Bulletin of Environment, Pharmacology and Life Sciences
Bull. Env. Pharmacol. Life Sci., Vol 10 [5] April 2021 : 92-99

Online ISSN 2277-1808
Journal's URL:http://www.bepls.com
CODEN: BEPLAD

ORIGINAL ARTICLE **OPEN ACCESS**

Stability Indicating HPLC Method Development and Validation for Simultaneous Estimation of Selected Drugs in their Combined Pharmaceutical Dosage Form

Gurdeep Singh[1, 2], Sunil Shivhari Jaybhaye*[1]
1Oriental College of Pharmacy and Research, Oriental University, Indore, Madhya Pradesh, 453555.
2School of Pharmaceutical Sciences, Lovely Professional University, Phagwara-144411, Punjab, India.
Corresponding Author's Email: jaybhayesunil89@gmail.com

ABSTRACT
The new method for simultaneous establishment of paracetamol (PCM), cetrizine(CTZ) and phenylephrine (PNP) has been evolved by reverse phase HPLC from combination drug product. The separation achieved on C18 (4.6 x 250mm, 5µm particle size) column with Isocratic elution of mobile phase comprising methanol: 0.05% triethyl amine, in the ratio of 25:75 v/v (pH 2.70adjusted with OPA). The mobile phase flow rate was maintained at 1.0 ml/min and the analyte concentration was measured at detection wavelength 239 nm. The calibration curves were linear over the concentration range of 32.5–195µg/ml, 0.5-3µg/ml and 1-6 for PCM (n = 2), CTZ (n = 2) and PNP (n = 2) respectively. The PCM, CTZ and PNP were exposed to different stress condition like thermal, photolytic, hydrolytic, and oxidative stress conditions and samples were analyzed by proposed method. The stressed sample demonstrated the specificity of assay method in presence of degradant products with no interferences was observed from its stress degradation products. Analytical performance of the proposed HPLC procedure was thoroughly validated in terms of linearity, precision, accuracy, specificity, robustness, detection and quantification limits. The proposed method was suitable for quantitative determination and stability study ofPCM, CTZ and PNP in commercial tablets.
Key words: *Paracetamol, Cetirizine, Phenylephrine, RP-HPLC, Diode Array Detection*

Received 21.01.2021 Revised 22.03.2021 Accepted 24.03.2021

INTRODUCTION

Stability testing forms an important part of drug product process development. The purpose of stability testing is to provide evidence on how the quality of a drug substance or drug product varies with time under the influence of a variety of environmental factors such as temperature, humidity and light, enables recommendation of storage conditions, retest periods. The assay of drug product in stability test sample needs to be determined using stability indicating method. [1]In recent times, there is an increasing tendency towards the development of stability-indicating assays, using the approach of stress testing as incorporated in the International Conference on Harmonization (ICH) guideline. Even this approach is being extended to drug combinations, to allow accurate and precise quantitation of multiple drugs, their degradation, and interaction of products.

Paracetamol (PCM) is also known as acetaminophen it's causes reduction in the amount of prostaglandin, therefore, helps to prevent fever, headache and other pain like migraine headache, muscular aches, neuralgia, backache, joint pain, rheumatic pain, general pain, toothache, teething pain, period pain, and also used for the reduction of fever of bacterial or viral origin. It is suitable for most people, including elderly and young children, because it has very few side effects. Paracetamol (PCM) is chemically it is N-(4-hydroxyphenyl) acetamide (Fig.1). PCM,an antipyretic agent. Literature survey revealed the most recent methods for determination of paracetamol like chromatographic [2-7]

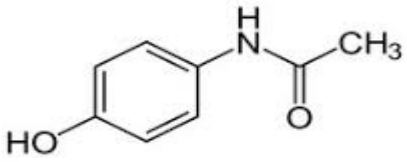

Fig. 1. Chemical Structure of Paracetamol (PCM)

Cetirizine HCl or 2-[2-[4-[(4-chlorophenyl)phenylmethyl]-piperazin-1-yl]ethoxy]aceticacid dihydrochloride (fig.2), Cetirizine is a piperazine derivative and metabolite of hydroxyzine, is an antihistamine, reported to be a long acting and with some mast-cell stabilizing activity. It is used for the symptomatic relief of hypersensitivity reactions including rhinitis and chronic urticaria.4-8. Cetirizine is rapidly absorbed from the gastro- intestinal tract after oral administration.There are several UV, and HPLC method reported for analysis of cetirizine individually or in combination with other drugs. [8-11]

