Treatability of Pharmaceutical Wastewater by Using Combined Ultrasound Cavitation and Persulfate Process

Karan Pandya
Pandit Deendayal Petroleum University

Anantha Singh T S (singh87@nitc.ac.in)
National Institute of Technology Calicut  https://orcid.org/0000-0002-7735-497X

Pravin Kodgire
Pandit Deendayal Energy University

Research Article

**Keywords:** Ultrasound, Cavitation, Persulfate, Box-Behnken design, Optimization, Pharmaceutical wastewater.

**Posted Date:** May 6th, 2021

**DOI:** https://doi.org/10.21203/rs.3.rs-297267/v1

**License:** This work is licensed under a Creative Commons Attribution 4.0 International License. Read Full License
Treatability of Pharmaceutical Wastewater by Using Combined Ultrasound Cavitation and Persulfate Process

Karan Pandya, Anantha Singh T.S., Pravin Kodgire

1Department of Civil Engineering, School of Technology, Pandit Deendayal Energy University, Gandhinagar, Gujarat, India,
2Department of Civil Engineering, National Institute of Technology Calicut, India
3Department of Chemical Engineering, School of Technology, Pandit Deendayal Energy University, Gandhinagar, Gujarat, India

(*singh87@nitc.ac.in; pravin.kodgire@sot.pdpu.ac.in)

Abstract

In recent years industrialization caused, magnificent leaps to high profitable growth of pharmaceutical industries, however, simultaneously it has given rise to environmental pollution. Pharmaceutical processes like extraction, purification, formulation etc. generates huge volume of wastewater with high COD, biological oxygen demand, auxiliary chemicals, and different pharmaceuticals substance or their metabolites in the active or inactive form imparting intensive color, which necessitates its proper treatment before being discharged. This study focuses on the feasibility analysis of utilization of ultrasound cavitation assisted with persulfate oxidation approach for the treatment of such complex effluent. Process parameters like pH, amplitude intensity, oxidant dosage was optimized for COD removal applying response surface methodology-based Box Behnken design. The optimum value observed for pH, amplitude intensity, oxidant dosage is 5, 20%, 100 mg/L respectively with 39.5% removal of COD and 6.5% removal of TOC in 60 min of fixed processing time. Study confirms that a combination of ultrasound cavitation and persulfate is a viable option for the treatment of pharmaceutical
wastewater than individual treatment and it can be used as an intensification technique in existing treatment plants for achieving maximum COD removal.

Keywords–Ultrasound, Cavitation, Persulfate, Box -Behnken design, Optimization, Pharmaceutical wastewater.

INTRODUCTION

Environmental pollution is one of the global challenge of today's world (Spina et al., 2012; Singh & Prashant, 2017). Amongst that, industrial effluent and other hazardous discharge from industries is one of the prime concerns for developing countries like India. In India one-third portion of water pollution in the natural water bodies and marine pollution are induced by industrial wastewater (Kansal et al., 2013; R. Singh & Prashant, 2017), U.S EPA reported daily effluent produced from pharmaceutical unit as $1.0068 \times 10^9$ L (Adishkumar et al., 2012). Because of these effluents, containing highly biological active compound which is likely cause health harm to human and animals, and also promote the development and spreading of antibiotic resistance genes although the concentration of pharmaceutical residue present in effluent is less.

This antibiotic resistance gene interrupt the ecological balance of aquatic environment by initiating irreversible transformation to aquatic fauna (Ng et al., 2014; Tiwari et al., 2020).

Industrial wastewater quality is estimated based on the amount of organic matter present as COD (chemical oxygen demand), total carbon, biological oxygen demand, and other wastewater quality parameter and nowadays the high amount of pharmaceutical substances used for the protection and cure of diseases for humans and animals therefore, huge amount of wastewater generated in pharmaceutical industries (Mohapatra et al., 2014; Ghafoori et al., 2015). Over 60% of pharmaceutical sectors meet country's demand and is one of rapid expanding sectors of Indian economy. The produced wastewater from pharmaceutical sectors are complex and hazardous in
nature, high COD, biological oxygen demand, solid containing supplementary chemicals and
presence of pharmaceuticals secondary metabolites leads the wastewater to be a under “red
category” (Gadipelly et al., 2014; Martínez et al., 2018; Changotra et al., 2017, 2019).
Pharmaceutical wastewater contains the majority of pollutants recalcitrant or bio-refractory
substances which are very difficult to degrade (Grandclément et al., 2019). Thus it is necessary
to treat pharmaceutical wastewater efficiently sooner than discharging it into any water bodies to
avoid hazards to the environment and ecosystem (Gadipelly et al., 2014; Martínez et al., 2018;
Changotra et al., 2017, 2019).

