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Degradation of Ampicillin and Penicillin G using Anodic Oxidation

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The degradation of ampicillin and penicillin G has been carried out by oxidation method using mixed metal oxides (MMO) electrodes as the anode. The objective of this paper was to study the electrochemical properties of several types of antibiotic drugs using electroanalytical techniques and to evaluate the efficiency of commercial MMO electrodes for the degradation of the drugs by anodic oxidation. For electrochemical studies, the determination of ampicillin and penicillin G has been carried out by differential pulse cathodic stripping voltammetry (DPCSV) at a hanging mercury drop electrode (HMDE) using Britton Robinson buffer (BRB). Ampicillin showed a clear peak current at potential -0.25 V at BRB pH 7 with initial and accumulation potential of 0 V, accumulation time of 30 seconds and with 0.02 V/s of scan rate. For penicillin G determination, the following optimum conditions were used: BRB pH 12, initial potential -0.3 V, accumulation potential of 0 V, and accumulation time of 30 seconds with 0.02 V/s of scan rate. For electrodegradation studies, two mixed metals oxide (MMO) titanium based electrodes have been used in three different mediums: BRB pH 4, tap water and BRB pH 10. For MMO electrode based on (Ru-Ir-TiO_2 (20:30:50)-10 micron), the best medium for degradation of ampicillin was at pH 4 with 100 % degradation in 15 minutes: for penicillin G, pH 10 is the best medium for the degradation. For (Ru-Ir-TiO_2 (40:10:50)-10 micron, similar results were obtained i.e. pH 4 was the best medium for ampicillin and pH 12 for penicillin G.

Keywords: Mixed metal oxide (MMO), electrodegradation, ampicillin, penicillin G, DPCSV

1. INTRODUCTION

In recent years, there has been an increasing concern about the presence of new emerging pollutants such as pesticides, drugs and endocrine disrupting chemicals (EDC) in aquatic environment [1-2]. These may cause a tremendous effect in the environment which will affect human health. The

number of pharmaceutical compounds including antibiotics has been observed in the water cycle including surface water [3-5], and even in drinking water [3]. Among them, drugs need a lot of attention due to their wide use in both human and veterinary medicine, unrestricted use and the negative effects such as proliferation of antibiotic-resistant bacteria [6-8]. Indeed, the presence of antibiotics in wastewaters is increasing and the treatment for removing the antibiotics will be a challenge in the future.

A lot of studies have been carried out to remove or degrade pharmaceuticals in various media. Methods such as Fenton process [9-11], UV/ZnO photocatatylic process [12] and advanced oxidation processes [13] were designed to degrade pharmaceutical waste in the water cycle. However, electrochemical methods are supposed to be the best method for antibiotic drugs removal because of the simultaneous oxidation-reduction process taking place at the electrodes without the need to add other reagents. Indeed, the electrochemical methods have been suggested as a useful method of removing harmful organic materials such as pesticides, drugs and EDC in wastewaters and effluents.

Electrochemical methods (electrochemical oxidation, electrocoagulation, electroflotation, etc.) have achieved great interest in water treatment. Electrochemical oxidation has been applied successfully to degrade different organic pollutants [14], pharmaceuticals [15-16] and pesticides [17]. The electrochemical properties such as wide potential window in aqueous and non-aqueous electrolytes, chemical and physical stability and small background current made them apparently a popular choice in this field [18]. Most of commonly used electrode materials are unsuitable for this application due to their toxicity (e.g. mercury), instability or affordability. Fortunately, the unique properties of MMO successfully overcame these problems. Mixed metal oxide electrodes (MMO) have shown very promising results in the field of electroanalysis [19-21], electrocatalysis [22-23], electrochemical waste treatment [24-28] and pesticide treatment [29]. This paper is focused at evaluation of the effectiveness of MMO electrodes for electrodecomposition of ampicillin and penicillin G before discharge to the environment and at the development of a new method for the decomposition of ampicillin and penicillin G using an electro-oxidation method.

