Larhyss Journal, ISSN 1112-3680, n°61, March 2025, pp. 321-341

EFFICIENT REMOVAL OF PHARMACEUTICAL CONTAMINANTS BY ALUMINIUM SULPHATE INSIGHTS ON DICLOFENAC AND PH INFLUENCE

BACHA N.[1, 2], ACHOUR S.[2]

[1] Scientific and Technical Research Center on Arid Regions (CRSTRA), Campus of Mohamed Khider University, Biskra, Algeria
[2] Research Laboratory in Subterranean and Surface Hydraulics (LARHYSS), Faculty of Science and Technology, Mohamed Khider University, Biskra, Algeria

bachanaima@yahoo.fr

Research Article – Available at http://larhyss.net/ojs/index.php/larhyss/index
Received May 12, 2024, Received in revised form January 5, 2025, Accepted January 7, 2025

ABSTRACT

The widespread presence of pharmaceutical residues, particularly non-steroidal anti-inflammatory drugs (NSAIDs) like diclofenac, in aquatic environments poses significant risks to both ecosystems and human health. This study aimed to evaluate the effectiveness of coagulation-flocculation using aluminum sulfate for the removal of diclofenac from distilled water under different pH conditions. Experimental procedures involved jar-test coagulation-flocculation trials at pH levels of 4, 7, and 9, with varying initial diclofenac concentrations and coagulant dosages. Diclofenac removal efficiency was analyzed using UV-visible spectrophotometry.

The results indicated that pH and coagulant dosage significantly influenced the removal efficiency. The highest removal efficiency (64.44%) was achieved at near-neutral pH (pH 7) with a coagulant dosage of 150 mg/L for a diclofenac concentration of 15 mg/L. At acidic (pH 4) and alkaline (pH 9) conditions, the removal efficiencies were lower, reaching up to 60.74% and 31.49%, respectively, for higher diclofenac concentrations. Reaction mechanisms varied with pH due to changes in aluminum speciation and diclofenac interactions, with strong complexation and ligand exchange observed at near-neutral pH. A stoichiometric relationship was identified between the initial diclofenac concentration and the optimal coagulant dosage, with variations based on pH.

This study highlights the importance of pH optimization in coagulation processes and provides valuable insights for improving water treatment strategies to mitigate pharmaceutical contamination.

Keywords: Pharmaceuticals, Diclofenac, coagulation-flocculation, aluminium sulphate, pH optimization, stoichiometry.

INTRODUCTION

Nowadays, one of the major environmental concerns is the growing water contamination by humans' activities, technological developments and rapid industry expansion (Handayani et al., 2023). Water contamination might be both organic and inorganic (Harrat and Achour, 2016). Governments and water agencies worldwide are becoming increasingly concerned about trace organic contaminants.

As a type of trace organic contamination, a variety of pharmaceutical items may be found in wastewater and natural rivers as a result of a range of waste sources, such as hospital and pharmaceutical company waste and household waste (Alexander et al., 2012). Fig. 1 shows how pharmaceutical compounds are released into the environment.

The primary source of these residues is human and animal pharmaceuticals, which are frequently only partially metabolised and eliminated as chemical compounds or metabolites in urine and faeces (Taft, 2009).

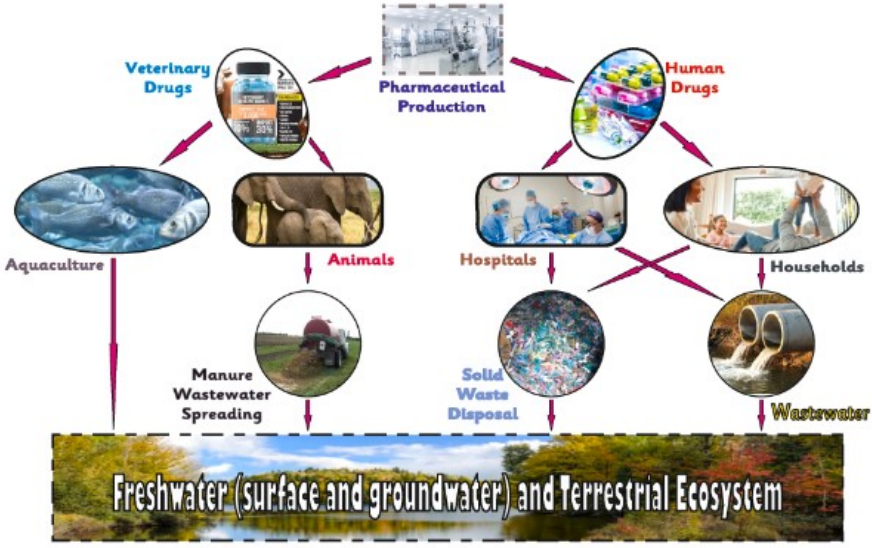


Figure 1: Origins of drug residues in the environment

Chemicals known as pharmaceutical compounds are utilised to cause a biological effect in the human or animal body that is advantageous to health. Their classification is as follows:

- The drug's mechanism of action describes how it alters certain biochemical processes in the body.
- The way a medicine affects an organ, like your skin, brain, or digestive tract, is known as its physiological effect.

- Chemical structure: This is how a drug's chemical composition is specifically organised.

Their extensive use is the cause of widespread contamination of aquatic environments by a broad spectrum of molecules. They can be considered persistent or recalcitrant pollutants due to their continuous release into the environment and, sometimes, their intrinsic properties (Bocaly, 2010). Pharmaceuticals are one form of trace organic contamination that has been demonstrated to have detrimental effects on both human health and the environment when found in water (Ortuzar et al., 2022).

Furthermore, in aquatic environments, these chemicals persist for longer periods of time at low concentrations (ng L^{-1} to µg L^{-1}), and their lipophilicity harmful effects are more inclined to be chronic than acute (Hernandez-Tenorio et al., 2022).

They may have a potent mutagenic and genotoxic effect on exposed living organisms and are referred to as endocrine disruptors (WHO, 2012; Sharif et al., 2016).

Their intact form directly correlates with the potential hazards of such chemicals in water. Nevertheless, in natural water reservoirs or during sewage treatment, parent compounds may undergo additional transformations through biotic and abiotic processes (microbiological transformation, hydrolysis, or photolysis) (Hejna et al., 2022). As a result, intact medications and their byproducts may accumulate in the tissues of plants, animals, and algal varieties and be hazardous to them. Efficient water treatment methods must be employed with the goal to remove trace organic contaminants and ensure that any potential health risks to people are minimised prior to consumption of water.

