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Research Article

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Chemometric-assisted UV spectrophotometric method for determination of diacerein and aceclofenac in pharmaceutical formulation

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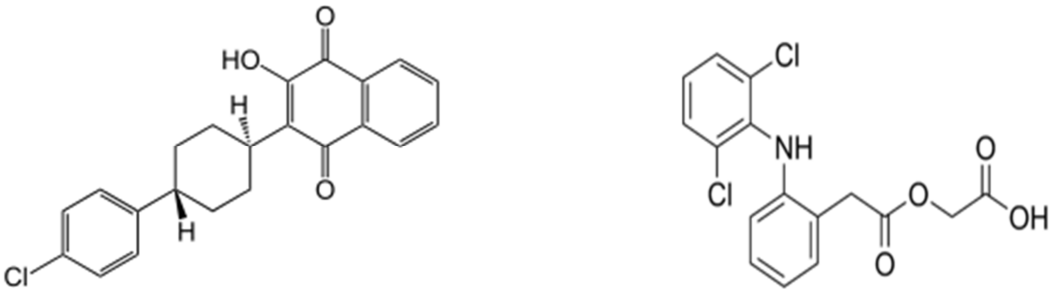
ABSTRACT

In this work a numerical method, based on the use of spectrophotometric data coupled to Principal component regression (PCR) and Partial least squares (PLS) multivariate calibration, is evaluated for the simultaneous determination of Diacerein and Aceclofenac in bulk and tablet dosage form. Spectra of Diacerein and Aceclofenac were recorded at concentrations within their linear ranges 2-12 µg/ml and 5-30 µg/ml, respectively and were used to compute a total of 51 synthetic mixtures involving 36 calibration and 15 validation sets in the wavelength range of 200-400 nm with the wavelength interval of λ=0.5 nm in methanol. The analytical performances of these chemometric methods were characterized by relative prediction errors and recovery studies (%) and were compared with each other. These two methods were successfully applied for estimation of drugs and pharmaceutical formulation (tablet) with no interference with excipients as indicated by the recovery study results. The proposed methods are simple, rapid and can be easily used as an alternative analysis tool in the quality control of drugs and formulation.

Key words: Diacerein, Aceclofenac, PCR, PLS

INTRODUCTION

Diacerein(DIA) is *trans*-2-[4-(4-chlorophenyl)cyclohexyl]-3-hydroxy-1,4-naphthalenedione [Fig. 1(a)] class anthraquinone used to treat joint diseases such as osteoarthritis (swelling and pain in the joints). It works by inhibiting interleukin-1 beta. Aceclofanac (ACECLO) 2-[2-[2-[(2,6-dichlorophenyl)amino]phenyl]acetyl] oxyacetic acid [Fig. 1(b)] well known NSAIDS a cytokine inhibitor works by blocking the action of COX, used to treat pain & inflammation. It is official in USP, BP. Literature survey reveals that many analytical methods have been reported like HPTLC [1-2], RP-HPLC [3-6] and UV Spectrophotometry [7-11] for the determination of diacerein and aceclofenac as individual and in combination with other drugs. There are no reports on chemometric analysis of these drugs. Multivariate calibration is a chemometric method which has been employed for determination of drugs in combined dosage form [12,13]. The present work aim to develop an alternative numerical based analytical procedure on chemometric assisted spectrophotometric methods for analysis of diacerein&aceclofenac in bulk & tablet dosage form.



(a) **(b)**

Figure 1: Chemical Structure of (a) Diacerein and (b) Aceclofenac

EXPERIMENTAL SECTION

Instrumentation

Double beam UV- Vis spectrophotometer (Jasco V-730) with matched pair of 1 cm quartz cells were used to record spectra of all solutions. The spectra were recorded at spectral band width of 2.0 nm, scanning speed 100 nm/min and data pitch 0.5 nm. Unscrambler X (10.3) (64-bit) trial version and Microsoft Excel 2007 were used for model generation and application of chemometric.

Material and Reagents

Reference standard of Diacerein and Aceclofenac were obtained from GlenmarkPvt. Ltd, Nashik&Twilight LitakaPharma Ltd, Mumbaias gift samples and methanol used was of AR grade (LOBA Chemie, India, LOT NO. B156501502). Tablets (Dycerin tablets) marketed by Glenmark Pharmaceuticals Ltd. (Mumbai, INDIA) containing Diacerein IP 50 mg and Aceclofenac IP 100 mg were procured from local pharmacy shop.