Conventional treatments cannot efficiently treat recalcitrant or bio-refractory molecules present
in industrial effluent and sometimes it also get converted in another complex by-product as
Fluoxetine and endocrine disruptors which has resulted multitude of undesirable problems like
harm the reproduction, metabolism of aquatic organism and feminization of fish population
(Ford & Fong, 2016; Huang et al., 2016) which are not easily biodegradable which further
pollutes water bodies (Singh & Prashant, 2017). Treatments like biological oxidation required
longer time because it is slower reaction rate (Crini & Lichtfouse, 2019) chemical coagulation is
useful for removal of waste material in form of colloidal or suspended that do not settle very
quickly it requires longer time & more sludge production (Verma et al., 2012) chemical
oxidations target selective bio resistant compound it can be used as pretreatment (Mantzavinos &
Psillakis, 2004) and adsorption reactors rapidly get clogged and its regeneration is costly and it
decreases acceptance of certain type of metal ions (Crini & Lichtfouse, 2019), due to this
demerits treatments are not efficient to remove all the hazardous compounds effectively from
pharmaceutical wastewater (Jeworski & Heinzle, 2000; Ayare & Gogate, 2019). In recent times
advance oxidation process (AOP) such as Fenton oxidation (Singh et al., 2013) ozonation
ultraviolet/hydrogen peroxide (Hu et al., 2011) ultrasound cavitation (Gągol et al., 2018) have been considered as a useful process for treatment of bio-refractory pollutants (Q. Yang et al., 2015). Among the AOP, ultrasound cavitation-based process has seen as a promising process for the oxidation of various pollutants in industrial wastewater. Principle behind ultrasonication process is pressure variation in liquid caused by inducing ultrasound which produces cavitation for the treatment of wastewater (Thanekar & Gogate, 2019). Cavitation occurs due to pressure difference in outer flow and inside the system pressure induced by sound waves as system pressure decrease or increase in flow velocity produce small cavities which starts to grow longer compare to higher system pressure (Dular et al., 2016). Furthermore, variation of pressure leads to cavity formation, growth, and its collapse over micro-scale duration. These three-stage occurs during ultrasound cavitation process which leads to generate free radicals and release a large amount of energy up to 5000K temperature and 1000 Atm pressure in wastewater known as “local hotspot” which can be extremely suitable for the oxidation of pollutants (Leighton, 1995; Thanekar & Gogate, 2019). The main advantage behind this treatment is it does not require any chemicals to promote oxidation, no sludge formation, no visible light require (Vega & Peñuela, 2018), break up agglomerates (Jordens et al., 2016; Dong et al., 2020). Ultrasound cavitation is useful for the treatment of active pharmaceutical compound like carbamazepine, diclofenac, ciprofloxacin (Beckett & Hua, 2001; Rayaroth et al., 2016). Ultrasound cavitation accelerates the degradation of pollutants in combination with other oxidation process like Fenton’s regent (Zhang et al., 2016), hydrogen peroxide (Chandak et al., 2020), carbon tetrachloride and persulfate ions (Anipsitakis & Dionysiou, 2003) to generate radicals (Rayaroth et al., 2016). Among the various oxidant, per-sulfate ion enhance degradation of organic matter in the wastewater though the use of combined ultrasound - persulfate system.
has been less studied (Monteagudo et al., 2015, 2018; Wang & Zhou, 2016). Alternative of hydrogen peroxide, Persulfate ion has gained more attention in the interest of higher redox potential of sulfate radical (2.5 V – 3.1V) and expanded life time than hydroxyl radical for advanced oxidation treatment in recent time. Formation of sulfate radical occurs by breakage of O-O bond of Persulfate ions using different activation method like heat (Tan et al., 2012), transitional metals (Liu et al., 2016), UV (Xie et al., 2015). Among them, activation by ultrasound acts as an emerging method and typically used for pharmaceuticals (Zou et al., 2014; Yang et al., 2019).

In Combined process multiple operating parameters influences or affects the removal efficiency. For complex system governed by several parameters, generally usage of one parameter optimization at a time could provide mis-interpretation due to lack of interaction effect, thus design of experiment is effective tool for optimization, there are various DOE available for optimization of parameters by reducing the number of experiment and cost (Dopar et al., 2011) like box Behnken method of response surface methodology design (RSM) which is a powerful design tool for modeling complex conditions (Tak et al., 2015) and it estimate the relation between manageable input parameter and response variable (Khorram & Fallah, 2018).

This current study focuses on the combined effect of Ultrasound cavitation and Persulfate oxidation on the treatment of pharmaceutical wastewater. The optimization of process parameters like pH, Amplitude intensity, Persulfate Dosage by Box Behnken design as a response surface methodology for treatment of pharmaceutical wastewater using ultrasound – persulfate system was also carried out. Optimization can be potentially considered for scaling up purposes as an intensification technique for industrial wastewater treatment.

MATERIAL AND METHODOLOGY
Pharmaceutical wastewater sample of 40 liters was collected from the pharmaceutical industry from Bharuch, Gujarat, India. Collected samples were stored in the refrigerator at 4°C to avoid further biodegradation. Characterization of the pharmaceutical wastewater was done as per the standard method (APHA, 2012) and given in Table 1. As given in Table 1, COD of the wastewater is as high as 13760 mg/L.

Chemicals

In this study chemicals of Analytical grade were used for the entire experimental process. The potassium persulfate purity 98% purity, potassium dichromate 99% purity, mercury sulphate 98% purity, silver sulphate 98% purity, ammonium ferrous sulphate 99% purity, manganous sulphate 98% purity, ferric chloride 98% purity, Di-potassium hydrogen phosphate 99% purity, potassium iodide 99% purity, potassium hydroxide 85% purity, sodium thiosulphate 98% purity were procured from M/s Merck India. Sulphuric acid of 98% purity, ferroin Indicator, calcium chloride 96% purity, magnesium sulphate 99% purity, starch as an indicator were procured from M/s Finar India. All the required reagents were prepared using double distilled water. For ultrasonic cavitation, probe-type sonicator was used with a microprocessor-based programmable probe (Model No: VCX 500 with 17 mm solid probe diameter) procured from Sonics Vibracell, USA.

Design of Experiment (DOE)

Design-expert software was used to prepare DOE. The removal of organic matter from pharmaceutical wastewater was optimized using Box- Behnke design as RSM. Table 2, represents coded and its real value for lower level (-1), mid-level (0), high level (+1) for removal
of organic matter as COD another Table 3 provides detail total number of experimental runs to perform for factors pH (A), Amplitude Intensity % (B), Persulfate Dosage (C). Initially, while performing experiment process parameter pH (A) was varied from 2 to 8, Amplitude Intensity (B) was varied from 20 to 80 (%), Persulfate oxidant dosage (C) was varied from 100 mg/l to 400 mg/l to obtain better COD removal efficiency. The selection of real value for different levels decides based on the given literature review.

Experimental Procedure

All experiments were conducted in a cylindrical batch glass reactor with 250 mL of working volume (capacity of 500 mL). The schematic diagram of the experimental process reactor is shown in Figure 1. The temperature of the sample was maintained at 30°C and the pH was adjusted using nitric acid and sodium hydroxide. The Persulfate Dosage was added according to the real value of factors suggested by DOE. All 15 experimental runs were conducted according to DOE suggested value. Treated samples were withdrawn during the experiment at a time interval of 15, 30, and 60 min and analyzed for COD. COD of the sample was analyzed as per the Standard method using closed reflux method.

