RESEARCH PAPER

Validated Stability indicating and assay method development of Zuranolone in formulation by RP-HPLC using Quality by Design Approach

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Abstract:
Using the QbD methodology, a new RP-HPLC technique was developed and validated for the assessment of Zuranolone concentration in a capsule formulation. The chromatographic separation was achieved on a column of 4.6 × 250 mm with methanol-OPA water (80.5:19.5) serving as a mobile phase. Column temperature was maintained at 25° C and analysis was conducted at λ = 290 nm. The retention time of Zuranolone was found to be between 3 and 4 minutes thereby ensuring separation between components. Step one of the QbD protocol included the identification of important parameters which were optimized thereafter in order to provide stable outcome. Steps in the method had been validated according to ICH rules and requirements concerning linearity, precision, accuracy, specificity, robustness, limit of detection and limit of quantification. The precision of the entire system is satisfactory as shown by repeatability values of 1.3 and 1.4. Results of the recovery study have shown a high average recovery value of 99.27 % while the assay provided 99.80 %. Limits of detection and quantification are 0.10 and 0.31 µg/ml correspondingly. The calibration curve showed excellent linearity defined by the following equation Y = 31.15x − 0.099. In conclusion, the RP-HPLC technique developed in this research has become a fast and inexpensive alternative which can be utilized in the quality control of Zuranolone in pharmaceutical formulation. The incorporation of Quality by Design principles into the process of method development has made the obtained technique reliable with respect to consistent efficiency under normal and difficult conditions of its application.

Keyword: Chromatographic separation, ICH rules, Quality by Design (QbD), Linearity, Regression equation, RP-HPLC technique.
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Introduction:

Zuranolone is a type of neuroactive steroid that positively alters the function of GABAA receptors by acting as a positive allosteric modulator (PAM) for these receptors. Zuranolone differs from the majority of peripherally acting PAM (e.g. Benzodiazepines) at GABAA receptors in that it can alter the function of both synaptic and extra synaptic GABAAreceptors, as it binds to a site on the receptor that is different than benzodiazepines.[1,2] The pharmacologic profile of Zuranolone was designed to represent a neuroactive steroid, while also having pharmacokinetic properties consistent with a once-daily oral dosing regimen.[3]

As of August 4, 2023, Zuranolone has been approved by the FDA as the first medication intended to treat postpartum depression[4]. This medication has received approval based on two successful Phase 3 clinical trials as shown in figure 1. Zuranolone is classified as a neuroactive steroid, and it exerts its impact through positive allosteric modulation of GABA A receptors, improving GABAergic inhibition and playing a role in restoring excitatory-inhibitory balance in neuronal signaling[5].

Preparative and analytical chromatography exist. Preparative chromatography is carried out with the objective of separating components in a mixture for further use[6]. Analytical chromatography is carried out with relatively smaller quantities of material, and its aim is to measure the relative composition of the analytes in the mixture[7].

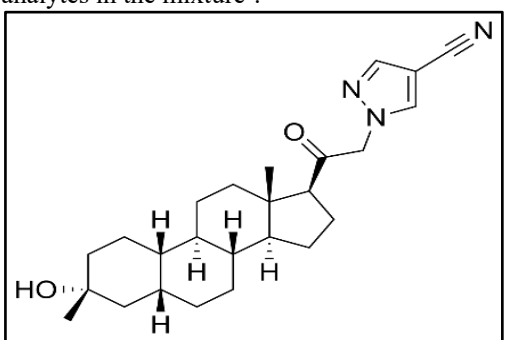


Figure 1. Chemical structure of Zuranolone

MATERIALS AND METHODS:

Chemicals:

Drug (Zuranolone) as an Active Pharmaceutical Ingredient (API), andAnesthetic (Zuranolone Injection). Drug made with an intravenous route. The other consciousness of the solvents used in this method are distilled water acetonitrile phosphate buffer methanol potassium dihydrogen ortho phosphate buffer ortho phosphoric acid. All the reagents/solvents for this method are supplied by Rankem.

Equipment:

The chromatographic analysis was performed using an Agilent Technologies 1100 Gradient HPLC system equipped with a DAD detector and ChemStation software. Separation was achieved on an RP-C18 (Waters) column (4.6 × 250 mm, 5 µm) maintained at 25°C. The mobile phase, consisting of Methanol: 0.1% OPA (80:20 v/v), was delivered at a flow rate of 1 mL/min in isocratic mode. Detection was carried out at 290 nm, and methanol was used as the diluent.

Methods:

Standard Solution Preparation

A standard stock solution (Stock-I) of Zuranolone was prepared by dissolving 10 mg of drug in 10 mL methanol to obtain 1000 µg/mL. Working standard solutions of 10–50 µg/mL were prepared by pipetting 0.1–0.5 mL of Stock-I into 10 mL volumetric flasks and making up the volume with mobile phase.

Sample Preparation

The average amount of the contents of Zurzuvae was found by weighing 20 capsules. 10 mg of Zuranolone (30 mg) of powder was transferred to a 100 mL volumetric flask and dissolved in methanol, sonicated for 15 minutes, diluted to volume (Stock-II). 3 mL of Stock II was then further diluted to 10 mL with mobile phase, yielding a solution containing 30 µg/mL for assay purposes.

HPLC Instrumentation

Chromatographic analysis was carried out using an Agilent Technologies HP-1100 HPLC system equipped with a G1310A IsoPump reciprocating pump, capable of operating up to 400 bar pressure with a flow range of 0.001–5 mL/min and four-solvent mobile phase mixing capability.

System Suitability Parameters

System suitability was evaluated by injecting 20 µg/mL Zuranolone standard solution six times. Parameters such as peak tailing, USP plate count, retention time, and resolution were assessed. The %RSD of peak area for six injections was found to be within 2%, indicating acceptable system performance.

Specificity:

Specificity of the developed method was assessed by checking interference from blank and placebo solutions at the retention time of Zuranolone. No interfering peaks were observed, confirming the specificity of the method.

Sample Preparation:

10 capsules of Zurzuvae were weighed and the average weight was calculated. Powder equivalent to 25 mg Zuranolone was transferred to a 100 mL volumetric flask, dissolved in diluent, sonicated for 25 minutes, diluted to volume, and filtered to obtain 250 µg/mL stock solution. Further dilution of 0.8 mL to 10 mL yielded 20 µg/mL working solution.

Linearity:

Linearity was established over the concentration range of 5–30 µg/mL by preparing six concentration levels (25%, 50%, 75%, 100%, 125%, and 150%) from a 200 µg/mL standard stock solution, demonstrating proportional response with concentration.

