID concentrations. Pharmaceutical effluents dispersed in the environment inflict chronic effects rather than acute symptoms on species. Reports from different geographic aquatic bodies indicated an exponential increase in NSAID concentrations soon [16].

According to Gaw et al. [17], pharmaceutical pollutants in aquatic bodies affect species in ways such as but not limited to reducing feeding rates and immune response. The toxicity of NSAIDs affects the cytoplasmic membrane of aquatic species, creating stress response and prompting negative adaptation mechanisms. Adverse effects are most apparent in invertebrates, which accumulate higher levels of NSAID residue than other drug classes [18]. Non-target species may also receive potential risk at different ecological hierarchies, presenting similar toxic effects as invertebrates [19]. All aquatic species are prone to the gradual increase of antibiotic resistance and long-term genetic and physiological malformations when exposed. Given the urgency to relieve the consequences, identifying the ecotoxicity and effects on the environment of NSAIDs was the research priority in the 2010s [17].

Ic. Ecotoxicity Overview

Research on the ecotoxicity of NSAIDs has been reviewed extensively in the existing literature. Acetylsalicylic acid, salicylic acid, and acetic acid – components of NSAIDs – are classified as harmful per the European Union Water Framework Directive [20]. Supplementing Gaw et al.'s [17] findings, Silva et al. [21] exemplified another NSAID, ibuprofen, as a high-risk threat due to its high occurrence in environmental samples. Other NSAID chemicals such as ethyl alcohol [22]. and citric acid monohydrate tablets [23] have also been cited for their ecotoxicity risks in different geographic aquatic bodies by various literature.

The majority of ecotoxicity reviews point to the increasing concentrations of NSAIDs in the environment towards the low efficiency of WWTPs in removing advanced contaminants [24]. WWTPs were not traditionally designed to treat pharmaceutical effluents and their biochemical reactions. Accumulation of concentrations near the environment of treatment plants is sometimes higher than other chemical concentrations. Ecotoxicity review of NSAIDs and their potential causes have led to the reconsideration of current wastewater treatment methods and the introduction of advanced removal technologies.

II. Advanced Methods of Pharmaceutical Wastewater Removal

Ila. Overview of Non-Electrochemical Removal Technologies

² Environmental buffer, defined by the US EPA [11], is “the land between the boundary of an area that may be used by an industrial land use, such as a wastewater treatment plant, and the boundary of the area within which unacceptable adverse impacts due to industrial emissions on the amenity of sensitive land use are possible.

³ Electrochemical oxidation and its magnitude are also referred as electroreduction or concentration reduction in this research paper.

⁴ Non-steroidal anti-inflammatory drugs, or NSAIDs, are “medicines that are widely used to relieve pain, reduce inflammation, and bring down a high temperature” [12].

There are currently four main advanced non-electrochemical removal methods – activated carbon, reverse osmosis, filtration, and ozonation – treating pharmaceutical effluent at WWTPs. Per Guo et al.'s (2017) synthesis review and many other research articles, the benefits of non-electrochemical treatment methods surround the flexibility to treat an array of harmful reactions. An example of non-electrochemical removal technology includes activated carbon, which uses its large surface area and multilevel pore structure, trapping pollutants through its high adsorption capacity [25]. Another popular technique, reverse osmosis, uses cellulose ester and aromatic polyamide to plate and frame harmful substances [26]. Ultrafiltration, microfiltration, and ozonation apply static pressure differences to prompt biochemical reactions that disinfect activated compounds, suspended particles, and pathogens [27].

Numerous benefits and the versatility of non-electrochemical technologies come with flaws that prevent the cost-efficiency of advanced treatments at WWTPs. According to the Water Research Foundation [28], high maintenance fees and efficiency of complex removal operations hinder the development and rollout of the technologies. Namely, reverse osmosis relies heavily on the constant flow of water while ozonation degrades the environment when mining for necessary materials [29]. These financial and infrastructural burdens had directed current research toward the newly electrochemical technologies at WWTPs.

