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Electrochemical Study of Theophylline-Creatinine Interaction Using Square Wave Voltammetry

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Abstract: In this work, the interaction between theophylline (TP) and creatinine was studied. A three electrode detection system was used, 2mm diameter glassy carbon electrode as working electrode, 1mm diameter platinum wire as auxillary electrode and Ag/AgCl. saturated KCl as reference electrode. Square wave voltammetric technique (SWV) also used, the voltammogram of theophylline shows a stable well - defined reduction peak at (1.07) V versus Ag/ AgCl Sat. KCl/ in phosphate buffer solution (pH=7) using glassy carbon electrode. The voltammograms were recorded for theophyline with serious addition of creatinine, interaction of theophyline with the sequence addition of creatinine were examined at different temperatures (288, 293, 298, 298, 303, 308 and 310) ºK and the thermodynamics parameters were calculated. The binding constant (K) between theophylene and creatinine was also measured. The results showed that the binding constant (K) decreased with increasing temperature, this is as a result of the negative value of enthalpy change (-46.6) KJ. mol-1 (exothermic binding). Negative value of Gibbs energy (-275.338 x 102 _ -36384.961 x102) KJ. mol-1 indicates that the interaction is spontaneous and could be due to van der waals forces or hydrogen bonds effect i. e the low value of Gibbs energy indicates weak interaction between the studied compounds.

Keywords: Theophylline, Cratinine, Interaction, Modified electrode

Introduction

Theophylline (1,3-dimethylxanthine) as a xanthine derivative has been commonly used as an additional treatment drug in the asthmatic acute phase in children and bronchospasm in adults (Kawai and Kato, 2000; Kanehara et al., 2008; Igarashi and Iwakawa, 2009; Fuyong Jiao et al., 2018). It is also used clinically as diuretic, cardiac stimulant and smooth muscle relaxant (Shruti et al., 2019). Thus, more and more scientists have paid increasing attention to the techniques for the quantitative determination of theophylline. The chemical structure of theophylline is shown in Fig. (1).

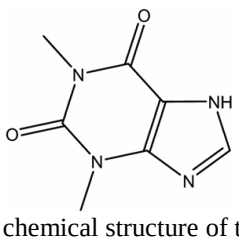

Fig. 1. The chemical structure of theophylline

At present, many methods have been employed for measuring theophylline quantitatively, such as liquid chromatography (Kalyani and Chava, 2017; Srdjenovic et al., 2008; Huang and Xu, 2005), UV spectrometry

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(Sujana, 2016; Culzoni, 2005), chemiluminescent immunoassay (Zhou et al., 2005), gas chromatographymass spectrometry (GC–MS)and gas chromatography–isotope dilution mass spectrometry (GC– IDMS) (Kress et al., 2002; Arinobu et al., 2009). Nevertheless, some of these methods, such as chromatography and mass spectrometry, are time-consuming, expensive and need complicated preconcentration or multisolvent extraction as well as trained technicians. Instead, electrochemical methods are characterized by simplicity, high sensitivity, good stability, low-cost instrumentation on-site monitoring (Sadik et al., 2003). Thus, they are exploited for the determination of theophylline.

Creatinine is a metabolic waste product of the breakdown of muscle creatine. The creatinine levels in the blood serum indicate an equilibrium between production and excretion by the kidney and is an indicator of kidney function (Horne and Swearingen, 1993) . Normal concentrations of creatinine in the blood serum for adult males is 0.62 to 1.10 mg/dL and 0.45 to 0.75 mg/dL for adult women(Skurup et al., 2008). Increased serum creatinine levels, comparable to the decline in the quality of the kidneys, so that the analysis of creatinine levels in the blood is very important to know the kidneys quality work.

