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Review

Slurry photocatalytic membrane reactor technology for removal of pharmaceutical compounds from wastewater: Towards cytostatic drug elimination

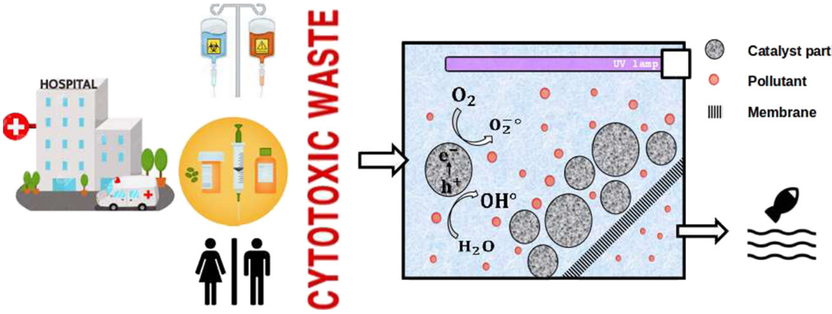
Raphael Janssens [a,*], Mrinal Kanti Mandal [b], Kashyap Kumar Dubey [c], Patricia Luis [a]

[a] *Materials & Process Engineering (iMMC-IMAP), Université catholique de Louvain, Place Sainte Barbe 2, 1348 Louvain-la-Neuve, Belgium*
[b] *Department of Chemical Engineering, National Institute of Technology Durgapur, M.G. Avenue, Durgapur, West Bengal 713209, India*
[c] *Department of Biotechnology, Central University of Haryana, Jant-Pali, Mahendergarh 123031, Haryana, India*

HIGHLIGHTS

- Photocatalytic membrane reactor efficiently removes common cytostatic compounds.
- Ceramic membranes have high resistances towards abrasion of catalyst particles.
- Doping of photocatalyst allows efficient PhCs degradation with visible light.
- Treatment of HWW with sunlight based on self-powered PMR is technologically feasible.

GRAPHICAL ABSTRACT



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ABSTRACT

The potential of photocatalytic membrane reactors (PMR) to degrade cytostatic drugs is presented in this work as an emerging technology for wastewater treatment. Cytostatic drugs are pharmaceutical compounds (PhCs) commonly used in cancer treatment. Such compounds and their metabolites, as well as their degraded by-products have genotoxic and mutagenic effects. A major challenge of cytostatic removal stands in the fact that most drugs are delivered to ambulant patients leading to diluted concentration in the municipal waste. Therefore safe strategies should be developed in order to collect and degrade the micro-pollutants using appropriate treatment technologies. Degradation of cytostatic compounds can be achieved with different conventional processes such as chemical oxidation, photolysis or photocatalysis but the treatment performances obtained are lower than the ones observed with slurry PMRs. Therefore the reasons why slurry PMRs may be considered as the next generation technology will be discussed in this work together with the limitations related to the mechanical abrasion of polymeric and ceramic membranes, catalyst suspension and interferences with the water matrix. Furthermore key recommendations are presented in order to develop a renewable energy powered water treatment based on long lifetime materials.

Abbreviations: PMR, photocatalytic membrane reactor; PhCs, pharmaceutical compounds; WWT, wastewater treatment; AOP, advanced oxidation process; UF, ultrafiltration; NF, nanofiltratoin; RO, reverse osmosis; LED, light emitting diode.

[*] Corresponding author.
E-mail address: raphael.janssens@uclouvain.be (R. Janssens).

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Contents

1. Introduction

Most countries around the word have strict regulations concerning wastewater treatment. Usually environmental agency sets the water quality standards to be achieved by municipal wastewater treatment plants as it is the case in U.S.A. (USEPA, 2011) or in Europe (European Commission, 1991). Even if one might believe that household wastewater composition remained unchanged throughout decades, the reality is different due to the increasing worldwide production of pharmaceutical and personnel care products used to meet the modern civilization needs. In addition during the last decades, chemical detection methods have significantly improved and the presence of pollutants in the environment can be detected at parts-per-trillion/parts-per-billon levels (ng-μg/L) (Daughton and Ternes, 1999). Thus, the environmental fate of those pollutants can be more easily monitored leading to an enhanced awareness of their emission and possible consequences on the environment and human health.

The occurrence of micropollutants in surface waters depends on unexpected environmental parameters. For instance, heavy rainfall induces diverse effects such as dilution of the pollutant emission from point sources or leaching of biocides or bisphenols initially trapped in building materials. Beside natural events, the concentration in micropollutants in rivers increase significantly when passing through large cities as it is the case for caffeine and nonylphenol in rivers running through large cities in the USA and China, respectively (Luo et al., 2014). Therefore modeling of surface water contamination is not an easy matter. And the emergence of contaminating compounds in surface water forces the authorities to be reactive on the calculation of the 'predicted environmental concentrations' and to adapt water treatment methods in order to meet the 'predicted no-effect-concentrations' (European Commission, 2003). Apart from agricultural and aquaculture runoff most of the micropollutants pass during their lifetime through wastewater treatment plants (WWTP). Hence wastewater treatments should be adapted to the local pollution sources.

In comparison to wastewater released by households, recent analyses have recorded significant concentrations of pharmaceutical compounds (PhCs), disinfectants, X-ray contrast media and resistant microbiological loads in hospital wastewater (HWW) (Verlicchi et al., 2015). In a study on Spanish surface waters high PhCs concentrations were detected in rivers located downstream of a university campus, pharmaceutical plant, hospital and a large retirement home. The samples had a total PhCs concentration of 78.7 μg/L with a single contribution of the antiepileptic drug carbamazepine of 67.7 μg/L (Valcarcel et al., 2011).

Antineoplastic or cytostatic drugs comprise an emerging part of persistent micropollutants. These PhCs are used as oncological treatments to destroy cancerous cells by diverse mechanisms of action. For instance, the alkylating agent class corresponds to drugs able to crosslink the two DNA spins by covalent bonds leading to disruptions of DNA synthesis and prevention of the mutant cells replication (Goodman and Gilman, 1991). Cytostatic drugs are thus genotoxic, mutagenic, cyanogenic, teratogenic and fetotoxic. But metabolites may be more toxic than the parent compounds because certain drugs are designed to be activated by reactions with patient's metabolism (Negreira et al., 2014a). For these reasons cytostatic drugs and their excretions must be handled following strict safety procedures depending on the applied concentrations. Especially the preparation of stock solutions requires the highest level of safety in order to protect the personnel (Eitel et al., 1999; W.H.O., 2012). Concerning the stability of 26 cytostatic drugs and metabolites, storage in the dark at −20 °C from collection to analysis was shown to be the best option (Negreira et al., 2014b).

The cytotoxic actions on the human metabolism are diverse and well documented but their effects on ecosystems remain unclear (PILLS_Report, 2012). This is due to the absence of environmental risk assessment (ERA) study (Zhang et al., 2013). In addition, even if DNA is permanently damaged, ecotoxicity tests included in ERA may give false-negative results. Therefore an appropriate test for mutagenicity and genotoxicity detection should be selected with great care (Prasse et al., 2015). These drugs are designed to be persistent in order to remain inactivated until having their therapeutic effect in the patient's body (Sanderson et al., 2004). This is why wide scope antineoplastic drugs like cyclophosphamide and ifosfamide were shown to be non-biodegradable in laboratory tests (Kummerer et al., 2000) and are expected to run unchanged through municipal wastewater treatment plants based on biological treatment (Kummerer, 2001). As stated by Daughton and Ternes at the end of the 20th century: “major change goes undetected until the cumulative level of these effects finally cascades to irreversible change - change that would otherwise be attributed to natural adaptation or ecologic succession” (Daughton and Ternes, 1999).

The probable most concentrated source of cytostatic drugs is the oncological wards of large hospitals where patients are interned for cancer treatment. Indeed a concentration of the cytostatic carboplatin of 100 μg/L was measured in wastewaters coming form an oncological ward in Vienna (Negreira et al., 2014a). And downstream hospital wastewaters are discharged into the municipal sewer system without any pre-treatment which, once diluted, runs to the nearby wastewater treatment plant (Zhang et al., 2013). It is therefore understandable that a lower composition of anti-neoplastics ranging from 5 to 50 μg/L was typically recorded in hospital wastewaters (Verlicchi et al., 2015) and that a level of cyclophosphamide of 41 ng/L was detected in 2001 in Spanish surface waters (Valcarcel et al., 2011). Furthermore a second main pollution source comes from patients treated in one-day clinics, representing 75% of the patients treated with cytostatic drugs (Negreira et al., 2014a). Ambulant patients are sent home after receiving the treatment where they pollute municipal wastewaters. The stress on the environment is then of another kind, instead of few highly concentrated sources, pollution is released in a diffuse way on a large geographic area. A last point calling for the development of appropriate water treatments is the increase of genotoxic agents production throughout years related to the annual new cancer cases which are expected to rise from 14 million in 2012 to 22 million within the next two decades (Ferlay et al., 2013).