Iib. Overview of Electrochemical Removal Technologies

Electrochemical methods are popular due to their precision and simplicity to reduce pharmaceutical concentrations in the environment [30]. There are three emerging and popular electrochemical processes: electrodialysis, electrocoagulation, and electrochemical oxidation. Electrodialysis uses electrolytic and dialysis diffusion processes to allow anions and cations to move cathodes and anodes [31]. The advantage of electrodialysis is consuming low energy; its shortcoming is the constraint of only removing salt components of chemical compounds [32]. Electrocoagulation adds chemical agents into wastewater and uses coagulation techniques to remove pollutants [33]. The addition of chemical agents, under rapid mixing, makes pollutants into precipitable particles. The array of precipitable particles, nevertheless, varies depending on the chemical agents, which could easily miss out on removing certain pharmaceutical components in WWTPs. Applications of electrochemical oxidation, on the other hand, have emerged as a crucial research focus in the literature. The electrochemical oxidation process, where electrons are lost from the cathode to oxidize the pollutants in the anode, is cited for its environmentally friendly benefits and advantage over electrochemical technologies. It has high efficiency and can be used at WWTPs on a large-scale [34]. The large-scale implementation at WWTPs has a downfall where the volume treated per electrode is at a low ratio, hence preventing performance at the maximum reduction capacity. This downfall can be used to an advantage at the small-scale to increase the

functionality and the magnitude of electrochemical oxidation.

III. Current Approaches in Electrochemical Oxidation

Feier et al. [35] noted the importance of pretreating pharmaceutical effluents using electrochemical oxidation techniques before releasing them into the sewer system and WWTPs. The researchers coined conventional separation techniques of electrochemical oxidation as the gold standard for the detection and removal of accumulated pharmaceuticals. The scenario is attributed to the high oxidation potential of existing NSAIDs, which cannot be achieved through biodegradation [36]. Of all the NSAIDs, Wudarska et al. [37] contend that acetylsalicylic acid and its derivatives salicylic and acetylsalicylic acid pose a high interest in toxicity study, especially through electrochemical methods. They contended that the quasi-reversible relationship and level of electrochemical oxidation of acetylsalicylic acid's subcomponent makes it convenient enough to analyze since the oxidation part is irreversible.

III. Addressing the Literature Gap

Wudarska et al.'s [37] experiment solidified the supplementary relationship between cyclic voltammetric analysis and spectrophotometric analysis when analyzing concentration reductions of common NSAIDs and chemicals such as acetylsalicylic acid and salicylic acid. Chrzescijanska et al. [38] also drew a similar correlation while explaining the transfer and diffusion coefficient during electrochemical oxidation. These researchers haven't solidified whether different electrode meal plates, experiment scales, temperature, or pH levels – electrochemical properties – would contribute to a different magnitude of reduction. Existing literature on electrochemical oxidation treatment of pharmaceuticals, though addressed a significant gap in identifying cost-effective techniques for large-scale wastewater treatment, haven't considered pretreatment as the priority rather than design their experiments to apply to WWTPs. Therefore, this research aims to find the optimal conditions for electrochemically oxidizing pharmaceutical wastewater using conventional methods on the small scale to mitigate the environmental threat.

IV. Hypothesis

This research hypothesizes that the wavelength for analysis would be at the lower parameters of the machine per existing literature. High temperatures may derive a greater magnitude in electrochemical reduction due to the increase in energy whereas low pH levels and high reactivity plates increase oxidation due to favoring electron transferring conditions. We predict that the scale does not affect electrochemical oxidation given the limits on the small scale. But overall, when combining all optimal factors, we contend that the optimal conditions group would perform significantly better than the control group by at least 10%.

METHODOLOGY

I. Reagents

Ia. Procurement of Reagents

The following reagents were chosen based on their use in similar studies or as a component of NSAID pharmaceuticals. Pure ethyl alcohol and citric acid monohydrate were procured from Shimakyu's Pure Chemicals with a purity of over 99.5%. Acetylsalicylic acid was purchased from Choneye Pure Chemicals with an assay of over 98%. Buffer chemicals and salicylic acid were obtained from Emperor Chemicals Co., Ltd. Acetaminophen was purchased in a pharmacy in Hsinchu City, Taiwan. All the reagents were of analytical grade and used as received.

Ib. Preparation of Solutions

Two standardized concentration levels for solid and liquid reagents were set by adapting the methodology used by Wudarska et al. [37] and Chreścijańska et al. [38]. The concentration of solutions for solid substances was prepared with a weight (g) to distilled water volume (mL) ratio of 1:30. The concentration of solutions for liquid substances was prepared with a reagent volume (mL) to distilled water volume (mL) ratio of 1:10. Solutions used to determine the pH effect on concentration reduction were prepared by dissolving substrates in buffers.

