

APPLICATIONS OF MODERN ELECTROANALYTICAL TECHNIQUES IN PHARMACEUTICAL DRUG ANALYSIS: REVIEW

¹G. M. Shinde *, ²V.R. Biradar, ³M.S. Charde & ⁴R.D. Chakole.

M. Pharm, Research Scholar
Department of Pharmaceutical Chemistry,
Government College of Pharmacy, Vidyanagar Karad, Dist -Satara,
Maharashtra, India, Pin- 415124

For correspondence,

Mr. Gopal Macchindra Shinde

Department of Pharmaceutical Chemistry,
Government College of Pharmacy,
Vidyanagar Karad, Dist -Satara, Maharashtra, India, Pin- 415124.

ABSTRACT: In the pharmaceutical and medical sciences, drug determination in pharmaceutical preparations and biological fluids is essential. The cyclic voltammetric method used for the determination of vitamin c concentration in apple juices. Modern electroanalytical technique recently used for determination of anti HIV drugs, also used for the determination of Rutin. Some voltammetric technique helpful for determination of metals. Utilizing electrochemical detectors in conjunction with LC or flow injection systems is a recent trend in drug analysis. With significant advancement in electroanalytical instrumentation, these techniques are gaining popularity in determination of therapeutic agents and their metabolites in sample at very low concentrations (10-50ng/ml). The principle and theories of various modern electroanalytical technique with recent modern advancement regards to instrumentation are also included in this article.

Key Words: Modern electroanalytical techniques, Drug Analysis, Electrochemistry, Voltammetry, Columetry, Polarography, amperometry, conductometry, Pharmaceutical Analysis.

INTRODUCTION:

The electroanalytical technique used for determination of drugs and their metabolites in biological fluids is now a day increases its importance in the pharmaceutical and biomedical sciences (2) This article attempts to introduce the principle voltammetry, potentiometry, coulometry, amperometry, conductometry (1) Additionally, a number of these methods are currently being used to elucidate electrode operations by studying the mechanisms underlying organic redox reactions (1). The most challenging pharmaceutical analytical procedures required excellent specificity and the ability to identify pharmaceuticals in biological fluids with sub nanogram detection limits [2,20] More recently, monitoring blood levels and urinary excretion of drugs in low doses (up to 50-100 ng/ml) has been made possible using contemporary electroanalytical techniques combined with TLC or LC [2,21].

THEORY AND INSTRUMENTATION:

The term "electroanalytical chemistry" refers to the study of chemical reactions that take place in a system in response to electrical stimulation. It also refers to the analysis of chemical species using electrochemical methods. Some parameters —potential (E), current (I), charge (Q), and time—are measured in an electrochemical experiment (2) In this paper selectively reviews recent applications of the electrochemical modes of amperometry, conductometry, coulometry, ionselective electrodes, potentiometry, stripping voltammetry (anodic and cathodic), and voltammetry in the analysis of medications and

1] VOLTAMMETRY: Voltammetry is a class of electroanalytical techniques used in analytical chemistry and numerous industrial processes. Voltammetry uses current measurements to determine an analyte's properties while the potential is changed [6,7], very small amount of sample is required in this technique. This technique mainly used in determination of vitamin c in apple juices.

Key instrument components:

the principal components of a voltammetric analyzer are (fig.1): three electrodes in solution containing analyte

- **Working electrode:** microelectrode with varying potential throughout time. E.g. : Gold, Silver, Mercury drop
- **Reference electrode:** potential remains constant.
- **Counter electrode:** mercury that complete circuit, conduct e from signal source through solution to the working electrode.

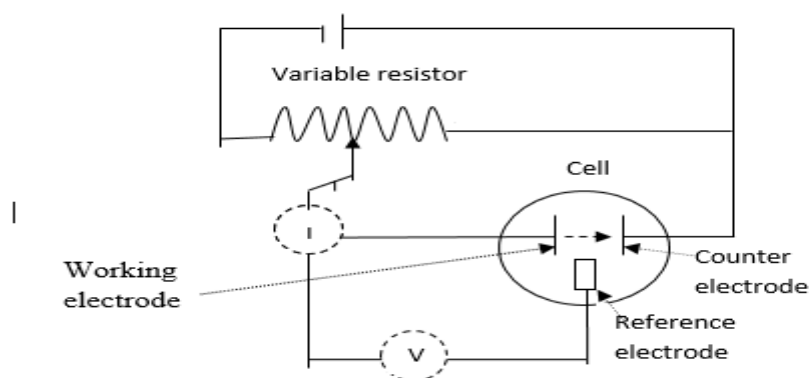


Figure 1: Schematic representation of a basic voltammetric system comprising of three electrodes (WE: working electrode, RE: reference electrode, CE: counter electrode, I: current signal, V: voltage)

