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Treatment of statins drug (pravastatin and rosuvastatin) in water by electro-Fenton process: Kinetics of degradation/mineralization and optimization of experimental conditions for a biological post-treatment

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Abstract: The treatment of pravastatin and rosuvastatin contaminated water as much as toxic and persistent organic pollutant was carried out by Electro-Fenton method EF. Several experiments were conducted in a cell compartment equipped with a platinum anode and a carbon felt cathode. The effects of several parameters such as the applied current and the catalyst Fe^{2+} concentration have been studied. Mineralization aqueous solutions of pravastatin followed by the chemical oxygen demand COD gave a higher degree of reduction of more than 90% for 6 hours of treatment at a current of 100 mA and Fe^{2+} concentration of 0.2 mM. The study of the degradation kinetics was followed during electrolysis by HPLC giving a pseudo first order reaction using a current of 100 mA and Fe^{2+} concentration of 0.1mM. A number of intermediate products for pravastatin and rosuvastatin have been identified using HPLC and liquid chromatography-mass spectrometry analyses. Biodegradability of the pre-treated solutions of two statins by EF was evaluated in order to decide the optimal moment to introduce the biological process. It was given by the ratio BOD_5/COD which increases from 0 initially to 1.3 after 2 hours for pravastatin and from 0 initially to 1.5 after 3 hours for rosuvastatin as the COD decreases. It implies that EF tends to enhance the biodegradability and could be used as a pre-treatment step for biological treatment.

Keywords: pravastatin; rosuvastatin; Electro-Fenton; degradation; mineralization; biodegradability.

Introduction

Pharmaceuticals account for a large group of human and veterinary drugs used in the world. The sale is estimated at 250 billion $ annually [1], hence their presence in the environment has become a major research topic and highlighted in the United States in the 1970s [2,3] and meadows a decade later in England [4]. The penetration of these products in the environment can occur through different routes leading to pollution. The sources of this contamination involve the elimination of drugs in waste production and water treatment [5]. The inefficiency of conventional physicochemical methods in sewage treatment plants for disposal of medicines leads to their accumulation in the environment [6]. Despite their very low content in natural waters, their presence is very toxic for the biological hierarchy. This finding was demonstrated by the production of multi-resistant strains of microorganisms by certain drugs and their adverse effects on the endocrine system of fish and invertebrates and algae [7]. Statins are a group of medicines used to lower cholesterol levels in the blood, prescribed to patients at risk of coronary heart disease for the reduction of morbidity and cardiovascular mortality. The presence of these medicines in water has been well-covered by several studies [8]. A recent research has shown that statins have potential anti-cancer effects [9,10]. Because of their reluctance in wastewater treatment systems, their widespread presence and their high persistence, these drugs have been detected in untreated wastewater to 4-49ng/L, in the treated wastewater 1-59 ng/L and even in the drinking water [8-11,12]. Due to their toxicity to humans and other forms of life, there is a strong need to treat all effluents contaminated by these pollutants before their admission in the environment [13].

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Previously, a number of advanced oxidation processes (AOP) were evaluated for the disposal of pharmaceuticals in water [14-18]. AOPs are effective methods that generate hydroxyl radicals *in situ* $^{\bullet}OH$ capable to oxidize organic molecules until their mineralization. These radicals may be produced by chemical, photochemical or electrochemical methods [19-21].

Recently, electrochemical methods based on the Fenton reaction such as electro-Fenton (EF) have shown promising results in the degradation of organic matter in water through their simplicity, high efficiency and relatively low cost [22,23]. This has been demonstrated for several pollutants, including phenols [24,25], synthetic dyes [26], herbicides and pesticides [27,28] and drugs [29-33].

EF method is based on the addition of a catalytic amount of Fe^{2+} in an acid solution contained in an electrolytic cell continuously producing H_2O_2 from O_2 injected at the cathode according to the reaction (1) [31]. The reaction between Fe^{2+} and H_2O_2 gives Fe^{3+} and the hydroxyl radical $^{\bullet}OH$ according to Fenton's reaction (2). $^{\bullet}OH$ is considered to be the strongest oxidizing following its high standard reduction potential (E ° ($^{\bullet}OH$ /H_2O) = 2.80 V/ENH) and has no selectivity for reacting with the organic compounds until mineralization giving carbon dioxide, water and inorganic ions.

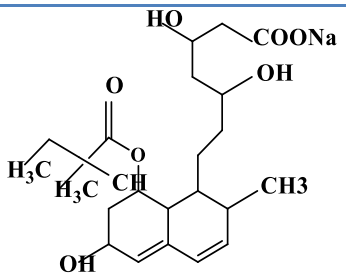
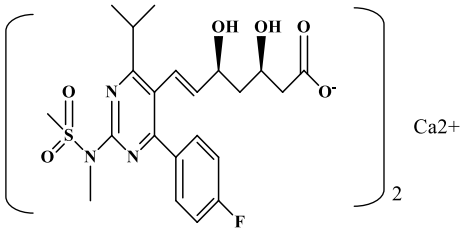
$$O_2 + 2e^- + 2H^+ \rightarrow H_2O_2 \quad (1)$$

$$H_2O_2 + Fe^{2+} \rightarrow Fe^{3+} + {}^{\bullet}OH + OH^- \quad (2)$$

$$Fe^{3+} + e^- \rightarrow Fe^{2+} \quad (3)$$

In the present paper, we choose to study the case of PRA of the first generation and ROS of the 3rd generation as a model of statin known by their large volume production, high consumption, highly toxic and potentially carcinogenic [34,35]. Our primary objectives are to determine the degradation kinetics and efficiency of mineralization of acidic aqueous solutions of PRA by Electro-Fenton process, knowing that this study was already done in the first article for ROS [17] which The decay kinetics of ROS followed pseudo-first order reaction and an optimum current of 300 mA and a catalyst (Fe^{3+}) concentration of 0.2mM were found to be optimal for an effective degradation. The identification of the intermediates and the study of the biodegradability were carried out for both statins.

Table 1. Pravastatin sodium (PRA) and Rosuvastatin calcium (ROS) properties

Compound	Structure	Molecular weight
monosodium salt of Pravastatin [1 S - [1 α (βS *, DELTA.S *) 2 α, 6 α, 8 β (R *, 8a α]] - 1, 2, 6, 7, 8, 8a - hexahydro - β, δ, -trihydroxy 6 -2 - methyl - 8 - (2 - methyl l - 1 - oxobutoxy) - 1 - acid naphtalèneheptanoïque	 $C_{23}H_{35}O_7.Na$	446.52 mg/l
calcium bis[(3*R*,5*S*,6*E*)-7-{4-(4-fluoro-phenyl)-6-(1-methylethyl)-2-[methyl(methylsulfony) amino]pyrimidin-5-yl}-3,5-dihydroxyhept-6-enoate]	 $C_{44}H_{54}F_2N_6O_{12}S_2{\bullet}Ca$	1001.14mg/l

Experimental Section

Chemicals

Pravastatin sodium PRA (98%) and Rosuvastatin calcium (98%) were purchased from Sigma Aldrich and used without purification. there chemical structures and physical properties were given in Table 1. Anhydrous sodium sulfate Na_2SO_4 used as supporting electrolyte is of analytical grade from Sigma Aldrich. Heptahydrated ferrous sulfate and pentahydrated ferrous sulfate used as catalyst is of analytical grade from Shangai Chemical Reagents Co. Solutions were prepared with high-purity water obtained from a Millipore Milli-Q system with resistivity > 18MΩ at 25°C and were adjusted to pH 3.0 with analytical grade sulfuric acid from Merck using HANNA pH-meter. Other chemicals such as methanol, Triéthylamin, and acetic acid (HPLC grade, Sigma Aldrich), Acetonitril (ACN)

(HPLC grade, Carlo erpa), were used as received. Potassium chloride (KCl), Mercuric sulfate $HgSO_4$, silver sulfate $AgSO_4$ and potassium dichromate K_2CrO_7 were purchased from Hach Lange Europe, Belgium.