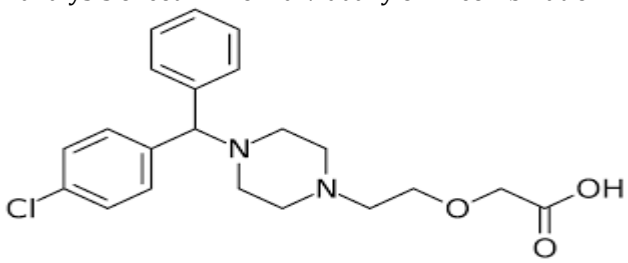

Fig. 2. Chemical Structure of Cetrizine (CTZ)

Phenylephrine hydrochloride (PE), (R)-1-(3-hydroxyphenyl)-2-methylaminoethanol hydrochloride (fig.3)(C9H13NO2, HCl) is useful as a nasal and sinus decongestant. Literature survey revealed the most recent methods for determination of paracetamol like chromatographic [12-14]

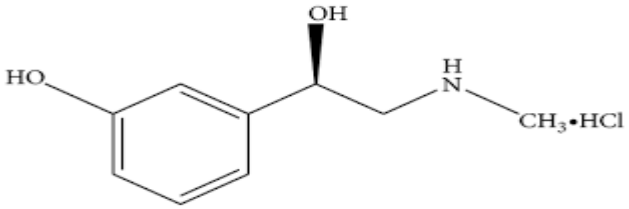

Fig. 3. Chemical Structure of Phenylephrine (PNP)

A developed HPLC method with high sensitivity and selectivity will be useful for the estimation of PCM, CTZ and PNPin combined pharmaceutical dosage form in presence of their degradation product. Therefore the aim of study was to develop and validate sensitive, precise, accurate and specific HPLC-DAD method for determination of PCM, CTZ and PNP in combined dose pharmaceutical formulation.

MATERIAL AND METHODS

Experimental

Chemicals and reagents

Working standards of pharmaceutical grade PCM,CTZ and PNP was received as a gift sample from Swapnroop drug and pharmaceutical, Aurangabad Maharashtra, India.A combination product containing the three drugs was purchased from local pharmacy shop. TEA, OPA, Sodium hydroxide, hydrochloric acid and hydrogen peroxide, HPLC grade Acetonitrile, water and methanol were purchased from Merck Ltd., India.

Equipment and chromatographic condition

The modular HPLC system used was equipped with Agilent Quaternary Gradient HPLC pump ((G130A) S.NO.DE9180834), An Auto injector, solvent degasser and DAD detector (G13148 S.NO. DE71365875). A Data Ace Chromatography data system was used to record and evaluate the data collected during and following chromatographic analysis. The chromatographic separation was achieved on an Eclipse XDE C-18 Agilent, (250 mm × 4.6 mm i. d., and 5µm particle size) column using a mixture of methanol: 0.05%TEA in the ratio 25:75 v/v (pH adjusted to 2.7 with OPA) as mobile phase at a flow rate of 1.0 ml/min. The eluent was monitored using Diode array detector (DAD) detection at a wavelength of 239 nm. The mobile phase was filtered through a 0.45 µm nylon filter prior to use and sonicated using an

ultrasonic bath (Ultrasonic electronic instrument). A precision water bath equipped with MV controller (i-therm, Biomedical, India) was used to carry out selected reactions in solution during stress degradation study. Thermal stability study was carried out in dry air oven. Other equipments used were analytical balance (WENSAR™ High Resolution Balance.) and Micro pipettes.

Preparation of standard and stock solution

A stock solution of PCM,CTZ and PNP (3250µg/ml),(50 µg/ml) and(100µg/ml) was prepared by accurately weighing approximately 325,5 mg of PCM,5 mg CTZ and 10mg PNP into a 100 ml A-grade volumetric flask and making up the volume with HPLC grade mobile phase. The stock solution was protected from light using aluminium foil. Aliquots of the standard stock solution of marketed formulation were transferred using A-grade bulb pipette into 100 ml volumetric flasks and the solutions were made up to volume with mobile phase to give final concentrations of 32.5,65,97.5,130,162.5and 195µg/ml for PCM, 0.5,1,1.5,2.0,2.5 and 3µg/ml for CTZ and 1,2,3,4,5 and 6µg/ml for PNP.

