# Removal of Aspirin, Salicylic Acid, Paracetamol and *p*-Aminophenol by Advanced Membrane technology Activated Charcoal and Clay Micelles Complex.

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***Abstract:***
*The stability of aspirin and paracetamol in sludge and the efficiency of advanced nano-membrane technology towards their removal from wastewater were investigated. The kinetics study revealed that aspirin and paracetamol were degraded in wastewater to salicylic acid and p-aminophenol, respectively. The kinetics at room temperature for the degradation reactions of both pharmaceuticals was first order kinetics with rate constants of 0.845 × $10^{-8}$ $Ms^{-1}$ and1.0 × $10^{-8}$ $Ms^{-1}$, respectively. These values are about 10-foldhigher than those obtained for both pharmaceuticals in pure water under the same conditions. The performance of Al-Quds University wastewater treatment plant has shown complete removal of both pharmaceuticals from spiked wastewater within the detection limit of the analytical method. In addition, the adsorption isotherms for aspirin and paracetamol, and their metabolites were studied using both activated carbon and a clay-micelle complex. The isotherms were found to fit Langmuir isotherm.*
***Keywords:*** *Aspirin, Paracetamol, p-Aminophenol, Pharmaceuticals, Wastewater, Membrane technology, Activated carbon, Clay micelles complex.*

## 1. Introduction

### 1.1. Background

In the Middle East, in general, and Palestine, in particular, water resources are very limited and currently a serious shortage problem exists [1-3]. This situation would be aggravated in the future since the water balance gap between the available water supplies and the water demand, as a result of population growth, rapid urbanization and industrialization associated with living standards improvement,will increase. This gap cause serious shortage of fresh water to be used in human purposes, agricultural, and other non-human purposes, Hence, water contamination and the production of large volume of wastewater are the expected results [3-7]. The principal fresh water resources available to Palestinians include groundwater, surface water, and springs. Additional water sources include rainwater harvesting. Groundwater and springs are the main source of fresh water in Palestine [1, 4, 7-8]. Therefore, water must be used wisely and efficiently not only to control the consumptive use of water but also to reduce the wastewater flows. Due to the expected increase in volume of wastewater in combination with a serious problem from its disposal, treatment and recycling of wastewater is critical when looking for new sources of water in water-scarce regions (Flow chart S1, Supplementary Data). Hence, wastewater flows must be managed effectively to prevent pollution and to protect the environment from hazardous chemical and biological pollutants. The purpose of wastewater treatment is generally to allow human and industrial effluents to be disposed without causing a danger neither to human health nor to the environment. The reuse of reclaimed wastewater in Palestine is a major priority, as confirmed by the Palestinian Water Policy recently adopted by the Palestinian Water Authority (PWA) and the Ministry of Agriculture [4, 7]. In addition, the Palestinian National Authority (PNA) has concern for the protection of the environment through the Ministry of Environmental Affairs (MENA) [4].

#### 1.1.1. Wastewater management in Palestine

Wastewater is one of the major sources of pollution that has serious adverse impact both on the environment and local residents. The wastewater sector status in Palestine is characterized by poor sanitation, different wastewater quality, insufficient treatment, and unsafe disposal of untreated or partially treated wastewater into the environment. Sewage collection networks in the West Bank are limited to major cities and to certain portions of these municipalities. Most of them are poorly designed and old [4, 9]. Therefore, the situation of the sewerage system is extremely critical [10]. Wastewater management in Palestine had been neglected for decades. Meanwhile, wastewater management is a tool to maintain environmental integrity, promote health, and protect from diseases[11]. No comprehensive data on wastewater characteristics and amounts discharged are yet available [12]. The effectiveness of the existing urban sewage collection and treatment facilities is usually constrained by limited capacity, poor maintenance, process malfunction, poor maintenance practices, and lack of experienced or properly trained staff [13-14].

Generally, treated wastewater has a long history of applications and can serve many purposes for which fresh water is used, primarily in agriculture, and additional areas of applications, including industrial, and domestic if undergo suitable treatment [15]. To ensure sustainable and successful wastewater reuse applications, the following requirements must be fulfilled [16-17]: (1) The potential public health risk associated with wastewater reuse are evaluated and minimized and (2) the specific water reuse applications meet the water quality objectives. Presently, raw or partially treated wastewater in many areas in Palestine is discharged to the

wades where it is used for irrigation purposes. Several studies have shown that the reuse of treated effluents for irrigated agriculture is possible in most areas in Palestine. However these projects are still on the pilot-scale. In general, Palestinians farmers lack the proper experience in using this resource in a safe way [2-6, 12-14, 18-21]. The reuse of treated wastewater must be combined with strategies to prevent health risks and environment from pathogens, heavy metals, pesticides, personal care products (PCPs), pharmaceuticals and endocrine disrupters. Therefore, the Palestinian Water Authority (PWA), the regulator of water sector, has newly developed national guidelines based on recommended rules issued by the World Health Organization (WHO) to ensure protection of public health and the environment from the discharge of untreated or inadequately treated wastewater effluents [22-23]. Development of appropriate and sustainable sewage treatment technologies will help to preserve biodiversity, maintain healthy environment and save freshwater supply [7]. Among the different treatment systems now available worldwide, the main types of treatment plant are used in Palestine: (i) stabilization ponds for small communities [4-5]; (ii) trickling filter [4-5]; (iii) oxidation ditches [4-5]; and (iii) activated sludge or extended aerated activated sludge for a large scale community [4-5]. Table S1 (Supplementary Data) lists the current status of the existing and planned wastewater treatment plants in the West Bank [4].

### 1.2. Definition of wastewater and its characteristics

Wastewater is defined as the liquid effluents which are discharged from a community after it has been contaminated by various ways. It is usually generated from residences, institutions, commercial, industrial establishments, and surface and ground water [17]. Wastewater consists of 99 percent water by weight and the remaining one percent includes suspended and dissolved organic and inorganic substances as well as microorganism [24].The wastewater from residences, institutions, commercial places, and farms are referred to as domestic wastewaters [25]. Domestic wastewater, or "sewage", can also be divided into two groups; black-water which is basically wastewater from toilets (urine and etc.) and grey-water refers to the household wastewater which has not been contaminated by toilet waste and which originates from bathrooms and laundries. Grey-water constitutes the largest flow of wastewater [26]. Industrial wastewater generated from industries varies in flow and composition depending on the type of industries. A combination of domestic and industrial wastewaters often referred to as municipal wastewater [17, 24-27]. Wastewater is characterized in terms of its physical, chemical, and biological composition [28]. Physical parameters include total solid contents, particle size distribution, turbidity, temperature, conductivity, transmittance, density, color, and odor. Total solid contents are subdivided into total suspended solids (TSS) and total dissolved solids (TDS). Chemical parameters associated with the organic content of wastewater include biochemical oxygen demand (BOD), chemical oxygen demand (COD), total organic carbon (TOC), and total oxygen demand (TOD). Inorganic chemical parameters include salinity, hardness, pH, acidity and alkalinity, as well as concentrations of ionized metals such as iron and manganese, and anionic entities such as chlorides, sulfates, sulfides, nitrates, and phosphates. Bacteriological parameters include coliforms, fecal coliforms, specific pathogens, and viruses [17,28].

### 1.3.Overview of wastewater treatment

Wastewater treatment is the process of removing varying amounts of contaminants from wastewater, depending on the level and type of treatment they provide. Its objective is to optimize the benefits of wastewater as a resource of both water and nutrients, and to ensure protection of public health and the environment from the discharge of untreated or inadequately treated wastewater effluents [29]. Also, in wastewater reclamation and reuse, water quality requirements may call for reduction in suspended solids, total dissolved solids, pathogenic microorganism (i.e. bacteria, protozoan, and viruses), as well as selected constituents such as nitrates, chlorides, and natural and synthetic organic compounds [17].

#### 1.3.1. Wastewater treatment plant process

Wastewater treatment process includes physical, chemical, and biological units to remove physical, chemical, and biological contaminants. Typically, wastewater treatment process (Flow chart S2, Supplementary Data) can be broken down into four basic steps: preliminary, primary, secondary, and tertiary. These treatments are to achieve different levels of contaminant removal. Primary and secondary unit operations and processes are called conventional wastewater treatment. After conventional wastewater treatment, tertiary (advanced treatment) treatment improves the quality of secondary wastewater and produces an effluent that can be used as a substitute of freshwater sources for household and industrial needs [17,28,30-31]. The initial steps are collectively known as preliminary treatment, in which oils, grease, fats and gross objects such as large objects, rags, and grit are removed through combination of screening and settling by gravity [17,30]. Primary treatment involves partial removal of suspended solids and organic matter found in wastewater by means of physical operations such as screening and sedimentation prior to biological treatment. Primary treatment acts as a precursor for 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 processes. In secondary treatment unit, three types of technologies can be applied to break down organic material with agitation and aeration. These are: activated sludge process, trickling filters, and lagoon systems [17,30]. The activated sludge process use a variety of mechanisms to utilize dissolved oxygen to promote the growth of a biological flock that substantially breaks down and removes organic material, then allows these solid flocks to settle out. Bacteria-containing "activated sludge" is continually re-circulated back to the aeration basin to increase the rate of organic decomposition [27,32]. After primary and secondary treatment, several physical–chemical processes have been investigated as tertiary treatment of secondary effluents, including ozonation [33], photo-catalytic degradation of recalcitrant compounds ($UV/TiO_2$) [33], and adsorption [28, 31-

[32]. Tertiary treatment is often performed by a sequence of coagulation/flocculation, membrane filtration, and disinfection [31]. The effluents obtained from the combination of tertiary treatment processes are generally of good quality and can be used in different sectors: industry, agriculture, and urban consumption. This treated wastewater contains low concentrations of organic matter, inorganic ions (nitrates, sulfates and phosphates), and pathogenic microorganism which meets the requirements for the reuse criteria for wastewater so that it minimizes its potential negative impact on public health and to reduce environmental damage [31,34]. Any settled solids (sludge) from any treatment process are given further treatment and undergone several options for disposal [17,24]. Application of sewage sludge to agricultural land may be beneficial because it can improve and maintain productive soils which may enhance plant growth. In addition, the use of sludge as a fertilizer would decrease the amounts of chemical fertilizers needed in agriculture [17,24,35].

**1.3.2. Membrane filtration**

Membranes filtration are frequently used for tertiary treatment of wastewater before discharge to surface water, recover materials in industry before they enter waste streams, and to treat waters for potable use [36]. Nowadays, membrane processes can play a key role in reducing water scarcity mainly in areas with scarce water supplies. These membranes are also increasingly being considered as essential additions to conventional water and wastewater treatment methods in anticipation of future demands for high standards and reduced environmental impact [31-40]. Membranes are semi-permeable barriers that are used to separate and remove constituents from a fluid stream ranging from large visible particles to molecular and ionic chemical species including bacteria, viruses, and other pathogenic microorganisms [17, 36]. In membrane separation process, the feed water is separated into a stream that can pass through the membrane, i.e., permeate and a fraction of feed that cannot pass through the membrane, i.e., the concentrate. Membrane process can be classified in terms of the size of the membrane pores or molecular weight cutoff (MWCO) which specifies the maximum molecular weight of solute to be rejected, the separation mechanism, the nature of the driving force, the chemical structure and composition of membranes, and the geometry of construction [36]. A schematic representation of a membrane separation process is given in (Flow chart S3, Supplementary Data).

**1.3.2.1. Types of membranes**

Most commercial membrane modules are manufactured in four configurations as spiral wound, hollow fibers, plate-and-frame, and tubular [41-42]. The principal types of membrane modules used for water and wastewater treatment are hollow fiber and spiral wound [17, 43]. In a hollow fiber element (Figure 1a, Appendix), fibers made of porous polymer material are bundled together and sealed in a cylindrical pressure vessel. The feed flows into the module, the permeate flows into or out of the hollow fibers and is collected, while the retentate exits the module for further treatment [42]. As shown in (Figure 1b, appendix), spiral wound elements consist of two flat membrane sheets separated by a thin, mesh-like porous support or spacer and are sealed on three sides like an envelope. The fourth side is fixed onto a perforated plastic center tube that collects the product water (permeate). The membranes are rolled up around the tube in the form of a spiral. Feed water is pumped through the layers and the product water (permeate) passes through the membrane into the permeate spacer and then is collected in the central perforated collection tube. The retentate exits from the feed spacers at the opposite end of the spiral sheet. Hollow fiber and spiral elements are used for microfiltration (MF), ultrafiltration (UF), and reverse osmosis (RO) [42]. The driving force for membrane process can be external pressure, electrical potential gradient [17, 36], concentration gradient [17, 36], or other driving forces. The most commonly used membrane systems in water and wastewater treatment are pressure-driven membranes, therefore, most of the discussion in this section focuses on them. Pressure-driven membrane processes are typically classified into four common categories depending on their pore size: microfiltration (MF), ultrafiltration (UF), nanofiltration (NF), and reverse osmosis (RO) [36, 38, 41-43]. The various pressures-driven membrane processes and their separation characteristics are shown in Table S2 (Supplementary Data).

**1.3.2.1.1. Microfiltration (MF) and Ultrafiltration (UF)**

Low-pressure driven membranes (LPMs) include MF and UF which are typically operated under trans-membrane pressures of 100 pound per square inch (psi) or less (700 kPa). They are characterized by their ability to reduce turbidity, and remove suspended or colloidal particles *via* sieving mechanism. In wastewater reclamation, MF and UF are considered as a pretreatment step for RO and NF, so that fouling potential of the less permeable membranes is minimized and can be realized. MF have a pore size ranging between approximately 0.08-2.0µm, although there are exceptions, as MF with pores sizes of up to 10µm are available, with MWCO greater than of approximately 100 kD (D; g $mol^{-1}$). While UF pore size generally ranges from 0.005- 0.2µm, with MWCO of approximately 10 to 100 kD. UF membranes are designed to remove dissolved macromolecules solutes from feed water, such as colloids, proteins, and carbohydrates. Therefore, UF offers higher removals efficiency than the MF; however, UF membranes do not remove ultra small substances such as sugar and salts [17,36,37,41].

**1.3.2.1.2. Nanofiltration (NF) and Reverse Osmosis (RO)**

High-pressure driven membranes (HPMs) generally refer to NF and RO which are required for the removal of ultra-small dissolved contaminants via a softening or desalination mechanisms. NF also called "membrane softening" is designed for the removal of selected dissolved constituents from wastewater such as multivalent ions (i.e. calcium and magnesium) responsible for water hardness [17]. RO is used primarily for desalination, in which water is transferred through a dense membrane to retain salts and low molecular weight solutes [17, 36, 41]. Therefore, pushing water through membrane pores requires a higher operating pressure than MF and UF. The required operating pressure can range from less than 150 psi (1000 kPa) for some NF applications to more

than 1,000 psi (7000kPa) for RO. Commercially available HPMs employed in wastewater reclamation usually have small pore sizes ranging between approximately 0.01-0.001µm and between 0.001-0.0001µm for NF and for RO membranes, respectively. With this ultra small pore size, the attainable range of MWCO levels is less than 100 D for RO membranes and between 200 and 1,000 D for NF membranes [16, 39]. Reverse osmosis (Figure 2, Appendix) is the reversal of the natural osmotic process, accomplished by applying pressure in excess of the osmotic pressure to the more concentrated solution. This pressure forces the water through the membrane against the natural osmotic gradient, thereby increasingly concentrating the water on one side (i.e., the feed) of the membrane and increasing the volume of water with a lower concentration of dissolved solids on the opposite side (i.e., the filtrate or permeate) [17,42].

### 1.4. Occurrence of Pharmaceuticals in wastewater

In recent years, the occurrence of pharmaceuticals and personal care products (PPCPs) and their metabolites in the aquatic environment has been recognized as being an important part of the chemicals that are present in low concentrations in the environment. A variety of pharmaceuticals have been detected in many environmental samples worldwide. Their occurrence has been reported in sewage treatment plant effluents, surface water, seawater, groundwater, soil, sediment and fish [44-51].

#### 1.4.1. Pharmaceuticals and personal care products (PPCPs) Background

Pharmaceutically active compounds (sometimes called active pharmaceutical ingredients or APIs) cover a wide-range of compounds with substantial variability in structures, function, behavior and activity, in which they are developed and designed to interfere with biological systems, and have an important role in diagnosis, treatment, prevention the disease, health conditions, or functions of human body and/or animals [44, 51]. These substances include both inorganic and organic compounds, although most of the modern pharmaceuticals are small organic compounds with a molecular weight below 500 Daltons. These chemicals are moderately water soluble as well as lipophilic to be bioavailable and biologically active [52]. Pharmaceuticals are produced and used in increasingly large volumes every year [53]. Examples of pharmaceutical compounds include antipyretics, analgesics, blood lipid regulators, antibiotics, antidepressants, chemotherapy agents, and contraceptive drugs. Personal care products (PCPs) are defined as chemicals marketed for direct use by the consumer in order to alter odor, appearance, and touch without displaying significant biochemical activity (except over-the-counter, OTC, medications) and having intended end uses primarily on the human body (products not intended for ingestion with exception of food supplements) [44]. They include cosmetics, bath additives, shampoo, skin care products, oral hygiene products, hair sprays, sun screens, hair dyes, deodorants, perfumes, soaps, fragrances, veterinary drugs, insect repellents and lotions. The expectations of the amounts of these products will continue to increase due to the increase in the standards of living as reflected by the improvement in the health care system and longer life expectancy. The term endocrine disrupters (EDs) refer, in general, to the synthetic chemicals and natural compounds that may affect the endocrine system (the communication system of glands, hormones, and cellular receptors) that control the body's internal functions [54]. Endocrine disrupters has recently attracted much attention since many of these disrupters cause negative reproductive and developmental health effects for the human or animals and its offspring [55-56].

#### 1.4.2. Analytical methods

Although pharmaceuticals and endocrine disrupters have been detected in a wide variety of environmental samples including wastewater effluents, rivers, lakes, surface waters, groundwater and drinking water for decades, researchers have recently begun to quantify their levels in the environment due to the development of new analytical technologies that result in the detection of minute traces of pharmaceuticals and other organic chemicals [57]. These analytical methods have become sufficiently sensitive to identify and quantify their presence in wastewater treatment plant (WWTP) effluents, surface waters, drinking water, and ground water. Investigations carried out in many countries have detected more than 80 pharmaceuticals, their metabolites, and pharmaceuticals care products in aquatic environment at concentrations in the range of mg\L to ng\L levels [58-59]. Reported compounds include wide range of classes of pharmaceuticals: Analgesics, anti-inflammatory compounds, beta-blockers, lipid regulators, anti-epileptics, antibiotics, x-ray media contrast agents, cytostatic agents, and contraceptives [59].

Because PPCPs and EDs represent structurally diverse classes of compounds, the different analytical methods have been used and applied for identification and quantification of these chemicals in water samples. The measurement of these compounds in water most commonly consist of an extraction of the chemicals from water, concentration of the resulting extract, and chromatographic separation by gas or liquid chromatography followed by high sensitivity and detection. Due to the complexity of wastewater samples, the extraction techniques such as liquid-liquid and steam distillation have been used to extract these compounds from wastewater and water, however solid phase extraction (SPE) is the most common technique employed for sample enrichment. Variations of SPE include solid phase micro-extraction (SPME) and various on-line and automated SPE techniques [60-61].

#### 1.4.2. Sources in the environment

After the administration, drug molecules are absorbed, distributed, metabolized, and finally excreted from the body. To be used safely most of the pharmaceuticals are designed in a way to undergo metabolism (enzymatic transformations) in organs such as liver, intestine, kidney, and lungs after they have achieved desired pharmacological effects. In most cases, pharmaceuticals are excreted as one or several metabolites. These metabolites are typically the result of either phase 1 or phase 2 metabolic reactions [62]. They excreted to the sewer system *via* urine and feces and reach WWTPs where they do not undergo further degradation to a satisfactory degree.

Hence, WWTPs play a key role in the introduction of pharmaceuticals into the environment. Veterinary and human pharmaceuticals and their metabolites enter the environment by two main pathways. The first is *via* the effluents from wastewater treatment plants (WWTPs) (Flow chart S4, Supplementary Data)[53]. The second route by which pharmaceuticals can enter the environment is by the disposal of unwanted medicines and/or medications that have expired and ended in the sink/toilet or in household waste which subsequently are taken to landfill sites (Flow chart S4, Supplementary Data) [53]. Entry into the environment by this route is dependent on the habits of the society and level of education.

### 1.4.3. Physicochemical properties

The fate of organic substance, once released in the environment is determined by their physicochemical and biodegradability properties, water solubility, hydrophobicity, and tendency to volatilize [63].These properties will influence whether compounds will remain in the aqueous phase or adsorb to sewage sludge. The tendency for organic compounds to accumulate in sludge solids can be assessed using octanol-water Partition Coefficient $K_{ow}$ (or log P). Table S3, (Supplementary Data) shows the adsorption potential of organic substances depending on their $K_{ow}$ values [64].

