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Electrochemical Behaviour of Selected β-Amino Alcohols and Amino Acids

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Abstract

In the present work, the electrochemical behaviour of a series of 17 commercially available compounds was investigated at a glassy carbon working electrode under different conditions. The effect of specific and non-specific solute-solvent interactions affecting the oxidation potentials of the investigated compounds was confirmed by employing Modified Linear Solvation Energy Relationship (LSER) analysis. The role of ionization to the electrochemical oxidation of the investigated β-amino alcohols and their derivatives was also established, using oxidation potentials obtained at the pH values of 4.0, 7.4, 9.0 and 11.0. In all cases, a linear decrease of oxidation potential by increasing the pH was observed. Chronoamperometric signal of 300, 500 and 800 mV and radical scavenging activity towards DPPH of the compounds were further employed as additional measurements for the evaluation of their antioxidant profile. The obtained electroanalytical data imply that the β-amino alcohols, amino acids and a biogenic amine studied in this work possess moderate to strong antioxidant properties.

Keywords: β- Amino alcohols; Amino acids; Antioxidant activity; Voltammetry; Oxidation potentials; DPPH; Radical scavenging

Introduction

Antioxidant activity of novel bioactive compounds is of paramount importance in medicinal chemistry. Indeed, unbalance between pro-oxidants and antioxidants in profit of pro-oxidants causes elevated oxidative stress. Pro-oxidants are able to readily damage biological molecules [1]. In addition, a pro-oxidant can be an oxidant of pathological importance [2]. Even though pro-oxidants are considered as harmful molecules [2], they can play a beneficial role as signal transduction messenger cells to mediate signal transduction. In addition, they have the physiological function in the non-phagocytic cells to mediate signal transduction of some growth factors and cytokines to achieve certain cellular function, named as "redox signaling". Pro-oxidants are also considered as powerful oxidative stress biomarkers and they have been shown in many cases as cancer chemo-preventive agents [3, 4].

The β-amino alcohol moiety is a common structural component in a vast group of naturally occurring and synthetic molecules possessing a wide range of biological activities [5]. Especially, β-amino alcohols have been widely reported to act as chemical indicators stimulating the plant self-defence mechanism against oxidative stress, while they can act as pro oxidants under certain conditions [6-13]. Oxidative stress has been implicated in the pathogenesis of several human diseases, such as atherosclerosis, diabetes mellitus, chronic inflammation, neurodegenerative disorders and certain types of cancer [14].

Antioxidant activity of bioactive species can be studied by means of electrochemical parameters. Electroanalytical data can be correlated with those derived from antioxidant protocols [15], because redox behaviour of an antioxidant at an electrode is related to its behaviour in chemical redox reaction with a radical [16]. In particular, oxidation potentials provide an estimation of the energy required for a compound to donate an electron. Indeed, the more negative oxidization potential is, the more easily the compound will donate an electron and the higher its expected antioxidant activity [17, 18]. The determination of the oxidation potential and, generally, the investigation of the electrochemical behaviour of a compound can easily be performed by applying cyclic voltammetry. The latter has been considered in recent years as a conventional methodology for evaluating the antioxidant capacity of human and horse plasma, animal tissues, edible plants, wines and different types of tea and coffees [15, 16, 19]. Another electroanalytical technique for the evaluation of antioxidant profile of bioactive species is chronoamperometry, whose results can be correlated with antioxidant protocols such as the evaluation of the scavenging ability against stable free radicals like 1,1- diphenyl-2-dipicrylhydrazyl (DPPH) [20, 21]. Electroanalytical studies of β-amino alcohols and amino acids [22] can possibly contribute to the development of a useful measure for the evaluation of their biological properties such as antioxidant capacity.

In the present work, the electrochemical behaviour of a series of commercially available amino-compounds and their derivatives was investigated under different conditions. In order to study the parameters affecting the oxidation potential of the investigated compounds in physiological conditions, Modified Linear Solvation Energy Relationships (LSER) analysis was employed. The effect of pH on the oxidation potentials was also established. The chronoamperometric signal of the compounds under investigation at oxidation potentials of 300, 500 and 800 mV was also determined. The antioxidant activity of selected compounds was evaluated in vitro by measuring their ability to scavenge the stable free radical 1,1-diphenyl-2-dipicrylhydrazyl (DPPH).

