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Research Article

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Kinetic simultaneous spectrophotometric determination of paracetamol and ibuprofen using H-point standard addition method

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ABSTRACT

A very simple and sensitive Spectrophotmetric method for simultaneous kinetic determination of paracetamol and ibuprofen using H-point standard addition method (HPSAM) was described. The method was based on difference in the rate of oxidation of these compounds with alkaline potassium permanganate to produce a bluish green colored measurable at 610 nm. Different experimental parameters were carefully studied and optimized for getting results with minimum errors. Paracetamol and ibuprofen can be determined in the range of 1.0-20.0 and 5.0-25.0 µgm1^{-1} respectively and minimum detectability of 0.29 and 0.92 µgm1^{-1}. Correlation coefficients were greater than 0.9971 in all cases. The maximum value of relative standard deviation did not exceed 1.25 (n=5). The recovery was between 98.0 to 101.2% with relative error of 0.09 and 0.1 for paracetamol and ibuprofen, respectively. The proposed method has successfully been applied for simultaneous determination of paracetamol and ibuprofen in synthetic samples and pharmaceutical preparations

Keywords: Paracetamol, Ibuprofen, H-point standard addition method (HPSAM), spectrophotometry-

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INTRODUCTION

For kinetic determination by HPSAM, the reaction of paracetamol (analyte) should be faster than that of ibuprofen (interferent). This method is based on the assumption that only paracetamol reacts with time and the analytical signal for ibuprofen does not change with time [1,2]. The requirements for the application of HPSAM is that only to work at two times where the analytical signals due to the interference are constant and for the analyte to be different as possible as. By plotting the analytical signals versus added analyte concentration, two straight lines are obtained that have a common point with coordinates H ($-C_H$, S_H), where $-C_H$ is the unknown analyte concentration and S_H is the analytical signal due to the interference.

Various simultaneous methods including proton magnetic resonance [3], thin layer chromatography [4], HPLC [5-9], GLC [10,11] and spectrophotometry [12-17] are available for the determination of paracetamol and ibuprofen. However, there is no kinetic application of HPSAM for analysis of paracetamol and ibuprofen in a binary mixture. This paper describes new simple, rapid, accurate, reproducible and economical method for the simultaneous kinetic Spectrophotmetric determination of paracetamol and ibuprofen using H-point standard addition method.

EXPERIMENTAL SECTION

2.1. Apparatus

A shimadzu (Kyoto, Japan) UV-1650 PC, UV-Visible double-beam spectrophotometer with two matched 1cm path-length quartz cells was used. The subsequent statistical manipulation was performed by transferring the spectral data to Microsoft Excel 2007 program and processing them with the standard curve fit package and matrix calculation.

2.2. Materials and reagents

Paracetamol and ibuprofen samples were kindly provided by middle east pharmaceuticals and Cosmetics laboratories , Gaza ,Palestine. Tablets containing the drugs were obtained from the local market. Potassium permanganate (AnalaR,BDH) 0.125M stock solution in 0.1 M NaOH and 10.0 M sodium hydroxide stock solution(Merck, Darmstat,Germany) were used. Stock 20.0 $\mu gm1^{-1}$ paracetamol and 50.0 $\mu gm1^{-1}$ ibuprofen solution in 0.1M NaOH were prepared. Further dilutions were made as and when required.

2.3. Procedure

2.3.1. Individual calibration

1.0ml of $1.25x10^{-3}$ M potassium permanganate , 1.0 ml of 0.1 M sodium hydroxide and appropriate volumes of paracetamol and ibuprofen standard solutions were added into a 5.0 ml standard flask and volume was made up to the mark with 0.1M NaOH. A portion of the solution was transferred into a quartz cell and variations of absorbance with time were recorded at 610nm at a time intervals of 1.0 min for each sample. The final concentration of paracetamol and ibuprofen must be between 1.0-20.0 and 5.0 - 25.0 $\mu gm1^{-1}$, respectively.

2.3.2.Kinetic-HPSAM

In a 5.0ml volumetric flask, 1.0 ml of $1.25x10^{-3}$ potassium permanganate, 1.0 ml of 0.1M sodium hydroxide and appropriate amounts of paracetamol and ibuprofen standard solution were added. Standard additions of paracetamol were made and volume was completed to the mark with 0.1M NaOH. The absorbance was measured at 1 and 4 min for performing kinetic-HPSAM in the proposed system.