Forced degradation studies of API and tablet contents

In order to determine whether the analytical method and assay were stability-indicating PCM, CTZ and PNP active pharmaceutical ingredient (API) powder were stressed under various conditions to conduct forced degradation studies. In all cases, API (130µg/ml PCM, 2µg/ml for CTZ and 4µg/ml for PNP) subjected to forced degradation and prepared for analysis. The same stress conditions were applied to placebo and blank solution. Methanol was used as co-solvent in all studies. All stressed solutions of API and marketed formulation were withdrawn periodically during stress study and subjected to analysis after suitable dilution of stressed samples to yield final concentrations of 130,2 and 4µg/ml for PCM, CTZ and PNP respectively and filtered before injection in the chromatographic system.

Acid degradation studies

Solutions for acid degradation studies were prepared in mobile phase and 0.1N hydrochloric acid (50:50v/v)take 0.4 ml sample(from API stock) and the resultant solutions refluxed for 30min, 60 min and 24 hr at 70^{o}C.

Alkali degradation studies

Solutions for alkali degradation studies were prepared in mobile phase and 0.1N sodium hydroxide (50:50v/v)take 0.4 ml sample(from API stock) and the resultant solutions refluxed for 30min, 60 min and 24hr at 70^{o}C.

Neutral degradation studies

Solutions for neutral degradation studies were prepared in mobile phase and water (50:50v/v)take 0.4 ml sample (from API stock)and the resultant solutions refluxed for 30min, 60min 70^{o}C.

Oxidation

Solutions for oxidation studies were prepared in mobile phase and 3% H_2O_2 (50:50 v/v)take 0.4 ml sample (from API stock)and the resultant solutions were kept for 30min,60min,120 min and 24hr at room temperature.

Photolytic degradation

API in solid form were exposed to shorter and longer UV radiation to determine the effect of light irradiation on the stability of PCM, CTZ and PNP.Approximately 50 mg of API powder was spread on a glass dish in a layer that was less than 2mmthick. All samples for photostability testing were placed in a light cabinet and exposed to light for 24h. Control sample protected with aluminium foil was also placed in the light cabinet and exposed concurrently. Following removal from the light cabinet, all samples were prepared for analysis as previously described.

Temperature stress studies

API powder was exposed to dry heat in an oven at 70^{o}C for 24 h. The API powder was removed from the oven. Weight API powders were then prepared for analysis as previously described.

Development of method

HPLC studies were carried out on all the reaction solutions containing API individually, and on a marketed formulation. The separations were achieved by isocratic elution using methanol: 0.05%TEA (25:75 v/v, pH adjusted to 2.70 with OPA) as a mobile phase. It was filtered through 0.45 µm nylon filter and degassed before use. The injection volume was 20µl and mobile phase flow rate was 1.0 ml/min. The detection was carried out at 239 nm.

Preparation of tablets for assay

Twenty tablets were weighed, crushed and mixed in a mortar and pestle for 20 min. A portion of powder equivalent to 325mg PCM, 5mgCTZ and 10mg PNP was accurately weighed and transferred into100 ml A-grade volumetric flasks, up to 100 ml mobile phase was added and sonicated for 20 min for complete dissolution of the PCM, CTZ and PNP the solutions were then diluted up to volume with mobile phase. Aliquots of the solution were filtered through a 0.45µm nylon filter. From the filtrate, 0.4ml of the filtered solution was transferred to a 10ml A-grade volumetric flask and made up to volume with mobile phase,

to yield final concentrations of drugs in the range of linearity.

