Efficiency of Membrane Technology Activated Charcoal and a Clay Micelle Complex for the Removal of Ibuprofen and Mefenamic Acid.

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Abstract:
Kinetic studies on the stability of two non-steroids anti-inflammatory drugs (NSAIDs), ibuprofen and mefenamic acid, in pure water and activated sludge indicated that both pharmaceuticals were resistant to degradation for one month. The efficiency of sequential advanced membrane technology wastewater treatment plant towards removal of both drugs from wastewater was investigated. The sequential system included activated sludge, ultrafiltration (hollow fiber membranes with 100 kDa cutoff, and spiral wound membranes with 20 kDa cutoff), activated carbon column and reverse osmosis (RO). The overall performance of the integrated plant demonstrated complete removal of ibuprofen and mefenamic acid from spiked wastewater samples. Activated carbon column was the most effective component in removing these NSAIDs with a removal efficiency of 98.8% for both ibuprofen and mefenamic acid. Batch adsorption of both NSAIDs by activated charcoal and a composite micelle (octadecyltrimethylammonium (ODTMA)–clay (montmorillonite) was determined at 25 ˚C. The results revealed that both adsorptions fit Langmuir isotherm with Q_{max} of 66.7 mg/g and 62.5 mg/g for ibuprofen using activated carbon and clay-micelle complex, respectively, and with Q_{max} of 90.9 mg/g and 100.0 mg/g for mefenamic acid using activated charcoal and clay-micelle complex, respectively. These results suggest that an integration of ODTMA-clay-micelle complex column in wastewater treatment plant is highly promising and can lead to an improvement of the removal efficiency of these drugs from wastewater.

Keywords: *Ibuprofen; Mefenamic acid; Wastewater treatment; Stability in sludge; HF-membranes; Activated carbon; Micelle–clay complex.*

List of Abbreviations

PNA	Palestinian National Authority
PWA	Palestinian Water Authority
WHO	World Health Organization
NSAIDs	Non-steroidal anti-inflammatory drugs
BOD	Biological Oxygen Demand
CMC	Critical Micelle Concentration
COD	Chemical Oxygen Demand
Da (g mol^{-1})	Dalton
HF	Hollow Fiber
HPLC	High Pressure Liquid Chromatography
Ko/w	Octanol-water Partition coefficient
KD	Kilo Dalton
KP	Kilopascal
M F	Microfiltration
MWCO	Molecular weight Cutoff
NF	Nanofiltration
O DTMA	Octadecyltrimethylammonium
OTC	Over the counter
OWCs	Organic Wastewater Contaminants
PCPs	Personal Care Products
PPCPs	Pharmaceuticals and Personal Care Products
ppm	Part per million
RO	Reverse Osmosis
SPE	Solid Phase Extraction
SPME	Solid Phase Micro-extraction
STP	Sewage Treatment Plants
SW	Spiral Wound
TDS	Total Dissolved Solids
TSS	Total Suspended Solids
TOC	Total organic carbon
TOD	Total Oxygen Demand
UF	Ultrafiltartion
UV	Ultra Violet
UV/TiO_2	Ultra Violet/Titanium dioxide
WWTPs	Waste Water Treatment Plants
LPMS	Low-Pressure driven membranes

1. Introduction

The consumption of water over the world is increasing, and the demand on water resources for household, commercial, industrial, and agricultural purposes are in rise as well. This soaring in demand is due to a rapidly expanding population, industrial expansion, and the need to expand irrigated agriculture. However, this expanding in population is offset by a decrease in fresh water resources and low water availability [1].

In the Middle East, in general, and in Palestine in particular, water resources are very limited[2-4].This situation will be aggravated in the future, since the water balance gap between the available water supplies and water demands, as a result of population growth, rapid urbanization and industrial associated with living standards improvement, will increase. This gap along with a contamination of ground water and surface water by industrial effluents, and agricultural chemicals, will cause serious shortage of fresh water and high production of wastewater [1, 4-7].

The water consumption in Palestine which is considered as a semi-arid country is divided among three principle sectors: (1) agricultural sector consumes around 70%, and represents the largest consumer of water in Palestine, (2) domestic sector which consumes about 27% of the water consumption, and finally (3) industrial sector which consumes only 3% of the total water use (Figure 1, appendix A) [5].

The ground water is the main source of fresh water in Palestine, the aquifer system comes from three main ground water drainage basins, the first in the western, the second in the northeastern, and the third in the eastern part of the West Bank (Palestine).The sources of fresh water in Palestine suffer from Israeli confiscation and control [8].

The surface water is considered to be very important to the Palestinians due to complete Israeli confiscation of the Jordan River basin, which is the only source of surface water in

Palestine [2]. This situation requires preserving all water supplies that currently exist, and control water usage and use it efficiently, minimize water pollution and water contamination by reducing wastewater flows, and finding solutions for disposal, treatment and recycling of wastewater.

Reducing wastewater flows which is the major source of pollution of fresh water will contribute in increasing adverse effects, because untreated or partially treated wastewater causes health and environmental hazard [9-10].Therefore, the Palestinian National Authority (PNA) and the Palestinian Water Authority (PWA) have put the reuse of wastewater as a major priority in their agenda [5].

1.1 Wastewater management in Palestine

The major sources of wastewater pollution can be classified as municipal, industrial and agricultural. Municipal water pollution consists of wastewater from homes and commercial establishments. The main goal of treating wastewater is to reduce its adverse content of suspended solids, oxygen-demanding materials, dissolved inorganic compounds and harmful bacteria [11]. In Palestine during the occupation period, wastewater sector was much neglected; as a result the status of wastewater sector is characterized by poor sanitation, insufficient treatment, and unsafe disposal of untreated or partially treated wastewater into the environment. Approximately 60% of the houses in urban communities are connected to sewage systems, some large towns and cities have no sewage system at all, and wastewater is discharged into septic tanks and/or emptied into valleys (wades), therefore the situation of sewage system is extremely critical [12]. In the villages no sewage networks exist, and wastewater is collected in cesspits or septic tanks, most of Israeli settlements in the West Bank discharge the wastewater in wades without any treatment and only 1% of the collected wastewater are properly treated [13].

The existing urban sewage collection and treatment facilities are constrained by limited capacity, poor maintenance, process malfunction and lack of experienced or a poor trained staff [14-15]. Generally water reuse application can serve many purposes, such as landscape irrigation which is considered as the largest field in using reclaimed wastewater [1, 16-17].Therefore, in order to achieve a sustainable and effective application of water reuse, the treatment system process must be able to isolate industrial toxins, pathogens carbon, and nutrient to prevent public health hazards that might be caused by wastewater reuse [18].

The treated or partially treated wastewater that is discharged in many areas in the West Bank is presently used for irrigation purposes, however, this use still in small-scale projects due to the lack of experience that is required for safe usage [18]. The reuse of treated wastewater must be combined with strategies, to prevent health and environment risks from pathogens, heavy metals, pesticides, and pharmaceuticals. Therefore, the Palestinian National Authority (PNA) has commenced acting aggressively in the field of water and wastewater management in terms of legislation, policies, and strategies, design and implementation of projects, as well as approving environmental laws that regulate the wastewater usage. Furthermore, the Palestinian Water Authority (PWA) has established guidelines extracted from rules issued by the World Health Organization (WHO) to ensure protection of the public health and environment from discharge of untreated or inadequately treated wastewater effluents [19-21].

The efficient sewage treatment systems are urgently needed in Palestine, because appropriate and sustainable sewage treatment technologies will help to preserve biodiversity and maintain healthy ecosystems [5]. Various methods for wastewater treatment have been used in some of the Mediterranean countries, many are conventional such as activated sludge and biofilters and others slightly less conventional, such as oxidation ditches, aerated lagoons and natural treatment system such as waste stabilization ponds [6]. In Palestine, two types of treatment plant systems: conventional and less conventional are used; stabilization ponds for small communities, tickling filter, oxidation ditches, and activated sludge for large scale community. Table S1 (Supplementary data) lists the current status of existing and planned wastewater treatment in the West Bank [5].

The main goal of this research study was to investigate the performance of advanced treatment technologies which include integration of activated sludge process with ultra-filtration membranes (hollow fiber and spiral wound membranes), activated carbon adsorbent, micelle-clay filters, and reverse osmosis for the removal of some non-steroidal anti-inflammatory drugs, such as ibuprofen and mefenamic acid.

In this study the efficiency of the integrated membranes assembled in the wastewater treatment plant at Al-Quds University was tested for removing representative examples of non-steroidal anti-inflammatory drugs (NSAIDs) [22] namely ibuprofen (structure 1 in Figure 2, appendix A) and mefenamic acid (structure 2 in Figure 2, appendix A) from wastewater. A clay micelles-complex, octadecyltrimethylammonium (ODTMA, structure 3 in Figure 2, appendix A) and activated charcoal membranes were also included in the membranes plant system.

It should be indicated that ibuprofen and mefenamic acid are extensively used as non-prescription drugs, with an annual consumption of several hundreds of tones in developed countries, as they are widely used for painful and inflammatory conditions [22].

1.2 Wastewater

Wastewater contains the following broad grouping of constituents: 1) organic matter such as feces, hair, food, vomit, paper fibers, plant material, urea, 2) nutrients (nitrogen, phosphorus potassium), 3) inorganic matter (dissolved mineral), 4) toxic chemicals such as pharmaceuticals and drugs and 5) pathogens. This composition in fact may differ from community to community, it depends on the source. For example the composition of wastewater coming from residential communities is not the same as in areas having industrial units, the time also play a vital role in wastewater composition, because the largest amount of water entering municipal wastewater system during the diurnal interval and holidays, other factors such as the size of community may also affect the wastewater composition [23-24].

1.2.1 Definition and Characteristics of Wastewater

In general wastewater can be defined as any water that has been used, and affected in quality by anthropocentric influence [25]. The more specific definition of wastewater is a combination of water carried wastes removed from residence, institution, commercial, industrial establishments, and ground water [23].Wastewater is about 99% water by weight referred as influent, and the remaining one percent includes suspending and dissolved organic substances, as well as microorganisms [25, 26], but this ratio may varies according to the activity that wastewater resulted from, but the constituents ratio is not less than 95% water, as water is often added during the flushing to carry the waste down a drain [23]. The wastewater sources can be domestic wastewater or "sewage" and this type resulted from homes, commercial places, and farms [27]. Domestic wastewater can be divided into two elements, black water which originates from toilets and kitchens and is highly contaminated and grey water which originates from baths, showers, wash basins and washing machine and is generally less contaminated. Grey water makes up to 40% - 60% of the total domestic wastewater volume [28]. Industrial/commercial wastewater is flow generated and discharged from manufacturing and commercial activities, a combination of domestic and industrial wastewater constituents is known as municipal wastewater [29]. The principal elements for which wastewater is prescribed are the physical, chemical, and biological elements, the physical parameters include total solid contents which consist of total suspended solid (TSS) and total dissolved solids (TDS), particle size distribution, turbidity, temperature, conductivity, transmittance, density, color and odor. The chemical parameters include biochemical oxygen demand (BOD), chemical oxygen demand (COD) and all of these parameters are considered organic chemical parameters, and other parameters like hardness, pH, salinity, ionized ions and metals are considered inorganic chemical parameters as well as the biological parameters such as coliform, fecal coliforms, viruses, and pathogens [29-31].

1.2.2 Wastewater treatment process

Treatment facilities incorporate numerous processes, which in combination achieve the desired water quality objectives. These processes involve the separation, removal and disposal of pollutants present in wastewater. The treatment of wastewater is accomplished by four basic methods or techniques; physical, mechanical, biological and chemical. The physical method of treatment is unit operations used in wastewater treatment which include; flow-metering, screening, mixing, sedimentation, accelerating gravity settling, floatation, filtration gas transfer and volatilization. Mechanical treatment methods involve the use of machines and chemical treatment methods include many processes such as chemical precipitation, adsorption, disinfection and dechlorination [11, 29]. Water treatment usually consists of four stages: preliminary, primary, secondary, and tertiary. But the primary and secondary stages are considered the major steps, and the tertiary stage is required to achieve complete removal for pollutants which have not been removed by secondary treatment [26].

1.2.2.1 Preliminary treatment

The influent that flows to treatment plant contains pieces and wood, rags, plastic and other debris in addition to sand, eggshells and other coarse inorganic materials, as well as organic matter from household, industrial, commercial and institutional water use. All these components are removed through combination of screening and settling [29-30, 32].

1.2.2.2 Primary treatment

In primary treatment, the objectives such as large debris, grit and sands from wastewater by screening, settling, or floating are physically removed [26]. During primary treatment wastewater flows into and through large settling tanks or clarifiers where the flow velocity is reduced. Here initial separation occurs, with 40% to 50% of the heavier settle-able solids forming primary sludge on the bottom of the settling tanks, and lighter materials float to the tanks surface [29].

1.2.2.3 Secondary treatment

The secondary treatment is designed for removal of biodegradable dissolved and colloidal organics and suspended solids that have escaped the primary treatment by utilizing biological treatment process. In the secondary treatment unit, three types of technologies can be applied to break down organic material with agitation and aeration. There are: activated sludge process, trickling filters, and lagoon system [30, 32]. Activated sludge process removes the dissolves organic material and converts colloidal matter to a biological sludge which rapidly settles. The activated sludge process uses a variety of mechanisms to utilize dissolved oxygen to promote the growth of biological flock that substantially breaks down and removes organic material, then allows these solids flock to settle out [29, 33-34].

1.2.2.4 Tertiary treatment

Any addition processing after secondary treatment is called tertiary treatment which is physical-chemical processes applied to remove more suspended solids, organic matter, nitrogen, phosphorous, heavy metals and bacteria. These processes include, ozonation, photo-catalytic degradation of recalcitrant compounds (UV/TiO_2, and adsorption) [31, 34-36]. Tertiary treatment may also involve physical-chemical separation techniques such as carbon adsorption, flocculation/precipitation, membranes for advanced filtration, ion exchange, dechlorination and reverse osmosis [35].

1.3 Membrane filtration

Membrane filtration technology is a separation process, in which a semi-permeable membrane acts as a filter that allows water flow through, while removing suspended solids and other substances [37]. Membrane technology has been used for a tertiary wastewater treatment process after secondary biological wastewater treatment as an advanced wastewater treatment stage. Application of membrane technology to wastewater treatment has expanded due to increasingly stringent legislation and continuing advancement of membrane technology [38]. The semi-permeable membranes which act as a filter or barriers used to separate and remove constituents from wastewater ranging from large visible

particles to molecular and ionic chemical species including bacteria, viruses, and other pathogenic microorganisms [30, 39]. In membrane separation process, the feed water is separated into stream that can pass through the membrane known as permeate, and a fraction of feed that cannot pass through the membrane known as retentate or concentrate [40]. The removal of suspended or colloidal particles based on the size of membrane pores relative to that of the particulate matter, in the applications that require the removal of dissolved contaminants, the molecular weight cutoffs (MWCO) is considered the main criteria for effective separation, because it specifies the maximum molecular weight of solute to be rejected, the removal process is in the range of 100 to 500 Daltons [37], other parameters such as the kind of driving force (pressure, chemical structure and composition of membrane, geometry of construction and type of feed flow) play a vital role in the membrane filtration process [39].

1.3.1 Membrane modules

There are four main types of modules: 1) plate 2) frame, 3) tubular spiral wound, and 4) hollow fiber [41]. Hollow fiber and spiral wound modules constructions involve sealing the membrane material into an assembly; these types of modules are designed for long-term use (a number of years).These modules are used in drinking water treatment and also in wastewater treatment [30, 42]. Hollow fiber and spiral wound are made from organic material (synthetic polymers i.e. polyamide and polysulphone). Hollow fibers is narrow tube made of non-cellulosic polymer, in this type a bundles of individual fibers are sealed into a hydraulically housing as shown in Structure A (Figure 3, appendix A).The fiber usually has a small diameter, around 100 µID and ~ 200 µmod. In hollow fiber the feed flows into the module, the permeate flow into or out of the hollow fiber and is collected, while retentate exits the module for further treatment [43-44]. Spiral wound is one of the most compact and inexpensive membrane, in this type two flat sheet membranes are placed together with their active sides facing away from each other. Each flat sheet membrane has one active side through which the smaller molecules permeate through, a feed spacer which is a mesh like material is placed between the two flat sheet membranes. The two flat sheet membranes with feed spacer separating them are rolled around perforated tube which is called collection tube as shown in Structure B (Figure 3, appendix A). Membrane filtration can basically be divided into four main technologies based on the driving force used for filtration: microfiltration (MF), ultrafiltration (UF), nanofiltration (NF), and reverse osmosis (RO). Hollow fiber and spiral wound are used for microfiltration (MF), ultrafiltration and reverse osmosis (RO) as well [45].The driving force can be external pressure, electrical potential gradient, concentration gradient, or other driving forces. The most commonly used membrane system in water and wastewater treatment are pressure-driven membrane. Microfiltration (MF), ultrafiltration (UF), nanofiltration (NF), and reverse osmosis (RO) use the pressure-driven force and are classified according to their pore size. Table S2 (Supplementary Data) shows the separation characteristics for various pressures-driven membrane processes [39, 46].

