

## Removal of psychoactive pharmaceuticals from wastewaters using microbial electrolysis cells producing hydrogen

Dilan Akagunduz<sup>a</sup>, Rumeysa Cebecioglu<sup>a</sup>, Murat Ozdemir<sup>b</sup> and Tunc Catal<sup>a,c,\*</sup>

<sup>a</sup> Istanbul Protein Research-Application and Innovation Center (PROMER), Uskudar University, Uskudar, 34662 Istanbul, Turkey

<sup>b</sup> Personalized Medicine Application and Research Center (KIMER), Uskudar University, Uskudar, 34662 Istanbul, Turkey

<sup>c</sup> Department of Molecular Biology and Genetics, Uskudar University, Uskudar, 34662 Istanbul, Turkey

\*Corresponding author. E-mail: tunc.catal@uskudar.edu.tr

 TC, 0000-0003-2990-8680

### ABSTRACT

In this study, hydrogen production was analyzed along with methane and carbon dioxide generation using paroxetine, venlafaxine, and o-desmethylvenlafaxine (ODV) as substrates in single-chamber microbial electrolysis cells (MECs). Combinations of all three drugs were examined at concentrations of 750 ng/mL and 170 ng/mL. At the beginning of MEC operations using a 750 ng/mL mixture of drugs, there was no hydrogen or methane, but carbon dioxide was detected. When the concentration of the drug mixture was reduced to 170 ng/mL, MECs produced hydrogen and methane gas. Removal of the drugs during MEC operations was also analyzed using liquid chromatography coupled with tandem mass spectrometry (LC-MS/MS). Paroxetine, venlafaxine and ODV drugs were removed up to 99% by MECs. In conclusion, MECs could offer an alternative treatment method for wastewaters containing psychoactive pharmaceuticals with the added benefit of fuel hydrogen generation.

**Key words:** antidepressant drugs, hydrogen, microbial electrolysis cells, wastewater

### HIGHLIGHTS

- Psychoactive pharmaceuticals generated hydrogen in microbial electrolysis cells.
- 99% of paroxetine, venlafaxine and ODV drugs were removed with MECs.
- Cytotoxic analysis was performed on the ECV-304 cell line using the MTT assay.
- MECs could be used for wastewater contaminated with psychoactive drugs.
- Additionally, simultaneous hydrogen generation could be achieved.

## 1. INTRODUCTION

Renewable energy sources are being researched to meet the energy needs of increasing populations, and recent efforts have focused on the production of biohydrogen from wastewaters and organic wastes (Digman & Kim 2008). Hydrogen is a valuable gas, often obtained by different technologies from the most common water, biomass, and fossils. However, using water to produce hydrogen is expensive so hydrogen production from wastewater for sustainable energy generation is of interest (Nath & Das 2004; Obeid *et al.* 2009). Unlike other fuels, hydrogen is an environmentally friendly energy carrier that has a high energy value and low merit for power consumption, and does not cause environmental pollution. Fossil fuels are not renewed and cause many environmental problems. Hydrogen can also turn into electricity or water when burned. For this reason, hydrogen is thought to be the most attractive alternative fuel to replace fossil fuels (Das & Veziroglu 2001; Wang & Wan 2009). Although hydrogen is a renewable and efficient, clean energy source, there are several drawbacks such as production cost and storage.

Microbial electrolysis cells (MECs) represent new technology related to biofuel and microbial fuel cells that treat waste materials while recovering energy (Bermek *et al.* 2013; Catal 2015; Catal *et al.* 2018a, 2018b; Atasever-Arslan *et al.* 2020). Whereas MFCs generate electricity using organic materials, MECs partly back the process in order to produce hydrogen from organic compounds by applying a potential (Wagner *et al.* 2009; Lu & Ren 2016). Agricultural wastes, domestic

This is an Open Access article distributed under the terms of the Creative Commons Attribution Licence (CC BY 4.0), which permits copying, adaptation and redistribution, provided the original work is properly cited (<http://creativecommons.org/licenses/by/4.0/>).

wastes and food processing wastes have great potential for hydrogen production since they contain high amounts of carbon sources, and contaminants found in wastewaters can be efficiently removed (Digman & Kim 2008; Kumru *et al.* 2012; Bermek *et al.* 2013; Abourached *et al.* 2014; Sen *et al.* 2019). It is well known that various drug metabolites contaminate wastewaters, and some drugs are discharged into our ecosystem through urine and feces negatively affecting aquatic life. Selective serotonin reuptake inhibitors (SSRIs) and serotonin norepinephrine reuptake inhibitors (SNRIs), which are used in the treatment of diseases such as depression and anxiety, also diffuse into the nature with urine. SSRIs and SNRIs are among the most commonly prescribed drugs in the world for the treatment of recurrent depressive disorder (Galecki *et al.* 2018; Doron *et al.* 2019). Hospital wastewater, manufacturing wastewater, domestic wastewater, and leachate contain excreted drugs and their active metabolites (Hernando *et al.* 2006). SSRI and SNRI group drugs are mixed with wastewater causing bioaccumulation in the long term and damaging the ecosystem. For this reason, it is very important to detect and remove drugs from wastewater (Blaha *et al.* 2019). However, until now, there has been no information about the biodegradation of SSRI and SNRI drugs in microbial electrochemical cells.

In this study, it was aimed (i) to analyze the hydrogen, methane, and carbon dioxide production from the SSRI/SNRI group of drugs consisting of paroxetine, venlafaxine and ODV produced in MECs, (ii) to remove the examined pharmaceuticals simultaneously as an alternative technique to other conventional methods, and (iii) to evaluate the cytotoxicity of the SSRIs/SNRIs using ECV 304 (human endometrial) cell line. In addition, since there are no data on the possibility of obtaining hydrogen from wastewater contaminated with these drugs, this environmentally important issue has been investigated for the first time.

