State of the Art Wastewater Treatment in Pharmaceutical and Chemical Industry by Advanced Oxidation

Martin Sörensen, Frank Zegenhagen, Jürgen Weckenmann

Enviolet GmbH, Karlsruhe

Abstract

This article shows potential and practical implementation of UV-oxidation for destruction of pollutants and micropollutants, like endocrine or antibiotic compounds in strong chemical and pharmaceutical wastewater. An overview of typical technologies used for treatment of industrial wastewater with assets and drawbacks is given. Compounds that need to be oxidized in the described applications are 1,4-dioxane, EDTA, pyrolidones, aromatics (phenols, toluene, ...), VOCs, EE2, various Active Pharmaceutical Ingredients (API), surfactants and FOG (= Fat, Oil and Grease). The examples presented of UV-oxidation are located at BASF, Enva, Haupt Pharma, GSK, Merck and Pharma Action. Besides photos of the installed UV-plants, flow rates, concentrations and operating costs are listed as well. Understanding possible reaction pathways and mechanisms described enabled Enviolet to develop optimized processes and produce plants designed on base of a single lab investigation.

Zusammenfassung

Dieser Artikel zeigt die Möglichkeiten und den praktischen Einsatz der UV-Oxidation zur Zerstörung von Microverunreinigungen und Schadstoffen, wie endokrin oder antibiotisch wirksame Substanzen in konzentriertem chemischem oder pharmazeutischem Abwasser. Ein Überblick zeigt die Vor-und Nachteile typischer Verfahren für die Behandlung von industriellem Abwasser auf. Die in den dargestellten Anwendungsbeispielen abzubauenden Inhaltstoffe sind 1,4-Dioxan, EDTA, Pyrolidon, Aromaten (Phenole, Toluol, ...), VOCs, EE2, verschiedene Wirkstoffe, Tenside und FOG (= fat, oil, grease). Die aufgeführten Beispiele befinden sich bei BASF, Enva, Haupt Pharma, GSK, Merck und Pharma Action. Neben Bildern der installierten Anlagen werden Durchfluss, Konzentrationen und Betriebskosten genannt. Reaktionswege und Mechanismen werden beschrieben, deren Verständnis es Enviolet ermöglicht auf Basis einer Laboruntersuchung optimierte Prozesse zu entwickeln und anhand einer einzigen Labor Analyse Anlagen zu realisieren.

Introduction

This article presents a modern approach for treating concentrated wastewater from chemical production, pharmaceutical production and formulation directly at the place of processing to avoid contaminated sewage.

Micropollutants are getting more and more into focus of public discussion, especially those being endocrine or showing other problematic side effects i. e. the development of resistance and antibiotic resistant genes [1, 2].

These micropollutants are highly diluted (anthropogenic) xenobiotic substances from many different industries and applications. Due to their persistence, bioaccumulation potential, and toxicity, it is necessary to minimize their input into the sewage system and water bodies. Additionally lipophilic xenobiotics might be adsorbed in sediments where they inflict damage to sediment dwelling organisms [3].

Potential emissions of micro pollutants into the environment may occur by:

- domestic wastewater polluted by the patient
- hospitals wastewater

- animal husbandry and veterinary medicine
- industrial production of pharmaceuticals

Usually domestic wastewater and wastewater from hospitals are treated in sewage treatment plants (STP). Additionally in doctors' surgeries used drugs, especially contrast media are excreted by patients and lead to significant concentrations in STPs. As these have no barrier for micropollutants, they are directly passing into the water body or indirectly via sewage sludge used as fertilizer [4].

Veterinary drugs and their metabolites can be found in the manure of animals and are washed into the soil and ground water or entering surface waters directly.

Due to GMP (Good Manufacturing Praxis) at least in Europe and Northern America pharmaceutical and chemical production sites have reduced their emissions of active substances dramatically in contrast to countries like e.g. India [5].

Considerable efforts are undertaken by companies following GMP regulations to meet requirements and avoid any pollution and so best technologies are still required.

The growing concern about a class of substances, which are suspected to interfere with the endocrine system, has led to the first consequences on legal base. The commission of the European Union has received an increasing number of parliamentary questions since 1997 on the following topics on pharmaceuticals:

- use and regulation of a range of suspected endocrine disrupting substances [6]
- investigation and prevention of hormones and hormonal effect acting chemicals in the environment
- antibiotics in aquatic environment [7]

Pharmaceutical wastewater treatment means that in general no recycling has to be taken into account, as this would violate GMP rules for the manufacturing of medicinal products. An exception might be recovering and reuse of solvents, nitrates, etc. [8, 9]. Therefore, manufacturers need to know how to deal with pharmaceutical wastewater and be aware of regulatory requirements.

A good example for the possibility of recycle/reuse of residuals is from production of x-ray Contract Media (CM) containing organic bound iodine where iodide can be extracted from the solutions after incineration or UV-oxidation [10] by gas scrubbing. The recovered iodine can be sold on the world marked [11].

There are (local) rules of discharge for various parameters, that are defined by EPA (Environmental Protection Agency, e.g.: USA, UK, Ireland …), EEA (European Environmental Agency in Europe), SEPA (State Environmental Protection Agency, China) and by various institutions in many other countries.

In the EU there are actually no binding legal limits for APIs, but defining them is under process and actually many manufacturers of APIs are tending to apply the PNEC (Predicted No Effect Concentrations), where available, as future legal values will not be lower than those and Water Frame Work Directive is the actual common base [11, 12, 13].

Significance of micro pollutants and possibilities to prevent their emission into the environment

Considering the consumption of human pharmaceutics per year (e.g. 2009) in Germany the following classes are the most important: Analgesics: 2647 to, anti-diabetic medication 1310 to, antibiotics 571 to, x-ray contrast media 395 to.

In veterinary medication, anti-inflammatories and antibiotics dominate the quantitative consumption, however due to their ecotoxicological or environmental significance prescribed hormones deserve special attention.

On base of ecotoxicological data, impact analyses have been carried out to evaluate relevance of various substances. Important parameters are PNEC and MEC (Measured Environmental Concentration). The ratio from MEC and PNEC characterizes the risk for the environment. In case of resulting ratios above 1, measures to avoid and minimize risks are required. Figure 1 shows these values of various APIs analyzed in German surface waters on base of worst-case estimations [14].

