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Simultaneous Estimation of Aspirin and Lansoprazole in Synthetic Mixture by Q-Absorption Ratio Method And dual Wavelength Method

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ABSTRACT

Simple, rapid, accurate, precise and economical UV-spectrophotometric methods have been developed and validated for simultaneous estimation of Aspirin and Lansoprazole in a Synthetic mixture. The first method is the Q-Absorption ratio method, which involves formation of Q-absorption equation at 299.2 nm (isoabsorptive point) for Aspirin and Lansoprazole and also at 276.6 nm (λmax of Aspirin). The Second method is Dual Wavelength Method. The method was based on determination of Aspirin at the absorbance difference between 272.28 nm and 286.41 nm and Lansoprazole at the absorbance difference between 269.20 nm and 294 nm. Developed methods were validated according to ICH Q2 (R1) guidelines. The methods were found to be linear between the range of 33.3-166.6 µg/ml for Aspirin and 5-25µg/ml for Lansoprazole for both methods. The precision (intra-day, inter-day) of methods were found within limits (RSD <2%). Accuracy was determined by recovery studies and showed % recovery between 98 to 102%.

Keywords : Aspirin and Lansoprazole, Synthetic mixture, Spectrophotometric methods.

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INTRODUCTION[1, 2, 3]

Aspirin, 2-(acetyloxy)benzoic acid, (Figure 1), acts as an inhibitor of cyclooxygenase which results in the inhibition of the biosynthesis of prostaglandins. It also inhibits platelet aggregation and is used in the prevention of arterial and venous thrombosis. Aspirin is official in IP, BP, and USP. Acetylsalicylic acid is an analgesic, antipyretic, antiplatelet, antirheumatic, and anti-inflammatory agent. Lansoprazole, chemically known as 2-([3-methyl-4-(2,2,2-trifluoroethoxy)pyridin-2-yl]methylsulfinyl)-1 *H*-benzimidazole, is a strong anti-secretory agent that acts on gastric H^+/K^+ ATPase of parietal cells. It is used to treat ulcers, gastroesophageal reflux disease and peptic ulcer caused by stress, non-steroidal inflammatory disease. In addition to its acid-suppressing effects, Lansoprazole has been shown to modulate the inflammatory status, oxidative stress and ameliorate mucosal injuries in the esophagus, intestine and lungs.

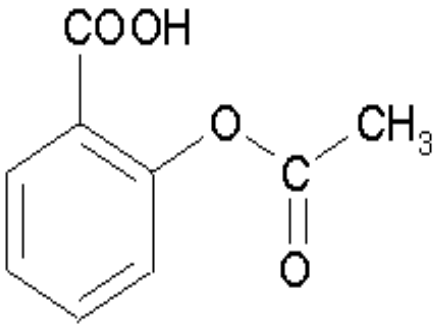


Figure 1 : Structure of Aspirin

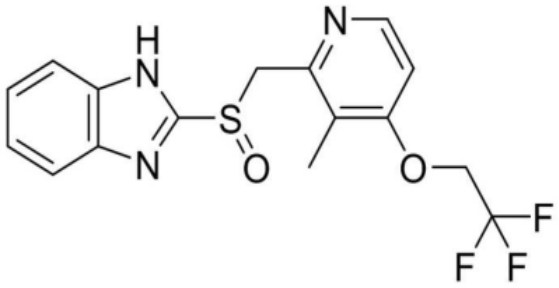


Figure 2 :Structure of Lansoprazole

Aspirin is used to prevent the thrombus and embolism, the recurrence of cerebral infarction or myocardial infarction or treatment of rheumatoid arthritis and osteoarthritis in low-dose. Due to longer use of Aspirin, there is possibility of the onset of ulcer. So, to prevent inflammation and to prevent gastric or duodenal ulcer administration of Aspirin in low dose and Lansoprazole in high dose is given in one combination. So, combination of these two drugs shows synergic effect. Based on literature survey it is found that various analytical methods like UV spectroscopy, High Performance Thin Liquid Chromatography (HPTLC), Reverse Phase High performance Liquid Chromatography (RP–HPLC), Liquid Chromatography and Mass Spectroscopy (LC-MS) have been reported for the determination and estimation of as Aspirin individual drug and combination with other drug. Similarly, various methods like RP-HPLC, HPTLC, UV spectroscopy were reported for the analysis of Lansoprazoleas individual drug and in combination with other drug. But, No method was reported for selective estimation of these two drugs in combination. Therefore, it is a thought of interest to develop simple, accurate and precise methods for the simultaneous estimation Asprin and Lansoprazole in combination.

