RESEARCH PAPER

Quality by design based UPLC method development and validation for simultaneous estimation of albuterol and budesonide in pharmaceutical dosage forms

T. Mallika[1*], P. Aparna[1*]

[1]Department of Chemistry, JNTUH-College of Engineering, Kukatpally, Hyderabad, Telangana, India

[*]**Corresponding author:** T. Mallika, Email: tmallikaphd2021@gmail.com https://orcid.org/0000-0002-2748-1057

[*]Dr. P. Aparna, Email: aparnapasula@jntuh.ac.in https://orcid.org/0000-0001-6724-1835

ABSTRACT

The combination of albuterol and budesonide is used to prevent and treat asthma, breathing problems, tightness in the chest, coughing, wheezing, and shortness of breath in adults. In the current work, a QBD based UPLC method was developed and verified for the assessment of Albuterol and budesonide in the pharmaceutical dosage form. A CHS column (100 nm × 2.1 mm × 1.7 µm) was employed containing a mobile phase that includes acetonitrile and a 7.8 g solution of $NaHPO_4$ in a 66.4:33.6 (v/v) ratio. At 0.3 mL/min, the flow rate was kept constant, and the optimized detection wavelength was set at 240.0 nm. The retention times for Albuterol and Budesonide were observed at 1.180 minutes and 1.657 minutes, accordingly. The technique was proved following the ICH Q2 guidelines confirming its reliability. For accuracy and intermediate precision, the relative standard deviation (RSD) studies of Albuterol and Budesonide was within 2.0%. The accuracy for quantification ranged from 99.08% to 99.90%, utilizing a regression coefficient exceeding 0.999. The research results indicate that developed Albuterol and budesonide UPLC method can be employed for formulation evaluation and clinical studies.

Keywords: Albuterol, Budesonide, UPLC, Robustness, Degradation, Method validation.

How to cite this article: Mallika T, Aparna P. Quality by design based UPLC method development and validation for simultaneous estimation of albuterol and budesonide in pharmaceutical dosage forms. Int J Drug Deliv Technol. 2026;16(9s): 181-191. DOI: 10.25258/ijddt.16.9s.18

INTRODUCTION

Bronchodilators represent a central approach in the pharmacological management of airway diseases such as chronic obstructive pulmonary disease (COPD). In COPD, these agents are primarily used to ease breathing difficulties, optimize lung performance, and minimize the frequency and impact of symptom flare-ups. Current research into bronchodilators focuses on enhancing their safety and developing agents with once-daily dosing to improve patient convenience and treatment outcomes. The primary classes—beta-2 agonists, anticholinergics, and theophylline—are essential in managing respiratory conditions, and combination therapies are frequently employed to control and prevent asthma symptoms [1-4]. Budesonide and albuterol are used together to prevent and treat adult dyspnoea, breathlessness and wheezing, coughing, and chest tightness. Budesonide is a member of steroids class. It works by decreasing respiratory oedema [5]. Significant morbidity is linked to untreated asthma. Fast-acting bronchodilators can quickly alleviate the symptoms of asthma [6], but they don't address the underlying inflammation when used as a rescue medication. As a rescue medication, combining a short-acting beta2-agonist, such as albuterol (salbutamol), with an inhaled corticosteroid, like budesonide, in a single inhaler may help control swelling and bronchoconstriction while reducing the risk of asthma flare-ups [7-10]. The literature review outlines various analytical techniques for figuring out the dosage forms of Albuterol and budesonide [11-13]. The current work's goal is to create a new UPLC method based on QBD technique and validate the developed technique for simultaneous determination of Albuterol and budesonide in the dosage form.

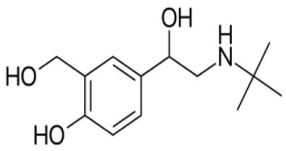


Figure 1: Chemical structure of Albuterol

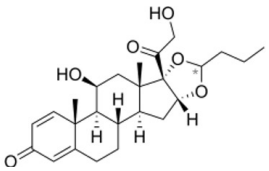


Figure 2: Chemical structure of Budesonide

MATERIALS AND METHODS

Chemicals:

Albuterol and Budesonide, Acetonitrile, Methanol, Orthophospharic acid, Disodium hydrogen Phosphate (NaHPO4), Milli-Q Water.

Instrument:

pH meter (BVK Enterprises, India), electronic balance (Denver), ultrasonicator (BVK Enterprises), Waters Acquity UPLC system with Auto Injector and Accquity TUV detector with Empower 3 software, the absorbance of solutions containing Albuterol, Budesonide, was measured using a UV-VIS spectrophotometer (PG Instruments T60) and Design export 13.

Diluent and Mobile phase preparation Diluent

preparation:

A diluent comprising water and acetonitrile with a 50:50 (V/V) ratio was used.