Creatinine analysis methods that are generally used in the medical field is the Jaffe method. Analysis of creatinine using the Jaffe method has a principle, namely by forming a colored complex solution which can be analyzed by UV-Vis spectrophotometer. The advantages of this method as an analytical process is easy and simple, while the drawback is the low selectivity. Other common methods used for the analysis of creatinine is the enzymatic method. Analysis of creatinine with this method is hardly bothered by another matrix, but it takes a long time for the analysis and the cost is quite expensive (Guo and Guo; 2005).

Another method that has been used for the analysis of creatinine is potentiometric method. In the potentiometric method used two electrodes, the working electrode and reference electrode(Darmokoesoemo, et al.; 2017). The function of the working electrode is sensoring the analyte in the solution being analyzed, so that the working electrode must be selective and sensitive to analyte. Electrodes used for potentiometric analysis can be modified with the aim to increase the selectivity and sensitivity to analyte.

In this work the determination of creatinine through its interaction with theophylline was carried out using square wave voltammetry technique (SWV).

Experiment

Apparatus

All the electrochemical experiments were performed using a797VA computrace instrument (Metrohm, Switzerland). The reference electrode was an Ag/AgCl with saturated KCl, 1.0 mm a platinum wire was used as the auxiliary electrode and 2.0 mm a glassy carbon electrode GC used as the working electrode. pH measurements were performed by using a digital pH meter (HANNA, Italy, calibrated with standard buffers.The Haake Heated Water Bath Circulator is Model G, USA.

Chemicals and Reagents

All chemicals used in this work (creatinine, theophylline, dipotassium hydrogen phosphate K2HPO4, and potassumdihydrogen phosphate KH2PO4) were of analytical grade and used without further purification, and were purchased from Fluka, and BDH.

Preparation of the Theophylline Electrode

Electropolymerisation of Theophylline at the surface of bare glassy carbon electrode GC was carried out by using cyclic voltammetric method in aqueous solution containing (1.960 x 10-4)M TP in 0.2 M PBS of pH 7.0. The TP molecules are reduced and rapidly combine with the GC surface. A uniform film is produced on GC surface, which indicates that the TP has been deposited on the GC surface by electropolymeriztion method.

Results and Discussion

Electrochemical Behaviour of Theophylline

The square wave voltammogram was recorded using (9.090 x10-5) M theophylline (TP) in phosphate buffer solution under the default instrument. After that the optimum conditions of TP has been studied, and the voltammograms of (9.090 x 10-5) M of TP Fig. (2) were recorded under each effective parameter and the results obtained are summarized in (Table 1).

Table 1. Default and the optimum conditions of TP

Condition	Defaultconditions	Optimum conditions of TP
Start Potential (V)	0.4	0.4
End Potential (V)	1.4	1.4
Deposition potential (V)	-0.9	-1.5
Deposition time (s)	60	50
Equilibration time (s)	5	5
Voltage step (V)	0.006	0.002
Amplitude (V)	0.02	0.03
Frequency (Hz)	50	100
Sweep rate (V/s)	0.3	0.1984

