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DEVELOPMENT AND VALIDATION OF STABILITY INDICATING UPLC METHOD FOR THE SIMULTANEOUS ESTIMATION OF NETUPITANT AND PALONOSETRON IN CAPSULE

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Keywords:

Netupitant, Palonosetron, RP-UPLC, Stability studies, Precision

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ABSTRACT: A simple, accurate, and precise stability-indicating method was developed for the simultaneous estimation of the Netupitant (NTPT) and Palonosetron (PLSN) in a capsule by UPLC. Chromatographic elution was processed through an HSS C18 (100 × 2.1 mm, 1.8µ) reverse phase column, and the mobile phase composition of 0.01N KH_2PO_4 buffer (4.0 pH) and acetonitrile in the ratio of 55:45 was pumped through a column at a flow rate of 0.3 ml/min. The column oven temperature was maintained at 30 °C, and the detection wavelength was processed at 274 nm. Retention times of NTPT and PLSN were found to be 1.682 min and 1.288 min, respectively. Repeatability of the method was determined in the form of %RSD, and findings were 0.9 and 1.0 for NTPT and PLSN, respectively. The percentage recovery of the method was found to be 99.98% and 99.61% for NTPT and PLSN, respectively. LOD, LOQ values obtained from regression equations of NTPT and PLSN were 2.174, 6.587µg/ml and 0.02, 0.05 µg/ml respectively. Regression equation of NTPT was y = 4923.1x ± 1915.4 and PLSN was y = 40065x ± 224.19. Two analytes were subjected for acid, peroxide, photolytic, alkali, neutral, and thermal degradation studies, and the results show that the percentage of degradation was found between 0.85% and 6.50%. Retention times and total run time of two drugs were decreased, and the developed method was simple and economical. So, the developed method can be adopted in industries as a regular quality control test for the quantification of NTPT and PLSN.

INTRODUCTION: NTPT/PLSN (trade name Akynzeo) is a combination drug for the prevention of acute and delayed chemotherapy-induced nausea and vomiting. NTPT is a selective neurokinin 1 (NK1) receptor antagonist with potential antiemetic activity.

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NTPT competitively binds to and blocks the activity of the human substance P/NK1 receptors in the central nervous system (CNS), thereby inhibiting NK1-receptor binding of the endogenous tachykinin neuropeptide substance P (SP), which may result in the prevention of chemotherapy-induced nausea and vomiting (CINV).

SP is found in neurons of vagal afferent fibers innervating the brain-stem nucleus tractus solitarii and the area postrema, which contains the chemoreceptor trigger zone (CTZ), and maybe elevated in response to chemotherapy.

The NK-receptor is a G-protein receptor coupled to the inositol phosphate signal-transduction pathway and is found in both the nucleus tractus solitarii and the area postrema [1, 2]. NTPT chemically designated as 2- [3, 5-Bis(trifluoromethyl)phenyl]-*N*,2-dimethyl-*N*- [4- (2- methylphenyl)- 6- (4-methyl-1- piperazinyl)-3- pyridinyl] propanamide with molecular weight and formula of 578.59 g/mole and $C_{30}H_{32}F_6N_4O$ respectively **Fig. 1**.

PLSN is an antinauseant and antiemetic agent indicated for the prevention of nausea and vomiting associated with moderately-emetogenic cancer chemotherapy and for the prevention of post-operative nausea and vomiting. PLSN is a highly specific and selective serotonin 5-HT_3 receptor antagonist that is pharmacologically related to other 5-HT_3 receptor antagonists, but differs structurally [3-5]. PLSN has a high affinity for 5-HT_3 receptors, but has little to no affinity for other receptors. The serontonin 5-HT_3 receptors are located on the nerve terminals of the vagus in the periphery, and centrally in the chemoreceptor trigger zone of the area postrema. It is suggested that chemo-therapeutic agents release serotonin from the entero-chromaffin cells of the small intestine by causing degenerative changes in the GI tract. The serotonin then stimulates the vagal and splanchnic nerve receptors that project to the medullary vomiting center, as well as the 5-HT3 receptors in the area postrema, thus initiating the vomiting reflex, causing nausea and vomiting [6-8]. PLSN chemically designated as (3*aS*)-2-[(3*S*)-1-Aza-bicyclo[2.2.2] oct-3-yl]-2,3,3*a*,4,5,6-hexahydro-1*H*-benz[*de*] iso-quinolin-1-one with molecular weight and formula of 296.407 g/mole and $C_{19}H_{24}N_2O$ respectively **Fig. 1**.

