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Applications Ultraviolet Spectrophotometry Method with Multiple Wavelength for Simultaneous Determination Binary Mixture of Pseudoephedrine Hydrocloride and Triprolidine Hydrocloridein Tablet

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Abstract : The mixture of pseudoephedrine hidrocloride (PSE) and triprolidine hidrocloride (TRI) which is one kind of anti-influenza tablets combination.The aim of study to determination of binary mixture PSE and TRI in tablet by ultraviolet spectrofotometry with multiple wavelength technique in the matrix calculation.The metodology used to determine of PSE and TRI in tablet by spectophotometric method with wavelength in the matrix calculation.The metodology used to determine of PSE and TRI in tablet by spectrophotometric method with wavelength in matrix calculation with 0.1 N HCL as a solvent. The multiple wavelength method measured at wavelength 220 nm, 245 nm, 251 nm, 256 nm, and 264 nm. Theresults were obtained the PSE and TRI in T tablet was (101.90 ± 0.52)% and (96.99 ± 1.55)% respectively.The resultsobtained were accurate and precise.The conclusions of this studies is this spectrophotometric method with multiple wavelengths in the matrix calculations can beused to determination of binary mixture PSE and TRI in tablet.
Keywords: *Pseudoephedrine HCl, TriprolidineHCl, Tablet,Multiple Wavelength, Ultraviolet Spectrophotometry.*

1. Introduction

Pharmaceutical preparations on the market nowadays, for example tablet dosage, contains more than one active substances. The aims of this mixture is to improve the therapeutic effect and to facilitate its use. One of the active substances mixture that is commonly used is the mixture of PSE andTRI which is one kind of anti-influenza. Examination of the quality of a drug preparation is absolutely necessary to ensure that the dosage contains ingredients with quality and a predetermined amount and following standard analytical procedures. Terms for tablet dosage form binary mixturePSE and TRIwhich contains PSE and TRI is not less than 90.0% and not more than 110.0% of the amount listed on the labeland determination by using High Performance Liquid Chromatography[1].This method requires tools and operating costs are relatively expensive and relatively longtimes analysis.

Therefore, it is necessary to require alternative methods of analysis tools and operational costs are cheaper, easier in practice, but can give results with good accuracy and precision.Modifications spectrophotometric method ultraviolet can be used for multicomponent analysis in the context of quality control by setting the content of the mixture can be done together without having to be separated and a short time analysis

with the tools and the cost is relatively cheaper[2-4]. The most common procedure used in the determination of the mixture of subtances that the spectrum is overlapping is the zero crossing method[5-11].The methodcan be developed is multicomponent analysis method more practical spectrophotometrywith the principle of multiple regression equation by calculating matrix method at multiple wavelengths[12-14]. Wavelength selection based on the wavelength of absorption to barely give uptake, where the absorption fulfill the law of Lambert and Beer which is 0.2 to 0.8. Determining the wavelength by selecting a five-point wavelength independent variables.Several studies on the assay of the PSE and TRI had been done beforeby derivative spectrophotometry with zero crossing using aquadest[5]and 0.1 N HCL solution[6].The aims of this studies is to determination binary mixture of PSE and TRI by derivative ultraviolet spectrophotometry method with multiple wavelength. Chemical structure of PSE and TRI can be seen in Figure 1.

(a) (b)

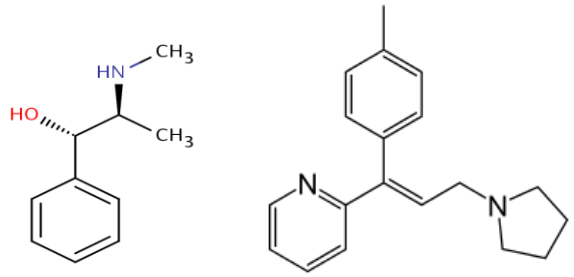

Figure 1. Chemical Structure of (a) Pseudoephedrine and (b)Triprolidine

2. Experiment

2.1 Apparatus

UV- Visible Spectrophotometer(Shimadzu 1800) with a computer equipped with UV Probe 2.34 software (UV-1800 Shimadzu), analytical balance (Mettler Toledo),sonicator (Branson 1510), pH meter (Hanna), glass tools, mortar and other tools required in sample preparation.

