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ELECTROCHEMICAL STUDIES USING ACTIVATED GLASSY CARBON. I. MELOXICAM

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The meloxicam was investigated in water-methanol solution by using cyclic voltammetry (CV) at anodically activated GCE. Two different times for application of the anodic activation electrode potential were used and six different times for application of three different accumulation electrode potentials were used in each case in order to obtain better cyclic voltammetric behaviour of meloxicam in comparison with that at inactivated GCE. It results an enhancement of the electron transfer ability to anodically activated GCE surface leading to a better electrochemical response (much better defined and more stable peak currents) regarding both peak current heights, which are higher, and peak potentials, which are anticipated, in comparison with the behaviour of meloxicam at inactivated bare GCE. The peak current ratio, defined as $r_{pa} \quad \frac{I_{pa,act}}{I_{pa,inact}}$, increases with increasing accumulation time for each activation potential used and for each accumulation electrode potential used. A change in the electrode mechanism from diffusion control (at bare GCE) to adsorption control (at anodically activated GCE) occurs.

INTRODUCTION

Oxicams as meloxicam, piroxicam and tenoxicam are enolic acid derivatives belonging to the non-steriodal anti-inflammatory drugs. These drugs have diverse chemical structures and different therapeutic activities but three common features: identical basic pharmaceutical properties, similar mechanism of action, and similar adverse effects.[1,2] They exhibit acidic properties due to their enolic structure with pK_a in the range of medium acidic strength (3-5). The enolic structure is preferred due to the greater extent of conjugation.[3] In the gastric juice they act in their protonated form but in the plasma they are highly ionized due to their amphiphilic properties.

Oxicams derive from benzene(thieno)thiazine heterocyclic system, where the group of N-heterocyclic carboxamide includes the triazine sulphur, and in position 4 there is an enolic group. Condensation of benzene ring or thiophene ring with the heterocyclic system as well as substitution of the amide group in position 3 imparts acidic properties to the enolic group. For their redox properties, amide and enol groups seem to be responsible.[4] Usually, the oxicams were studied by using especially polarographic methods in their different variants[5-8] or at GCE.[4] The aim of this study was to obtain a better cyclic voltammetric behaviour of meloxicam at anodically activated GCE in comparison with that at inactivated bare GCE by using the same activation potential at different activation times and different accumulation potentials at different accumulation times.

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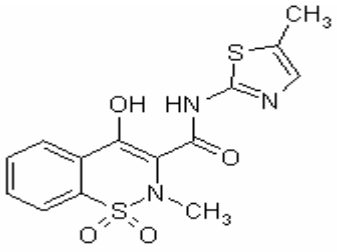

Fig. 1 – Meloxicam structure.

EXPERIMENTAL

Apparatus: Electrochemical experiments were carried out using the potentiostat-galvanostat system AutoLab PGStat 12, controlled by General Purpose Electrochemical System (GPES) electrochemical interface for Windows (version 4.9.007). Three electrodes in one-compartment cell (10 ml) were used in all experiments. Glassy carbon electrode served as a working substrate electrode. All potentials were measured and given referred to SCE electrode used as reference electrode. The counter electrode was a glassy carbon electrode.

Measurements: All measurements were carried out at room temperature. All solutions were deaerated by dry argon stream for 5 min before every experiment and an argon atmosphere was maintained above the solution during the experiment

Chemicals: All chemicals were reagent grade, methanol (Chimopar), the components of the phosphate buffer solution (PBS) (Carlo Erba) and the oxicams as meloxicam (high purity kindly offered by LaborMed Pharma S.A.- from manufacturer) were used without further purification; the aqueous solutions have been prepared using doubly-distilled water. Before modification, the glassy carbon surface was polished with alumina slurry on a polishing pad, washed with distilled water and sonicated for 3 minutes in doubly distilled water.

