J. Flow Injection Anal., Vol. 22, No. 2 (2005) 123–128

Sequential injection spectrophotometric kinetic method for the determination of Paracetamol in dosage forms

Abubakr M. Idris[a]*, Salah M. Sultan[b], Kamal E. E. Ibrahim[c] and F.N. Assubaie[a]

[a]Chemistry Department, King Faisal University, P.O. Box 400, Al-Ahssa 31982, Saudi Arabia *e-mail: abubakrmi@yahoo.com, Fax: 00966-3-5886437

[b]Chemistry Department, King Fahad University for Petroleum and Minerals, P.O. Box 2026, Dhahran 31261, Saudi Arabia

[c]Department of Pharmaceutical Chemistry, Faculty of Pharmacy, University of Khartoum, P.O. Box 321, Khartoum, Sudan

Abstract

A simple, rapid, selective and sensitive kinetic method for the determination of Paracetamol utilizing sequential injection analysis (SIA) technique was explored. The method was based upon comprehensive kinetic investigation of oxidation reaction of paracetamol with potassium permanganate in sulphuric acid media. The absorbance decrease of permanganate was measured at the wavelength 526 nm to monitor the reaction kinetics. The reaction orders with respect to the concentration of sulphuric acid, permanganate and paracetamol were found to be inverse one (-1), positive one (+1), and positive one (+1), respectively. The activation energy was examined and the reaction mechanism was postulated. The fixed time kinetic approach was used for the determination of the drug. The calibration equation "A = 0.0038C + 0.1209", with 0.9931 correlation coefficient (r) was found to be linear for paracetamol concentration ranging between 6.61×10^{-5} to 1.32×10^{-3} mol l^{-1} at the fixed time of 70 s at room temperature. This equation was obtained when injecting 35 µl of 1.0 mol l^{-1} H_2SO_4, 30 µl of 2.0×10^{-3} mol l^{-1} potassium permanganate, 20 µl of paracetamol and 25 µl water and by adjusting the flow rate at 25 µl s^{-1}. The newly adopted method was applied for the determination of paracetamol in dosage forms of tablets and capsules containing other drugs. No interference was observed neither from the other drugs of diphenylamine hydrochloride, chloroxazone and pseudophedrine hydrochloride nor from excipients. The proposed SIA kinetic method was found to be accurate and repeatable when the results were statistically compared with the results obtained by the BP standard method.

***Key words**:* Sequential injection analysis, Paracetamol, Potassium permanganate, Kinetics

1. Introduction

Paracetamol (Acetoamniophen) is chemically known as N-(4-hydroxyphenyl) acetamide (fig. 1). It is a white, crystalline powder and sparingly soluble in water. It is well known as analgesic and antipyretic drug. Quantitative determination of paracetamol in dosage forms has received wide attention and several methods were developed involving spectroscopy [1-14], chromatography [15-20] and electrochemistry [21-24]. In the BP [25] method, paracetamol is assayed in the generic form by titration with ammonium cerium(IV) sulphate in the presence of hydrochloric acid and tris(1,10-phenanthroline)iron(II) sulphate complex (ferroin) while it is assayed in tablets by spectrophotometrically measuring the resulting buffered solution at 257 nm. Some methods already proposed required high sophistication and very expensive cost of equipments [15-20]. A variety of spectrophotometric methods cited in the literature were based on oxidation reaction required long heating time and critical acid and reagent concentration [1-3]. Recently, permanganate, as the superior oxidizing agent as well as enjoying high molar absorptivity, has been widely used for the determination of many drugs in dosage forms and it was found to be selective in highly controlled conditions. This paper describes, for the first time, the application of acidic permanganate to the spectrophotometric determination of paracetamol utilizing sequential injection analysis (SIA) technique.

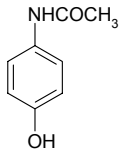

Fig. 1. Paracetamol structure

2. Experimental

2.1 Chemicals and reagents

2.1.1. Paracetamol

Sigma reference standard A3035 (USA) was used here. 6.61×10^{-3} mol l^{-1} as a standard stock solution of paracetamol was prepared weekly and stored in brown bottle, while standard working solution were prepared daily.

2.1.2. Potassium permanganate

Ready prepared concentrated potassium permanganate solution for redox titration by Titrisol 9935 (Merck, Germany) was diluted to 1:l to obtain 0.02 mol l^{-1}. The stock solution was standardized weekly. The standard working solutions were prepared daily.

