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Electrochemical oxidation of D-glucose in alkaline medium: impact of oxidation potential and chemical side-reactions on the selectivity to D-gluconic and D-glucaric acid

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Abstract: The electrocatalytic oxidation of D-glucose was studied in alkaline medium on copper, platinum and gold electrodes with particular emphasis on the synthesis of a high value added product: glucaric acid. An initial ranking of the three different materials, with respect to their electrochemical activity towards glucose oxidation, was performed utilizing cyclic voltammetry. To determine which functional group can react on which metal, cyclic voltammetry experiments were performed in three different solutions containing 0.04 M of gluconic acid, glucuronic acid or glucaric acid in 0.1 M aqueous NaOH. The observations drawn based on these initial experiments were then verified by analyzing the product solutions (obtained after prolonged electrolysis experiments) with HPLC analysis. The oxidation of glucose on copper at high potentials leads predominantly to C-C cleavage products, mainly formic acid, with a selectivity of 54.2%, while at lower potentials the oxidation of the aldehyde group on C1 and of the hydroxymethyl group on C6 produces moderate yields of gluconic and glucaric acid. On platinum the oxidation of the aldehyde group on C1 is the most relevant process, therefore the selectivity towards gluconic acid obtained is as high as 78.4%. Nevertheless, at lower potentials, a higher selectivity to glucaric acid (12.6%) and a lower selectivity to gluconic acid (68.0%) are the result of a more effective oxidation of also the hydroxymethyl group on C6. Gold is the most active and selective electrocatalyst of the ones examined in this work. On Gold, at lower potentials, the oxidation of the aldehyde group on C1 produces 86.6% of selectivity to gluconic acid while, at higher potentials, the oxidation of the hydroxymethyl group on C6 also takes place, promoting the further oxidation to glucaric acid (13.5% of selectivity is reached after 65 h of reaction at 5°C, with a residual gluconic acid equal to 65.8%). The demonstrated dependence of the selectivity on the oxidation potential suggests new future perspectives for the electrocatalytic oxidation of D-glucose to D-glucaric acid on bare metal electrodes. Moreover, the low selectivity of this process, very often claimed in literature, has been ascribed here for the first time to two chemical processes which are in competition with the electrochemical one and both consume the reactant and promote the formation of undesired side-products.

Introduction

One of the major challenges in the current political and socioeconomical context is the reduction of the societal dependence on fossil resources. The steady decrease of fossil fuel reserves, together with the widespread concerns for pollution and global warming, have made the search for alternatives to the traditional petroleum-derived resources a must over the last decades. Amongst the most promising and recognized alternatives, the conversion of renewable biomass into fuels and high value chemicals is especially interesting due to its low cost and high availability.

Carbohydrates are widely available, renewable organic materials constituting the major part of the total biomass, e.g. 75% of the dry weight of herbaceous and woody biomass are carbohydrates [1]. However, despite the low costs and easy access, only 3-5% of carbohydrates have industrial use, with the great majority remaining unused [2]. This has consequently led to an increase of the research efforts focused on harvesting the potential of lignocellulosic biomass residues resulting from the forestry and agricultural activities [2-3]. Among various carbohydrates, cellulose and glucose are of particular interest in green chemistry since they can be used to generate a wide range of valuable compounds. Cellulose is a polysaccharide consisting of a linear chain of D-glucose units and constitutes 45% of the total annual production of biomass [3]; glucose is the monosaccharide obtained by depolymerisation of said cellulose.

Glucaric acid, the aldaric acid obtained by the oxidation of glucose, is one of the most valued chemical products that can be derived from biomass [4]. It's market size was estimated at USD 550.4 million in 2016 and its demand is expected to grow because of the stringent regulations on the use of harmful chemicals (like the ban on the use of phosphates in detergents due to their toxic nature) [5]. Among others, its use as a raw material for the development of metal complexation agents, biodegradable polymers and detergents, has shown great potential [6-7]. In fact, an important characteristic of glucaric acid that makes it so industrially relevant is that the carboxylic groups can react selectively with different amines, alcohols, and vinyl derivatives to form products with new application profiles such as aldonolactones, which are used in the preparation of N-alkyl aldonamide surfactants [8]. Moreover, glucaric acid derivatives have also been studied in the pharmaceutical industry in applications relevant to cholesterol reduction and cancer chemotherapy [9-11].

However, the current synthesis methods suffer from various disadvantages [12]. In particular, chemical routes involve drastic conditions (high temperature and pressures), more than one synthetic stage and/or production of mixtures that require further, usually complex, workup. For example, chemical oxidation of glucose using strong oxidants, such as nitric acid, is a non-selective and expensive process that, moreover, produces NO_x emissions [12]. The use of electrochemical methods in organic chemistry represents a promising alternative to the chemical routes. These methods, in fact, are based on the transfer of electrons in mild conditions, not requiring any oxidizing or reducing agents [13-15]. Most importantly, the selectivity can be controlled by adjusting the operating voltage or current density.

The mechanism of the electrocatalytic oxidation of glucose on different metal and metal oxide electrodes has been broadly explored. Platinum has been the most widely studied electrocatalyst [16-25]; in particular Beden et al. applied a reflectance IR spectroscopic technique to study the electro-oxidation of D-glucose at platinum electrodes in alkaline medium [21]. Their studies were based on mechanistic considerations and

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it is recurrent in literature to attribute the first step of action to dehydrogenation upon adsorption of glucose. The same authors compared the electro-reactivity of D-glucose in neutral and alkaline media. They found out that, in neutral solution, D-glucose is in its poorly active anomeric form, α-D-glucopyranose, while in alkaline solution it converts to the more active β-D-glucopyranose [21].

Gold is another metal that has been extensively investigated for the oxidation of glucose [26-41]. Kokoh et al. [37] performed an "on line" chromatographic analysis of the products of the electrocatalytic oxidation of D-glucose on pure and adatoms modified platinum and gold electrodes in alkaline, buffer, and acidic media, with the aim to study the reaction mechanism and kinetics [37]. The authors proved in the first place that gluconic acid is not the sole and final product of D-glucose electrochemical oxidation as several reaction products, i.e. carboxylic acids, were detected by chromatographic analysis. Their results suggested that the applied potential, the nature of the electrode, as well as the nature of the adatoms are important parameters for determining the selectivity of D-glucose oxidation. In the conclusions, they envisage further investigations in order to obtain valuable commercial products other than gluconic acid (such as glucaric and keto-gluconic acids). Pasta et al. [40] investigated the electrocatalytic properties of nanostructured gold electrodes for glucose electro-oxidation by cyclic voltammetry and compared it to commercially available polycrystalline gold electrodes underlining the influence of the morphology on the electrocatalytic performance in glucose alkaline fuel cell applications. Moreover, they investigated the role of the pH and found a strong improvement of substrate reactivity obtained by increasing the OH$^-$ concentration.