Electrolytic system

The experiments were performed using a cylindrical and open undivided cell of 6 cm diameter and 250 ml capacity in which statins aqueous solutions were placed. The cathode is **70 cm² (10 cm × 7 cm**) carbon felt piece (carbon Lorraine) with a thickness of 0.5cm, and the anode is a platinum **5 cm².** The anode is centered in the electrolytic cell and surrounded by the cathode. The electrodes were connected to a Potentiostat model / Galvanostat PGZ301 associated with "VoltaLab" to control the current intensity. A saturated calomel electrode (SCE) was used as reference. Electrolysis was conducted with a volume of 200ml of aqueous solution, while stirring vigorously with a magnetic stirrer and a rotation rate of 700 revolutions / minute for mass transfer. Sparging with compressed air for 10 minutes through the solution is needed to saturate the aqueous solution before the electrolysis. The aqueous solutions contain 0.05 M of Na_2SO_4, 0.1mM of Fe^{2+} and 0.2mM of Fe^{3+} were added for PRA and ROS, respectively. The study was brought to room temperature and applying a constant current in the range of 30 to 300 mA at pH 3 considered as the recommended value for the EF process [36].

Analytical procedures

The PRA concentration during electrolysis was quantified by high performance liquid chromatography (HPLC), using a waters 2695, fitted with Thermo Hypersil C18 column 250mm/4.6mm/5µm at 25 °C, and coupled with photodiode array PDA 2998 detector selected at optimum wavelengths of 238 nm. The sample volumes were 50 µL. Acetic acid/triéthylamin/methanol/water 1:1:450:550 (v/v/v/v) mixture was used as a mobile phase at a flow rate of 1.3 ml/min. the corresponding retention time (t_r) for PRA was 18min.

The evolution of Rosuvastatin concentrations was detected using a Waters 2695, fitted with Zorbax eclipse XDB C18 column (150mm/4.6mm/3.5µm) at 25°C, equipped with an isocratic pump and photodiode array PDA 2260 detector selected at optimum wavelength of 248 nm. The mobile phase was a mixture of ACN/acetic acid (30 :70, v/v). It was eluted with a rate of 1 ml.min^{-1}. The injection volume was 130 µL.

Mineralization of solutions was followed by the reduction of chemical oxygen demand (COD) using the Lovibond® Vario-MD200 Photometer. After oxidation with $K_2Cr_2O_7$ at an acidic pH, quantification of the amount of oxygen required for oxidation of the organic material was carried out at 150°C for 2 hours [37]. COD values have been measured colorimetrically using DR/125 spectrophotometer (Hach Company, USA).

For LC/MS analysis of oxidation by-products in the study, we used an LC surveyor HPLC system coupled with an LCQ Advantage triple quadrupole mass spectrometer equipped with a pneumatically assisted electro spray ionization source (ESI) in positive ion mode and a Waters photodiode array detector (PDA). A sample volume of 20 µL was injected into Inertsil BDS Hypersil C18(150×2.1)mm×5µm column which thermostated at 35 °C. the mobile phase was a mixture of water/ formic acid – methanol/formic acid 0.1% with gradient program as follows: 0 min 90% A; 1 min 90% A; 21 min 40% A, 26 min 0% A36 min 0% A; 37 min 90% A; 57 min 90%. The flow rate was equal to 0.2 mL min^{-1} and Detection was performed at 200-600 nm.

The biological oxygen demand was measured by an Oxdirect BSB BOD Lovibond thermostated at 20 °C. The pH of the samples was adjusted to a value between 6.5 and 7.5 after the addition of the bacterial seed and the necessary nutrients for bacterial growth. We note that we used domestic wastewater obtained from National Office of Electricity and Drinking Water, Rabat, Morocco and all the experiments are aerated to reach oxygen saturation.

Results and Discussion

Kinetic study of PRA degradation

The effect of the current applied to the oxidative degradation was studied for 200 ml of the aqueous solution of PRA (0.13mM) with 0.1 mM of Fe^{2+} at pH 3. According to the results in Figure 1, the kinetics of degradation is accelerated by increasing the applied current from 30 to 100 mA. This influence can be explained by the increase in the speed of the electrochemical reactions 1 and 3, leading to the generation of more $^{\bullet}OH$. The complete disappearance of PRA was observed at 9min, 7min, and 4min for 30, 60, 100mA, respectively. Therefore, 100 mA appears to be the optimal value of the current.

It was also observed that the decrease in PRA concentration can be described by a pseudo-first order reaction kinetics. The values of the apparent rate constants were determined by 0.57 min^{-1} (R^2 = 0.972) for 30 mA, 0.73min^{-1} (R^2 = 0.967) for 60mA, and 2.13 min^{-1} (R^2= 0.999) for 100mA. Increasing k_{app} is related to an expected acceleration of the production of $^{\bullet}OH$. The value of k_{app} for 300 mA (0.88 min^{-1}) was significantly lower compared to that of 100 mA. This can be explained by the acceleration of wasteful reactions at higher current values such as reduction of O_2, evolution of H_2 at the

cathode or oxidation of H_2O_2 at the anode (reactions 4, 5 and 6).

$$O_2 + 4e^- + 4H^+ \rightarrow 2H_2O \quad (4)$$

$$2H_2O + 2e^- \rightarrow H_2 + 2OH^- \quad (5)$$

$$H_2O_2 \rightarrow O_2 + 2H^+ + 2e^- \quad (6)$$

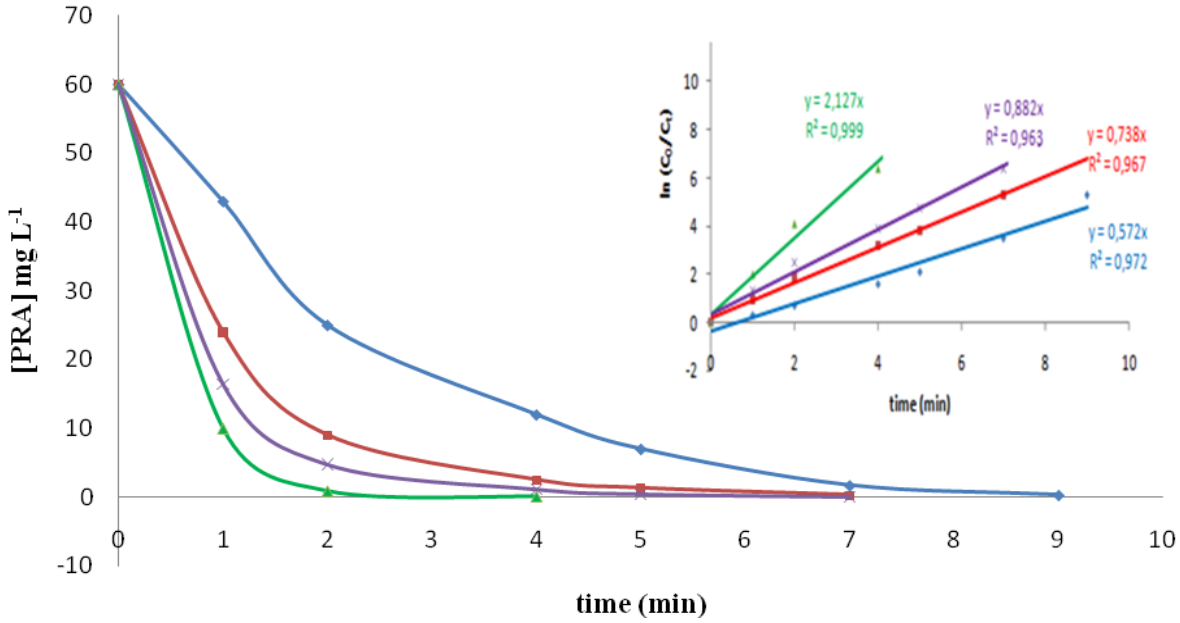


Figure 1. Effect of the current applied on PRA concentration decay by Electro-Fenton treatment at pH 3 in 0.05 M Na_2SO_4 and 0.1 mM Fe^{2+}. Applied current I (mA): 30 (-♦-), 60 (-▪-), 100 (-▲-), 300 (-×-).

