Environmental Technology

ISSN: 0959-3330 (Print) 1479-487X (Online) Journal homepage: http://www.tandfonline.com/loi/tent20

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*Environmental Technology*, 2014
Vol. 35, No. 15, 1945–1955, http://dx.doi.org/10.1080/09593330.2014.888097



# Stability and removal of dexamethasone sodium phosphate from wastewater using modified clays

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(*Received 7 July 2013; accepted 20 January 2014*)

Stability and removal of dexamethasone sodium phosphate (DSP) from wastewater produced at Al-Quds University Campus were investigated. Kinetic studies in both pure water and wastewater coming from secondary treatment (activated sludge) demonstrated that the anti-inflammatory DSP underwent degradation to its hydrolytic derivative, dexamethasone, in both media. The first-order hydrolysis rate of DSP in activated sludge at 25°C ($3.80 \times 10^{-6}$ s$^{-1}$) was about 12-fold larger than in pure water ($3.25 \times 10^{-7}$ s$^{-1}$). The overall performance of the wastewater treatment plant (WWTP) installed in the University Campus was also assessed showing that 90% of spiked DSP was removed together with its newly identified metabolites by the ultra-filtration (UF) system, which consists of a UF hollow fibre (HF) with a 100-kDa cutoff membrane as the pre-polishing stage for the UF spiral wound with a 20-kDa cutoff membrane. In testing other technologies, the effectiveness of adsorption and filtration by micelle–clay (MC) preparation for removing DSP was ascertained in comparison with activated charcoal. Batch adsorption in aqueous suspensions of the MC composite and activated carbon was well described by Langmuir isotherms showing the best results for MC material. Filtration of DSP water solutions demonstrated a significant advantage of columns filled in with a mixture of sand and MC complex in comparison with activated carbon/sand filters.

**Keywords:** dexamethasone sodium phosphate; wastewater treatment; activated sludge; activated charcoal; micelle–clay complex; column filtration



## Nomenclature

| | |
|---|---|
| DSP | dexamethasone sodium phosphate |
| FAC | fine powder activated charcoal |
| GAC | granular activated charcoal |
| HF | hollow fibre UF membrane |
| HP | hydrolysis product |
| MC | micelle–clay complex |
| ODTMA | octadecyl trimethyl ammonium |
| RO | reverse osmosis |
| SW | spiral wound UF membrane |
| UF | ultra-filtration |
| WWTP | wastewater treatment plant |

## 1. Introduction

Despite the progress in water treatment methods, varying amounts of chemicals exist in what is referred to as 'clean' water.[1] Organic contaminants in the environment, especially in water, have become a major concern due to their toxicity. To remediate this pollution problem, various chemical, physical and biological processes have been developed, such as microbial degradation, filtration, adsorption, coagulation and membrane separation. However, all these remediation methods have suffered from certain limitations and disadvantages such as high cost, poor removal efficiency and possibility of desorption.[1] This is an ever growing problem including the so-called 'emerging pollutants', which comprise a large number of pharmaceuticals. For the past three decades, data have been accumulated on the concentrations of pharmaceutical residues in drinking water.[2]

The occurrence of pharmaceutically active substances in the environment has become an important issue in the last few years. These compounds along with their metabolites, which can be even more harmful than the original compounds, are continuously released into the environment, mainly through disposal of unused or expired drugs or directly from pharmaceutical discharges.[3]

Pharmaceuticals are generally excreted after being partially or completely converted to metabolites with enhanced

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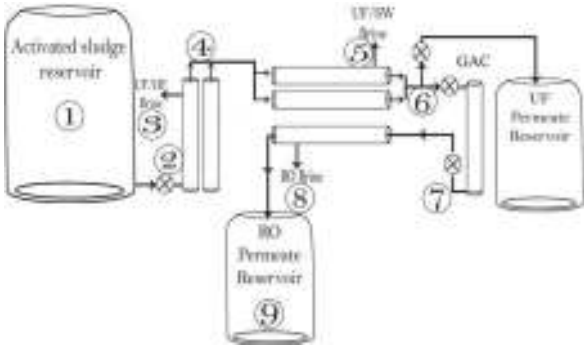



Figure 1. Flow diagram schematizing the WWTP at Al-Quds University. Sampling sites are indicated by numbers. UF/HF, hollow fibre ultra-filtration membrane; UF/SW, spiral wound ultra-filtration membrane; RO, reverse osmosis; GAC, granular activated charcoal filter.



solubility in water, but a significant quantity of the parent drug may also be excreted unchanged.[4] Most of these compounds come either from domestic sewage or from hospitals, or industrial discharges, and enter municipal wastewater treatment plants (WWTPs). The removal efficiency of WWTPs is influenced by the chemical properties of each specific compound to be removed, microbial activity in the activated sludge (AS) unit, use of membrane units and environmental conditions realized in the plant.[5–7]

Recent studies have clearly shown that the elimination of pharmaceutically active compounds in municipal WWTPs is often incomplete,[8] with efficiencies ranging between 60% and 90% for a variety of polar compounds.[9–12]

To evaluate the efficiency of different traditional and innovative tools for the elimination of pharmaceutical residues, we are performing a series of water purification experiments by using the WWTP installed at the Al-Quds University in Palestine (Figure 1), which includes sequential units, such as AS, ultra-filtration (UF), granular activated charcoal (GAC) and reverse osmosis (RO).[4]

Problems arising from the management of such a plant can be referred to the capability of the AS unit to favour the bio-degradation of organic pollutants as well as the fouling phenomenon affecting membrane units, which must be often replaced with high costs.

In the present work, we are reporting about the efficiency of advanced wastewater treatment technologies adopted in the Al-Quds plant for the removal of 'dexamethasone sodium phosphate' (DSP), which was used as the model pharmaceutical compound due to its high solubility in water and large consumption in many Countries. Nevertheless, because of the tendency of DSP to undergo hydrolysis in a large range of pH, we were also concerned with the removal of its hydrolysis product 'dexamethasone'.