Pharmaceuticals may be removed to variable degrees by wastewater and drinking water treatment processes, despite the fact that these processes are not expressly built to do so. Non-steroidal anti-inflammatory medications, hormones, antibiotics, endocrine disruptors, and painkillers are among the examples of these hazardous contaminants. While some of these compounds may be eliminated using conventional processes, others are challenging for wastewater treatment facilities to break down.

Numerous factors may affect removal during treatment because wastewater and surface water are complex and variable media and pharmaceuticals have a wide spectrum of physical-chemical characteristics.

Various conventional technologies can be used to remove pharmaceutical wastes in the water, such as adsorption separation, precipitation, and coagulation-flocculation (Bukhtawar et al., 2024). In addition, the degradation techniques used are biodegradation, electro catalysis, chlorination, ozonation and advanced oxidation process (AOP) such as photocatalysis (Sharma et al., 2023).

To remove pharmaceutical residues from wastewater and surface water, existing treatment systems must be optimised and improved.

Steps of traditional water treatment includes coagulation treatment as a fundamental component. Coagulation treatment has long been used to treat water in order to reduce turbidity and colour and to eliminate pathogens (Matilainen et al., 2010; Vieno et al.,

2010; Achour et al., 2019). By using coagulation, it is possible to effectively remove the hydrophobic and high molar mass fractions of natural organic matter, such as humic substances. (Matilainen et al., 2010; Bacha et Achour, 2023).

Coagulation-flocculation is becoming more generally accepted as a removal treatment that can, to some extent, compete with more expensive treatments like oxidation via ozone or adsorption using activated carbon, in addition to being a method of clarification (Achour et Guesbaya,2005; Alexander et al., 2012).

Many studies (Vieno, 2006) has demonstrated the effectiveness of the coagulation-flocculation process for the removal of pharmaceuticals, both in wastewater and in fresh water. The process's efficiency in eliminating trace organic contaminants, including pharmaceuticals, can be enhanced by optimising parameters such as pH, coagulant dosage, and initial concentration of pollutant (Vieno et al., 2010; Alexander et al., 2012).

In order to achieve this, our study aims to evaluate how effectively pharmaceutical-type organic compounds may be eliminated from water by conventional coagulation treatment.

Since it influences both the speciation of the coagulant's hydrolysed forms and the dissociation of the functional groups included in the organic compound's structure, the pH parameter is significant. (Rezeg and Achour, 2005; Afoufou and Achour, 2017; Bacha and Achour ,2013; Naceradska et al., 2019).

Therefore, this work aims to demonstrate the significance of pH in the removal of recalcitrant chemical compounds, such as diclofenac, which is part of the class of non-steroidal anti-inflammatory drugs (NSAIDs). This involves carrying out coagulation flocculation tests using aluminum sulfate on diclofenac dissolved in distilled water. Different parameters are varied such as the dose of coagulant, the initial concentration of the organic product but especially the pH. The influence of pH is also be examined on the stoichiometry that can be established between the initial concentration of diclofenac and the optimal dose of coagulant.

OVERVIEW ON OCCURRENCE AND TOXICITY OF ANTI-INFLAMMATORY PHARMACEUTICALS IN ENVIRONMENT

NSAIDs, or non-steroidal anti-inflammatory drugs, are medications that are frequently used to lower fever, reduce inflammation, and treat pain. Because NSAIDs are so widely used, their adverse effects are becoming more frequent. NSAID use raises the risk of renal disease, unfavourable cardiovascular events, and a variety of gastrointestinal (GI) issues. (Brune and Patrignani, 2015).

The prevalence and toxicity of anti-inflammatory pharmaceuticals, particularly non-steroidal anti-inflammatory drugs (NSAIDs), in the environment has emerged as an increasing issue due to their extensive use and potential adverse impacts on ecosystems and human health. NSAIDs are thought to be bio-accumulative, persistent, and non-biodegradable.

Commonly used NSAIDs such as Diclofenac, Ibuprofen, and Naproxen are frequently detected in surface water, wastewater, and even drinking water. Examples of NSAID concentrations in waters on various continents are compiled in Table 1.

These pharmaceutical compounds are among the most often reported in aquatic environments and account for around 15% of all pharmaceuticals identified in worldwide monitoring surveys.

Aquatic environments have been reported to contain nanogrammes to microgrammes per litre of several anti-inflammatory medications, including mefenamic acid, naproxen, diclofenac, ibuprofen, and ketoprofen. Most of these medications are sourced from wastewater treatment plants. Several aquatic environments, such as surface waters, seawaters, groundwaters, wastewater, and sludge, have been shown to include diclofenac, naproxen, ketoprofen and ibuprofen. (Lakshmi et al., 2024).

Studies have revealed that non-steroidal anti-inflammatory drugs (NSAIDs) can negatively affect aquatic species, including fish, amphibians, and invertebrates, thereby disrupting their reproductive processes, growth, and behavior (Schwaiger et al., 2004).

Marine microorganisms, algae, aquatic invertebrates, and various trophic levels have all shown acute NSAID toxicity, with phytoplankton showing the highest susceptibility (Ruiz and Font, 2011). The liver, kidneys, gills, and muscle all indicated bioaccumulation of diclofenac and ibuprofen. In rainbow trout, renal lesions and subcellular effects have been noted. The LOEC for fish toxicity and environmental concerns was met by the levels of diclofenac in surface water and wastewater. The metabolites of ibuprofen and naproxen may become more hazardous than the original substance following photodegradation (Kümmerer, 2009).

Prior research has demonstrated that pharmaceutical pollutants are frequently not completely reduced during the wastewater treatment process. Pharmaceuticals' capacity to interact with solid particles is a key feature in their removal during treatment processes because it allows for physical-chemical (coagulation, settling, flotation) or biological (biodegradation) methods to remove them (Roberts and Thomas, 2006).

Data on drinking and tap water is scarcer than that on surface waters and wastewater, particularly in developing and emerging nations.