RESULT AND DISCUSSION

ANOVA Analysis

ANOVA Table 4, provides the details of various coefficient values of process parameters and other details for COD removal from pharmaceutical wastewater with ultrasound cavitation treatment. The table shows that the Model (Fischer test value) F value is 9.42 and it shows model value is significant as the p value is less than 0.0500 which implies the model is significant. The significance of p value fixes the error probability of regression co-efficient as significant. For optimized condition of parameter quadratic and some other interaction term are significant, the
parameter pH (A) is slightly significant another parameter Persulfate Dosage (C) is significant, an interaction effect of Amplitude Intensity (B) and Persulfate Dosage (C), is also significant with respect to model terms. According to the analysis of variance (ANOVA) selected parameters P-value is less than 0.0500 (P< 0.0500) than selected parameters are significant for the process efficiency and the P-value of parameters is greater than 0.100 (P>0.100) than selected parameters is not significant for the process efficiency.

Mathematical representation of independent variable to the dependent response by coded terms shown by this Eqn. (1).

\[ \text{COD (mg/l)} = 30 + 2197.7A + 19.62B - 6.013C - 3.55AB + 0.88AC + 0.256BC - 240.2A^2 - 0.620B^2 - 0.0319C^2 \ldots \] (1)

From the above equation, it is noticed that the terms have a positive effect on yield or COD removal and persulfate concentration (C) has a negative impact on the yield. The quadratic terms with a negative sign show a negative impact on yield which means the percentage of COD yield will decrease with the increase in concentration of persulfate. Other interaction terms as AB, AC & BC shows a combined effect on the percentage of yield. The Persulfate Dosage (C) term shows a positive impact on yield as interaction term AC, BC & interaction term AB shows a negative impact on yield percentage.

For identification order of each process parameters and its effect while keeping the other process parameter constant indicated in perturbation plots Fig.2 (a) then factors sensitivity on COD removal is indicated by nature of the curve for each process parameter and the factor with more slope has more noticeable effects on COD removal (Muthukumaran et al., 2017; Milano et al., 2018). Hence, the plot shows that factor B has a prominent effect on COD removal followed by A and C similar to that reflected in the Table of ANOVA.
The individual effect of parameter effect plots shown in Fig.3(a),3(b), & 3(c) the plots are made by taking one factor as variable and the other two factors fixed at constant levels and the experimental results are shown at three different levels compare to predicated plots.

Effect of pH on COD removal

One of the important parameters that affect the process efficiency is pH, it plays a vital role in the generation of intermediate oxidants for the oxidation of various compounds it can also affect their state during the cavitation process (Keenan & Sedlak, 2008; Barik & Gogate, 2017; Thanekar & Gogate, 2019). Effect of pH on the degradation of organic pollutants were studied by varying pH from 2 to 8 with fix Amplitude as 50% and Persulfate Dosage of 250 mg/L. The plot shown in Fig. 3 (a) generated using Design of Expert shows the variation of pH from the lower level to a higher level and its effect on COD removal (mg/L). As shown in Fig. the maximum COD removal of 39.5% at pH 5 at a reaction time of 60 min was observed. Increasing pH from the lower level at pH 2 to mid-level pH 5 removal efficiency has also increased after achieving maximum removal at mid-level pH 5 with 50% of Amplitude Intensity and 250 mg/l dosage of Persulfate oxidant further increasing pH to a higher-level pH 8 reduced removal efficiency.

The plot Fig.4, shows the individual and combined effect of ultrasound cavitation and persulfate oxidation on COD removal. The individual effect of the ultrasound cavitation process under the optimum condition of pH 5 and Amplitude 20% shows the removal of 8.10% and Persulfate oxidation under 100 mg/l dosage show removal of 5%. Standalone effect of both processes for removal of COD is less significant compare to combine effect of Ultrasound cavitation with Persulfate process which was more significant (L. Yang et al., 2019) with the removal of 39.5% under the optimum condition of pH 5 Persulfate Dosage of 100 mg/l and Amplitude of 20%.
This was due to the production of synergistic effect which leads to higher amount of cavitation yield and effective generation of sulfate radicals by persulfate oxidant. Maintaining the mid-level value of factors Amplitude Intensity of 50% and Persulfate Dosage of 250 mg/l at pH 2 and pH 8 and the corresponding predicated removal efficiency was 19.5% and 20.6% respectively. Excessive loading of Persulfate Dosage above 250mg/l has proven as a scavenger for the process under acidic condition as given in Eqn. (2) (Peyton 1993; Wei et al. 2018). The observed results shows acidic condition as more effective compare to alkaline conditions for the degradation of pollutants under similar kind of analysis as shown in some literature (Thanekar & Gogate, 2019). Due to that removal was low at a higher level of pH 8. Especially, at mid-level pH 5 shows maximum removal efficiency rather than another highly acidic pH 2 due to a higher amount of cavitation yield and effective generation of sulfate radicals by persulfate oxidant. At pH 2 higher amount of proton present in form of $H_3O^+$ which decreases effective decomposition of persulfate oxidant while increasing pH, quantity of $H_3O^+$ ions decreases in solution which leads to effective generation of sulfate radicals from persulfate as in shown in given Eqn. (3) & (4) (Romero et al., 2010; Sarath et al., 2016).

\[ S_2O_8^{2-} \rightarrow 2SO_4^{2-} \] \hspace{1cm} (2)

\[ S_2O_8^{2-} + H^+ \rightarrow HS_2O_8^{2-} \] \hspace{1cm} (3)

\[ HS_2O_8^{2-} \rightarrow H^+ + SO_4^- + SO_4^{2-} \] \hspace{1cm} (4)

Effect of Amplitude on COD removal

Effect of Power dissipation is one of the important influences in the ultrasound cavitation production rate, increasing amplitude generates more violent collapse of bubbles (Vega & Peñuela, 2018). In this study effect of power dissipation on COD removal was studied by
varying Amplitude Intensity from 20 to 80% (Power dissipation – 18W to 78W) with fixed pH of 5 and Persulfate Dosage of 250 mg/l. The plot shown in Fig. 3 (b), shows the variation of Amplitude Intensity at different levels and its effect on COD removal. A maximum removal estimate at a lower level of 20% (18W) shows that generation of cavitation yield is higher at the lower amplitude and lower at higher amplitude (Feng et al., 2002). The trend of the plot shows that it is not much sensitive towards process efficiency from the lower level to higher level it shows slight curvature, therefore amplitude intensity variation shows least significant favorable by ANOVA as shows in Table 4. The COD removal at 50% and 80% of Amplitude intensity is 31.6% and 29.9% respectively. Higher power intensity at lower frequency decoupling effect occurs between sample solution and transducer, thus bubble cloud formation occurs at the surface of the horn or transducer resulting in a reduction of sound waves in the solution, hence at a lower frequency power cavitation becomes more effective (Sunartio et al., 2007).