II. Spectrophotometric Analysis

Spectrophotometric analysis is a practical standard for measuring the change in concentration through absorbance levels. Prado et al. [39] and Wudarska et al. [37] have coined the interchangeability of cyclic voltammetry and spectrophotometry in detecting the sensitive changes in concentration during electrochemical oxidation processes of NSAID pharmaceuticals. Therefore, a spectrophotometric analysis was chosen and carried out in Prema Pro-779 Vis-NIR Spectrophotometer (range: 330 nm to 1100 nm). The spectrophotometer was first warmed for twenty minutes, then calibrated using a cuvette filled with respective solutions. Approximately 5 mL of solution was injected into the cuvette and placed into the sample chamber for analysis.

III. Electrochemical Cell

A two-electrode electrochemical cell of platinum plates with a surface area of 5 mm² was employed. Approximately 50 mL of solutions were added into the beaker with supporting electrolyte of Na₂SO₄ and then purged to remove dissolved gasses. Solutions were then electrochemically oxidized by two 1.5-volt batteries, connected by alligator clips to the electrodes, for two minutes before being stirred and sampled for spectrophotometric analysis. Constant monitoring of experimental parameters through an ammeter and voltmeter were conducted to minimize error.

IV. Control Group

This research's control group has the following parameters carried out under STP conditions: platinum

electrodes, pH 7, and electrode area (mm²) to solution volume ratio (mL) of 1:10 [40].

V. Data Analysis

All statistical analyses were conducted using the IBM® SPSS® Statistics Software [41]. Jupyter Notebook (Python) was employed to generate tables and graphs. Pre-conditions were evaluated using Levene's Homogeneity of Variances before carrying out the F-Test and Tukey-Kramer (Tukey's W) post-hoc test [42]. Statistical analysis of datasets in this research meets all pre-conditions. Independent variables are inspected individually per solution and in combination for all experiments [43]-[44]. Post-hoc tests on individual solutions must show individual homogeneous subsets for all manipulated variables, indicating the independency of results before being analyzed collectively. All analyses were performed at the 95% confidence level.

VI. Experimental Procedure

VIa. Pre-Experiment

A pre-experiment was first conducted to identify the respective wavelengths of solutions for future experiments. Solutions were scanned in wavelengths of 25 nm intervals from 330 nm to 1100 nm. Subsequent intervals are scanned if there appears to be a local maximum between the 25 nm intervals using derivative tests. To ensure the absorbance data complies with Beer Lambert's Law, only wavelengths in the UV-VIS range (300 nm to 800 nm) are considered [45].

VIb. Experiment One to Four

Independent variables were manipulated from the control group in each experiment. Data were collected and analyzed from five trials per solution and twenty-five trials in combination for all solutions. Experiment one tests temperature levels at intervals of 5°C from 5°C to 50°C. This simulates the water temperature in the environment from normal to extreme conditions [46]. Experiment two explores the effects of pH levels by 3 pH intervals from pH 1 to pH 13, mimicking the extreme and average wastewater conditions in the environment or sewage system. A pH meter was utilized to detect the changes in pH levels, ensuring the accuracy of the experiment. The effect of electrode plates (zinc, aluminum, iron, and copper metals) on electrochemical reduction magnitude was tested in experiment three. Lastly, experiment four manipulates the solution volume to electrode surface area ratio from 1:5, 1:10, 1:15, to 1:20 to derive the effect of scale on reduction. 1:5 is the smallest possible ratio for the electrochemical cell to function; 1:20 is the maximum capacity of the electrochemical cell.

VIc. Experiment Five

Experiment five was carried out after analyzing the results from experiments one to four. Optimal independent variables of electrode area (mm²) to solution volume (mL) ratio of 1:20, zinc electrode, pH 1, and 5°C were selected to compare with the control group. Data were collected and

analyzed from forty trials per solution and fifty trials in combination.

RESULTS

I. Pre-Experiment: Optimal Wavelength for Spectrophotometric Detection

Table I shows the optimal wavelength and maximum absorbance of tested solutions in the UV-VIS range. Salicylic acid, acetylsalicylic acid, and citric acid monohydrate presented their maximum absorbance at approximately 980 nm in the near-IR range. These data points are omitted due to a violation of Beer Lambert's Law. Follow-up procedures for the three solutions were conducted, finding the optimal wavelength at 330 nm. Ethyl alcohol and acetaminophen, similarly, present an optimal wavelength at 330 nm. Overall, the results in the pre-experiment direct the following experiments to analyze solutions at 330 nm for the best sensitivity.