## 2. MATERIAL AND METHODS

### 2.1. Chemicals

The following drugs were used in the experiments: paroxetine (paroxetine hydrochloride hemihydrate, batch no. 5301-17018M2, Zhejiang Huahai Pharmaceutical, Zhejiang, 317,024, China), venlafaxine (D,L-venlafaxine, cat. no. V119995, Toronto Research Chemicals, Toronto, Canada), ODV (D,L-O-desmethyl venlafaxine, cat. no. D296500, Toronto Research Chemicals, Toronto, Canada). The drugs were obtained from Uskudar University Advanced Toxicology Analysis Laboratory. Sodium acetate trihydrate, 99% [NaOOCCH<sub>3</sub>·3H<sub>2</sub>O] was obtained from VWR (Alfa Aesar, CAS 6131-90-4, Karlsruhe, Germany). D(+)-Glucose [C<sub>6</sub>H<sub>12</sub>O<sub>6</sub>] was obtained from VWR (Alfa Aesar, Karlsruhe, Germany). All other chemicals used in the study were analytical grade and obtained from commercial sources. The study was approved by the Non-Interventional Research Ethics Board of Uskudar University (No. 61351342-/2019-144).

### 2.2. MEC construction and operation of MECs

Single-chamber MECs were set up as described in the literature (Catal *et al.* 2015). Four MECs were used, two main and two controls. MECs were made from narrow-mouthed media bottles sealed with caps (VWR International, LLC) on the butyl septum top. The volume of the MECs was 15 mL. Anodes (Lot: 14032102, FuelCells, Texas, USA, 4 cm<sup>2</sup>) and cathodes (CTO32414, FuelCells, Texas, USA, 2 cm<sup>2</sup>) were placed inside the MECs. The anode material of the MECs was coated with carbon. One side of the cathodes was coated with 0.5 mg/cm<sup>2</sup> Pt catalyst (20 wt% Pt/C Vulcan XC-72, FuelCell Store, USA) using Nafion (7 mL per mg of Pt/C catalyst, 5%, Sigma-Aldrich). MECs were inoculated with a mixed microbial culture enriched from a local wastewater treatment plant (Pasakoy Advanced Biological Wastewater Treatment Plant, Istanbul, Turkey) using sodium acetate as the sole carbon source. Sodium phosphate buffer (100 mM ionic strength; pH 7.0) was prepared as a stock solution in 2 L according to a previously published method (Lovley & Phillips 1988). The buffer consisted of the followings; 8.19 g/L Na<sub>2</sub>HPO<sub>4</sub> (CALBIOCHEM, Cat: 567550, Darmstadt, Germany) and 6.601 g/L NaH<sub>2</sub>PO<sub>4</sub>·2H<sub>2</sub>O (Alfa Aesar, Cat: A11316, Karlsruhe, Germany). For the 50 mM inoculum solution, 0.675 g sodium acetate trihydrate was dissolved in 80 mL 100 mM sodium phosphate buffer (NaPO<sub>4</sub>, pH 7). The inoculum solution (12 mL) was added to each MEC. Then, they were purged with nitrogen (N<sub>2</sub>:CO<sub>2</sub> mixture, 80:20) gas to maintain anaerobic conditions. Voltage (0.7 V) was applied to the experimental groups using a power supply connecting its positive pole to the anode and negative pole to the cathode (Catal *et al.* 2017). A platinum wire was used to connect electrodes to the power supply. No voltage was applied to the control groups. Combinations of all three drugs were examined at concentrations of 750 ng/mL and 170 ng/mL, respectively. The 750 ng/mL drug sample contained 260 ng/mL paroxetine, 280 ng/mL venlafaxine and 210 ng/mL ODV. The 170 ng/mL drug sample contained 60 ng/mL paroxetine, 60 ng/mL venlafaxine and 50 ng/mL ODV (Table 1). All operations were performed in a cabinet with a temperature control (32 ± 2 °C).

**Table 1** | Drug concentrations

Drugs	750 ng/mL	170 ng/mL
Paroxetine	260	60
Venlafaxine	280	60
ODV	210	50

### 2.3. Analyses and calculations

The voltage data were recorded every 11 min with a data acquisition system (Keithley, KickStart Software, Version 1.9.8.21, Oregon, USA). Analysis of the gas produced by MECs was performed using gas chromatography (GC) equipment (Agilent, 7820A; J&W Scientific, USA) with a thermal conductivity detector (AGT-64332A) and a column. Argon was used as the carrier gas (113-3133 GS-CARBONPLOT, 30 m, 0.32 mm, 3 mm, J&W Scientific, USA). The following conditions were applied during the gas analysis: column flow 2.8 mL min<sup>-1</sup>, and 185 °C heater (Catal *et al.* 2015).

The Agilent HP-1200 LC series (Santa Clara, CA, USA) system was used for chromatographic separation with an ACE-3 C8 (3 µm, 3.0 mm × 150 mm) column. The column temperature was maintained at 45 °C, while the auto-sampler was maintained at 10 °C and the sample injection volume was 5.0 µL. Mobile phase A was 2 mM ammonium formate in water, and mobile phase B was 2 mM ammonium formate in methanol:acetonitrile (50:50 v/v). The flow rate was maintained at 0.5 mL/min using gradient conditions. The gradient consisted of linear from 5% B to 95% B (1–5 min), held constant at 95% B (5.1–8 min) and back to 5% B (8.1 min) and held constant at 5% B (8.1–12 min). The chromatographic separation was 12 min in total. An Agilent 6,470 tandem mass spectrometer with an electrospray ionization source in positive ionization mode was used to determine ODV, venlafaxine, and paroxetine content. The mass spectrometer parameters were optimized, including capillary voltage (4 kV), source temperature (300 °C), gas flow (10 L/min), nebulizer (40 psi), sheath gas temperature (350 °C) and sheath gas flow (10 L/min). Quantification was performed using the multiple reaction monitoring (MRM) mode to study precursor ion → product ion (m/z) transitions, respectively of ODV, venlafaxine, and paroxetine (264.3 → 107.0), (278.2 → 58.1) and (330.2 → 192.2) (Yang *et al.* 2014).