Pharmaceuticals are synthetic or natural chemicals that can be found in medicines, over-the-counter drugs and veterinary drugs. Pharmaceuticals contain active ingredients that have been designed to have pharmacological effects and confer significant benefits to society [30]. The presence of pharmaceuticals in the environment and the water cycle at trace level has been widely discussed and published in the past decade. There are many studies and reports stating that the presence of pharmaceuticals in waste water is increasing year by year [30]. For this reason, lots of analytical methods have been developed to determine the presence of the pharmaceuticals in waste water. Pharmaceuticals enter the environment through many routes, including human or animal excreta, wastewater effluent, treated sewage sludge, industrial waste, and medical waste from health-care landfill, leachate and biosolids [30].

Many reports stated that the presence of new emerging pollutants in pharmaceutical effluents and surface waters have raised substantial concern in the public and regulatory agencies. Because of potential risk to humans and wildlife, removal of these pollutants will likely become more important in hospital and clinical wastes to protect the environment and human health. Due to the concern, a lot of new methods such as biological degradation, photodegradation and the application of activated carbon

have been developed. However, most of these methods still do not satisfy all the requirements. Therefore, new method must be developed in order to reduce and eliminate these chemicals.

2. EXPERIMENTAL

2.1 Chemicals and Glassware

All chemicals used were analytical reagent grades (ANALAR). Antibiotic drugs (ampicillin, (2*S*,5*R*,6*R*)-6-([(2*R*)-2-amino-2-phenylacetyl]amino)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0] heptane-2-carboxylic acid) and penicillin G, (2*S*,5*R*,6*R*)-3,3-dimethyl-7-oxo-6-(2-phenylacetamido)-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid) were reagent grade from Fluka. The organics and other chemicals (glacial acetic acid, ortophosphoric acid, sodium hydroxide) were analytical grade from Merck. Double distilled deionized water (DDDW) was obtained from a Water Purification System from Millipore. Britton-Robinson buffer (BRB) solutions were prepared in a usual way. A stock solution of 0.01 mol/L ampicillin and penicillin G were prepared by dissolving 0.743 g (ampicillin) or 0.713 g (penicillin G sodium salt) of the pure substance in 0.25 L of DDDW. More diluted solutions of both antibiotics were prepared by precise dilution of stock solutions. All glassware was soaked in 10 % nitric acid and rinsed several times with DDDW.

2.2 Instrumentation

Voltammetric experiments were carried out using Autolab PGSTAT with hanging mercury drop electrode (HMDE) as the working electrode; a silver–silver chloride (Ag/AgCl/3 M KCl) electrode as a reference and a platinum wire as an auxiliary electrode (all supplied by Metrohm, Switzerland). Nitrogen gas was used to remove dissolved oxygen. pH measurements were performed with laboratory pH meter Cyber Scan 500 (Eutech instruments).

2.3 Electrodes

A series of commercial titanium based electrodes (Tianode) with different metals composition has been used during the electrodegradation of antibiotic drugs. These mixed metals oxide act as anode during the electrodegradation process. The MMO electrodes that have been used during this electrodegradation included Ru-Ir-TiO_2 (40:10:50)-10 micron and Ru-Ir-TiO_2 (20:30:50)-10 micron. The electrochemical cell system consisted of titanium cathode and mixed metal oxide (MMO) titanium based anode. A power supply DC-Power Supply SMM-12 (Teletron) and a stirrer hotplate of H10707V2 model (Favorit) were used for electrochemical degradation of antibiotic drugs.

2.4 Electrochemical Procedures

A 200 mL aliquot of antibiotic aqueous solution was placed in a 0.25 L beaker with 0.1 g of NaCl and mixed using a magnetic stirrer. The pH of BRB (electrolyte) was adjusted to the required

values (pH 4 and pH 10) by 1.0 mol/L NaOH. The voltage was adjusted to 10.0 V and the current was 0.2 A. The treatment times (electrolysis) were then set to 15 minutes, 30 minutes and 60 minutes. The solutions after the electrochemical degradation were analyzed using DPCSV at HMDE in a BRB solution.