Obviously, estrogens and antibiotics constitute so far the most challenging classes of pharmaceuticals due to their properties and their effect to the environment.

Synthetic 17α-ethinylestradiol (EE2) is probably the most effective estrogen-active substance to fish as it leads already at concentrations of 0.32 ng/L to reduced egg fertilization success and sexual ratio skewed towards females in fathead minnows' populations [15]. The estrogenic activity of sewage is the reason for the reduced fertility of fish, despite a reduction of about 80 to 90 % by conventional purification with activated sludge process [16].

This demonstrates the need to avoid any possible emissions from industrial production or plants by appropriate technology. A good example for destruction of ethinylestradiol and other APIs in wastewater from production of contraceptives, thyroid hormones and narcotics is Haupt Pharma in Münster, Germany, using UV-oxidation for this task (cf. below) [17].

Design requirements for municipal STPs are to eliminate mainly organics from sanitary wastewater and industrial wastewater being non-toxic and showing a good bio-degradability. The volume rate of STPs is high and the level of contamination is relatively low (Table 1).

The task of STPs is to reduce the load of substrate and nutrients before the treated wastewater is rejected into our aquatic environment at lowest possible costs. Nearly all

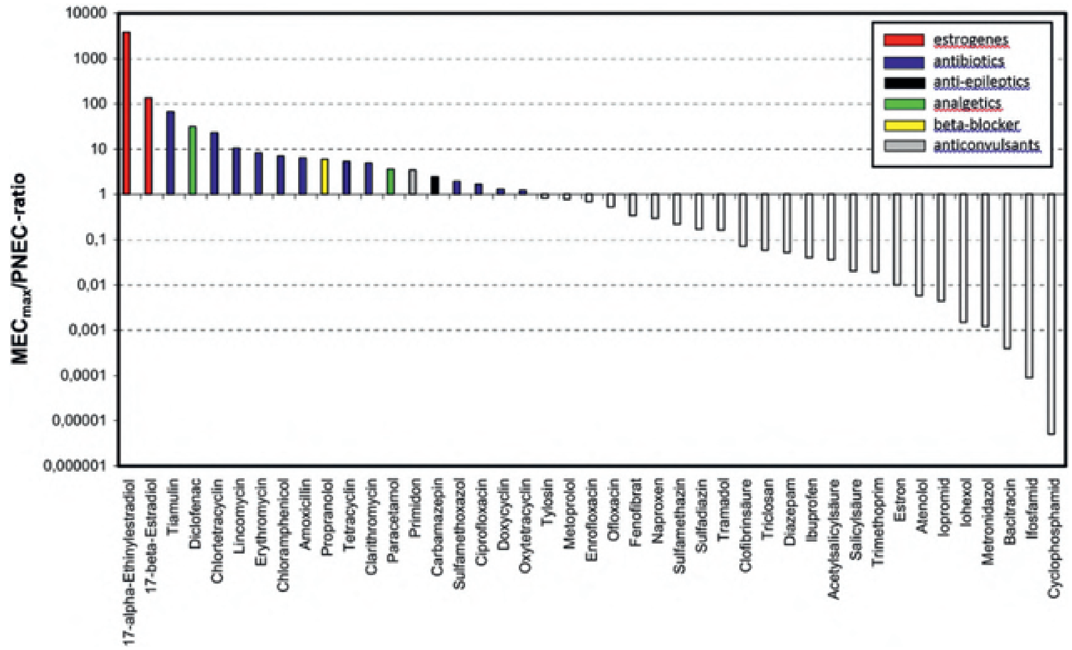

Fig. 1: MEC/PNEC ratio of pharmaceuticals with very good to sufficient ecotoxicological database (Source: [14]).

STPs have no barrier for anthropogenic substances as they show different chemical behavior on biological degradation, which in STPs is the main cleaning-tool flanked by simple mechanical separation.

Most xenobiotic substances show no or a poor bio-availability and degradation of some APIs could be improved by extended retention times, which is in practice difficult considering the typical flow rates. Depending on the APIs' structure a seemingly elimination of APIs is often a result of adsorption on sewage sludge [18]. The best way to treat xenobiotics, thus also of APIs, is directly by special designed wastewater treatment installations integrated on site where APIs are synthesized or formulated.

Table 2 gives an overview of typical techniques used for treatment of industrial wastewater. All these techniques have their advantage, but as in pharmaceutical applications special requirements are defined, Table 2 extracts these under aspects important for pharmaceutical wastewater treatment.

Table 2 shows clearly that only techniques based on oxidation can solve the problem of API sustainably, xenobiotics, or recalcitrant organics, as operating costs are low and no concentrate has to be disposed of.

In practice, there is often not only one technique as tool for state-of-the-art wastewater treatment. BASF (Ludwigshafen) for example operates as final treatment a big biological wastewater treatment plant with very sophisticated sludge removal by flocculation filtration. For a successful operation, within the factory many different techniques of pre-treatment are used to support the biological wastewater treatment. UV-oxidation for example is used to eliminate 1,4-dioxane, EDTA, pyrrolidones, aromatics, and other substances which cannot be removed in a biological process. This successful concept it copied in many bigger chemical plants.

Examples in chemical and pharmaceutical industry

■ BASF (Ludwigshafen)

Wastewater from synthesis of chelating agents for detergents and cleaners, pulp and paper and agriculture contain mostly EDTA.

The effluent of the EDTA-manufacturing line at BASF in Ludwigshafen shows a completely bio-available wastewater, with the exception of EDTA remaining after an extraction step. Therefore, BASF [19] was focusing on a highly selective treatment for elimination of this single substance only. The reason was that

■ Table 1

Typical range of flow and concentration of STPs.

Parameter	Untreated WW	Treated WW
Flow in m^3/d	1 000–1 000 000	
COD in mg/L	50–100	Ca. 30
P in mg/L	< 16 (1–5)	2 (0.5–1)
N in mg/L	30–100	5–10
Micropolutants in mg/L	n.n.–0.01	No significant change

■ **Table 2**

Overview on treatment techniques for industrial wastewater from chemical production.

