

An overview on cyclic voltammetry and its application in pharmaceutical analysis

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ABSTRACT

Cyclic voltammetry is the most widely used technique for acquiring qualitative information about electrochemical reactions. The power of cyclic voltammetry results from its ability to rapidly provide considerable information on the thermodynamics of redox processes and the kinetics of heterogeneous electron-transfer reactions, and on coupled chemical reactions or adsorption processes. Cyclic voltammetry is often the first experiment performed in an electroanalytical study. In particular, it offers a rapid location of redox potentials of the electro active species, and convenient evaluation of the effect of media upon the redox process.

Keywords: Cyclic voltammetry, Electrochemical reactions, Thermodynamics, Redox potential.

1. INTRODUCTION

Electrochemical analyses can be thought of in terms of two broad classes of measurement, one in which the potential that develops between two electrodes is measured (potentiometry) and another in which the current that flows between two electrodes is measured (amperometry). In potentiometry, it often proves helpful to arrange things such that the current is very low (e.g., by placing a high-resistance voltmeter in series between two electrodes).^[1] The electrochemical potential of one electrode (the reference electrode) is usually fixed, so the measured cell potential can be interpreted in terms of an equilibrium half-cell reaction involving an analyte species in contact with the other electrode (the working electrode). In favourable cases, one can use data from potentiometric measurements to calculate analyte concentrations directly from the Nernst equation. Potentiometry is a simple and straightforward analytical method, and is routinely used to solve many problems in the analysis of electrochemically active and/or charged analytes^[2].

Cyclic voltammetry is the most widely used technique for acquiring qualitative information about electrochemical reactions. The power of cyclic voltammetry results from its ability to rapidly provide considerable information on the thermodynamics of redox processes and the kinetics of heterogeneous electron-transfer reactions, and on coupled

chemical reactions or adsorption processes.^[3] Cyclic voltammetry is often the first experiment performed in an electroanalytical study. In particular, it offers a rapid location of redox potentials of the electro active species, and convenient evaluation of the effect of media upon the redox process.

1.1. History

Historically, the branch of electrochemistry we now call voltammetry developed from the discovery of palaeography in 1922 by the Czech chemist Jaroslav Heyrovsky, for which he received the 1959 Nobel Prize in chemistry. The early voltammetry methods experienced a number of difficulties, making them less than ideal for routine analytical use. However, in the 1960s and 1970s significant advances were made in all areas of voltammetry (theory, methodology, and instrumentation), which enhanced the sensitivity and expanded the repertoire of analytical methods. The coincidence of these advances with the advent of low-cost operational amplifiers also facilitated the rapid commercial development of relatively inexpensive instrumentation^[4].

The common characteristic of all voltammetric techniques is that they involve the application of a potential (E) to an electrode and the monitoring of the resulting current (i) flowing through the electrochemical cell. In many cases the applied potential is varied or the current is

monitored over a period of time (t). Thus, all voltammetric techniques can be described as some function of E , i , and t . They are considered active [5] techniques (as opposed to passive techniques such as potentiometry) because the applied potential forces a change in the concentration of an electro active species at the electrode surface by electrochemically reducing or oxidizing it.

The analytical advantages of the various voltammetric techniques include excellent sensitivity with a very large useful linear concentration range for both inorganic and organic species (10^{-12} to 10^{-1} M), a large number of useful solvents and electrolytes, a wide range of temperatures, rapid analysis times (seconds), simultaneous determination of several analytes, the ability to determine kinetic and mechanistic parameters, a well-developed theory and thus the ability to reasonably estimate the values of unknown parameters, and the ease with which different potential waveforms can be generated and small currents measured [6,7].

Analytical chemists routinely use voltammetric techniques for the quantitative determination of a variety of dissolved inorganic and organic substances. Inorganic, physical, and biological chemists widely use voltammetric techniques for a variety of purposes, including fundamental studies of oxidation and reduction processes in various media, adsorption processes on surfaces, electron transfer and reaction mechanisms, kinetics of electron transfer processes, and transport, speciation, and thermodynamic properties of solvated species. [8] Voltammetric methods are also applied to the determination of compounds of pharmaceutical interest and, when coupled with HPLC, they are effective tools for the analysis of complex mixtures.

The electrochemical cell, where the voltammetric experiment is carried out, consists of a working (indicator) electrode, a reference electrode, and usually a counter (auxiliary) electrode. In general, an electrode provides the interface across which a charge can be transferred or its effects felt. Because the working electrode is where the reaction or transfer of interest is taking place, whenever we refer to the electrode, we always mean the working electrode [9]. The reduction or oxidation of a substance at the surface of a working electrode, at the appropriate applied potential, results in the mass transport of new material to the electrode surface and the generation of a current. Even though the various types of voltammetric techniques may appear to be very different at first glance, their fundamental principles and applications derive from the same

electrochemical theory. Here we summarize some of the electrochemical theory or laws common to all of the voltammetric techniques.