3. RESULTS AND DISCUSSION

3.1. Determination of Ampicillin and Penicillin G using Differential Pulse Cathodic Stripping Voltammetry (DPCSV)

Forsman [31] studied the behavior of penicillin by cathodic stripping voltammetry using HMDE at -0.1 V vs SCE in a pH 4 acetate buffer containing excess of copper(II). The studies concluded that the reduction of penicillin group can possibly occur at the S-H bond and the final reduction products are penicillamine and penilloaldehyde. Therefore, we have tried to find optimum conditions for voltammetric determination of penicillin at HMDE.

3.1.1. Effect of pH

At first, voltammograms of ampicillin and penicillin G were investigated using BRB between pH 3 and pH 12. The effects of other voltammetric parameters were then investigated for the optimization of conditions for the determination of this drug. It was observed that reduction peaks of both drugs were shifted to more negative potentials with increasing pH.

Ampicillin adsorbed strongly on HMDE and showed two well-developed peaks between pH 5 and pH 12. However, at higher pH, more positive peaks (potential from 0 V to -0.1V) were too close to mercury dissolution current and therefore not suitable for analytical purposes. So, the more negative peak (potential between -0.2 V and -0.5 V) was used for ampicillin determination.

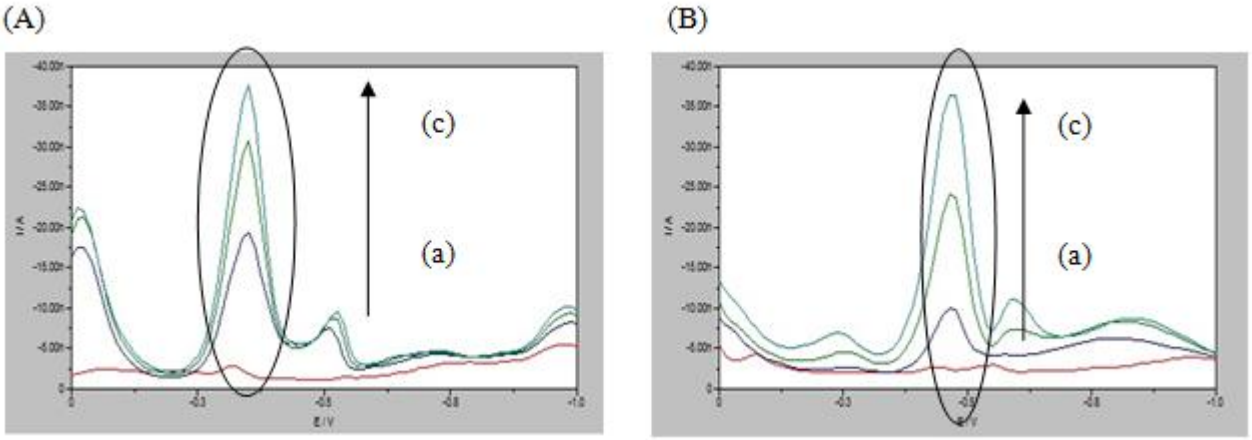

Figure 1. DPCS voltammograms at HMDE in 0.04 mol/L BRB for (A) ampicillin at pH 7 (B) penicillin G at pH 12, E_i = 0 V, E_{acc}= 0 V, t_{acc}= 30 s, scan rate = 0.02 Vs^{-1} ; (a) 1×10^{-7} mol/L (b) 3×10^{-7} mol/L (c) 5×10^{-7} mol/L

The highest peak for ampicillin was found at pH 7 and this pH was used for optimization of other voltammetric parameters. As for penicillin G, two peaks at potential -0.3 V to -0.5 V and -0.8 V to -0.9 V have been observed. However, reduction peak at potential -0.3 V was better developed than the peak at -0.8 V and thus better suitable for analytical purposes. The highest peak for penicillin G was found at pH 12. Therefore, this pH 12 was chosen for optimization of other voltammetric parameters. Figure 1 shows the voltammogram of ampicillin and penicillin G at optimum pH while Figure 2 shows the voltammograms of ampicillin and penicillin G at various pH. The graphs for peak current and peak potential versus pH of BRB solution for both drugs are shown in Figure 3.

