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Development and validation of stability indicating RP-HPLC method for determination of aspirin and pantoprazole sodium in synthetic mixture stability indicating HPLC method

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ABSTRACT

The present study describes a new accurate and precise stability indicating reverse phase HPLC method for quantitative computation of pantoprazole sodium and Aspirin from physical simulated mixture. The proposed chromatographic method employs Hypersil ODS C18 column (250 x 4.6 mm, 5 μ) as the stationary phase and combination of methyl alcohol and water in ratio of 70: 30 v/v as the elution medium. Overall separation was carried out at 0.8 ml/minute flow rate and elution was monitored at 254 nm. The proposed system gave well resolved peak of Aspirin and Pantoprazole sodium with elution time of 2.32 and 5.85 minute respectively. Same system was effective in separation of active components and degradation products when the components were subjected to forced degradation as per regulatory guidelines (ICHQ1). Finally, the optimized method was successfully validated as per ICH Q2R1 guidelines and applied for quantitative analysis of both active components in synthetic mixture.

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1. Introduction

When we discuss about aspirin (ASP), it is chemically acetyl derivative of benzoic acid having wide spectrum of physiological action that includes anti-inflammatory, analgesic and direct platelet aggregation inhibitory action. Previous actions are mediated through inhibition of cyclooxygenase pathways.¹ Currently it is having legal status in Indian Pharmacopeia (IP), British Pharmacopeia (BP) and United State Pharmacopeia (USP). Extensive literature search highlights majorly UV spectroscopy,²⁻⁵ HPLC⁶⁻⁸ and HPTLC⁹⁻¹¹ as analytical methods for analysis of Aspirin from bulk and pharmaceutical dosage form.

On contrast, pantoprazole sodium (PAN) is benzimidazole derivative which preliminary decrease the gastric acid secretion by suppressing Na⁺/K⁺ ATP pump that is again having legal status in Indian Pharmacopeia (IP) and United State Pharmacopeia (USP).¹² Detailed literature review revealed UV,¹³⁻¹⁶ HPLC^{17,18} and HPTLC¹⁹⁻²¹ method for determination of Pantoprazole sodium in bulk and pharmaceutical dosage form.

At present, the proposed combination of pantoprazole sodium and aspirin is in clinical phase III and trials have been initiated by Alkem laboratories at clinical dose level of 20 mg and 80 mg respectively and it has been rationalized that co-administration of pantoprazole sodium enhances antiplatelet aggregation activity and decrease associated gastrointestinal complication like ulcers.

At present there is no analytical method available for determination of Aspirin and pantoprazole and hence it

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was decided to develop and validate a new, simple, precise and accurate, stability indicating RP-HPLC method for determination of ASP and PAN in synthetic mixture. Simulated mixture, which actually resembles to the formulation was used, as commercial formulation is not available in the market because of phase III trial (i.e., encapsulation of all contents in the hard gelatine capsules in required proportion). The dose of Pantoprazole and Aspirin was decided as per disclosure made in clinical trial initiated by Alkem laboratories.²²

2. Materials and Methods

2.1. Materials

Both active components ASP (99.46% w/w) and PAN (99.67% w/w) were received as gift samples from to RMS Scientific services, Anand Gujarat. while other solvents like methyl alcohol and water were of HPLC grade and procured from Merck life sciences private limited, Mumbai. Hard gelatin shells were procured purchased from shashwat herbal, Anand, Gujarat. Inactive agents used in the study are selected as per IIG limits and were available at the institute level. Other chemicals like hydrogen peroxide, HCl and NaOH were also available at institute level.

2.2. Instrument and experimental conditions

Shimadzu 20ATVp HPLC unit equipped with autosampler having provision of UV-VIS detector and capable of quaternary gradient operation was used to process the samples, while LC Solution® software was used to process and integrate the obtained chromatogram. Hypersil ODS C18 column (250 x 4.6 mm, 5 μ) was employed as analytical column. Mettler Toledo weighing balance was used to weigh accurate quantities of samples having sensitivity of 0.1 mg. All the solutions were sonicated by using sonicator having make of Labtronik.