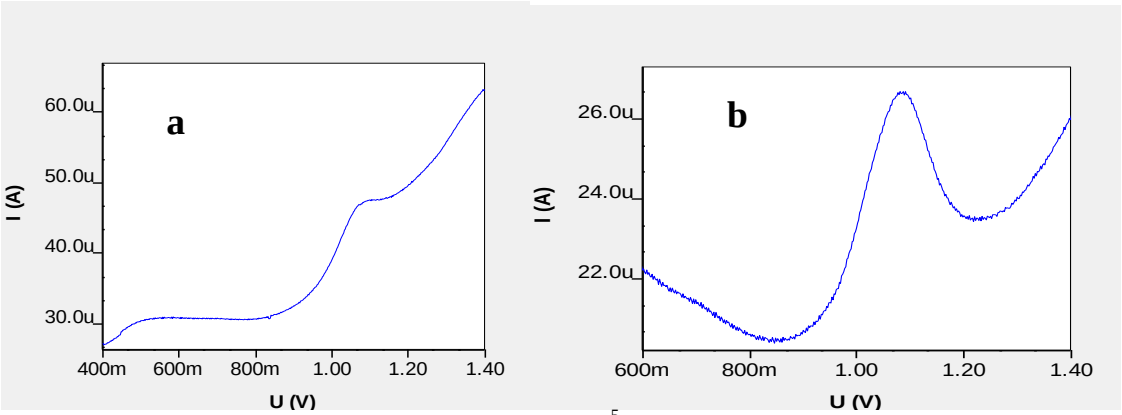

Fig. 2. The voltammogram of TP (9.090 x 10^{-5}) M (a)under the default conditions, (b) under the studied optimum conditions

Effect of pH on the TP reduction peak

The Effect of pH on the reduction potential and diffusion current of TP reduction peak in the 0.2 M phosphate buffer (pH 4.0-9.0) was studied by square-wave voltammetry. A significant decrease of the peak current is observed at pH 4.0 to 9.0. The obtained peak shifts to the less positive potentials with the increase in the pH, and the plot of Ep versus pH is linear as shown in Fig. (3) with correlation coefficient value(R2= 0.9172), and solpe value(0.0312 V.pH-1) which is near of the theoretical value calculated by Hillson,. this is indicate a complex electrode process in which electron exchange is significantly influenced by protons.

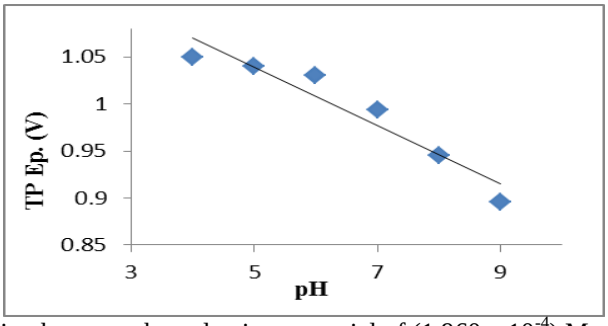

Fig. 3. The relation between the reduction potential of (1.960 x 10^{-4}) M of TP and the pH

Electropolymeriztion of TP onto glassy carbon electrode

Electropolymeriztion is a facile and efficient approach to immobilize a film onto solid state electrode surface because film properties, such as thickness, permeation and charge transportation, can be adjusted by controlling electrochemical parameters. Fig. (4) shows the successive cyclic voltammetric CV curves during the electropoly- meriztion of TP from a phosphate buffer solution (pH 7.0) containing (1.960 x 10-4)M TP. A uniform film is produced on GE surface, which indicates that the TP has been deposited on the glassy carbon electrode GC surface by electropolymeriztion method.

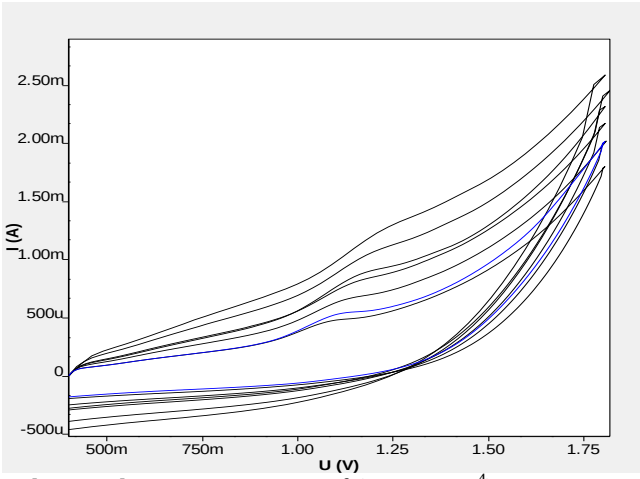

Fig. 4. Electropolymerization curve of (1.960 x10^{-4}) M TPat GC

Electrochemical Behaviour of creatinine

The square wave voltammogram was recorded using (17.333 x10-5) M creatinine in phosphate buffer solution, the creatinine shows a reduction peak at (0.109) V Fig. (5).