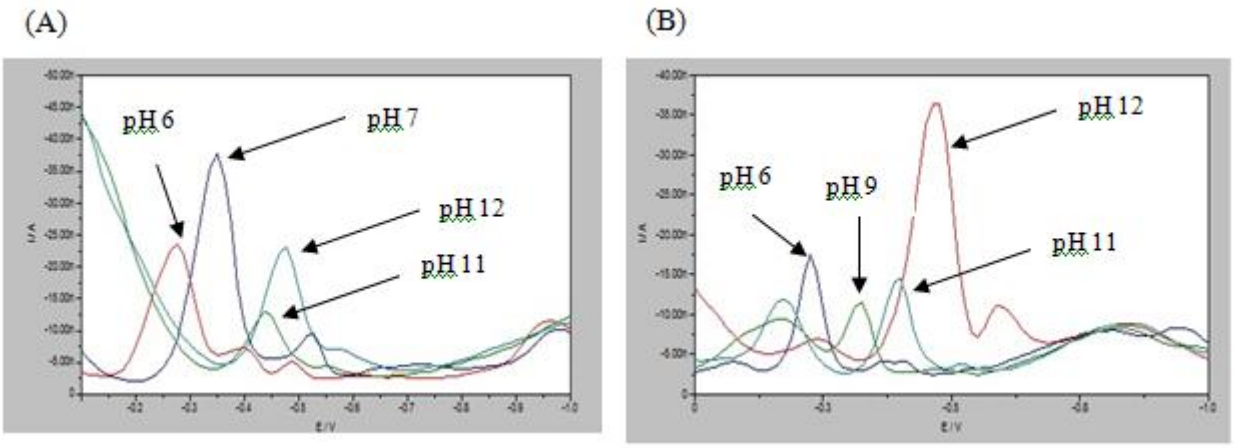

Figure 2. DPCS voltammograms at HMDE in 0.04 mol/L BRB for (A) ampicillin (B) penicillin G at various pH, E_i = 0 V, E_{acc}= 0 V, t_{acc}= 30 s, scan rate = 0.02 Vs^{-1}; concentration of ampicillin and penicillin G = 5×10^{-7} mol/L.

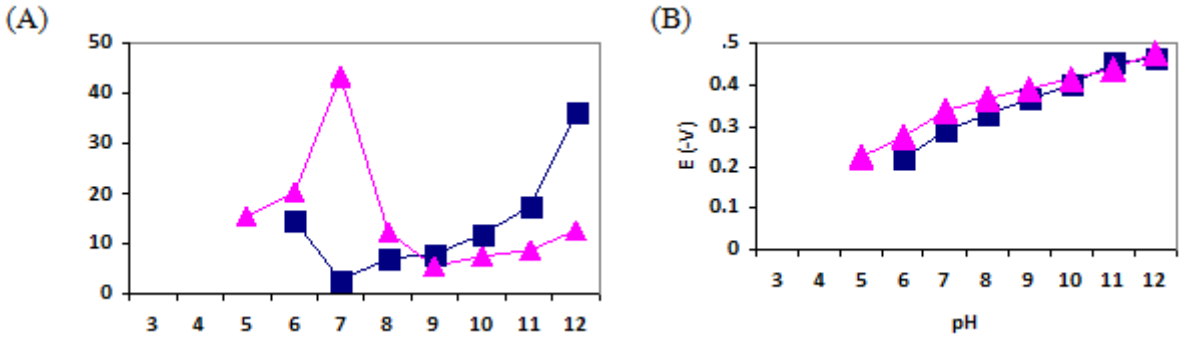

Figure 3. The peak current (A) and peak potential (B) versus pH of BRB for ampicillin (▲) and penicillin G (■), E_i = 0 V, E_{acc}= 0 V, t_{acc}= 30 s, scan rate = 0.02 Vs^{-1}. Concentrations of ampicillin and penicilin G were 5×10^{-7} mol/L.