MODERN VOLTAMMETRIC TECHNIQUES [2]

- Rapid Scan Linear sweep voltammetry
- Normal Pulse Voltammetry
- Differential pulse Voltammetry
- Fast Cyclic voltammetry
- Square wave voltammetry
- Constant Potential amperometry
- Chronopotentiometry
- Chronoamperometry
- Adsorptive stripping voltammetry
- Anodic stripping voltammetry
- Cathodic stripping voltammetry
- Adsorptive stripping voltammetry

A] Anodic stripping voltammetry:

Anodic-stripping analysis is the most delicate electroanalytical method currently in use. For solutions containing metal ions in the range of 10^{-6} to 10^{-12} M, trace level analysis is possible. Stripping voltammetry can also be used for simultaneous multi-element determination. In addition, compared to other spectroscopic techniques, it is a cost-effective instrumentation technique. The main purpose of anodic stripping voltammetry (ASV) is to estimate the concentration of trace metals that can be reduced and preconcentrated at an electrode. The process works particularly well for metals that amalgamate with mercury to dissolve in it.

B] Cathodic stripping voltammetry:

CSV has shown to be effective for determining halides (iodide, bromide, and chloride) and sulphides as well as a variety of organic substances, such as biological components (cystine, glutathione), drugs (penicillin), and insecticides. Ethynylestradiol, a synthetic steroid hormone, is used in pharmaceutical medicines known as combination low-dose oral contraceptives. Bond and al el [8] developed method that combines reverse-phase liquid chromatography and cathodic stripping voltammetry, The working electrode was an HMDE, while the reference electrode was a NaCl-saturated with Ag/AgCl. Data for the investigation of two dosage forms, both of which contained a mixture of ethynylestradiol and levonorgestrel, revealed remarkable recoveries. The detection limits for the steroids were about 5×10^{-9} M., which were within the limits allowed for biological media [1].

C] Rapid Scan Linear sweep voltammetry: It is the most basic approach, in which a rapid potential scanning in one direction at the working electrode fluctuates linearly (20-100 mV/s) with time [2].

D] Normal Pulse Voltammetry: A series of periodic constant pulses of potential are superimposed on a linear scanning to provide consistent signal amplification. The difference in current between just before and after the pulse is measured to reduce the influence of capacitive current on the reading [2].

E] Differential Pulse Voltammetry (DPV):

Is a mix of linear sweep and pulsed voltammetry? It is a very sensitive approach with a detection limit of ppb or below. It has found widespread application in the analysis of trace levels of organic substances. However, the many pulses in the waveform make it a somewhat slower process, with individual scans requiring minutes to complete [2].

F] Chronoamperometry:

The chronoamperometric (also called potentiostatic) measurement is a technique in which an electrode is subjected to a constant current or a current step, and the resulting potential change is plotted vs time. Its capacity to measure larger concentrations makes it superior to more typical polarographic/voltammetric approaches.[2]

2] Coulometry:

Coulometry, both at constant potential and with constant current (coulometric titrations), is typically performed in stirred solution and should be considered in this section. These approaches have high sensitivity and accuracy in analysis. Purdy's monograph covers these methods in depth (9).

Instrumentation: As aforementioned, a simple voltage divider polarograph applied to a two-electrode setup is inadequate for quick and precise voltammetric observations. For such work, the true potential at the working electrode must be precisely controlled to within a few millivolts. This is implemented with a potentiated, which, as the name implies, keeps the potential static (constant). A proper sweep circuit controls the potentiated for dynamic operations, and it correctly and rapidly maintains any desired potential as a function of time. A three-electrode technique is used. The complete polarograph is typically built from operational amplifiers, which are ubiquitous in electrochemical studies. Detailed discussions of operational amplifier polarographs are to be found in the literature [10,11]¹

ANALYTICAL APPLICATIONS OF ELCTROANALYTICAL TECHNIQUES:

Having examined the basic techniques of modern electrochemical practice, the purpose of this section is to review briefly some of the applications that have been made and to evaluate critically the potentialities of electrochemistry applied to compounds of pharmaceutical systems [1].

Main application of modern electroanalytical techniques in pharmaceutical analysis is for the determination of drugs and their metabolites in pharmaceuticals and biological fluids.

