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Removal of simvastatin from aqueous solution by electrochemical process using graphite-PVC as anode: A case study of evaluation the toxicity, kinetics and chlorinated by-products

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ABSTRACT

As far as we know, the electrochemical degradation of simvastatin, a widely used as a cholesterol lowering drug, has not been reported yet. The oxidation process has been investigated in pure water and wastewater using graphite-Poly Vinyl Chloride (PVC) composite electrode as anode. Effects of initial concentration of simvastatin, NaCl loading, type of sample and applied voltage were tested to evaluate the electrochemical oxidation process. The results revealed that the electrochemical oxidation rates of simvastatin followed pseudo first-order kinetics, with rate constant values ranged from 0.006–0.23 min^{-1} depending on the operating parameters. Simvastatin was completely removed, after 40 min of treatment, at 4 g/L NaCl and 10 V indicating high concentration of OCl^- produced in the solution but at the same time energy consumption (EC) was very high. However, 6 V was selected for further experiments (90% removal and 0.093 Wh/mg energy consumption) after 40 min. The low concentration of simvastatin (30 mg/L) exhibited better removal of 97% compared to 50 mg/L which gives removal 90% after 40 min. In this work the electrochemical oxidation process of simvastatin has been studied by monitoring the by-products and their toxicity using the time–of–flight (TOF/MS) technology. Chlorinated by-products were separated and identified accurately using isotope modern software. Simvastatin was transformed within 20–80 min, however, after 100 min most of by-products have been removed. Eleven new by-products of simvastatin were identified and monitored in both positive and negative ionization mode.

1. Introduction

The occurrence of pharmaceutical in the aquatic environment has been recognized as one of emerging issue in environment chemistry. The widespread presence in the aquatic environment can be explained by their extensive use in medical practice and incomplete removal in wastewater treatment plants (WWTPs) [1–5]. These compounds are present in the environment at trace levels (ng/L-μg/L), hence it is known as micro pollutants. One of these micro pollutants is simvastatin ($C_{25}H_{38}O_5$) which is a cholesterol-lowering drug. It belongs to a class of drugs called HMG-CoA reductase inhibitors, commonly called "statins". Simvastatin reduces cholesterol by inhibiting an enzyme in the liver (HMG-CoA reductase) that is necessary for the production of cholesterol. In the blood, simvastatin lowers total and low density lipoprotein (LDL) or "bad" cholesterol as well as triglycerides [drugbank [6]]. It is low polar, highly water soluble compound and is among the top selling pharmaceuticals in Malaysia. Toxicity studies for simvastatin is rather scarce in aquatic environment. Kaufmann et al. [7] investigated mitochondrial toxicity of simvastatin in L6 cells (rat skeletal muscle cell line), 100 micromol/L of simvastatin induced death in 27–49% of the cells.

In Malaysia, simvastatin was detected in influent, effluent STP and hospital, and surface water [8–10]. The reason may be attributed to the conventional treatments which are unable to degrade simvastatin and other pollutants efficiently. Many

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advanced oxidation processes including ozonation, photo-Fenton, neutral photo Fenton, photo-oxidation, sonoelectrolysis and photoelectrolysis are applied for oxidation and treatment of organic pollutants from wastewater [11–16]. However, the capital, operational and maintenance costs associated with these processes make them less attractive. Specifically, the ozonation process is considered slow so many reaction intermediates and transformation products are found.

Consequently, it is necessary to look for alternatives so electrochemical process is considered a promising technology for treatment of pollutants in water. For our knowledge, electrochemical degradation of simvastatin has not reported yet so this study may achieve this purpose.

Recently, there has been an increasing interest in the application of electrochemical oxidation method for the wastewater treatment. Moreover, more and more attention has been focused on the exploration of novel anodes where the degradation of organic compounds mostly happens [17–20].

A big challenge for the degradation of the pharmaceuticals in water samples is the identification the by-products which are generated after treatment of the parent compounds. The identification of by-products in water samples requires an accurate analytical tool which is capable of providing the complementary information about the by-products in order to find the final expected structure.

The most powerful tool to collect more information about by-products is liquid chromatography combined with mass spectrometry (LC–MS) and other related technologies (Calza et al. [21], Kosjek and Heath, 2008 Hu 2 [22]). Of course, the by-products have different physico-chemical properties, and concentration range so it could bring a serious difficulties. Moreover, the extraction protocol and chromatographic separation are influenced by the variation of the polarity for these compounds. The elucidation of the proposed structure of the by-products is based on the origin structure of the parent compound and the fragmentation patterns (Garcia-Reyes and Fernandez-Alba [23]). Furthermore, understanding the reactions that take place during the treatment also plays an important role to predict the possible structure for the by-product. LC-TOF-MS is very valuable analytical technique for the identification of by-products (Gomez et al. Hu2 [24]). Combination of LC-TOF-MS with other complementary techniques, like GC–MS, has also been reported (Aguera et al. hu2 [25]), hybrid Q-TOF-MS or Q-Linear ION TRAP-MS (QqLIT-MS), Ion Trap-MS (IT-MS), Triple quadrupole-MS (QqQ-MS) are also of interest for MS/MS or MS3 fragmentation, since they provide additional structural information for fragmentation assignment (Eichhorn and Aga Hu 2, al-qaim et al. review [26,27]).