Table 1: Some examples of NSAIDs identified in different types of water

Location	NSAIDs concentration (µg/l)	Common NSAIDs detected	Reference
Selected rivers, Germany	0.0011-15.033; 0.0051–0.032	Diclofenac; Ibuprofen	Thomas et Langford, 2007
Ceyhan River, Turkey	0.086-0.176; 0.034-0.473	Diclofenac; Etodolac	Gusel et al., 2018
Edo River, Japan	0.002; 0.01; 001; 0.264; 0.002.	Diclofenac; Felbinac; Ibuprofen, acetylsalicylique acid; Mefenamic acid.	Nishi et al., 2015

3 Rivers of Western Himalaya	0.01-2.05	Diclofenac	Sharma et al., 2024
Coastal marine water, France	0.032-0101; 0.010-0.214	Diclofenac, Naproxen	(Bocaly, 2010)
wastewater, Province of Castellon, Spain	1.17-39.8 (Influents); 0.62-0.74 (Effluents)	Diclofenac, Ibuprofen, Naproxen, ketoprofen	Garcia-Lor et al., 2010
Wastewater, Durban, KwaZulu-Natal Province, South Africa	23.5-115.1; 67.9-220.9; 14.4-109.3	Diclofenac; Naproxen; Ibuprofen	Madikizela & Chimuka, 2017

MATERIAL AND METHODS

Preparation of solutions

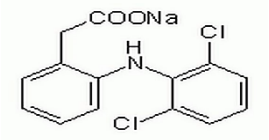
Solution of diclofenac

Diclofenac, which is a common non-steroidal anti-inflammatory drug, was obtained from Pharmalliance. Diclofenac was available as a sodium salt. Diclofenac's chemical structure and properties are listed in Table 2.

A 100 mg/L stock solution served as the basis for all of the Diclofenac solutions that were analysed. This solution was utilised both in the preparation of standard solutions and in trials conducted with synthetic solutions.

The distilled water used, during our tests, has a conductivity of about 5 µs/cm and a pH ranging from 6.07 to 6.79. The pH of the solutions was adjusted using 0.1N HCl and NaOH solutions.

Table 2: Main phhysico-chemical properties of diclofenac sodium (O'Neil, 2006; Anses, 2019)

Diclofenac (DFC)	
Chemical formula	
Molecular formula	$C_{14}H_{10}Cl_2NNaO_2$
Molecular weight	318.13 g mol^{-1}
Water solubility	Soluble in water to 50mg/ml.
Log Kow	0.7-1.2
pKa	4.15
log Dow	1.15

Coagulant solution

The coagulant reagent used is aluminum sulfate ($Al_2(SO4)_3$, $18H_2O$) for which a stock solution of 10 g/l is prepared periodically in distilled water.

Diclofenac analysis

DFC, an aromatic organic compound, was determined using an OPTIZEN 2120 UV UV-visible spectrophotometer equipped with quartz cells and a 1 cm optical path. The wavelength used is 276 nm and corresponds to the maximum absorbance.

The residual concentrations were determined from the absorbance calibration curves (Fig.2).

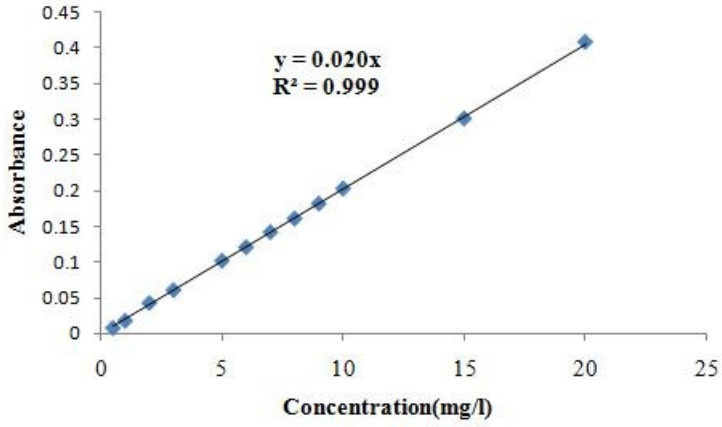


Figure 2: Calibration curves of diclofenac in distilled water (Wave length λ=276nm)

Description of Jar-Test

One laboratory-scale test that can replicate the coagulation/flocculation process in water treatment facilities is the jar-test. A set of six transparent jars placed in a row on a gang stirrer makes up the Jar Test apparatus. Samples of the aqueous solution to be treated are placed inside each jar. In order to provide uniform test conditions, the gang stirrer enables all of the jars to be stirred simultaneously at the same pace.

The "Jar-Test" procedure was followed for all coagulation-flocculation tests on a flocculator (Ficher 1198 Flocculator). It provides the simultaneous agitation of distilled water solutions supplemented with DFC and increased aluminium sulphate doses.

For three minutes, the solutions were rapidly stirred at 200 rpm. After then, the speed is lowered to 60 rpm for 30 minutes. The supernatant is extracted and vacuum-filtered on an OSMONICS INC membrane with a porosity of 0.45 µm following a 30-minute settling period (Bacha and Achour, 2015). A spectrophotometer is then used to analyse the filtrate.

Diclofenac acid was dissolved in distilled water at amounts of 2, 5, 8, 10, and 15 mg/l in an attempt to establish relationships between the initial Diclofenac concentration and increasing coagulant dosage carried out. The pH is gradually raised to 4, 7, and 9 during these trials by adding sodium hydroxide solution or hydrochloric acid. The pH varied during the three (3) minutes of rapid shaking.

The removal efficiency of the organic chemical DFC from the samples can be computed as a percentage using the following formula, where R% refers for efficiency in percentage, C_0 and C_f refer for the initial and final concentrations of the DFC in milligrams per litre, respectively:

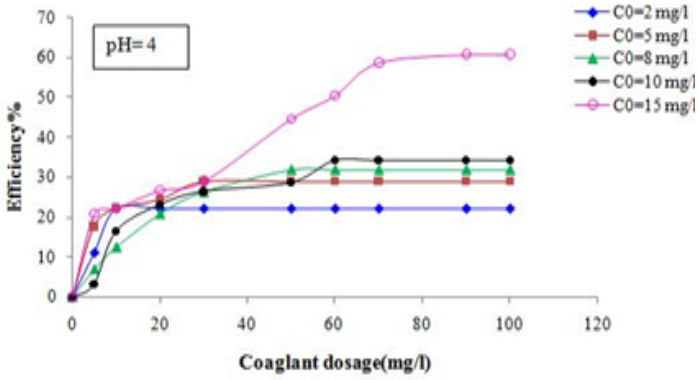
$$R(\%) = \frac{C_0 - C_f}{C_0} \times 100 \quad (1)$$