Aiming at the assessment of bacterial culture, which normally develops in the AS unit of Al-Quds WWTP, the stability of DSP in pure water as well as in the AS collected from the plant was investigated and the DSP degradation products were identified.

Finally, to check for different tools to be used instead of UF membranes, the effectiveness of micelle–clay (MC) filter for removing DSP was ascertained and compared with a filter filled with GAC. Besides, the DSP adsorption equilibrium parameters and the adsorption Langmuir coefficients were determined by using both MC and fine powder activated charcoal (FAC) as the adsorbent materials.

DSP, 9-fluoro-11β,17-dihydroxy-16α-methyl-21-(phosphonooxy) pregna-1,4-diene-3,20-dione disodium salt (structure **1** in Scheme 1), a synthetic adrenocortical steroid, is a white or slightly yellow, crystalline powder. It is highly soluble in water and is exceedingly hygroscopic. It is widely used to treat inflammation, allergy and diseases related to adrenal cortex insufficiency. DSP is also known to reduce neointimal hyperplasia in arteries.[13,14] It is used for coating drug-eluting stents for local drug delivery to prevent restenosis [15–17] and is 5–14 times more potent than prednisolone and 25–75 times more potent than cortisone and hydrocortisone.[18] The corticosteroids cause alterations in metabolism of fats, proteins and carbohydrates, and affect a range of organs in the body including the heart, muscle and kidneys. Blood chemistry may change and there is decreased activity and shrinkage of the thymus gland, adrenal glands, spleen and lymph nodes. The liver becomes enlarged, thyroid activity decreases and mineral is drawn away from bone. Muscle wasting occurs, and the immune system is adversely affected causing the person to be more susceptible to infections, especially of the eye.[13–17] DSP is one of the most water-soluble adrenocorticosteroidal agents. It is, therefore, suitable for intravenous use and particularly for ophthalamic formulations.[19]

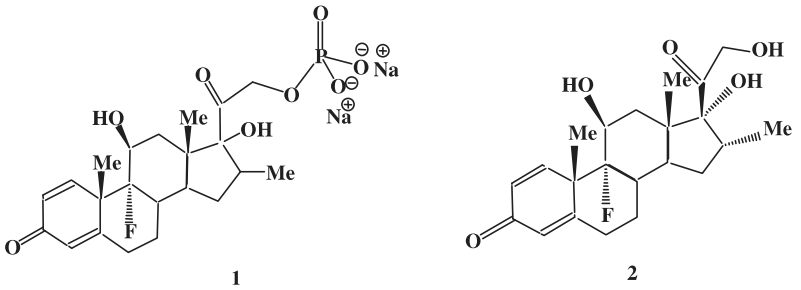
The MC composite, which was used in this study, is positively charged, has large surface area and includes large hydrophobic domains.[20] Micelle–clay composites have already been proven useful in the removal of about 20 neutral and anionic pollutants.[20–25]

## 2. Experimental

### *2.1. Materials and equipment*

#### *2.1.1. Materials*

All chemicals were of analytical grade. The clay used was Wyoming Na-montmorillonite SWY-2 clay; obtained from the Source Clays Registry (Clay Mineral Society, Colombia, MO, USA). Quartz sand (grain size 0.8–1.2 mm) was obtained from Negev industrial minerals (Israel). Octadecyl trimethyl ammonium (ODTMA) bromide was obtained from Sigma–Aldrich. Pure DSP and its hydrolysis product dexamethasone (structure **2** in Scheme 1) were obtained from Birzeit Pharmaceutical Company (Palestine) with 99% purity, and both were used as received. FAC with particle size $\leq 60.0\,\mu m$, and GAC with particle size $\leq 700.0\,\mu m$ were obtained from Sigma (Sigma




Scheme 1. Structures of DSP (**1**) and its hydrolysis product dexamethasone (**2**).

Chemical Company, USA). The powder was used for batch adsorption experiments while the granules were used in column experiments. Magnesium sulphate anhydrous, potassium dihydrogen phosphate as well as methanol and water for analysis (HPLC grade) were purchased from Sigma–Aldrich (Munich, Germany). High-purity diethyl ether (>99%) was purchased from Biolab (Israel).

For sample enrichment and purification, SPE 1 g C–18 6 mL disposable cartridges (Waters, Milford, MA, USA) were used.

### 2.1.2. *Equipment*

Samples were shaken using Big Bill, (Banstaed/Themolyne, USA). The disappearance of DSP and its hydrolysis product were determined by using a high-pressure liquid chromatography system model 2695 HPLC from Waters (Israel), equipped with a Waters 2996 Photodiode array. Data acquisition and control were carried out using Empower™ software (Waters, Israel). Analytes were separated on a 4.6 mm × 150 mm C18 XBridge® column (5-μm particle size) used in conjunction with a 4.6 mm, 20 μm, XBridge® C18 guard column.

HPLC conditions: mixture of 0.01 M $KH_2PO_4$: methanol (1:1; v/v) as mobile phase; flow rate of 1.2 mL $min^{-1}$; UV detection at a wavelength of 254 nm Acrodisc® syringe filters with GHP membrane (hydrophilic polypropylene 0.45-μm porosity) from Waters were always used for all analytical filtration requirements. The identification of DSP degradation products was performed using a liquid chromatography system coupled to a hybrid linear quadrupole ion trap–Fourier-transform ion cyclotron resonance (FT-ICR) mass spectrometer (Thermo Fisher Scientific, Bremen, Germany).

The advanced WWTP employed in this study is located at Al-Quds University-Palestine and was described in detail elsewhere.[24] Normally, the effluent from this plant is recycled for the irrigation of plants cropped in the field of university campus.

## 2.2. *Methods*

Linearity of the proposed analytical method was verified by analysing standard solutions in the range of 0.1–100 mg $L^{-1}$ for both DSP and its hydrolysis product in pure water. The calibration curves were obtained with a determination coefficient $R^2$ of 0.9996 and 0.9998, respectively. The repeatability of triplicate subsequent injections was ranging from 98.8% to 99.5%, depending on the sample concentration and type of analyte. The repeatability of morning/evening injections on the basis of 6-hours elapsed time was ranging from 97.6% and 98.2%, and was also affected by the concentration and type of analyte. Correction coefficients were used for experimental samples.