Torto et al. also investigated the electrochemical oxidation of mono- and disaccharides at fresh as well as oxidized copper electrodes in alkaline media [42]. From their experimental data and previously reported work [42-49] it is shown that Cu can also oxidize aldohexoses and their acid derivatives electrochemically via a mechanism which proceeds stepwise from aldohexoses to their acid derivatives [44]. In these studies, despite performing exhaustive electrolysis experiments, no concrete evidence for the production of gluconic or glucaric acids was obtained. The authors ascribe it to either the detection limits of the analysis technique employed or to a rapid complete oxidation of the glucose molecule to formate and carbonate products on the copper surface.

The selective transformation of D-glucose into the corresponding aldaric acid has only recently been attempted by means of homogenous and heterogeneous catalysis [50-53]. The authors Solmi et al. [50] employed highly active Au and AuBi nanoparticles supported on activated carbon as catalyst to perform the chemical oxidation with O$_2$ as oxidant. The best yield of glucaric acid obtained was 31%, with 18% of gluconic acid and 40% by-products. The authors Merbouh et al. obtained a yield of glucaric acid as high as 85% by employing a TEMPO-like nitroxide oxidation catalyst, 4-acetamido-2,2,6,6-tetramethyl-1-piperidinyloxy (4-acetamido-TEMPO), in combination with several oxidizing agents and co-catalyst in mild conditions [51]. Subsequently the authors employed TEMPO as homogeneous mediator for the electrochemical oxidation of D-glucose to D-glucaric acid [52-53], as the electrochemical method allowed to limit the amount of non-recyclable side-products generated during the reaction. However very effective, the use of homogenous mediators in catalytic reactions causes considerable drawbacks when thought of industrial applications. The use of mediators, or homogeneous catalysts, in fact, requires considerable downstream processing of the product stream: i.e separation of the mediator from the products and recycling. Additionally, to the best of our knowledge, there is only one recent publication where heterogeneous electrocatalysis is applied successfully for this purpose [13]. The authors employed an electrocatalytic membrane reactor with MnO$_2$/Ti as the anode to selectively convert glucose into glucaric acid in neutral media (99% conversion of glucose and 99% total selectivity to gluconic and glucaric acids). The authors attributed the excellent performances obtained using this reactor configuration to the convection-enhanced mass transfer and to the timely removal of the desired products in the reactor that prevents their further conversion into by-products. The success obtained by these authors encourages further efforts, on the one hand, to understand the mechanism of electrochemical, selective, transformation of glucose into glucaric acid and on the other hand, to design a process that could be implemented industrially and is thus easily up-scalable.

The first challenge encountered during the electrocatalytic oxidation of D-glucose in alkaline media is the low selectivity of the overall process which results in several reaction products including D-fructose and low molar mass carboxylic acids where the structure of the glucose molecule is disrupted [37]. It has been reported in literature that, in alkaline conditions, D-glucose is consumed by two chemical reactions [54]: the isomerization of D-glucose into D-fructose and its thermal oxidative degradation. The former is a reaction controlled by a thermodynamic equilibrium and for which bases are common homogenous catalysts. The latter is a set of irreversible temperature-catalyzed reactions (aldolization/retroaldolization, β-elimination, and benzylic rearrangement) that take place simultaneously to isomerization and lead to several by-products [54]. In our work, we preliminary investigate the stability of the reaction solution to find the operating conditions less favorable for these side-reactions so to limit their impact on the process (i.e. low temperature and concentration of the base). The second challenge refers more specifically to the production of D-glucaric acid from glucose, passing through the formation of the intermediate product, gluconic acid, and in limiting the oxidation process to the two terminal anomeric carbons in the glucose molecule, while keeping the six-atom structure otherwise unaltered. In an uncontrolled process, i.e., at high temperatures or in presence of high concentration of strongly reactive oxidants (radicals, ions), any carbon atom in the glucose backbone becomes a reactive site, leading to the cleavage of C-C bonds and formation of low molar mass carboxylic acids. Our objective was to develop an electrochemical method, using only heterogeneous catalysts, that allows a controlled oxidation with high selectivity towards the desired products (gluconic and glucaric acid) while at the same time preventing the formation of undesired side-products. In this work, we want to demonstrate that, by adjusting an electrochemical parameter (applied potential), it is possible to achieve a region-selective oxidation of glucose to gluconic and glucaric acid.

The electro-reactivity of the two terminal functional groups of D-glucose was investigated by cyclic voltammetry in alkaline medium for three different metal electrodes, in order to find a relationship potential-reactivity of the functional group. Once the optimal reaction conditions, maximally avoiding undesired chemical side-reactions, were selected, this relationship was finally verified by analyzing the products of long-term electrolysis.

Results and Discussion

Oxidation of D-glucose at copper, platinum and gold electrodes

The cyclic voltammograms of copper, platinum and gold recorded at ambient temperature in 0.1 M NaOH in the absence and presence of glucose (0.04 M) are given in Fig. 1.

For copper, four oxidation peaks can be observed during the positive potential sweep, at 0.61 (peak A), 0.84 (peak B), 1.11 (peak C) and 1.80 V_{RHE} (peak D) (Fig. 1(a)). The oxidation at peak