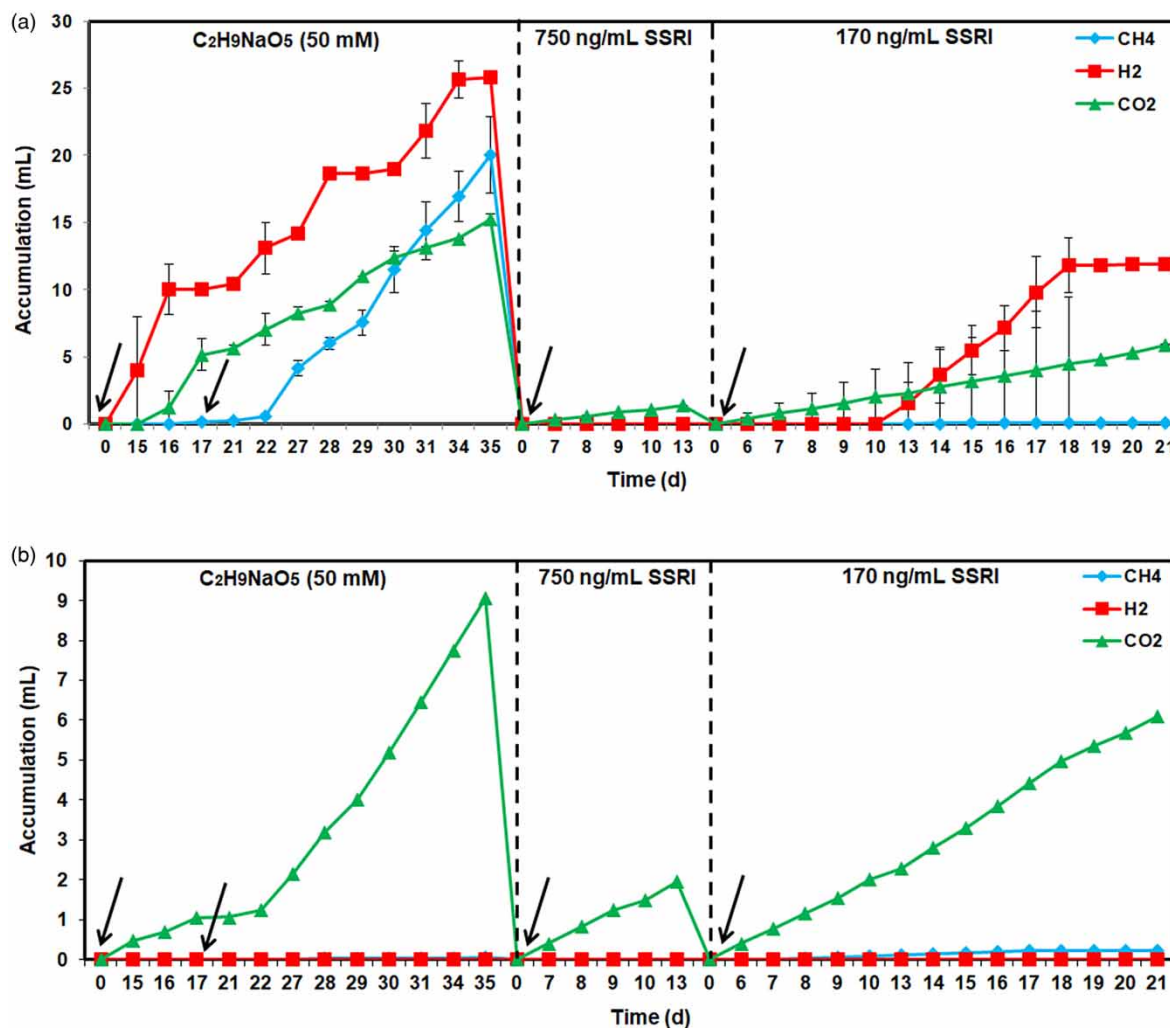
The removal rate (R) was calculated using the following formula:

$$R(\%) = 100 \times \frac{(I_1 - I_2)}{I_1} \quad (1)$$

where  $I_1$  is drug concentration before being added to MECs, and  $I_2$  is the concentration after being added to MECs (Catal *et al.* 2017).

### 2.4. Cytotoxic analyses

Cytotoxic analysis was performed to examine the effect of drugs (paroxetine, venlafaxine and ODV) on healthy cell lines. A literature search was conducted to determine the doses (Bielecka & Obuchowicz 2016; Cobanoglu *et al.* 2017). The following concentration range was determined: 0–200 µM (0–66 ng/mL). The ECV 304 (human endometrial) cell line was used in the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay to determine the effect of drugs on cell viability (Cebeçioğlu *et al.* 2019). The cells were grown in a 5% CO<sub>2</sub> incubator at 37 °C. The cells were diluted to 10<sup>5</sup> cells/mL with Gibco DMEM (1×) medium containing 10% FBS (Gibco, cat. no. 10,500, South America), L-glutamine, and penicillin/streptomycin. Next, 90 µL of the cells were added to 96-well plates and incubated for 24 h at 37 °C in a 5% CO<sub>2</sub> in air incubator. Then, 10 µL drug doses of paroxetine (60-30-15-8 ng/mL), venlafaxine (60-30-15-8 ng/mL), and ODV (60-30-15-8 ng/mL) were administered to the cells after 24 h. No drug dose was administered to the control group. MTT solution (Invitrogen Thermo Fisher Scientific, cat. no. M6494, Eugene, OR, USA) dissolved in sterile phosphate-buffered saline (PBS) (VWR, Lot No. 1206C155, Solon, OH, USA) was added to all wells at a concentration of 5 mg/mL after 24 h. Here, 100 µL of the mixture were then taken from each well, and 100 µL of DMSO (50%) (VWR, cat. no. 161054006, France) was added. Incubation took place at room temperature for 50 min. The optical density (OD) of each well was measured with an ELISA multi-well spectrophotometer set at 540 nm. A