Buffer phase preparation:

Dissolve 7.8 g of Na_2HPO_4 (disodium hydrogen phosphate) in 900 mL of Milli-Q water. Set the pH to 4.0 ± 0.1 using dilute orthophosphoric acid, then dilute the solution to 1000 mL with Milli-Q water.
Mobile phase: The mobile phase is made up of acetonitrile and buffer in ratio of 30:70 which is Pass through a suitable filter.

Standard and sample solution preparations:

Standard solutions: 2.25 mg of albuterol and 2 mg of budesonide were precisely measured and then shifted to separate 50 ml volumetric flasks. After adding 40 mL of the diluents to the flask, it was subjected to 10 minutes of sonication and then used the diluent to adjust the volume. Concentration obtained was 45µg/mL of Albuterol and 40µg/mL of Budesonide. Further on from this solution 1ml of solution was taken and added in to a 10-milliliter volumetric flask and added diluent to make up the volume. Obtain concentrations are 4.5µg/mL of Albuterol and 4.0µg/mL of Budesonide
Sample solutions: Pressurized meter dose inhaler = (LI-pMDI) 10 actuations from to (Albuterol (90mcg) and Budesonide (80mcg) were carefully taken and shifted into a 10 mL volumetric flask then added 2.5 ml of diluents, and then sonicated the flask for 25 minutes. Diluent was then used to modify the volume, and 0.45 µm filters were used for filtering.
Obtain concentration was 9µg/mL of Albuterol and 8µg/mL of Budesonide. Further from this solution taken 5ml and transferred in to a 10-milliliter volumetric flask and added diluent to make up the volume. Obtain concentrations are 4.5µg/ml of Albuterol and 4.0µg/ml of Budesonide

Validation of the method:

According to the ICH Q2 guideline, the suggested method was confirmed for assay by UPLC [14], and a number of papers, including forced degradation tests, were published in compliance with the criteria [15-20].

System Adequacy: The system appropriateness characteristics were assessed by generating standard solutions of Albuterol (4.5 ppm) and Budesonide (4 ppm). The solutions were injected six times, and the parameters such peak tailing, resolution, and USP plate count were evaluated. The percentage RSD for the six standardised injection findings should not exceed 2%.
Details: examining any disturbance with the process that has been optimized. This method should not be used to observe conflicting peaks in blank and placebo over the retention periods of these drugs. It was said that this strategy was particular.
Precision:

To determine repeatability, six spiked samples were prepared at 100% assay level. To assess intermediate accuracy, six spiked solutions were prepared by separate analysers on various days with an average RSD of less than 2%.

Linearity:

From the mixed standard stock solution, aliquots of approximately 0.25, 0.5, 0.75, 1, 1.25, and
1.5 mL were taken and subsequently placed into various volumetric flasks with a 10 mL capacity. The final concentrations of these solutions are 1.125ppm to 6.75 ppm for Albuterol and 1ppm to 6ppm for Budesonide. Regression coefficient should also fall between 0.999 and 0.999.

Accuracy:

Accuracy was evaluated by preparing triplicate drug product solutions spiked with Albuterol and Budesonide at three levels (50%, 100%, and 150%); each sample was injected thrice. The recovery ranged from 98% to 102%.

Robustness:

The temperature, mobile phase ratio, and flow rate are among the few specific modifications made to the procedure; nonetheless, no appreciable change in drug elution were observed, and all of parameters within the permissible range as specified by guidelines of ICH.

Force Degradation Oxidation:

Separately, 1ml of 20% H_2O_2 and 1 ml of the stock solutions of Albuterol and Budesonide were added. The solutions were maintained at 60^0C for 30 minutes. The final solution was diluted to provide a (4.5ppm and 4 ppm) solution for the UPLC analysis. The 1 µL sample was injected and the chromatogram was obtained.

Studies on Acid Degradation:
Separately, 1 ml of 2N HCl and the stock solutions in 1 milliliter of Albuterol and Budesonide were added. The solutions were reflux at 60^0C for 30 minutes. The final solution was diluted to provide a (4.5ppm and 4 ppm) solution for the UPLC analysis. The 1 µL sample was injected and the chromatogram was obtained.

Alkaline degradation:

1 mL of 2N NaOH and 1 mL of Albuterol and Budesonide stock solutions were each added individually. The solutions were held at 60 degrees Celsius for half an hour. The final solution was diluted to (4.5ppm and 4 ppm). A 1 µL sample was injected, and the chromatogram was produced.

Degradation of dry heat:
The normal pharmaceutical solution was roasted at 105 °C for six hours to investigate deterioration by dry heat. After

diluting the sample to a (4.5ppm and 4 ppm) solution, 1µl was injected into the system to evaluate its stability for UPLC analysis. Following that, the chromatograms were documented.