### 1.4.4 Environmental occurrence, fate, and removal of PPCPs

Many scientific articles clearly document the release of PPCPs into the environment, and their presence in ground water, surface waters, and wastewater treatment plant effluents. Furthermore, the occurrence, fate and the concentration of these pharmaceuticals in the environments were also documented [44-51, 53, 55, 56]. Currently, intensive research is underway to investigate the effect of human and animal's medications on the environments. A brief summary of relevant studies in this field is outlined in the following paragraph. A very comprehensive review is given by Daughton and Ternes about the occurrence, fate and causes of PPCPs in aquatic environment. They concluded, in 1999, that the most frequently PPCPs found in environmental sample are acetaminophen, acetylsalicylic acid, betaxol, bezafibrate, biphenylol, bisoprolol, carazolol, carbamazepine, and chlorophene [44]. Studies on tertiary wastewater treatment plant effluents and nearby wells and creeks in the Sequim-Dungeness area of northwest Washington detected 16 compounds in wastewater samples. These compounds are acetaminophen, caffeine, carbamazebine, cimetidine, codeine, cotinine (metabolite of nicotine), diltiazem, hydrocodone, ketoprofen, metformin, nicotine, paraxanthine, salbutamol, sulfamethoxazole, trimethoprim, and estrone [58]. Kolpin *et al.* provided the first U.S nationwide reconnaissance of the occurrence of pharmaceuticals, hormones, and other organic wastewater contaminants (OWCs) in streams. The U.S Geological Survey (USGS) found 80% of the sampled streams contained organic contaminants, and the compounds most frequently detected were pharmaceuticals. The most frequently detected compounds are steroids (including cholesterol), nonprescription drugs (such as caffeine, nicotine metabolites, and pain relievers), triclosan (antiseptic), and DEET (*N*,*N*-Diethyl-*meta*-toluamide is the most common active ingredient in many insect repellents) [49]. Other Studies indicate that PPCPs are already harming wildlife at levels found in water and have shown a potential negative effects on fish, plants, algae, bacteria, earthworm, and dung invertebrates [57]. Example of negative impacts of EDs to aquatic organism is the contribution of synthetic estrogens, also known endocrine disruptors, to the feminization of male fish in waters receiving treated wastewater effluents [56, 65]. On the other hand, it was proven that drinking water contaminated by wastewater is a potential source of exposure to mammary carcinogens and endocrine disrupting compounds from commercial products, natural as well as pharmaceutical hormones. These contaminants are hypothesized to increase breast cancer risk [66]. Also, it has been reported that the effect of the pharmaceuticals and Edson human body are: reduction of the amount of sperm, increase of the incidence of testicle and prostate cancers; and increased endometriosis [67].

Although concentrations of many pharmaceuticals residues in potable drinking water are so low that they do not pose high risks to human beings [68], the main concern is the chronic and/or synergistic effects of the "cocktail" of pharmaceuticals that humans have released to water-body. Some published reports raised issues related to the possible development of antibiotic-resistant bacteria upon exposure to untreated hospital and domestic sewage effluent [69], the genotoxic effects of some drugs [70], and endocrine disruption by therapeutically administered synthetic and natural hormones [48, 70-72].

Effluents from wastewater treatment plants can be considered as one of the most important sources of pharmaceuticals in the environment [44, 73-74]; therefore, the need for wastewater treatment technologies is required and plays an important role in removing pharmaceuticals and other contaminants [45]. Effective treatment technologies are also needed in order to ensure a safe use for reclaimed wastewater because Palestine suffers from an increase demand for water due to the rising population with very limited resources for water supply [1-3]. The methods of treatment used for the removal of pharmaceuticals from wastewater are the following: (1) biodegradation: biological degradation (aerobic/anaerobic by micro-organisms) of drug substances leading to a reduction of the parent compounds and/or their metabolites during wastewater treatment. (2) Deconjugation: conjugates of organic compounds such as steroid hormones have been shown to be readily deconjugated in domestic wastewater and within sewage treatment plants (STPs) due to the large amounts of β-glucuridase enzyme present (produced by the fecal bacterium Eacherichia coli). It seems probable that glucuronide and sulfate conjugates of drug compounds will be degraded by the same process. The effect will be to increase the excreted contribution of the active drugs to sewage and effluents. (3) Partitioning: Partitioning between the aqueous and organic biomass phases is a key component in determining the ultimate concentrations of organic pollutants. Compounds with high log P (lipophilic molecules) values are known sorbed 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. (4) Removal during sludge treatment: drugs may also be degraded by abiotic process (hydrolysis) during sewage treatment processes. Many pharmaceuticals are not thermally stable and so might be expected to break down during processes such as composting due to heat (as well as chemical and biodegradation). (5) Photodegradation: several pharmaceutical compounds have been shown to degrade due to the action of sunlight. The most extensively studied of these compounds is the analgesic/anti-inflammatory drug diclofenac, which has been shown to degrade in the aquatic environment due to ultraviolet (UV) light [74-75].

Because of an incomplete elimination in wastewater-treatment plants, residues of many toxic organic compounds, including pharmaceutical products, are also found in surface waters. Advanced treatments have to be considered to overcome this problem. Several processes have been studied to remove pharmaceuticals from water. Researchers reported a significant efficiency of nanofiltration and reverse osmosis membrane filtration [74], advanced oxidation processes [72] and activated carbon adsorption [74-75].

In Palestine, this study is the first to report on the removal of pharmaceuticals by ultrafiltration membranes (hollow fiber and spiral wound), their adsorption by activated carbon and clay-micelle filters, and removal by reverse osmosis technology.

The main goal of this research study is to investigate the performance of advanced treatment technologies which include integration between activated sludge process with ultra-filtration membranes (hollow fiber and spiral wound membranes), activated carbon adsorbent, micelle-clay filters, and reverse osmosis in terms of removal of aspirin (acetylsalicylic acid) and paracetamol (acetaminophen). The wastewater treatment plant located at Al-Quds University main campus in Abu-Dies is made from such integrations and samples will be taken from different compartments of this plant. Aspirin and paracetamol are chosen since both pharmaceuticals are widely consumed and are found to be frequently used medicines in Palestine.

The sub-goals of this study are: (i) identifying the most popular drugs prescribed in Palestine and preparing a ranking list of these drugs and (ii) studying the stability of aspirin and paracetamol in pure water and in presence of sludge.

## 2. Experimental

### 2.1. Identification of the most popular drugs in Palestine

In the first stage of this study, we have evaluated the most popular drugs in Palestine by conducting a search on 7000 members of Kubat Holeim Klalit using "Omri" program. This program stores the medication files for all population in Israel and East Jerusalem [76].

### 2.2. Instrumentation

#### 2.2.1. High Pressure Liquid Chromatography

High Pressure Liquid Chromatography (HPLC-PDA) system consists of an alliance 2695 HPLC from (Waters: Israel), and a waters Micromass® Masslynx ™ detector with Photo diode array (PDA) (Waters 2996: Israel). Data acquisition and control were carried out using Empower ™ software (Waters: Israel). Analytes were separated on a 4.6mm x150mm C18 XBridge ® column (5 µm particle size) used in conjunction with a 4.6mmx20 µm XBridge ™ C18 guard column. Microfilter was used with 0.45µm (Acrodisc® GHP, Waters).

#### 2.2.2. UV-Spectrophotometer

The concentrations of samples were determined spectrophotometrically (UV-spectrophotometer, Model: UV-1601, Shimadzu, Japan) by monitoring the absorbance at $\lambda_{max}$ for each drug.

#### 2.2.3. pH meter

pH values were recorded onpH meter model HM-30G: TOA electronics ™ was used in this study to measure the pH value for each sample.

#### 2.2.4. Centrifuge and Shaker

Labofuge®200 Centrifuge was used, 230 V 50/60 Hz. CAT. No. 284811. Made in 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.

#### 2.2.5. 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 ultrafiltration membrane (Hollow fiber and Spiral wound). After the ultrafiltration 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 ultrafiltration process is made of two small scale membrane treatment plants with a capacity of 12 $m^3$ /day. The first UF unit is equipped with 2x4 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 1.5$m^3$/h. The reverse osmosis (RO) membranes are 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.). Membrane 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.

**2.3. Chemicals and Reagents**

Pure standards (>99 %) of aspirin, salicylic acid, paracetamol and *p*-aminophenol are commercially available (Sigma–Aldrich). Methanol and water are both HPLC grade and purchased from Sigma Aldrich. Magnesium sulfate and Charcoal were purchased from Sigma-Aldrich. Octadecyltriethylammonium clay-micelle complex (ODTMA) was obtained as a gift[77]from Professor Nir at the Hebrew University. High purity diethyl ether (>99%) was purchased from Biolab, Hydrochloric acid (37%), and orthophosphoric acid (OPA) were obtained from Riedel-De Haen. Tap water was filtered using 0.22µm filter.

**2.4. Methods (aspirin and salicylic acid)**

**2.4.1. Sample and standards preparation**

**(a) Stock solution**: Stock solution was prepared by dissolving aspirin and salicylic acid standards in a mixture of methanol: water that adjusted to pH 3.45 in a ratio (45:55 v\v) to a concentration of 200 ppm for the use in (b).

**(b) Calibration curves**: A 200 ml stock solution of 1:1 mixture of aspirin and salicylic acid with a final concentration of 200 ppm was prepared in the same manner as for (a). The following diluted solutions were prepared from the stock solution: 1, 2, 3, 5, 10, 20, 40, 60, 100, 120, 140, and 160 ppm. Then, each diluted solution was extracted three times with ether. The ether extracts were combined, dried with anhydrous magnesium sulfate ($MgSO_4$), filtered and evaporated. For HPLC-PDA analysis, the dried residue after evaporated ether was dissolved with methanol: water (adjusted to pH 3.45) (45:55 v\v) and was injected to the HPLC apparatus.

**2.4.2. Kinetic studies on the stability of aspirin in pure water and wastewater**

**(a) Kinetic study on the stability of aspirin in pure water:** For the hydrolysis reaction of aspirin in pure water, a 500 ppm solution was used. The reaction progress was followed by monitoring the disappearance of aspirin and the appearance of salicylic acid with time at ($20^o$ C) using the HPLC method.

**(b) Kinetic study on the stability of aspirin in presence of sludge:** The same procedure as described in (a) was used for the hydrolysis of aspirin in the presence of sludge. However, in this case water was replaced with a suspended sludge in plain water at $20^o$ C.

Samples at specific time intervals were taken. Then, the sample aqueous layer was extracted three times with ether. The ether extracts were combined, dried with anhydrous $MgSO_4$, filtered and evaporated. For HPLC-PDA analysis, the dried residue was dissolved in a mixture of methanol: water (adjusted to pH 3.45) (45:55 v\v) and was injected to the HPLC apparatus.

**2.4.3. Liquid-liquid extraction**

Liquid-liquid extraction procedure was applied to the diluted solutions (samples of calibration curve) and wastewater samples using diethyl ether solvent. Each sample was extracted three times with ether. The ether extracts were combined, dried with anhydrous $MgSO_4$, filtered and evaporated. For HPLC-PDA analysis, the dried residue was dissolved in a mixture of methanol: water (adjusted to pH 3.45) (45:55 v\v) and was injected to the HPLC apparatus. (See Flow chart S5) (Supplementary Data).

**2.4.4. Salicylic acid wastewater spiking and sampling**

Sample of 60 g of salicylic acid was dissolved in a minimum amount of methanol and was poured immediately into the wastewater tank. Then, eight wastewater samples were collected from different locations of wastewater treatment plant (WWTP) (Figure 3, Appendix). Samples were kept on ice during transportation to the laboratory. Once received, conventional wastewater parameters including total suspended solids (TSS), temperature, and pH were measured then the samples were filtered and adjusted to pH (< 2) by the addition of concentrated hydrochloric acid, and then stored at 4 ºC until extraction. (See Flow chart S5) (Supplementary Data).

**2.4.5. Chromatographic conditions for the separation of aspirin and salicylic acid**

All samples were analyzed using HPLC-PDA. The optimal HPLC conditions that was found for the analysis of salicylic acid are: a C-8 as the column, a mixture of water: methanol (water pH adjusted to 3.4 using dilute *o*-phosphoric acid) (55:45 v/v) as a mobile phase, a flow rate of 2 mL/ minute and a UV detection at a wavelength of 230 nm.

**2.4.6. Adsorption studies onto micelle-clay complex and charcoal**

**2.4.6.1. Sample and Standards preparation**

**(a) Stock solution**: Stock solution was prepared by dissolving salicylic acid standard in distilled water of 500 ppm concentration, which similar to that used in (b).

**(b) Calibration curves**: A 500 ml stock solution of salicylic acid with a final concentration of 500 ppm that was prepared in (a) used to prepare the following diluted solutions: 1ppm, 2ppm, 4ppm, 6ppm, 8ppm, 10ppm, 20ppm,40ppm,60ppm, 80ppm, and 100ppm. Then, absorption of each solution was determined using UV-spectrophotometer at wavelength (**λ** max) 296.6nm.

**2.4.6.2. Adsorption experiment**

Salicylic acid was used as adsorbate. Stock solution of salicylic acid was prepared using filtered tap water. All working solutions were prepared by diluting the stock solution with filtered tap water. The amount of adsorbent was 0.5g in

100mL of salicylic acid solutions with the concentration in the range of 100 to 400ppm. The salicylic acid solutions were shaken at 250rpm until the solutions have reached their equilibrium for 3hours. Then, the samples were centrifuged and filtered.

The equilibrium concentrations of unabsorbed salicylic acid in the supernatant solutions were measured by UV-visible spectrophotometer. Wavelength of 296.6nm was used to analyze the concentration of salicylic acid. The mass of pharmaceutical (salicylic acid) sorbet, $Q_{e,}$ was determined by mass balance as shown below:

$$Qe = \left[\left(\frac{Ci - Ce}{M}\right)\right] \times (Vt)$$

Where $Q_e$ is the mass of pharmaceutical (salicylic acid) sorbet (mg $g^{-1}$); $C_i$ is the initial concentration (mg $L^{-1}$); $C_e$ is the equilibrium concentration (mg $L^{-1}$); M is the mass of adsorbent (g); and $V_t$ is the total volume of liquid in sample (L).

### 2.5. Methods (paracetamol and *p*-aminophenol)

#### 2.5.1. Sample and standards preparation

**(a) Stock solution:** Stock solution was prepared by dissolving paracetamol standard and *p*-aminophenol standard in acetonitrile and water that adjusted to pH 3.45 in a ratio (10:90) to a concentration 200 ppm that used in (b).

**(b) Calibration curves**: A 500mL stock solution of 1:1 mixture of paracetamol and *p*-aminophenol with a final concentration of 100 ppm was prepared in the same manner as in (a).The diluted solutions that were prepared from the stock solution are: 10ppm, 20ppm, 40ppm, 60ppm, 80ppm and 100ppm. Then, each diluted solution was extracted three times with ether. The ether extracts were combined, dried with anhydrous magnesium sulfate ($MgSO_4$), filtered and evaporated. For HPLC-PDA analysis, the dried residue after evaporated ether was dissolved with a mixture of water: acetonitrile (water adjusted to pH 3.45 using dilute *o*-phosphoric acid) in a ratio (90:10 v\v) and was injected to the HPLC apparatus.

#### 2.5.2. Kinetic studies on the stability of paracetamol in pure water and wastewater

**(a) Kinetic study on the stability of paracetamol in pure water:** For the hydrolysis reaction of paracetamol in pure water, a 200 ppm solution was used. The reaction progress was followed by HPLC method.

**(b)Kinetic study on the stability of paracetamol in the presence of sludge:** The same procedure as described in (b) was used for the hydrolysis of paracetamol in the presence of sludge. However, in this case water was replaced with a suspended sludge in plain water. Samples at specific time intervals were taken. Then, the sample aqueous layer was extracted three times with ether. The ether extracts were combined, dried with anhydrous $MgSO_4$, filtered and evaporated. For HPLC-PDA analysis, the dried residue was dissolved in a mixture of acetonitrile water (adjusted to pH 3.45) (10:90 v\v) and was injected to the HPLC apparatus.

#### 2.5.3. Liquid-Liquid extraction

Liquid-liquid extraction procedure was applied to the diluted solutions (samples of calibration curve) and wastewater samples using diethyl ether solvent. Each sample was extracted three times with ether. The ether extracts were combined dried with anhydrous $MgSO_4$ filtered and evaporated. For HPLC-PDA analysis, the dried residue was dissolved in a mixture of acetonitrile: water (adjusted to pH 3.45) (10:90 v\v) and was injected to the HPLC apparatus. (See Flow chart S5) (Supplementary Data).

#### 2.5.4. Paracetamol and p-aminophenol wastewater spiking and sampling

A sample of a mixture of 60g of paracetamol and 60g of *p*-aminophenol was dissolved in minimum amount of methanol and were poured immediately into the wastewater tank. Then, eight wastewater samples were collected from different locations of wastewater treatment plant (WWTP) (Figure 3, Appendix). Samples were kept on ice during transport to the laboratory. Once received, conventional wastewater parameters including total dissolved solids (TDS), temperature, and pH were measured, the samples were filtered, and then stored at 4 ºC until extraction (See Flow chart S5) (Supplementary Data).

#### 2.5.5. Chromatographic conditions for the separation of paracetamol and p-aminophenol

The optimal HPLC conditions that were efficient for the separation of paracetamol and *p*-aminophenol are: C-18 as the separation column, a mixture of water: acetonitrile (water pH adjusted to 3.45 using dilute *o*-phosphoric acid) (90:10 v/v) as a mobile phase, flow rate of 1.0 ml/ minute and a UV detection at a wavelength of 247.0 nm.

#### 2.5.6. Adsorption studies of parcetamol and p-aminophenol onto micelle-clay complex and charcoal

#### 2.5.6.1. Sample and Standards preparation

**(a) Stock solution**: Each stock solution of paracetamol and *p*-aminophenol standard was prepared in a separated two volumetric flask by dissolving them in distilled water to a concentration 500ppm that used in (b).

**(b) Calibration curves**: Each 500ml stock solution of paracetamol and *p*-aminophenol with a final concentration of 500ppm was prepared in (a) used to prepare the following diluted solutions: 1ppm, 2ppm, 4ppm, 6ppm, 8ppm, and 10ppm. Then, the absorption of each solution of paracetamol and *p*-aminophenol was determined using UV-spectrophotometer at wavelength (**λ** max) 243nm and 195nm, respectively.

#### 2.5.6.2. Adsorption experiment

The paracetamol and *p*-aminophenol were used as adsorbate. Each stock solution of each one of adsorbate was prepared

using filtered tap water. All working solutions were prepared by diluting the stock solution with filtered water. The concentrations of paracetamol and *p*-aminophenol were determined spectrophotometrically by monitoring the absorbance at 243nm and 195 nm, respective, where maximum absorbance was observed. All solutions were shaken with an electronic shaker at 250rpm in 250mL conical flasks. In the adsorption isotherm tests, 0.5g adsorbent was thoroughly mixed into 100 mL paracetamol solution in the range 200 to 700ppm, while 0.5g adsorbent was thoroughly mixed into 100 mL *p*-aminophenol solution in the range 10 to 100ppm. After the flasks had been shaken for 3 hours, the solution was centrifuged for the separation of solid particles before spectrophotometric measurements of paracetamol and *p*-aminophenol.

## 3. Results and discussion

### 3.1. Identification of the Most Popular Drugs in Palestine

Pharmaceuticals are used in large quantities throughout Palestine as prescription and non-prescription drugs and they reach the environment. So the application of advanced membrane wastewater treatment plant to ensure the efficient removal of these pharmaceuticals from wastewater is considered the important and the first study in Palestine. In future, this study will be the corner stone for conducting other studies which may concentrate on (1) the occurrence, fate and the concentration of these pharmaceuticals once arrived wastewater; (2) the quantitative information on pharmaceuticals concentrations in WWTPs effluents and their removal; and (3) the investigation the effect of human and animals medications on the environment (i.e. environmental risk assessment) in Palestine.

The data in Table S4 (Supplementary Data ) was obtained from a research conducted using the group of KupatHoleemKlalit that includes 7000 of its members in Israel and East Jerusalem. In this search, Omri program was utilized to evaluate the top twenty consumed drugs in the year 2009. This data is applicable also for the Palestinian population due to the similarity in the use of drugs in the two regions. Table S4 (Supplementary Data) lists a wide range of pharmaceutical classes including analgesics, vitamin supplements, anti-inflammatory compounds, antibiotics, anti-hypertensive agents, hypoglycemic agents, and lipid regulators[76].

Based on the above results, this research is concerned with two pharmaceuticals aspirin (acetylsalicylic acid, "ASA") and paracetamol (acetaminophen). Both pharmaceuticals are widely sold as an over-the-counter (OTC) and prescribed medications and therefore, were anticipated to occur in wastewater influents. Some physicochemical properties of aspirin and its metabolite, salicylic acid, and paracetamol, and its metabolite, *p*-aminophenol, are summarized in Table S5 (Supplementary Data). Section 3.2 and 3.3 describes the fate of these pharmaceutical in wastewater and the efficiency of the different wastewater treatment processes in removing them from environment.

### 3.2. Aspirin (acetylsalicylic acid)

Aspirin is a member of a family of chemicals called salicylates. It is chemically known as acetylsalicylic acid "ASA" and is commonly prescribed for its analgesic, antipyretic and anti-rheumatic actions. In addition, aspirin is used once daily in low doses, 75 mg and 100 mg, as prophylactic medicine for the prevention of blood aggregation [62]. The latter (blood aggregation) is the most common cause for heart attack among people over the age of 40. Aspirin is among the top twenty medicines that have been found to be frequently used in East Jerusalem due to its activity as a pain killer [76].