Throughout this review slurry photocatalytic membrane reactor (PMR) will be presented as a key technology for micro-pollutant removal (Molinari et al., 2001; Mozia et al., 2015a). Discussion on light sources, catalyst photo-activity, membrane fouling control and resistance to abrasion will be presented together with several recommendations to overcome the current limitations of slurry PMR systems.

2. Slurry photocatalytic membrane reactor (PMR)

A photocatalytic membrane reactor is a hybrid technology merging a photocatalytic reactor with a filtration process. Photocatalytic reactions occurring at the catalyst surface enable the system to degrade organic matter while a membrane module can be used as a support layer and/or a separation step. A first class of photocatalytic membrane reactor is characterized by immobilization of the catalyst on a membrane surface. In this case advantages like fouling alleviation or high permeate quality are pointed out (Zhang et al., 2016). However the catalyst active surface area is limited and catalyst regeneration is only possible by replacing completely the photocatalytic membrane. To overcome those limitations a second class of PMR was developed by bringing in suspension catalyst particles. Called slurry PMR, this novel technology must include an additional filtration step in order to recover the suspended catalyst (Molinari et al., 2008). The working principle of slurry PMR is represented in Fig. 1: when irradiated by light, electrons of the catalyst material are excited from the valence band to the conduction band leading to the formation of a free electron-hole pair. As these free charges encounter the species absorbed on the catalyst surface, active radicals are formed such as hydroxyl and hydrogen peroxyl (OH• and H_2O_2•, respectively) which have high oxidizing potentials to degrade organic/inorganic matter in solution (Lan et al., 2013). Simultaneously thanks to a membrane module, the catalyst particles are confined in the system and a treated stream free of catalyst is obtained at the permeated side (Ganiyu et al., 2015).

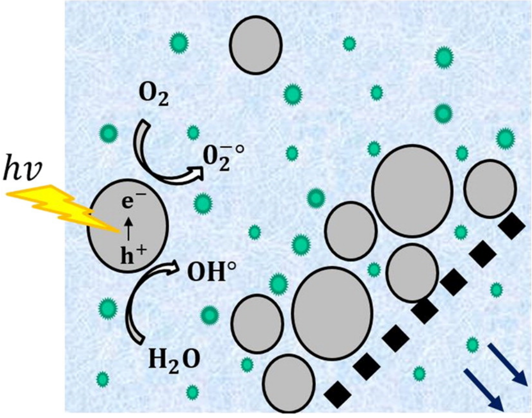

Fig. 1. Scheme of slurry PMR operation with catalyst particles in grey and pollutant in green. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

As summarized in Table 1 slurry PMRs are already studied at laboratory and pilot plant scales for PhCs removal (Plakas et al., 2016a). Nevertheless many challenges remain to be addressed in order to develop low energy consuming slurry PMRs having long lifetimes.

2.1. Photocatalyst

Photocatalyst particles are the core of slurry PMR systems because they enhance degradation kinetics. The following sections summarize the main light sources currently in use and the main characteristics of catalyst affecting its photo-activity.

2.1.1. Light source

One of the most common lamps is called mercury lamp and exists in two kinds: low pressure (LP Hg) and medium pressure (MP Hg) mercury lamps. Studies have inferred that at similar powers and without catalyst in suspension, LP lamps induce higher degradation rates of the cyclophosphamide drug than MP lamps because the emitted photons have higher energies or, in other words, shorter wavelengths around 254 nm (Kim and Tanaka, 2009). Beside mercury lamps light-emitting diodes (LEDs) can be used as light source (Wang et al., 2008). Such diodes have the great advantage to avoid mercury disposal problem and have higher energy efficiencies. In addition the lifetime of mercury lamps being 9000–12,000 h is extended when using LED to 35,000–50,000 h (Eskandarian et al., 2016). Currently diodes having emission peaks from 255 up to 405 nm are available on the market.

2.1.2. Photo-catalytic material

Photocatalyst materials have to be selected depending on the available light source. One of the most studied photocatalyst is titanium oxide due to its availability on the market in various crystalline forms, high photo-activity efficiencies, non-toxicity and high photochemical stability (Hilles et al., 2012). Cytostatic drug degradation have been reported using slurry UV/TiO_2 system on ifosfamide and cyclophosphamide (Lutterbeck et al., 2015; Ofiarska et al., 2016). In the case of TiO_2 two crystalline forms are used as catalyst: anatase and rutile which have band gaps of 3.2 and 3.02 eV leading to absorption edges of 416 nm and 280–400 nm, respectively. Hence titanium based catalysts are excited by UV wavelengths not higher than 387 nm, which represents around 3% of the solar spectrum received on earth (Lan et al., 2013). Several ways exist to extend the activity of a photocatalyst

Table 1
Literature research on photocatalytic membrane reactor of degradation of pharmaceutical compounds.

Ref.	Technology feature	Target compound	Degradation (%) of target compounds or drug rejection	Experimental conditions	Analytical methods
Separated membrane reactor					
Plakas et al. (2016a) pilot plant	Diclofenac 0.5 mg/L	UV-C/TiO_2 (P25 0.5–0.75 g/L)/ UF (0.03 μm) hollow fiber 4.19 m^2 PVDF	56–100% degraded 52% removal of TOC	Tap water as matrix pH = 7.5–8 $V_{tot} = 25$ L $V_{photo} = 15$ L $V_{mem} = 10$ L TMP = 8–34 kPa HRT = 30–60 min	TOC HPLC-DAD
Doll and Frimmel (2005)	Carbamazepine 2 mg/L	UV_{254} (LP)/TiO_2 (P25, 1 g/L)/ UV_{254} (LP)/TiO_2 (Hombikat UV100, 1 g/L)/ MF (0.4 μm) tubular module AlO_x 6/10 × 250 mm MF (0.2 μm) flat module PVDF - MF (0.2 μm) flat module polypropylene - MF (0.24 μm) flexible ceramic membrane foil	98% degraded after 1 h Drug degradation rates observed with the catalyst Hombikat UV100 are higher than with catalyst P25 AlO_x was resistant to abrasion and back-washing The 3 last studied membranes were not resistant to the abrasion of TiO_2	Demineralized water as matrix pH = 6.8 $V_{tot} = 15.9$ L $V_{photo} = 0.132$ L CFV = 0.3 m/s $F_{photo} = 40$ L/h $F_{mem} = 16.7$ L/h $F_{perm} = 1$ L/h Mean irradiation time = 3 min $V_{recycled} = 97\%$	DOC HPLC-DAD
Mozia and Morawski (2012)	Ibuprofen 11 mg/L	UV_{365}/TiO_2 (P25, 0.5 g/L)/ membrane distillation (0.2 μm) polypropylene 0.0127 m^2	100% degraded after 5 h 100% drug reject.	Artificial fresh water as matrix T = 20 °C	TOC pH HPLC-UV/Vis
Szymański et al. (2015)	Humic acids 5 mg/dm^3	UV_{254} (LP)/TiO_2 (P25, 0.5–2 g/L)/ UF 100 kDa tubular membrane TiO_2 Filtanium	Absorbance = 0 after 30 min 65–73% humic acid reject.	Synthetic surface water as matrix pH = 6.5 CFV = 3–6 m/s TMP = 0.1 MPa T = 20 °C	TOC UV_{254} abs. Turbidity HPLC
Molinari et al. (2006)	Furosemide 10 mg/L Ranitidine 10 mg/L	UV (MP 120 W)/TiO_2 (P25, 1 g/L)/ nanofiltration (0.05–0.1 μm) sulfonated polysulfone	>80% furosemide degraded after 120 min >50% ranitidine degraded after 120 min Furosemide: 10–60% reject. Ranitidine: 5–30% reject.	Ultrapure water as matrix pH = 11 $V_{photo} = 0.5$ L $[O_2] = 20$ mg/L TMP = 4–8 bar T = 30 °C	pH Spectrophoto-meter
Sarasidis et al. (2014)	Diclofenac (anti-inflam. drug) 2 mg/L	UV_{365}/TiO_2 (P25, 0.5 g/L)/UF: PVDF hollow fibers 0.097 m2 (0.04 μm)	99.5% degradation 69% mineralization after 60 min	Synthetic ultrapure water, ground water, surface water. pH = 6 $V_{photo} = 2.3$ L $J_{o2} = 1.2$ L/min $V_{mem} = 0.7$ L	TOC pH Radiometer HPLC-UV/Vis HPLC-GC/MS

(continued on next page)

Table 1 (*continued*)