Photo stability:

The photochemical stability of the medication was further tested by subjecting the (4.5ppm and 4 ppm) solution to ultraviolet light and retaining the beaker in an ultraviolet chamber for seven days, or 200 watt hours per square metre in a photo stability laboratory. To test the sample's stability, 1 µl of the resulting solution was diluted into solutions with concentrations of 0.2 ppm and 500 ppm using an UPLC. Following that, chromatograms were recorded.

Neutral degradation:

Medication stress testing were conducted in neutral circumstances via refluxing the medication in 60ºC water for six hours. After diluting the solution to 4.5ppm and 4 ppm concentrations, 1 µl was injected into the UPLC system to test the sample's stability. Following that, chromatograms were recorded.

3.7 optimized Method

Different organic modifiers, such as acetonitrile and methanol, as well as UPLC columns. Optimisation of the procedure The approach was optimised utilising the Central Composite Design (CCD). Initial experiments are required to optimise the final procedure. Total Three parameters, namely % organic content, temperature of the column and flow rate required to be optimised. So CCD was used to optimise these conditions, which were adjusted across three levels (high, medium, and low). Various ranges of four parameters (26.6-43.4%, Acetonitrile, column temperature 25 and 35 0C, and 0.25-0.35ml/min flow rate) were selected, and counter and 3D surface plots were generated to show the impact of every parameter on theoretical plates, retention time, area, and asymmetry (CQA). A desirability function is used to optimised circumstances to estimate retention duration, asymmetry, theoretical plates, and peak area.

RESULTS

4.1 Design of experiment.

Central composite design (CCD) in conjunction with response surface methodology (RSM) is employed in the experimental design for HPLC method optimization since RSM may solve with HPLC separation. Design Expert version 13 software implements this response surface method central composite design. Three factors (dependent variables) were used in this work to optimize RP-HPLC separation: temperature, flow rate and the composition of the mobile phase. Three dependent variables (factors) were used in the CCD process, which involved 20 runs: flow rate (X1), composition of mobile phase (X2), and column temperature (X3). Response variables for the following were employed in UPLC optimization for the separation of Albuterol and Budesonide utilizing these factors: Retention time of (Albuterol) (Y1), Retention time of (Budesonide) (Y2), Resolution between Albuterol and Budesonide (Y3), Number of theoretical plates (Albuterol) (Y4), Number of theoretical plates (Budesonid) (Y5), Number of Tailing factor of Albuterol (Y6) and Number of Tailing factor of Budesonid (Y7) The values were expressed in table 1

Table I. Central Composite design using dependent variables

		Factor 1	Factor 2	Factor 3	Response 1	Respons e 2	Respons e 3	Respons e 4	Respons e 5	Response 6	Respons e 7
Std	Ru n	A:FR	B:MP (Organi c phase)	C:Temp	RT1	RT2	RS	NTP1	NTP2	TF1	TF2

1	10	0.27	30	27	1.467	2.384	5.6	3140.7	2768.1	1.26	1.9
2	8	0.33	30	27	1.203	1.966	5	2606.8	2121	1.2	1.8
3	14	0.27	40	27	1.421	1.887	2.8	3050.6	2244	1.2	1.5
4	11	0.33	40	27	1.15	1.364	1.9	2636.3	1878.3	1.1	1.3
5	13	0.27	30	33	1.367	2.233	5.1	2948.2	2510.7	1.17	1.5
6	17	0.33	30	33	1.144	1.875	4.8	2512.1	1818.8	1.2	1.57
7	9	0.27	40	33	1.324	1.696	3.1	2925.4	2216.1	1.2	1.5
8	7	0.33	40	33	1.087	1.266	2.8	2488.8	1732	1.2	1.4
9	15	0.2495	35	30	1.5	2.019	3.3	3214.7	2578.4	1.21	1.5
10	19	0.3504	35	30	1.052	1.399	2.7	2481.2	1623.8	1.15	1.34
11	4	0.3	26.591	30	1.315	2.489	7.6	2885.4	2541	1.2	1.98
12	1	0.3	43.409	30	1.241	1.436	3	2888.2	2042.9	1.15	1.5
13	12	0.3	35	24.9546	1.366	1.968	3.2	2852.9	2359.1	1.2	1.5
14	5	0.3	35	35.0454	1.184	1.612	3.1	2537	2042.1	1.2	1.26
15	18	0.3	35	30	1.284	1.749	3.5	2946.5	2356	1.16	1.14
16	20	0.3	35	30	1.288	1.764	3.6	2988.5	2374	1.16	1.15
17	6	0.3	35	30	1.295	1.709	3.5	2950.3	2365	1.16	1.14
18	3	0.3	35	30	1.298	1.769	3.6	2969.2	2366	1.16	1.13
19	2	0.3	35	30	1.298	1.769	3.6	2971.2	2326	1.16	1.12
20	16	0.3	35	30	1.281	1.781	3.7	2975.9	2366	1.15	1.13