Calibration curves and repeatability trials were repeated preparing new calibration solutions by using wastewater taken from the AS reservoir of Al-Quds WWTP. Results suffered from a major inaccuracy due to the variability of recovery percentages. The determination coefficients of calibration curves were 0.9985 for DSP and 0.9989 for dexamethasone. Repeatability normally was not reduced. The limit of detection, based on a signal/noise of 3, was 0.02 mg $L^{-1}$ for DSP and 0.01 mg $L^{-1}$ for dexamethasone. The limit of quantification, based on a signal/noise of 10, was 0.06 and 0.03 mg $L^{-1}$ for DSP and its hydrolysis product, respectively.

### 2.2.1. *Characterization of wastewater used*

The wastewater was characterized before the experiments according to American Public Health Association procedures [26,27] by performing measurements listed in Table S1 (Supplementary material).

The initial relatively high values of COD and TSS may be attributed to residues of chemicals in the wastewater from laboratories, which were not well removed by the secondary biological treatment.

Table S2 (Supplementary material) summarizes chemical, physical and biological characteristics of wastewater sampled from the AS reservoir of Al-Quds WWTP (sampling site #2 in Figure 1). This table reveals that the wastewater contained high amounts of suspended solids and large populations of bacteria, which are responsible for the fouling phenomena affecting UF and RO membranes. Moreover, high values of electrical conductivity and total dissolved solids are typical for municipal wastewaters and should be reduced if WWTP effluents are re-used for crop irrigation purposes.

#### 2.2.2. *Efficiency of WWTP for DSP and dexamethasone removal*

The efficiency of different treatment units was ascertained by spiking separately the secondary effluent with 1.0 mg $L^{-1}$ of either DSP or its hydrolysis product dexamethasone in the AS reservoir (1000 L). Samples were collected from different locations of the WWTP as depicted in Figure 1. Before analysis of DSP, 1 mg of $KH_2PO_4$ was added to 100 mL of sample to stabilize pH, the acidic form of DSP and the ionic strength of the solution. SPE-C18 disposable cartridges were used to pre-concentrate 10 mL of each sample by adsorption of analytes. A part (20 μL) of the methanolic solution eluted from SPE cartridge was injected into the HPLC and analysed using the same conditions for the determination of both DSP and dexamethasone. Recovery tests were performed using triplicate solutions of both substances, and values ranging from 98% to 102% were obtained.

#### 2.2.3. *Stability of DSP*

Stability study of DSP was performed using 100 mg $L^{-1}$ solutions in pure water, or AS taken from the WWTP installed at Al-Quds University. Samples at specific time intervals (0–14 days) were collected from the stability solutions (maintained under continuous orbital shaking), filtered and analysed by HPLC. The degradation by-products of DSP were investigated using liquid chromatography/Fourier-transform ion cyclotron resonance/mass spectrometry.

#### 2.2.4. *Micelle–clay complex preparation*

The ODMTA MC complex was prepared by mixing a smectitic clay mineral (montmorillonite) with the cationic surfactant ODTMA (as bromide salt) with a critical micelle concentration value of 0.3 mM as described previously.[21] The added surfactant was mostly in micellar form. The obtained complex by virtue of its positive charge and hydrophobic region is capable of efficiently binding neutral and negatively charged organic molecules.[21–25,28]

#### 2.2.5. *Batch adsorption experiments*

Batch adsorption experiments were carried out on DSP at different concentrations. Experiments were performed in 250 mL Erlenmeyer flasks containing 200 mg of either MC complex or FAC; 100 mL of DSP solutions having known initial concentration was then introduced into each flask. The flasks were shaken in an oscillating shaker for 3 hours at room temperature, and then the content of each flask was centrifuged (10,000 *g*) for 5 min and filtered using 0.45-μm filters. The equilibrium concentrations of DSP were then obtained by HPLC, using the conditions reported above. The retention time of DSP was 6 min.

#### 2.2.6. *Column filtration experiments*

Column filtering experiments were performed using 50:1 (w/w) mixtures of quartz sand and either ODTMA–clay complex, or GAC, 20 cm layered in borosilicate columns of 25-cm length and 5-cm diameter. Each column contained 13 g of complex, or GAC. The bottom of the column was covered with 3-cm layer of quartz sand. Quartz sand was thoroughly washed by distilled water and dried at 105°C for 24 h before its use. Solutions in pure water (1 L each) containing different DSP concentrations (0.01, 1, 10 and 100 mg $L^{-1}$) were passed through either MC or GAC columns (one column for each solution). In all cases, the flow rate was 2.0 mL $min^{-1}$. Eluted fractions were collected in all column experiments and analysed.

All experiments reported in Sections 2.2.1–2.2.6 were performed in three replicates, and average values and standard deviations were calculated.

## 3. Results and discussion

### 3.1. *Efficiency of WWTP for DSP and dexamethasone removal*

The efficiency of WWTP at Al-Quds University for the removal of DSP and dexamethasone was studied. The AS reservoir (site 1 in Figure 1) was separately spiked with either DSP or dexamethasone at a concentration of 1.0 mg $L^{-1}$, which is an amount close to literature findings.[8,11] Samples were taken from different collecting sites of WWTP as described in Section 2.2.2 and Figure 1. Analytical results of water effluent from UF system indicated that the efficiency of the UF process is about 63–95% (sample nos 4 and 6, see also Figure 1 and Table 1).[24,25] DSP was completely removed in the effluent from GAC filter. However, it should be outlined that the concentration of DSP (or dexamethasone) influent in the treatment units was diminishing along their sequence. This relationship reflected upon 100% removal by GAC filter, where influent water contained only 0.06 mg $L^{-1}$ of DSP, or 0.07 mg $L^{-1}$ of dexamethasone, on average, after the passage through the UF filters. This finding made unnecessary the use of RO for any further purification. Nevertheless, the advanced technology adopted in the WWTP of Al-Quds University did not overcome a problem common to all plants: the production of brine, in which a large portion of the contaminants ends up being concentrated there. For this reason, different methods of water filtration and purification should be experimented.