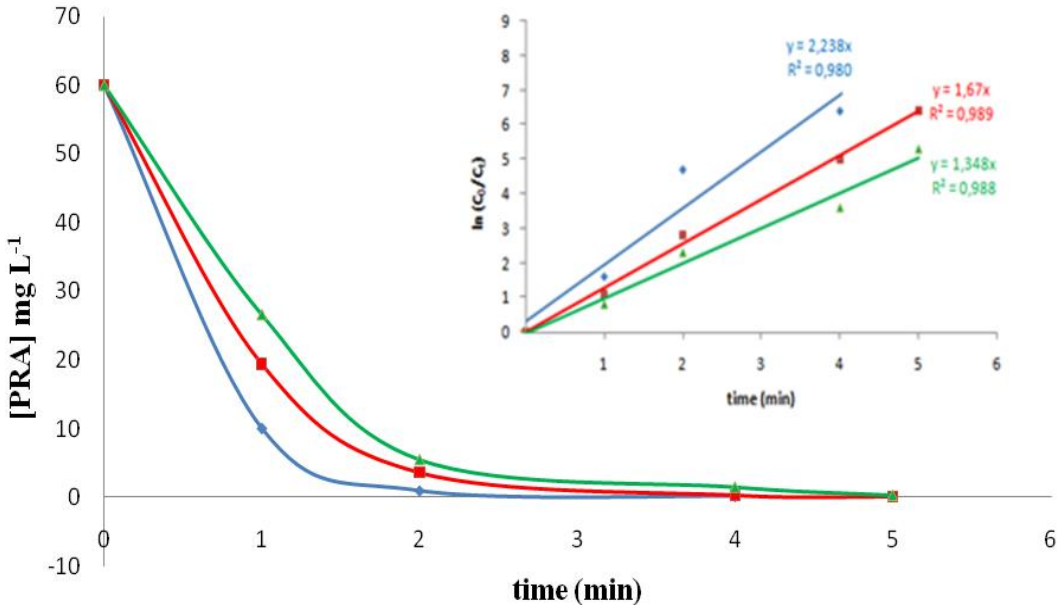


Figure 2. Effect of catalyst concentration Fe^{2+}on PRA concentration decay during Electro-Fenton treatment in 0.05M Na_2SO_4 at pH 3 and applied current 100mA. [Fe^{2+}] = 0.1mM (-♦-), 0.2 mM (-▪-), 0.5mM (-▲).

The catalyst concentration Fe^{2+} is another important parameter in EF process. Degradation of 0.13 mM of PRA was studied in the presence of various concentrations of Fe^{2+} at pH 3 and applying a constant current of 100 mA. The results are reported in Figure 2.

The complete disappearance of PRA was reached at 4min for catalyst concentration 0.1mM and 5min for catalyst concentrations 0.2mM and 0.5mM. The higher apparent rate constant was observed for 0.1mM (2.23 min^{-1}). In contrast, the decrease of this value was observed for 0.2mM (1.67min^{-1}) and 0.5mM (1.35 min^{-1}). This can be explained by the fact that the highest concentrations of Fe^{2+} hinder process efficiency due to the improvement in the rate of its reaction with $^{\bullet}OH$ (Reaction 7) [37] below:

$$Fe^{2+} + {}^{\bullet}OH \rightarrow Fe^{3+} + OH^- \quad (7)$$

Study of the mineralization process

The electrolysis of aqueous solutions of PRA was performed to see the evolution of the COD as a function of time and thus study the process of mineralization. Various parameters influence the effectiveness of mineralization, the most important are: pH of the solution, applied current, catalyst concentration, supporting electrolyte and temperature. Note that the optimum pH value is about 3 and the sodium sulfate is considered as the best supporting electrolyte [38-40].

Influence of applied current on the EF

Aqueous solutions of PRA were electrolyzed using 0.05 M Na_2SO_4, Fe^{2+} concentration of 0.1 mM at pH 3 and applied current range between 30mA and 300mA. The results are shown in Figure 3.

As can be seen, an increase in the current applied causes a decrease in COD values. This relation is explained by the generation of hydroxyl radicals from the Fenton reaction (reaction 2) due to increased production of H_2O_2 from reaction (1) [41-42]. The degree of reduction of PRA is 68%, 82%, 93%, 89% for 30, 60, 100 and 300mA respectively after 6 hours of treatment. The best current obtained for maximum mineralization is 100mA. By against it was observed a decrease in the efficiency of the mineralization for the 300mA, this increase of current probably leads to side reactions 4,5,6 and 7 that harm generation of Fenton's reagent.

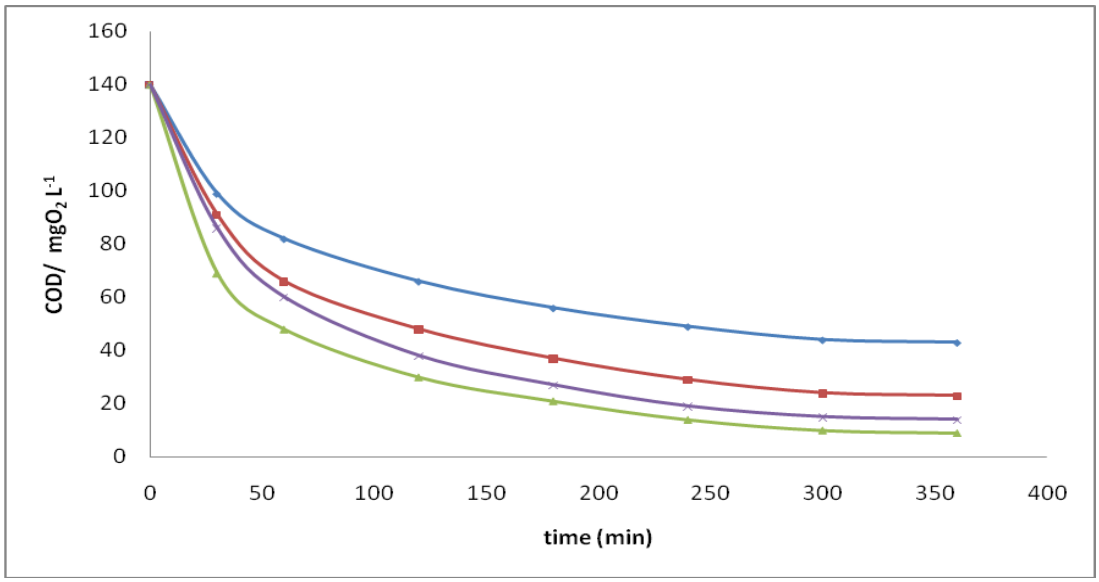


Figure 3. Removal of solution COD as a function of applied current during EF treatment on 0.13 mM PRA in 0.05 M Na_2SO_4 at pH 3 and room temperature with [Fe^{2+}] = 0.1 mM. Applied current (mA): I: 30(-♦-), 60(-▪-), 100(-▲-) 300(-×-).

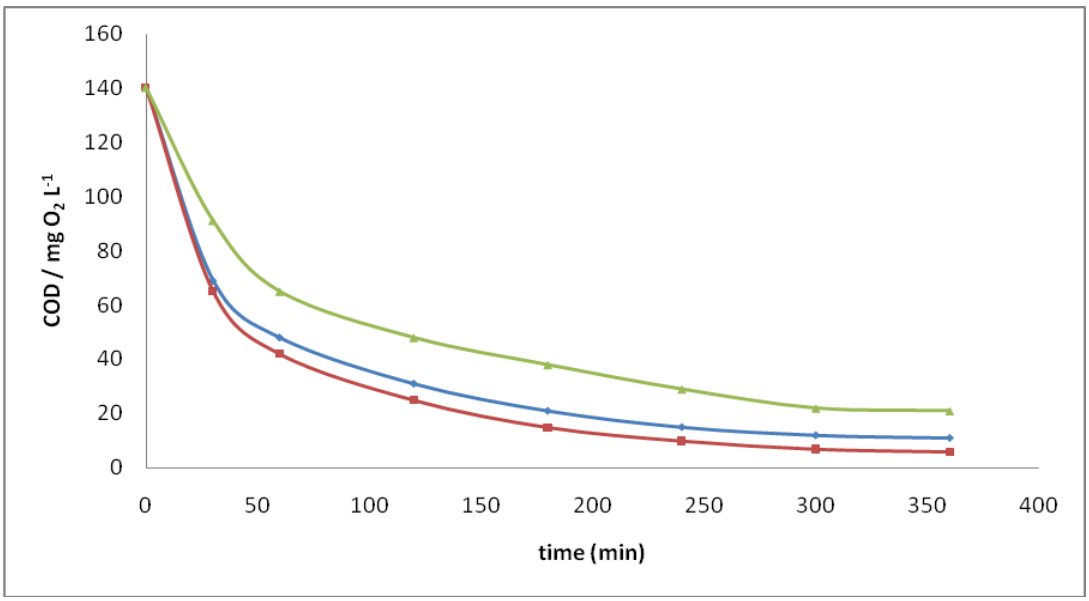


Figure 4. Removal of solution COD as a function of catalyst concentration during EF treatment of 0.13 mM PRA in 0.05 M Na_2SO_4 at pH 3 and room temperature with 100 mA. [Fe^{2+}] = 0.1 mM (-♦-); 0.2 mM (-▪-); 0.5mM (-▲-)

Influence of Fe^{2+} concentration on the EF

The catalyst concentration Fe^{2+} is another essential parameter to the Electro-Fenton. Its regulatory effect of the production of hydroxyl radicals $^{\bullet}OH$ of the reaction (2) plays an important role. The influence of this parameter on the degradation of PRA was clarified for 200ml of 0.13mM PRA solution using 0.05M Na_2SO_4 at pH 3, 100 mA and a concentration of Fe^{2+} between 0.1 and 0.5mM.