**Figure 1** | Total gas accumulation of drugs (a) and control groups (b) on MECs. Arrows indicate electrolyte refreshment.

cytotoxicity index (CI) was calculated based on ODs according to the following formula (Cebecioglu *et al.* 2019):

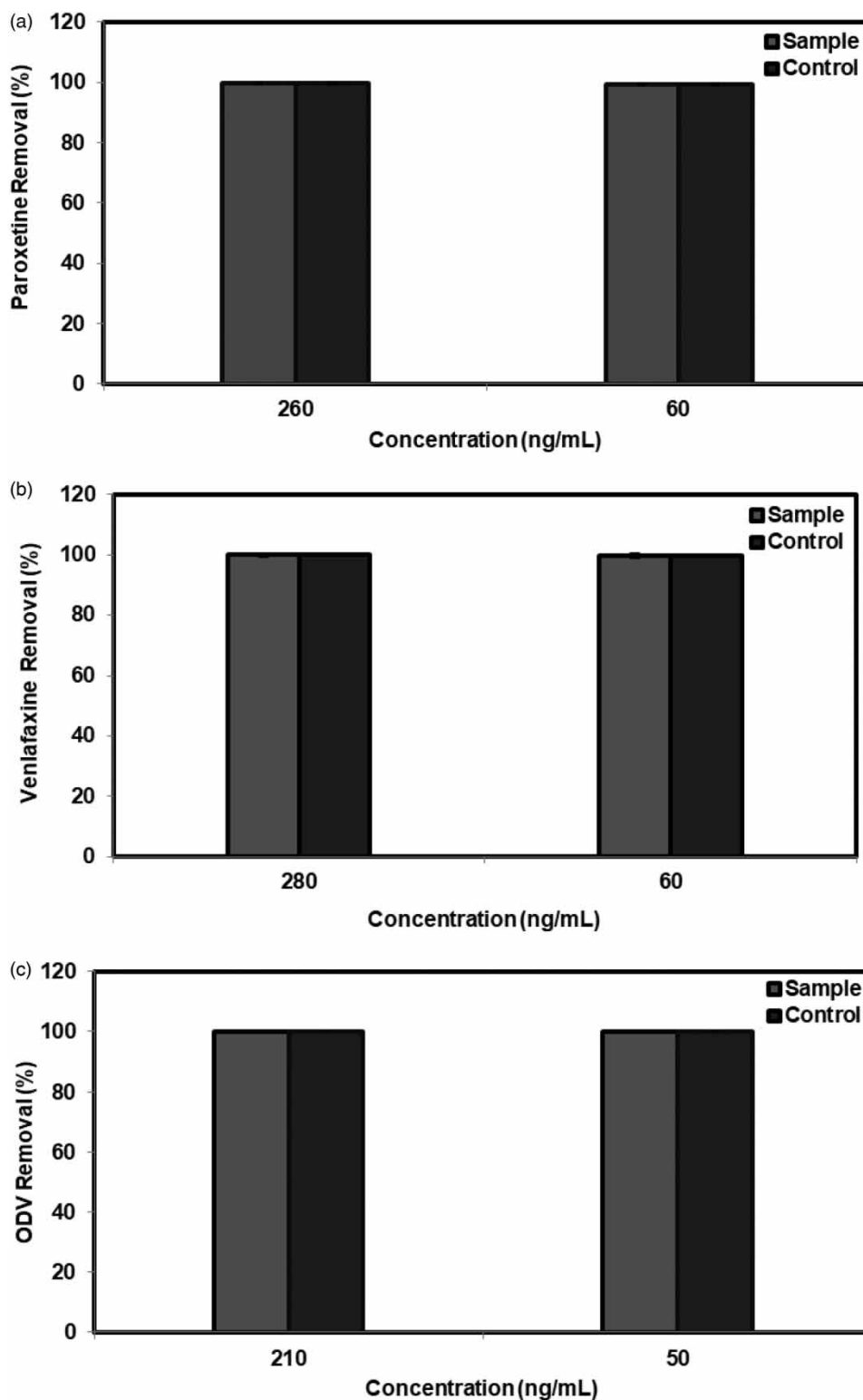
$$CI \% \left( \left( \frac{OD \text{ of the treated wells}}{OD \text{ the control wells}} \right) - 1 \right) \times 10$$

### 3. RESULTS AND DISCUSSION

#### 3.1. Gas production results

MECs were operated in batch modes, and the gas production was measured daily. Figure 1 shows total gas accumulation of in the presence and absence of the drugs in MECs. MECs were fed with sodium acetate trihydrate (50 mM), and operated in the absence of drugs for 35 days (Figure 1). On the 17th day, sodium acetate trihydrate (50 mM) was refreshed. Hydrogen production was observed in MECs applied voltage of 0.7 V. Total hydrogen production was 25.8 mL on the 35th day. MECs produced 20 mL of methane (CH<sub>4</sub>) gas and 15 mL of carbon dioxide (CO<sub>2</sub>) gas along with hydrogen gas. No hydrogen production was observed in the controls without voltage and only 9 mL of CO<sub>2</sub> gas was accumulated. Hydrogen production was not observed in the control and voltage applied samples when 750 ng/mL drugs were applied to MECs. While 1.3 mL CO<sub>2</sub> accumulated in the voltage applied samples, 1.9 mL CO<sub>2</sub> accumulated in the control. These results indicate that 0.7 V voltage application is suitable for hydrogen production in MECs in the absence of the drugs, but SSRI and SNRI drugs at high

concentration may inhibit hydrogen production possibly because of negative impacts on microorganisms. Conversely, hydrogen production was observed when the concentration was reduced to 170 ng/mL (60 ng/mL paroxetine, 60 ng/mL venlafaxine and 50 ng/mL ODV). MECs were treated with 170 ng/mL drugs for 21 days; 12 mL of hydrogen accumulated