Accuracy:

Accuracy was determined by recovery studies at 50%, 100%, and 150% levels using spiked solutions. The % recovery was found within the acceptable range of 98–102%, indicating accuracy of the method.

Robustness:

Robustness was evaluated by introducing deliberate variations in flow rate, mobile phase composition, and temperature. Parameters including flow rate (±0.1–0.3 mL/min) and temperature (21°C and 31°C) were altered. No significant changes in chromatographic performance were observed, and %RSD remained within acceptable limits.

Sensitivity (LOD & LOQ):

The Limit of Detection (LOD) and Limit of Quantification (LOQ) were determined using diluted standard solutions prepared from stock solutions of Zuranolone, confirming the sensitivity of the developed method.

Forced Degradation Studies:

Forced degradation studies were carried out under acidic, alkaline, oxidative, thermal, photolytic, and neutral conditions to evaluate method stability. Samples were subjected to stress conditions such as 2N HCl, 2N NaOH, 20% H_2O_2, heat (105°C), UV exposure, and water reflux at 60°C, followed by chromatographic analysis to assess degradation behavior and stability of Zuranolone.

ANOVA for Quadratic model:

The Factor Coding was as follows: Code. The sum of squares was used from Type III – Partial The Model F-value was 5016.89; this indicates that the model is significant. The probability that such a large F-value would occur due only to "noise" would be 0.01% -- therefore, we have a good feeling (there is strong evidence) that the model is indeed "Fit". The P-values of < 0.0500 indicted that the Terms (A-B-AB-A^2-B^2) were statistically significant factors in the model (each was < 0.0500); while those > 0.1000 were not (statistically). Furthermore, if there are many insignificant factors present, we may be able to reduce the model and improve upon it as a result (excluding those factors required to maintain the hierarchy of the factors in the model).

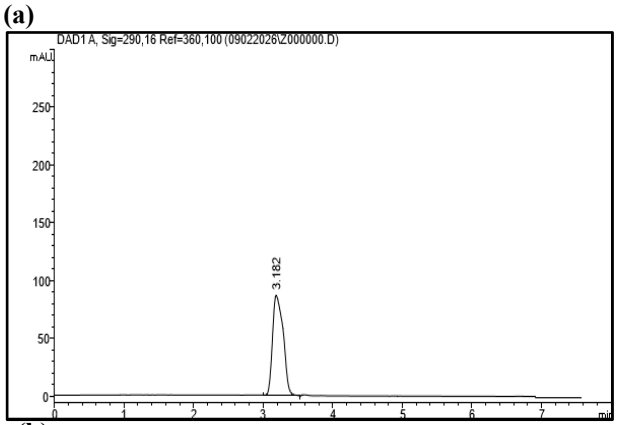
RESULTS:

Chromatographic conditions: The trials are shown in Figure 2 and given in Table 1

Table 1. Chromatographic Conditions

Trial	Mobile Phase (Methanol : 0.1% OPA Water)	Flow Rate (mL/min)	RT (min)	Key Result / Observation
Trial 1	95:5	0.7	3.182	Plate count: 1744; satisfactory performance; further

				optimization required
Trial 2	90:10	0.7	3.382	Plate count: 1796; improved peak symmetry
Trial 3	85:15	0.7	3.438, 3.729	Resolution: 0.80; poor separation
Trial 4	85:15	0.7	3.739	Plate count: 11255; resolution: 2.28; improved separation
Trial 5	80:20	0.7	4.128	Plate count: 8539; satisfactory peak shape but longer retention
Trial 6	80:20	0.9	3.237	Plate count: 7708; peak symmetry: 0.90; satisfactory performance; selected as optimized condition



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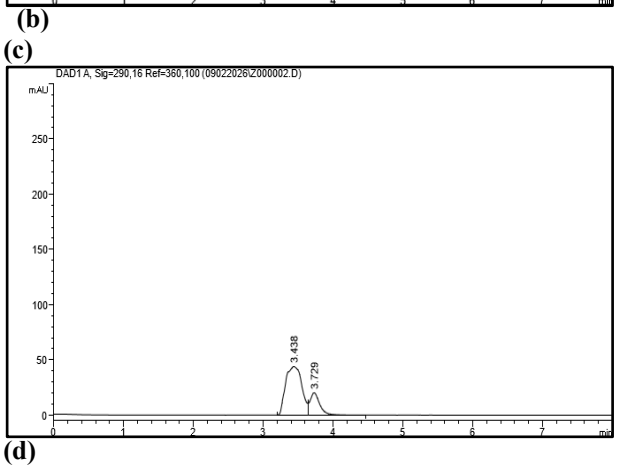

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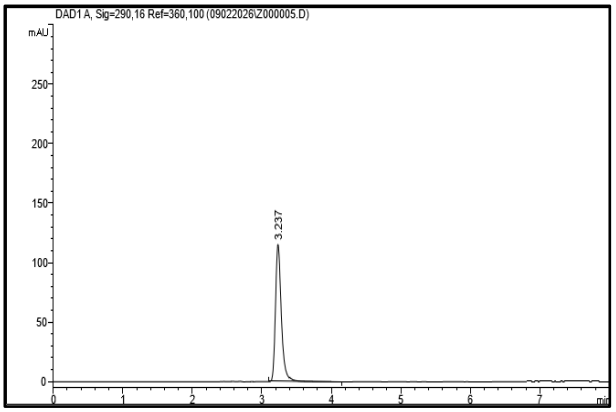

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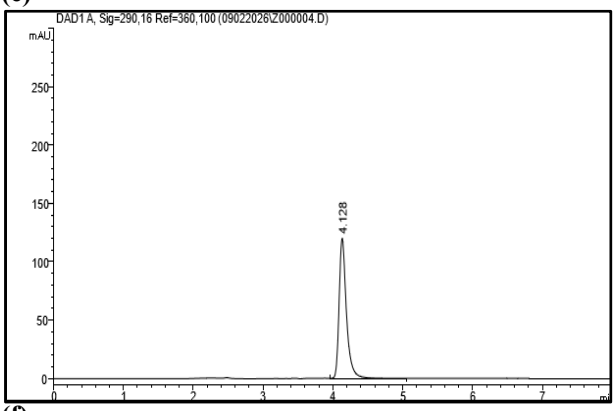

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Figure 2. Chromatographic condition Trial 1-6 of Zuranolone analysis