Where necessary, more specific details are given later under the discussion of each technique cyclic voltammetry (CV) has become an important and widely used electroanalytical technique in many areas of chemistry. It is rarely used for quantitative determinations, but it is widely used for the study of redox processes [10], for understanding reaction intermediates, and for obtaining stability of reaction products.

This technique is based on varying the applied potential at a working electrode in both forward and reverse directions (at some scan rate) while monitoring the current. For example, the initial scan could be in the negative direction to the switching potential [11]. At that point the scan would be reversed and run in the positive direction. Depending on the analysis, one full cycle, a partial cycle, or a series of cycles can be performed.

1.2. Cyclic voltammetry principle

Cyclic voltammetry consists of scanning linearly the potential of a stationary working electrode, using a triangular potential waveform. Depending on the information sought, single or multiple cycles can be used. During the potential sweep, the potentiostat measures the current resulting from the applied potential. The resulting plot of current vs. potential is termed a cyclic voltammogram [12]. The cyclic voltammogram is a complicated, time-dependent function of a large number of physical and chemical parameters.

The utility of cyclic voltammetry is highly dependent on the analyte being studied. The analyte has to be redox active within the experimental potential window. It is also highly desirable for the analyte to display a reversible wave. A reversible wave is when an analyte is reduced or oxidized on a forward scan and is then reoxidized or reproduced in a predictable way on the return scan [12].

Even reversible couples contain polarization over potential and thus display a hysteresis between absolute potential between the reduction (E_{pc}) and oxidation peak (E_{pa}). This over potential emerges from a combination of analyte diffusion rates and the intrinsic activation barrier of transferring electrons from an electrode to analyte. A theoretical description of polarization over potential is in part described by the Butler-Volmer equation and Cottrell equation. Conveniently in an ideal system the relationships reduces to, $E_{pc}-E_{pa}=57\text{-mv}/n$, for an n electron process [13].

Reversible couples will display ratio of the peak currents passed at reduction (i_{pc}) and oxidation (i_{pa}) that is near unity ($1 = i_{pa}/i_{pc}$). This ratio can be perturbed for reversible couples in the presence of a following chemical reaction, stripping wave, or nucleation event.

When such reversible peaks are observed thermodynamic information in the form of half cell potential $E^{0}_{1/2}$ can be determined. When waves are semi-reversible such as when i_{pa}/i_{pc} is less than or greater than 1, it can be possible to determine even more information especially kinetic processes like following chemical reaction [14].

When waves are non-reversible it is impossible to determine what their thermodynamic $E^{0}_{1/2}$ is with cyclic voltammetry. This $E^{0}_{1/2}$ can be determined; however it often requires equal quantities of the analyte in both oxidation states. When a wave is non-reversible cyclic voltammetry can not determine if the wave is at its thermodynamic potential or shifted to a more extreme potential by some form of over potential. The couple could be irreversible because of a following chemical process; a common example for transition metals is a shift in the geometry of the coordination sphere [15]. If this is the case, then higher scan rates may show a reversible wave. It is also possible that the wave is irreversible due to a physical process most commonly some form of precipitation as discussed below. Some speculation can be made in regards to irreversible waves however they are generally outside the scope of cyclic voltammetry [16].

In cyclic voltammetry, one sweeps the potential of the working electrode at a specific sweep rate (in volts / second), and measures the resulting current vs. time curve. Usually the sweep is reversed at a specific switching potential, hence the name cyclic voltammetry. Since the sweep rate is constant and the initial and switching potentials are known, one can easily convert time to potential, and the usual protocol is to record current vs. applied potential. The resulting current vs. applied potential curve (a cyclic voltammogram) is predicted for an ideal, reversible system [17].

Cyclic voltammetry (CV) is very similar to LSV. In this case the voltage is swept between two values at a fixed rate, however now when the voltage reaches V_2 the scan is reversed and the voltage is swept back to V_1 . A typical cyclic voltammogram recorded for a reversible single electrode transfer reaction. Again the solution contains only a single electrochemical reactant [18]. The forward sweep produces an identical

response to that seen for the LSV experiment. When the scan is reversed we simply move back through the equilibrium positions gradually converting electrolysis product (Fe^{2+} back to reactant (Fe^{3+}). The current flow is now from the solution species back to the electrode and so occurs in the opposite sense to the forward sweep but otherwise the behaviour can be explained in an identical manner. For a reversible electrochemical reaction the CV recorded has certain well defined characteristics [19].