Ref.	Technology feature	Target compound	Degradation (%) of target compounds or drug rejection	Experimental conditions	Analytical methods
				T = 20 °C	
Separated membrane photoreactor (SMPR)					
Molinari et al. (2008)	Gemfibrozil 10 mg/L Tamoxifen 8 mg/L	UV (MP 120 W)/TiO_2 (P25, 0.1 g/L)/ nanofiltration 600–800 Da polyethersulfone flat sheet	98.9% gemfibrozil degraded in 40 min 60% gemfibrozil mineralized 100% tamoxifen degraded in 60 min 42% gemfibrozil reject. 62.5% TOC rejection	Ultrapure water as matrix pH = 4–10 $V_{photo} = 0.7$ L $C_{o2} = 22$ ppm $V_{mem} = 0.095$ L TMP = 4–8 bar T = 30 °C	TOC DOC pH Particle size analyzer HPLC-UV
Ho et al. (2009)	Biologically treated sewage effluent (BTSE) containing 11–13 mg/L of TOC	UV_{352}/TiO_2 (P25, 0.5–1.5 g/L)/ MF: polyethylene hollow fiber membrane 0.05 m^2 (0.1 μm)	80% DOC degradation Lower reject. of smaller molecules (100–200 Da)	Study of the removal of effluent organic matter in BTSE pH = 6.5–7 $V_{photo} = 1.5$ L $J_{o2} = 19.2\ m^3/h \cdot m^2$ $V_{mem} = 6$ L TMP = 2–10 kPa T = 28 °C	TOC DOC Turbidimeter Radiometer SPE HPLC-MS/MS
Integrated membrane reactor (IMPR)					
Augugliaro et al. (2005)	Lincomycin (common antibiotic) 75 μM	Sunlight/TiO_2 (P25, 0.2 g/L)/ NF tubular membrane: DK2540C DL2540C	Complete degradation 97.78% lincomycin reject. 91.3% lincomycin reject.	Ultrapure water as matrix pH = 6.3 $V_{photo} = 22$ L $V_{tot} = 39$ L $J_{recycl} = 334$ L/s TMP = 1–12 bar T = 25 °C	TOC HPLC-MS/MS
Fernandez et al. (2014)	33 PhCs cumulated concentration of 500 ng/L	UV_{365}/TiO_2 (P25, 0.5 g/L)/ PVDF hollow fiber membrane 100 cm^2 (0.04 μm)	100% degradation of 18 PhC after 60 min. 50–88% degradation of 14 PhCs after 60 min Variable reject.	Organic-based model surface water as matrix pH = 6.5–7 $V_{photo} = 2.4$ L TMP = 300 mbar T = 25 °C	TOC Radiometer SPE HPLC-MS/MS

DAD: diode array detection.
F_{photo}: liquid flow entering the photoreactor.
F_{mem}: liquid flow entering the membrane module.
F_{perm}: permeate liquid flow.
F_{recycl}: liquid flow recycled to the photoreactor.
J_{O2}: oxygen flux.
V_{tot}: total liquid volume in the system.
V_{photo}: liquid volume in the photoreactor.
PVDF: polyvinylidene fluoride.
TOC: total organic carbon.

under visible light: doping, band-gap nanoengineering, and crystal morphology tuning.

2.1.3. Methods to improve catalyst efficiency

Dopants improve the separation of electron from holes, introduce intermediary energy levels, and may improve surface-absorption of species. Following this strategy titanium oxide particles have been doped with carbon, nitrogen, or sulfur, reducing the band gap to <3.0 eV (Lan et al., 2013). In addition as represented in Fig. 5, doping TiO_2 by simple sol-gel method with platinum (0.15%) induced an elimination increase of cyclophosphamide and ifosfamide from 66 and 59% to 99 and 98% under irradiation with artificial visible light (Ofiarska et al., 2016). In laboratories a filter removing wavelengths shorter than 420 nm is used to remove the non-visible part of a spectrum emitted by a lamp. Another study investigated doping with palladium by deposition precipitation, which improved the photocatalytic activity of commercial TiO_2 illuminated with artificial visible light by a factor five (Molinari et al., 2015). Consequently it is clear that further researches are possible in order to treat wastewaters directly with sunlight.

A second way to improve catalyst efficiencies is to reduce the recombination of electrons with holes by driving them towards opposite directions. Thanks to heterojunctions between two different crystalline lattices of a same material, pair separation is favored as it is the case for the commercially available catalyst Degussa P25 containing anatase 80% and rutile 20% (Klavarioti et al., 2009). Moreover the heterojunction formatted by the deposition of Cu_2O and Ag nanoparticles (p-type) on ZnO nanotubes (n-type) allowed to increase the kinetic constant by a factor 3.2 in comparison to non-modified ZnO nanotubes (Chiang and Lin, 2015). Similar results were obtained by another study working with TiO_2 nanotubes and with TiO_2 supported on carbon nanotubes. Under UV irradiation, kinetic constant of phenol degradation and total organic carbon removal were 0.39 h^{-1} and 16.7% but increased to 0.75 h^{-1} and 53.7% for the double-materials nanotubes (Yu et al., 2008). Combining band-gap nanoengineering and doping improve thus catalyst activity: prepared surface-fluorinated TiO_2 ($FTiO_2$)/graphene oxide hybrid nanosheets gave degradation efficiencies of methyl blue 3–4 times higher than single TiO_2 nanosheet under 365 nm UV light (Reddy et al., 2015).

A last way to improve the photo-activity is to modify the morphology of nanoparticles. During synthesis of photocatalytic particles operating parameters can be tuned in order to obtain particles of different crystal sizes and morphologies, which modify the recombination rate of electrons with holes (Lan et al., 2013). The finely tuned morphology of crystals in TiO_2 P25 particles may be one of the explanations for their high photocatalytic performance (Klavarioti et al., 2009).

2.2. Membrane fouling

The deposition of matter on the membrane surface leads to a reduction of transmembrane fluxes. This reduction depends on the nature of the fouling matter.

2.2.1. Bio-fouling

Proliferation of micro-organisms on membranes occurs during filtration of streams loaded in non-toxic organic matter. This event called bio-fouling is unlikely to occur in PMR systems for diverse reasons: high toxicity of wastewaters, presence of radical species and collision of catalyst particles on the membrane surface (Zhang et al., 2016).

2.2.2. Organic fouling

Beside bio-fouling, the role of suspended organic matter in fouling mechanisms was pointed out by a study on critical flux of a microfiltration (MF) membrane. The transmembrane fluxes obtained with a biologically treated sewage effluent increased if a pretreatment by photocatalysis was performed (Ho et al., 2009). This reveals the significant advantage of coupling oxidation with filtration in PMR technology. In addition the authors observed that standalone MF could not reject small molecular weight organics (100–200 Da), but prior to filtration a TiO_2/UV treatment could remove both small molecular weight and large organic molecules (1500–2000 Da) (Ho et al., 2009).

Beside negative impacts, organic fouling was shown to improve drug rejections: an interesting study showed an increase of cyclophosphamide rejection by nanofiltration (NF) from 30 to 60% during filtration of a membrane bioreactor (MBR) effluent instead filtration of ultrapure water matrix. The performance improvement observed with MBR effluents were attributed to the organic cake layer build-up at the membrane surface (Wang et al., 2009).

2.2.3. Inorganic fouling

To be efficiently confined in PMR systems, catalyst particles must form aggregate and the size of these aggregates depend directly on the pH of the slurry solution. This was observed by a study measuring TiO_2 catalyst rejection with a 0.2 μm pore size membrane: below pH 4 particles attract each other leading to the formation of large aggregates which precipitates and are hardly dispersed in solution. While over a pH of 10 the repulsion is so high that particles cannot be efficiently rejected by a 0.2 μm pore size membrane. Therefore a study suggested to perform PMR experiments in a pH range of 7 ± 3 in order to obtain efficient catalyst rejection (Molinari et al., 2008).

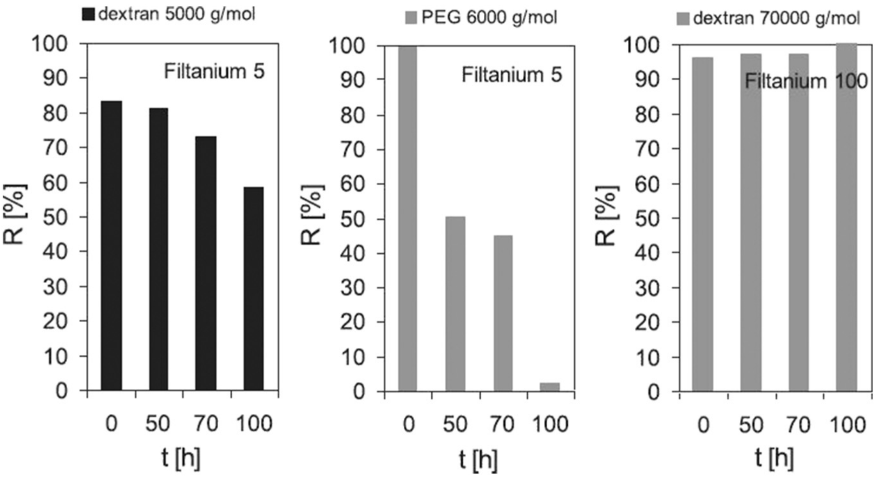

Fig. 2. Changes of separation properties of the Filtanium 5 and the Filtanium 100 membranes during long term operations in PMR.
Reprinted from (Mozia et al., 2015a).