Table 2: The experimental design's factors and level

Factor	Name	Units	Type	Sub Type	Minimum	Maximum	Coded Low	Coded High	Mean	Std. Dev.
A	FR	ml/min	Numeric	Continuous	0.2495	0.3505	-1 ↔ 0.27	+1 ↔ 0.33	0.3000	0.0254
B	MP	%	Numeric	Continuous	26.59	43.41	-1 ↔ 30.00	+1 ↔ 40.00	35.00	4.24
C	Temp	0 C	Numeric	Continuous	24.95	35.05	-1 ↔ 27.00	+1 ↔ 33.00	30.00	2.54

RSM employing CCD along with statistical parameters was performed. A factor was deemed to significantly affect the responses if the value of the determination coefficient (R2) ≥ 0.8 and the Adjusted R^2 value > 0.8. Less than 0.2 must separate the Predicted R2 from the Adjusted R2. The results from CCD and the real experiments were compared using the independent t-test statistical test.

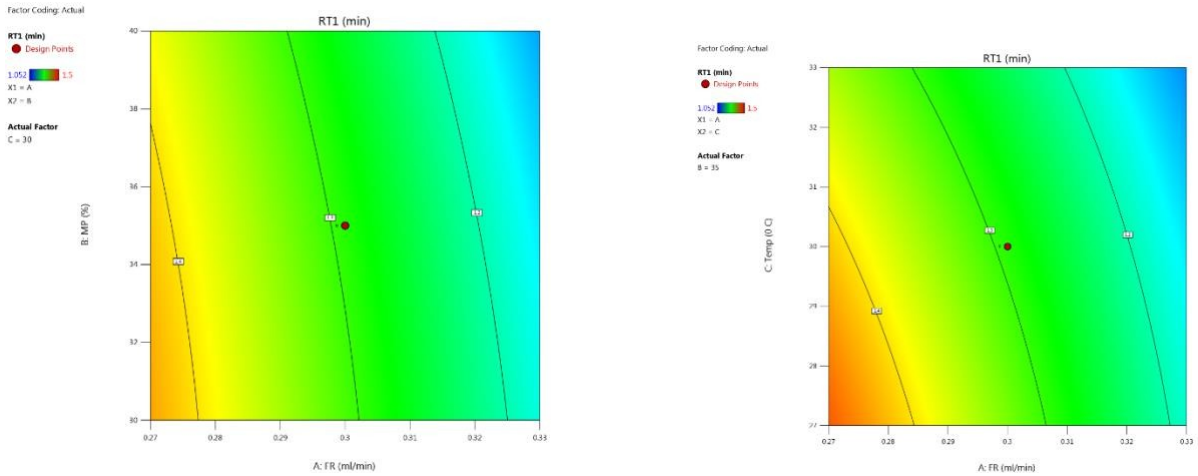


Figure 3: The contour plot of Retention time and 2D surface graph of Response-1 of variables of mobile phase composition and temperature and flowrate.

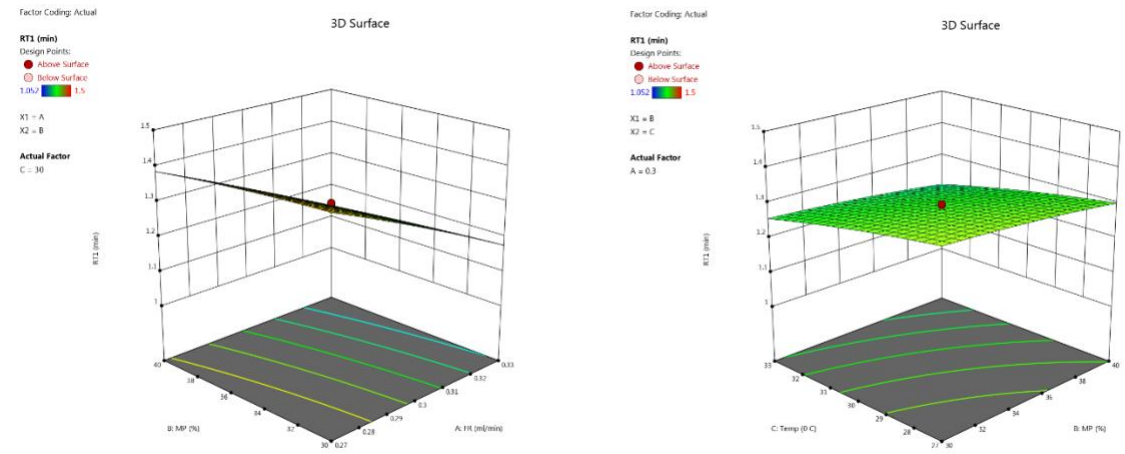
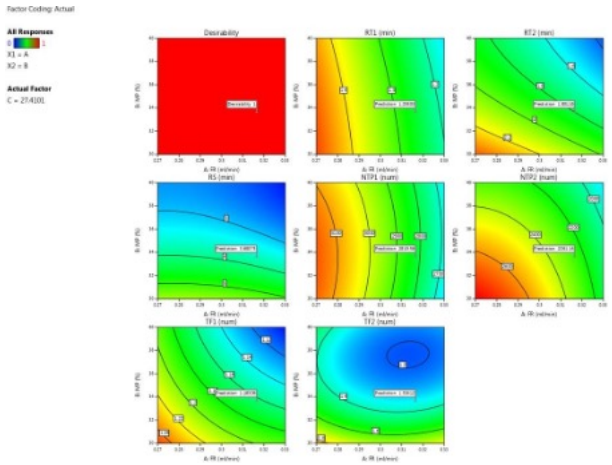