Preparation of standard stock solution

Diacerein (10 mg) and Aceclofenac were accurately weighed and transferred (10 mg) into two different 10 ml of volumetric flask and volume was made up to 10 ml with methanol (1000 µg /ml). Further 1 ml was pipetted and diluted to 10 ml to achieve final concentration of 100 µg/ml of DIA and ACECLO, respectively.

Preparation of working stock solution

From standard stock solution of (100 µg /ml) 0.2,0.4,0.6,0.8,1,1.2 ml of DIA & 0.5,1,1.5,2,2.5,3 ml of ACECLO pipetted and diluted to 10 ml with methanol to obtain final concentration of 2, 4, 6, 8, 10 and 12 µg /ml for DIA and 5, 10, 15, 20, 25 and 30 µg /ml for ACECLO, respectively.

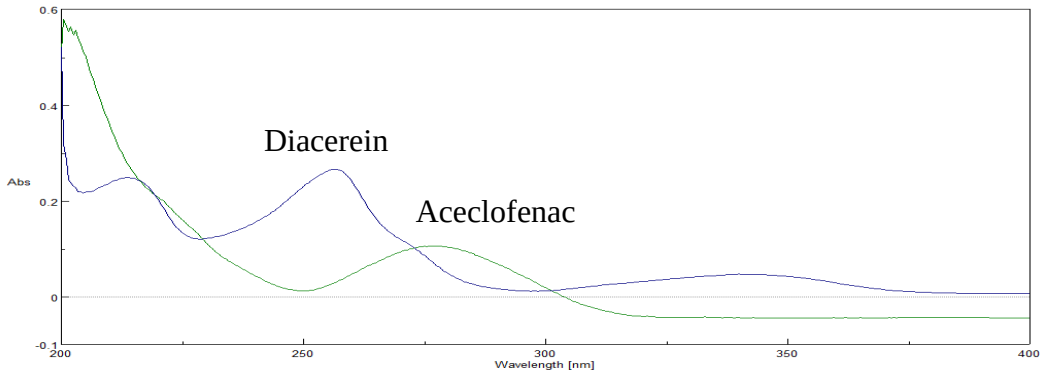


Figure 2: Overlay spectra of DIA and ACECLO (10 µg /ml each)

Construction of calibration and validation set

Two sets of standard solutions, a calibration set (Table No.1) and a validation set(Table No.2) were prepared. Thirty six calibration standards and fifteen validation standard mixtures were prepared by mixing appropriate volumes of the working standard solutions of DIA and ACECLO and diluting to volume with methanol. The combinations of DIA and ACECLO are illustrated in table 1. The absorption spectra of the prepared solutions were measured from 200-400 nm with 0.5 nm intervals. The spectra were saved as ASCII (.txt) format which were further extracted in MS-Excel as required by Unscrambler software for model generation.The absorbance data of the calibration set were then processed by the Unscrambler® program for the development of PCR & PLS models. For validation of the PCR & PLS models, the concentrations of DIA and ACECLO in the validation set were predicted which is

shown in the Table No.3 by using the proposed PCR & PLS models. validation of all the methods was performed by ICHQ2 (R1).

Table 1: Calibration set

SN	ACECLO (µg/ml)	DIA (µg/ml)	SN	ACECLO (µg/ml)	DIA (µg/ml)
1	5	2	19	20	2
2	5	4	20	20	4
3	5	6	21	20	6
4	5	8	22	20	8
5	5	10	23	20	10
6	5	12	24	20	12
7	10	2	25	25	2
8	10	4	26	25	4
9	10	6	27	25	6
10	10	8	28	25	8
11	10	10	29	25	10
12	10	12	30	25	12
13	15	2	31	30	2
14	15	4	32	30	4
15	15	6	33	30	6
16	15	8	34	30	8
17	15	10	35	30	10
18	15	12	36	30	12

Table 2: Validation set

SN	DIA (µg/ml)	ACECLO (µg/ml)	SN	ACECLO (µg/ml)	DIA (µg/ml)
1.	3	5	9	11	22
2.	6.5	15	10.	8.5	10
3.	0	15	11.	10	11
4.	2	5	12.	4	10
5.	6	15	13.	8	20
6.	12	24	14.	4	0
7.	8	18	15.	12	30
8.	10	20			