However even at appropriate pH, filtration can be hindered by the buildup of a catalyst cake layer at the membrane surface. Thus starting from the non-fouled situation, a step increase of transmembrane pressure drop (TMP) leads to a proportional step increase of water flux until the catalyst drag force overcomes the lift force induced by turbulent flow in the membrane channel (Jiang et al., 2013). At this point a maximum flux is reached corresponding to the sudden cake layer formation. The method described here to obtain the critical flux is called critical flux stepping method and is widely used to define safe operating conditions which ensures no fouling (Xu and Gao, 2010).

Beside pH and hydraulic conditions in membrane modules, catalyst load is an important parameter of PMR systems. At low concentration a part of the light emitted may leak out of the reactor while at high catalyst load a proportion of catalyst particles may not be activated due to short penetration length of light in the solution. Different studies have found an optimal catalyst load for PMR systems as being 1–1.5 g/L (Szymański et al., 2015; Ho et al., 2009). Thus a non-negligible catalyst amount may be immobilized at the membrane surface as inorganic-fouling depending on the hydraulic conditions applied in the module.

2.3. Polymeric membranes

Thanks to the properties of polymer materials, it is possible to manufacture membranes having small and defined pore sizes. This feature allows high rejections of small molecular weight compounds such as cytostatic drugs. In the case of cyclophosphamide (261.01 g/mol), 90% rejection were observed using the most dense kind of membranes called reverse osmosis (RO) membrane (Wang et al., 2009). However the energy consumed for RO filtration is non-negligible (120 kWh per 100 m^3 of polluted water treated) in comparison to less dense membrane like NF (85 kWh) or UF (5 kWh) (Athanasekou et al., 2015).

In PMR systems membranes operate in a particularly aggressive environment being exposed to UV irradiation, oxidative species produced by photocatalytic reactions, direct chemical cleaning agents or even oxidizing compounds such as peroxides. In addition repetitive contacts by catalyst particles with the surface weaken membranes by abrasion. The importance of this mechanical degradation depends on the chemical and mechanical membrane strength as well as the shape and size of the catalyst particles. In this scope two independent studies pointed out the important weaknesses of polymeric membrane in PMR applications: one evidenced an increase of water flux and organic matter permeation after 30 days of direct UV light irradiation with 10 different membranes (Chin et al., 2006). The second showed that catalyst abrasion affects significantly the membranes having the smallest pores size (Mozia et al., 2015b).

2.4. Ceramic membranes

In long term operations, ceramic membranes were shown to be more resistant to mechanical abrasion and photocatalytic reactions than polymeric ones (Doll and Frimmel, 2005). This is why ceramic membranes were implemented in PMR (Mozia et al., 2015a; Doll and Frimmel, 2005; Jiang et al., 2013) leading to successful PhCs elimination (Doll and Frimmel, 2005; Szymański et al., 2015; Mozia et al., 2014; Benotti et al., 2009). Nevertheless, the ceramic material does not remain intact after long filtration runs. This was observed by Mozia et al. on 3 different titanium oxide membranes: a 0.2 μm microfiltration (MF) membrane, a 5 kDa Filtanium ultrafiltration (UF) and a 100 kDa Filtanium ultrafiltration membrane. In this work, separation properties of membranes were assessed by the rejection of polyethylene glycol (PEG) and dextran having different molecular weights: 5000 g/mol, 6000 g/mol and 70,000 g/mol. Interestingly the MF membrane with maximum pore size of 0.2 μm showed an increase of rejection properties together with a decrease of flux caused by piling up of catalyst particles inside pores (Mozia et al., 2015a). Thus before implementing the MF membrane in PMR, the authors recommended to investigate the long term separation and flux properties of MF membranes before to implement them in PMR. The second membrane studied (Filtanium 5) showed an important drop of dextran (5000 g/mol) and PEG (6000 g/mol) rejections after 100 h of operation as represented in Fig. 2. This information added to the observation of a surface roughness increase led the authors to conclude that the thin layer active during the separation had been scraped by catalyst particles. Fig. 2 shows also that the third membrane studied (Filtanium 100) presented stable dextran rejection and fluxes after 100 h operation. Then the authors concluded that the 100 kDa ultrafiltration membrane is the only one which did not suffer of separation layer damage or unstable fluxes due to catalyst particles entering its pores (Mozia et al., 2015a).

Another study evaluated the stability of the Filtanium 100 kDa membrane on longer filtration run. After 400 h the rejection of 70,000 g/mol and 110,000 g/mol dextrans decreased from 95 to 46% and from 99 to 81%, respectively (Szymański et al., 2015). Based on the SEM image of Fig. 3 the authors observed that the separation layer was not completely removed after >2 weeks of continuous operation. Therefore they attributed the rejection reductions to the opening of new pores on the membrane surface and not to complete damage of the skin layer. The major conclusion is that the membrane was still able to reject catalyst particles after 400 h operation (Szymański et al., 2015).

Even if ceramic membranes are more stable than polymeric ones for PMR applications, further studies should be conducted in order to determine which ceramic materials and membrane geometries have the highest resistance to mechanical abrasion. In the future the two main advantages of polymeric and ceramic materials could be combined in one membrane having high PhC rejections and mechanical resistance. For instance researches could aim to synthesize a composite membrane having a ceramic layer placed over a polymeric membrane for protective purpose.

3. System configuration

As represented in Fig. 4, two main configurations of slurry PMR systems have been developed in order to meet specific needs and

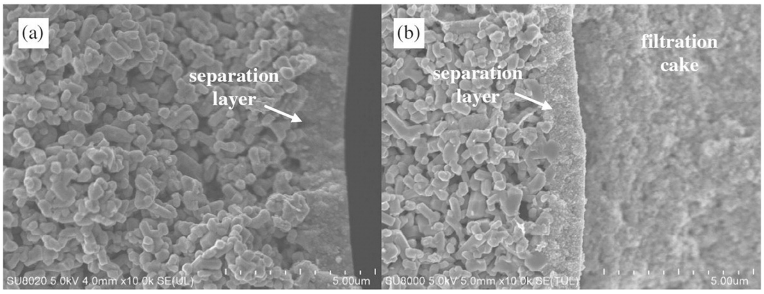

Fig. 3. Cross section of the 100 kDa UF membrane: initially (a) and after 400 h of operation in PMR (b). Reprinted from (Szymański et al., 2015).

constraints such as catalyst irradiation, membrane resistance and fouling: (a) a separated membrane photoreactor and (c) an integrated membrane photoreactor.

3.1. Separated membrane photoreactor (SMPR)

This configuration is obtained by coupling side by side the photoreactor and the separation module as represented in Fig. 4.a. The setup works as follows: the polluted stream is fed in the photoreactor where a light source activates the catalyst suspended by vigorous steering. The activation of catalyst leads to the formation of oxidizing radicals which degrade the organic matter. Meanwhile oxygen bubbling favors the oxidation process and a temperature control is ensured by a cooling liquid running in the reactor double jacket. Once oxidized, the mixture is sent to a separated membrane module where the catalyst is filtered and recirculated to the photoreactor.

As represented in Fig. 4.b, another SMPR configuration is possible: firstly by replacing the photoreactor by a compounds parabolic collector (CPC) in order to collect natural sunlight for photocatalyst activation (Augugliaro et al., 2005). Thanks to the parabolic shape of a mirror, sun rays are reflected towards a UV-transparent glass tube in which the photocatalytic effluent runs in a plug flow. For maximal performances the tube radius has to be adapted to the light penetration length. The reactor should also face the sun with an appropriate inclination in order to maximize the daily light collection. This collector was successfully tested at the Plataforma solar of Almeria in Spain where a common antibiotic (lincomycin) was degraded in a CPC pilot plant (Augugliaro et al., 2005). Secondly the SMPR setup can be modified by placing the membrane module vertically in the mixture coming from the photoreactor as shown in Fig. 4.3. By this way the mixture is enriched in oxygen and turbulences are induced at the membrane surface leading to fouling reduction as it was shown by Molinari et al. (2008).