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Experimental

Instrumentation

The electrochemical investigation of the β-amino alcohols and their derivatives was performed using the polarograph 797 VA Computrace (Metrohm). As working electrode, a glassy carbon (GC) was employed. The reference electrode was an Ag/AgCl one, filled with 3M KCl (≥99.5% p.a., Merck) in High Purity Water (HPW) supplied by an EASYpure II (Model D 7381, Barnsted International) water purification system, and the auxiliary a Pt electrode. Working electrode was polished at the beginning of each measurement with alumina powder (0.3 mm) for 3min, using a polishing cloth, and it was rinsed with deionized water and ethanol. Furthermore, in the end of each working day, it was sonicated firstly for 5 min in distilled water and, secondly, for another 5 min in acetone. The condition of the electrode was frequently checked using a 0.1M solution of $Fe(CN)_6^{4-}$. The determination of the free-radical scavenging capacity was evaluated with the stable radical 2,2-diphenyl-1-picrylhydrazyl (DPPH•). A spectrophotometer (Helios Unicam, USA) was used to measure the absorbance at 517 nm where the delocalisation gives rise to the deep violet colour, characterised by an absorption band in methanol solution.

Reagents

All reagents were of analytical grade. *L*-DOPA (≥98%, Sigma-Aldrich), dopamine hydrochloride (99%, Alfa Aesar), *L*-tyrosine hydrochloride (99%, Alfa Aesar), tyrosol (≥ 99.5%, FlukaChemika), tyramine (97%, Acros Organics), serinol (≥ 98%, Sigma-Aldrich), *L*-serine (≥ 98%, Sigma-Aldrich), Boc-tyrosine (≥ 98%, Alfa Aesar), ethanolamine (≥ 98%, Sigma-Aldrich), 2-amino-2-methyl-1-propanol (≥ 90%, Sigma-Aldrich), 2-amino-1-phenylethanol (≥ 98%, Sigma-Aldrich), 2-amino-3- phenyl-1- propanol (≥ 98%, Sigma-Aldrich), *L*-phenylalanine (≥ 98%, Sigma-Aldrich), *L*-cysteine (≥ 99%, FlukaChemika), 2-(methylamino)ethanol (≥ 98%, Sigma-Aldrich), (S)-(+)-2-amino-1-propanol (≥ 98%, Sigma-Aldrich) and norepinephrine (≥ 98%, Sigma-Aldrich) were the compounds under investigation. Their structures are presented in Table 1. *L*(+) ascorbic acid (≥99.7%, Carlo-Erba) was used as the reference compound.

Buffer solutions were prepared by dissolution of the appropriate amounts of CH_3COOH (Merck), CH_3COONa (≥99% Sigma Aldrich), $NaH_2PO_4 \cdot H_2O$ (≥98% Sigma Aldrich), Na_2HPO_4 (Acros Organics), HCl (37% Fluca), Na_2CO_3 (Acros Organics), $NaHCO_3$ (Acros Organics) in HPW. DPPH (1, 1-diphenyl, 2-picrylhydrazyl) was obtained by Sigma-Aldrich and methanol used for the assay was of analytical grade (Fisher Scientific).

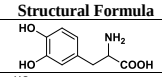
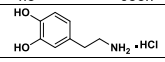
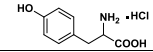
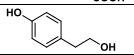
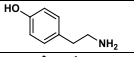
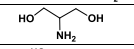
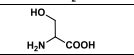
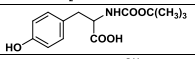
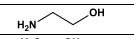
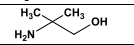
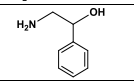
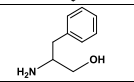
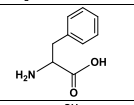
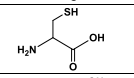
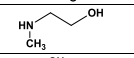
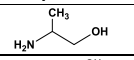
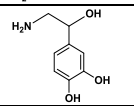
Electrochemical studies

All studies were carried out in room temperature (22±1°C). The electrochemical investigation, involving cyclic voltammetry and chronoamperometry was performed by spiking micro-amounts of the compounds under investigation in different buffers in a 10 mL Metrohm polarographic cell. The final concentration of the investigated species in the polarographic cell was about 1.0 mM. As buffers, the following solutions were tested:

(A) CH_3COOH / CH_3COONa, pH=4.0

(B) NaH_2PO_4 / Na_2HPO_4, pH=7.4

Table 1: Structural formula of the investigated compounds.