Table 3: Results for validation set by PCR and PLS methods were predicted

METHOD		PCR				PLS			
DIA	ACECLO	DIA		ACECLO		DIA		ACECLO	
Actual (µg/ml)		Predicted	% R*	Predicted	% R*	Predicted	% R*	Predicted	% R*
3	5	2.979	96.6	4.965	99.2	2.979	96.6	4.965	99.2
6.5	15.5	6.603	101.5	15.62	100.7	6.603	101.5	15.62	100.7
0	15	1.039	-0.05	15.19	101.2	1.039	-0.05	15.19	101.2
2	5	2.255	110	4.893	97.86	2.255	110	4.893	97.86
6	15	5.964	98.33	14.95	99.7	5.964	98.33	14.95	99.7
12	24	12.03	100.2	24.39	101.2	12.03	100.2	24.39	101.2
8	18	8.278	102.5	18.20	101.1	8.278	102.5	18.20	101.1
10	20	10.26	102.6	20.79	103.9	10.26	102.6	20.79	103.9
11	22	10.81	98.3	22.55	102.5	10.81	98.3	22.55	102.5
8.5	10	8.322	97.90	10.33	103.3	8.322	97.90	10.33	103.3
10	11	9.715	97.15	11.49	104.4	9.715	97.15	11.49	104.4
4	10	4.497	110	10.02	100.2	4.497	110	10.02	100.2
8	20	7.913	98.91	19.77	98.85	7.913	98.91	19.77	98.85
4	0	4.150	103.7	-0.085	0.000	4.150	103.7	0.0083	0.000
12	30	11.81	98.41	29.76	99.2	11.81	98.41	29.76	99.2

Assay of marketed formulation

Twenty tablets were accurately weighed and finely powdered. Tablet powder equivalent to 5 mg of DIA (10 mg ACECLO) was accurately weighed and transferred into 100 ml volumetric flask and 70 ml of methanol was added. The mixture was sonicated for 10 min and diluted up to the mark with methanol and filtered through a whatman filter paper no. 41. From this solution 0.8 ml & 1ml aliquot was withdrawn into different 10 ml volumetric flask and diluted up to the mark with methanol to get solutions which contains DIA 4 µg/ml and ACECLO 10 µg/ml. The analysis procedure was repeated six times for Tablet formulation.

Accuracy study

The accuracy study was carried out at three levels 80 %, 100 % and 120 % of concentration. Calculated amount of DIA and ACE from standard solutions were spiked into sample solution and scanned in range of 200-400 nm. Concentrations were predicted by using developed PCR and PLS models

RESULTS AND DISCUSSION

Linearity

The linearity of measurement was evaluated by analyzing different concentration of the standard solution of DIA and ACECLO. Linearity results were found at 6 different concentrations ranging from 2-12 µg/ml for DIA and 5-30 µg/ml for ACECLO.

Precision

Precision was measured in terms of repeatability of application and measurement. Repeatability of standard application was carried out using three replicates of the standard solutions of DIA & ACECLO. Method precision was done by taking 4, 6, 8 µg/ml for DIA and 10, 15, 20 µg/ml for ACECLO in three replicates at each level. The results of which are presented in Table 4.

Table 4: Precision results obtained using developed PCR and PLS models

Amount Taken µg/ml		Predicted Conc. µg/ml				R %				% RSD			
		DIA		ACECLO		DIA		ACECLO		DIA		ACECLO	
DIA	AC-ECLO	PCR	PLS	PCR	PLS	PCR	PLS	PCR	PLS	PCR	PLS	PCR	PLS
4	10	4.04	4.04	10.01	10.02	100	100	100.1	100.1				
4	10	4.20	4.20	10.24	10.24	102	102	102.4	102.4	3.38	3.38	1.50	1.50
4	10	3.93	3.93	9.956	9.956	99.5	99.5	99.56	99.56				
6	15	6.14	6.14	15.04	15.04	100	100	100.2	100.2				
6	15	6.07	6.0746.0	15.11	15.01	100	100	100	100.2	0.78	0.78	0.133	0.133
6	15	6.05		15.00	15.00	100	100	100	100				
8	20	8.16	8.16	20.06	20.06	100	100	100.3	100.3				
8	20	8.16	8.16	20.03	20.02	101	101	100.1	100.1	1.70	1.70	0.332	0.332
8	20	7.92	7.92	20.04	19.93	99.6	99.6	99.65	99.65				

Assay

Six replicates at assay concentration were carried out results of which are presented in Table 5.