3.2. Integrated membrane photoreactor (IMPR)

A second slurry PMR system was proposed by Chin et al. integrating the membrane module inside the photoreactor (Chin et al., 2006). As shown in Fig. 4.c the footprint of the installation is thus reduced. However in this case the membrane is subject to direct light irradiation as well as oxidizing agents produced by the photocatalytic reaction. Consequently polymeric membranes used in IMPR were reported to suffer from important deterioration (Chin et al., 2006). Membrane resistance is thus currently a limiting factor for the development of this setup.

To summarize a separation between photoreactor and membrane module is recommended if sensitive polymeric membranes are used (Mozia et al., 2015a). In addition separated membrane photoreactor allows for easier maintenance operations as the parts of the systems are more accessible than in an integrated system. However IMPR has higher compactness but presents an issue of fast deterioration of polymeric modules which could be solved by using ceramic membranes.

4. Evaluation of treatment performance

Following up the amount of carbon contained in aromatic rings before and after treatment is a way to observe drug degradation. This can be done by recording light absorption at wavelength 254 nm corresponding to the absorption peak of aromatic cycles (Liu et al., 2014). During treatment the value of specific UV absorbance (SUVA) decreases as aromatic rings are opened faster than carbon leaves the system in the gaseous CO_2 state. SUVA is defined as the ratio of light absorbance at 254 nm over dissolved organic carbon (DOC):

$$\mathrm{SUVA} = 100 \times \frac{\mathrm{UV}_{254}}{\mathrm{DOC}} \tag{1}$$

In addition, it is possible to measure the biodegradability of an effluent via the biodegradability index which is the ratio between the

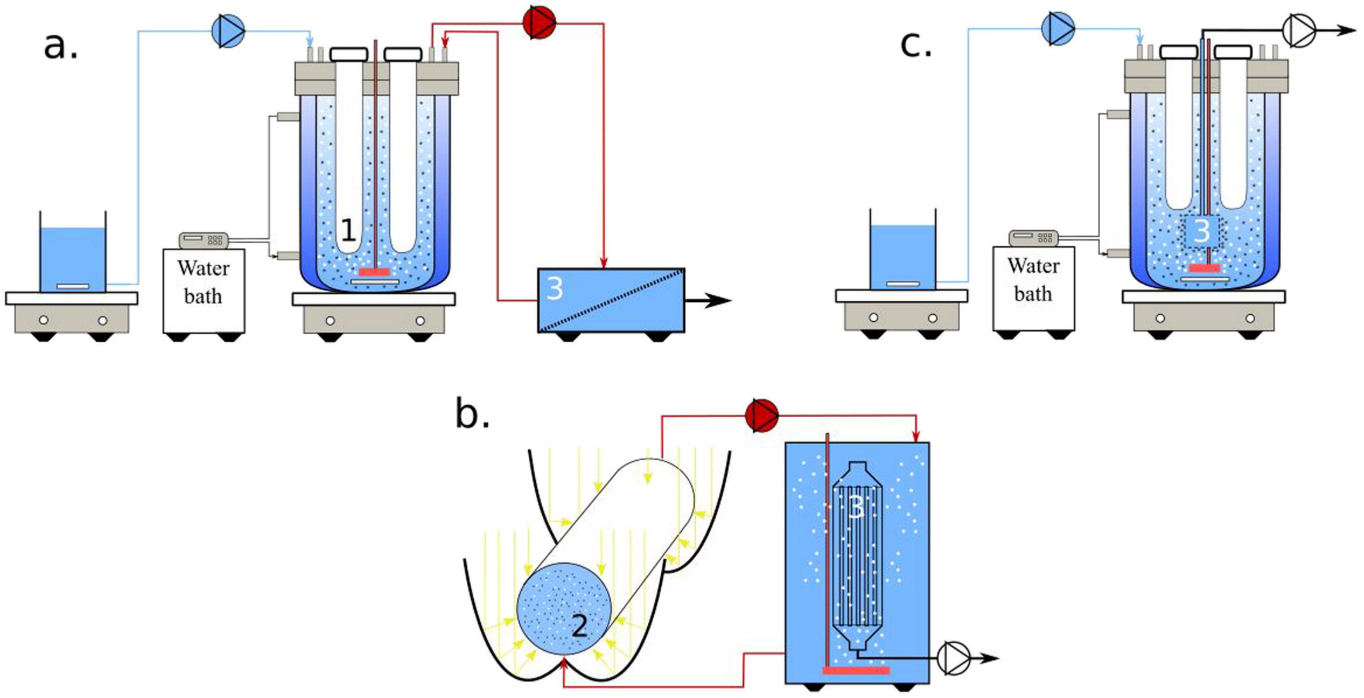

Fig. 4. Scheme of a separated membrane photoreactor (a), a modified separated membrane photoreactor (b), an integrated membrane photoreactor (c); a lamp (1), a compound parabolic collector (2) and a membrane module (3).

biological oxygen demand and the chemical oxygen demand (BOD_5/COD). An efficient treatment should increase this ratio as the persistent pollutants having low bio-degradability are broken down into smaller and more biodegradable molecules (Liu et al., 2014).

The degradation rates of a pollutant by photocatalysis are generally described via the pseudo-first-order rate constant (k'_t). This constant corresponds to the slope of the following linear regression:

$$-\frac{d[C]}{dt} = k'_t[C] \rightarrow \ln\frac{[C]}{[C_0]} = -k'_t \times t \tag{2}$$

In other words the pollutant concentration $[C]$ decreases over time t as degradation occurs. Most of the research papers presented in Tables 1 and 3 express removal efficiencies as degradation percentages after a certain amount of time. Some indicates the time required to remove 100% of a molecule and others gives degradation percentages obtained after 120 min. However the use of k'_t would facilitate the comparison of performance as this rate constant is independent of time and initial concentration.

In addition drug degradation rate depends on the lamp power and reactor design in PMR systems. This is why scientists have defined the electrical energy per order (EOO) corresponding to the energy required to decrease the pollutant concentration of one order of magnitude in a treated volume of 1 m^3 (Benotti et al., 2009):

$$\text{EEO} = \frac{\ln(1)}{k}\left[\frac{\text{kWh}}{\text{m}_w^3}\right] \tag{3}$$

The use of EEO allows to compare operating costs between high and medium pressure mercury lamps at fixed removal efficiency (Benotti et al., 2009).

Another interesting specific parameter is the radiant power per unit volume (P_r) which indicates the energy sent per second and per volume delivered to the reactor:

$$P_r = \frac{P_{lamp}}{V_r}\left[\frac{\text{kW}}{\text{m}_r^3}\right] \tag{4}$$

The removal constant (k'_t) divided by P_r plotted for different lamps configurations allows to determine the optimum light intensity for a given reactor (Karabelas et al., 2013). However, this number does not include data about the quantity of water treated, which is an intention of the photocatalytic space-time yield (PSTY). PSTY has been proposed to reflect the mass and photon transfer rates and light utilization efficiency in relation with the reactor volume (V_r) and treated volume (V_w) (Leblebici et al., 2015):

$$\text{PSTY} = \frac{\text{STY}}{P_r}\left[\frac{\text{m}_w^3}{\text{m}_r^3\text{ day kW}}\right] \tag{5}$$

where STY is the space-time yield standardized to the quantity of water processed from 100 (C_{a0}) to 0.1 (C_a) mmol/L of pollutants. STY includes into PSTY a notion of depollution efficiency per volume of wastewater (V_w):

$$\text{STY} = \frac{V_w}{\tau} = -\frac{V_w k}{\ln\frac{C_a}{C_{a0}}} = \frac{V_w k}{6.908}\left[\frac{\text{m}_w^3}{\text{day}}\right] \tag{6}$$

Some benchmarks calculated by a study on various PMR configurations are summarized in Table 2 (Leblebici et al., 2015). Among the studied designs annular reactor gave the lowest PSTY value. The authors imputed these poor results to the fact that no mixing of the solution was applied. The second design considered is based on the same photoreactor but connected to a membrane module in order to confine the suspended catalyst in the system allowing for continuous treatment. The last configurations presented in the Table 2 are agitated tubular reactors illuminated externally by multiple lamps and equipped with a membrane module. This configuration gave the highest PSTY scores. In the case of the two membrane/multi lamp reactors, the photoreactor volumes appeared to be of most importance as the pilot plant system (11,400 mL) gave 10 times higher PSTY value than the laboratory system (135 mL). This observation led the authors to conclude that the lamp power of laboratory installations is often oversized leading to leak out of lights from reactors.

The main drawback of all the benchmarks previously mentioned is that they do not take into account the energy required for liquid recirculation, mixing, bubbling nor for pressurizing membrane modules. For more accurate indications, these expenses should be accounted in energy consumption balances.