2.2 Materials

Material used were 0.1 N Hydrocloride, Pseudoephedrine Hydrocloride BPFI, TriprolidineHydrocloride BPFIand T tablets(each tablet contains60 mg of PSE and 2.5mg of TRI).

2.3 Preparation of Pseudoephedrine HydroclorideStock Solution

An accurately weighed 50 mg of PSE was dissolvedwith 0.1NHCL solution and the volume was made up to 25 mL to obtain a solution with a concentration of2000 µg/mL stock solution I (SS I). From this solutions pipette 12.5 mL was put into a 25 mL with0.1N HCLsolution to obtain a solution with a concentration of 1000 µg/mL (SS II).

2.4 Preparation of TriprolidineHydroclorideStock Solution

An accurately weighed 50 mg of TRI was dissolved in 0.1 N HCl solution and the volume was made up to 25 mL to obtain concentration2000 µg/mL stock solution I (SS I). From this solutions pipette2.5 mL was put into a 25 mL with 0.1 N HCl solution to obtain a solution with a concentration of100 µg/mL(SS II).

2.5 Preparation of Calibration Curve of Pseudoephedrine Hydrocloride

Taken as much as 1.8 mL; 2.5 mL; 3.2 mL; 3.9 mL; and 4.6 mL of SS II were diluted to 10 mL with 0.1 N HCl solution to produce concentration 180 µg/mL; 250 µg/mL, 320 µg/mL; 390 µg/mL; and 460 µg/mL respectively.Measured absorbance in the 200-400 nm wavelength to create a calibration curve. Absorption spectrum calibration curve as much as six repetitions.

2.6 Preparation of Calibration Curve of Triprolidine Hydrocloride

Taken as much as 0.75 mL; 1.05 mL; 1.35 mL; 1.65 mL; and 1.95 mL of SS II were diluted to 10 mL with 0.1 N HCl solution to produce concentration 7.5 mg/mL, 10.5 µg/mL, 13.5 µg/mL, 16.5 µg/mL, and 19.5 µg/mL respectively.Measured absorbance in the 200-400 nm wavelength to create a calibration curve. Absorption spectrum calibration curve as much as six repetitions.

2.7 Determination of Absorption Maximum Spectrum Pseudoephedrine Hydrocloride

Taken as much as 9.1 mL from SSII (concentration 1000 µg/ml) was diluted to 25 mL with 0.1 N HCl solution to obtain concentration 370 µg/mL of PSE. Absorbance was measured at a wavelength of 200-400 nm.

2.8 Determination of Absorption Maximum SpectrumTriprolidine Hydrocloride

Taken 3.1 mL from SS II (concentration 100 µg/mL) was diluted to 25 mL with 0.1 N HCl solution to obtain concentration 12.5 µg/mL ofTRI. Absorbance was measured at a wavelength of 200-400 nm.

2.9 DeterminationWavelength Analysis of Pseudoephedrine Hydrocloride and Triprolidine Hydrocloride

Make PSEsolutionwith a concentration of 370.0 µg/mL and TRI solution with a concentration of 12.5 µg/mL.Then both these solutions was measured absorbance at a wavelength of 200-400 nm. Furthermore absorption spectrum of each of the components in the overlapping overlaid, spectral readings is done in the wavelength range 215-265 nm, because the wavelength range is PSE and TRIoverlap overall. Then searched fivepoint wavelenghtsto be used. Wavelength selection is taken from the absorption spectrum of componentsranging provide uptake until barely give uptake and the absorbance measured at predetermined multiple wavelengths.

