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Rapid communication

Corrosion inhibitors from expired drugs

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ABSTRACT

This paper presents a method of expired or unused drugs valorization as corrosion inhibitors for metals in various media. Cyclic voltammograms were drawn on platinum in order to assess the stability of pharmaceutically active substances from drugs at the metal–corrosive environment interface. Tafel slope method was used to determine corrosion rates of steel in the absence and presence of inhibitors. Expired Carbamazepine and Paracetamol tablets were used to obtain corrosion inhibitors. For the former, the corrosion inhibition of carbon steel in 0.1 mol L^{-1} sulfuric acid solution was about 90%, whereas for the latter, the corrosion inhibition efficiency of the same material in the 0.25 mol L^{-1} acetic acid–0.25 mol L^{-1} sodium acetate buffer solution was about 85%.

1. Introduction

One of the most common types of corrosion inhibitors for metals and their alloys are adsorption inhibitors. They are generally organic compounds containing N, O, S heteroatoms or structures containing π electrons in their molecules (Rohwerder et al., 2002; Schweitzer, 2010). By adsorption on the metal surface, the organic molecules form a protective layer that prevents diffusion of the chemical species involved in the ionization of the metal. Adsorption of such compounds is achieved due to interactions between metal (low unoccupied molecular orbitals – LUMO) and non-participant electrons of heteroatoms or π electrons (high occupied molecular orbitals – HOMO) (Bockris and Reddy, 2004).

The research performed mainly in the past years identified numerous active drug components that fulfill the above-mentioned conditions, thus showing inhibitory activity on the corrosion of metals and alloys (Abdallah, 2004; Arslan et al., 2009; Tamborin et al., 2011; Xuehui et al., 2010). In a recent review, Gece has identified 17 classes of drugs that can be used as corrosion inhibitors for various metals and alloys (carbon steel and stainless steel, Al and Al alloys, Cu, Zn, Ti), in various corrosive environments (solutions of HCl, H_2SO_4, H_3PO_4, NaCl) (Gece, 2011).

Most of the pharmaceutical active substances are far more expensive than the organic inhibitors currently implemented. Therefore, our study was focused on the usage of expired drugs or unused drugs because of patient's non-compliance that contain in their composition active substances with inhibitory properties. This method of unused medicines valorization can solve two major environmental and economical problems: limitation of environmental pollution with pharmaceutically active compounds and reduction of the disposal costs of expired drugs.

On the one hand, releasing even a small amount of unused drugs in the environment is a risk for humans as well as for aquatic and terrestrial eco-systems (Ruhoy and Daughton, 2007; Patwary et al., 2011; Kotchen et al., 2009; Feitosa-Felizzola and Chiron, 2009; Schlüsener and Bester, 2006; Bound and Voulvoulis, 2006; Kümmerer and Hempel, 2010; Khetan and Collins, 2007). On the other hand, neutralization of unused drugs is generally performed by incineration with the risk of polluting the atmosphere with toxic compounds containing N, S, P or halogen atoms.

In most cases expired drugs can be tested as corrosion inhibitors, whereas the active substance degrades only infinitesimally. An important proof in this respect is the study requested by the Pentagon and conducted by the FDA in 1985, to determine whether the massive drug stock of the U.S. Army became ineffective. The results showed that 90% of the drugs maintained stability long time after the expiration dates (Gebhart, 2005).

It is necessary to take into account that pharmaceutical dosage forms of drugs contain frequently several active compounds, but also a number of excipients designed to ensure stability and bioavailability. Currently, in the pharmaceutical industry, hundreds of excipients are used (Rowe et al., 2006). Under these circumstances, the nature and sequence of operations for inhibitors formulation is customized according to the products composition. During the

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process of the corrosion inhibitors formulation a large number of excipients may be separated by a simple operation, settling or filtration, due to solubility differences between active substance and excipients. In the study of the inhibitory effect of drugs, it is necessary to take into consideration the possible chemical reactions of the pharmaceutically active compound in the corrosive environment. In this respect, a common example is that of aspirin in corrosive aqueous solution, which hydrolyses into salicylic acid and acetic acid. The metal corrosion inhibition in this case is given by the mixed effect of hydrolysis products. Furthermore, synergistic effects must be taken into account when drugs contain several active substances.

Following the foregoing arguments and in order to illustrate the proper approach for obtaining the corrosion inhibitors from expired drugs, our experimental study has been focused on two common drugs: Carbamazepine (active substance 5*H*-dibenz[*b*,*f*]azepine-5-carboxamide) and Paracetamol (active substance *N*-acetyl-4-aminophenol), produced and used in large amounts, for a wide range of diseases.

2. Materials and methods

Carbamazepine tablets and Paracetamol tablets expired for about 12 months have been tested.