LINEARITY: Five linear concentrations of Zuranolone (10–50 µg/mL) were injected in triplicate, and the a
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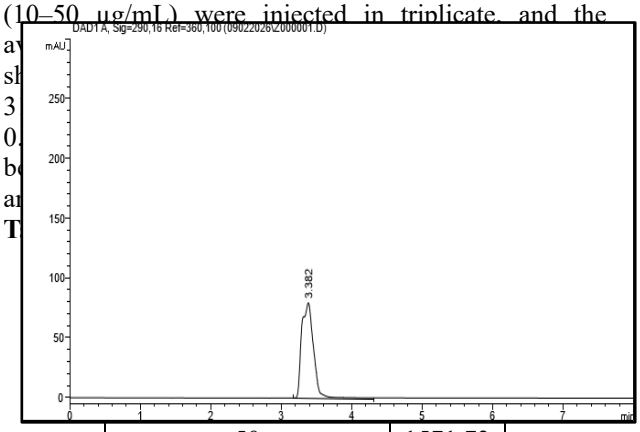
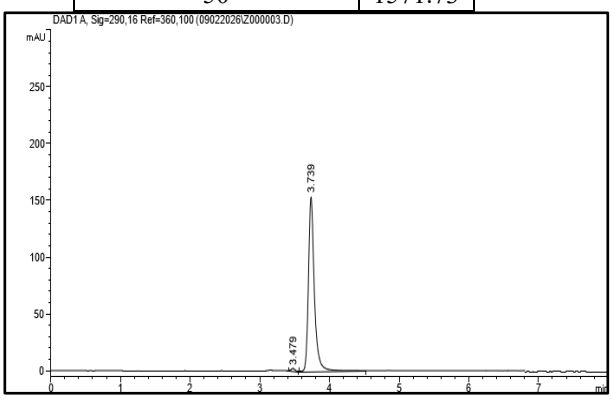


50	1571.73



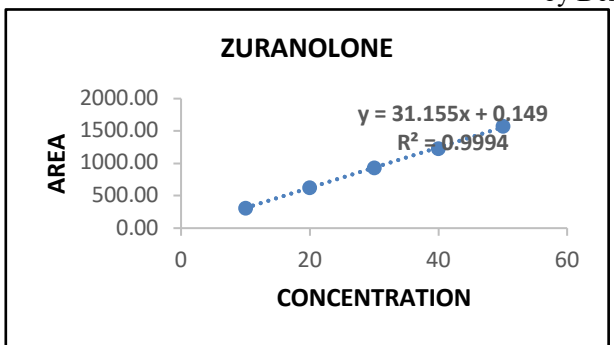


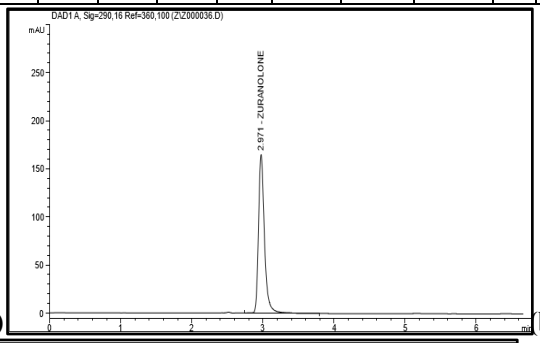
Figure 3. Concentration of Zuranolone

PRECISION: Precision concentration Interday is shown in Figure 4 and given in Table 3 and Intraday is shown in Figure 5 and Table 4.

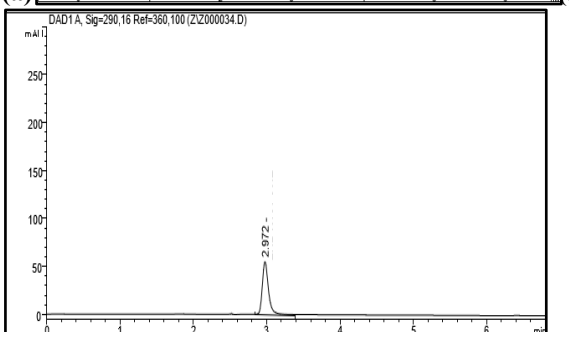
Concentration	Area I	Area II	Area III	Mean	Amt Found	AM	%Amt Found	SD	%RSD
10	310.97733	310.47883	310.78222	310.74	9.98	0.998053291	99.81	0.25	0.08
30	934.73719	933.83396	935.65519	934.74	30.01	1.00417467	100.04	0.91	0.10
50	1570.126	1567.488	1568.241	1568.62	50.36	1.007234194	100.72	1.36	0.09

Table 3. Precision concentration of Interday

Concentration	Area I	Area II	Area III	Mean	Amt Found	AM	% Amt Found	SD	%RSD
10	315.06777	316.80556	316.52516	316.13	10.15	1.015347127	101.53	0.93	0.29
30	950.36	944.28	945.42	946.69	30.40	1.013207	101.32	3.2	0.34
	85	52	56			66		3	
50	1559.48	1556.025	1558.732	1558.08	50.02	1.004673 45	100.05	1.82	0.12



(a) (b)



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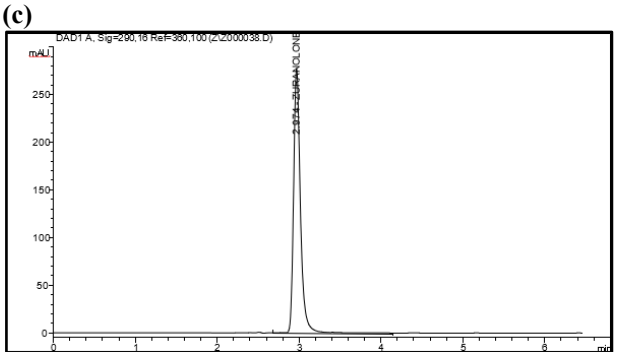
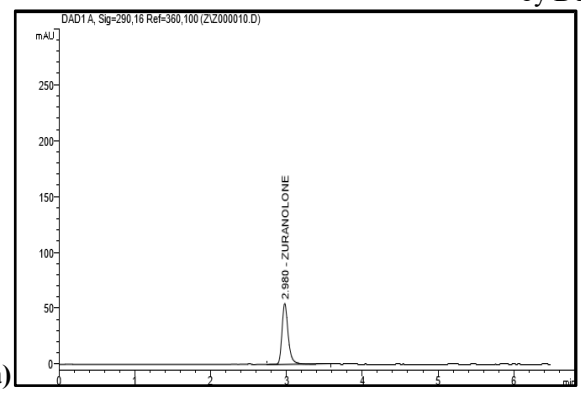