2.3. Optimization of chromatographic conditions

For optimizing separation, initially working solutions of ASP and PAN were prepared at concentration of 10 μ g/ml in methyl alcohol owing to similar solubility in that solvent. For method development purpose 254 nm was selected as analytical wavelength as both the components possess significant absorbance at that wavelength. When the components were handled on Hypersil ODS C18 column (250 x 4.6 mm, 5 μ) as the separation phase and combination of methyl alcohol and water in ratio of 70: 30 on volume basis as the elution medium at flow rate of 0.8 ml/minute, well resolved peak of both the actives were observed. So, for this purpose isocratic mode on former conditions was preferred. All the system suitability parameters (SSTs) were observed on above mentioned chromatographic condition.

3. System Suitability Parameters

The applicability of optimized condition was further assessed by system suitability testing. The same was executed by chromatographing standard mixture having concentration of 24+6 μ g/ml of ASP and PAN for five times and parameters like resolution (Rs), elution time (Tr), number of theoretical plates (N) and tailing factor (T) were monitored with associated relative standard deviation.

4. Preparation of Solutions for Forced Degradation Studies

4.1. Acid induced hydrolysis

Accurately weighed amount corresponding to 80 mg of ASP and 20 mg of PAN were transferred to 50 ml volumetric flask and volume of same was raised to the mark with 50 ml 0.1 N HCl. Same solution was heated under refluxed condition at 80°C for 1 hour. After any loss was compensated by addition of 0.1 N HCl. 1.5 ml of previously cooled solution was transferred to 10 ml volumetric flask and 5 ml diluent (mobile phase) was added. The same contents were neutralized with 1 M NaOH and volume was raised to mark with diluent. 1 ml of previous solution was further diluted to 10 ml with diluent. The resulting solution have concentration of 24 μ g/ml of ASP and 6 μ g/ml of PAN (Treated sample). In similar way 0 hour sample (Only difference was heating condition was not provided) and blank (Only difference is there is no addition of API) were prepared. % Degradation of both components was calculated by comparing area of treated sample and control.

4.2. Base induced hydrolysis

Same amount of API like in former case were transferred to 50 ml volumetric flask and volume of same was raised to the mark with 50 ml 0.1 N NaOH. Same solution was heated under refluxed condition at 80°C for 1 hour. After any loss was compensated by addition of 0.1 N HCl. 1.5 ml of previously cooled solution was transferred to 10 ml volumetric flask and 5 ml diluent (mobile phase) was added. The same contents were neutralized with 1 M HCl and volume was raised to mark with diluent. 1 ml of previous solution was further diluted to 10 ml with diluent. The resulting solution have concentration of 24 μ g/ml of ASP and 6 μ g/ml of PAN (Treated sample). In similar way 0 hour and blank sample were prepared. % Degradation of both components was computed by comparing area of treated sample and control.

4.3. Hydrogen peroxide induced stress (Oxidative)

Same amount like in acid and base hydrolysis were subjected to oxidative stress by exposing them to 50 ml of 1% H₂O₂ and the contents were refluxed at 80°C for 1 hour. 1.5 ml of previously cooled solution was transferred

to 10 ml volumetric flask and 5 ml diluent was added. 1 ml of previous solution was further diluted to 10 ml with diluent. In similar way 0 hour and blank sample were prepared. % Degradation of both components was computed by comparing area of treated sample and control.

4.4. Thermal stress

Exact quantity of ASP and PAN like in previous cases were transferred to petri dish and exposed to 80 °C for 3 hours in hot air oven and residues were reconstituted with help of methyl alcohol and transferred into 50 mL volumetric flask and volume of flask was raised with the mark with same solvent. 1.5 ml of resulting solution was diluted to 10 ml with diluent and 1 ml of resulting solution was further diluted to 10 ml with diluent. Above solution was chromatographed and % degradation was computed by comparing against standard concentration of PAN and ASP.