In order to study the electrochemical behavior of active substances carbamazepine standard (Sigma, 98% HPLC purity) and *N*-acetyl-4-aminofenol (Fluka, 98% HPLC purity) have been used. Test solutions for the corrosion rate evaluation of carbon steel were prepared starting from sulfuric acid p.a. (Merck, 95–97%), glacial acetic acid p.a. (Fluka, 99.8%) and sodium acetate p.a. (Fluka, 99%), and the effect of active substances on the corrosion rate has been tested on carbon steel with the following composition of main elements: Fe, 95.79%; C, 0.413%; Cu, 0.181%; Ni, 0.242%; Mn, 0.975%; Cr, 1.004; Si, 1.37%. Test media were as follows: 0.1 mol L^{-1} H_2SO_4 solution and 0.25 mol L^{-1} acetic acid–0.25 mol L^{-1} sodium acetate buffer solution.

The electrochemical behavior of the active substances was investigated by cyclic voltammetry and Tafel slope method was used to determine corrosion rates. In order to extend the potential range of the electrochemical characterization, the cyclic voltammograms were drawn on platinum electrode. The electrochemical experiments were carried out using an AUTOLAB Potentiostat/Galvanostat PGSTAT 302N, in a thermostated 100 mL cell with three electrodes assembly, at 25 °C, controlled by an ultrathermostat. Platinum and carbon steel specimens with 1 cm^2 exposed area were used for electrochemical measurements as working electrode, a Ag/AgCl as reference electrode and two graphite rods as counter electrodes. Working electrodes were polished, washed and ultrasonicated in distilled water for 3 min. Prior to each experiment, solutions were degassed with high purity nitrogen, and a nitrogen blanket was kept above the solution during measurements. Potentiodynamic polarization curves were obtained with a scan rate of 100 mV s^{-1} for cyclic voltammograms and 1 mV s^{-1} for Tafel slope curves in the potential range of −250 to +250 mV relative to the corrosion potential. Several runs were performed for each set of experiments in order to obtain reproductive results. Corrosion currents and rates were determined using GPES AUTOLAB software.

3. Results and discussion

In addition to the stability in the environment they are used in, another condition that corrosion inhibitors have to accomplish is the stability at the metal–solution interface in the corrosion potential domain. The stability of corrosion inhibitors and their electrochemical behavior at the metal–test solution interface is revealed by cyclic voltammetry. To avoid interferences with the corrosion processes taking place at the steel–solution interface and in order to extend the potential domain, polarization curves were drawn on a platinum electrode, in basic solution, as well as in the presence of inhibitors. Since carbamazepine is less soluble in water, a solution of 0.1 mol L^{-1} H_2SO_4 saturated with carbamazepine was prepared. Fig. 1 shows the polarization curve drawn on the platinum electrode in 0.1 mol L^{-1} H_2SO_4 solution and in 0.1 mol L^{-1} H_2SO_4 solution saturated with carbamazepine.

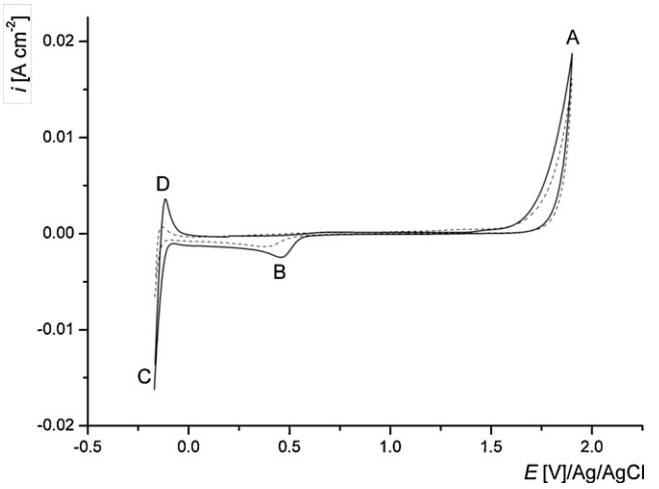

Fig. 1. Cyclic voltammograms on Pt in 0.1 mol L^{-1} H_2SO_4 (solid line) and in 0.1 mol L^{-1} H_2SO_4 saturated with carbamazepine (dashed line); scan rate: 100 mV s^{-1}.

As depicted in Fig. 1, carbamazepine does not undergo major changes. Branch A of the curve corresponds to the oxygen evolution, peak B to oxygen reduction, and branch C to the hydrogen evolution, while peak D is attributed to the oxidation of adsorbed hydrogen. Accordingly, carbamazepine is stable in the range of carbon steel corrosion potential. Electrode processes are inhibited due to the adsorption of the organic compound on the working electrodes surface.