Figure 4: The contour plot of Retention time-2 and 3D surface graph of Albuterol and Budesonide because of variables of mobile phase composition and temperature and flowrate.



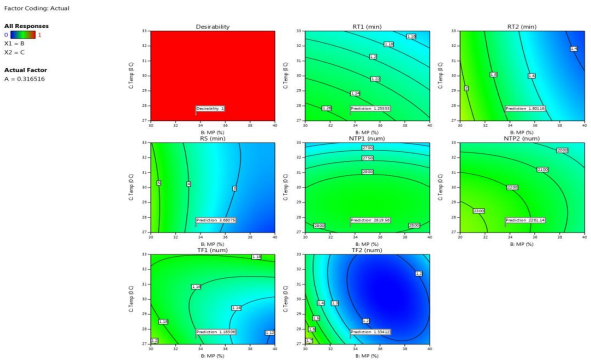
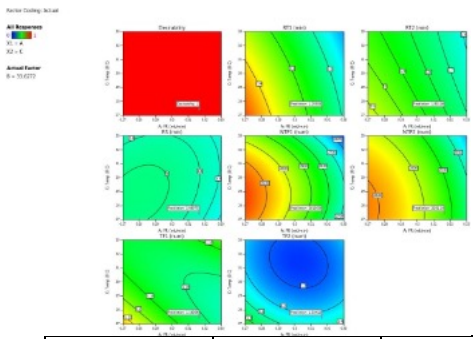


Figure 5: Overall Desirability plot of Albuterol and Budesonide because of variables of mobile phase composition and temperature and flowrate.



Tabel 3: RT, NTP, RS values of Albuterol and Budesonide

Solution 1 of 100 Response	Predicted Mean	Predicted Median	Observed	Std Dev	n	SE Pred	95% PI low	95% PI high
RT1	1.25503	1.25503	1.284	0.0114738	1	0.012614	1.22693	1.28314
RT2	1.80116	1.80116	1.749	0.0396273	1	0.0435651	1.70409	1.89822
RS	3.68075	3.68075	3.5	0.125522	1	0.137995	3.37327	3.98822
NTP1	2819.56	2819.56	2946.5	25.2438	1	27.7523	2757.72	2881.39
NTP2	2261.14	2261.14	2303.0	22.1277	1	24.3265	2206.93	2315.34
TF1	1.16306	1.16306	1.2	0.00429254	1	0.00471909	1.15254	1.17357
TF2	1.33412	1.33412	1.2	0.0180523	1	0.0198462	1.2899	1.37834

design

Table 4: Factors and level utilised in the experimental

Factor	Level (-1)	Level (0)	Level (+1)
Flow rate (ml/min)	0.2700	0.3	0.3300
Organic Phase (Ratio)	30.00	33	40.00
Temperature (°C)	27.00	30	33.00

4.2 Optimized Chromatogram Table 5: optimized conditions

Flow rate	0.3 mL/min

Column	CHS C18 100 x 2.1mm, 1.7 µm
Wavelength	240.0 nm
Temperature	30°C
Injection volume	1.0 µL
Run time	3.0 minutes
Mobile phase	66.4 volumes of Acetonitrile , 33.6 volumes of 7.8 g of dibasic sodium phosphate in water, adjusted to pH 4.0 with OPA