Aspirin is a white powder that is stable in dry conditions but is hydrolyzed to salicylic acid and acetic acid under humid or mist conditions (Figure 4, Appendix). Salicylic acid itself, which is derived naturally from willow tree bark, has also been used as an antipyretic since ancient times, and it is still used as an additive of some skin-care products and as a food preservative [59]. When aspirin is ingested, it is quickly and effectively hydrolyzed to the major excretion product, salicylic acid. Then, salicylic acid is metabolized primarily to two major inactive metabolites: salicyluric acid (75%) arises from conjugation of salicylic acid with glycine, and glucuronide ether and ester (15%) arises from conjugation with glucuronic acid. In addition to these metabolites, small amounts of gentisic acid (1%) metabolites resulting from *p*-hydroxylation mediated by cytochrome P450. These metabolites are then excreted in the urine. Only 5%-10% of a dose is excreted as free salicylic acid (Figure 5, Appendix) [80-81]. The occurrence of aspirin was reported in treated wastewater in many countries around the world. Nakada and coworkers, reported that aspirin had the highest concentrations among other pharmaceuticals, ranging from 470 to 19400 $ngL^{-1}$ in the sewage treatment plants (STPs) influents in Tokyo, Japan, and were removed efficiently during primary and secondary treatments (> 90% efficiency) [82]. Terns and coworkers reported average concentrations of salicylic acid in public owned wastewater treatment plants (POTWs), which received influents from domestic, municipal, and industrial sewage system 54 $\mu gL^{-1}$ influents and in effluents of 0.5 $\mu gL^{-1}$[83]. The removal of salicylic acid (hydrolytic product of aspirin) has been studied by different research groups. Gagnon and coworkers studied the disinfection processes in terms of removing salicylic acid. They found that salicylic acid was eliminated at a rate greater than 50% at an ozone dose of 10 $mgL^{-1}$, and a higher rate (70%) was observed when 20 $mgL^{-1}$ of ozone was used. The ozone technology is better than ultraviolet (UV) radiation in removing salicylic acid [84]. A high biodegradation of salicylic acid (>94%) during biologically activated sludge (BAC) process supported that salicylic acid was removed efficiently by BAC [85]. Whereas according to Heberer (2002b), there are several other sources of salicylic acid in sewage, besides to the active metabolite of aspirin. These sources such as the use of salicylic acid as keratolytic, dermatic or preservative of food are even more likely to be responsible for the occurrence of this compound in the aquatic environment [59].

#### 3.2.1. Calibration curve for Aspirin and Salicylic acid with extraction

The calibration curve was obtained by plotting peak area versus concentration and is displayed in Figures 6 and 7 (Appendix) (ten data points) for aspirin and salicylic acid, respectively. They showed excellent linearity with correlation coefficient ($R^2$) of 0.998 for aspirin and 0.999 for salicylic acid.

**3.2.2. Kinetic studies on the stability of aspirin in pure water and wastewater**

Since many pharmaceuticals might undergo degradation upon their standing in aqueous medium and wastewater environment, kinetic studies on aspirin in pure water and wastewater conditions have been undertaken. The kinetic results which were monitored by HPLC revealed that aspirin undergoes hydrolysis to salicylic and acetic acids (Figure 4, Appendix). The rate of hydrolysis of aspirin is a function of temperature, amount of moisture present, and pH-dependent. Figures 8 and 9 (Appendix) display the HPLC chromatograms of aspirin hydrolysis in pure water after 5 days incubation at 25$^o$ C and of aspirin hydrolysis in the presence of wastewater after 8 days at 25$^o$ C, respectively. The peak at retention time of 4.3 minutes belongs to aspirin and that at 5.5 minutes to the hydrolysis product, salicylic acid. The kinetic data was examined for linear relationship. A linear correlation with a high correlation coefficient ($R^2$) was found between ln [aspirin] (logarithms of aspirin concentration) and time. The correlation results obtained are illustrated graphically in Figure 10 (Appendix). In pure water, the linear correlation between ln [aspirin] and time is shown in Figure 10 (Appendix) (blue points) where the correlation coefficient ($R^2$) was 0.9532. The rate constant for the hydrolysis of aspirin in pure water obtained from the slope of the plot in Figure 10 (Appendix) is 0.357 x $10^{-8}$ $Ms^{-1}$. Similarly, kinetic study on the stability (hydrolysis) of aspirin in wastewater was conducted. The HPLC monitoring results for the hydrolysis of aspirin after incubation in wastewater for 10 days were examined for correlations. The correlation of ln [aspirin] versus time gave a straight line with a correlation coefficient ($R^2$) of 0.9892 as shown in Figure 10 (pink points). The first order rate calculated from the slope of the curve gave a value of 0.845 x $10^{-8}$ $Ms^{-1}$.

The following calculations of the initial rate of hydrolysis of aspirin in pure water and wastewater further illustrate this point.

Rate of first order reaction = dC/dt = k [C]

Concentration of aspirin = weight of aspirin/Molecular weight of aspirin in 1 liter = 500ppm =0.5g ÷ (180/M) = 0.00278M.

Initial Rate of the hydrolysis of aspirin in pure water at 25 °C = 0.1104 M x 0.00278/ day = 3.069x$10^{-4}$ M $day^{-1}$ = 3.069 x $10^{-4}$M/(24 x 60 x 60) sec = 8.6 x $10^4$ = 0.357 x $10^{-8}$ $Ms^{-1}$.

Initial Rate of the hydrolysis of aspirin in the presence of wastewater at 25° C = 0.2617 M x 0.00278day = 7.269x$10^{-4}$ M $day^{-1}$ = 7.269 x $10^{-4}$ M /(24 x 60 x 60) sec. = 8.6 x $10^4$ = 0.845 x $10^{-8}$ $Ms^{-1}$.

The literature value for the rate constant for the hydrolysis of aspirin (Fersht and Kirby, 1967) at 39˚C is 1.1 x $10^{-5}$ $Ms^{-1}$ [86]. The initial rate at this temperature for the 500 ppm was equal to 0.29 x$10^{-8}$ $Ms^{-1}$. This value is similar to that obtained in pure water and is significantly less than that in wastewater.

Comparison of the hydrolysis reaction rate values in pure water and in wastewater solution (0.357 x $10^{-8}$ $Ms^{-1}$ vs. 0.845 x $10^{-8}$ $Ms^{-1}$) revealed that the hydrolysis in wastewater proceeds at faster rate than in pure water. The accelerations in rate can be attributed to the content nature of the wastewater (consisting of variety of enzymes, bacteria and heavy metals) which can act as a catalyst for such reactions.

**3.2.3. The efficiency of membranes and activated carbon adsorbent in terms of removal of salicylic acid**

Since aspirin is not a stable chemical entity and undergoes a fast hydrolysis in presence of wastewater, our goal was to find a suitable method for removing the aspirin hydrolyzed products, salicylic and acetic acids. It is known that acetic acid has a low boiling point and it is expected that within a short time of its formation it will be evaporated. On the other hand, the solid un-volatile salicylic acid has to be removed by one of the well-known filtration methods. Therefore, efforts in this research were concentrated on a membrane removal of the hydrolyzed product (salicylic acid) from wastewater samples rather than the removal of the parental drug (aspirin). The use of membranes for wastewater treatment, especially coupling the membrane systems with other technologies such as pretreatment using activated sludge treatment process and/or ultrafiltration membranes followed by the use of reverse osmosis technologies could be the most efficient method in treating wastewater and removing a variety of pharmaceuticals [87].

**3.2.3.1. Salicylic acid wastewater spiking and sampling**

Sixty gram salicylic acid standard was dissolved in a minimum amount of methanol then poured into the wastewater treatment plant (WWTP). Eight wastewater samples were collected from different locations of the wastewater treatment plant located at Al-Quds University main campus at Abu-Dies using pre-cleaned 500 ml glass containers. Figure 3 (Appendix) illustrates the sampling points (s.p.) which are as follows: Blank sample "before the addition of salicylic acid sample" (s.p. 1); AST ultrafiltration "hollow fiber" (AST-UF-HF) influent (s.p. 2) and effluent (s.p. 4), Nirosoft ultrafiltration "spiral wound" (Nirosoft UF-SW) effluent (s.p. 6), activated carbon adsorbent effluent (s.p. 7), and reverse osmosis membrane effluent (s.p. 8). The eight samples were kept in an ice bath during transportation to the laboratory. Conventional wastewater parameters for the eight samples including total dissolved solids (TDS= 630 $mgL^{-1}$), temperature (27$^o$ C), and pH were measured (pH= 7.3), then the samples were filtered and adjusted to pH < 2 by the addition of concentrated hydrochloric acid (HCl) to improve the recovery for the acidic drug (salicylic acid), and then the sample was centrifuged for 15 minutes to remove suspended materials prior to extraction of acidic drugs, and then stored at 4$^o$ C. The samples solutions were extracted by ether in order to clean up samples and this step is required in order to concentrate the target compound (salicylic acid) to a detectable level, and after evaporation were analyzed by HPLC (see Flow chart S5) (Supplementary Data).

The results obtained are summarized in Table S6 (Supplementary Data).

**3.2.3.1. The efficiency of (UF-HF) and (UF-SW), activated carbon and RO membranes at the removal of salicylic acid.**
Figures 11, 12, 13 and 14 (Appendix) display the chromatograms of concentration of salicylic acid after passing through UF-HF, UF-SW membranes, activated carbon adsorbent, and reverse osmosis, respectively. Table S6 (Supplementary Data) shows the efficiency of the removal of salicylic acid during ultrafiltration by hollow fiber (UF-HF), spiral wound (UF-SW), activated carbon adsorbent, and reverse osmosis. Examination of the results listed in Table S6 (Supplementary Data) reveals that the efficiency of the hollow fiber and spiral wound ultrafiltration process is more than 70% (samples No. 4 and 6) at the removal of salicylic acid in the effluent sample. The rejected salicylic acid was found and accumulated in the brine and concentrate of this machine. On the other hand, the efficiency for the removal of salicylic acid during activated carbon adsorbent is more than 98% (Sample No. 7). The removal of salicylic acid from wastewater could rely on two types of processes which are based on mass transfer separtion accomplished by the transfer of mass from one phase to another (i.e. UF and RO membranes) and the sorption "i.e. adsorption" mechanism (activated carbon). It can be concluded that using a consequent system of the two types of UF membranes followed by activated carbon adsorbent is highly efficient to remove salicylic acid and hence there was no need to pass it through a reverse osmosis membrane.

**3.2.4. Adsorption studies of salicylic acid onto a clay micelle complex and activated charcoal**
Adsorption mechanism depends on the physicochemical properties of the pharmaceutical and the aquifer media properties. Adsorption of salicylic acid onto a clay micelle complex and charcoal adsorbents was investigated and described in this section.

**3.2.4.1. Calibration curve for salicylic acid using UV-visible spectrophotometer**
The calibration curve for salicylic acid was obtained by plotting absorption of the drug versus its concentration, and is displayed in Figure 15 (Appendix). The results shown in the figure indicate an excellent linearity with a correlation coefficient ($R^2$) of 0.9999.

**3.2.4.2. Adsorption isotherm**
A clay micelle complex is prepared by mixing a specific type of a clay mineral (montmorillonite) with a cationic surfactant. In this study, octadecyltrimethylammonium (ODTMA) (Figure 16, Appendix) with a critical micelle concentration (CMC) value of 0.3 mM was employed for a complex formation. A certain mass of clay was introduced into a solution of ODTMA until reaching a concentration of $1x10^{-2}$ M then stirred for 24 hours. The complex was filtered and dried then mixed with excess sand [77].
Equilibrium relationships between adsorbents (i.e. clay micelle complex and charcoal) and adsorbate (i.e. salicylic acid) are described by adsorption isotherms. The most common model for adsorption process is Langmuir adsorption isotherm. The latter is the most widely used for modeling equilibrium data and determination of the adsorption capacity [88]. Its linear form is represented by equation (1):

$$Ce/Qe = 1/(k \times Qmax) + Ce/Qmax \dots Eq(1).$$

Where $C_e$ is the equilibrium concentration of the pharmaceutical (salicylic acid) (mg $L^{-1}$); $Q_e$ is the equilibrium mass of the adsorbed pharmaceutical (salicylic acid) per gram of complex (mg $g^{-1}$); k is the Langmuir constant; and $Q_{max}$ is the maximum mass of pharmaceutical (salicylic acid) removed per gram of complex (mg $g^{-1}$) and it represents the adsorption capacity of the pharmaceutical onto adsorbents.
Tables S7 and S8 (Supplementary Data) list the initial and final equilibrium concentrations of salicylic acid obtained from the adsorption test. Also, the tables include the fixed mass of the clay micelle complex and charcoal used in the test. Figure 17 (Appendix) shows a linear correlation between the terms $C_e/Q_e$ and $C_e$ which indicates that the adsorption of salicylic acid onto the clay micelle complex and charcoal follows the Langmuir isotherm model.

$Q_{max}$ and k parameters for the removal of salicylic acid by the clay micelle complex were determined from the slope and the intercept of (red points) shown in Figure 17 (Appendix). The calculated values of $Q_{max}$ and k are shown in the following equations 2-3:

$$Slope = 1/Qmax = 0.0177;$$
$$Qmax = 56.49 \frac{mg}{g} \dots\dots\dots\dots\dots\dots Eq\ (2).$$
$$Intercept = 1/(k \times Qmax) = 0.1209;$$
$$k = 0.1464 \dots\dots\dots\dots\dots\dots Eq\ (3).$$

Langmuir isotherm for the removal of salicylic acid by charcoal adsorbent was done in order to compare it with the efficiency for the removal by a clay micelle complex. Blue points shown in Figure 17 (Appendix) describe the Langmuir isotherm for the removal of salicylic acid by charcoal. The calculated values of $Q_{max}$ and k are shown in the following equations 4-5:

$$Slope = 1/Qmax = 0.0165;$$
$$Qmax = 60.60 \frac{mg}{g} \dots\dots\dots\dots\dots\dots Eq\ (4).$$
$$Intercept = 1/(k \times Qmax) = 0.2012;$$
$$k = 0.0820 \dots\dots\dots\dots\dots\dots Eq\ (5).$$

Comparison between the calculated values of the $Q_{max}$ for the adsorption of salicylic acid on the clay micelle complex and charcoal reveals that both have comparable efficiency. However, since the quantity of the cationic surfactant in the clay micelle is about three times smaller than the quantity of activated carbon in charcoal the adsorption efficiency of the clay micelle is much superior than charcoal. This complex by

virtue of its positive charge with hydrophobic region is capable of binding negatively charged organic molecules and bacteria as well [77]. Meanwhile, from the results in Table S9 (Supplementary Data), it can be observed that the activated carbon in charcoal has a higher capacity than the clay micelle complex in sorption of salicylic acid. This demonstrates that hydrophobic interactions are significant even for polar salicylic acid compound.

### 3.3. Paracetamol (acetaminophen)

Paracetamol was chosen for this study because it is widely used as an over-the-counter analgesic and antipyretic drug in Palestine. It is among the top twenty medicines that were found to be frequently used in the West Bank and Jerusalem [76]. Also, it is heavily used all over the world [89]. Paracetamol is metabolized primarily in the liverinto non-toxic products. Three metabolic pathwaysare notable as shown in Figure 18 (Appendix) .Glucuronidation is believed to account for 40% to 60% of the metabolism of paracetamol. Sulfation (sulfate conjugation) may account for 20–40% [90]. N-hydroxylation and rearrangement, then Glutathione (gamma-glutamyl-L-cysteinylglycine: GSH) conjugation, accounts for less than 15%. The hepatic cytochrome P450 enzyme system metabolizes paracetamol, forming a minor yet significant alkylating metabolite known as NAPQI (*N*-acetyl-*p*-benzo-quinone imine). NAPQI is then irreversibly conjugated with the sulfhydryl groups of glutathione. All three pathways yield final products that are inactive, non-toxic, and eventually excreted by the kidney. In the third pathway; however, the intermediate product NAPQI is toxic. NAPQI is primarily responsible for the toxic effects of paracetamol [80]. Paracetamol has been found with a concentration of up to 6 mg $L^{-1}$ in European sewage treatment plants (STP) effluents [49] up to 10 mg $L^{-1}$ in natural waters in USA [91], and even more than 65 mg $L^{-1}$ in the Tyne River, UK. Furthermore, according to a reconnaissance study of organic wastewater contaminants in USA waters, paracetamol was determined to occur at a frequency of 23.8% in surface water at a maximum concentration of 10 $\mu gL^{-1}$ [49]. Recently removal of aqueous paracetamol by electrochemical [92], ozonation, $H_2O_2$-UV oxidation, and semiconductor photo catalysis have been reported for degradation of paracetamol [93].

#### 3.3.1 Calibration curve for paracetamol and *p*-aminophenol

The calibration curve was obtained by plotting peak area versus concentration and is displayed in Figures 19 and 20 (Appendix) (seven data points) for paracetamol and *p*-aminophenol, respectively. The figures show excellent linearity with a correlation coefficient ($R^2$) of 0.997 for paracetamol and 0.986 for *p*-aminophenol.

#### 3.3.2.Kinetic studies on the stability of paracetamol in pure water and wastewater

Paracetamol is available in different dosage forms: tablet, capsules, drops, elixirs, suspensions, and suppositories. Its saturated aqueous solution has a pH of about 6 and is stable (half-life over 20 years), meanwhile under abnormal conditions (heat, pH, temperature, etc.) its stability decreases and it degrades slowly forming a mixture of contaminants, such as *p*-aminophenol and acetic acid, (Figure 21, Appendix). This reaction could also be carried out by enzymatic cleavage or by microwave assisted alkaline hydrolysis of amide bond[90].

In a similar manner to that of aspirin, kinetic studies on paracetamol in pure water have been carried out at 25° C. The kinetic results which were monitored by HPLC revealed that paracetamol was completely stable in pure water due to the high activation energy needed to break down the amide bond. No degradation products were observed after incubation for more than two weeks as presented in Figures 22 and 23 (Appendix). On the other hand, HPLC monitoring of a solution of paracetamol in the presence of wastewater gave a gradual disappearance of a peak characterized as the reactant at a retention time of 3.92 minutes and a gradual appearance of a new peak at a retention time of 1.97 minutes characterized as a product. Figure 24 (Appendix) shows a representative chromatogram for the hydrolysis of paracetamol to products. Characterization of the compound that showed a peak at 1.97 minutes revealed that the hydrolyzed product of paracetamol is *p*-aminophenol. This result was supported by the fact that when a standard solution of *p*-aminophenol was injected to HPLC at the same conditions of the kinetic experiments. Only one peak at a retention time of 1.97 minutes was obtained. Figure 24 and 25 (Appendix) display the HPLC chromatograms of paracetamol in wastewater after 2 days incubation at 25°C and the hydrolysis of paracetamol in presence of wastewater after 7 days at 25°C, respectively. The hydrolysis of paracetamol in the presence of wastewater can be attributed to the content nature of the wastewater (consisting of variety of enzymes, bacteria and heavy metals, etc.) which can act as a catalyst for the cleavage of the amide bond (Figure 21, Appendix). The kinetic data obtained from the HPLC monitoring (7 days) was examined for linear correlation. The correlation results indicates a linear correlation between ln [paracetamol] and time with a correlation coefficient ($R^2$) = 0.8855 (Figure 26, Appendix). The rate constant for the hydrolysis of paracetamol obtained from the slope of the plot in Figure 25 is $0.8466 \times 10^{-8}$ $Ms^{-1}$. The rate constant for the hydrolysis of paracetamol in wastewater was calculated as follows:

Concentration of paracetamol = weight of paracetamol/Mw of paracetamol in 1 liter = 200ppm = 0.2g/151.1 = $1.3230 \times 10^{-3}$ M.

Rate of first order reaction = dC/dt = k [C].

Initial Rate of the hydrolysis of paracetamol in the presence of wastewater at 25°C = 0.5529 M x $1.3230 \times 10^{-3}$day = 7.3148 $\times 10^{-4}$ M/day = 7.3148 x $10^{-4}$M /(24 x 60 x 60) sec = 0.8466 x $10^{-8}$ $Ms^{-1}$.

#### 3.3.3. The efficiency of membranes and activated carbon adsorbent in terms of removal of paracetamol and *p*-aminophenol

##### 3.3.3.1. Paracetamol and its hydrolyzed product (p-aminophenol) wastewater spiking and sampling

Samples of sixty gram of paracetamol and sixty gram of its hydrolyzed product (*p*-aminophenol) were dissolved in a minimum amount of methanol and were introduced to WWTP.

Then, eight wastewater samples were collected from different locations of WWTP located in Al-Quds University main campus at Abu-Dies using pre-cleaned 500 mL amber glass bottles. Samples from the sampling points 2, 4, 6, 7 and 8 (Figure 3, Appendix) were collected for observing the membranes removal efficiency: ultrafiltration (hollow fiber and spiral wound), then followed by activated carbon and reverse osmosis membrane.

**3.3.3.2. The efficiency of HF-UF (hollow fiber), SW-UF (spiral wound), activated carbon and RO membranes at the removal of paracetamol and p-aminophenol.**

Since paracetamol was found to undergo hydrolysis to *p*-aminophenol when kept standing for extended time in wastewater we sought to study the efficiency of the different membranes on the removal of both paracetamol and *p*-aminophenol. Figures 27, 28, 29, and 30 (Appendix) display the chromatograms of concentration of paracetamol and *p*-aminophenol after passing HF-UF , SW-HF membranes, activated carbon adsorbent, and reverse osmosis, respectively. While Table S10 (Supplementary Data) summarizes the results of the efficiency of HF-UF, SW-UF, activated carbon adsorbent and reverse osmosis membranes in removing paracetamol and *p*-aminophenol.

Inspection of the results listed in Table 10 (Supplementary Data) indicates that the efficiency of the ultrafiltration process is about 40% (samples No. 4 and 6) at the removal of paracetamol and about 70% at that of*p*-aminophenol in the effluent samples. On the other hand, both the activated carbon adsorbent and the reverse osmosis membranes were significantly superior in the removal of paracetamol and *p*-aminophenol. In the case of acetaminophen a removal of 99% was observed by both membranes whereas a 100% removal was achieved when 4-aminophenol was tested (Sample No. 7 and 8).