1.3.2 Microfiltration (MF) and ultrafiltration (UF)

Microfiltration (MF) and ultrafiltration (UF) are filtration processes, that operate on a physical sieving separation process [47], in terms of pore size, MF has the largest pore size (0.1- 3.0 microns), but UF pore sizes range from 0.01- 0.1 microns; for that MF is typically used for turbidity reduction, removal of suspended solids, giardia and cryptosporidium. On the other hand, UF membranes which have smaller pore size are used to remove some viruses, color, odor, and some colloidal natural organic matter [48]. In addition, both processes (MF and UF) require low trans-membrane pressure (1 -30 psi) to operate (LPMS), and both are used as pretreatment to desalination technologies such as reverse osmosis (RO), nano-filtration (NF) and electro-dialysis [48].

1.3.3 Nanofiltration (NF) and Reverse osmosis (RO)

Nanofiltration is a medium to high-driven membrane filtration process (150 - 1000 Kpa), and has a pore size around 0.001 micron. Nanofiltration removes most organic molecules, nearly all viruses, most of the natural organic matter and some salts, where large ionic species, including divalent and multivalent ions, and more complex molecules are highly retained [30], while allows the diffusion of certain ionic solutes, such as sodium and chloride and monovalent ions in general. In reverse osmosis (RO) a high-driven pressure against a semi-permeable membrane is required (more than 1000 Kpa), due to the great osmotic difference between the solutions on each side of the membrane, which is greater than in the nanofiltration case. In terms of pore size RO filters have pore size around 0.0001 micron, the molecular weight cutoff (MWCO) levels is less than 100 D for RO membranes, and between 200 and 1000 D for NF membranes [49-50]. Osmosis occurs when a semi-permeable membrane separates two salts solutions of different concentrations, the water will migrate from dilute solution to a concentrated solution, and this will create what is called “osmotic pressure” (Figure 4, appendix A). In RO membranes, the force is exercised against the osmotic pressure to make the water to move from the more concentrated solution to the much diluted one, this will increase the volume of water with lower concentration of dissolved solid (Figure 4, appendix A)[30, 45].

1.4 Occurrence of Pharmaceuticals and personal care products (PPCPs) in wastewater

At present, there is an increasing concern on the presence of pharmaceuticals in the environment, the occurrence of drugs and their metabolites, and also personal care products (PPCPs) in our water became important issue, due to their potential risk to the aquatic environment. Thousands of tons of pharmaceuticals are used yearly with different purposes, such as prevention, diagnosis, care, and mitigation of diseases or to improve the state of health. The same quantity or more consumed from PPCPs which include analgesics, fragrances, sun screen shampoos and cosmetics. All these pharmaceuticals and PPCPs can end up in the aquatic environment, where the discharge of therapeutic agents from production facilities, hospitals and private household effluent, as well as improper

disposal of unused drugs pose a burden on the environment [51-53]. The fate of these pharmaceuticals and PPCPs will be in the wastewater treatment plants (WWTPs), where the conventional wastewater treatment in WWTPs are based on primary, secondary and tertiary treatment in some cases, but these conventional treatments are not specifically designed to remove pharmaceuticals [51]. Therefore, effluents from wastewater treatment plants (WWTPs) can be considered as one of the most important sources of pharmaceuticals in aquatic environment, since these compounds are not fully eliminated during the conventional treatment process, and they are only partially eliminated [54].

1.4.1 Analytical methods

A number of studies indicated the presence of pharmaceuticals and personal care products (PPCPs) traces in the aquatic environmental at different concentrations. For example, a study carried out in Australia, Brazil, Canada, Croatia, England, Germany, Greece, Italy, and USA detected more than 80 pharmaceuticals and their corresponding metabolites in the aquatic environment at concentrations in the μgL^{-1} range or lower [76]. Another study performed in Spain reported the presence of 13 pharmaceuticals and personal care products (PPCPs) in municipal wastewater, eight compounds were detected in raw wastewater in the range of 0.6 – 6.6 μgL^{-1} [55]. Another reported study demonstrated that 27 of 32 pharmaceuticals and four metabolites were detected in European municipal wastewater treatment plant effluents at values of over 1 μgL^{-1} [75]. Generally, it was reported that drug residue concentrations found in receiving water fall in the low ngL^{-1} to low μgL^{-1}[61].

The presence of pharmaceuticals and personal care products (PPCPs) at trace levels (ngL^{-1}) and in complex water matrices, such as wastewater and surface water, makes their analysis difficult [56]. Currently, no standardized analytical methods are available for the analysis of pharmaceuticals and organic micropollutants in the environmental waters, because these pharmaceuticals represent structurally diverse classes of compounds, and owing to the diversity of physic-chemical properties. Hence, different analytical methods have been used for the identification and quantification of these chemicals in water samples [57]. The most common sample isolation and pre-concentration technique is solid phase extraction (SPE) [53]. SPE also is used for cleanup of pharmaceuticals in water samples [58]. Variations of SPE include solid phase micro-extraction (SPME) and various on-line and automated SPE techniques [59].

1.4.2 Method of treatment

Even that pharmaceuticals residue and their metabolites are usually detectable in the environment at trace levels, the low concentration level (ngL^{-1} - μgL^{-1}) can induce toxic effects, as in the cases of antibiotic and steroids that cause resistance in natural bacterial populations or endocrine disruption effects [60]. Pharmaceuticals are designed to interact with receptors in humans and animals, but in aquatic environment the organisms exhibiting the same enzyme receptors as humans and therefore they could experience similar pharmacodynamic effects [61]. Although concentrations of many pharmaceuticals residues in potable drinking water are so low and do not pose high risks to human beings, the main concern is the chronic and/or synergistic effects of the "cocktail" of pharmaceuticals that human have released to water body [62-63].

The methods of treatment used for the removal of pharmaceuticals from wastewater are the following: (1) biodegradation, (2) deconjugation, (3) partitioning, (4) removing during sludge treatment and (5) photodegradation [64].

(1) Biodegradation: biological degradation can take place in wastewater by means of aerobic/anaerobic microbial degradation of the drug substance leading to reduction of parent compounds and/or their metabolites during wastewater treatment [64]. The microbes include bacteria, yeasts, fungi, protozoa, and unicellular plants and rotifers, some of these organisms have the ability to degrade some of most hazards and recalcitrant chemicals [65].

(2) Deconjugation: pharmaceuticals compounds are often metabolized in the liver, and as a consequence glucuronide and sulfate conjugates of the parent drug are excreted. Deconjugation of organic compounds such as steroid hormones in domestic wastewater and within sewage treatment plans (STPs) occur due to the large amounts of β-glucosidase enzyme present.

(3) Partitioning: partitioning between the aqueous and organic biomass phase is considered the key component in determining the ultimate concentration of organic pollutants. Compounds with high log $K_{o/w}$ (lipophilic molecules) values are known to sorb to sludge, while substances with lower values are more likely to stay in the aquatic phase, depending on the individual compound, and substances sorbing to solids may also be remobilized if they are not strongly bound [64].

(4) Removal during sludge treatment: drugs may also be degraded by a biotic process (hydrolysis and oxidation) during sewage treatment process. Many pharmaceuticals are not thermally stable, and might be expected to break down during processes such as compositing due to heat as well as chemical and biodegradation processes [64].

(5) Photodegradation: several pharmaceuticals have proven to degrade due to the action of sunlight. Some pharmaceuticals such as diclofenac which is analgesic/anti-inflammatory drug, has been shown to degrade in aquatic environment due to ultraviolet (UV) light [64]. Due to incomplete elimination in wastewater treatment plants (WWTPs) using the conventional treatment method, residues of pharmaceuticals and PPCPs are found in both wastewater and surface water [66].Therefore, an improvement of this situation requires the application of advanced treatment techniques, such as membrane filtration technology, nanofiltration and reverse osmosis [67, 72-74], advanced oxidation processes [68], and activated carbon adsorption [64, 67, 72-74].

This study reports the efficiency of advanced technology for the removal of selected pharmaceuticals, ibuprofen and mefenamic acid, at the wastewater treatment plant at Al-Quds University which includes ultrafiltration (hollow fiber and spiral wound), activated carbon and reverse osmosis. In

addition, the adsorption of both pharmaceuticals using ODTMA-clay-micelles complex is reported.

2. Experimental

2.1. Instrumentation

2.1.1. High Performance Liquid Chromatography

High Performance Liquid Chromatography (HPLC-PDA) system consists of an alliance 2695 HPLC (Waters: Milford, MA, USA), and a waters Micromass® Masslynx™ detector with Photo diode array (Waters 2996: Milford, MA, USA). Data acquisition and control were carried out using Empower ™ software (Waters: Milford, MA, USA). Analytes were separated on a 4.6 mm ×150 mm C18 XBridge® column (5 µm particle size) used in conjunction with a 4.6 mm × 20 µm XBridge™ C18 guard column. Microfilter was used with 0.45 µm (Acrodisc® GHP, Waters).

2.1.2 pH meter

pH meter model HM-30G: TOA electronics™ was used in this study to measure the pH values for the samples

2.1.3 Centrifuge and Shaker

Labofuge®200 Centrifuge was used, 230 V 50/60 Hz. CAT. No. 284811 (Germany). Some of pharmaceuticals solutions were shaken with an electronic shaker (Bigbill shaker, Model No.: M49120-26, 220-240 V 50\60 Hz.) at 250 rpm.

2.1.4 Description of Wastewater Treatment Plant (WWTP)

The wastewater treatment plant (WWTP) at Al-Quds University collects a mixture of black, gray, and storm water. The treatment plant consists of a primary treatment (two stage primary settling basin), and a secondary (activated sludge with a hydraulic retention time of 16-20 hours, coagulation and chlorination) treatment. Then, the secondary effluent is introduced to the sand filter before entering the ultra- filtration membrane (Hollow fiber and Spiral wound). After the ultra-filtration process, the effluent is subjected to activated carbon column followed by a reverse osmosis (advanced treatment). Then, a blend of all effluents is used for irrigation. The ultra-filtration process is made of two small scale membranes with a capacity of 12 m^3 /day. The first UF unit is equipped with 2 x 4 inch pressure vessels with pressure resistance up to 150 psi. Each vessel holds two separation membranes (spiral wound with 20 kD cutoffs which is equivalent to 0.01 micron separation rate). The designed permeate capacity of the system is 0.5-0.8 m^3/h. This membrane can remove bacteria, suspended solids, turbidity agents, oil, and emulsions. The second unit is equipped with two pressure vessels made from Vendor (AST technologies, model number 8000 WW 1000-2M) that houses the hollow fiber membranes with 100 kD cutoff (Vendor, AST technologies, Model no. 8000-WWOUT-IN-8080). The two units are designed to deliver 1.5m^3/h. The reverse osmosis (RO) membrane is made from thin film polyamide which consists of 1 x 4 inch pressure vessel made from composite material with pressure resistance up to 400 psi. The vessel holds two 4 inches special separation membranes (manufactured in thin film polyamide with pH range 1-11 models BW30-4040 by DOW Film Tec.). Membranes anti-scalent (Product NCS-106-FG, made of phosphate in water with active ingredient of phosphonic acid disodium salt) are continuously dosed to the RO feed at concentration of 4 ppm in order to prevent deposition of divalent ions. The system is designed to remove major ions and heavy metals. The designed RO permeate capacity of the system is 0.45- 0.5 m^3/h.

2.2. Chemicals and Reagents

Pure standards of ibuprofen (> 99%), mefenamic acid (> 99%) were obtained from local pharmaceutical company. Acetonitrile, methanol HPLC grade, orthophosphoric acid, magnesium sulfate, Charcoal activated fine powder with particle size (≤ 60.0 micron), charcoal activated granules with particle size (≤ 700.0 micron), and octadecyltrimethylammonium (ODTMA) complex were purchased from Sigma chemical company, C_{18} (1 g) cartridges 6cc single use for general laboratory use were purchased form Waters company (Milford, MA, USA).

2.3. Methods (Ibuprofen and mefenamic acid)

2.3.1. Calibration curves using the solid phase cartridge

The C_{18} cartridges were preconditioned by passing first 10 mL of water through the cartridge and then 10 mL of acetonitrile. The cartridges were then air dried. Several solutions of ibuprofen and mefenamic acid with different concentrations (1.0, 5.0, 10.0, 20.0, 30.0, 40.0, and 50.0 ppm) were prepared. 10 mL of each of these solutions was passed through the cartridge. The adsorbed mefenamic acid or ibuprofen was eluted from the adsorbent of the cartridge using 10 mL of acetonitrile. Afterwards, 20 µl of the eluate was injected into the HPLC and analyzed using the HPLC conditions for ibuprofen and mefenamic acid. Peak areas vs. concentration of ibuprofen and mefenamic acid was then plotted, and correlation coefficient of the plots were recorded.

2.3.2 Stability study of ibuprofen and mefenamic acid

2.3.2.1. Stability study in pure water

For this study, a 50 ppm solution of ibuprofen (prepared by dissolving ibuprofen in distilled water adjusted to pH 8.0 by using 1N sodium hydroxide) was used. Samples at specific time intervals (0, 1, 2, 4, 5, 10, 15, 20, 25, 30 days) were taken, and analyzed by HPLC method for ibuprofen. The concentration of ibuprofen at each time interval was calculated from a calibration curve and compared to the original concentration (50 ppm), and then the percentage of ibuprofen degraded was calculated. The same procedure was applied for mefenamic acid; HPLC method for mefenamic acid was used.

2.3.2.2 Stability study in the presence of sludge

The same procedure described in section (2.3.2.1) was applied for studying the stability of ibuprofen and mefenamic acid in the presence of sludge but water was replaced with a suspended sludge in plain water. In this experiment aeration was performed to maintain the bacterial growth within the sample during the whole study period.

2.3.3 Micelle-clay complex preparation

The micelle–clay complex was prepared by stirring 12mM of ODTMA with 10g/L clay for 72 hours. Suspensions were centrifuged for 20 min at 15 000 g, supernatants were discarded, and the complex was lyophilized.

2.3.4 Calibration curves

(a) Stock solution: Stock solution was prepared by dissolving ibuprofen and mefenamic acid standards in water that adjusted to pH 8.0 to a concentration of 1000 ppm for the use in (b).

(b) Calibration curves: The following diluted solutions were prepared from the stock solution of ibuprofen (1.0, 5.0, 10.0, 25.0, 50.0, 100, 200, 500 and 1000.0 ppm). 20 µl of each solution was injected into the HPLC and the peaks for ibuprofen were recorded using the following HPLC conditions: C18 column, wavelength = 220 nm, Flow rate = 2.0 mL/min, mobile phase: 50 % of 0.07 % phosphoric acid solution/ 50 % acetonitrile. For mefenamic acid, the same procedure was followed but using the following HPLC conditions: C_{18} column, wavelength = 350 nm, flow rate = 1.0 mL/min. Peak areas vs. concentration of ibuprofen and mefenamic acid (in ppm) was then plotted, and R^2 of the plots are recorded.

2.3.5 Batch adsorption isotherms

Equilibrium relationships between adsorbents (clay micelle complex and activated charcoal) and adsorbate (ibuprofen and mefenamic acid) are described by adsorption isotherms. This was done by studying the percentage removal of the adsorbate by both adsorbents (clay micelle complex and activated charcoal) at different concentrations (50, 100, 200, 500 and 1000 ppm) prepared in distilled water at pH = 8.0 adjusted by using 1M sodium hydroxide. The following procedure was applied: 100 mL from each solution was transferred to 200 mL Erlenmeyer flask, 0.5 g of the clay micelle complex was then added to the flask. Then the flask was placed on a shaker for 180 minutes. Afterwards, each sample was centrifuged for 5 minutes, and filtered using 0.45 µm filter. Then 20 µl of the filtered solution was injected into the HPLC and the peak areas of ibuprofen and mefenamic acid were recorded.