MATERIALS AND METHOD

A Double Beam U.V. Spectrophotometer (UV-1800, Shimadzu) having two matched quartz cells with 1 cm light path, 1.8 mm bandwidth and 2 mm wavelength accuracy was used to measure absorbance of the resulting solutions. Aspirin and Lansoprazole sample were received as a gift sample by West-coast Pharma, Ahmedabad, Gujarat. Solvent Methanol (AR Grade) was used in the study. All chemicals and reagents of analytical grade were used.

Selection of solvent

Aspirin is soluble in Methanol, Acetonitrile and Chloroform. Lansoprazole is also soluble in Methanol, Acetonitrile, Chloroform. Both the drugs are freely soluble in Methanol. So, Methanol was used as a Solvent for estimation of Aspirin and Lansoprazole.

- **Preparation of Standard solutions and Synthetic mixture:**

For Stock solution of Aspirin: Accurately weigh 100 mg of Aspirin and transferred in to a 100 ml volumetric flask and diluted with Methanol (1000 µg/ml).

For Stock solution of Lansoprazole: Accurately weigh 10 mg of Lansoprazole and transferred in to a 100 ml volumetric flask and diluted with Methanol (100µg/ml).

- **Preparation of synthetic mixture of Aspirin and Lansoprazole:**

  Dosage Form: 100 mg Aspirin

  15 mg Lansoprazole

The synthetic mixture of Aspirin and Lansoprazole was prepared in the ratio 6.66:1. Accurately weighed Aspirin(66.66 mg) and Lansoprazole (10mg) were transferred in 100 ml volumetric flask and dissolved in Methanol (70 ml). Common excipients like, Lactose, Corn starch, Hydroxyl Propyl Methyl cellulose, Talc were added in this mixture and sonicated for 20 mins. This solution was filtered through Whatman filter papers(0.45µm)and residue was washed thoroughly with Methanol. The filtrate and washing were combined and diluted to the mark with Methanol to get solution of Aspirin(66.66 µg/ml) and Lansoprazole (100 µg/ml).

- **Preparation of sample solution**

Synthetic mixture (3.3 ml) was taken in to a 10 ml volumetric flask and the volume was adjusted up to mark with Methanol to get a final concentration of Aspirin (66.6 µg/ml) and Lansoprazole (10 µg/ml).

- **Selection of Analytical wavelength**

Method I (Q- Absorption ratio method)

The solution of Aspirin was prepared in Methanol by pipette out 0.9 ml from the stock solution (1000µg/ml) in10ml volumetric flask and dilute upto the mark with Methanol.(99.99 µg/ml).and scanned in the wavelength range of 200-400 nm. Lansoprazole was also prepared in Methanol by pipetting out 1.5 ml from stock solution (100 µg/ml) in10ml volumetric flask and dilute upto the mark with Methanol (15 µg/ml).and scanned in the wavelength range of 200-400 nm. Two wavelengths were selected, from the overlain spectrum of Aspirin and Lansoprazole: one Wavelength at 299.2 nm which is the isoabsorptive point for both drugs and the other λ max at 276.6 nm which is λmax of Aspirin. The method employs Q-values and the concentration levels of drugs in sample solution were determined by using the following formulae:

$$Cx = \frac{Qm - Qy}{Qx - Qy} * \frac{A}{ax}, Cy = \frac{Qm - Qx}{Qy - Qx} * \frac{A}{ay}$$

Where,

Cx and Cy are concentration of Aspirin and Lansoprazole respectively,

A = The absorbance of mixture at isoabsorptive point.

Qx = The ratio of absorptivity of Aspirin at 276.6 and 255.9 nm.

Qy = The ratio of absorptivity of Lansoprazole at 276.6 and 255.9 nm.

Qm = The ratio of absorbance of mixture at 255.9 nm and 276.6nm.

ax = The absorptivity value of Aspirin at isoabsorbtive point.

ay =The absorptivity value of Lansoprazole at isoabsorptive point.