**3.3.4. Adsorption studies of paracetamol and *p*-aminophenol onto a clay micelle complex and activated charcoal.**

**3.3.4.1. Calibration curve for paracetamol using UV-visible spectrophotometer**

The calibration curve was obtained by plotting the absorption of paracetamol versus its concentration and is illustrated in Figure 31 (Appendix). The Figure shows excellent linearity between the two variables with a correlation coefficient ($R^2$) of 0.998.

**3.3.4.2. Calibration curve for p-aminophenol using UV-visible spectrophotometer**

The calibration curve was obtained by plotting the absorption of *p*-aminophenol versus its concentration and is illustrated in Figure 32 (Appendix). The figure indicates excellent linearity with a correlation coefficient ($R^2$) of 0.994.

**3.3.4.3 Adsorption isotherm**

In a test similar to that conducted for salicylic acid, the sorption for the removal of paracetamol and its hydrolysis product *p*-aminophenol by a clay micelle complex and charcoal is well described by Langmuir adsorption isotherm as shown by the correlation of Ce\Qe versus Ce (Figure 33, Appendix). Tables S11, S12, S13 and S14 (Supplementary Data) list the initial and final equilibrium concentrations of both chemicals obtained from the adsorption test. Also, the tables include the fixed mass of the clay micelle complex and charcoal used in the test. The sorption of paracetamol and *p*-aminophenol onto both adsorbents are well fitted with Langmuir sorption isotherm since the correlation coefficients for the Langmuir sorption of paracetamol and *p*-aminophenol were found in the range of 0.9921-0.9968 (Table S15, Supplementary Data), which are close to unity. The calculated $Q_{max}$ and k values for the removal of paracetamol by a clay micelle complex are 185.185 mg $g^{-1}$, 0.0325, respectively. The values for *p*-aminophenol are 15.33 mg $g^{-1}$ and 0.461, respectively. The Langmuir isotherms for the removal of both chemicals by charcoal gave $Q_{max}$ values 129.87 mg $g^{-1}$ for paracetamol and 12.5 mg $g^{-1}$ for *p*-aminophenol and the calculated k values were 0.35 for paracetamol and 4.82 for *p*-aminophenol. Comparison of the calculated $Q_{max}$ values of both chemicals using a clay micelle complex and charcoal reveals that the former is more efficient than the later in removing paracetamol and *p*-aminophenol. The results can be explained by the mean of physicochemical properties of the organic drug, that is, water solubility and octanol-water partition coefficient ($K_{ow}$). These properties can play a major role in the mobility of the drug in the subsurface adsorbents. The water solubility of paracetamol is 12,743 mg $L^{-1}$, while that of *p*-aminophenol is 15,000 mg $L^{-1}$. Moreover, *p*-aminophenol has a low log $K_{ow}$ of 0.04, while that of the paracetamol is higher (0.46), as shown in Table 5. (Supplementary Data). *P-Aminophenol* with low $K_{ow}$ values tends to dissolve more readily in water than paracetamol, and thus tends to adsorb less. As a result, paracetamol shows greater sorption ability when compared to *p*-aminophenol in both adsorbents (Figure 33, Appendix). In addition, it can be concluded that the adsorption of both chemicals onto activated carbon surface is due mainly to dispersive forces causing the hydrophobic interaction between adsorbate and adsorbent. The hydrophobic part of pharmaceuticals tends to associate with the non-polar surface of activated carbon with the hydrophilic group directed toward the aqueous phase. Although the water solubility of these two pharmaceuticals is high, substantial sorption is still realized due to the hydrophobic part of both chemicals onto the non-polar surface of the activated carbon. The interactions caused by the affinity between polar and charged moieties of both organic compounds and a clay micelle complex appear to play an important role in the sorption of those compounds onto this complex.

**4. Summary and conclusions**

The following conclusions emerged from this study:

(i) Both aspirin and paracetamol are not stable in wastewater conditions and they undergo a relatively fast hydrolysis to the corresponding hydrolysis products. Therefore, efforts should be concentrated on finding suitable methods for the removal of salicylic acid (aspirin product) and *p*-aminophenol (paracetamol product) rather than to focus on the parental drug.

(ii) The efficiency of hollow fiber and spiral wound membranes at the removal of the pharmaceutical studied herein (paracetamol and aspirin) is not satisfactory (40-70%), whereas, the activated carbon, clay micelle complex and reverse osmosis membranes were completely efficient in removing both pharmaceuticals (about 100%). Hence, we conclude that a clay micelle complex and activated carbon filters can effectively remove pharmaceuticals of the kind described herein and there is no need to use more expensive method such as a reverse osmosis membrane.

(iii) Activated charcoal and a clay micelle complex are considered to be effective methods for the removal of aspirin, paracetamol, and their degradation products from aqueous solution because both membranes characterized by a large surface area, micro-porous nature, high adsorption capacity, high purity, and easy availability.

**References**


[1] Nazer, D.; Siebel, M.; Van der Zaag, P.; Mimi, Z.; , Gijzen, H., 2008. Water footprint of the Palestinians in the west bank. American Water Resources Association 44, 2, 449-458.

[2] McNeill, L.S.; Almasri, M.N.; Mizyed, N., 2010.A sustainable approach for reusing treated wastewater in agricultural irrigation in the West Bank-Palestine. Desalination 251, 315-321.

[3] Lonergan, S.; Brooks; D., 1994. Watershed: The Role of Fresh Water in the Israeli Palestinian-Conflict. International Development Research Centre, Ottawa. pp. 1-329.

[4] Birzeit University, 2005. Prospects of efficient wastewater management and water reuse in Palestine. EMWATER-Project Efficient Management of Wastewater, its Treatment and Reuse in the Mediterranean countries, Institute for water studies, Birzeit, West Bank, Palestine.

[5] Bdour, A.; Hamdi, M.; Tarawneh Z., 2009. Perspectives on sustainable wastewater treatment technologies and reuse options in the urban areas of the Mediterranean region. Desalination 237, 162-174.

[6] German-Israeli-Palestinian project submitted to Friends of Environment and Water (FEW) and House of Water and Environment (HWE), 2006. Collective water study. Experiences with Use of Treated Wastewater for Irrigation in Palestine.

[7] United Nations Environmental Program (UNEP), 2003. Desk study on the environment in the occupied Palestinian Territories. Task. N-4808,Arendal. Available online at:http://www.unep.org/download_file.multilingual.asp?FileID=105. Accessed, October , 2010.

[8] Abu-Zahra, B. A. A., 2001. Water crisis in Palestine. Desalination 136, 93-99.

[9] Al-Tamimi, A.; Rabi, A.; Abu-Rahma, A., 2008. The Palestinian Hydrology Group's Experience in Grey Water Treatment and Reuse in the Palestinian Rural Areas. Proceedings of the first Symposium on wastewater reclamation and reuse for water management in Palestine.

[10] Abu-Madi, M.; Al-Saed, R.; Braadbart, O.; Alaerts, G., 2000. Selection criteria for appropriate sanitation in the Palestinian rural and semi-urban communities. The International Symposium on Water Sector Capacity Building and Research in Palestine, Birzeit University, Palestine.

[11] Daibis, F., 2000. Towards sustainable development in the water sector: a perspective from Palestine. Water Sci. Technol. 42 , 81–86.

[12] Mahmoud, N.; Amarneh, M.; Al-Sa'ed, R.; Zeeman, G.; Gijzen, H.; Lettinga, G., 2003. Sewage characterization as a tool for the application of anaerobic treatment in Palestine. Environmental Pollution. 126, 115-122.

[13] Al-Saed, R., 2005. Obstacles and chance to cut pollution load discharges from urban Palestine. International Water Resources Association 30, 4, 538-544.

[14] Al-Saed, R., 2000. Wastewater management for small communities in Palestine. Proceedings of the Technical expert consultation on appropriate and innovative wastewater management for small communities in EMR countries, Amman, Jordan.

[15] Al-Zubi, Y., 2007. Effect of irrigation water on agricultural soil in Jordan valley: An example from arid area conditions. Journal of Arid Environments 70, 63–79.

[16] United Nations Environmental Program (UNEP) and Global Environment Centre Foundation (GEC) (2004).Water and wastewater reuse: An Environmentally Sound Approach for Sustainable Urban Water Managements. Available online at: http://www.unep.or.jp/ietc/Publications/Water_Sanitation/wastewater_reuse/Booklet Wastewater_Reuse.pdf. Accessed :October,2010.

[17] Metcalf and Eddy, Inc., 2003. Wastewater engineering. Treatment, disposal and reuse.4th ed., McGraw-Hill. New York.

[18] Swaileh, K.; Hussein, R.; Abulhej, S., 2004. Assessment of heavy metal contamination in road side surface soil and vegetation from the west bank. Archives of environmental and technology. 47, 23-40.

[19] Al-Sa`ed, R., 2007. Pathogens Assessment in Reclaimed Effluent Used for Industrial Crops Irrigation. Int. J. Environ. Res. Public Health. 4, 68-75.

[20] Samhan, S.; Al-Sa`ed, R.; Mahmoud, N., 2007. Removal of Pathogenic Microorganisms in Pilot-scale Uasb-septic Tanks and Albireh Urban Wastewater Treatment Plant in Palestine. International Water Resources Association. 32, 787-798.

[21] Bakir, H., 2001. Sustainable wastewater management for small communities in the Middle East and North Africa. Journal of Environmental Management 61, 319–328.

[22] World Health Organization (WHO), 2000. Guidelines for wastewater reuse in agriculture and aquaculture:

recommended revisions based on new research evidence. WELL Study. Task No. 68 (1). Available online at: http://www.bvsde.paho.org/bvsacd/cd25/well.pdf. Accessed: October, 2010.

[23] World Health Organization (WHO), 2006. Guidelines for the Safe Use of Wastewater, Excreta and Greywater: Wastewater Use in Agriculture. 3rd ed., Vol. (1), Geneva Available online at:http://whqlibdoc.who.int/publications/2006/9241546824_eng.pdf. Accessed: October, 2010.

[24] Vigneswaran, S.; Sundaravadivel, S., 2009. Recycle and reuse of domestic wastewater. Faculty of Engineering, University of technology, Sydney, Australia, pp. 2-10.

[25] Scott, C.; Faruqui, N.; Sally, L., 2004. Wastewater use in irrigated agriculture: Confronting the livelihood and environmental realities. 1st ed., CABI, Canada. pp. 1-206.

[26] Emmerson, G., 1998. Every drop is precious: Greywater as an alternative water source. Queensland Parliamentary Library.

[27] Bielefeldt, A.R., 2009. Water Treatment, Industrial. Encyclopedia of Microbiology, 3rd edition. M. Schaechter, editor, et al. Academic Press. Pp. 569-586.

[28] Environmental Protection Agency (EPA), 1997. Wastewater Treatment Manuals: Primary, Secondary and Tertiary treatment. (EPA, Ireland). Available online at: http://www.epa.ie/downloads/advice/water/wastewater/EPA. Accessed: October,2010.

[29] World Health Organization (WHO), 2006. Guidelines for the Safe Use of Wastewater, Excreta and Greywater: Wastewater Use in Agriculture. 3rd ed., Vol. (1), Geneva. Available online at: http://whqlibdoc.who.int/publications/2006/9241546824_eng.pdf/ Accessed: October,2010.

[30] United States Environmental Protection Agency (US.EPA), 2004. Primer for Municipal Wastewater treatment systems .U.S. EPA, Washington.

[31] Acero, J.; Benitez, F.; Leal, A.; Real, F., Teva F., 2010. Membrane filtration technologies applied to municipal secondary effluents for potential reuse. Journal of Hazardous Materials 177, 390–398.

[32] Okoh, A.; Odjadjare, E.; Iqbinosa, E.; Osode A., 2009. Wastewater treatments plants as a source of microbial pathogens in receiving watersheds. Africans Journals of Biotechnology 6, 25, 2932-2944.

[33] Benitez, F.; Acero, J.; Leal, A.; Real, F., 2007. Ozone and membrane filtration based strategies for the treatment of cork processing wastewaters. Journal of Hazardous Materials 152, 373-380.

[34] Goren, U.; Aharoni, A.; Kummel, M.; Messalen, I.; Brenner, A.; Gitis, V., 2008. Role of membrane pore size in tertiary flocculation/adsorption/ultrafiltration treatment of municipal wastewater. Sep. Purif. Technol. 61, 193–203.

[35] United States Environmental Protection Agency (US.EPA), 1993. Standards for the use or disposal of sewage sludge; Final Rules. 40 CFR Part 257 et al. Available online at: http://water.epa.gov/scitech/wastetech/biosolids/upload/fr2-19-93.pdf\.

[36] Mallevialle, J.; Odendaal, P.; Wiesner, M., 1996. Water Treatment Membrane Processes. New York: McGraw-Hill.

[37] Owen, G.; Bandi, M.; Howell, J.; Churchouse, S., 1995. Economic assessment of membrane processes for water and wastewater treatment. Journal of Membrane Science 102, 77-91.

[38] Wintgens, T.; Melin, T.; Schafer, A.; Khan, S.; Muston, M.; Bixio, D.; Thoeye, C., 2005. The role of membrane processes in municipal wastewater reclamation and reuse. Desalination. 178, 1-11.

[39] Zhou, H.; Smith, D., 2002. Advanced technologies in water and wastewater treatment. J. Environ. Sci. 1 , 247-264.

[40] Nicholas C., 1998. Liquid Filtration.2nd ed., Elsevier.

[41] United States Environmental Protection Agency (US.EPA), 2005. Membrane Filtration Guidance Manual. Office of water, EPA/815/R-06/009. Available online at: http://www.epa.gov/ogwdw/disinfection/lt2/pdfs/guide_lt2_membranefiltration_final.pdf/Accessed: October ,2010.

[42] United States Environmental Protection Agency (US.EPA), 1996. Capsule Report: Reverse Osmosis Process. Office of research and development, EPA/625/R-96/009. Available online at: http://www.epa.gov/nrmrl/pubs/625r96009/625r96009.pdf/ Accessed: October, 2010.

[43] Tansel, B., 2008. New technologies for water and wastewater treatment: A survey of recent patents. Recent patents on chemical engineering 1, 17-26.

[44]Daughton, C.; Ternes, T., 1999. Pharmaceuticals and personal care products in the environment: agent of subtle change?. Environ health perspective 107, 907-785.

[45] Heberer, T., 2002. Occurrence, fate, and removal of pharmaceuticals residues in the aquatic environment: a review of recent research data. Toxicology letters 131, 5-17.

[46] Ternes, T., 1998. Occurrence of drugs in German sewage treatment plants and rivers. Water Res. 32 , 3245–3260.

[47] Kummerer, K., 2001. Drugs in the environment: emission of drugs, diagnostic aids and disinfectants into wastewater by hospitals in relation to other sources-a review. Chemosphere 45, 957-969.

[48] Halling-Sorensen, B.; Nielsen, N.; Lansky, P.; Ingerslev, F.; Hansen, L.; Lutzhoft, H., 1998. Occurrence, fate and effects of pharmaceutical substances in the environment- a review. *Chemosphere*. Vol. 36, pp. (357-394).

[49] Kolpin, D.; Furlong, E.; Meyer, M.; Thurman, E.; Zaugg, S.; Barber, L.; Buxton, H., 2002. Pharmaceuticals, hormones and other organic wastewater Contaminates in U.S. streams, 1999-2000: a national reconnaissance. Environ. Sci. Technol 36, 1202-1211.

[50] Schwarzenbach, R.; Escher, B.; Fenner, K.; Hofstetter, T.; Johnson, C.; Gunten, U.; Wehrli B., 2006. The Challenge of Micropollutants in Aquatic Systems. Science. 313, 1072-1077.

[51] Kummerer, K., 2009.The presence of pharmaceuticals in the environment due to human use –present knowledge and

future challenges- a review. Journal of Environmental Management 90, 2354–2366.
[52] Lipinski, C.; Lombardo, F.; Dominy, B.; Feeney, P., 1997. Experimental and Computational Approaches to Estimate Solubility and Permeability in Drug Discovery and Development Settings. Adv. Drug Deliv. Rev. 23, 3–25.
[53] Bound, J.; Voulvoulis N., 2005. Household disposal of pharmaceuticals as a pathway Contamination in the United Kingdom, Environ health perspective 113, 1705-1711.
[54] United States Environmental Protection Agency (US. EPA) 1997.special report on environmental endocrine disruption: An effects assessment and analysis. Washington, DC: Office of Research and Development, EPA/630/R-96/012.
[55] Helland, J., 2006. Endocrine Disrupters as Emerging Contaminants in wastewater, Minnesota House of Representatives Research Department. Available online at: www.house.mn/hrd/hrd.htm/.
[56] Escher, B.; Baumgartner, R.; Koller, M., Treyer, K.; Lienert, J.; McArdell, C.; 2010. Environmental toxicology and risk assessment of pharmaceuticals from hospital wastewater. Water Research 45, 75-92.
[57] Boxall, A., 2004. The environmental side effects of medication. EMBO reports 5, 7-9.
[58] http:// www.ecy.wa.gov/biblio /0403051..html./ Accessed: Aug. 2008.
[59] Heberer, T., 2002b. Tracking persistent pharmaceutical residues from municipal sewage to drinking water. Journal of Hydrology 266, 175-189.
[60] Ternes, T.; Hirsch, R.; Mueller, J.; Haberer, K., 1998. Methods for the determination of neutral drugs as well as beta blockers and β2- sympathomimetic in aqueous matrices using GC/MS and LC/MS/MS. Fresenius Journal of Analytical Chemistry 362, 329-340.
[61] Grosi, M.; Petrovic, M.; Barcelo, D., 2008. Analysis of Emerging Contaminants of Municipal and Industrial Origin. Hdb Env Chem. 5, 37-104.
[62] Harvey, R.; Champe, P.; Howland, R.; Mycek, M., 2006. Pharmacology, 3rd ed. Lippincott Williams and Wilkins.
[63] Drewes, J., 2007. Removal of pharmaceuticals in wastewater and drinking water treatments. In :Petrovic M., Barcelo D., (Eds.). comprehensive Analytical chemistry: fate and removal of pharmaceuticals in the water cycle. Elsevier, Amesterdam, The Netherlands.
[64] Baleen, S. I., 2007. Municipal wastewater treatment plant (WWTP) effluents.RIWA . Netherlands.
[65] Kallaos, J.; Wheeler, K.; Wong, C.; Zahller, M., 2007. Pharmaceuticals in wastewater streams: Disposal practices and policy options in Santa Barbara, Donald Bren School of environmental science and management.
[66] Brody, J.; Aschengrau, A.; McKelvey, W.; Swartz, C.; Kennedy, T.; Rudel, R., 2006. Breast cancer risk and drinking water contaminated by wastewater: a case control study, Environmental Health: a Global Access Science Source.
[67] Esplugas, S.; Bila, D.; Krause, L.; Dezotti, M., 2007. Ozonation and Advanced Oxidation Technologies to Remove Endocrine Disrupting Chemicals (EDCs) and Pharmaceuticals and Personal Care Products (PPCPs) in Water Effluents. Journal of Hazardous Materials 149 , 631-642.
[68] Webb, S.; Ternes, T.; Gilbert, M.; Olejniczak, K., 2003. Indirect human exposure to pharmaceuticals via drinking Water. Toxicology Letters 142, 3, 157-167.
[69] Juvancz, Z.; Barna, S; Gyarmathy, D; Konorót, F., 2008, Study of Endocrine Disrupting Chemicals in Environment, Acta Polytechnica Hungarica 5, 49-58.
[70] Nikolaou, A.; Meric, S.; Fatta, D., 2007. Occurrence patterns of pharmaceuticals in water. Anal Bioanal Chem. 387, 1225-1234.
[71] Kummerer, K., 2004. Resistance in the Environment.J. of Antimicrob. Chemother 54, 311–320.
[72] Ikehata, K.; Naghashkar, N.; Ei-Din, M., 2006. Degradation of aqueous pharmaceuticals by ozonation and advanced oxidation processes: a review. Ozone Sci. Eng. 28, 353–414.
[73] Petrovic, M.; Alda, M.; Diaz-cruz, S.; Postigo, C.; Radjenovic, J.; Gros, M.; Barcelo, D., 2009. Fate and removal of pharmaceuticals and illicit drugs in conventional and membrane bioreactor wastewater treatment plants and by riverbank filtration. Phil. Trans. R. Soc. A. 367, 3979-4003.
[74] Zhou, H.; Smith, D., 2002. Advanced technologies in water and wastewater treatment. J. Environ. Eng. Sci. 1, 247-264.
[75] Jones, O.; Voulvoulis, N.; Lester, J., 2005. Human pharmaceuticals in wastewater treatment processes, Critical Reviews in Environmental Science and Technology 35, 401-427.
[76] Henry, J. A., 2005. Abstracts of the European Association of Poisons Centres and Clinical Toxicologists XXV International Congress. Clinical Toxicology 43, 387–538.
[77] Polubesova, T.; Zadaka, D.; Groisman, L.; Nir, S., 2006. Water remediation by micelle-clay system: case study for tetracycline and sulfonamide antibiotics, Water Res. 40, 2369-2374.
[78] British pharmacopoeia (BP 2007).
[79] Champman and Hall, 1982).Dictionary of organic compounds. 5th ed. (Vol. 1-6).
[80] Williams, D.; Lemke, T., 2002. Foye's Principles of medicinal chemistry, 5th ed. Philadelphia: Lippincott Williams and Wilkins.
[81] Henschel, K.; Wenzel, A.; Diedrich, M.; Fliedner, A., 1997. Environmental hazard assessment of pharmaceuticals. Regulatory toxicology and Pharmacology 25, 220-225.
[82] Nakada, N.; Tanishima, T.; Shinohara, H.; Kiri, K.; Takada, H., 2006. Pharmaceuticals chemicals and endocrine disrupters in municipal wastewater in Tokyo and their removal during activated sludge treatment, Water Res. 40 , 3297-3303.
[83] Ternes, T.A.; Stumpf, M.; Schuppert, B.; Haberer, K., 1998. Simultaneous Determination of antiseptics and acidic drugs in sewage and river.VomWasser. 90, 295-309.
[84] Gagnon, C.; Lageunesse, A.; Cejka, P.; Gagne F.; Hausler, R., 2008. Degradation of selected acidic and neutral pharmaceutical products in a primary- treated wastewater by disinfection processes. Ozone science and engineering 30, 387-392.