IMPACT OF PH AND ALUMINIUM SULPHATE DOSAGE ON THE ELIMINATION OF DIFFERENT DICLOFENAC CONCENTRATIONS

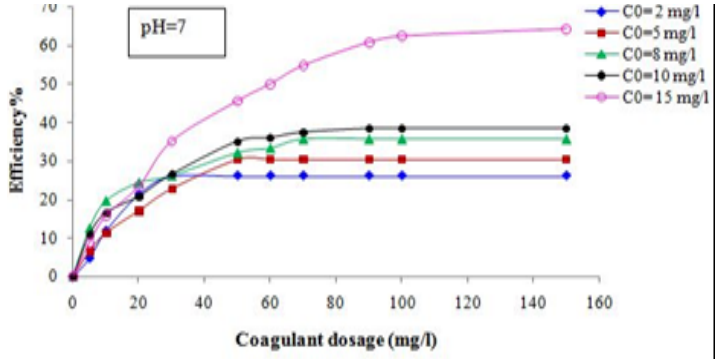
This study step focusses at how aluminium sulfate's coagulation-flocculation affects the removal efficiencies of DFC dissolved in distilled water. This is accomplished by studying various reaction parameters throughout the experiment (coagulation pH, DFC concentration, coagulant dose). A discussion of possible reaction mechanisms may also be based on these findings.

Results

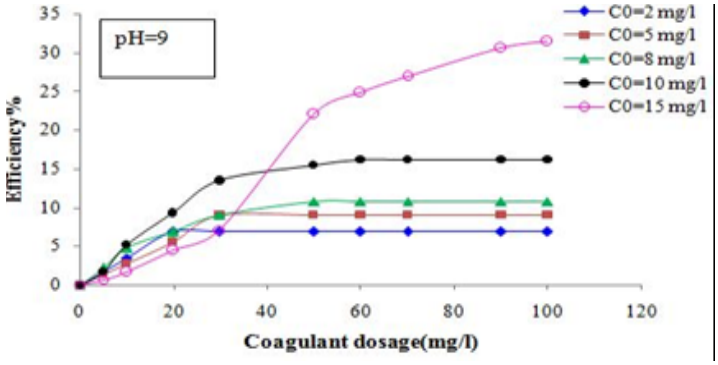
Increasing diclofenac concentrations were added to distilled water, and different amounts of aluminium sulphate were used to coagulate the mixture. The solutions' pH ranged from 4 to 9. Fig. 3 illustrates the results for each pH.



(a)



(b)



(c)

Figure 3: Diclofenac removal efficiency with aluminum sulfate at varying pH levels. (a) pH=4; (b) pH = 7; (c) pH = 9

Based on the coagulation-flocculation results for all tested concentrations of diclofenac across the studied pH levels, the following observations can be made:

- Regardless of the diclofenac concentration or the pH level, the curves exhibit a similar shape. Overall, two distinct zones can be identified:

  i) The first zone, where the yield R% increases significantly until reaching a value corresponding to the optimal removal of diclofenac.

  ii) The second zone, where the yield stabilizes, even with an excess amount of coagulant.

- For all initial concentrations (C0), the efficiency improves with increasing coagulant dosage, reaching an optimum point for diclofenac removal. Beyond this point, the yield remains unchanged, even with additional coagulant dosage.

- As the initial concentration (C0) increases, the optimal coagulant dosage and removal efficiency (R%) also increase for all pH values, with the efficiencies following the order: R% (pH = 7) > R% (pH = 4) > R% (pH = 9).
- Effective removal of higher pollutant concentrations require a higher coagulant dosage.

Discussion of results

The reaction mechanisms of diclofenac (a non-steroidal anti-inflammatory drug, NSAID) with the coagulant aluminum sulfate ($Al_2(SO_4)_3$) in water can vary depending on the pH of the system.

pH-dependent hydrolysis reactions of aluminum sulfate

Aluminum sulfate is commonly used in water treatment for coagulation, and its behavior is strongly pH-dependent. Numerous studies by scientists (Stumm and Morgan, 1996; Zhao et al., 2009; Duan et Gregory, 2003; Mensah-Akkuteh et al., 2022) have concentrated on the hydrolysis of aluminium salts and the by-products of that hydrolysis. According to several studies, pH is one of the most crucial variables influencing the aluminium species found in the aqueous solution (Bacha and Achour, 2015; Khelili and Achour, 2015).

Depending on the pH, aluminium sulphate added to water may generate the following monomers: Al^{3+}, $Al(OH)^{2+}$, $Al(OH)_2^{+}$, $Al(OH)_3$, and $Al(OH)_4^{-}$. Additionally, a variety of polymers is produced using the generic formula: $Me_n(OH)_y^{3n-y}$ (Dentel et Gosset, 1988; Van Benschoten et Edzwald, 1990).

Table 3 is based on the previously mentioned studies. The following table provides a summary of the hydrolysis reactions of aluminium sulphate ($Al_2(SO_4)_3$) in water, highlighting the relevant pH range, reactions, and approximate pKa values for each phase of the hydrolysis process.

At low pH (<4), aluminum predominantly exists as Al^{3+}. At high pH (>8), it shifts to the aluminate ion $[Al(OH)4]^-$, reducing coagulation efficiency. Precipitation of $Al(OH)_3$ (aluminum hydroxide) occurs near its minimum solubility at pH 5.5–7.5, making this range the most effective for coagulation and adsorption processes.

pKa values are approximate because they depend on the ionic strength and temperature of the solution. The **pKa values** presented in the table are widely reported in scientific literature and derived from experimental studies and thermodynamic data on the hydrolysis of aluminum in water (Baes and Mesmer, 1976; Brown and Ekberg, 2016).

Table 3: Hydrolysis Reactions of Aluminum Sulfate with Associated pH and pKa Values

Reaction	pH range	pKa (Baes and Mesmer, 1976)	Description
$Al^{3+} + H_20 \leftrightarrow Al(OH)^{2+} + H^+$	3-5	4.98	Initial hydrolysis of aluminum ion to monohydroxy complex.
$Al^{3+} + 2H_20 \leftrightarrow Al(OH)_2^+ + H^+$	4-6	10.63	Formation of dihydroxy aluminum species.
$Al^{3+} + 3H_20 \leftrightarrow Al(OH)_{3(S)} + H^+$	5-8	15.66	Precipitation of aluminum hydroxide.
$Al^{3+} + 4H_20 \leftrightarrow Al(OH)_4^- + H^+$	> 8	22.91	Dissolution of $Al(OH)_3$ to form soluble aluminate ions.