Method II(Dual Wavelength Method)

The solution of Aspirin was prepared in Methanol by pipette out 0.9 ml from the stock solution (1000µg/ml) in10ml volumetric flask and dilute upto the mark with Methanol.(99.9 µg/ml).and scanned in the wavelength range of 200-400 nm. Lansoprazole was also prepared in Methanol by pipetting out 1.5 ml from stock solution (100 µg/ml) in10ml volumetric flask and dilute upto the mark with Methanol (15 µg/ml).and scanned in the wavelength range of 200-400 nm. For dual wavelength Method, the spectrum shows identical absorbance at 272.28 nm (λ1) and 286.413(λ2) therefore these two wavelengths were selected for the analysis of Aspirin. All the solutions of series A were scanned to ensure that the difference between λ1 and λ2 is zero. So these two wavelength selected for determination of concentration of Lansoprazole Similarly, the Lansoprazolesolutions were scanned to determine the two wavelengths, where absorbance is zero. These two wavelengths were found to be 294 nm (λ3) and 269.2 nm (λ4). All the solution of series B were scanned to ensure that difference between (λ1) and (λ2) is zero. So this two Wavelength selected for determination of concentration of Aspirin.

RESULTS AND DISCUSSION

Applicability of proposed methods was tested by analyzing the synthetic mixture of Aspirin and Lansoprazole.

- **Calibration curve for Aspirin and Lansoprazole:**

For Aspirin

An aliquots of stock solution of Aspirin (0.3,0.6,0.9,1.3,1.6 ml) were pipettes out from 1000 µg/ml stock solution in five different 10ml volumetric flasks and further diluted to attain concentration of about 33.3,66.6,99.9,133.3,166.6 µg/ml respectively.

Graph of Absorbance Vs Concentration was plotted for Method I

Graph of Absorbance Diff. Vs Concentration was plotted for Method II.

For Lansoprazole

An aliquots of stock solution of Lansoprazole(0.5, 1.0, 1.5, 2.0, 2.5 ml) were pipettes out in five different 10ml volumetric flasks and further diluted to attain concentration of about 5, 10, 15, 20, 25 µg/ml respectively.

Graph of Absorbance Vs Concentration was plotted for Method I

Graph of Absorbance Diff. Vs Concentration was plotted for Method II.

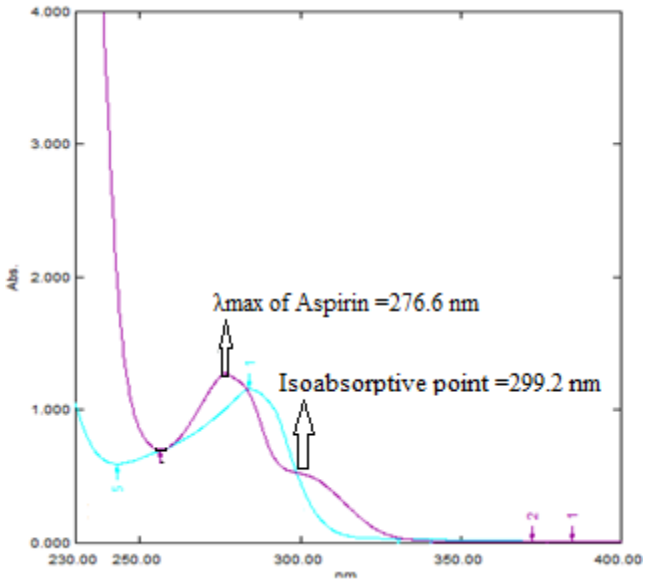


Figure 3 : Overlain Spectra of Aspirin (99.9 µg/ml) and Lansoprazole (15µg/ml), Method I.

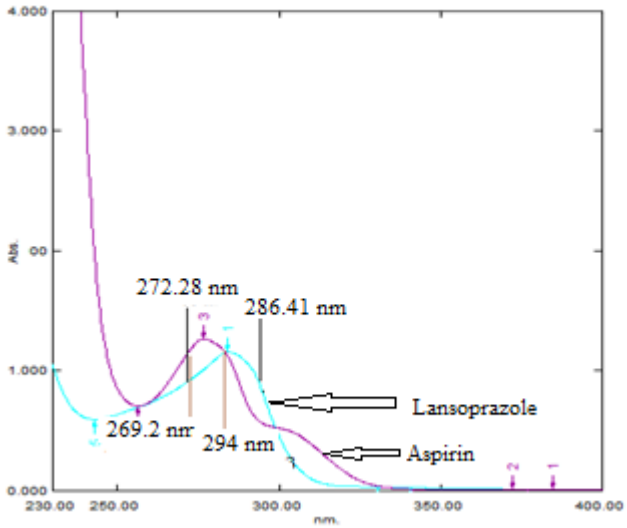


Figure 4: Overlain Spectra of Aspirin (99.99µg/ml) and Lansoprazole (15µg/ml), Method II.