2.3.3. Procedure for tablets

An accurately weighed amount of the powder of the tablets was transfer into a small conical flask and extracted with 3x10ml of acetone [10]. The extract was filtered and evaporated using a rotatory evaporator at 50 C^0 till dryness. The residue was dissolved in 0.1M NaOH and then the general procedure was applied.

RESULTS AND DISCUSSION

3.1. Optimization of experimental parameters

Paracetamol and ibuprofen were found to react with alkaline potassium permanganate producing a bluish green color with absorption maximum at 610 nm .The reaction of paracetamol with potassium permanganate was found to be faster than that of ibuprofen in the same conditions. Figure1. shows the absorbance time graph for the reaction of paracetamol and ibuprofen with potassium permanganate. This difference in the kinetic behavior was used for simultaneous determination of paracetamol and ibuprofen in the present work.

The various experimental factors were studied and optimized. The order of addition of the reagents is very important. Mixing potassium permanganate with sodium hydroxide and addition of paracetamol and ibuprofen gave very high sensitivity [20]. For more simplicity and better control of temperature, all the studies were performed at room temperature. The influence of the concentration of potassium permanganate was studied using different concentrations ranging from $5.0x10^{-3}$ to $5.0x10^{-4}$.. The highest results was obtained with $1x10^{-4}$ M . Complete reaction takes place only in alkaline medium. Different concentrations of NaOH ranging from0.01 to 0.2 M were tested. It was found that the reaction took place starting from 0.075M upwards. However, to ensure a complete reaction, $2.5x10^{-4}$M $KMnO_4$ and 0.1M NaOH (final concentration) were chosen for the simultaneous determination of 1.0-20.0 $\mu gm1^{-1}$ paracetamol and 5.0-25.0 $\mu gm1^{-1}$ ibuprofen.

3.2. Absorbance- Time behavior

Under optimized conditions, the characteristics of calibration graphs, for the individual determination of paracetamol and ibuprofen, are given in table1.

3.3. Applying kinetic-HPSAM

In this system, paracetamol and ibuprofen are the analyte and interferent respectively. Difference in the rate of oxidation of paracetamol and ibuprofen with alkaline potassium permanganate is the main reason for applying kinetic-HPSAM.

3.3.1. Selection of appropriate time

The best pair of time (t_1 and t_2) selected is the one which gives greatest slope increment for paracetamol and the change in absorbance (ΔA) for ibuprofen is negligible. To select the appropriate times, time pairs of 1-3, 1-4, 1-5, 2-5, 2-6, 3-5 and 3-6 min were examined. The time pair of 1- 4 min was employed for obtaining the highest accuracy as shown from table 2 and the plot of H-point standard addition method as shown in figure 2.

According to the theory of HPSAM at H-point ($-C_H$, S_H) C_H (concentration of paracetamol) is independent on the concentration of ibuprofen (Figure3) and S_H, the analytical signal due to ibuprofen, is also independent on the paracetamol concentration (Figure 4).

3.3.2 Reproducibility and accuracy of the method

Under optimum conditions simultaneous determination of paracetamol and ibuprofen were made by using kinetic-HPSAM. To check the reproducibility and accuracy of the method, five replicate experiments were performed in different samples and the results are given in Table3. The relative standard deviation for a mixture of 2.0 $\mu gm1^{-1}$ paracetamol and 5.0 $\mu gm1^{-1}$ ibuprofen were 1.25 and 0.38, respectively. The recovery was between 98.0 and 101.2% with relative error of 0.09 and 0.1 for paracetamol and ibuprofen, respectively. Limits of detection were 0.29 and 0.92 $\mu gm1^{-1}$, respectively for paracetamol and ibuprofen. It was calculated as LOD= $C_H + 3SD_H$, where C_H and SD_H are the mean and standard deviation of five replicate measurements of a blank sample using HPSAM [19]. As evident from the results, the accuracy and precision of the method are within acceptable limits

3.3.3. Effect of interferences

Selectivity in kinetic methods is achieved by choosing reagents and conditions that amplify difference in the rates at which the analyte and potential interferences react. In general, most of reductants which react with potassium permanganate under the experimental conditions interfere [20]. Different sensitizers and surfactants react strongly with the $KMnO_4$/NaOH system [20].Therefore paracetamol and ibuprofen should be extracted and separated before applying the simultaneous kinetic method.