### 3.2. *Stability of DSP in pure water and in sludge*

Literature survey on the stability of DSP indicates that the drug undergoes degradation in aqueous solutions buffered at various pH values, temperature, light exposure and oxidative conditions.[29] Furthermore, DSP cleaves into four major degradation products.

Table 1. Removal of DSP and dexamethasone (hydrolysis product – HP) from wastewater by different treatment units in Al-Quds WWTP; average values of three replicates.

| | | | Concentration of DSP and dexamethasone (HP) (mg $L^{-1}$) | | | |
|---|---|---|---|---|---|---|
| | | | Means ± SD | | Remaining (%) | |
| Sample description | | Sampling site as in **Figure 1** | DSP | HP | DSP | HP |
| AS spiked amount | | 1 | 1.0 | 1.0 | | |
| UF-HF | Influent | 2 | 0.83 ± 0.05 | 0.81 ± 0.02 | | |
| | Concentrates produced | 3 | 0.46 ± 0.04 | 0.43 ± 0.04 | | |
| | Effluent | 4 | 0.31 ± 0.03 | 0.24 ± 0.02 | 37.3 | 29.6 |
| UF-SW | Concentrates produced | 5 | 0.19 ± 0.02 | 0.17 ± 0.02 | | |
| | Effluent | 6 | 0.06 ± 0.03 | 0.07 ± 0.04 | 5.3 | 8.6 |
| GAC effluent | | 7 | b.l.d. | b.l.d. | ≈0.0 | ≈0.0 |

b.l.d., below the limit of detection.

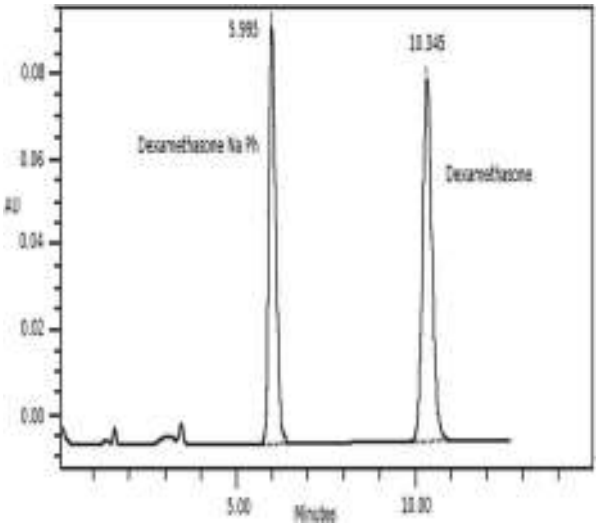



Figure 2. Chromatogram showing the appearance of an intense peak attributable to dexamethasone, the hydrolysis product of dexamethasone sodium phosphate risen after 2 weeks of incubation in pure water.

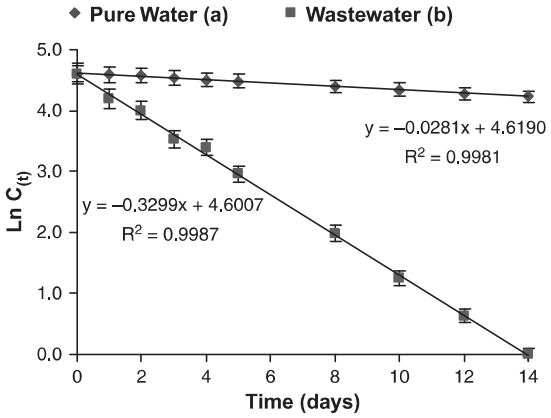



Figure 3. Kinetics of DSP degradation in pure water (plot a) and activated sludge (plot b). Data are reported as natural logarithm of concentrations ($C_{(t)}$) vs. time. Initial concentration ($C_{(0)}$) = 100 mg $L^{-1}$. Plotted values are the means of three replicates; bars represent the standard deviations calculated for each average value.

They were identified as dexamethasone-21-oic acid, 17-oxodexamethasone, 6β-hydroxy dexamethasone and 16,17-unsaturated dexamethasone.[30]

Figure 2 illustrates the HPLC chromatogram of DSP after 2 weeks of incubation in pure water at room temperature ($C_{(0)}$ = 100 mg $L^{-1}$). The peak at 6-min retention time is characteristic of the acidic form of DSP, and the peak at 10.3-min can be attributed to its hydrolysis product dexamethasone. The kinetic data of DSP hydrolysis in pure water are plotted in Figure 3 (plot a) as natural logarithm of DSP concentration vs. time (days). The determination coefficient $R^2$ of the first-order hydrolysis reaction was 0.9981, and the kinetic constant was 3.25 $10^{-7}$ $s^{-1}$.

Similarly, a kinetic study on the stability of DSP was conducted in the AS at room temperature. The determination coefficient $R^2$ in this case was 0.9987 (Figure 3, plot b), and the kinetic constant was 3.80 × $10^{-6}$ $s^{-1}$. The degradation half-life was diminished from 24.7 days in pure water to 2.1 days in the AS, where the concentration of the parent molecule was found at the level of 1 mg $L^{-1}$ after 2 weeks of incubation. The degradation rate in the sludge medium was about 12-fold faster than in pure water. The accelerated degradation can be attributed to bioactivity of the AS.

Monitoring the derivative substances arising from the degradation of DSP in the AS showed that the first degradation product, dexamethasone, underwent further degradation to other by-products as identified-by mass spectrometrical analysis. Extracted ion chromatogram (XIC) of the 14-day biodegraded sample is shown in Figure 4. Using very selective XICs by FT-ICR/MS, generated with a tight mass-to-charge ratio window of ±0.0010 units around each selected protonated molecule (i.e. $[M + H]^+$ ± 1.0 mDa), greatly reduced the signal complexity of the total ion current trace (data not shown) allowing to completely characterize all degradation products.