Validation of the method

The method was validated for linearity, precision (inter-day, intra-day), accuracy, specificity, selectivity, LOD, LOQ and robustness. Standard plots were constructed for both PCM, CTZ and PNP in the range of 32.5-195µg/ml,0.5-3µg/ml and 1-6µg/ml, respectively. The system precision was evaluated by six replicate injections of the standard solution. The method precision was studied by injecting two standard solutions of same concentration. The results for method precision and system precision were expressed in terms of percent relative standard deviation. The intraday precision was evaluated by analyzing the API sample at three times on the same day. The inter-day precision of the method was studied by analyzing the API samples on different days. Accuracy was determined by fortifying the marketed formulations with three known concentrations of the pure drugs. Further, the specificity of the method was assessed by study of the resolution factor of the drug peaks from nearest resolving peaks. The selectivity was determined by checking peak purity of all the peaks, including those of degradation products, using a DAD detector.

RESULTS AND DISCUSSION

The immediate interest in developing present stability indicating HPLC method was to accomplish resolution between PCM, CTZ and PNP and its degradation product. The preferred chromatographic condition chosen was established on symmetry of peak shape and contraction of chromatographic analysis. The mobile phase consisting mixture of methanol: 0.05%TEA in the ratio 25:75 v/v (pH adjusted to 2.70 with OPA) as mobile phase at a flow rate of 1.0 ml/min. The selection of organic solvent based on its affinity towards supportive UV transmittance, low viscosity and provides acceptable resolution between two drugs. The recommended chromatographic conditions applied an available C18 column with least use of organic solvent. The established method demonstrates no interferences from any possible forced degradation products. The results obtained from the study it can be concluded that our proposed method was closer to the ideal conditions of an assaying method for routine industrial use.

Development and optimization of stability-indicating HPLC method with degradation Behavior

Anisocratic method was found necessary to optimize the separation of major degradation products formed under various stress conditions. The best resolution was achieved with initial run of methanol: 0.05%TEAin the ratio of (25:75v/v, pH 2.70 adjusted with OPA). The obtained chromatogram is represented in fig. 4 shows the Rt of PCM, CTZ and PNP at 3.21, 9.10and respectively.

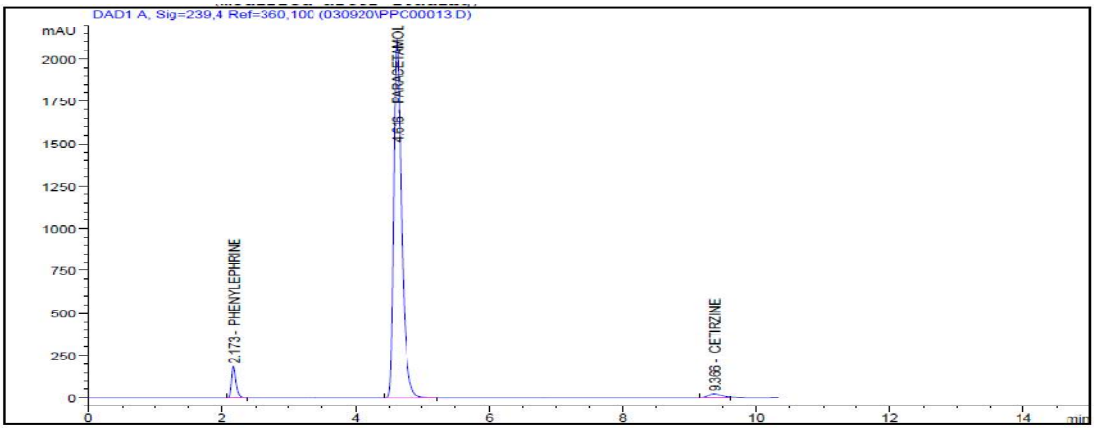

Fig. 4. Typical Chromatogram of PCM (Rt = 4.616 min) CTZ (Rt= 9.10 min)and PNP(Rt= 9.366 min) respectively.

The method worked well with the mixture of degradation solutions and was even applicable to degraded formulations. Fig. 5(a–f) shows the obtained chromatographic resolution of PCM, CTZ and PNP from its degradation product generated during various stress conditions. HPLC studies on API (PCM, CTZ and PNP) different stress conditions indicated the following degradation behavior. Both the drugs were found to be highly labile and showed degradation within 1 hr at 70oC in 0.1N HCl. CTZ showed higher degradation as compared to PCM. The major degradation products formed were at retention times (RTs) 2.2, and5.178 min. The API was refluxed in alkaline condition. PCM showed degradation within 0.73% at 70°Cin 0.1N NaOH, while CTZ was found within 20.05% at 70°Cin alkaline condition and PNP was found 100% degradation at 70°Cin alkaline condition. The major products appeared at RTs 2.761min.