2.2.3. **Sulphuric acid**

95-98 % (w v^{-1}), 1.84 g l^{-1}, extra pure grade supplied from Barcelona, Spain was used for preparing working solution.

2.2 **Sample preparation**

For the determination of paracetamol in dosage forms, 20 tablets were crushed and the required amount of powdered tablets and capsules were dissolved in water and filtered. The filtrate was diluted to the required volume.

2.3. **Apparatus**

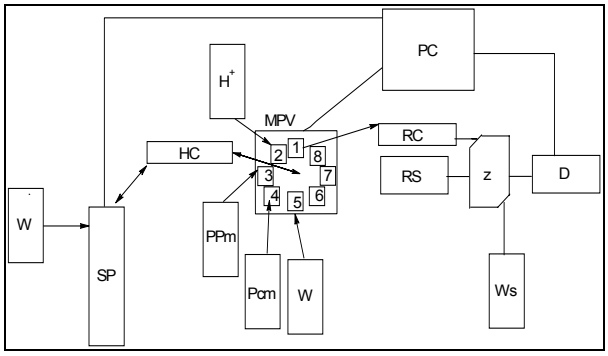

Fig. 2. SIA manifold diagram, W: water; SP: syringe pump; HC: holding coil; H^+: sulphuric acid; PPm: potassium permanganate; Pcm: paracetamol; MPV: multi-position valve; 1-8: ports; PC: personal computer; RC: reaction coil; RS: radiation source; Z: Z-flow cell; D: detector; Ws: waste.

The manifold used in this method consists of SIA combined with a fibre optic spectrometer. The full components of the manifold are diagrammed in fig. 2. The SIA system is the *FIALab 3500* (Medina, WA USA). It is composed of a syringe pump, a multi-position valve, a Z-flow cell with SMA fibre optic connectors as well as pump tubing and PC. The *Syringe Pump* is 24,000 steps with an optical encoder feedback and 1.5 seconds to 20 minutes per stroke of 2.5 ml size. It is > 99% accuracy at full stroke. The *Multi-Position Valve* has eight ports with a standard pressure of 250 psi (gas)/600 psi (liquid); zero dead volume; chemically inert; port selection is usually done using the software program. *The Z-Flow Cell* is 10 mm path length plexiglass compatible with standard SMA terminated fibre optics was used. *Pump Tubing* of 0.30" ID Teflon type supplied by Upchurch Scientific, Inc. (Oak Harbor, WA, USA) was used for connecting the different units; and making both the holding coil (200 cm long) and the reaction coil (100 cm long).

The fibre optic spectrometer is composed of a light source, 200 micron fibre optic connectors and a detector. The light source is *LS-1 Tungsten Halogen* (Ocean Optics, USA) optimized for VIS-NIR (360nm-2µm) wavelength range. The detector is *USB2000 Spectrometer* (Ocean Optics, USA) adapted to 200-1100nm wavelength range.

2.4 **Software Packages**

FIALab for Windows version 5.0 from FIAlab® (Medina, WA USA) was utilised for programming, controlling the SIA manifold and data acquisition.

SigmaPlot 2004 for Windows version 9.01 from Systat Software, Inc. was employed for constructing kinetic curves and calculating linear regression equations.

SPSS for Windows version 10.0.1 was used for calculating t-test values.

2.5. **Method and Procedure**

The following steps are the protocol applied for kinetic investigation and samples analysis for paracetamol:

1. Working solutions of sulphuric acid, potassium permanganate, paracetamol as well as water (for total volume adjustment and as a spacer solution for mixing and dilution process) were linked to the selector valve through ports 2, 3, 4 and 5, respectively and also water as a carrier was linked to the syringe at the in-position valve.
2, The syringe was filled with 2000 µl of the carrier by directing the two-way valve to the (in-position) mode with flow rate of 100 µl s^{-1}.
3. Tubes were loaded with their respective reagents by performing aspiration runs and directing the two-way valve to the (out-position) mode with flow rate of 100 µl s^{-1}.
4. With a 100 µl s^{-1} flow rate, the syringe was emptied and step 2 was repeated.
5. The required volumes of sulphuric acid, potassium permanganate and water were sequentially aspirated into the holding coil and short reverse strokes were performed repeated three times to allow reagents to mix and dilute keeping the flow rate fixed at 50 µl s^{-1}.
6. With a flow rate adjusted at 25 µl s^{-}1, a 1800 µl volume was dispensed to the Z-flow cell passing through the reaction coil and, simultaneously, the reference and absorbance scan were performed by the spectrometer at 526 nm wavelength and the maximum value of the monitored peak was recorded as absorbance-1 (A_1).
7. Step 5 was repeated.
8. With 100 µl s^{-1} flow rate, a 180 µl volume was allowed to dispense towards the detector thus trapping all reagents in the reaction coil for the required delay time to allow reaction to take place.
9. 1500 µl was dispensed to the Z-flow cell at a flow rate of 25 µl s^{-1} and, simultaneously, the reference and absorbance were scanned at fixed wavelength at 526 nm. The maximum value of the monitored peak was recorded as absorbance-2 (A_2).