In addition to dexamethasone, which was formed from hydrolysis of DSP, seven major biodegradation products

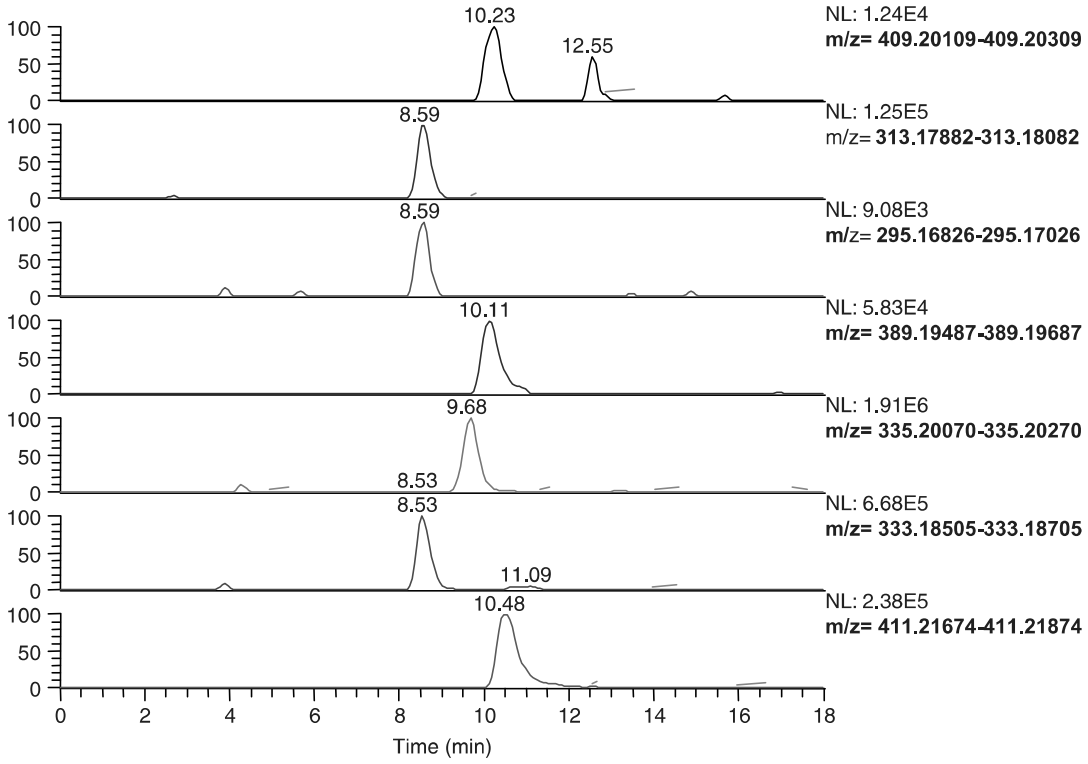



Figure 4. Extracted ion chromatograms (XICs) acquired by LC/ESI-FTICRMS in positive ion mode for the aqueous sample collected after 2 weeks of biodegradation from the activated sludge spiked with 100 mg $L^{-1}$ of DSP. The ions monitored are displayed in each trace and correspond to the most abundant protonated moieties $[M+H]^+$, using a restricted window of $\pm 0.0010$ $m/z$ unit centred around each selected ion (Table S1 in Supplementary material).

were identified arising from dexamethasone biodegradation at retention times 8.53 (**3**), 10.23 (**4**), 9.68 (**5**), 10.11 (**6**), 8.59 (7), 8.59 (**8**) and 10.48 (**9**) minutes. Based on the accurate $m/z$ values (Table S1, in Supplementary material) and relevant literature,[30] we propose the following structures for all degradation products evolved (Figure 5):

$C_{20}H_{25}FO_3$ [17-oxodexamethasone] (**3**),
$C_{22}H_{29}FO_6$ [6′-hydroxy dexamethasone] (**4**),
$C_{20}H_{27}FO_3$ [testosterone] (**5**),
$C_{22}H_{28}O_6$ [3′,4′-dihydroxy-10,13-dimethylspiro[1,2,6,7,8,9,12,14,15,16-deca hydro cyclo penta [a] phenanthrene-17,5′-oxolane]-2′,3,11-trione] (**6**),
$C_{20}H_{22}O_2$ [(8S,13S,14S,17S)-13-methyl-3-oxo-2,6,7,8,14,15,16,17-octahydro-1H-cyclopenta [a] phenanthren-17-yl] (**7**),
$C_{20}H_{24}O_3$ [(8S,13S,14S,17R)-17-ethynyl-17-hydroxy-13-methyl-1,2,6,7,8,14,15,16-octahydrocyclopenta[a]phenanthren-3-one] (**8**),
$C_{22}H_{31}O_6F$ [6-Fluoro-11,14,17,21-tetrahydroxy-16-methylpregn-4-ene-3,20-dione (**9**).

Figure 6 describes the suggested pathway by which dexamethasone degrades to metabolites (**4**) and (**9**). The hydroxyl group can attack two different positions on the dexamethasone moiety. Figure 7 illustrates the proposed pathways for the degradation of (**4**) to the other degradation products (**3**, **6**, **7** and **8**).

The FT-ICR infrared multiphoton dissociation MS/MS spectrum, reported in Figure S1 (Supplementary material), shows that compound (**8**) gives a molecular peak at $m/z$ 313 and three fragments with $m/z$ 295 $[M\text{-}H_2O + H]^+$, 277 $[M\text{-}2H_2O + H]^+$ and 267 $[M\text{-}H_2O - CO + H]^+$, due to the loss of $H_2O$ and CO. In Figure 7, the first pathway (A–B) leads from compound (**4**) to compound (**3**) by the loss of $H_2O$, formaldehyde and CO moieties, then to compound (**8**) through the loss of hollow fibre (HF). The second pathway (C–D) leads from compound (**4**) to compound (**6**) by the loss of HF molecule, and successively to compound (**8**) with the loss of water, formaldehyde and CO groups.

