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Research Article

SIMULTANEOUS ESTIMATION AND VALIDATION OF PARACETAMOL, CHLORPHENIRAMINE MALEATE, PHENYLEPHRINE HYDROCHLORIDE, CAFFEINE AND ITS STRESS DEGRADATION STUDIES USING UV VISIBLE SPECTROSCOPY

Amrita Natekar *, Siddhi Naroji
Dnyanprassarak Mandal's College and Research Centre, Assagao-Bardez-Goa, India
*Corresponding Author Email: amritanatekar@yahoo.in

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ABSTRACT

A simple, precise, accurate and economic simultaneous UV spectrophotometric method has been developed for the estimation of Paracetamol, Chlorpheniramine Maleate, Phenylephrine Hydrochloride and Caffeine in tablet formulation. The estimation was based upon the measurement of absorbance at absorbance maxima of 245 nm, 260 nm, 269 nm and 275 nm for Paracetamol, Chlorpheniramine Maleate, Phenylephrine Hydrochloride and Caffeine in water, respectively in tablet dosage form. The method was then validated for different parameters as per ICH (International Conference on Harmonization) guidelines.

Keywords: Paracetamol, Chlorpheniramine Maleate, Phenylephrine Hydrochloride, Caffeine, UV spectrophotometry.

INTRODUCTION

Paracetamol (PARA) is chemically N-(4-hydroxyphenyl)acetamide with chemical formula $C_8H_9NO_2$. It has analgesic and antipyretic activity. Various methods such as UV spectrophotometry, HPLC, HPTLC was reported for the estimation of Paracetamol from its formulation[1,2,3,4]. Phenylephrine Hydrochloride is chemically (*R*)-3-[-1-hydroxy-2-(methyl amino) ethyl] phenol with chemical formula $C_9H_{13}NO_2$. It is used as α_1 – adrenergic receptor agonist. It was determined alone or in combination by using UV spectrophotometry, HPLC, RP-HPLC methods[1,2,6]. Chlorpheniramine Maleate is chemically 3-(4-chlorophenyl)-N,N-dimethyl-3-pyridin-2-yl-propan-1-amine with chemical formula $C_{16}H_{19}ClN_2$. It has anti histaminic activity. From the literature survey Chlorpheniramine Maleate was determined alone or in combination by using UV spectrophotometry, HPLC, RP-HPLC methods[1,3,6]. Caffeine is chemically ,3,7-Trimethylpurine-2, 6-dione with chemical formula $C_8H_{10}N_4O_2$. It is a central nervous system stimulant. UV-spectrophotometry, HPLC methods have been reported for the estimation of caffeine[3]. A mixture of this combination is widely used for the relief of sinus congestion and headache. The literature reveals that no analytical method is available for simultaneous estimation of these 4 drugs in combination. So the aim of the study was to develop and validate UV spectrophotometric method for simultaneous estimation of Paracetamol, Phenylephrine Hydrochloride, Caffeine and Chlorpheniramine maleate in bulk and combined dosage form.

MATERIALS AND METHODS

UV – Visible spectrophotometer, Make: Lab India, Model: UV 3000$^+$, equipped with spectral bandwith of 2.0 nm and 1cm matched quartz cells. Commercially available tablet: Sinarest (Label claim: Paracetamol- 500mg, Caffeine- 30mg , Phenylephrine Hydrochloride- 10mg , Chlorpheniramine Maleate- 2mg) was procured from local market.

Selection of common solvent

After assessing the solubility of drugs in different solvents water was used as common solvent for developing spectral characteristics.

DETERMINATION OF λmax

The tablet solution were suitably diluted with diluent and subjected for determination of λmax in the range of 200-400 nm. Spectrum is shown in Figure 1.