2.3.6 Efficiency of the wastewater treatment plant (WWTP) of Al-Quds University for removal of ibuprofen and mefenamic acid

The efficiency of different membranes (hollow fiber (HF-UF), spiral wound (SW-UF), activated carbon and reverse osmosis (RO) membranes) for the removal of ibuprofen from wastewater was studied by spiking ibuprofen in the storage tank of the wastewater treatment plant at a concentration of 40 ppm (by dissolving 25 g of ibuprofen in the storage tank containing 625 liters of activated sludge wastewater). Samples were taken from the following points of the WWTP: (1) storage tank (before running wastewater treatment plant) (2), (3), and (4) feed-, brine- and product-points of the HF-UF membrane, respectively (5) and (6) concentrated -, and permeated-UF point of the HF- SW membrane, respectively (7) activated carbon point, and (8) reverse osmosis point. These sampling points are shown in (Figure 5, appendix A). These samples were treated using SPE C_{18} cartridge as follows: 10 mL of sample was loaded into the C_{18} cartridge, and allowed to pass through the cartridge by effect of gravity. Ibuprofen adsorbed on the C_{18} cartridge was then eluted using 10 mL of acetonitrile. 20 µl of the eluted solution was injected into the HPLC, and analyzed using the HPLC conditions for ibuprofen method of analysis. The concentration of ibuprofen in each sample was calculated using the calibration curve for ibuprofen (see section 2.3.1). The same procedure was applied to study the efficiency of the WWTP for the removal of mefenamic acid where 40 ppm of mefenamic acid was spiked into the storage tank (by dissolving 25 g mefenamic acid in the storage tank containing 625 liters of activated sludge wastewater). Sampling procedure and treatment of the samples by SPE cartridges was followed as described for ibuprofen. The procedure for the calculation of the concentration of mefenamic acid in the tested samples was followed as described for ibuprofen, but using the HPLC conditions and calibration curve for mefenamic acid.

3. Results and discussion

3.1. Ibuprofen

Ibuprofen is a stable white crystalline powder and is only very slightly soluble in water. Less than 1 mg of ibuprofen dissolves in 1 mL water (< 1 mg/ mL). It is soluble in organic solvents like acetonitrile and alcohols. Ibuprofen is a member of the class of agents commonly known as nonsteroidal anti-inflammatory drugs (NSAIDs). It is used to relief the symptoms of a wide range of illnesses such as headaches, backache, period pain, dental pain, neuralgia, rheumatic pain, muscular pain, migraine, cold and flu symptoms and arthritis. Ibuprofen is an over the counter drug (OTC) and is consumed with large quantities daily [69].

3.1.1 Calibration curve for ibuprofen using solid phase extraction cartridge (SPE)

The calibration curve was obtained by plotting peak area versus concentration (in ppm) and is displayed in (Figure 6, appendix A) (seven data points) in the range 1.0 ppm – 50 ppm) of ibuprofen. The plot shows excellent linearity with correlation coefficient (R^2) of 0.99.

3.1.2 Stability study of ibuprofen

3.1.2.1. Stability of ibuprofen in pure water

Stability study of ibuprofen in pure water has carried out with ibuprofen concentration of 50 ppm in pure water and at 25 C° for 30 days. Samples were taken at different time intervals (0, 1, 2, 4, 5, 10, 15, 20, 25, and 30 days). The kinetic results showed that ibuprofen was stable at these conditions and no degradation products of the drug was detected (Figures 7 and 8, appendix A).

3.1.2.2 Stability study in the presence of sludge

Stability studies of ibuprofen was also conducted (as in section 3.1.2.1) in wastewater containing sludge with total plate count (TPC) = 25 $X10^7$ cfu/100 mL at 25 C° for 30 days. The results revealed that ibuprofen was stable in this media, and no

ibuprofen degradation products was observed (Figures 9 and 10, appendix A).

3.1.3 HPLC conditions for analysis of ibuprofen

C_{18} column, wavelength = 220 nm, Flow rate = 2.0 mL/min, mobile phase: 50 % of 0.07 % phosphoric acid solution/50% acetonitrile.

3.1.4 Adsorption studies of ibuprofen on a clay micelle complex (ODTMA) and activated charcoal

The adsorption mechanism depends on the physicochemical properties of the pharmaceutical and the aquifer media properties. Adsorption of ibuprofen onto a clay micelle complex and charcoal adsorbents was investigated and described in the following sections.

3.1.4.1 Adsorption of ibuprofen on the clay micelle complex (ODTMA)

The clay micelle complex (ODTMA) is prepared by mixing certain type of clay mineral (montmorillonite) with cationic surfactant. In this study octadecyltrimethylammonium (ODTMA), (Structure 3 in Figure 2, appendix A) with a critical micelle concentration (CMC) value of 0.3 mM was employed for the complex formation. A certain mass of clay was introduced into a solution of ODTMA until reaching a concentration of 1×10^{-2} M then stirred for 24 hours at 37 ˚C. The complex was filtered, dried and mixed with excess sand. This complex by virtue of its positive charge with hydrophobic region is capable of binding negatively charged organic molecules [70].

3.1.4.1.1 Adsorption of ibuprofen on (ODTMA) at pH 4.0

The efficiency of octadecyltrimethylammonium (ODTMA) complex for a removal of ibuprofen form a spiked sample was studied by preparing a solution of ibuprofen with 200 ppm concentration by dissolving ibuprofen in distilled water at pH = 4.0 adjusted by using 1M sodium hydroxide. A 100 mL from this solution was then transferred to 200 mL Erlenmeyer flask, 0.5 g of the complex was added to the Erlenmeyer flask containing the sample of ibuprofen, and then the Erlenmeyer flask was shacked for 180 minutes. Samples were taken according to determined intervals. Each sample was centrifuged for 5 minutes, and then it was filtered through 0.45 µ Millipore filter. Then 20 µl of each solution was injected into the HPLC and the peaks were recorded using the same HPLC conditions used in section 3.1.3. Table S3 (Supplementary Data) and (Figure 10, appendix A) showed incomplete removal of ibuprofen. The pK_a of ibuprofen is 4.4 and the pH of the spiked samples is 4.0. Therefore at pH 4 a solution of ibuprofen will exist approximately 50% in the ionized and 50% in the non-ionized forms. Results have shown that the percentage removal of ibuprofen in spiked samples at pH 4.0 was about 59.0%. This percentage of removal might be attributed to the interaction between the ionized forms of ibuprofen with the positively charged clay micelle complex. At pH 4, ibuprofen is 50% negatively charged and 50 % uncharged, so only the negative form of ibuprofen interacts with the positively charged complex indicating that the type of interaction between ibuprofen and the complex is electrostatic, while the hydrophobic interaction is negligible. It is worth noting that the removal of ibuprofen is relatively fast: about 59% in 5 minutes, however after this period the percentage removal remains constant up to three hours.

3.1.4.1.2 Adsorption of ibuprofen on (ODTMA) at pH 8.0

The percentage removal of ibuprofen by a clay micelle complex was also studied at pH 8.0.The same procedure was applied as in section 3.1.4.1.1, by preparing a solution of ibuprofen at a concentration of 200 ppm in distilled water at pH = 8.0 adjusted by 1M sodium hydroxide**,** where ibuprofen at pH 8.0 completely exists in the ionized form. Results have shown that ibuprofen is 90 % removed at pH 8.0. Table S4 (Supplementary Data) and (Figure 12, appendix A) demonstrated that the mode of interaction between ibuprofen and the clay micelle complex is mainly electrostatic, and the hydrophobic interactions are scarily involved. It is worth noting that about 84.0% of ibuprofen is eliminated in the first 5 minutes, and only 6.5% of ibuprofen was removed during the remaining time (about three hours).This indicates that the removal process by the clay micelle complex (ODTMA) is very fast.

3.1.4.2 Adsorption of ibuprofen on the activated charcoal

The efficiency of activated charcoal for the removal of ibuprofen form a spiked sample was studied by preparing 200 ppm concentration of ibuprofen in distilled water at pH = 8.0 adjusted by using 1M sodium hydroxide, then 100 mL from this solution was transferred to 200 mL Erlenmeyer flask, 0.5 g of the activated charcoal was added to an Erlenmeyer flask containing the sample of ibuprofen, then the Erlenmeyer flask was put on a shaker for 180 minutes. Samples were taken according to determined intervals. Each sample was centrifuged for 5 minutes, and then was filtered by 0.45 µ Millipore filter. 20 µl of each solution was injected into the HPLC and the peaks were recorded using the same HPLC conditions used in previous sections. Table S5 (Supplementary Data) and (Figure 13, appendix A) illustrate the removal of ibuprofen by activated charcoal. The results revealed that activated charcoal is effective for the removal of ibuprofen from spiked samples (200 ppm) at pH = 8.0. The removal was about 98% and achieved after two hours. The capacity of the clay micelle complex and activated charcoal towards adsorption of ibuprofen was quite comparable. The results demonstrated that the adsorption of ibuprofen on a clay micelle complex is faster when compared to that with the activated charcoal (about 84% of ibuprofen was removed in the first 5 minutes while only 49% of ibuprofen was removed by the activated charcoal). However, after three hours the adsorption capacity of the clay complex and activated charcoal was about similar (90% for the clay complex and 99% for activated charcoal).

3.1.4.3 Analysis of adsorption isotherms

Equilibrium relationships between adsorbents (clay micelle complex and charcoal) and adsorbate (i.e. ibuprofen) are described by adsorption isotherms. The most common model for adsorption process is a Langmuir adsorption isotherm which is considered as the most widely used modeling for equilibrium data and determination of the adsorption capacity [71]. It is a linear form and represented by the following equation:

$C_e/Q_e = 1/ (K\ Q_{max}) + C_e/Q_{max}$…… Eq. (1)

Where:

C_e: equilibrium concentration of ibuprofen (mg/L).
Q_e: the equilibrium mass of the adsorbed ibuprofen per gram of complex ($mg.g^{-1}$)
($mg.g^{-1}$).
K:Langmuir constant

Q_{max}: maximum mass of Ibuprofen removed per gram of complex ($mg.g^{-1}$)

For this study the adsorption of ibuprofen of five concentrations (50, 100, 200, 500, and 1000 ppm) on the clay micelle complex and activated charcoal were studied, then C_e, and Q_e were calculated as in Tables S6 and S7 (Supplementary Data). C_e/Q_e vs. C_e was plotted for ibuprofen adsorbed onto both clay micelle complex and activated charcoal (Figure14, appendix A).

The two parameters Q_{max} and K values for the adsorption of ibuprofen on the clay micelle complex and activated charcoal can be calculated from the slopes and y-intercepts of the equations obtained from the plots (Q_{max} = slope^{-1}, K = (y-intercept)$^{-1}$(Q_{max})$^{-1}$). Table 1 (appendix B) shows the values for Q_{max} and k for ibuprofen adsorbed on both clay micelle complex and activated charcoal. Q_{max} and K parameters for the removal of Ibuprofen by the clay micelle complex were calculated as follows:

Slope = 1/ Q_{max} =0.016;Q_{max} = 62.5 mg/g Eq. (2)

Intercept = (1/ K x Q_{max}) = 0.025; K = 0.64Eq.(3)

The same procedure was applied for calculation of the Q_{max} and K for removal of ibuprofen by the activated charcoal. The results demonstrated that both adsorbents, the clay micelle complex and activated charcoal, have the same efficiency for the removal of ibuprofen as both Q_{max} are comparable (62.5 mg of ibuprofen per gram of complex, and 66.7 mg of ibuprofen per gram of activated charcoal) , As shown in (Figure 14, appendix A) the relationship between C_e/Q_e and C_e is linear for both the clay micelle complex and activated charcoal with R^2 greater than 0.99 which indicates that the adsorption of ibuprofen onto clay micelle and charcoal follows the Langmuir isotherm model.

3.1.5 Efficiency of the wastewater treatment plant (WWTP) at Al-Quds University for the removal of ibuprofen

The efficiency of the wastewater treatment plant (WWTP) at Al-Quds University for ibuprofen removal was studied. Result demonstrated that ibuprofen was 59.8% removed at hollow fiber stage (UF-HF), while about 94.7% of ibuprofen was removed at spiral wound (SW) stage, (Tables S8 and S9)(Supplementary Data). At the activated carbon adsorbent point of the wastewater treatment plant, 98.8% of ibuprofen was removed. The results also indicate that complete removal (99.9%) of ibuprofen was achieved after passing through the reverse osmosis membrane , RO (Figures 15, 16 , 17 and 18). These findings demonstrate that the WWTP at Al-Quds University is effective for the removal of ibuprofen. UF-HF and UF-SW are responsible for 60% and 95% removal, respectively, while activated carbon and RO are responsible for 99% and 99.9%, respectively. Hence, activated carbon and RO system are crucial components for the removal of ibuprofen such that the environmental acceptable standards could be reached.

3.2 Mefenamic acid

Mefenamic acid is a non-steroidal anti-inflammatory drug (NSAIDs), used to treat pain; it is typically prescribed for oral administration. Mefenamic acid decreases inflammation (swelling) and uterine contractions, and is consumed with large quantities every day, and used in large quantities throughout Palestine [69].

3.2.1 Calibration curve for mefenamic acid using solid phase extraction cartridge (SPE)

The calibration curve was obtained by plotting peak area versus concentration (in ppm) and is displayed in (Figure 18, appendix A) (seven data points) in the range 1.0 ppm – 50 ppm for mefenamic acid. The plot shows excellent linearity with correlation coefficient (R^2) of 0.99.

3.2.2 Stability study of mefenamic acid

3.2.2.1. Stability of mefenamic acid in pure water

Stability study of mefenamic acid in pure water has carried out where the concentration of mefenamic acid in pure water was 50 ppm and the temperature of the solution was kept at 25 °C for 30 days. Samples were taken at different time intervals (0, 1, 2, 4, 5, 10, 15, 20, 25 and 30 days). The kinetic results showed that mefenamic acid was stable at these conditions and no degradation products was detected as shown in Figures 20 and 21 (appendix A).

3.2.2.2 Stability study in the presence of sludge

Stability studies of mefenamic acid was also conducted (as in section 3.2.2.1) in wastewater containing sludge with total plate count (TPC) = 25 X 10^7 cfu/100 mL at 25 °C for 30 days. The results revealed that mefenamic acid was also stable in this media, and no degradation products was observed as shown in Figures S1 and S2 (Supplementary Data) .

3.2.2.3 Calibration curve

The calibration curve was obtained by plotting peak area versus concentration and is displayed in (Figure 22, appendix A) (eleven data points) for mefenamic acid. The figure shows excellent linearity in the range (0.8 -1000.0 ppm) with correlation coefficient (R^2) of 1.0.

3.2.3 Adsorption studies of mefenamic acid on the clay micelle complex (ODTMA) and activated charcoal

Adsorption of mefenamic acid onto a clay micelle complex and charcoal adsorbents was investigated in the same manner to that of ibuprofen.

3.2.3.1 Adsorption of mefenamic acid on the clay micelle complex (ODTMA)

The efficiency of octadecyltrimethylammonium (ODTMA) complex for the removal of mefenamic acid form a spiked sample was studied by preparing a solution of mefenamic acid with a concentration of 200 ppm, prepared by dissolving mefenamic acid in distilled water at pH = 8.0 adjusted by using 1M sodium hydroxide, then (as in ibuprofen) 100 mL from this solution was transferred to 200 mL flask, 0.5 g of the complex was added to the Erlenmeyer flask containing the sample of mefenamic acid, then the flask was shaken for 180 minutes. Samples were taken according to determined intervals. Each sample was centrifuged for 5 minutes, and then was filtered by 0.45 µ Millipore filter. 20 µl of each solution was injected into the HPLC and the peaks were recorded using the same HPLC conditions for mefenamic acid used in the previous sections. Table S10 (Supplementary Data) and (Figure 23, appendix A) indicate complete removal for mefenamic acid by ODTMA complex. The results of this study revealed that only 5 minutes were needed for a complete removal of mefenamic acid (97.3% removal). Similarly to ibuprofen, the results of mefenamic acid showed that electrostatic interaction between mefenamic acid and the clay micelle complex is the predominate mode of interaction rather than hydrophobic interaction. Comparison of the removal of mefenamic acid and ibuprofen on the clay micelle complex demonstrated that the removal of mefenamic acid is faster and more efficient than that of ibuprofen.

3.2.3.2 Adsorption of mefenamic acid on activated charcoal

The capacity of activated charcoal for adsorption of mefenamic acid was studied, in the same manner as that for ibuprofen (section 3.1.4.2).The results demonstrated that activated charcoal is quite effective in removing mefenamic acid from spiked samples of (200 ppm) (97.2 % removal after 3 hours) (Table S11, Supplementary Data and Figure 24, appendix A). The combined results revealed that the capacity of the clay micelle complex and activated charcoal for mefenamic acid removal was quite comparable. In addition, the results demonstrated that the adsorption of mefenamic acid on a clay micelle complex is very fast compared to that of mefenamic acid on activated charcoal, 96 % of mefenamic acid was removed in the first 5 minutes by a clay complex vs. only 28 % by activated charcoal. Furthermore, the adsorption of mefenamic acid on a clay micelle complex was faster than that of ibuprofen (96% vs. 84% in the first 5 minutes). It should be indicated that the adsorption mode of these two pharmaceuticals on activated charcoal is somewhat different. The percentage of the removal for mefenamic acid in the first 5 minutes by activated charcoal was only 28 % whereas that of ibuprofen was 49.6%. However, after 3 hours, the adsorption capacity of the clay complex and activated charcoal was almost similar (97.3% when using clay micelle complex and 97.2 % when using activated charcoal).