To the best of our knowledge, no publication has appeared on biodegradation of DSP or dexamethasone in wastewater. However, there are some *in vitro* and *in vivo* studies in rat and human livers on DSP metabolism to 17-oxodexamethasone and 6-hydroxy dexamethasone, which are two of main derivative substances we report in Figure 5 as number (**3**) and (**4**), and side chain cleaved metabolites [30] having a structure different from derivatives identified in our work.

### 3.3. *Adsorption isotherms*

The adsorption of DSP at several initial concentrations on MC complex and activated charcoal was investigated.

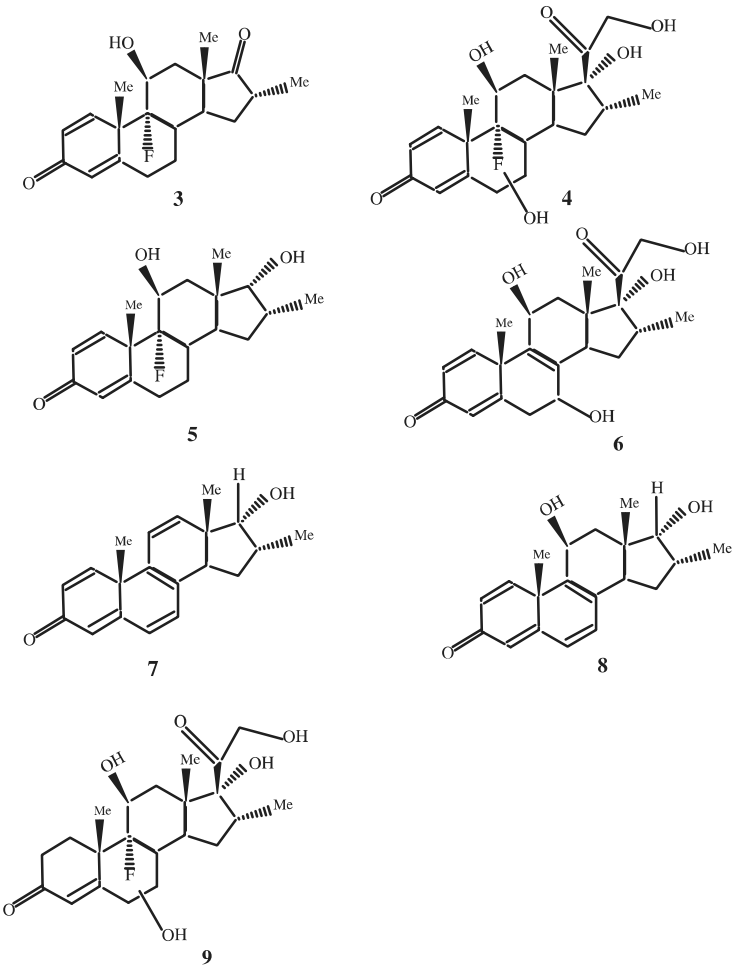



Figure 5. Chemical structures of dexamethasone biodegradation products. 17-Oxodexamethasone $C_{20}H_{25}FO_3$, exact MW 332.17822 (**3**); 6-hydroxy dexamethasone $C_{22}H_{29}FO_6$, exact MW 408.19427 (**4**); testosterone $C_{20}H_{27}FO_3$, exact MW 334.19387 (**5**); 3′, 4′-dihydroxy-10,13-dimethylspiro[1,2,6,7,8,9,12,14,15,16-deca hydro cyclo penta [a] phenanthrene-17, 5′-oxolane]-2′,3,11-trione $C_{22}H_{28}O_6$, exact MW 388.18804 (**6**); [(8S,13S,14S,17S)-13-methyl-3-oxo-2,6,7,8,14,15,16, 17-octahydro-1H-clopenta[a]phenanthren-17-yl] acetate $C_{20}H_{24}O_3$, exact MW 312.17200 (**7**); (8S,13S,14S,17R)-17-ethynyl-17-hydroxy-13-methyl-1,2,6,7,8,14,15,16-octahydrocyclopenta[a]phenanthren-3-one $C_{20}H_{22}O_2$, exact MW 294.16143 (**8**); [6-Fluoro-11,14,17, 21-tetrahydroxy-16-methylpregn-4-ene-3,20-dione $C_{22}H_{31}O_6F$, exact MW 410.20992 (**9**).

Equilibrium relationships between adsorbent and adsorbate can be described by Langmuir adsorption isotherm,[24,31–33] represented by the following equation:

$$\frac{C_e}{Q_e} = \frac{1}{(k\,Q_{max})} + \frac{C_e}{Q_{max}} \quad (1)$$

where $C_e$ (mg $L^{-1}$) is the equilibrium concentration of the drug in the solution, $Q_e$ (mg $g^{-1}$) is the equilibrium mass of the adsorbed drug per gram of complex or activated charcoal, $k$ (L $mg^{-1}$) is the Langmuir binding constant and $Q_{max}$ (mg $g^{-1}$) is the maximum mass of drug removed per gram of complex.

The data fitted well the Langmuir equation giving $R^2 = 0.9953$ for activated charcoal and 0.9997 for the MC (Figure 8). Langmuir constants $Q_{max}$ and $k$ were determined from the slope and intercept in Figure 8. These values for MC complex are 652.1 mg $g^{-1}$ and 2.795 L $mg^{-1}$, respectively, whereas the values for activated charcoal are 103.4 mg $g^{-1}$ and 0.184 L $mg^{-1}$, respectively. The Langmuir binding constant '$k$' for the MC complex was about 15-fold greater compared with the activated charcoal, and the value of $Q_{max}$ was nearly sixfold higher for the former. The values of $k$ and $Q_{max}$ parameters suggest that the MC complex is a better adsorbent of DSP than the activated charcoal.