10. The response (R) of the reaction was calculated using the following equation expressed as follows:

$$R = A_1 - A_2 / A_1 1 \times 100$$

3. Results and discussion

A preliminary investigation on the paracetamol oxidation by acidified permanganate gave different response values depending on the flow rate, the concentration of reactants, the reaction time and temperature. It was therefore decided to study the kinetics of the reaction and hence validate the method for quantitative assay of paracetamol. The reaction order with respect to each reactant and the activation energy were determined and the mechanism was postulated. A

kinetic optimized method for the determination of paracetamol in generic form was adopted. Eventually, the method was applied for the determination of paracetamol in dosage forms and the performance characteristics of the adopted method were evaluated.

The next three sections discuss the reaction order with respect to the concentration of each reactant of sulphuric acid, permanganate and paracetamol. Volumes reacted were 30 µl for each reactants and 20 µl for the spacer solution (water). The concentrations of all reactants except the examined reactant are kept constant and the rate of the reactant being examined was obtained by varying its concentration. Kinetic curves between delay time and the response (R) for each reactant were plotted. The reaction rates for each reactant were calculated from the plot as "$\Delta A/\Delta t$" and the reaction order was obtained throughout the linear regression of log rate versus log concentration of the examined reactant.

Values for "$\Delta A/\Delta t$" were calculated by taking a fixed region in the y-axis to represent fixed absorbance value which intersects at different values on the time scale as the rate changes by changing the concentration of reactant concentration. This explains why we usually get different values of time at fixed absorbance, a method called the fixed absorbance method.

3.1 Reaction order with respect to sulphuric acid concentration

The acid concentrations of 0.2, 0.4, 0.6, 0.8 and 1.0 mol l^{-1} were allowing for possible kinetic investigation to be monitored spectrophotometrically, while the convenient concentrations of permanganate and paracetamol were $2.0x10^{-3}$ and $5.0x10^{-4}$ mol l^{-1} respectively. The obtained results were calculated and the kinetic curves are plotted in fig. 3. The rates of reaction were calculated and the results obtained are presented in table 1. Linear regression of Log rates versus Log acid concentrations gave the following equation:

log rate = -1.0491 Log $[H^+]$ - 2.9748, r = 0.9967

The above linear equation clearly indicates that the reaction order with respect to hydrogen ion concentration is inverse one indicating that the reaction rate increases as acid decreases and that the hydrogen ion is one of the reaction product

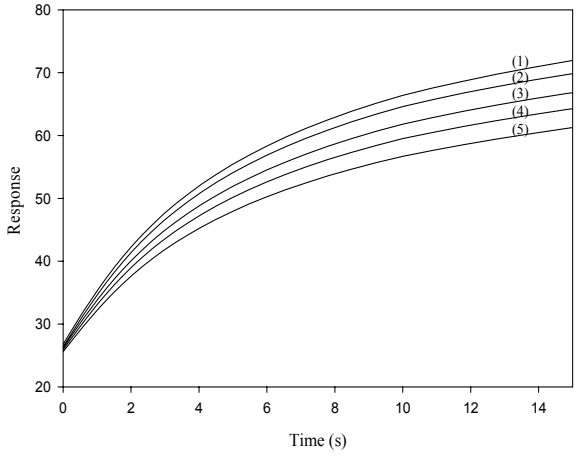

Fig. 3. Kinetic curves for the determination of the reaction order with respect to sulphuric acid concentration. [Potassium permanganate] = $2.0x10^{-3}$ mol l^{-1}; [paracetamol] = $5.0x10^{-4}$ mol l^{-1}; $[H_2SO_4]$ = (1) 0.2, (2) 0.4, (3) 0.6, (4) 0.8 and (5) 1.0 mol l^{-1}.

