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Review Article

Electrochemical methods for ascorbic acid determination

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ABSTRACT

The present review focuses on electrochemical methods for ascorbic acid assessment. The occurence, role, biological importance of vitamin C, as well as the non-electrochemical methods for its assessment are firstly reviewed. The electrochemical behavior of ascorbic acid is then illustrated, followed by a description of the potentiometric, voltammetric and amperometric methods for vitamin C content estimation in various media. Different methods for the development of electrochemical sensors are reviewed, from unmodified electrodes to different composites incorporating carbon nanotubes, ionic liquids or various mediators. From this perspective, the interaction between the functional groups of the sensor's material and the analyte molecule is discussed, as it is essential for the analytical characteristics obtained. The analytical performances of the potentiometric, voltammetric or amperometric chemical and biochemical sensors (linear range of analytical response, sensitivity, precision, stability, response time etc) are highlightened. The numerous applications of ascorbic acid electrochemical sensors in fields like food, pharmaceutical or clinical analysis, where vitamin C represents a key analyte, are also presented.

Contents

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1. Introduction

Vitamin C is a hydrosoluble, antioxidant vitamin, which has a γ-lactone structure, and represents the L enantiomer of ascorbic acid, the biochemically and physiologically active form. Ascorbic acid is a hexanoic sugar acid with two dissociable protons (p*K*a 4.04 and 11.34). Therefore, under physiological conditions, it occurs as an ascorbate anion.

Ascorbic acid (AA) is known for its reductive properties, being easily oxidated to dehydroascorbic acid. It acts as a powerful antioxidant which fights against free-radical induced diseases [1–6]. Plants and most animals synthesize ascorbate from glucose. In primitive fish, amphibians and reptiles, ascorbate synthesis takes place in kidney, whereas for mammals liver is the site of synthesis, where the enzyme L-gulonolactone oxidase converts glucose to ascorbic acid [7,8]. Due to a genetic mutation that induce a L-gulonolactone oxidase deficiency, humans, some other primates, and guinea pigs are unable to synthesize ascorbic acid, so they need to take it from diet [9].

Ascorbic acid can scavenge singlet oxygen, or act as chelating agent. This is claimed as the basis of its ability to protect oxidizable constituents, including phenolic and flavor compounds, therefore being largely used as an antioxidant in foods and drinks. Studies performed on wine showed that the benefit of ascorbic acid as an antioxidant consists in its capacity to scavenge molecular oxygen, before the oxidation of phenolic compounds. Ascorbic acid also appears to be an ideal free-radical scavenger, because it reacts rapidly with hydroxyl (and other) radicals to form relatively unreactive radicals that do not readily propagate [10].

Vitamin C can be found in many biological systems and foodstuffs, namely fresh vegetables and fruits, as the most ubiquitous water-soluble vitamin ever discovered. Rich sources include blackcurrant, citrus fruit, leafy vegetables, tomatoes, green and red peppers, etc. Vitamin C is involved iron absorption, collagen synthesis and immune response activation and participates in wound healing and osteogenesis, helps maintaining capillaries, bones, and teeth [1–6].

Ascorbic acid excess can lead to gastric irritation, and one of its metabolites, oxalic acid, causes renal problems [11]. In some cases, excessive quantities of ascorbic acid may result in the inhibition of natural processes occurring in food and can contribute to taste/aroma deterioration; [12]. Another drawback of ascorbic acid excess is its ability to act as a strong antioxidant only in aqueous media and in the absence of heavy metal cations. In the presence of heavy metal cations, it can even act as a prooxidant: ascorbate ion is an excellent reducing agent that can reduce ferric (Fe^{3+}) to ferrous (Fe^{2+}) iron, while being oxidized to dehydroascorbate [7,13,14].

$$2Fe^{2+} + \text{Ascorbate} \rightarrow 2Fe^{3+} + \text{Dehydroascorbate}$$

The metal ion resulted can be subsequently reduced, reoxidated and again reduced, entering a redox cycle generating reactive oxygen species [7,13,14]. Thus, depending on the coordination environment, Fe^{2+} can react with O_2, reducing it to superoxide radical anion, which dismutes to H_2O_2 and O_2 [7].

$$Fe^{2+} + O_2 \rightarrow Fe^{3+} + O_2^{\bullet -}$$

$$2O_2^{\bullet -} + 2H^+ \rightarrow O_2 + H_2O_2$$

In a classic Fenton reaction, Fe^{2+} reacts with H_2O_2 to generate Fe^{3+} and the strongest reactive oxygen species (ROS), namely the very oxidizing hydroxyl radical.

$$Fe^{2+} + H_2O_2 \rightarrow Fe^{3+} + OH\cdot + OH^-$$

The presence of ascorbate can allow the recycling of Fe^{3+} back to Fe^{2+}, which in turn will catalyse the formation of highly reactive oxidant species. This prooxidant activity may be displayed in the presence of heavy metal cations and in the absence of other antioxidant compounds, such as SO_2 [10].

Ascorbic acid is a labile substance as it is easily degraded by enzymes and atmospheric oxygen. Its oxidation is accelerated by excessive heat, light, and heavy metal cations [2]. Ascorbic acid is frequently used as an antioxidant in food industry to prevent unwanted changes in color or flavor. As an electron donor, ascorbic acid serves as one of most important small-molecular-weight antioxidants which contributes to the total antioxidant capacity-an important quality indicator of foods and drinks [15–17]. Due to the crucial role of vitamin C in biochemistry and in industrial applications, the determination of vitamin C still presents research interest. Quick monitoring of vitamin C levels during production and quality control stages is important [18].

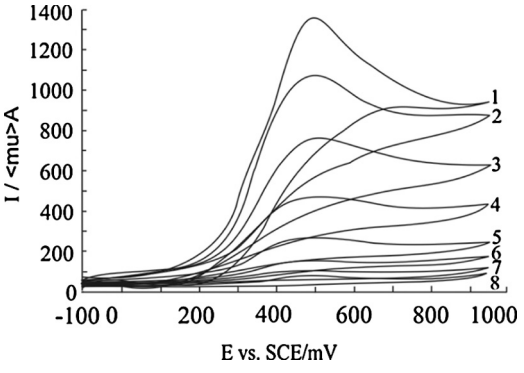


Figure 1. Cyclic voltammograms obtained with a Pt working electrode for different ascorbic acid concentrations, expressed as mmol L^{-1}: 20 (line 1), 15 (2), 10 (3), 5 (4), 2.5 (5), 1.25 (6), 0.625 (7) and 0.31 (8); potential scan rate 50 mV/s; a 0.1 mol L^{-1} KCl solution was used as supporting electrolyte [60].

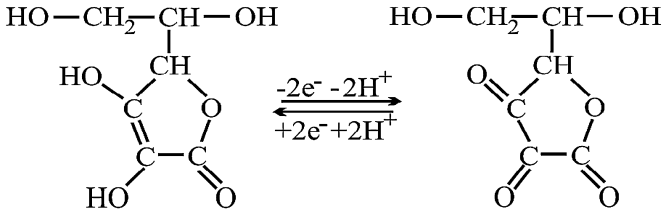
2. Ascorbic acid determination by non-electrochemical techniques.

Traditional methods for ascorbic acid assessment involve titration with an oxidant solution: dichlorophenol indophenol (DCPIP) [19], potassium iodate [20] or bromate [21]. Chromatographic methods, like liquid chromatography [22–24] and particularly HPLC with electrochemical detection [25–27], have been used in ascorbic acid assessment in foodstuffs and biological fluids. Fluorimetric methods based on dehydroascorbic acid reaction with o-phenylene diamine and requiring strict control of the pH value [28,29] and UV-VIS absorbance-based determinations [30] were also applied. Ascorbic acid was assessed spectrophotometrically, based on its reaction with hexacyanoferrate (III) [31–33], on its oxidation using the Cu(II)-neocuproine complex [34], or on the determination of iodine reacted with ascorbic acid [35]. Other optical methods for vitamin C estimation include chemiluminescence [36].

3. Electrochemical behavior: the irreversibility of ascorbic acid/dehydroascorbic acid redox couple

Ascorbic acid is the most common electroactive biological compound, being easily oxidated, and this constitutes the basis of its electrochemical determination. Ascorbic acid forms with dehydroascorbic acid an irreversible redox couple. Its electrocatalytical oxidation showed only the anodic oxidation peak [1,37–39], for which Randles Sevčic equation described the observed direct dependece between the current intensity corresponding to ascorbic acid electrooxidation and the square root of the potential sweep rate [40,41].

Regarding ascorbic acid/dehydroascorbic acid redox couple irreversibility, studies have been devoted to the investigation of ascorbic acid oxidation mechanism, which describe an electrochemically reversible electron transfer coupled to irreversible chemical reactions, determining an overall irreversible process: the oxidation of ascorbic acid involves the release of two electrons and two protons, to produce dehydroascorbic acid, which was proved to be followed by an irreversible solvation reaction at pH lower than 4.0 [1].



This irreversible reaction yields an electroinactive product, 2,3-diketogulonic acid, formed when dehydro-L-ascorbic acid opens its lactone ring [42–49], easily adsorbable on the electrode surface, which can result in electrode fouling [50–52].

Literature data on ascorbic acid oxidation at pH < 8 mention two successive one electron oxidation steps accompanied by rapid dehydration rendering the oxidation process irreversible [49,53–55]. A detalied description of ascorbic acid oxidation at gold electrode describes two clearly defined stages producing two waves. The first wave is produced by a bielectronic process in which two protons interchange at the pH range of 2-4.5, one proton at pH 4.5-8 and finally two protons at pH >8. Namely, at pH values inferior to the first pKa value of L-ascorbic acid (approximately 4.5), two protons interchange globally during the process. At higher pH values, a single proton interchanges, with ascorbate anion as electroactive species. These considerations are consistent with the variation of the peak potential with pH, observed up to pH 8 [49]. It was diffficult to identify the products of ascorbic acid oxidation or to carry out a detailed study of the second oxidation wave at pH higher than 8, given the instability of the basic solutions of both L-ascorbic and dehydro-L-ascorbic acids. It was found that the intermediate, ascorbate anion is electrochemically oxidized to a diketolactone, subsequently dehydrated to dehydroascorbic acid which rearranges to another ene-diol further oxidized at higher potentials [49].

For this irreversible redox couple the anodic peak height correlated with analyte concentration corresponds to the oxidation of the reduced form [56–60] (Figure 1).

3.1. Electrochemical behavior at unmodified electrodes

The polarographic behavior of ascorbic acid was first investigated in acid medium, using a mercury capillary as working electrode [43]. It was established that the limiting current is independent of the pH value, and it is also diffusion - controlled. The value of the half-wave potential $E_{1/2}$ was found independent of L-ascorbic acid concentration, but varies with pH. The values of the slopes of the linear ranges were - 59 and - 27 mV/H^+ concentration decade [43]. Studies carried out in basic solution showed that L-ascorbic acid is unstable in this medium and therefore the current decrease is not only caused by the electrochemical oxidation of the analyte, but also by its homogeneous decomposition in solution [44].

Cyclic voltammetry studies at a glassy carbon electrode, showed only the anodic oxidation peak, recorded at about 580 mV in 0.1 mol L^{-1} phosphate buffer pH = 2.0, containing 0.1 mmol L^{-1} disodium EDTA [56], for which the height increases with ascorbic acid concentration, and no cathodic peak current was observed in the potential range studied, 200-1000 mV, using a 50 mV/s potential scan rate.