Analytical chemists create methods for quality control, stability testing, pharmacokinetics, identification, and clinical trials in order to bring a drug product from the discovery stage to the commercial market [2].

1] Rutin analysis

Based on cetyltrimethylammonium chloride (CTAC) functionalized graphene (Gr) and palladium nanoparticles (Pd) (CTAC-Gr-PdNPs), a new and sensitive electrochemical sensor for rutin detection was designed [3]. A flavonoid glycoside **rutin** is that found in some plants such black tea, buckwheat tea, It is also known as **vitamin P** [3,12,13] the determination of voltammetric properties of rutin in pharmaceutical fluids is done by using cyclic voltammetry [3]

The method was successfully applied to the measurement of rutin in rutin tablets in order to assess its viability.

Table No1: Determination result of rutin in rutin tablet by Square wave voltammetry (SWV)[3]

Native concentration ^a (x10 ⁻⁷ mol/L)	Standard added (x10 ⁻⁷ mol/L)	Total found ^a (x10 ⁻⁷ mol/L)	R.S.D(%)	Recovery (%)
2.135			1.8	
	2	4.097	2.4	98.6
	4	6.120	2.1	99.8
	6	8.164	2.7	101.5

^aAverage value of three replicate measurements

Table No2: Determination of results of rutin in the human blood serum [3]

Samples	Added ^b (10 ⁻⁷ mol/L)	Found ^c (10 ⁻⁷ mol/L)	Recovery (%)	R.S.D(%)
Human blood serum	1	0.988	98.8	2.4
	3	3.101	103.4	1.8
	5	5.021	100.4	1.2

^a0.5ml human blood serum was mixed with 9.5 ml pH 2.0 PBS.

^b10 µL or 30 µL or 50µ L rutin solution (1 x 10⁻⁴ mol /L) was added to the mixed solution.

^cAverage value of three replicate measurements.

The experimental part covered the sample treatment procedures. The rutin content of the rutin tablets was determined to be 20.0 ± 0.28 mg per tablet using the response signal and calibration curve. This value was consistent with the label values of 20 mg per tablet, and the RSD for three parallel determinations was 1.8 percent. In order to evaluate the recovery, known quantities of standard

solutions were additionally added to the sample solution. The outcomes are shown in Table 1. The recovery rate, which ranged from 98.6 to 101.5%, points to a precise and dependable procedure [3].

Human blood serum was chosen as the actual sample to assess the applicability of the suggested approach in biological samples. Rutin was not clearly detected in the initial sample. Before the analysis, some rutin standard solutions were introduced to the blood serum for the purpose of verifying the accuracy. Table 2 provided a list of the evaluation findings. Rutin recovery rates ranged from 98.8 to 103.4 percent, and the RSD was determined using three parallel determinations [3].

2] For the determination of anti HIV drugs

Electroanalytical technique also used for the determination of anti-HIV drugs from dosage form for e.g., Efavirenz, Zidovudine, Abacavir, Didanosine, Electrochemical techniques also aid in the identification of the redox mechanism of drugs and provide crucial information related to the DNA-drug interactions [4,14].

3] Simultaneous Electroanalytical Determination of Analyzed Drugs:

In analytical methods for single component, some of the simultaneous determination included. Capillary zone electrophoresis was used to determine lamivudine, didanosine, and saquinavir all at the same time [4,15].

4] Determination of Metals:

Analyzing the levels of all dissolved metals in samples that have been filtered and oxidized (i.e., organic material removed) [16,17,18,19]. Analysis of fresh, filtered samples to determine the (operationally defined) labile dissolved metal fraction [5,16,22,23].

5] To determine the concentration of vitamin c in apple juices by using cyclic voltammetry

Two methods were used to determine concentration of vitamin c, the voltammetric method as reference the titration method by using 2,6 dichlorophenolindophenol (Tillmans reagent) as self indicator. Ascorbic acid concentration was determined using the standard addition method. Ascorbic acid oxidation current was measured on voltammogram and was linearly related to ascorbic acid concentration (a linear calibration curve was found in the range up to 150mg ascorbic acid/100cm³ SOLUTION). The titrimetric approach was utilized to confirm the results. Vitamin C concentration differences between tests utilizing the cyclic voltammetric and titrimetric techniques are less than one mg.

Conclusion: The present review expresses that electroanalytical technique determine vitamin C in apple juices, also determine Anti-HIV drugs. It is also applicable for Rutin analysis, helpful in metal detection.

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