Reaction mechanisms by pH

The reaction mechanisms of diclofenac (a non-steroidal anti-inflammatory drug, NSAID) with the coagulant aluminum sulfate ($Al_2(SO_4)_3$) in water can vary depending on the pH of the system.

Below is an outline of potential mechanisms at different pH levels:

Low acidic pH < 5

Regardless of the initial Diclofenac concentration and coagulant dosage, the elimination efficiencies appear to be minimally impacted at pH 4, and the efficiencies do not surpass 60.74% for higher Diclofenac concentrations. Specifically, a higher initial Diclofenac content results in a higher percentage of elimination (Fig. 3a) but also a higher demand for coagulant.

Aluminum speciation: Al^{3+} is the dominant species in solution.

At acidic pH, aluminum sulfate dissolves to produce aluminum ions (Al^{3+}) and sulfate ions: $Al_2(SO_4)_3 \leftrightarrow 2Al^{3+} + 3SO_4^{2-}$

Diclofenac speciation: Diclofenac (a weak acid) remains largely protonated as neutral molecules under acidic conditions. It exists in its protonated form H-diclofenac or Na-diclofenac, with its carboxylic acid group remaining neutral.

Reaction mechanisms: Protonated diclofenac may interact weakly with Al^{3+} through hydrogen bonding or electrostatic interactions, but these are not significant mechanisms for removal since diclofenac's hydrophobicity dominates at low pH.

Complexation involves the formation of coordination bonds between aluminum species and diclofenac, primarily through the carboxylic acid and aromatic amine groups in diclofenac. At low pH, complexation is less pronounced because the carboxylic acid group on diclofenac is not deprotonated, reducing its ability to coordinate with Al^{3+}.

Any complexation would involve weak interactions between the aromatic nitrogen or oxygen atoms in diclofenac and Al^{3+}.

Ligand exchange involves replacing water or hydroxide ligands in aluminum complexes with diclofenac. Aluminum exists as highly hydrated $[Al(H_2O)_6]^{3+}$ complexes.

Diclofenac (in its neutral form) may weakly replace water molecules through ligand exchange, but this is limited because diclofenac is less nucleophilic in its protonated state.

Near neutral pH (5< pH<8)

The efficiency curves (Fig.3b) demonstrate that higher coagulant demand and improved yield are the outcomes of increasing the Diclofenac concentration. Furthermore, there is always an optimal dosage of aluminium sulphate for all Diclofenac concentrations, beyond which the elimination efficiency stabilises. In general., pH 7 exhibits better Diclofenac elimination efficiency than pH 4.

Reaction mechanisms between diclofenac and aluminum sulfate (or its hydrolysis products) are key additional considerations, especially because diclofenac has functional groups capable of interacting with aluminum. These mechanisms are influenced by pH, as the speciation of both aluminum and diclofenac changes.

Aluminum speciation: At near-neutral pH, aluminum sulfate hydrolyzes to form various aluminum hydroxide species, including: $Al(OH)^{2+}$, $Al(OH)_2^{+}$, $Al(OH)_3$.

Diclofenac speciation: In this pH range, diclofenac mostly exists as its anionic form ($diclofenac^-$) due to deprotonation of its carboxylic acid group (pKa ~4.2).

Reaction mechanisms: The negatively charged $diclofenac^-$ can bind to positively charged aluminum hydrolysis products (e.g., $Al(OH)^{2+}$, $Al(OH)_2^{+}$) through electrostatic interactions.

Adsorption of $diclofenac^-$ onto the precipitated aluminum hydroxide, $Al(OH)_3$, is a primary removal mechanism. The high surface area and charge properties of $Al(OH)_3$ facilitate this process (Alexander et al., 2012).

The deprotonated carboxylate group on diclofenac strongly interacts with aluminum species. Complexation occurs between $diclofenac^-$ and soluble partially hydrolyzed species (e.g., $Al(OH)^{2+}$, $Al(OH)_2^{+}$)).

The aromatic rings and amine groups may also contribute to additional coordination (Koslowska et al., 2017).

Moreover, hydrolyzed species like $Al(OH)^{2+}$ and $Al(OH)_2^{+}$ readily undergo ligand exchange. $Diclofenac^-$ can replace hydroxide or water ligands in these species. This contributes to adsorption onto aluminum hydroxide precipitates and enhances removal from solution.

Alkaline pH (>8):

The pH 9 yields curves demonstrate that raising the DFC concentration leads to higher coagulant demand and improved yield, much like at pH 4 and pH 7. Diclofenac is slightly removed at pH = 9, according to the results provided in (Fig.3c). Even though the coagulant dose is greater than what is needed at pH = 4, the optimal yield ranges from 6.89 to 31.49%.

Aluminum speciation: At alkaline pH, aluminum hydroxide precipitates dissolve to form soluble aluminate ions: $[Al(OH)_4]^-$

Diclofenac speciation: Diclofenac remains in its anionic form ($diclofenac^-$).

Reaction mechanisms: Precipitation and adsorption mechanisms are less effective at higher pH values. At high pH, electrostatic repulsion occurs between $diclofenac^-$ and negatively charged aluminate ions $[Al(OH)4]^-$, reducing the effectiveness of diclofenac removal. Complexation is inhibited at high pH due to the negative charge on both $diclofenac^-$ and the aluminate ions.

Ligand exchange is limited because aluminum exists as the aluminate ion ($[Al(OH)4]^-$, which is highly stable and does not easily exchange ligands (Rezeg and Achour, 2017).

Summary of results by pH

For each pH under study, Table 4 summarises the outcomes of varying the initial diclofenac concentration and the coagulant dosage.