Table 1 Reaction rates of different concentrations of sulphuric acid in mol l^{-1}, and constant concentrations of permanganate ($2.0x10^{-3}$ mol l^{-1}) and paracetamol ($5.0x10^{-4}$ mol l^{-1})

Exp. No.	$[H^+]$	Log $[H^+]$	Δt/s	$(\Delta A/\Delta t) \times 10^{-3}$	Log ΔA / Δt
1	0.2	-0.699	1.5	6.531	-2.185
2	0.4	-0.398	2.8	3.594	-2.444
3	0.6	-0.222	4.6	2.434	-2.613
4	0.8	-0.097	5.2	1.901	-2.721
5	1.0	0.000	7.2	1.368	-2.864

3.2 Reaction order with respect to permanganate concentration

The reaction order with respect to permanganate was determined using constant concentration of sulfuric acid and paracetamol that are 0.4 and $5.0x10^{-4}$ mol l^{-1} respectively and different concentration of permanganate ranging from 1.6 to 2.0×10^{-3} mol l^{-1}. The kinetic curves were run (fig. 4) and the rates of reaction were calculated (table 2). Linear regression of Log rate versus Log permanganate concentration gave the following equation:

log rate = 0.9378 Log $[KMnO_4]$– 0.4778, r = 0.9948

The linear regression revealed that the reaction order with respect to permanganate is positive one.

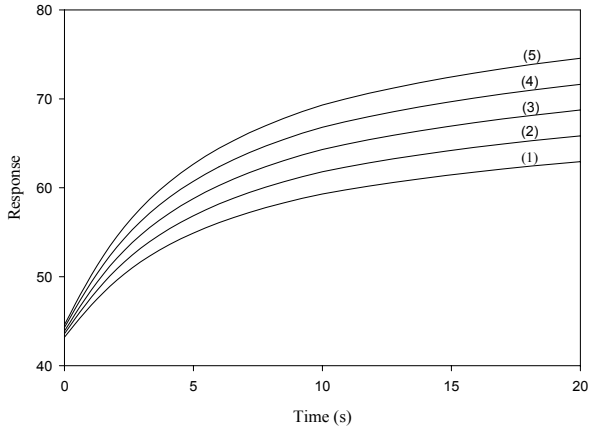

Fig.4. Kinetic curves for the determination of the reaction order with respect to permanganate; $[H_2SO_4]$ = 0.4 mol l^{-1}, [paracetamol] = $5.0x10^{-4}$ mol l^{-1} and $[KMnO_4]$ = (1) 1.6×10^{-4}, (2) $1.7x10^{-4}$, (3) $1.8x10^{-4}$, (4) $1.9x10^{-4}$ and (5) $2.0x10^{-4}$ mol l^{-1}.

Table 2 Reaction rates of different concentrations of permanganate, in mol l^{-1}, and constant concentrations of sulphuric acid (0.4 mol l^{-1}) and paracetamol (5.0×10^{-4} mol l^{-1})

Exp. No.	$[KMnO_4]$ $\times 10^{-3}$	Log $[KMnO_4]$	Δt/s	$\Delta A/\Delta t$ $\times 10^{-3}$	Log $\Delta A/\Delta t$
1	1.6	-2.796	3.0	3.404	-2.468
2	1.7	-2.770	2.7	3.565	-2.448
3	1.8	-2.745	2.6	3.837	-2.416
4	1.9	-2.721	2.5	4.009	-2.397
5	2.0	-2.699	2.1	4.315	-2.365

3.3 Reaction order with respect to paracetamol concentration

The reaction order with respect to paracetamol was determined using different concentrations of paracetamol that are 3.0×10^{-4}, 4.0×10^{-4}, 5.0×10^{-4}, 6.0×10^{-4}, and 7.0×10^{-4} mol l-1 and constant concentrations of sulphuric acid and potassium permanganate that are 0.4 mol l^{-1} and 2.0×10^{-3}, respectively. Fig. 5 graphs the kinetic curves and the results of calculated reaction rates are shown in table 3. Linear regression of Log rate versus Log paracetamol concentration gave the following equation:

log rate = 1.0154 Log [Pcm] +1.6002, r = 0.9825

From the slope of the equation above, the reaction order with respect to paracetamol was positive one, which indicates that the reaction rate increases as paracetamol increases.

