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Biosensor-based real-time monitoring of paracetamol photocatalytic degradation

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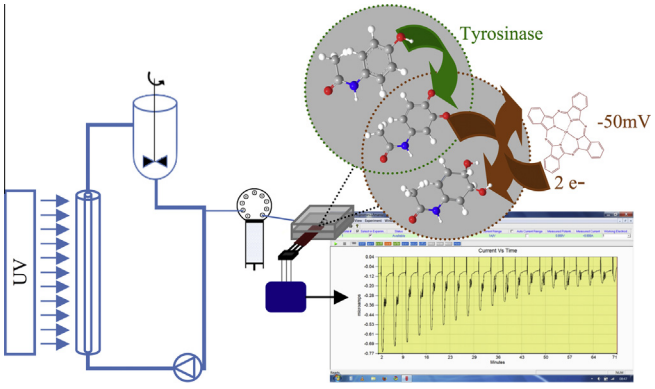
HIGHLIGHTS

- A flow-cell biosensor was developed for monitoring a photocatalytic process.
- The biosensor was based on tyrosinase immobilization on CoPC-modified SPCE.
- The photocatalytic degradation of paracetamol was successfully monitored.

GRAPHICAL ABSTRACT



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ABSTRACT

This paper presents for the first time the integration of a biosensor for the on-line, real-time monitoring of a photocatalytic degradation process. Paracetamol was used as a model molecule due to its wide use and occurrence in environmental waters. The biosensor was developed based on tyrosinase immobilization in a polyvinylalcohol photocrosslinkable polymer. It was inserted in a computer-controlled flow system installed besides a photocatalytic reactor including titanium dioxide (TiO_2) as photocatalyst. It was shown that the biosensor was able to accurately monitor the paracetamol degradation with time. Compared with conventional HPLC analysis, the described device provides a real-time information on the reaction advancement, allowing a better control of the photodegradation process.

1. Introduction

Pharmaceuticals, personal care products and their degradation compounds are organic contaminants that have been detected in wastewater and surface waters throughout the world (Benotti et al., 2009). These emerging pollutants, like many other anthropogenic compounds, are continuously introduced into the aquatic environment from several sources like industries, urban and hospital wastes (Langford and Thomas, 2009). Paracetamol (4-acetaminophen) is commonly used as analgesic and antipyretic drug for human beings. At therapeutic doses, it is considered a safe drug. Therefore, in most countries, paracetamol can be purchased in retail stores as an over-the-counter preparation, and it is

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currently the most widely used drug worldwide (An et al., 2009). This molecule is easily accumulated in aquatic environments; it has been shown to be present in surface waters, wastewaters, and drinking waters throughout the world (Wu et al., 2012).

Paracetamol-contamined waters are mainly treated by usual oxidation processes (Tunay et al., 2010) e.g. H_2O_2/UV (Vogna et al., 2002; Andreozzi et al., 2003) and ozonation (Andreozzi et al., 2003). In 2004, Sirés et al. have described the use of UV light associated to electrochemical methods for paracetamol mineralization in water by catalytic action of Fe^{2+} and Cu^{2+} on electrogenerated hydrogen peroxide (Sirés et al., 2004, 2006). Although these methods may be efficient for treating this pollutant, the harsh reaction conditions, the generation of secondary products, and the high operational cost associated with these techniques have often made them not a desirable choice (Wu et al., 2012). Recently, the photocatalytic oxidation of paracetamol has been investigated (Yang et al., 2008) and main reaction intermediates have been identified (Zhang et al., 2008). Heterogeneous photocatalysis appears as a promising alternative to degrade organic micropollutants in a non-selective manner. In photocatalysis, the excitation of a photocatalyst with UV rays allows the creation of electron–hole pairs that triggers the formation of hydroxyl radicals, thus enabling chemical species to be broken down and finally, mineralized into CO_2 and water (Galvez et al., 2003). The use of solar radiations as UV source would allow obtaining energetically-autonomous, self-sufficient water treatment processes (Malato et al., 2009). An efficient use of UV light thus represents a major challenge in the conception and the development of this technology adapted for a sustainable water treatment (Bahnemann et al., 2004). Basically, such efficiency is highly dependent of the photocatalytic media implemented in the reactor that may be added in a slurry free form or immobilized on an adapted support (Plantard and Goetz, 2014).