Effect of Persulfate oxidant on COD removal

Persulfate ($S_2O_8^{2-}$) is one of the strong oxidizing agents (Yang et al., 2019) for the degradation of organic matter. It gets activated in the presence of metal (Liu et al., 2016), heat (Tan et al., 2012) or ultrasound (Yang et al., 2019) as in given below in Eqn. (5) and produces sulfate radicals ($SO_4^{2-}$) with an oxidation potential of 2.40 V. The persulfate radical is more stable radical compare to hydroxyl radical (Romero et al., 2010). Persulfate oxidation has strong oxidation ability and efficient performance in a wide range of pH (Amor et al. 2019).

\[ S_2O_8^{2-} + \text{activator(Heat,US,Metal,Heat)} \rightarrow 2SO_4 \]  \hspace{1cm} (5)

Organic compounds + $SO_4^{2-} \rightarrow $ Oxidation Product \hspace{1cm} (6)
In this study effect of combined ultrasound activated and persulfate oxidation on COD removal was studied by varying Persulfate Dosage from 100 mg/l to 250 mg/l with fix factors pH 5 and amplitude of 50% as shown in Fig. 3 (c). Maximum COD removal of 32% was observed at a lower level of Persulfate Dosage of 100 mg/l. Predicted removal at mid-level of 250 mg/l dosage and higher-level of 400 mg/l dosage of persulfate was 31.3% and 21% respectively. Higher removal was reported at 100 mg/l dosage and with further increasing dosage from 250 mg/l to 400 mg/l removal efficiency starts decreasing which shows degradation rate is higher at 100 mg/L concentration of Persulfate Dosage. It shows that, increase in persulfate concentration lead to existence of excess persulfate in the system with which sulfate radicals in system react and produce sulfate ions and also extra sulfate radicals react itself, as given in Eqn. (7) and Eqn. (8) (Vu et al., 2004; Wei et al., 2018). The additional persulfate loading under particularly acidic solution reported as scavenger, thus rate of reaction slightly decreases with increase in dosage (Peyton 1993; Wei et al. 2018).

\[ SO_4^- + SO_4^- \rightarrow S_2O_8^{2-} \] \hspace{1cm} (7)

\[ SO_4^- + S_2O_8^{2-} \rightarrow SO_4^{2-} + S_2O_8^{2-} \] \hspace{1cm} (8)

Effect of pH and Amplitude on COD removal

The interaction effect of pH (A) and Amplitude (B) on COD removal is not significant approved by ANOVA as shown in Table 4, its P-value is higher than 0.005 (P > 0.005). Combined effect of pH and amplitude on COD removal was studied by maintain other parameters constant and the results are as shown in Fig. 6. The increasing amplitude at pH 2, removal of COD increased to 30.8% and on other hand middle level pH 5 with amplitude up to 50% removal efficiency increases further as a result of generation of effective cavitation and effective decomposition of persulfate (Sarath et al., 2016). Further increasing amplitude to 80% at pH 5, reduces removal
due to reduced cavitation yield, thus increasing or decreasing amplitude beyond or below 50% under near acidic condition (Thanekar & Gogate, 2019).

Effect of Amplitude and Persulfate Dosage on Yield Removal

Interaction effect of Amplitude (B) and Persulfate Dosage (C) on COD removal is a significant effect as indicated by ANOVA outputs shown in Table 4, its P-value is lower than 0.005 (P > 0.005). Fixing pH at 5, the interaction effect for Amplitude and dosage of persulfate on COD removal is shown in Fig. 7. For Amplitude of 20% and Persulfate Dosages of 100 mg/l shows much significant removal in COD due to amount of activation energy required for breakage of O-O bond and generation of sulfate radicals (Wacławek et al., 2017) was achieved under lower amplitude. Under higher amplitude of 50% and 80% persulfate amount of 250 mg/l and 400 mg/l became excessive loading for the system thus it reported as a scavenger for the process and it reduces the removal (Wei et al., 2018) compared to 20% amplitude and 100 mg/l of dosage.

Effect of pH and Persulfate Dosage on COD Removal

The interaction effect of pH (A) and Persulfate Dosage (B) on COD removal was not significant as indicated by ANOVA output as shown in Table 4, its P-value is higher than 0.005 (P > 0.005). Fixing amplitude at mid-level 50%, the interaction effect of pH and dosage of persulfate on COD removal is shown in Fig. 8. Under acidic pH of 2 and 5 with 100 mg/l dosage, shows much significant COD removal efficiency when compared to removal achieved at 250 mg/l and 400 mg/l dosage. Excessive loading of persulfate leads to less utilization of persulfate ions under acidic conditions (Wei et al., 2018), persulfate loading above some extent proven scavenger under acidic condition (Peyton 1993; Wei et al. 2018). Increasing dosage under the alkaline condition has not shown significant removal in COD removal.
CONCLUSION

The optimized parametric condition of pH 5, Amplitude Intensity of 20% and Persulfate Dosage of 100 mg/l shows 5440 mg/L removal of COD and 6.6% removal of TOC at 60 min of reaction time. Observed result shows that process parameter pH and Persulfate oxidant dosage shows much significance on COD removal efficiency. Synergistic effect of ultrasound Cavitation and Persulfate oxidation was more efficient for the degradation of organic matter from pharmaceutical wastewater compare to stand-alone process effect under optimum condition. It can potentially consider for scaling up purposes as an intensification technique for industrial wastewater treatment.