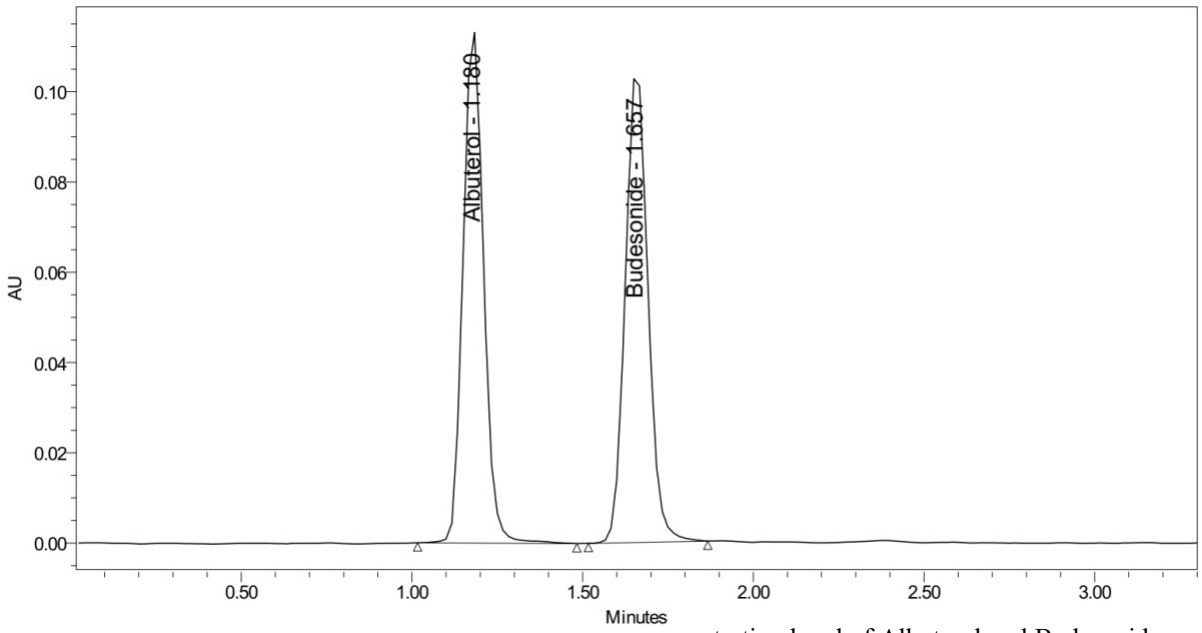


Figure 6: Optimized Chromatogram

Budesonide and albuterol eluted at 1.657 and 1.180 minutes, respectively, and were both well- resolved. Optimisation and validation followed the exceedingly satisfactory USP plate count and TF.

Linearity:

The detector respond was shown to be linear in the concentration band of Albuterol and Budesonide peak areas are measured. The calibration curves of Albuterol and Budesonide are shown in figures 7-8 respectively and calibration data is Table 6.

Table 6 Calibration data of Albuterol and Budesonide

	Albuterol		Budesonide	
s.no	Conc (µg/mL)	Peak area	Conc (µg/mL)	Peak area
1	0	0	0	0
2	1.125	196358	1	165650
3	2.25	384007	2	336473
4	3.375	572163	3	506086
5	4.5	764662	4	672573
6	5.625	960840	5	832613
7	6.75	1142359	6	999051
Conc range (µg/mL)	1.125-6.75		1-6	
Regression Equation	y = 169419x + 2552.5		y = 166685x + 1723.1	
Co-relation	0.999		0.999	

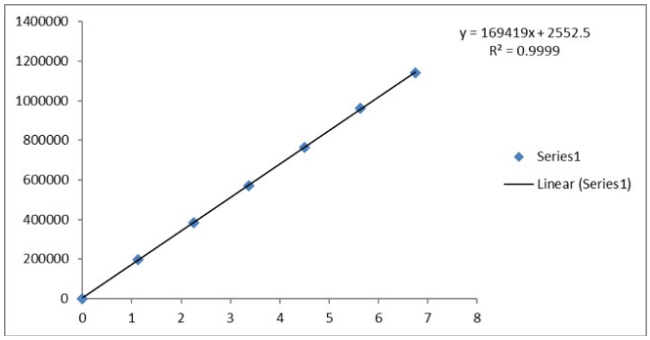


Figure 7: Calibration data of Albuterol

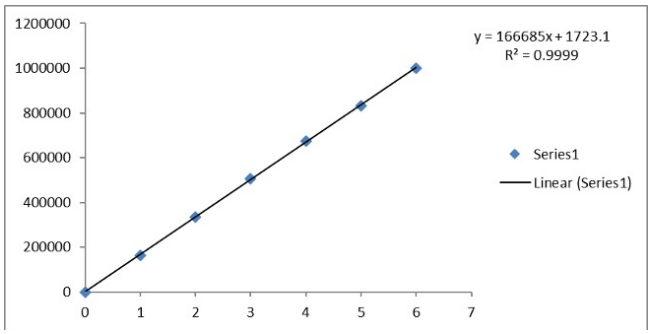


Figure 8: Calibration data of Budesonide Precision:

From a vf which contain standard solution 6 injections were injected and the area was obtained.

The %RSD was below 2% so the Precision was passed.

Table 7: System Precision of Albuterol and Budesonide

s.no	Albuterol			Budesonide		
1.	767898			672495		
2.	767528			676462		
3.	768096			674812		
4.	765210			673880		
5.	767770			669225		
6.	763306			671478		
Avg	766635			673059		
100%	4.5	4.46	99.1	4	3.964	99.09
	4.5	4.49	99.8	4	3.981	99.51
	4.5	4.50	99.9	4	3.978	99.45
150%	6.75	6.74	99.8	6	5.948	99.14
	6.75	6.73	99.7	6	5.951	99.18
	6.75	6.71	99.4	6	5.945	99.08
% recovery	99.69%			99.21%		

Limits of detection and quantification.