These results show the effect of Fe^{2+} concentration in COD decay. Using 0.2mM of Fe^{2+}, the oxidation of PRA was accelerated because The formation of radicals $^{\bullet}OH$ Was effective satisfactorily, by the Fenton's reaction (2) [40] Removing 95% of COD for 6h of treatment. The inhibition of the mineralization process at the higher concentration 0.5mM can be explained by the associated loss of generated $^{\bullet}OH$ with Fe^{2+} from the following parasitic reaction **7** [43]. It has been reported that an excess of ferrous ions would consume hydroxyl radicals [31,44], for this reason, no improvements have been achieved when an increase on Fe^{2+} concentration was attained, 0.5mM removing just 84.2% of COD.

Apparent Current Efficiency (ACE) is defined as the percentage of applied current utilized to reduce COD:

$$ACE\ \% = \frac{(COD_0 - COD_t)FV}{8It} \times 100$$

Where COD_0 and COD_t are the COD at times 0 and t (s), respectively, F is Faraday's constant (96,487 C mol^{-1}), V is the volume of the electrolyte (dm^3), I is the current (A), and 8 is the equivalent mass of oxygen (g. eq^{-1}).

In fact, as shown by ACE vs. time curves in Fig. 5, During the electrolytic treatment, ACE decreases over time, ACE values were the highest in the first 30 minutes with 18.31%, 10.94%, 9.51%, 2.41 % for currents 30, 60, 100, and 300mA respectively, but decreased significantly during the remainder of the electrolysis duration. This observed decrease could be explained by the decrease in the concentration of aromatic compounds in the solution and subsequently the formation of by-products that are more difficult and resistant to mineralize such as short-chain carboxylic acids, in addition to the domination of parasitic reactions (4) and (6).

Apparent current efficiency

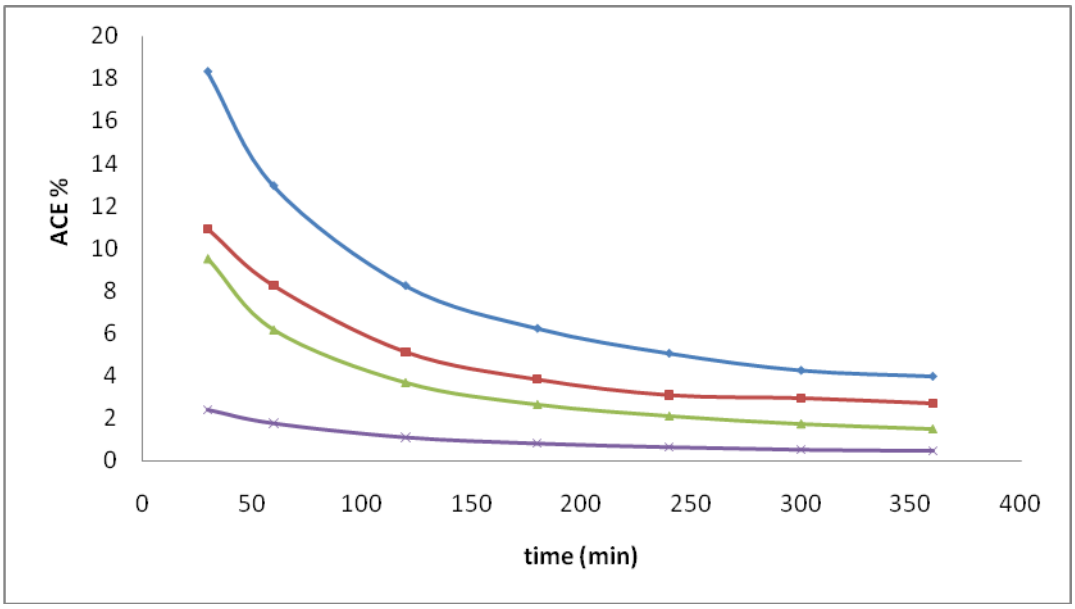


Figure 5. Evolution of ACE % during EF treatment of 0.13 Mm PRA in 0.05 mM Na_2SO_4 at pH 3 and room temperature with [Fe^{2+}] = 0.2 mM. Applied current (mA): I: 30 (-♦-), 60(-▪-), 100(-▲-) 300(-×-).

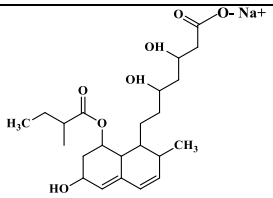
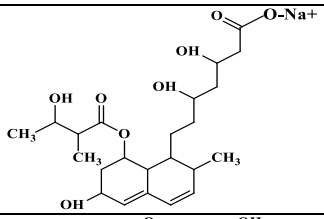
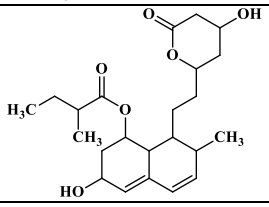
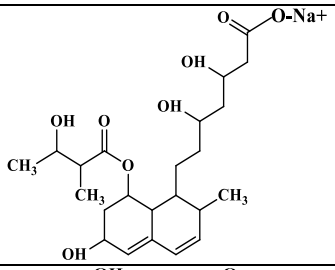
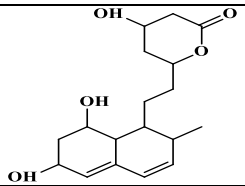
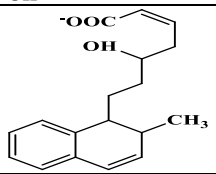
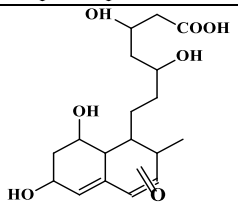
Identification of reaction intermediates

During our analysis of the samples, the first 10 minutes of the electrolysis were marked by the gradual disappearance of PRA and ROS and training of aromatic intermediates which in turn gradually disappear during the electrolysis. The optimum conditions for the electrolysis of aqueous solutions of ROS are determined according to the results obtained in the study of the degradation of this statin [17]. The intermediates obtained were identified by HPLC according to the European Pharmacopoeia 7.1 and LC/MS. Tables 2 and 3 summarizes the name, molecular formula and characteristics of the identified intermediaries and their HPLC chromatorgrams and mass spectra are given in Figures SI-1, SI-2, SI-3, SI-4 (Supplementary Information at the end).