Technique	Principle	Elimination of Xenobiotics/APIs	Remark on process	CAPEX	OPEX
Activated Carbon	Sorption	Concentration on fixed phase	Good sorption properties are required.Generation of waste	Low	High
Advanced oxidation	Chemical Oxidation	YES	Different elimination levels can be achieved	Low-medium	Medium
Biological treatment	Biological Oxidation	Only in rare cases			
Evaporation	Concentration	Concentration	Distillate often polluted as many ingredients are purgeable or steam-purgeable	High	High, also due to concentrate disposal
Flocculation/ Filtration	Mechanical	NO, bad efficiency on removal of organics	No relevance in pharmaceutical industry	Low	Low
High pressure Oxidation	Chemical Oxidation	YES		Very High	Low
External Incineration	Thermal Oxidation	YES		Low, as storage only	Very High
Incineration on site	Thermal Oxidation	YES		High	Very High
Membrane	Mechanical separation	Concentration of API with lower flow rate	Membranes are sensible for fouling, Concentrate has to be disposed externally	Medium	High, also due to concentrate disposal

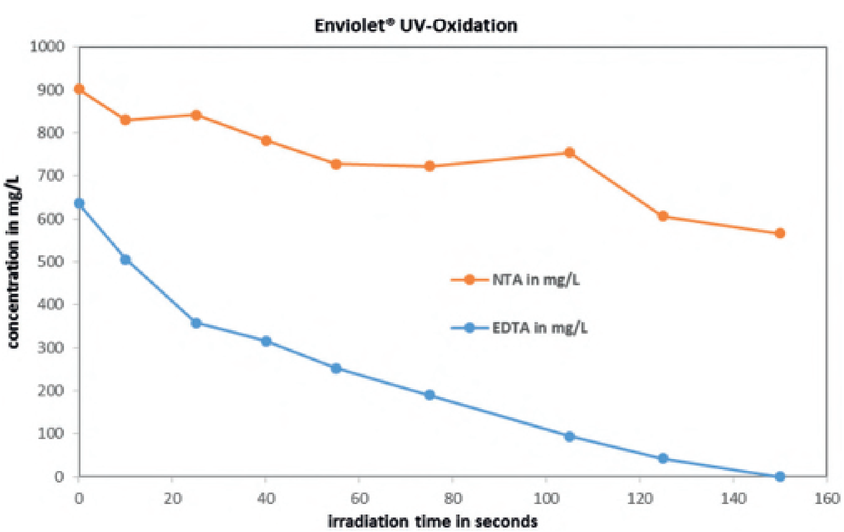

Fig. 3: Selective destruction of EDTA at BASF Ludwigshafen, Germany.

Fig. 2: UV-oxidation unit for selective destruction of EDTA at BASF in a flow between 10–12 m^3/h with adjustment of treatment intensity regarding degradation and flow rate (Source: Fig. 2–4, 6, 8–12, 14–20 Enviolet).

the existing biological wastewater treatment plant at BASF is one of the most developed wastewater treatment plants at a chemical manufacturing site. However, as known EDTA cannot be removed by any biological treatment. Therefore, a highly selective UV-treatment, reducing the concentration of EDTA without any detectable change of the matrix was selected as pretreatment (see Fig. 2). This process keeps operational costs at a minimum (see Table 3). This type of treatment is applied as well for selective removal of API from industrial wastewater at many pharmaceutical manufacturing sites of leading pharmaceutical companies.

In Fig. 3 the degradation curve of EDTA is displayed. Striking is the relatively small reduction of NTA, that is well bio available whereas EDTA is eliminated [20].

■ Enva Ireland

Enva provides technical solutions for the treatment of waste and wastewater to clients across all types of industry in Ireland and UK. This includes being service providers to many of the world's leading pharmaceutical companies. Enva provides services at its own licensed waste treatment facilities, and also provides services and technology at its customer sites. In 2012 Enva installed 2 UV based AOP (Advanced Oxidation Process) systems at their specialised chemical waste treatment facility in Shannon, Ireland (see Fig. 4). These units were designed to be

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■ **Table 3**

Data of treatment at BASF Ludwigshafen, Germany.

Parameter	Data	Result
Flow rate	240–280 m^3/d	
COD	≈ 3 000 mg/L	no significant impact
EDTA	400–600 mg/L	≈ 50 % reduction rate
Bioavailability of target	0 %	≈ 90 % of photo transformed molecules [20]
OPEX	≈ 0.5 €/m^3	

■ **Table 4**

Data of treatment at Enva, Ireland.

Parameter	Data	Result
Flow rate	10–40 m^3/d – depending on application	
COD	1 000–50 000 mg/L	Depending on treatment focus
API	Various types and concentration	target depending on API
Bioavailability	Mostly low	Usually > 60 %
OPEX	Varying with application	

Fig. 4: Multi purpose treatment installation at enva.

Fig. 5: Selective UV-Photo-oxidation of high potential hormones at Haupt Pharma (Source: Haupt Pharma).

multi-functional, so that Enva can receive a wide variety of aqueous wastes for treatment and can operate different campaigns depending on the customer's requirements. These units are used for the treatment of a variety of organics-contaminated wastes, e. g. API removal, toxicity reduction, COD (Chemical Oxygen Demand) reduction & VOC (Volatile Organic Compound) reduction. Due to good and efficient treatment at Enva two Irish pharmaceutical companies have installed own installations at their production site for treating the full factory wastewater with specific technology.

■ Haupt Pharma

Haupt Pharma [17] in Münster as job-shop manufacturer is operating the biggest site for formulation of high potential sexual hormones in Europe. In 8 formulation lines all types of sexual hormones like EE2 are formulated and packed for final application. The wastewater from Cleaning in Place (CIP) is treated by AOP (see Fig. 5) to remove all hormones in a proper way to release clear and clean water into the municipal sewer (see Table 5 and Fig. 6).

■ GSK (Singapore)

Amoxicillin manufacturing site of GSK in Singapore is one of the biggest sites for production of antibiotics worldwide. It is well known that biological treatment plants are not very capable treating the strong wastewater from antibiotic manufacturing lines, due to the effect of its ingredients, which resulted at GSK Singapore in incinerating the wastewater. GSK-manufacturing site was searching for a more suitable process to be applied for removal of several substances from the strong wastewater. A treatment system has been installed (see Fig. 7 and 8) where the capacity of strong wastewater was increased from 54 m^3/d stepwise to 100 m^3/d.