METHOD DEVELOPMENT

Twenty tablets of marketed formulation were accurately weighed and powdered in mortar and pestle. A quantity of powder equivalent to 50mg was weighed and was dissolved in 20 ml of 0.1N NaOH. Sonicated for 2 minutes. Then it was diluted upto the mark with water in 100 ml standard measuring flask. The solution was filtered using Whatman filter paper 42. From this 1ml of the solution was again diluted to 100ml with distilled water. Absorbance was recorded. Results are shown in Table 1.

METHOD VALIDATION

Validation is a process that demonstrates whether the analytical procedure is suitable for the intended use and that it supports the purity, potency and quality of drug product and drug substances[5,8,9].

Accuracy: Accuracy of the method was determined by calculating recovery of PARA, CHLOR, CAFF, PHEN at 90%, 95%, 100%, 105% and 110% level of sample solutions of each API respectively. Absorbance was noted down and standard

deviation was found out for each API. Results are shown in Table 1 which indicates that the method is accurate as the statistical results are within the acceptable range (S.D.< 2..0)

Linearity: Linearity of the method was determined at five concentration levels 1-4 µg/ml for PARA, CHLOR, CAFF and PHEN independently. Absorbance at each concentration level was noted down and regression equation was found out. Calibration curves were plotted (Figure 2-5) and results are reported in Table 1.

Precision:

Repeatibility (Intraday): To check the degree of repeatability of the methods, suitable statistical evaluation was carried out. Repeatability was performed for three times with tablets formulation with the interval of 1 hour. The coefficient of variation was calculated. Results are shown in Table 1.

Intermediate precision (Interday): Intermediate precision was determined by assay of sample solution on two different days. Absorbance was recorded. The coefficient of variation was calculated. % C.O.V not more than 1.0 indicates good precision (Table 1)

Specificity: Commonly used excipients (starch, and sodium stearate) were spiked into a pre weighed quantity of drugs. The specificity of the method was investigated by observing any interference of drug with the excipients. Absorbance was recorded. (Table 1)

Limit of Detection (LOD): The limit of detection was determined by preparing solutions of different concentrations. The detection limit of the individual analytical procedure is the lowest amount of analyte in the sample that can be detected but not neccesarily quantitated as an exact value. Results of the same are shown in Table 1.

Limit of Quantification (LOQ): It is the concentration that can be quantitated reliably with a specified level of accuracy and precision. The LOQ was calculated using formula involving slope of calibration curve and standard deviation of response. (Table 1)

STRESS DEGRADATION STUDIES

The International Conference on Harmonization (ICH) guideline entitled stability testing of new drug substances and products requires that stress testing be carried out to elucidate the inherent stability characteristics of the active substances[7].

Acidic condition: Twenty tablets of marketed formulation were accurately weighed and powdered in mortar and pestle. A quantity of powder equivalent to 500mg of Paracetamol was weighed and was dissolved in 20 ml of 0.1N NaOH. Sonicated for 2 minutes. Then it was diluted up to the mark with water in 100ml standard measuring flask. The solution was filtered using Whatman filter paper 42. From this 1ml of the solution was taken and to it 1ml of 3N HCl was added and was diluted up to the mark in 100ml standard measuring flask. Absorbance of this solution was noted down after 4 hours. (Table 2)

Alkaline conditions: Twenty tablets of marketed formulation were accurately weighed and powdered in mortar and pestle. A quantity of powder equivalent to 500mg of Paracetamol was weighed and was dissolved in 20 ml of 0.1N NaOH. Sonicated for 2 minutes. Then it was diluted up to the mark with water in 100ml standard measuring flask. The solution was filtered using Whatman filter paper 42. From this 1ml of the solution was taken and to it 1ml of 3N NaOH was added and was diluted up to the mark in 100ml standard measuring flask and the solution was taken in a cuvette for the UV- Analysis. Absorbance was noted down after 4 hours. (Table 2)