5. Preparation of Solutions for Analytical Method Validation

5.1. Preparation of solution for linearity and range

To study linearity and range, accurately weighed quantities of 20 mg PAN and 80 mg ASP was diluted to 100 ml with diluent to produce stock solution containing 200 µg/ml PAN and 800 µg/ml of ASP. Various aliquotes were transferred to 10 ml volumetric flask and volume of each raised to 10 ml to give mixtures having concentration of 8-40 µg/ml to 2-10 µg/ml of ASP and PAN respectively. Each concentration was injected at 20 µl injector volume and response obtained was plotted against concentration to observe linear regression coefficient.

5.2. Intermediate precision (Repeatability)

For adjudging repeatability of method, solution of linearity studies were analyzed 5 times and each level is observed for relative standard deviation (RSD).

5.3. Method precision

This parameter was studied by injecting individual concentration that represents overall range are studied on same day and between days and for the same Mixture of ASP and PAN that represents overall range (8+2,16+4 and 24+6 µg/ml) were analyzed on same day at different time interval for Intraday precision and different day for Interday precision. Each concentration was analyzed for three times and was monitored for RSD at each level.

5.4. Accuracy study

As it refers to the % recovery of analyte in presence of excipients, it was practiced by spiking of placebo with standard at 50, 100 and 150% of target concentration.

Each concentration was injected for three times and % recovery was calculated on the basis of served area at each spiking level (By utilization of linear regression analysis). Composition of placebo: Microcrystalline cellulose (30mg), Eudragit (25mg), Polyethylene Glycol (15mg), Dicalcium phosphate (40mg). (Table 1)

5.5. Assay

For the said purpose, 80 mg of ASP and 20 mg of PAN were weighed accurately and mixed with commonly used excipient (same used in accuracy study). All the contents were diluted to 100 ml with methyl alcohol, sonicated for 5 minutes and filtered from 0.45 micron membrane filter under positive pressure. 0.3 ml of previously filtered solution was further diluted to 10 ml with diluent (mobile phase) to give final concentration of 24 µg/mL of ASP and 6 µg/mL of PAN. Above solution was chromatographed in triplicates by employing optimized chromatographic conditions.

6. Result and Discussion

6.1. Optimized chromatographic conditions

When method was operated using optimized chromatographic condition a well resolved peak of ASP and PAN was observed at 2.286 and 5.859 minutes respectively (Figure 1). All the system suitability parameters were within USP guidelines with RSD less than 1 and have been highlighted in Table 2.

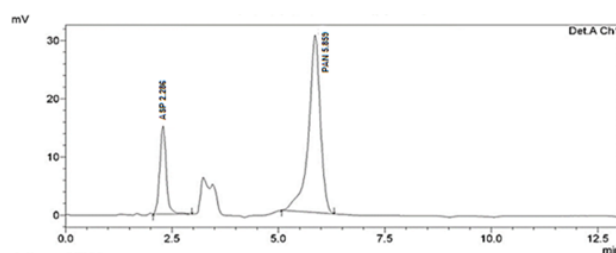


Fig. 1: Chromatogram of mixture of ASP and PAN using optimized chromatographic

7. Forced Degradation Studies

Optimized method was found to be stability indicating as it is able to separate all the degradation products in the presence of active ingredient. (Figures 2, 3, 4 and 5) No degradation product found to interfere with estimation of ASP and PAN in stressed samples. Even the stress given found to be optimum as % degradation observed was predictive in nature (below 15%). (Table 3)