The specific UV-process is removing toxicity and phenol-based active structures and is increasing the bioavailability of the strong wastewater resulting GSK stopping incineration of this wastewater (see Fig. 9 and 10, Table 6). Due to pre-treatment by photo-oxidation, the existing biological system at GSK is also able to handle this wastewater. For all environmental activities of GSK including the installation of the photo-oxidation GSK (together with other sustainability projects) was labeled with

■ **Table 5**

Data of treatment at Haupt Pharma Münster.

Parameter	Data	Result
Flow rate	12 m^3/d	No change
COD	2 000–4 000 mg/L	Ca. 20 % reduction rate
Sexual hormones like EE2	≈ 10–100 mg/L	< 0.01 mg/L
Bioavailability	≈ 65 %	≈ 90 %
OPEX	≈ 1–3 €/m^3	

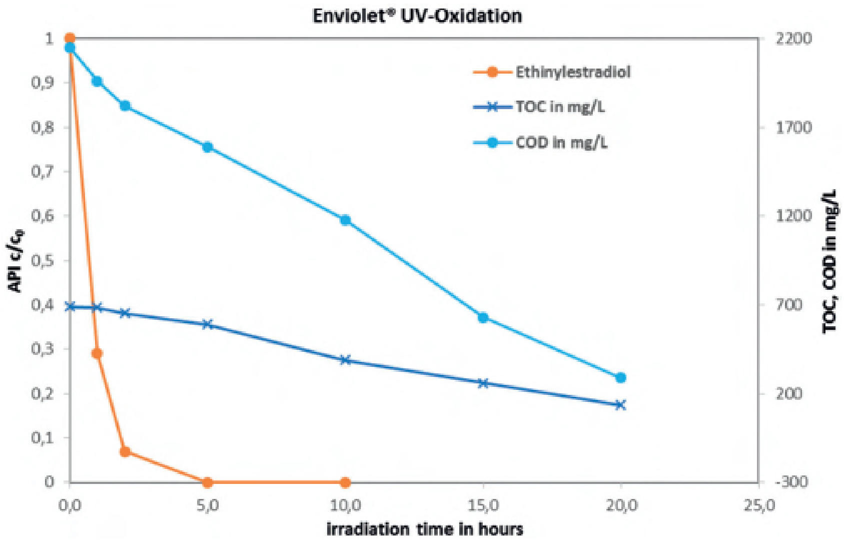

Fig. 6: Selective destruction of EE2 and concentrations of COD and TOC at Haupt Pharma Münster.

Fig. 7: Treatment installation at GSK Singapore (Source: GSK).

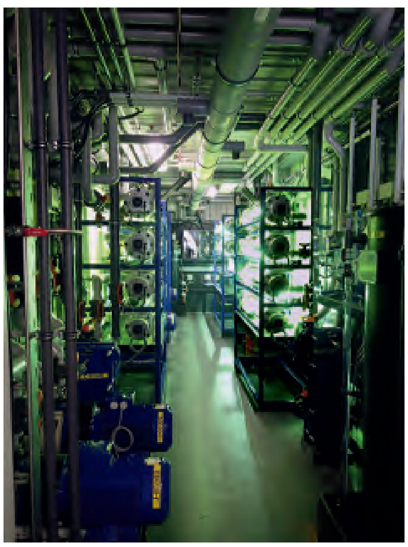

Fig. 8: Photo-oxidation installation placed at GSK for elimination of residual Amoxicillin and non bio-available organics in strong process wastewater.

a Singapore Environment Achievement Award.

■ BASF (Ireland)

Wastewater from synthesis of Phenol-based functional chemicals with a background of surfactants is released with flow rates between 250 and 700 m^3/d, depending on the actual wastewater composition.

The effluent of the plant was discharged to a biological plant on site, but presence of not biodegradable surfactants and several non-biodegradable organics prevented a constant and acceptable operation for BASF. Therefore a UV-based AOP was installed on site (see Fig. 11 and 12) and wastewater treated by this process is discharged to the municipal wastewater treatment plant. The UV-based AOP effectively destroys all aromatic structures by opening the aromatic ring and generation of small organic acids with good bioavailability. FOG (= Fat, Oil and Grease) also being part of this effluent are separated before AOP and also in the first step of oxidation, as by destruction of surfactants FOG can be easily floated and removed, as surfactants are destroyed in the first step of UV-oxidation.

■ Merck

The pharmaceutical manufacturing site of Merck KGaA in Altdorf Switzerland is producing an antihypertensive containing a phenolic structure. This production is generating some wastewater. This stream of wastewater originally was collected and sent to incineration for significant costs. A process treating this wastewater successfully by elimination of all aromatic structures, all solvents and huge increase of bioavailability of remaining organics has been developed (see Fig. 13 and 14). Toxicity was removed completely. For best oxidation at highest efficiency, also a recuperation system was integrated into the UV-plant. As control, system is fully integrated into Merck's factory management the

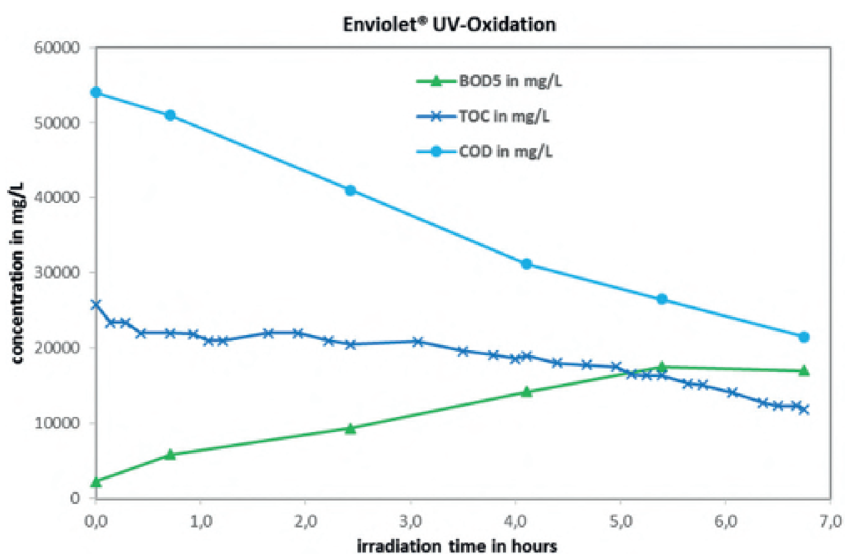

Fig. 9: Parameters TOC, COD and BOD_5 during the treatment at GSK Singapore.