3.1.2 Effect of potential and time of accumulation

For ampicillin, the initial potential from 0 V to -0.15 V has been tested at pH 7. As the initial potential moves towards more negative values, the peak current decrease slightly showing reduced amount of analyte adsorbed on the mercury surface. Therefore, 0 mV was chosen as the optimum

accumulation potential for ampicillin. For penicillin G no significant change in peak currents was observed when the E_i was set from 0 V to -0.2 V. However, a slight increase in current occurred when E_i was set at -0.3 V. Thus, the initial potential of -0.3 V was chosen as the optimum initial potential for penicillin G.

The effect of accumulation time (t_{acc} = 1, 10, 30, 45, 60, 90, 120, 150, 180, and 210 seconds) was studied at the initial potential and accumulation potential set at 0 V at pH 7 and pH 12. Ampicillin peak current increased linearly from 0 to 30 seconds with slow decrease afterwards showing electrode passivation, desorption of analyte from the mercury electrode or formation of multiple layer at the surface of the mercury electrode which affects the stripping process. For this reason, 30 s was chosen as the optimum accumulation time.

Penicillin G seems to accumulate for the first 30 s. Afterwards, the peak current decreases due to passivation, desorption or formation of a double layer which affects the peak height. Therefore, the optimum accumulation time for penicillin was set at 30 second. Figure 4 shows the graph of peak current versus initial potential and accumulation time for both antibiotics.

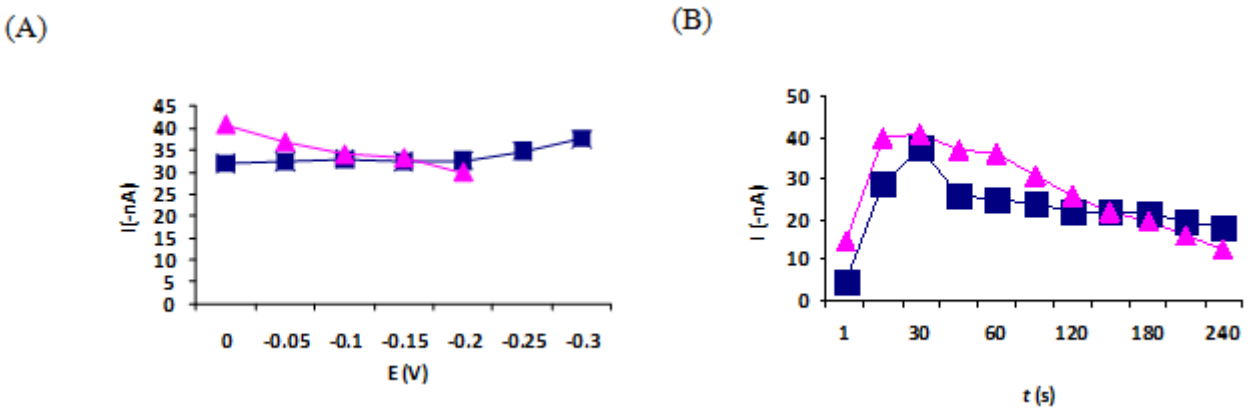

Figure 4. The effect of (A) initial potential and (B) accumulation time in 0.04 mol/L BRB on ampicillin (▲) and penicillin G (■) reduction peak at optimum pH. E_{acc}= 0 V, t_{acc}= 30 s, scan rate = 0.02 Vs^{-1}. Concentration of ampicillin and penicillin G were 5 × 10^{-7} mol/L.

3.1.3. Calibration curve of Ampicillin and Penicillin G

The voltammograms for various concentrations of ampicillin and penicillin G in BRB solutions of pH 7 and pH 12 were recorded. The reduction peak currents versus concentration of the analytes plots showed a good linearity in the concentration range of 1.0 - 5.0 × 10^{-8} mol/L as shown in Figure 5. The linear regression equations for both drugs can be represented as:

I_p (-nA) = 0.8176 × c – 0.694 for ampicillin

I_p(-nA) = 0.7372 × c + 1.32 for penicillin G

with a correlation coefficient of 0.9934 and 0.9909, respectively. The limit of detection (LOD) of these drugs (3 SD/*b*, where SD is the standard deviation of the peak currents and *b* is the slope of the related calibration equation) is shown in Table 1.