ACKNOWLEDGEMENTS

Authors are thankful to the Director, Pandit Deendayal Energy University, Gandhinagar, India and Director, National institute of Technology, Calicut, India for providing encouragement and kind permission for publishing the article. The authors also would like to thank Centre for Biofuels and Bioenergy Studies (CBBS) in PDEU for providing laboratory facilities for perform characterization and property estimation.

CRediT authorship contribution statement

Karan Pandya: Methodology, Formal analysis, Writing - original draft, Writing & editing.

T. S. Anantha Singh: Conceptualization, Methodology, Formal analysis, Supervision, Writing - original draft, Writing – review & editing.

Pravin Kodgire: Conceptualization, Methodology, Formal analysis, Supervision, Writing - original draft, Writing – review & editing.
Ethical approval: This study follows all ethical practices during writing.

Consent to participate: The author declares consent to participate.

Consent to publish: The author consents to publish this article in Environmental Science and Pollution Research.

Competing interests: The author declares that there are no conflicts of interest.

Transparency: The author confirms that the manuscript is an honest, accurate and transparent account of the study reported; that no vital features of the study have been omitted; and that any discrepancies from the study as planned have been explained.
REFERENCES

Adewuyi, Y. G., & Oyenekan, B. A. (2007). Optimization of a sonochemical process using a novel reactor and Taguchi statistical experimental design methodology. Industrial and Engineering Chemistry Research, 46(2), 411–420. https://doi.org/10.1021/ie060844c

Adishkumar, S., Sivajothi, S., & Rajesh Banu, J. (2012). Coupled solar photo-fenton process with aerobic sequential batch reactor for treatment of pharmaceutical wastewater. Desalination and Water Treatment, 48(1–3), 89–95. https://doi.org/10.1080/19443994.2012.698799

Amor, C., Rodríguez-Chueca, J., Fernandes, J. L., Domínguez, J. R., Lucas, M. S., & Peres, J. A. (2019). Winery wastewater treatment by sulphate radical based-advanced oxidation processes (SR-AOP): Thermally vs UV-assisted persulphate activation. Process Safety and Environmental Protection, 94–101. https://doi.org/10.1016/j.psep.2018.11.016

Anipsitakis, G. P., & Dionysiou, D. D. (2003). Degradation of organic contaminants in water with sulfate radicals generated by the conjunction of peroxymonosulfate with cobalt. Environmental Science and Technology, 37(20), 4790–4797. https://doi.org/10.1021/es0263792

Ayare, S. D., & Gogate, P. R. (2019). Sonocatalytic treatment of phosphonate containing industrial wastewater intensified using combined oxidation approaches. Ultrasonics Sonochemistry, 51, 69–76. https://doi.org/10.1016/j.ultsonch.2018.10.018

Barik, A. J., & Gogate, P. R. (2017). Hybrid treatment strategies for 2, 4, 6-trichlorophenol degradation based on. Ultrasonics - Sonochemistry. https://doi.org/10.1016/j.ultsonch.2017.07.029

Beckett, M. A., & Hua, I. (2001). Impact of ultrasonic frequency on aqueous sonoluminescence and sonochemistry. Journal of Physical Chemistry A, 105(15), 3796–3802. https://doi.org/10.1021/jp003226x

Chandak, S., Ghosh, P. K., & Gogate, P. R. (2020). Treatment of real pharmaceutical wastewater using different processes based on ultrasound in combination with oxidants. Process Safety and Environmental Protection, 137, 149–157. https://doi.org/10.1016/j.psep.2020.02.025

Changotra, R., Rajput, H., & Dhir, A. (2017). Natural soil mediated photo Fenton-like processes in treatment of pharmaceuticals: Batch and continuous approach. Chemosphere, 188, 345–353. https://doi.org/10.1016/j.chemosphere.2017.09.016

Changotra, R., Rajput, H., & Dhir, A. (2019). Treatment of real pharmaceutical wastewater using combined approach of Fenton applications and aerobic biological treatment. Journal of Photochemistry and Photobiology A: Chemistry, 376, 175–184. https://doi.org/10.1016/j.jphotochem.2019.02.029

Chu, W., Choy, W. K., & Kwan, C. Y. (2007). Selection of supported cobalt substrates in the presence of ozone for the oxidation of monuron. Journal of Agricultural and Food Chemistry, 55(14), 5708–5713. https://doi.org/10.1021/jf063754r

Cortez, S., Teixeira, P., Oliveira, R., & Mota, M. (2010). Ozonation as polishing treatment of mature landfill leachate. Journal of Hazardous Materials, 182(1–3), 730–734. https://doi.org/10.1016/j.jhazmat.2010.06.095
Crimi, M. L., & Taylor, J. (2007). Experimental evaluation of catalyzed hydrogen peroxide and sodium persulfate for destruction of BTEX contaminants. Soil and Sediment Contamination, 16(1), 29–45. https://doi.org/10.1080/15320380601077792

Crimi, G., & Lichtfouse, E. (2019). Advantages and disadvantages of techniques used for wastewater treatment. Environmental Chemistry Letters, 17(1), 145–155. https://doi.org/10.1007/s10311-018-0785-9

Dong, Z., Udepurkar, A. P., & Kuhn, S. (2020). Synergistic effects of the alternating application of low and high frequency ultrasound for particle synthesis in microreactors. Ultrasound Sonochemistry, 60(September 2019), 104800. https://doi.org/10.1016/j.ultsonch.2019.104800

Dopar, M., Kusic, H., & Koprivanac, N. (2011). Treatment of simulated industrial wastewater by photo-Fenton process. Part I: The optimization of process parameters using design of experiments (DOE). Chemical Engineering Journal, 173(2), 267–279. https://doi.org/10.1016/j.cej.2010.09.070

Dular, M., Griessler-Bulc, T., Gutierrez-Aguirre, I., Heath, E., Kosjek, T., Krivograd Klemenčič, A., Oder, M., Petkovšek, M., Rački, N., Ravnikar, M., Šarc, A., Širok, B., Zupanc, M., Žitnik, M., & Kompare, B. (2016). Use of hydrodynamic cavitation in (waste)water treatment. Ultrasound Sonochemistry, 29, 577–588. https://doi.org/10.1016/j.ultsonch.2015.10.010

