APPLICATION OF A VOLTAMETRIC FLOW-THROUGH CELL TO FLOW-INJECTION-ANALYSIS (FIA)

Ari IVASKA[a] and TOM H. RYAN[b]

[a] *Department of Analytical Chemistry, Åbo Akademi, 20500 Turku (Åbo) 50, Finland and*
[b] *EDT Research, 14 Trading Estate Rd, London NW10, 7LU, England*

Received August 28th, 1980

A new voltammetric flow-through cell has been designed to be used as an electrochemical detector in HPLC (high performance liquid chromatography) and may also be used as a voltammetric detector of FIA (flow-injection-analysis). The cell is of wall jet type and has a volume of approximately 1 µl. Performance of the cell was tested and the flow-characteristic determined by analysing paracetamol which is oxidized at a glassy carbon electrode and is frequently used as a pain-killing drug. Application of d.c. (direct current) and n.p. (normal pulse) voltammetric working modes in FIA were studied. D.c. was found to be more sensitive and should be used when low sample concentrations are determined. N.p. was, however, found to give more reproducible results at high concentrations. A known tablet formulation containing paracetamol was analysed by the proposed method and a good agreement was found between the result obtained and the manufacturer's certificate.

FIA is a new and novel method and can be used in many different kind of analysis[1,2]. The sample is introduced into a carrier stream *via* a valve or syringe and mixing takes place by diffusion while the plug is moved in the tubing. A continous concentration gradient is developed at the sample-carrier interface and depending on the type of analysis limited, medium or large dispersion is desired. The stream may also be mixed with a reagent which reacts with the sample forming a product detectable by an analytical method. FIA differs from the traditional analytical methods in that the measurements are not made at equilibrium. The response signal do not reach the steady state value but have the form of sharp peaks.

Spectrophotometric and potentiometric detectors have mainly been used in FIA. Some voltammetric detectors have also been devised[3-5]. A new voltammetric detector will be described in this paper and applied in FIA for an organic compound.

EXPERIMENTAL

Apparatus

Flow injection analysis was done with the arrangement shown in Fig. 1. The carrier stream C is pumped by the pump P (Gilson Minipuls HP-4) through the detector D after which the stream is discharged to the waste. At point S the sample is introduced by an electrically operating, double-injection valve (Bifok) to the carrier stream where it is transported as a plug to the detector.

Injection volume of 50 µl was used in this study. The flow should have limited dispersion[1] in order to maintain the sample integrity. No mixing coils are needed and short tubings allow fast analysis. The detector is of a new wall jet design (EDT) and shown in Fig. 2. The working electrode is of Tokai glassy carbon. The reference electrode is a silver/silverchloride electrode in a KCl gel and separated from the stream by a ceramic plug. The auxiliary electrode is of stainless steel and forms the cell bottom. The incoming solution flows through the auxiliary electrode and impinges normally on the surface of the working electrode. This design allows a short distance between the working and auxiliary electrodes giving a minimum potential drop in the solution which is of great importance when organic solvents are used. The cell volume is approximately 1 µl. The signals were measured with the EDT Pulsed Potentiostatic Control Unit LCA 10 and recorded with a strip chart recorder.

The oxidizing mechanism of *p*-aminophenol and paracetamol were studied in quiescent soutions by linear sweep voltammetry. A conventional polarograph was used and the electrodes were glassy carbon as working electrode, double-junction saturated calomel as reference electrode and platinum wire as auxiliary electrode.

Reagents

All the chemicals in this study were of reagent grade quality. The carrier stream was a 0·1M acetate buffer of pH 4·7 and containing 10% methanol in order to aid the dissolution of the possibly adsorbed electrochemical reaction products from the working electrode. The tablet formulation containing paracetamol (4-hydroxyacetanilide) was a product from Boots (Boots B.p. 500 mg).

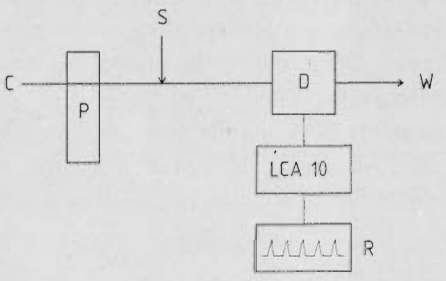


FIG. 1

Arrangement for the voltammetric FIA, C carrier stream, P pump, S sample injection, D detector, LCA 10 = EDT Pulsed Potentiostatic Control Unit, R recorder, W waste