The irreversibility of the ascorbic acid redox couple, was proved also at Pt [59,60], as well as unmodified carbon paste electrodes [60]. The peak corresponding to ascorbic acid oxidation appeared at 490 mV (versus SCE) at a Pt strip electrode, and at 510 mV at an unmodified carbon paste electrode, using 0.1 mol L^{-1} KCl solution as electrolyte [60]. A comparative study of ascorbic acid determination at bare gold electrodes in a phosphate buffer solution at pH 6.90, showed for the single-crystal Au(111) electrode much better electrocatalytic activity in comparison with the gold disk electrode [61].

The difficulties in obtaining good reproducibility in direct electrochemical oxidation of ascorbic acid and the problems of electrode fouling have led to interest in the investigation of the role of various mediators and consecutively modified electrodes (metallic or carbonaceous), to catalyse the electrochemical oxidation of ascorbic acid.

3.2. Electrochemical behavior at chemically modified electrodes

The electrochemical behavior of ascorbic acid on a cobalt hydroxide modified glassy carbon electrode in alkaline solution was investigated and compared with the performances of the unmodified electrode [57]. The oxidation process and its kinetics were studied and it was found that the presence of the cobalt hydroxide modifier film obtained from carbonate solutions containing Co(II)-tartrate complexes [62], resulted in increased oxidation rate and peak current intensity, therefore ascorbic acid was oxidized at lower potentials, reaction thermodynamically more favorable. The modified electrode presented good electrocatalytic activity for the oxidation of ascorbic acid at approximately 565 mV *vs.* SCE, in 100 mmol L^{-1} sodium hydroxide solution used as supporting electrolyte and with a scan rate which varied from 5 to 300 mV s^{-1}. The cyclic voltammograms and chronoamperograms indicated a catalytic electrogeneration of Co(IV) and the current–time responses followed a Cottrellian behavior [57].

On a poly 3,4-ethylenedioxythiophene (PEDOT)-modified glassy carbon electrode, ascorbic acid oxidation peak occured at around -0.035 V, indicating a cathodic shift of 0.25 V when compared with the bare electrode. Furthermore, a sharper oxidation peak was obtained with the modified electrode. The low oxidation peak potential and the enhanced oxidation current were attributed to electrostatic interactions between the electrode surface groups and the analyte: the cationic PEDOT film interacted with the negatively charged ascorbate, which resulted in an effective analyte preconcentration at a less anodic value [40]. The development of an electrochemical sensor based on the incorporation of a ferricyanide mediator with a polyelectrolyte–calcium carbonate microsphere, embedding of the aforementioned electrode materials and subsequent modification of the glassy carbon electrode resulted in pronounced electrocatalytic oxidation of AA by ferricyanide with a peak at 270 mV, in 0.1 mol L^{-1} PBS (pH 7.0) which represented a negative-shift, compared with direct electrochemical oxidation of AA on glassy carbon [63].

The potential electrocatalytic activity of ascorbic acid was also investigated, at unmodified carbon paste and at tetrabromo-p-benzoquinone modified carbon paste electrodes (TBQ-MCPE), in phosphate buffer pH 7.0. and the direct oxidation of ascorbic acid at the unmodified carbon paste electrode showed an irreversible wave. The cyclic voltammetric responses were also recorded with the modified electrode: in the absence of ascorbic acid, a pair of well-defined redox peaks were obtained with the tetrabromo-p-benzoquinone modified carbon paste electrode; the addition of 1.0 mmol L^{-1} ascorbic acid, determined a drastic enhancement of the anodic peak current, and no cathodic current was noticed in the reverse scan. This behavior is consistent with a very strong electrocatalytic effect. The catalytic peak potential of the modified electrode was found at about 105 mV, whereas that of the unmodified electrode was about 535 mV, an enhancement of the peak current being also achieved with the modified electrode [58].

The presence of an anionic surfactant as modifier conferred excellent electrocatalytic activity to a dodecylbenzene sulfonate modified carbon paste electrode (DDBSMCPE). The cyclic voltammogram showed a single irreversible oxidation peak at both modified and bare electrodes. Ascorbic acid oxidation occurred at around 182 mV at the BCPE, whereas at the DDBSMCPE it occured at about −25 mV in phosphate buffer pH 7.40. It was stipulated that this shift in the oxidation potential could be due to the repulsive force between the negatively charged SO_3 layer of the modified electrode and the anionic form of ascorbic acid [39].

Cyclic voltammetry studies performed on Pt electrodes proved that the growth of Pt surface oxides was greatly surpressed by the use of fluorosurfactants as modifiers [64].

Recent studies performed on various modified electrodes such as norepinephrine modified glassy carbon electrode [65], tryptophan derivatives modified glassy carbon electrode [66], poly (2-amino-1,3,4-thiadiazole) deposited glassy carbon electrode [67], gold nanoparticles self-assembled onto the l-cysteine modified glassy carbon electrode [68], multiwall carbon nanotubes modified glassy carbon electrode [69] or poly(orthanilic acid) coated multiwalled carbon nanotubes modified glassy carbon electrode [70], tetraoctylammonium bromide stabilized gold nanoparticles-1,6-hexanedithiol modified Au electrode [71], multi-walled carbon nanotubes with methylene blue composite film-modified electrode [72], 3-mercaptopropyl-functionalized silica network gold nanoparticles modified electrode [73], thiocytosine/guanine-gold nanoparticles based modified gold electrodes [74], carbon paste/cobalt Schiff base composite electrode [75] not only decrease the overvoltage and enhance the electrocatalytic peak current, but also solve a common problem encountered at unmodified surfaces, such as the peak overlapping.

4. Potentiometric ascorbic acid sensors and biosensors

Potentiometric determination of ascorbic acid relies on its determination by the ascorbate oxidase catalysed reaction. Ascorbate oxidase is a metalloprotein, containing about 8 atoms of copper per mole of enzyme [76,77], bound in three different chemical complexes forming the active sites. This enzyme catalyses the oxidation of L-ascorbic acid in the presence of molecular oxygen in accordance to the following reaction mechanism [77]:

$$Enzox + Asc \underset{K_{-1}}{\overset{K_1}{\longleftrightarrow}} Enzox \cdot Asc \xrightarrow{K_2} Enzred + P$$

$$Enzred + O_2 \underset{K_{-3}}{\overset{K_3}{\longleftrightarrow}} Enzred \cdot O_2 \xrightarrow{K_4} Enzox + H_2O$$

where Enzox and Enzred represent the oxidized and reduced forms of enzyme, respectively; Asc stands for the ascorbate ion (primary substrate) and P is ascorbate free radical [76,77].

4.1. Composites

This principle was applied in the development of a biosensor, where the potential variation is caused by the reduction of Cu^{2+} present in the enzyme structure to Cu^{+}, by the ascorbate anion. This redox mechanism induces changes in the electronic density on the electrode surface, which are sensed by the potentiometric transducer. On this basis, a potentiometric biosensor for ascorbic acid was constructed, by ascorbate oxidase immobilization in a poly(ethylene-co-vinyl acetate) matrix, fixed on a graphite-epoxy composite electrode. The electrode showed a sub-Nerntian slope (50.3 ± 0.6 mV), within the range 8.0×10^{-6} and 4.5×10^{-4} mol L^{-1} for ascorbate, in 0.1 mol L^{-1} KH_2PO_4 solution at pH 5.0. After continuous testing during 15 days (about 300 analyses), no decrease in the analytical response was noticed [76].

4.2. Screen printed electrodes

The potentiometric determination of ascorbic acid was also performed by a sensor array fabricated by screen printing, with a RuO_2 film deposited on the working area of each sensor. The potential response of the enzyme based biosensor depended linearly on L-ascorbic acid concentration between 0.02 mmol L^{-1} and 1 mmol L^{-1} with a sensitivity of 13.85 mV L $mmol^{-1}$ [78].

4.3. Modified field effect transistors

Horseradish peroxidase immobilized on the surface of an Ion Sensitive Field Effect Transistor (ISFET) can be used for the determination of L-ascorbic acid in fruit juices and beverages. Peroxidase reduces hydrogen peroxide to water in the presence of hydrogen donors (antioxidant molecules), and this enzyme reaction can be used for the detection of either hydrogen peroxide or antioxidant species. The hydrogen donor, L-ascorbic acid is converted to dehydro-L-ascorbic acid during the peroxidase-catalysed reaction, in the presence of H_2O_2. The consumption of L-ascorbic acid during the enzyme-catalysed H_2O_2 reduction, causes a local pH increase in the biomembrane, which is sensed by the ISFET. Because peroxidase activity is pH dependent and reported to be maximal at pH 6.0, the sensor response versus ascorbic acid in buffers with different pH values has been discussed. The sensor sensitivity in phosphate buffer is strongly pH dependent and reaches its minimum at pH 6.70-7.20. This tendency was first ascribed to the buffer capacity change, as potassium phosphate monobasic with a pK_a value of 7.21 was used in the buffer preparation. On the other hand, the sensor response increased linearly with pH when citrate buffers were used. When sodium citrate was used in buffer preparation, pK_a values were: 3.12, 4.76, 6.40, and the buffer capacity in the measured pH range was almost constant. Thus, it was concluded that changes in the sensor response have been caused by enzyme activity variation [79].

Volotovsky et al. [80] developed a two-ISFET biosensor, containing horseradish peroxidase immobilized into bovine serum albumin gel, as well as glucose oxidase and urease, co-immobilized under a polymeric film, which could be used for determination of glucose, ascorbic and citric acids in fruit juices and beverages. To determine ascorbic acid contents, measurements with the biosensor were carried out in 10 mmol L^{-1} phosphate buffer, pH 6.0. The biosensor response to hydrogen peroxide in media with various ascorbic acid concentrations was recorded, with 1 mmol L^{-1} hydrogen peroxide concentration chosen for injection, as appropriate to determine ascorbic acid up to 2 mmol L^{-1}. The sensor was characterized by a long-term stability: after 1 month storage in phosphate buffer at 4 °C the biomembrane has maintained 60% of its original catalytic activity [80].

Another ascorbic acid sensor based on an ion-sensitive field-effect transistor was prepared by modifying the sensitive area of the transducer with MnO_2 nanoparticles [81]. An additional Nafion membrane coated on top of the sensor was used to immobilize the MnO_2 nanoparticles and control the amount of ascorbic acid entering the membrane. The reaction of the MnO_2 nanoparticles with ascorbic acid produced a local pH change, which was correlated with the ascorbic acid concentration and could be monitored by the ISFET.

$$Ascorbic\ acid + MnO_2 \rightarrow Dehydroascorbic\ acid + Mn^{2+} + 2OH^-$$

Thus, one ascorbic acid molecule gives two hydroxyl ions, resulting in the pH increase. A decrease in the response was noticed with the increase of the solution pH, from 5.5 to 8.0. Acidic environment proved more appropriate for the reaction of MnO_2 nanoparticles with the analyte, while basic conditions suppressed the reaction to some extent. It was found that the increase of phosphate concentration in the buffer induced a dramatic decrease of the analytical signal [81].

5. Voltammetric and amperometric sensors

Voltammetry is a potentiodynamic technique, based on measuring the current arising from oxidation or reduction reactions at the electrode surface, when a controlled potential variation is imposed [82]. Amperometry is based on the application of a constant potential to a working electrode, and the subsequent measurement of the current generated by the oxidation/reduction of an electroactive analyte [83–85].

