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Chemometric assisted RP-HPLC quantitative estimation and validation of hydrochlorothiazide and triamterene in tablet dosage form

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ABSTRACT

A new chemometric assisted by high-performance liquid chromatography (HPLC) with photodiode array (PDA) detection was implemented for the simultaneous determination of Hydrochlorothiazide and Triamterene in tablet dosage form. Two chemometric calibration techniques, principle component analysis (PCA) and partial least square analysis (PLS) were applied to the peak area at 276 nm of PDA detector responses. The method was carried out on a Luna C18, 250mm x 4.6mm, 5µm, column with a mobile phase consisting of Acetonitrile and Buffer in the ratio of (25 :75v/v) and flow rate of 1.0 ml/ min. The detection was carried out at 272 nm. The retention time for Hydrochlorothiazide and Triamterene were found to be 4.1and 6.2min respectively. The method was validated according to the ICH guidelines for specificity, LOD, LOQ, precision, accuracy, linearity and robustness. The method showed good reproducibility and recovery with %RSD less than 2. So the proposed method was found to be simple, specific, precise, accurate and linear. The 'UNSCRAMBLER -X(camo)' software was used for the numerical calculations. All of the two-chemometric analysis methods in this study can be satisfactorily applied for the quantitative analysis of Hydrochlorothiazide and Triamterene in pharmaceutical tablet dosage form.

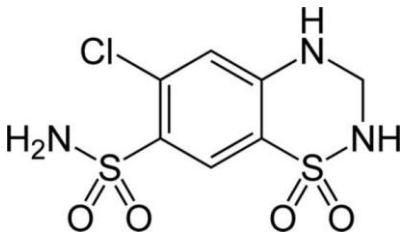
Keywords: PCA, PLS, HPLC, Hydrochlorothiazide, Triamterene.

INTRODUCTION

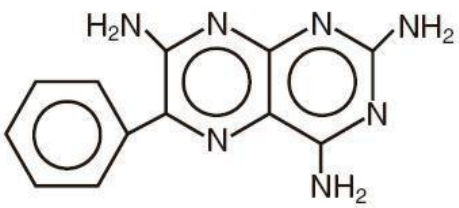
Data analysis plays a major role in assuring the quality of the bulk drug and Pharmaceutical preparations which contributes to safety issue. Standard analytical procedure for the determination of newer drugs or formulation may not be available in pharmacopoeias. Therefore it is essential to develop the chemometric assisted RP-HPLC methods to provide a rapid quantitative analysis of pharmaceutical properties of intermediate and finished dosage forms. The chemometric analytical methods are accurate, precise, specific, linear, simple and rapid. Many spectrophotometric and chromatographic methods have been reported for the determination of Hydrochlorothiazide and Triamterene in Pharmaceutical dosage forms. In

some of these methods the data analysis is time consuming and lengthy process. Chemometric assisted RP-HPLC techniques involve the applying of methods like PCA, PLS to redundancy of noise and to determine the correlation between variables, covariance between different sets of variables.

This drug is used to treat high blood pressure. Lowering high blood pressure helps prevent strokes, heart attacks, and kidney problems. This medication is a combination of two "water pills" (diuretics): triamterene and hydrochlorothiazide. This combination is used by people who have developed or are at risk for having low potassium levels on hydrochlorothiazide. It causes you to make more urine, which helps your body get rid of extra salt and water. This medication also reduces extra fluid in the body (edema) caused by conditions such as heart failure, liver disease, or kidney disease. This can lessen symptoms such as shortness of breath or swelling in your ankles or feet [1, 2, 3].



Hydrochlorothiazide



Triamterene

Hydrochlorothiazide is a 6-chloro-1,1-dioxo-3,4-dihydro-2H-1,2,4-benzothiadiazine-7-sulphomanide. CAS number is 58-93-5, and its acts as a Thiazide Diuretic and it is white crystalline powder and it is soluble in dilute ammonia, slightly soluble in water [1].

Triamterene is a 2,7-Diimino-6-phenyl-1,2,3,7-tetrahydro-4-pteridinamine CAS number is 396-01-0 and its acts as a Potassium sparing diuretic and it is white crystalline powder and Soluble in formic acid, DMSO, insoluble in water [2]

Literature survey reveals that spectrophotometric analysis of triamterine [4], HPLC method for hydrochlorthiazide [5] alone and spectrophotometric method [7] and HPLC [6, 8-14] in combinations are available. However scanty methods are available for simultaneous determination of Hydrochlorothiazide and Triamterene in literature. Hence a novel HPLC method has been proposed in this present research.