TABLE I

OPTIMAL WAVELENGTH FOR EXPERIMENTAL SOLUTIONS		
Sample Solution	Optimal Wavelength (nm)	Maximum Absorbance (Au)
Salicylic Acid	330	.16830
Ethyl Alcohol	330	.45925
Citric Acid Monohydrate	330	.05763
Acetylsalicylic Acid	330	.05876
Acetaminophen	330	.43246

II. Experiment One: Optimal Temperature for Electrochemical Oxidation

Figure I provide the magnitude of mean difference as a function of temperature for all solutions. Table II supplements Figure I by displaying the linear regression formulas of Figure I and the R² value for the solutions. Table III shows the post-hoc homogeneous subsets under the Tukey-Kramer test.

A negative correlation was found between the mean difference of concentration and temperature for most solutions. An inspection of the data in Figure I reveals that citric acid monohydrate, on contrary, maintained a positive correlation with a slope of .00041 – the smallest in magnitude. When acetylsalicylic acid is examined separately in two ranges – 5°C to 25°C and 30°C to 50°C – higher R² values are derived showing a stronger negative correlation. Ethyl alcohol has the highest ability to reduce NSAID concentrations with a slope of -.00751 below 40°C. The difference with the smallest electrochemical oxidation magnitude is approximately .28 Au.

The Tukey-Kramer post-hoc test derived three groups of homogeneous subsets: low temperatures (5°C ≤; ≤ 25°C), warm temperatures (25°C ≤; ≤ 35°C), and high temperatures (>= 25°C). The low-temperature subset has a concentration reduction ranging from .05563 Au to .10335 Au with an average of .08315 Au, which is approximately 0.05 Au greater than the lowest subset. These results suggest that low temperatures, specifically for ethyl alcohol, are best for electrochemical oxidation.

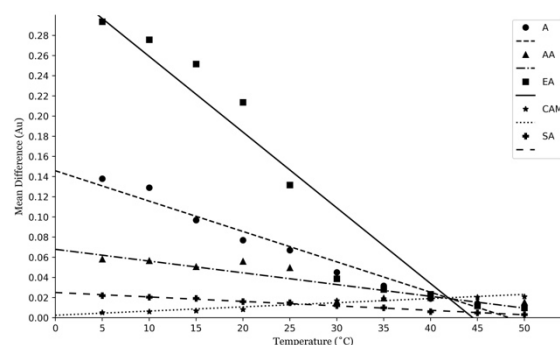


FIGURE I
THE MAGNITUDE OF MEAN DIFFERENCE AS A FUNCTION OF TEMPERATURE

TABLE II

LINEAR REGRESSION EQUATION AND R² VALUE OF FIGURE I

Sample Solution	Regression Equation	R ²
Salicylic Acid	-.02504x + .02460*	.98949
Ethyl Alcohol	-.00751x + .33428*	.90601
Citric Acid Monohydrate	.00041x + .00251*	.92071
Acetylsalicylic Acid	-.00117x + .06786*	.81612
Acetaminophen	-.00301x + .14577*	.95623

* p < .05

TABLE III

TUKEY-KRAMER POST-HOC RESULTS OF EXPERIMENT ONE

Tukey HSD ^{a, b}		Subset for alpha = .05		
Temperature (°C)	N	1	2	3
5	25	-.10335		
10	25	-.09758		
15	25	-.08503		
20	25	-.07418	-.07418	
25	25	-.05563	-.05563	-.05563
30	25		-.02579	-.02579
35	25		-.02162	-.02162
40	25			-.01770
45	25			-.01345
50	25			-.01229
Significance		.165	.083	.282

Note. The F-Test multi-comparison data analysis (ANOVA) has a significance value of p < .05. Means for groups in homogeneous subsets are displayed.

^a Uses Harmonic Mean Sample Size = 25.000

^b Confidence level = 95%

III. Experiment Two: Optimal pH Level for Electrochemical Oxidation

Figure II displays the magnitude of reduction as a function of pH levels, supplemented by the linear regression formulas in Table II. Table V presents the results of the Tukey-Kramer post-hoc test.

The figure illustrates that lower pH levels are easier for NSAID solutions to electrochemically oxidize. The table is quite revealing in several ways. First, acetylsalicylic acid has the weakest R² value of .55548 with a slope of .06100. Other solutions presented a high R² value showing a strong correlation. Ethyl alcohol has the highest electrochemical oxidation magnitude of all pH levels with a slope of 0.22341. Salicylic acid, oppositely, has the lowest concentration reduction magnitude with a slope of 0.03462.

Homogeneous subsets of low pH levels (pH 1 ≤; ≤ pH 4), medium-low pH levels (pH 4 < < pH 7), medium-

high pH levels (pH 7 \leq ; \leq pH 10), and high pH levels (pH 10 \leq ; \leq pH 13) was produced through the Tukey-Kramer post-hoc test. The highest average electrochemical reduction is .08658. The average of each homogeneous subset differs from one another by approximately .02 Au. Overall, these results indicate that lower pH levels aid concentration reduction, specifically for ethyl alcohol.