Activation of GCE

The bare GCE was polished using 0.05 μm alumina slurry until a mirror-like finish was obtained; then it was rinsed with twice distilled water, cleaned by ultrasonication in twice distilled water for 3 min and finally dried in air. Then the GCE was anodically activated at +1.8 V for 60 s and, respectively, for 120 s. This procedure can improve the electrochemical response of biological compounds, increasing both the activity and reproducibility of carbon electrodes.[9-11] In addition, at the pretreated GCE some biological compounds can be adsorbed and, as a consequence, accumulated at the electrode surface prior to CV and/or DPV experiments. Anodic activation of the surface of GCE at high anodic electrode potential results in an oxidized film containing functional groups, especially of carbon-oxygen type (maybe of quinone type[11]). As a result the number of active sites at the GCE surface increases and the rate of the electron transfer reaction can be increased.[12-14] The anodization of GCE results in more stable peak currents. It is also possible to increase the effective surface aria of the GCE due to the porous films formation at the electrode surface. Meloxicam (Fig. 1) containing aromatic rings could give adsorption to the GCE surface. This adsorption at an anodically activated GCE could be used as a preconcentration or accumulation step before any electrochemical study or determination.

RESULTS AND DISCUSSION

As can be seen in Fig. 1, at low scan rate it seems to appear three anodic peaks but at large scan rate the second and especially the third anodic peaks turn into a shoulder appearance, probably due to the increase of the capacitive current contribution to the total current.

The first anodic peak is developed at E_{pa} from 410 mV for 100 mV/s to 415 mV for 500 mV/s and the second anodic peak, much better defined, at E_{pa} from 735 mV for 100 mV/s to 866 mV for 500 mV/s. The third anodic peak, ill-defined with increasing scan rate, appears at E_{pa} from 919 mV for 100 mV/s to 1020 mV for 500 mV/s. All three anodic peaks shift anodically with increasing scan rate, all of them being less and less defined.

Of course, the cyclic voltammetry experiment at an inactivated GCE in the background solution (containing 20% MeOH and 80% PBS, but no meloxicam) shows no peak in the potential range explored as can be seen from Fig. 2 B.

As concerns the peak currents behaviour with the scan rate, both of them exhibit a linear dependence between the peak current and the square root of scan rate (I_p against $v^{1/2}$) (regression coefficients: R=0.996 and, respectively, R=0.999) and a slope of 0.5 for the plots $\ln I_p$ versus $\ln v$ (regression coefficients: R=0.997 and, respectively, R=0.999), indicating that meloxicam participates to the electrode reaction like a diffusional species (alternatively, the plots I_p against v are not linear). Also, the multicycling of the electrode potential shows that the peak currents decrease slowly with the increasing number of the cycle, probably due to a weak fouling effect of the oxidation products which can be adsorbed to the electrode surface, for both recorded anodic peaks.

On the negative-going sweep there is no cathodic peak due to the fact that the oxidation of meloxicam is irreversible at the bare GCE.

The effect of anodic activation of a bare GCE, at 1.8 V (vs. SCE) either for 60 s (Fig. 3, curve 2) or for 120 s (Fig. 3, curve 3) and of a preconcentration electrode potential of – 0.5 V applied for 60 s, can be seen in Fig. 3, in comparison with the bare GCE response (Fig. 3, curve 1, the bare GCE response). The electroactive species gives rise to a much better defined cyclic voltammogram having both peak currents increased and peak potentials anticipated in

comparison with the response recorded for an inactivated GCE. It can be noticed that simultaneously the hysteresis of the cyclic voltammogram at GCE modified by anodic activation increases as it is usually expected for chemically modified electrodes. The activation of GCE for 120 s seems to lead to a better electrochemical response (as regarding definition of the peak and the peak current height but not as regarding the peak potential position for both anodic peaks) comparing with the activation for only 60 s. The peak current ratio, defined as $r_{pa} = \frac{I_{pa,act}}{I_{pa,inact}}$, is 1.07 for the first anodic peak and 1.16 for the second anodic peak, an enhancement due to the increase of the activity of the anodically activated GCE.