2.10 Determination Binary Mixture of Pseudoephedrine Hydrocloride and Triprolidine Hydrocloride

Carefully weighed 10.0 mg of reference materials of PSE and TRI and then insertedinto the10.0 ml flask respectively, diluted with 0.1 N HCL until dissolved.Taken 3.0 mL of PSE and 0.13 ml TRI and mixture, and then inserted into the 10.0 ml flask, diluted with 0.1 N HCL until dissolved.Absorbance was measured at a wavelength of 200-400 nm. It should be measured up to six repititions.

2.11Determination Binary Mixture of Pseudoephedrine Hydrocloride and Triprolidine Hydrocloride in Tablet Dosage Form

Twenty tablets are weighed and crushed homogeneous. Furthermore, weighed amount of powder equivalent to 50 mg of PSE and TRI an the equality of TRI contained in there is calculated. It should be weighed up to six repititions.Subsequently incorporated into the flask50 mLand diluted with 0.1NHCl (with sonicator for 15 minutes), and then paid back with 0.1 N HCl until the line mark, shaken until homogeneous. The solution is then filtered, approximately 10 mL of the first filtrate discarded. Taken 3 mL, put in a 10 mL flask and paid back withdiluted with 0.1 N HCl until the line marks to obtained solution in which there are PSE and TRI concentration of 300 µg / mL and 12.5 µg/mL, respectively. Measured absorption at a wavelength of 200-400 nm.

2.12 Calculation of Pseudoephedrine Hydrocloride and Triprolidine Hydrocloridelevels in The Binary Mixture

The calculation of the levels of each component in the mixture on the basis of the absorbance of the mixture (Ac) and uptake types of each component in the multi wavelength known from the measurement results using the matrix equation[12]:

$[C] = [[a] \times [a^1]]^{-1} \times [A] \times Ac]$

Description :

[C] : the levels of components of the mixture

[A] : matrix absorption of compounds making up the mixture

[A^1] : matrix transpose absorption of compounds making up the mixture

[[A] X [a^1]] $^{-1}$:inverse matrix transpose matrix times the absorption of compounds making up the mixture

Ac : sample uptake value analysis

3. Results and Discussion

3.1 Determination of Maximum Absorption Spectrum

Measurement of maximum absorption spectrum PSE and TRI at a concentration of 370.0 µg/mL and 12.5 µg/mL, respectively. Based on the research results, obtained maximum wavelength PSE at 251 nm and 256 nm and then for TRI at 290 nm. Absorption maximum spectrum of PSE (concentration 370.0 µg / mL) and TRI(concentration 12.5µg / ml) can be seen on Figure 1 and Figure 2.

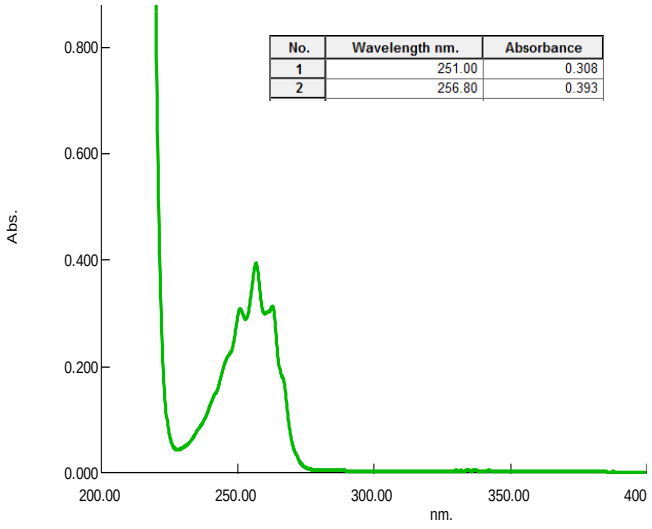

Figure 1. Absorption maximum spectrum of PSE (concentration 370.0 µg / ml)