Feng, R., Zhao, Y., Zhu, C., & Mason, T. J. (2002). Enhancement of ultrasonic cavitation yield by multi-frequency sonication. Ultrasound Sonochemistry, 9(5), 231–236. https://doi.org/10.1016/S1350-4177(02)00083-4

Ford, A. T., & Fong, P. P. (2016). The effects of antidepressants appear to be rapid and at environmentally relevant concentrations. Environmental Toxicology and Chemistry, 35(4), 794–798. https://doi.org/10.1002/etc.3087

Gadipelly, C., Pérez-González, A., Yadav, G. D., Ortiz, I., Ibáñez, R., Rathod, V. K., & Marathe, K. V. (2014). Pharmaceutical industry wastewater: Review of the technologies for water treatment and reuse. Industrial and Engineering Chemistry Research, 53(29), 11571–11592. https://doi.org/10.1021/ie501210j

Gągol, M., Przyjazny, A., & Boczkaj, G. (2018). Wastewater treatment by means of advanced oxidation processes based on cavitation – A review. Chemical Engineering Journal, 338(January), 599–627. https://doi.org/10.1016/j.cej.2018.01.049

Gao, Y. qiong, Gao, N. yun, Deng, Y., Yang, Y. qiong, & Ma, Y. (2012). Ultraviolet (UV) light-activated persulfate oxidation of sulfamethazine in water. Chemical Engineering Journal, 195–196, 248–253. https://doi.org/10.1016/j.cej.2012.04.084

Ghafoori, S., Mowl, A., Jahani, R., Mehrvar, M., & Chan, P. K. (2015). Sonophotolytic degradation of synthetic pharmaceutical wastewater: Statistical experimental design and modeling. Journal of Environmental Management, 150, 128–137. https://doi.org/10.1016/j.jenvman.2014.11.011

Grandclément, C., Seyssiecq, I., Píram, A., Wong-Wah-Chung, P., Vanot, G., Tiliacos, N., Roche, N., Doumenq, P., Chang, C. Y., Chang, J. S., Vigneswaran, S., Kandasamy, J., Martínez, F., Molina, R., Rodríguez, I., Pariente, M. I., Segura, Y., Melero, J. A., Ganzenko, O., … Kanematsu, W. (2019). Combined hydrodynamic cavitation based processes as an efficient treatment option for real industrial effluent. Ultrasound Sonochemistry, 52(1), 89–
Hu, X., Wang, X., Ban, Y., & Ren, B. (2011). A comparative study of UV-Fenton, UV-H2O2 and Fenton reaction treatment of landfill leachate. Environmental Technology, 32(9), 945–951. https://doi.org/10.1080/09593330.2010.521953

Huang, G. Y., Liu, Y. S., Chen, X. W., Liang, Y. Q., Liu, S. S., Yang, Y. Y., Hu, L. X., Shi, W. J., Tian, F., Zhao, J. L., Chen, J., & Ying, G. G. (2016). Feminization and masculinization of western mosquitofish (Gambusia affinis) observed in rivers impacted by municipal wastewaters. Scientific Reports, 6(February), 1–11. https://doi.org/10.1038/srep20884

Jeworski, M., & Heinzle, E. (2000). Combined chemical-biological treatment of wastewater containing refractory pollutants. Biotechnology Annual Review, 6, 163–196. https://doi.org/10.1016/S1387-2656(00)06022-1

Jordens, J., Appermont, T., Gielen, B., Van Gerven, T., & Braeken, L. (2016). Sonofragmentation: Effect of Ultrasound Frequency and Power on Particle Breakage. Crystal Growth and Design, 16(11), 6167–6177. https://doi.org/10.1021/acs.cgd.6b00088

Kansal, A., Siddiqui, N. A., & Gautam, A. (2013). Assessment of heavy metals and their interrelationships with some physicochemical parameters in eco-efficient rivers of Himalayan region. Environmental Monitoring and Assessment, 185(3), 2553–2563. https://doi.org/10.1007/s10661-012-2730-x

Keenan, C. R., & Sedlak, D. L. (2008). Ligand-enhanced reactive oxidant generation by nanoparticulate zero-valent iron and oxygen. Environmental Science and Technology, 42(18), 6936–6941. https://doi.org/10.1021/es801438f

Khorram, A. G., & Fallah, N. (2018). Treatment of textile dyeing factory wastewater by electrocoagulation with low sludge settling time: Optimization of operating parameters by RSM. Journal of Environmental Chemical Engineering, 6(1), 635–642. https://doi.org/10.1016/j.jece.2017.12.054

Kim, H. Y., & Jung, G. H. (2018). Paraplegia by Acute Cervical Disc Herniation after Shoulder Arthroscopic Surgery in Beach-Chair Position. Open Journal of Anesthesiology, 08(11), 280–283. https://doi.org/10.4236/ojanes.2018.811028

Lastre-Acosta, A. M., Cruz-González, G., Nuevas-Paz, L., Jáuregui-Haza, U. J., & Teixeira, A. C. S. C. (2015). Ultrasonic degradation of sulfadiazine in aqueous solutions. Environmental Science and Pollution Research, 22(2), 918–925. https://doi.org/10.1007/s11356-014-2766-2

Leighton, T. G. (1995). Bubble population phenomena in acoustic cavitation. Ultrasonics - Sonochemistry, 2(2), 123–136. https://doi.org/10.1016/1350-4177(95)00021-W

Lin, Y. T., Liang, C., & Chen, J. H. (2011). Feasibility study of ultraviolet activated persulfate oxidation of phenol. Chemosphere, 82(8), 1168–1172. https://doi.org/10.1016/j.chemosphere.2010.12.027

Liu, H., Bruton, T. A., Li, W., Buren, J. Van, Prasse, C., Doyle, F. M., & Sedlak, D. L. (2016). Oxidation of Benzene by Persulfate in the Presence of Fe(III)- and Mn(IV)-Containing Oxides: Stoichiometric Efficiency and Transformation Products. EnvironmentalScienceandTechnology, 50(2), 890–898. https://doi.org/10.1021/acs.est.5b04815