In addition to biodegradability, ecotoxicological aspects are of great importance in depollution treatments. A commonly used ecotoxicity test is the inhibition of the bioluminescence of the bacteria *Vibrio fischeri* (Lutterbeck et al., 2015; Liu et al., 2014; Niu et al., 2013). However, this non-specific test does not give information about DNA damages. This is why genotoxicity and mutagenicity tests were developed as the Ames test (Prasse et al., 2015). This last test is relevant when studying compounds like genotoxic cytostatic compounds, metabolites and degradation by-products (Molinari et al., 2008; Ho et al., 2009; Lutterbeck et al., 2015).

Finally, a life cycle analysis (LCA) permits to evaluate different scenarios with a system of scores representing the energy spent, the carbon dioxide equivalent avoided or even the avoided impact on environment due to water treatment. In addition, data bases include information about the materials required to produce a lamp, reactor, pump or even hydrogen peroxide. On this basis the scores obtained by different PMR systems, different lamps or on diverse wastewater qualities can be plotted for comparison. For instance a LCA study showed that the use of H_2O_2 for PhCs removal has a significant impact on the environment due to its production process (Köhler et al., 2012). The output of LCA always depends on the database used therefore great care should be taken during source data selection.

5. Cytostatic drugs removal

Fig. 5 compares drug removal efficiencies obtained with PMR systems and other advanced oxidation processes. This graph includes two different literature surveys: a first one on PMR system (see Table 1) and a second one on chemical oxidation, photolysis, photocatalysis and combined processes (see Table 3). Because few studies were published on cytostatic drug degradation, the scope of the survey was extended to PhCs removal. Data presented in Fig. 5 are to be used qualitatively because many parameters can vary from one study to another, such as the targeted drug, its concentration, reaction time, wastewater matrix and pH, photo-catalyst type and load, membrane material and pore size, light source and intensities, reactor volume and configuration, etc. Therefore quantitative comparisons will be only done on experiments having the same operating conditions.

Cyclophosphamide and ifosfamide are often studied as model cytostatic compounds for degradation test because of their stability. A study measured the degradation of 30 drugs spiked at μg/L concentrations in pure water when irradiated by UV light and found that cyclophosphamide was one of the two most stable compounds leading to classify it as slowly-degradable (Kim and Tanaka, 2009). The 30 drugs were selected for their high occurrence in hospital wastewaters. The results summarized in Fig. 5 indicate moderate performance of cytostatic degradation by ozonation and single photolysis. Indeed 21% degradation of cyclophosphamide was obtained by photolysis and 42% by ozonation but an increase to 59% was observed when these two processes were combined together. Degradation was even improved to 99% by hydrogen peroxide addition (Cesen et al., 2015). In fact, UV light accelerates the homogeneous breaking of chemical bonds leading to faster radical production. Despite higher removal efficiencies obtained with $UV/O_3/H_2O_2$ than with TiO_2 systems, photocatalytic processes have the

Table 2
PSTY data for various slurry PMR configurations. Data taken from (Leblebici et al., 2015).

Reactor	$V\,(\mathrm{m}^3)$	$k'_t\,\left(\frac{1}{\mathrm{day}}\right)$	STY $\left(\frac{\mathrm{m}_w^3}{\mathrm{m}_r^3\ \mathrm{day}}\right)$	LP $\left(\frac{\mathrm{kW}}{\mathrm{m}_r^3}\right)$	PSTY $\left(\frac{\mathrm{m}_w^3}{\mathrm{m}_r^3\ \mathrm{day\ kW}}\right)$
Annular reactor	8.0^*10^{-4}	50.4	5.1^*10^{-2}	500	1.0^*10^{-4}
Membrane/annular reactor	3.0^*10^{-3}	100.8	0.10	155	6.52^*10^{-4}
Membrane/multi lamp reactor	0.135	14.4	1.44^*10^{-2}	0.22	6.49^*10^{-2}
Membrane/multi lamp reactor	11.4	N/A	3.04	4.23	0.72

great advantage to be non-dispersive. Therefore treatment by photocatalytic operations is more sustainable in regards to the high environmental impact related to the production of oxidizing chemicals (Köhler et al., 2012).

Experimental conditions summarized in Tables 1 and 3 deviate much from conditions encountered in wastewater samples. Often cytostatic concentrations investigated are well above the μg/L concentrations recorded in hospital wastewaters (Verlicchi et al., 2015) and matrices in which drugs are spike are far less complex than real cases. However successful degradation were obtained with PhCs spiked (ng/L) in matrices such as Colorado river (Benotti et al., 2009) and organic-based model solution (Fernandez et al., 2014). These results comfort scientists in the idea that degradation of PhCs spiked in ternary wastewaters is possible by PMR treatment.

Even if up to date the removal of cytostatic drugs by PMR system has not been studied, together the performances of photocatalytic processes in complex matrices and the PMR results on various PhCs represented in Fig. 5 indicate that slurry membrane reactors may become a leading advanced technology for specific wastewater treatment.

6. Recommendations to overcome PMR limitations

As the advantages of PMR are double due to the combination of membrane modules and photocatalytic reactors in a single process, the drawbacks follow a similar tendency. Therefore, many challenges still remain to be addressed.

6.1. Fouling regulation strategies

In order to minimize fouling, several strategies are proposed in the literature (Zhang et al., 2016): self-cleaning process, feed pretreatment (Ho et al., 2009), aeration, operating parameters optimization (Chin et al., 2006), back-washing, chemical-washing. The efficiency of back-washing for flux restoration is related to catalyst-membrane

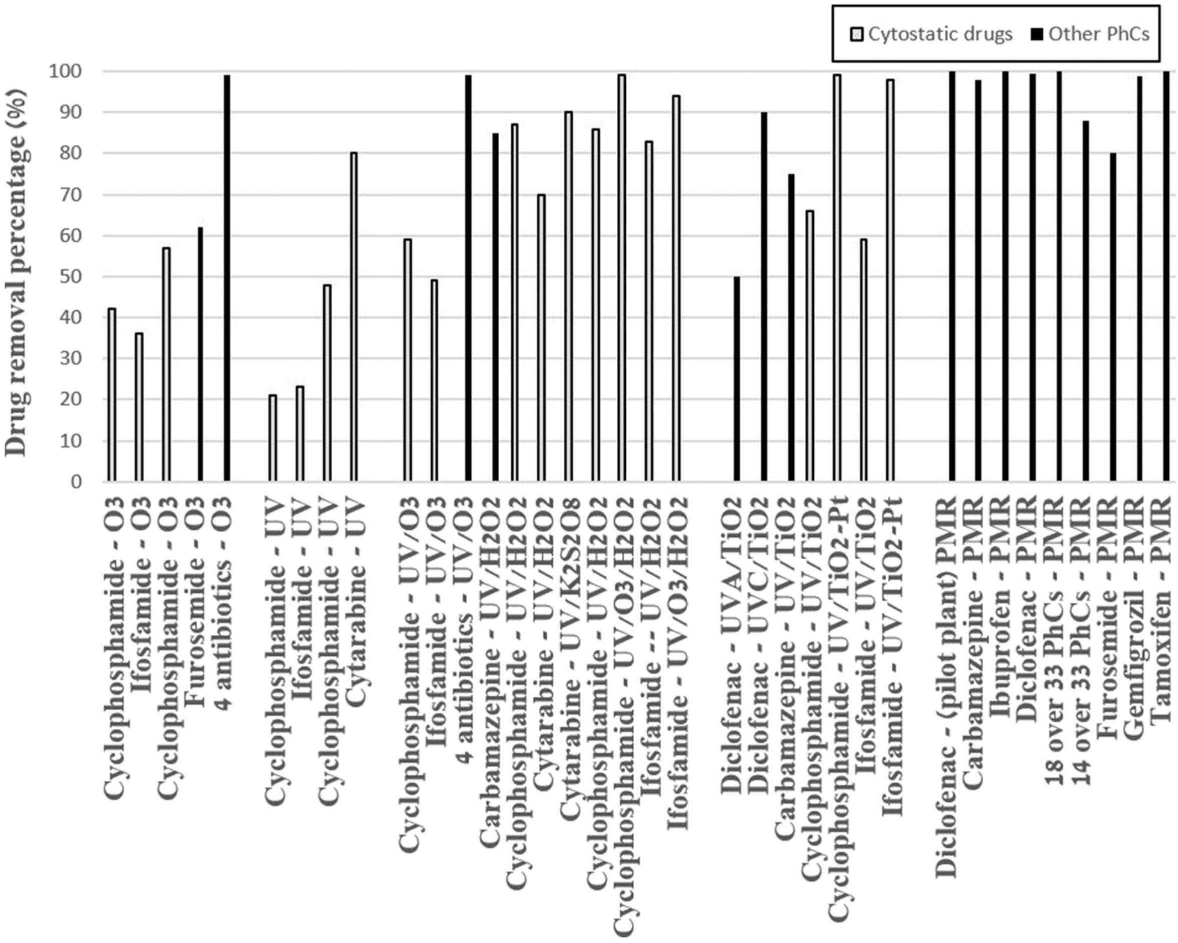

Fig. 5. Drug removal efficiencies observed by studies presented in Tables 1 and 3. X-axis.