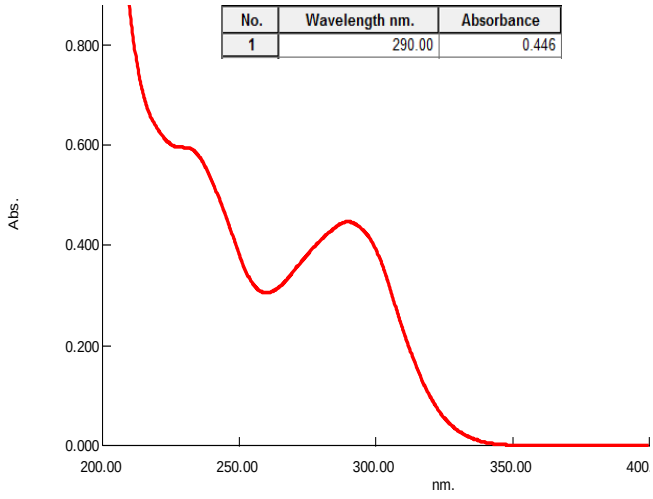

Figure 2. Absorption maximum spectrum of TRI (concentration 12.5µg / ml)

3.2 Absorption Spectra

Absorption spectra PSE with a concentration of 180-460 µg/ml and TRI at a concentration of 7.5 to 19.5 µg/ml can be seen on Figure 3 and Figure 4.

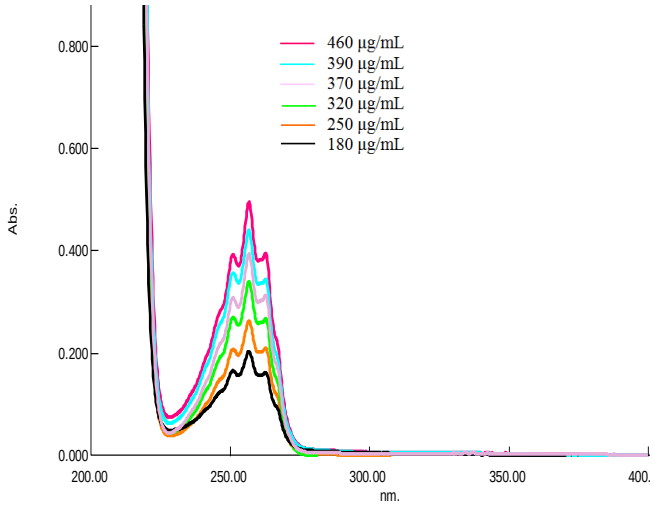

Figure 3. Absorption spectra PSE with a concentration of 180-460 µg/mL

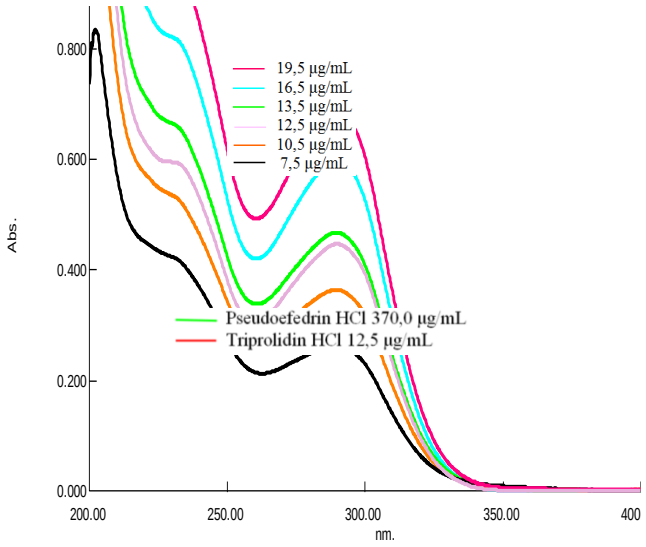

Figure 4. Absorption spectra TRI at a concentration of7.5-19.5 µg/mL

3.3 Determination of Multiple Wavelength Analysis

Overlapping absorption spectrum of PSE with a concentration of 370.0 ug/ mland TRI with a concentration 12.5 µg/ml can be seen in the Figure 5 and the result measurements on some chosen absorption point for the determinations of the measurement matrix by multiple wavelength can be seen in the Figure 6.