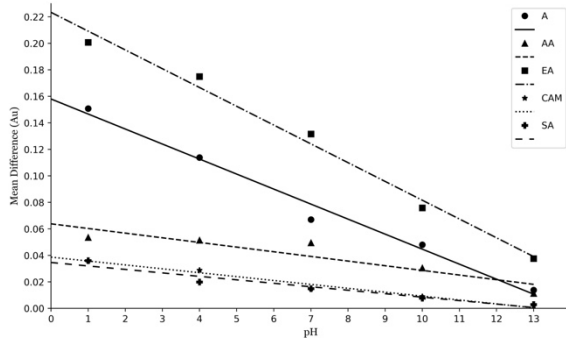


FIGURE II

THE MAGNITUDE OF MEAN DIFFERENCE AS A FUNCTION OF pH LEVEL

TABLE IV

LINEAR REGRESSION EQUATION AND R² VALUE OF FIGURE II

Sample Solution	Regression Equation	R ²
Salicylic Acid	-.03462x + .03200*	.93641
Ethyl Alcohol	-.22341x + .20923*	.98741
Citric Acid	-.03869x + .03574*	.98148
Monohydrate		
Acetylsalicylic Acid	-.06100x + .04772*	.55548
Acetaminophen	-.15802x + .14669*	.98514

* p < .05

TABLE V

TUKEY-KRAMER POST-HOC RESULTS OF EXPERIMENT TWO

Tukey HSD ^{a, b}	N	1	2	3	4
pH					
1	25		-.095412		
4	25		-.077776		
7	25		-.055632	-.055632	
10	25			-.034176	-.034176
13	25				-.01345
Significance		.679	.464	.496	.532

Note. The F-Test multi-comparison data analysis (ANOVA) has a significance value of p < .05. Means for groups in homogeneous subsets are displayed.

^a Uses Harmonic Mean Sample Size = 25.000

^b Confidence level = 95%

IV. Experiment Three: Optimal Electrode for Electrochemical Oxidation

Table VI shows the results of the Tukey-Kramer post-hoc test of mean difference concerning different electrode metals. Post-hoc analysis has indicated two homogeneous subsets grouped by reactivity: zinc, platinum, and aluminum (group 1); and platinum, copper, and iron (group 2). Group 1 has an average of .07109 Au in concentration reduction, which is .03636 Au greater than group two. Zinc has the strongest reduction magnitude of .08160 Au; Iron has the weakest concentration reduction magnitude of .02035. In summary, these results show that higher reactivity, specifically zinc, better facilitates concentration reduction.

TABLE VI

TUKEY-KRAMER POST-HOC RESULTS OF EXPERIMENT THREE

Tukey HSD ^{a, b}	Subset for alpha = .05		
Electrode	N	1	2
Zinc	5	-.08160	
Aluminum	5	-.07605	
Platinum	5	-.05563	-.05563
Copper	5		-.02820
Iron	5		-.02035
Significance		.406	.127

Note. The F-Test multi-comparison data analysis (ANOVA) has a significance value of p < .05. Means for groups in homogeneous subsets are displayed.

^a Uses Harmonic Mean Sample Size = 25.000

^b Confidence level = 95%

V. Experiment Four: Optimal Scale for Electrochemical Oxidation

Figure III provides the magnitude of mean difference as a function of scale for solutions. Linear regression formulas of Figure III are presented in Table VII. Table VIII shows the Tukey-Kramer post-hoc result of concentration mean difference.

A higher electrode area to solution volume scale has a higher level of electrochemical oxidation on the pharmaceuticals. As shown in Table VII, ethyl alcohol presents the highest electrochemical oxidation magnitude with a slope of .04887 and an average of .02 Au greater than the second-highest solution. Citric acid monohydrate and salicylic acid, on a similar scale, displayed weak magnitudes of concentration reduction with a slope of .00179 and .00419 respectively.

The post-hoc test derived two groups of homogeneous subsets 1:20, 1:15, 1:10 (group 1); and 1:15, 1:10, 1:5 (group 2). The highest homogeneous subset has an average of .296928 Au of reduction whereas the smallest reduction subset has an average of 0.05147. Overall, the higher scale has the highest magnitude in electrochemical reduction, evident through the 1:20 dataset.