Sensitive and cost-effective detection techniques are fundamental in order to accurately determine the level of waters contamination before, during and after treatment process. Conventional methods involve HPLC, GC/MS and 2D ^{1}H ^{13}C ^{15}N NMR analysis (Vogna et al., 2002; Espinosa Bosch et al., 2006). These methods are highly sensitive and allow the determination of a large number of compounds, but they are costly, long and/or require time-consuming pre-treatment procedures that may cause a partial loss or transformation of the target, thereby leading to underestimated results (Espinosa Bosch et al., 2006). Moreover, these methods are not suitable for on-line and real-time analysis.

Alternative methods are mainly based on the biosensor technology, they have already been developed for the detection of several pharmaceutical compounds in water (Adrian et al., 2009) including paracetamol (Odaci et al., 2006; González-Sánchez et al., 2011). However, enzymatic biosensors, one of the most promising advanced monitoring methods (Istamboulie et al., 2010a), have not been reported yet for the control of pharmaceuticals degradation processes. Valero et al. showed that paracetamol can be oxidized by the monophenolase activity of tyrosinase to its corresponding o-quinone (Valero et al., 2002, 2003a). This group has also studied the use of tyrosinase for paracetamol quantification, mentioning the possibility to immobilize this enzyme for designing a specific biosensor (Valero et al., 2003b). Based on this idea, a biosensor including avocado tissue as a source of tyrosinase has been developed (Vieira et al., 2013), and applied to the chronoamperometric determination of paracetamol in pharmaceutical formulations (Fatibello-Filho, 2001).

In the current study, an enzymatic biosensor was developed by immobilizing tyrosinase on specially-tailored screen-printed electrodes allowing the fast and accurate determination of paracetamol. The biosensor was incorporated in a flow-cell system that was associated to the photocatalytic process, thus allowing the real-time monitoring of paracetamol photodegradation. The validation of the monitoring system was performed using conventional chromatographic analysis (HPLC-UV).

2. Materials and methods

2.1. Chemicals and materials

Tyrosinase (Tyr, EC.1.14.18.1 from mushroom) having 4276 U mg^{-1} and paracetamol (4-acetaminophen) were obtained from Sigma–Aldrich (France). Poly (vinyl alcohol) azide-unit water pendant photo-crosslinkable polymer (PVA-AWP) was provided by Toyo Gosei Kogyo Co (Chiba, Japan). The enzyme was dissolved in distilled water containing 0.1% albumin at 50 U mL^{-1}, and the stock solution was dispensed into several aliquots that were stored frozen at −20 °C. The pastes used for screen-printing, Electrodag 423SS and 6037SS, were obtained from Acheson (Plymouth, UK), cobalt phthalocyanine (CoPC)-modified carbon paste was purchased from Gwent Electronic Materials, Ltd (Gwent, UK). A glycerophthalic paint (Astral, France) was used as insulating layer. Transparent PVC sheets (200 mm × 100 mm × 0.5 mm) (SKK, Germany) were used as screen-printing supports.

2.2. Photocatalytic reactor

The photo-reactor was a cylindrical borosilicate glass tube (internal diameter 1.2 cm, length 80 cm) operating in a closed recirculation circuit with a stirred reservoir tank, with a total working volume of 1 L (Goetz et al., 2009). The solution flowed through the reactor inside the annular space formed between the inner tube and the reactor inside wall and was mixed in the recirculation tank. The solution was continuously re-introduced by means of a volumetric pump. Temperature inside the chamber containing the system was kept almost constant by means of a fan blowing the warm air out. The radiation source was a UV lamp (VL-330) with emission centred at 365 nm and the radiation flux density at the reactor axis was fixed at 10 W m^{-2}. To illuminate the total surface of the reactor, an aluminium parabolic collector was positioned just behind the reactor.