3.3.4 Application

To evaluate the applicability of the proposed method , it was applied to simultaneous determination of paracetamol and ibuprofen in commercially available tablets. Table 4 shows a good agreement between the obtained results and certified amounts, which indicates the successful applicability of the HPSAM for simultaneous determination of paracetamol and ibuprofen

Table1 Calibration graph characteristics, for the determination of paracetamol and ibuprofen.

Compound	linear range, $\mu gm1^{-1}$	slope	intercept	R^2	detection limit, $\mu gm1^{-1}$
Paracetamol	1.0-20.0	0.1517	0.0056	0.9993	0.16
Ibuprofen	5.0-25.0	0.0201	-0.0035	0.9994	0.55

Table 2. Application of signal increment version of HPSAM in a synthetic mixture of 2.0 $\mu gm1^{-1}$ paracetamol and 5.0 $\mu gm1^{-1}$ ibuprofen.

Time interval (min)	Paracetamol found ±SD ($\mu gm1^{-1}$)	Recovery,%	RSD (n=5)
1-3	2.15±0.028	108.0	1.4
1-4	2.01±0.026	100.5	1.3
1-5	2.05±0.030	102.5	1.5
2-5	2.13±0.032	106.5	1.6
2-6	2.20 ±0.030	110.0	1.5
3-5	2.12±0.028	106.0	1.4
3-6	2.10±0.032	105.0	1.6

Table3. Result of five replicates for the analysis of Paracetamol and ibuprofen in different samples

A-C equations	R^2	Taken (µgm1^{-1}) Paracetamol	Ibuprofen	Found ± SD (n=5) Paracetamol (RSD)	Ibuprofen (RSD)	Recovery% Paracetamol	Ibuprofen
A_2= 0.1033C+ 0.2641 A_4 =0.1422C+ 0.3761	0.9992 0.9997	2.0	5.0	1.99± 0.025 (1.25)	5.01±0.019 (0.38)	99.5	100.2
A_2=0.0982C+ 0.4632 A_4 =0.01451C+ 0.6680	0.9984 0.9979	4.0	5.0	3.98 ±0.031 (0.78)	4.96±0.021 (0.42)	99.5	99.2
A_2=0.0991C+ 0.6558 A_4 =0.1491C+ 0.9780	0.9988 0.9979	6.0	5.0	5.99 ±0.035 (0.58)	5.02 ±0.023 (0.46)	99.8	100.4
A_1=0.1010C+ 0.8862 A_4 =0.1455C+ 1.2820	0.9971 0.9985	8.25	5.0	8.27 ±0.051 (0.62)	4.99 ±0.041 (0.82)	100.2	99.8
A_1=0.1009C+ 1.3082 A_4 =0.1439C+ 1.9022	0.9982 0.9973	12.5	5.0	12.34 ±0.073 (0.58)	5.06 ±0.044 (0.88)	98.7	101.2
A_1=0.1000C+ 0.3160 A_4 =0.1450C+ 0.4776	0.9980 0.9971	2.0	10.0	1.96 ±0.022 (1.10)	9.93 ±0.066 (0.66)	98.0	99.3
A_1=0.0989C+ 0.3844 A_4 =0.1467C+ 0.5472	0.9974 0.9991	2.0	15.0	2.02 ±0.023 (1.15)	15.06 ±0.081 (0.54)	101.0	100.4

Table 4. Simultaneous determination of paracetamol and ibuprofen in pharmaceutical samples

Sample No.	Certified amount (mg)		Found ± SD (n=5)		Recovery %	
	Paracetamol	Ibuprofen	Paracetamol	Ibuprofen	Paracetamol	Ibuprofen
Parofen tablet (UNIPHARMA,Egypt)	500.0	400.0	505±3.71	400.8.±2.71	101.0	100.2
Mepabrufen tablet (Medifood, Egypt)	500.0	400.0	495.5±2.22	398.8±2.63	99.1	99.7