Compound	Common Name	Structural Formula
1.	*L*-Dihydroxy-Phenylalanine (*L*-DOPA)	
2.	Dopamine hydrochloride	
3.	*L*-Tyrosine hydrochloride	
4.	Tyrosol	
5.	Tyramine	
6.	Serinol	
7.	*L*-Serine	
8.	*Boc*-tyrosine	
9.	Ethanolamine	
10.	2-amino-2-methyl-1-propanol	
11.	2-amino-1-phenylethanol	
12.	2-amino-3-phenyl-1-propanol	
13.	*L*-phenylalanine	
14.	*L*-cysteine	
15.	2-(methylamino)ethanol	
16.	(S)-(+)-2-amino-1-propanol	
17.	Norepinephrine	

(C) Na_2HPO_4 adjusted at pH=9.0 with HCl

(D) Na_2CO_3 / $NaHCO_3$, pH=11.0

Cyclic voltammograms were recorded between -400 and 1200 mV with a scanning rate of 20 mVs^{-1}, while for chronoamperometric measurements, the potentials of 300, 500 and 800 mV were selected. All measurements were carried out at least in triplicate, and the mean value was considered.

Solvation properties

Solvation parameters were taken from the module Absolv, included in ADME Boxes version 3.0 software (Pharma Algorithms) and they are presented in Table S1, in supplementary material. These parameters involve the hydrogen-bond acidity (A), the hydrogen-bond basicity (B), the dipolarity/ polarizability (S), the excess molar refraction (E) and the McGowan molecular volume (V).

Statistical analysis

Linear regression analysis was performed using the Statistica-Axa 7.0 software package (StatSoft, Tulsa, OK, USA). The following statistic data were provided for the obtained equations: N is the number of data points, s is the standard deviation, R is the correlation

Table S1: The Abraham descriptors of the investigated compounds.

Compound	A	B	S	E	V
1	1.56	1.44	1.77	1.33	1.43
2	0.98	1.08	1.35	1.15	1.22
3	1.28	1.29	1.60	1.18	1.37
4	0.81	0.67	1.12	1.01	1.12
5	0.71	0.94	1.17	1.01	1.16
6	0.74	1.29	0.96	0.64	0.75
7	1.03	1.30	1.15	0.60	0.76
8	1.28	1.33	1.93	1.22	2.15
9	0.46	0.94	0.72	0.42	0.55
10	0.46	0.98	0.66	0.40	0.83
11	0.46	1.19	1.10	1.03	1.16
12	0.46	1.06	1.17	1.00	1.30
13	0.78	1.02	1.39	0.95	1.31
14	0.78	1.05	1.12	0.83	0.87
15	0.38	0.84	0.58	0.37	0.69
16	0.46	0.97	0.71	0.43	0.69
17	1.23	1.61	1.49	1.40	1.27

coefficient, R^2 is the adjusted square of the correlation coefficient and F is the Fisher test, calculated for a significance level of 0.05.

Antioxidant protocol – DPPH assay

The DPPH scavenging assay was performed according to Brand-Williams et al. (1995) [23, 24]. Briefly, 0.1 mL of appropriately diluted samples was added to 3.9 mL of DPPH• (3.0 mg/100 ml) in methanol in the spectrophotometric cuvette. After stirring vigorously for 30 s, the absorbance at the wavelength of 517 nm was recorded at 20 and 60 minutes. The changes in absorbance were measured at 25 °C. The percent radical scavenging was calculated as follows:

$$\% \text{ Scavenging} = 100 * (A_0 - A_t) / A_0$$

Where A_0 is the initial DPPH absorbance and A_t is the absorbance at 20 min or 60 min of reaction. IC_{50} (the half maximal inhibitory concentration of the substance that produces 50% scavenging) was extrapolated from the plot of the percent radical scavenging versus the substance concentration, obtained for the different substrates.