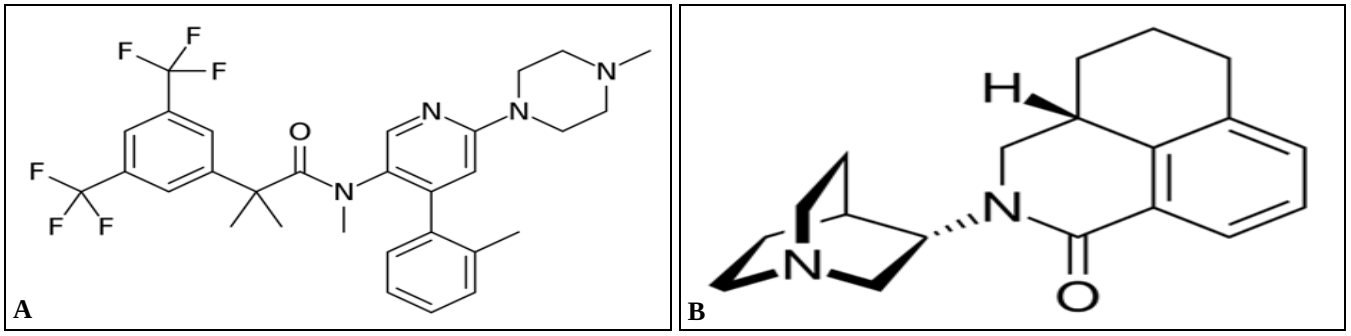

FIG. 1: CHEMICAL STRUCTURES OF A) NTPT AND B) PLSN

The literature review unveils that a very less spectrometric [9], LC-MS/MS [10,] and reverse-phase high-performance liquid chromatographic [11-19] techniques have been reported for the estimation of NTPT and PLSN. Based on the reported HPLC methods, there is a need to develop a stability-indicating RP-UPLC method for the simultaneous determination of NTPT and PLSN in bulk and capsule form with less retention times.

MATERIALS AND METHODS:

Chemicals and Reagents: API of NTPT and PLSN were obtained from spectrum Pharma Research Solutions, Hyderabad. HPLC-grade methanol and acetonitrile were procured from Merck chemical division, Mumbai, India; potassium dihydrogen orthophosphate, orthophosphoric acid, sodium dihydrogen orthophosphate and HPLC-grade water were bought from Rankem, avantor performance material India limited. Akynzeo capsules were obtained from a local pharmacy.

Chromatographic System: Liquid chromato-graphic UPLC system of Waters equipped with PDA (photodiode array detector), auto-sampling unit and HSS C18 (100 × 2.1 mm, 1.8µ) reverse phase column. The mobile phase composition of 0.01N KH_2PO_4 buffer (4.0 pH) and acetonitrile in the ratio of 55:45 was pumped through a column at a flow rate of 0.3 ml/min. The column oven temperature was maintained at 30°C, and the detection wavelength was processed at 274 nm. Integration of output signals was monitored and processed by waters Empower software-2.0.

Diluent: Depending up on the solubility of the drugs, diluent was optimized. Acetonitrile and water in the ratio of 50:50% v/v were used as diluent.

Preparation of Standard Stock Solutions: Exactly weighed 150mg of NTPT and 0.25mg of PLSN poured into two 50ml volumetric flasks

alone. 10ml of diluent was added and vortexed for 20 min. Flasks were made up with diluent and marked as standard stock solutions 1 and 2 (3000µg/ml of NTPT and 5.0 µg/ml PLSN). 1ml from each stock solution was pipetted out and taken into a 10ml volumetric flask and made up with diluent to get 300µg/ml of NTPT and 0.5µg/ml of PLSN.

Preparation of Sample Stock Solutions: 20 capsules were weighed, and the average weight of each tablet was calculated. The weight equivalent to 1 capsule was transferred into a 100ml volumetric flask, and 25 ml of diluent was added and sonicated for 25 min. Further, the volume was made up with diluent and filtered through a 0.45 µ filter (3000µg/ml of NTPT and 5.0 µg/ml PLSN). 1ml of the resultant solution was poured into a 10ml volumetric flask and made up with diluent (300µg/ml of NTPT and 0.5µg/ml of PLSN).

Preparation of Buffer: Accurately weighed 1.36gm of potassium dihydrogen orthophosphate in a 1000ml of volumetric flask consisting of about 900ml of milli-Q water and sonicated to degasify and make up the volume with water. Then 1ml of Triethylamine was added and PH adjusted to 4.0 with a dilute orthophosphoric acid solution**.**

Method Validation: The developed method for NTPT and PLSN was subjected for validation for the parameters like system suitability, linearity, robustness, the limit of detection (LOD), the limit of quantification (LOQ), precision, and accuracy as per the guidelines of ICH [20-24].