Oxidative degradation: Twenty tablets of marketed formulation were accurately weighed and powdered in mortar and pestle. A quantity of powder equivalent to 500mg of Paracetamol was weighed and was dissolved in 20 ml of 0.1N NaOH. Sonicated for 2 minutes. Then it was diluted up to the mark with water in 100ml standard measuring flask. The solution was filtered using whatman filter paper 42. From this 1ml of the solution was taken and to it 1ml of 3% H_2O_2 was added and was diluted up to the mark in 100ml standard measuring flask and the solution was taken in a cuvette for the UV- Analysis. Absorbance was noted down after 4 hours. (Table 2)

Dry heat induced degradation: Twenty tablets of marketed formulation were accurately weighed and powdered in mortar and pestle. A quantity of powder equivalent to 500mg of Paracetamol was weighed and was dissolved in 20 ml of 0.1N NaOH. Sonicated for 2 minutes. Then it was diluted up to the mark with water in 100ml standard measuring flask. The solution was filtered using Whatman filter paper 42. From this 1ml of the solution was again diluted to 100ml with distilled water. This solution was exposed to temperature of 70^0C for 4 hours and the solution was taken in a cuvette for the UV- Analysis. (Table 2)

Photolytic degradation: Twenty tablets of marketed formulation were accurately weighed and powdered in mortar and pestle. A quantity of powder equivalent to 500mg of Paracetamol was weighed and was dissolved in 20 ml of 0.1N NaOH. Sonicated for 2 minutes. Then it was diluted up to the mark with water in 100ml standard measuring flask. The solution was filtered using Whatman filter paper 42. From this 1ml of the solution was again diluted to 100ml with distilled water. This solution was kept in sunlight for 4 hours and the solution was taken in a cuvette for the UV- Analysis. (Table 2)

CONCLUSION

The proposed method for simultaneous estimation of Paracetamol, Chlorpheniramine Maleate, Phenylephrine Hydrochloride and Caffeine tablet dosage form were found to be accurate, simple and rapid which can be well understood from validation data and stress degradation studies as given in table 1 and 2. Hence it can be used for the routine analysis of four drugs in combined dosage form. By comparing the absorbance the stress degradation studies showed that the drug product undergoes degradation in acidic, heat induced, oxidative and photolytic conditions whereas it is relatively stable when exposed to alkaline conditions. The developed method is validated according to ICH guidelines. The correlation coefficient of the drugs were found to be close to 1.00, indicating good linearity. %RSD indicates that the method gives sufficient accuracy. % correlation of variation for intra-day and inter-day precision were found to be in acceptable range. Thus this method was found to be precise. There was no interference from tablet excipients that was observed in this method. The method was found to have good sensitivity indicating that the developed method can be easily and conveniently adopted for the routine quality control analysis

Table 1: Optical characteristics data and validation parameters

Parameter	Values			
Drugs	**PARA**	**CAFF**	**PHEN**	**CHLOR**
Working (nm)	245	275	269	260
Absorptive	0.324	0.195	0.236	0.303
Correlation Coefficient	0.990	0.984	0.971	1.022
Slope	0.0675	0.014	0.0165	0.016
LOD	0.069	0.179	0.319	0.437
LOQ	0.104	0.543	0.968	1.325
Intra-day precision (% COV)	0.239	0.499	0.881	0.876
Inter-day precision (% COV)	0.477	0.545	0.536	0.536
Specificity	Specific	Specific	Specific	Specific
Linearity (Correlation Coefficient)	0.990	0.984	0.971	1.022
Accuracy (Standard deviation)	0.0183	0.0260	0.0294	0.0240

Table 2: STRESS DEGRADATION STUDIES

Degradation condition	Time (hours)	PARA	CAFF	PHEN	CHLOR
Acidic	4	0.288	0.096	0.120	0.206
Basic	4	0.310	0.182	0.211	0.278
Oxidative	4	0.299	0.145	0.175	0.255
Dry heat induced	4	0.301	0.083	0.106	0.189
Photolytic	4	0.267	0.102	0.184	0.201