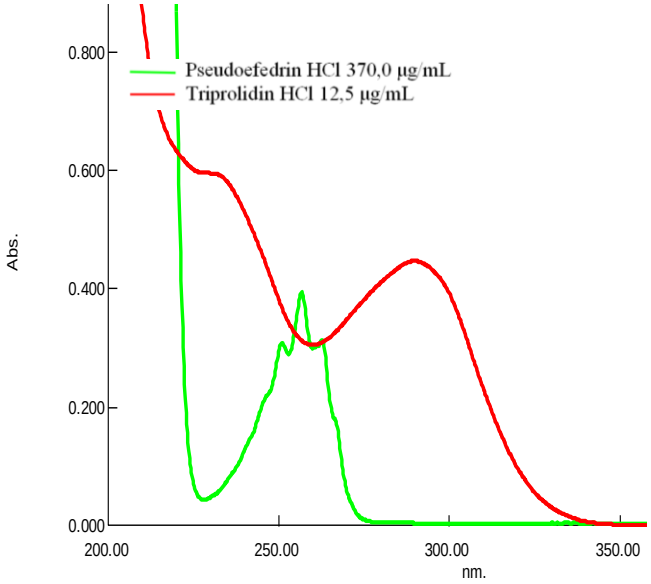

Figure5 Overlapping absorption spectrum of PSE (concentration of 370.0 ug / ml) and TRI (concentration of 12.5 µg/mL)

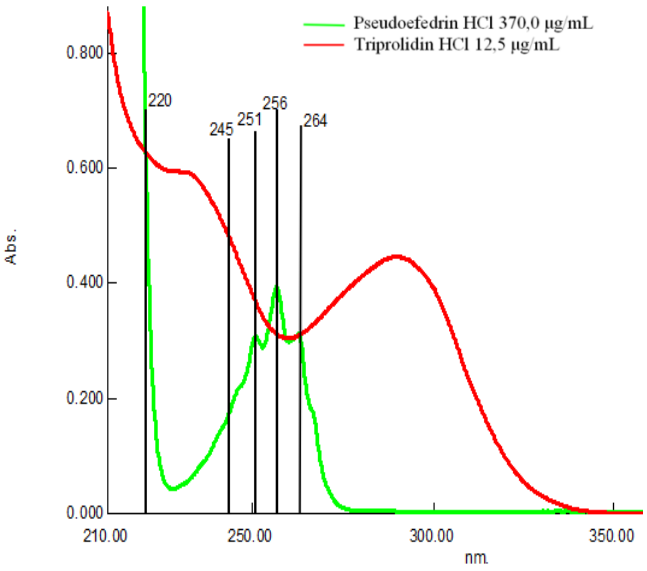

Figure 6. Five point of wavelength to determination PSE and TRI by multiple wavelength

3.4 Determinations Absorbance Spectrum of Multiple Wavelength

Absorption spectrum PSE and TRI with various concentrations in 0.1N HCl solution showed that the concentration, does not change the shape of the spectrum of each substance and purity of the substance being measured, so that it can be said solvent 0.1N HCl can be used in the assay binary mixture.PSE has an absorption maximum at wavelengths of 251 and 256 nm and TRI at 290 nm. Both of these compounds have the wavelength difference is not too large so that absorption curve of each component of the overall overlapping multicomponent analysis can be performed by spectrophotometry ultravioletwith multiple wavelength applications. The absorbance value is a value that indicates how big the contributions of a substance absorbance to the mixture at particularry wavelength[12].