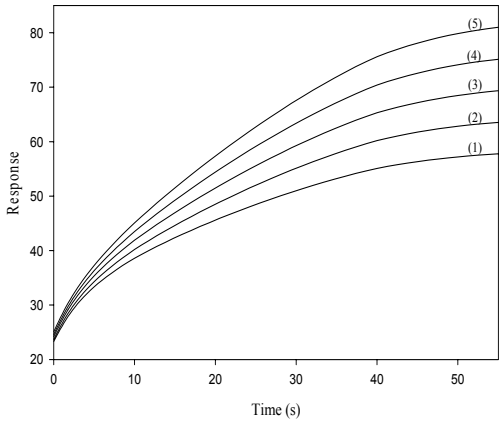

Fig. 5 Kinetic curves for the determination of the reaction order with respect to paracetamol concentration; $[H_2SO_4]$ = 0.4 mol l^{-1}; $[KMnO_4] = 2.0 \times 10^{-3}$ mol l^{-1}; [paracetamol] = (1) 3.0×10^{-4}, (2) 4.0×10^{-4}, (3) 5.0×10^{-4}, (4) 6.0×10^{-4} and (5) 7.0×10^{-4} mol l^{-1}.

Table 3 Reaction rates of different concentrations of paracetamol in mol l^{-1}, and constant concentration of sulphuric acid (0.4 mol l^{-1}) and permanganate (2.0×10^{-3} mol l^{-1})

Exp. No.	$[Pcm] \times 10^{-4}$	Log [Pcm]	Δt/s	$\Delta A/\Delta t \times 10^{-2}$	Log $\Delta A/\Delta t$
1	3.0	-3.523	1.5	1.023	-1.990
2	4.0	-3.398	1.1	1.408	-1.851
3	5.0	-3.301	0.7	1.977	-1.704
4	6.0	-3.222	0.7	2.012	-1.696
5	7.0	-3.155	0.6	2.449	-1.611

3.4 Proposed reaction mechanism

The reaction rate measurements as indicated by the figures 3, 4, and 5 above clearly proves that the reaction takes place in two steps. The reaction orders with respect to the concentration of sulphuric acid, permanganate and paracetamol were found to be inverse one (-1), positive one (+1), and positive one (+1), respectively giving the following rate law:

$$\text{Rate} = k[Mn^{3+}]\,[\text{aminophenol}]/\,H^+$$

The stoichiometry of the reaction of paracetamol with permanganate in sulphuric acid proved to be 1:2, respectively when a classical titration was carried out while heating the solution at 35^0C.

It is proposed that paracetamol is first protonated fastly in acidic media to *p*-aminophenol, which is then oxidized to *p*-aminoquinonoe in the second step and this step is considered the rate determining step; and finally oxidized to *p*-quinone (Fig 6).

It is worth mentioning here that the manganese(III) is considered the active oxidant in permanganate reactions as manganese(VII) diamarizes with manganese(II) produced immediately at the very beginning of the reaction thus generating manganese(III) stable species[26,27].

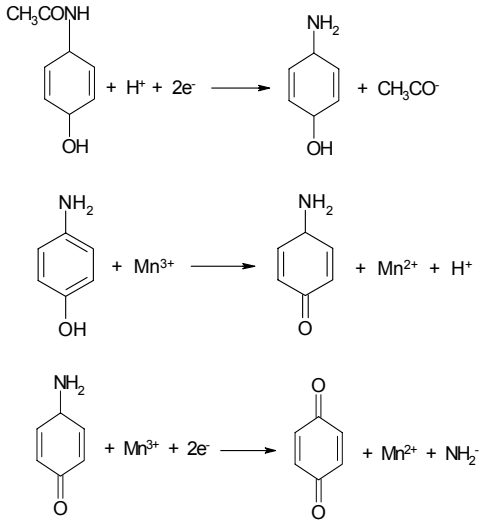

Fig. 6 Proposed reaction mechanism of the paracetamol oxidation by acidified permanganate