Figure 4. Precision concentration at 10%(a), 30%(b), 50%(c) Interday

Table 4. Precision concentration of Intraday



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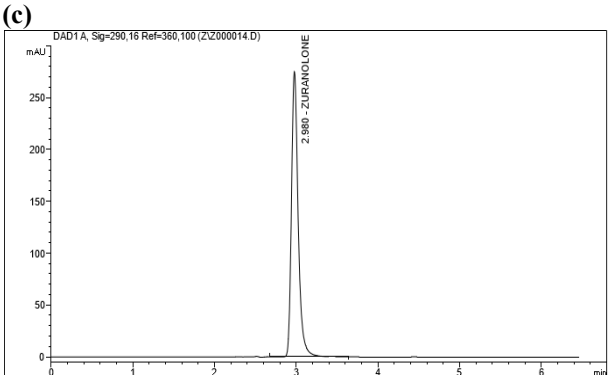


Figure 5. Precision concentration of 10%(a), 30%(b), 50%(c) Intraday

REPEATABILITY:

For the repeatability study (50 µg/mL), Zuranolone exhibited a retention time of 2.972 min with a peak area of 1581.60950 mAUs, symmetry factor of 0.91, and plate count of 6915. The results indicated good repeatability and precision of the developed HPLC method as shown in Figure 6 and Table 5.

Table 5. Repeatability concentration of Zuranolone

Concentration	Area I	Area II	Area III	Mean	Amt. Found	AM	% Amt Found	SD	%RSD
50	1581.60910	1577.09867	1578.67676	1579.12151	50.70	1.0140037 6	101.40	2.31	0.15

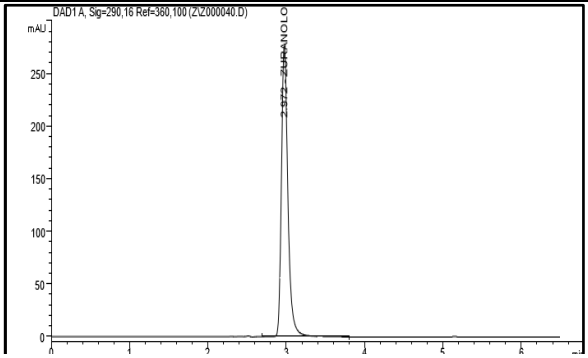


Figure 6. Repeatability concentration graph of Zuranolone

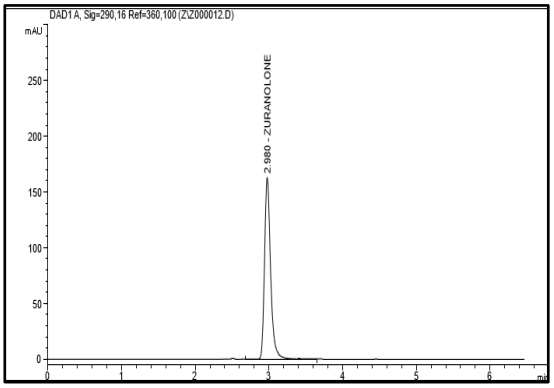
ACCURACY:

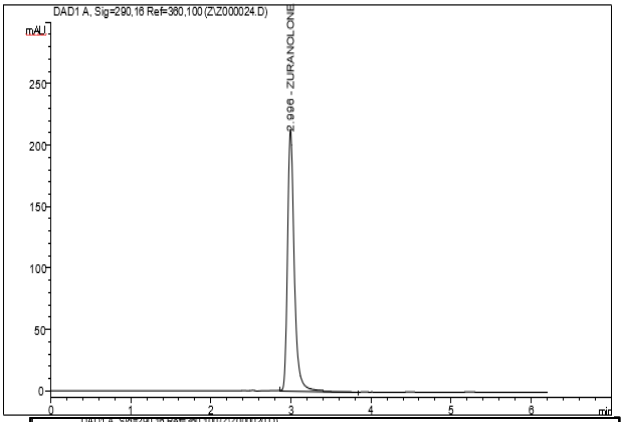
The Accuracy of Zuranolone is given in Table 6 and shown in Figure 7.

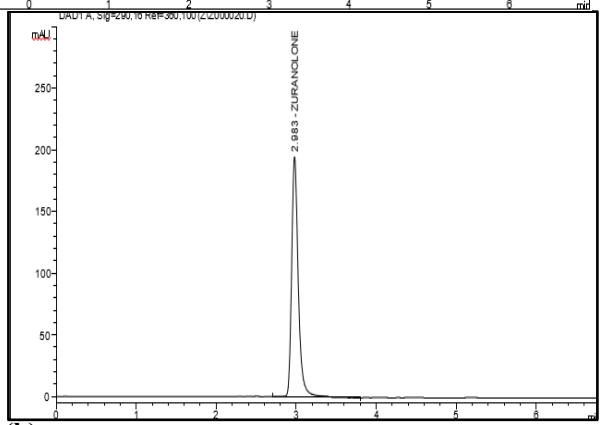
Table 6. Accuracy of Zuranolone

Level	Amount Added	Mean % Recovery	%RSD
80%	16	99.15 ± 0.02	0.02
100%	20	99.42 ± 0.28	0.28
120%	24	99.28 ± 0.74	0.74

(a)







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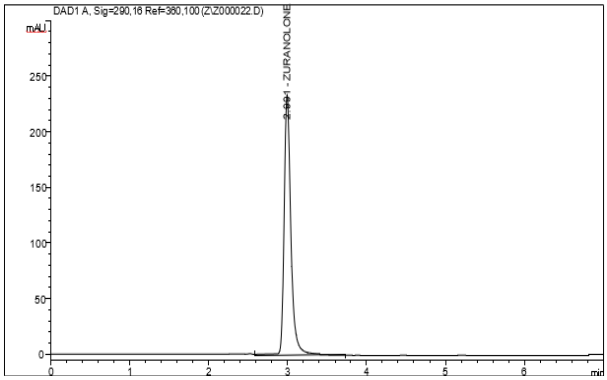


Figure 7. Accuracy graph of Zuranolone at 80%(a), 100%(b),120%(c)

ASSAY:

Assay of Zuranolone: The assay of Zuranolone was carried out under optimized chromatographic conditions using an RP-C18 column with detection at 290 nm. Zuranolone showed a sharp peak at a retention time of 3.031 min with a peak area of 925.97620 mAUs, symmetry factor of 0.93, and plate count of 7575, indicating satisfactory chromatographic performance and suitability of the method for assay determination as shown in Figure 8 and Table 7.