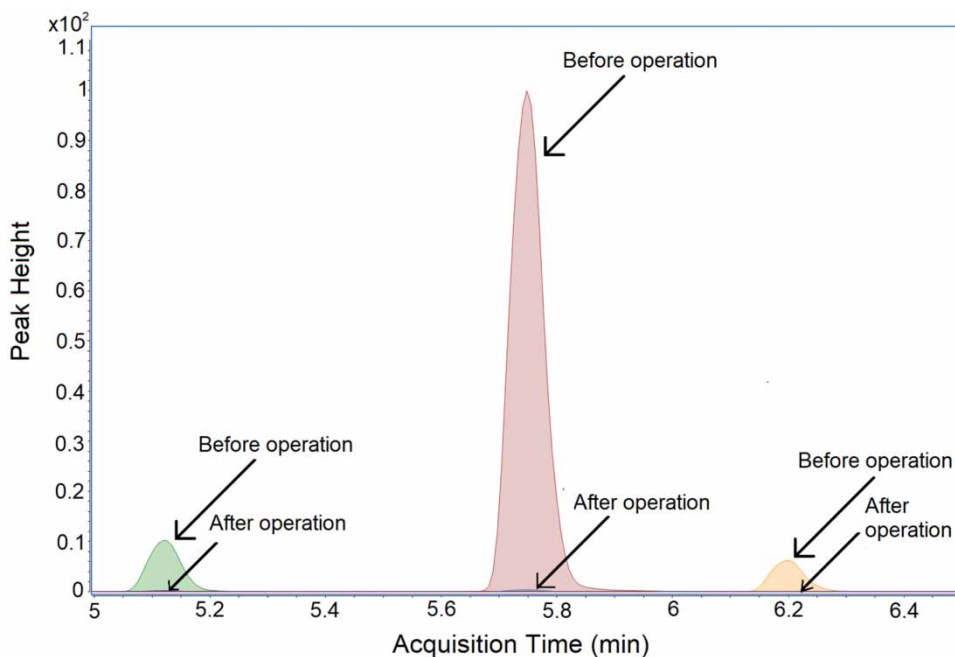
**Figure 2** | Removal rate of drugs during MEC operation. Paroxetine (a), venlafaxine (b), ODV (c).

until 18th day of the operation, and then MECs stopped producing hydrogen. Additionally, 6 mL of CO<sub>2</sub> gas and 0.06 mL of CH<sub>4</sub> gas accumulated. While producing hydrogen in samples treated with 170 ng/mL drugs, methane production was suppressed. No hydrogen production was observed in the controls without voltage, and only 6 mL of CO<sub>2</sub> gas accumulated. These results indicate that methanogenesis could be inhibited in the presence of SSRI/SNRI drugs while fermentative activities could be continued in MECs. Studies using human urine containing metabolites as a substrate in MECs have been reported previously. Microbial electrochemical cells can detect and remove metabolites in wastewater and also produce energy (Catal *et al.* 2019; Ozdemir *et al.* 2019). It was reported that hydrogen production in MECs using sodium acetate, monosaccharaides, disaccharides and cellulosic wastes as carbon sources (Catal 2015; Catal *et al.* 2015, 2017). Previously, 18 mL of hydrogen gas was produced using maltose and 20 mL of hydrogen was produced using cellobiose after 14 d of operation (Catal 2015). Possibly, the substrates used on hydrogen production might affect the production yield, and the examined drugs seem to have an impact on the gas profile produced in MECs affecting fermentation and methanogenesis metabolisms. Interestingly, after treatment with antidepressant drugs, suppression of methane production was observed in both the experimental group and the control group. These results suggest that the combination of antidepressant drug administered in the study might have methanogen inhibitor properties. In particular, the methanogen inhibitory properties of venlafaxine, paroxetine and ODV could be investigated in future studies. There have been reports that the microbiota is affected in individuals using antidepressants used for treatment (Lukić *et al.* 2019). However, which drug or drug combination has methanogen inhibitory properties should be investigated in more detail.