[85] Nugrohoi, W.; Reungoat, J.; Keller, J., 2010. The performance of biological activated carbon in removing pharmaceuticals in drinking water treatment. Journal of Applied Sciences in Environmental Sanitation 123, 123-133.

[86] Fersht, A.; Kirby, A., 1980. The hydrolysis of aspirin: intramolecular general base catalysis of ester hydrolysis. Adv. Phys., Org. Chem. 17, 183–278.

[87] Radcliff, R.; Zarnadze, A., 2004. Application of Membrane Technology to the Production of Drinking Water. Water Conditioning & Purification, 23-25.

[88] Dakiky, M.; Khamis, M., Manasra, A.; Mereb, M., 2002. Selective adsorption of chromium (VI) in industrial waste water using low cost abundantly available adsorbents, Adv. Environ. Res. 6, 533-540.

[89] Ternes, T. A., 1998. Occurrence of drugs in German sewage treatment plants Ami River, Water Res. 32, 3245–3260.

[90] Nelson, L. H.; Flomenbaum, N.; Goldfrank, LR., 2006. Goldfrank's Toxicologic Emergencies, 9$^{th}$ed.New York: McGraw-Hill.

[91] Roberts, P.; Thomas, K., 2006. The occurrence of selected pharmaceuticals in wastewater effluent and surface waters of the lower Tyne catchment.Sci. Total Environ. 356 , 143–153.

[92] Vogna, D.; Marotta, R.; Napolitano, A.; d'Ischia, M., 2002. Advanced oxidation chemistry of paracetamol.UV/H2O2-induced hydroxylation/ degradation pathways and 15N-aided inventory of nitrogenous breakdown products.J. Org. Chem. 67, 6143–6151.

[93] Carp, O.; Huisman, C. L.; Reller, A., 2004. Photo-induced reactivity of titanium dioxide. Prog. Solid State Chem. 32, 33–177.

## Appendix

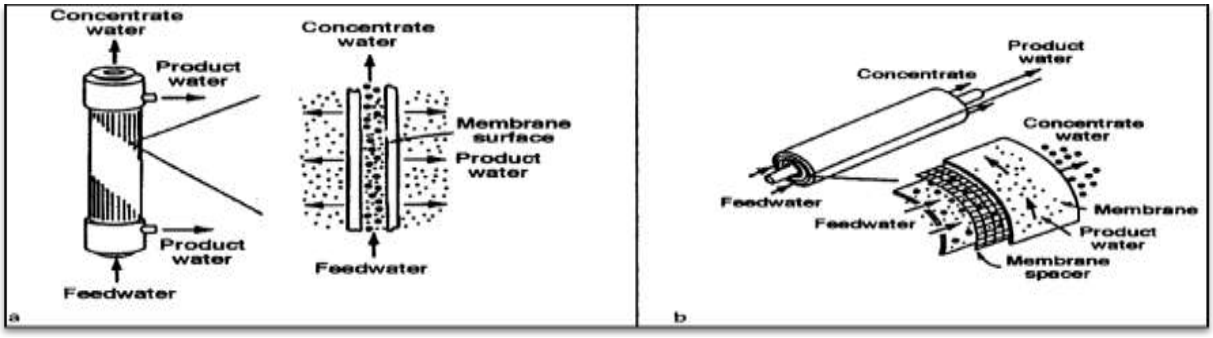



**Figure 1:** Hollow fiber **(a)** and spiral wound **(b)** modules.

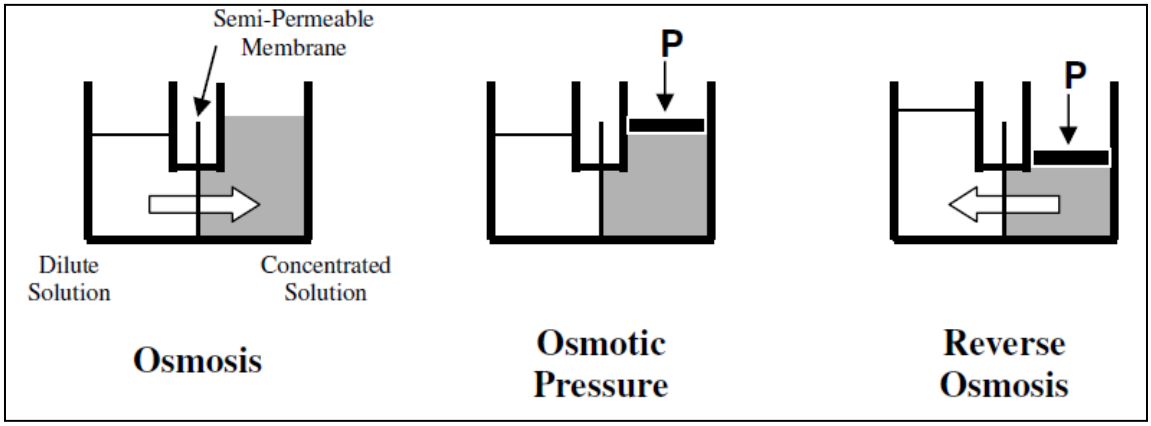



**Figure 2:** The principle of reverse osmosis process.

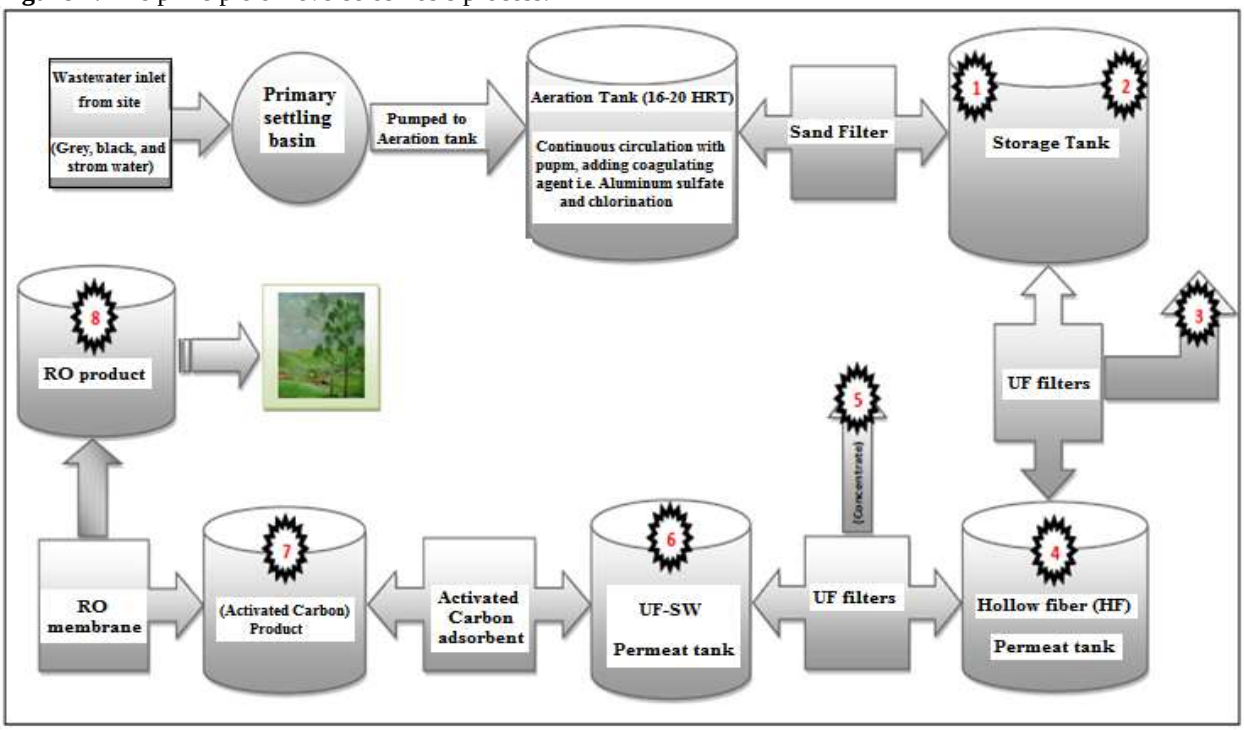


**Figure 3:** Flow diagram showing the process of wastewater treatment plant which consists of HF-UF filters (hollow fiber) and SW-UF (spiral wound), activated carbon and RO filters. The sampling locations in the plant are indicated by red printed Arabic numbers.

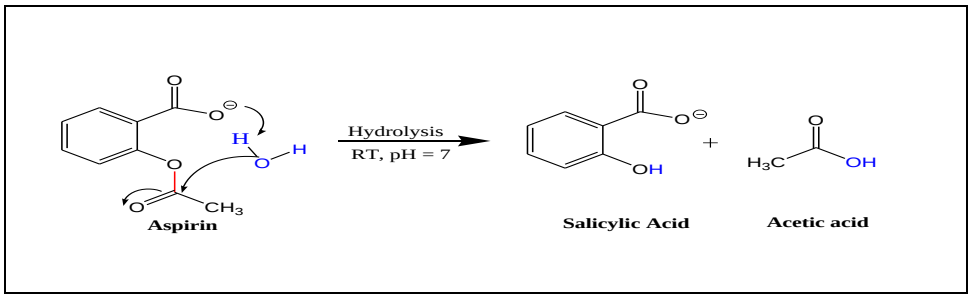



**Figure 4:** Hydrolysis of aspirin (acetylsalicylic acid) to salicylic acid and acetic acid.

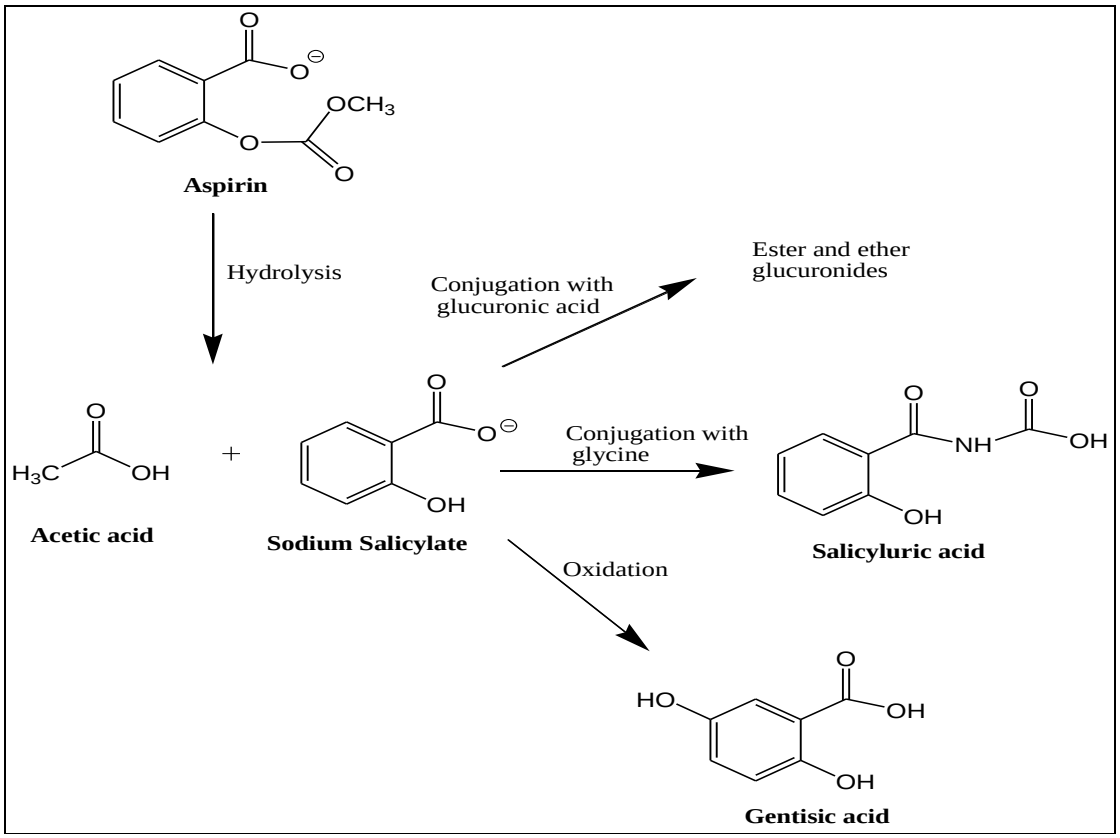



**Figure 5:** Major metabolism pathways for aspirin.

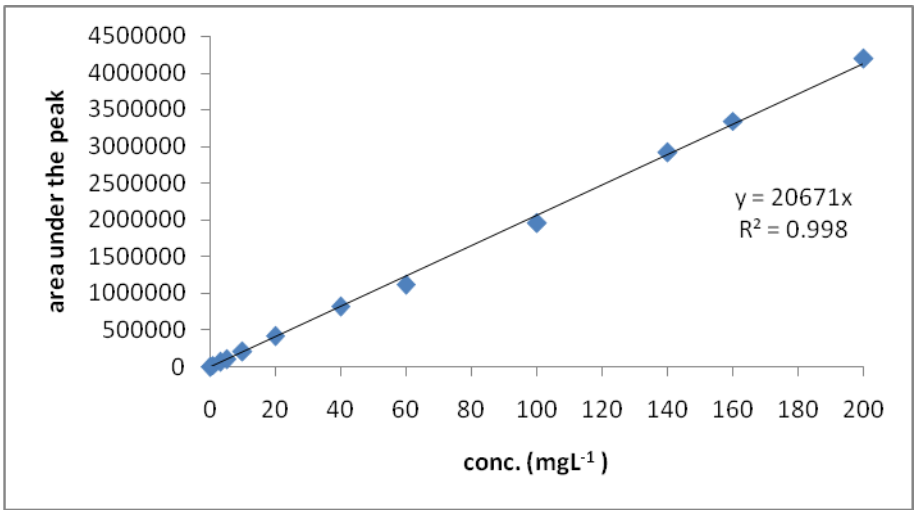



**Figure 6:**Aspirin calibration curve

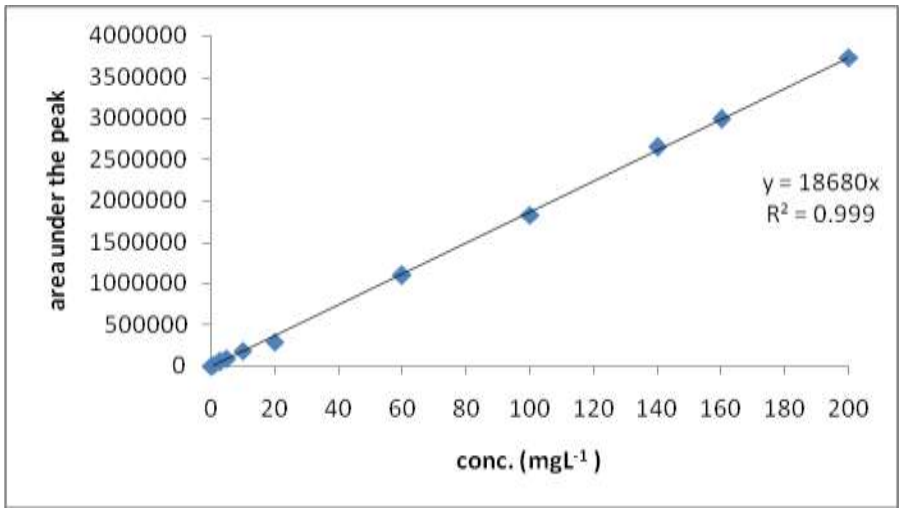



**Figure 7:**Salicylic acid calibration curve for.

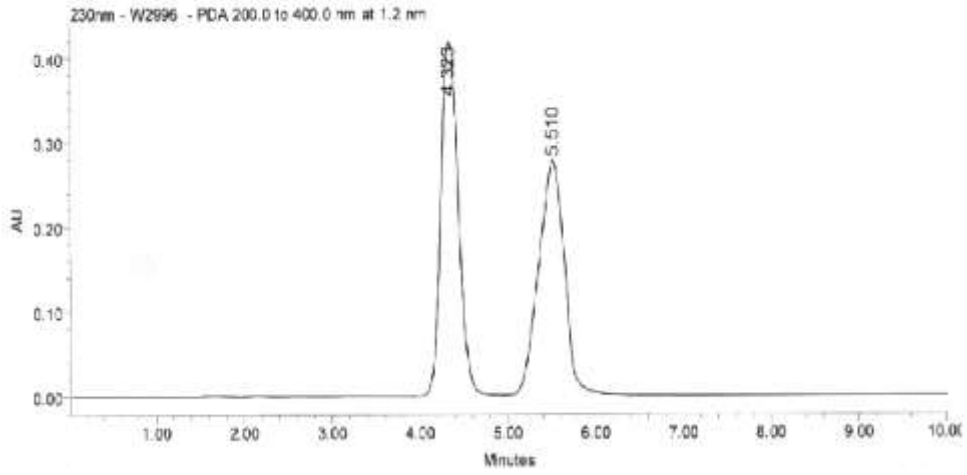


**Figure 8:** Chromatogram showing the hydrolysis of aspirin after 5 days in pure water.

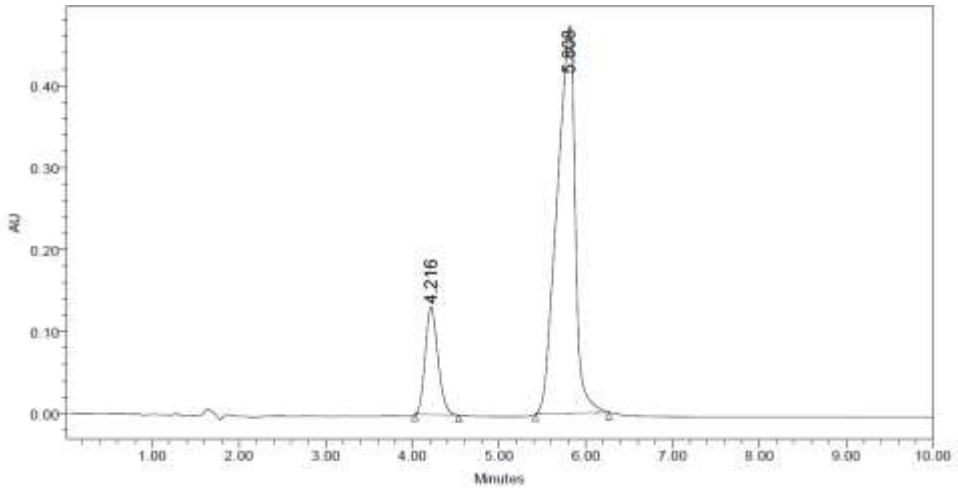



**Figure 9:** Chromatogram showing the hydrolysis of aspirin after 8 days in presence of wastewater.

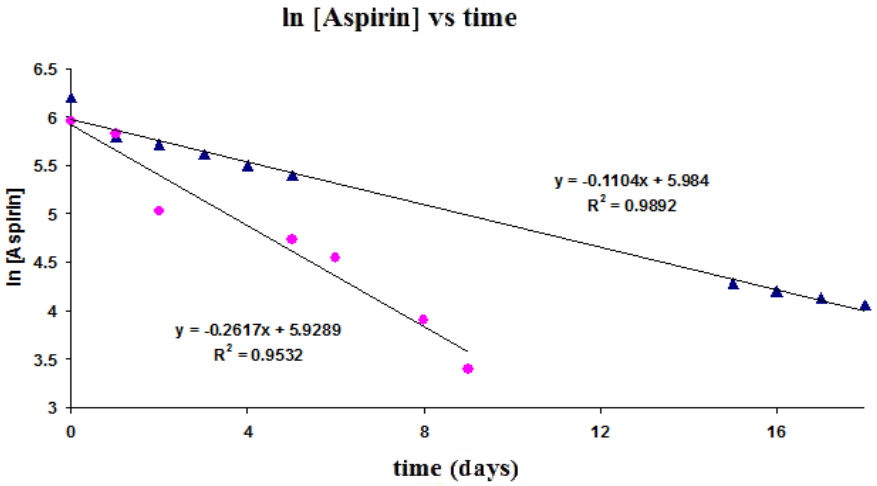



**Figure 10:** Plot of ln [Aspirin] vs. time (days). ▲ (Blue points) is for the hydrolysis of aspirin in pure water at 25° C and ● (pink points) is for the hydrolysis of aspirin in the presence of wastewater at 25° C.