Two TiO_2 catalyst materials with different properties were investigated: a powder supplied by Degussa and a cellulose support impregnated with TiO_2 provided by Alhstrom. Degussa P-25 is the most widely used photocatalyst, it is considered as the reference material according to its photocatalytic behavior. Its specific surface area (BET) was 54 m^2 g^{-1} and the particles of TiO_2 had an average diameter of about 20 nm. The catalyst in a powder form was dispersed in solution to obtain a suspension. As described in a previous work, an optimum concentration of 0.7 g L^1 was used, allowing the total absorption of the radiation entering the tubular reactor (Plantard and Goetz, 2014). The Ahlstrom photocatalytic material consisted of TiO_2 (Millenium PC-500) immobilized on a flat and flexible non-woven support of cellulose fibers (paper grade 1048). Its specific surface area referenced with the total photocatalytic material mass was equal to 98 m^2 g^{-1}. More precisely, this photocatalytic material consisted of cellulosic fibers (38 g m^{-2}), TiO_2 (16.7 g m^{-2}), zeolite (2 g m^{-2}) and SiO_2 (13.3 g m^{-2}). The photocatalytic media was wrapped around a tube (diameter 5 mm) at the axial center of the reactor. The useful surface of the photocatalytic media in the reactor was 0.02 m^2.

2.3. Tyrosinase-based sensors and flow system

Screen-printed electrodes (SPE) were prepared using a semi-automatic DEK 248 screen-printing system (Weymouth, UK) according to a procedure previously described (Istamboulie et al., 2010b). The working electrode was a 4 mm diameter disk, the counter electrode was a 16 mm × 1.5 mm curved line and the Ag/AgCl

pseudo-reference electrode was a 5 mm × 1.5 mm side straight layer. The CoPC-modified paste was directly screen-printed on the working electrode. The electrodes were left to dry during 30 min at 60 °C.

Biosensors were prepared by physical entrapment of the enzyme in a biocompatible photopolymer (PVA-AWP). PVA-AWP was mixed with Tyr solution in a ratio 1:1 (v/v) and gently vortex-mixed to obtain homogeneous enzyme/polymer dispersion. A volume of 4 µL was deposited onto each working electrode of biosensors and sets of electrodes were left for photo-polymerization by exposition to neon light (2 × 8 W) for minimum 3 h at 4 °C. After about 7 d of storage in 4 °C in moisture-less environment, the biosensors were ready to use. The amount of tyrosinase finally entrapped in the sensing layer was calculated to be 100 U/electrode, according to the theoretical activity mentioned by the supplier (Sigma–Aldrich).

Electrochemical measurements were performed using an electrochemical analyzer (Potentiostat – Galvanostat PG581, Uniscan, UK). Cyclic voltammograms were recorded over potentials ranging from −300 to 500 mV with a scan rate of 20 mV s^{-1}. All measurements were performed in 0.1 M phosphate-buffer pH 6 containing 0.1 M KCl using SPE modified with CoPC, a mediator commonly used for phenolic compounds detection (Moczko et al., 2012).

Initial trials of amperometric measurements were carried out in stirred solution by injecting 1 mL sample in 3 mL buffer, these assays are called "batch measurements" in the following text. The electrodes were tested in 0.1 M phosphate buffer at pH 6, at four different applied working potentials (−150 mV, −100 mV, −50 mV, 0 mV vs. Ag/AgCl). The current intensity was recorded before and after injection of paracetamol when the current stabilization reached the plateau, the measured signal corresponding to the difference between the baseline and the plateau level. The developed biosensors were integrated in a flow system consisting of a poly (methyl methacrylate) (PMMA) flow cell connected using Teflon® tubing to a Cavro® XCalibur pump (Tecan, Switzerland) fitted with a 2.5 mL syringe. All the parameters such as flow rate, washing step, injection volumes and signal measurements were optimized and completely controlled using a special programme written using HyperTerminal for Windows 7 (see Supplementary data and Fig. S1). The optimized system allowed performing a measurement within 3.5 min.