RESULTS AND DISCUSSION:

Method Development and Optimization: We tried different mobile phase combinations with methanol, water, acetonitrile, and buffer. At all the combinations, the resulting chromatograms got poor resolution, theoretical plates, and peak shape. Finally, excellent chromatographic efficiency parameters were obtained with the mobile phase composition of 0.01N KH_2PO_4 buffer (4.0 pH), and acetonitrile in the ratio of 55:45%v/v pumped through an HSS C18 (100 × 2.1 mm, 1.8µ) reverse phase column, at a flow rate of 0.3 ml/min. The column oven temperature was maintained at 30°C, and the detection wavelength was processed at 274 nm. Based on the solubility, all the dilutions were made with acetonitrile and water in the ratio of 50:50% v/v. Retention times of NTPT and PLSN were found to be 1.682 min. and 1.288 min. respectively. An injection volume of 1.0 µl was infused through a UPLC system to get better performance.

System Suitability: The system suitability variables were estimated by preparing standard solutions of NTPT and PLSN, and the same was injected 6 times into the chromatographic system. The variables like peak tailing, resolution, and USP plate count were estimated [25, 26]. The results were shown in **Fig. 2** and **Table 1**.

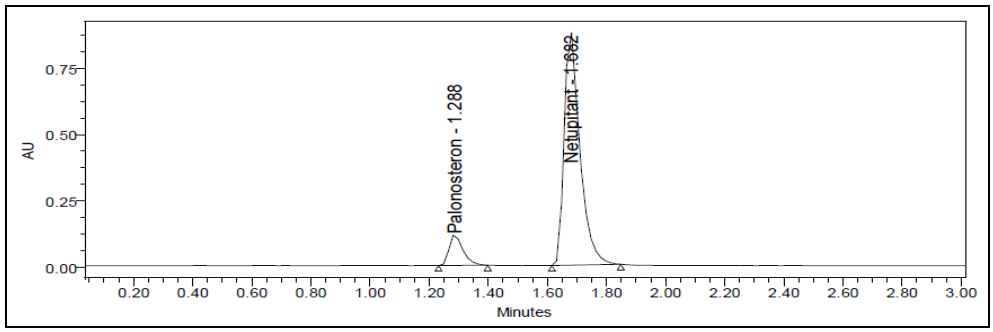

FIG. 2: SYSTEM SUITABILITY CHROMATOGRAM OF NTPT AND PLSN

TABLE 1: SYSTEM SUITABILITY PARAMETERS FOR NTPT AND PLSN

S.	PLSN			NTPT			
no.	RT(min)	USP Plate Count	Tailing	RT(min)	USP Plate Count	Tailing	USP Resolution
1	1.293	2970	1.25	1.685	6606	6606	6606
2	1.296	3002	1.25	1.687	6397	6397	6397
3	1.300	2897	1.19	1.690	5927	5927	5927
4	1.302	2827	1.19	1.691	5660	5660	5660
5	1.302	2959	1.21	1.691	5701	5701	5701
6	1.313	3149	1.17	1.705	6960	6960	6960

Specificity: Method specificity was determined by infusing the blank, placebo, standard, and sample solutions into a chromatographic system, and the resulting chromatograms were evaluated for interference with the excipients, degradants, and other components may expect to be present [20]. Blank, standard, formulation, and placebo chromatograms were represented in **Fig. 3**.