Table 1: Preparation of solutions for accuracy studies

Preparation of solutions for Accuracy studies			
Unspiked	50%	100%	150%
Placebo	Placebo	Placebo	Placebo
-	Weigh accurately 40 mg of ASP and 80 mg of PAN in 100 ml calibrated volumetric flask (400+100 $\mu\text{g/ml}$)	Weigh accurately 80 mg of ASP and 20 mg of PAN in 100 ml calibrated volumetric flask (800+200 $\mu\text{g/ml}$)	Weigh accurately 120 mg of ASP and 30 mg of PAN in 100 ml calibrated volumetric flask (1200+300 $\mu\text{g/ml}$)
-	To achieve final concentration, 0.2 ml of from above solution was diluted up to 10 ml with Mobile Phase (8+2 $\mu\text{g/ml}$)	To achieve final concentration, 0.2 ml of from above solution was diluted up to 10 ml with Mobile Phase (16+4 $\mu\text{g/ml}$)	To achieve final concentration, 0.2 ml of from above solution was diluted up to 10 ml with Mobile Phase (24+6 $\mu\text{g/ml}$)

Table 2: System suitability parameters ASP + PAN = 24 + 6 $\mu\text{g/mL}$

Parameter	ASP	RSD	PAN	RSD
Retention time (R_t)	2.46 \pm 0.02	0.8130	5.87 \pm 0.0076	0.1299
Tailing Factor	0.991 \pm 0.001	0.1009	0.996 \pm 0.00152	0.1533
Number of theoretical plate	2232.333 \pm 2.516	0.1127	3005.333 \pm 4.509	0.1500
Resolution (R_s)		8.887 \pm 0.0025		0.0283

Table 3: Summary of data derived from forced degradation study by proposed HPLC method

Stress Condition	Area (mv. sec)	ASP	Pa	% Degradation (Asp)	% Degradation (Pan)
Acid Hydrolysis	Area of Control	254267	8435	10.30%	13.38%
	Area of treated	228067	7306		
Base Hydrolysis	Area of Control	92545	82178	12.84%	9.77%
	Area of treated	80655	74148		
Oxidative Stress	Area of Control	166955	2598	10.44%	15.62%
	Area of treated	149509	2192		
Thermal Degradation	Area of Control	81456	75564	5.88%	4.46%
	Area of treated	76663	72236		

Table 4: Linearity data of ASP

Sr. No.	Concentration ($\mu\text{g/ml}$)	Mean area ($\mu\text{V.s}$) \pm SD	RSD
1	8	32312 \pm 333.30	1.032
2	16	81844 \pm 721.68	0.881
3	24	147389.4 \pm 931.625	0.632
4	32	219374.6 \pm 1003.108	0.457
5	40	275195.8 \pm 1021.303	0.371

Table 5: Linearity data of PAN

Sr. No.	Concentration ($\mu\text{g/ml}$)	Mean area ($\mu\text{V.s}$) \pm SD	RSD
1	2	28475 \pm 293.2	1.03
2	4	79202 \pm 579.68	0.731
3	6	145310.2 \pm 945.15	0.650
4	8	217634.2 \pm 983.01	0.451
5	10	281486.8 \pm 1042.89	0.370

Table 6: Repeatability data of ASP

Sr. No.	8	16	24	32	40
1	32145	81256	147819	219450	274085
2	31135	81961	146711	218571	276199
3	32154	83021	147022	218679	274099
4	32219	81705	146579	221055	275755
5	32905	81279	148816	219118	275841
Mean	32312	81844	147389.4	219374.6	275195.8
SD	333.3	721.68	931.625	1003.108	1021.303
%RSD	1.032	0.8818	0.6320	0.4572	0.3711

Table 7: Repeatability data of PAN

Sr. No.	Concentration ($\mu\text{g/mL}$)				
	2	4	6	8	10
1	28695	79642	145910	216409	281069
2	28759	79567	144842	216890	281921
3	28596	79496	145953	217998	281233
4	28219	79058	143855	218878	283001
5	28108	78248	145991	217996	280210
Mean	28475	79202	145310.2	217634.2	281486.8
SD	293.2	579.68	945.153	983.010	1042.895
%RSD	1.03	0.7319	0.6504	0.4516	0.3704