5.1. Voltammetry/amperometry at bare/unmodified electrodes

The stoichiometry hydrogen peroxide formation from ascorbic acid in a model wine system has been examined by square-wave voltammetry on a hanging mercury drop electrode. Ascorbic acid and hydrogen peroxide could both be determined in the same test sample by first employing an anodic scan for ascorbic acid and then a cathodic scan for hydrogen peroxide. The potential was scanned from 0 mV to 400 mV for ascorbic acid. The minimum and maximum current range settings were 1 nA and 1 mA respectively. The step duration was 0.1 s, with a step amplitude of 5 mV and a pulse amplitude of 50 mV. Under these conditions, linear calibration plots were obtained for ascorbic acid (up to 235 mg L^{-1}, that is 1.335×10^{-3} mol L^{-1}) and hydrogen peroxide (up to 1.20×10^{-4} mol L^{-1}), both ranges being proper to the proposed real sample analysis given the concentrations likely to occur in white wine. Square-wave voltammetry with the hanging mercury drop electrode yielded voltammograms with a high degree of consistency, as each experiment is conducted with a fresh mercury drop. The peak current repeatability for ascorbic acid was illustrated by the value of the relative standard deviation, less than 1% [86].

Though L-ascorbic acid is one of the most electroactive biomolecule, it is generally difficult to determine its concentration value at unmodified carbon or bare metal electrodes, given the occurence of surface problems previously mentioned at the description of its electrochemical behavior [49–51]. Nevertheless, several studies were conducted, aiming at the viable ascorbic acid determination at bare metal or unmodified carbonaceous electrodes, with the necessity of electrode pretreatment [61], or mechanical and electrochemical repetitive cleaning steps [59,60].

L-ascorbic acid was determined in aqueous media by linear-scan voltammetry at a gold electrode; the optimum conditions for pH and sweep rate were determined as 3.2 and 7500 mV s^{-1}, respectively [82]. A single-crystal Au(111) electrode was used for the simultaneous determination of dopamine and ascorbic acid in a phosphate buffer solution at pH 6.9. The single-crystal Au(111) electrode displayed excellent electrocatalytic activity for dopamine and ascorbic acid oxidation in comparison with the gold disk electrode. In this latter case, the peak potential of ascorbic acid was shifted to more negative values in both cyclic and differential pulse voltammetry. The single-crystal Au(111) electrode exhibited this excellent electrocatalytic activity towards both ascorbic acid and dopamine, because hydrogen flame treatment has provided for the single-crystal electrode surface a well-defined atomic structure, which results in more AuOH sites, identified as the active species responsible for the oxidation process at the single crystal electrode surface, in neutral and alkaline media [61].

The vitamin C content of apple juices has been monitored by cyclic voltammetry at a Pt working electrode [12]. The oxidation current of ascorbic acid was linearly dependent on the ascorbic acid concentration (the linear calibration curve was found in the range of up to 150 mg ascorbic acid/100 mL solution). The results obtained by cyclic voltammetry were consistent with the ones obtained by the titrimetric method. The method is easy for automation and can be applied without special preparation of the studied apple juices samples. The performances of bare Pt and unmodified carbon paste electrodes in ascorbic acid determination were investigated: when a Pt electrode was used as working electrode, the limit of detection (LOD) and the limit of quantification (LOQ) obtained by cyclic voltammetry were 0.075 mmol L^{-1} and 0.25 mmol L^{-1}, respectively. Lower LOD and LOQ values were obtained when a carbon paste electrode was employed as working electrode: the limits of detection and the limit of quantification obtained by cyclic voltammetry were 0.018 mmol L^{-1} and 0.062 mmol L^{-1} respectively. The performances of bare Pt and unmodified carbon paste electrodes were also compared in differential pulse voltammetry. The limit of detection (LOD) and the limit of quantification (LOQ) obtained by differential pulse voltammetry were 0.087 mmol L^{-1} and 0.29 mmol L^{-1} respectively, when a Pt electrode was used. Lower values were obtained when a carbon paste electrode was employed as working electrode: LOD and LOQ obtained by differential pulse voltammetry were 0.02 mmol L^{-1} and 0.068 mmol L^{-1}, respectively. The sensitivities given by the slopes of the calibration graph were lower than in cyclic voltammetry experiments: for a Pt working electrode, 65.42 μA L $mmol^{-1}$ was the sensitivity obtained in CV studies, whereas 21.839 μA L $mmol^{-1}$ was the sensitivity obtained in DPV [60].

The levels of ascorbic acid in 50 tropical fruit samples were determined by cyclic voltammetry using a glassy carbon working electrode [56]. The unmodified glassy carbon electrode was also applied to the electrochemical oxidation and selective voltammetric determination of ascorbic acid. Conditions employed were: pulse amplitude 25 mV; frequency 15Hz; potential step 4 mV. The peak potential of ascorbic acid moved to less positive potentials with increasing pH. Good agreement with the HPLC determinations was obtained for effervescent, chewable vitamin C tablets, as well as for different *Rosa* species extracts. The method is rapid, requiring less than 2 min to run a sample [1].

The electrochemical oxidation behavior of ascorbic acid was studied by differential pulse voltammetry (DPV) at a glassy carbon electrode in an extended pH range (between 0.64 and 11.15), in diluted H_2SO_4 and different buffered aqueous media (Britton-Robinson, acetate, phosphate). The voltammetric response was found to be strongly pH dependent: the anodic peak potential was shifted to positive values with increasing pH [87].

In a study aiming at the voltammetric comparison of different carbonaceous materials, the background signal and analytical responses of ascorbic acid were evaluated by DPV at different carbon electrodes [88]. The transient currents associated with small potential steps have been examined, and it was concluded

that they are attributed mainly to redox reactions of various groups on the electrode surface. Instrumental parameters have been thoroughly investigated and optimized for improving the signal-to-background response. Glassy-carbon and carbon-paste disk electrodes have been compared. It was stipulated that the current-time profile depends on the potential domain, because of potential-dependent reactions of different surface groups (surface reactions of the quinone-hydroquinone couple) and formation of carboxyl groups, identified by cyclic voltammetry [88]. Secondly, although the two electrodes have the same surface area, much larger currents are observed at the glassy carbon electrode. Electrode reactions occuring at carbon paste are generally slower than at glassy carbon electrodes, yet the signficantly lower background current of the paste rendered it superior to glassy carbon from the signal-to-background characteristics standpoint. Thus, combined with the low price and easy preparation, these features make carbon paste a suitable electrode material for many applications. Although larger currents are observed at the glassy-carbon electrode, they decay faster than those recorded with the carbon paste electrode. It was concluded that in most cases, the currents decay faster as the potenial region becomes less anodic [88].

5.2. Voltammetry/amperometry at chemically modified electrodes

The need for overpotential diminution and fouling minimization led to the need of electrode modification aiming at increased sensitivity and more neat peak separation, required mainly in complex media such as biological samples particularly prone to interferences, where ascorbic acid coexists with other electroactive species.

5.2.1. Modified metal electrodes

Linear sweep voltammograms obtained at a gold electrode with dimercaptothiadiazole layers formed from methanol and from several methanol–water mixtures at different ratios, showed that thin dimercaptothiadiazole monolayers formed from non-aqueous solvents, separate the voltammetric signals of uric acid and ascorbic acid [89]. The fabrication of gold nanoparticles (GNs)-modified gold electrode was reported, based on the self-assembly of gold nanoparticles at the surface of a mixed film of 1,6- hexanedithiol and 1-octanethiol, which is self assembled at a gold electrode. Free —SH groups of hexanedithiol were used as scaffold to immobilize GNs, the film formed by this technique having the advantages of high organization and uniformity.This GNs chemically modified electrode was used for electrochemical determination of ascorbic acid and dopamine in aqueous media [90].

The use of a metallic modified microelectrode array lead to the successful flow injection amperometric quantification of ascorbic acid, dopamine, epinephrine and dipyrone in mixtures: the four groups of microelectrodes included a pure gold electrode and electrodes modified by electrodeposition of platinum, palladium or a mixture of platinum and palladium. The multivariate calibration method eliminates the need for previous separations or for chemical reactions to attain more favorable conditions to quantify each constituent of the samples. For mixtures with lower concentrations, it was possible to use, in the present study, only four of the 24 microelectrodes to increase the current. The use of a multipotentiostat with the capacity to control a larger number of working electrodes can provide even more information, favoring the analysis of even more complex mixtures with optimized reliability [91].

5.2.2. Modified carbonaceous electrodes

One of the most convenient and easy to use materials for the preparation of modified electrodes is represented, undoubtedly, by carbon pastes. The modifier can be dissolved in a binder or admixed mechanically to the paste during its homogenization. Carbon pastes are dynamic and renewable materials endowed with excellent conductivity and electrocatalytic properties, with wide applicability in electrochemical or bioelectrochemical sensors [92,93]. Therefore, cyclic voltammetric responses of ascorbic acid were recorded at an unmodified carbon paste electrode and at a tetrabromo-p-benzoquinone modified carbon paste electrode. Cyclic voltammetry studies achieved a decrease in the overvoltage of approximately 430 mV and an enhancement of the peak current with the modified electrode, that was quite effective not only in detecting ascorbic acid, dopamine and uric acid, but also in the simultaneous differential pulsed voltammetric determination of each component concentration in mixture. The peak current increased linearly for 10.0 to 600.0 $\mu mol\,L^{-1}$ ascorbic acid concentration [58].

A series of carbonaceous amperometric sensors were developed: carbon paste, modified carbon paste and glassy carbon electrodes and used for ascorbic acid quantification. Modified carbon paste electrodes were obtained from carbon paste incorporating 10% vanadate as modifier. The device is integrated in a flow injection analysis set-up. Hydrodynamic and amperometric parameters were optimized: glassy carbon electrodes exhibit slopes of $4.75 \times 10^5\,nA\,L\,mol^{-1}$ (± 6.4%) under optimum conditions. Carbon paste and modified carbon paste electrodes proved more sensitive, with slopes of $6.37 \times 10^5\,nA\,L\,mol^{-1}$ (± 6.6%) and $7.32 \times 10^5\,nA\,L\,mol^{-1}$ (± 4.4%) [94].

The electrocatalytic behaviors of a methionine-modified carbon paste electrode and bare carbon paste electrode for the electrooxidation of ascorbic acid were studied and compared, by using cyclic voltammetry. The obtained results showed good enhancement in the anodic peak current in the case of the modified electrode, compared to the bare electrode. The anodic peak current showed an increase with ascorbic acid concentration, with linearity in the range of $5.0 \times 10^{-6}\,mol\,L^{-1}$ to $12 \times 10^{-5}\,mol\,L^{-1}$. The proposed method was adapted for the determination of the concentration of ascorbic acid present in real samples and the results were found to be satisfactory [95]. A carbon paste electrode modified with a 2,2′-(1,8-octanediylbisnitriloethylidine)-bis-hydroquinone showed high electrocatalytic activity towards ascorbic acid; the current was enhanced significantly, relative to the situation encountered when an unmodified electrode was used [96].