3.2.4 Analysis of adsorption isotherms

As for ibuprofen (section 3.1.4.3) the adsorption of mefenamic acid in different concentrations (50, 100, 200, 500, and 1000 ppm) on the clay micelle complex and activated charcoal was studied. The C_e, and Q_e were calculated, then C_e/Q_e was plotted against C_e and the linear relationships obtained are illustrated in (Figure 25, appendix A). As shown in (Figure 25, appendix A), the relationship between C_e/Q_e and C_e is linear for both the clay micelle complex and activated charcoal with R^2 greater than 0.99. The two parameters Q_{max} and K values for the adsorption of mefenamic acid on a clay micelle complex and activated charcoal was calculated from the slops and y-intercepts of the equations obtained from the plots (Q_{max} = slop^{-1}, K = (y-intercept)$^{-1}$(Q_{max})$^{-1}$). Table 2 (appendix B) shows the values for Q_{max} and K for mefenamic acid adsorbed on both clay micelle complex and activated charcoal. Qmax and K parameters for the removal of mefenamic acid by the clay micelle complex were calculated as follows:

Slope = 1/ Q_{max} = 0.010; Q_{max} = 100 mg/g …..Eq. (4)

Intercept = (1/ K x Q_{max}) = 0.095; K = 0.105 L/mg … Eq. (5)

The same procedure was applied for the calculation of Q_{max} and K for removal of mefenamic acid by the activated charcoal (Tables S12 and S13, Supplementary Data). The combined results demonstrated that both adsorbents, clay micelle complex and activated charcoal were quit efficient in the removal of mefenamic acid with both having close Q_{max} values (100 mg of mefenamic per gram of complex vs. 91 mg of mefenamic acid per gram of activated charcoal). It is noteworthy here to compare the efficiency of both adsorbents for removal of ibuprofen and mefenamic acid by comparing Q_{max} values. It is clear from these values Table S14 (Supplementary Data) that both adsorbents have higher efficiency for removal of mefenamic acid compared to ibuprofen.

3.2.5 Efficiency of the WWTP at Al-Quds University for removal of mefenamic acid

The efficiency of the wastewater treatment plant at Al-Quds University for a removal of mefenamic acid was studied in the same manner as described for ibuprofen, where mefenamic acid was spiked in a concentration of 40 ppm, and the experiment was repeated three times for the repeatability of the results. Samples were taken from the same locations as described in section 3.1.5. The samples results taken from hollow fiber points (UF-HF), demonstrated that mefenamic acid was approximately 74.0% removed at this stage, while about 94.3% of mefenamic acid was removed after passing the spiral wound (SW) stage (Tables S15 and S16)

(Supplementary Data). The sample taken after passing activated carbon adsorbent point showed that mefenamic acid is almost completely removed (98.8%). Finally analysis of the samples taken after passing the RO membrane stage which includes brine RO and permeated RO indicated that approximately complete removal of mefenamic acid was achieved in this stage (99.5%) (Figures 26-29, appendix A). It is interesting here to compare the efficiency of the WWTP at Al-Quds University for the removal of ibuprofen and mefenamic acid. Referring to (Tables S9 and S16) (Supplementary Data), it is clear that ultrafiltration points of the WWTP are not sufficient for complete removal of ibuprofen and mefenamic acid; however activated carbon and RO are crucial for a complete removal of ibuprofen and mefenamic acid. Therefore, it is safe to conclude that the RO membrane of the wastewater treatment plant is required for the removal of ibuprofen and mefenamic acid to reach the acceptable environmental standards.

4. Summary and Conclusions

In this study, two acidic pharmaceuticals, ibuprofen and mefenamic acid were found to be stable in wastewater (for 30 days).Therefore, it is necessary to find a method for the removal of these pharmaceuticals from wastewater. Advanced wastewater treatment plant utilizing ultra filtration, activated carbon and RO showed that UF_HF and UF_SW are not efficient in removing both drugs to safe level. Whereas activated carbon and RO are efficient. Adsorption studies on clay- micelle complex (ODTMA) and charcoal revealed that both adsorbents are efficient in the removal of ibuprofen and mefenamic acid at pH 8. The removal efficiency for ibuprofen are 90.3% and 99.1%, respectively, whereas the removal efficiency for mefenamic acid are 97.3% and 97.2%, respectively. These results indicate that an integration of clay-micelle complex filters within the existing advanced membrane treatment system is very promising in improving removal efficiency and minimizing cost of treatment

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Appendix A

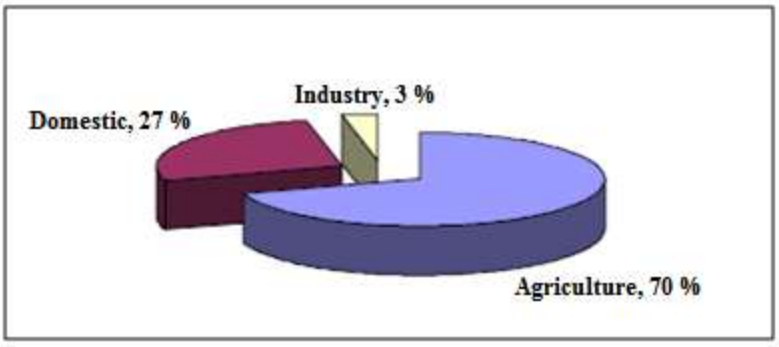
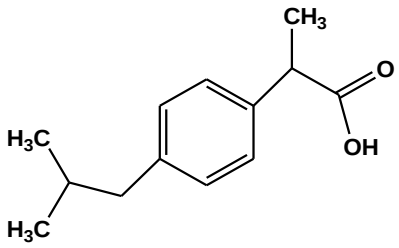


Fig. 1. Water consumption in Palestine [5].



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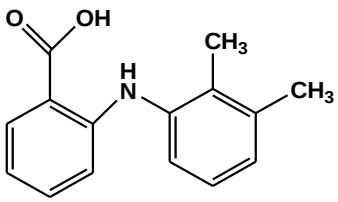

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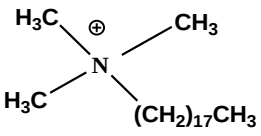

3

Fig. 2. Chemical structures for Ibuprofen (1), Mefenamic acid (2) and ODTMA (3).

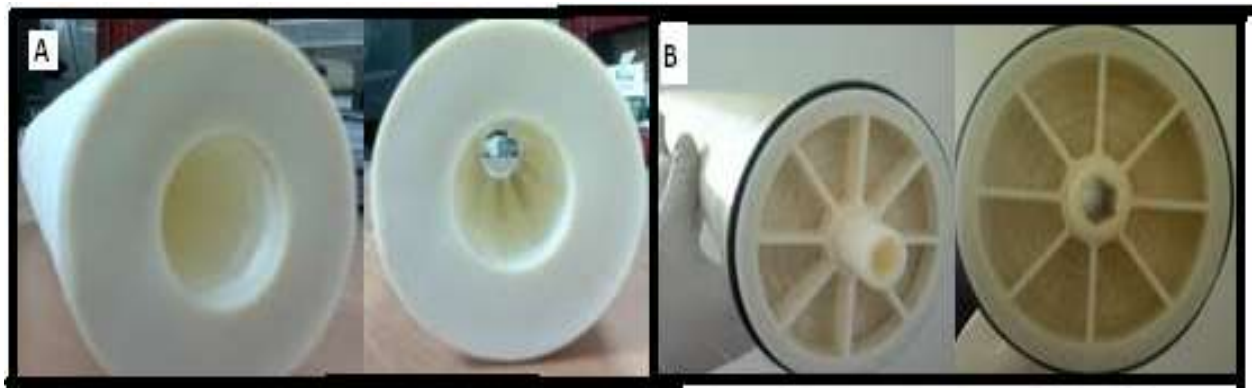

Fig. 3. Hollow fiber (A) and spiral wound (B) modules.

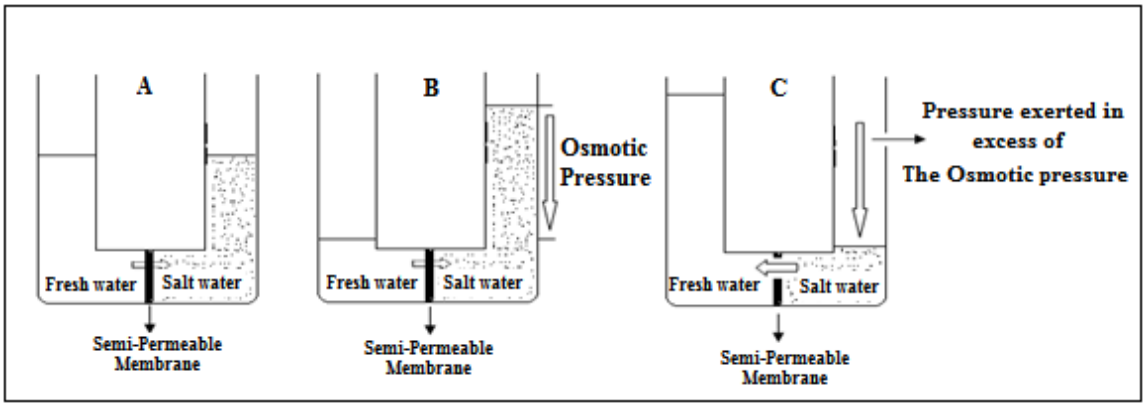

Fig. 4. Osmosis (A), osmotic pressure (B) and reverse osmosis (c)

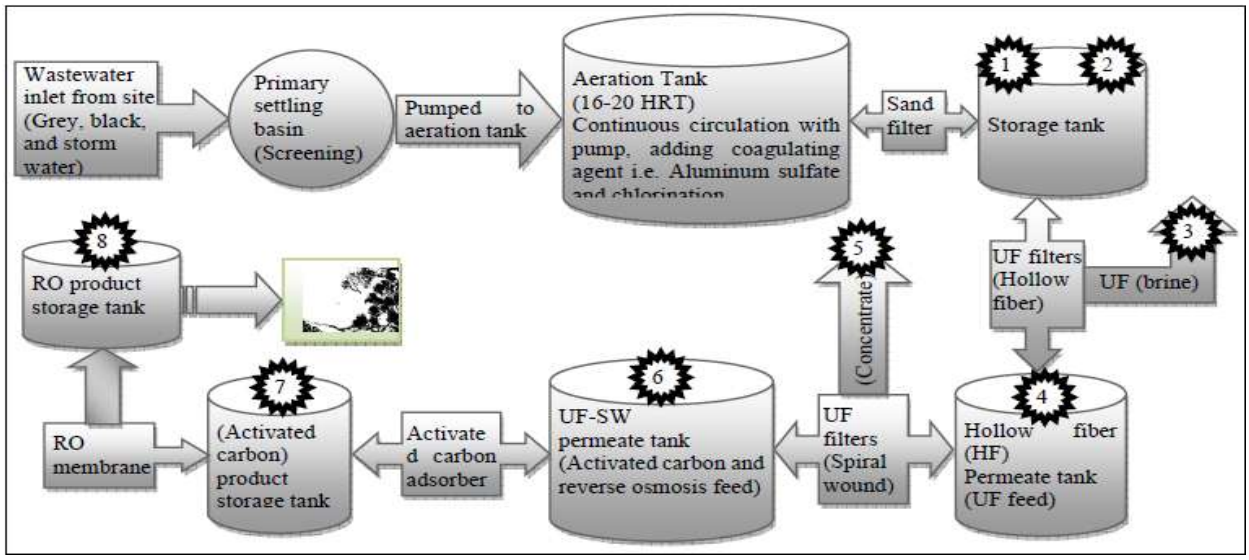

Fig. 5. Flow diagram showing the process of wastewater treatment plant which consists of HF-UF filters (hollow fiber) and SW-UF (spiral wound), activated carbon and RO filters.

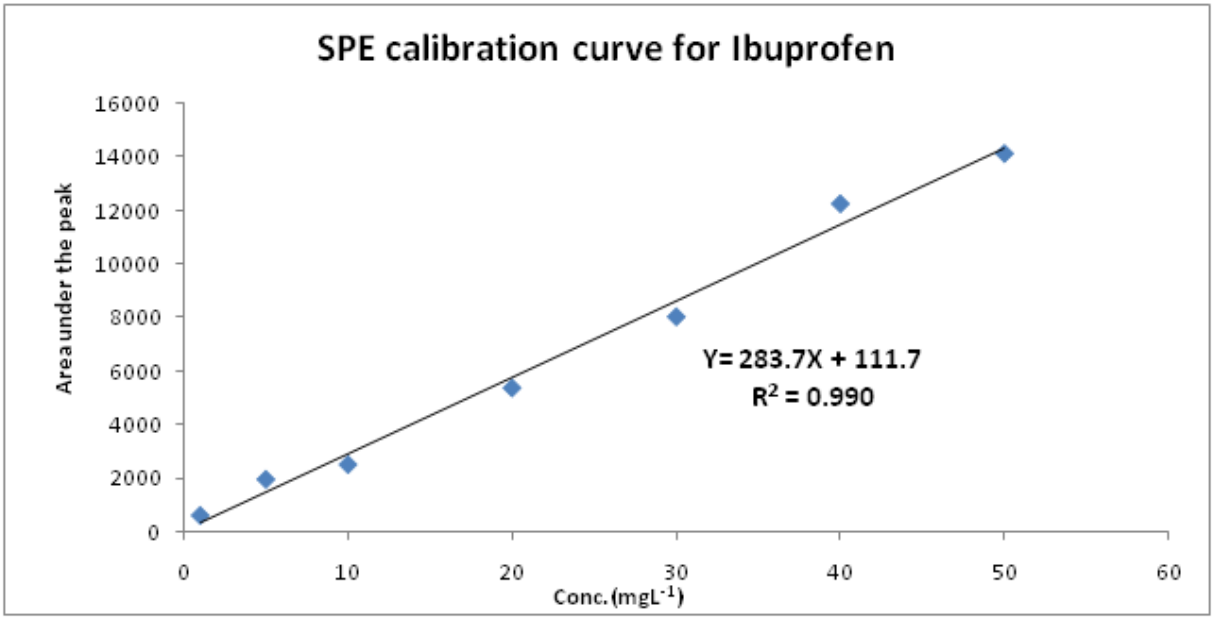

Fig. 6. Calibration curve for ibuprofen using SPE.

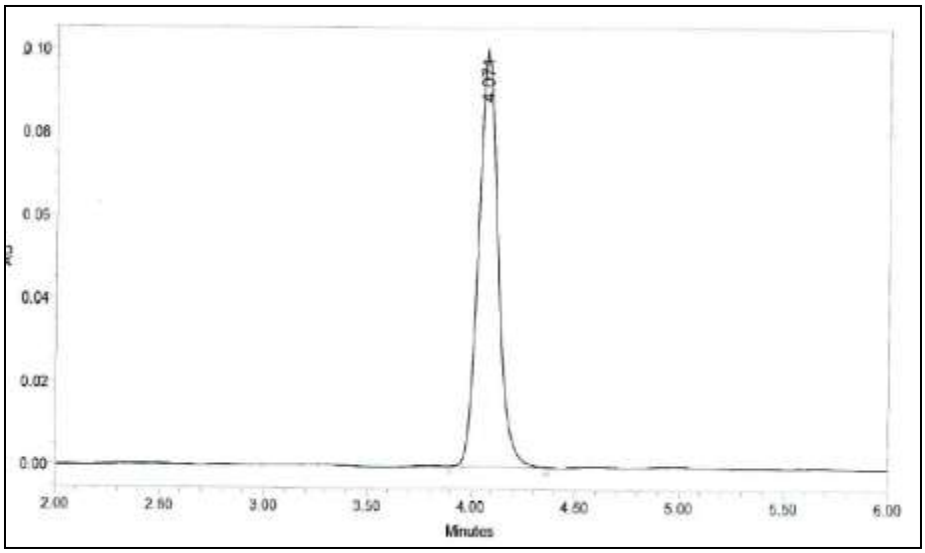

Fig. 7. Chromatogram showing ibuprofen after 0 days in pure water.