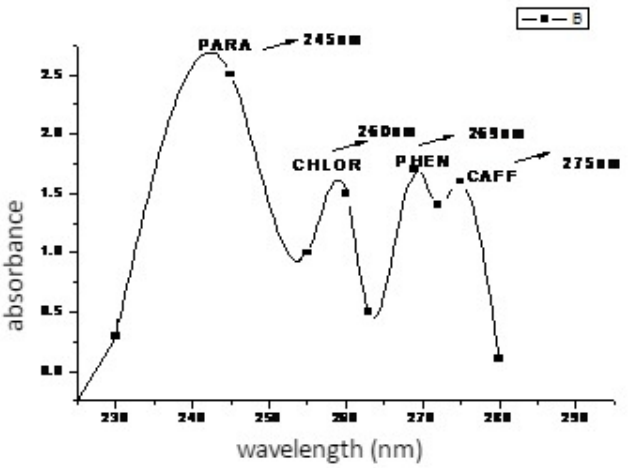

Figure 1: Determination of λmax

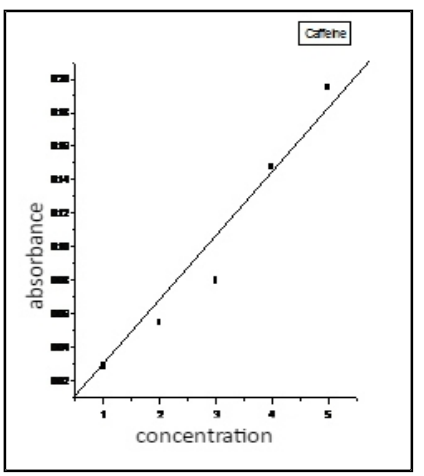

Figure 2: Linearity graph of CAFF

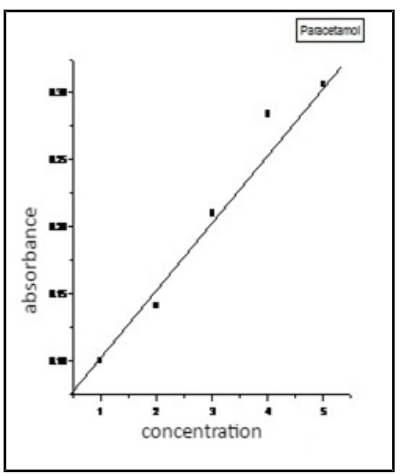

Figure 3: Linearity graph of PARA

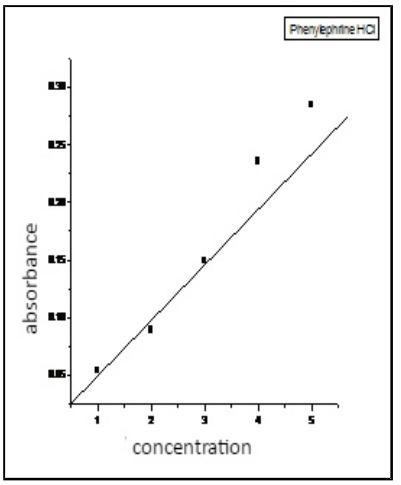

Figure 4: Linearity graph of PHEN

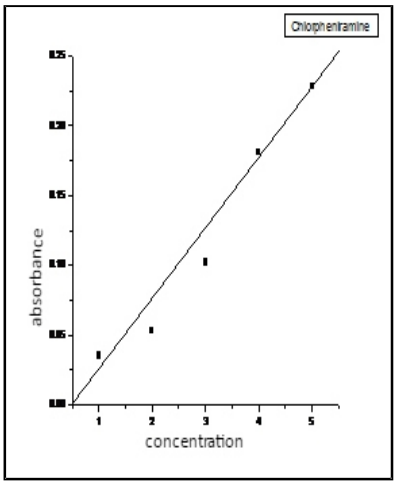

Figure 5: Linearity graph of CHLOR

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