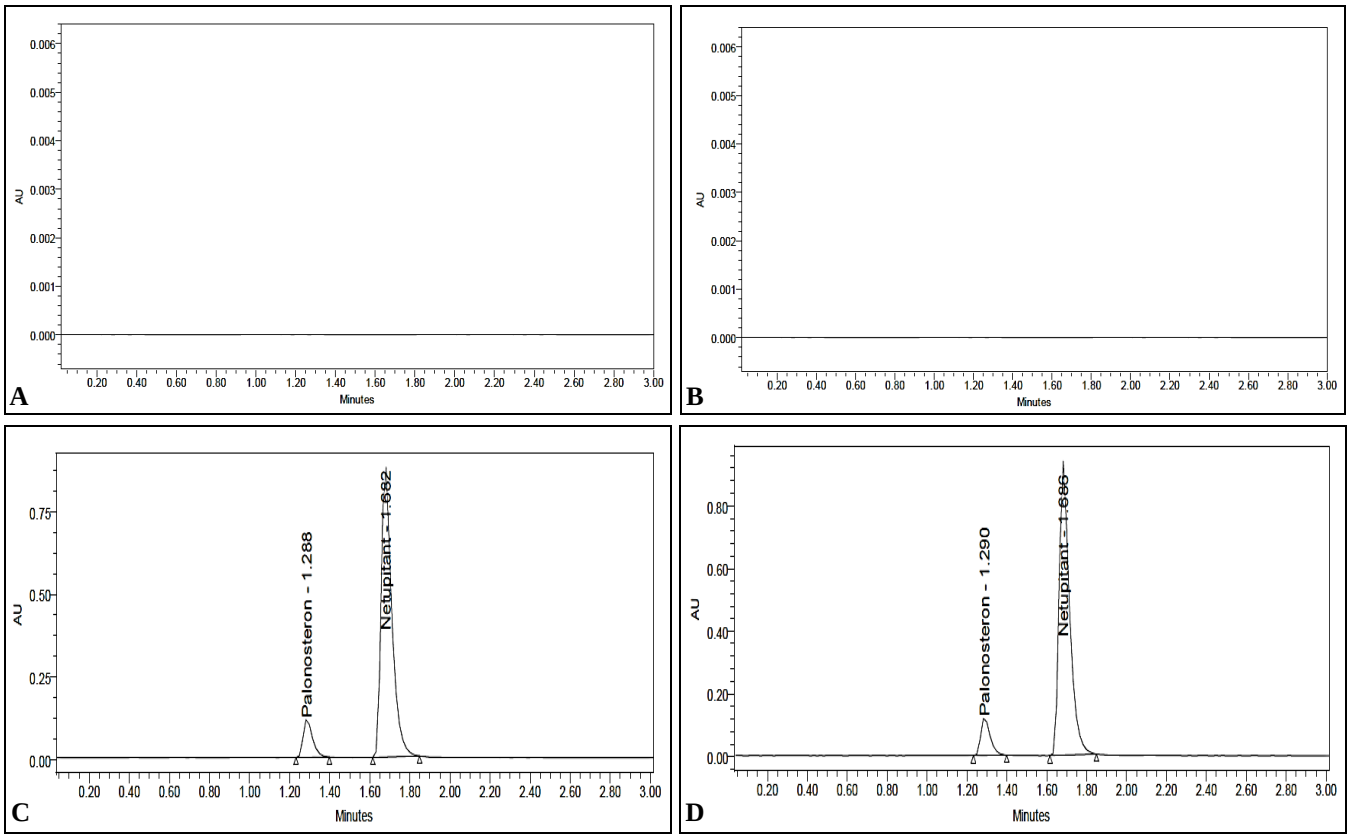

FIG. 3: CHROMATOGRAMS OF A) BLANK, B) PLACEBO, C) STANDARD AND D) SAMPLE

TABLE 2: REPEATABILITY RESULTS OF NTPT AND PLSN

S. no.	Area of NTPT	Area of PLSN
1	1475960	19938
2	1467092	20243
3	1476887	20289
4	1472173	20112
5	1498861	19915
6	1462369	20425
Mean	1475557	20154
SD	12665.2	202.5
%RSD	0.9	1.0

SD: Standard deviation; RSD: Relative standard deviation

Precision: The precision of the method was evaluated in terms of method precision and intermediate precision. The method precision (repeatability) was estimated by infusing 6 standard solutions and 6 sample solutions. Intermediate precision was evaluated by infusing 6 standard solutions and 6 sample solutions on different days by different employees on different chromatographic systems [23, 25]. The peak responses of all the chromatograms were taken, and standard deviation, % RSD (relative standard deviation), and percentage assay of sample solutions were calculated. The findings were represented in **Table 2** and **3**.

TABLE 3: INTERMEDIATE PRECISION RESULTS OF NTPT AND PLSN

S. no.	Area of NTPT	Area of PLSN
1	1414182	19232
2	1388187	19105
3	1375020	18991
4	1399247	18960
5	1386258	19438
6	1379109	18991
Mean	1390334	19120
SD	14352.1	185.9
%RSD	1.0	1.0

SD: Standard deviation; RSD: Relative standard deviation

Accuracy: Method accuracy was estimated at three variable concentrations of 50%, 100%, and 150% level by spiking the known amount of the drug analytes [26]. The % recovery at each level was calculated, and the findings were represented in **Table 4**.

TABLE 4: ACCURACY RESULTS OF NTPT AND PLSN

	PLSN				NTPT			
% Level	Amount Spiked (µg/ml)	Amount recovered (µg/ml)	% Recovery	Mean %Recovery	Amount Spiked (µg/ml)	Amount recovered (µg/ml)	% Recovery	Mean %Recovery
50%	0.25	0.248	99.5	99.61%	150	149.856	99.90	
	0.25	0.25	100.0		150	148.957	99.30	
	0.25	0.247	99.0		150	149.591	99.73	
100%	0.5	0.497	99.5		300	299.675	99.89	99.98%
	0.5	0.495	99.1		300	299.944	99.98	
	0.5	0.507	101.4		300	298.962	99.65	
150%	0.75	0.753	100.4		450	449.892	99.98	
	0.75	0.741	98.9		450	448.685	99.71	
	0.75	0.747	99.6		450	451.107	100.25	

Linearity: The linearity of the developed method was evaluated by processing 6 different concentration levels of both NTPT and PLSN over the concentration of 75 to 450 µg/ml and 0.125 to 0.75 µg/ml. Each concentration level was processed in triplicates [20, 24]. The linearity plots were acquired by plotting peak response (on X-axis) versus concentration (on Y-axis). The results of the linearity were represented in **Fig. 4, 5,** and **Table 5**.