Mantzavinos, D., & Psillakis, E. (2004). Enhancement of biodegradability of industrial wastewaters by chemical oxidation pre-treatment. Journal of Chemical Technology and...
Martínez, F., Molina, R., Rodríguez, I., Pariente, M. I., Segura, Y., & Melero, J. A. (2018). Techno-economical assessment of coupling Fenton/biological processes for the treatment of a pharmaceutical wastewater. Journal of Environmental Chemical Engineering, 6(1), 485–494. https://doi.org/10.1002/jce.2017.12.008

Milano, J., Ong, H. C., Masjuki, H. H., Silitonga, A. S., Chen, W. H., Kusumo, F., Dharma, S., & Sebayang, A. H. (2018). Optimization of biodiesel production by microwave irradiation-assisted transesterification for waste cooking oil-Calophyllum inophyllum oil via response surface methodology. Energy Conversion and Management, 158(August 2017), 400–415. https://doi.org/10.1016/j.enconman.2017.12.027

Mohapatra, D. P., Brar, S. K., Tyagi, R. D., Picard, P., & Surampalli, R. Y. (2014). Analysis and advanced oxidation treatment of a persistent pharmaceutical compound in wastewater and wastewater sludge-carbamazepine. Science of the Total Environment, 470–471, 58–75. https://doi.org/10.1016/j.scitotenv.2013.09.034

Monteagudo, J. M., Durán, A., González, R., & Expósito, A. J. (2015). In situ chemical oxidation of carbamazepine solutions using persulfate simultaneously activated by heat energy, UV light, Fe2+ ions, and H2O2. Applied Catalysis B: Environmental, 176–177, 120–129. https://doi.org/10.1016/j.apcatb.2015.03.055

Monteagudo, J. M., El-taliawy, H., Durán, A., Caro, G., & Bester, K. (2018). Sono-activated persulfate oxidation of diclofenac: Degradation, kinetics, pathway and contribution of the different radicals involved. Journal of Hazardous Materials, 357(April), 457–465. https://doi.org/10.1016/j.jhazmat.2018.06.031

Muthukumaran, C., Praniesh, R., Navamani, P., Swathi, R., Sharmila, G., & Manoj Kumar, N. (2017). Process optimization and kinetic modeling of biodiesel production using non-edible Madhuca indica oil. Fuel, 195, 217–225. https://doi.org/10.1016/j.fuel.2017.01.060

Nejumal, K. K., Manoj, P. R., Aravind, U. K., & Aravindakumar, C. T. (2014). Sonochemical degradation of a pharmaceutical waste, atenolol, in aqueous medium. Environmental Science and Pollution Research, 21(6), 4297–4308. https://doi.org/10.1007/s11356-013-2301-x

Ng, K. K., Shi, X., Tang, M. K. Y., & Ng, H. Y. (2014). A novel application of anaerobic bio-entrapped membrane reactor for the treatment of chemical synthesis-based pharmaceutical wastewater. Separation and Purification Technology, 132, 634–643. https://doi.org/10.1016/j.seppur.2014.06.021

Peyton, G. R. (1993). The free-radical chemistry of persulfate-based total organic carbon analyzers. Marine Chemistry, 41(1–3), 91–103. https://doi.org/10.1016/0304-4203(93)90108-Z

Rao, Y., Yang, H., Xue, D., Guo, Y., Qi, F., & Ma, J. (2016). Sonolytic and sonophotolytic degradation of Carbamazepine: Kinetic and mechanisms. Ultrasonics Sonochemistry, 32, 371–379. https://doi.org/10.1016/j.ultsonch.2016.04.005

Rayaroth, M. P., Aravind, U. K., & Aravindakumar, C. T. (2016). Degradation of pharmaceuticals by ultrasound-based advanced oxidation process. Environmental Chemistry Letters, 14(3), 259–290. https://doi.org/10.1007/s10311-016-0568-0

Rodríguez-Chueca, J., Laski, E., García-Cañibano, C., Martín de Vidales, M. J., Encinas, Kuch, B., & Marugán, J. (2018). Micropollutants removal by full-scale UV-C/sulfate radical
based Advanced Oxidation Processes. Science of the Total Environment, 630, 1216–1225. https://doi.org/10.1016/j.scitotenv.2018.02.279

Romero, A., Santos, A., Vicente, F., & González, C. (2010). Diuron abatement using activated persulphate: Effect of pH, Fe(II) and oxidant dosage. Chemical Engineering Journal, 162(1), 257–265. https://doi.org/10.1016/j.cej.2010.05.044

Sarath, K., Gandhimathi, R., Ramesh, S. T., & Nidheesh, P. V. (2016). Removal of reactive magenta-MB from aqueous solution by persulphate-based advanced oxidation process. Desalination and Water Treatment, 57(25), 11872–11878. https://doi.org/10.1080/19443994.2015.1054886

Singh, R., & Prashant, R. (2017). A review on characterization and bioremediation of pharmaceutical industries’ wastewater: an Indian perspective. Applied Water Science, 1–12. https://doi.org/10.1007/s13201-014-0225-3

Singh, S. K., Tang, W. Z., & Tachiev, G. (2013). Fenton treatment of landfill leachate under different COD loading factors. Waste Management, 33(10), 2116–2122. https://doi.org/10.1016/j.wasman.2013.06.019

Spina, F., Anastasi, A., Prigione, V., Tigini, V., & Varese, G. C. (2012). Biological treatment of industrial wastewaters: A fungal approach. Chemical Engineering Transactions, 27, 175–180. https://doi.org/10.3303/CET1227030

Sunartio, D., Ashokkumar, M., & Grieser, F. (2007). Study of the coalescence of acoustic bubbles as a function of frequency, power, and water-soluble additives. Journal of the American Chemical Society, 129(18), 6031–6036. https://doi.org/10.1021/ja068980w

Tak, B. yul, Tak, B. sik, Kim, Y. ju, Park, Y. jin, Yoon, Y. hun, & Min, G. ho. (2015). Optimization of color and COD removal from livestock wastewater by electrocoagulation process: Application of Box- Behnken design (BBD). Journal of Industrial and Engineering Chemistry, 28, 307–315. https://doi.org/10.1016/j.jiec.2015.03.008