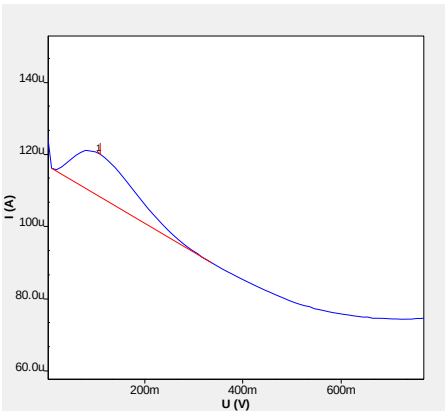

Fig. 5. Shows the creatinine reduction peak at (0.109) V.

Effect of creatinine on Theophylline Reduction Peak

The effect of creatinine on TP peak was studied by adding sequence additions of creatinine (1.470 x 10^{-5} - 38.066 x 10^{-5}) M to a voltammetric cell containing (1.666 x 10^{-3}) M of TP; a decrease in the TP current peek value was observed with the sequence additions of creatinine Fig. (6).

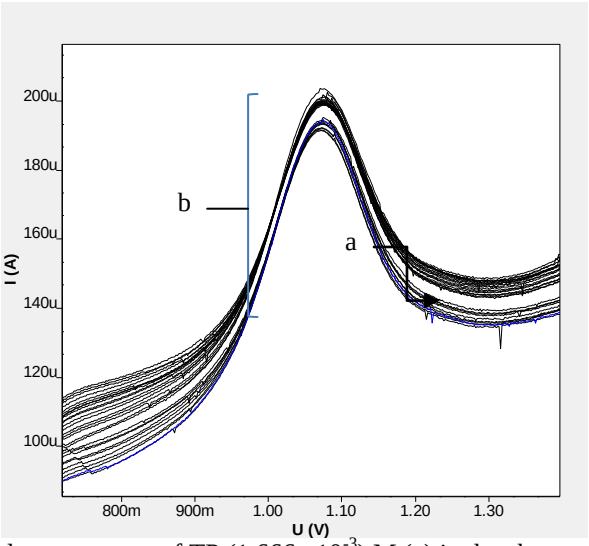

Fig. 6. The voltammograms of TP (1.666 x10^{-3}) M (a) in the absence of creatinine (b) in the presence of creatinine (1.470x10^{-5} - 38.066x10^{-5}) M

Stability of Theophylline Reduction Peak in the Presence of Creatinine

The stability of TP voltammogram (3.849 x10^{-4}) M in the presence of creatinine(9.305 x 10^{-4}) M was measured at different times, using phosphate buffer solution (pH=7) under the previous optimum conditions of TP and the results are shown in (Table 2). The results indicate that the interaction peak was stable within the studied time (110) min.

Table 2. Stability of theophylline reduction peak in the presence of creatinine

Time (min)	Ep.(V)	Ip. (nA)
0	1.05	27200
10	1.05	26000
20	1.05	26800
30	1.05	26800
40	1.05	26400
50	1.05	26700
60	1.05	26800
70	1.05	27500
80	1.05	26600
90	1.05	27700
110	1.05	27600

Thermodynamic Calculations

The binding constant of theophylline- creatinine was calculated according to the equation (1).

$$\ln (Ip/(Ip^{o} - Ip)) = \ln (1/[Conc.(M)]) - \ln (K) \quad \ldots\ldots\ldots\ldots \quad (1)$$

Where Ip^{o} is the reduction current of TP alone, Ip is the reduction current of TP- creatinine complex, Conc. is the molar concentration of TP, and (K) is the binding constant of TP- creatinine complex.

The binding constant was calculated at different temperatures (288, 293, 298, 303, 308, 310) K°, and the results are shown in Fig. (7).