Table 1: Calibration data for Aspirin :Method I

Aspirin (299.2 nm)			Aspirin (276.6 nm)		
Conc. (µg/ml)	**Mean Absorbance ± SD**	**% RSD**	**Conc. (µg/ml)**	**Mean Absorbance ± SD**	**% RSD**
33.3	0.142±0.0015	1.10	33.3	0.226± 0.0020	0.88
66.6	0.214± 0.0017	0.80	66.6	0.434± 0.0025	0.57
99.9	0.283± 0.0025	0.88	99.9	0.637± 0.0040	0.63
133.3	0.351± 0.0020	0.59	133.3	0.851± 0.0035	0.41
166.6	0.437± 0.0030	0.69	166.6	1.071± 0.0055	0.51

Table 2: Calibration data forLansoprazole, Method I

Lansoprazole (299.2 nm)			Lansoprazole (276.6 nm)		
Conc. (µg/ml)	**Mean Absorbance ± SD**	**% RSD**	**Conc. (µg/ml)**	**Mean Absorbance ± SD**	**% RSD**
5	0.080±0.0006	0.79	5	0.170± 0.0010	0.61
10	0.177± 0.0011	0.64	10	0.357± 0.0026	0.74
15	0.255± 0.0015	0.59	15	0.512± 0.0030	0.59
20	0.332± 0.0025	0.75	20	0.711± 0.0032	0.45
25	0.423± 0.0022	0.52	25	0.869± 0.0045	0.51

Table 3: Calibration data for Aspirin and Lansoprazole, Method II

Aspirin			Lansoprazole		
Conc. (µg/ml)	**Absorbance Diff.(294-269.20 nm)± SD**	**% RSD**	**Conc. (µg/ml)**	**Absorbance Diff.(286.41-272.28 nm)± SD**	**% RSD**
33.3	0.047± 0.0005	1.21	5	0.070± 0.0005	0.82
66.6	0.267± 0.0020	0.74	10	0.145± 0.0011	0.79
99.9	0.464± 0.0025	0.54	15	0.222± 0.0020	0.93
133.3	0.713± 0.0057	0.80	20	0.295± 0.0026	0.89
166.6	0.934± 0.0056	0.60	25	0.375± 0.0032	0.85

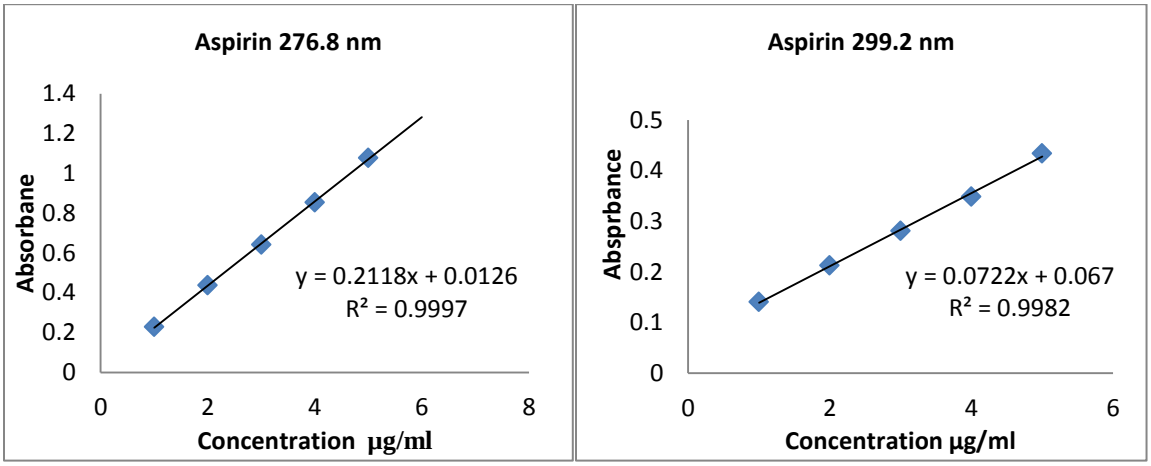


Figure 5 : Calibration curve of Aspirin (Method I)