To test carbamazepine as corrosion inhibitor expired pills were grinded and dissolved in absolute alcohol, in order to obtain a 0.1 mol L^{-1} solution. The resulting solution was filtered to remove insoluble excipients (colloidal silicon dioxide, magnesium stearate, starch, polyethilenglicol, etc.). Polyethylene glycol, possible excipient, remained in solution, possesses inhibitory activity on the corrosion process of carbon steel in sulfuric acid (Ashassi-Sorkhabi and Ghalebsaz-Jeddi, 2005). Starting from the above solution, 0.1 mol L^{-1} H_2SO_4 with 5×10^{-3} mol L^{-1} carbamazepine test solution was prepared.

The inhibitory effect of carbamazepine was studied by means of Tafel polarization method, determining the corrosion rates in 0.1 mol L^{-1} H_2SO_4 solution and in 0.1 mol L^{-1} H_2SO_4 with carbamazepine. Tafel polarization curves for the steel sample in 0.1 mol L^{-1} H_2SO_4 solution without (curve A) and with carbamazepine (curve B) are shown in Fig. 2.

Tafel slopes emphasize that carbamazepine affects both the cathodic hydrogen evolution and the anodic process of iron ionization, consequently the corrosion potential does not shift significantly when carbamazepine was added. Corrosion currents determined from the Tafel slopes, are: 1.58×10^{-4} A cm^{-2} in 0.1 mol L^{-1} H_2SO_4 solution and 1.59×10^{-5} A cm^{-2} in 0.1 mol L^{-1} H_2SO_4 solution with carbamazepine, which correspond to corrosion rates of 1.8 mm/year and 0.19 mm/year, respectively.

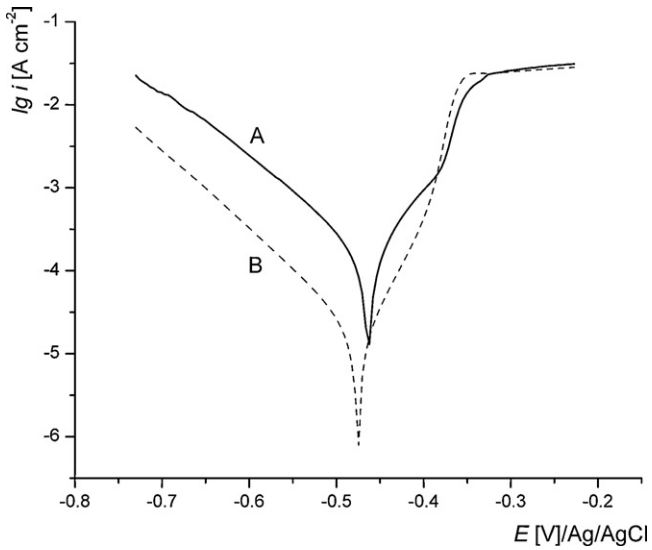

Fig. 2. Tafel polarization curve for carbon steel in 0.1 mol L^{-1} H_2SO_4 solution without (curve A) and with carbamazepine (curve B).

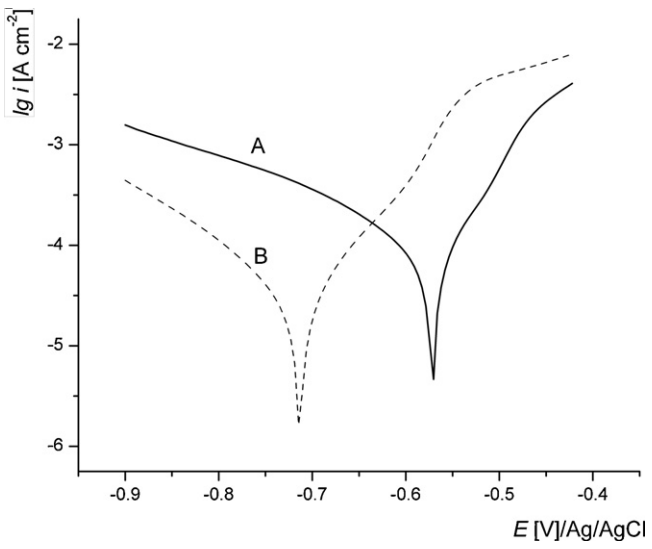

Fig. 4. Tafel polarization slope for carbon steel in acetic acid-sodium acetate buffer solution without (curve A) and with paracetamol (curve B).

Inhibition efficiency of carbamazepine is calculated with the following relation (Sastri, 2001):

$$IE\ \ (\%) = \left(\frac{i_{corr} - i'_{corr}}{i_{corr}}\right) \times 100 \qquad (1)$$

where i_{corr} and i'_{corr} are the corrosion current or rate in the absence and in the presence of the inhibitor, respectively.

For carbamazepine, the inhibition efficiency is about 90%.