3.5 Activation energy

To examine that activation energy of paracetamol oxidation by acidified permanganate, five experiments were conducted at different temperatures varied between 23 to 35°C and different delay times with constant concentration of reactants that are 1.812 mol l^{-1} H_2SO_4, 2.0 × 10^{-3} mol l^{-1} $KMnO_4$ and 3.307 × 10^{-4} mol l^{-1} paracetamol. The reaction rates were calculated and presented in table 4. Linear regression of log *k'* versus T^{-1} was plotted using the Arrhenius equation as expressed below:

Log K' = $-E_a/2.303$ RT + Log [A]

where *K*' is the pseudo rate of the reaction, *R* is the gas constant = 8.314 J K^{-1} mol^{-1}, *Ea* is the activation energy, *T* is the temperature in Kelvin and A is the pre-exponential factor. The equation was applied and the activation energy was found to be 101.9 KJ mol^{-1}.

Table 4 Calculated rate constant values for the reaction of 1.812 mol l^{-1} H_2SO_4, 2.0×10^{-3} permanganate and 3.307×10^{-4} paracetamol at variable temperatures.

T (°C)	1/T x 10^{-3}k	K' x 10^{-3}	Log K'
23	3.378	12.5	-1.903
26	3.344	17.9	-1.747
29	3.311	27.7	-1.558
32	3.279	41.7	-1.380
35	3.247	60.8	-1.216

3.6 Analytical appraisals

To obtain the best and widest linear calibration curve for paracetamol analysis, different fixed times and a wide range of paracetamol concentration were applied at room temperature keeping constant concentration of the other reactants at 1.0 mol l^{-1} H_2SO_4 and 2.0 × 10^{-3} mol l^{-1} $KMnO_4$. The volumes of the reactants applied were 35, 30, 20 and 25 µl for H_2SO_4, $KMnO_4$, paracetamol and water ,respectively, with a flow rate of 25 µl s^{-1} and the results obtained are presented in table 5. As shown from the table, the shortest fixed time achieved the best linearity is 70 s in the range of paracetamol concentration of 6.61 × 10^{-5} - 1.32 × 10^{-3} mol l^{-1}. The above conditions were selected on the light of the thorough investigation of the reaction conditions and reaction rate measurements outlined in the preceding sections thus validating the present method and justifying the conditions stated without necessitating optimization study. Therefore, the calibration equation expressed bellow was applied for the quantitative determination of paracetamol in dosage forms.

$$A = 0.0038C + 0.1209$$

Table 5 Calibration equations at different fixed times using 35 µl of 1.0 mol l^{-1} H_2SO_4, 30 µl of 2.0 × 10^{-3} mol l^{-1} potassium permanganate, 20 µl of paracetamol and 25 µl water.

Time (s)	Calibration equation	r
30	R = 0.0039C + 0.1285	0.9439
40	R = 0.0036C + 0.1016	0.9622
70	R = 0.0038C + 0.1209	0.9931
120	R = 0.0033C + 0.1650	0.9862
200	R = 0.0037C + 0.1836	0.9696

Table 6: Results obtained by the methods of and BP for the determination of paracetamol in proprietary drugs.

Drug	Supplier	Content (mg)	Mean recovery ± RSD(%)* SIA method	Mean recovery ± RSD(%)* BP method	t*
Panadol, tablets	Dungarvan, Irland	Paracetamol, 500mg	99.6 ± 0.2	99.8 ± 1.3	0.90
Samfadol, tablets	Samfs, Sudan	Paracetamol, 500mg	99.5 ± 0.7	99.6 ± 1.5	1.05
Panadol Night, tablets	Dungarvan, Irland	Paracetamol, 500 Diphenylamine HCl, 25	99.2 ± 0.4	99.1 ± 2.0	1.45
Panadol Sinus, tablets	Dungarvan, Irland	Paracetamol, 500 Pseudoephedrine HCl,	99.3 ± 0.5	99.1 ± 1.3	1.37
Parafon capsules	Cilag, Switzerland	Paracetamol, 300 Clorzoxazone, 250	98.4 ± 0.7	98.1 ± 1.2	2.10

*relative standard deviation for 5 replicates

** Student t-test values

3.7 Application

In order to examine the interferences of paracetamol with other drugs and excipients in dosage forms, the proposed SIA method was applied in some proprietary drugs collected from the local dispensaries. The BP method for the assay of paracetamol tablets was performed for the same batch samples. The results of the comparative study are introduced in table 6. The statistical calculation of the Student t-test indicates high accuracy and repeatability. The proposed SIA method shows high selectivity, which other ingredients in dosage forms such as diphenylamine hydrochloride, pseudophedrine hydrochloride and chloroxazone beside excipients such as starch. Codeine phosphate was found to be chemically interfered with paracetamol in dosage forms. Despite the oxidizing power of permanganate, the method was found to be selective for paracetamol determination under such sulfuric acid concentration