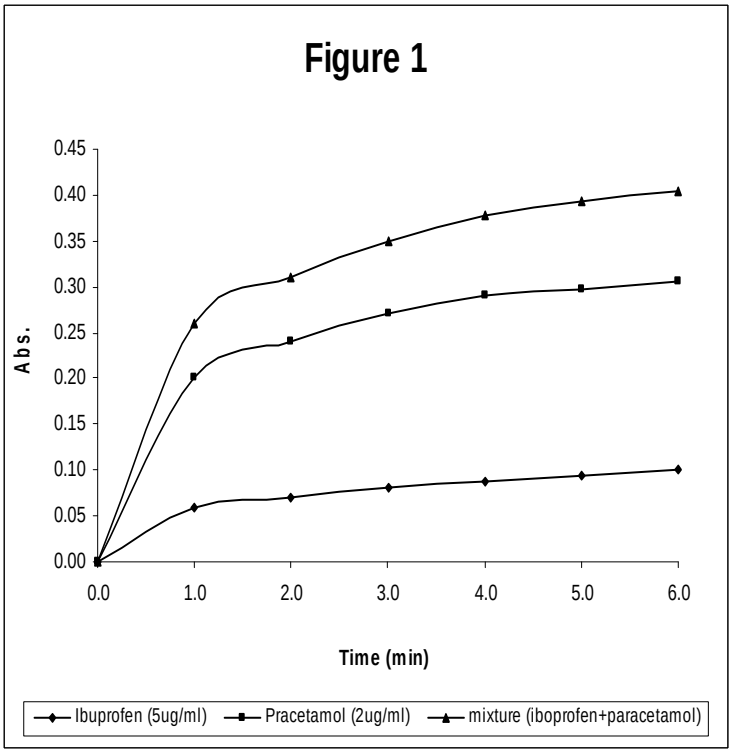

Figure 1. Absorbance-time curve for paracetamol (2.0 µgml^{-1}) , and ibuprofen (5.0 µgml^{-1}) and mixture of paracetamol (2.0 µgml^{-1}) and (5.0 µgml^{-1}) ibuprofen.