ARTICLE

A has been reported by Kano et al. [49] to correspond to a one-electron transfer reaction between Cu and OH^- ions in solution with the formation of a Cu_2O monolayer as a result. Peak B has been mainly attributed to a two-electron transfer reaction directly from Cu, in combination with (to a smaller extent however) a one-electron transfer reaction from Cu_2O, resulting in the formation of CuO [49]. This species, in which copper has oxidation state +2, appears to be reactive towards glucose oxidation since the current density corresponding to its peak, in presence of glucose, is slightly higher than in blank solution.
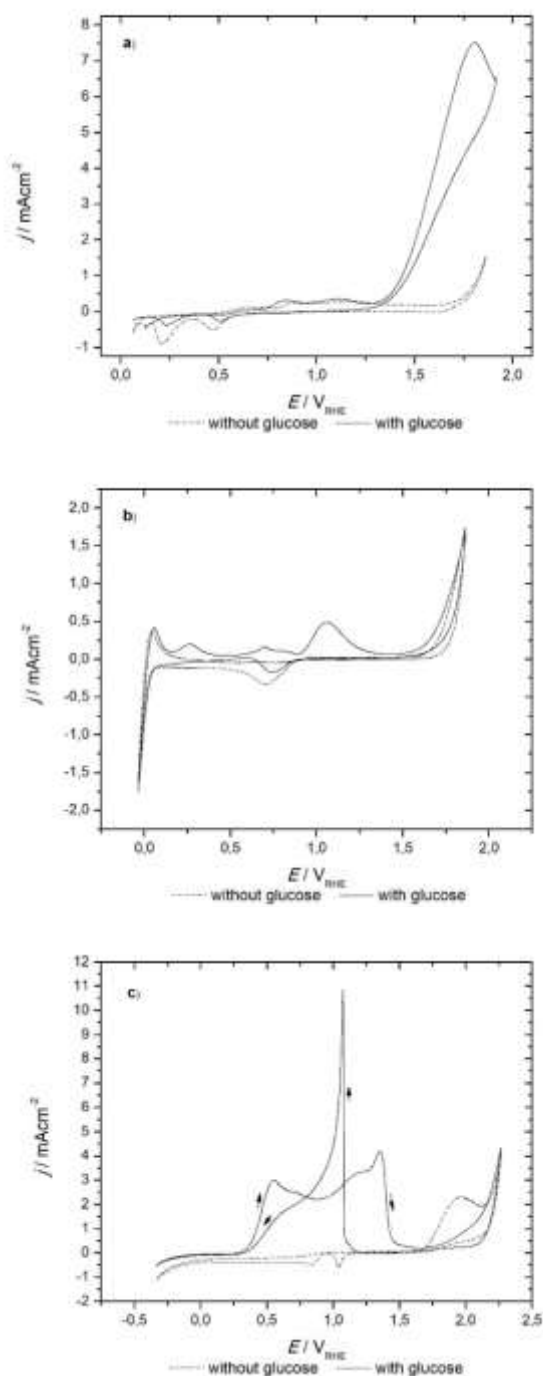

Figure 1. Voltammograms of: (a) copper, (b) platinum and (c) gold electrodes in alkaline medium (0.1 M NaOH) recorded at 10mV s^{-1}, at 20°C without (dashed lines) and with (solid lines) 0.04 M D-glucose.

Peak C has been found to increase with the solution alkalinity (up to 0.1 M NaOH) [49]; at higher NaOH concentrations it appears at less anodic potentials and eventually overlaps with B. Kano et al. did not attribute a specific reaction to this peak, but they hypothesized the formation of a soluble product, either chemically or electrochemically, which diffuses away from the electrode surface and hence is not recovered in the cathodic sweep [49]. In our case, peak C is slightly more pronounced in presence of glucose and shows a reactivity similar to that of peak B, pointing us in direction of the formation of a soluble product from CuO. Finally, Peak D has been attributed to the formation of soluble reaction products, namely cuprite CuO_2^{2-}, from either Cu, through an (electro)chemical reaction from CuO, which diffuse away from the electrode surface, and hence are not recovered in the cathodic half-cycle [49]. We found that these species show the highest current density in presence of glucose and are thus the most interesting Cu species to perform the oxidation of glucose, which we believe results in the cleavage of the C-C bonds and formation of low molar mass carboxylic acids, i.e. formic acid, as will be confirmed by HPLC analysis. The two reduction peaks in the cathodic scan represent the reduction of, respectively, Cu(II) to Cu(I) and Cu(I) to Cu(0), which can be observed both in presence and in absence of glucose.

Three oxidation peaks are visible on the platinum electrode during the positive potential sweep, at 0.26 (peak A), 0.70 (peak B) and 1.10 V_{RHE} (peak C) (Fig. 1(b)) all in the presence of glucose. The presence of shoulders (which affect peak B especially) suggests that the peaks are complex and result from different contributions. Yei et al. [18] thoroughly studied the mechanism of glucose electrooxidation on platinum in alkaline medium. They concluded that: peak A corresponds to the oxidation of the adsorbed hydrogen produced by chemisorption of the glucose molecule, without poisoning of the surface and peak B corresponds to the direct oxidation of glucose from the bulk. Finally, for peak C it is more difficult to determine the involved reaction. This peak was hypothesized to correspond to the oxidation of the adsorbed species resulting from the chemisorption of glucose in the range of peak A [18]. The reduction peak in the cathodic half-cycle corresponds to the reduction of the oxidized Pt.

Finally, the CV curve of the gold electrode in glucose alkaline solution shows three clear electrochemical processes during the anodic sweep and two during the cathodic return scan (Fig. 1(c)). Pasta et al. [40] concluded that glucose electrooxidation on gold follows the same mechanism as on platinum. According to the authors: peak A (around 0.55 V_{RHE}) corresponds to the dehydrogenation of anomeric carbon under adsorption control; peak B at 1.34 V_{RHE}, with a large left shoulder has been attributed to several oxidative processes taking place in the potential range from 1 V_{RHE} to 1.34 V_{RHE} that lead to gluconate as oxidation product [40]; at 1.50 V_{RHE} (peak C) gold surface oxidation occurs, as demonstrated by Xiang et al. [41]. The oxidative peak around 1 V_{RHE} in the cathodic scan (peak D) is obtained as soon as the oxide layer is reduced to generate free O^{2-} anions which react with glucose and then the Au surface undergoes re-oxidation by OH$^-$ in solution [40]. Pasta et al. didn't give an explanation for the oxidation process taking place at E, 0.55 V_{RHE}, in the cathodic scan. It might be attributed, as further explained in the following paragraph, to the same oxidation process taking place at A.

From these studies, it is clear that the electrocatalytic glucose oxidation is strongly influenced by the nature of the applied catalyst. For each examined metal, the different potential windows correspond with different oxidation processes. In some cases the metal is itself involved in the oxidation reaction (i.e. at peak B on Pt or at peak A and B on Au) in some other cases it is an oxide species of the metal that acts as catalytic mediator (i.e. the two oxides of Cu formed at peaks B and C or the platinum oxide at peak C) and, finally, soluble species can be generated at certain potentials that react with glucose in solution (namely the

species cuprite CuO_2^{2-} at peak D on Cu or the free O^{2-} anions generated by the reduction of the gold oxide layers at peak D).

Voltammetry study on glucose derivatives

The structural formulas of D-glucose (for simplicity we show the open-chain form) and its three derivatives, gluconic, glucuronic and glucaric acid, are shown in Fig.2.
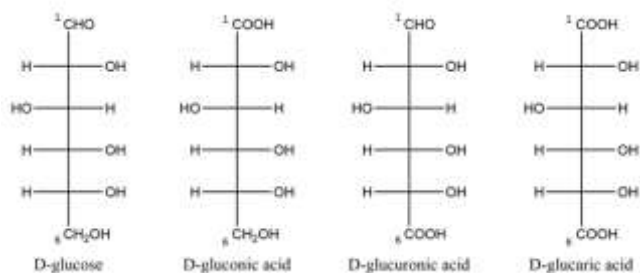

Figure 2. Structural formulas of D-glucose and its three derivatives.