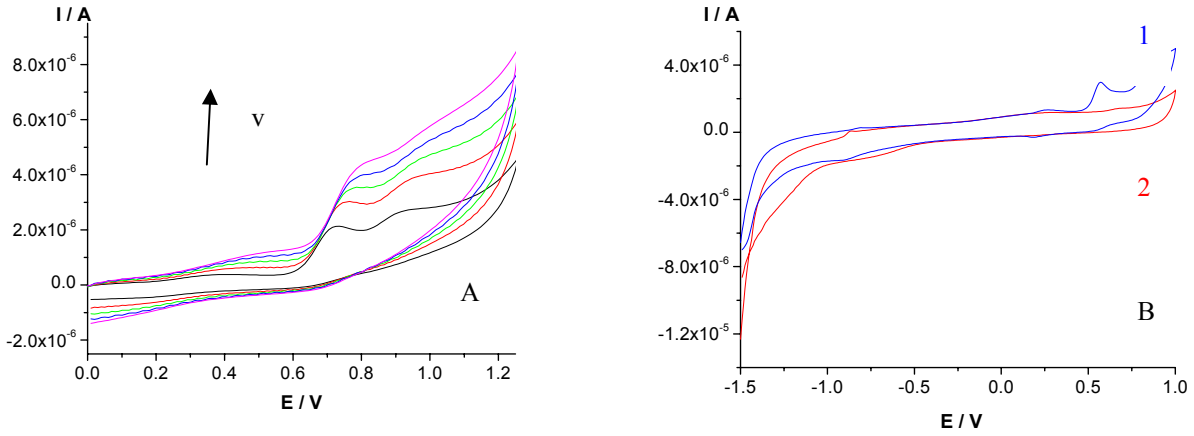

Fig. 2 – Cyclic voltammograms of 10^{-4} M meloxicam illustrating the scan rate dependences (100-200-300-400-500 mV/s) at a inactivated, bare GCE, recorded between 0.0 V and 1.25 V potential range (A) and a comparison between two cyclic voltammograms illustrating the difference between the voltammetric response of a solution containing 20% MeOH and 80% PBS (line 1) and the same solution containing meloxicam (line 2), recorded at a scan rate of 50 mV/s, and between -1.5 – 1.0 V potential range on a inactivated (B).

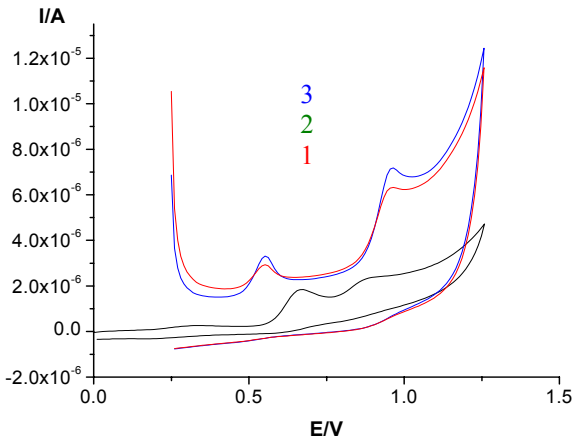

Fig. 3 – Cyclic voltammograms (scan rate of 50 mV/s, potential range from 0.25 V to 1.25 V) for illustrating the different electrochemical responses of an inactivated GCE (1) and of an activated GCE (2) and (3). The activation electrode potential was 1.8 V, applied either for 60 s (2) or for 120 s (3), and the accumulation electrode potential was -0.5 V with an accumulation/preconcentration time of 60 s.

The anticipation of the first anodic peak is better for an activation time of 60 s than for 120 s, as can be seen from the comparison between the peak potentials of the first anodic peak given in Table 1, irrespective of the accumulation time used and in Table 2, irrespective of the accumulation potential used but the same accumulation time.

For an activation time of 60 s (see Fig. 4 A) and of 120 s (see Fig. 4 B), at activation potential of +1.8 V (vs. SCE), the preconcentration time has been changed in the range 10 s-60 s, with a step of 10 s, and the cyclic voltammograms were recorded at 50 mV/s. The first anodic peak current is well-shaped in both case, but the second anodic peak

current is better defined for 120 s accumulation time, the latter turning into a shoulder-shaped appearance with increasing scan rate. Again, there is no cathodic peak on the cathodic sweeping electrode potential, the two anodic processes keeping their irreversibility.