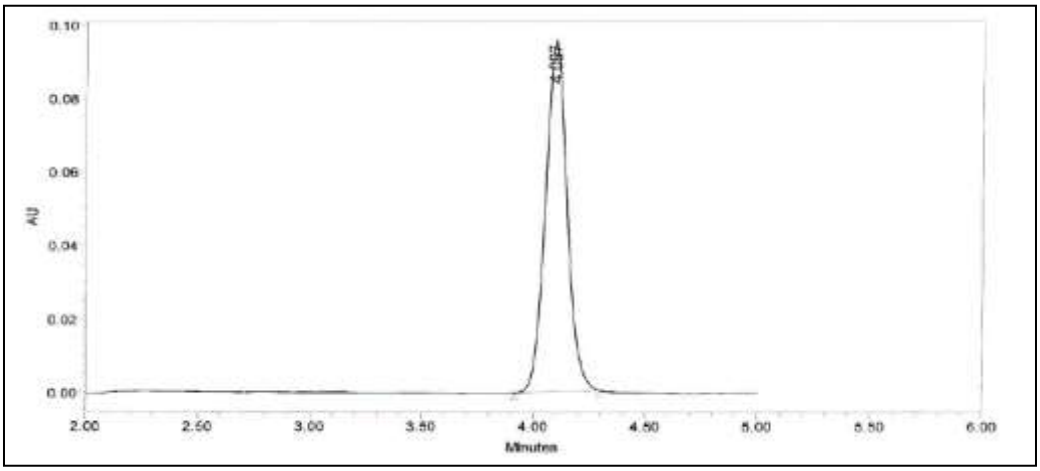

Fig. 8. Chromatogram showing ibuprofen after 30 days in pure water.

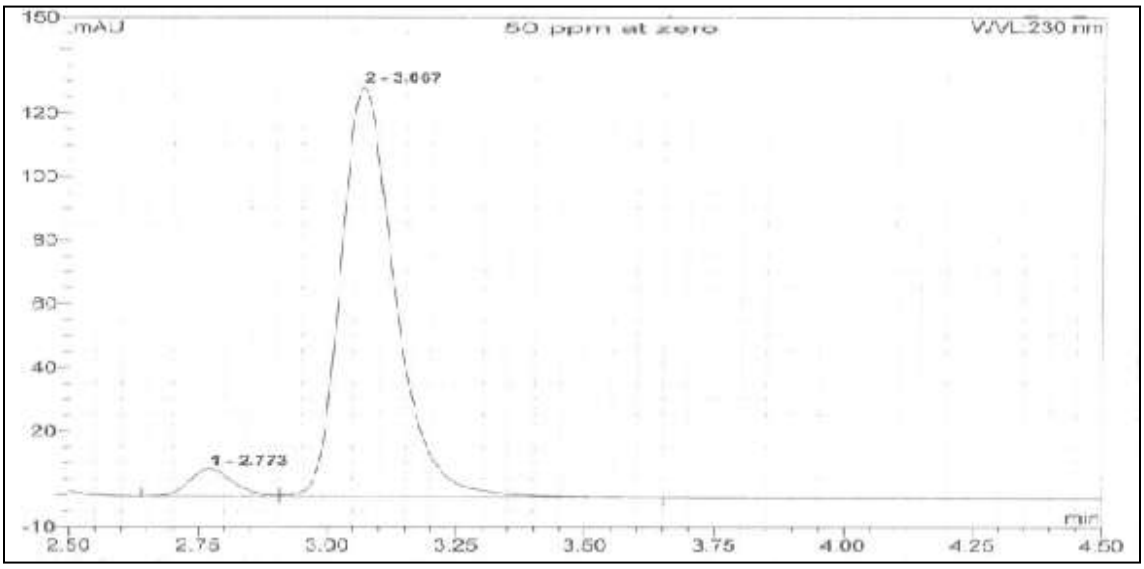

Fig. 9. Chromatogram showing ibuprofen after 0 days in wastewater.

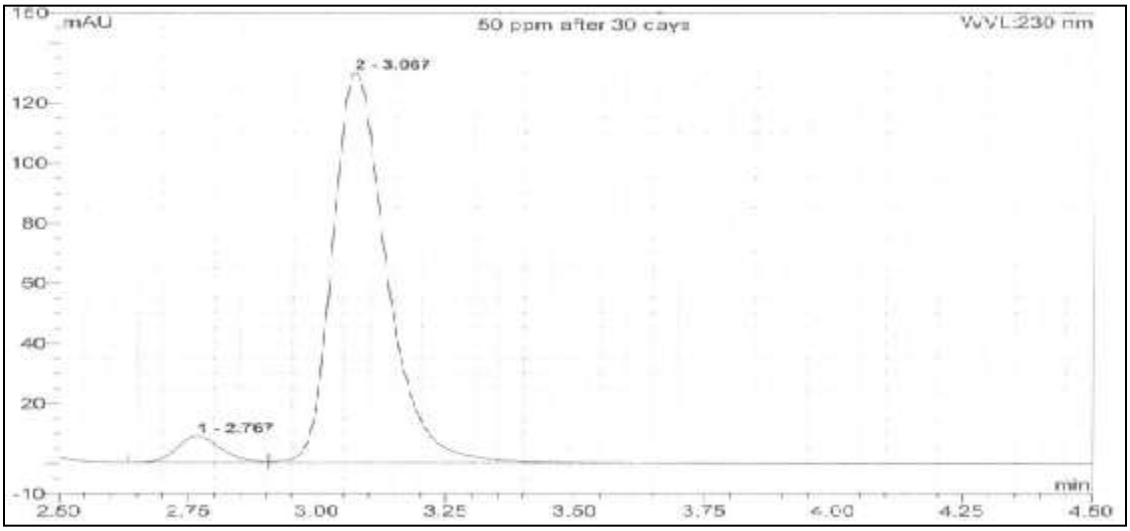

Fig. 10. Chromatogram showing ibuprofen after 30 days in wastewater.

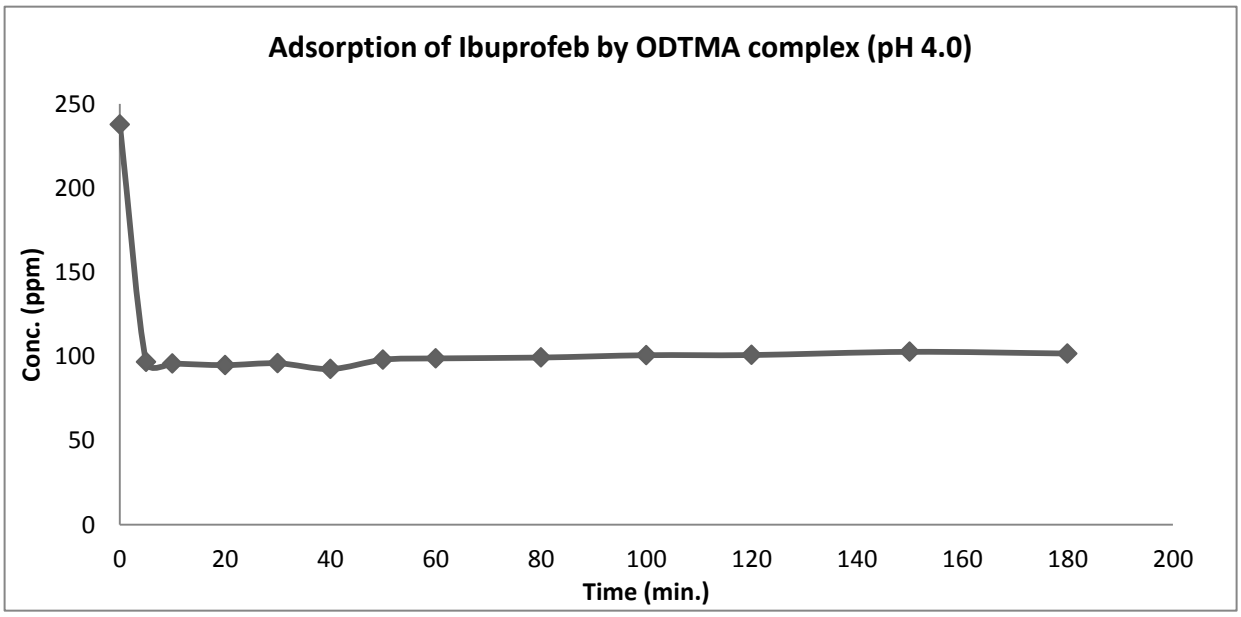

Fig. 11. Adsorption of ibuprofen by clay micelle complex (ODTMA) at pH 4.0.

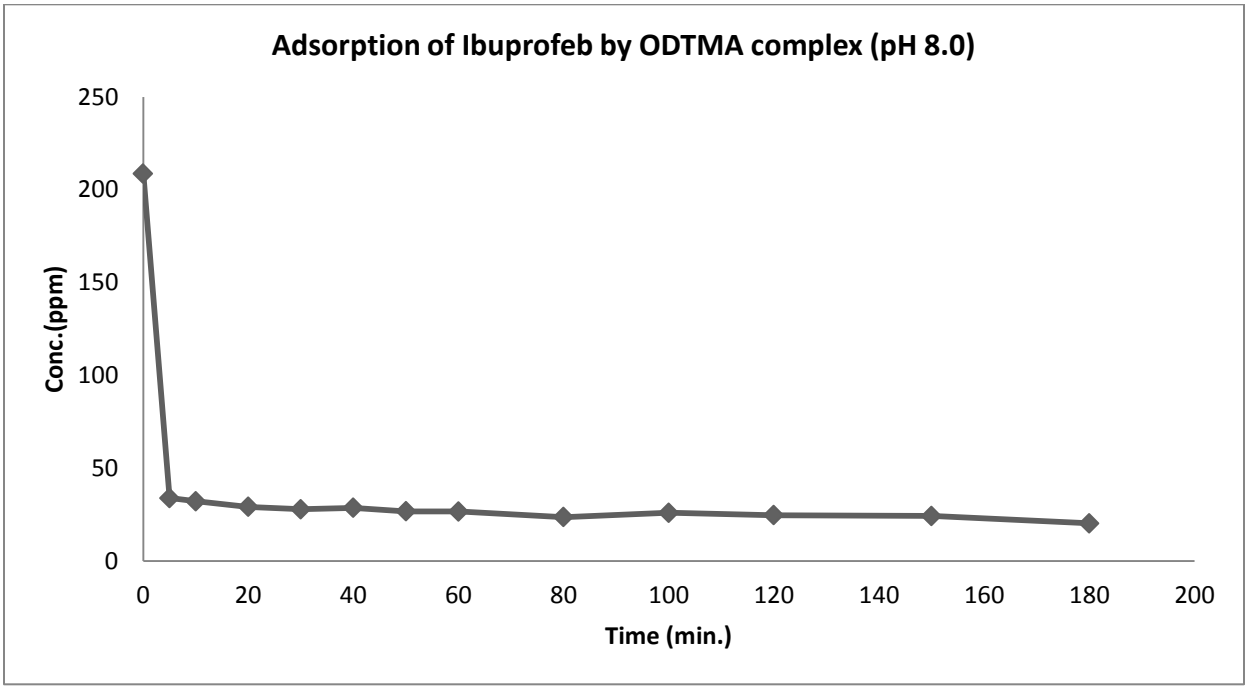

Fig. 12. Adsorption of ibuprofen by clay micelle complex (ODTMA) at pH 8.0.

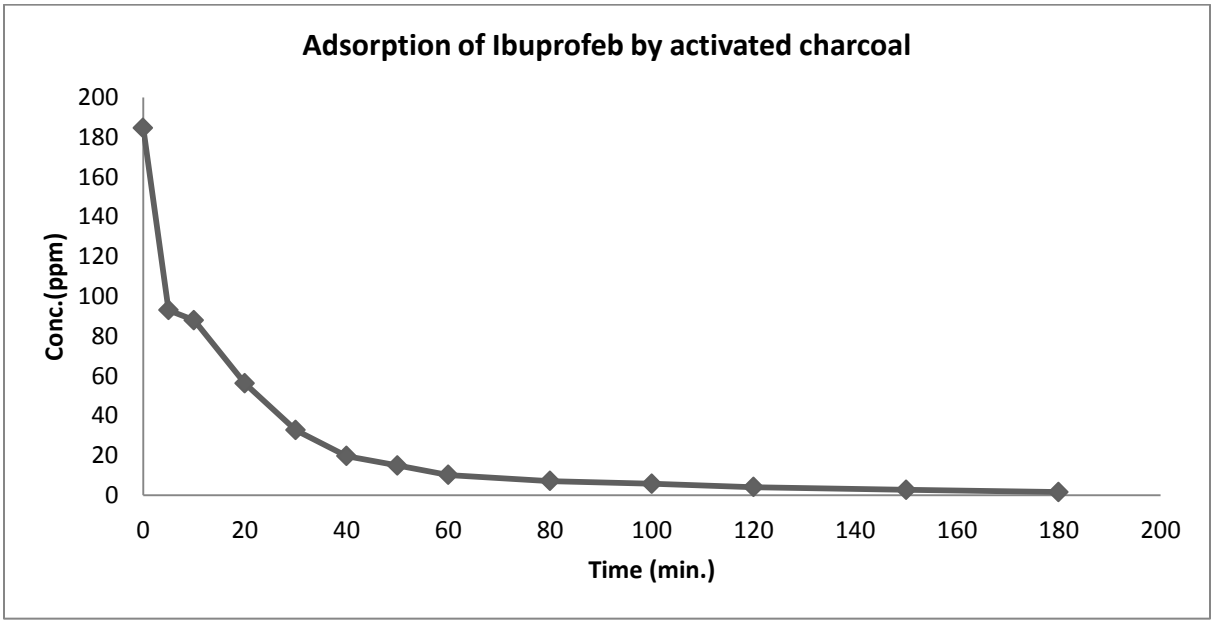

Fig. 13. Adsorption of ibuprofen by activated charcoal.

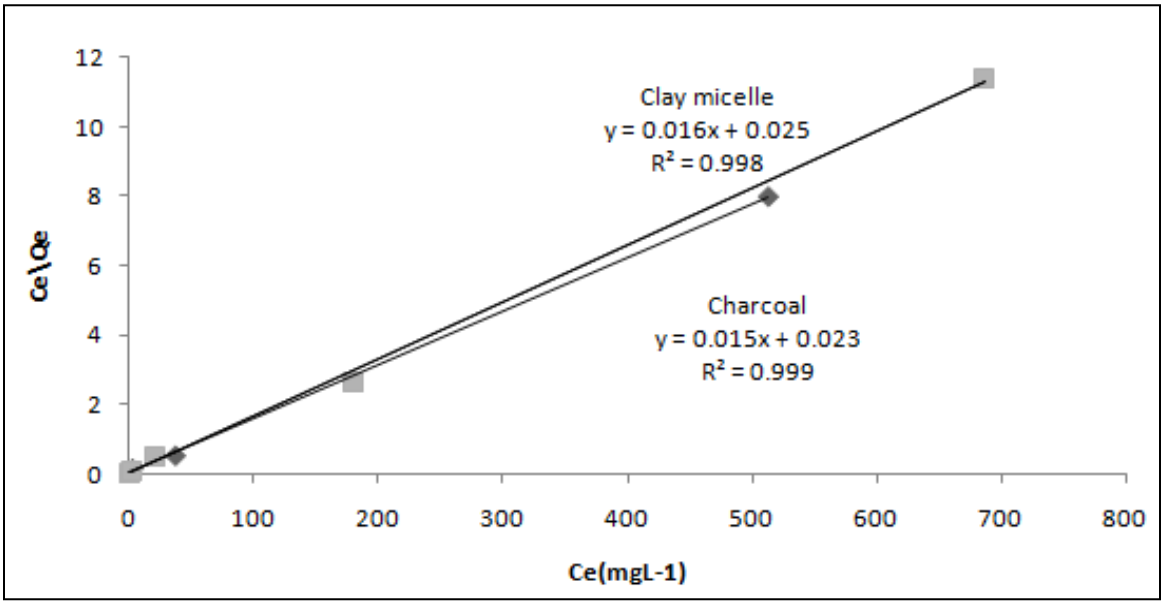

Fig. 14. Langmuir isotherms for the removal of ibuprofen.