Gluconic acid is the glucose derivative resulting from the oxidation of the aldehyde group on C1, so it only has one oxidizable functional group, on C6: the hydroxymethyl group; glucuronic acid is the glucose derivative that would result from the oxidation of the hydroxymethyl group on C6, so it only has one functional group, on C1: the aldehyde group; finally, glucaric acid is the derivative resulting from the complete oxidation of both groups, in C1 and C6, to carboxyl groups, leaving it without directly accessible and oxidizable sites.

In the next paragraph, the reactivity of each derivative in function of the oxidation potential was investigated by cyclic voltammetry on the three electrodes under investigation. Fig.3 shows the cyclic voltammograms of copper in the presence of glucose (Fig. 3(a)), glucuronic acid (Fig. 3(b)), gluconic acid (Fig. 3(c)) and glucaric acid (Fig. 3(d)).
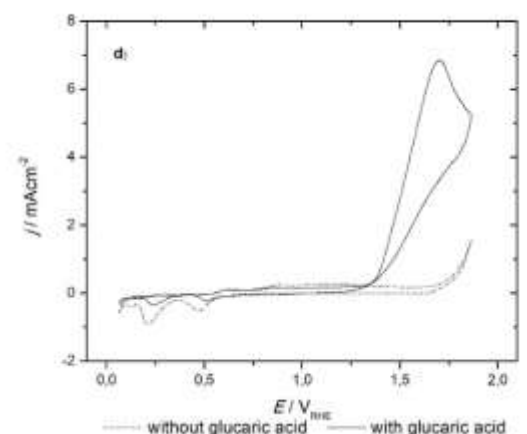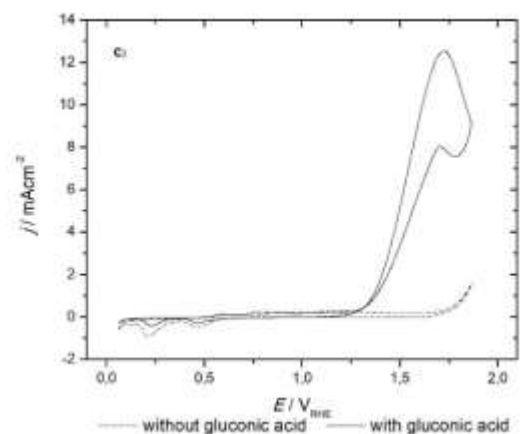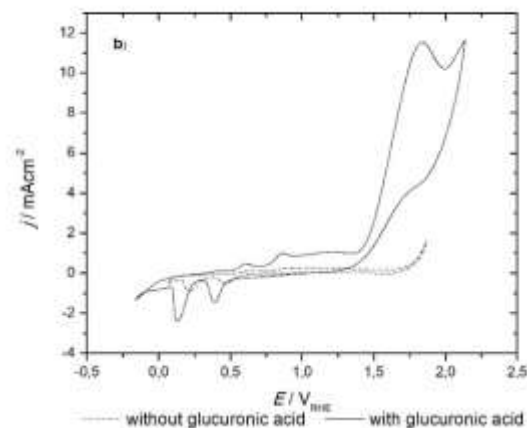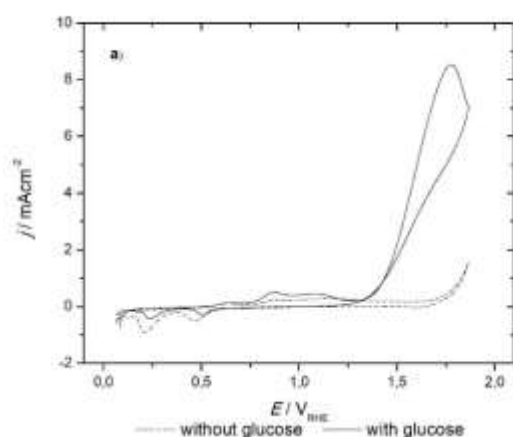

Figure 3. Voltammograms of copper electrode in 0.04 M (a) glucose, (b) glucuronic acid, (c) gluconic acid and (d) glucaric acid (solid lines) in alkaline medium (0.1 M NaOH) recorded at 10mV s^{-1}, at 20°C, compared with the blank solution (dashed lines).

Peaks A and B appear in all the voltammograms of the four solutions, as well as in the blank solution, and correspond to the oxidation of Cu(0) to Cu(I) and Cu(II), respectively [49]. Peak B was already found to increase upon addition of glucose, and the same is true in presence of glucuronic acid. On the other hand, no increase is visible when gluconic and glucaric acids are added to the solution. This could signify that Cu(II), which is formed at this oxidation potential, is able to predominantly oxidize the aldehyde group at C1, which is absent for gluconic and glucaric acid. The same explanation

can be given for Peak C that can only be observed in the voltammograms of glucose and glucuronic acid, and is thus expected to originate from the oxidation of the aldehyde group by a soluble species of copper similar to CuO. Based on these first observations, we believe that at peaks B and C, a reaction involving a two-electrons transfer takes place, leading to the oxidation of the C1 aldehyde group into a carboxyl group, generating gluconic acid. Finally, peak D, characterized by a much higher current density, is present in the voltammograms of all the four carbohydrates and thus clearly does not depend on the nature of the available functional groups present in the molecules. This can be explained by assigning this peak to the (undesired) cleavage of the C-C bond, which can possibly take place at this high overpotentials and is independent of the available functional groups. This ultimately leads to the formation of lower carboxylic acids, i.e. formic acid and is therefore undesirable.