2.4. HPLC analysis

Chromatographic determination of paracetamol was carried out using a VWR-Hitachi HPLC-unit LaChrom Elite (VWR, France), fitted with a HTA L-2130 pump with piston flushing, Hamilton HxSil C18 5 µm reversed phase column, auto-sampler L-2200, DAD-detector L-2450, ND-Gradient L-2130, Degasser L-2130 and piloted using EZChrom Elite datasystem for Hitachi DAD-system. The elution was carried out using a 3-step gradient elution program with flow of 1 mL/min. The initial mobile phase consisted in 8% acetonitrile/92% acidified water (containing 0.1% trifluoroacetic acid) and was changed linearly to 15% acetonitrile/85% acidified water within 15 min. Acetonitrile ratio was then reverted back to 8% in 3 min and finally, this ratio was kept constant for the last 5 min. Injections of 20 µL sample were performed, and the detection of paracetamol was carried out at 245 nm at room temperature.

3. Results and discussion

3.1. Electrochemical properties of developed biosensors

The electrochemical properties of SPE modified or not with CoPC (respectively CoPC-SPE and SPE) were studied using cyclic voltammetry. Fig. 1 shows the voltammograms obtained in presence of 1 mM paracetamol. Preliminary experiments carried out in the absence of tyrosinase showed that paracetamol was readily oxidized at potentials higher than 350 mV vs Ag/AgCl, but no significant reduction peak was observed. In presence of tyrosinase, a characteristic wave was observed, corresponding to the reduction of the orthoquinone produced upon enzymatic oxidation of paracetamol. The intensity of this reduction peak was particularly enhanced when using CoPC-modified electrodes (Fig. 1). Orthoquinone was thus reduced at low-reducing potentials, close to 0 mV vs Ag/AgCl, therefore preventing the reduction of other undesirable contaminating substances. Based on these results, Tyr/CoPC-SPEs were thus selected for paracetamol detection.

3.2. Characterization of Tyr/CoPC-SPE in batch conditions

Preliminary batch experiments were performed in chronoamperometric mode to evaluate the real effect of operating potential on the biosensor response. Fig. 2 shows the response of Tyr/CoPC-based sensors to 1 µM paracetamol at potentials ranging from 0 to −150 mV vs Ag/AgCl. As expected, an increase of the reduction signal was observed when decreasing the applied potential. In order to reach the best compromise between selectivity and sensibility, the optimal potential was found to be −50 mV vs Ag/AgCl, as it allows reaching a good sensitivity while minimizing potential interferences.

The operational stability of immobilized tyrosinase was estimated by successively measuring the response of the same biosensor to 4 µM paracetamol at −50 mV vs Ag/AgCl. In these batch conditions, the sensors were washed between tests with distilled water. Tyr/CoPC-based sensors were shown to be stable for at least 15 consecutive measurements and presented a good reproducibility with a signal variation of 5%. The average response to 4 µM paracetamol for $n = 5$ electrodes prepared in the same experimental conditions was −44 ± 2 nA. The sensitivity of the biosensor, calculated for concentrations up to 33 µM, was equal to −88 mA M^{-1} cm^{-2}. Such sensitivity is comparable with the one reported in literature using a peroxidase-based biosensor (González-Sánchez et al., 2011).

3.3. Characterization of Tyr/CoPC-SPE integrated in the flow system

Preliminary experiments were carried out to study the effect of TiO_2 nanoparticles on Tyr/CoPC-based sensors. It was shown that