Table 7. Concentration for Assay of Zuranolone

Concentration	I	C	M	CM	Amt Found	LC	% Label Claim
30.00	925.976	0.149	31.15	926.13	29.73115	0.9910388	99.10
30.00	928.437	0.149	31.15	928.59	29.81015	0.9936772	99.37
30.00	929.243	0.149	31.15	929.39	29.83602	0.9945344	99.45
30.00	930.476	0.149	31.15	930.63	29.87256	0.9958533	99.59
30.00	931.725	0.149	31.15	931.87	29.91257	0.99719	99.72
Mean	929.17				29.77		99.24
SD	2.178				0.056		0.186
%RSD	0.234				0.188		0.188

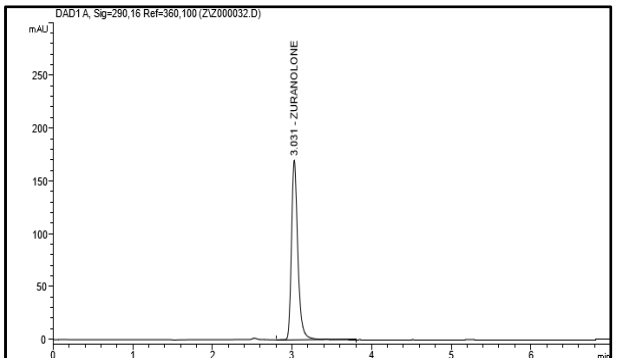


Figure 8. Assay of Zuranolone

ROBUSTNESS:

Robustness study at concentration79.5:20.5 v/v: For the robustness study (mobile phase change: Methanol 79.5% : 0.1% OPA water 20.5%, 30 µg/mL), Zuranolone showed a retention time of 3.019 min with a peak area of 934.86633 mAUs, symmetry factor of 0.99, and plate count of 5491. The results indicated that slight changes in mobile phase composition did not significantly affect chromatographic performance, confirming the robustness of the method as shown in Table 8 and Figure 9.

Table 8. Parameter changed for robustness at concentration 79.5:20.5 v/v

Parameter Changed	Condition	Conc. (µg/mL)	Peak Area I	Peak Area II	Mean Area	SD	%RSD
Mobile Phase Change	Methanol: 0.1% OPA water (**79.5:20.5 v/v**)	30	934.8663	939.9870	937.43	3.621	0.386
Wavelength Change	**289 nm**	30	913.7065	918.0828	915.895	3.095	0.3379

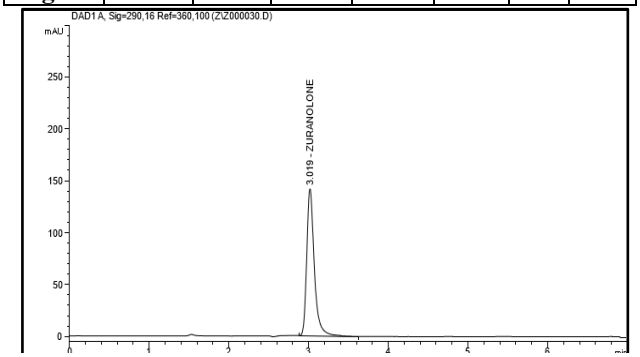


Figure 9. Robustness graph at concentration 79.5:20.5 v/v

Robustness study at concentration 81.5:18.5 v/v: For the robustness study (mobile phase change: Methanol 81.5% : 0.1% OPA water 18.5%, 30 µg/mL), Zuranolone showed a retention time of 2.930 min, peak

area of 938.25128 mAUs, and plate count of 6974, indicating satisfactory chromatographic performance and method robustness as shown in Figure 10 and Table 9.

Table 9. Parameter changed for robustness at concentration 81.5:18.5 v/v.

Parameter Changed	Condition	Concentration (µg/mL)	Peak Area I	Peak Area II	Mean Area	SD	%RSD
Mobile Phase Change	Methanol: 0.1% OPA water **(81.5:18.5 v/v)**	30	938.2513	939.9398	939.096	1.19	0.1271
Wavelength Change	**291 nm**	30	957.75183	959.1783	958.47	1.01	0.11

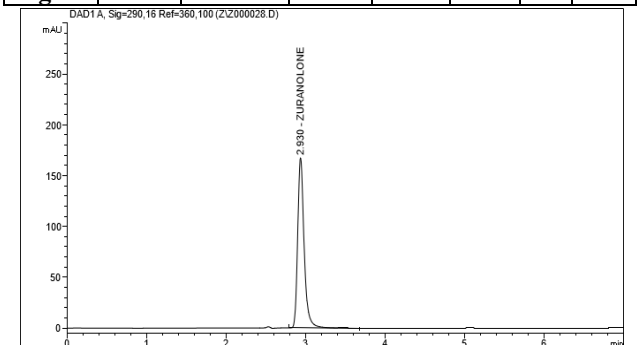


Figure 10. Robustness graph at concentration 81.5:18.5 v/v

Wavelength change for robustness of Zuranolone: For the robustness study (wavelength change: 289 nm, 30 µg/mL), Zuranolone exhibited a retention time of 2.997 min, peak area of 913.70648 mAUs, and plate count of 6805, indicating satisfactory chromatographic performance and robustness of the developed method as shown in Figure 11.

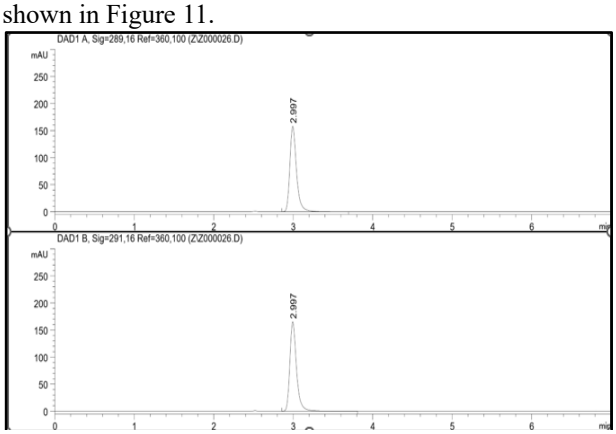


Figure 11. Wavelength change graph for robustness of Zuranolone

RUGGEDNESS:

For the study of ruggedness (30 µg/mL), Zuranolone exhibited a retention time of 2.973 min, peak area of 937.51093 mAUs, symmetry factor of 0.91, and plate count of 6898, indicating satisfactory chromatographic performance and ruggedness of the developed HPLC method as given in Table 10 and Figure 12.