Table 3
Literature research on advance oxidation process for PhC degradation.

Ref.	Target compound	AOP feature	Drug degradation (%)	Experimental conditions	Analytical methods
Cesen et al. (2015)	Cyclophosphamide (CP) 10 µg/L Ifosfamide (IF) 10 µg/L	Bioreactor	59% of CP 35% of IF	Artificial wastewater as matrix V = 1.8 L T = 20 °C	Solid phase extraction-GC/MS DOC
		O_3 (36 g_{O3}/g DOC)	After 2 h of irradiation: 42% of CP 36% of IF		
		O_3/H_2O_2 (2.5 g_{H2O2}/L)	40% of CP 39% of IF		
		H_2O_2 (5 g_{H2O2}/L)	30% of CP 26% of IF		
		UV_{254}	21% of CP 16% of IF		
		UV_{254}/O_3	59% of CP 49% of IF		
		UV_{254}/H_2O_2 (2.5 g_{H2O2}/L)	86% of CP 83% of IF		
		$UV_{254}/O_3/H_2O_2$ (5 g_{H2O2}/L)	99% of CP 94% of IF		
McArdell et al. (2011)	Cyclophosphamide 150 ng/L Furosemide 313 ng/L	O_3 (1.08 g_{O3}/g_{DOC})	57% of CP with hydraulic residence time (HET) = 23 min 62% for FU with HRT = 23 min	HWW treated by membrane bioreactor as matrix V = 200 L pH = 8 T = 22 °C	HPLC-MS/MS
Liu et al. (2014)	4 antibiotics cumulate concentration of 600 µg/L (norfloxacin, ofloxacin, roxithromycin, azithromycin)	O_3 (4 mg_{O3}/L)	Complete degradation after 20 min	BTSE as matrix pH = 7–7.5 V = 4 L	HPLC-MS/MS UV_{254} abs. COD SEM STLI test
		UV_{254} (LP)	Negligible		
		UV_{254} (LP)/O_3 (4 mg_{O3}/L)	Complete degradation after 10 min		
Kim et al. (2009)	Cyclophosphamide 10 mg/L	UV_{254} (LP Hg)	After 1 h of irradiation: 48% of CP	BTSE as matrix pH = 6.7–7 V = 4.8 L	
		UV_{254}/H_2O_2 (6 mg_{H2O2}/L)	87% of CP 97% of CP in pure water as matrix		
Ocampo-Pérez et al. (2016)	Cytarabine (CYT) 10 mg/L	$UV_{238–334}$ (MP Hg)	After 1 h of irradiation: V = 22 L 80% of CYT in Ultrapure water (pH = 5.7)		LC/MS/MS
		UV/H_2O_2 (100 μM_{H2O2})	90% of CYT in Ultrapure water (pH = 5.7) 91% of CYT in wastewater (pH = 8)		
		$UV/K_2S_2O_8$ (100 μM_{K2S2O2})	99% of CYT in Ultrapure water (pH = 5.7) 97% of CYT in wastewater (pH = 8)		
Eskandarian et al. (2016)	4 PhCs cumulate concentration of 20 mg/L (acetaminophen, diclofenac, ibuprofen, sulfamethoxazole)	UV_A (LED)/TiO_2 (P25, 0.5 g/L)	50% of diclofenac degraded after 160 min	Ultrapure water V = 0.150 L	HPLC-UV TOC DOC
		UV_B (LED)/TiO_2 (P25, 0.5 g/L)	70% diclofenac degraded after 160 min		
		UV_C (LED)/TiO_2 (P25, 0.5 g/L)	90% diclofenac degraded after 160 min		
Ofiarska et al. (2016)	Ifosfamide 50 mg/L	$UV_{>290}/TiO_2$	After 1 h of irradiation: 59% of IF 66% of CP	Ultrapure water as matrix pH = 5.5 V = 0.05 L Catalyst load 5 g/L	HPLC-UV
	Cyclophosphamide 50 mg/L	$UV_{>420}/TiO_2$	43% of IF		
		$UV_{>290}/TiO_2$-Pt (0.15%)	98% of IF 99% of CP		
		$UV_{>420}/TiO_2$-Pt (0.15%)	84% of IF		
Benotti et al. (2009)	Carbamazepine 220 ng/L	$UV_{185–254}$/UF	With 1 kWh/m^3: Over 75% degraded	Colorado River water, USA as matrix pH = 8.0 Photo-cat™ reactor V = 11,500 L	HPLC-MS/MS TOC DOC pH Yeast estrogen screen
		$UV_{185–254}/TiO_2$ (P25, 0.05 g/L)	Over 85% degraded		
		$UV_{185–254}/H_2O_2$ 10 ppm/UF	With 0.5 kWh/m^3: Over 85% degraded		
		$UV_{185–254}/H_2O_2$ 20 ppm/UF	Over 95% degraded		

interactions. In fact, the larger the membrane pore size, the deeper the catalyst penetration and thus, catalyst deposition has a stronger influence. Hence, back-washing was reported to be more effective for fouling reduction in the case of membrane having large pore size as microfiltration (Zhao et al., 2002). For smaller pore size like UF modules an increase of the feed cross flow velocity has a higher impact on the water flux improvement than back-washing (Mozia et al., 2015a). Chemical cleaning agents can also be used to dissolve and oxidize fouling agents. After membrane cleaning, pure water fluxes were reported to be as high as or higher than the fluxes obtained initially on modules depending on the damage caused to the membrane (Molinari et al., 2008). Interestingly oxidization by cleaning agents of the cake layer expanded by back-washing is a very effective way to restore initial flux (Zhao et al., 2002).

6.2. Degradation enhancement by chemical oxidation

The formation of radicals in photocatalytic reactor can be accelerated by addition of oxidizing agents in the liquid mixture (Ocampo-pérez et al., 2010). Different works evidenced the positive effect of chemical addition on cyclophosphamide degradation: low removals were recorded by O_3/H_2O_2 (Chen et al., 2008) but irradiation with UV permitted to reach 99% degradation (Cesen et al., 2015). As represented in Fig. 5 peroxodisulfate is another strong oxidizing agent which once irradiated by UV induces the production of OH• and SO_4• radicals (Von Gunten, 2003). Consequently higher cytarabine removal efficiencies and mineralization rates were obtained by UV/$S_2O_8^{2-}$ than by UV/H_2O_2 treatment (Ocampo-Pérez et al., 2016). An important feature of this oxidizing agent is the fact that its final product (sulfate ion) is virtually inert (Ocampo-pérez et al., 2010).

Despite high treatment performances chemical oxidation processes are based on constant consumption of chemicals. Consequently we recommend to use oxidizing agents only to face emergency events such as pollution peaks which would overtake the maximal treatment capacity of the plant. Another particular case permitting chemical consumption stands in the frame of industrial ecosystems as many chemical processes produce oxygenated water as by-product. Therefore in order to minimize the transport and packing costs of oxidizing solutions, treatment plants should be placed nearby pollution sources and units producing aqueous flows having a high oxidizing potential (Erkman, 2001; Tonn et al., 2014).

6.3. Transformation products and metabolites

Extinction of the chromatographic peaks corresponding to a certain drug is a first indication of an effective treatment. However in most of the cases parent compounds are transformed into smaller stable by-products which may exhibit higher polarities. This has important consequences in PMR applications as a decrease of membrane rejection (Szymański et al., 2015; Sarasidis et al., 2014) or inversely an accumulation of by-products in PMR systems (Sarasidis et al., 2014; Augugliaro et al., 2005). In addition by-products (Lutterbeck et al., 2015; Liu et al., 2014) and metabolites (Negreira et al., 2014b) can have higher toxicities than their parent compounds. Hence the toxic character of treated effluent may arise from various reaction routes.

6.4. Wastewater composition

Slurry PMRs have been tested on different water matrices leading to significant variation of performances. At first a comparison between pure and surface water evidenced a 15% difference of removal efficiencies (Fernandez et al., 2014). This is related to the presence of anions like Cl^-, HCO_3^-, NO_3^- and SO_4^{2-} (Pastrana-Martinez et al., 2015) having higher reaction rates with hydroxyl radicals than pollutants. In addition other species as HCO_3^- and CO_3^- act as radical scavengers (Sarasidis et al., 2014).