Table 8: Intraday and inter day precision data of ASP (n = 3 determinations)

Concentration ($\mu\text{g/ml}$)	Intraday Mean + SD	%RSD	Inter-Day Mean + SD	%RSD
8	32228 \pm 354.192	1.0990	32511 \pm 387.284	1.1912
16	80939 \pm 717.843	0.8868	81052 \pm 770.283	0.9503
24	146222.3 \pm 928.846	0.6352	147403.7 \pm 1110.605	0.7534

Table 9: Intraday and inter day precision data of PAN (n = 3 determinations)

Concentration ($\mu\text{g/ml}$)	Intraday Mean + SD	%RSD	Inter-Day Mean + SD	%RSD
2	28473 \pm 300.231	1.0544	28253 \pm 314.019	1.1114
4	79078 \pm 600.722	0.7596	79105.67 \pm 658.472	0.8323
6	145200.7 \pm 926.550	0.6381	145259.3 \pm 1027.148	0.7071

Table 10: Accuracy data of ASP and PAN by HPLC method

Level of spiking	Total placebo (mg)	Amount of std. drug added ($\mu\text{g/ml}$)		Amount of drug recovered ($\mu\text{g/ml}$)		% Rsecovery	
		ASP	PAN	ASP	PAN	ASP	PAN
Unspiked	110	-	-	-	-	-	-
50 %	110	8	2	7.966 \pm 0.037	1.997 \pm 0.012	99.583 \pm 0.743	99.86 \pm 0.660
100 %	110	16	4	15.92 \pm 0.096	3.970 \pm 0.026	99.520 \pm 0.599	99.25 \pm 0.661
150 %	110	24	6	23.93 \pm 0.105	5.997 \pm 0.007	99.721 \pm 0.441	99.95 \pm 0.115

Table 11: Assay of synthetic mixture of ASP and PAN by HPLC method

Drug	Amount of drug taken ($\mu\text{g/mL}$)	Amount of drug found ($\mu\text{g/mL}$)	% Assay
ASP	16	15.91 \pm 0.0458	99.435 \pm 0.283
PAN	4	3.970 \pm 0.0152	99.416 \pm 0.381

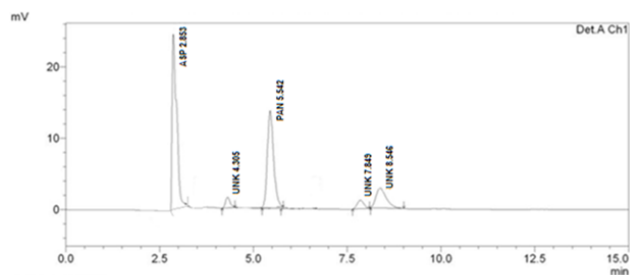


Fig. 2: Chromatogram of treated sample (Acid hydrolysis)

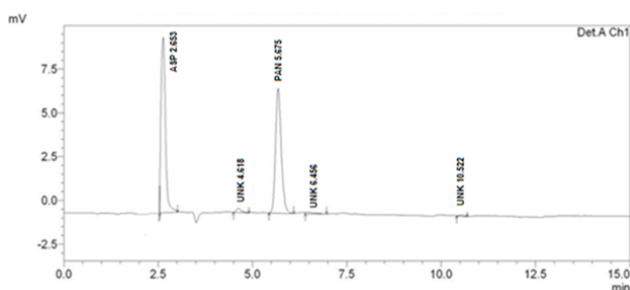


Fig. 3: Chromatogram of treated sample (Base hydrolysis)