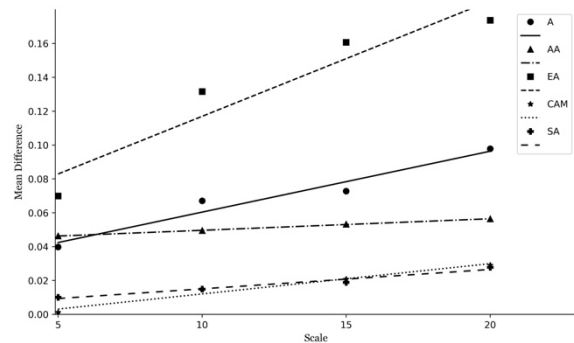


FIGURE III

THE MAGNITUDE OF MEAN DIFFERENCE AS A FUNCTION OF SCALE MULTIPLES

TABLE VII

LINEAR REGRESSION EQUATION AND R² VALUE OF FIGURE III

Sample Solution	Regression Equation	R ²
Salicylic Acid	.00419x + .00115*	.96666
Ethyl Alcohol	.04887x + .05568*	.90556
Citric Acid	.00179x + -.0058*	.96791
Monohydrate		
Acetylsalicylic Acid	.00068x + .04285*	.99879
Acetaminophen	.02444x + .02804*	.95038

* $p < .05$

TABLE VIII

TUKEY-KRAMER POST-HOC RESULTS OF EXPERIMENT FOUR

Tukey HSD ^{a, b}	Subset for alpha = .05		
Scale	N	1	2
20	25	-.076984	
15	25	-.065312	-.065312
10	25	-.055632	-.055632
5	25		-.033472
Significance		.362	.076

Note. The F-Test multi-comparison data analysis (ANOVA) has a significance value of $p < .05$. Means for groups in homogeneous subsets are displayed.

^a Uses Harmonic Mean Sample Size = 25.000

^b Confidence level = 95%

VI. Experiment Five: Optimal Condition Group vs Control Group

Table IX provides the F-Test ANOVA results comparing the control group with the optimal conditions group. At the 95% confidence level, the optimal conditions group performed approximately 50% greater electrochemical oxidation on the NSAID solution than the control group. Taken together, these results suggest that with 5°C, pH 1, 1:20 scale, and zinc electrode, a greater concentration reduction magnitude can be reached.

TABLE IX

TUKEY-KRAMER POST-HOC RESULTS OF EXPERIMENT FIVE

	Sum of Squares	df	Mean Square	F	Significance
Between Groups	.435	1	.435	52.829	<.00a
Within Groups	3.258	396	.008		
Total	3.693	397			

^a Confidence level = 95%

DISCUSSION

I. Pre-Experiment: Optimal Wavelength for Spectrophotometric Detection

Our aim in this experiment was to measure the effect of temperature on concentration reduction magnitude. The analysis results revealed that all solutions should be analyzed at 330 nm, the lowest wavelength possible by our spectrophotometer. The low wavelength findings are consistent with existing literature: salicylic acid [47], acetylsalicylic acid [48], ethyl alcohol [49], citric acid monohydrate [50], and acetaminophen [51]. The absorption bands in the near IR spectrum represent and correspond with the interactions between groups, rings, and substituents per Wudarska et al.'s [37] research. It's worth noting that derivative tests have presented various local maxima throughout the UV-VIS spectrum, however, none of them were greater than the global maximum at 330 nm.

We cannot exclude the possibility that more sensitive changes could be detected due to the limitation of the spectrophotometer. Many of the NSAID pharmaceuticals in this research have an optimal wavelength ranging from 250 nm to 350 nm per existing literature. Considering that optimal wavelength is the wavelength in which the change in concentration of the solution could be detected most

sensitively, the choice of the lowest possible wavelength in this experiment suffices the requirement. It could be argued that more subtle changes – beyond this research's accuracy to 5 decimal points – can be detected through other advanced apparatuses. Future directions addressing the limitations and improving this experiment include using more sophisticated equipment and other spectrophotometric techniques.

II. Experiment One: Optimal Temperature for Electrochemical Oxidation

The objective of this experiment was to identify the effect of different temperature levels on electrochemical oxidation magnitudes. A negative, linear relationship between reduction magnitude and the temperature was found for most solutions. This contrasts with our hypothesis that higher temperatures produce greater magnitudes.

A plausible explanation for low-temperature electrochemical oxidation having greater magnitudes is the ease of electron transfer. Lopez & Poul [52] suggest that electrochemical oxidation of substances at low temperatures offers more possibilities for electron transfer reactions and mechanistic pathways of chemical coupled reactions. Though the experiment was conducted on coordination compounds, the results confirm and shed light on our findings in experiment one. Santos et al. [24] concur with the explanation, noting the derivatives of compounds in this research such as acetylsalicylic acid are coordination compounds, which are easily reduced at lower temperatures from emerging chemical pathways. Other existing literature has also cited chemicals and batteries having better electron transfer pathways.