In conclusion, the oxidation of the hydroxymethyl group on C6 is not visible in the cyclic voltammogram, so we expect copper to selectively oxidize the C1 aldehyde group at low potentials (0.8 - 1.2 V_{RHE}).
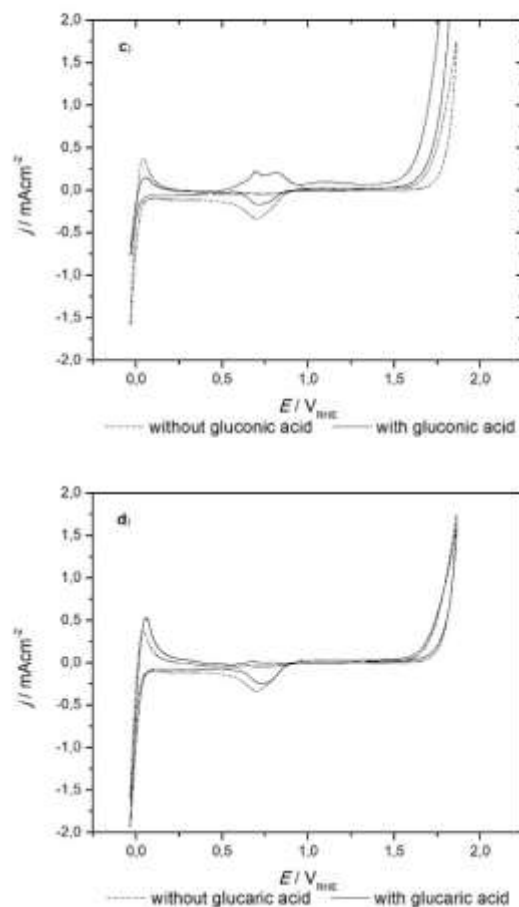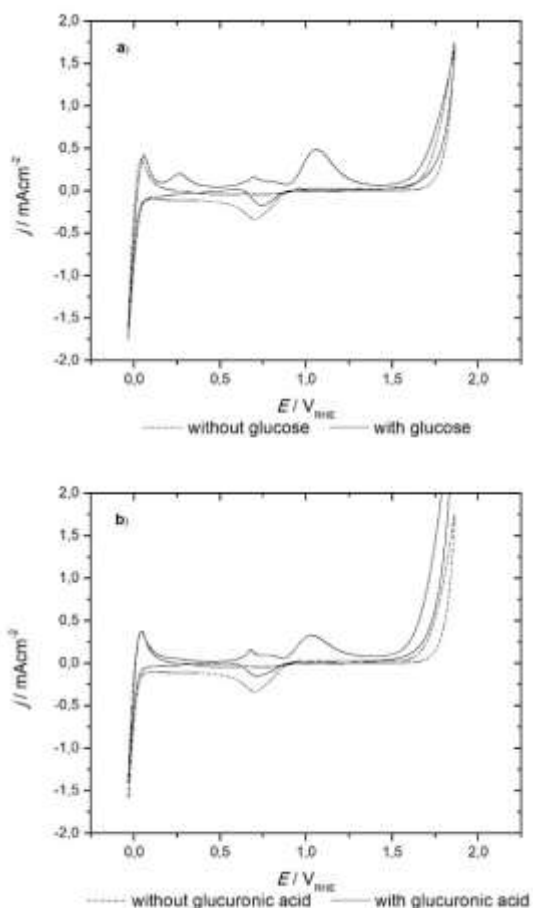
without glucose —— with glucose

without glucuronic acid —— with glucuronic acid

without gluconic acid —— with gluconic acid

without glucaric acid —— with glucaric acid

Figure 4. Voltammograms of platinum electrode in 0.04 M (a) glucose, (b) glucuronic acid, (c) gluconic acid and (d) glucaric acid (solid lines) in alkaline medium (0.1 M NaOH) recorded at 10mV s^{-1}, at 20°C, compared with the blank solution (dashed lines).

The same study was then performed on platinum (Fig.4). None of the glucose oxidation peaks appear in the solution containing glucaric acid, meaning that neither oxidation processes nor cleavage of the C-C bond takes place on the Pt electrode. On the contrary, both peak B and C are present in the solution containing glucuronic acid and a more pronounced peak B appears in the solution containing gluconic acid. This might be explained by stating that peak C, that was assigned by Yei at al. [18] to the oxidation of adsorbed glucose on an already oxidized platinum surface, corresponds mainly to the oxidation of the aldehyde group, present in the glucuronic acid molecule but not in the gluconic one. Peak B, which is present in the voltammograms of both hydrocarbons, and that had been attributed by Yei at al. to the direct oxidation of glucose from the bulk, might be assigned to both oxidations, of the aldehyde and of the hydroxymethyl groups. In conclusion, both the oxidation of the hydroxymethyl group on C6 and of the aldehyde group on C1 are visible in the cyclic voltammogram of platinum, that can therefore oxidize C6 at lower overpotentials and C1 at higher overpotentials.

Finally, the electrocatalytic activity of gold was also studied in the solutions of the three glucose derivatives (Fig.5).
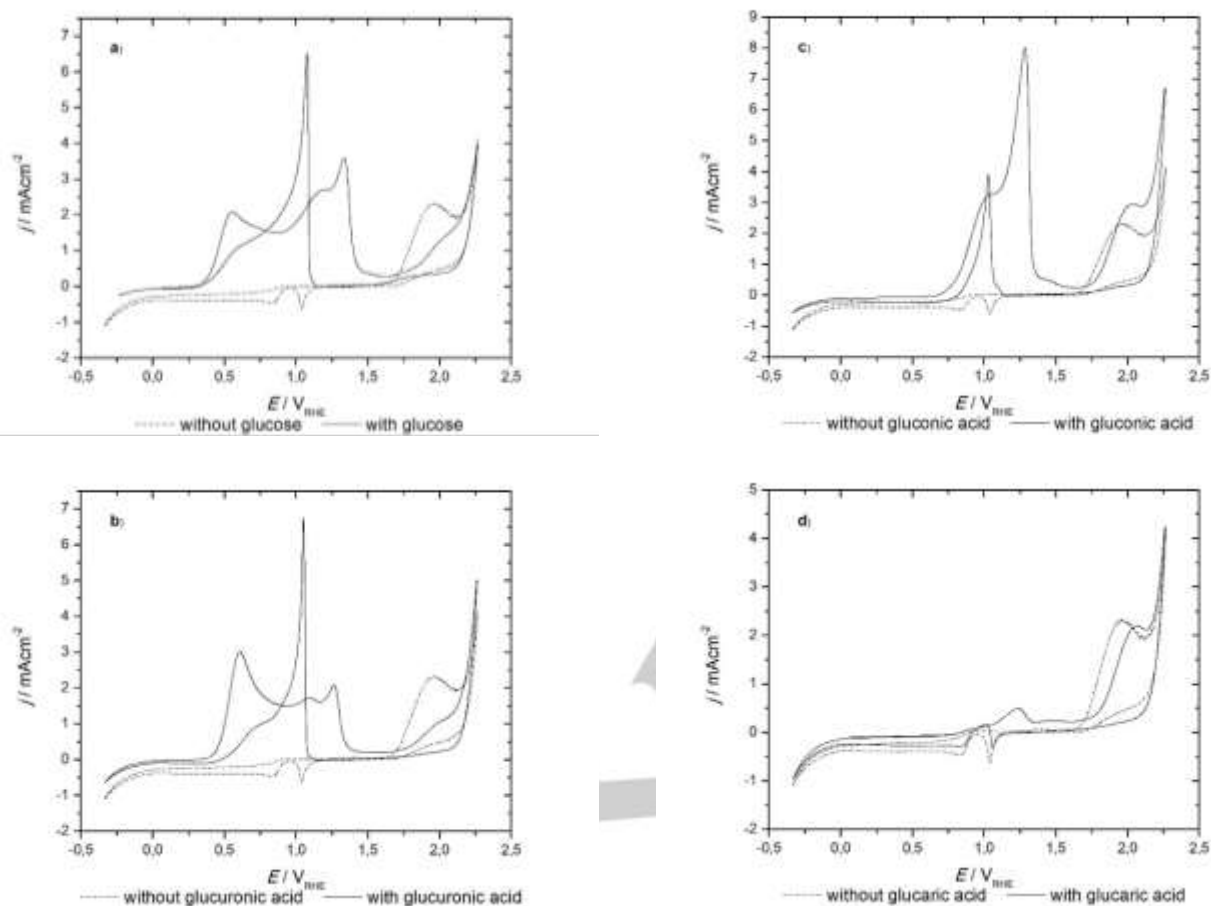
Figure 5. Voltammograms of gold electrode in 0.04 M (a) glucose, (b) glucuronic acid, (c) gluconic acid and (d) glucaric acid (solid lines) in alkaline medium (0.1 M NaOH) recorded at 10mV s^{-1}, at 20°C, compared with the blank solution (dashed lines).