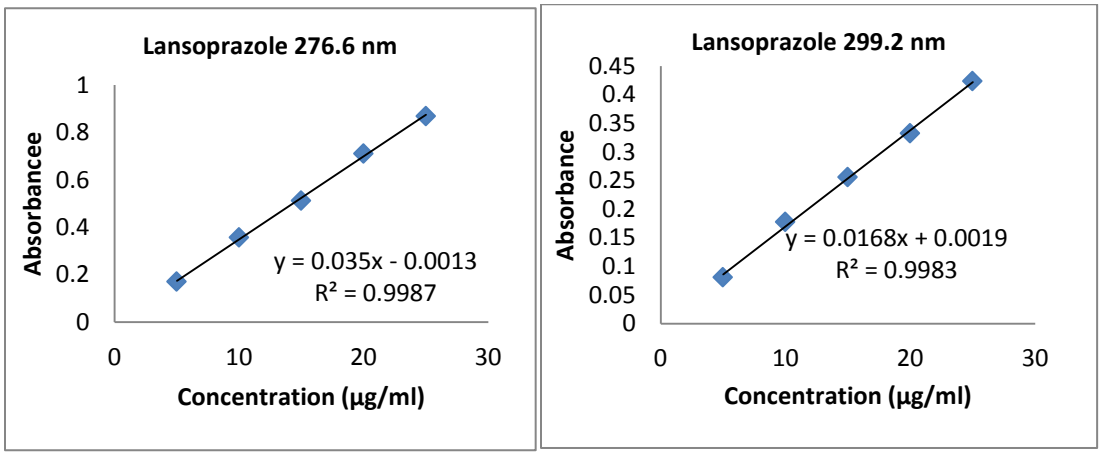
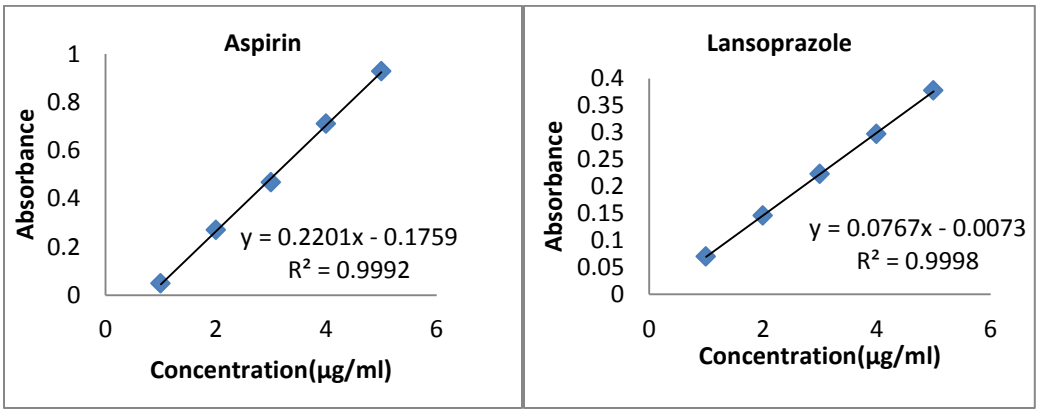


Figure 6 : Calibration curve of Lansoprazole(Method I)



(A) **(B)**

Figure 7 :A. Calibration Plot of Aspirin at Difference of absorbance between 269.20 nm And 294 nm.