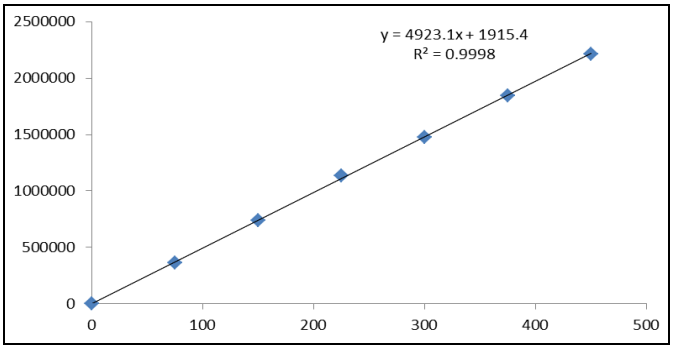

FIG. 4: CALIBRATION CURVE OF NTPT

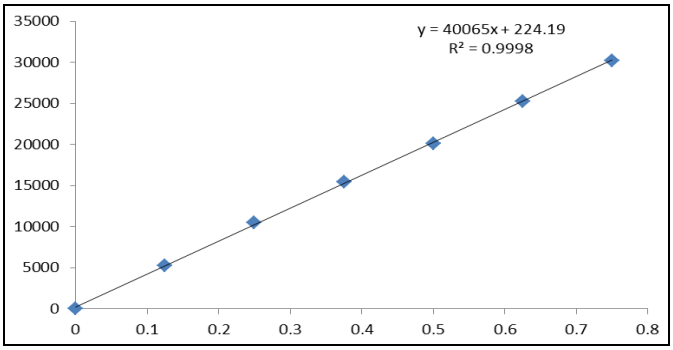

FIG. 5: CALIBRATION CURVE OF PLSN

TABLE 5: LINEARITY RESULTS FOR NTPT AND PLSN

NTPT		PLSN	
Conc. (µg/ml)	Peak area	Conc. (µg/ml)	Peak area
0	0	0	0
75	363525	0.125	5254
150	736887	0.25	10462
225	1134680	0.375	15451
300	1475001	0.5	20123
375	1844025	0.625	25277
450	2213099	0.75	30173

LOD and LOQ: LOD is the lowest quantity of drug in a sample that can be identified but cannot be quantified exactly. LOQ is the lowest quantity of a drug in an analyte which can be quantitatively estimated with suitable accuracy and precision. The LOD and LOQ values were calculated from the linearity data by utilizing the standard deviation and slope of the curve [20, 23]. The resulting LOD and LOQ findings were represented in **Table 6**.

TABLE 6: LOD AND LOQ RESULTS FOR NTPT AND PLSN

Analyte	LOD (µg/ml)	LOQ (µg/ml)
NTPT	2.174	6.587
PLSN	0.02	0.05

Robustness: The method robustness was processed by introducing small variation in the optimized LC conditions such as organic phase in the mobile phase (±5%), flow rate (-0.27 and +0.33 ml/ min), and column temperature (±5°C). The findings were shown in **Table 7**.

TABLE 7: ROBUSTNESS DATA FOR NTPT AND PLSN

S. no.	Variation in LC conditions	% RSD for NTPT	% RSD for PLSN
1	Flow rate (-) 0.27ml/min	1.3	1.4
2	Flow rate (+) 0.33ml/min	1.1	0.9
3	Organic phase -5%	0.7	1.4
4	Organic phase + 5%	1.5	1.1
5	Temperature at 25°C	1.3	1.4
6	Temperature at 35°C	0.9	1.1

Degradation Studies:

Alkali Degradation Studies: To 1 ml of each stock solution of NTPT and PLSN, 1 ml of 1N NaOH was added to a 10 ml volumetric flask and kept at 60 °C for 30 min. The resulting solution

was neutralized with 1ml of 1N HCl, and further, the solution was made up to the mark to get 300µg/ml and 0.5µg/ml concentrations of NTPT and PLSN, respectively. From that 1.0 µl of the solution was infused into a UPLC system, and the resultant chromatograms were analyzed for the stability of analytes [21]. The findings were represented in **Table 8** and **Fig. 6**.