Depending on the water pH significant PhCs adsorption were recorded on membranes (Molinari et al., 2006) and suspended catalyst particles. In the case of titanium oxide particles the point of zero charge (pH_{pzc}) is 6.8. Consequently below a pH of 6.8 catalyst particles are positively charged and attract negatively charged humic acids leading to high adsorption levels (Szymański et al., 2015). Inversely at pH over 6.8 low absorption rates were recorded for the anion of the drug gemfibrozil due to repulsion with the negatively charged particles (Molinari et al., 2008). A study on diclofenac estimated that 166 mg were adsorbed per m^2 of polymeric membrane surface and 2 mg/g_{TiO_2} (Sarasidis et al., 2014). Consequently rapid change of the pH of wastewater (due to e.g., heavy rainfall) could induce a drop of membrane rejection or even desorption of drugs. Therefore situations where the PMR module releases more compounds than what it receives are practically possible.

6.5. Urine source separation

The strategy of separating urine at the source is not a recent idea for reduction of pharmaceutical contamination and treatment costs (Escher et al., 2007; Lienert and Larsen, 2010). As urine represents 1% of the total domestic wastewaters (Zhang et al., 2013) this strategy could be very effective in hospitals which administrated drugs having high urine excretion percentages. For instance X-ray contrast media, analgesics and antiepileptic agents have percentage of intact drugs excreted in the urines higher than 80%. However little excretion via urines (average urine excretion of 49% for 13 cytostatic drugs (Escher et al., 2007)) does not necessary mean failure of separation strategies. In fact compounds preferentially excreted in faeces are probably lipophilic therefore the part of drug non-collected in urine may end up in activated sludge and pollute sludge-amended soils (Escher et al., 2007). If this assumption is validated by future studies, improvements of current environmental risk assessment are highly recommended focusing on PhCs leachates from sludge-amended soils and regarding chronic toxicity of drugs mixture on organisms (Verlicchi and Zambello, 2015). In this case urine collection would be an effective system to remove pharmaceuticals currently dissolved in domestic wastewaters. In order to maximize the pollutant collection, drugs and administration modes leading to short urine excretion rates should be preferentially selected (Zhang et al., 2013). Beside pollution in hospitals, important drug amounts are excreted at home by out-patients. In the case of cytostatic compounds the part of drugs delivered to ambulant patients was recorded to be as high as 75% in a Swiss hospital (McArdell et al., 2011). In order to tackle this diffuse pollution of domestic wastewaters, patients could be asked to collect their urines in urine bags designed for this purpose. Once returned to the hospitals, this liquid waste mixed with urines collected from no-mix toilets (separating urine from faeces), waterless urinals and catheters could be sent through a specific parallel sewage system to slurry PMR for treatment.

Even if No-Mix toilet still presents many issues such as social acceptance, technical availability and large infrastructure investments (Lienert and Larsen, 2010), the coupling a support from the authorities with technical developments could lead to the development of specific parallel wastewater systems.

6.6. Self-powered PMR system

In regards to the world increase of energy demand it is wise to design low energy consuming devices. Therefore the development of small self-powered units able to level up the wastewater quality without any fossil fuel dependency is an interesting field of study (Richards et al., 2014). In the case of PMR two main parts require energy supply: membrane pump and light. A first environmental sustainable source possible to be harvested is the sunlight. Therefore photovoltaic panels were installed in Iran and directly connected to LED's emitting UV with a maximum wavelength of 395 nm. The polycrystalline solar panel used had a power range of 225–250 W, an efficiency as high as 13.8–15.3% and was able to power 6 pieces of 3 W LED. After only 20 min the concentration (20 mg/L) of cefixime (antibiotic) and phenazopyridine (analgesic drug) was divided by two thanks to a titanium oxide photocatalyst (Reza et al., 2016). This laboratory scale system demonstrated the possibility of powering a photocatalytic treatment with sunlight. Another approach to reduce environmental impact of the system would be to remove the lamp: collection of light thanks to a compounds parabolic collector in order to irradiate a TiO_2 catalyst led to degradation of the lincomycin antibiotic (Augugliaro et al., 2005). Moreover catalyst having higher UV–Vis photo-activity than TiO_2 are being developed (Pastrana-Martinez et al., 2015).

Beside the energy consumed for light production, a large energy amount is required by the filtration process in systems. At first photovoltaic panels were used to power desalination membrane modules. And it was shown possible to produce 250 L/h of drinking water from brackish water in Central Australia with four 24 V_{DC} photovoltaic panels as the only power source. This treatment process combined ultrafiltration and reverse osmosis operating at 0.5 and 12 bar, respectively (Schäfer et al., 2007). In addition the wind has also been studied as sustainable resource for drinking water production from brackish water: by using a wind turbine simulator based on real German wind speed data (average wind speed 6.1 m/s) searchers showed possible to power a reverse osmosis membrane operating at 10 bar leading to the production of 800 L/day of drinking water (Richards et al., 2014). Surprisingly wind fluctuation or intermittency does not only lead to negative impacts on filtration performances. A study concluded that a reverse osmosis system was not affected by important turbulences over an average wind speed of 7.0 m/s. However below this speed limit further control strategies should be developed in order to deal with intermittent operation (Park et al., 2011). Another work studied the consequences of wind interruption on transmembrane fluxes. Restoration of transmembrane pressure after a standstill period induced an increase of flux. This odd phenomenon was related to the relaxation and expansion of the biofouling layer at the membrane surface (Peter-Varbanets et al., 2012). Similarly, a brief flux increase was recorded in PMR system after pressure restoration. This is related to the decompression of the catalyst cake layer during the standstill period (Mozia et al., 2015a). Therefore membrane filtration takes benefits of fluctuating power sources. The case of light production is else: if less power is available then less light will be emitted to the photoreactor. Thus external energy should be brought into the system via addition of oxidizing chemicals such as persulfate (Reza et al., 2016) or by outspreading the hydraulic residence time of the PMR system (Sanches et al., 2013).

Most of the renewable sources are fluctuating with time depending on the timescale considered: geothermal heat, plant growth, hydroelectricity from tides, rivers, dam or even swell. A major challenge is thus to design processes able to adapt themselves to the fluctuation rate of their energy source.

6.7. Economic limitations

A lack of economic studies has been observed in the literature, which makes difficult to conclude on the economic viability of this technology. Nevertheless, it is interesting to highlight the study by Plakas et al. that compared the economic impact of four ternary wastewater treatments: O_3/UV, PMR, RO with MF pretreatment, and powdered activated carbon adsorption coupled with UF membrane (PAC-UF) (Plakas et al., 2016b). Results indicated that the investment costs for PMR systems are 20 times lower than for O_3/UV under similar operating and maintenance costs (0.4 ± 0.8 €/m^3) and energy consumption (3.3 ± 0.3 KWh/m^3) (Plakas et al., 2016b). Therefore, PMR outstands O_3/UV treatment on an economic basis but it seems to be more expensive than PAC-UF. The reason is related to the 10 times lower operating and maintenance costs and energy consumption in comparison to PMR (Plakas et al., 2016b). Nevertheless, beside these studies and to the knowledge of the authors, little data are available concerning the economic evaluation of PMR systems. This is probably related to the fact that this treatment has not yet been studied intensively. Hence, significant work remains to be done. First of all, a sustainable economic analysis should include all costs during processes comparison. Costs such as regeneration of absorbent, treatment of retentate from membrane processes and management of waste should not be forgotten as it is an advantage of PMR to reduce these costs close to zero. Secondly, the economic advantage of using expensive photocatalyst active under renewable visible light could motivate the scientific community to operate PMRs without artificial light source. Other research could also enhance water treatments using PMR to produce high quality and reusable water, closing the loop of water consumption and avoiding costly pollution assessment and depollution campaign.

7. Conclusions

Cytostatic compounds are a class of pharmaceutical compounds (PhCs) used in cancer treatment. These drugs are designed to be persistent because they need to remain inactivated until having their therapeutic effect in the patient's body. This probably explains why cytostatic drugs were found at μg/L levels in wastewaters released by a hospital oncological ward and at ng/L levels in Spanish surface waters. Furthermore, most of them were shown to be mutagenic, cytotoxic and genotoxic. Together high environmental toxicities and persistence's are a cocktail calling for appropriate treatment to be developed.

Slurry photocatalytic membrane reactors (slurry PMRs) are presented in this work as a promising technology for wastewater treatment. This hybrid system put together the high degradation rates obtained with suspended photocatalyst and the separation properties of membranes. By this union, catalyst particles can be successfully confined in the system. During PMR operation, membrane modules are subject to contact with oxidizing species and mechanical abrasion caused by catalyst particles. For this reason, resistant ceramic membranes were implemented in PMR systems even though they do not reject efficiently cytostatic drugs. The rejection of small molecular weight compounds such as cytostatic compounds, metabolites and their transformation-products is currently a feature belonging to dense polymeric membranes. Nevertheless, future work could be conducted in order to manufacture composite polymeric membranes protected by a ceramic layer. This work presented also how PMR configurations can be adapted to delay inorganic fouling occurrence.

The recent development of photocatalyst active under real sunlight together with the possibility to power filtration module with wind opens the door towards a new generation of self-powered treatment plants working on sustainable resources.

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