Adsorptive Stripping Anodic Voltammetric Determination of Thioctic Acid in Bulk and Pharmaceutical Formulations

Nawal A. Alarfaj

الطرق الكهربية) بحساسيتها وانتقائيتها ودقتها كما تمتاز بانخفاض التكلفة مقارنة بطرق التحليل الأخرى، كما أن هذه الطرق لها تطبيقات واسعة في معظم مجالات الحياة حيث تستخدم لتحليل المركبات العضوية وغير العضوية في العينات المختلفة ومنها المستحضرات الصيدلية في كافة أشكالها سواء كانت أقراصاً دوائية أو حقن أو كبسولات أو غيرها. كما يمكن استخدامها لتحليل الأدوية في السوائل

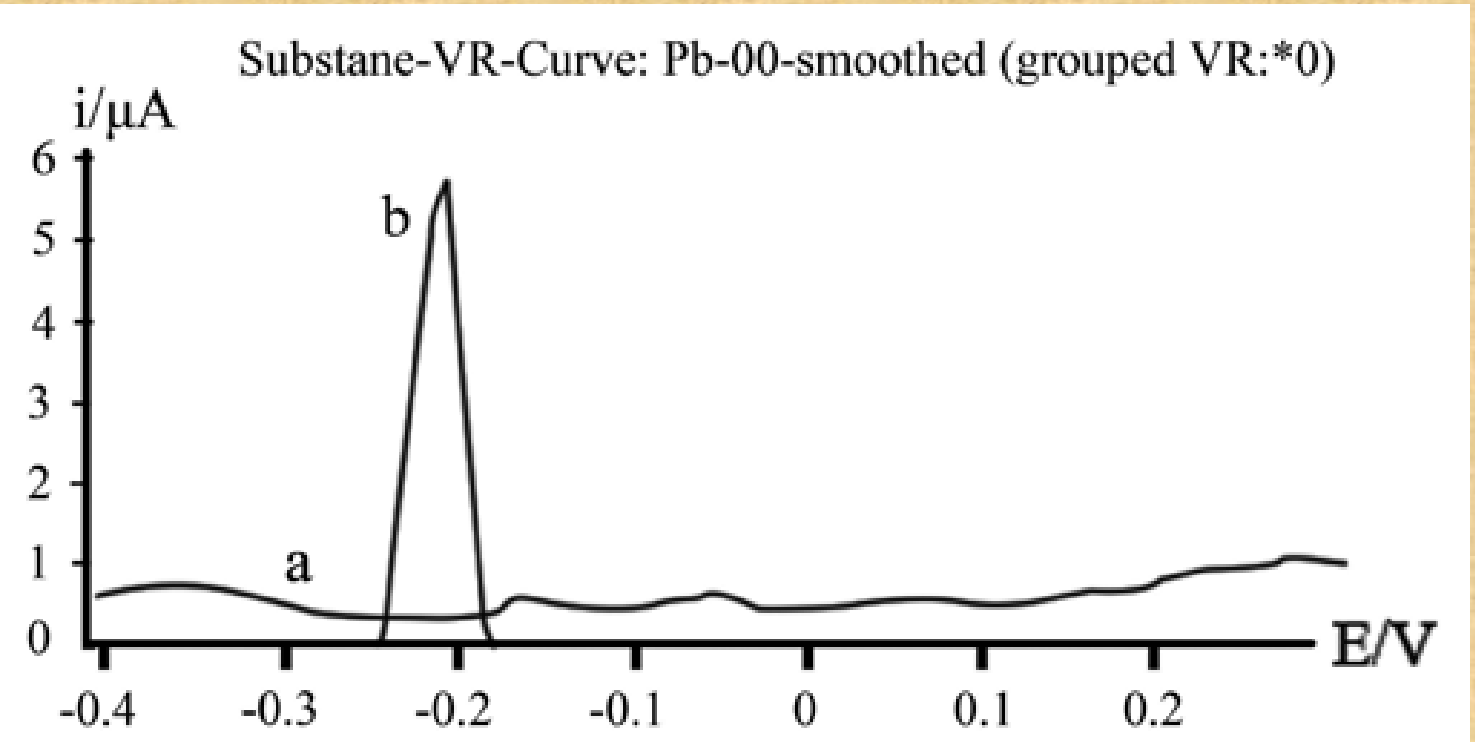
وفي هذا البحث تم اختيار مركب حمض الثيوكتيك لأهميته وتمت دراسة السلوك الكهروكيميائي له وتحليله بطريقة فولتاميترية عند قطب قطرة الزئبق المعلقة

Thioctic acid is used for treatment of liver dysfunction and diabetic neuropathy and as antidote to poisonous mushrooms .

Adsorptive stripping voltammetric analysis is simple and sensitive technique that can be used for analysis of drugs without the necessity for extraction steps prior to the assay . The major advantage of square – wave voltammetry is its great speed .