Table 4: Behavior of the coagulation process for Diclofenac removal

pH=4	pH=7	pH=9
Removal efficiency is minimally affected and does not exceed 60.74% for high DFC concentrations.	The DFC elimination efficiencies are higher in pH7 than in pH4. For high Diclofenac concentration, it reached 64.44% by applying an aluminium sulphate dose of 150 mg/L.	DFC is weakly eliminated at pH = 9. The optimum yield varies between 6.89 and 31.49% although the coagulant dose is higher than that required at pH = 4.
Higher initial concentrations lead to increased removal efficiency but require higher coagulant dosages.	Higher initial concentrations lead to increased removal efficiency but require higher coagulant dosages.	Higher initial concentrations lead to increased removal efficiency but require higher coagulant dosages.
There is an optimal dosage for all DFC levels, beyond which removal efficiency stabilizes.	There is an optimal dosage for all DFC levels, beyond which removal efficiency stabilizes.	There is an optimal dosage for all DFC levels, beyond which removal efficiency stabilizes.

Depending on the pH range, Table 5 summarises the mechanisms that are expected to take place during the reaction between diclofenac and aluminium sulphate.

Table 5: Summary of Reaction mechanism hypothesis between aluminium sulphate and DFC

pH Range	Complexation	Ligand Exchange
<5	ak complexation with Al^{3+}; limited by protonation of diclofenac.	inimal; FC remains mostly neutral.
5<pH<8	Strong complexation with hydrolyzed aluminum species (e.g., Al $(OH)^{2+}$).	Significant; DFC replaces hydroxide/water.
pH >8	Negligible due to repulsion between diclofenac$^-$ and $[Al(OH)4]^-$	Minimal; stable aluminate ions dominate.

ALUMINIUM SULPHATE AND DICLOFENAC'S STOICHIOMETRIC RELATIONSHIP IN DISTILLED WATER AT DIFFERENT PH VALUES.

The results of the coagulation-flocculation of DFC throughout our studies demonstrated that, in every case, the organic compound's elimination efficiencies increased simultaneously with the compound's initially concentrations. As a result, we can presume that the reaction between aluminium sulphate and DFC may be stoichiometric. We utilised the findings in Fig. 3 to demonstrate a stoichiometric relationship between the optimal amount of aluminium sulphate and the initial level of DFC.

Diclofenac removal efficiencies and optimum coagulant doses

Table 6 summarizes the results concerning the efficiencies (R%) and the optimum doses for each pH and each initial concentration C_0 of DFC. Each concentration tested has an optimal coagulant dosage where effectiveness reaches its maximum.

Table 6: Optimum yields and doses of aluminum sulfate during diclofenac flocculation trials in distilled water.

C_0 (mg/l)	pH=4		pH=7		pH=9	
	Optimum coagulant dosage(mg/l)	Ropt%	Optimum coagulant dosage (mg/l)	Ropt%	Optimum coagulant dosage(mg/l)	Ropt%
2	10	22.22	30	26.19	20	6.89
5	30	28.89	50	30.48	30	8.97
8	50	31.94	70	35.71	50	10.78
10	60	34.44	90	38.57	60	16.21
15	90	60.74	150	64.44	100	31.49

At the optimum, these results highlight that the yields and the coagulant demand increase with the increase in the concentrations of the organic compound. Furthermore, the pH determines the optimal dosage, with pH = 4 < pH = 9 < pH = 7. This indicates that the reaction mechanisms vary and become complex dependent on the medium's pH.

This data set offers insightful information about how to best optimise coagulation procedures in a range of operational conditions. It becomes clear that coagulant dosage and removal effectiveness are significantly influenced by pH and (C_0).

Diclofenac concentration and coagulant dosage at varying pH values: a stoichiometric relationship

Linear stoichiometric relationships can be obtained by using the linear least squares method by adjusting each pair of values of the two parameters (the initial concentration of DFC and the optimal dose of aluminium sulphate).

The "optimal dose of coagulant versus initial concentration of diclofenac" relationship has a high correlation coefficient (r^2).

These are the stoichiometric relationships between the initial concentration of DFC and the optimal dosage of aluminium sulphate for each pH. These correlations only hold valid when diclofenac is dissolved in distilled water.

The stoichiometric relationships between the optimal dose of aluminum sulfate and the initial concentration of DFC are as follows:

Y = Optimal coagulant dosage (mg/L)

X= Initial concentration of DFC (mg/L)

For pH = 4, Y = 6 X with r^2 = 0.997

For pH = 7, Y = 10 X with r^2 = 0.991

For pH = 9, Y = 6 X with r^2 = 0.977

The resulting regression lines' slope indicated that 6 mg of Al/DFC was needed to treat 1 milligramme of DFC at pH = 4 and 9 and 10 mg of Al/mg DFC at pH = 7.

Black et al. first reported coagulation reactions in 1963. These reactions were based on the stoichiometry between the coagulant and organic materials, such as humic compounds. The ratio of the concentration of NOM or DOC to the Al dosage needed for coagulation depends on pH. The organic compound's negative charge generates a coagulant demand. Higher coagulant dosage is required for the dissolved organic fraction than that for the insoluble organic fraction.

O'Melia et al., (1999), suggested that the stoichiometry depends on the types of organic substances to be treated, coagulant types and solution conditions.

Furthermore, alum coagulation at low pH can be accomplished with lesser dosages than at higher pH, while coagulation at pH above 7 is challenging and expensive, particularly when the water temperature is greater.

The increased concentration of $AI(OH)^{+2}$ and Al^{+3} in cold water coagulation at pH 5.5 reduces the dosage for charge neutralisation; however, coagulation at this low pH may result in issues with residual Al and particle stability, leading to inadequate clarity and filtration (Edzwald et Tobiason, 1999).

For DFC, their physicochemical characteristics also have a significant impact on coagulation. Thus, hydrophobicity, molecular size or weight (MW), and functional groups -which provide the negative charge that boosts the reactivity with aluminium-are crucial.

CONCLUSION

This study explored the effectiveness of coagulation-flocculation using aluminum sulfate to remove diclofenac, a common non-steroidal anti-inflammatory drug (NSAID), from distilled water. The experimental parameters included varying diclofenac concentrations, coagulant dosages, and pH levels (4, 7, and 9). Results demonstrated that the efficiency of diclofenac removal is strongly influenced by pH and the dosage of the coagulant.

At near-neutral pH (pH 7), the highest removal efficiency of 64.44% was achieved for a diclofenac concentration of 15 mg/L using an aluminum sulfate dosage of 150 mg/L. This efficiency was attributed to favorable reaction mechanisms, including strong complexation and effective ligand exchange between aluminum hydroxide species and the deprotonated form of diclofenac. In contrast, at acidic (pH 4) and alkaline (pH 9) conditions, removal efficiencies were lower, reaching 60.74% and 31.49%, respectively. These variations are explained by differences in aluminum speciation and diclofenac interactions.