TABLE 8: DEGRADATION DATA OF NTPT AND PLSN

Type of degradation	NTPT			PLSN		
	Area	%Recovered	% Degraded	Area	%Recovered	% Degraded
Acid	1401393	94.78	5.22	18916	93.67	6.33
Alkali	1425724	96.43	3.57	19453	96.33	3.67
Peroxide	1409975	95.36	4.64	18881	93.50	6.50
Thermal	1440170	97.41	2.59	19875	98.42	1.58
UV light	1461415	98.84	1.16	19897	98.53	1.47
Neutral	1465976	99.15	0.85	20027	98.53	1.47

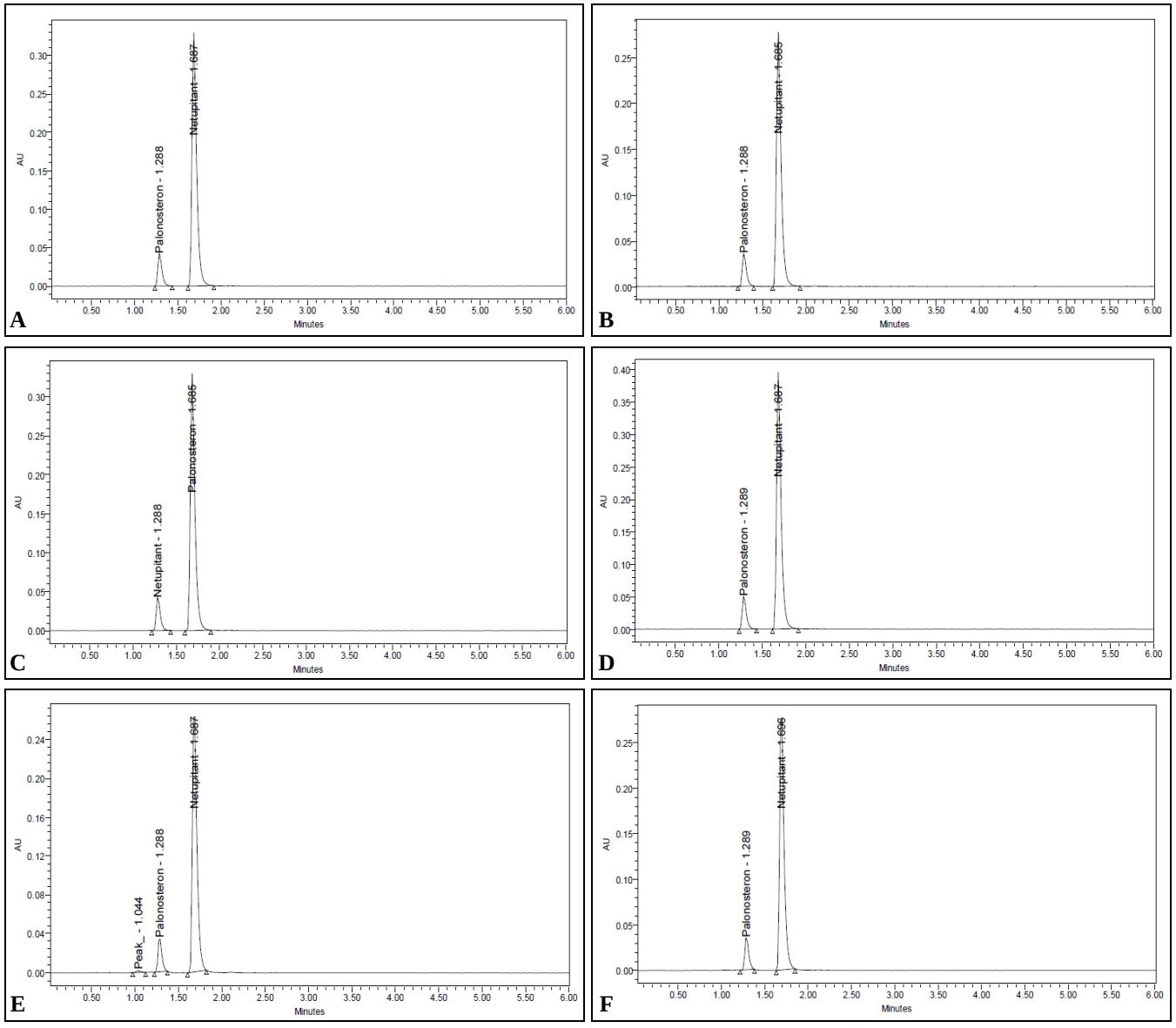

FIG. 6: REPRESENTATIVE CHROMATOGRAMS OF A) UV-DEGRADATION, B) PEROXIDE DEGRADATION, C) THERMAL DEGRADATION, D) NEUTRAL DEGRADATION, E) ACID DEGRADATION AND F) ALKALI DEGRADATION

Photolytic Stability Study: For the photolytic stability study, NTPT 3000µg/ml and PLSN 5.0µg/ml solutions were exposed to UV-light by placing the solutions in UV cabinet for 1day or 200

Watt-hours/m^2 in photostability chamber. The resulting solutions were combined in a 10ml volumetric flask and made up to the mark with diluent to get 30µg/ml and 0.5µg/ml concentrations of NTPT and PLSN, respectively. From that 1.0 µl of the solution was infused into a UPLC system, and the resultant chromatograms were analyzed for the stability of analytes. The findings were represented in **Table 8** and **Fig. 6**.