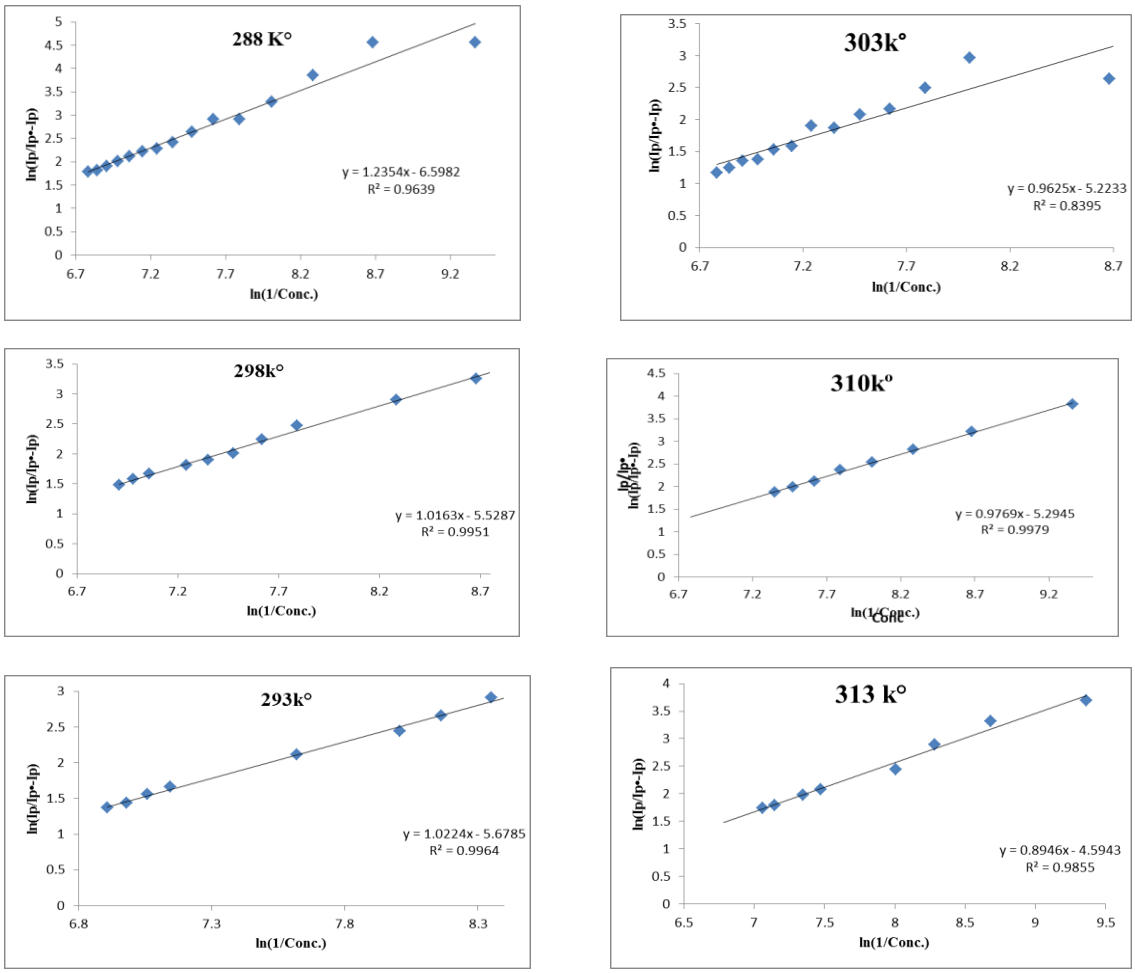

Fig. 7. Plot of ln (Ip/(Ipº –Ip)) vsln (1/[Conc.(M)]) at (288, 293, 298, 298, 303, 308, 310)ºK