- The square – wave voltammetry is a large – amplitude differential technique in which a waveform composed of a symmetrical square waves is applied to the working electrode . The current is sampled twice during each square – wave cycle , once at the end of the forward pulse and once at the end of the reverse pulse . The resulting peak current is proportional to the concentration of the analyte

The electrochemical behavior of thioctic acid at the hanging mercury drop electrode was studied in different supporting electrolytes . In Britton - Robinson buffer pH 3.29, the square – wave adsorptive anodic stripping voltammogram of thioctic acid exhibited a single well – defined anodic peak at about – 0.21 V vs Ag / AgCl .



SW- AdAS voltammogram for 6 x 10^{-7} M thioctic acid in Britton Robinson buffer of pH 3.29 ; f = 60 Hz ; $\triangle E_s$ = 10 mV , E_{sw} = 20 mV. (a) without preconcentration and (b) following preconcentration for 60 s at – 0.4V

The peak response was characterized with respect to pH, preconcentration time , accumulation potential , supporting electrolytes , frequency , scan increment and pulse amplitude .

Under the optimized conditions a fully validated , simple , high sensitive , precise and inexpensive square – wave adsorptive anodic stripping voltammetric procedure was described for determination of thioctic acid in bulk form and tablets .

All measurements were carried out with the Electrochemical Trace Analyzer . A three – electrode system , composed of a HMDE as the working electrode , an Ag /AgCl reference electrode and a platinum wire as auxiliary electrode , was used . Stirring of the solution in the electrolysis cell was performed to provide the convective transport during the preconcentration step .

General analytical procedure

Stock solution (1 x10^{-3} M) of thioctic acid was prepared in methanol . This solution was further diluted with methanol to give the appropriate concentrations of working standard solutions . Aliquots of these solutions in the concentration range 5 x 10^{-8} – 9 x 10^{-7} M were transferred into a series of 25 ml volumetric flasks and diluted to the mark with Britton - Robinson buffer of pH 3.29 . Each solution was transferred into the electrolysis cell , then was purged with pure nitrogen

The accumulation potential of – 0.4V versus Ag /AgCl was applied to a new mercury drop while the solution was stirred at 400 rpm for 60s . At the end of the accumulation period , the stirring was stopped and a 5s rest period was allowed for the solution to become quiescent . Then the voltammogram was recorded by scanning the potential toward the positive direction over the range – 0.4 to + 0.2V using the SW mode . All measurements were made at room temperature

Analysis of tablets

An accurately weighed quantity of the mixed contents of ten pulverized tablets equivalent to 10.0 mg of the drug was transferred into a 50 ml volumetric flask . Then methanol was added to the mark. The flask with its contents were sonicated for 15 min and filtered . The desired concentrations of the drug were obtained by further dilution with methanol . An aliquot volume of this solution was transferred into a 25 ml volumetric flask and diluted to the mark with Britton - Robinson buffer of pH 3.29 . The above general analytical procedure was followed .

RESULTS AND DISCUSSION

The determination of thioctic acid was done on the HMDE by SW-ASV. During a preconcentration step of 60 s at -0.4 V on the electrode surface , the disulfide present in the analyte is reduced to mercaptan in the adsorption process and by the transfer of two electrons

$$RSSR + Hg \rightarrow [(RS)_2 Hg]_{(ads)}$$

$$[(RS)_2 Hg]_{(ads)} + 2e^- + 2H^+ \rightarrow 2\,RSH + Hg$$

The produced mercaptan gives a well – defined anodic peak at a potential of – 0.21 V vs. Ag /AgCl . This anodic peak results from the electrochemical oxidation of mercaptan to produce disulfide by the transfer of two electrons :

$$2\,RSH + Hg \rightarrow Hg (RS)_2 + 2\,H^+ + 2e^-$$

Effect of type and pH of the supporting electrolyte

The influence of pH on the square – wave voltammetric response for 6 x 10^{-7} M thioctic acid was examined in Britton – Robinson buffers of different pH values and following pre - concentration for 60 s . The voltammograms exhibited a single well – defined two – electrons reversible anodic peak over the pH range 2 - 9 . The peak current intensities (i_p) were recorded at different pH values

A much higher peak current intensity was achieved in Britton - Robinson buffers of pH 3 - 4 . Other supporting electrolytes such as acetate buffer , sodium sulphate , sodium nitrate and potassium chlolride were also tested but the peak current intensity was less developed compared to that obtained in Britton - Robinson buffers of pH 3 - 4 . Therefore Britton - Robinson buffer of pH 3.29 was used as a supporting electrolyte in the rest of present work .

Optimization of the proposed analytical procedure

The optimum instrumental conditions , frequency f , scan increment ΔE_s and pulse amplitude E_{sw} were studied for 6×10^{-7} M thioctic acid in Britton - Robinson buffer, the optimal instrumental operational conditions of the proposed square – wave procedure can be concluded as : frequency f = 60 Hz , scan increment ΔE_s = 10 mV and pulse amplitude E_{sw} = 20 mV .