Based on Figure 6.it can be determined five points wavelength to be used. Wavelength selection based on the wavelength of absorption to barely give uptake, where absorbance fulfill Lambert and BeerLawwhich is 0.2 to 0.8[15]. Five points wavelength used are 220 nm, 245 nm, 251 nm, 256 nm and 264 nm.At a wavelength 220 nmis the point of intersection of both uptake, ata 245 nm PSE and TRI was equally provide absorption is large enough.At a251nmand 256 nm is maximum absorption for PSE andat a 264 nm is the wavelength of PSE still leave a smaller uptake and TRI still provide a sizeable uptake. The absorbance spectrum of PSE and TRI can be seen at Table 1 and Table 2.

Table 1. The absorbance spectrum of PseudoepedrineHydrocloride

Concentration µg/mL	**λ1**	**λ2**	**λ3**	**λ4**	**λ5**
	220 nm	**245 nm**	**251 nm**	**256 nm**	**264 nm**
180	0.507	0.115	0.165	0.196	0.142
250	0.630	0.136	0.207	0.253	0.182
320	0.768	0.175	0.269	0.326	0.231
390	0.904	0.236	0.356	0.424	0.300
460	0.999	0.255	0.387	0.471	0.339
	a = 0.00217	a = 0.00056	a = 0.00086	a = 0.00104	a =0.00074
	b = 0.0567	b = -0.0029	b = -0.0017	b = -0.0013	b =-0.0014
	r = 0.9913	r = 0.9944	r = 0.9965	r = 0.9981	r =0.9984

Table 2. The Absorbance Spectrum of Tripolidine Hydrocloride

Concentration µg/mL	λ1 220 nm	λ2 245 nm	λ3 251 nm	λ4 256 nm	λ5 264 nm
7.5	0.450	0.324	0.264	0.227	0.212
10.5	0.574	0.407	0.331	0.285	0.273
13.5	0.715	0.507	0.408	0.353	0.342
16.5	0.882	0.631	0.509	0.438	0.427
19.5	1.036	0.738	0.593	0.512	0.501
	a = 0.05238	a = 0.03730	a = 0.02995	a = 0.02585	a =0.02540
	b = 0.0203	b = 0.0149	b = 0.0139	b = 0.0117	b = 0.0067
	r = 0.9985	r = 0.9952	r = 0.9978	r = 0.9979	r =0.9990

The used absorbance value (a) can be determine based on the price of (r) count, and then, (r) count value compared with (r) table with a level of 95% is 0.8114.Based on these data it appears that the value of r count of PSE and TRI is greater than the value of (r) table.This means that the equation has good linearity, because the value of (r) count ranges with values $-1 \leq r \leq 1$[12].

3.5 Determination of Levels, Coefficient of Variation, and Acuracyof Pseudoephedrine Hydroclorideand Triprolidine Hydrocloride in Tablet.

Data absorbance of the sample solution that has been obtained at a wavelength220 nm, 245 nm, 251 nm, 251 nm and 264 nm are used to calculate the levels of each, by entering the data available on the matrix calculation formula. Then from the calculation will be obtained by concentration of each component thereof to the accuracy of the results of the matrix and the coefficient of variation (CV).

Accuracy of matrix calculations are used to determine the accuracy of an analytical method while the coefficient of variation (CV) is used to determine the precision of an analytical method. The accuracy of an analytical method for the drug substance with low concentrations considered good when the value range between 90-107% accuracy, while an analytical method is said to have good

precision if the coefficient of variation (CV) 2%[15-16].