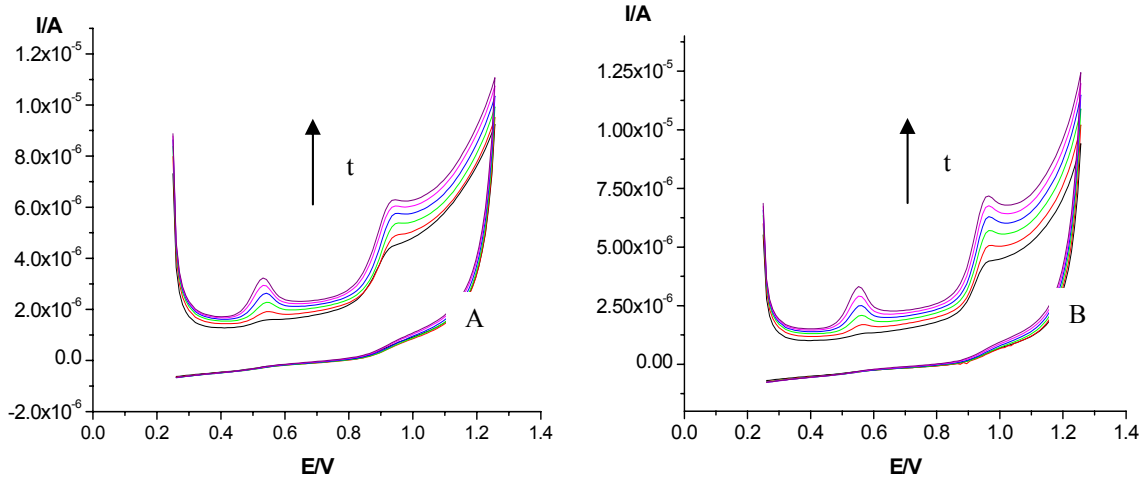

Fig. 4 – Cyclic voltammograms illustrating the dependence on the GCE accumulation/preconcentration time (10, 20, 30, 40, 50 and 60 s) at the preconcentration potential (-0.5 V), recorded at 50 mV/s scan rate, 1.8 V activation electrode potential for 60 s (A) and for 120 s (B). The arrows indicate the increasing time.

The influence of different accumulation time (from 0 s to 60 s, with 10 s time step) on the peak currents and peak potentials is given in Table 1, for anodic activation at 1.8 V carried out for two different activation times, 60 s and 120 s. In both cases, the accumulation electrode potential was -0.5 V. As can be noticed, the peak currents increase with increasing accumulation time and the peak potential is either almost constant (for first anodic peak at 60 s duration of activation and for the second anodic peak at 120 s duration of activation) or varies anodically (for second anodic peak at 60 s duration of activation) or cathodically (for first anodic peak at 120 s duration of activation).

Table 1

Peak currents and peak potentials at different accumulation time but the same accumulation potential (-0.5 V) for two different anodic activation times (60 s, and, respectively, 120 s) and the same anodic activation electrode potential (1.8 V)

	Activation time 60 s						Activation time 120 s					
t (s)	10	20	30	40	50	60	10	20	30	40	50	60
E_{pa1} (V)	0.512	0.512	0.512	0.512	0.512	0.512	0.560	0.560	0.560	0.560	0.555	0.555
I_{pa1} (μA)	1.65	2.11	2.31	2.60	2.81	3.01	0.69	0.93	1.07	1.19	1.30	1.37
E_{pa2} (V)	0.874	0.874	0.884	0.884	0.894	0.894	0.950	0.950	0.950	0.950	0.950	0.950
I_{pa2} (μA)	1.31	1.66	2.07	2.48	2.89	3.29	0.95	1.30	1.65	1.97	2.15	2.35

In the linear case behaviour, one may affirm that the amount of the accumulated meloxicam in the interfacial region increase linearly with the increasing accumulation time, while for the curved case of decreasing slope it is possible as, in the time scale of the cyclic voltammetry experiments, especially at longer duration of accumulation, an equilibrium between the diffusional and the adsorbed concentrations of the electroactive compound to be settle down. In the range of explored accumulation time, no decrease in the peak current occurs, so it seems probably that the saturation coverage of the electrodic interface is not yet obtained. At anodically activated GCE usually an adsorption of electroactive species may occur as a result of the functionalized surface of

the electrode and of the aromatic moieties of the electroactive species, as it was noticed to occur at mercury surface.[15] So that the oxidation process could be accomplished by both diffusional and adsorbed electroactive species at anodically activated GCE. Alternatively, it could be possible as a blockage of the electrode surface by absorption of the oxidation products to occur, the oxidation products fouling the electrode surface. In the anodically pretreated GCE case this fouling process seems to not play an important role due to the oxidized film containing functional groups which increases both the activity and the reproducibility of the GCE.[9-11]

The accumulation time influence on the peak currents and peak potentials was also studied at another two accumulation electrode potentials, -0.6 V and, respectively, -0.7 V. Both peak currents increase and peak potentials shift in the negative direction occur irrespective of the accumulation time used for preconcentrating the compound and the activation time used for anodic activation of the bare GCE. In each case, the peak currents increase with the increasing application time of the accumulation potential for an accumulation time in the range from 0 s to 60 s, showing an electroactive action of the activated bare GCE. In all three cases considered above, the increases of the two anodic peak currents were either linear (i.e., with a constant slope) or tend to lower (i.e., the curve increases with a decreasing slope).