Tan, C., Gao, N., Deng, Y., An, N., & Deng, J. (2012). Heat-activated persulfate oxidation of diuron in water. Chemical Engineering Journal, 203, 294–300. https://doi.org/10.1016/j.cej.2012.07.005

Thanekar, P., & Gogate, P. R. (2019). Combined hydrodynamic cavitation based processes as an efficient treatment option for real industrial effluent. Ultrasonics Sonochemistry, 53(January), 202–213. https://doi.org/10.1016/j.ultsonch.2019.01.007

Tiwari, B., Drogui, P., & Tyagi, R. D. (2020). Removal of emerging micro-pollutants from pharmaceutical industry wastewater. In Current Developments in Biotechnology and Bioengineering. Elsevier B.V. https://doi.org/10.1016/b978-0-12-819594-9.00018-8

Vega, L. P., & Peñuela, G. A. (2018). High Frequency Sonochemical Degradation of Benzophenone-3 in Water. Journal of Environmental Engineering (United States), 144(8), 1–7. https://doi.org/10.1061/(ASCE)EE.1943-7870.0001406

Verma, A. K., Dash, R. R., & Bhunia, P. (2012). A review on chemical coagulation/flocculation technologies for removal of colour from textile wastewaters. Journal of Environmental Management, 93(1), 154–168. https://doi.org/10.1016/j.jenvman.2011.09.012

Vu, X. Y., Bao, Z. C., & Barker, J. R. (2004). Free Radical Reactions Involving Cl₂, Cl₂−, and SO₄− in the 248 nm Photolysis of Aqueous Solutions Containing S 2O 82− and Cl−. Journal of Physical Chemistry A, 108(2), 295–308. https://doi.org/10.1021/jp036211i
Waclawek, S., Lutze, H. V., Grübel, K., Padil, V. V. T., Černík, M., & Dionysiou, D. D. (2017). Chemistry of persulfates in water and wastewater treatment: A review. Chemical Engineering Journal, 330, 44–62. https://doi.org/10.1016/j.cej.2017.07.132

Wang, S., & Zhou, N. (2016). Removal of carbamazepine from aqueous solution using sono-activated persulfate process. Ultrasonics Sonochemistry, 29, 156–162. https://doi.org/10.1016/j.ultsonch.2015.09.008

Wei, L., Chen, W., Li, Q., Gu, Z., & Zhang, A. (2018). Wastewater in heat-activated persulfate system †. 20603–20611. https://doi.org/10.1039/c8ra01995a

Xie, P., Ma, J., Liu, W., Zou, J., Yue, S., Li, X., Wiesner, M. R., & Fang, J. (2015). Removal of 2-MIB and geosmin using UV/persulfate: Contributions of hydroxyl and sulfate radicals. Water Research, 69, 223–233. https://doi.org/10.1016/j.watres.2014.11.029

Yang, L., Xue, J., He, L., Wu, L., Ma, Y., Chen, H., Li, H., Peng, P., & Zhang, Z. (2019). Review on ultrasound assisted persulfate degradation of organic contaminants in wastewater: Influences, mechanisms and prospective. Chemical Engineering Journal, 378(April). https://doi.org/10.1016/j.cej.2019.122146

Yang, Q., Zhong, Y., Zhong, H., Li, X., Du, W., Li, X., Chen, R., & Zeng, G. (2015). A novel pretreatment process of mature landfill leachate with ultrasonic activated persulfate: Optimization using integrated Taguchi method and response surface methodology. Process Safety and Environmental Protection, 98, 268–275. https://doi.org/10.1016/j.psep.2015.08.009

Zhang, M. F., Qin, Y. H., Ma, J. Y., Yang, L., Wu, Z. K., Wang, T. L., Wang, W. G., & Wang, C. W. (2016). Depolymerization of microcrystalline cellulose by the combination of ultrasound and Fenton reagent. Ultrasonics Sonochemistry, 31, 404–408. https://doi.org/10.1016/j.ultsonch.2016.01.027

Zou, X., Zhou, T., Mao, J., & Wu, X. (2014). Synergistic degradation of antibiotic sulfadiazine in a heterogeneous ultrasound-enhanced Fe0/persulfate Fenton-like system. Chemical Engineering Journal, 257, 36–44. https://doi.org/10.1016/j.cej.2014.07.048
Figures

Figure 1

Schematic diagram of Experimental Process
Figure 2

(a) Comparison of Predicted COD removal (Box Behnken design) to Actual COD removal (b) Profile of Perturbation Plot showing significant parameter affecting COD removal with factors pH (A) 2 to 8, Amplitude (B) 20% to 80%, Persulfate Dosage 100 to 400 mg/l (C) with middle level values
Figure 3

(a) Profile of Individual Parameter Plot with two reference curves based on ANOVA for Process Parameter pH from 2 to 8, with fix parameter amplitude of 50%, and Persulfate Dosage of 250 mg/l on Removal of COD with 95% of confidence interval band. (b) Profile of Individual Parameter Plot two reference curve based on ANOVA for Process Parameter Amplitude from 20% (18W) to 80% (78W) with fix parameter pH of 5, and Persulfate Dosage of 250 mg/l at mid-level on Removal of COD (mg/l) with 95% of confidence interval band. (c) Profile of Individual Parameter Plot two reference curve based on ANOVA for Process Parameter Persulfate Dosage 100 to 400 (mg/l) with fix parameter of pH 5 and amplitude of 50% on Removal of COD with 95% of confidence interval band.
Figure 4

Profile of percentage COD removal with Individual treatment; ultrasound at pH 5, amplitude 20%; Persulfate of 100 mg/l; Combine Effect of ultrasound with persulfate at pH 5 & Persulfate Dosage of 100 mg/l, Amplitude of 20% within 60 min reaction time.
Figure 5

(a) Profile of Interaction effect plot for process parameter pH 2-8 to Amplitude 20%-80% (AB) maintaining Persulfate Dosage (mg/l) at middle level
(b) Profile of Interaction effect plot for Amplitude 20%-80% to Persulfate Dosage 100-400 (mg/l) (BC) maintaining pH at middle level
(c) Profile of Interaction effect plot for pH 2-8 and Persulfate Dosage 100-400 (mg/l) (AC) maintaining Amplitude % at middle level