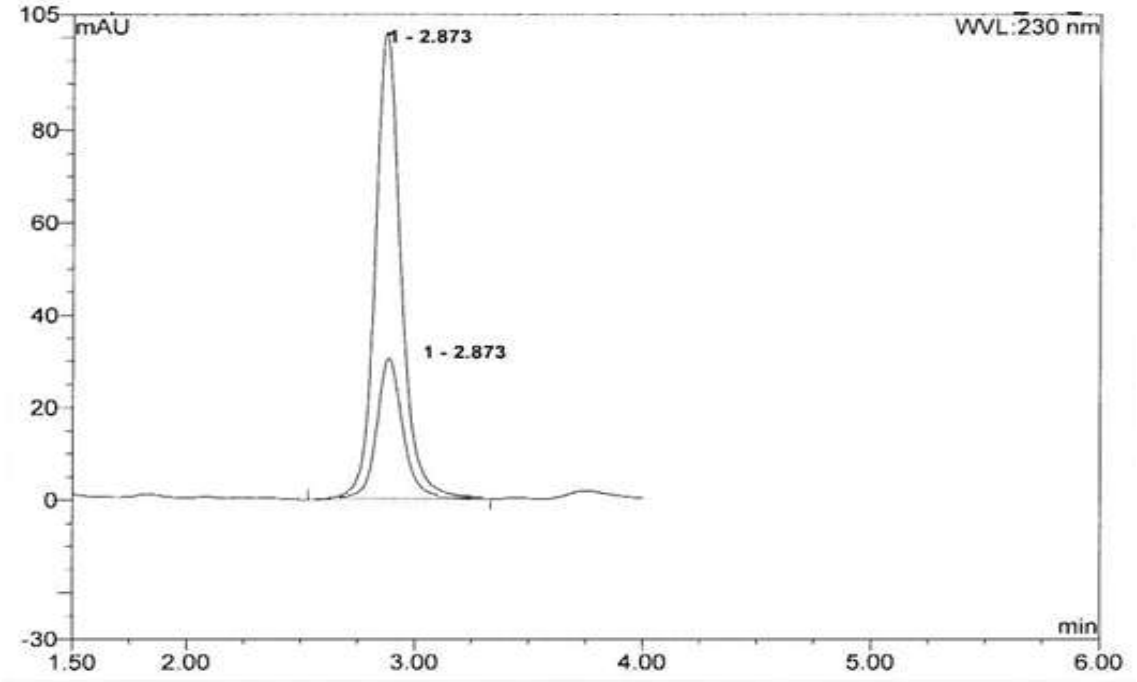

Fig. 15. Chromatograms showing the initial concentration of ibuprofen and after running the HF-UF point (see Fig. 5).

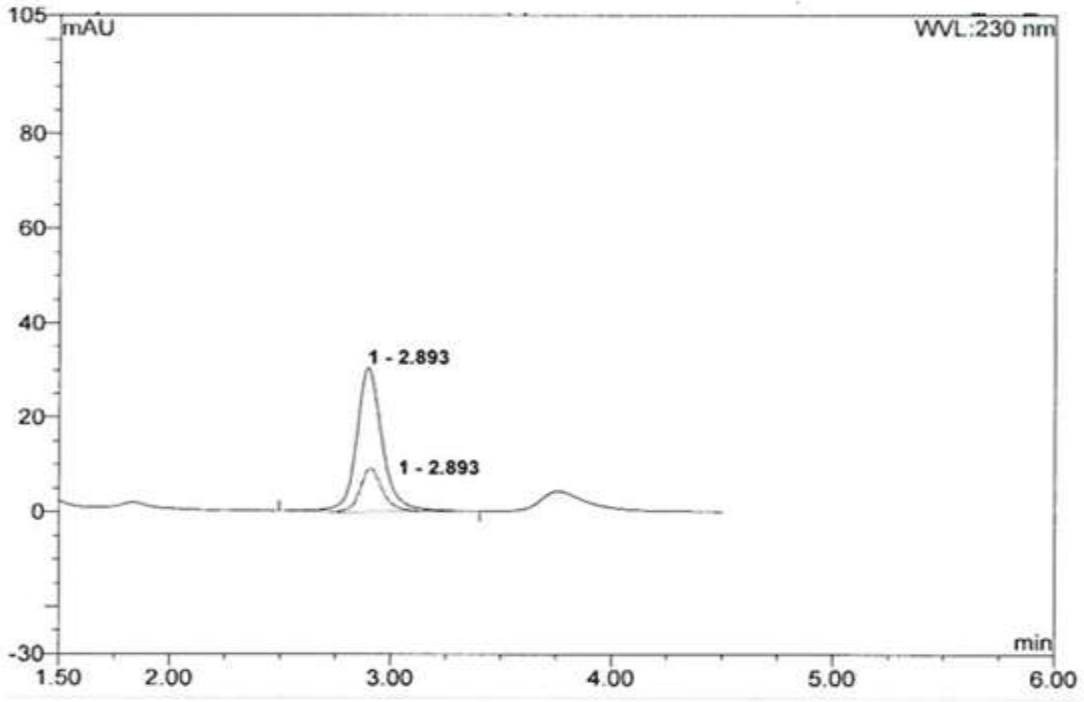

Fig. 16. Chromatogram showing the concentration of ibuprofen before and after running the SW-UF point (see Fig. 5).

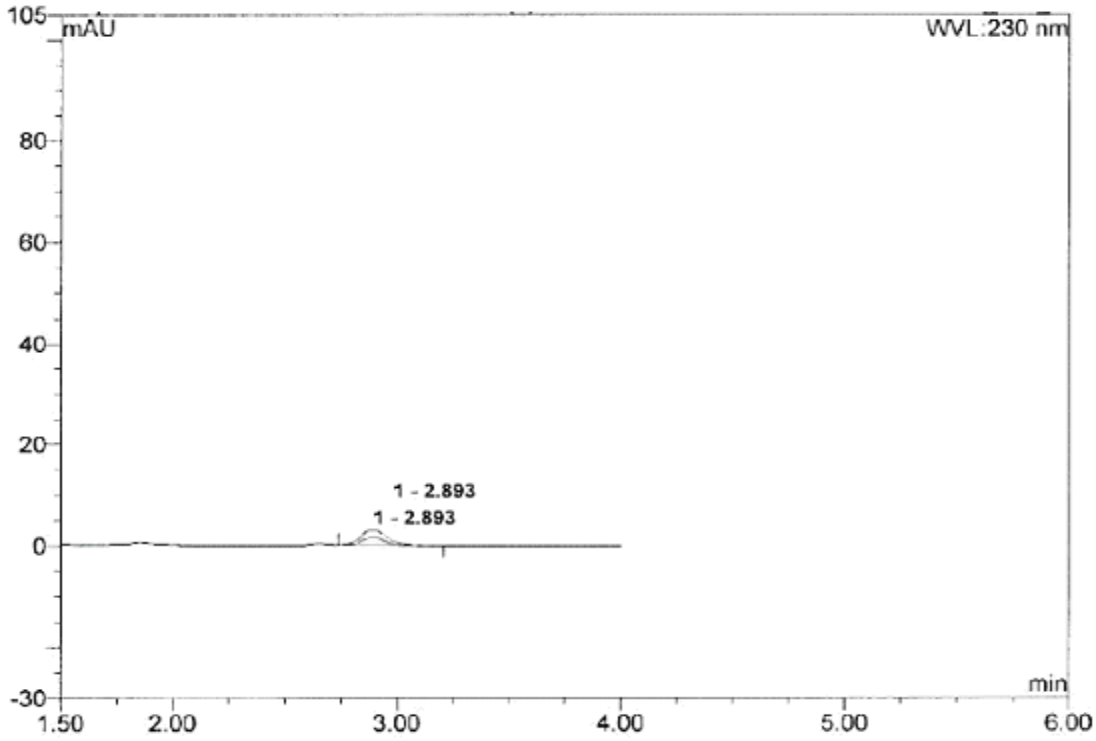

Fig. 17. Chromatogram showing the concentration of ibuprofen before and after running activated charcoal adsorbent point (see Fig. 5).

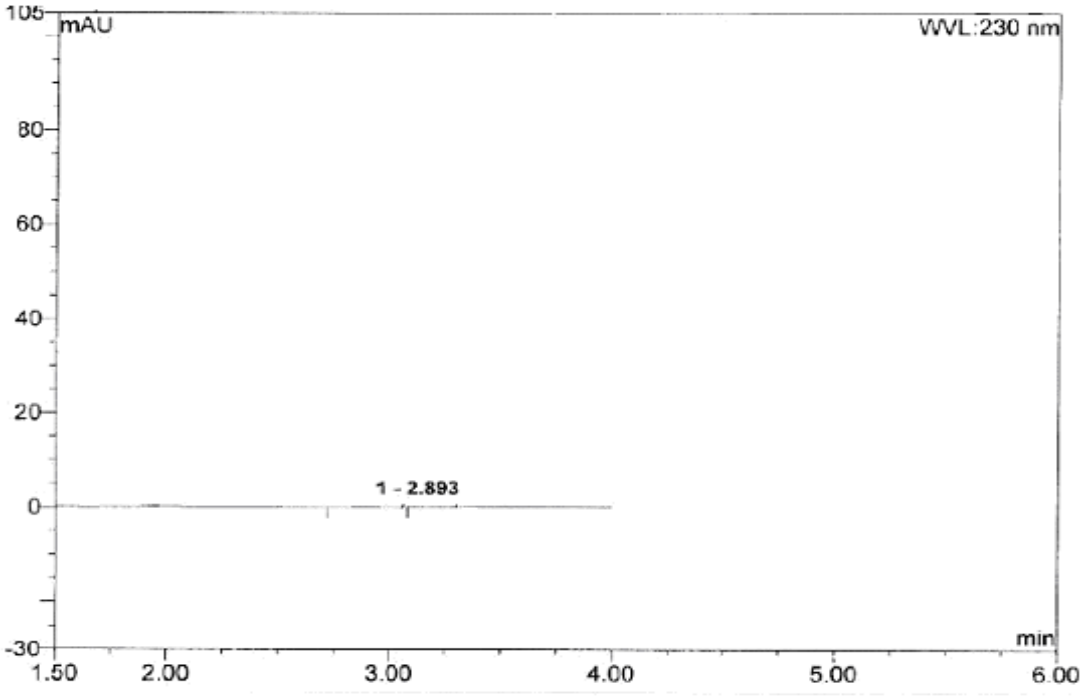

Fig. 18. Chromatogram showing the concentration of ibuprofen after passing reverse osmosis (RO) membrane(see Fig. 5).

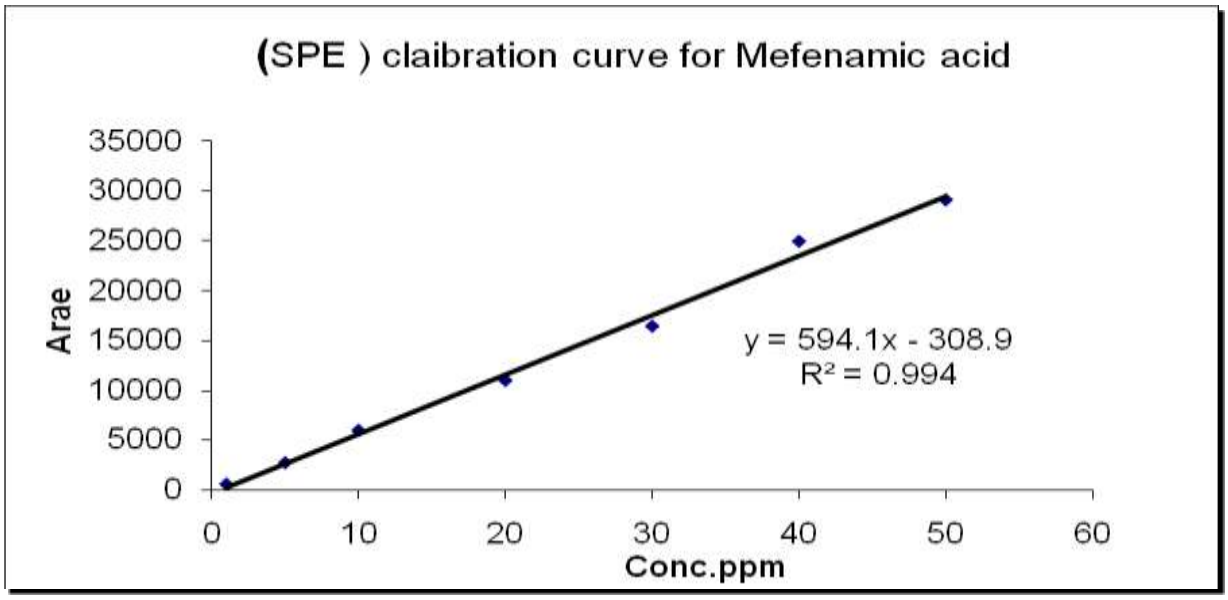

Fig. 19. Calibration curve by using SPE for mefenamic acid.

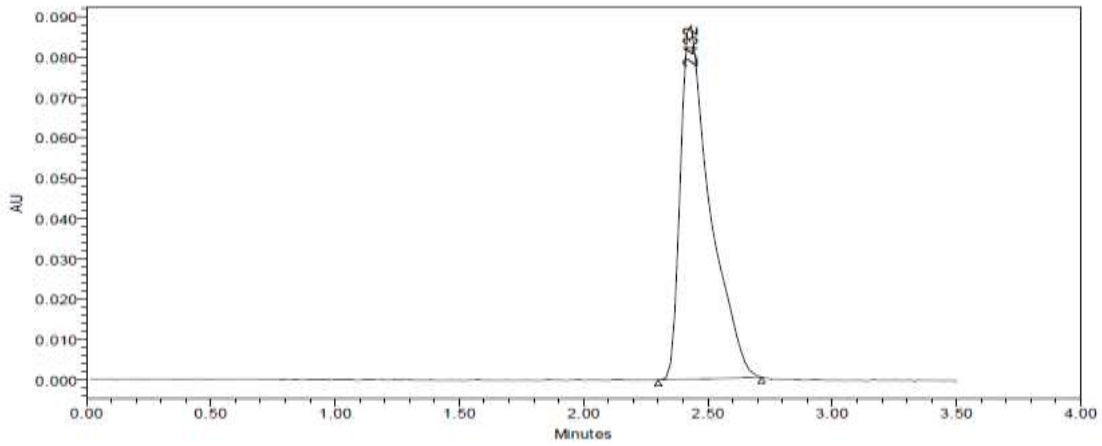

Figure 20. Chromatogram showing mefenamic acid at 0 days in pure water.

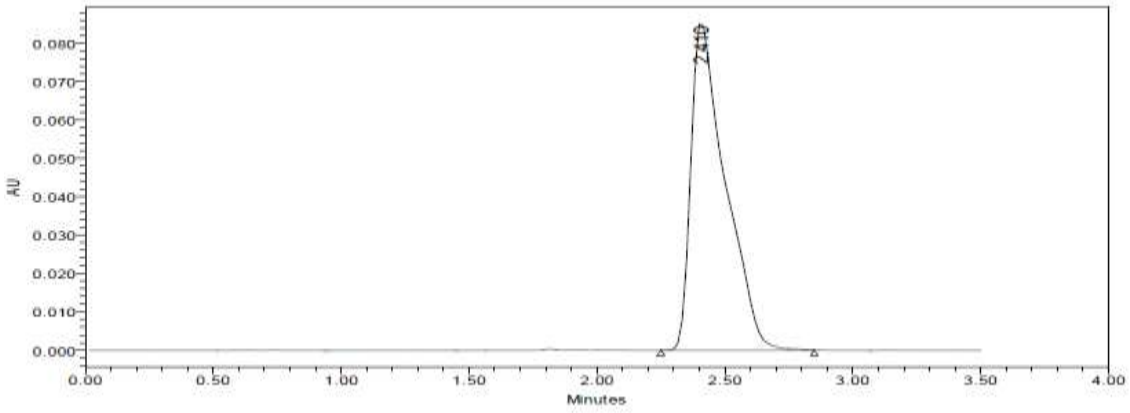

Figure 21. Chromatogram showing mefenamic acid at 30 days in pure water.

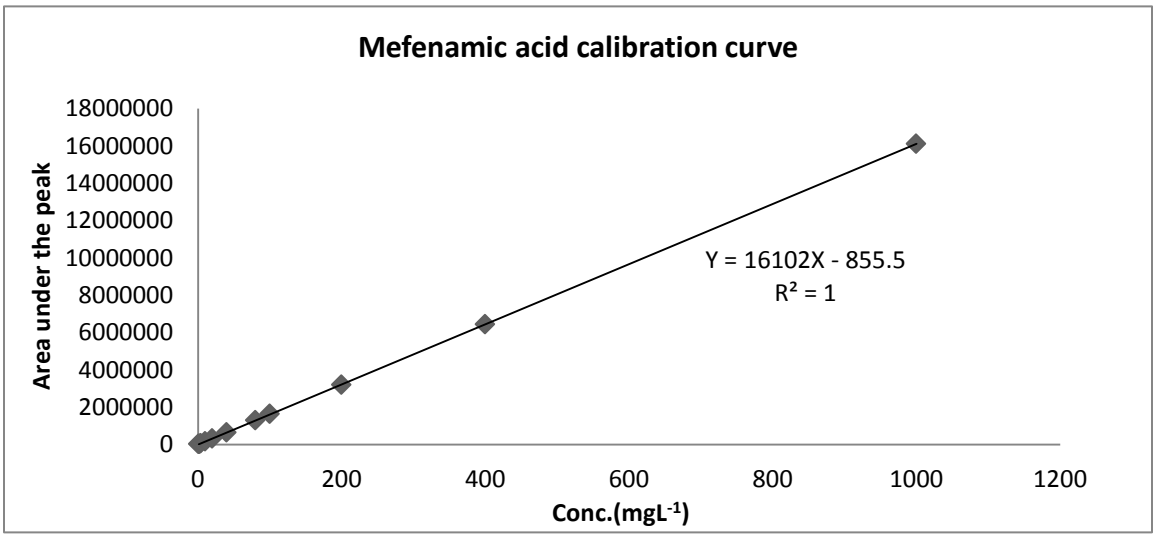

Fig. 22. Calibration curve for mefenamic acid.