Acetylsalicylic acid is only temperature-dependent in certain temperatures in the results section. The result may be explained by the fact that the energy required for acetylsalicylic acid to be reduced has a higher barrier, thus harder to transfer electrons. An observation of residue and gas products clustered around the electrode was apparent in acetaminophen and ethyl alcohol. The observation could be due to its higher magnitude of electrochemical oxidation, as supported by Figure I.

This experiment has not situated itself within the literature in terms of high-temperature electrochemical oxidation due to its scarcity. Deviations from existing literature also appeared in citric acid monohydrate, which presented a positive, linear relationship. Suggestions for future directions of this experiment include consolidating the slow electron transfer rate at high temperatures (in contrast to low temperatures), sampling more reagents to explain the behavior of citric acid monohydrate, or analysis of the results on the atomic level.

III. Experiment Two: Optimal pH Level for Electrochemical Oxidation

The experiment set out to assess the correlation between pH level and electrochemical oxidation was assessed in this experiment. A negative, linear correlation between pH level and concentration reduction magnitude

was found. These results on the small-scale were like the large-scale according to Dao et al. [53].

Our analysis has discovered that acetylsalicylic acid is not pH-dependent despite the trend in all other solutions. Ethyl alcohol and acetaminophen, sample solutions reduced at higher magnitudes, could be attributed to the substance's original pH level in contrast with its adjusted pH level. Acidic substances are easier to transfer electrons compared with basic substances, thus maintaining their original states ease the reduction process [54].

It is important to bear in mind the other possible sampling factors when considering pH level effects. In the environment, pharmaceutical pollution is mixed, creating oscillating pH levels and new biochemical reactions. Despite this limitation, the original intention of this experiment was to analyze the solutions independently for data analysis, ensuring that they could be used for pretreatment individually. This gap indicates future directions of research focusing on mixture toxicity on the effect on pH levels during electrochemical oxidation. The pH characteristics can also be further analyzed by researching the structural and functional components of NSAIDs and other pharmaceuticals.

IV. Experiment Three: Optimal Electrode for Electrochemical Oxidation

For the effect of electrodes on the magnitude of electrochemical oxidation, it was found that electrodes with higher reactivity traits reduce NSAIDs more readily than those with lower reactivity. Besides the easiness of electron transfer with high reactivity plates, according to Talbot [55], electrode potential, Gibbs free energy, ionization potential, and ionization energy could be the reasons behind the difference in the magnitude of electrochemical oxidation. Further review of the existing literature has indicated that higher acidity correlates with higher reactivity in many chemicals and metals. Comparing the study with our F-Test analysis, copper and iron demonstrated a lower level of reduction whereas aluminum and zinc, having high reactivity with acids, performed better. Overall, the results debunk our hypothesis that higher conductivity metals better oxidize substances with iron as an exception.

Advanced electrodes for electrochemical oxidation such as boron-doped diamond and carbon-based electrodes are hard-to-get and expensive materials as pretreatment devices. Therefore, using commonly accessible and cheap electrodes in this experiment, we can determine the effects of electrodes on a small scale. Future directions for this experiment include a cost-effective analysis of different electrodes, finding the relationship between conductivity and reactivity for NSAIDs, and testing different pairs of conventional electrodes to find a more optimal combination to reduce pharmaceutical concentrations.

V. Experiment Four: Optimal Scale for Electrochemical Oxidation

The fourth experiment in this research was to uncover the relationship between scale and electrochemical oxidation magnitude. A positive, linear trend of higher

sample solution to electrode area ratio was presented in the results. The trend can be explained by the increased area allowing more electron transferring to happen between electrodes. Observatory evidence from the gas-like bubbles formed around the electrodes for numerous solutions was increased as the scale was increased.

A limitation of this study is the interval of scale. It could be further minimized to analyze the more subtle changes in concentration changes. The limitation does not affect the overall result of this study since the Tukey-Kramer F-Test analysis displayed a homogeneous mean between higher-level scales.

VI. Experiment Five: Optimal Conditions Group vs Control Group

The aim of experiment five was to compare the electrochemical oxidation magnitude of all the optimal conditions combined with the control group. The current study has found that the optimal group performed, on average, 50% better than the control group. The result may be explained by the fact that combining all variables, creates more electron transfer pathways and favorable conditions.