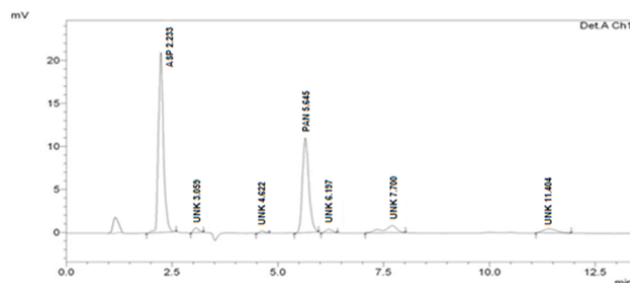


Fig. 4: Chromatogram of treated sample (Oxidative stress)

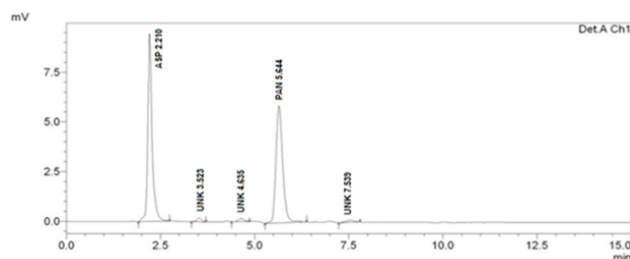


Fig. 5: Chromatogram of treated sample (Thermal stress)

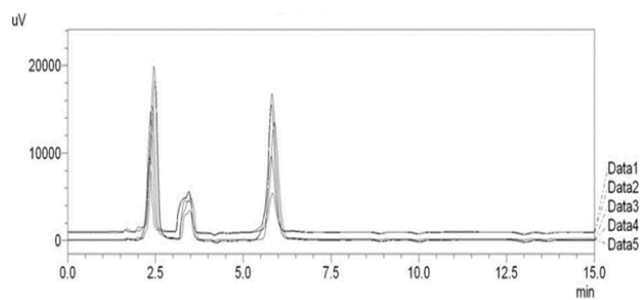


Fig. 6: Overlain chromatogram of standard mixtures for linearity studies

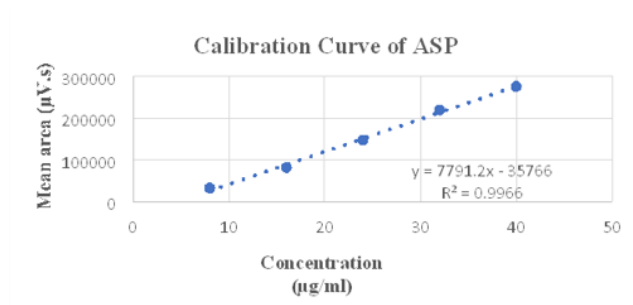


Fig. 7: Regression analysis of ASP (8-40 µg/ml)

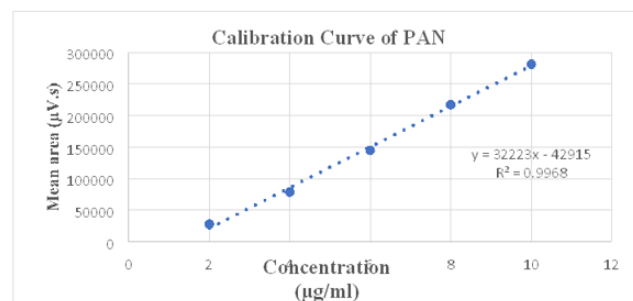


Fig. 8: Regression analysis of PAN (2-10 µg/ml)

8. Analytical Method Validation

8.1. Linearity and range

As per ICH guidelines, the value of R^2 should be greater than 0.995 and observed R^2 for given concentration range for ASP and PAN is 0.996 and 0.997 respectively. Hence, we can say that developed method is linear over the range of 8 - 40 µg/mL and 2 - 10 µg/mL for ASP and PAN respectively show in Figures 6, 7 and 8. Linearity data for both drugs is shown in Tables 4 and 5.