The main objective pursued in this study is treatment of simvastatin in aqueous samples using electrochemical oxidation treatment applying graphite–PVC electrode as anode. LC-TOF-MS was used for separation, identification and elucidation the proposed by-products. Moreover, assessment of toxicity for simvastati n before and after treatment was also considered.

2. Materials and methods

2.1. Chemicals and reagents

Sodium chloride (NaCl) used as supporting electrolyte was purchased from Merck with purities of more than 99.5%. Tetrahydrofuran (THF) (CAS No 109-99-9), polyvinylchloride (PVC) were purchased from Sigma Aldrich. Simvastatin (SMV) (CAS no. 79902-63-9) were obtained from Sigma-Aldrich (USA). Deionized water (DIW) used was supplied by EASYPure RODI (USA). HPLC-grade acetonitrile (ACN), HPLC grade acetone, HPLC grade methanol and formic acid (FA) were supplied by Merck (Germany). For toxicity experiments, *Escherichia coli* (*E. coli*) bacteria was obtained from Laboratory of Microbiology, Faculty of Sciences and Technology, University Kebangsaan Malaysia, Bangi, Malaysia, Mueller Hinton broth (nutrient broth) was obtained from (Merck, Germany).

Stock standard solution of simvastatin was prepared by dissolving 0.01 g SMV in 10 mL of HPLC-grade methanol (1000 mg/L) and stored at −18 °C to minimize the degradation of simvastatin. Further dilutions of simvastatin were prepared in pure water (50 mL) for treatment purpose. Prior to use, all glassware were boiled with water at 100 °C, rinsed with distilled water, dried in an oven at 200 °C for 2 h, subsequently rinsed with MeOH, and dried in the oven at 200 °C for 2 h.

2.2. Electrolytic system

The Platinum (Pt) metal foil electrode was prepared using its metal foil (99.98% purity, Aldrich chemical company). A 0.5 thickness Pt foil was cut into approximately 1 cm × 1 cm piece connected to a silver wire with silver conducting paint and sealed in a glass rod. Subsequently, epoxy gum was applied to cover the silver wire connecting surface. The graphite–PVC electrode was prepared by mixing a weighed portion of graphite carbon powder and polyvinyl chloride (PVC) in 4 mL tetrahydrofuran (THF) solvent and swirled flatly to homogeneous followed by drying by left it one night at room temperature. The mixture was placed in 1 cm diameter stainless steel mould and pressed at 10 t/cm^2 using hydroulic machine (Carver HYDRAULIC unit model 3912). A typical pellet contained approximately 95% of graphite and 5% of PVC. The total weight of pellet obtained is approximately 1.5 g. Graphite −PVC pellet connected to a silver wire with silver conducting paint and sealed to a glass rode. Subsequently, epoxy gum was applied to cover the silver wire connected surface [28].

The reaction mixture was carried out using 100 mL pyrex glass inserted inside a glass pyrex vessel provided with two points; inlet and outlet water stream to control the temperature. The glass pyrex (cell reactor) was placed on magnetic stirring block in order to keep its contents well mixed during the experiment. Graphite-PVC pellet and Pt plate were used as anode and cathode, respectively. The distance between the electrodes was approximately 2.5 cm. The electrodes were then connected to a direct current (DC) power supply (CPX200 DUAL, 35V 10A PSU).

Comparative electrochemical degradations of 50 mL solutions of simvastatin (50 mg/L) in deionised water were made for graphite-PVC. The influence of applied voltage, initial concentration of SMV and concentration of NaCl was examined at the predetermined time intervals of 0, 10, 20, 30 and 40 min. Solutions were always kept between 22–24 °C, which was the maximum temperature that can be used in the cell without significant water evaporation during prolonged electrolysis. All the trials were carried out under vigorous stirring with a magnetic bar (600 rpm) to ensure mixing and the transport of reactions toward/from the electrodes. However, aliquots of the solutions were withdrawn from the reactor and filtered using 0.25 μm then transferred to 250 μL deactivated glass insert with polymer feet inserted in amber glass vials from Agilent Technologies (USA), 30 μL was automatically injected into LC-ESI/TOF/MS system for analysis.

2.3. Instruments and analytical procedures

The LC analysis were performed using a Dionex Ultimate 3000/LC 09115047 (USA) system equipped with a vacuum degasser, a quaternary pump, an auto sampler and a UV–vis diode array detector. Chromatography was performed on a Thermo Scientific C18 (250 mm × 2.1 mm, i.d.: 5 μm) column. The injection volume was 30 μL. Simvastatin were analysed in positive ion (PI) mode and