B. Calibration Plot of Lansoprazoleat Difference of absorbance between 272.28and286.41 nm .(Method II)

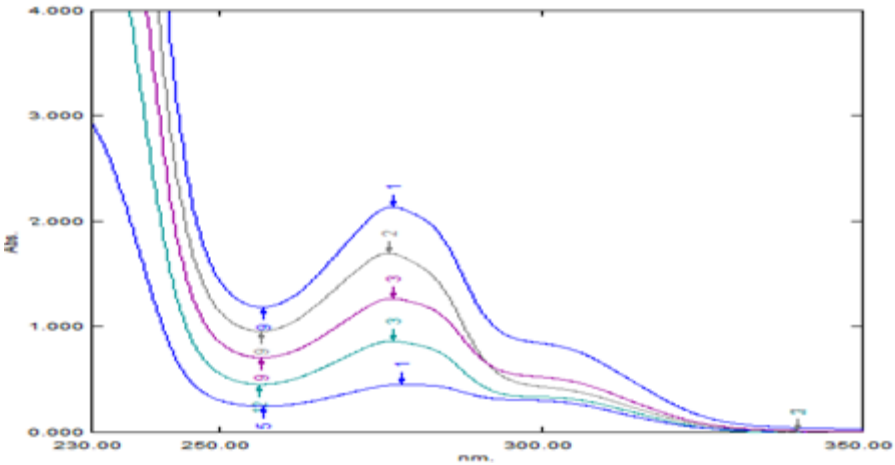


Figure 8: Overlain Spectra ofAspirin (33.3-166.6µg/ml)

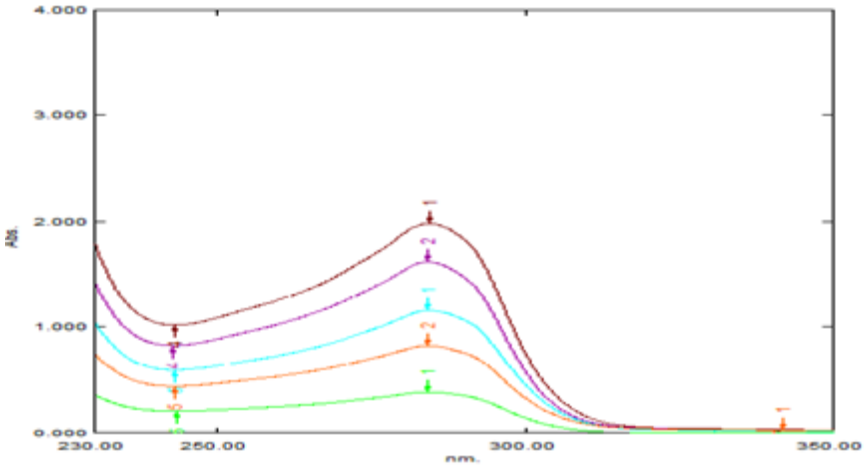


Figure 9: Overlain Spectra of Lansoprazole (5-10 µg/ml).

Method Validation[4]

Validation of the analytical method is the process that establishes by laboratory studies in which the performance characteristics of the method meet the requirements for the intended analytical application. UV spectrophotometric method developed was validated according to International Conference on Harmonization (ICH) guidelines for validation of analytical procedures. The methods were validated for the parameters like linearity, accuracy, system precision, intra-day precision, inter-day precision/ intermediate precision/ ruggedness, robustness, limit of detection(LOD) and limit of quantitiation (LOQ).

Accuracy

To determine the accuracy of the proposed method, recovery studies were carried out by standard addition method. Different amounts (80%, 100%, and 120%) from standard mixture of Aspirin and Lansoprazole within the linearity range were taken and added to the pre-analyzed synthetic

mixture of concentration 100 µg/ml Aspirin and 15µg/ml Lansoprazole. From that percentage recovery values were calculated.

Table 4: Accuracy Data

Table 4: Accuracy Data

Drug name	Level of addition	Amount spiked (µg/ml)	Total amount (µg/ml)	Total amount obtained (n=3) ±SD		% Recovery±SD	
				Method I	Method II	Method I	Method II
Aspirin (66.6 µg/ml)	80 %	53.2	119.8	120.39± 0.52	119.53± 0.85	100.49% ±0.43	99.77%± 0.71
	100 %	66.6	133.2	134.2± 0.99	133.50± 0.88	100.75% ±0.70	100.22%± 0.66
	120 %	79.9	146.5	147.20± 0.65	146.8± 0.70	100.48% ±0.44	100.20%± 0.54
Lansoprazole (10 µg/ml)	80 %	8	18	18.30± 0.19	18.26± 0.03	100.31 %±0.56	101.66%± 0.55
	100 %	10	20	20.13± 0.24	20.1± 0.26	100.28% ±0.81	101.00%± 0.50
	120 %	12	22	22.96± 0.12	21.96± 0.26	101.34% ±0.54	99.84%± 0.94

Precision

The precision of a method is defined as the closeness of agreement between independent test results obtained under optimum conditions. Three different concentrations of Aspirin and Lansoprazolein the linear range were analyzed in 3 independent series in the same day (intra-day precision) and 3 consecutive days (inter-`day precision). The precision of the analysis was determined by calculating the relative standard deviation (RSD %).