It should be noted that the pathway of the intermediate products obtained in Tables 2 and 3 formed by the oxidative degradation is illustrated in

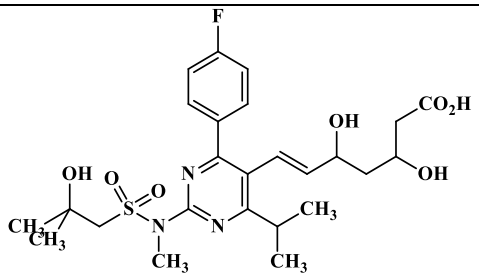
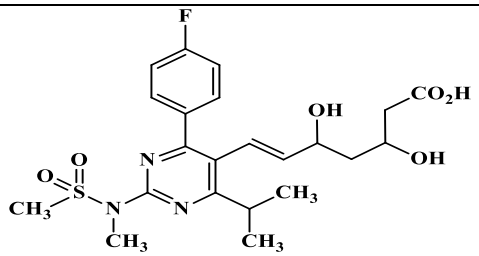
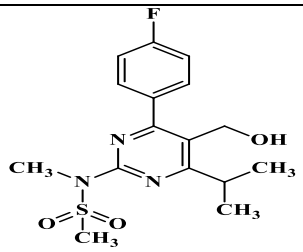
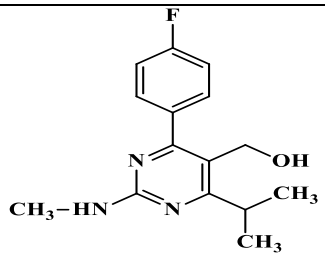
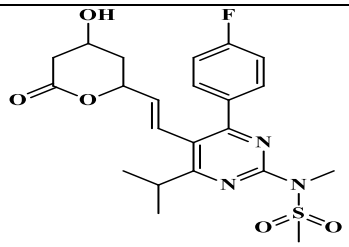
the overall diagram of the elimination of the two statins in the Figures 6 and 7. It comprises two stages; the first step is characterized by the degradation of the product in aromatic intermediates by $^{\bullet}OH$, followed by the second stage characterized by the presence of aliphatic intermediates which continue to degrade by the attack of the $^{\bullet}OH$ until the total mineralization ($H_2O + CO_2$).

Table 2. Intermediate products identified using HPLC and LC-MS during the degradation of PRA by EF treatment.

Intermediates compounds	**T_R (min)**	**m/z**	**Chemical formula**
Compound A [a]	**11.16**	**446**	
Compound B [a,b,c]	**3.38**	**439**	
Compound D [a ,b,c]	**34.21**	**406**	
Compound E [a,b,c]	**5.57**	**439**	
1 [d]	**-**	**320**	
2 [e]	**-**	**284.9**	
3 [d]	**-**	**354**	

Notes: a = Obtained by HPLC retention time in agreement with method European Pharmacopoeia 7.1
b = Obtained by LC/MS in agreement with data reported in S.L. Syed et J. Siji [45]
c = Obtained by LC/MS in agreement with data reported in S.L. Syed [46]
d = Obtained by LC/MS in agreement with data reported in B. Ravazi B et al.[47]
e = Obtained by LC/MS in agreement with data reported in A. Kocijan A et al.[48]

Table 3. Intermediate products identified using HPLC and LC-MS during the degradation of ROS by EF treatment.

Intermediates compounds	T_R (min)	m/z	Chemical formula
Compound A [f]	48	539.62	
Compound B [f,g]	56	482.15	
4 [g,h]	-	352.13	
5 [g,h]	-	274.16	
6 [i]	-	462.15	

Notes: f = Obtained by HPLC retention time in agreement with method European Pharmacopoeia 7.1
g = Obtained by LC/MS in agreement with data reported in T.C. Machado et al.[49]
h = Obtained by LC/MS in agreement with data reported in J. Segalin et al. [50]
i = Obtained by LC/MS in agreement with data reported in S. Sulaiman et al. [51]

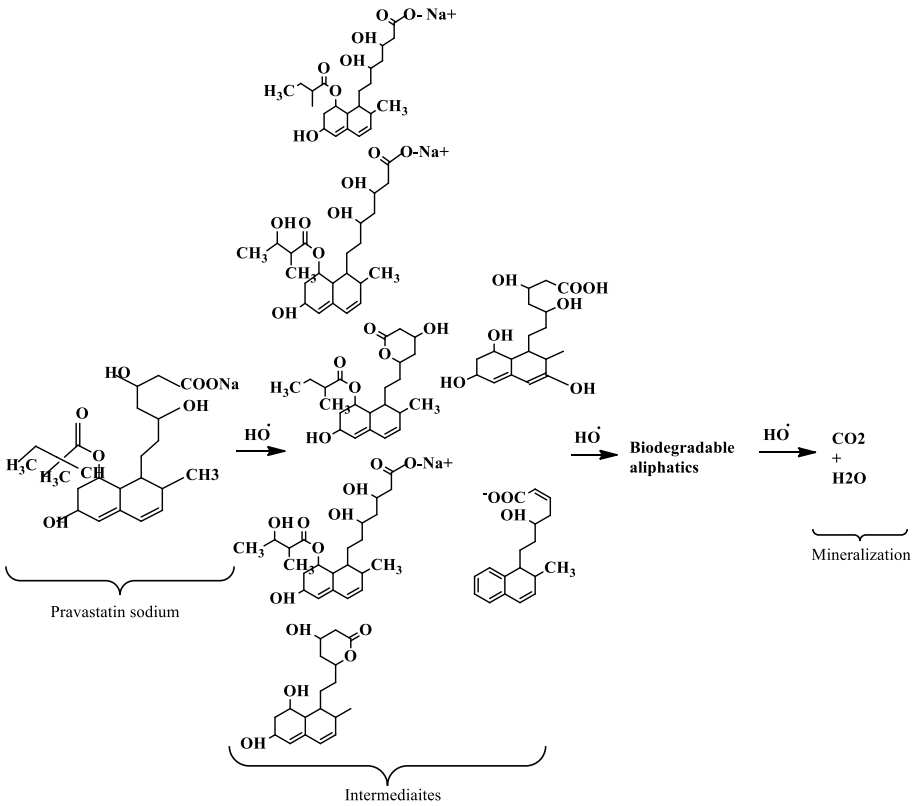


Figure 6. Global diagram of degradation/mineralization of pravastatin in an aqueous medium using the EF process. Optimal conditions (100 mA, $[Fe^{2+}]$ = 0.1 mM

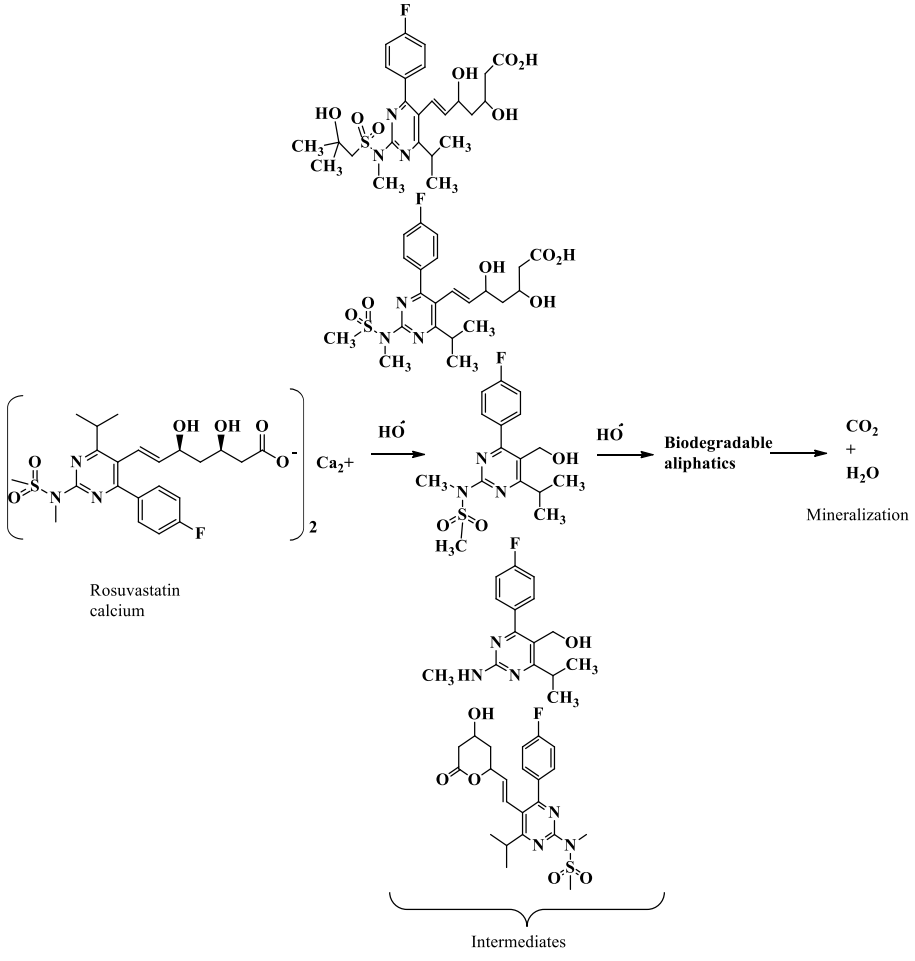


Figure 7. Global diagram of degradation/mineralization of rosuvastatin in an aqueous medium using the EF process. Optimal conditions (300 mA, $[Fe^{3+}]$ = 0.1 mM)

Biodegradability assays and Study of feasibility of the coupling EF with the biological treatment

The biodegradability was characterized by the ratio between Biochemical Oxygen Demand at 5 days (BOD_5) and COD [52]. This ratio must be greater than 0.4 to consider that the solution is easily biodegradable [53]. All the bottles containing the solutions were equipped with a rubber sleeve in which 3 to 4 drops of KOH solution were added to trap the CO_2 formed during biodegradation. This generates a decrease in pressure within the system. The samples were incubated at 20 °C during 5 days in dark conditions.