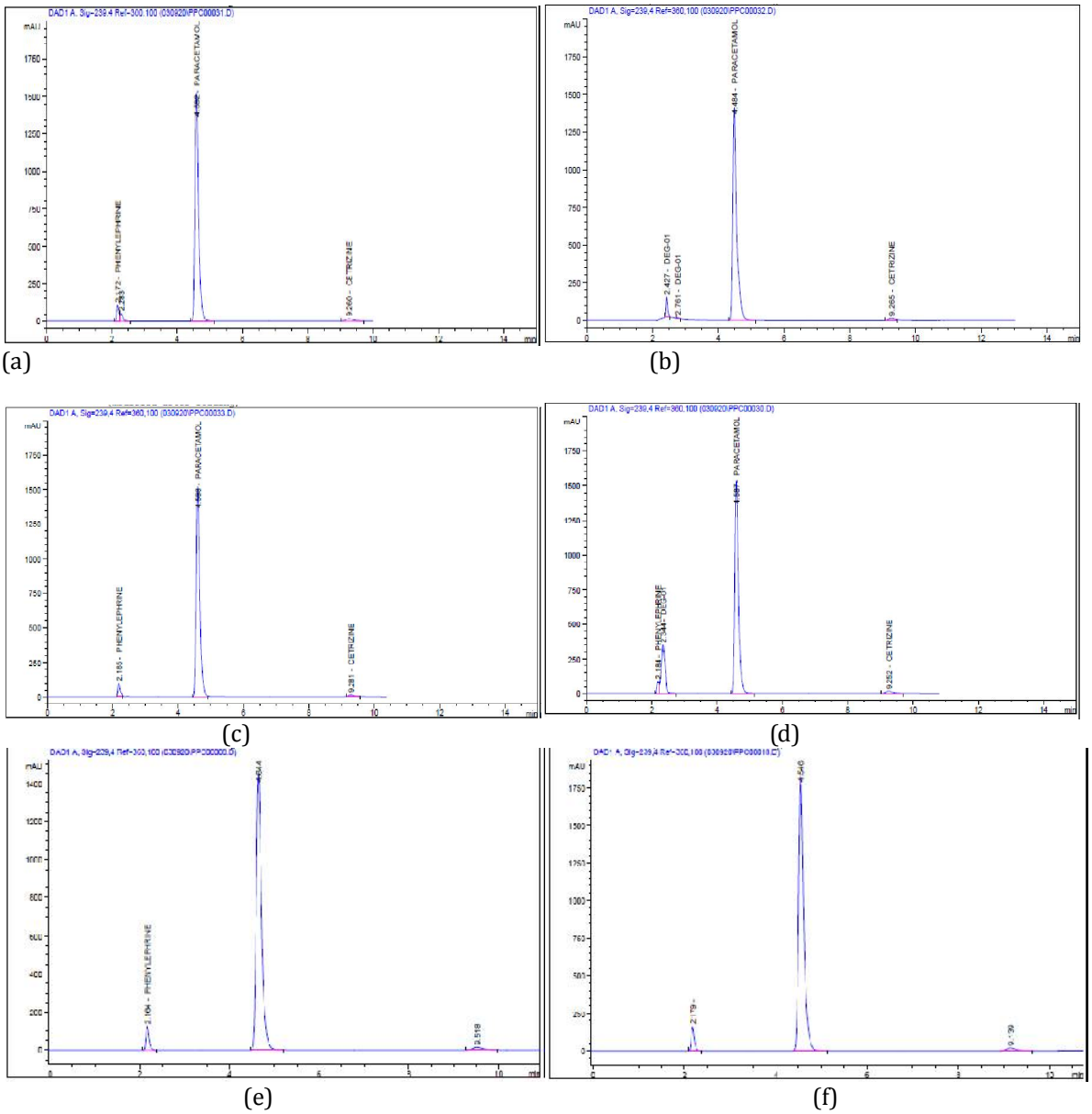

Fig. 5.Indicates the obtained chromatograms of stress studies of PCM, CTZ and PNP as: a) Acid degradation b) Alkali Degradation) Neutral degradation d) Oxidative degradation e) Photolytic degradation f) Thermal degradation