### *3.4. Modified clay adsorption*

DSP solutions were passed through filters that included the MC complex or activated charcoal mixed with excess sand at 1:50 ratios (w/w). Results (Table 2) indicate a significant advantage of the MC filter in removing DSP compared with

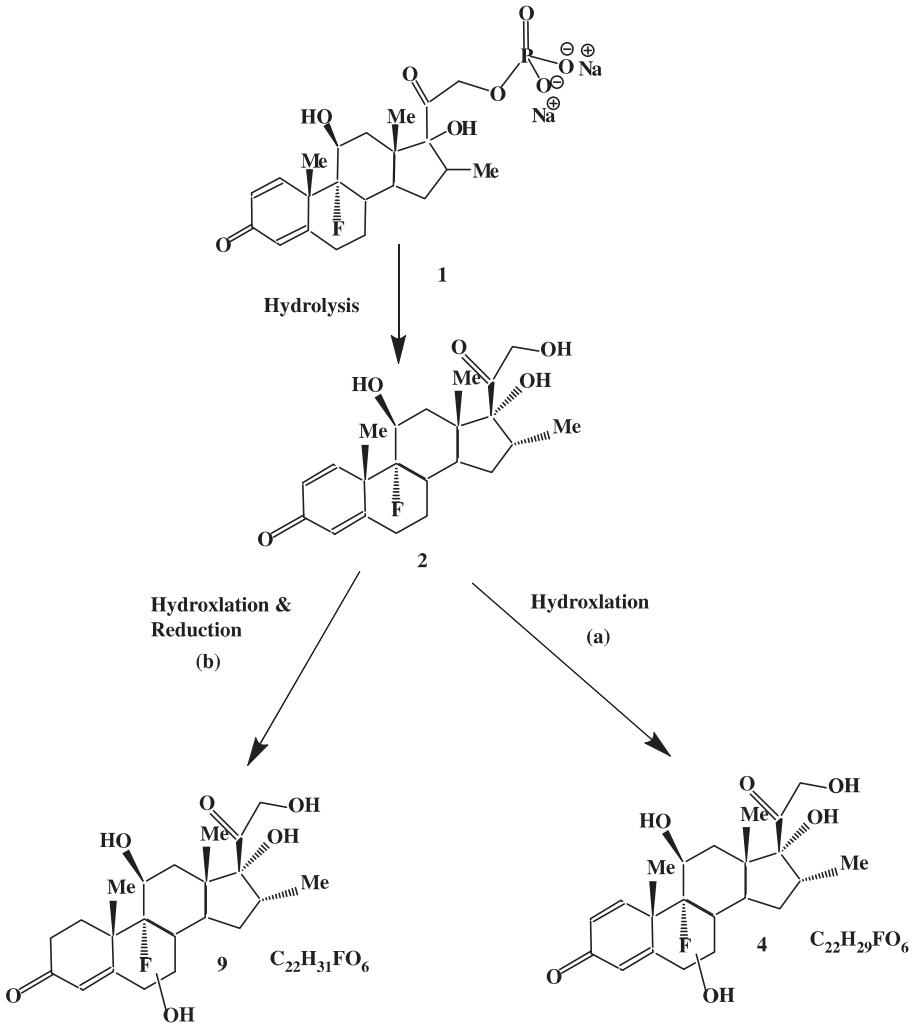



Figure 6. Proposed transformation pathway for the biodegradation of dexamethasone sodium phosphate (**1**).

the removal by activated charcoal. This finding was not surprising, since parameters obtained for adsorption isotherms have clearly shown that the MC complex was more efficient than the activated charcoal in adsorbing DSP from water.

Previous reported experiments demonstrated the advantage of the MC filters in removing anionic and certain neutral pollutants.[21–23]

Polubesova et al. [21] found a very efficient removal from water of neutral and anionic herbicides by micelle–clay complexes. In another study,[22] column filters filled with a mixture of quartz sand and micelle–clay complex provided a very efficient result for the retention of tetracycline and sulphonamide pharmaceuticals from wastewater. Zadaka et al. [23] tested column filters with either a mixture of quartz sand and organic micelle—montmorillonite or zeolite; both filters were capable of removing well ethylene dibromide, anionic pollutants as sulphosulphuron, imazaquin and sulfentrazone, and neutral compounds such as bromacil and chlorotoluron from aqueous environments; in contrast, a filter filled with the same weight of activated carbon and sand only partially removed these pollutants.

In a recent paper, Karaman et al. [24] showed that MC filters were more efficient towards the removal of diclofenac potassium from wastewater than activated carbon. Morover, Khamis et al. [1] concluded that the incorporation of MC filters in sewage treatment systems with loose tertiary capability can be a promising technology. More recently, Khalaf et al. [25] suggested that the integration of clay–micelle complex filters in existing WWTPs may be helpful for improving the removal efficiency of recalcitrant residues of non-steroid anti-inflammatory drugs.

In laboratory study, Qurie et al. [32] found that micelle–clay complex filters under continuous naproxen-spiked water flowing are efficient in removing naproxen, suggesting that the efficiency of the existing advanced WWTP could be improved by including filtration columns filled with suitable sand/micelle–clay mixtures.