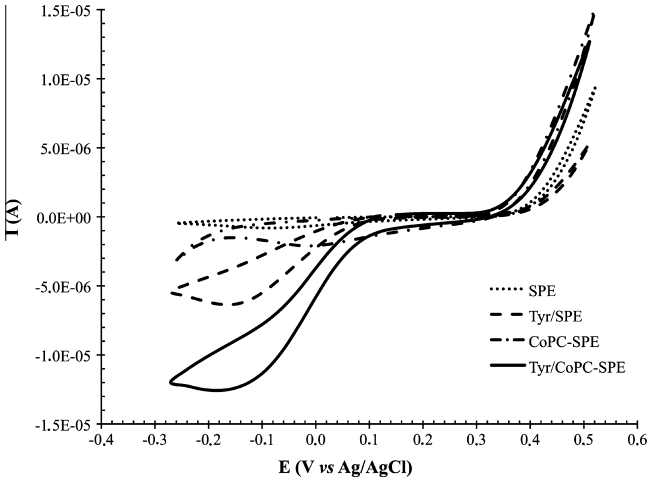

Fig. 1. Cyclic voltammograms obtained in presence of 1 mM paracetamol in 0.1 M phosphate-buffer pH 6 containing 0.1 M KCl (scan rate 20 mV s^{-1}).

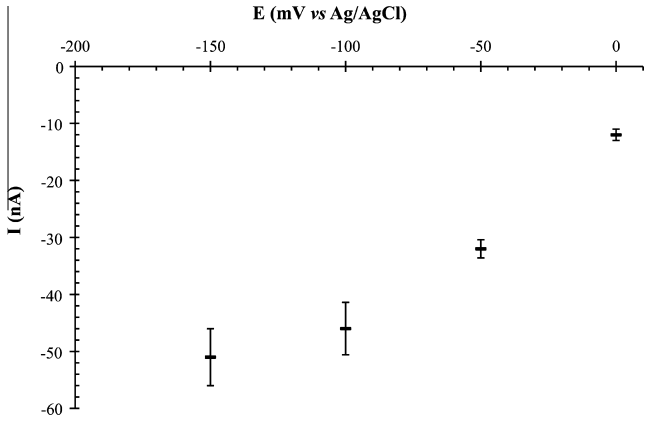

Fig. 2. Chronoamperometric response of Tyr/CoPC-based sensor to 1 μM paracetamol as a function of applied potential.

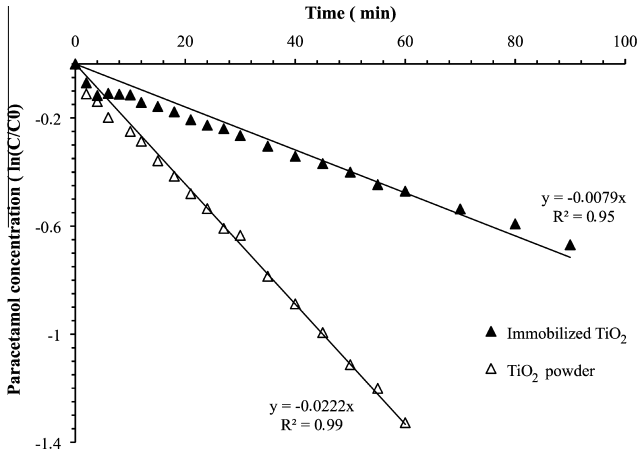

Fig. 4. Linearized representations of paracetamol photodegradation kinetics, evaluated by HPLC analysis, using the two forms of TiO_2 catalyst.

TiO_2 at 700 mg L^{-1} did not interfer with the biosensor measurements when working at −50 mV vs Ag/AgCl. The stability of Tyr/CoPC-based sensors in the flow system was studied. No decrease in biosensor response was observed after a sequence of 40 automatic injections of paracetamol, the average response being equal to −195 ± 15 nA. Calibration curves were established for paracetamol concentrations up to 40 μM, showing a sensitivity of −111 mA M^{-1} cm^{-2}. The detection limit, calculated according to the paracetamol concentration leading to a response corresponding to a signal/noise ratio of 3, was 0.5 μM.

3.4. Monitoring of paracetamol degradation using an off-line biosensor

Experiments were first performed using a paracetamol initial concentration of 5 mg L^{-1} (33 μM) and TiO_2 catalyst immobilized on cellulosic fibers. Samples were collected and analyzed at time intervals of 2 min during the first 12 min, then 3 min until 30 min, and finally 5 min until 90 min. Fig. 3 illustrates the kinetics of paracetamol photocatalytic degradation established by HPLC analysis and using the biosensor in batch conditions.