■ Table 6

Data of treatment at GSK Singapore.

Parameter	Data	Result
Flow rate	54–100 m^3/d	
COD	58 000–70 000 mg/L	≈ 40 … 50 % reduction rate
Phenol-based organics from Amoxicillin process	≈ 1 000–5 000 mg/L	< 0.5 mg/L
Bioavailability	≈ 0 %	≈ 70 … 90 %
OPEX	≈ 20 €/m^3	

■ Table 7

Data of treatment at BASF Ireland.

Parameter	Data	Result
Flow rate	360–700 m^3/d	
COD	10 000–17 000 mg/L	≈ 30 %
VOC	≈ 1 000 mg/L	< 1 mg/L
Bioavailability	5 %	≈ 60 %
OPEX	≈ 4–5 €/m^3	

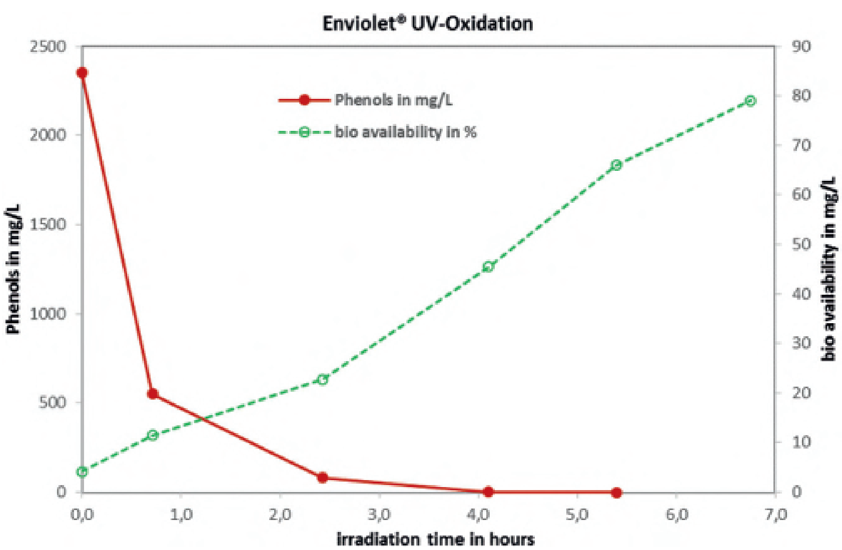

Fig. 10: Parameters Phenols and Bioavailability during the treatment at GSK Singapore.

Fig. 11: UV-plant for treatment of aromatic process wastewater.

unit is operated with minimum personal effort. Taking this unit into operation was significant environmental improvement for Merck combined with huge cost saving (see Table 8).

■ Pharma Action

The new GMP compliant heparin processing plant of Pharma Action (Toennies Group) has achieved a supply chain, in which the entire process: from animal slaughter via extraction of prime raw material to refinement into API occurs within one single company. Putting a focus on sustainability, process solution is treated with UV-Oxidation to break down organic substance like amino acids and eliminate organic background (see Fig. 15). With this method, treated

Fig. 12: Treatment tanks for AOP.

Fig. 13: Containerized UV-installation at Merck for treatment of strong wastewater from pharmaceutical manufacturing (Source: Merck).

Fig. 14: Photos of samples during various stages during UV-treatment at Merck (left to right: untreated to treated).

Fig. 15: Unit at Pharma Action for the purification of process solution and recovery of extraction salt (Source: Pharma Action).

■ **Table 8**

Data of treatment at Merck Altdorf, Switzerland.

Parameter	Data	Result
Flow rate	37 m³/d	
TOC	≈ 50 000 mg/L	≈ 5 000 mg/L
Phenols	15 000–24 000 mg/L	< 5 mg/L
DCM	≈ 5 000 mg/L	< 1 mg/L
Bioavailability	< 5 %	≈ 95 %
OPEX	≈ 20 €/m³	

■ **Table 9**

Data of treatment at a production site Pantoprazole and other APIs.

Parameter	Data	Result
Flow rate	36 m³/d	
COD	≈ 20 000 mg/L	≈ 5 000 mg/L
Pantoprazole	≈ 1 000 mg/L	< 0.01 mg/L
Bioavailability	5 %	≈ 95 %
OPEX	≈ 8 €/m³	

solution can be recovered and reused in the same process, resulting in savings of 1 000 MT/a of salt.

■ Multiple API Production

A production site for Pantoprazole and others of a leading Japanese pharmaceutical company has been using UV-oxidation for years for treating their effluent (see Fig. 16). Different API (e.g. Pantoprazole see Fig. 17 and Tab. 9) need to be degraded below the detection limit. The special challenge for developing this application was handling polymerization of degradation products in the wastewater matrix. Due to the specific reactor design, there are no layers or deposits on the UV-lamps, however to avoid deposits in the tanks precautions had to be taken and successfully implemented by appropriate treatment parameters.

■ API-manufacturer

A leading American pharmaceutical company operates a production site that produces wastewater with high COD amounts containing various API and solvents. The aim of treatment is elimination of API and reduction of the COD load by at least 60 % to lowest possible operating costs and unstaffed operation. To achieve this an online TOC-analyzer system was implemented for monitoring degradation and piloting process by adjustment of process parameters like number of UV-reactors, dosage of oxidant and operation conditions (see Fig. 18 and Table 10).

Fig. 16: UV-installation for Pantoprazole destruction.