Results and Discussion

Electrochemical study at physiological conditions (pH 7.4)

The electrochemical behaviour of the investigated compounds was studied by cyclic voltammetry using a GC electrode, which has been the working electrode of choice in analogous studies [17, 21, 25]. The electrochemical investigation was firstly performed in phosphate buffer at pH=7.4 in order to mimic the physiological pH conditions. All compounds gave one well-defined anodic peak with no cathodic steps, which implies an irreversible electrochemical process. This can be explained on the basis that the oxidation process is probably followed by a chemical reaction that rapidly removes the generated product [26, 27]. A representative cyclic voltammogram for serinol at pH 7.4 is illustrated in Figure 1. The first cycle curves of cyclic voltammogram were used to determine the anode peak voltages (E_{ap})

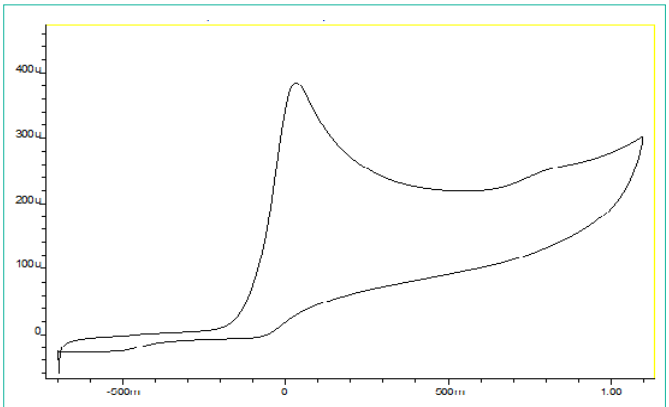


Figure 1: Cyclic voltammograms at a glassy carbon electrode of Serinol at pH 7.4. Sweep rate: 20mV·s^{-1}.

of the investigated compounds, as well as their half-peak voltages ($E_{1/2}$), considered as the voltage at which the current equals the half of the maximum anode peak current. In Table 2, E_{ap} and $E_{1/2}$ values are presented. Among the investigated amino acids, L-DOPA (1) and L-serine (7) showed the lowest oxidation potentials (0.25 and 0.26V, respectively) whereas among the studied amino alcohols the lowest E_{ap} were found for serinol (6) and 2-amino-2-methyl-1-propanol (10) (0.19 and 0.28V, respectively). These E_{ap} values are comparable with the one found for the reference compound, ascorbic acid (E_{ap}=0.21V), which is a well-known antioxidant thus; they could be considered as an indication for significant antioxidant activity. Oxidation potentials between 0.32 and 0.50 V were found for the amino acids Boc-tyrosine (8), and L-cysteine (14), and the amino-alcohols dopamine (2), 2-amino-1-phenylethanol (11), 2-(methylamino)ethanol (15), (S)-(+)-2-amino-1-propanol (16) and norepinephrine (17). These E_{ap} values imply intermediate antioxidant properties. The rest of the studied compounds showed E_{ap} higher than 0.50V therefore they are expected to be weak antioxidants. The $\Delta E = E_{ap} - E_{1/2}$ values, presented also in Table 2 are around 70 mV which corresponds the removal of one electron during the first step of the electrochemical oxidation [21].

Modified linear solvation energy relationships (LSER) analysis

The Abraham's Linear Solvation Energy Relationships (LSER) are widely utilized to characterize many biological and physicochemical processes, governed by forces, such as hydrophobic interactions, steric and electronic effects and hydrogen bond formation [28]. In the case of electro active species, selective solvation of both initial compounds and their intermediates is likely to occur, including non-specific solute-solvent interaction (stabilization of a charge or a dipole by virtue of its dielectric effect) and specific solute-solvent interaction, such as hydrogen bonding and electron pair donor or acceptor mechanism. The general equation proposed by Abraham et al. is presented in Eq. (1) [29, 30].

$$S.P. = a \cdot A + b \cdot B + s \cdot S + e \cdot E + v \cdot V + c \quad (1)$$

Where SP is a dependent solute property in a given system, such as the E_{ap} values.

In the case of electrochemical oxidation, the coefficients a, b, s, e and v reveal the differences between the phases of the solution in the electrolytic cell and the electrode. For LSER analysis the E_{ap} values of

Table 2: Anodic peak voltages (E_{ap}), half-peak potentials ($E_{1/2}$) and their differences $\Delta E = E_{ap}-E_{1/2}$ of the compounds under investigation obtained at a glassy carbon electrode under different pH values.