Table10. Ruggedness of Zuranolone by HPLC method.

Concentration	I	Amount Found	LC	% Label Claim
30.00	937.511	30.09188	1.003063	100.31
30.00	938.016	30.10808	1.003603	100.36
Mean	937.76	30.10		100.33
SD	0.357	0.011		0.038
%RSD	0.038	0.038		0.038

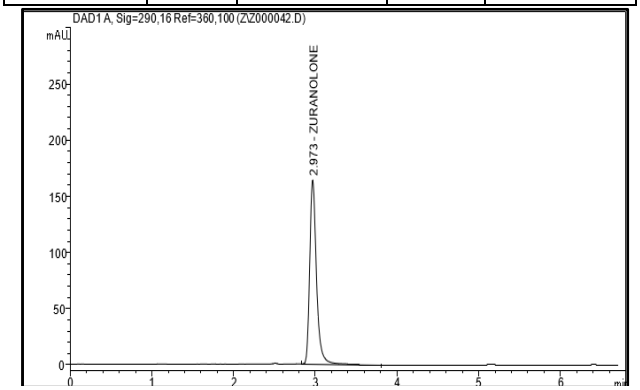


Figure 12. Ruggedness of Zuranolone by HPLC method

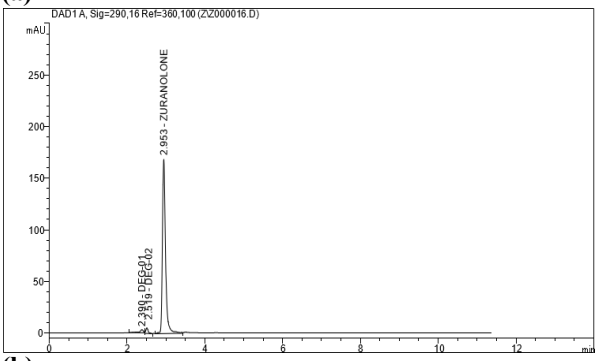
FORCED DEGRADATION:

Forced Degradation After -2 Hours: The forced degradation is given in Table 13 and shown in Figure 13.

Table 13.Forced Degradation After -2 Hours (0.1n HCL)

Sr. No.	Degradation	Area of Standard	Area of degraded Sample	%Degraded	Actual % Degradation
1	Acid Degradation	935.75079	919.84741	98.30	1.70
2	Basic Degradation	935.75079	916.14551	97.90	2.10
3	H_2O_2 Degradation	935.75079	891.09622	95.23	4.77
4	Neutral	935.75079	930.51703	99.44	0.56

(a)



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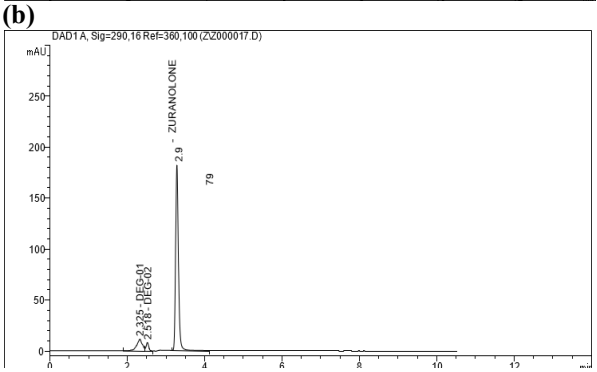
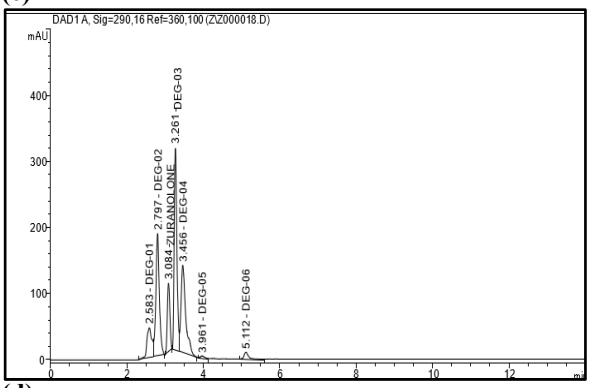
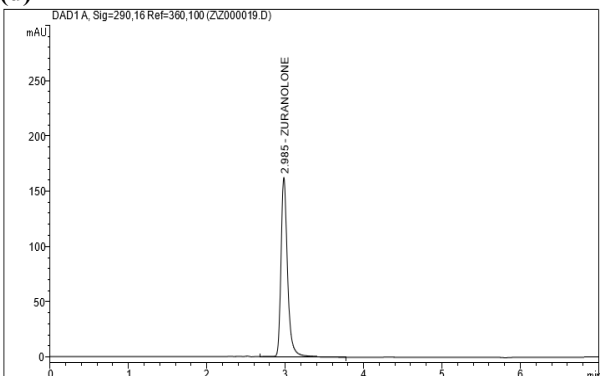


(a)Forced Acid Degradation (0.1n HCL)
(b) Forced Base Degradation (0.1N NaOH)

(c)



(d)



(c) Forced H_2O_2 Degradation (3% H_2O_2)
(d) Forced Neutral Degradation

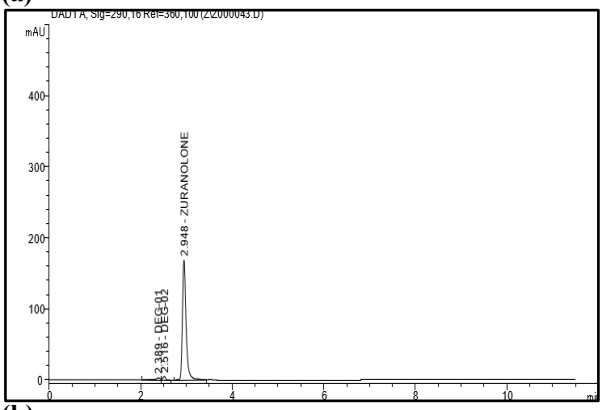
Figure 13. Forced Degradation After -2 Hours

Forced Degradation After -24 Hours: The forced degradation is given in Table 14 and shown in Figure 14