8.2. Repeatability

When all mixtures were analyzed at all concentration, calculated relative standard deviation at each level was found to be less than 2 so that method was found to be

repeatable over the range of 8 - 40 $\mu\text{g/mL}$ and 2 - 10 $\mu\text{g/mL}$ for ASP and PAN respectively. Repeatability data are shown in table 6 and 7 for ASP and PAN respectively.

8.3. Method precision

For determining inter day and intraday precision, %RSD was monitored at selected concentration level which was found to be less than 2 so method was found to be precise for estimation of ASP and PAN. Data for intermediate precision are given in table 8 and 9 for ASP and PAN respectively.

8.4. Accuracy study

Spiked placebo with standard solution at 50, 100 and 150% level was analyzed for % recovery which was found within 98 to 102, so method was found to be accurate (Table 10).

8.5. Assay

When prepared synthetic mixture was analyzed by developed and validated method, % assay was found to be 99.435 for ASP and for 99.416 PAN (Table 1)

9. Summary and Conclusion

As the proposed combination of ASP and PAN is in clinical phase III, no analytical method is available yet for simultaneous quantitative expression of both the components from synthetic mixture. The proposed stability indicating RP-HPLC method not only separates and quantify the components from synthetic mixture with at most accuracy but also gives idea about the stability of mentioned components under variety of conditions as per ICHQ1 guidelines. It can be concluded that both the components are highly susceptible to oxidative stress (10.44 for ASP and 15.62 for PAN) and hence formulation of both can be made and packaging can be made in such a way that it can be protected from exposure to atmospheric oxygen. Finally, method was successfully validated as per ICHQ2R1 guidelines and applied for determination of ASP and PAN from synthetic mixture. Still there is scope of improvement in method as there is limitation of working with UV-VIS detector and hence limitation of not having peak purity is major drawback with stability indicating method.

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11. Author Contributions

1. Preeti Yadav: Collection of all the data after the completion of the research work and the preparation of manuscript was done by Preeti Yadav.
2. Pinak Patel: The design of the study from choosing the drug to choosing the method was done by Pinak Patel. Protocol for execution of validation parameters and stability studies was also prepared by Pinak Patel.
3. Anamika Singh: Execution of Stability studies as per the protocol was done by Anamika Singh.
4. Rashmi Shukla: Execution of validation studies as per the protocol was done by Rashmi Shukla.
5. Krunal Detholia: During the study, synthetic mixture preparation according to the dose of the drugs was done by Krunal Detholia.

12. Source of Funding

None.

13. Conflict of Interest

The authors declare no conflicts of interest.