Compound	pH=4			pH=7.4			pH=9			pH=11		
	E_{ap} (V)	$E_{1/2}$ (V)	ΔE (mV)	E_{ap} (V)	$E_{1/2}$ (V)	ΔE (mV)	E_{ap} (V)	$E_{1/2}$ (V)	ΔE (mV)	E_{ap} (V)	$E_{1/2}$ (V)	ΔE (mV)
1	0.47 ± 0.02	0.41 ± 0.03	60 ± 5	0.25 ± 0.03	0.18± 0.02	70 ± 5	0.15 ± 0.04	0.09 ± 0.02	60 ± 5	0.07 ± 0.03	0.01 ± 0.01	65 ± 5
2	0.51 ± 0.02	0.44 ± 0.02	65 ± 5	0.35 ± 0.02	0.27 ± 0.04	75 ± 5	0.27 ± 0.03	0.2 ± 0.02	70 ± 5	0.22 ± 0.02	0.14 ± 0.03	75 ± 5
3	0.71 ± 0.03	0.64 ± 0.02	65 ± 5	0.51 ± 0.03	0.44 ± 0.04	70 ± 5	0.42 ± 0.03	0.35 ± 0.03	65 ± 5	0.35 ± 0.02	0.27 ± 0.03	75 ± 5
4	0.65 ± 0.04	0.59 ± 0.04	60 ± 5	0.52 ± 0.03	0.44 ± 0.03	75 ± 5	0.46 ± 0.03	0.4 ± 0.03	60 ± 5	0.43 ± 0.02	0.35 ± 0.03	80 ± 5
5	0.70 ± 0.04	0.62 ± 0.02	75 ± 5	0.56 ± 0.02	0.48 ± 0.02	80 ± 5	0.50 ± 0.02	0.42 ± 0.03	75 ± 5	0.44 ± 0.03	0.37 ± 0.02	70 ± 5
6	0.77 ± 0.04	0.7 ± 0.03	65 ± 5	0.19 ± 0.02	0.11 ± 0.03	75 ± 5	-0.05 ± 0.03	0.02 ± 0.02	75 ± 5	-0.36 ± 0.03	-0.29 ± 0.02	70 ± 5
7	0.63 ± 0.02	0.57 ± 0.02	60 ± 5	0.26 ± 0.04	0.18 ± 0.03	75 ± 5	0.08 ± 0.02	0.01 ± 0.04	70 ± 5	-0.19 ± 0.02	-0.11 ± 0.04	80 ± 5
8	0.7 ± 0.03	0.64 ± 0.03	60 ± 5	0.44 ± 0.02	0.37 ± 0.02	70 ± 5	0.34 ± 0.04	0.27 ± 0.02	70 ± 5	0.13 ± 0.02	0.46 ± 0.04	80 ± 5
9	1.11 ± 0.03	1.02 ± 0.02	75 ± 5	0.6 ± 0.03	0.52 ± 0.02	80 ± 5	0.32 ± 0.04	0.25 ± 0.02	70 ± 5	0.11 ± 0.04	0.03 ± 0.02	80 ± 5
10	0.86 ± 0.02	0.79 ± 0.02	70 ± 5	0.28 ± 0.03	0.2 ± 0.03	80 ± 5	0.16 ± 0.02	0.08 ± 0.04	75 ± 5	-0.11 ± 0.03	-0.03 ± 0.02	75 ± 5
11	0.77 ± 0.04	0.7 ± 0.02	70 ± 5	0.5 ± 0.02	0.42 ± 0.02	75 ± 5	0.38 ± 0.02	0.31 ± 0.04	65 ± 5	0.29 ± 0.03	0.22 ± 0.03	70 ± 5
12	0.9 ± 0.03	0.82 ± 0.03	75 ± 5	0.58 ± 0.03	0.50 ± 0.02	75 ± 5	0.43 ± 0.03	0.36 ± 0.03	70 ± 5	0.31 ± 0.02	0.23 ± 0.02	80 ± 5
13	1.2 ± 0.03	1.12 ± 0.03	80 ± 5	0.72 ± 0.02	0.64 ± 0.04	75 ± 5	0.5 ± 0.03	0.42 ± 0.03	75 ± 5	0.33 ± 0.02	0.25 ± 0.03	75 ± 5
14	0.82 ± 0.02	0.75 ± 0.04	65 ± 5	0.38 ± 0.04	0.30 ± 0.02	75 ± 5	0.17 ± 0.03	0.1 ± 0.03	70 ± 5	-0.01 ± 0.02	0.06 ± 0.03	70 ± 5
15	0.74 ± 0.04	0.67 ± 0.02	70 ± 5	0.45 ± 0.02	0.37 ± 0.03	80 ± 5	0.33 ± 0.03	0.26 ± 0.02	70 ± 5	0.23 ± 0.03	0.15 ± 0.02	80 ± 5
16	0.74 ± 0.02	0.66 ± 0.02	75 ± 5	0.42 ± 0.03	0.34 ± 0.03	75 ± 5	0.27 ± 0.02	0.20 ± 0.02	65 ± 5	0.18 ± 0.03	0.10 ± 0.04	75 ± 5
17	0.75 ± 0.02	0.69 ± 0.02	60 ± 5	0.32 ± 0.02	0.25 ± 0.02	70 ± 5	0.15 ± 0.02	0.08 ± 0.02	65 ± 5	-0.01 ± 0.03	0.06 ± 0.02	70 ± 5
Ascorbic acid	0.29 ± 0.02	0.22 ± 0.02	70 ± 5	0.21 ± 0.02	0.15 ± 0.02	65 ± 5	0.15 ± 0.02	0.13 ± 0.02	70 ± 5	0.19 ± 0.02	0.13 ± 0.02	65 ± 5