Chemical Background [21]

For the major part of UV-oxidation treatments, we find curves like shown in Fig. 19 as an example:

The degradation process starts by oxidizing the carbon of organic molecules, whereby oxygen-containing functional groups are formed. However, no carbon dioxide is formed at first, which is why TOC reduction is rather insignificant at the beginning. But, since C-atoms of the molecules already have obtained a higher oxidation number, less oxygen is needed for a complete oxidation to carbon dioxide and, therefore, COD concentration is reduced faster. With COD oxidation (=feeding molecules with oxygen) the bio-availability is typically improving which is noticeable

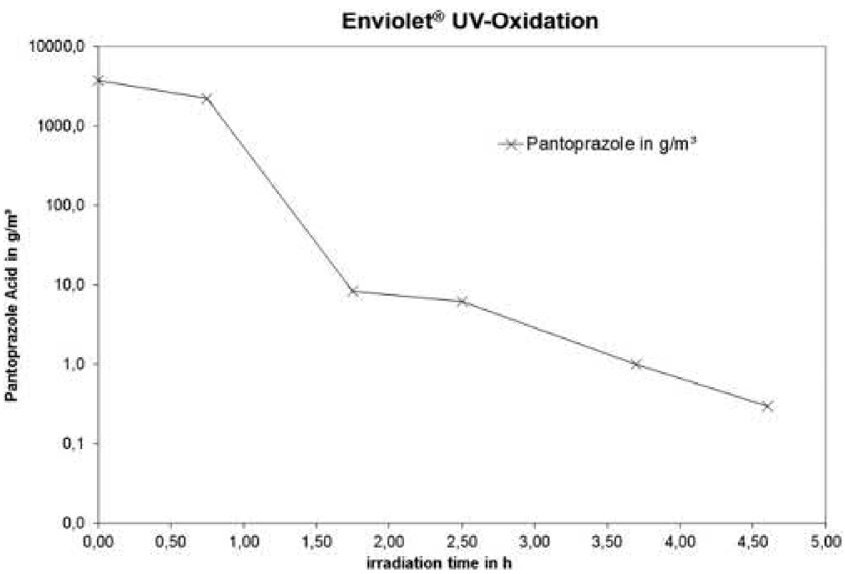

Fig. 17: Degradation of Pantoprazole (logarithmic scale).

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Table 10

Data of treatment (American pharmaceutical company).

Parameter	Data	Result
Flow rate	40 m^3/d	
API (various)	≈ 10–4 000 mg/L	≈ 100 % removal rate
COD	≈ 35 000 mg/L	≈ 10 000 mg/L
Bioavailability	Low	> 80 %
OPEX	≈ 7–9 €/m^3	

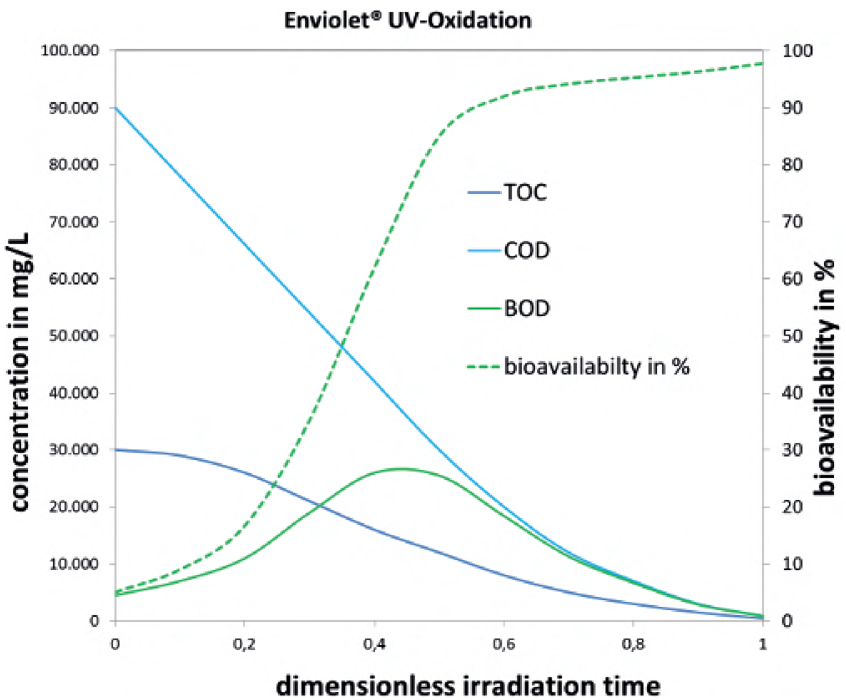

Fig. 19: Typical degradation of TOC, COD, BOD and resulting increase of bio-availability versus irradiation time.

by an increasing BOD. The changes of COD and BOD can be described as bio-availability in % (= ratio BOD/COD x 100 %). A bio-availability of 60 % can be considered "good" and between 40–60 % it is typically sufficient for the water to be discharged to a sewage treatment plant.

An example for UV-oxidation of a complex mixture of toxic organic compounds in a real wastewater (fine chemicals industry) containing phthalic acid derivates is illustrated in the following diagrams (Fig. 20 and 21). This example is presented because detailed analyses of degradation products and bio availability exist. Concentrations of carboxylic acids are rising during the treatment by UV-oxidation and, after reaching a maximum their concentration, is dropping as well. At this stage complete bio availability is already achieved. This was shown by measurement of BOD5 (Biological Oxygen Demand after 5 days) and comparing it with the COD. An adapted activated sludge would lead to an even a higher bio availability.

The above given measurable results are based on following reaction chains:

Light of proper wavelength splits hydrogen peroxide (H_2O_2) into highly reactive hydroxyl radicals by photolysis (UV/H_2O_2-process), which re-

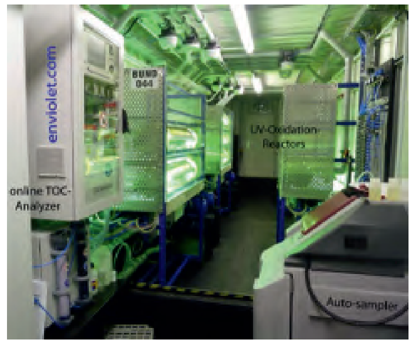

Fig. 18: UV-oxidation system with integrated online analytics for automatic operation.

acts quickly with organic and inorganic water compounds:

$$H_2O_2 \xrightarrow{h\nu} 2\ HO^{\bullet}$$

Such hydroxyl radicals (OH-radicals) are not only generated with the least amount of chemicals [22] but also with the most economical energy input by the UV/H2O2-process [23]. For this reason AOP is also at high target-concentrations very well suited for effective treatment of pollutants in aqueous solutions such as, highly contaminated wastewater, electroplating baths and even ultrapure process water.