Although biological treatment is an economically profitable process, its effectiveness is limited by recalcitrant organic compounds and the time required when a long period of acclimation is required. On the other hand, during the mineralization of the recalcitrant organic compounds by electro-Fenton process, the electrical energy consumption and relatively the cost of treatment are even higher than the electrolysis time is quite long. Therefore, the coupling of these two methods allows an effective and less expensive treatment.

The coupling of an advanced oxidation process such as EF to a biological treatment is particularly recommended to improve the biodegradability of a substrate [54,55]. Several studies have confirmed the efficacity of this combination in the elimination of recalcitrant organic compounds [56,57].

- **Case of PRA**

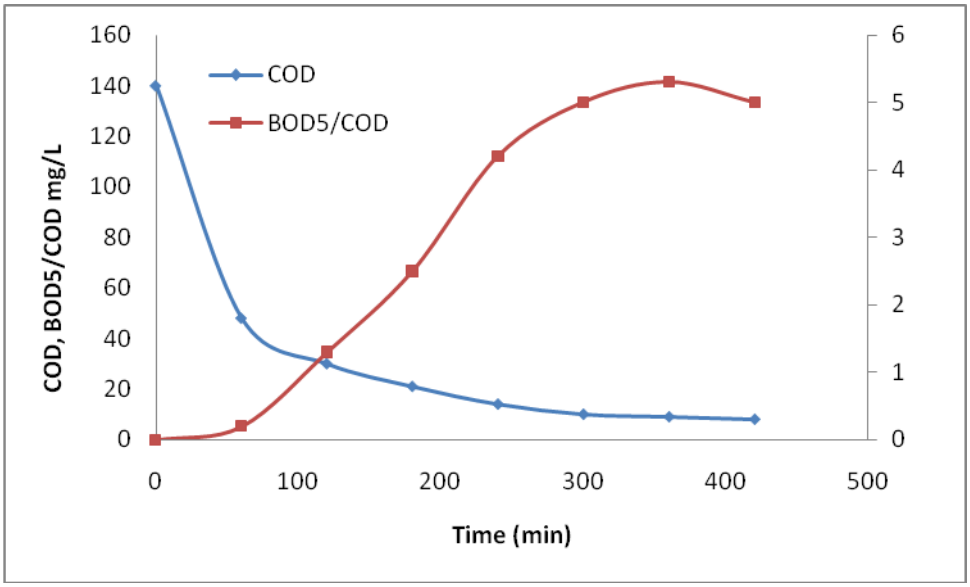


Figure 8. Evolution of BOD_5/COD ratio and COD abatement rate during the treatment of PRA (I= 100mA, $[Fe^{2+}]$ = 0.1 Mm)

Exploitation of the results shows that the untreated solutions of PRA are non-biodegradable due to the BOD_5/COD ratio that tends to 0 and that the biodegradability of PRA increases as the COD decreases at different times during 7 hours of preprocessing (420 min).

After 60 minutes of electrolysis, the biodegradability is still limited since the ratio BOD5/COD is equal to 0.2. This behavior is mainly due to the total disappearance of PRA and the formation of aromatic intermediates characterized by their toxicity and low biodegradability.

At 120 min, the ratio BOD5/COD increases to 1.3, this is explained by the formation of readily biodegradable substances such as aliphatic molecules, following the opening of aromatic rings by oxidation reactions.

Finally, from 120 min to 420 min, the oxidation reactions continue in the medium and consequently improve the biodegradability to 5.3.

According to the results noted previously, it was found that the PRA is non-biodegradable and its total disappearance of the aqueous solutions is after 4 min of electrolysis by EF (Fig. 1), giving rise to aromatic products still non-biodegradable (Table 3) but which can be transformed into biodegradable aliphatic intermediates as the oxidation by $^{\bullet}OH$ continues. It should also be noted that the mineralization of solutions of PRA gave an abatement rate equal to 78% after 2 hours of treatment while the remaining 22% requested a longer time (5 hours) to reach complete mineralization. explaining the presence of aliphatic products characterized by their resistance to the mineralization by $^{\bullet}OH$, thus requiring a large energy consumption.

For this purpose, it implies that EF tends to improve the biodegradability of PRA solutions and could be used as a pretreatment step for biological treatment for 2 hours.

- **Case of ROS**

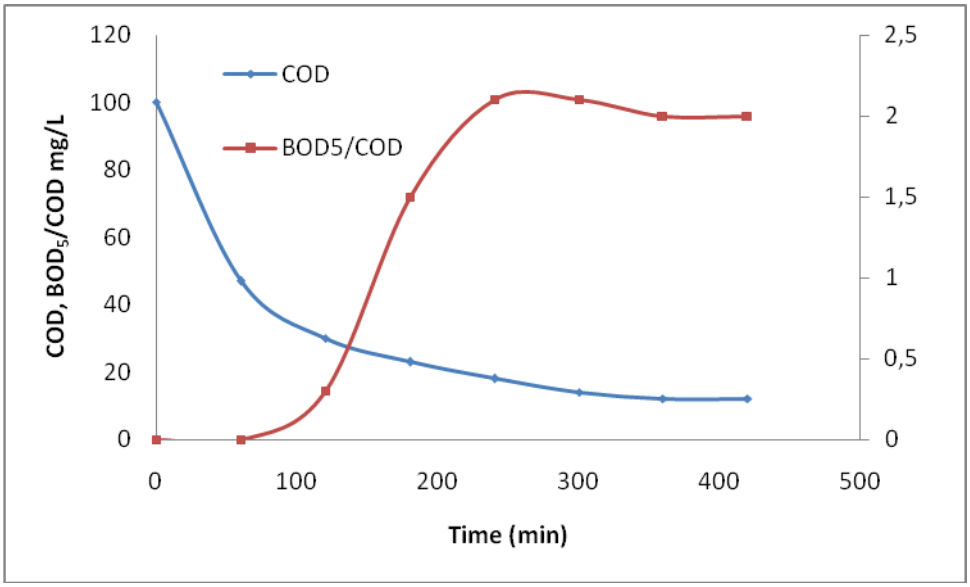


Figure 9. Evolution of BOD_5/COD ratio and COD abatement rate during the treatment of ROS (I=300mA, $[Fe^{2+}]$ = 0.2 Mm)

According to the results, the ROS solution is non-biodegradable at the beginning and at 60 min of the electrolysis with a BOD_5 / COD ratio equal to 0. A very slight increase of the biodegradability was observed after 120 min of the electrolysis with a BOD5 / COD ratio of 0.3, thus showing that the primary and aromatic by-products are relatively resistant to microorganisms. However, an easily biodegradable solution was obtained with a ratio of 1.5 after 180 min, this can be explained by the transformation of the aromatic intermediates into biodegradable aliphatic products following oxidation by the hydroxyl radicals generated.

On the other hand, the mineralization rate of the ROS solutions reached 77% after 3 hours of treatment, while the remaining 23% mineralized completely after 4 hours of electrolysis because of the difficulty of oxidizing the by-products. aliphatic by $^{\bullet}OH$, resulting in a high consumption of unnecessary energy that can be avoided by involving biological treatment after 3 hours of EF electrolysis.

Conclusion

In this study, we employed Electro-Fenton process to oxidize PRA, the experiments were performed using cells with a carbon felt cathode and Pt anode. They show that Fe^{2+} and applied current have an important effect in EF. The degradation of this statin followed pseudo-first order reaction kinetics. The highest COD removal was achieved when a current of 100 mA is applied in the presence of 0.2 mM Fe^{2+} at 5h of treatment. A number of stable intermediate products have been identified for PRA and ROS using HPLC and LC-MS analyses. Biodegradability tests shows that the relevance of EF pretreatment has been confirmed and electrolysis of 180 min of the ROS solution and 120 min of the PRA solution is required for efficient biological treatment.