the 17 investigated compounds obtained at pH= 7.4 were used. The obtained relationship is presented in Eq. (2):

$$E_{ap} = (0.628 \pm 0.134) - (0.545 \pm 0.204)\cdot A - (0.360 \pm 0.149)\cdot B + (0.738 \pm 0.369)\cdot S - (0.035 \pm 0.165)\cdot E - (0.166 \pm 0.195)\cdot V \quad (2)$$

(N=17, R= 0.816, R^2= 0.666, s= 0.098, F= 4.39)

As shown, the coefficients of the parameters E and V are not statistically significant (t<2.0). Therefore, regression analysis was repeated taking into account only the statistically significant parameters of A, B and S. The obtained relationship is presented in Eq. (3):

$$E_{ap} = (0.621 \pm 0.126) - (0.431 \pm 0.147)\cdot A - (0.332 \pm 0.138)\cdot B + (0.457 \pm 0.127)\cdot S \quad (3)$$

(N=17, R= 0.802, R^2= 0.644, s= 0.093, F= 7.823)

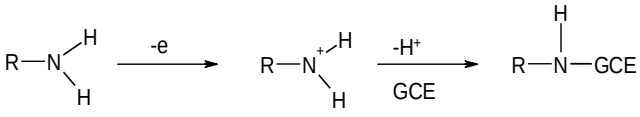
As shown, oxidation potential data greatly correlate with solvatochromic parameters, implying that both specific and non-specific solute-solvent interactions influence the reactivity of the studied compounds towards the working electrode. More to the point, the statistically significant coefficient of A reveals the influence of hydrogen bond donor interactions of the reactants with the solvent. This observation is in agreement with the role of amino groups in the first step of oxidation on a GC electrode, as shown in Scheme 1 [31].

Moreover, the significance of coefficient of B may reflect the solvation of the polar intermediates of amino alcohols through hydrogen bond acceptor interactions. However, electrochemical reactivity of amino alcohols is also influenced by non-specific interactions, which are more evident in the case of the reactants' intermediates (positive sign of S). It should be noted that analogous observations were found for a series of oxicams, reported in a previous work by some of us [20].

Effect of ionization

It is well known that the electrochemical oxidation is affected greatly by the pH value in the case of ionizable compounds. In the case of amino alcohols, their oxidation can be performed either at the amino-group, or at the hydroxyl group. Under basic or neutral conditions oxidation usually starts at the nitrogen atom [32], as confirmed by the solvatochromic analysis. However, change of pH can lead to alteration of ionization of the amino group, from neutral at basic pH values to fully protonated state at acidic conditions.

In order to gain insight into the effect of ionization to the oxidation potentials of the compounds under study, the electrochemical investigation was also performed at the pH values of 4.0, 9.0 and 11.0. The E_{ap}, $E_{1/2}$ and $\Delta E = E_{ap}-E_{1/2}$ values of the investigated species are presented in Table 2. As shown, a considerable decrease of their oxidation potential by increasing the pH was observed. It is interesting that a linear correlation E_{ap}=f(pH) followed by good statistics was found for the investigated compounds. Results of the linear regression E_{ap}/pH are shown in Table 3. Slopes may reflect chemical structures.



Scheme 1: Proposed mechanism of oxidation of amino-group on a GC electrode [31].