Different porphyrins were also used for the design of seven carbon paste and seven diamond paste based microelectrodes, employed for the differential pulse voltammetric determination of ascorbic acid. Low detection limits were obtained, namely between 1.1×10^{-14} and $5.1 \times 10^{-7}\,mol\,L^{-1}$, while the sensitivities were between $3.07\,pA\,L\,mol^{-1}$ and $1285.18\,A\,L\,mol^{-1}$. Ascorbic acid assay in pharmaceutical and beverages samples yielded degrees of recovery higher than 92.0% and 91.50%, respectively. The surface of the microelectrodes is easily renewable by simple polishing, becoming ready for use in a new assay [97]. A graphene-doped carbon paste electrode [98] was prepared by the addition of graphene into the carbon paste mixture. Compared with the conventional carbon paste electrode, an improved electrochemical response of graphene doped carbon paste electrode was proved, due to the excellent electrical conductivity of graphene. The graphene doped carbon paste electrode was further used for the determination of ascorbic acid with low overvoltage, enhanced current response, and good sensitivity. Typical amperometric responses of the bare carbon paste electrode and graphene doped carbon paste electrode to successive additions of ascorbic acid in $0.1\,mol\,L^{-1}$ phosphate buffer solution pH 7.0, were obtained within 5 s [98].

The voltammetric response of a manganese dioxide graphite composite electrode towards ascorbic acid was recorded, in a pH 7.2 phosphate buffer solution. The oxidation current was

found to increase with increasing of ascorbic acid amount; distinct voltammetric peaks are obtained for concentrations as low as 250 μmol L^{-1} ascorbic acid [99].

Other carbonaceous materials (e.g. glassy carbon) were also used as modifiable electrode materials, due to the high electrical conductivity, resistence to chemical attack, suitability in a large potential range and compatibility with acidic media. A glassy carbon electrode (GCE) has been modified by electrochemical oxidation in mild acidic media (0.1 mol L^{-1} H_2SO_4) and could be applied for individual and simultaneous determination of ascorbic acid, dopamine and uric acid. The cyclic voltammetry responses of bare and oxidized (modified) GCE were recorded, in phosphate buffer solution pH 7.0. The oxidized glassy carbon electrode showed a single redox couple (E_0 = −2.5 mV), determined by the formation of functional groups during the electrochemical pretreatment. Particularly, the presence of these functional groups generates the successful decrease of overpotentials in the oxidation process compared with the bare GCE, allowing simple and sensitive simultaneous determination of three analytes [100].

Polymeric films were proved to enhance the electrocatalytical activity towards ascorbic acid, increasing the electron transfer rate between the glassy carbon electrode and the polymeric film. A stable modified glassy carbon electrode based on the poly 3-(5-chloro-2-hydroxyphenylazo)-4,5-dihydroxynaphthalene- 2,7-disulfonic acid (CDDA) film was prepared by electrochemical polymerization technique to investigate its electrochemical behavior by cyclic voltammetry. The properties of the films electrodeposited during preparation under different conditions, as well as their stability were examined. The homogeneous rate constant for the electron transfer between CDDA and glassy carbon electrode was calculated as 5.25 (± 0.20) x 10^2 cm s^{-1}. The modified electrode showed electrocatalytic activity towards ascorbic acid, dopamine and uric acid oxidation in buffer solution pH 4.0 with a diminution of their overpotential of about 0.12, 0.35, and 0.50 V for ascorbic acid, dopamine and uric acid, respectively [101].

A poly(caffeic acid) thin film was deposited on the surface of a glassy carbon electrode by the potentiostatic technique in aqueous solution. The poly(caffeic acid)-modified electrode was used for the determination of ascorbic acid, dopamine, and their mixture by cyclic voltammetry. The modified electrode shows good sensitivity, selectivity, and stability and has been applied to the analysis of pharmaceutical samples with satisfactory results [102].

Another voltammetric method for determination of ascorbic acid was reported, by using a glassy carbon electrode modified with poly(bromocresol purple), poly(BCP)/GCE. Cyclic voltammetry studies showed that, compared with the bare GCE, the poly(BCP) film exhibited an obvious electrocatalytic effect towards ascorbic acid oxidation, which reduced the oxidation overpotential for about 240 mV, with an increased current response, in 0.1 mol L^{-1} phosphate buffer solution (pH 6.50). Good degrees of recovery were obtained for known ascorbic acid amounts added to the analysed samples, between 97.78 and 102.54% [103].

The use of conducting polymers offers numerous opportunities to transduce analyte–receptor interactions into measurable responses. The advantages of conducting polymers-based sensors over devices using small molecule elements (chemosensors) are the ability of conducting polymers to exhibit properties that respond to even minor perturbations in the system [40]. Under these circumstances, the oxidation behaviors of ascorbic acid and dopamine were investigated at bare glassy carbon and poly(3,4-ethylenedioxythiophene)-modified glassy carbon electrodes. The PEDOT film was deposited on a glassy carbon electrode by electropolymerization from an acetonitrile solution [40]. An amperometric sensor for ascorbic acid determination from foodstuffs and pharmaceutical preparations was developed by aniline electropolymerisation on both glassy carbon and screen printed working electrodes [104].

Thin films of polyaniline containing the dopant ions polyvinylsulfonate and polystyrenesulfonate have been prepared on 25 μm Pt disk microelectrodes and tested for ascorbic acid oxidation in various buffers, as well as in wine and orange juice containing solutions. Polyaniline-based microelectrodes incorporating polyvinylsulfonate and polystyrenesulfonate as dopant ions maintain conducting polymer electroactivity in neutral pH solutions. The acquired differences in the size of the plateau currents (twice as large with polyvinylsulfonate over polystyrenesulfonate) point to an effective influence of the dopant ion on the polyaniline redox mediator properties, possibly through a modification of the conductivity and/or morphology of the conducting polymer [105]. Aniline containing suspended silicotungstic acid and carbon nanotubes, was electropolymerized on the surface of a glassy carbon electrode in a single step, providing a simple, controllable and sensitive amperometric sensor, greatly improving the electrocatalytic oxidation of ascorbic acid [106].

A significant catalytic effect in ascorbic acid oxidation was obtained in the presence of a cationic surfactant (cetyl trimethyl ammonium bromide) absorbed on the glassy carbon electrode surface: the peak potential in the cationic micellar medium was lower than that obtained in aqueous medium, accompanied with the increase of the intensity measured for the anodic oxidation peak [107]. Another surfactant-based glassy carbon electrode was modified with a film composed of chitosan incorporating cetylpyridine bromide used to determine uric acid and ascorbic acid by differential pulse voltammetry. This modified electrode shows an efficient electrocatalytic activity and fairly selective separation ability for ascorbic and uric acid [108].

A novel binuclear copper complex modified glassy carbon electrode was fabricated using a cyclic voltammetric method in phosphate buffer solution and it showed a very efficient electrocatalytic activity for anodic oxidation of dopamine and ascorbic acid with a significant decrease in the overpotentials. The binuclear copper complex modified GCE was stable and reproducible. To this aim, the electrode was renewed by CV scans in 100 mmol L^{-1} phosphate buffer, in the potential window 0.0–0.8 V after each experiment. satisfactory results were obtained at ascorbic acid and dopamine determination in medicine and foodstuff samples [109].

Aspartic acid was covalently grafted on to a glassy carbon electrode by amine cation radical formation through the electrooxidation of the amino-acid. Voltammetric experiments proved that aspartic acid was immobilized as a monolayer on the glassy carbon electrode [110].

At the surface of a $LaFeO_3$ nanoparticles - modified glassy carbon electrode, the calibration curves for ascorbic acid, dopamine and uric acid were linear for the whole concentrations ranges investigated (500–3,000 μmol L^{-1} for ascorbic acid, 1.00–6.00 μmol L^{-1} for dopamine and 100–600 μmol L^{-1} for uric acid) with good correlation coefficients [111].

A cathodically pretreated boron-doped diamond electrode was used for the simultaneous anodic determination of ascorbic acid and caffeine by differential pulse voltammetry. This method was successfully applied for the determination of ascorbic acid and caffeine in pharmaceutical formulations, with results consistent with those obtained using a HPLC reference method [112].

Carbon nanotubes (CNT) are endowed with remarkable electrical, chemical, mechanical and structural properties. Their unique properties recommend them as highly attractive for the task of chemical sensors in general, and, particularly, electrochemical detection. In addition to the enhanced electrochemical reactivity, CNT-modified electrodes have proven useful to accumulate important biomolecules and to alleviate surface fouling. The remarkable

sensitivity and conductivity enables the use of carbon nanotubes as sensitive nanoscale sensors [113].

Thus, a new electrochemical method was investigated for the *in vivo* measurements of ascorbic acid in rat brain, by means of a multiwalled carbon nanotubes (MWNTs)-modified carbon fiber microelectrodes. The technique relied on the electrochemical property of MWNTs of promoting ascorbic acid oxidation [42]. The simultaneous voltammetric determination of ascorbic acid and rutin has been achieved at an acetylene black paste electrode modified with a multi-walled carbon nanotubes–chitosan composite film (MWCNTs–CHIT/ABPE) [114].

A selective and simultaneous square wave voltammetric determination of ascorbic acid, acetaminophen and tryptophan has been explored at a multiwall carbon nanotube modified paste electrode [115]. A novel modified, graphite-multiwall carbon nanotube paste electrode for the determination of ascorbic acid, based on a cationic surfactant, cetrimonium iodide-iodine was proposed. The electrochemical response characteristics of the modified electrode towards AA were investigated by cyclic voltammetry and differential pulse voltammetry in buffer solution (pH 2.0). When compared with activated carbon or graphite, the developed multiwall carbon nanotube modified paste electrode not only shifted the oxidation potential of AA to less positive potentials, but also enhanced its peak current. Furthermore, the oxidation of AA was highly stable at the modified paste electrode, which allowed the successful quantification of AA in pharmaceutical and food samples [116].

The differential pulse voltammetric technique was further employed for simultaneous determination of ascorbic acid, dopamine and uric acid, with a sensor based on helical carbon nanotubes (HCNTs). A water soluble cationic polymer, poly(diallyl dimethylammonium chloride) (PDDA), is used to functionalize the nanotubes' surface, aiming to improve the dispersability and adhesion to substrates of the helical carbon nanotubes. The current responses achieved at the GC electrode coated with PDDA@HCNTs were higher in DPV than in CV. The analytical performances of this sensor enable the simultaneous detection of ascorbic acid, dopamine and uric acid in the fetal bovine serum samples [117].

A novel carbon composite electrode consisting of n-octylpyridinum hexafluorophosphate ionic liquid and single-walled carbon nanotube (SWCNT) was fabricated and investigated. Compared with other composite electrodes using graphite or paraffin oil, the ionic liquid–SWCNT (IL–SWCNT) composite electrode exhibited remarkable increase in the electron transfer rate for the electroactive compound and a significant overpotential decrease in ascorbic acid reaction. Furthermore, the IL–SWCNT electrode endowed with pronounced electrocatalytic activity, was applied to determine ascorbic acid levels in real food samples [118].

A new type of modified electrode sensor for ascorbic acid has been prepared by deposition of multi-walled carbon nanotubes (MWCNT) and poly(Nile blue A) on the surface of glassy carbon electrodes. Nile blue A was electropolymerised either beneath (directly on glassy carbon) or onto the MWCNT layer by potential cycling in phosphate buffer solution at pH 6.0. The characterization of the modified electrodes was carried out by cyclic voltammetry and electrochemical impedance spectroscopy [119]. The best results were obtained with the modified electrodes prepared with polyNile Blue (PNB) films beneath the thinnest MWCNT layer at 100 mV. A thicker polyNile Blue underlying film in the MWCNT/PNB electrodes was more suitable for electrochemical sensing, since it gave a stable signal. Quantitative determination of ascorbate was achieved by cyclic voltammetry and fixed potential amperometry in phosphate buffer solution at pH 5.3. The modified electrodes exhibited good sensitivity, wide linear range, a detection limit of 1.6 $\mu mol\,L^{-1}$ and good stability, showing that they can be used as sensors for ascorbic acid. The quantitative amperometric determination of AA using MWCNT/PNB and PNB/MWCNT modified electrodes was performed using the standard addition method. Because by amperometry a higher sensitivity than by CV was obtained, this method was chosen to perform an interference study and to determine ascorbate in pharmaceutical samples. [119].