These findings could be somewhat limited by the interdependency of the variables based on the solution. For instance, pH levels and temperature, when applied to a solution, may produce different, non-linear effects contradicting our results from previous experiments. However, this does not disrupt the focus of the experiment on comparing the overall effects. Future directions include uncovering the dependency between the variables and finding its effect separately on the effect of electrochemical oxidation.

CONCLUSION

I. Overall Results

This research has deduced the conclusion that at low temperatures and pH levels, high solution volume to electrode area scale, and using electrodes with high reactivity series produces an approximately 50% greater electrochemical oxidation in a conventional setting. The optimal results presented are as follows: 5°C, pH 1, 1:20 scale, zinc electrode, and analyzed at 330 nm. The limitations of this research have been addressed separately in the discussion section of each experiment.

II. Future Directions and Implications

Besides the future directions listed individually in each experiment, this research aims to catalyze the development of small-scale pretreatment devices implemented in the household. Two proposed easy-to-build models are presented in Figure IV and Figure V. Figure IV demonstrates a self-assembled electrochemical cell that could be implemented in areas where wastewater treatment for pharmaceuticals isn't developed and without a steady source of electricity. Figure V displays a more advanced version of the electrochemical cell with a monitor showing real-time data and electricity sources from a cord. These two models could be further implemented by fixing their

shape and size into different locations, making them a flexible and reliable device to pretreat pharmaceutical wastewater. Research in the future is suggested to focus on the implementation and other cost-efficient techniques to improve the function of small-scale pretreatment electrochemical oxidation cells, mitigating the environmental threat from pharmaceuticals.

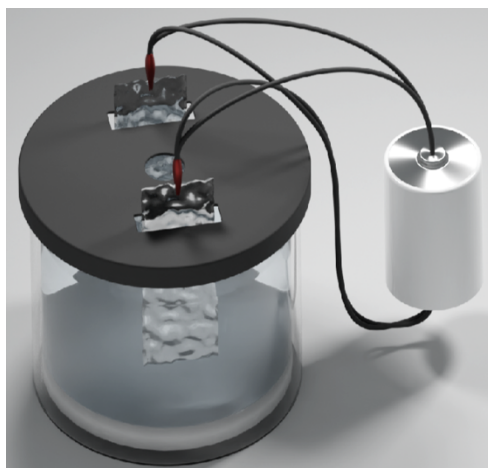


FIGURE IV

MODEL ONE PROTOTYPE OF A CONVENTIONAL ELECTROCHEMICAL OXIDATION PRETREATMENT APPLIANCE

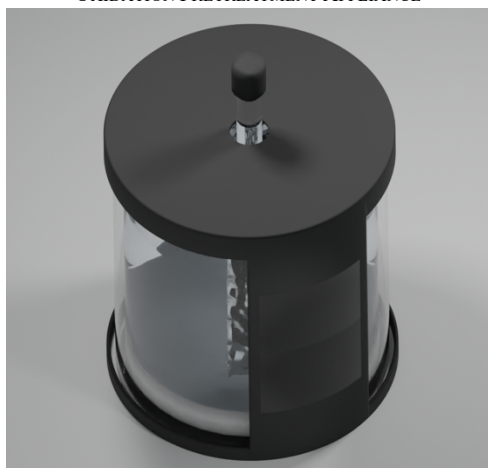


FIGURE V

MODEL TWO PROTOTYPE OF A CONVENTIONAL ELECTROCHEMICAL OXIDATION PRETREATMENT APPLIANCE

ACKNOWLEDGMENT

The author thanks Dr. Toulouse Antonin Roy and Mr. Johnson Ting from Pacific American School for their unwavering support in providing constructive feedback and review.

AUTHOR CONTRIBUTIONS

Benjamin Chang contributed to the design and implementation of the research, the analysis of the result, and the writing of the manuscript.

SOURCES OF FUNDING

This study was not funded by any institution or entity.

POTENTIAL CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

STUDY ASSOCIATION

Part of this research was adopted and submitted to the 2022 Taiwan Science Exploration Fair under the topic of *Conditions for Building an Electrochemical Oxidation Model Pretreating Common Non-Steroidal Anti-Inflammatory Drugs* by Elizabeth Huang, Benjamin Chang, and Jeffrey Huang from Pacific American School.

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APPENDIX

- Graphs and tables of individual solutions can be accessed at: tinyurl.com/AP-Research-Appendix.
- Programming code in Jupyter Notebook and SPSS results can be accessed at: github.com/borbeneal233/AP-Research.