Gold, in addition to exhibiting the highest electro-activity (excluding the undesired C-C cleavage at 1.8 V$_{RHE}$, which is more pronounced on copper), also shows distinct oxidation peaks for the aldehyde and for the hydroxymethyl groups. It is easy to see that the oxidation processes at 0.55 V$_{RHE}$, both in the anodic and in the cathodic scan (peaks A and E, respectively) only take place in the glucose and glucuronic acid solutions. For this reason we believe that they correspond exclusively to the oxidation of the aldehyde group. Peaks B and D, instead, are present in all the solutions. Nevertheless, peak B is significantly higher in the gluconic acid solution, and might thus be related to the oxidation of the hydroxymethyl group. Peak D, which was attributed to the reaction between free O^{2-} anions and glucose from the bulk, is slightly less pronounced in the gluconic acid solution, so might be attributed predominantly to the oxidation of the aldehyde group, and in a lesser extent to the hydroxymethyl functional group. In conclusion, as for platinum, both the oxidation of the hydroxymethyl group on C6 and of the aldehyde group on C1 are visible in the cyclic voltammogram of gold, that can therefore oxidize C1 at lower overpotentials and C6 at higher overpotentials.

ARTICLE

Long-term Electrolysis

In order to find the reaction conditions that inhibit the base-catalysed isomerization of D-glucose to D-fructose and oxidative degradation to lower molar mass carboxylic acids, preliminary experiments were performed in absence of the catalysts at two different temperatures, 5 and 20°C. In absence of the base, glucose conversion did not occur, but in 0.1 M NaOH the sugar was quickly converted into a variety of products, mainly fructose but also gluconic acid, glycolic acid, tartaric acid glucaric acid, oxalic acid and formic acid. Except for one minor product that remained unidentified, the carboxylic acids were analyzed by HPLC: the selectivity % and the conversion of glucose after 65 h of reaction in absence of the catalyst are presented in Table 1. The products whose concentration is below 100 ppm are indicated as "traces".

Table 1. Chromatographic analyses of the solutions of D-glucose after 65 h of reaction in absence of the catalyst at 5 and 20°C.

Product	Selectivity (%)	
	5°C	20°C
Glucaric acid	traces	traces
Gluconic acid	10.7	4.6
Formic acid	traces	traces
Oxalic acid	traces	traces
Tartaric acid	traces	2.6
Glycolic acid	traces	6.0
Fructose	79.8	84.5
Glucose conversion (%)	18.4	46.3

In the absence of the catalyst, the predominant product is D-fructose, as a consequence of the NaOH-catalyzed isomerization of D-glucose, and the conversion to this product increases with the reaction temperature. Besides, in accordance with previous studies [54], the aldose-ketose isomerization is accompanied by sugar degradation reactions, which lead to the production of low molar mass carboxylic acids (i.e. formic, oxalic, tartaric and glycolic acids) [54]. The authors [54] reported that the rate and extent of these side reactions are controlled mainly by the type of base cation, base concentration, and temperature. In particular, they indicate alkali and alkaline earth hydroxides as very active catalysts towards the isomerization reaction, but also unselective, promoting the oxidative degradations of glucose, especially when used at high concentration or increased time and reaction temperature.

In accordance with these previous studies, our experiments demonstrate that, at high concentration of the base and ambient temperature, the base-catalyzed isomerization reaction, together with the (thermal) oxidative degradation of glucose, affect dramatically the performance of the electrocatalytic process since they consume almost 50% of the glucose in the solution.

Therefore, mild reaction conditions and a low alkali concentration are advisable to limit these undesired side-reactions, which is why all following experiments were performed at 5°C.

In order to determine the electrooxidation products, D-glucose (0.04 M) was oxidized at copper, platinum and gold electrodes in 0.1 M NaOH medium (pH 13) by means of long-term electrolysis (65 h) at a temperature of 5°C. After electrolysis, samples from the electrolyzed solutions were analysed by HPLC (Fig. S1). In all the experiments, the identified products were the same as the ones obtained in absence of the catalyst. The long-term electrolysis of D-glucose on copper was carried out at 0.84, 1.11, and 1.80 V_{RHE}. The selectivity % of the products in the liquid phase after 65 h of reaction at 5°C is given in table 2. The products whose concentration is below 100 ppm are indicated as "traces".

Table 2. Chromatographic analyses of the solutions of D-glucose after 65 h electrolysis on Cu at 0.84 V_{RHE}, 1.11 V_{RHE} and 1.80 V_{RHE} at 5°C.

Product	Selectivity (%)		
	E_{ox}=0.84 V_{RHE}	E_{ox}=1.11 V_{RHE}	E_{ox}= 1.80 V_{RHE}
Glucaric acid	38.4	26.8	12.2
Gluconic acid	30.4	44.5	17.8
Formic acid	13.9	15.2	54.2
Oxalic acid	traces	traces	traces
Tartaric acid	traces	traces	traces
Glycolic acid	traces	traces	traces

Although a good selectivity to glucaric acid is achieved at the lower potentials, 0.84 and 1.11 V_{RHE}, the catalyst activity is too low to achieve acceptable conversions. From the Cyclic Voltammetry study it was concluded that copper, at these potentials, corresponding to peak B and C in Fig. 1(a), oxidizes the C1 aldehyde group, which is confirmed by the results of the electrolysis. Moreover, the percentage of glucaric acid suggests that, at these potentials, also the C6 hydroxymethyl group is able to complete its oxidation to carboxyl, which was not easily deducible from the CV. Finally, our hypothesis (based on CV combined with a literature study) that cuprite species, formed at 1.80 V_{RHE}, are responsible for the cleavage of the C-C bonds and thus the formation of mainly formic acid is confirmed by the obtained high selectivity (>50%) to this product.