### 3.2. Removal results of the antidepressant drugs in MECs

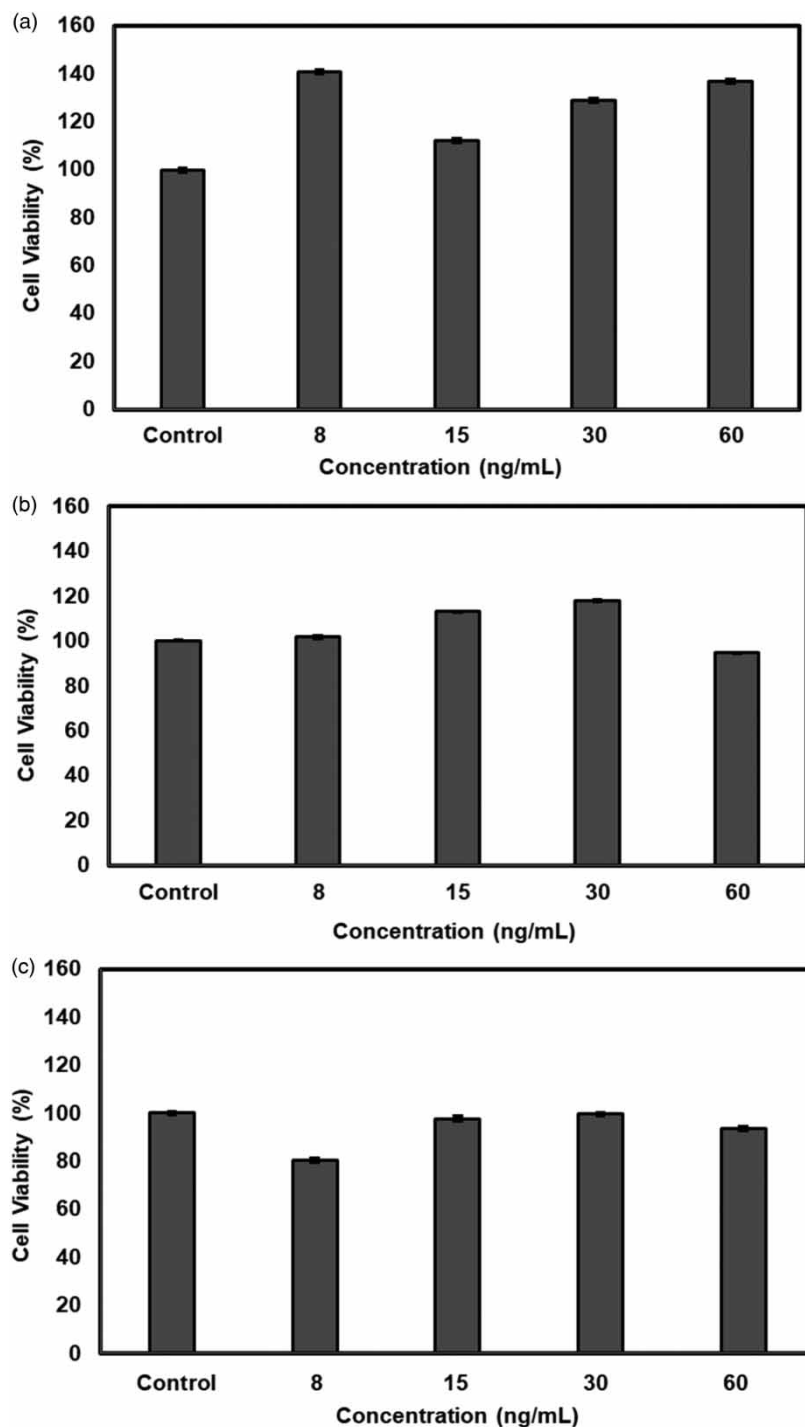
All samples were collected before and after the MECs operations to understand the removal ratios of the drugs. The removal of drugs was analyzed using an LC-MS/MS setup (Figure 2). The 750 ng/mL drug sample contained 260 ng/mL paroxetine, 280 ng/mL venlafaxine and 210 ng/mL ODV. In the 170 ng/mL drug sample, there was 60 ng/mL paroxetine, 60 ng/mL venlafaxine and 50 ng/mL ODV. There was no drug in the sodium acetate trihydrate samples. Removal of samples containing 260 ng/mL and 60 ng/mL paroxetine was 99.7% and 99.3%, respectively. The removal of samples containing 280 ng/mL and 60 ng/mL venlafaxine was 99.9% and 99.6%, respectively. The removal of samples containing 210 ng/mL and 50 ng/mL ODV was 100% and 99.8%, respectively. As a result, over 99% of paroxetine, venlafaxine and ODV drugs were removed by MECs.

The results of drug removal and the LC-MS/MS chromatogram results are complementary (Figure 3). These results indicate that SSRI/SNRI drugs could be efficiently removed in MECs, and even control MECs showed high removal ratios. The



**Figure 3** | LC-MS/MS chromatogram of 170 ng/mL drugs (the peaks show, respectively: 1st ODV, 2nd venlafaxine, 3rd paroxetine).

removal efficiencies of several pharmaceutically active compounds have been compared using membrane biological reactors in previous studies, and showed efficient removal ratios depending on the drugs examined (Ceconet *et al.* 2017). On the other hand, biological electrochemical systems have shown both good removal efficiencies and simultaneous energy generation to support wastewater treatment plants' operational costs. Previously, the removal efficiencies of the drugs such as cocaine and cannabinoid metabolites found in urine were examined in microbial electrochemical cells, and over 90% of removal rates were reported (Catal *et al.* 2019; Ozdemir *et al.* 2019). These results indicate that MECs could be used to



**Figure 4** | Cytotoxicity of drugs on ECV-304 cell line. Paroxetine (a), venlafaxine (b), ODV (c).

remove drugs found in urine, providing a clean approach for wastewater treatment, and supporting the operation costs of the wastewater treatment plants generating hydrogen.

### 3.3. Cytotoxicity results

To investigate the effects of paroxetine, venlafaxine and ODV on healthy cell lines, doses of 8, 16, 30, and 60 ng/mL were studied (Figure 4). The 8 ng/mL dose of paroxetine increased cell viability by approximately 40%, whereas 15 ng/mL increased viability by approximately 10%. The other doses, 30 ng/mL and 60 ng/mL, increased cell viability by approximately 30% compared to the control group (Figure 4).

Jahromi and co-workers investigated the effects of paroxetine on the human adipose-derived stem cells (hAD-SCs) cell line using the MTT assay (Jahromi *et al.* 2016). Here, 1  $\mu$ M paroxetine was applied to the cells for 2, 4, or 6 days. As a result, they reported that paroxetine administered at 4 and 6 days significantly increased cell viability. It was observed that 15 ng/mL of venlafaxine increased cell viability by approximately 10%, while 30 ng/mL increased cell viability by about 20% compared to the control group. Doses of 8–60 ng/mL venlafaxine had no effect on cell viability. Wang and co-workers examined the effects of venlafaxine on PC12 cell lines with typical neuronal properties (Wang *et al.* 2013). The cells were first treated with corticosterone and then venlafaxine was applied with MTT assay. They reported corticosterone-induced cell death as a protective feature of venlafaxine and enhancing cell viability. Kruk and co-workers investigated the effects of venlafaxine on human mesenchymal stem cells (MSC) with MTT assay (Kruk *et al.* 2018). They reported that venlafaxine did not change significantly in the viability of MSC cells. Our results indicate that paroxetine, venlafaxine and ODV have no toxic effects on the cell viability of ECV304 cells. However, the toxicity of the metabolites mixed into wastewaters through human urine should be investigated in advance considering the whole ecosystem.