Table 1. Analytical parameters of calibration curves for ampicillin and penicillin G

Analytical Parameters	Ampicillin	Penicillin G
Linear Range	1.0 - 5.0 × 10^{-8} mol/L	1.0 - 5.0 × 10^{-8} mol/L
Slope	0.82 A L/mol	0.74 A L/mol
Intercept	-0.69 nA	0.13 nA
Correlation coefficient	0.9934	0.9909
Limit of Detection	1.7 × 10^{-9} mol/L	2.3 × 10^{-9} mol/L

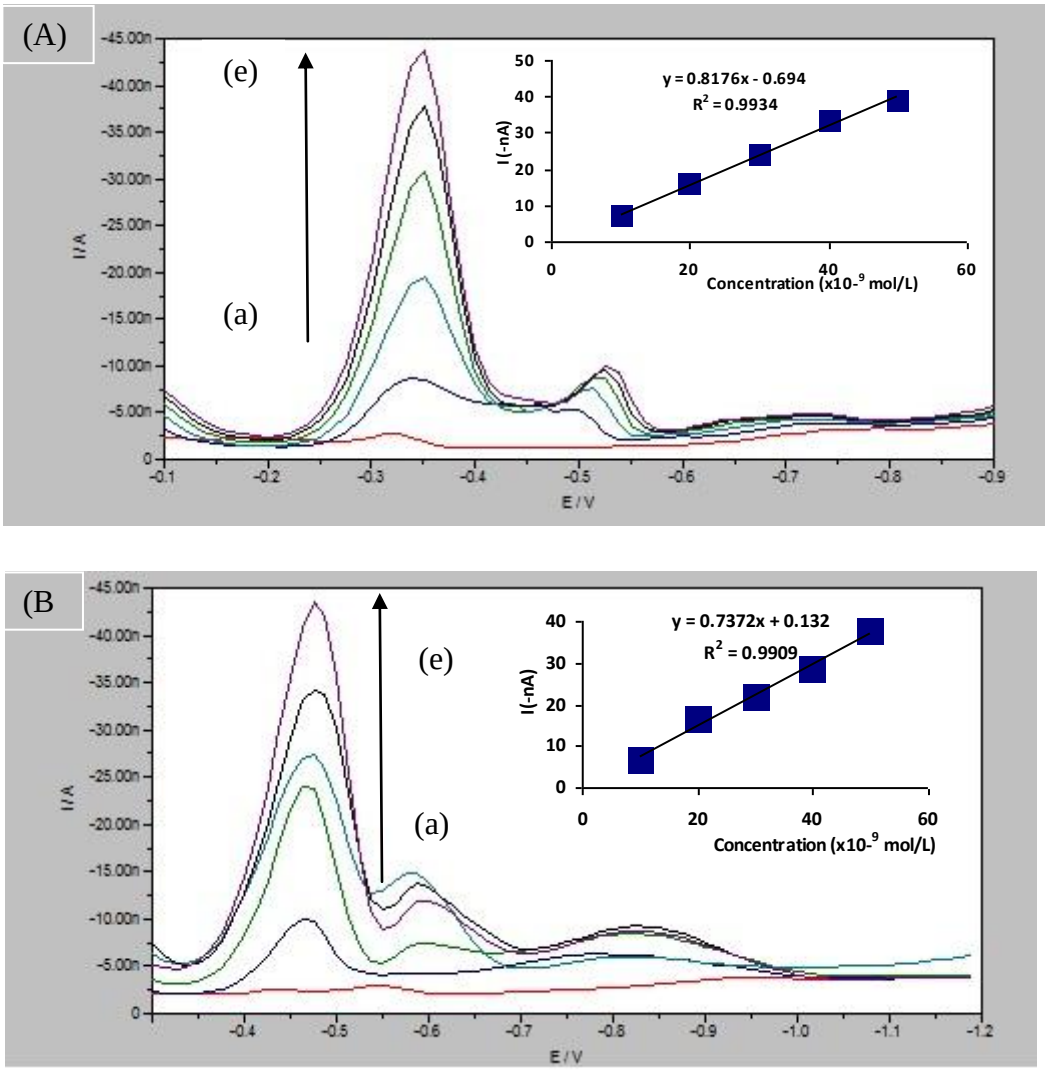

Figure 5. DPCSV at HMDE calibration for (A) ampicillin and (B) penicillin B in concentration of 1.0 - 5.0 × 10^{-8} mol/L in 0.04 mol/L BRB solution at pH 7 and pH 12 with optimum conditions for each drugs and with scan rate = 0.02 Vs^{-1}.

3.2. Electrodegradation of Ampicillin and Penicillin G

The second part of the study focuses on electro-oxidation of ampicillin and penicillin G. The aim of this study was to remove the antibiotic drugs via electro-degradation. The parameters that were monitored in this study were the type of anode, medium and the effect of treatment (electrodegradation) time. Three different media used were: pH 4, tap water, and pH 10 with the treatment time of 15, 30, and 60 minutes. A series of MMO titanium based mixed metal oxide electrodes (Ru, Ir, TiO_2) with different ratios of the metal oxides were used as an anode. Based on previous studies, there are two possible pathways for the degradation of ampicillin [29,32,33] and penicillin G [34]. Path 1 starts with the formation of penicilloic acid, followed by decarboxylation, possibly via attachment of primary COO^- group, while path 2 begins with de-ammonification of parent ampicillin.