The inhibitory properties of *N*-acetyl-4-aminofenol were tested in acetic acid 0.25 mol L^{-1}–sodium acetate 0.25 mol L^{-1} buffer solution in order to avoid the hydrolysis to 4-aminophenol and acetic acid. Fig. 3 shows polarization curves on Pt in acetic acid–sodium acetate buffer solution with and without addition of *N*-acetyl-4-aminophenol standard.

The cyclic voltammograms depict the anodic A and cathodic C domain, corresponding to oxygen and hydrogen evolution reaction, respectively. Peaks B and D are assigned to oxygen reduction and hydrogen oxidation, respectively. The addition of *N*-acetyl-4-aminophenol leads to the appearance of E and F peaks due to the partial oxidation processes of the active substance. It may be noted that *N*-acetyl-4-aminophenol is not active in a wide range of potential, and it is resistant to oxidation in the studied solution up to +0.5 V/Ag-AgCl. During the corrosion rate measurements the potential does not exceed the value of 0.25 V/Ag-AgCl.

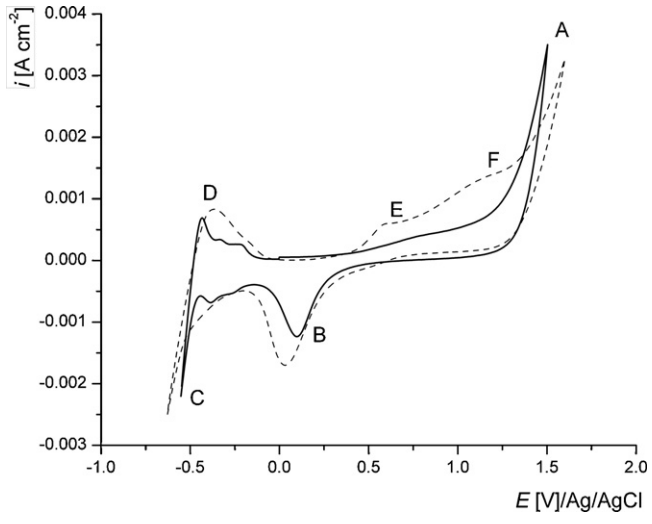

Fig. 3. Cyclic voltammograms on Pt in acetic acid–sodium acetate buffer solution: without (solid line) and with *N*-acetyl-4-aminophenol 0.01 mol L^{-1} (dashed line).

In order to test the inhibitory effect of Paracetamol, expired pills were grinded and dissolved in acetic acid 0.25 mol L^{-1}–sodium acetate 0.25 mol L^{-1} buffer solution. The insoluble excipients were removed by filtration. Fig. 4 shows Tafel polarization slopes for carbon steel in acetic acid–sodium acetate buffer solution and emphasizes the influence of paracetamol on the cathodic process of hydrogen evolution, significantly shifting the corrosion potential towards more negative values.

Corrosion current densities obtained from Tafel slopes were 6.49×10^{-5} A cm^{-2} for the buffer solution without inhibitor and 9.65×10^{-5} A cm^{-2}, in the same solution in the presence of inhibitor. Hence, corrosion rates were 0.73 mm/year for the solution without inhibitor and 0.11 mm/year in the solution with inhibitor, respectively. Thereby, the inhibiting efficiency, calculated using relation (1), is about 85%.

4. Conclusions

The present paper showed that an optimal formulation with corrosion inhibiting properties for metals or alloys can be identified by means of a suitable approach for each drug. Thus, when Carbamazepine was used as corrosion inhibitor for carbon steel, the inhibition efficiency went up to 90% in strong acid medium, while Paracetamol reported an efficiency of about 85% when tested as corrosion inhibitor for carbon steel in weak acid environment.

It is expected that not all active substances from drugs possess inhibitory properties in the corrosion process of metals. In this respect, it is known that some organic compounds containing the amino group can be corrosion accelerators due to the catalytic effect in the hydrogen evolution reaction (Vaduva et al., 2011), connected with the anodic ionization of iron. On the other hand, the active substance must be stable at the metal–corrosive solution interface, and therefore the study of the electrochemical behavior by cyclic voltammetry is strongly recommended.

The development of various ways to collect unused drugs, currently promoted only as an action to limit environmental pollution, supports their valorization also as corrosion inhibitors.

A systematic study on available unused drug classes is necessary to get a complete image of the possibilities to obtain corrosion inhibitors and to determine the most suitable

formulation approach. Moreover, it is mandatory to mention that inhibitors obtained from unused drugs could be applied in: water cooling systems, deicing solutions for aircraft, airports, ways, etching and degreasing solutions, oil pipelines, paints and coatings, inhibitors for concrete, fuels and lubricants, metal processing solutions.

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