Investigation of microbial species in microbial electrochemical cells is important for effective removal of drugs from wastewater. The degradation of the antibiotic sulfamethoxazole and microbial community analysis in single-chamber MECs were previously investigated, and *Proteobacteria*, *Bacteroidetes* and *Chlorobi* were reported as the dominant phyla in the anode (Xue *et al.* 2019). Zhang *et al.* (2017) analyzed the bacteria involved in the degradation of the antibiotic chloramphenicol using double-chamber MFC reactors separated by cationic exchange membranes, and the dominant genera in the MFC anode biofilm were found as *Azonexus*, *Comamonas*, *Nitrososphaera*, *Chryseobacterium*, *Azoarcus*, *Rhodococcus* and *Dysgonomonas*. The dominant microbial community changes after antibiotic tobramycin introduction in MFCs, and the antibiotic tobramycin was found to be effective against *Geobacter* spp., *Aminiphilus* spp. and *Acetoanaerobium* spp. (Wu *et al.* 2014). In a literature research, no study was found in which microbial community analysis of MECs and microbial fuel cells fed with SSRI and SNRI drugs was performed. Therefore, the identification of microorganisms that play an effective role in SSRI/SNRI removal in microbial electrochemical cells may contribute to the effective removal of such pollutants together with energy production in the future.

## 4. CONCLUSIONS

A potential approach for removal of SSRI/SNRI drugs (paroxetine, venlafaxine and o-desmethylvenlafaxine) from wastewaters was demonstrated in single-chamber MECs. SSRI/SNRI drugs were almost completely degraded in the MECs. Hydrogen was generated simultaneously using the drugs without pretreatment. The drugs at concentration level of 170 ng/mL slightly decreased hydrogen production, nonetheless, did not inhibited. Drugs had no significant effect on cell viability. Degradation mechanism of the drugs in the MECs could be investigated individually in the future. In conclusion, MECs could offer an alternative treatment method for wastewater containing SSRI/SNRI drug metabolites, with the added benefit of fuel hydrogen generation.

## DATA AVAILABILITY STATEMENT

All relevant data are included in the paper or its Supplementary Information.

## REFERENCES

- Abourached, C., Catal, T. & Liu, H. 2014 Efficacy of single-chamber microbial fuel cells for removal of cadmium and zinc with simultaneous electricity production. *Water Research* **51**, 228–233.
- Atasever-Arslan, B., Akdogan, E., Cakmak Cebeci, F. & Catal, T. 2020 Bioelectricity generation using human neuronal-like cells in single chamber biofuel cells. *Journal of Cleaner Production* **271**, 122505.