1. The voltage separation between the current peaks is
2. The positions of peak voltage do not alter as a function of voltage scan rate
3. The ratio of the peak currents is equal to one
4. The peak currents are proportional to the square root of the scan rate

1.3. Instrumentation in cyclic voltammetry

A CV system consists of an electrolysis cell, a potentiostat, a current-to-voltage converter, and a data acquisition system. The electrolysis cell consists of a working electrode, counter electrode, reference electrode, and electrolytic solution. The working electrode's potential is varied linearly with time, while the reference electrode maintains a constant potential [20]. The counter electrode conducts electricity from the signal source to the working electrode. The purpose of the electrolytic solution is to provide ions to the electrodes during oxidation and reduction. A potentiostat is an electronic device which uses a dc power source to produce a potential which can be maintained and accurately determined, while allowing small currents to be drawn into the system without changing the voltage. The current-to-voltage converter measures the resulting current, and the data acquisition system produces the resulting voltammogram [21].

1.4. Electrodes of cyclic voltammetry

A typical electrochemical cell consists of the sample dissolved in a solvent, an ionic electrolyte, and three (or sometimes two) electrodes. Cells (that is, sample holders) come in a variety of sizes, shapes, and materials. The type used depends on the amount and type of sample, the technique, and the analytical data to be obtained. The material of the cell (glass, Teflon, polyethylene) is selected to minimize reaction with the sample. The method uses reference electrode, working electrode, and counter electrode which in combination are sometimes referred to as a three-electrode setup. Electrolyte is usually added to the test solution to ensure sufficient conductivity [22]. The combination of the solvent, electrolyte and

specific working electrode material determines the range of the potential.

Electrodes are static and sit in unstirred solutions during cyclic voltammetry. This "still" solution method results in cyclic voltammetry's characteristic diffusion controlled peaks. This method also allows a portion of the analyte to remain after reduction or oxidation where it may display further redox activity. Stirring the solution between cyclic voltammetry traces is important as to supply the electrode surface with fresh analyte for each new experiment. The solubility of an analyte can change drastically with its overall charge. Since cyclic voltammetry usually alters the charge of the analyte it is common for reduced or oxidized analyte to precipitate out onto the electrode. This layering of analyte can insulate the electrode surface, display its own redox activity in subsequent scans, or at the very least alter the electrode surface. For this and other reasons it is often necessary to clean electrodes between scans [23].

Common materials for working electrodes include glassy carbon, platinum, and gold. These electrodes are generally encased in a rod of inert insulator with a disk exposed at one end. A regular working electrode has a radius within an order of magnitude of 1 mm. Having a controlled surface area with a defined shape is important for interpreting cyclic voltammetry results [24].

To run cyclic voltammetry experiments at high scan rates a regular working electrode is insufficient. High scan rates create peaks with large currents and increased resistances which result in distortions. Ultra microelectrodes can be used to minimize the current and resistance. The counter electrode, also known as the auxiliary or second electrode, can be any material which conducts easily and won't react with the bulk solution. Reactions occurring at the counter electrode surface are unimportant as long as it continues to conduct current well. To maintain the observed current the counter electrode will often oxidize or reduce the solvent or bulk electrolyte [25].

In most cases the reference electrode should be as close as possible to the working electrode; in some cases, to avoid contamination, it may be necessary to place the reference electrode in a separate compartment. The unique requirements for each of the voltammetric techniques are described under the individual techniques [26].

1.5. Reference electrodes

The reference electrode should provide a reversible half-reaction with Nernstian behaviour, be constant over time, and be easy to assemble and maintain. The most commonly used reference electrodes for aqueous solutions are the calomel electrode, with potential determined by the reaction $\text{Hg}_2\text{Cl}_2(\text{s}) + 2\text{e}^- = 2\text{Hg}(\text{l}) + 2\text{Cl}^-$ and the silver/silver chloride electrode (Ag/AgCl), with potential determined by the reaction $\text{AgCl}(\text{s}) + \text{e}^- = \text{Ag}(\text{s}) + \text{Cl}^-$. The potentials of the commonly used calomel electrodes, along with those of some other reference electrodes. These electrodes are commercially available in a variety of sizes and shapes [27].

1.6. Counter electrodes

In most voltammetric techniques the analytical reactions at the electrode surfaces occur over very short time periods and rarely produce any appreciable changes in bulk concentrations of R or O. Thus, isolation of the counter electrode from the sample is not normally necessary [28]. Most often the counter electrode consists of a thin Pt wire, although Au and sometimes graphite have also been used.