References

1. Eric HA, Joseph L. Aspirin Circulation AHA. *Circulation*. 2000;101(10):1206–18.
2. Dolores M, Morales-Hipolito EA, Garduno-Rosas JA, Villaseñor A, Lopez-Arellano R. Development and validation of an alternate stability-indicating UV spectrophotometric analytical method for aspirin in tablets. *Indian J Pharm Sci*. 2017;78(6):810–5.
3. Murtaza G, Khan SA, Shabbir A, Mahmood A. Development of a UV-spectrophotometric method for the simultaneous determination of aspirin and paracetamol in tablets. *Sci Res Essays*. 2011;6(2):417–21.
4. Kokot Z, Burda K. Simultaneous determination of salicylic acid and acetylsalicylic acid in aspirin delayed-release tablet formulations by second- derivative UV spectrophotometry. *J Pharm Bio Anal*. 1998;18(4-5):871–5.
5. Salomi P, Sultana A, Sharmila, Nagarajan C, Prakash G. Simultaneous estimation of aspirin and omeprazole (yosprala) in bulk by UV-spectroscopy. *J Drug Deliv Ther*. 2017;7(3):87–91.
6. Sawyer M, Kumar V. A rapid high performance liquid chromatographic method for the simultaneous quantitation of aspirin, salicylic acid and caffeine in effervescent tablet. *J Chromatogr Sci*. 2003;41:393–7.
7. Patel D, Patel N. Development and validation of RP-HPLC method for simultaneous estimation of aspirin and esomeprazole magnesium tablet dosage form. *J Chem*. 2012;751940:1–5.
8. Shinde R, Kachave S. Method development and validation of aspirin and ticlopidine hydrochloride in bulk drug and tablet formulation by RP-HPLC. *Int J Pharm Res*. 2013;5(3):19–22.
9. Patel JV, Patel CN, Patel PU, Prajapati PH, Patel MB. Simultaneous estimation of cilostazol and aspirin in synthetic mixture using HPTLC method. *Int J Chem Sci*. 2018;6(3):1377–84.
10. Tank PH, Vadalia KR, Dedania ZR. Development and validation of HPTLC method for simultaneous estimation of rosuvastatin calcium and aspirin in capsule dosage form. *Int J Pharm Sci Res*. 2012;3(10):3867–70.
11. Bhusari VK, Dhaneshwar SR. Validated HPTLC Method for Simultaneous Estimation of Atenolol and Aspirin in Bulk Drug and Formulation. *ISRN Anal Chem*. 2012;3:1–5.
12. The United State Pharmacopoeia, 26th Revision. *US Pharmacopoeial convention Inc*. 2012;p. 4211–4211.

13. Nagaraju C, Samy K, Madhukumar C, Dilipkumar G, Bushra S, Sheeba S. Development and validation of differential spectrophotometric method for determination of pantoprazole in tablet dosage form. *Asian J Pharm Anal Med Chem*. 2013;1(2):98–103.
14. Barri S, Subramanyam B, Dharmateja B, Haribabu M, Kiran D. Development and validation of new analytical method for the simultaneous estimation of pantoprazole and domperidone by UV-spectrophotometry. *Indo Am J Pharm Res*. 2019;9(5):1993–2000.
15. Shailendra SS, Zaranappa, Chaluvvaraju KC, Veena MK, Rajani S. Development and Validation of UV-Spectrophotometric Method for Simultaneous Estimation of Aceclofenac and Pantoprazole in Bulk and Tablet Dosage Forms Using Hydrotropic Solvent. *Int Pharma Pharma Res*. 2016;6(3):331–44.
16. Khushbu N, Gunjansinh P, Jalpesh A, Kunjan, Shailesh S. Development and Validation of Derivative Spectrophotometric Method for simultaneous Estimation of Diclofenac and Pantoprazole in Combined Capsule Dosage Form. *Asian J Res Chem*. 2013;6(2):155–7.
17. Battu PR, Reddy NK. Development and validation of RP-HPLC for the pantoprazole sodium sesquihydrate in pharmaceutical dosage forms and human plasma. *Int J Chem Technol Res*. 2009;1(2):195–8.
18. Safwan A, Soulaifa A. modified high-performance liquid Chromatographic method for the analysis of pantoprazole sodium in pharmaceutical dosage forms using lansoprazole as internal standard. *Arabian J Chem*. 2016;9(1):114–9.
19. Patel SA. High Performance Thin Layer Chromatographic Method for Estimation of Pantoprazole Injection. *Int Res J Pharm*. 2011;2(8):132–5.
20. Patil A, Mulla S. Development and validation of HPTLC method for the simultaneous estimation of Naproxen and Pantoprazole in combined dosage form. *Int J Pharm Pharm Sci*. 2013;5:223–5.
21. Patel GH, Prajapati ST, Patel CN. HPTLC Method Development and Validation for simultaneous Determination of Cinitapride and Pantoprazole in Capsule Dosage Form. *Res J Pharm Technol*. 2011;4(9):1428–31.
22. Moukarbel G, Bhatt DL. Antiplatelet therapy and proton pump inhibition: clinician update. *Circulation*. 2012;125(2):375–80.

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