Using the immobilized catalyst, approximately 50% of paracetamol contained in the photo-reactor was eliminated within 90 min. The results were compared with similar experiments carried out using the P-25 TiO_2 powder. In this case, an additional filtration step was required for removing TiO_2 nanoparticles before HPLC analysis. Taking into account the high efficacy of paracetamol degradation, the measurement was stopped after 60 min.

These results confirm the tendency usually accepted: the 2D material was probably limited by its insufficient exchange interface, whereas suspended particles ensure that nanomaterial-based catalysts are distributed homogenously throughout the reactor volume-space. The powder in suspension represents the best option on the basis of the kinetic criterion.

The data obtained from HPLC allowed confirming that the concentration profiles as a function of time follow a pseudo-first order kinetic law (Eq. (1)):

$$\frac{C}{C_0} = \exp(-kt), \tag{1}$$

where C_0 is initial concentration of the target molecule (mg L^{-1}), C is its actual concentration (mg L^{-1}), t is the duration of irradiation (s), and k is the kinetic constant (s^{-1}).

Whatever the material used, it was shown that the kinetic model fitted the experimental results with a reasonable degree of accuracy (Fig. 4). The calculated kinetic constants were 0.47 s^{-1} and 1.33 s^{-1} for immobilized and free TiO_2 catalyst, respectively.

Concerning amperometric analysis realized with biosensors, it was observed that the found concentrations oscillated with acceptable variations around the values determined by HPLC analysis. The kinetic constants calculated from biosensors analysis were 0.46 s^{-1} and 1.14 s^{-1}, using immobilized and free TiO_2 catalyst, respectively. Therefore, the biosensor appears as a reliable tool for the analysis of paracetamol degradation, with the advantage that it does not require any sample pre-treatment.

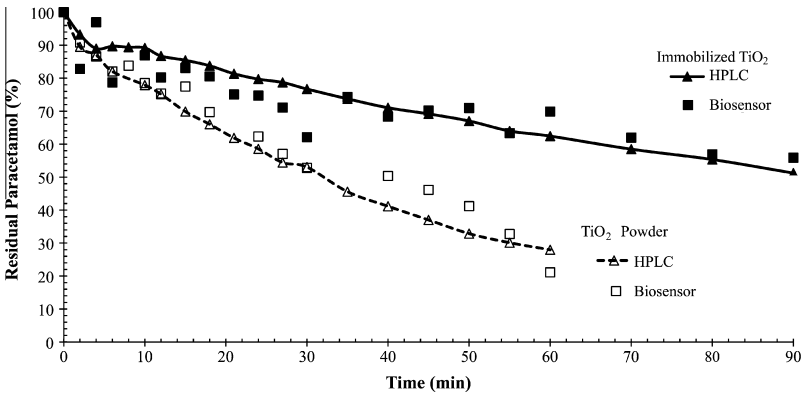

Fig. 3. Monitoring of paracetamol photodegradation as a function of irradiation time, using either HPLC or biosensor analysis, and considering the two forms of TiO_2 catalyst.