Table 5: Repeatability Data(n=6) : Method I

Drug Name	Aspirin	Lansoprazole
Concentration	99.9 µg/ml	15µg/ml
MEAN±SD(n=3)	0.283± 0.0025	0.254± 0.0013
%RSD	0.91	0.52

Table 6: Repeatability Data (n=6) :Method II

Drug Name	Aspirin	Lansoprazole
Concentration	99.9 µg/ml	15 µg/ml
MEAN±SD(n=3)	0.470± 0.0017	0.226± 0.0011
%RSD	0.36	0.50

Table 7 : Intraday Precision Data (n=3) : Method I

Aspirin			Lansoprazole		
Conc. (µg/ml)	**Mean Absorbance ± SD**	**% RSD**	**Conc. (µg/ml)**	**Mean Absorbance ±SD**	**% RSD**
33.3	0.142± 0.0015	1.07	5	0.081± 0.0010	1.23
99.9	0.283± 0.0030	1.05	15	0.256± 0.0020	0.80
166.6	0.437± 0.0036	0.82	25	0.424± 0.0025	0.59

Table 8 : Intraday Precision Data (n=3) : Method II

Aspirin			Lansoprazole		
33.3	**Mean Absorbance ± SD**	**% RSD**	**Conc. (µg/ml)**	**Mean Absorbance ±SD**	**% RSD**
99.9	0.047± 0.0005	1.21	5	0.071± 0.0010	1.40
166.6	0.470± 0.0040	0.85	15	0.226± 0.0026	1.17
	0.934± 0.0065	0.69	25	0.381± 0.0035	0.92

Table 9:Interday Precision Data(n=3) :Method I

Aspirin			Lansoprazole		
Conc. (µg/ml)	**Mean Absorbance ± SD**	**%RSD**	**Conc. (µg/ml)**	**Mean Absorbance ± SD**	**% RSD**
33.3	0.143± 0.0020	1.45	5	0.081± 0.0015	1.87
99.9	0.284± 0.0040	1.41	15	0.256± 0.0022	0.88
166.6	0.439± 0.0055	1.25	25	0.425± 0.0035	0.82

Table 10:Interday Precision Data (n=3) : Method II

Aspirin			Lansoprazole		
Conc. (µg/ml)	**Mean Absorbance ± SD**	**% RSD**	**Conc. (µg/ml)**	**Mean Absorbance ± SD**	**% RSD**
33.3	0.048± 0.0008	1.65	5	0.071± 0.0011	1.54
99.9	0.472± 0.0055	1.16	15	0.227± 0.0036	1.58
166.6	0.938± 0.0097	1.03	25	0.381± 0.0047	1.23

Limit of Detection (LOD):

LOD was estimated from the set of calibration curves to determine method linearity.

LOD = 3.3 * S.D / Slope

Where,

S.D= Standard deviation of the Y intercept of calibration curve.

Slope = Mean slope of calibration curve.

Limit of Quantification (LOQ):

LOQ was estimated from the set of calibration curves to determine method linearity.

LOQ = 10 * S.D / Slope

Where,

S.D= Standard deviation of the Y intercept of calibration curve.

Slope = Mean slope of calibration curve.

Table 11:LOD and LOQ data of Aspirin and Lansoprazole : Method I

Drug Name	LOD (µg/ml)	LOQ (µg/ml)
Aspirin	0.229	0.695
Lansoprazole	0.117	0.356

Table 12: LOD and LOQ data of Aspirin and Lansoprazole: Method II

Drug Name	LOD (µg/ml)	LOQ (µg/ml)
Aspirin	0.104	0.315
Lansoprazole	0.09	0.269

Table 13 : Applicability to synthetic mixture Data

	Drug	Amount in synthetic mixture	Amount found(mg) (n=3) ± SD.		% Amount found± SD.	
Synthetic mixture			**Method I**	**Method II**	**Method I**	**Method II**
	Aspirin	100 mg	100.26± 0.50	99.86±0.66	100.26%±0.50	99.86%±0.66
	Lansoprazole	15mg	15.15± 0.007	14.93±0.15	100.98%±0.45	100.44%±1.01