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SUPPLEMENTAY INFORMATION

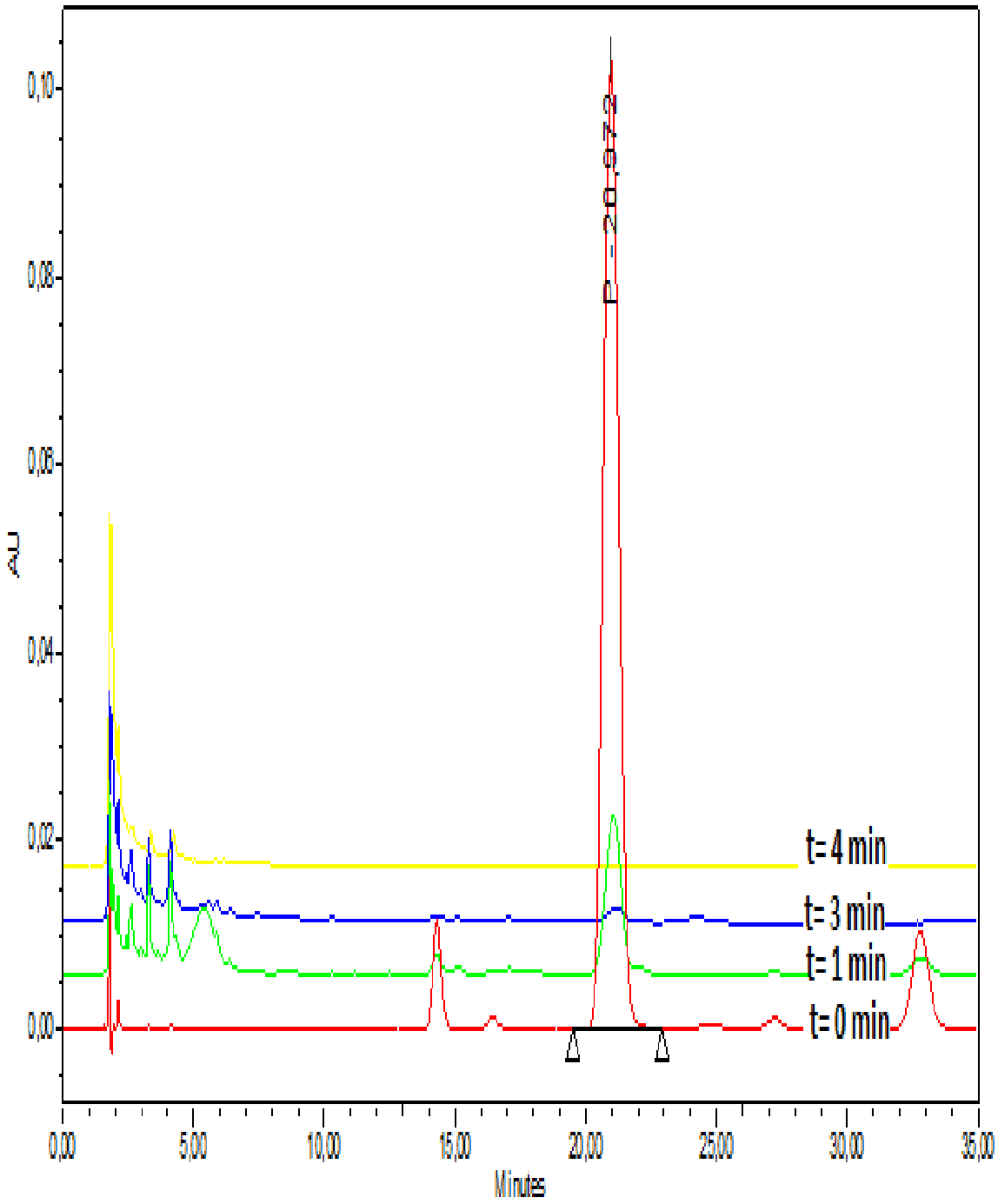

Figure SI-1. Chromatograms showing the decrease of the existence of pravastatin in the solution during the first 5 min of treatment by electro-Fenton process. [Fe^{2+}]= 0.1 mM, I = 100 mA, [Na_2SO_4] = 0.05 M, V = 200 ml.

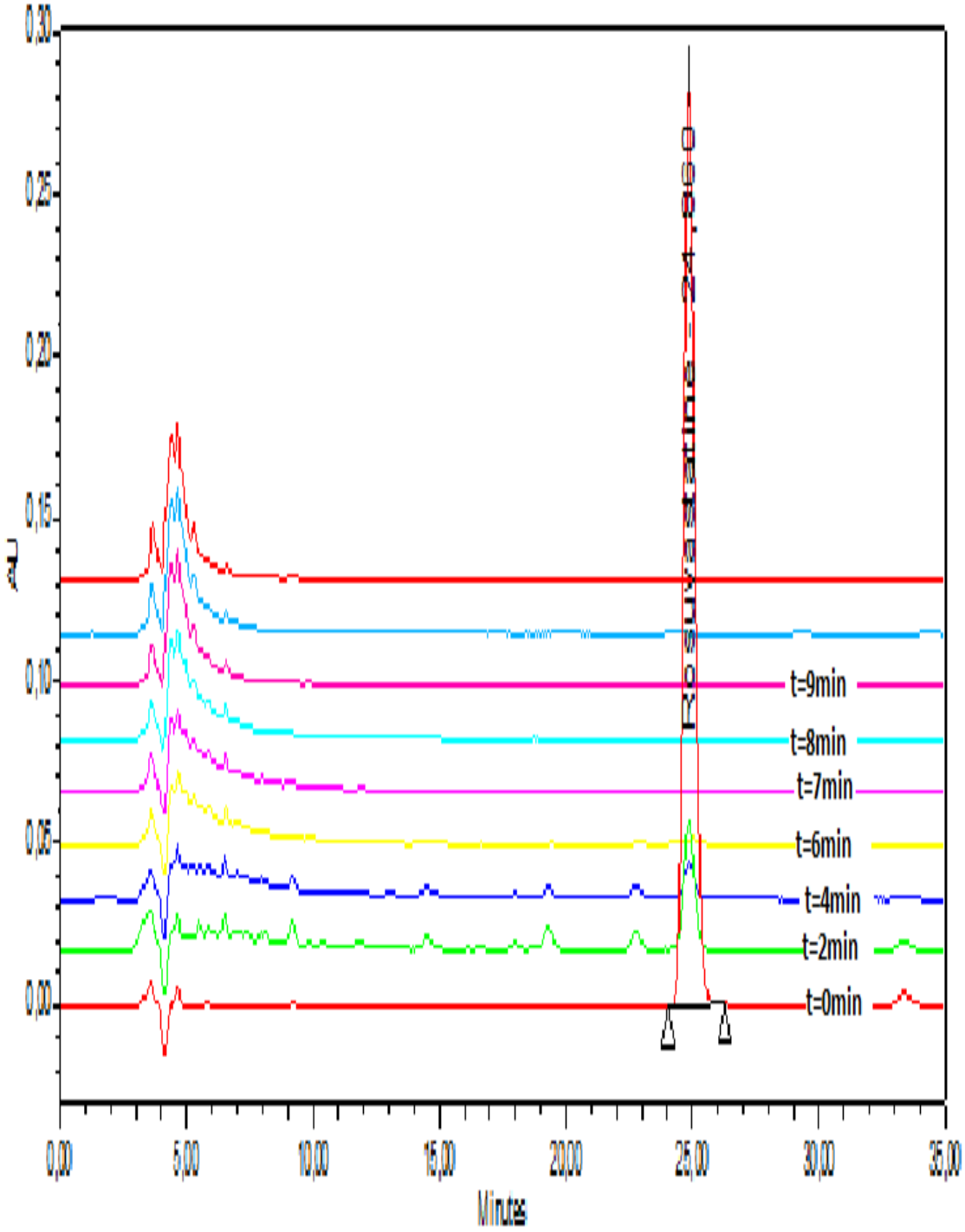

Figure SI-2. Chromatograms showing the decrease of the existence of rosuvastatin in the solution during the first 15 min of treatment by electro-Fenton process. $[Fe^{2+}]$= 0.1 mM, I = 300 mA, $[Na_2SO_4]$ = 0.05 M, V = 200 ml