MATERIALS AND METHODS

Optimised chromatographic conditions

The developed RP-HPLC method for the estimation of Hydrochlorothiazide, Triamterene was carried out on Agilent C18, 250mm x 4.6mm, 5µm column using mobile phase composition (mixture of 0.1% Ortho Phosphoric acid and Acetonitrile in the ratio of (75:25V/V). Adjusted to PH2.5 with flow rate of 1.0 ml /min at 276 nm. Software (Empower, Version 2.0, Unscrambler-X).

Preparation of buffer solution

Mixed 1ml Ortho Phosphoric acid in 1litre water, filtered through 0.45µm nylon membrane filter. Mobile phase: A mixture of Acetonitrile and 0.1%OPA in the ratio of 25:75%v/v was sonicated to degas and filtered through 0.45µm nylon membrane filter. Retention time of Hydrochlorothiazide is about 5.121 min. Retention time of Triamterene is about 3.368 min.

Preparation of standard stock solution

Hydrochlorothiazide

Weighed accurately 82.5mg of Hydrochlorothiazide working standard into a 20 mL volume tricflask. Added 15 mL of diluent sonicate to dissolved and diluted to volume with diluent.

Triameterene

Weighed accurately 124.2 mg Triamterene working standard into a 20 mL volumetric flask. Added 15 mL of diluent, sonicate to dissolve and diluted to volume with diluent. Further diluted each 1mL of Solution-A, B to 10 mL with the diluent.

Preparation of Sample solution

Weighed 10 capsules or tablets and weigh and crush to powder then take 5 capsules or tablets equivalent of sample into a 50 mL volumetric flask. Added 40 mL of diluent, sonicate to dissolve and diluted to volume diluent. Further 5 mL was diluted to 50 mL with the diluent. Filter through 0.45µ Nylon syringe filter.

Procedure

Injected 5µL of Standard preparation five times and sample preparation in the Chromatograph. Recorded the chromatograms and measure the peak responses of Hydrochlorothiazide, Triamterene. The system suitability parameters should be met. From then peak responses, calculated the content of Hydrochlorothiazide and Triamterene in the sample.

RESULTS AND DISCUSSION

The results are summarized in Tables 1-3 and Figures 1-7 and are self explanatory. The complexity of problems encountered in pharmaceutical analysis with the importance of achieving is the selectivity, speed, low cost, simplicity, sensitivity, specificity, precision and accuracy in estimation of drugs. Chemometric methods are less expensive methods and they do not require sophisticated instrumentation and any prior separation step. This can be considered a superiority of these chemometric techniques over HPLC. But they need software for resolution and determination of active ingredients in the mixtures. The chemometric methods proposed for hydrochlorothiazide and triamterene are very powerful methods for the simultaneous analysis of these two drugs in combined dosage form.

Table 1: Assay of hydrochlorothiazide and triamterene

Drug	Area	Labeled amount(mg)	Amount present(mg)	% Assay
Hydrochlorothiazide	860421	25	25.1±0.86	100.5
Triameterene	1208900	37.5	37.52±1.04	100.8

Table 2: Validation parameters of proposed method

Parameter	Acceptance criteria	Hydrochlorothiazide	Triamterene
Linearity Range Correlation Coefficient	Correlationcoefficient $r^2 > 0.999$	$r^2 = 0.9998$	$r^2 = 0.9993$
System Precision	RSD < 2%	%RSD = 0.128	%RSD = 0.177
Intermediate Precision	RSD < 2%	%RSD = 0.161	%RSD = 0.123
Method precision	RSD < 2%	%RSD = 0.16	%RSD = 0.15
Accuracy	Recovery 98- 102% (individual)	% recovery=100.4	% recovery=100.4
Solution Stability	> 12 h	Stable up to 24 h %RSD = 0.782	Stable up to 24 h %RSD = 0.761
Robustness	RSD NMT 2% in modified condition Flow minus Flow plus Organic plus Organic minus WavelengthplusWavelength minus	Complies%RSD= 0.241%RSD= 1.618%RSD=0.142%RSD=0.080%RSD= 0.646%RSD= 0.471	Complies%RSD= 1.618%RSD= 0.410%RSD=0.113% RSD=0.406%RSD= 0.412%RSD= 0.213