Poly(xanthurenic acid) and multi-walled carbon nanotubes (MWCNT) hybrid composites have been successfully prepared to form polyXa-MWCNT for glassy carbon modification, aiming at ascorbic acid determination. A well defined redox couple has been identified, as a result of the polyxanthurenic acid redox processes. This composite is stable at various scan rates and different pH conditions and has a surface coverage of $2.3 \times 10^{-9}\,mol\,cm^{-2}$ at the poly(xanthurenic acid) multi-walled carbon nanotubes modified glassy carbon electrode. This electrode presents lower over-potential and higher current responses vs ascorbic acid when compared to the bare electrode. At a value of the applied potential of +300 mV, it has a sensitivity of 160.2 $\mu A\,L\,mmol^{-1}\,cm^{-2}$ [120].

Recently, a graphene/Pt-modified glassy carbon electrode was constructed and studied, to simultaneous estimation of ascorbic acid, dopamine, and uric acid levels via cyclic voltammetry and differential pulse voltammetry. Size-selected Pt nanoparticles with a mean diameter of 1.7 nm were self-assembled onto the graphene surface. An optimized adsorption of size-selected Pt colloidal nanoparticles onto the graphene surface results in a graphene/Pt nanocomposite that can constitute the basis for glassy carbon modification and amperometric routine analysis of three analytes in 0.1 $mol\,L^{-1}$ phosphate buffer solution pH = 7.0, at 0.5 V [121].

A highly responsive ascorbic acid sensor was constructed, utilizing over-oxidized polypyrrole and palladium nanoparticles composites (OPPy–PdNPs). In the presence of palladium nanoparticles, polypyrrole was coated on a gold electrode through cyclic voltammetry and over-oxidized, at a fixed potential in NaOH solution [122]. Results revealed that the over-oxidized polypyrrole and palladium nanoparticles composites-modified gold electrode (OPPy–PdNPs/Au) had the capacity to catalyse the oxidation of ascorbic acid by lowering its oxidation potential at 0 V. The OPPy–PdNPs/Au electrode exhibited two different linear concentration ranges. In the low concentration range (1–520 $\mu mol\,L^{-1}$), the OPPy–PdNPs/Au electrode proved a direct linear dependence of current responses on concentration and had high sensitivity (570 $\mu A\,L\,mmol^{-1}\,cm^{-2}$) and a high correlation coefficient (0.995). In contrast, in the higher concentration range (120–1600 $\mu mol\,L^{-1}$), the relationship between current responses and concentration of AA can be represented by a two-parameter sigmoidal equation. In addition, the sensor exhibited a short response time (less than 2 s) and a detection limit as low as 1 $\mu mol\,L^{-1}$. Thus, the proposed sensor has great potential for the assessment of AA in complex biosystems and can be applied in various fields, particularly neuroscience [122].

A simple and effective strategy was proposed for synthesis of nickel nanoparticles dispersed in a poly1,5-diaminonaphthalene(NiNPs@P-1,5-DAN) matrix. The electrochemical characterization of this modified electrode exhibits a stable redox behavior of the Ni(III)/Ni(II) couple in 0.1 $mol\,L^{-1}$ NaOH aqueous solution. The electrooxidation of glucose, ascorbic acid and dopamine in alkaline solution was studied by using square-wave voltammetry. The detection limits for ascorbic acid was 0.010 $\mu mol\,L^{-1}$ [123].

5.2.3. Nanoparticle composites and ceramic composites

Functional nanoparticles - carbon nanotube composite films combine the advantages of enhanced electrocatalytic activity and

large surface area and carbon nanotubes (CNTs) are advanced ideal materials for supporting nanosized metallic particles in electrocatalysis. Hence, a unique bimetallic, nano platinum with nano gold, on nafion incorporated with functionalized multiwall carbon nanotubes composite film was developed by the potentiostatic method. The composite film exhibits efficient catalytic activity towards the oxidation of biocompounds and allows the determination of ascorbate anion, epinephrine and urate anion in buffer solution (pH 6.75) [124].

A carbon–ceramic material, $SiO_2/C/Nb_2O_5$ was used for electrode development, and it showed the ability to improve the electron transfer between the electrode surface and the analyte, ascorbic acid [125]. The presence of Nb_2O_5 at the SiO_2/C surface reduces the overvoltage of ascorbic acid oxidation, shifting the oxidation potential to a value by about 180 mV more negative. The peak current is considerably enhanced compared with the response of ascorbic acid on the SiO_2/C electrode surface. This behavior clearly demonstrates the electrocatalytic function of the $SiO_2/C/Nb_2O_5$ electrode towards ascorbic acid oxidation. The voltammetric response of ascorbic acid on the $SiO_2/C/Nb_2O_5$ electrode may be attributed to the interaction between Nb_2O_5 and ascorbic acid, which includes the formation of covalent bonds between the niobium oxide and ascorbic acid, this leading to a very fast kinetics of ascorbic acid oxidation on the $SiO_2/C/Nb_2O_5$ surface. Moreover, niobium oxide is an n-type semiconductor; the conduction band is formed from the 3d orbital of Nb atoms and the valence band, from the 2p orbitals of oxygen. Thus, the electrical conductivity at potentials above the conduction band edge may facilitate electron transfer in ascorbic acid oxidation. The $SiO_2/C/Nb_2O_5$ electrode presented good repeatability for selective ascorbic acid determinations [125].

Single-walled carbon nanotube-modified carbon–ceramic electrodes (SWCNT/CCE) were employed for the simultaneous determination of acetaminophen and ascorbic acid. The SWCNT/CCE displayed excellent electrochemical catalytic activities towards acetaminophen and ascorbic acid oxidation compared with bare GCE. The modified electrode greatly catalysed the electrooxidation reactions of acetaminophen and ascorbic acid [126].

5.3. Amperometric enzymic assay: biosensors

Amperometric biosensors rely on electron transfer reactions - the reduction/oxidation of an electroactive species, generated in an enzyme reaction. The role of the enzyme is to generate/consume an electroactive species, which can stoichiometrically be correlated to the analyte concentration [83–85,127]. Amperometric ascorbic acid biosensors were obtained by ascorbate oxidase immobilization on a nylon net [128] or on a collagen membrane [129], using a Clark oxygen electrode as transducer [128–130].

The ascorbate oxidase membrane was coupled to an O_2 electrode and the yielding reaction was monitored by oxygen depletion at -600 mV using flow injection analysis optimized to 0.1 mol L^{-1} phosphate buffer pH 5.8, with a carrier solution flow-rate of 0.5 mL min^{-1}. The ascorbic acid calibration curve was linear from 1.2×10^{-4} to 1.0×10^{-3} mol L^{-1}. The evaluation of biosensor lifetime leads to 500 injections. Commercial pharmaceutical samples were analysed with the proposed method and the results were in accordance with those obtained by high-performance liquid chromatography (HPLC) [128]. Ascorbate oxidase isolated from the epicarp of *Cucumis sativus* was also immobilized on a collagen membrane mounted on a Clark oxygen electrode, for ascorbic acid content assessment in fruit juices [129]. Another amperometric biosensor was developed by immobilizing ascorbate oxidase on a nylon semipermeable membrane, fixed on an oxygen electrode. An optimum enzyme loading of 100 U ascorbate oxidase immobilized on the enzyme membrane was obtained. The sensitivity (given by the slope of the calibration graph) was 4.15 + 0.114 nA L $mmol^{-1}$ [130].

Ascorbate oxidase was immobilised on cyanogen bromide activated-Sepharose 4B and incorporated in a flow-injection system with amperometric detection at a glassy carbon electrode at +600 mV. On passage through the immobilized ascorbate oxidase, a fraction of the L-ascorbic acid was converted into dehydroascorbic acid and the resulted signal decrease was measured and correlated to the amount of analyte present, allowing simple and rapid determination of L-ascorbic acid in fruit and vegetable juices. The sampling throughput was 30 samples h^{-1} [131].

Ascorbic and uric acid were determined by coupling the amperometric technique with flow analysis. Uric acid and ascorbic acid present in urine were rapidly determined by an amperometric method coupled with flow injection analysis [132]. An array of gold microelectrodes modified by electrochemical deposition of palladium was employed as working electrode. This method is based on three steps involving the flow injection of: (1) the sample spiked with a standard solution, (2) the pure sample, and (3) the enzymatically treated sample. The enzymatic treatment was carried out with ascorbate oxidase, uricase, and peroxidase at pH = 7.0. Uric and ascorbic acids were quantified in urine using amperometric differential measurements at +750 mV and +550 mV, respectively [132].

The advantages and peculiarities of carbon nanotubes, discussed at the voltammetric methods, recommend them also for incorporation in amperometric biosensors. Due to their enhanced structural, mechanical, electrical and electromechanical properties, carbon nanotubes are known for their considerable use in the area of sensors as high strength conductive composite materials, characterized by good biocompatibility and possibility of renewal [133,134].

One possible approach is to improve the interaction of the biomolecule of interest with CNTs, leading to the improvement of the performance of biosensor materials. Ferritin protein was non-covalently immobilized onto single wall carbon nanotubes (SWNTs) [133,134]. Ferritin can be dispersed in polar matrices, thus combining ferritin with SWNTs enhances the nanotube interaction with water and improves the dispersion of SWNTs in aqueous solution [133]. The affinity of CNTs for proteins and their electrocatalytic activity, were exploited in ascorbate oxidation: the carbon nanotube/ferritin film was used in the construction of an amperometric ascorbic acid biosensor. The investigation of the oxidation of ascorbic acid was carried out by sequential additions of 1.0 mmol L^{-1} ascorbic acid to a phosphate buffer solution, using the SWNT/ferritin electrode. It could be observed that the current increased continuously with sequential ascorbic acid additions. The developed biosensor allows the determination of ascorbic acid with a sensitivity of 767 μA mg^{-1} (for a 1 mmol L^{-1} solution). Ferritin protein bound to SWNTs was proved to enhance the oxidation reaction of ascorbic acid over 11-fold [133].

An ascorbate biosensor was fabricated by covalently immobilizing ascorbate oxidase from *Lagenaria siceraria* fruit onto a carboxylated multiwalled carbon nanotubes and polyaniline (c-MWCNT/PANI) layer, electrochemically deposited on the surface of an Au electrode [134]. The diffusion coefficient of ascorbic acid was determined as 3.05×10^{-4} cm^2 s^{-1}. The biosensor showed optimum response at pH = 5.80 in a broad temperature range (30–45^{0}C), polarized at +0.6 V. For the amperometric response of the AsOx/c-MWCNT/PANI/Au electrode, the current variation was due to the reduction of molecular oxygen nonconsumed in the ascorbic acid oxidation catalysed by ascorbate oxidase [134]:

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

The biosensor was employed for determination of ascorbic acid level in sera, fruit juices and vitamin C tablets with good correlation with results provided by the 2,6-dichlorophenolindophenol method. It had advantages over earlier enzyme sensors, such as no leakage of enzyme due to the covalent coupling with the support, lower response time, wider working range, higher storage stability (was used 200 times over a period of two months, when stored at 4^0 C) [134].