Another important way for studying the improvement of the electrochemical response of meloxicam at an anodically activated GCE was to change the accumulation electrode potential in order to study its influence on the allure of the anodic peaks.

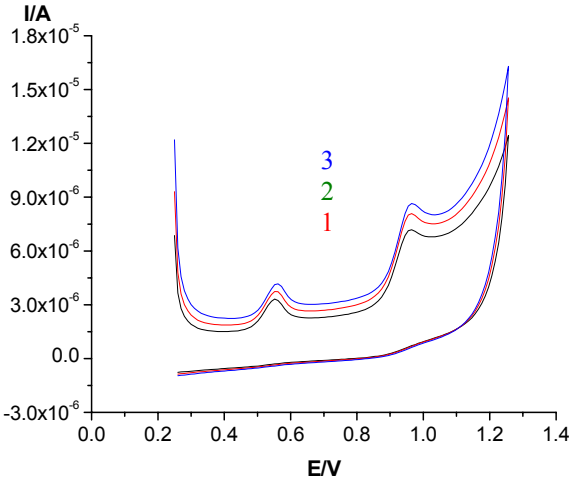

Fig. 5 – Comparison between three cyclic voltammograms (scan rate of 50 mV/s, potential range from 0.25 to 1.25 V) illustrating the influence of value of the second conditioning potential (-0.5 V (line 1), -0.6 V (line 2), -0.7 V (line 3)) maintained for 60 s. The first conditioning potential is 1.8 V applied for 60 s.

Fig. 5 shows the cyclic voltammograms obtained at the same activation of the GCE (so at 1.8 V electrode potential vs. SCE) and at the same accumulation time (60 s) but at different accumulation electrode potentials: -0.5 V, -0.6 V and -0.7 V (all of them referred to SCE). One can see the same well-shaped anodic peaks in all the three cases, a very small increase in peak current heights and, also, a small anodic shift of peak potentials for both anodic peaks recorded.

The results of the different accumulation electrode potentials used in cyclic voltammetry studies are summarized in Table 2.

Table 2

Peak currents and peak potentials at different accumulation potentials (-0.5 V, -0.6 V and, respectively, -0.7 V) for 60 s accumulation time for two different anodic activation times (60 s, and, respectively, 120 s) but the same anodic activation electrode potential (1.8 V)

	Activation duration 60 s			Activation duration 120 s		
E (V)	-0.5 V	-0.6 V	-0.7 V	-0.5 V	-0.6 V	-0.7 V
E_{pa1} (V)	0.512	0.532	0.532	0.555	0.555	0.562
I_{pa1} (μA)	3.01	3.21	3.21	3.29	3.71	4.15
E_{pa2} (V)	0.894	0.925	0.925	0.950	0.950	0.950
I_{pa2} (μA)	1.37	1.57	1.57	2.35	2.62	2.71

CONCLUSIONS

In order to obtain a better electrochemical response to a cyclic voltammetry perturbation, it is customary to improve the electrochemical behaviour of a bare GCE. The choice for the enhancement of the electron transfer ability was to anodically activate the surface of the GCE with the obtaining of an oxidized film containing functional groups, especially of carbon-oxygen type, which confer an improved redox activity and having a larger active area due to its porosity. Both the enhancement of peak currents and the cathodic shift of the anodic peak potentials were obtained at the anodically activated GCE versus inactivated bare GCE. Also a better peak definition resulted. Both the accumulation electrode potential (-0.5, -0.6 and -0.7) influence and different accumulation time (10-20-30-40-50-60 s) within the same accumulation electrode potential used were explored for an anodic activation made either for 60 s or for 120 s activation time. In each studied case, the peak currents increase with increasing activation time of the bare GCE or with increasing cathodic accumulation electrode potential of meloxicam.

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