The study also revealed a stoichiometric relationship between the initial diclofenac concentration and the optimal coagulant dosage, with 6 mg of aluminum sulfate required per mg of diclofenac at pH 4 and 9, and 10 mg of aluminum sulfate per mg of diclofenac at pH 7. This finding underscores the need for careful optimization of coagulant dosage based on pH conditions to achieve effective diclofenac removal.

These findings highlight the critical role of pH in optimizing coagulation processes and provide valuable insights for enhancing water treatment methods to address the growing concern of pharmaceutical contamination. Future research could investigate the application of these findings to real wastewater samples containing complex mixtures of contaminants and explore the combined use of coagulation-flocculation with other treatment technologies for improved removal efficiency.

REFERENCES

ACHOUR S., GUESBAYA N. (2005). Coagulation-flocculation by aluminum sulphate of organic phenolic compounds and humic substances, Larhyss Journal., No 4, pp.153- 168. (In French).

ACHOUR S., MODJAD H., HELLAL A., KHELILI H. (2019). Tests to optimize clarification and disinfection processes for dam water in the Khenchela region (eastern Algeria), Larhyss Journal, No 37, pp. 151-174. (In French)

AFOUFOU F., ACHOUR S. (2017). Elimination of aniline by aluminum sulfate and effect of mineral salts, Larhyss Journal, No 32, pp. 285-299.

ALEXANDER J.T., HAI F.I., AL-ABOUD T.M. (2012). Chemical coagulation-based processes for trace organic contaminant removal: Current state and future potential, Environmental Management, pp. 195-207.

ANSES (2019). (Environmental and Occupational Health Safety on the assessment of health risks Opinion of the French National Agency for Food, Environmental and Occupational Health Safety on the assessment of health risks linked to the presence of diclofenac in water intended for human consumption, Maisons-Alfort, France. (In French).

BACHA N., ACHOUR S. (2013). Influence of reactional parameters on aluminum sulfate/pyromellitic acid stoechiometry in distilled water, Larhyss Journal., No 13, pp.2521-9782 (In French).

BACHA N., ACHOUR S. (2015). Influence of reaction parameters on the stoichiometry of aluminum sulphate/natural organic matter in distilled water, Larhyss Journal., No 21, pp. 141-148. (In French)

BACHA N., ACHOUR S. (2023). Polymeric humic material removal by coagulation-flocculation, Stoichiometric dosage aluminum sulphate/humic acid in saline aqueous media, Larhyss Journal., No 53, pp. 199-217.

BAES C.F., MESMER R.E. (1976). The Hydrolysis of Cations, Book, Edited by Wiley-Interscience, New York, USA.

BLACK A.P., SINGLEY J.E., WHITTLE G.P., MOULDING J.S. (1963). Stoichiometry of the coagulation of color-causing organic compounds with ferric sulphate, Journal American Water Works Association (JAWWA), Vol. 55, No 10, pp. 1347-1366.

BOCALY M. (2010). Impacts of pharmaceutical substances on water and aquatic environments, documentary synthesis, National Office for Water and Aquatic Environments (ONEMA), International Office for Water (OIEAU), France. (In French).

BROWN P.L., EKBERG C. (2016). Hydrolysis of metal ions, Book, Edited by Wiley, Weinheim, Germany.

BRUNE K., PATRIGNANI P. (2015) New insights into the use of currently available non-steroidal anti-inflammatory drugs, Journal of Pain Research, pp. 105-118.

BUKHTAWAR F., USMAN M., HAQ A.U., SAEED M., SALEEM A. (2024). Optimization of multi-stage micellar-enhanced flocculation process for removal of Levofloxacin hemihydrate in wastewater, Journal of Water Process Engineering, Vol. 59, Paper ID 104971.

DENTEL S.K., GOSSETT J.M. (1988). Mechanisms of Coagulation with Aluminum Salts, Journal American Water Works Association (JAWWA), Vol. 80, No 4, pp. 187-198.

DUAN J., GREGORY J. (2003). Coagulation by hydrolysing metal salts, Advances in Colloid & Interface Science, Vols. 100-102, pp. 475- 502.

EDZWALD J.K., TOBIASON J.E. (1999). Enhanced coagulation: US requirements and a broader view, Water Science and Technology, Vol. 40, Issue 9, pp. 63-70.

GRACIA-LOR E., SANCHO J.V., HERNÁNDEZ F. (2010). Simultaneous determination of acidic, neutral and basic pharmaceuticals in urban wastewater by ultra high-pressure liquid chromatography-tandem mass spectrometry, Journal of Chromatography A, Vol. 1217, No 5, pp. 622–632.

GUZEL E.Y., CEVIK F., DAGLIOGLU N. (2018): Determination of pharmaceutical active compounds in Ceyhan River, Turkey: Seasonal., spatial variations and environmental risk assessment, Human and Ecological Risk Assessment: An International Journal., Vol. 25, No 8, pp. 1-16.

HANDAYANI T., EMRIADI E., DESWATI D., RAMADHANI P., ZEIN, R. (2023). Effective Removal of Indigo Carmine in Aqueous Solutions using a Low-Cost Adsorbent Developed from Corn Husk Waste: Synthesis, Batch, and Optimization Studies, Pollution, Vol. 9, No 4, pp. 1396-1413.

HARRAT N., ACHOUR S. (2016), Behavior of humic substances in the water of the Zit El Amba dam during coagulation-flocculation in the presence of aluminum sulfate and activated carbon, Larhyss Journal, No 26, pp. 149-165. (In French)

HEJNA M., KAPUSCI NSKA D., AKSMANN A. (2022). Pharmaceuticals in the Aquatic Environment: A Review on Eco-Toxicology and the Remediation Potential of Algae, International Journal of Environmental Research and Public Health, Vol. 19, Paper ID 7717.

HERNÁNDEZ-TENORIO R., GONZÁLEZ-JUÁREZ E., GUZMÁN-MAR J.L., HINOJOSA-REYES L., HERNÁNDEZ-RAMÍREZ A. (2022). Review of occurrence of pharmaceuticals worldwide for estimating concentration ranges in aquatic environments at the end of the last decade, Journal of Hazardous Materials Advances, Vol. 8, Paper ID 100172.