1.7. Working electrodes

The working electrodes are of various geometries and materials, ranging from small Hg drops to flat Pt disks. Mercury is useful because it displays a wide negative potential range (because it is difficult to reduce hydrogen ion or water at the mercury surface), its surface is readily regenerated by producing a new drop or film, and many metal ions can be reversibly reduced into it. Other commonly used electrode materials are gold, platinum, and glassy carbon [29].

Cyclic voltammetry is carried out in quiescent solution to ensure diffusion control. A three-electrode arrangement is used. Mercury film electrodes are used because of their good negative potential range. Other working electrodes include glassy carbon, platinum, gold, graphite, and carbon paste an arrangement where different electrodes with specific functions are put together in an electrolyte solution that contain an electro active species ,working electrode, reference electrode and auxiliary electrode [30].

1.8. Applications

Cyclic voltammetry (CV) has become an important and widely used electro analytical technique in many areas of chemistry. It is widely used to study a variety of redox processes, for obtaining stability of reaction products, the presence of intermediates in oxidation-reduction reactions, reaction and electron transfer kinetics and the reversibility of a reaction. CV can also be used to determine the electron stoichiometry of a

system, the diffusion coefficient of an analyte, and the formal reduction potential ^[31], which can be used as an identification tool. In addition, because concentration is proportional to current in a reversible, Nernstian system, concentration of an unknown solution can be determined by generating a calibration curve of current vs. concentration.

Cyclic Voltammetry (CV) is an electrochemical technique which measures the current that develops in an electrochemical cell under conditions where voltage is in excess of that predicted by the Nernst equation. CV is performed by cycling the potential of a working electrode, and measuring the resulting current. The laboratory experiment will introduce to cyclic voltammetry as a simple, rapid, and powerful method for characterizing the electrochemical behavior of analytes that can be electrochemically oxidized or reduced ^[32].

Cyclic voltammetry can be used to study qualitative information about electrochemical processes under various conditions, such as the presence of intermediates in oxidation-reduction reactions, the reversibility of a reaction. CV can also be used to determine the electron stoichiometry of a system, the diffusion coefficient of an analyte, and the formal reduction potential, which can be used as an identification tool. ^[33] In addition, because concentration is proportional to current in a reversible, Nernstian system, concentration of an unknown solution can be determined by generating a calibration curve of current vs. concentration.

The difference between the two materials, and the importance of removing oxygen from solutions to be analyzed. Second, acquire voltammetric data for the electrochemical reduction of the herbicide N, N'-dimethyl-4, 4' bipyridine, commonly known as methyl viologen or paraquat. The herbicidal action of this molecule derives from its ability to act as an electron acceptor, thereby disrupting the metabolic electron transport chain in plants, it is therefore important to know what the redox potential is for reduction of methyl viologen ^[34].

Cyclic voltammetry is a powerful technique for the study of the extracellular electron-transfer of electro active microbial bio films. Useful thermodynamic information as well as qualitative information on the nature of the electron-transfer process can be extracted from CV experiments, including: 1) formal potentials of redox species, 2) the reversibility of redox species and its dependency on the scan rate, 3) studying the influence of the mass transfer, 4) elucidating which redox couples are responsible for the

development of turnover currents, i.e. the identification of the bioelectrocatalytically active sites, and 5) distinguishing between adsorbed and diffusive natures of the mediators ^[35].

Kinetic parameters may also be extracted, albeit less reliably than for the abiotic electrochemical systems. Here, the coupling of CV with mathematical modeling is the tool of choice for the next level of data analysis. The kinetic parameters can only be reliably estimated if the mechanisms and limiting steps of complex microbe-electrode interactions can be fully elucidated furthermore ^[36].

2. CONCLUSION

Cyclic voltammetry is a type of potentiodynamic electrochemical measurement. In a cyclic voltammetry experiment the working electrode potential is ramped linearly versus time like linear sweep voltammetry. Cyclic voltammetry takes the experiment a step further than linear sweep voltammetry which ends when it reaches a set potential. When cyclic voltammetry reaches a set potential, the working electrode's potential ramp is inverted. Cyclic voltammetry is generally used to study the electrochemical properties of an analyte in solution. Cyclic voltammetry (CV) has become an important and widely used electroanalytical technique in many areas of chemistry. It is widely used to study a variety of redox processes, for obtaining stability of reaction products, the presence of intermediates in oxidation-reduction reactions, reaction and electron transfer kinetics, and the reversibility of a reaction. CV can also be used to determine the electron stoichiometry of a system, the diffusion coefficient of an analyte, and the formal reduction potential, which can be used as an identification tool. In future cyclic voltammetry plays an important role in analysis of biochemical compounds.

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