It can be argued that in addition to DSP residues wastewater usually includes other recalcitrant organic

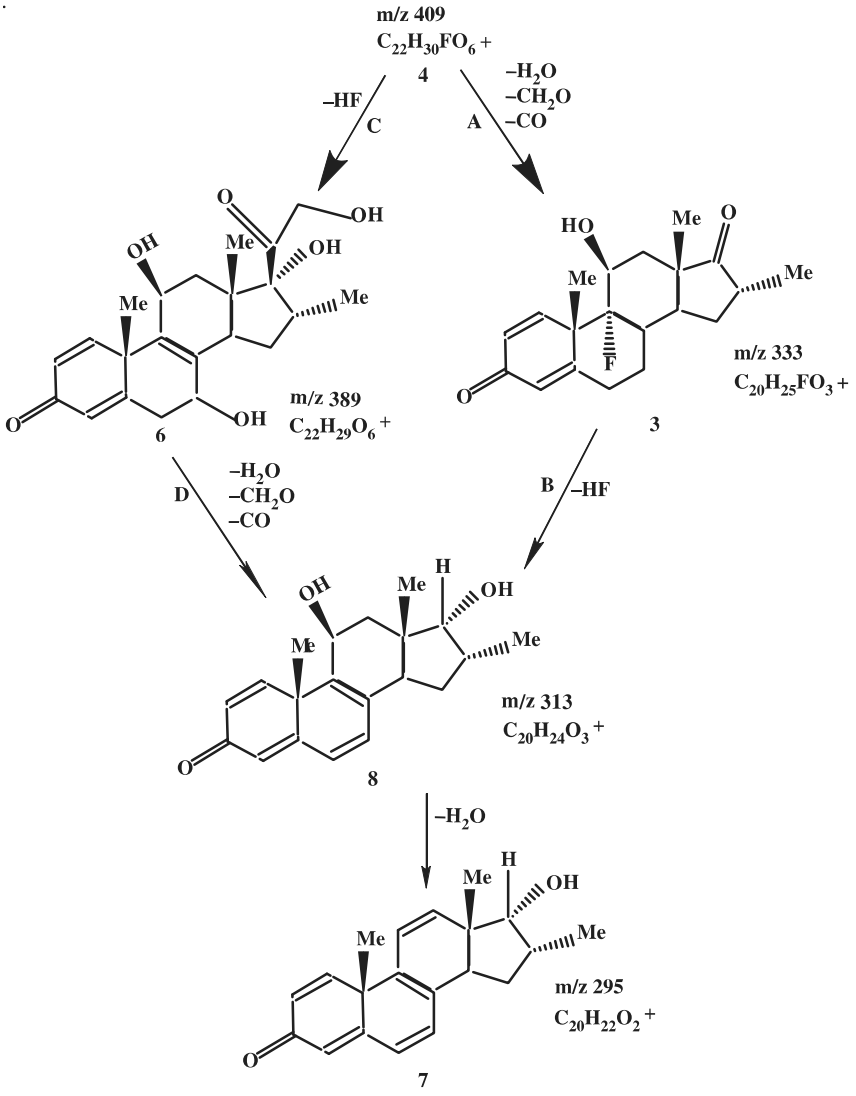



Figure 7. Proposed transformation pathways for dexamethasone (**4**).

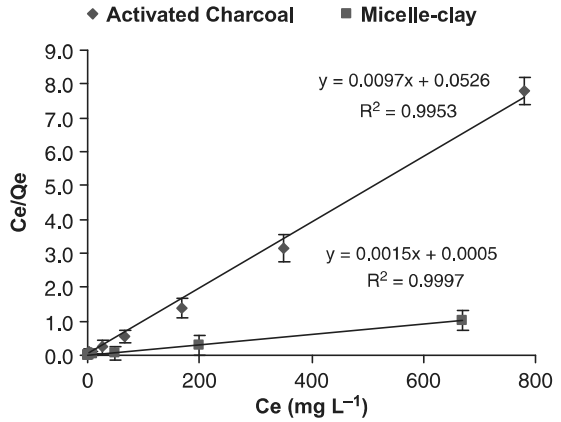



Figure 8. Langmuir isotherms for the adsorption of DSP by micelle–clay complex (■) and by activated charcoal (♦). Dosage of adsorbent (0.2 g). Data reported are means of three replicates. Bars represent standard deviations of means.

Table 2. Removal of DSP by filtration of 1 L of pure water solutions (100, 10, 1.0, 0.01 mg $L^{-1}$) through laboratory filters, which included either MC or GAC mixed with excess sand at 1:50 (w/w) ratio; means of three replicates.

| Initial concentration (mg $L^{-1}$) | Column type[a] | Average eluted concentration (mg $L^{-1}$) | ±SD |
|---|---|---|---|
| 100 | MC | b.l.d. | – |
| 100 | GAC | 64.3 | 1.2 |
| 10 | MC | b.l.d. | – |
| 10 | GAC | 3.1 | 0.5 |
| 1.0 | MC | b.l.d. | – |
| 1.0 | GAC | 0.17 | 0.08 |
| 0.01 | MC | b.l.d. | – |
| 0.01 | GAC | b.l.d. | – |

[a]Flow rate, 2 mL $min^{-1}$; temperature, 25°C; b.l.d., below the detection limit of the analytical method used.

pollutants.[33–36] In such cases, GAC filters can be used as a first-stage tertiary process to remove the majority of neutral pollutants, and additional MC filters can be adopted as the second stage to eliminate anionic pollutants, and neutral compounds not retained by GAC filters.

## 4. Conclusions

In this study, we determined the rates of degradation of DSP in pure water and in sludge. The degradation products, which were identified by LC–MS and LC/MS/MS techniques, were found to include not only the already known metabolites 17-oxodexamethasone and 6′-hydroxy dexamethasone but also many others derivatives not previously investigated.

The study demonstrated that the advanced treatment technologies installed at the WWTP of Al-Quds University were effective for the complete removal of both DSP and its hydrolysis product from 1 mg $L^{-1}$ spiked wastewater.

The filtration performed using the mixture sand/MC complex was able to remove and retain very high concentrations of DSP from aqueous solutions. The large effectiveness and removal capacity of the MC complex are due to the high adsorption affinity towards the anionic DSP by the relatively large number of positively charged and hydrophobic sites of the MC complex based on ODTMA.

## Funding

This work was partially supported by a generous grant from Sanofi Pharmaceutical Company (France) managed through Peres Center for Peace. S.A.B. and S.N. thank the European Commission in the framework of the Project 'Diffusion of nanotechnology based devices for water treatment and recycling – NANOWAT' [ENPI CBC MED I-B/2.1/049, Grant No. 7/1997] for supporting a part of this work.

## Supplemental data

Supplemental data for this article can be accessed 10.1080/09593330.2014.888097.

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