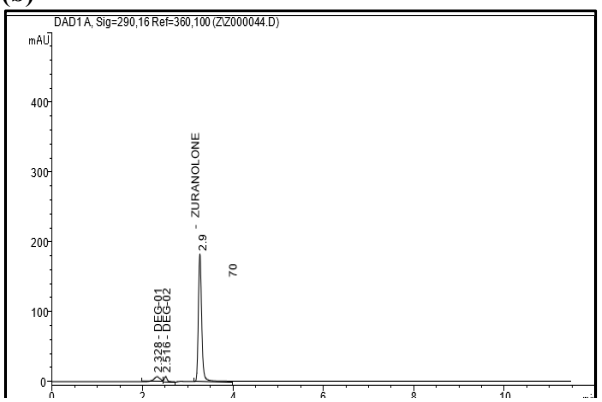
Table 14. Forced Degradation After -24 Hours

Sr. N	Degradation	Area of Stand	Area of degraded Sample	Degraded upto	Actual % degrada
O.		ard		%	tion
1	Acid Degradation	935.75079	902.83636	96.48	3.52
2	Basic Degradation	935.75079	879.27814	93.96	6.04
3	H_2O_2 Degradation	935.75079	775.08298	82.83	17.17
4	Neutral	935.75079	930.45673	99.43	0.57
5	Photolytic	935.75079	932.24869	99.63	0.37

(a)

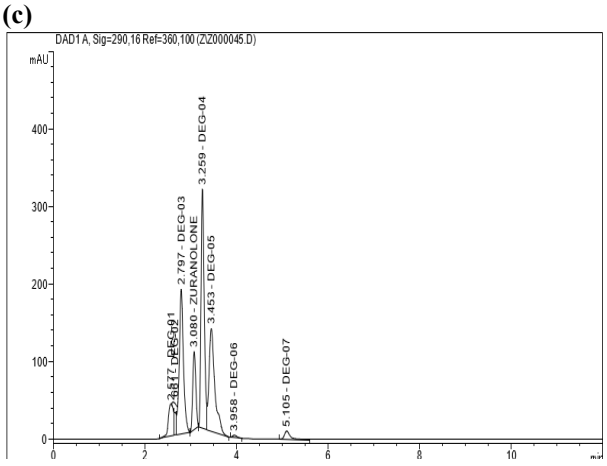


(b)

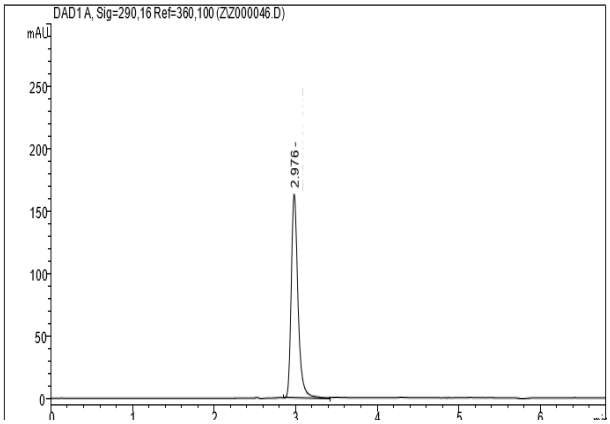


(a) Forced Acid Degradation (0.1n HCL)
(b) Forced Base Degradation (0.1N NaOH)

(c)



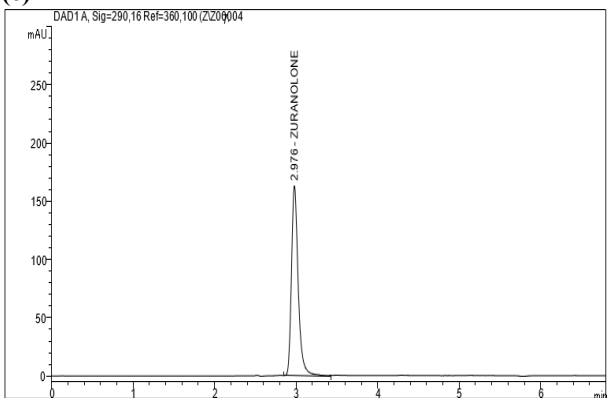
(d)



(c) Forced H_2O_2 Degradation (3% H2O2)

(d) Forced Neutral Degradation

(e)



(e)Forced Degradation After (Photolytic)

Figure 14. Forced Degradation After -24 Hours

QbD experimental design:

Table 15. QbD design

Run	Factor 1	Factor 2	Response R1	Response R2	Response R3
	A:Mobile Phase	B:Flow Rate	(Retention Time)	(Area)	(Theoretical Plates)
	%	ml/min	minutes	AUC	TP
1	80	0.9	3.242	678.504	7603
2	80	0.9	3.243	678.959	7631
3	85	1	2.654	643.662	7806
4	80	0.7	3.884	818.75	8882
5	87	0.9	2.848	691.559	9356
6	85	0.8	3.3	794.263	9700
7	80	0.9	3.244	678.512	7613
8	80	1	2.812	585.135	6835
9	75	1	3.419	612.22	6462
10	80	0.9	3.246	679.869	7632
11	80	0.9	3.249	679.14	7643
12	75	0.8	4.261	768.447	7438
13	72	0.9	4.116	682.664	6692

Table 16. Fit Summary

Std. Dev.	0.0105	**R^2**	0.9997
Mean	3.35	**Adjusted R^2**	0.9995
C.V. %	0.3150	**Predicted R^2**	0.9981
		Adequate Precision	227.6367

Figure 15. ANOVA Graph for Quadratic model R1(RT)

Table 17. Fit Summary

Std. Dev.	8.66	**R^2**	0.9902
Mean	691.67	**Adjusted R^2**	0.9832
C.V. %	1.25	**Predicted R^2**	0.9302
		Adequate Precision	38.2921