Matrix calculation of PSE and TRI in T Tablet, for example sample preparation number one:

$$\begin{pmatrix} C1 \\ C2 \end{pmatrix} = \left[\begin{pmatrix} 0.00219 & 0.0006 & 0.00089 & 0.00107 & 0.00076 \\ 0.05215 & 0.03728 & 0.02986 & 0.02577 & 0.02539 \end{pmatrix} \begin{pmatrix} 0.00219 & 0.05215 \\ 0.0006 & 0.03728 \\ 0.00089 & 0.02986 \\ 0.00107 & 0.02577 \\ 0.00076 & 0.02539 \end{pmatrix} \right]^{-1} \begin{pmatrix} 0.00219 & 0.0006 & 0.00089 & 0.00107 & 0.00076 \\ 0.05215 & 0.03728 & 0.02986 & 0.02577 & 0.02539 \end{pmatrix} \begin{pmatrix} 1.365 \\ 0.67 \\ 0.615 \\ 0.649 \\ 0.544 \end{pmatrix}$$

$$\begin{pmatrix} C1 \\ C2 \end{pmatrix} = \begin{pmatrix} 320.728785 \\ 12.31467773 \end{pmatrix}$$

Table 3. The result of the calculation of the levels and the coefficient of variation of PSE and TRI levels in the T tablet

Sample	PSE			TRI		
	Measurable levels (µg/mL)	Theoretical levels (µg/mL)	Accuracy of the results matrix (%)	Measurable levels (µg/mL)	Theoretical levels (µg/mL)	Accuracy of the results matrix (%)
1	320.73	315	101.82	12.315	13.125	93.82
2	326.94	318	102.81	12.774	13.25	96.40
3	314.30	312	100.73	12.759	13.00	98.14
4	322.14	315	102.27	13.382	13.125	101.95
5	323.09	318	101.60	13.166	13.25	99.35
6	321.73	315	102.13	12.113	13.125	92.28
Accuracy matrix results			101.90%	Accuracy matrix results		96.99%
%CV			0.5236	%CV		1.5472

Table 4. Level of PSE and TRI in T Tablet

No	Substances	T Tablet	Label claim/ tablet (mg)	Requirement (%)
1	PSE	(101.90 ± 0.52)% (60.82-61.45) mg	60	90-110
2	TRI	(96.99 ± 1.55) % (2.38-2.46) mg	2.5	90-110

Based from Table 3 and Table 4 can be seen that the levels of PSE and TRI in tablets are not less than 90.0% and notmore than 110.0% of the amount listed on the label[1]. The coefficient of variation (CV) obtained in PSE and TRI is 0.5236 and 1.5472 respectively. It means having a good precision.

Table 5. Several studies on the assay of PSE and TRI

	References[5]	References[6]	This work
Methods	***zero crossing***	***zero crossing***	**multiple wavelength**
Solvent	**Aquadest**	**0.1 N HCl**	**0.1 N HCl**
Wavelength	PSE at 227.6 nm, TRI at 230 nm	PSE at 271 nm, TRI at 318 nm	220 nm, 245 nm, 251 nm, 256 nm, and 264 nm
Level of PSE	(97.39 ± 0) %	(99.3 ± 1.72)% 58,50-60,57 mg	(101.90 ± 0.52)% 60.82-61.45 mg
Level of TRI	(96.32 ± 1.19)%	(93.78 ± 0.89)% 2.32-2.36 mg	(96.99 ± 1.55)% 2.38-2.46 mg

4. Conclusion

Based on this research, it can be concluded that multiple wavelength ultraviolet spectrophotometric method with matrix calculation can be used to determination binary mixture of PSE and TRI. The level of PSE and TRI in T Tablet were (101.90 ± 0.52)%and(96.99 ± 1.55)%respectively is meets the requirements are listed in the USP 30[1] . The proposed method is simple, rapid, low cost and can be applied successfully to assay simultaneously of binay mixture.