Std dev	1945.7	2563.0
%RSD	0.3	0.4

Table 8: Intraday and inter day Precision

Intra-day Precision		Inter-day Precision	
Albuterol	Budesonide	Albuterol	Budesonide
764414	674103	756701	660963
766798	673432	757142	663276
760977	671584	755056	666428
760323	670482	759717	665639
760117	675094	760452	662744
766321	674809	760426	662483
763158	673251	758249	663589
3061.8	1845.5	2261.2	2058.8
0.4	0.3	0.3	0.3

Accuracy

%recovery was found in 3 different level as 50%, 100% 150% and the sample was injected in triplicate manner and the findings was displayed in table 9.

Table 9: Accuracy of Albuterol and Budesonide

	Albuterol			**Budesonide**		
% Level	Amount taken (µg/mL)	Recovered (µg/mL)	% Recovery	Amount taken (µg/mL)	recovered (µg/mL)	% Recovery
50%	2.25	2.24	99.3	2	1.986	99.29
	2.25	2.23	99.1	2	1.981	99.04
	2.25	2.23	99.3	2	1.982	99.12

Tabel 10: LOD and LOQ of Albuterol and Budesonide

Molecule	**LOD**	**LOQ**
Albuterol (µg/mL)	0.01	0.04
Budesonide (µg/mL)	0.01	0.03

Robustness

Table 11 Robustness data of Albuterol

Conditions	Optimized method	Condition applied	area	RT	Plate Count	Tailing factor
Flow rate (±0.1ml/min)	0.3ml/min	0.27ml/min	752966	1.232	2526	1.25
		0.3ml/min	767898	1.278	2834	1.16
		0.33ml/min	768549	1.314	2630	1.22
Column temp. (±3^{0}c)	30^{0}c	27^{0}c	773222	1.257	2594	1.23
		30^{0}c	767528	1.278	2815	1.17
		33^{0}c	787823	1.281	2596	1.24
Mobile phase Composition (5%v/v)	66.4: 33.6	61.4: 38.6	760353	1.257	2620	1.19
		66.4: 33.6	768096	1.278	2822	1.17
		71.4: 28.6	786138	1.295	2661	1.23

Table 12 Robustness data of Budesonide

Conditions	Optimized method	Condition applied	area	RT	Plate Count	Tailing factor
Flow rate (±0.1ml/min)	0.3ml/min	0.27ml/min	654967	1.650	2014	1.26
		0.3ml/min	676462	1.716	2202	1.24
		0.33ml/min	678715	1.761	2203	1.33
Column temp. (±3^{0}c)	30^{0}c	27^{0}c	676326	1.604	2223	1.39
		30^{0}c	676462	1.719	2260	1.24
		33^{0}c	666773	1.765	2159	1.25
Mobile phase Composition (5%v/v)	66.4: 33.6	61.4: 38.6	670632	1.567	2291	1.43
		66.4: 33.6	674812	1.719	2258	1.24
		71.4: 28.6	678716	1.928	2130	1.45

Force Degradation Studies

Table 13 Degradation data of Albuterol and Budesonide

Forced degradation data of both Albuterol and Budesonide shown in table 13.

Conc of degradation study	Albuterol		Budesonide	
	% drug degraded	% drug Undegraded	% drug degraded	% drug Undegraded
2N HCl	4.95	95.05	3.69	96.31
2N NaOH	8.57	91.43	7.77	92.23
Oxidative	8.29	91.71	6.65	93.35
Thermal	3.28	96.72	3.39	96.61

Photostabilty	1.97	98.03	2.63	97.37
Humidity	0.92	99.08	0.57	99.43

Assay data:

Albuterol. And Budesonide assay data was performed and the obtained findings were noted in table 14

Table 14: Assay data

	Albuterol	Budesonide
S.no	% Assay	% Assay
1	99.61	100.06
2	99.92	99.96
3	99.16	99.68
4	99.08	99.52
5	99.05	100.20
6	99.86	100.16
Avg.	99.45	99.93
Std.dev.	0.40	0.27
%RSD	0.4	0.27

CONCLUSION:

An UPLC method developed with the implementation of Quality by Design (QBD) principles offers a dependable, efficient, and robust technique for the accurate quantification of Budesonide and Albuterol in pharmaceutical formulations. The method exhibits high precision, accuracy, and sensitivity, ensuring reliable analysis of these active ingredients across various dosage forms. By applying QBD, the method parameters were optimized, reducing variability and improving reproducibility. This approach has great potential for use in routine quality control and stability testing, ultimately aiding in the production of safer and more effective pharmaceutical products.