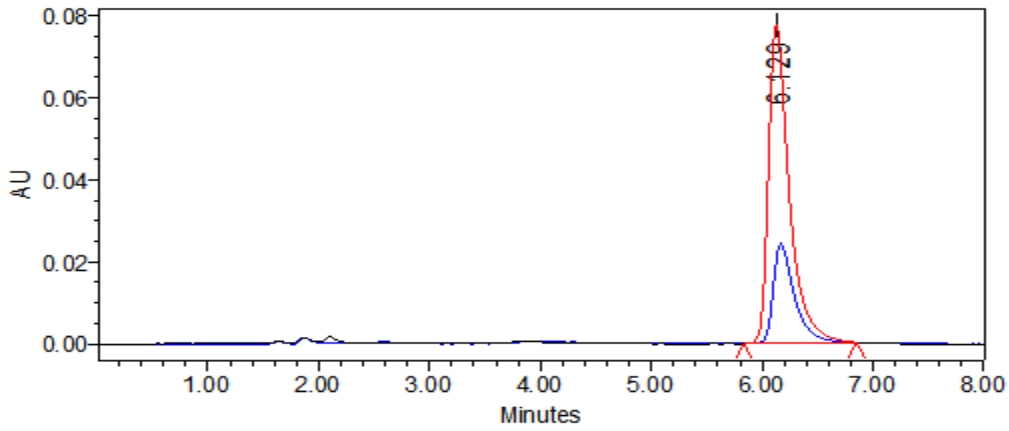


**Figure 11:** Chromatogram showing the initial concentration of salicylic acid and after running the HF-UF (it represents the concentration of samples number 2 and 4, "see Figure 3").

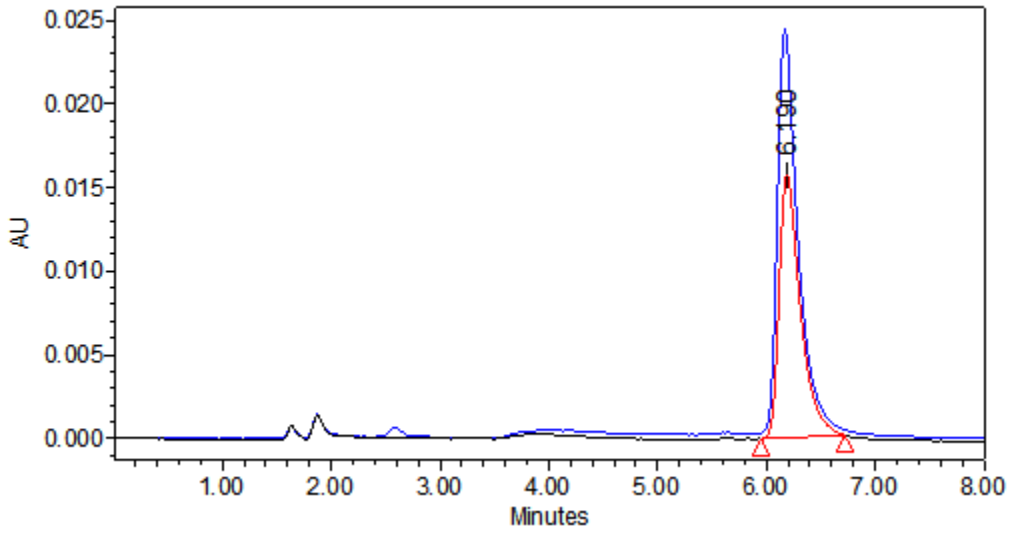



**Figure 12:** Chromatogram showing the concentration of salicylic acid before and after running the SW-UF (it represents the concentration of samples number 4 and 6, "see Figure 3").

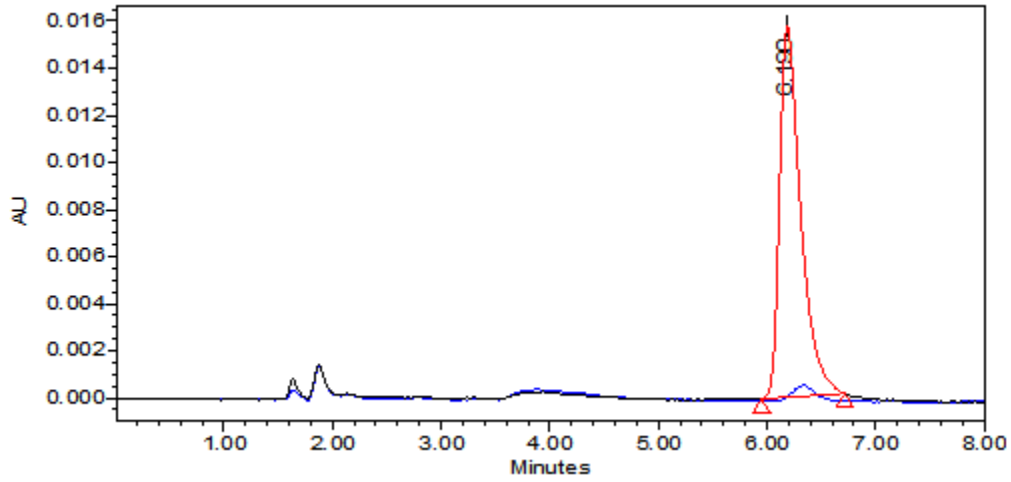



**Figure 13:** Chromatogram showing the concentration of salicylic acid after passing activated carbon adsorbent(it represents the concentration of samples number 6 and 7 "see Figure 3").

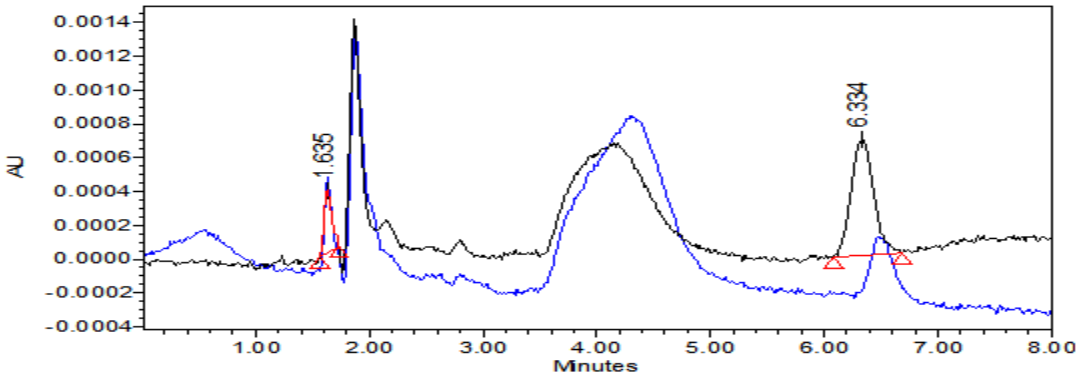


**Figure 14:** Chromatogram showing the concentration of salicylic acid before and after passing reverse osmosis (it represents the concentration of samples number 7 and 8 "see Figure 3).

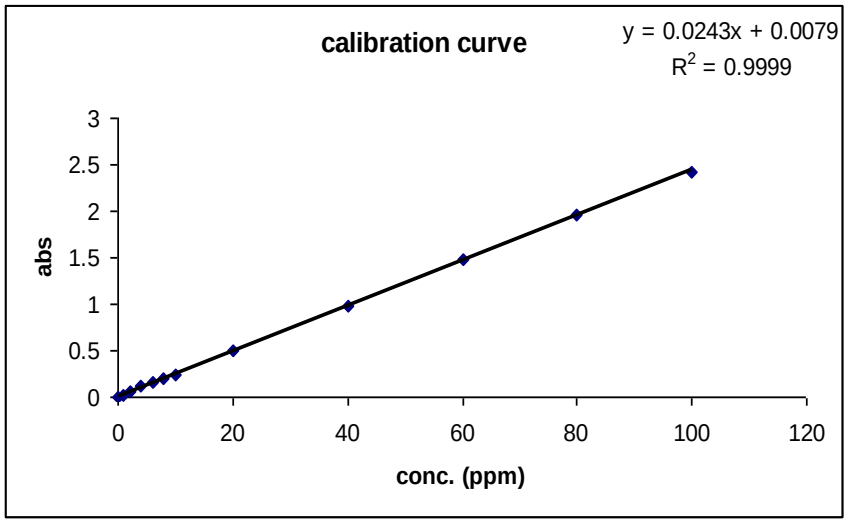
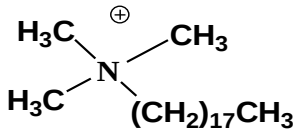



**Figure 15:** Absorption versus concentration ($mgL^{-1}$) of salicylic acid ($\lambda_{max}$ = 295nm).




**Octadecyltrimethylammonium (ODTMA)**

**Figure 16**: Structure of octadecyltriethylammonium (ODTMA).

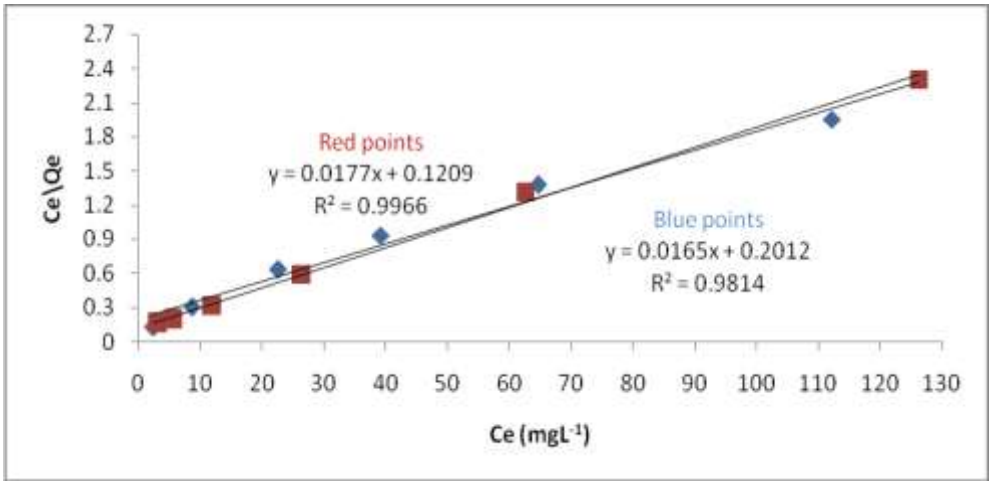


**Figure 17**: Langmuir isotherms for the removal of salicylic acid by a clay micelle complex (■) and by charcoal (♦).

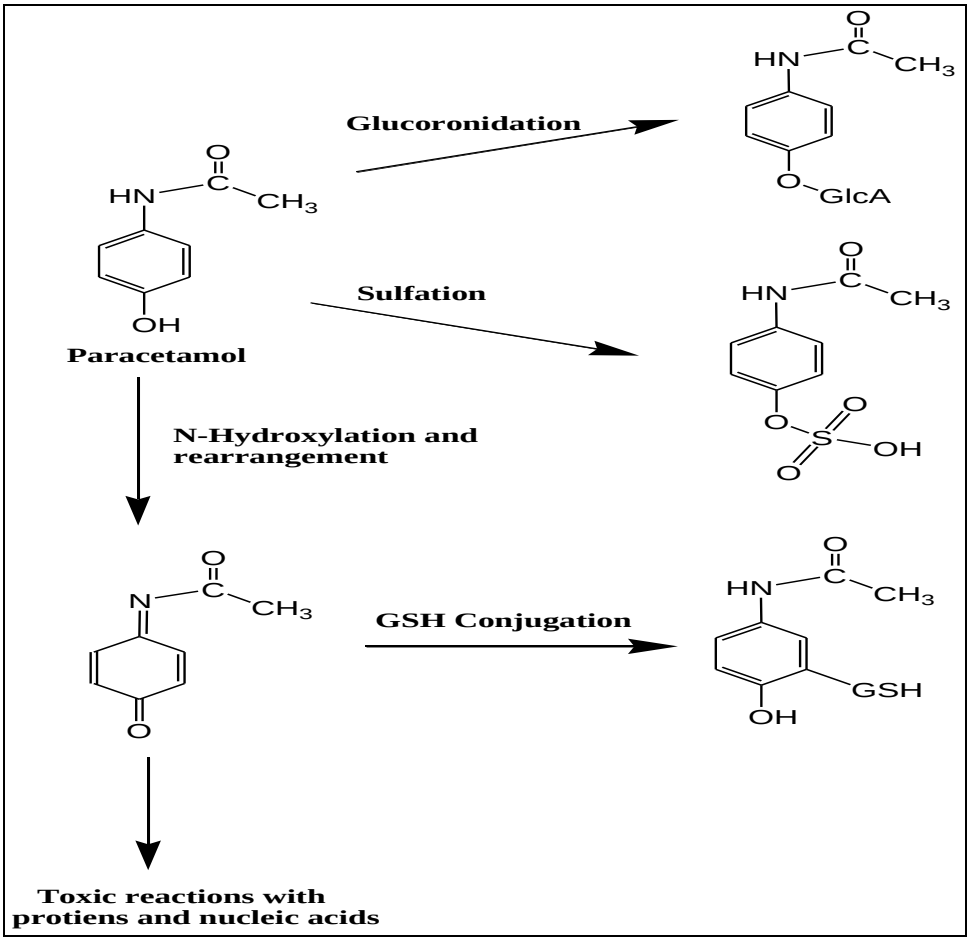



**Figure 18:** Metabolic pathways for paracetamol.

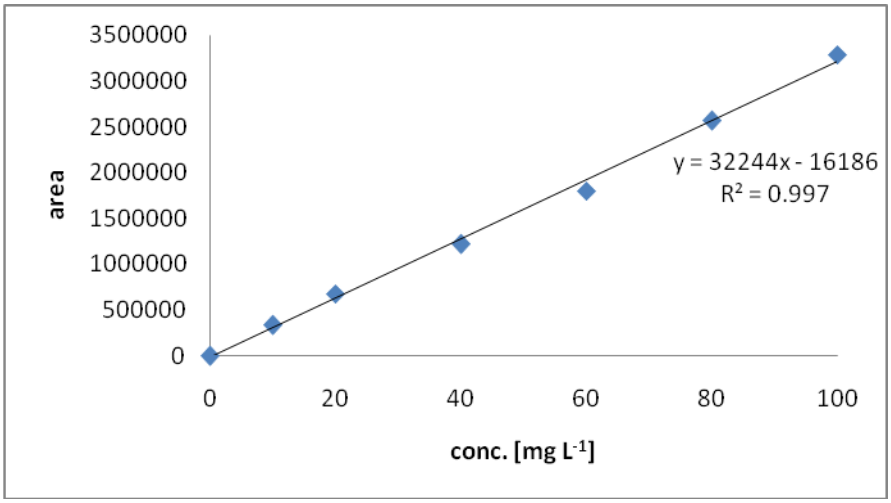


**Figure 19:**paracetamol calibration curve

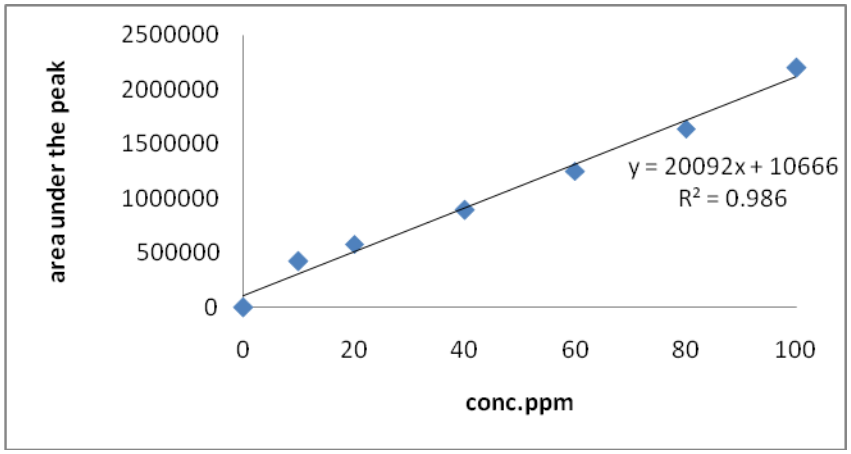



**Figure 20**: *p*-aminophenol. calibration curve.

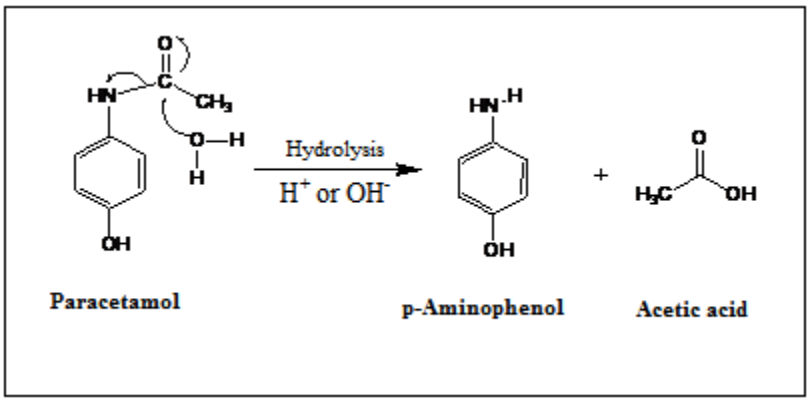



**Figure 21:** Hydrolysis pathway for paracetamol.

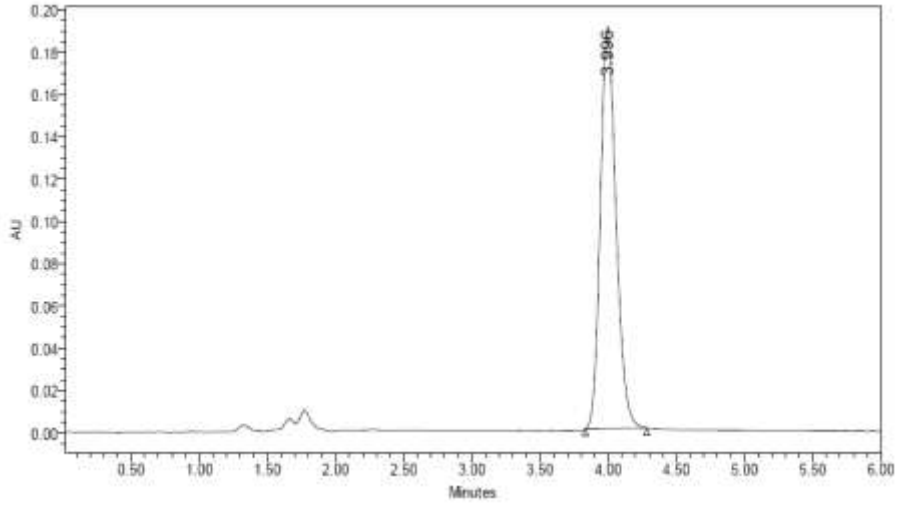


**Figure 22**: Chromatogram showing paracetamol in pure water.

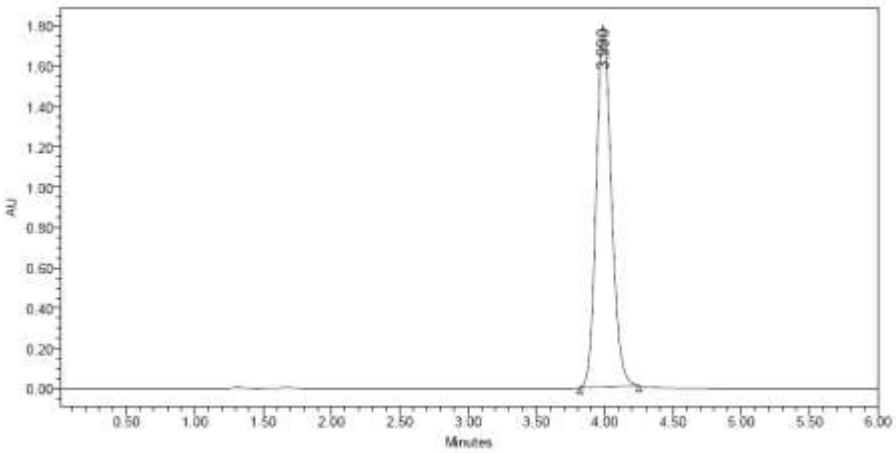



**Figure 23:**Chromatogram showing the hydrolysis of paracetamol after 2 weeks in pure water.

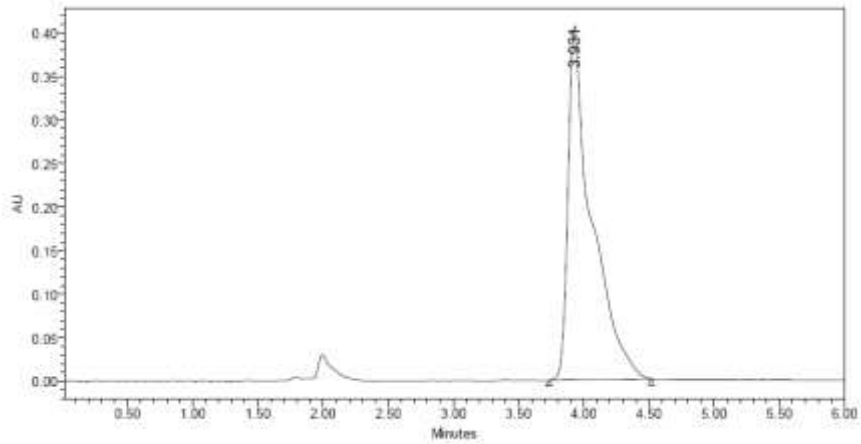



**Figure 24:** Chromatogram showing the hydrolysis of paracetamol after 2 days in presence of wastewater at 25$^{o}$C.

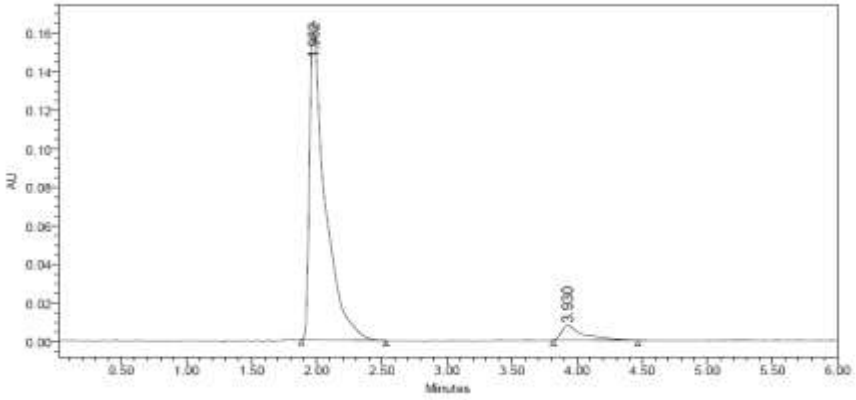


**Figure 25**: Chromatogram showing the hydrolysis of paracetamol after 7 days in presence of wastewater at 25°C.

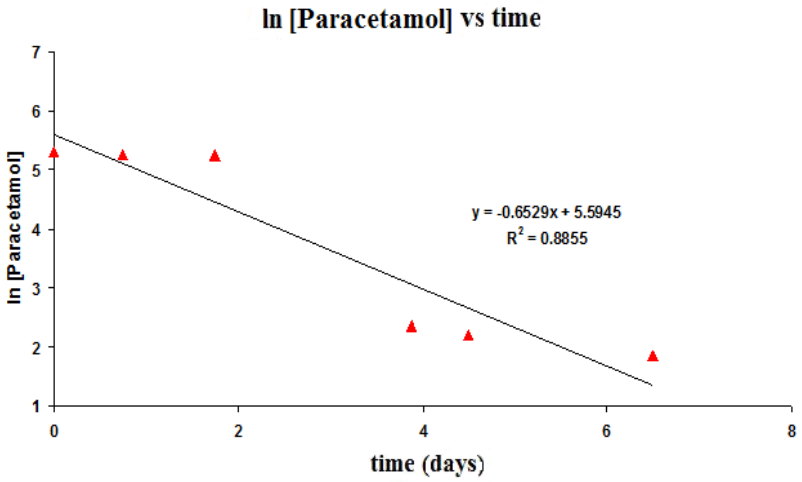



**Figure 26:**Plot of ln [Paracetamol] vs. time (days) for the hydrolysis of paracetamol in the presence of wastewater at 25°C.