RESULTS AND DISCUSSION

Aspirin and Lansoprazole are freely soluble in methanol. So, Methanol was selected for both the Methods for the estimation of Aspirin and Lansoprazole. The first method is the Q-Absorption ratio method, which involves formation of Q-absorption equation at 299.2 nm (isoabsorptive point) for Aspirin and Lansoprazole and also at 276.6 nm (λmax of Aspirin). The Second method is Dual Wavelength Method. The method was based on determination of Aspirin at the absorbance difference between 272.28 nm and 286.41 nm and Lansoprazole at the absorbance difference between 269.20 nm and 294 nm. The Methods were validated as per ICH Q2(R1) and found to be linear as for both the methods, R^2 value is not less than 0.99. The methods were found to be precise as %RSD for both the methods found to be < 2%. The methods were found to be accurate as %recovery 99.5- 100.9% for both the methods.

Table 14: Optical Regression Characteristics and Validation Parameters for Method I And Method II.

Sr. No.	Parameters	Method I Aspirin	Lansoprazole	Method II Aspirin	Lansoprazole
1	Wavelength (nm)	299.2 nm, 276.6 nm	299.2 nm, 276.6 nm	272.28 nm,286.4 nm	269.20 nm, 294 nm
2	Beer's Law Limit (µg/ml)	33.3-166.6	5-25	33.3-166.6	5-25
3	Regression equation	y = 0.211x + 0.0126(276.6)	y = 0.035x - 0.0013(276.6)	y = 0.220x - 0.175	y = 0.076x - 0.007

	(y = mx +c)	y = 0.0722x + 0.067(299.2)	y = 0.0168x + 0.001 (299.2)		
6	Correlation Coefficient (r^2)	0.999, 0.992	0.998, 0.998	0.999	0.999
7	Repeatability (% RSD, n=6)	0.91	0.52	0.36	0.50
8	Interday (n=3) (% RSD) (µg/ml)	1.25-1.45	0.82-1.87	1.03-1.65	1.23-1.54
9	Intraday(n=3) (% RSD) (µg/ml)	0.82-1.05	0.59-1.23	0.69-1.21	0.92-1.40
10	LOD(µg/ml)	0.229	0.117	0.104	0.315
11	LOQ(µg/ml)	0.695	0.356	0.315	0.269
13	Accuracy	100.48-100.75%	100.32- 100.34%	99.77-100.22%	99.84-101.666%

Statistical Comparison

Table 15 : Result of compared Recovery study data by Student t-test

t- test Value (Between UV Method I and Method II)	Aspirin	Lansoprazole
t calculated	0.75	0.84
t tabulated	1.745	1.745
t-test 95% confidence interval ($p \leq 0.05$ &d.f = 4)		

Table 16 : Assay comparison by Paired t-test

t- test Value (Between UV Method I and Method II)	Aspirin	Lansoprazole
t calculated	0.92	0.19
t tabulated	2.131	2.131
t-test 95% confidence interval ($p \leq 0.05$ &d.f = 4)		

Statistical Comparison

Simultaneous estimation of Aspirin and Lansoprazole in synthetic mixture by Q-absorption ratio method and Dual wavelength method were developed and validated. For comparison, statistical test (Student t-test) was applied and it was found that the tabulated values were greater than calculated values. So, there was no significant difference between the Assay parameter obtained through Q-absorption ratio method and Dual wavelength method. The results indicate that both methods are equally sensitive, reliable and can routinely apply for Simultaneous estimation of Aspirin and Lansoprazole in synthetic mixture.

CONCLUSION

Simple, accurate, rapid and precise Q- Absorption Ratio and Dual Wavelength Method were developed and validated for simultaneous estimation of both these drugs. These methods developed in Methanol. The plot of absorbance versus respective concentration was found to be

linear in the concentration range of 33.33-166.66 µg/ml for Aspirin and 5-25 µg/ml for Lansoprazole respectively for both the methods. Accuracy of method was found between 98-101 %. The precision (intra-day, inter-day and repeatability) of method was found within limits. This method can be successfully applied for the simultaneous estimation of in Aspirin and Lansoprazole. This method can be successfully applied for the simultaneous estimation of Aspirin and Lansoprazole synthetic mixture.

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