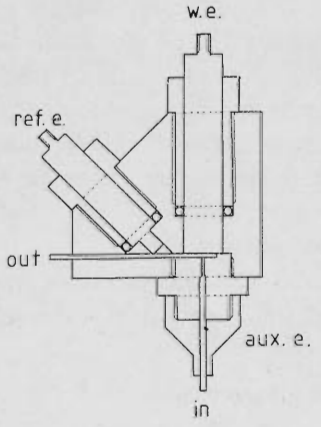
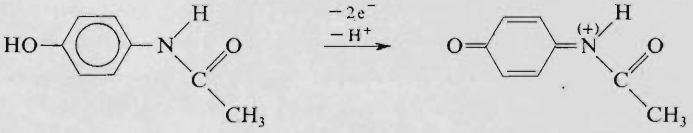


FIG. 2

Voltammetric flow-through cell used in this study, w.e. = working electrode, ref.e. = = reference electrode, aux.e. = auxiliary electrode

RESULTS AND DISCUSSION

Performance and the flow-characteristic of the described voltammetric flow--through cell were studied using paracetamol, 4-hydroxyacetanilide, as the test compound. It is a pain-killing drug and used in many tablet formulations and hence a rapid method for its analysis is of importance. Paracetamol is oxidized on a glassy carbon electrode[6] and in the hydrodynamic system at pH 4·7 $E_{1/2}$ was found to be +0·5 V. The peak heights in quiescent solutions of 10^{-4}M *p*-aminophenol and paracetamol are 3·3 and 3·4 μA resp. indicating that the same number of electrons are involved in oxidation of both compounds assuming that diffusion coefficients of both compounds are approximately the same. Number of electrons and protons involved in the oxidation of paracetamol were determined by the method proposed by Zuman[7]. Following values were obtained: $\alpha n = 1{\cdot}03$ and number of protons 0·9. Because *p*-aminophenol is known to undergo two-electron oxidation[8] the following reaction for paracetamol may be postulated:



The dependence of the signal on flow-rate was studied in using 500 ng injections of paracetamol. D.c. was used as the voltammetric mode and +1·2 V as the working potential. The flow-characteristic, current (i) *vs* flow-rate (w), is shown in Fig. 3*a* and in Fig. 3*b* log i is plotted as the function of log w. As can be seen, between flow-

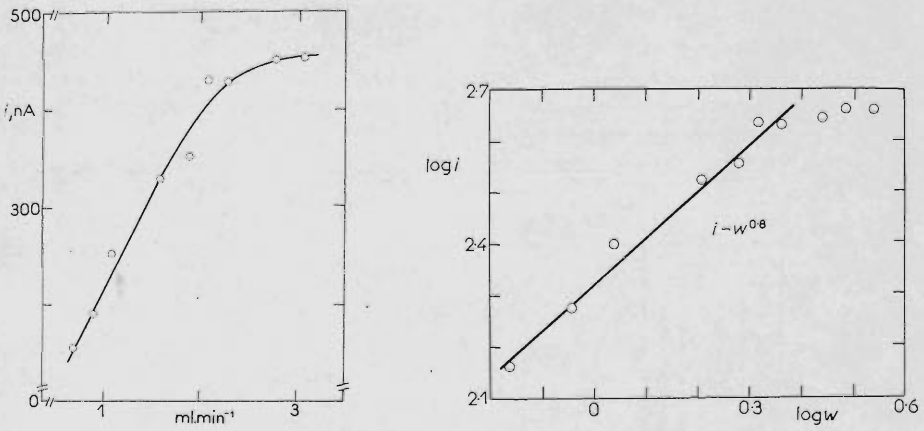


FIG. 3

Flow-characteristics *a* current, i, *vs* flow-rate, w, *b* log i *vs* log w. D.c. mode +1·2 V ans 500 nh injections of paracetamol

rates of 0·7 and 2·5 ml min^{-1} the current is dependent on the flow-rate to the power of 0·8 which is near the theoretical value 0·75 for wall jet cells[9]. With increasing flow-rate the current becomes constant.

Reproducibility of the detector signal in FIA was studied by using repeted sample injections. Both d.c. and m.p. working modes were studied. Injections of 500 ng paracetamol were used. The d.c. signal decreases with number of injections. This is obviously caused by gradual fouling of the electrode surface signals of the original height were obtained after mechanical cleaning of the surface by rubbing the electrode against a soft tissue paper moistened with methanol. A good reproducibility was found with 100 ng injections and with 5 ng the relative standard deviation in 10 determinations was 1·6%.