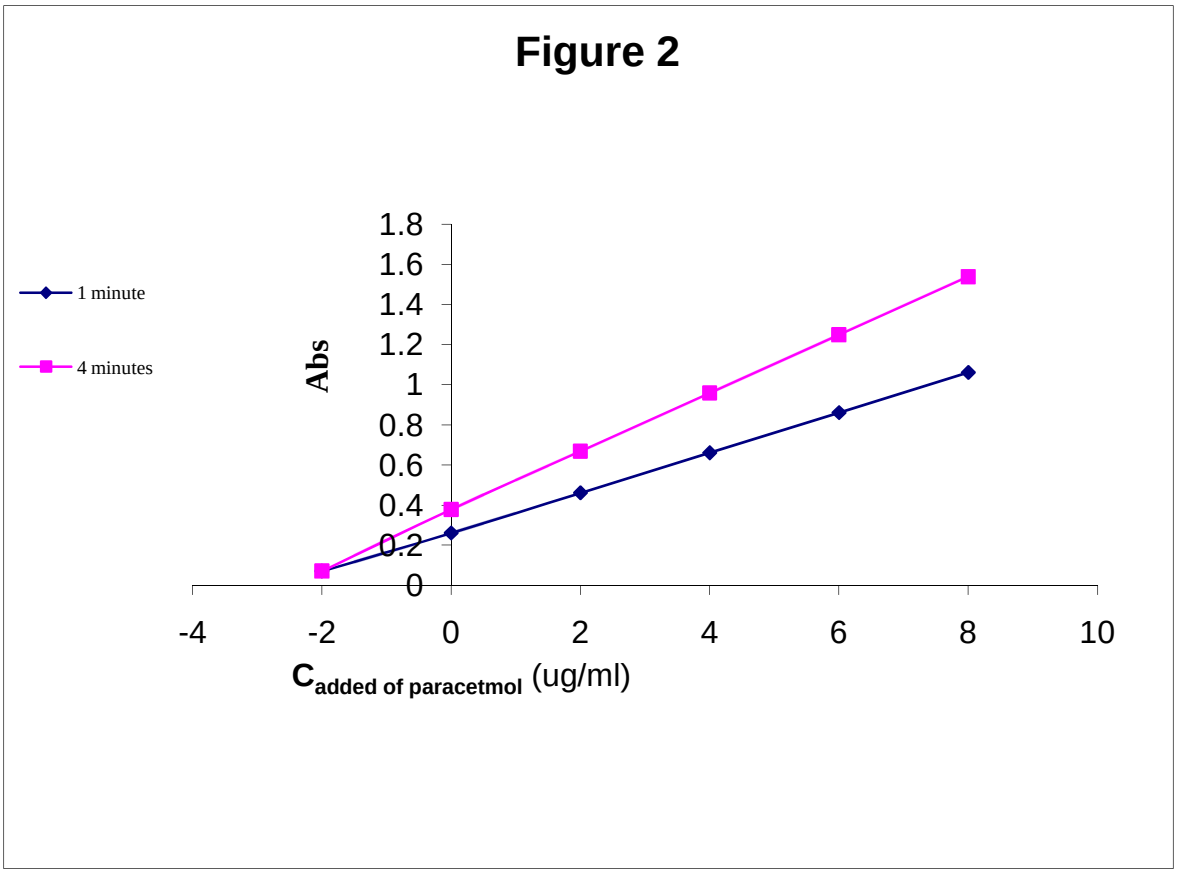

Figure 2. Plot of HPSAM for simultaneous determination of paracetamol (2.0 µgml^{-1}) and ibuprofen (5.0 µgml^{-1}).