Acid Degradation Studies: To 1 ml of each stock solution of NTPT and PLSN, 1ml of 1N Hydrochloric acid was added into a 10 ml volumetric flask and refluxed at 60 °C for 30 min. The resulting solution was neutralized with 1ml of 1N NaOH, and further, the resulting solution was made up to the mark to get 30µg/ml and 0.5µg/ml concentrations of NTPT and PLSN, respectively. From that 1.0 µl of the solution was infused into a UPLC system, and the resultant chromatograms were analyzed for the stability of analytes. The findings were represented in **Table 8** and **Fig. 6**.

Neutral Degradation Studies: To 1 ml of each stock solution of NTPT and PLSN, 5 ml of water was added into a 10 ml volumetric flask and kept for refluxing at 60 °C for 6 h. Further, the resulting solution was made up to the mark to get 30µg/ml and 0.5µg/ml concentrations of NTPT and PLSN, respectively. From that 1.0 µl of the solution was infused into a UPLC system, and the resultant chromatograms were analyzed for the stability of analytes. The findings were represented in **Table 8** and **Fig. 6**.

Oxidation: To 1 ml of each stock solution of NTPT and PLSN, 1 ml of 20% hydrogen peroxide (H_2O_2) was added to a 10 ml volumetric flask and kept at 60°C for 30 min. Further, the resulting solution was made up to the mark to get 30µg/ml and 0.5µg/ml concentrations of NTPT and PLSN, respectively. From that 1.0 µl of the solution was infused into a UPLC system, and the resultant chromatograms were analyzed for the stability of analytes. The findings were represented in **Table 8** and **Fig. 6**.

Dry Heat Degradation Studies: To a 10 ml volumetric flask, add 1ml of each stock solution of NTPT and PLSN and monitored at 105 °C for 6 h in a hot air oven to perform the dry heat stability study. Further, the resulting solution was made up to the mark to get 30µg/ml and 0.5µg/ml concentrations of NTPT and PLSN, respectively. From that, 1.0 µl of the solution was infused into a UPLC system, and the resultant chromatograms were analyzed for the stability of analytes. The findings were represented in **Table 8** and **Fig. 6**.

CONCLUSION: A simple, accurate and precise method was developed for the simultaneous estimation of the NTPT and PLSN in Tablet dosage form by RP-UPLC technique. Retention times of NTPT and PLSN were found to be 1.682 min and 1.288 min, respectively. Chromatographic elution was processed through an HSS C18 (100 × 2.1 mm, 1.8µ) reverse phase column, and the mobile phase composition of 0.01N KH_2PO_4 buffer (4.0 pH) and acetonitrile in the ratio of 55:45 was pumped through a column at a flow rate of 0.3 ml/min. Repeatability of the method was determined in the form of %RSD, and findings were 0.9 and 1.0 for NTPT and PLSN, respectively. LOD, LOQ values obtained from regression equations of NTPT and PLSN were 2.174, 6.587µg/ml and 0.02, 0.05 µg/ml respectively. Two analytes were subjected for acid, peroxide, photolytic, alkali, neutral, and thermal degradation studies, and the results show that the percentage of degradation was found between 0.85% and 6.50%. Retention times and total run time of two drugs were decreased, and the developed method was simple and economical. So, the developed method can be adopted in industries as a regular quality control test for the quantification of NTPT and PLSN.

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REFERENCES:

1. Darmani NA, Zhong W, Chebolu S and Mercadante F: Differential and additive suppressive effects of 5-HT3 (palonosetron)- and NK1 (netupitant)-receptor antagonists on cisplatin-induced vomiting and ERK1/2, PKA and PKC activation. Pharmacol Biochem Behav 2015; 131: 104-11.
2. Rizzi A, Campi B, Camarda V, Molinari S, Cantoreggi S, Regoli D, Pietra C and Calo G: *In-vitro* and *in-vivo* pharmacological characterization of the novel NK(1) receptor selective antagonist netupitant. Peptides 2012; 37: 86-97.