Thermodynamic parameters were calculated Fig. (8) according to the equations (2) for Van't Hoff eq. and (3), the binding constant at different temperatures are shown in (Table 3).

$$\ln K = \frac{\Delta H}{RT} + \frac{\Delta S}{R} \quad \ldots\ldots\ldots\ldots \quad (2)$$

$$\Delta G = -R\,T\,\ln K \quad \ldots\ldots\ldots\ldots \quad (3)$$

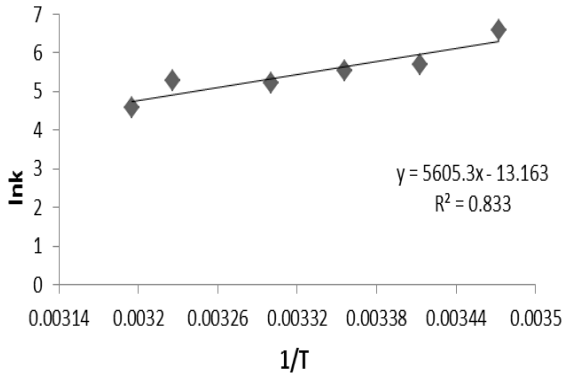

Fig. 8: Plot of ln K vs 1/T

Table 3. The relation between binding constant and temperature

T (C°)	T(K°)	Ln K_b	The binding constant K_b (10^2) M	ΔH (KJ.mol^{-1})	ΔG (KJ.mol^{-1})	ΔS (J.mol^{-1}.K^{-1})
15	288	6.598	733.773		-36384.961	
20	293	5.678	292.510		-31857.024	
25	298	5.528	251.816	-46.6	-31545.923	-0.109
30	303	5.223	185.545		-30303.413	
37	310	5.294	199.237		-31426.108	
40	313	4.594	98.9188		-27533.894	

The negative value of ΔS indicates that the interaction is ordered. The negative value of ΔH means that the interaction is exothermic. From the values of ΔG,the spontaneity of interaction is decreased with increasing temperature. This agrees with the negative value of ΔH showing that the type of interaction is hydrogen bonding or vander Waals forces. From the binding constant and thermodynamic results, we find that the interaction between TP and creatinine is week, exothermic, spontaneous and stable (Ross and Subramanian, 1981).

Conclusion

Square wave voltammetry technique is a good technique to study the interaction between TP and creatinine. Thermodynamics parameters give an idea about interaction type, negative value of enthalpy change means that the interaction was exothermic, negative value of entropy change indicates that the interaction became more ordered and the shifting of Gibss free energy value to more positive caused the spontaneouity decrease. From the thermodynamics parameters we can conclude that the interaction between TP and creatinine may be due to hydrogen bonding or vander Waals forces.

References

Arinobu, T.; Hattori, H.; Kumazawa, T.; Lee, X.P.; Mizutani, Y.; Katase, T.; Kojima, S.; Omori, T.;
Kaneko, R.; Ishii, A.; Seno, H. (2009). High-throughput determination of theophylline and caffeine in human serum by conventional liquid chromatography-mass spectrometry. Forensic. Toxicol.; 27(1), 1-6.

Blake, K.; Kamada, A.K. (1996). "Textbook of Therapeutics: Drug and Disease Management".
Williams and Wilkins: Baltimore; 6, 651 p.

Culzoni, M.J.; De Zan, M.A.; Robles, J.C.; Mantovani, V.E.; Goicoechea, H.C. (2005). Chemometries-assisted uv-spectroscopic strategies for the determination of theophylline insyrups. J. Pharmaceut. Biomed., 39(5),1068-1074.

Darmokoesoemo, H.; Khasanah, M.; Sari, N.M.; Kusuma, H.S.; (2017). Analysis of creatinine by potentiometric using electrode carbon paste modified by molecularly imprinted polymer as sensor. Rasayan Journal of Chemistry • 10(2), 450 – 453.