3.2.1. Electrodegradation of Ampicillin

The electrodegradation of ampicillin was monitored using DPCSV at HMDE at pH 7. Degradation was carried out in acidic medium (pH 4), tap water and alkaline medium (pH 10). The percentage of ampicillin removal after the electrolysis was calculated from the current peak height before and after the electrolysis. Two types of Ru-Ir-TiO_2 electrode with different ratios (20:30:50 and 40:10:50) were used. At pH 4, both MMO electrodes showed 100 % degradation in 15 minutes. However, there were two non-identified peaks observed at potential -0.95 V which indicates that some electrochemically active byproducts were produced. In tap water, both electrodes showed 100 % degradation after 60 minutes. Different results were obtained in the alkaline medium. Ampicillin was not fully degraded after 60 minutes in ratio of Ru-Ir-TiO_2 (20:30:50) compared to Ru-Ir-TiO_2 (40:10:50) ratio. However, there were still two unidentified peaks at -0.45 V and -0.76 V suggesting formation of some other byproducts.

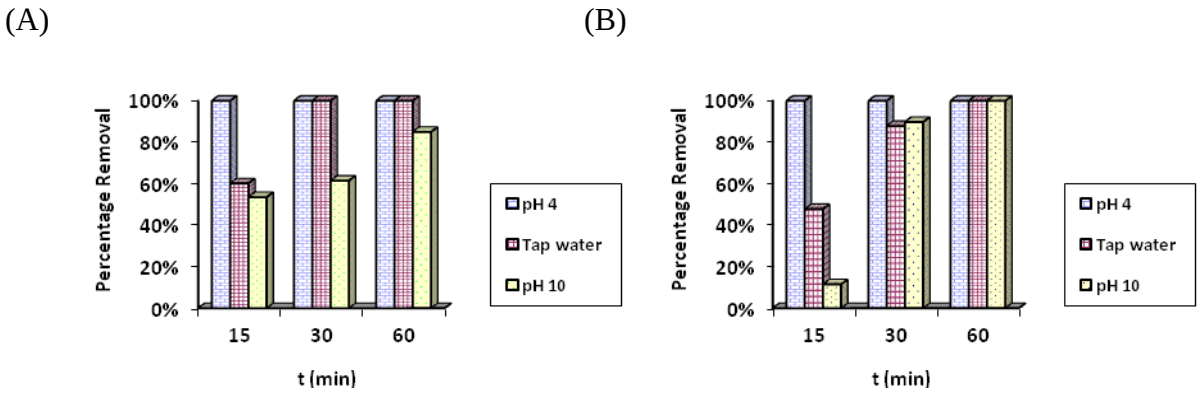

Figure 6. The degree of degradation (%) of ampicillin versus treatment time in three different media using (A) Ru-Ir-TiO_2 (20:30:50) and (B) Ru-Ir-TiO_2 (40:10:50) anode.