For gold and platinum a constant decrease of current density was observed during the electrolysis process, which was ascribed to active surface poisoning during the oxidation process. To avoid this poisoning, the electrolysis were carried out using an optimized program of potential which included three potential plateaus, in order to maintain the electrode activity at a sufficient level [36]. The oxidation plateau over 30 s was followed by a reactivation procedure consisting of two short potential pulses (1 s): one at 2.40 V_{RHE} , that allowed to reactivate the electrode by clearing out the poisoning species, and the second at 0 V_{RHE} that served to reduce the metal surface and allowed the adsorption of the organic molecule. These steps were repeated at the length of the experiments until 65 h passed.

The electrolysis experiments of D-glucose on platinum were carried out at two oxidation potentials: 0.70 and 1.10 V_{RHE} . The selectivity % of the products in the liquid phase after 65 h of reaction at 5°C are given in table 3. The products whose concentration is below 100 ppm are indicated as "traces".

Table 3. Chromatographic analyses of the solutions of D-glucose after 65 h electrolysis on Pt at 0.70 V_{RHE} (Potential program 1) and 1.10 V_{RHE} (Potential program 2) at 5°C.

Product	Selectivity (%)	
	Potential program 1 [a]	Potential program 2 [b]
Glucaric acid	12.6	6.3
Gluconic acid	68.0	78.4
Formic acid	12.0	7.8
Oxalic acid	traces	traces
Tartaric acid	traces	traces
Glycolic acid	traces	traces

[a] Potential program 1: 0.70 V_{RHE} for 30 s, 2.40 V_{RHE} for 1 s, 0 V_{RHE} for 1 s. Initial conditions: 0.04 M D-glucose in 0.1 M NaOH.
[b] Potential program 2: 1.10 V_{RHE} for 30 s, 2.40 V_{RHE} for 1 s, 0 V_{RHE} for 1 s. Initial conditions: 0.04 M D-glucose in 0.1 M NaOH.

For both oxidation potentials, gluconic acid is the main product of the electrochemical reaction as expected based on previous literature. Nevertheless, at the end of the electrolysis at 0.70 V_{RHE} , a higher amount of glucaric acid and a lower amount of gluconic acid were detected, while the total amount of lower molar mass products remained the same. This confirms the results obtained from the cyclic voltammetry study: at this potential, corresponding to peak B in the voltammogram of platinum electrode (Fig. 1(b)), both oxidations, of the aldehyde and of the hydroxymethyl groups, are promoted so that the intermediate product, D-gluconic acid, is able to further convert into the corresponding aldaric acid more effectively than at higher overpotentials (1.10 V_{RHE}, peak C).
The electrolysis of D-glucose on gold were carried out at two oxidation potentials: 0.55 and 1.34 V_{RHE} . The selectivity % of the products in the liquid phase after 65 h of reaction at 5°C is given in table 4. The products whose concentration is below 100 ppm are indicated as "traces".

Table 4. Chromatographic analyses of the solutions of D-glucose after 65 h electrolysis on Au at 0.55 V_{RHE} (potential program 3) and 1.34 V_{RHE} (potential program 4) at 5°C.

Product	Selectivity (%)	
	Potential program 3 [a]	Potential program 4 [b]
Glucaric acid	traces	13.5
Gluconic acid	86.6	65.8
Formic acid	6.0	8.8
Oxalic acid	traces	traces
Tartaric acid	traces	traces
Glycolic acid	traces	traces

[a] Potential program 3: 0.55 V_{RHE} for 30 s, 2.40 V_{RHE} for 1 s, 0 V_{RHE} for 1 s. Initial conditions: 0.04 M D-glucose in 0.1 M NaOH.
[b] Potential program 4: 1.34 V_{RHE} for 30 s, 2.40 V_{RHE} for 1 s, 0 V_{RHE} for 1 s. Initial conditions: 0.04 M D-glucose in 0.1 M NaOH

At lower oxidation potential, 0.55 V_{RHE}, glucose converts exclusively to gluconic acid, while at higher potential, 1.34 V_{RHE}, part of the glucose further converts into glucaric acid through oxidation of both, the aldehyde and the hydroxymethyl group. Again, the results of the electrolysis confirm our hypothesis based on the cyclic voltammogram of gold, that can therefore oxidize C1 at lower overpotentials, and C1 and C6 at higher overpotentials. As expected, for both oxidation potentials, gluconic acid is the main product of the electrochemical reaction.

The electrolysis of D-glucose on Pt and Au over 65 h at 5°C lead to high yields of D-gluconic acid. The further oxidation of the latter to D-glucaric acid in these conditions was promoted at lower potentials on Pt (0.70 V_{RHE}) and at higher potentials on Au (1.34 V_{RHE}) and in both cases was accompanied by the formation of lower molar mass carboxylic acids (mainly formic acid). We suspect that the formation of products in which the molecular structure of D-glucose is disrupted (tartaric, glycolic, formic and oxalic acids), in all the experiments, might also occur due to the formation of small quantities of D-fructose in the reaction system. Indeed, despite minimalizing the chemical side-reaction by optimizing the reaction conditions, an undeniable amount of D-fructose is still detected in the reaction solution at the end of the electrolysis. A participation of the ketose in the electrochemical reaction, could, indeed, have an impact on the product distribution.

Our results demonstrate that the sole electrochemical reaction, performed in a simple H-cell on bare (unmodified) metal electrodes, i.e. platinum and gold, is able to convert into gluconic and glucaric acid more than 80% of the glucose reacted and that the selectivity towards one product or the other can be controlled by adjusting the electrochemical parameters.

Conclusions

The results of the cyclic voltammetry study performed in the three solutions containing 0.04 M of gluconic acid, glucuronic acid and glucaric acid in 0.1 M aqueous NaOH are confirmed by the electrolysis: the selectivity of the electrooxidation of D-glucose on copper, platinum and gold is potential-dependent. The relationship potential-reactivity of the functional group is verified for the three catalysts examined in this work.
Gold is the catalyst, of the ones examined in this work, with the highest selectivity to gluconic and glucaric acid. For this electrode, at low potentials, i.e. 0.55 V_{RHE}, D-gluconic acid is the final oxidation product (with a selectivity of 86.6%). At higher potentials, i.e. 1.34 V_{RHE}, D-gluconic acid is still the main product but a 13.5% of D-glucaric acid is the sign that, at this potential, the produced gluconic acid undergoes further oxidation. An important applied potential effect was also found for the oxidation on platinum. As for gold, the main oxidation product is the intermediate D-gluconic acid, but, in this case, it is at lower potentials, i.e. 0.70 V_{RHE} that it further oxidizes to D-glucaric acid (with a 12.6% of selectivity after 65h). Copper is the least active catalyst of the ones examined in this work: even though the selectivity to D-glucaric acid is quite high at low potentials (38.4% at 0.84 V_{RHE} and 26.8% at 1.11 V_{RHE}), its activity (current density) is too low and the formation of C-C cleavage products too high. At the highest potential, i.e. 1.80 V_{RHE}, the current density is high but here formic acid becomes the main oxidation product and the selectivity to D-gluconic acid and D-glucaric acid is very low.