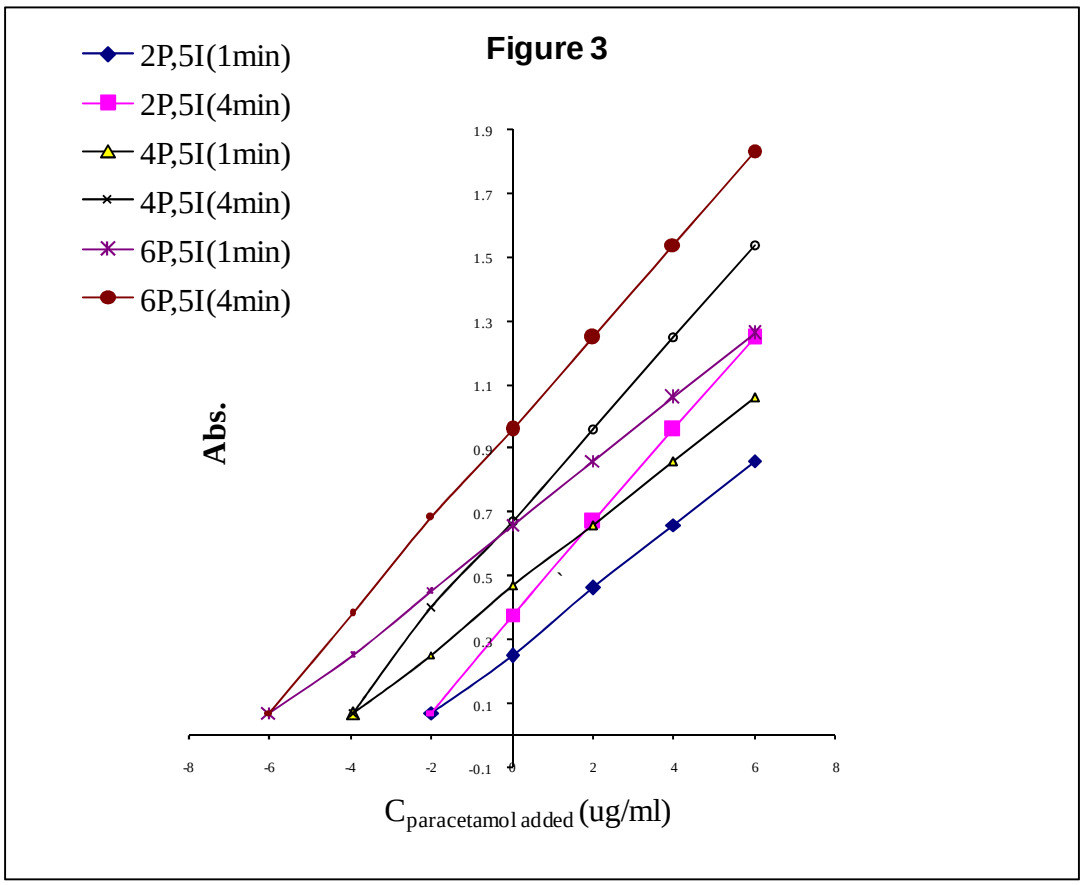

Figure 3. Plot of HPSAM for fixed ibuprofen (5.0 µgml^{-1}) and paracetamol (2.0, 4.0 and 6.0 µgml^{-1}) (P: paracetamol, I: Ibuprofen).

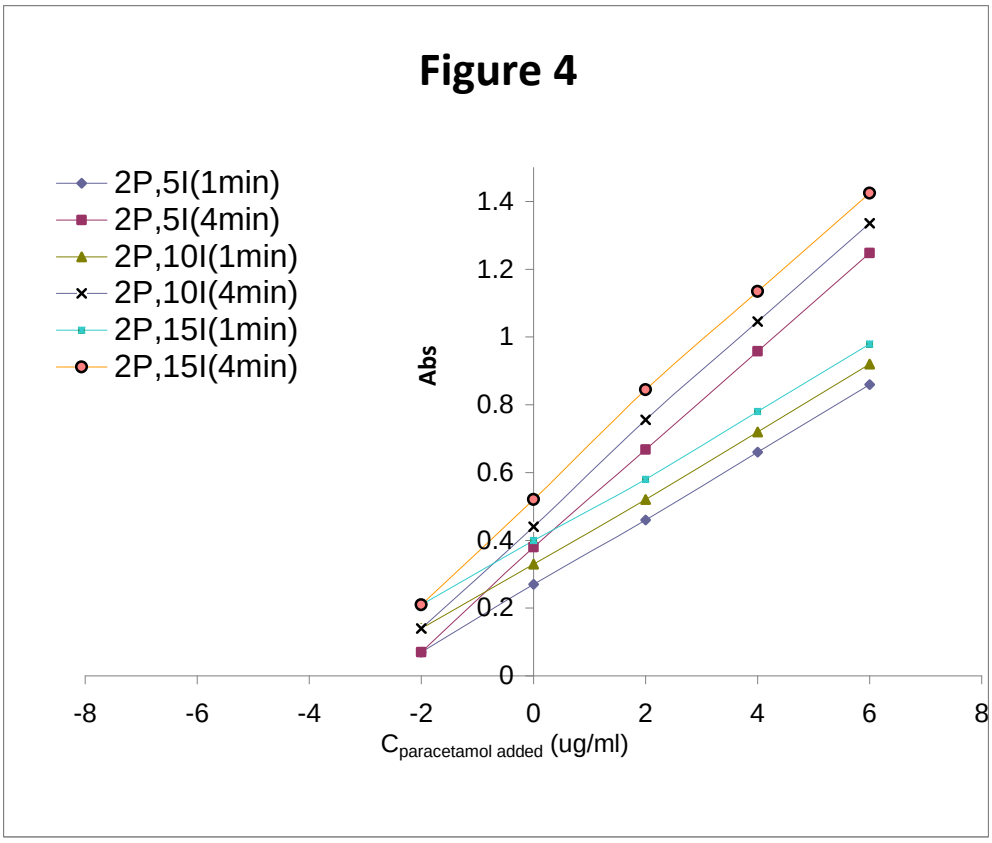

Figure 4. Plot of HPSAM for fixed paracetamol (2.0 µgml^{-1}) and ibuprofen (5.0, 10.0 and 15.0 µgml^{-1}), (P: paracetamol, I: Ibuprofen).

CONCLUSION

Simultaneous determination of paracetamol and ibuprofen without the use of any expensive instrument has been done . this reduces the cost of applied method. Although of the adequate selectivity of the proposed method, it is simpler than the time consuming HPLC methods and is more sensitive than the UV-vis Spectrophotmetric methods.

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