Figure 6 shows the degradation percentage of ampicillin (%) versus treatment time in three different media using both electrodes. It is possible to conclude that ampicillin can be successfully degraded at pH 4 in a shorter time and Ru-Ir-TiO_2 anode with ratio of 40:10:50 is the best one due to complete degradation.

3.2.2. Electrodegradation of Penicillin G

The degree of destruction of penicillin G was monitored by DPCSV at HMDE at pH 12. Again, two MMO electrodes with different ratio were used. At pH 4, 100 % degradation was observed after 60 minutes. The same is valid for destruction in tap water. However, in alkaline medium the degradation was more efficient. For 20:30:50 ratio, 68 % of penicillin G was degraded after 15 minutes, 83 % after 30 minutes and 100 % after 60 minutes. For 40:10:50 ratio, the values were 47.45 % after 5 minutes and 100 % after 60 minutes (see Fig. 3,6). Thus, it can be concluded that pH 10 is optimal. The degradation percentages of penicillin G (%) versus treatment time in three different media using both electrodes are shown in Figure 7. The products of the degradation were not identified. This could be the subject of further study.

(A) (B)

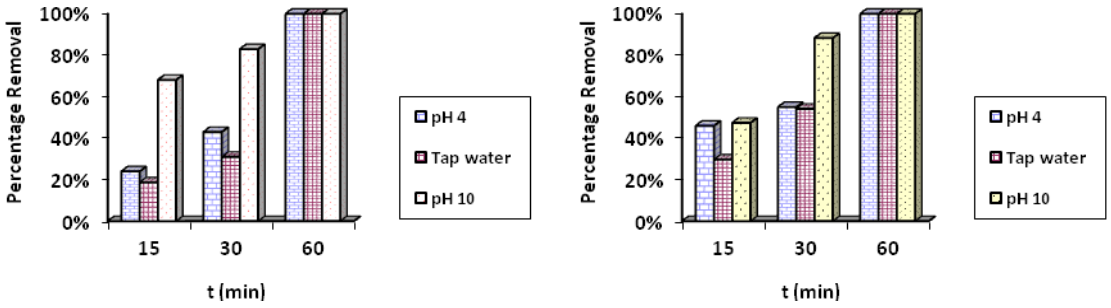

Figure 7. The degree of degradation of penicillin G (%) versus treatment time in three different media using (A) Ru-Ir-TiO_2 (20:30:50) and (B) Ru-Ir-TiO_2 (40:10:50) anode

4. CONCLUSION

A differential pulse cathodic stripping voltammetric (DPCSV) method at a hanging mercy drop electrode (HMDE) has been developed for monitoring the efficiency of electrochemical destruction of ampicillin and penicillin G. The optimum conditions for ampicillin were found to be: pH 7, initial potential E_i = 0 V, accumulation potential E_{acc} = 0 V, accumulation time, t_{acc} = 30 s and scan rate 0.02 Vs^{-1}. For the determination of penicillin G the optimum conditions were: pH 12 with initial potential E_i = 0 V, accumulation potential E_{acc} = -0.3 V, accumulation time, t_{acc} = 30 s and scan rate 0.02 Vs^{-1}.

In the electrodegradation studies, two mixed metals oxide (MMO) titanium based electrodes have been used in three different media (pH 4, tap water and pH 10). For MMO electrode with Ru-Ir-TiO_2 (20:30:50)-10 micron, the best medium for degradation of ampicillin was at pH 4. Total degradation (100 % degradation) was achieved in 15 minutes of electrolysis time, while for penicillin G, pH 10 was found to be the best medium for the degradation. For Ru-Ir-TiO_2 (40:10:50)-10 micron, similar results were obtained, i.e. pH 4 was the best medium for ampicillin and pH 12 for penicillin G.

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