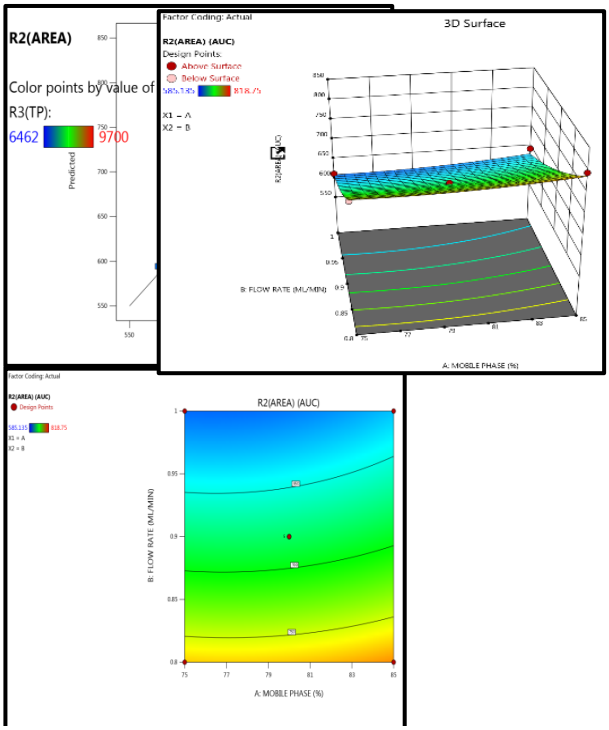
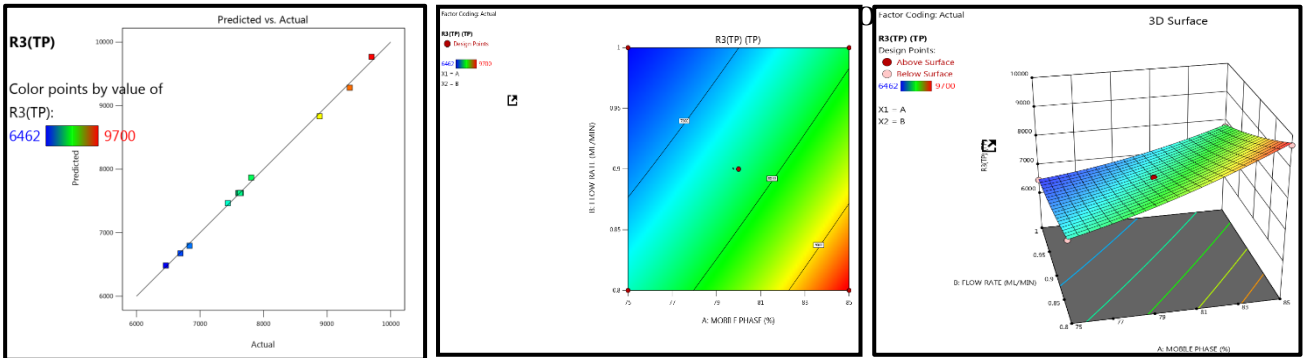


Figure 16. ANOVA Graph for Quadratic model R2 (AREA)

Table 18. Fit Summary

Std. Dev.	54.09	**R^2**	0.9982
Mean	7791.77	**Adjusted R^2**	0.9969
C.V. %	0.6942	**Predicted R^2**	0.9878
		Adequate Precision	89.3807



Final Equation in Terms of Coded Factors:

It was found that the two independent variables (the amount of A) = 0.84591e45, the amount of B = 6.69977e22) both had the effect of decreasing the RT of Zuranolone. Therefore, if more A is added to the mobile phase than B, there would be a decrease in the RT of Zuranolone that was found that the two independent variables (the amount of A) = 0.84591e45, the amount of B = 6.69977e22) both had the effect of decreasing the RT of Zuranolone. Therefore, if more A is added to the mobile phase than B, there would be a decrease in the RT of Zuranolone.

According to the interaction term's coefficient (AB = +0.0490), mobile-phase composition (A) and flow-rate (B) had combined interactive effects (on chromatographic behavior). The quadratic coefficient of both factors (A^2 = +0.1170 and B^2 = +0.0500) demonstrate curvature (indicating extreme-values for factors A or B would result in increasing RT). Because the coefficient of A was greater than that of B, the mobile phase composition (A) plays a more significant role in influencing the retention time than the flow rate (B). Overall, therefore, this equation is used to predict and optimize the chromatographic conditions necessary to obtain satisfactory separation of Zuranolone this is given in table 15-21 and shown in Figure 15-17.

Conclusion:

We have developed and validated a reliable, simple, precise, accurate and robust RP-HPLC method for the determination of Zuranolone in accordance with a QbD approach. The optimal chromatographic conditions were: Methanol:0.1%OPA (80:20 v/v) as mobile phase; a flow rate of 0.9 mL/min; a 4.6×250 mm RP-C18, 5 µm column; and detection at 290 nm. This provided all satisfactory parameters such as: Column parameters: peak symmetry; retention time; theoretical plate count. The RP-HPLC method was validated as pe ICH guidelines with linearity (10–50 µg/mL) of R^2=0.9994, good precision, accuracy, repeatability, ruggedness, robustness (%RSD < 2%). The results of the forced degradation (acid, base, oxidation and neutral) indicated the stability-indicating capability of the method in separating the degradation product(s) from the active drug peak. The results from the QbD study showed that the mobile phase composition and flow rate significantly affected retention time. and found the quadratic model produced a high-level predictability (R^2=0.9997) of these parameters. In summary, the developed RP-HPLC method is reliable and reproducible for the quantitative analysis and stability of Zuranolone in pharmaceutical formulations on a routine basis.

Reference:

1) Althaus AL, Ackley MA, Belfort GM, Gee SM, Dai J, Nguyen DP, Kazdoba TM, Modgil A, Davies PA, Moss SJ, Salituro FG. Preclinical characterization of zuranolone (SAGE-217), a selective neuroactive steroid GABAA receptor positive allosteric modulator. Neuropharmacology. 2020 Dec 15;181:108333.
2) Clayton AH, Lasser R, Nandy I, Sankoh AJ, Jonas J, Kanes SJ. Zuranolone in major depressive disorder: results from MOUNTAIN-a Phase 3, multicenter, double-blind, randomized, placebo-controlled trial. The Journal of Clinical Psychiatry. 2023 Feb 20;84(2):22m14445.
3) Salituro FG, Harrison BL, Beresis RT, Bai Z, Blanco MJ, Belfort GM, Dai J, Loya CM, Ackley MA, Althaus AL, Grossman SJ. Neuroactive Steroids. 2. 3α-Hydroxy-3β-methyl-21-(4-cyano-1H-pyrazol-1'-yl)-19-nor-5β-pregnan-20-one (SAGE-217):A Clinical Next Generation Neuroactive Steroid Positive Allosteric Modulator of the (γ-Aminobutyric Acid) A Receptor. Journal of Medicinal Chemistry. 2017 Aug 17;60(18):7810-9.
4) Perez AG, Saaraswat M, Oldak SE. A Brief Review of the Postpartum Depression Medication Zuranolone.
5) Liu J, Hong L, Qian Y, Chen R, Lin W. Modeling the efficacy of a novel antidepressant zuranolone for major depressive disorder. Journal of Affective Disorders. 2025 Aug 26:120158.
6) McNaught AD, McNaught AD. Compendium of chemical terminology.
7) Hostettmann K, Hostettmann M, Marston A. Preparative chromatography techniques. Applications in Natural Product Isolation. 198