Sufficient amount of degradation was observed upon refluxing the combination for 3h at 70°C. CTZ showed little higher degradation as compared to PCM. The major degradation products appeared at RTs 0.3, 4.3 and4.8 min. The drugs showed sufficient amount of degradation in 3% H_2O_2 for 1h at room temperature. CTZ found to be 25.31% oxidation and PCM was found to be 1.96% oxidation and PNP was found to be 64.63% oxidation. The major degradation products appeared at 2.344 min.API and tablet formulation oxidation n were exposed to UV radiation for 24 h, similar to oxidative degradation, CTZ was found to be more susceptible to photolytic degradation than PCM and PNP was found to be 1.13% photolytic degradation. The major degradation products are not found. CTZ showed appreciable stability and did not influence to thermal degradation while PCM and PNP undergone degradation. The major degradation products are not found.

Validation of the developed stability-indicating method

The analytical method was validated with respect to parameters such as linearity, limit of Quantitation (LOQ), limit of detection (LOD), precision, accuracy, selectivity, recovery and robustness/ruggedness.

Linearity

Linearity was established by least squares linear regression analysis of the calibration curve The six point constructed calibration curves were linear over the concentration range of 32.5–195µg/ml,0.5–

3µg/ml for PCM and 1–6µg/ml for PNP (*n* = 2) and CTZ (*n* = 2), respectively. Peak areas of PCM, CTZ and PNP were plotted versus their respective concentrations and linear regression analysis was performed on the resultant curves. Correlation coefficients (*n*=3) were found to be 0.999 for both the drugs with %RSD was found to be < 2. Typically, the regression equations were: $y = 88.30\ xs + 336.2$ ($r^2 = 0.999$) for PCM, $y = 91.02x - 7.835$ ($r^2 = 0.999$) for CTZ and $y = 139.7x - 9.323$ ($r^2 = 0.999$) for PNP respectively.

LOD and LOQ

The detection and quantification limits were evaluated from calibration curves plotted in concentration ranges of32.5–195.0µg/ml for PCM (*n* = 2),0.5–3µg/ml for CTZ(*n* = 2),1–6 µg/ml for PNP(*n* = 2). The approach based on the standard deviation of the response and the slope was used for determining the detection and quantitation limits and the formulae used were LOD= 3.3σ/S and LOQ= 10σ/S (where σ = standard deviation of response and S = slope of calibration curve). The LOD for PCM, CTZ and PNP were found to be 0.2716µg/ml,0.1769µg/ml and 0.0101µg/ml, respectively. The LOQ that produced the requisite precision and accuracy was found to be 0.8233µg/ml,0.5363 µg/ml and 0.0307 µg/ml for PCM, CTZ and PNP respectively.

Precision

The intra- and inter-day variability or precision data were summarized in table 1 and 2, respectively and were assessed by preparation of standard solutions to produce solutions of three different concentrations of PCM,CTZ and PNP. Repeatability or intra-day precision was investigated by injecting two replicate samples of each of the samples of three different concentrations. Inter-day precision were assessed by injecting the sample of three different concentrations over next days.

Table.No.1: Intra-day Precision Data

Parameters	PCM			CTZ				PNP	
	Conc (µg/ml)			**Conc (µg/ml)**			**Conc (µg/ml)**		
	32.5	**97.5**	**162.5**	**0.5**	**1.5**	**2.5**	**1**	**3**	**5**
% Estimated	98.03	100.61	99.82	101.76	99.42	99.84	100.00	101.09	100.68
S. S. D.	± 2.361	± 9.850	± 1.626	± 0.04	± 0.035	± 1.66	± 0.21	±0.46	± 0.40
C. V	0.0750	0.1095	0.0111	0.078	0.025	0.707	0.13	0.10	0.05

* Mean of two determinations, S.D: Standard Deviation, C.V: Coefficient of variance