REFERENCES:

1. Mak G, Hanania NA. New bronchodilators. Curr Opin Pharmacol. 2012 Jun;12(3):238- 45.
2. Matera MG, Page CP, Cazzola M. Novel bronchodilators for the treatment of chronic obstructive pulmonary disease. Trends Pharmacol Sci. 2011 Aug;32(8):495-506.
3. Cazzola M, Rogliani P, Matera MG. Bronchodilators in airway diseases: a comprehensive review. Pharmacol Ther. 2021 May;223:107805.
4. Matera MG, et al. Pharmacology and Therapeutics of Bronchodilators Revisited. Pharmacol Rev. 2020 Jan;72(1):132-156.
5. Erbay M, Ayçiçek O, Bektaş Hocek A, Özdemir KN. The diagnostic value of bronchodilator response in differentiating asthma, COPD, and ACO in fixed airflow obstruction: a retrospective study. Pulm Med. 2025 Jul;2025:123456.
6. Knox-Brown B, et al. Bronchodilator responsiveness and future chronic airflow obstruction risk in a general population. EClinicalMedicine. 2025 Feb 28;50:101225.
7. Chipps BE, Albers FC, Reilly L, Johnsson E, Cappelletti C, Papi A. Efficacy and safety of as-needed albuterol/budesonide versus albuterol in adults and children aged ≥4 years with moderate-to-severe asthma: rationale and design of the randomised, double-blind, active-controlled MANDALA study. BMJ Open Respir Res. 2021;8(1). :e001077.
8. Global Initiative for Asthma. Global strategy for asthma management and prevention. 2022. Available from: https://ginasthma.org/gina-reports/. Accessed: Dec 11, 2024.
9. O'Byrne PM, Jenkins C, Bateman ED. The paradoxes of asthma management: time for a new approach? Eur Respir J. 2017;50:1701103.
10. National Asthma Education and Prevention Program Coordinating Committee Expert Panel Working Group. 2020 focused updates to the asthma management guidelines: a report from the National Asthma Education and Prevention Program Coordinating Committee Expert Panel Working Group. 2020.
11. Bloom CI, Cabrera C, Arnetorp S, et al. Asthma-related health outcomes associated with short-acting β2-agonist inhaler use: an observational UK study as part of the SABINA Global Program. Eur Respir J. 2020;55(5):2000251.
12. Sridhar Siddiraju, Analytical Method Development and Validation Strategies for Quantitative Determination of Novel Drugs Using High Performance Liquid Chromatography, Int. J. of Pharm. Sci., 2026, Vol 4, Issue 2, 2304-2310. https://doi.org/10.5281/zenodo.18640178.
13. Alkhateeb FL, Wilson I, Maziarz M, Rainville P. Ultra high-performance liquid chromatography method development for separation of formoterol, budesonide, and related substances using an analytical quality by design approach. J Pharm Biomed Anal. 2021 Jan 30;193:113729.
14. Erram SV, Fanska CB, Asif M. Determination of albuterol sulfate and its related substances in albuterol sulfate inhalation solution, 0.5% by RP-HPLC. J Pharm Biomed Anal. 2006 Mar 3;40(4):864-74.
15. Varshosaz J, Emami J, Tavakoli N, Minaiyan M, Rahmani N, Ahmadi F, Dorkoosh F. Development and validation of a rapid HPLC method for simultaneous analysis of budesonide and its novel synthesized hemiesters in colon specific formulations. Res Pharm Sci. 2011 Jul-Dec;6(2):107-16.
16. International Conference on Harmonisation. ICH Q2 (R1); Validation of Analytical Procedures: Text and Methodology. 2005.
17. Cholleti V, Ravindra Kumar Y, Pasula A, Surya PRP. Stability-indicating HPLC method development and validation of rivaroxaban impurities and identification of forced degradation products using LC–MS/MS. Biomed Chromatogr. 2022;36(9):e5424. doi:10.1002/bmc.5424.
18. Vijaykumar C, Kumar YR, Aparna P, Rao PSP. Development and validation of a stability-indicating, single HPLC method for sacubitril-valsartan and their stereoisomers and identification of forced degradation products using LC-MS/MS. Biomed Chromatogr. 2022;37(3):e5550. doi:10.1002/bmc.5550.
19. Vijaykumar C, Kumar YR, Aparna P, Marisetti VM. Enantioselective Green HPLC Method for Simultaneous Determination of Enantiomer, and Potential Impurities in Apremilast Drug Substance. Anal Chem Lett. 2022;12(6):691-714. doi:10.1080/22297928.2022.2155071.
20. Cholleti VK, Pasula A, Pavan KV, Kumar YR, Nitin HD. A new and enantioselective chromatographic method for linagliptin on amylose coated chiral stationary phase. AJAC. 2016;7:556-67. doi:10.4236/ajac.2016.77051.