3. De Leon A: Palonosetron (Aloxi): a second-generation 5-HT(3) receptor antagonist for chemotherapy-induced nausea and vomiting. Proc (Bayl Univ Med Cent) 2006; 19: 413-6.
4. Stoltz R, Cyong JC, Shah A and Parisi S: Pharmacokinetic and safety evaluation of palonosetron, a 5-hydroxytryptamine-3 receptor antagonist, in U.S. and Japanese healthy subjects. J Clin Pharmacol 2004; 44: 520-31.
5. Rubenstein EB: Palonosetron: a unique 5-HT3 receptor antagonist indicated for the prevention of acute and delayed chemotherapy-induced nausea and vomiting. Clin Adv Hematol Oncol 2004; 2: 284-9.
6. Yang LP and Scott LJ: Palonosetron: in the prevention of nausea and vomiting. Drugs 2009; 69: 2257-78.
7. Siddiqui MA and Scott LJ: Palonosetron. Drugs 2004; 64: 1125-32.
8. Eisenberg P, MacKintosh FR, Ritch P, Cornett PA and Macciocchi A: Efficacy, safety and pharmacokinetics of palonosetron in patients receiving highly emetogenic cisplatin-based chemotherapy: a dose-ranging clinical study. Ann Oncol 2004; 15: 330-7.
9. Parambi DGT, Mathew SRM and Ganesan V: Estimation of palonosetron hydrochloride (a 5-ht3 antagonist) in pharmaceutical dosage form by U.V. spectrophotometric method. Int J Chem Sci 2011; 9: 1619-24.
10. Mingzhen X, Yang i, Shihong L, Juan D, Huqun L, Ying Z, Weiyong L and Hui C: Development and validation of a rapid LC-MS/MS method for simultaneous determination of netupitant and palonosetron in human plasma and its application to a pharmacokinetic study. J Chromatogr B Analyt Technol Biomed Life Sci 2016; 1027: 187-93.
11. Panigrahy UP and Reddy ASK: A novel validated RP-HPLC-DAD method for the simultaneous estimation of Netupitant and Palonosetron in bulk and pharmaceutical dosage form with forced degradation studies. Int J ChemTech Res 2015; 8: 317-37.
12. Kalavati T, Shyamala and Sharma JVC: Development and validation of stability indicating UPLC method for the estimation of palonosetron in bulk and its pharmaceutical dosage form. Int J Pharm Pharmac Res 2019; 14: 144-54.
13. Singh NP, Goud VM, Sharma JVC, Sirisha P and Devi CHP: A review on analytical methods for the determination of palonosetron in pharmaceutical formulation. Int J Pharm Sci Rev Res 2020; 60: 91-93.
14. Kumar GV, Sravanthi B and Aparna NG: Development and validation of RP HPLC method for simultaneous estimation of netupitant and palonosetron in pharmaceutical dosage form. Indo Am J P Sci 2018; 05: 21-29.
15. Bhagavanji NVMS, Satyanarayana PVV, Karanam S and Naniprasad D: Development and validation of stability indicating RP-HPLC method for the estimation of netupitant and palonosetron in combined tablet dosage form. Int J Pharm Sci Rev Res 2016; 41: 81-87.
16. Manoranjani M: Method development and validation for simultaneous quantification of netupitant and palonosetron in bulk and pharmaceutical dosage form and their forced degradation study by RP-HPLC. Asian J Pharm Clin Res 2019; 12: 119-23.
17. Harole M, Patil RN, Gaware D, Suryawanshi G and Pise K: A validated stability indicating RP-HPLC method for simultaneous determination of netupitant and palenoserton in pharmaceutical formulations. World Journal of Pharmacy and Pharmaceutical Sciences 2016; l5: 878-87.
18. Mubeena S and Kumar KP: A novel development of RP-HPLC method for the estimation of netupitant and palonosetron in bulk and their combined dosage form. European J of Biomedical and Pharm Sci 2019; 6: 300-04.
19. Shilpa NV and MashruRC: Chemometrics assisted and RP-HPLC methods for quantification of netupitant and palonosetron hydrochloride by qbd approch: development and validation. World Journal of Pharmaceutical Research 2016; 5: 1173-97.
20. ICH: Q2 (R1), Validation of analytical procedures: text and methodology; 2005.
21. ICH: Q2B. Harmonized Tripartite Guideline, Validation of Analytical Procedure: Methodology, IFPMA, in: Proceedings of the International Conference on Harmonization, Geneva; 1996.
22. Guguloth R, Madhukar A, Kannappan N and Ravinder A: Method development and validation of new RP- HPLC method for the determination of sofosbuvir tablet. J Pharma Res 2016; 5: 161-63.
23. Charde MS, Welankiwar AS and Chakole RD: Development of validated RP-HPLC method for the simultaneous estimation of atenolol and chlorthalidone in combine tablet dosage form. International Journal of Advances in Pharmaceutics 2014; 3: 1-11.
24. de Mendoza AEH and Imbuluzqueta I: Development and validation of ultra-high performance liquid chromato-graphy-mass spectrometry method for LBH589 in mouse plasma and tissues. J Chromatogr B: Anal Technol Biomed Life Sci 2011; 879: 3490-6.
25. Ngwa G: Forced degradation studies as an integral part of HPLC stability indicating method development. Drug Delivery Technol 2010; 10: 56-9.
26. Mule KKL: Rapid analytical method for assay determination for prochlorperazineedisylate drug substances by Ultra performance liquid chromatography. Int J Curr Pharm Res 2017; 9: 118-22.

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