Table.No.2: Inter-Day Precision Data

Parameters	PCM			CTZ				PNP	
	Conc (µg/ml)			**Conc (µg/ml)**			**Conc (µg/ml)**		
	32.5	**97.5**	**162.5**	**0.5**	**1.5**	**2.5**	**1**	**3**	**5**
% Estimated	98.03	100.56	99.74	98.80	99.04	99.04	99.64	100.90	100.51
S. S. D.	± 4.1012	± 2.064	± 5.656	± 0.3111	± 0.6081	± 0.71	± 0.10	±0.50	± 1.37
C. V	0.1302	0.0230	0.0386	0.5893	0.4251	0.3062	0.07	0.11	0.19

* Mean of two determinations, S.D: Standard Deviation, C.V: Coefficient of variance

Accuracy

Accuracy study was performed by standard addition method by adding pure drug in a powder of marketed formulation at three different levels 80%, 100% and 120%. In each case, the percent relevant error and %RSD was calculated and found to be less than 0.56for PCM, 0.82 for CTZ and 0.78 for PNP The data obtained from recovery study for the determination of each compounds of interest are summarized in table 3.

Table No.3: Statistical Validation for Recovery Study

Level of recovery	% Mean Recovery			Standard Deviation			% R.S.D.		
	PCM	**CTZ**	**PNP**	**PCM**	**CTZ**	**PNP**	**PCM**	**CTZ**	**PNP**
80 %	99.0	99.16	100.1	± 0.55	± 0.81	0.03	0.556	0.821	0.03
100%	99.2	99.84	100.9	± 0.43	± 0.05	0.78	0.434	0.056	0.78
120%	98.9	99.68	101.5	± 0.14	± 0.25	0.20	0.142	0.250	0.19

Average of three determinations, R.S.D: Relative Standard deviation

Specificity

The results of stress testing studies in addition to that of monitoring standard solutions of each drug in the presence of their degradants indicated a high degree of specificity of this method for both PCM,CTZ and PNP The degradation product(s) of each of the parent compounds was found to be similar for both the tablets and API powders assessed. The method has sufficient specificity and selectivity as the two

drugs and even degradation products were well separated from each other, with the resolution factor of >2 in all cases. All the peaks were pure, which was proved through DAD purity studies. Data of peak purity index and purity threshold values indicates the degradants peaks are well separated from the drug peak. The established mass balance study ensured that all degradants were adequately detected. The above study is shown in table 4.

Table No. 4: Peak Purity study

Stress Condition	% degradation			Degradation upto(%)		
	PCM	**CTZ**	**PNP**	**PCM**	**CTZ**	**PNP**
Acid 0.1N HCl for 1h at 70°C.	0.98	9.73	64.63	99.02	90.28	35.57
Alkaline 1N NaOH for 1h at 70°C	0.73	20.05	100.0	99.27	79.95	0.00
Neutral H_2O for 1 h at 70°C	0.49	16.44	11.54	99.51	91.33	88.46
Oxidative 3% H2O2 for 1h at 70°C	1.96	25.31	64.63	98.04	74.69	35.37
Photolytic 24h in UV- radiation	0.01	0.44	1.13	99.99	99.56	98.87
Thermal 24hr at 70°C	0.0	0.0	0.0	100	100	100

*Average of three determinations

Robustness

The robustness of the method was investigated under a variety of conditions including changes of detection wavelength, flow rate and of organic phase composition. The degree of reproducibility of the results obtained as a result of small deliberate variations in the method parameters and by changing analytical operators has proven that the method is robust as R.S.D was found to be <2%.

CONCLUSION

In this work proposed and efficient HPLC DAD method was established validated for its simultaneous assessment of PCM, CTZ and PNP. It was observed from the literature survey that no official method was reported for present combination. Hence sincere efforts were plan to validate quantitative determination of PCM, CTZ and PNP. In summary method was validated and gratifying results were obtained for all components tested. The retrieve data declared current approach was linear response in fixed range with accurate and precise. The establish method reports least possible use of organic solvents thus contribute superlative security and environmental concerns. The results indicated the suitability of method to study stability of PCM, CTZ and PNP under various forced degradation conditions. The result of stress testing undertaken according to the International Conference on Harmonization (ICH) guidelines reveals that the developed method was selective and stability-indicating. The proposed method has the ability to separate these drugs from their degradation products. The method could be applied with success even to the analysis of marketed products, as no interference was observed due to excipients or other components present. It can be accomplished that the recommended methods has extreme assurance as rapid analytical tools for simultaneous estimation of PCM, CTZ and PNP in their combined pharmaceutical formulations, principally for quality control laboratories.