On the other side , the effect of varying accumulation potential (E_{acc}) from – 0.1 to – 0.6 V on the peak current intensity of the SW – Ad AS voltammogram of 6 x 10^{-7} M thioctic acid in Britton - Robinson buffer of pH 3.29 following preconcentration for 60 s was also evaluated. A maximum developed peak current was achieved at the potential – 0.4 V. The observed gradual decrease in peak current intensity may be attributed to the consequence of desorption of the drug at higher or lower potential values . Hence , a preconcentration potential of – o.4 V vs. Ag /AgCl was chosen throughout the present study.

The effect of accumulation time parameter was studied for 6×10^{-7} M at E_{acc} = - 0.4 V. Preconcentration potential initiated a remarkable enhancement for the SW – Ad ASV peak current up to 60 s accumulation time and then it becomes nearly constant up to 150 s. However at higher accumulation time , 300 s ,there is a decrease in peak current intensity. This may be due to desorption phenomena. Thus , for further quantitative studies for thioctic acid , an accumulation time of 60 s was selected as optimal value since it provided relatively high current with adequate practical time .

Analytical performance of the developed procedure
Calibration graph and detection limit

Under the optimum experimental conditions a good linear correlation was obtained between thioctic acid electrochemical response and its concentration in the range 5×10^{-8} - 9×10^{-7} M . The parameters of the concentration – current straight line were calculated by the least squares method.

The standard curve was linear with correlation coefficient (r) not less than 0.9997 . The regression analysis gave the following equation :

i_p (µA) = 0.724 x 10^7C + 1.625 (r = 0.9997) .

Validation of the method was evaluated by statistical analysis of the regression line regarding standard deviation of the intercept (Sa = 0.029) and the slope (S_b = 0.006) . The small values given point to the low scattering of the points around the calibration curve .

The limit of detection (LOD) was calculated using the relation 3 (S_a/ b) and was found to be 1.2 x10^{-8} M where S_a is the standard deviation of the intercept and b is the slope of the calibration curve .

Accuracy, precision and selectivity

The accuracy of the proposed method was checked by calculating the recovery of known amounts of thioctic acid added to Britton - Robinson buffer solution of pH 3.29 and analysed via the proposed method . A mean recovery of 100.7 ± 1.23 was achieved.

The analytical precision of the developed method was verified from the reproducibility of 10 determinations of 3×10^{-7} M thioctic acid and the estimated relative standard deviation was 1.05% .

The selectivity of the optimized procedure for assay of thioctic acid was examined in the presence of some common excipients usually present in formulations e.g. starch , lactose , talc and magnesium stearate. There is no significant effects on the SW-AdASV response of thioctic acid. Accordingly, the proposed procedure can be considered selective .

Analytical applications

The proposed method was further applied to the determination of thoictic acid in its dosage forms . The analytical results achieved by the proposed SW- Ad ASV procedure were in good agreement with those obtained using the comparison method, Statistical analysis of the results obtained using the students't – test and variance ratio F – test revealed no significant difference between the performance of the two methods regarding the accuracy and precision respectively (Table) .

SW- AdASV determination of thioctic acid and its dosage forms.

Drug form	% Found [a]	
	Proposed method	Reference method [5]
Thioctic acid (pure sample)	102 .5	101 .5
	101 . 0	101.1
	99.4	99 .8
	101 .0	
	99.6	
Mean ± S.D.	100. 7 ± 1.23	100.8 ± 0.89
Student's t- value	0.132 (2.447)[c]	
Variance ratio F-test	1.91 (19.25)[d]	
Thiotacid tablet [b]	98,0	99. 1
(300 mg / tablet)	99.0	98.6
	98.5	98.3
Mean ± S . D .	98.5 ± 0.50	98.7 ± 0.40
Student's t – value	0.543 (2.776)[c]	
Variance ratio F- test	1.56 (119)[d]	
Thiotacid tablet [b]	99.8	99.7
(600 mg / tablet)	98.8	98.6
	98.5	99.2
Mean ± S . D .	99.0 ± 0. 68	99.2 ± 0.55
Student's t- value	0.398 (2.776) [c]	
Variance ratio F- test	1.53 (19) [d]	

[a] Each result is the average of three separate determinations

[b] Products of Eva Pharma for Pharmaceuticals & Medical Appliance , Egypt .

[c] Tabulated t – values (at P = 0.05)[31]

[d] Tabulated F – values (at P = 0.05)[31]

CONCLUSION

The present work describes a validated SW-AdASV method for the determination of thioctic acid without interference from common excipients. Hence , it could be applied for the routine quality control of the studied drug either in bulk or in its corresponding dosage forms. The methodology appears to be more sensitive than the reported adsorptive cathodic stripping voltammetry.