The degradation of organic compounds via OH-radicals is initiated by hydrogen abstraction

$$R\text{-}H + HO^{\bullet} \longrightarrow R^{\bullet} + H_2O$$

or electrophilic addition of OH-radicals takes place:

$$R{=}R + HO^{\bullet} \longrightarrow {}^{\bullet}R\text{-}ROH$$

These initiated reactions follow various reaction possibilities of the generated radicals. In presence of oxygen an organic peroxyl-radical is formed:

$$R^{\bullet} + O_2 \longrightarrow RHO_2^{\bullet}$$

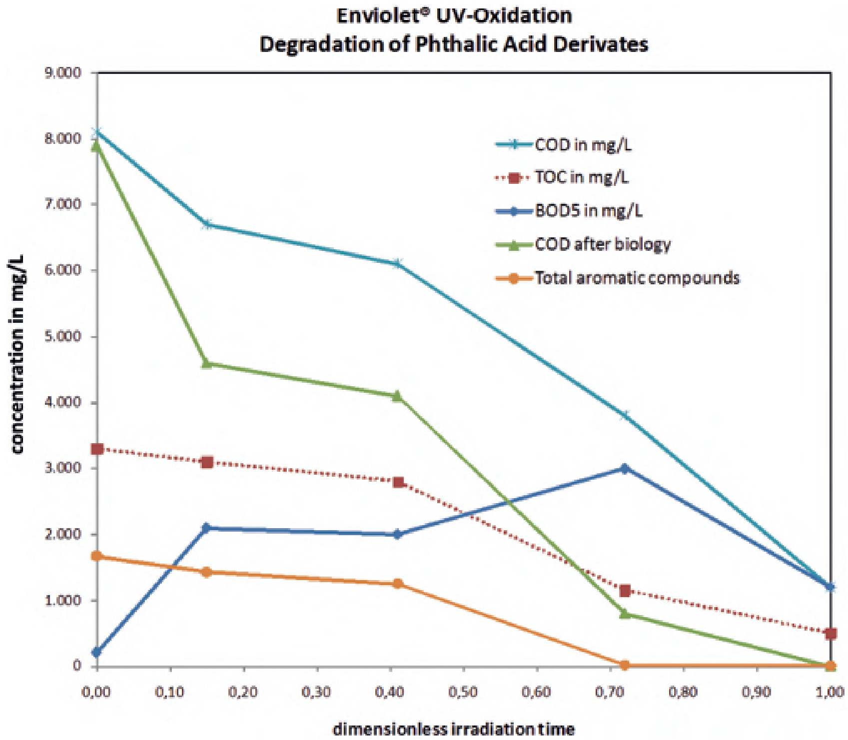

Fig. 20: Destruction of toxic compounds, COD, BOD_5 and TOC during UV-treatment of real wastewater.

Furthermore, various competitive reactions can occur:

$$R^{\bullet} + H_2O_2 \longrightarrow ROH + HO^{\bullet}$$

$$R^{\bullet} + HO^{\bullet} \longrightarrow ROH$$

$$R^{\bullet} + R^{\bullet} \longrightarrow \text{R-R (Polymerization)}$$

In general, polymerization is not a favored reaction because polymerized products may lead to precipitation issues on the UV lamp surface. For this reason it is important to avoid such polymerization by proper process control design and UV reactor construction. Also the peroxyl-radical ($RHO_2^{\bullet}$) may for instance continue its reaction as follows:

$$2\ RHO_2^{\bullet} \longrightarrow RO + RH^{+} + HO^{-}$$

Resulting aldehydes respectively ketones are oxidized into carboxylic acids by the subsequent reaction processes, which are subject to either a thermic or photo-chemical decarboxylation.

$$R'\text{-}CO_2\text{-}H \longrightarrow R'H + CO_2$$

Besides initiating reactions via OH-radicals (generated from H_2O_2) direct photolysis of water ingredients by UV irradiation plays a major role. However, sufficient absorption of these substances is required, which can be selectively destroyed under proper process conditions. Especially the possibility of a selective oxidation of toxic ingredients is a big advantage in regard to efficiency and economics.

Another possibility of the UV-induced degradation processes is the use of metal ions as catalysts, which, depending on the treatment objective and wastewater ingredients, may lead to a better process efficiency. The best-known process is the Photo-Fenton-Process, in which iron-containing solutions are used as catalyst. Based on various photo reactions hydroxyl-radicals are generated via photo reduction of metal ions and initiate the above described degradation process. In addition, many other reactions play a role and also resulting to the degradation

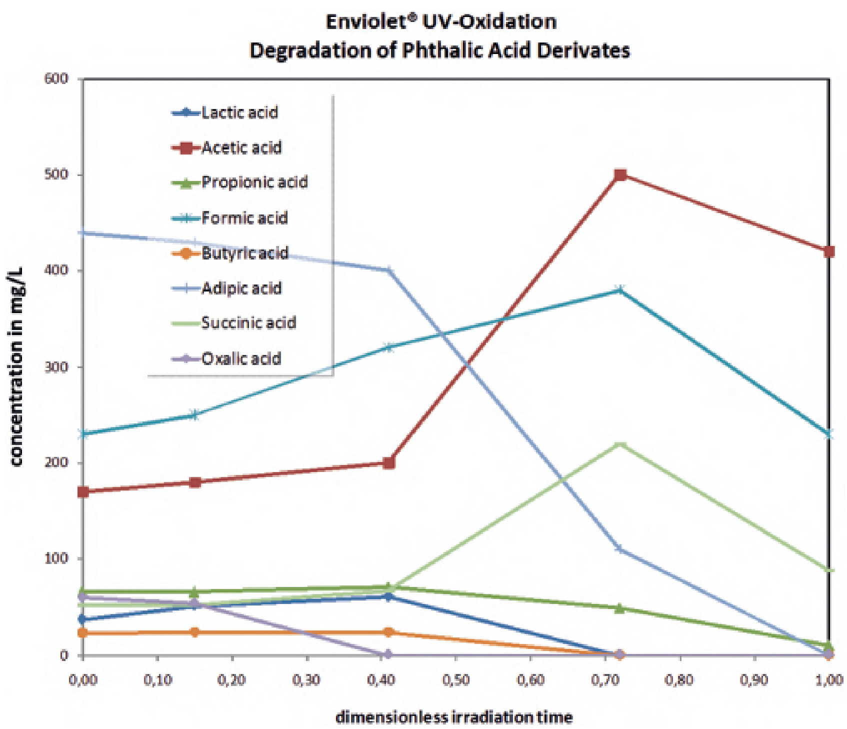

Fig. 21: Generation of bio available degradation products.