CONFLICT OF INTEREST

We have no conflict of interest to declare.

ACKNOWLEDGMENTS

The authors are thankful to Swapnroop drug and pharmaceutical, Aurangabad Maharashtra India for providing gift sample paracetamol, cetrizine and phenylephrine respectively as a pure drug.

REFERENCES

1. Bakshi, M., Singh, B., Singh, A., & Singh, S. (2001). The ICH guidance in practice: stress degradation studies on ornidazole and development of a validated stability-indicating assay. *Journal of pharmaceutical and biomedical analysis*, *26*(5-6), 891-897.
2. Vaidya, V. V., Singh, G. R., Choukekar, M. P., & Kekare, M. B. (2010). Simultaneous RP HPLC determination of aceclofenac, paracetamol and tizanidine in pharmaceutical preparations. *E-journal of Chemistry*, *7*(1), 260-264.

3. Birajdar, A. S., Meyyanathan, S. N., & Suresh, B. (2010). Method Development and validation for the simultaneous determination of paracetamol and tramadol in solid dosage form by RP-HPLC. *Int J Pharm Res Dev*, *1*, 1-6.
4. Mallah, M. A., Sherazi, S. T. H., Mahesar, S. A., & Khaskheli, A. R. (2012). Simultaneous quantification of ibuprofen and paracetamol in tablet formulations using transmission Fourier transform infrared spectroscopy. *Am J Anal Chem*, *3*(8), 503-511.
5. Rodenas, V., Garcıa, M. S., Sanchez-Pedreno, C., & Albero, M. I. (2000). Simultaneous determination of propacetamol and paracetamol by derivative spectrophotometry. *Talanta*, *52*(3), 517-52
6. Devi, T. A., Setti, A., Srikanth, S., Nallapeta, S., Pawar, S. C., & Rao, J. V. (2013). Method development and validation of paracetamol drug by RP-HPLC. *Journal of Medical & Allied Sciences*, *3*(1).
7. Hadad, G. M., Emara, S., & Mahmoud, W. M. (2009). Development and validation of a stability-indicating RP-HPLC method for the determination of paracetamol with dantrolene or/and cetirizine and pseudoephedrine in two pharmaceutical dosage forms. *Talanta*, *79*(5), 1360-1367.
8. Maithani, M., Raturi, R., Gautam, V., Kumar, D., Gaurav, A., & Singh, R. (2010). Simultaneous estimation of ambroxol hydrochloride and cetirizine hydrochloride in tablet dosage form by RP-HPLC method. *International Journal of Comprehensive Pharmacy*, *1*(2), 1-3.
9. Chaudhari, V., & Ubale, M. A Validated Stability-Indicating HPLC Assay Method for Cetrizine HCl in Bulk Drug.
10. Olmo, B., García, A., Marín, A., & Barbas, C. (2005). New approaches with two cyano columns to the separation of acetaminophen, phenylephrine, chlorpheniramine and related compounds. *Journal of Chromatography B*, *817*(2), 159-165.
11. Maithani, M., Raturi, R., Gautam, V., Kumar, D., Chaudhary, A. K., Gaurav, A., & Singh, R. (2010). Development and validation of a RP-HPLC method for the determination of chlorpheniramine maleate and phenylephrine in pharmaceutical dosage form.*International Journal of Comprehensive Pharmacy*, *1*(5), 1-4.
12. Dewani, A. P., Barik, B. B., Chipade, V. D., Bakal, R. L., Chandewar, A. V., & Kanungo, S. K. (2014). RP-HPLC-DAD method for the determination of phenylepherine, paracetamol, caffeine and chlorpheniramine in bulk and marketed formulation.*Arabian journal of chemistry*, *7*(5), 811-816.

CITATION OF THIS ARTICLE

G Singh, S S Jaybhay,. Stability Indicating HPLC Method Development and Validation for Simultaneous Estimation of Selected Drugs in Their Combined Pharmaceutical Dosage Form. Bull. Env. Pharmacol. Life Sci., Vol 10[5] April 2021 : 92-99.