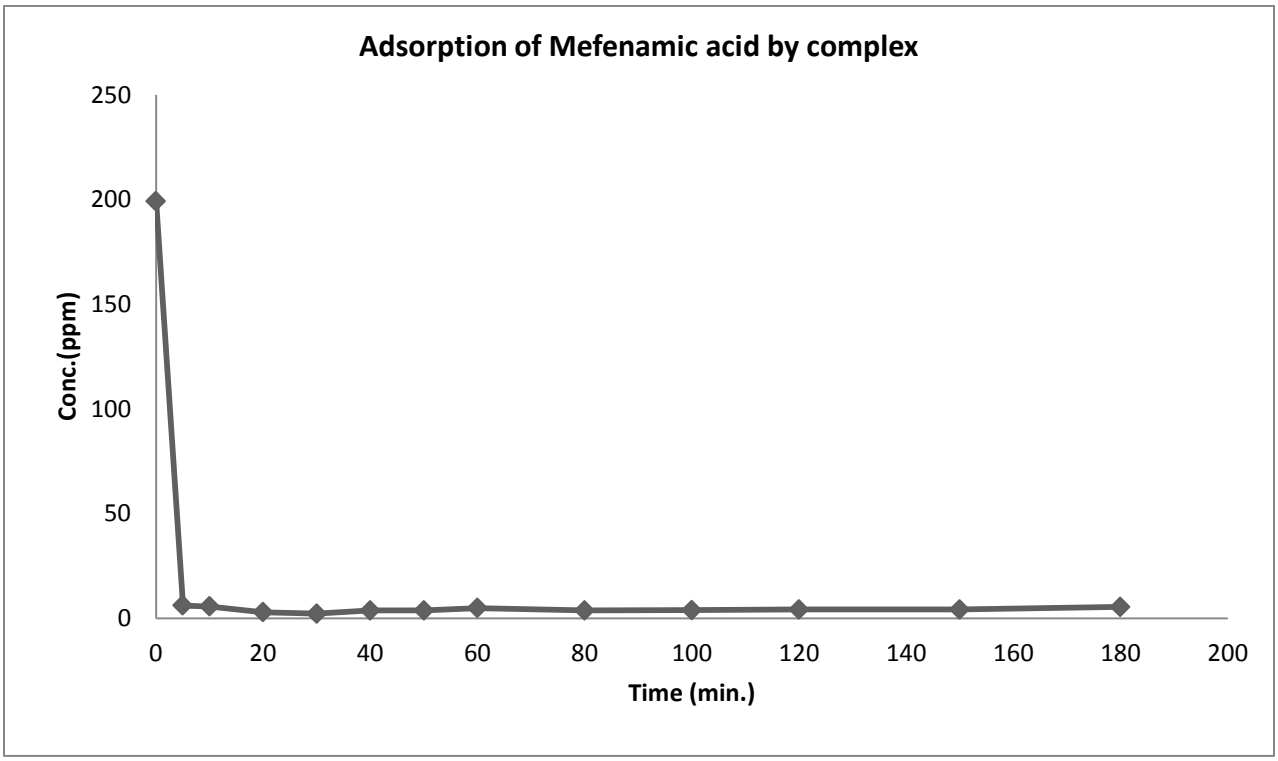

Fig. 23. Adsorption of mefenamic acid by clay micelle complex (ODTMA).

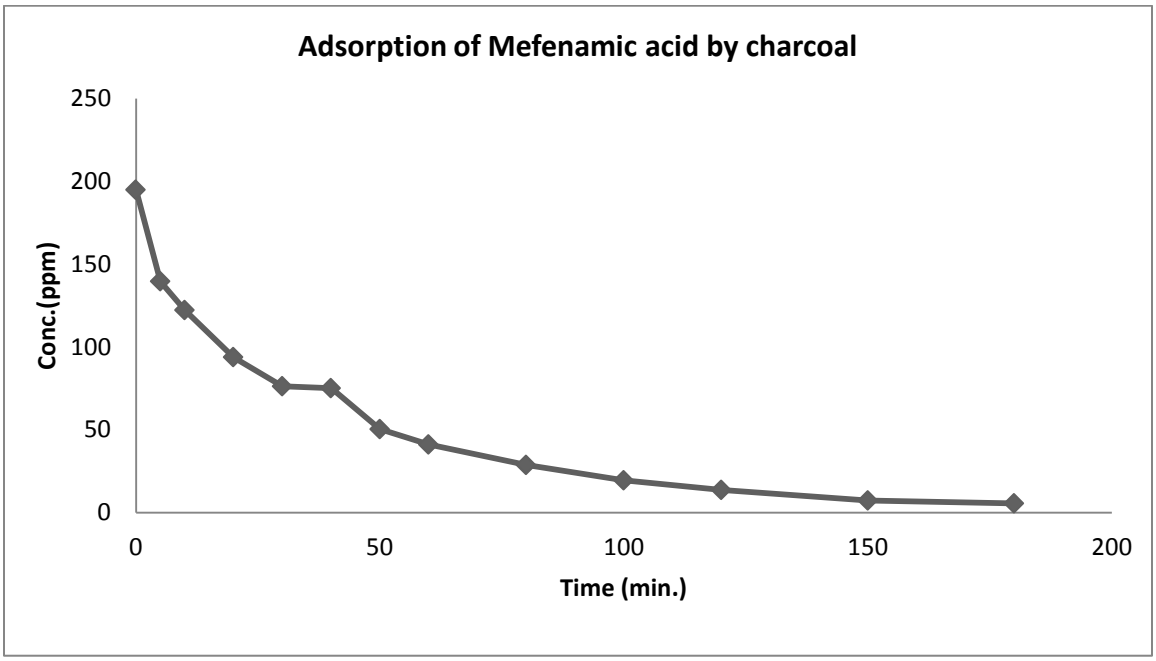

Fig. 24. Adsorption of mefenamic acid by activated charcoal.

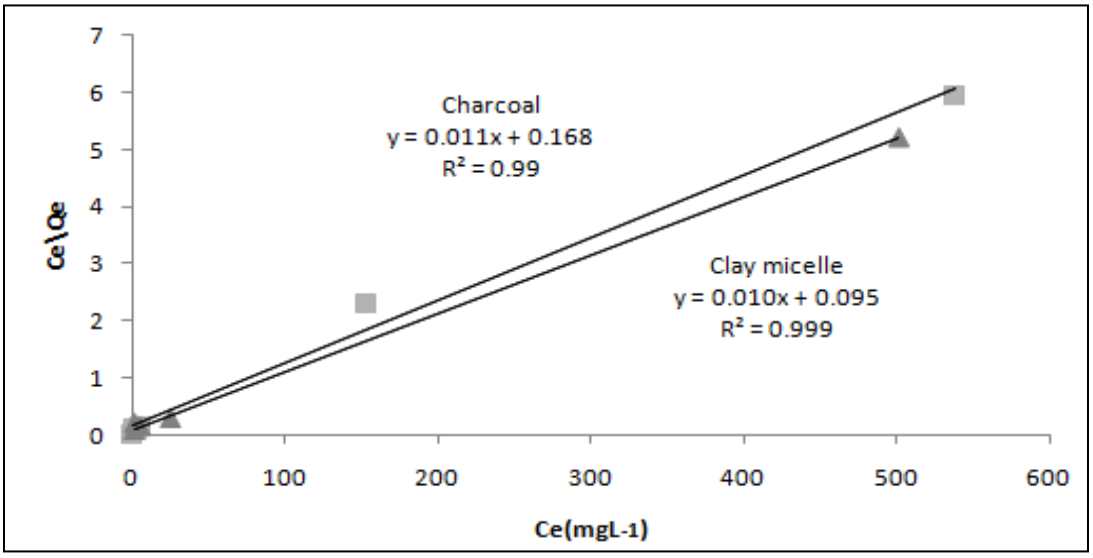

Fig. 25. Langmuir isotherms for the removal of mefenamic acid.

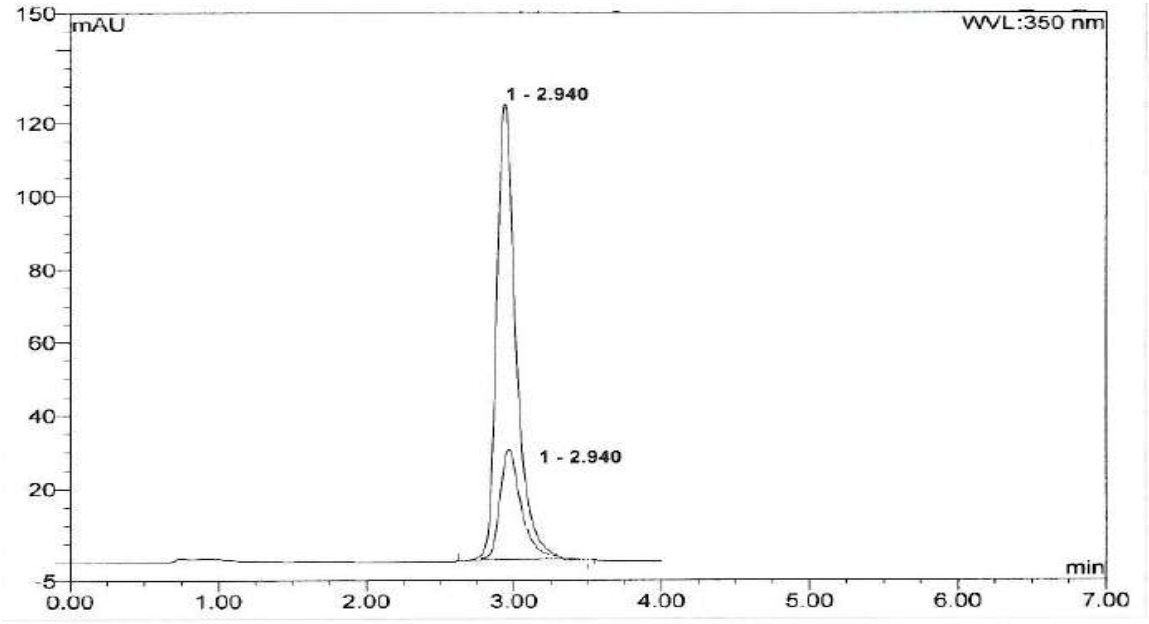

Fig. 26. Chromatogram showing the initial concentration of mefenamic acid before and after running the HF-UF point (Fig. 5).

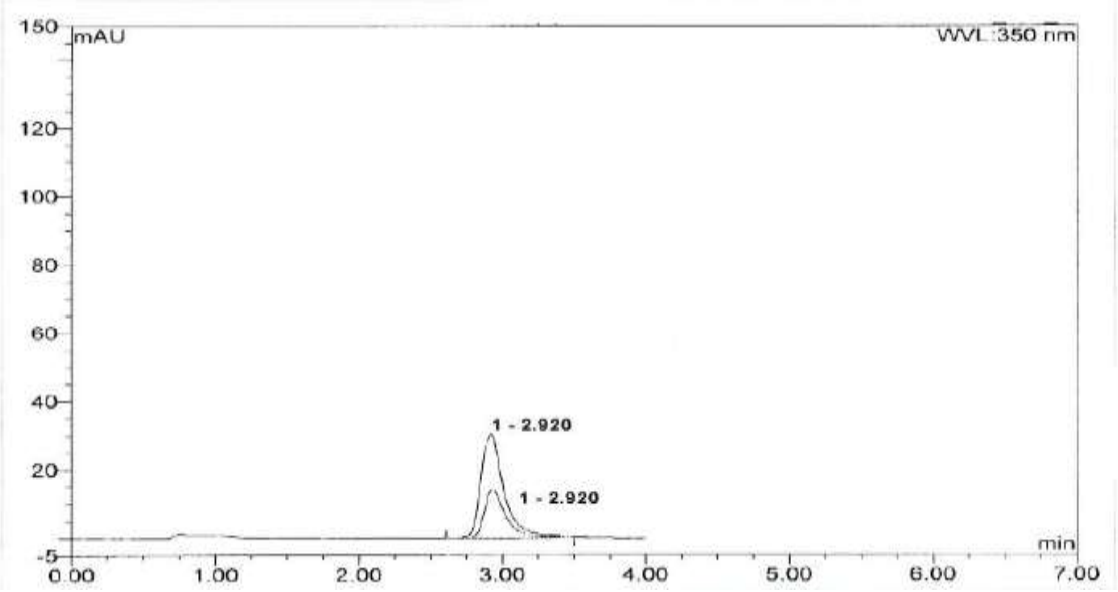

Fig. 27. Chromatogram showing the concentration of mefenamic acid before and after running the SW-UF point (Fig. 5).

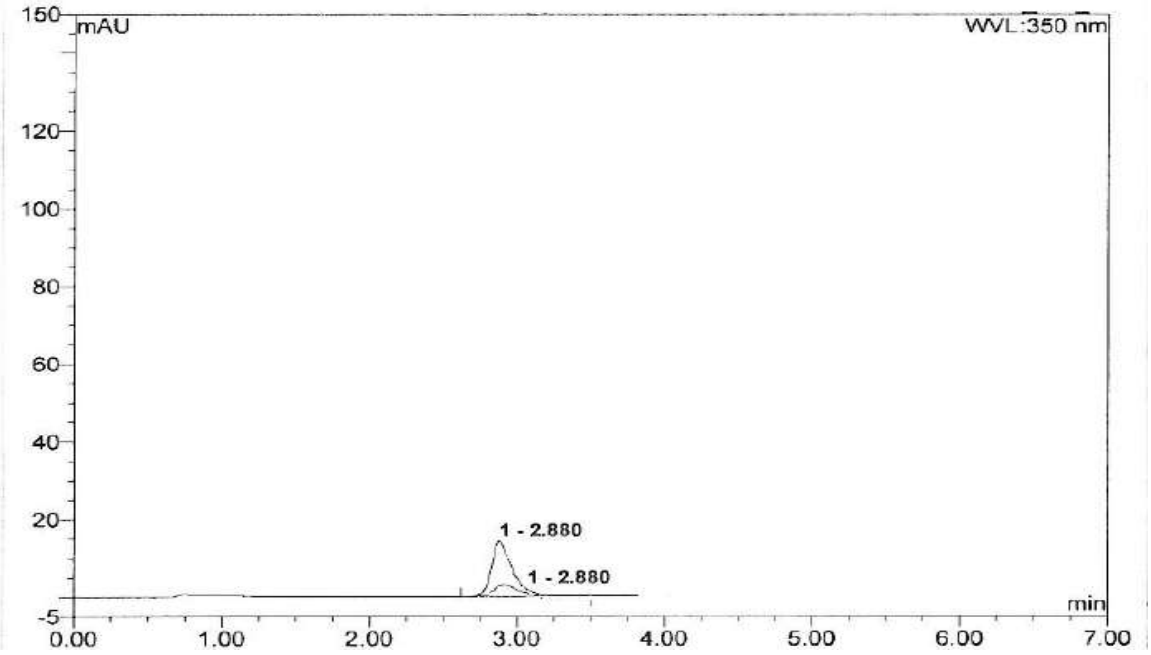

Fig. 28. Chromatogram showing the concentration of mefenamic acid before and after running activated charcoal adsorbent point (Fig. 5).

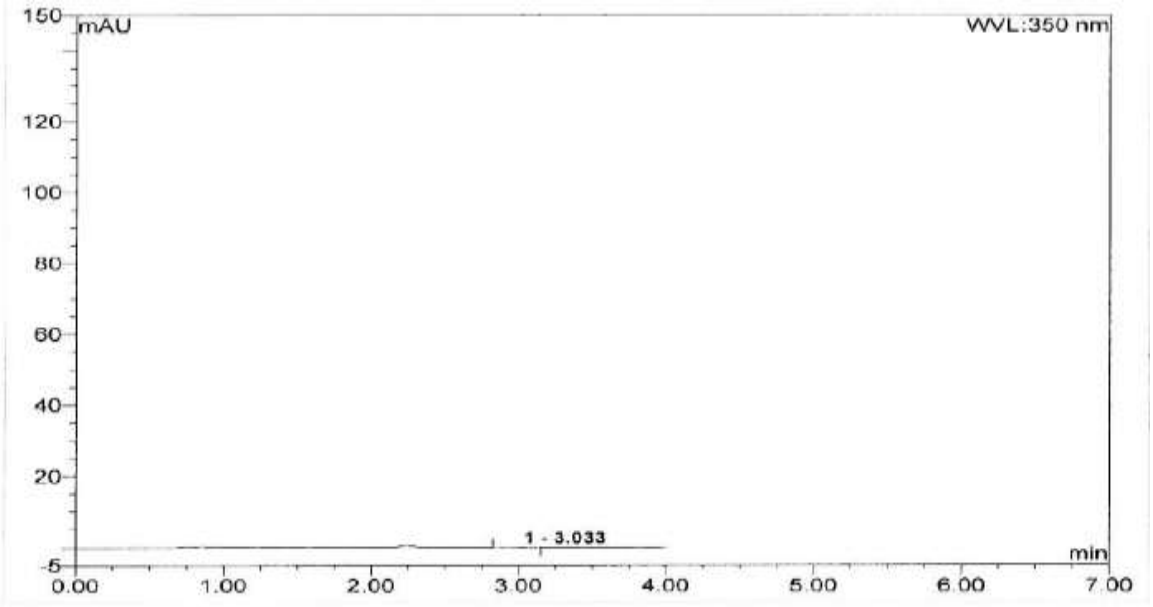

Fig. 29. Chromatogram showing the concentration of mefenamic acid after passing reverse osmosis (RO) membrane (Fig. 5).