Table 3: Linearity data of Hydrochlorothiazide and Triamterene

Linearity	Solution taken	Hydrochlorothiazide		Triamterene	
		Concentration µg/ml	Area counts	Concentrationµg/ml	Area counts
Linearity-1	0	0.00	0	0.00	0
Linearity-2	0.1	41.40	180277	62.10	1051577
Linearity-3	0.25	103.50	456425	155.25	243081

Linearity-4	0.5	207.00	925108	310.50	488126
Linearity-5	1	414.00	1858908	621.00	953245
Linearity-6	1.25	517.00	22785363	776.25	1198542
Linearity-7	1.5	621.00	2784563	931.50	1485431

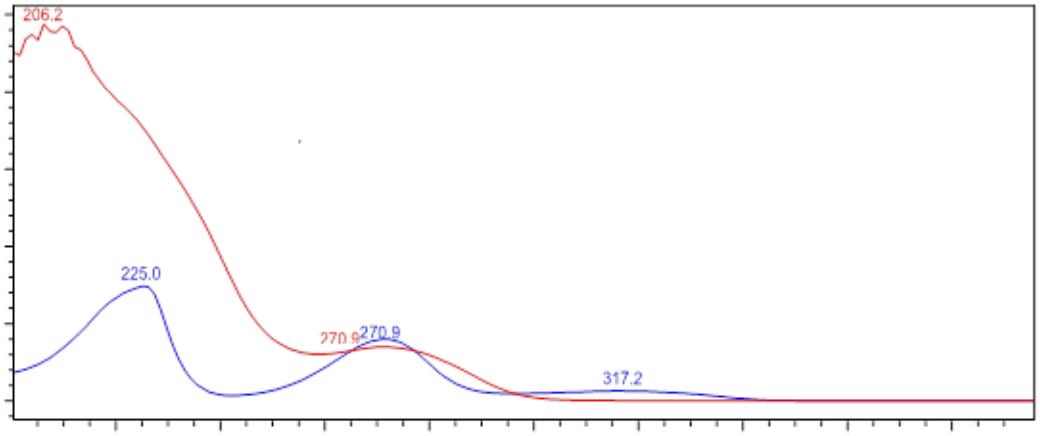


Fig. 1: Overlay spectrum of hydrochlorothiazide and triamterene

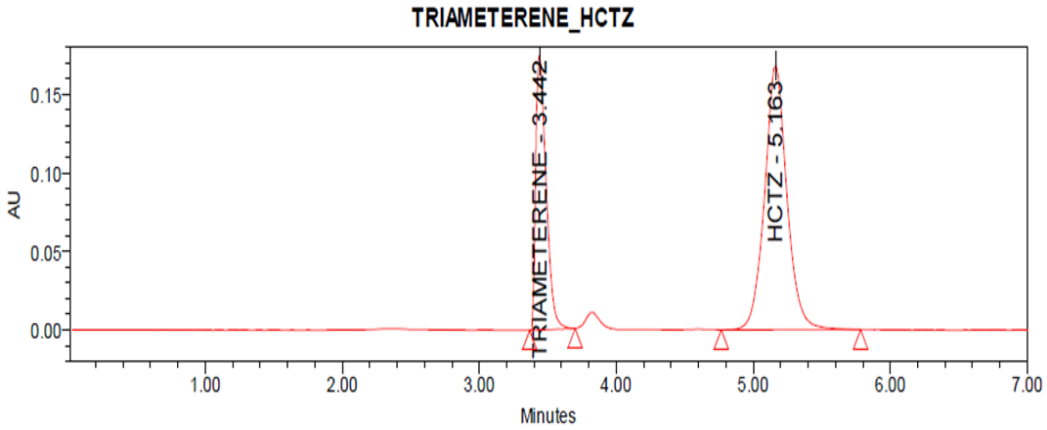


Fig. 2: A Representative chromatogram of Sample

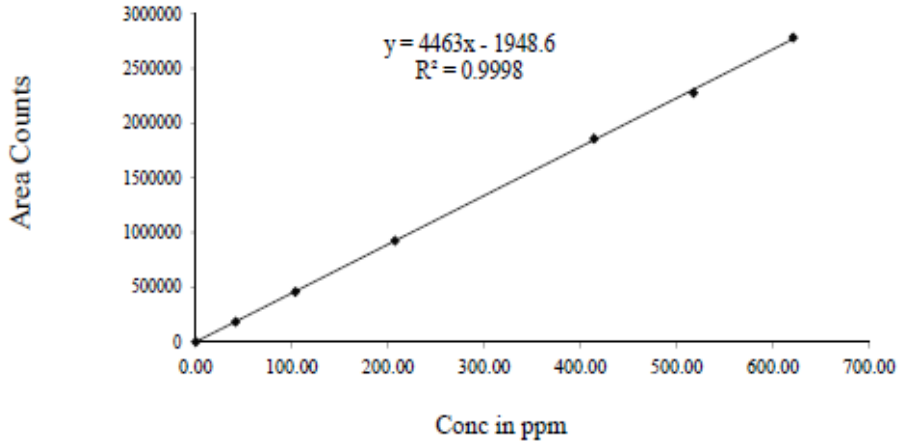


Fig. 3: Linearity plot of Hydrochlorothiazide

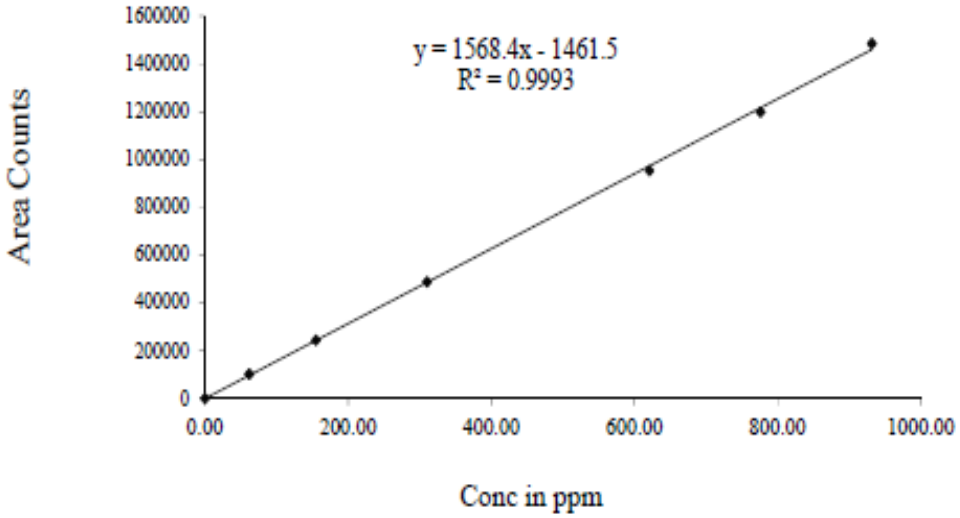