5. References

1. United State Pharmacopeia (USP). The National Formulary. 30th edition. The United States Pharmacopoeia Convention. 2007. 3426.
2. Nurhidayati, L. Spectrophotometric Derivative and Its Application in Pharmaceutical Sector. *Journal of Pharmaceutical Sciences* Indonesia. 2007. 5 (2): 93-99.
3. Sinaga, S.M., Tarigan, T.O, and Muclisyam. Determination of Mixture of Theophylline and Ephedrine Hydrocloride in Tablets by Derivative Spectrophotometric Method. *International Journal of PharmTech Research*. 2015: vol. 8(6): 273-283.
4. Shailendra, B., Shravan, B., and Deepti, J., Simultaneous Determination of Nitazoxanide and Ofloxacin in Tablet by Ultraviolet Spectrophotometry (Dual Wavelength Method).*International Journal of ChemTech Research*. 2010: vol. 2(1): 11-15.
5. Hayun, Harianto, and Yenti. Simultaneous Determination of Triprolidine HCl and Pseudoephedrine HCl as Anti-influenza Tablet by Derivative Spectrophotometry. *Majalah Ilmu Kefarmasian*. 2006: 1(3): 94-105.
6. Dongoran, R., A. Simultaneous Determination of Pseudoefedrine Hydrocloride and Triprolidine Hydrochloride in Tablet by Zero Crossing Derivative Spectrofotometry Method. Thesis. Medan. Faculty of Pharmacy. University of North Sumatera. 2011.
7. Vivek, M. P., Jigar A. P., Shweta S. H., Sunil, R. D.First and Second Derivative Spectrophotometric Methods For Determination of Olanzapine in Pharmaceutical Formulation. *International Journal of ChemTech Research*. 2010: vol. 2(1): 756-761.
8. Madhuri D.Game and D. M. Sakarkar. Quantitative Analysis for Clopidogrel Bisulphate and Aspirin by Second Derivative Spectrophotometric Method in Pharmaceutical Preparation. *International Journal of ChemTech Research*. 2010: vol. 2(4): 1886-1891.
9. Manzoor Ahmed, Maanasa Rajan.B.N., Sathish Kumar Shetty A, Rajesh.M. Zero order and First order Derivative Spectrophotometric methods for determination of Cisapride in Pharmaceutical Formulation. *International Journal of ChemTech Research*. 2011: vol. 3(3): 1020-1024.
10. Swati, D. A Stability indicating First Order Derivative Spectroscopic Method development and Validation for Estimation of Pioglitazone. *International Journal of PhramTech Research*. 2014: vol. 6(2): 468-475.
11. Bhavini, N., Chaganbhai, N. P., Nisha, B. P., Development and Validation of First Order Derivative Spectroscopic Method for Content Uniformity for Simultaneous Estimation of Ebastine and Phenylephrine Hydrochloride in Combined Tablet Dosage Form. *International Journal of PhramTech Research*. 2014: vol. 6(2): 537-545.
12. Zainuddin, M. Application of Multiple Wavelength Multicomponents Analysis to The Mixtutre Spectrofotometrycally of Phenylbutazone and Methampirone. *Indonesian Pharmacy Magazines*. 1999.10(4). 217-218.
13. Adrianto, Y.C. Validation of Ultraviolet Spectrofotometry Method with Multiple Wavelength for Determination of Mixture of Paracetamol and Ibupropen. Thesis. Yogyakarta: Faculty of Pharmacy University Sanata Dharma. 2009.
14. Muchlisyam, Sinaga, S.M., Haro, G. Two Novel Ultraviolet Spectrofotometry Method for Determination Binary Mixture of Isoniazid and Rifamficin in Tablet Dosage Form. *International Journal of PharmTech Research*. 2016. Vol.9(8).301-312.
15. Day, RA., and Underwood, AL. *Quantitative Analysis* Sixth Edition. Translator: Sopyan, L. (2002). Analysis of Quantitative Chemical Sixth Edition. Jakarta: Publisher.1998. 419.
16. Ermer, J., and McB. Miller, J.H. *Method Validation in Pharmaceutical Analysis, A Guide to Best Practice*. Weihheim: Wiley-Vch Verlag GmbH&Co. KgaA. 2005: 99.

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