Appendix B

Table 1. Langmuir adsorption parameters (K and Q_{max}) of ibuprofen onto clay micelle complex and activated charcoal adsorbents

Pharmaceutical	*Adsorbents*	*Langmuir*		
		K(L/mg)	**Q_{max} (mg/g)**	**R^2**
Ibuprofen	Clay micelle complex	0.64 ± 0.03	62.5 ± 0.68	0.998
	Charcoal	0.65 ±0.03	66.7 ± 0.35	0.999

* Results of K and Q_{max} are repeated as value ± SD; SD: standard deviation of three replicates

Table 2. Langmuir adsorption parameters (K and Qmax) of Mefenamic acid onto clay micelle complex and activated charcoal adsorbents.

Pharmaceutical	*Adsorbents*	*Langmuir*		
		K(L/mg)	**Q_{max} (mg/g)**	**R^2**
Mefenamic acid	Clay micelle complex	0.105 ± 0.004	100.0 ± 0.67	0.999
	Charcoal	0.065 ± 0.003	90.9 ± 0.74	0.99

* Results of K and Q_{max} are repeated as value ± SD; SD: standard deviation of three replicates

Supplementary data

Table S1. Wastewater treatment plants (WWTP) in the West Bank

Name of WWTP	Effluent Quantity m^3/d	Type of Treatment
Al Aroub	12-15	-Duckweed-based pond system -Small-scale biochemical system (JOHKASOU system) -Aeration tank
Birzeit University	100	-Screen -Equalization tank -Activated sludge -Sand filters
Deir-Samit-Hebron	40	-Sedimentation tank -Bio-filters
Ieensnya-Nablus	40	-Septic tank -Anaerobic filter
Nablus-west Salfit	25205	-Extended aeration
Kharas- Hebron	120	-Anaerobic stage -Wetlands -Sludge drying -Effluent storage tank
Sarha-Nablus	40	-Septic tank -Constructed wetland
Al-Bireh	3200	-Screening -Aeration tanks -Disinfection by UV radiation
Jenin	1500	-Aerated lagoon
Ramallah	1370	- Two aerated lagoons
Tulkarem	6742	-Stabilization ponds
Tafuh	1370	-Anaerobic rock filtration
Abu-Dees	2740	- Oxidation ditch
Halhul	2740	-Aerated pond system
Jarico	3290	----------
Biddya	3000	----------
Al-Ram	9000	-Aerobic sludge -Stabilization -Activated sludge

Table S2. Comparison of pressure-driven systems

Parameters	Membrane system			
	Low- pressure membrane		High- pressure membrane	
	Microfiltration (MF)	Ultrafiltration (UF)	Nanofiltration (NF)	Reverse Osmosis (RO)
Product particle size (µm)	0.08 to 2.0	0.005 to 0.2	0.001 to 0.01	0.0001 to 0.001
Retained compounds	Very small suspended particles, some colloids, most bacteria	Organic compounds > 1000 Da, pyrogen, viruses, bacteria, colloids	Organic compounds > 200 Da, some dissolved solids (i.e. multivalent ions)	Ions, Organic compounds >100 MW
Operating pressure, psi	1 to 15	30 to 100	80 to 125	≥ 1,000

Table S3. Percentage removal of ibuprofen by clay micelle complex (ODTMA) at pH 4.0.

No. sample	*Time (minutes)*	*% Removal*
1	0	0
2	5	59.3
3	10	59.7
4	20	59.0
5	30	59.6
6	40	59.1
7	50	58.8
8	60	58.4
9	80	58.2
10	100	59.8
11	120	59.1
12	150	59.2
13	180	59.6

Table S4. Percentage removal of ibuprofen by clay micelle complex (ODTMA) at pH 8.0.

No. sample	*Time (minutes)*	*% Removal*
1	0	0
2	5	83.8
3	10	84.6
4	20	86.0
5	30	86.7
6	40	86.3
7	50	87.2
8	60	87.2
9	80	88.7
10	100	87.6
11	120	88.2
12	150	88.4
13	180	90.3

Table S5. Percentage removal of ibuprofen by activated charcoal.

No. sample	*Time (minutes)*	*% Removal*
1	0	0
2	5	49.6
3	10	52.3
4	20	69.6
5	30	82.3
6	40	89.3
7	50	91.9
7	60	94.5
8	80	96.1
9	100	96.7
10	120	97.8
11	150	98.5
12	180	99.1

Table S6. Concentrations in equilibrium obtained for adsorption of ibuprofen onto the adsorbent clay micelle complex.

Conc. (initial) (mgL^{-1})	Mass (initial) (mg)	Conc. (final) (mgL^{-1}) (C_e)	Mass (final) (mg)	M initial - M final	Q_e= (M initial - M final) /0.5 g	C_e/Q_e
48.8 ppm	4.88	0.56 ppm	0.056	4.824	9.648	0.06
103.8 ppm	10.38	1.8 ppm	0.18	10.2	20.4	0.09
208.6 ppm	20.86	20.2 ppm	2.02	18.84	37.68	0.54
519.0 ppm	51.9	180.3 ppm	18.03	33.87	67.74	2.66
988.6 ppm	98.86	686.6 ppm	68.66	28.62	60.4	11.36

Table S7. Concentrations in equilibrium obtained for adsorption of ibuprofen onto the adsorbent activated charcoal.

Conc. (initial) (mgL^{-1})	Mass (initial) (mg)	Conc. (final) (mgL_{-1}) (Ce)	Mass (final) (mg)	M initial - M final	Qe= (M initial - M final) /0.5 g	Ce/Qe
52.0 ppm	5.2	0.28 ppm	0.028	5.172	10.344	0.027
86.4 ppm	8.64	2.4 ppm	0.24	8.4	16.8	0.14
184.6 ppm	18.46	1.6 ppm	0.16	18.3	36.6	0.043
394.8 ppm	39.48	36.9 ppm	3.69	35.8	71.6	0.52
835.6 ppm	83.56	513.3 ppm	51.33	32.23	64.46	8.0

Table S8. Removal of ibuprofen through the hollow fiber (UF-HF), spiral wound (UF-SW), activated carbon adsorbent and reverse osmosis from the wastewater treatment plant at Al-Quds university.

No.	Sample location name		Conc. of Ibuprofen (ppm) First trial	Conc. of Ibuprofen (ppm) Second trial	Conc. of Ibuprofen (ppm) Third trial
1	Blank (before addition of ibuprofen)		0	0	0
2	The initial concentration of ibuprofen in storage tank (after addition of ibuprofen)		37.1	42.4	40.0
3	HF-UF	*Feed point*	35.1	42.4	40.0
		Brine point	35.7	41.9	40.1
		Product point	9.7	15.3	23.4
4	HF-SW	*Concentrated UF point*	2.0	15.3	23.4
		Permeated UF point	1.1	4.4	1.0
5	Activated carbon point		0.27	0.37	0.83
6	Reverse osmosis (RO)	*Brine RO point*	0.24	0.04	0.82
		Permeated RO point	0.0	0.0	0.0

Table S9. Accumulative % removal of ibuprofen.

Trial No.	Hollow fiber (HF)	Spiral wound (SW)	Activated carbon	Reverse osmosis (RO)
1	73.9 %	97.1 %	99.3 %	99.8 %
2	63.9 %	89.6 %	99.1 %	100.0 %
3	41.5 %	97.5 %	97.9 %	99.9 %
Average	**59.8 %**	**94.7 %**	**98.8 %**	**99.9 %**
SD	**16.6**	**4.5**	**0.76**	**0.1**

Table S10. Percentage removal of mefenamic acid by ODTMA complex

No. sample	*Time (minutes)*	*% Removal*
1	0	Zero
2	5	96.9
3	10	97.2
4	20	98.5
5	30	98.9
6	40	98.1
7	50	98.1
7	60	97.5
8	80	98.1
9	100	98.0
10	120	97.9
11	150	97.3
12	180	97.3

Table S11. Percentage removal of mefenamic acid by charcoal.

No. sample	*Time (minutes)*	*% Removal*
1	0	Zero
2	5	28.4
3	10	37.2
4	20	51.9
5	30	60.9
6	40	60.9
7	50	74.2
7	60	78.9
8	80	85.3
9	100	90.0
10	120	93.0
11	150	96.3
12	180	97.2

Table S12. Concentrations in equilibrium obtained for adsorption of mefenamic acid onto the adsorbent clay micelle complex.

Conc. (initial) (mgL^{-1})	Mass (initial) (mg)	Conc. (final) (mgL^{-1}) (Ce)	Mass (final) (mg)	M initial - M final	Qe= (M initial - M final) /0.5 g	Ce/Qe
48.1	4.81	1.9	0.19	4.62	9.24	0.206
99.4	9.94	1.6	0.16	9.78	19.56	0.082
199.2	19.92	5.5	0.55	19.37	38.74	0.15
458.6	45.86	25.3	2.53	43.33	86.66	0.292
983	98.3	501	50.1	48.2	96.4	5.20

Table S13. Concentrations in equilibrium obtained for adsorption of mefenamic acid onto the adsorbent activated charcoal.

Conc. (initial) (mgL^{-1})	Mass (initial) (mg)	Conc. (final) (mgL^{-1}) (Ce)	Mass (final) (mg)	M initial - M final	Qe= (M initial - M final) /0.5 g	Ce/Qe
49.3	4.93	0.16	0.016	4.914	9.83	0.016
98.7	9.87	1.96	0.196	9.674	19.35	0.101
194.7	19.47	5.5	0.550	18.92	37.84	0.145
485.0	48.50	153.5	15.35	33.15	66.30	2.315
989.0	98.90	537.8	53.78	45.12	90.24	5.960

Table S14. Langmuir adsorption parameters (k and Qmax) of ibuprofen and mefenamic acid onto clay micelle complex and activated charcoal adsorbents.

Adsorbent	**Ibuprofen**		**Mefenamic acid**	
	k (L/mg)	**Q_{max} (mg/g)**	**k (L/mg)**	**Q_{max} (mg/g)**
Clay micelle complex	0.64 ± 0.03	62.5 ± 0.68	0.105 ± 0.004	100.0 ± 0.67
Charcoal	0.65 ±0.03	66.7 ± 0.35	0.065 ± 0.003	90.9 ± 0.74

Table S15. Removal of mefenamic acid by the hollow fiber (UF-HF), spiral wound (UF-SW), activated carbon adsorbent and reverse osmosis from the wastewater treatment plant.

No.	Sample location name		Conc. of Mefenamic acid (ppm) First trial	Conc. of Mefenamic acid (ppm) Second trial	Conc. of Mefenamic acid (ppm) Third trial
1	Blank (before addition of Mefenamic acid)		0	0	0
2	The initial concentration of Mefenamic acid in storage tank (after addition of Mefenamic acid)		42.0	40.0	39.5
3	HF-UF	*Feed point*	42.0	37.9	38.3
		Brine point	18.0	38.0	36.0
		Product point	1.1	11.3	18.4
4	HF-SW	*Concentrated UF point*	1.1	11.3	16.0
		Permeated UF point	0.15	1.94	4.7
5	Activated carbon point		0.12	0.73	0.60
6	Reverse osmosis (RO)	*Brine RO point*	0.45	0.72	0.60
		Permeated RO point	0.07	0.0	0.5

Table S16. Accumulative % removal of mefenamic acid.

Trial No.	Hollow fiber (HF)	Spiral wound (SW)	Activated carbon	Reverse osmosis (R.O)
1	97.8 %	99.6 %	99.7 %	99.8 %
2	71.8 %	95.2 %	98.2 %	100.0 %
3	53.4 %	88.1 %	98.5 %	98.7 %
Average	**74.3 %**	**94.3 %**	**98.8 %**	**99.5 %**
SD	**22.3**	**5.8**	**0.79**	**0.7**

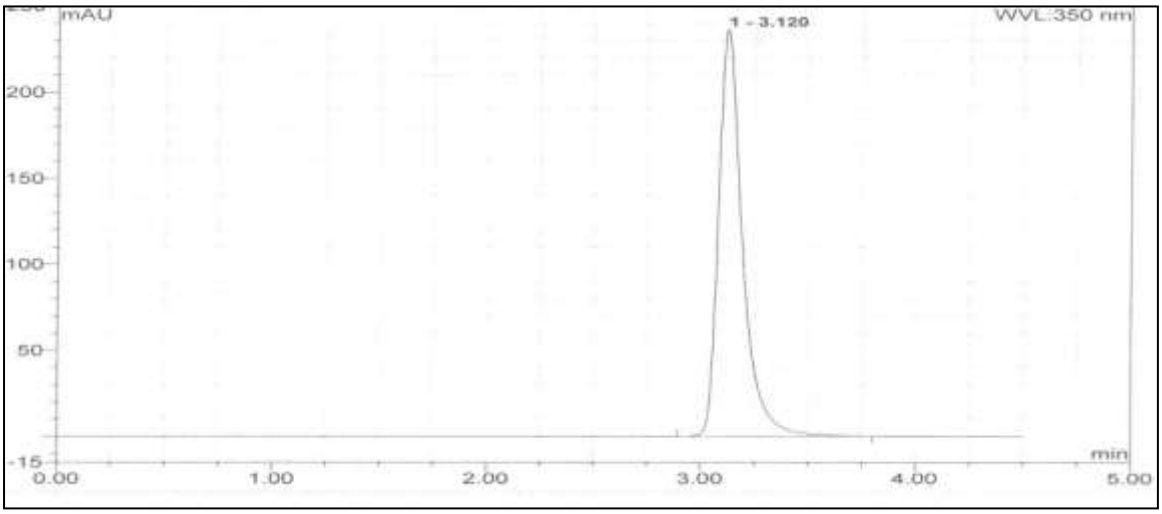

Fig. S1. Chromatogram showing mefenamic acid after 0 days in wastewater

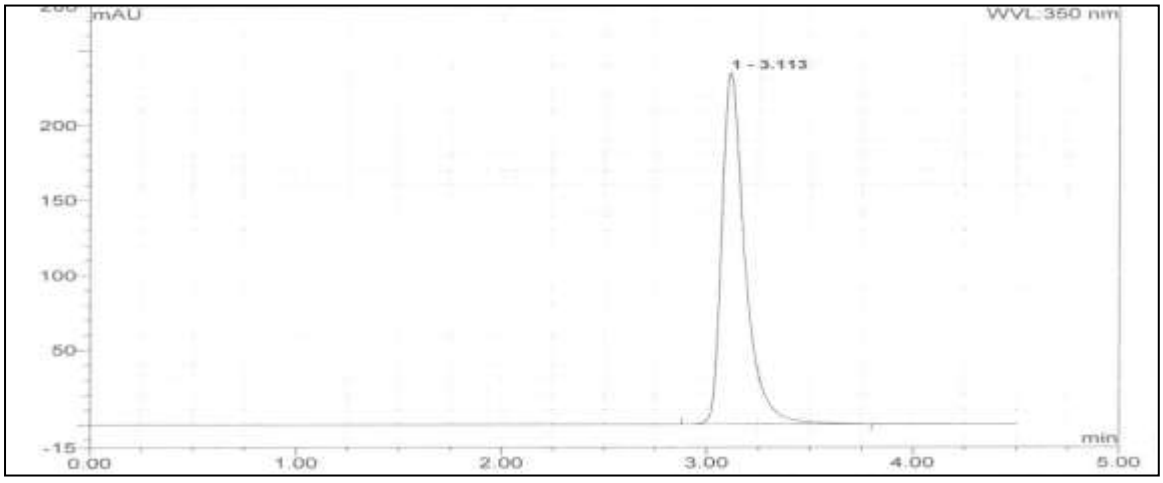

Fig. S2. Chromatogram showing mefenamic acid after 30 days in wastewater.