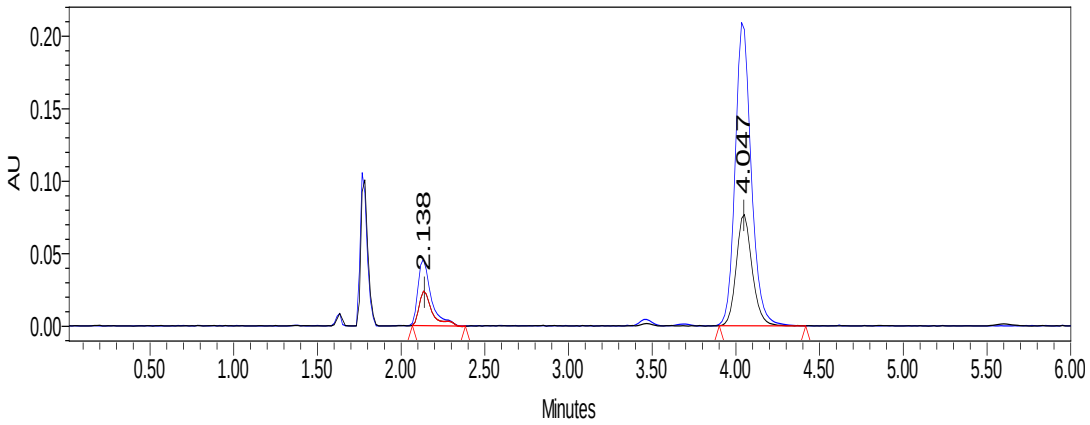



**Figure 27:** Chromatogram showing the initial concentration of paracetamol and *p*-aminophenol before and after running the HF-UF (it represents the concentration of samples number 2 and 4 "see Figure 3").

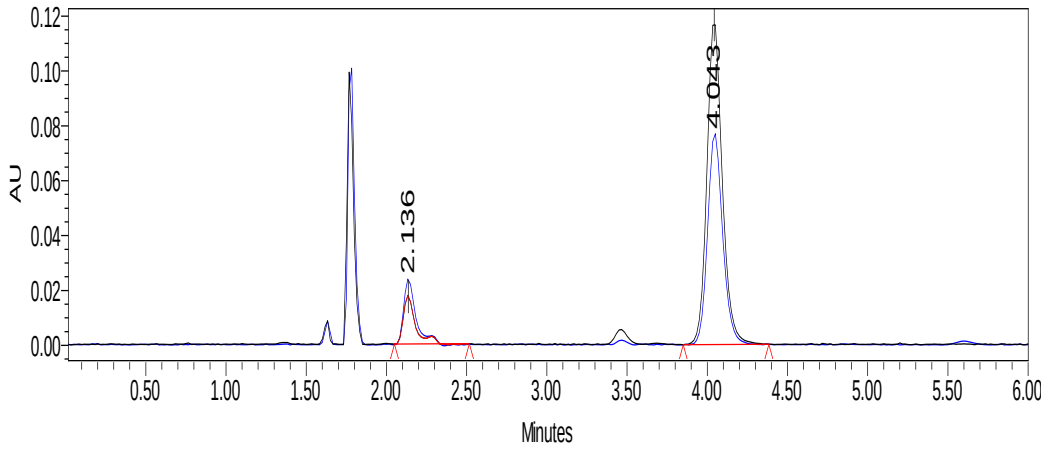


**Figure 28:** Chromatogram showing the concentration of paracetamol and *p*-aminophenol before and after running SW-UF (it represents the concentration of samples number 4 and 6 "see Figure 3").

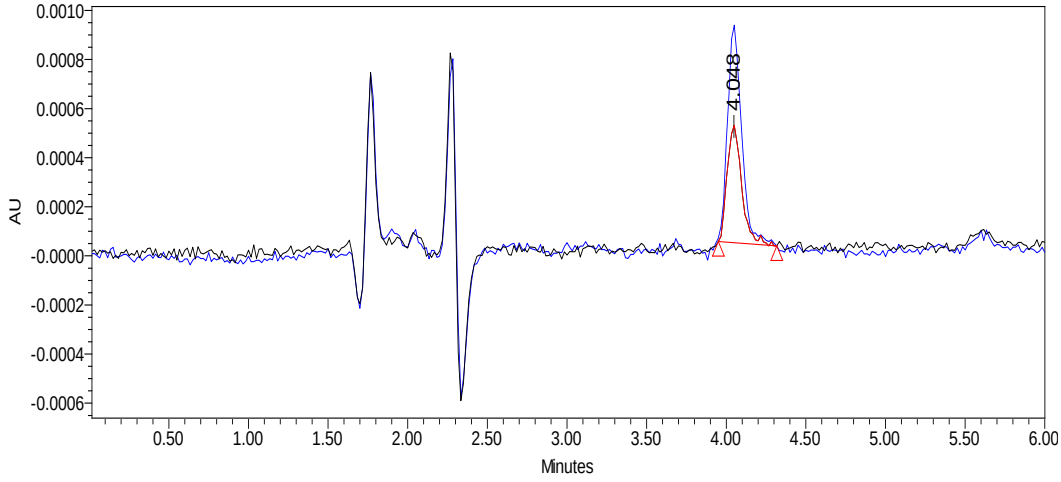



**Figure 29:** Chromatogram showing the concentration of paracetamol and *p*-aminophenol before and after passing activated carbon adsorbent(it represents the concentration of samples number 6 and 7 "see Figure 3").

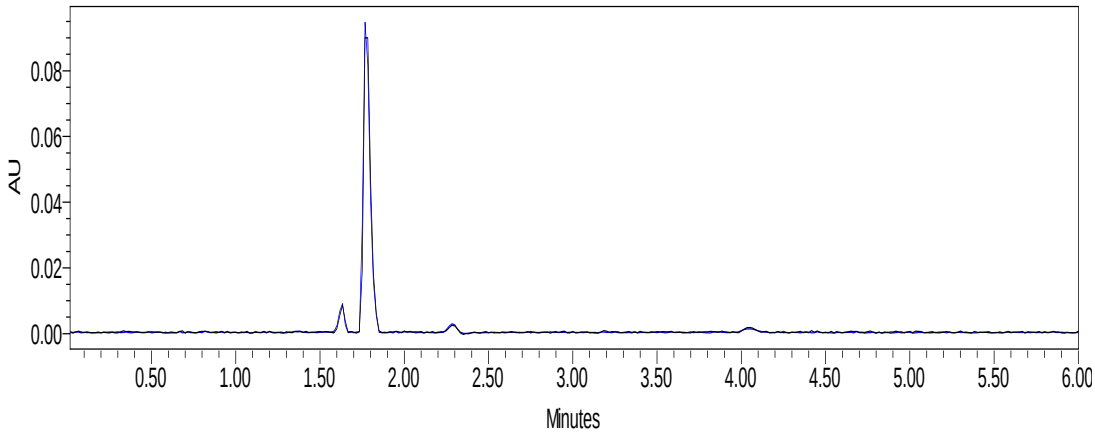



**Figure 30:** Chromatogram showing the concentration of paracetamol and *p*-aminophenol before and after passing Reverse Osmosis (RO) membrane(it represents the concentration of samples number 7and 8 "see Figure 3").

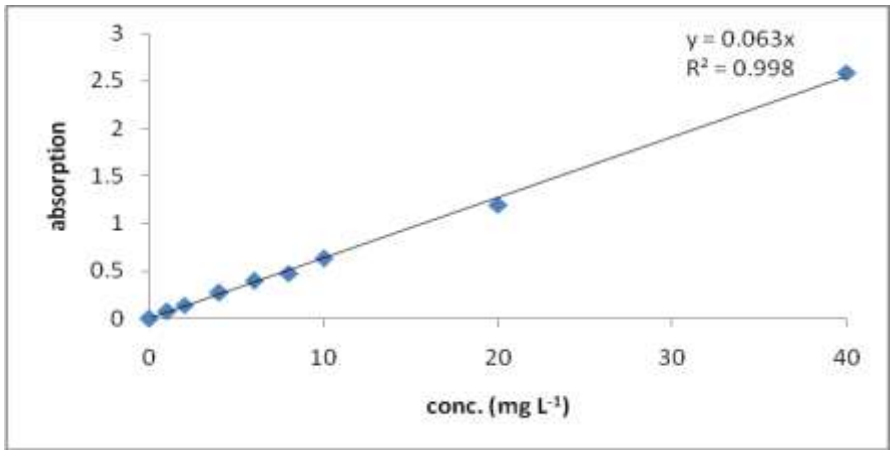


**Figure 31**: Absorption vs. concentration (mg $L^{-1}$) of paracetamol ($\lambda_{max}$= 243nm).

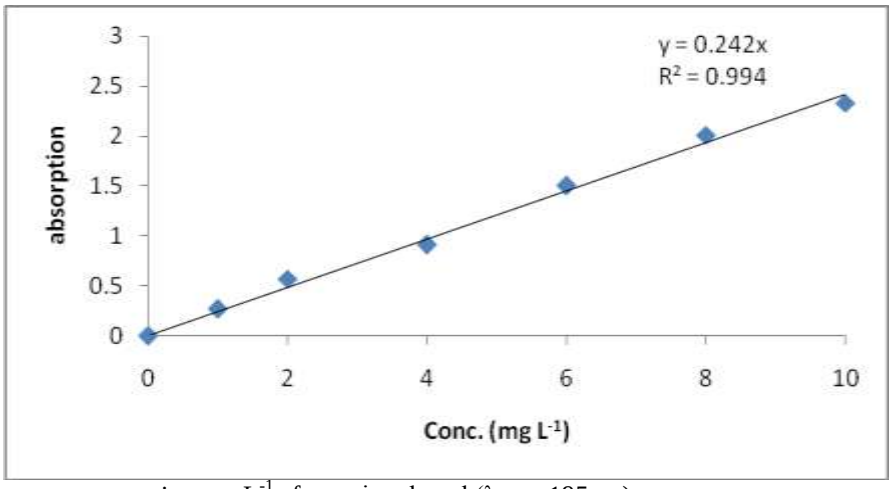



**Figure 32:** Absorption versus concentration mg $L^{-1}$ of *p*-aminophenol ($\lambda_{max}$= 195nm).

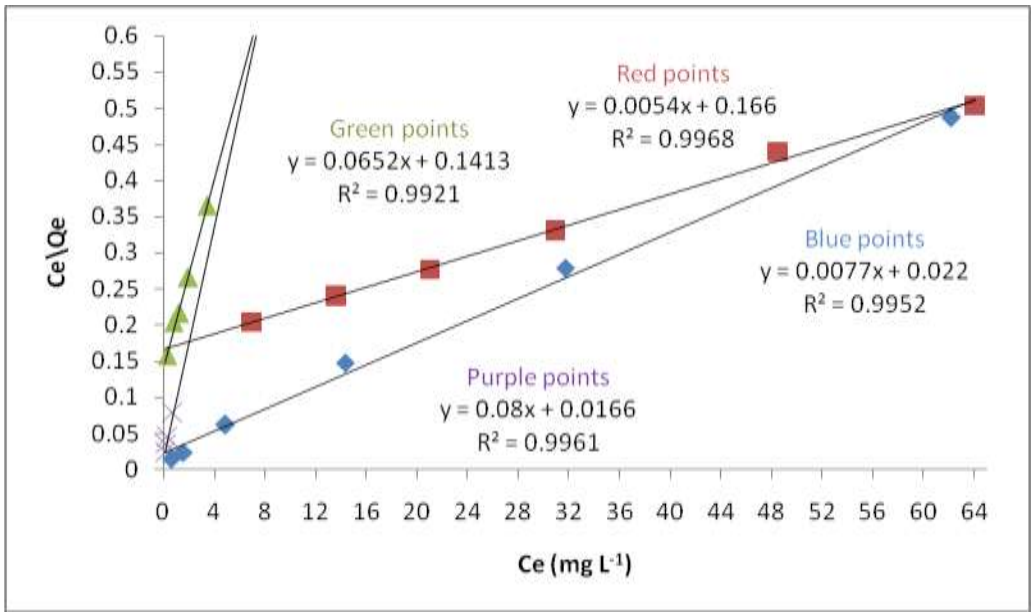



**Figure 33:** Langmuir isotherms for the removal of paracetamol and *p*-aminophenol by charcoal (blue points and purple points, respectively), and for removing paracetamol and *p*-aminophenol by a clay micelle complex (red points and green points, respectively).

## Supplementary Data

**Table S1:** Wastewater treatment plants (WWTP) in the West Bank (status and information)[4].

| Name of T.P | Status of T.P | No. of population served by T.P * 1000 (year) | Capacity of T.P (mcm/year) | Funding Agency | Estimated cost for construction (million US$) | Technology |
|---|---|---|---|---|---|---|
| Nablus East | Planning phase | 240(2021) | 9.2 | Germany KFW | 25 | Extended Aeration |
| Nablus West | Approved | 225(2021) | 9.0 | Germany KFW | 25 | Extended Aeration |
| Salfit | Detailed study | 24(2025) | 2.3 | Germany KFW | 13 | Extended Aeration |
| Jenin* | Rehabilitation is needed | 13.5(1997) | 0.5 | Israel | | Waste stabilization ponds |
| Al-Bireh | Constructed | 40(2000) | 1.1 | Germany KFW | 7 | Oxidation Ditch |
| Tulkarem** | No study yet | 223(2030) | 7.5 | Germany KFW | 50 | Extended Aeration Process |
| Abu-Dees | Feasibility study | 26(2020) | 1 | Norway | | Oxidation Ditch |
| Tafuh | Feasibility study | 16 | 0.5 | UNDP | | Anaerobic Rock Filter |
| Halhul | Preliminary design | 42(2020) | 1.0 | Not funded | 5.5 | Aerated Pond System |
| Birzeit area | Preliminary Study | 28(1994) | 1.2 | Not funded | 4.5 | Imhoff tank and trickling Filter |
| Hebron | Planning stage | 695(2020) | 25.0 | USA | 45 | Activated Sludge |
| Jericho | Preliminary Study | 26 (2000) | 1.2 | Not funded | | |
| Biddya | Preliminary Study | 24 (2000) | 1.1 | Not funded | 10.0 | |
| Ramallah*** | Feasibility Study | 40 (North) | 1.5 | Not funded | 7.0 | Extended Aeration |
| | | 40 (South) | 1.5 | | 7.0 | |
| Al-Ram | Preliminary Study | 86.5(2000) | 3.3 | Germany KFW | 11.0 | Aerobic sludge Stabilization+ Activated Sludge |
| **Total** | | **1789** | **66.3** | | **210** | |

**Note**: *Old and non-functioning sewage treatment plant exists. **Currently rehabilitation of the sewage treatment plant takes place. *** Currently rehabilitation of the old sewage treatment plant takes place as a partial solution. (KFW: KreditanstaltFuerWiederaufbau, T.P: Treatment Plant).

**Table S2:** Comparison of pressure-driven membrane systems

| Parameters | Membrane system | | | |
|---|---|---|---|---|
| | Low-pressure membranes | | High-pressure membranes | |
| | MF | UF | NF | 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, pyrogens, viruses, bacteria, | Organic compounds > 200 Da, some dissolved solids (i.e. multivalent ions) | Ions, Organic compounds >100 MW |
| **Operating pressure, psi** | 1 to 15 | colloids 30 to 100 | 80 to 125 | ≥ 1,000 |

**Table S3**: Adsorption potential dependence on log $K_{ow}$.

| | |
|---|---|
| Log $K_{ow} \leq 2.5$ | Low sorption potential |
| $2.5 <$ Log $K_{ow} < 4.0$ | Medium sorption potential |
| Log $K_{ow} \geq 4.0$ | High sorption potential |

**Table S4**: List of the most top twenty consumed pharmaceuticals in Israel and East Jerusalem.

| Drugs name<br><br>Brand Name, (Generic Name), Dosage form | Uses |
|---|---|
| Vitacal®+ D (Calcium + vit D) Capsules | Calcium deficiency |
| Disothiazide® (Hydrochlorthiazide) Tablets | Diuretic |
| Metformin® (Metformin) Tablets | Anti-diabetic agent |
| Augmentin® (Amoxycillin + Clavulanic acid) Caplets | Anti-bacterial |
| Zinnat® (Cefixime) Tablets | Anti-bacterial |
| Micropirin®, Aspirin® (Acetylsalicylic Acid) Tablets | Anti-coagulant |
| Moxypen® (Amoxycillin) Syrup | Anti-bacterial |
| Fusid® (Furosemide) Tablets | Diuretic |
| Tribemin ® (Vit B1, B2, B6) Tablets | Vitamin-B deficiency |
| Acamol® (paracetamol) Tablets | Anti-pyretic and pain killer |
| Ibufen® (Ibuprofen) Tablets | Anti-inflammatory |
| Ceforal® (Cephalexin) Capsules | Anti-bacterial |
| Normiten® (Atenolol) Tablets | Anti-hypertension |
| Omepradex® (Omeprazole) Capsules | Against stomach ulcer |
| Simvastatin® (Simvastatin) Tablets | Lowering cholesterol |
| Glibitic® (Glipizide) Tablets | Anti-diabetic agent |
| Optalgin® (Dyperone) Tablets | Anti-pyretic and pain killer |
| Enalpril® (Enalprilate) Tablets | Anti-hypertension |
| Bezafibrate® (Benzafibrate) Tablets | Lowering triglycerides |
| Amlodipine® (Amlodipine) Tablets | Anti-hypertension |

**Table S5**: Physicochemical properties [78-79].

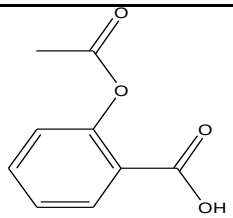
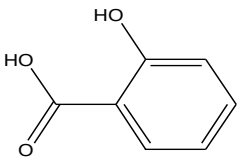
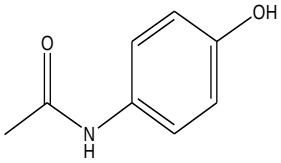
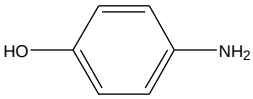
| Properties | Aspirin | Salicylic acid | Paracetamol (Acetaminophen) | *p*-aminophenol |
|---|---|---|---|---|
| Structure |  aspirin |  salicylic acid |  paracetamol |  p-aminophenol |
| Chemical formula | $C_9H_8O_4$ | $C_7H_6O_3$ | $C_8H_9NO_2$ | $C_6H_7NO$ |
| Molecular weight (MW, g $mol^{-1}$) | 180.16 | 138.12 | 151.16 | 109.13 |
| Water Solubility ($mgL^{-1}$), 25 $^oC$ | 3300 | 5000 | 12742.7 | 15000 |
| Log $K_{ow}$ | 0.46 | 1.19 | 0.46-0.89 | 0.04 |
| pKa at 25 $^oC$ | 3.49 | 2.98 | 9.5 | 5.75 |

**Table S6:** Performance of hollow fiber ultrafiltration (HF), spiral wound ultrafiltration (SW), activated carbon adsorbent, and reverse osmosis in terms of removal of salicylic acid from wastewater.