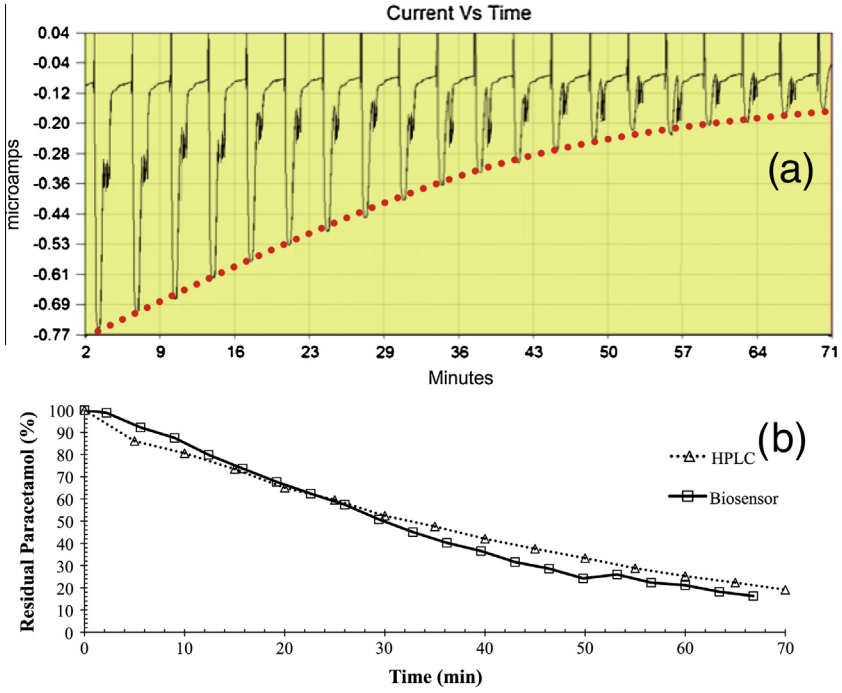

Fig. 5. (a) Intensity versus time monitoring of paracetamol photodegradation using the integrated flow Tyr/CoPC-based biosensor. (b) Kinetics of paracetamol photodegradation determined either with HPLC analysis or flow Tyr/CoPC-based biosensor, using TiO_2 powder as catalyst.

3.5. Monitoring of paracetamol degradation using an integrated flow biosensor

Based on the results obtained in batch conditions, P-25 TiO_2 powder was selected as photocatalyst for further experiments using Tyr/CoPC-SPE integrated in a flow system. The monitoring unit connected to the photoreactor allowed automatic and real-time recording of the biosensor response during photocatalysis experiments (see Supplementary data and Fig. S1). Using optimized sampling conditions, the monitoring was carried out in semi-continuous mode, one measurement being realized every 3.5 min.

Fig. 5a clearly shows the photocatalytic degradation of paracetamol recorded by the variation of the current intensities in time. As expected from preliminary batch experiment, the percentage of elimination was about 80% in 70 min. It was highlighted that a plateau was observed when 80% of paracetamol was eliminated, then the degradation was less effective. A control was performed at the end of experiments by injecting the initial paracetamol concentration, showing that the biosensor did not lose any activity during the whole test.

These data were exploited to calculate the paracetamol concentrations that were compared to those obtained by HPLC analysis. In this case, samples were manually taken-off, filtered, and injected after completion of the photodegradation experiment. The degradation curves obtained using the two analytical methods are shown in Fig. 5b. The results clearly validate the reliability of the developed biosensor for the monitoring of paracetamol photodegradation. The main advantage of using the on-line biosensor is related to its very fast response, which allows a real-time monitoring and therefore permits a better control of the process.

4. Conclusion

This work describes for the first time the integration of an enzymatic biosensor for the on-line, real-time monitoring of a photocatalytic degradation process. The enzyme tyrosinase was efficiently immobilized on cobalt-phthalocyanine-modified screen-printed electrodes, allowing the electrochemical detection of paracetamol at low potential. The obtained biosensor was integrated in a flow-cell that was connected to the photocatalysis tank, and automatically fed using a computer-controlled syringe pump. The biosensor response recorded in real time allowed determining paracetamol concentrations, which were in very good agreement with those obtained from HPLC analysis. It was shown that the use as a photocatalyst of TiO_2 nanoparticles in a slurry free form allowed degrading 80% of a 33 μM paracetamol solution within 70 min.

In conclusion, this work opens new possibilities in the integration of biosensing platforms for the monitoring of pollutants photodegradation. The main advantages of the described device consist in its full automation, as well as its ability to give real-time information on the reaction advancement, thus allowing a better control of the degradation process.

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Appendix A. Supplementary material

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.chemosphere.2015.03.019.

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