Fuyong, J.; Nan, G.; Sheng, Z.; Yuhua, Y. (2018). A Clinical Analysis and Study of 110 Pediatric Cases with Aminophylline Poisoning. Pharmacol. and Clin. Research, 5, 2473-5574.

Guo, M.D.; Guo, H.X., Journal of Electroanalytical Chemistry, 585, 28 (2005).

Haruta, Y.; Hattori, N.; Kohno, N. (2008). Anti-inflammatory effects and clinical efficacy of theophylline and tulobuterol in mild-to-moderate chronic obstructive pulmonary disease Pulm. Pharmacol. Ther.; 21, 874.

Hillson P.J.; and P.P. Birndaun, (1950), Trans. Faraday Soc., 48, 478.

Horne, M.M.; Swearingen, P.L.; Fluids, Electrolytes and Acid-Base Balance, 2nd ed., Mosby, St Louis (1993).

Igarashi, T.; Iwakawa, S. (2009). Effect of gender on theophylline clearance in japanese pediatric patients. Biol. Pharm. Bull., 32(2), 304-307.

Kalyani, L.; Chava, V.; Rao, N. (2017). Development and validation of stability-indicating RP-HPLC method for the simultaneous analysis of Salbutamol, Theophylline and Ambroxol. Saudi J. Med. and Pharm. Sci., 2413-4929.

Kanehara, M.; Yokoyama, A.; Tomoda, Y.; Shiota, N.; Iwamoto, H.; Ishikawa, N.; Taooka, Y.; Kawai, M.; Kato, M. (2000). Theophylline for the treatment of bronchial asthma: present status Find. Exp. Clin. Pharmacol., 22(5), 309-320.

Kress, M.; Meissner, D.; Kaiser, P.; Hanke, R.; Wood, W.G. (2002). Determination of theophylline by HPLC and GC-IDMS, the effect of chemically similar xanthine derivatives on the specificity of the method and the possibility of paracetamol as interfering substance. Clin. Lab., 48(9-10), 541-551.

Minton, N.A.; Henry, J.A. (1996). Acute and chronic human toxicity of theophylline. Human Exp. Toxicol., 15(6), 471-481.

Ross, D.P.; Subramanian, S. (1981). Thermodynamics of protein association reactions: forces contributing to stability. Biochemistry, 20, 3096-3102.

Sadik, O. A.; Land, W. H.; Wang, J. (2003). Targeting chemical and biological warfare agents at the molecular level. Electroanalysis., 15(14),1149-1159.

Skurup, A.; Kristensen, T.; Wennecke G., Clinical Chemistry and Laboratory Medicine, 46(1), 3(2008).

Shruti Mouryaa; Ramesh Bodlab; Ravikant Taureanb; Akanksha Sharmab; Simultaneous estimation of xanthine alkaloids (Theophylline, Theobromine and Caffeine): High-Performance Liquid Chromatography International Journal of Drug Regulatory Affairs. 2019; 7(2),35-41.

Srdjenovic, B.; Djordjevic-Milic, V.; Grujic, N.; Injac, R.; Lepojevic, C. (2008). Simultaneous HPLC determination of caffeine, theophylline in food, drinks, and herbal products. J. Chromatographic. Sci., 46(2), 144-149.

Sujana, K.; Venu, S.; Sravani, K.; Iswarya, P. (2016). simultaneous estimation of salbutamol and theophylline in bulk drugs and marketed formulation using simultaneous equation method. International J. Pharm. Tech. Research CODEN (USA)N; 9, 274-282.

Weinberger, M.; Hendeles, L. (1996). Theophylline in asthma. N. Engl, J. Med., 334(21), 1380-1388.

Zhou, M.X.; Guan, C.Y.; Chen, G.; Xie, X.Y.; Wu, S.H. (2005). Determination of theophylline concentration in serum by chemiluminescent immunoassay. J. Zhejiang. Univ. Sci. B., 6(12), 1148-1152.

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