- Bermek, H., Catal, T., Akan, S. S., Ulutaş, M. S., Kumru, M., Özgüven, M., Liu, H., Özçelik, B. & Akarsubasi, A. T. 2013 Olive mill wastewater treatment in microbial fuel cells. *World Journal of Microbiology and Biotechnology* **30**, 1177–1185.
- Bielecka, A. M. & Obuchowicz, E. 2016 Antidepressant drugs can modify cytotoxic action of temozolomide. *European Journal of Cancer Care* **26**, e12551.
- Blaha, M., Grabicova, K., Shaliutina, O., Kubec, J., Randák, T., Zlabek, V., Buřič, M. & Veselý, L. 2019 Foraging behaviour of top predators mediated by pollution of psychoactive pharmaceuticals and effects on ecosystem stability. *Science of the Total Environment* **662**, 655–661.
- Catal, T. 2015 Comparison of various carbohydrates for hydrogen production in microbial electrolysis cells. *Biotechnology & Biotechnological Equipment* **30**, 75–80.
- Catal, T., Lesnik, K. L. & Liu, H. 2015 Suppression of methanogenesis for hydrogen production in single-chamber microbial electrolysis cells using various antibiotics. *Bioresource Technology* **187**, 77–83.
- Catal, T., Gover, T., Yaman, B., Droguetti, J. & Yilancioglu, K. 2017 Hydrogen production profiles using furans in microbial electrolysis cells. *World Journal of Microbiology and Biotechnology* **33**, 115.
- Catal, T., Liu, H., Fan, Y. & Bermek, H. 2018a A novel clean technology to convert sucrose and lignocellulose in microbial electrochemical cells into electricity and hydrogen. *Bioresource Technology Report* **5**, 331–334.
- Catal, T., Yavaser, S., Enisoglu-Atalay, V., Bermek, H. & Ozilhan, S. 2018b Monitoring of neomycin sulfate antibiotic in microbial fuel cells. *Bioresource Technology* **268**, 116–120.
- Catal, T., Kul, A., Enisoglu-atalay, V., Bermek, H., Ozilhan, S. & Tarhan, N. 2019 Efficacy of microbial fuel cells for sensing of cocaine metabolites in urine-based wastewater. *Journal of Power Sources* **414**, 1–7.
- Cebecioglu, R., Yildirim, M., Akagunduz, D., Korkmaz, I., Tekin, H. O., Atasever-Arslan, B. & Catal, T. 2019 Synergistic effects of quercetin and selenium on oxidative stress in endometrial adenocarcinoma cells. *Bratislava Medical Journal* **120**, 449–455.
- Ceconet, D., Molognoni, D., Callegari, A. & Capodaglio, A. G. 2017 Biological combination processes for efficient removal of pharmaceutically active compounds from wastewater: a review and future perspectives. *Journal of Environmental Chemical Engineering* **5**, 3590–3603.
- Cobanoglu, H., Coskun, M., Çayir, A. & Coskun, M. 2017 In vitro genotoxic and cytotoxic effects of doxepin and escitalopram on human peripheral lymphocytes. *Drug and Chemical Toxicology* **41**, 238–244.
- Das, D. & Veziroglu, T. N. 2001 Hydrogen production by biological processes: a survey of literature. *International Journal of Hydrogen Energy* **26**, 13–28.
- Digman, B. & Kim, D. S. 2008 Review: alternative energy from food processing wastes. *Environmental Progress* **27**, 524–537.
- Doron, R., Versano, Z., Burstein, O., Franko, M., Shamir, A., Toledano, R. & Rehavi, M. 2019 Cerebral MAO activity is not altered by a novel herbal antidepressant treatment. *Journal of Molecular Neuroscience* **69**, 371–379.
- Galecki, P., Mossakowska-Wójcik, J. & talarowska, M. 2018 The anti-inflammatory mechanism of antidepressants – SSRIs, SNRIs. *Progress in Neuro-Psychopharmacology and Biological Psychiatry* **80**, 291–294.
- Hernando, M. D., Mezcuca, M., Fernández-Alba, A. R. & Barceló, D. 2006 Environmental risk assessment of pharmaceutical residues in wastewater effluents, surface waters and sediments. *Talanta* **69**, 334–342.
- Jahromi, M., Razavi, S., Amirpour, N. & Khosravizadeh, Z. 2016 Paroxetine can enhance neurogenesis during neurogenic differentiation of human adipose-derived stem cells. *Avicenna Journal of Medical Biotechnology* **8**, 152–158.
- Kruk, J. S., Bermeo, S., Skarratt, K. K., Fuller, S. J. & Duque, G. 2018 The effect of antidepressants on mesenchymal stem cell differentiation. *Journal of Bone Metabolism* **25**, 43–51.
- Kumru, M., Eren, H., Catal, T., Akarsubasi, A. T. & Bermek, H. 2012 Study of azo dye decolorization and determination of cathode microorganism profile in air-cathode microbial fuel cells. *Environmental Technology* **33**, 2167–2175.
- Lovley, D. R. & Phillips, E. J. P. 1988 Novel mode of microbial energy metabolism: organic carbon oxidation coupled to dissimilatory reduction of iron or manganese. *Applied and Environmental Microbiology* **54**, 1472–1480.
- Lu, L. & Ren, Z. J. 2016 Microbial electrolysis cells for waste biorefinery: a state of the art review. *Bioresource Technology* **215**, 254–264.
- Lukić, I., Getselter, D., Ziv, O., Oron, O., Reuveni, E., Koren, O. & Elliott, E. 2019 Antidepressants affect gut microbiota and *Ruminococcus flavefaciens* is able to abolish their effects on depressive-like behavior. *Translational Psychiatry* **9** (133), 1–16.
- Nath, K. & Das, D. 2004 Improvement of fermentative hydrogen production: various approaches. *Applied Microbiology and Biotechnology* **65** (5), 520–529.
- Obeid, J., Magnin, J., Flaus, J., Adrot, O., Willison, J. C. & Zlatev, R. 2009 Modelling of hydrogen production in batch cultures of the photosynthetic bacterium *Rhodobacter capsulatus*. *International Journal of Hydrogen Energy* **34**, 180–185.
- Ozdemir, M., Enisoglu-Atalay, V., Bermek, H., Ozilhan, S., Tarhan, N. & Catal, T. 2019 Removal of cannabis metabolite from human urine in microbial fuel cells generating electricity. *Bioresource Technology Reports* **5**, 121–126.
- Sen, P., Akagunduz, D., Aghdam, A. S., Cakmak Cebeci, F., Nyokong, T. & Catal, T. 2019 Synthesis of novel Schiff base cobalt (II) and iron (III) complexes as cathode catalysts for microbial fuel cell applications. *Journal of Inorganic and Organometallic Polymers and Materials* **30**, 1110–1120.
- Wagner, R. C., Regan, J. M., Oh, S., Zuo, Y. & Logan, B. E. 2009 Hydrogen and methane production from swine wastewater using microbial electrolysis cells. *Water Research* **43**, 1480–1488.
- Wang, J. & Wan, W. 2009 Factors influencing fermentative hydrogen production: a review. *International Journal of Hydrogen Energy* **34** (2), 799–811.

- Wang, H., Zhou, X. & Huang, J. 2013 The role of Akt/FoxO3a in the protective effect of venlafaxine against corticosterone-induced cell death in PC12 cells. *Psychopharmacology* **228**, 129–141.
- Wu, W., Lesnik, K. L., Xu, S., Wang, L. & Liu, H. 2014 Impact of tobramycin on the performance of microbial fuel cell. *Microbial Cell Factories* **13** (91), 1–7.
- Xue, W., Zhou, Q. & Li, F. 2019 Bacterial community changes and antibiotic resistance -gene quantification in microbial electrolysis cells during long-term sulfamethoxazole treatment. *Bioresource Technology* **294**, 122170.
- Yang, D. H. D., Murphy, M. A. & Zhang, S. 2014 *Highly Sensitive Detection of Pharmaceuticals and Personal Care Products (PPCPs) in Water Using an Agilent 6495 Triple Quadrupole Mass Spectrometer*. Agilent Technologies, Santa Clara, CA, USA.
- Zhang, Q., Zhang, Y. & Li, D. 2017 Cometabolic degradation of chloramphenicol via a meta-cleavage pathway in a microbial fuel cell and its microbial community. *Bioresource Technology* **229**, 104–110.

First received 6 May 2021; accepted in revised form 27 June 2021. Available online 8 July 2021