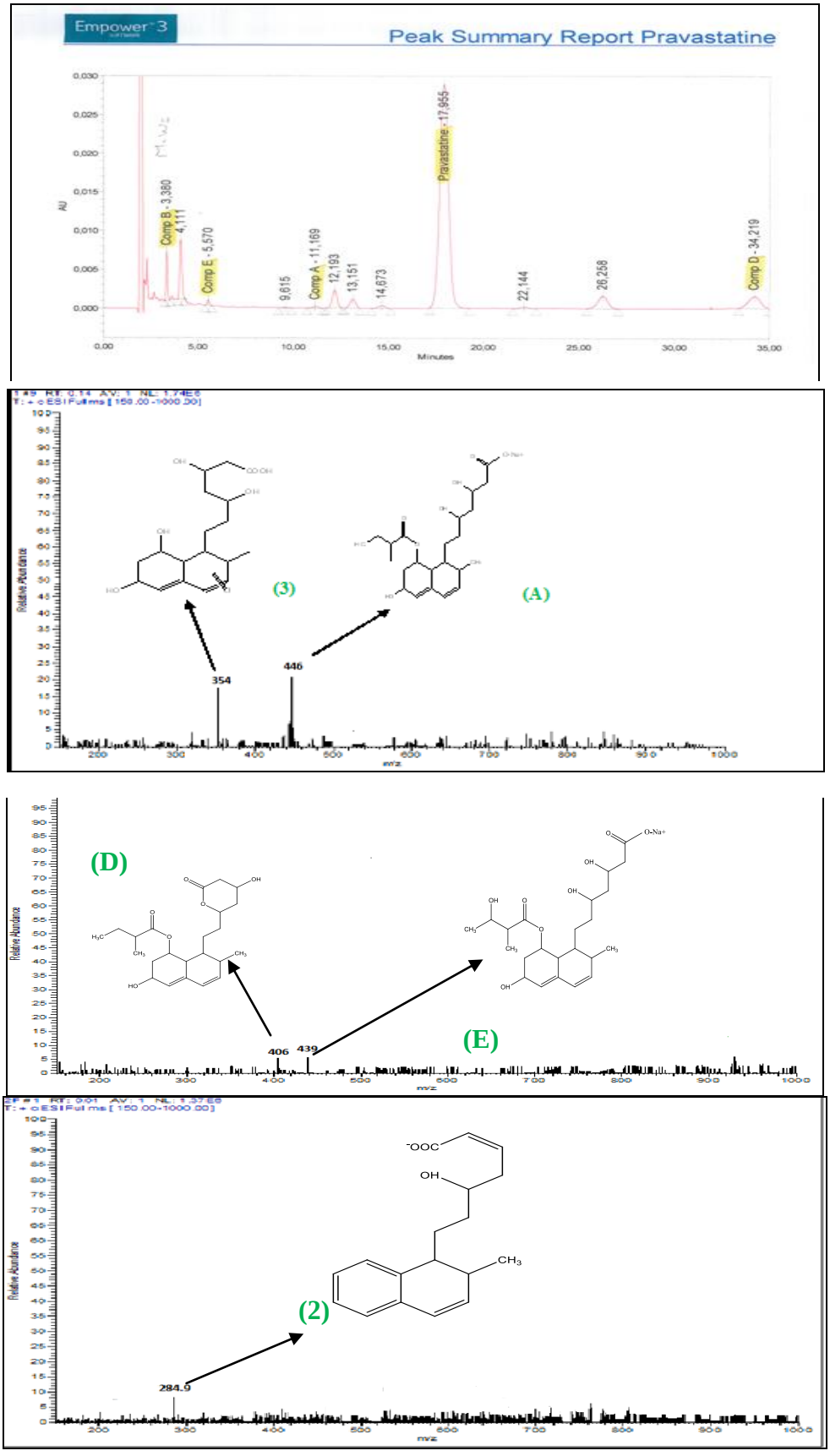

Figure SI-3. (A, B, D, E,1,2) HPLC chromatogram and Mass spectra of intermediate products present in the solution during 1 h of mineralization by electro-Fenton process of PRA. [Fe^{2+}] = 0.1 mM, I = 100 mA,

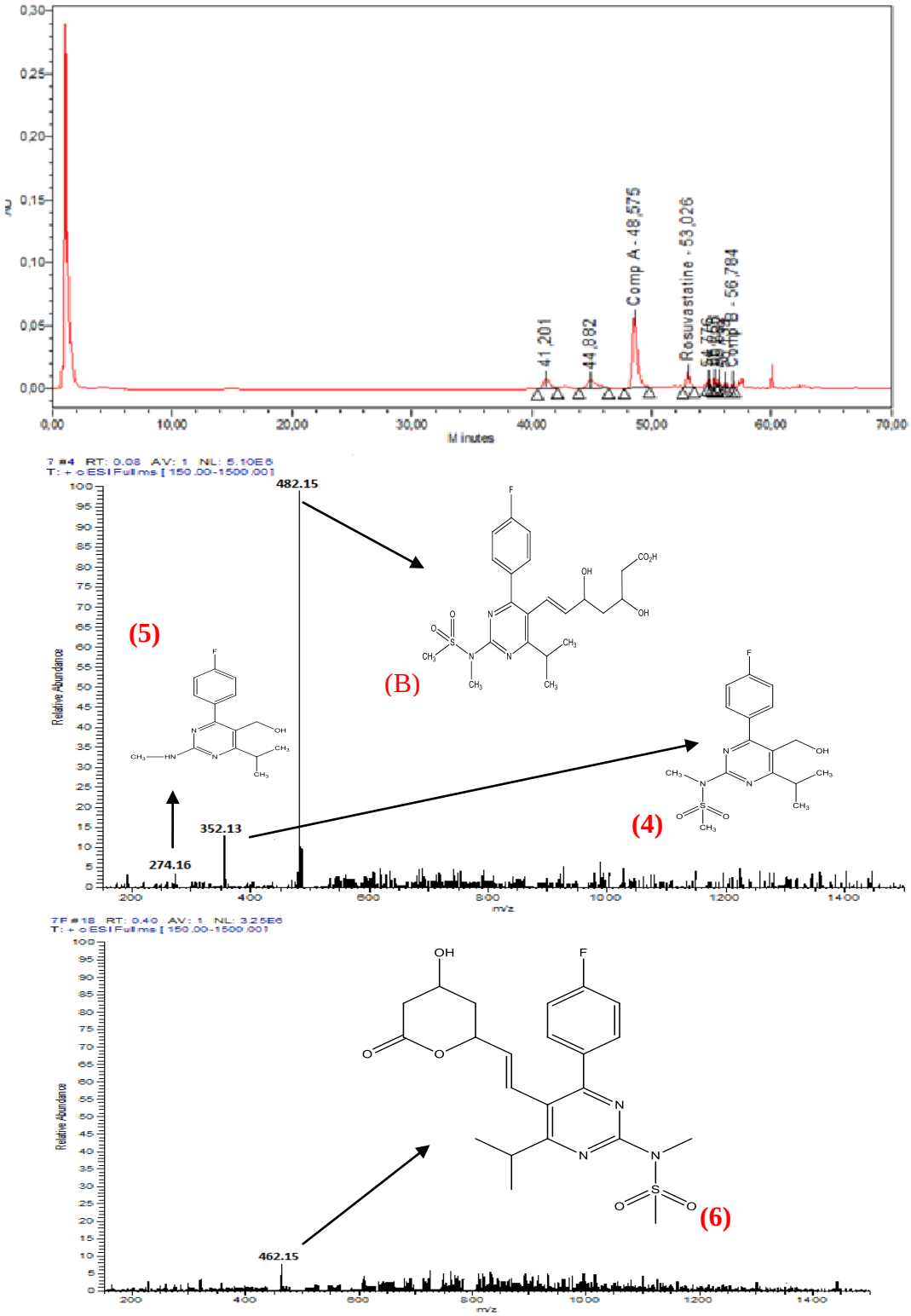

Figure SI-4. (A, B, 4,5,6) HPLC chromatogram and Mass spectra of intermediate products present in the solution during 1 h of mineralization by electro-Fenton process of ROS. [Fe^{2+}] = 0.1 mM, I = 300 mA,