In conclusion, in this work we developed a method that allows a controlled, selective, oxidation of a highly functionalized compound as D-glucose, into two value-added products, D-gluconic acid and D-glucaric acid, in batch, using bare metals as heterogeneous catalysts and without making use of any mediator/oxidizing agent/co-oxidant. The relationship between oxidation potential and reactivity of the functional groups demonstrated in this work, together with the findings on the role of the chemical side-reactions competing with the electrochemical process, open the doors to further developments, which will be the subject of our next studies: 1) the optimization of the operating

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conditions to maximize the yield of D-glucaric acid; 2) the up-scaling of the process through reactor design.

Experimental Section

Chemicals and reagents

The supporting electrolytes were prepared with ultrapure water (Synergy UV system) and sodium hydroxide (Sigma-Aldrich, 98%). Anhydrous D-glucose was purchased from VWR (99.5%), gluconic acid potassium salt (98%) and D-saccharic acid potassium salt (98%) from Sigma Aldrich, and D-glucuronic acid sodium salt (99%) from Acros Organics. All chemicals were used without further modifications.

Electrochemical setup

A thermostated three-electrode glass cell was used during the voltammetry study, while a two-compartment glass cell separated by a cation-exchange membrane (Nafion 117) was employed for the electrolysis. A silver-silver chloride electrode (Ag/AgCl) and a platinum rod were used as reference and counter electrodes, respectively. Copper (0.32 cm²), platinum (0.13 cm²) and gold (0.08 cm²) working electrodes used for the cyclic voltammetry experiments were purchased from AISI 304, Goodfellow. A copper rod (3.85 cm²), a platinum plate (2.91 cm²) and the gold 0.08 cm² working electrode were used for the long-term electrolysis. The electrochemical instrumentation consisted of a Bio-Logic VSP-300 Potentiostat. All the electrode activities are represented as current densities, utilizing the geometric area as active area and with respect to the reversible hydrogen electrode (V_{RHE}). Before every electrochemical measurement, the working electrodes' surface was carefully polished with aluminium (Φ 1 µm) slurry on a polishing cloth and then sonicated in MilliQ water for 5 min. Finally, the electrode was dried with high purity N_2 (99.999%). The cyclic voltammetry studies were conducted between 0 and 2 V_{RHE} at 10 mV/s at ambient temperature, while the long-term electrolysis experiments were performed for 65 hours at 5°C, in order to inhibit the thermal degradation of glucose in alkaline solution [54]. Solutions containing 0.04 M of glucose, gluconic acid, glucuronic acid and glucaric acid in 0.1 M aqueous NaOH were used for the cyclic voltammetry studies. All the voltammograms shown correspond to the cycle once a stable state is reached. An initial solution containing 0.04 M of glucose in 0.1 M NaOH (pH 13) was used for the electrolysis.

Product analysis

The identification of reaction products was carried out by gas chromatography coupled with mass spectrometry (GC-MS) using a RXI-1ms (Restek) capillary (30 m, 0.32 mm i.d. and 0.25 µm film thickness). The electrolytic solutions were treated before analysis according to the following procedure. The water was removed by lyophilization to leave dry samples of electrolyzed material. This material was trimethylsilylated using Supelco HMDS+TMCS+pyridine, 3:1:9 (Sylon HTP) Kit, as described in [55]. Authentic samples of the expected reaction products were also trimethylsilylated and their chromatographic data were used for the product identification.

The quantitative analysis of the reaction products was performed by high performance liquid chromatography (HPLC) using an ion-exclusion column (Shodex KC-811). A photodiode array (PDA) detector set to 210 nm was used to detect organic acids while a refractive index (RI) detector thermostated at 30°C was used to detect glucose and fructose. Gluconic acid and glucose peaks overlapped in the chromatograms obtained using the RI detector,

however, it was possible to perform a quantitative analysis of glucose, by subtracting the gluconic acid concentration obtained with the PDA detector from the total gluconic acid and glucose concentrations obtained with the RI detector, as already done by Solmi et al. [50]. The aqueous solutions of HPLC references were prepared from standard products >99% of pure gluconic, glucaric, lactic, tartaric, formic and oxalic acid. The selectivity (mol%) was calculated as the number of moles of product formed per number of moles of glucose consumed taking into account the stoichiometry:

$$Selectivity\ [mol\%] = 100 \cdot \frac{[mol\ of\ product\ formed]}{[mol\ of\ glucose\ consumed]} \cdot \frac{[\mu]}{[\nu]}$$

For the results of the electrolysis, the selectivity refers only to the contributions of the electrochemical reaction. All the measurements were performed two times and the errors measured on the values of selectivity of the products were, in all cases, lower than 3%. The analysis of the gas phase was performed by Gas Chromatography (GC) : no gaseous product was formed during the electrolysis.

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Table of Contents

A two-compartment glass cell separated by a cation-exchange membrane was employed in batch mode for the electrochemical oxidation of D-glucose in alkaline media. Three electrode materials (copper, platinum and gold) were examined with respect to their selectivity towards D-gluconic and D-glucaric acid. A strong dependence of the electro-reactivity of the two terminal functional groups of D-glucose on the oxidation potential demonstrated to be key for the control of the selectivity to the products of interest.

D-Glucose

D-Gluconic acid

D-Glucaric acid

2 e⁻ Ⓐ
4 e⁻ Ⓑ
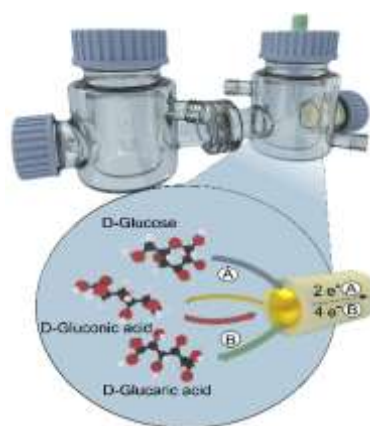
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Electrochemical oxidation of D-glucose in alkaline medium: impact of oxidation potential and chemical side-reactions on the selectivity to D-gluconic and D-glucaric acid

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