Fig. 4: Linearity plot of Triamterene

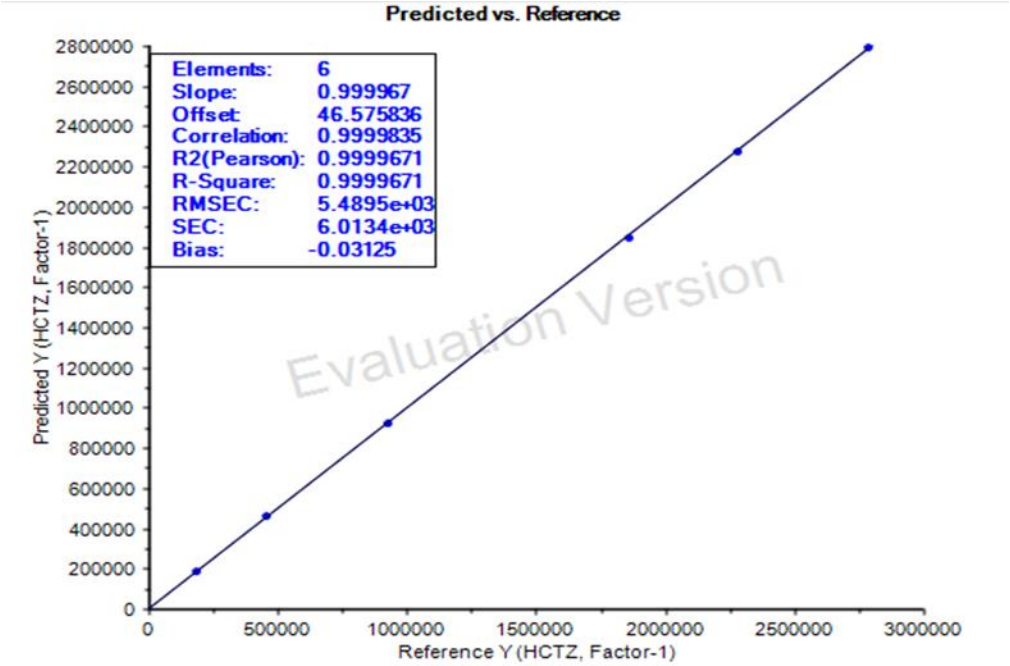


Fig. 5: PLS linearity spectral data of Hydrochlorothiazide

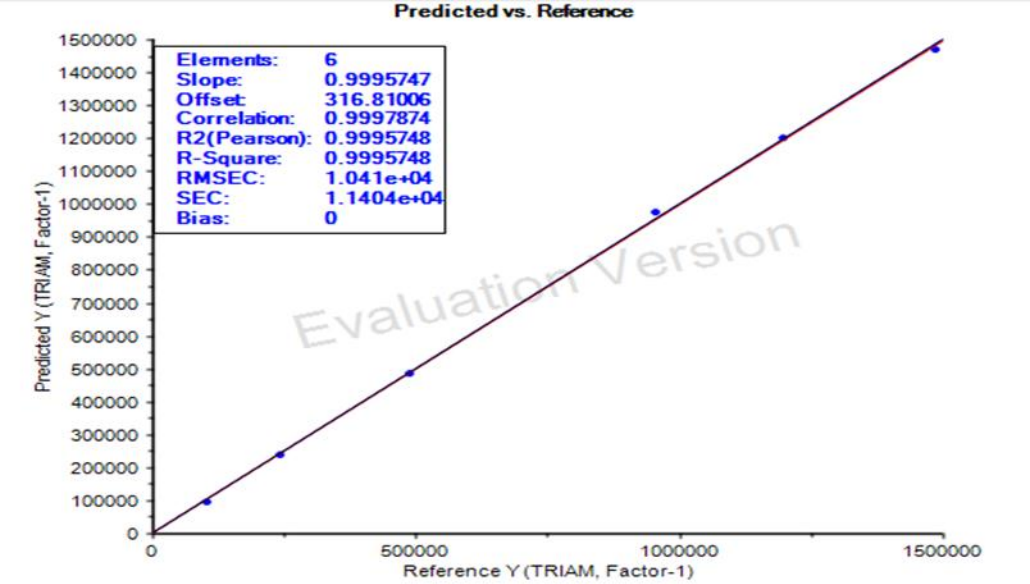


Fig. 6: PLS linearity spectral data of Triamterene

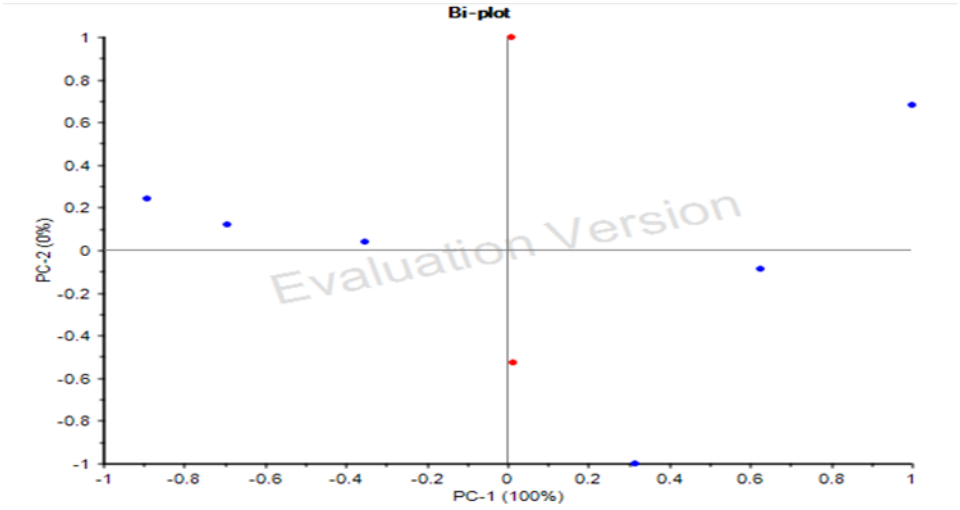


Fig. 7: PCA linearity spectral data of Hydrochlorothiazide and Triameterene

Acknowledgements

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