of organic water ingredients (see Fig. 22).

A common prejudice against UV-based oxidation is that wastewater has to be very transparent for light and should not contain any particles. That applies only to UV-disinfection but has no meaning for UV-oxidation. In contrast, often a strong color indicates already good absorption of light, which can be used by enhancing the above mentioned direct photolysis as initial reaction.

Above described possible reaction pathways lead consequently to the need of developing process parameters best suited for each task. Therefore, as a general rule, lab tests are carried out in the beginning of each industrial application.

The way from lab tests to industrial applications

Typically, wastewater projects start on a laboratory scale for establishment of the best available technology for a selected problem. A feasibility study starts with a classification test using several µL, which results with a degradation class. Then in the scale of 0.5–1 L a next step is done to verify the results from classification in a next scale. If again good results are achieved a complete process simulation is run with ca. 5–50 L also supplying a significant volume of (intermediate) samples for further testing on by-products and or biodegradability as well as analytics on single parameters like API, etc.

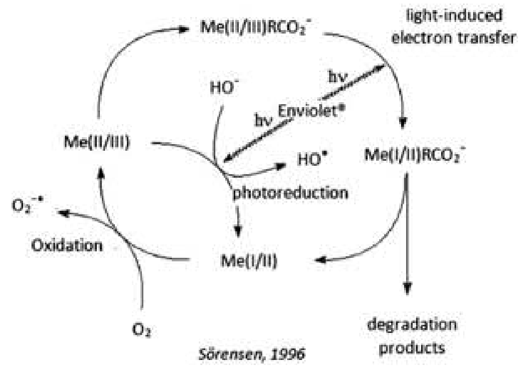

Fig. 22: Reaction of complex metal ions in oxygen saturated aqueous solution reduced by light-induced transfer of electrons (Source: [20]).

Based on this, customers can decide to go directly into a commercial project or run further test-work on site, up to 6 to per test, or rent a commercial scaled pilot installation.

During efficient and realistic testing procedures, reliable data for commercial installations are evaluated resulting in an appropriate treatment process including CAPEX and OPEX.

By that method reliable data can be supplied for:

1. establishing a strategy to treat pharmaceutical wastewater effectively
2. identifying the need for and advantages of the treatment of pharmaceutical wastewater at point of source

Table 11

Origins and properties of typical pharmaceutical wastewater.

	API-manufacturing	Formulation	
		Dry (Pills)	Liquid (Vials)
Origin of wastewater	Chemical synthesis of API and intermediates	CIP-cleaning of equipment	Residuals and CIP-cleaning of equipment
Note	Wide range of chemical mixture, due to reactions made	API at low concentration Starch (filling material) Wax (surface)Water	API at low concentration organic solvents, often recoveredWater
Typical existing solution	Incineration, Evaporation / Incineration		
Aim of treatment	Detoxification, increase of Bio-availability and direct discharge at low costs		
Treatment proposed	UV-Oxidation, UV-AOP often a special treatment, mostly with high flexibility for varying composition of effluent	UV-Oxidation able to handle suspended solids	UV-Oxidation able to handle some solvents
Following treatment	Often Biological treatment	none	non
COD in mg/L (range)	10 000–100 000	1 000–5 000	1 000–50 000
COD in mg/L (90 % percentil)	As above	2 000–3 000	5 000–10 000 (with good solvent recovery)
TSS in g/L	Up to 250	2–4	2–4
Flow rate	5–500 m^3/d	5–20 m^3/d	5–20 m^3/d

3. reducing investment, maintenance, and operating costs by selecting simple and effective wastewater treatment processes
4. relation between APIs and an easy-to-measure indicative parameter, like absorbance at a certain wavelength, TOC or COD...) easy to be operated by the customer, in the ideal case and at higher flow rates also by online-techniques
5. PLC controlled process, adjusting parameters based on instrumentation

Conclusion

In many cases, the integration of an AOP is supplied into existing structures for best CAPEX. Often good results are achieved by combination of biological and advanced oxidation in various ways, always depending on chemical character and already existing structures. Additional aspects are also future expansions or integration of other side streams into a new or modified treatment system based on UV-processes. By this approach more than 600 AOP-plants have been realized for these applications between 1997 and 2015.

Of course manufactures use all possibilities of wastewater savings (wastewater reductions) by optimized CIP rinsing processes by validating minimum rinsing time and number of rinsing steps needed. As well, reuse of wastewater for cooling processes in non-GMP areas or plant irrigation purposes, etc. are taken into account.

Typical Pharma applications can be roughly assigned to following origins and properties of wastewater as summarized in Table 11.

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Korrespondenz:

Dr. Martin Sörensen
Enviolet GmbH
Schenkenburgstr. 18
76135 Karlsruhe (Germany)
e-mail: MS@enviolet.com

Chefredaktion: Claudius Arndt. Sekretariat: Gudrun Geppert. Verlag: ECV · Editio Cantor Verlag für Medizin und Naturwissenschaften GmbH, Baendelstockweg 20, 88326 Aulendorf (Germany). Tel.: +49 (0) 75 25 94 00, Fax: +49 0) 75 25 94 01 80. e-mail: redaktion@ecv.de. http://www.ecv.de. Herstellung: Reemers Publishing Services GmbH / Holzmann Druck GmbH & Co. KG.