Table 3: Statistical analysis of the correlation $E_{ap} = E_{(pH=0)} - a \cdot pH$ for the 17 compounds under investigation.

Compound	Coefficients		Statistical parameters		
	E_{ap}	a	R^2	s	F
1	0.692 ± 0.034	0.061 ± 0.003	0.990	0.021	196.2
2	0.671 ± 0.031	0.043 ± 0.002	0.985	0.019	128.9
3	0.909 ± 0.033	0.058 ± 0.005	0.988	0.020	171.1
4	0.770 ± 0.032	0.042 ± 0.003	0.972	0.020	69.0
5	0.845 ± 0.016	0.045 ± 0.003	0.995	0.010	385.2
6	1.405 ± 0.029	0.173 ± 0.010	0.999	0.018	2103.4
7	1.106 ± 0.036	0.114 ± 0.012	0.997	0.023	639.2
8	1.028 ± 0.043	0.092 ± 0.006	0.992	0.026	238.1
9	1.679 ± 0.068	0.140 ± 0.012	0.994	0.042	309.9
10	1.373 ± 0.105	0.119 ± 0.005	0.983	0.065	116.4
11	1.035 ± 0.048	0.076 ± 0.006	0.986	0.030	146.0
12	1.229 ± 0.047	0.090 ± 0.004	0.991	0.029	223.5
13	1.682 ± 0.078	0.136 ± 0.009	0.989	0.048	180.0
14	1.327 ± 0.067	0.136 ± 0.012	0.992	0.042	236.1
15	0.991 ± 0.041	0.069 ± 0.005	0.990	0.025	206.5
16	1.048 ± 0.068	0.095± 0.006	0.980	0.042	99.0
17	1.166 ± 0.067	0.100 ± 0.004	0.989	0.041	185.3

Indeed, compounds with phenolic group, such as *L*-DOPA and dopamine exhibited values around 0.05 V/pH, while species with aliphatic hydroxyl group, such as serinol and ethanolamine as well as amino acids, such as phenylalanine and L-cysteine, showed values over than 0.10 V/pH. In all cases, the compounds studied gave one well-defined anodic peak, implying an irreversible process as observed at pH=7.4. It should be mentioned that ascorbic acid pka value is 4.20 therefore at pH 6.2 is fully ionised, so further increase of pH does not affect its ionisation and the standard error in E_{ap} corresponding value in pH 9 and pH 11 may be similar. Moreover, Tyrosol shows the lowest correlation (E_{ap}=f(pH)) apparently due to its structure which lacks an amino group and has a different oxidation mechanism.

Chronoamperometric investigation

There is evidence that a correlation between the chronoamperometric signal and reactivity towards reactive oxygen species and free radicals can be achieved in certain conditions [20, 21, 33]. In our previous investigation concerning a series of chalcone analogues [21], principal component analysis revealed the association of chronoamperometric signal with the ability of the compounds to scavenge H_2O_2 evaluated using the luminol chemiluminescence assay.

In the present work, chronoamperograms were recorded at the potentials of 300 mV, 500 mV and 800 mV, characterizing compounds with high, intermediate and weak antioxidant activity, respectively [34]. Measurements were performed at pH=7.4 with respect to the physiological conditions. Chronoamperometric signals for the studied compounds and the well known strong antioxidant ascorbic acid at the potentials of 300, 500 and 800 mV are presented in Table 4. As expected, L-DOPA (1), serinol (6), L-serine (7), 2-amino-2-methyl-1-propanol (10), norepinephrine (17) and ascorbic acid, which had shown E_{ap} in the range of 210-320mV, gave measurable signals at the glassy carbon electrode at all the three potentials that were used. Compounds 2, 8, 11, 14, 15 and 16 gave measurable signals at the glassy carbon electrode at 500mV whereas compounds 3, 4, 5, 9, 12 and 14 gave chronoamperometric signals only at 800mV.

Table 4: Amperometric signal (Ip) of the tested compounds measured with chronoamperometry at 300, 500 and 800 mV at pH 7.4 using glassy carbon electrode as working electrode.