| Sample location number (See Figure 3-1) | Name of sample location | Concentration of salicylic acid (mg $L^{-1}$) |
|---|---|---|
| Sample No. 1 | Blank (before addition 60 g of salicylic acid) | 0 |
| Sample No. 2 | Initial concentration of salicylic acid before running wastewater treatment plant | 54.303 |
| Sample No. 3 | Brine of AST(ultrafiltration-hollow fiber) | 38.619 |
| Sample No. 4 | Product of AST (ultrafiltration-hollow fiber) | 17.021 |
| Sample No. 5 | Nirosoft (ultrafiltration-spiral wound fiber) "concentrate" | 14.433 |
| Sample No. 6 | Permeate of Nirosoft (ultrafiltration-spiral wound fiber) | 11.42 |
| Sample No. 7 | Product of activated carbon adsorbent | 0.50 |
| Sample No. 8 | Product of reverse osmosis | 0.204 |

**Table S7:** Concentrations in equilibrium obtained for the adsorption test of salicylic acid onto the adsorbent clay micelle complex used.

| 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 |
|---|---|---|---|---|---|---|
| 100 | 10 | 3.17265 | 0.317265 | 9.68275 | 19.3655 | 0.1638 |
| 150 | 15 | 5.5595 | 0.55595 | 14.44405 | 21.66195 | 0.19245 |
| 200 | 20 | 11.97935 | 1.197935 | 18.80205 | 37.6041 | 0.31865 |
| 250 | 25 | 26.48555 | 2.648555 | 22.35145 | 44.7029 | 0.5925 |
| 300 | 30 | 62.51415 | 6.251415 | 23.7486 | 47.4972 | 1.31945 |
| 400 | 40 | 126.1151 | 12.61151 | 27.3885 | 54.777 | 2.2344 |

**Table S8:** Concentrations in equilibrium obtained for the adsorption test of salicylic acid onto the adsorbent charcoal used.

| 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 |
|---|---|---|---|---|---|---|
| 100 | 10 | 2.4528 | 0.24528 | 9.7547 | 19.5094 | 0.1258 |
| 150 | 15 | 8.6251 | 0.86251 | 14.1375 | 28.275 | 0.3068 |
| 200 | 20 | 22.65825 | 2.265825 | 17.7342 | 35.4684 | 0.6318 |
| 250 | 25 | 39.18125 | 3.918125 | 21.0819 | 42.1638 | 0.9333 |
| 300 | 30 | 64.613351 | 6.461335 | 23.53865 | 47.0773 | 1.3769 |
| 400 | 40 | 112.1438 | 11.21438 | 28.7856 | 57.57125 | 1.9526 |

**Table S9:** Langmuir adsorption parameters (k and $Q_e$), the square of correlation coefficient ($R^2$) of salicylic acid onto both adsorbents.

| *Pharmaceutical* | *Adsorbents* | *Langmuir sorption parameters* | | |
|---|---|---|---|---|
| | | **K** | **$Q_{max}$(mg $g^{-1}$)** | **$R^2$** |
| **Salicylic acid** | **Clay micelle complex** | 0.1464±0.00425 | 56.49±1.1596 | 0.9966±0.00219 |
| | **Charcoal** | 0.0820±0.0.01971 | 60.60±1.1563 | 0.9814±0.00205 |

**Table S10:** Performance of ultrafiltration hollow fiber (UF-HF), and ultrafiltration spiral wound (UF-SW), activated carbon adsorbent and reverse osmosis in terms of removal of paracetamol and *p*-aminophenol from wastewater.

| **Sample location No. (See Figure 3-1)** | **Sample location name** | **Concentration of paracetamol (mg $L^{-1}$)** | **Concentration of *p*-aminophenol (mg $L^{-1}$)** |
|---|---|---|---|
| Sample No. 1 | Blank (before addition of 25g paracetamol and *p*-aminophenol) | 0 | 0 |
| Sample No. 2 | Initial concentration of paracetamol and *p*-aminophenol before running wastewater treatment plant | 20.95 | 24.3 |
| Sample No. 3 | Brine of HF-Ultrafiltration | 20.92 | 20.4 |
| Sample No. 4 | Product of HF-Ultrafiltration | 12.47 | 6.87 |
| Sample No. 5 | SW-Ultrafiltration "concentrate" | 11.84 | 5.22 |
| Sample No. 6 | Permeate of SW-Ultrafiltration | 10.73 | 2.82 |
| Sample No. 7 | Product of activated carbon adsorbent | 0.223 | 0 |
| Sample No. 8 | Product of reverse osmosis | 0.11 | 0 |

**Table S11:** Concentrations in equilibrium obtained for the adsorption test of paracetamol onto the adsorbent charcoal used.

| 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 |
|---|---|---|---|---|---|---|
| 200 | 20 | 0.6035 | 0.06035 | 19.9394 | 39.7788 | 0.014925 |
| 300 | 30 | 1.568 | 0.1568 | 29.84315 | 59.6863 | 0.02389 |
| 400 | 40 | 4.907 | 0.4907 | 39.50915 | 79.0183 | 0.06228 |
| 500 | 50 | 14.3255 | 1.43255 | 48.56735 | 97.1347 | 0.14747 |
| 600 | 60 | 31.7325 | 3.17325 | 56.82695 | 113.6539 | 0.278965 |
| 700 | 70 | 62.1855 | 6.21855 | 63.78135 | 127.5627 | 0.48728 |

**Table S12:** Concentrations in equilibrium obtained for the adsorption test of paracetamol onto the adsorbent clay micelle complex used.

| 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 |
|---|---|---|---|---|---|---|
| 200 | 20 | 7.85 | 0.785 | 19.215 | 38.43 | 0.20425 |
| 300 | 30 | 13.69 | 1.369 | 28.631 | 57.262 | 0.239 |
| 400 | 40 | 20.99 | 2.099 | 37.901 | 75.802 | 0.27725 |
| 500 | 50 | 30.91 | 3.091 | 46.909 | 93.818 | 0.3295 |
| 600 | 60 | 48.545 | 4.8545 | 55.1455 | 110.291 | 0.44 |
| 700 | 70 | 64.125 | 6.4125 | 63.5875 | 127.175 | 0.504 |

**Table S13:** Concentrations in equilibrium obtained for the adsorption test of p-aminophenol onto the adsorbent clay micelle complex used.

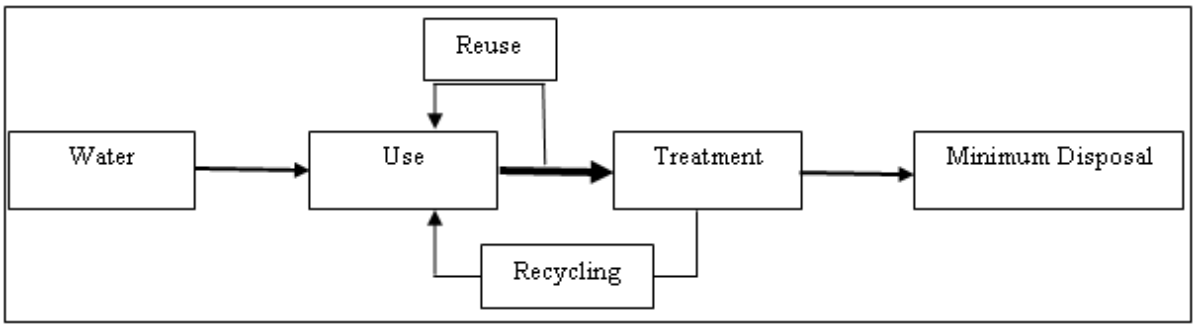
| Conc. (initial) ($mgL^{-1}$) | Mass (initial) (mg) | Conc. (final) ($mgL^{-1}$) (Ce) | Mass (final) (mg) | M initial - M final | Qe= (M initial - M final) /0.5 g | Ce/Qe |
|---|---|---|---|---|---|---|
| 10 | 1 | 0.305 | 0.0305 | 0.0305 | 0.061 | 0.1571 |
| 20 | 2 | 0.785 | 0.0785 | 1.9215 | 3.843 | 0.2041 |
| 30 | 3 | 1.245 | 0.1245 | 1.755 | 3.51 | 0.21635 |
| 40 | 4 | 1.945 | 0.1945 | 3.8055 | 7.611 | 0.2652 |
| 50 | 5 | 3.405 | 0.3405 | 4.6595 | 9.319 | 0.36495 |

**Table S14:** Concentrations in equilibrium obtained for the adsorption test of p-aminophenolonto the adsorbent charcoal used.

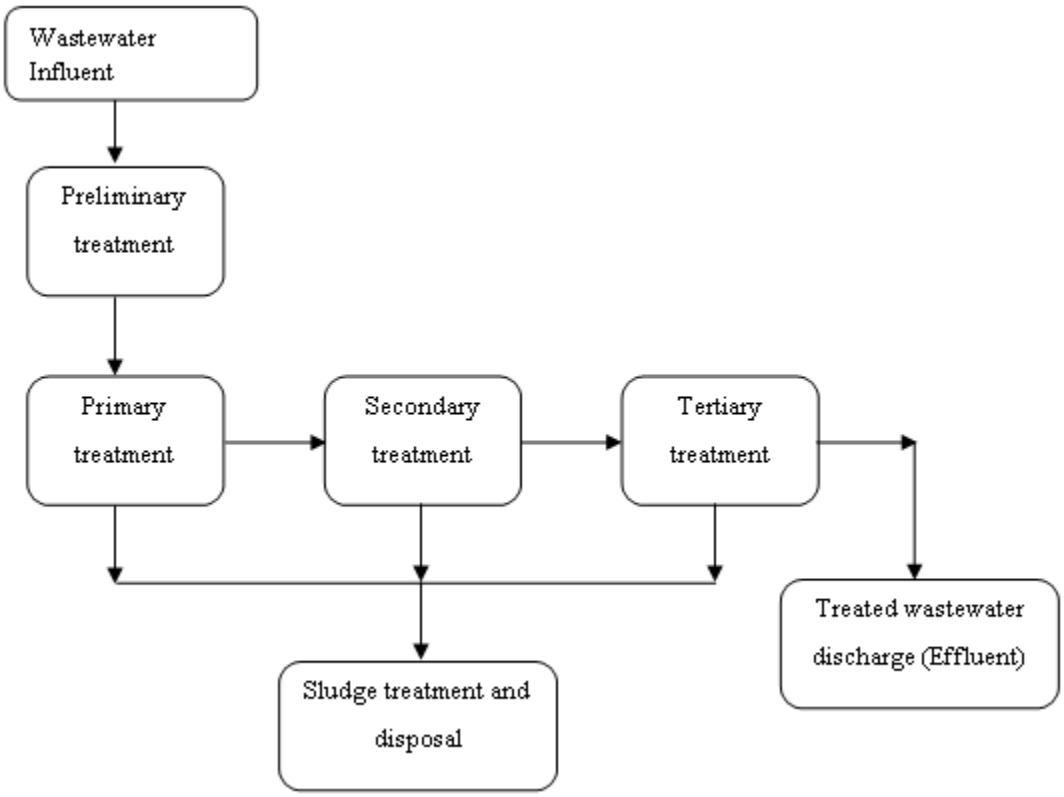
| Conc. (initial) ($mgL^{-1}$) | Mass (initial) (mg) | Conc. (final) ($mgL^{-1}$) (Ce) | Mass (final) (mg) | M initial - M final | Qe= (M initial - M final) /0.5 g | Ce/Qe |
|---|---|---|---|---|---|---|
| 20 | 2 | 0.0895 | 0.00895 | 1.9910 | 3.9821 | 0.02245 |
| 30 | 3 | 0.213 | 0.0213 | 2.9787 | 5.9574 | 0.035765 |
| 40 | 4 | 0.346 | 0.0346 | 3.9654 | 7.9308 | 0.04362 |
| 50 | 5 | 0.7645 | 0.07645 | 4.9235 | 9.8471 | 0.077655 |

**Table S15:** Langmuir adsorption parameters (k and Qe), the square of correlation coefficient (R2) of paracetamol and p-aminophenol onto both adsorbents.

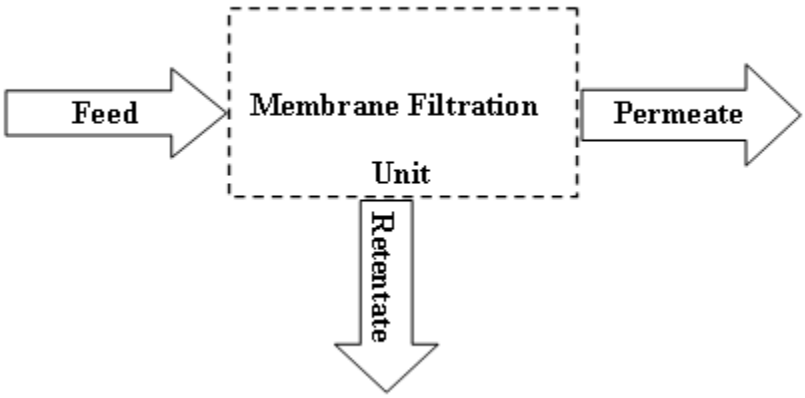
| *Pharmaceuticals* | *Adsorbents* | *Langmuir sorption parameters* | | |
|---|---|---|---|---|
| | | **K** | **$Q_{max}$(mg $g^{-1}$)** | **$R^2$** |
| **Paracetamol** | Clay micelle complex | 0.03253±0.00626 | 185.185±9.7142 | 0.9968±0.00485 |
| | Charcoal | 0.0350±0.0.05992 | 129.87±1.708 | 0.9952±0.0014 |
| ***p*-aminophenol** | Clay micelle complex | 0.4614±0.05505 | 15.3374±0.2163 | 0.9921±0.00133 |
| | Charcoal | 4.8192±1.6241 | 12.50±1.14320 | 0.9961±0.00399 |



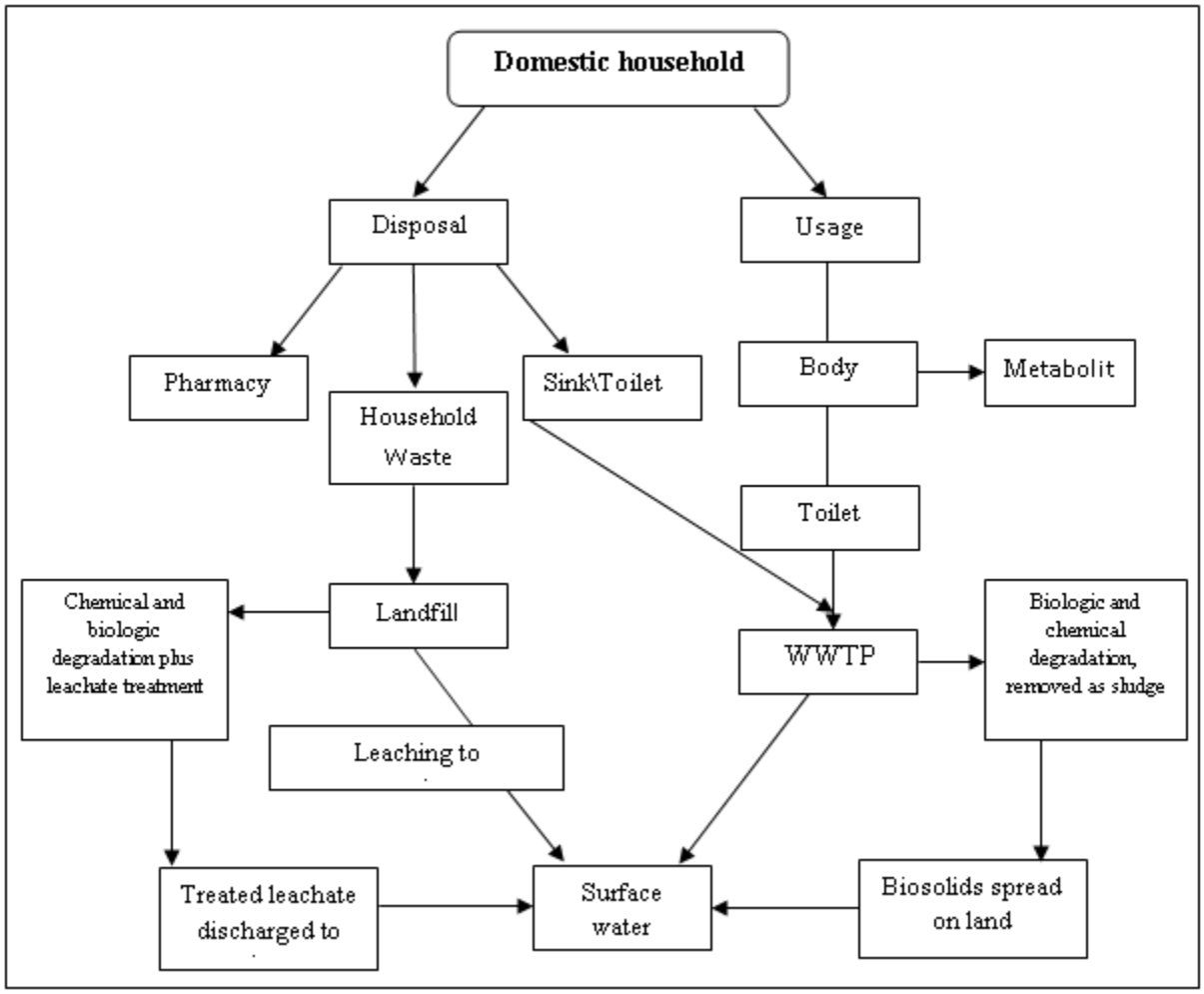
**Flow chart S1:** Future approaches of dealing with water (please note the size of the arrows).



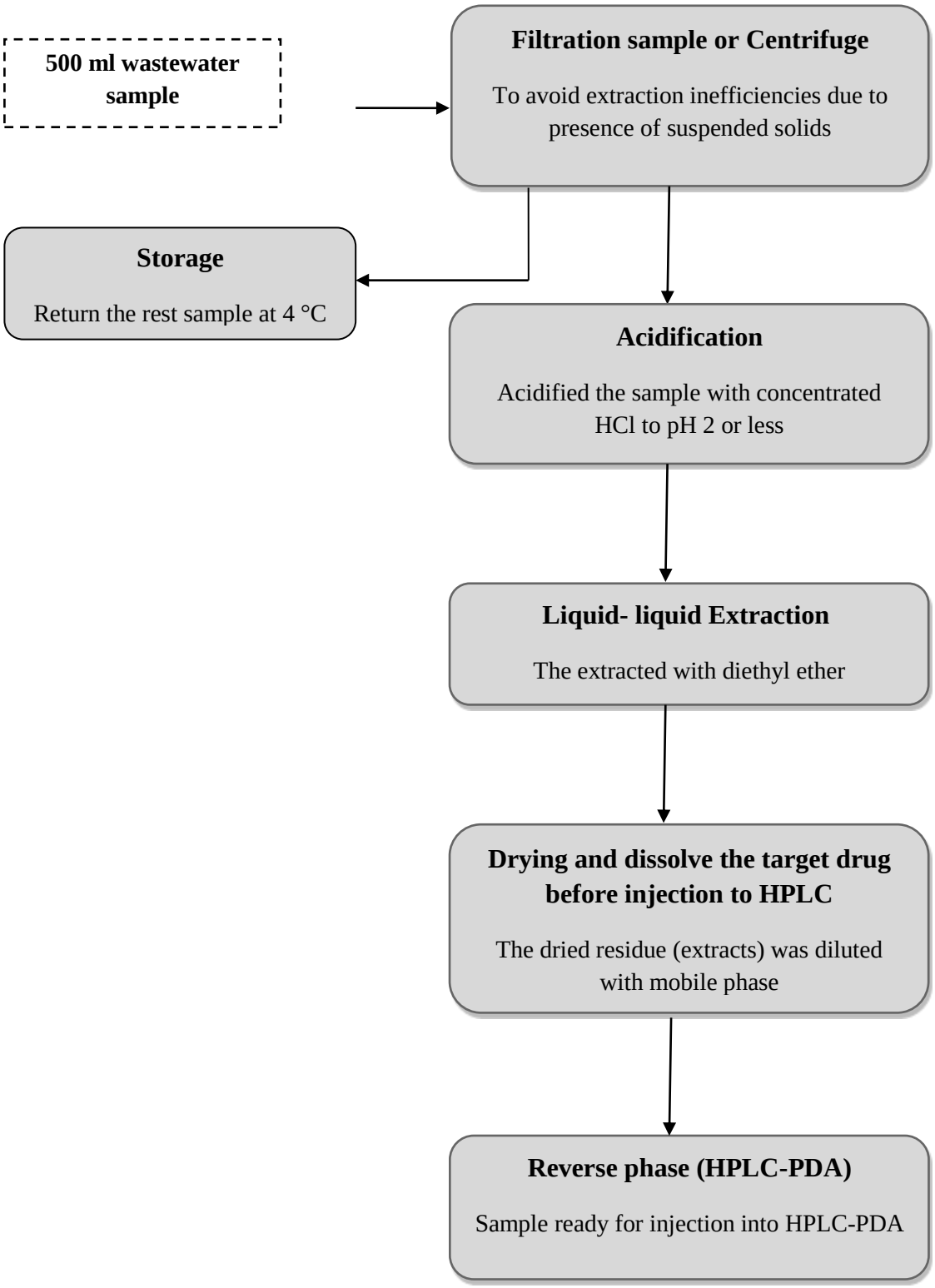

**Flow chart S2:** A schematic representation of a wastewater treatment classification.



**Flow chart S3:** A schematic of operation of a membrane process [38].



**Flow chart S4:**Pathways and fate of PPCPs from domestic households to the environment.




**Flow chart S5:** Schematic representation for the analysis process of salicylic acid, paracetamol, and *p*-aminophenol. (**Note:** paracetamol and *p*-aminophenol followed all steps without the acidification step)