4. Conclusion

A novel and simple method was explored for the determination of paracetamol in dosage forms by studying the kinetics of of paracetamol oxidation by potassium permanganate in sulphuric acid media comprehensively. The SIA as a superior fully automated technique empowers the newly adopted kinetic method to be highly accurate, reliable and selective method. In addition, permanganate as a superior oxidizing agent with high molar absorbtivity factor enjoying the method with rapidity and sensitivity. The fixed time method could not have been successfully applied if the traditional spectrophotmetric manual method was applied.

5. Acknowledgements

Thanks are due to the Department of Chemistry, College of Science, King Faisal University for allowing authors to perform this research. Mr. Abubakr M. Idris thanks University of Khartoum for registering him to study for awarding the PhD degree at the Faculty of Pharmacy.

6. References

1. M.K. Srivastava, S. Ahmed, D. Singh, C.I. Shukla, Analyst 110 (1985) 735.
2. S. M. Sultan, I.Z. Alzamil, A. M. Aziz-Alrahman, S. A. Altamrah, Y. Asha Analyst 111 (1986) 919.
3. S. M. Sultan, Talanta 34 (1987) 605.
4. J.M. Calatayud, C.G. Benito, Anal. Chem. Acta 231 (1990) 259.
5. F. Onur, N. Acar, STP Pharma. Sci. 5 (1995) 152.
6. Z. Bouhsain, S. Garrigues, M. Guardia, Analyst 121 (1996) 635.
7. N. Erk, F. Onur, Anal. Lett. 30 (1997) 1201.
8. Z. Bouhsain, S. Garrigues, M. Guardia, Fresenius J. Anal. Chem. 357 (1997) 973.
9. E. Dinc, F. Onur, Anal. Chim. Acta. 359 (1998) 93.
10. M.L. Ramos, J.F. Tayson, D.J. Curran, Anal. Chem. Acta 364 (1998) 107.
11. E. Dinc, F. Ounr, Sci. Phar. 67 (1999) 57.
12. A. Criado, S. Cardenas, M. Gallego, M. Valcarcel, Talanta 52 (2000) 417.
13. E. Dinc, C. Yucesoy, F. Onur, J. Pharm. Biomed. Anal. 28 (2002) 1091.
14. A.M. Wahbi, A.A. Gazy, O. Abdel-Razzak, H. Mahgoub, M.S. Moneeb, Saudi Pharm. J. 11 (2003) 192.
15. E. Dinc., J. Pharm Biomed Anal 21 (1999) 723.
16. J.L. Perez, M.A. Pello, Talanta 48 (1999) 1199.
17. C. Celma, J.A. Allue, J. Prunonosa, C. Peraire, R. Obach, J. Chromaotgr. A 870 (2000) 77.
18. L. A. Shervington, N. Sakhnini, J. Pharm. Biomed. Anal. 24 (2000) 43.
19. N. Erk, Y. Ozkan, E. Banoglu, S.A. Ozkan, Z. Senturk, J. Pharm. Biomed. Anal. 24 (2001) 469.
20. A. Garcia, F.J. Ruperez, A. Marin, A. Maza, C. Barmas, J. Chromatogr. B 785 (2003) 237.
21. D.J. Miner, J.R. Rice, R.M. Riggur, P.T. Kissinger, Anal. Chem. 5 (1981) 2258.
22. J. Zen, Y. Ting, Anal. Chem. Acta 342 (1997) 175.
23. H. Tanaka, P.K. Dasgupta, J. Huang, Anal. Chem. 72 (2000) 4713.
24. N. Wangfuengkanagul, O. Chailapakul, Pharm. Biomed. Anal. 28 (2002) 841.
25. BP, E-copy on CD, Ver. 6.0, 2002.
26. J.I Watters and I.M Kolthoff, J. Am. Chem. Soc., 70 (1948) 2455.
27. G.A. Rechnitz, G.N. Rao, Anal. Chem. 38 (1966) 1900.

(Received August 30, 2005)
(Accepted September 9, 2005)