The electrode fouling may partly be overcome by using n.p. working mode. In this technique the potential most of the time is held at a potential where no electrochemical reaction takes place. Only for short times pulses of the working potential are applied on the working electrode. When the potential returns to the rest or cleaning potential the adsorbed reaction products will be stripped off from the surface. By this way fouling is partly avoinded and the signal is more reproducible. Variation of the peak height is also partly due to the fact that the injection valve is not always working reproducibly. By keeping the working potential at +1·2 V and changing the cleaning

TABLE I

FIA of a tablet formulation for paracetamol. N.p. mode, working potential +1·2 V and cleaning potential —0·8 V

Value	Standard	Sample
i, μA	4·19 ± 0·17	4·17 ± 0·22
rel. st. d., %	4·2 (10)	5·3 (8)
(number of determinations)		

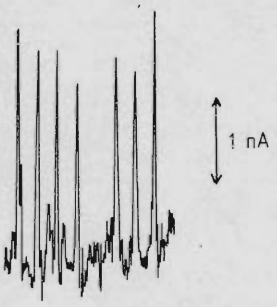


FIG. 4

Signals near the detection limit. D.c. at +1·2 V and 1 ng injections of paracetamol

potential reproducible results could be found only when the potential was −0·8 V or more negative. Cyclic voltammogram of paracetamol at pH 4·7 shows one oxidation peak on the anodic sweep. Upon the sweep reversal two broad peaks at *c.* +0·2 and −0·7 V were observed. This indicates that the electrochemical reaction products of the anodic oxidation of paracetamol are entirely stripped off first at potentials more negative than −0·7 V coinciding with the experimentally found most suitable cleaning potential.

Sensitivity of the method was studied in d.c. mode and a linear relationship between current and the ammount injected, m, over two orders of magnitude has been obtained. The detection limit is around 1 ng where the background noise makes the peak evaluation difficult as can be seen in Fig. 4.

When comparing the d.c. and n.p. working modes with each other it may be concluded that the detection limit for d.c. is lower and that technique should be used when low concentrations are analyzed[9,10]. In high concentrations the electrode surface will rapidly be fouled in d.c. and therefore n.p. should be used[10,11]. This conclusion is only a rule of thumb because different compounds behave differently especially in their surface adsorption properties.

The voltammetric FIA method was tested in analyzing a tablet formulation for paracetamol. The sample was dissolved in 100 ml 0·1M-HCl. Insoluble constituents were filtered and 1 ml of the clear solution was diluted to 100 ml with 0·1M acetate buffer pH 4·7 containing 10% methanol as well. Repeated injections of this solution were made and the signal compared with that of a standard solution of 50 μg ml^{-1}. The results are given in Table I. As can be seen a good agreement is found between the standard and the sample approving the manufacturer's certificate.

CONCLUSIONS

FIA is a fast method and allows a high sample frequency. It can easily be automated and interfaced with a computer[12] for data evaluation and results reporting. Such instruments will certainly be of great value in laboratories dealing with great numbers of samples like clinical, pharmaceutical, quality and process control laboratories.

As shown in this work, a voltammetric flow cell can also be used as the detector in FIA which advantages may be used in analysis for the great number of electrochemically active compounds. In this work an oxidation reaction has been used but by plating a thin film of mercury on the glassy carbon electrode the method can be extended to analysis for compounds which undergo reduction on mercury[10].

REFERENCES

1. Betteridge D.: Anal. Chem. *50*, 832A (1978).
2. Anal. Chim. Acta (*1980*) 114, Special Issue, Flow Analysis.
3. Brunt K., Bruins C. H. P., Doornbos D. A., Oosterhuis B.: Anal. Chim. Acta *114*, 257 (1980).

4. Dieker J. W., van der Linden W. E.: Anal. Chim. Acta *114*, 267 (1980).
5. Gilgen P., Rach P.: Chimia *32*, 345 (1978).
6. Shearer C. M., Christenson K., Mukherji A., Papariello G. J.: J. Pharm. Sci. *61*, 1627 (1972).
7. Zuman P.: in the book: *Advances in Analytical Chemistry and Instrumentation* (C. N. Reilley, Ed.), Vol. 2, p. 219. Wiley, New York, London 1965.
8. Adams R. N.: *Electrochemistry at Solid Electrodes*, p. 336. Marcel Dekker, New York 1969.
9. Yamada J., Matsuda H.: J. Electroanal. Chem. Interfacial Electrochem. *44*, 189 (1973).
10. Ivaska A., Smyth W. F.: Anal. Chim. Acta *114*, 283 (1980).
11. Dieker J. W., van der Linden W. E., Poppe H.: Talanta *26*, 511 (1979).
12. Stewart K. K., Brown J. F., Golden B. M.: Anal. Chim. Acta *114*, 119 (1980).