KOZLOWSKA M., RODZIEWICZ P., KACZMAREK-KEDZIERA A. (2017). Structural stability of diclofenac vs. inhibition activity from *ab initio* molecular dynamics simulations, Comparative study with ibuprofen and ketoprofen, Structural Chemistry, Vol. 28, pp. 999–1008.

KHELILI H., ACHOUR S. (2015). Influence of reaction parameters on the stoichiometry of aluminum sulfate/natural organic matter in distilled water, Larhyss Journal, No 23, pp. 287-304.

KÜMMERER K. (2009). The presence of pharmaceuticals in the environment due to human use – present knowledge and future challenges, Journal of Environmental Management, Vol. 90, Issue 8, pp. 2354-2366.

LAKSHMI D.S., GEETHA V.B., MURALI V. (2024). From prescription to pollution: The ecological consequences of NSAIDs in aquatic ecosystems, Toxicology Report, Vol. 13, Paper ID 101775.

MADIKIZELA L.M., CHIMUKA L. (2017). Occurrence of naproxen, ibuprofen, and diclofenac residues in wastewater and river water of KwaZulu-Natal Province in South Africa, Environmental Monitoring and Assessment, Vol. 189, Paper ID 348.

MATILAINEN A., VEPSÄLÄINEN M., SILLANPÄÄ M. (2010). Natural organic matter removal by coagulation during drinking water treatment: A review, Advances in Colloid and Interface Science, Vol. 159, pp. 189-197.

MENSAH-AKUTTEH H., BUAMAH R., WIAFE S. (2022). Optimizing coagulation–flocculation processes with aluminium coagulation using response surface methods, Applied Water Science, Vol. 12, Paper ID 188.

NACERADSKA J., PIVOKONSKA L., PIVOKONSKY M. (2019). On the importance of pH value in coagulation, Journal of Water Supply: Research and Technology-AQUA, Vol. 68, No 3, pp. 222-231.

NISHI I., KAWAKAMI T., ONODERA S. (2015) Monitoring the concentrations of nonsteroidal antiinflammatory drugs and cyclooxygenase-inhibiting activities in the surface waters of the Tone Canal and Edo River Basin, Journal of environmental science and health, Part A, Toxic/hazardous substances & environmental engineering, Vol. 50, No 11, pp. 1108–1115.

O'MELIA C.R., BECKER W.C., AU K.K., (1999). Removal of humic substances by coagulation, Water Science and Technology, Vol. 40, pp. 47– 54.

ORTÚZAR M., ESTERHUIZEN M., OLICÓN-HERNÁNDEZ D.R., GONZÁLEZ-LÓPEZ J., ARANDA E. (2022). Pharmaceutical Pollution in Aquatic Environments: A Concise Review of Environmental Impacts and Bioremediation Systems, Frontiers In Microbiology, Vol. 13, Paper ID 869332.

REZEG A., ACHOUR S. (2005). Elimination of aromatic organic acids by coagulation-flocculation with aluminum sulfate, Larhyss Journal, No 4, pp. 141-152. (In French)

REZEG A., ACHOUR S. (2017). Elimination of humic acid by the combination of aluminum sulfate/activated bentonite, Larhyss Journal, No 30, pp. 333-347.

ROBERTS P.H., THOMAS K.V. (2006). The occurrence of selected pharmaceuticals in wastewater effluent and surface waters of the lower Tyne catchment, Science of the Total Environment, Vol. 356, pp. 143 – 153.

RUIZ M.J., FONT G. (2011). Ecotoxicological effects of pharmaceuticals in the environment, in: Ecotoxicology around the Globe, Edited by Julia E. Visser, Nova Science Publisher, Chapter 8, pp. 227-246.

SHARIF A., ASHRAF M., ANJUM A.A. (2016). Pharmaceutical wastewater being composite mixture of environmental pollutants may be associated with mutagenicity and genotoxicity, Environmental Science Pollution Research, Vol. 23, pp. 2813–2820.

SHARMA D., CHOUDHARY P., GANDOTRA R. (2024). Assessment of diclofenac in three selected rivers of Western Himalayan Region, Ecology, Environment, & Conservation., Vol. 30, July Supplement Issue, pp. S354-S360.

SCHWAIGER J., FERLING H., MALLOW U., WINTERMAYR H., NEGELE R.D. (2004). Toxic effects of the non-steroidal anti-inflammatory drug diclofenac. Part I: histopathological alterations and bioaccumulation in rainbow trout, Aquatic toxicology, Vol. 68, No 2, pp. 141–150.

STUMM W., MORGAN J.J. (1996). Aquatic Chemistry: Chemical Equilibria and Rates in Natural Waters, Book, 3rd Edition**,** *Wiley-Interscience, New York, USA.*

TAFT D.R. (2009). Drug Excretion, Book Chapter 9, In Pharmacology, Edited by Hacker, Messer and Bachmann, Ohio, USA, pp.175–199.

THE MERCK INDEX. (2006). The Merck Index: An Encyclopedia of Chemicals, Drugs, and Biologicals, Edited by O'NEIL M.J., 14th Edition, Whitehouse Station, New Jersey: Merck, USA.

THOMAS K.V., LANGFORD K. (2007). Occurrence of pharmaceuticals in the aqueous environment, in: Comprehensive Analytical Chemistry, Edited by M. Petrović, D. Barceló, Elsevier, Vol. 50, pp.337-359.

VAN BENSCHOTEN S.E., EDZWALD S.K. (1990). Chemical aspects of coagulation using alurninurn salts-1, Hydrolytic reactions of alum and polyaluminum chloride, Water Research, Vol. 24, No 12, pp. 1519-1526.

VIENO N., TUHKANEN T., KRONBERG L. (2006). Removal of pharmaceuticals in drinking water treatment/Effect of chemical coagulation, Environmental Technology, Vol. 27, No 2, pp.183-192.

WHO (World Health Organization) (2012). Pharmaceuticals in drinking water, Editions World Health Organization, Geneva, Switzerland.

ZHAO H., LIU H., QU J. (2009). Effect of pH on the aluminum salts hydrolysis during coagulation process: Formation and decomposition of polymeric aluminum species, Journal of Colloid and Interface Science, Vol. 330, No 1, pp.105–112.