Carbon-supported PdNi nanoparticles (PdNi/C) were synthesized using a novel synthetic route, and characterized by transmission electron microscopy and X-ray diffractometry. The overall metallic content (Pd + Ni) was 10% (w/w) and uniformly distributed in the carbon black (90%) matrix. The PdNi/C modified glassy carbon electrode showed better catalytic activity than an equal amount of commercially available palladium carbon catalyst. This indicates that the PdNi/C nanomaterials are able to reduce the overpotential of AA oxidation with a peak shifted to -0.05 V, demonstrating the synergistic effect of Ni and Pd. These results show that Pd-based bimetallic catalysts have excellent enzymatic amperometric AA sensing capability, fast response, high reproducibility and stability. The biosensor based on carbon-supported PdNi nanoparticles yielded degrees of recovery comprised between 95.1 and 106.3% in tablets and serum [135].

6. Interferences from compunds present in biological media, pharmaceuticals and foodstuffs

6.1. Interferences in potentiometry

At a MnO_2 nanoparticles modified ion-sensitive field-effect transistor, the viable potentiometric determination of ascorbic acid in vitamin C injections, as well as in urine, was possible with no observed effect on the sensor's performances from other compounds present in the analysed media, such as glucose or uric acid [81].

6.2. Interferences in voltammetry/amperometry

6.2.1. Unmodified (bare) electrodes

In linear scan voltammetric assay of ascorbic acid at bare gold electrodes, the problem of interference effects in biological samples from uric acid and sugars was solved by the presence of copper ions [82]. The anodic peaks of ascorbic acid and dopamine, overlapping on a gold disk electrode, were well separated using the single-crystal Au(111) electrode. The procedure is characterized by low charge transfer resistance at the surface of the single crystal electrode. Hence, no homogeneous catalytic oxidation was noticed, and the oxidation signal of ascorbic acid was unaltered by the addition of dopamine [61].

6.2.2. Modified metal and carbonaceous electrodes

The bare gold electrode could not separate the voltammetric signals of ascorbic acid and uric acid, whereas the thin dimercaptothiadiazole monolayer formed from neat methanol most clearly separated the signals of the studied electroactive compounds: the oxidation of ascorbic acid occured at 230 mV while the oxidation of uric acid occured at 440 mV, enabling the determination of both analytes, simultaneously in mixture [89]. It was found that a methanol, ethanol, or DMSO solution of dimercaptothiadiazole behaves as a strong acid because these solvents are able to deprotonate dimercaptothiadiazole and thus, thin monolayers are formed on the gold electrode. On the other hand, an aqueous solution of dimercaptothiadiazole becomes less acidic due to weak deprotonation of dimercaptothiadiazole by water and thus, dimercaptothiadiazole forms a thick layer on the gold electrode. It was concluded that the thin dimercaptothiadiazole monolayer formed from non-aqueous solvents much better separates the voltammetric signals of uric acid and ascorbic acid than the thick layer formed in aqueous solution [89]. A gold nanoparticles-modified electrode could clearly differentiate the oxidation peaks of ascorbic acid and dopamine, with a peak-to-peak separation of 110 mV, enabling the determination of ascorbic acid and dopamine in the presence of each other, which was not possible at the bare Au electrode. On the modified Au electrode, 1,6-hexanethiol with pKa = 10.24 presents itself in protonated form at pH = 5.00, thus positively charged, while citrate ions as stabilizers, impair negative charge to GNs. Therefore, the authors stipulated that the resultant charge is a positive one, opposite to the charge of ascorbic acid form at this pH value. Furthermore, the stabilization of GNs was attributed to the replacement of the negative charges of ascorbic acid form at this pH value, by citrate ions. Therefore, the electrooxidation of ascorbic acid at the surface of this modified electrode shifted to a less positive potential. The magnitude of separation of the voltammetric peak potentials of ascorbic acid and dopamine is influenced by the solution pH: the oxidation peak potentials of dopamine and ascorbic acid were shifted to less positive values with decreasing acidity. This is a consequence of a deprotonation step involved in the oxidation processes of both analytes, that is facilitated at higher pH. The anodic peak potential difference increased with the pH increase from pH 3.0 to pH 5.0 and then decreased, so, to obtain a maximum peak separation for the anodic oxidation of ascorbic acid and dopamine, the pH was adjusted to 5.0. The observed 280 mV peak separation was more than enough to determine both analytes simultaneously [90].

A tetrabromo-p-benzoquinone modified carbon paste electrode could separate the oxidation peak potentials of ascorbic acid, dopamine and uric acid present in the same solution, whereas at the unmodified carbon paste electrode the peak potentials were indistinguishable [58].

The presence of functional groups on a glassy carbon electrode modified by electrochemical oxidation resulted in three well-defined voltammetric peaks at the potentials of 0.064, 0.227 and 0.354 V, for ascorbic acid, dopamine and uric acid, respectively. At the same time, the bare GCE fails to separate these peaks and gives a single oxidation peak at around 0.422 V [100]. A poly 3-(5-chloro-2-hydroxyphenylazo)-4,5-dihydroxynaphthalene-2,7-disulfonic acid modified glassy carbon electrode resolved the anodic peak overlapping of ascorbic acid, dopamine and uric acid into three well-defined differential voltammetric peaks. Interference studies showed that the modified electrode exhibits excellent selectivity towards ascorbic acid, dopamine and uric acid [101]. A poly(caffeic acid) thin film modified glassy carbon electrode is characterized by a pronounced electron-mediating behavior, followed by well-separated oxidation peaks towards ascorbic acid and dopamine at a scan rate of 10 mV s^{-1} with a potential difference of 135 mV, which was sufficient to determine ascorbic acid and dopamine individually and simultaneously [102]. A PEDOT film modified glassy carbon electrode has shown catalytic oxidation of dopamine and ascorbic acid and allowed a peak potential separation of 0.2 V [40].

The influence of some interferents commonly found in juices and pharmaceutical preparations, including 4-acetamidophenol, uric acid and citric acid is minimized at a polyaniline-modified glassy carbon amperometric sensor, which selectively catalyses the oxidation of L-ascorbic acid at low potentials (+100 mV) [104]. At polyaniline-based microelectrodes incorporating polyvinylsulfonate, a potential of 100 mV vs SCE was applied, in solutions obtained by mixing equal volumes of a (model) wine or juice with

a citrate/phosphate buffer pH = 6.7. Under these experimental conditions maximum plateau currents were generated from ascorbic acid oxidation, while minimizing the interference of other oxidizable beverage compounds: caffeic acid, catechin, glucose and SO_2. The repetitive quantitative analysis of wine and orange juice indicated a decrease of the sensor response, likely due to the adsorption of other unknown beverage components onto the active polyaniline layer redox sites [105].

Ascorbic acid oxidation at a glassy carbon electrode modified with a film composed of chitosan incorporating cetylpyridine bromide, was catalysed with a decrease of 200 mV in overpotential when compared to GCE, and the peak separation between ascorbic acid and uric acid was 260 mV [108]. Differential pulse and cyclic voltammetry at a binuclear copper complex modified glassy carbon electrode show two well-resolved anodic waves for the oxidation of dopamine and ascorbic acid in the same solution, which renders possible the simultaneous determination of both compounds. The tolerance limit was determined as the concentration causing ± 5% relative errors. For the potential interferent compounds studied, the following values were obtained: 0.03 mol L^{-1} Na^+, K^+, Cl^-; 0.01 mol L^{-1} Mg^{2+}, Ca^{2+}, SO_4^{2-}; 0.01 mol L^{-1} citric acid, lysine; 0.005 mol L^{-1} glucose, L-cysteine. At a concentration 30 times greater than that of the analyte, dopamine has no effect on the voltammetric signal of ascorbic acid oxidation [109]. Because of the electrostatic interactions established between negatively charged groups formed on the electrode surface and the analyte molecules, an aspartic acid modified glassy carbon electrode was proved to differentiate between dopamine and ascorbic acid in DPV [110]. A $LaFeO_3$ nanoparticles-modified GCE succeeded in resolving an overlapped voltammetric peak into three well defined DPV peaks at about −0.08, 0.09 and 0.22 V, in the oxidation of ascorbic acid, dopamine and uric acid, respectively. This separation of peaks was judged large enough to determine ascorbic acid, dopamine and uric acid individually and simultaneously [111].

Cyclic voltammetry results indicate that the developed multiwalled carbon nanotube-modified carbon fiber microelectrodes possess a remarkable electrocatalytic activity towards ascorbic acid oxidation and can be used for its selective measurement in the presence of other electroactive species coexisting in rat brain, such as 3,4-dihydroxyphenylacetic acid, uric acid, and 5-hydroxytryptamine [42]. Compared with the bare electrode, the peak currents of ascorbic acid and rutin at MWCNTs–CHIT/ABPE increased significantly and the anodic peak potential separation up to 342 mV between ascorbic acid and rutin was attributed to the unique characteristics of both acetylene black and multi-walled carbon nanotubes such as excellent conductivity, large surface area and strong adsorptive capacity, yielding higher accumulation efficiency of analyte molecules. The formation of π- π bonds between the electron rich- surface of carbon nanotubes and the analyte molecules, as well as the formation of hydrogen bonds between some functional groups present at the MWCNTs–CHIT/ABPE surface and the ascorbic acid or rutin molecules contributed to the better performances of the modified electrode [114]. A modified multiwall carbon nanotube paste electrode displayed a strong ability of resolving the overlapped voltammetric responses of ascorbic acid, acetaminophen and tryptophan into three well-defined voltammetric peaks. The three compounds can well be separated from each other in mixture with potential differences of 200, 330 and 530 mV between ascorbic acid and acetaminophen, acetaminophen and tryptophan and ascorbic acid and tryptophan, respectively, these values of peak separation being large enough to determine these analytes, individually and simultaneously [115].

A poly(diallyl dimethylammonium chloride) functionalized helical carbon nanotubes coated glassy carbon electrode can differentiate well-defined peaks for three key biocompounds: the peak potentials were obtained at about 376 mV, 224 mV, and 13 mV for uric acid, dopamine and ascorbic acid, respectively [117]. At the surface of a multi-walled carbon nanotubes (MWCNT) and poly(Nile blue A) modified glassy carbon electrode there was no interference from compounds commonly found in clinical and pharmaceutical samples, such as salicylic acid, paracetamol, dopamine, uric acid and aspirin in 0.1 mol L^{-1} phosphate buffer at pH 5.3, by 0.0 V amperometry [119].

When compared with the unmodified electrode, the large electrochemical potential difference achieved with a graphene/Pt nanocomposites modified glassy carbon electrode, was essential to distinguish ascorbic acid, uric acid and dopamine. At a graphene/Pt nanocomposites modified glassy carbon electrode the potential differences between the three detected peaks were 185 mV (ascorbic acid vs dopamine), 144 mV (dopamine vs uric acid) and 329 mV (ascorbic vs uric acid), in CV [121]. At a nano platinum/nano gold/nafion incorporated functionalized multiwall carbon nanotubes modified electrode, well defined voltammetric peaks were obtained for ascorbate, epinephrine and urate anions with separations of 0.222 and 0.131 V [124].