Compound	Chronoamperometric signal (μA)		
	300mV	500mV	800mV
1	7.2 ±0.5	7.7 ± 0.2	7.9 ± 0.3
2	–	4.7 ± 0.2	5.2 ± 0.3
3	–	–	2.1 ± 0.2
4	–	–	2.3 ± 0.3
5	–	–	2.0 ± 0.2
6	6.0 ± 0.5	6.6 ± 0.3	6.7 ± 0.2
7	3.7 ± 0.3	4.3 ± 0.6	4.5 ± 0.2
8	–	4.4 ± 0.3	5.2 ± 0.3
9	–	–	1.1 ± 0.2
10	4.0 ± 0.3	4.6 ± 0.2	4.7 ± 0.2
11	–	3.7 ± 0.3	4.2 ± 0.5
12	–	–	2.7 ± 0.3
13	–	–	3.9 ± 0.5
14	–	2.9 ± 0.2	3.6 ± 0.3
15	–	6.0 ± 0.4	6.3 ± 0.2
16	–	5.3 ±0.5	6.0 ± 0.2
17	4.6 ± 0.2	4.7 ± 0.2	5.0 ± 0.4
Ascorbic acid	2.1 ± 0.3	2.6 ± 0.4	2.8 ± 0.4

DPPH radical scavenging ability

In order to estimate the antioxidant activity of the studied compounds, their ability to scavenge the stable free radical DPPH was evaluated (Table 5). When the deep violet solution of DPPH radical was mixed with a solution of strong antioxidant it turned yellow and the degree of discoloration indicates the free radical scavenging potentials of the compound by their hydrogen donating ability. Compounds 1, 2, 4, 5, 6, 7, 8 and 10 were selected for this experiment. In the DPPH radical scavenging assay the decrease in DPPH absorbance was measured as a function of time (20 min and 60 min). For each compound, the concentration (mM) of the substance that produces 50% scavenging (IC_{50}) was measured.

The results of the DPPH assay show that L-DOPA (1) and dopamine (2) exhibit strong antioxidant activity (IC_{50} 1.04 and 0.32 mM, at 60min, respectively). These findings are in accordance with the E_{ap} measurements which implied that these compounds should exhibit important antioxidant activity. Dopamine (2) exhibits the highest antioxidant activity among the compounds tested in this work. On the other hand, tyrosol (4) and tyramine (5), with E_{ap} 520 and 510mV, respectively, show a significantly lower DPPH scavenging ability (IC_{50} 542.7 and 425.9mM, at 60min, respectively). It seems that in the case of these compounds there is a good correlation between the measured E_{ap} and their antioxidant activity. It is worth noting that all these compounds possess one or two phenolic hydroxyl groups, a

Table 5: DPPH radical scavenging ability of compounds 1, 2, 4, 5, 6, 7, 8 and 10.

Compound	$IC_{(50)}$ (mM)	
	20 min	60 min
1	1.14	1.04
2	0.34	0.32
4	843.4	542.7
5	771.4	425.9
6	>1000	>1000
7	>1000	>1000
8	>1000	>1000
10	>1000	>1000

structural feature that promotes interaction with the DPPH radical. In the case of the amino alcohols serinol (6) and 2-amino-2-methyl-1-propanol (10), as well as the amino acid L-serine (7), although their E_{ap} indicated a good antioxidant activity, the compounds failed to interact with the DPPH radical. This difference could be attributed to the mechanism of action of the DPPH assay, which involves mainly proton transfer. Neither of these compounds possesses a labile proton capable of giving this reaction at the conditions of the assay. Boc-tyrosine (8) (E_{ap}=440mV) did not show any interaction with DPPH.

Conclusions

Modified Linear Solvation Energy Relationship analysis at physiological conditions showed that both specific and non-specific solute-solvent interactions influence the reactivity of compounds towards glassy carbon electrode. Specific interactions involve influence of hydrogen bond donor interactions of the reactants with the solvent and solvation of the polar intermediates of amino alcohols through hydrogen bond acceptor interactions. The role of ionization to the electrochemical oxidation of the investigated β-amino alcohols and selected amino acids and amines was also established. A linear decrease of their oxidation potential by increasing the pH was observed. The obtained electro analytical data imply that some of the β-amino alcohols and amino acids studied in this work possess moderate to strong and intermediate antioxidant properties. The DPPH radical scavenging ability of selected compounds showed that, in the case of compounds possessing a catechol system, electrochemical data are in accordance with the antioxidant activity evaluated by the DPPH assay. As antioxidant activity is a multifactorial process, evaluation of the antioxidant activity of the compounds using other assays could shed more light to the correlation between electrochemical behavior and antioxidant ability.

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