It was found that dopamine, uric acid, paracetamol and ascorbic acid gave four separated peaks obtained at −0.06 V, 0.11 V, 0.21 V and 0.31 V, at a $SiO_2/C/Nb_2O_5$ electrode, indicating that the species oxidation took place independently at the modified ceramic composite [125]. Single-walled carbon nanotube-modified carbon–ceramic electrodes allowed selective determination of acetaminophen and ascorbic acid: both analytes gave sensitive oxidation peaks at 62 and 302 mV versus saturated calomel electrode, respectively. Common ions such as Na^+, K^+, Cl^-, NO_3^-, $H_2PO_4^-$, HPO_4^{2-}, CO_3^{2-} and SO_4^{2-} did not show interference. As for other usual interferences proper to biological samples and pharmaceuticals, dopamine (50-fold concentration), glucose, vitamin B6, tyrosine and cysteine had no significant influence on the current responses of acetaminophen and ascorbic acid (signal change <5%), suggesting that this method is selective in simultaneous determination of both analytes [126].

At an ascorbate oxidase/carboxylated multiwalled carbon nanotubes/polyaniline/gold electrode, it was proved that the value of the measured current intensity does not vary in the presence of common interferents such as oxalic acid, glucose, fructose, citric acid, lactose, starch, sucrose, tartaric acid and sodium chloride [134]. A PdNi/C modified glassy carbon electrode- based ascorbic acid biosensor is highly specific to AA in the presence of various organic and inorganic interfering species commonly found in food and biological samples: glucose, fructose, lactose, sucrose, uric acid, dopamine, glycine, tryptophan and nitrite [135].

7. Analytical performances of electrochemical ascorbic acid sensors

The analytical performances of electrochemical methods depend on the sensor's construction and some of the most illustrative examples are extensively reviewed below (see Table 1). It was proved that these analytical characteristics enabled the viable estimation of ascorbic acid content in various media (Table 2).

8. Some applications of electrochemical ascorbic acid sensors in food, pharmaceutical and biological fluid analysis

Electrochemical ascorbic acid sensors found widespread application in food, pharmaceutical and biomedical analysis, as shown below (Tables 2 and 3).

Table 1
Some analytical performances attained in vitamin C electrochemical determination.

Type of electrochemical detection	Transducer	Linear response	Detection limit	Relative standard deviation	Ref.
Potentiometric	Graphite-epoxy composite electrode	$8.0x10^{-6}$ - $4.5x10^{-4}$ mol L^{-1}	$4.5x10^{-6}$ mol L^{-1}	4%	[76]
Potentiometric	Two ISFETs	0.25–2.0 mmol L^{-1}	-	≤ 2.3%	[80]
Potentiometric	MnO_2 modified nanoparticles ISFET	0.02–1.27 mmol L^{-1}	0.01 mmol L^{-1}	-	[81]
Potentiometric	Iodine-modified platinum electrode; graphite and glassy-carbon electrodes coated with Prussian blue	10^{-5}-10^{-3} mol L^{-1}	-	7-10%	[136]
Linear scan voltammetry	Gold electrode	1-175 μg mL^{-1}	0.3 μg mL^{-1}	0.83-10.3%	[82]
Second order derivative linear scan voltammetry	Acetylene black paste electrode modified with a multi-walled carbon nanotubes–chitosan composite film	1 μmol L^{-1}–400 μmol L^{-1}	0.8 μmol L^{-1}	-	[114]
Voltammetric (CV)	Pt electrode	0.31-20 mmol L^{-1}	0.075 mmol L^{-1}	1.64%	[60]
Voltammetric (CV)	Carbon paste electrode	0.07-20 mmol L^{-1}	0.062 mmol L^{-1}	2.29%	[60]
Voltammetric (CV)	Manganese dioxide graphite composite electrode	0-2.5 mmol L^{-1}	0.4 μmol L^{-1}	-	[99]
Voltammetric (CV)	Modified glassy carbon electrode	$1.97–9.88\times10^{-4}$ mol L^{-1}	-	<1.5%	[100]
Voltammetric (CV)	Poly caffeic acid film modified glassy carbon electrode	$2.0\times10^{-5}–1.2\times10^{-3}$ mol L^{-1}	9.0×10^{-6} mol L^{-1}	-	[102]
Voltammetric (CV, DPV)	Cetrimonium iodide-iodine based graphite-multiwall carbon nanotube paste electrode	5.6×10^{-5} - 1.2×10^{-2} mol L^{-1}	1.2×10^{-6} mol L^{-1}	-	[116]
Voltammetric (CV, DPV)	Nano TiO2-PEDOT film modified glassy carbon electrode	-	0.02 μmol L^{-1}	-	[137]
Voltammetric (CV, DPV) and chronoamperometric	Cu-zeolite A/graphene-modified glassy carbon electrode	$2.0 x10^{-5}$–$2.0 x10^{-4}$ mol L^{-1}	$1.1x10^{-5}$ mol L^{-1}	-	[138]
Voltammetric (CV, DPV)	Gold nanoparticles/overoxidized polyimidazole composite modified glassy carbon electrode	210.0–1010.0 μmol L^{-1}	2.0 μmol L^{-1}	-	[139]
Voltammetric (DPV)	Glassy carbon electrode	3.52 - 176.1 μg mL^{-1}	0.88 μg mL^{-1}	-	[1]
Voltammetric (DPV)	Single crystal Au (III) electrode	1×10^{-6} - 5×10^{-4} mol L^{-1}	5×10^{-8} mol L^{-1}	-	[61]
Voltammetric (DPV)	Glassy carbon electrode	$6 x 10^{-6}$ - $8 x 10^{-4}$ mol L^{-1}	$5.16 x 10^{-7}$ mol L^{-1}	2.16%	[87]
Voltammetric (DPV)	Gold nanoparticles modified gold glassy carbon electrode	0.3–1.4 mmol L^{-1}	9.0×10^{-5} mol L^{-1}	-	[90]
Voltammetric (DPV)	2,2'-(1,8-octanediylbisnitriloethylidine)-bis-hydroquinone modified carbon paste electrode	5.0–30 μmol L^{-1} 40–1,500 μmol L^{-1}	0.6 μmol L^{-1}	-	[96]
Voltammetric (DPV)	Poly 3-(5-chloro-2-hydroxyphenylazo)-4,5-dihydroxynaphthalene- 2,7-disulfonic acid modified glassy carbon electrode	5.0–240 μmol L^{-1}	1.43 μmol L^{-1}	-	[101]
Voltammetric (DPV)	Glassy carbon electrode modified with poly(bromocre sol purple)	$2.0x10^{-5}$-$7.0x10^{-4}$ mol L^{-1}	$6.5x10^{-6}$ mol L^{-1}	3.5-3.8%	[103]
Voltammetric (DPV)	Polyaniline-modified glassy carbon and screen printed electrodes	0.4 μmol L^{-1} to 2 mmol L^{-1} (batch) 5 μmol L^{-1} to 100 μmol L^{-1} (flow injection)	0.4 μmol L^{-1} batch 2.45 μmol L^{-1} flow injection	-	[104]
Voltammetric (DPV)	Chitosan incorporating cetylpyridine bromide modified glassy carbon electrode	4.0×10^{-6} to 1.0×10^{-3} mol L^{-1}	8.0×10^{-7} mol L^{-1}	-	[107]
Voltammetric (DPV)	Binuclear copper complex-modified glassy carbon electrode	5.0–160.0 μmol L^{-1}	$2.8 x 10^{-6}$ mol L^{-1}	3.2%.	[109]
Voltammetric (DPV)	Cathodically pretreated boron-doped diamond electrode	1.9×10^{-5} to 2.1×10^{-4} mol L^{-1}	19 μmol L^{-1}	-	[112]
Voltammetric (DPV)	Poly(diallyl dimethylammonium chloride) modified helical carbon nanotubes coated glassy carbon electrode	25–1050 μmol L^{-1}	0.12 μmol L^{-1}	-	[117]
Voltammetric (DPV)	n-octylpyridinum hexafluorophosphate and single-walled carbon nanotube composite electrode	3.0 μmol L^{-1} - 4.2 mmol L^{-1}	1.0 μmol L^{-1}	-	[118]
Voltammetric (DPV)	Single-walled carbon nanotube-modified carbon–ceramic electrode	5.0-700.0 μmol L^{-1}	3.0 μmol L^{-1}	3.50%	[126]
Voltammetric (SWV)	Glassy carbon electrode	3.52 - 176.1 μg mL^{-1}	0.52 μg mL^{-1}	-	[1]

Table 1 (*Continued*)

Type of electrochemical detection	Transducer	Linear response	Detection limit	Relative standard deviation	Ref.
Voltammetric (SWV)	Carbon-paste electrode modified with multiwall carbon nanotubes	0.02–140.0 μmol L^{-1}	9.1 nmol L^{-1}	-	[115]
Amperometric	Graphene-doped carbon paste electrode	1.0×10^{-7} - 1.06×10^{-4} mol L^{-1}	7.0×10^{-8} mol L^{-1}	-	[98]
Amperometric	Glassy carbon electrode modified with polyaniline doped with silicotungstic acid and carbon nanotubes	1 μmol L^{-1} - 10 μmol L^{-1}	0.51 μmol L^{-1}	3.6%	[106]
Amperometric and cyclic voltammetry	Glassy carbon electrode modified by deposition of multi-walled carbon nanotubes and poly(NileblueA)	0.05–1.0 mmol L^{-1}	1.6 μmol L^{-1}	Less than 5%	[119]
Amperometric and linerar sweep voltammetry	Poly(xanthurenic acid) multi-walled carbon nanotubes composite -modified glassy carbon electrode	1×10^{-6}–1.52×10^{-3} mol L^{-1}	0.1 μmol L^{-1}	-	[120]
Amperometric	Over-oxidized polypyrrole and palladium nanoparticles composites-coated Au electrode	1–520 μmol L^{-1}	1 μmol L^{-1}	-	[122]
Amperometric	Clark oxygen electrode	$5x10^{-5}$ mol L^{-1} - $5x10^{-4}$ mol L^{-1}	-	2.3%	[129]
Amperometric	Clark oxygen electrode	0.10-0.55 mmol L^{-1}	0.023 mmol L^{-1}	2.67%	[130]
Amperometric	Glassy carbon electrode	0–400 ng mL^{-1}	4 ng mL^{-1}	1.0%	[131]
Amperometric	Gold microelectrodes array	0.44–2.64 mg L^{-1}	-	1.0%	[132]
Amperometric	Carboxylated multiwalled carbon nanotubes and polyaniline modified gold electrode	2–206 μmol L^{-1}	0.9 μmol L^{-1}	2.24-14.2%	[134]
Amperometric	Carbon-supported PdNi nanoparticles (PdNi/C) electrode	1.0×10^{-5} M - 1.8×10^{-3} mol L^{-1}	0.5 μmol L^{-1}	1.8%	[135]
Amperometric and voltammetric (CV)	Glassy carbon electrode modified with palladium nanoparticles supported on graphene oxide	0.02–2.28 mmol L^{-1}	-	4.32- 9.61%	[140]
Amperometric	Carbon fiber microelectrode modified with nickel oxide and ruthenium hexacyanoferrate	10–1610 μmol L^{-1}	1.0 μmol L^{-1}	4- 5%	[141]

Table 2
Examples of applications of electrochemical methods in ascorbic acid determination in various media.

Biorecognition element	Detection mode	Transducer	Analysed matrix	Application	Ref.
-	Potentiometric	Graphite-epoxy composite electrode	Vitamin C tablets	Pharmaceutical analysis	[76]
Horseradish peroxidase	Potentiometric	Two ISFETs	Fruit juices and beverages	Food analysis	[80]
-	Potentiometric	MnO_2 modified nanoparticles ISFET	Vitamin C injections	Pharmaceutical analysis	[81]
-	Potentiometric	MnO_2 modified nanoparticles ISFET	Biological fluids (urine)	Clinical analysis	[81]
-	Cyclic voltammetry and second-order linear scan voltammetry	Acetylene black carbon paste electrode modified with multi-walled carbon nanotubes–chitosan composite film	Pharmaceutical samples	Pharmaceutical analysis	[114]
-	Voltammetric (DPV and SWV)	Glassy carbon electrode	Chewable tablets	Pharmaceutical analysis	[1]
-	Voltammetric (DPV and CV)	Pt and carbon paste electrodes	Fruit juices	Food analysis	[60]
-	Voltammetric (DPV)	Glassy carbon electrode	Estervit tablets	Pharmaceutical analysis	[87]
-	Voltammetric (DPV)	Glassy carbon electrode	Fruit (citrus) juices	Food analysis	[87]
-	Voltammetric (DPV)	Glassy carbon electrode modified with poly(bromocre sol purple)	Vitamin C injections and tablets	Pharmaceutical analysis	[103]
-	Voltammetric (DPV)	Single-walled carbon nanotube-modified carbon–ceramic electrode	Ascorbic acid tablets	Pharmaceutical analysis	[126]
-	Voltammetric (DPV)	Single-walled carbon nanotube-modified carbon–ceramic electrode	Human serum samples	Clinical analysis	[126]
-	Voltammetric (DPV and CV)	Glassy carbon/multi-walled nanotubes–silica network–gold nanoparticles modified electrode	Vitamin C tablets and fruit juices	Pharmaceutical and food analysis	[142]
-	Voltammetric (SWV)	Carbon paste electrode modified with multiwall carbon nanotube	Tablets, fruit juices	Pharmaceutical and food analysis	[115]
-	Amperometric	Over-oxidized polypyrrole and palladium nanoparticles composites coated- Au electrode	Human serum samples and artificial cerebrospinal fluid	Clinical analysis	[122]
Ascorbate oxidase	Amperometric	Clark oxygen electrode	Fruit juices and soft drinks	Food analysis	[130]
Ascorbate oxidase	Amperometric	Array of gold microelectrodes modified by electrochemical deposition of palladium	Urine	Clinical analysis	[132]

Table 2 (*Continued*)

Biorecognition element	Detection mode	Transducer	Analysed matrix	Application	Ref.
Ascorbate oxidase	Amperometric	Carboxylated multiwalled carbon nanotubes/polyaniline modified Au electrode	Vitamin C tablets: Lamcea/Becozyme C forte (multivitamin)	Pharmaceutical analysis	[134]
Ascorbate oxidase	Amperometric	Carboxylated Multiwalled carbon nanotubes/polyaniline modified Au electrode	Human serum	Biomedical analysis	[134]
Ascorbate oxidase	Amperometric	Carboxylated multiwalled carbon nanotubes/polyaniline modified Au electrode	Fruit (citrus and apple) juices	Food analysis	[134]
-	Amperometric	Carbon fiber microelectrode modified with nickel oxide and ruthenium hexacyanoferrate	Human gastric juice	Clinical analysis	[141]

Table 3
Numerical data on ascorbic acid content determined in various analysed systems.

Electrochemical method	Electrode type	Analysed medium	Ascorbic acid content	Reference
Potentiometry	Polymeric membrane-based ion-selective electrode	Aspirin with vitamin C:	200.1 ± 0.5 mg- 200.8 ± 0.6 mg	[143]
Cyclic voltammetry	Glassy carbon	Cherry	54.86 mg/100g	[56]
Cyclic voltammetry	Glassy carbon	Guava	51.02 mg/100g	[56]
Cyclic voltammetry	Glassy carbon	Green pepper	182.34 mg/100g	[56]
Cyclic voltammetry	Pt strip	Orange juice	39.25 mg/100 mL	[60]
Cyclic and differential pulse voltammetry	Graphite-multiwall carbon nanotubes paste electrode	Baluchestani lemon juice	58.6 mg/100 mL	[116]
Cyclic and differential pulse voltammetry	Graphite-multiwall carbon nanotubes paste electrode	Egyptian orange juice	88.1 mg/100 mL	[116]
Cyclic voltammetry	Palladium-plated aluminum electrode	Effervescent tablets containing vitamin C and acetaminophen or acetaminophen tablets	0.206 mg per tablet	[144]
Differential pulse voltammetry	Carbon paste	Lemon juice	54.74 mg/100 mL	[60]
Differential pulse voltammetry	Glassy carbon	Grapefruit juice	13.14 ± 0.2 mg L^{-1}	[87]
Differential pulse voltammetry	Glassy carbon	Lemon juice	21.86 ± 0.32 mg L^{-1}	[87]
Differential pulse voltammetry	Glassy carbon	Orange juice	26.89 ± 0.49 mg L^{-1}	[87]
Differential pulse voltammetry	Poly(bromocresol purple) modified glassy carbon	Injections	75.60 x10^{-6} mol L^{-1}	[103]
Differential pulse voltammetry	n-octylpyridinum hexafluorophosphate ionic liquid single-walled carbon nanotube composite	Orange drink	48.96 ± 0.53 mg/100 mL	[118]
Differential pulse voltammetry	n-octylpyridinum hexafluorophosphate ionic liquid single-walled carbon nanotube composite	Tomato extract drink	24.31 ± 0.21 mg/100 mL	[118]
Differential pulse voltammetry	n-octylpyridinum hexafluorophosphate ionic liquid single-walled carbon nanotube composite	Green tea extract	14.27 mg/100 mL	[118]
Differential pulse voltammetry	Multi-wall carbon nanotubes and polyhistidine modified glassy carbon electrode	1000 mg Redoxon tablets	978 mg	[145]
Differential pulse voltammetry	Glassy carbon (GC) electrode modified by multi-walled carbon nanotubes (MWNTs) and bis(pyridyl -terpyridine) iron(II) thiocyanate complex	Injections (0.50 mmol L^{-1} declared content)	0.47 mmol L^{-1}	[146]
Differential pulse voltammetry	Copper(II)- phthalocyanine modified carbon paste	Supercarrot orange juice	8.56±0.62 mg/100 mL	[147]
Square-wave voltammetry	Multiwalled carbon nanotubes modified glassy carbon electrode	Orange juices	0.435 ± 0.011- 0.469 ± 0.017 mmol L^{-1} in (1/5) diluted sample	[148]
Amperometric	Vanadate modified carbon paste	Commercial soft drinks	206 - 214 mg L^{-1}	[94]
Amperometric	Ascorbate oxidase biosensor based on Clark type transducer	Fruit juices and soft drinks	0.48 - 1.98 mmol L^{-1}	[130]
Amperometric	Ascorbate oxidase/carboxylated multiwalled carbon nanotubes/polyaniline/gold	Apple juice	7.00 ± 1.00 mg dL^{-1}	[134]
Amperometric	Ascorbate oxidase/carboxylated multiwalled carbon nanotubes/polyaniline/gold	Human serum	29.0 ± 1.0 - 86.8 ± 0.44 μmol L^{-1}	[134]
Amperometric	Nickel nanoparticles poly1,5-diaminonaphthalene composite	Human serum	40 - 205 μmol L^{-1}	[123]
Amperometric	Multi-walled carbon nanotubes (MWCNT) and poly(Nile blue A) modified glassy carbon	250 mg aspirin tablet	246.0 ± 8.0 mg	[119]

Table 3 (*Continued*)

Electrochemical method	Electrode type	Analysed medium	Ascorbic acid content	Reference
Amperometric	Gold electrode modified by electrochemical deposition of palladium	Euphorbia milii var. splendens honey	5 mg/100 g	[149]
Amperometric	Gold electrode modified by electrochemical deposition of palladium	Eucalyptus tereticornis honey	6.20 mg/100 g	[149]
Amperometric	Glassy carbon electrode modified with the nickel(II)-bis(1,10-phenanthroline) complex and multi-walled carbon nanotubes	spiked fruit juices	1.28 μmol L^{-1}	[150]
Amperometric	Double-walled carbon nanotubes/choline-modified electrode	orange juice and lemon juice	recoveries in the range of 101.2–103.6% for known amount of standard	[151]
Amperometric	Poly-xanthurenic acid/multi-walled carbon nanotube/glassy carbon modified electrode	urine samples	recovery values of the spiked samples: 99.1% and 100.6%	[152]
Amperometric biosensor based on zucchini (Cucurbita pepo)	Oxygen electrode	lemon juice grapefruit juice apple juice tomato juice orange juice vitamin C tablet	3.52 mg/100 mL 2.86 mg/100 mL 2.14 mg/100 mL 5.68 mg/100 mL 37.9 mg/100 mL 0.774 mg/100 mL	[153]
Amperometric	Mesopore-rich active carbon-modified pyrolytic graphite electrode	human urine vitamin C tablet	1.63;1.58 mmol L^{-1} 48.5;51.3;49.7 mg	[154]
Amperometric	Screen-printed electrode modified with electrografted o-aminophenol film	fresh fruit vegetables commercial juices	lemon 4.3 μmol L^{-1} orange 5.0 μmol L^{-1} pineapple 15 μmol L^{-1} strawberry 4.7 μmol L^{-1} apple 3.4 μmol L^{-1} kiwi 3.4 μmol L^{-1} tomato 15 μmol L^{-1} green pepper 1.7 μmol L^{-1} lemon commercial juice 4.3 μmol L^{-1} orange commercial juice 3.9 μmol L^{-1} tomato commercial juice 2.8 μmol L^{-1}	[155]
Amperometric	Ethylene blue (NMB) encapsulated in mesoporous AlMCM-41 material	pharmaceuticals	tablet (effervescent) 243.6 mg g^{-1} tablet (chewable) 139.2 mg g^{-1} multivitamin syrup 65.3 mg mL^{-1} ampoule 49.1 mg mL^{-1}	[156]

9. Conclusions

The design and development of performant methods and sensors for vitamin C assessment is vital, given the constant importance and presence of this key analyte in foodstuffs, pharmaceutical and biological fluids, with implications in redox processes, human health and food quality. Due to the simplicity of the procedure and of the instrumentation, to the minimum requirements with respect to sample pre-treatment, as well as to fast response, sensitivity, and low cost, electrochemical techniques are often preferred to laborious instrumental methods in ascorbic acid determination, with accuracy and results obtained in real time, in complex media.

Different modalities of sensor development were applied, from bare to chemically modified sensors. Recent advances imply the use of carbon nanotubes and various composites, for which the large surface area and electrocatalytical activity greatly enhance the analytical signal, diminishes the peak potential corresponding to ascorbic acid oxidation and solves peak overlapping problems in complex samples. Yet, provided that adequate pretreatment and cleaning steps are included, several examples of viable ascorbic acid determination in various media by bare electrodes can be encountered, even in the presence of interferents. The methods' performances and application areas depend on the chosen electrochemical technique. It can be concluded that the different ways of construction and expected performances are adequate and tuned to the nature of the analysed compound and respective matrix.

The nature of the electrode material and surface groups formed, their interaction with the analyte molecules, along with the pH value of the analysed matrix and electrolyte type, greatly influence the electrooxidation rate, as well as the peak potential and height. The electrooxidation mechanism and rate are dependent on various factors: electrode nature and modifiers, electrode pre-treatment, surface groups, pH, electrolyte, presence of other compounds. The interaction between the respective form of analyte molecule present at that pH value (range) and the functional groups of the electrode/modifier layer is essential for determining electroxidation rate and electrode performance.

In complex media where interference occurence is expected, modifiers enhance the catalytic peak current of the analyte of interest, allowing better peak separation from interferent compounds.

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