Table 5: Assay result for DIA and ACECLO in tablet (Dycerin) by proposed methods

METHOD		PCR				PLS			
DIA	ACECLO	DIA		ACECLO		DIA		ACECLO	
Actual (µg/ml)		Predicted (µg/ml)	% R	Predicted (µg/ml)	% R	Predicted (µg/ml)	% R	Predicted (µg/ml)	% R
10	4	4.199	104.5	9.800	98.5	4.199	104.9	9.800	98
10	4	4.129	103	9.868	98.68	4.129	103.2	9.868	98.68
10	4	4.048	101.2	10.398	103.9	4.048	101	10.391	103.9
10	4	4.194	104.5	10.391	103.9	4.140	103.5	10.391	103.9
10	4	4.141	103.5	10.302	103	4.141	103.5	10.302	103
10	4	4.150	103.5	10.159	101.5	4.150	103.7	10.159	101.5
SD		0.054	1.219	0.262	0.262	0.0489	1.272	0.2612	2.606
MEAN		4.144	103.3	10.22	101.58	4.1345	103.3	10.15	101.4

3.4. Accuracy

Accuracy study was done by performing recovery studies by spiking different concentrations of pure drug (DIA & ACECLO) in the pre analyzed tablet sample at concentration levels of 80%, 100%, and 120 %**.** Result of recovery studies are given in Table 6 and 7.

Table 6: Accuracy data of DIA by PCR and PLS models

Level %	Sample Conc. µg/ml	Amount added µg/ml	Total Conc. µg/ml	Predicted Conc. µg/ml		% Recovery		% RSD	
				PCR	PLS	PCR	PLS	PCR	PLS
80 %	4	3.2	7.2	7.426 7.358 7.465	7.426 7.349 7.465	103.1 102.0 103.6	103.1 102 103.6	0.728	0.730
100 %	4	4	8	7.999 7.985 7.924	7.999 7.985 7.924	99.98 99.75 99.05	99.98 99.75 99.05	0.498	0.499
120 %	4	4.8	8.8	8.921 8.951 8.805	8.921 8.951 8.805	101.3 101.7 100.0	101.3 101.7 100.0	0.867	0.867

Table 7: Accuracy data of ACECLO by PCR and PLS models

Level %	Sample Conc. µg/ml	Amount added µg/ml	Total Conc. µg/ml	PREDICTED CONC. µg/ml		% Recovery		% RSD	
				PCR	PLS	PCR	PLS	PCR	PLS
80 %	10	8	18	17.914 17.879 17.157	17.914 17.879 17.157	99.4 99.13 101	99.5 99.1 101	0.166	1.013
100 %	10	10	20	20.129 19.957 20.052	20.129 19.957 20.052	100.6 99.75 100.25	100.6 99.75 100.2	0.431	0.431
120 %	10	12	22	21.684 21.752 21.652	21.684 21.752 21 .652	98.72 99.00 98.6	98.72 99 98.6	0.206	0.203

LOD and LOQ

LOD and LOQ were calculated as 3.3 σ/S and 10 σ/S, respectively; where σ is the standard deviation of the response (y-intercept) and S is the slope of the calibration plot. LOD & LOQ of DIA was found to be 0.39 & 1.20 and of ACECLO was found to be 0.5 & 1.5, respectively.

Two chemometric methods (PCR & PLS) were applied successfully to simultaneous determination of DIA and ACECLO in laboratory mixtures and pharmaceutical formulation. The applied methods confirm the suitability for simple, accurate and precise analysis of DIA and ACECLO in pharmaceutical preparations. The proposed methods can be applied for analysis of drugs in quality control lab as well as for in process quality control.

CONCLUSION

Two chemometric methods (PCR & PLS) were applied successfully to simultaneous determination of DIA and ACECLO in laboratory mixtures and pharmaceutical formulation. The applied methods confirm the suitability for simple, accurate and precise analysis of DIA & ACECLO in pharmaceutical preparations. The proposed methods can be applied for analysis of drugs in quality control lab as well as for in process quality control.

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REFERENCES

[1] S. Bhalerao; S.Tambe; V. Pareek; R.Shinde; L. Gupta,*Asian Journal of Pharmaceutical and Clinical Research*, **2010**, 3(1), 25- 30.

[2] H. William;B. Parimala Devi; J.Kurien; P. Valsalakumari; C. Mohandas, *International Journal Of Science And Research*,**2014**, 3(6), 2615- 2617.

[3] N. Nyola; G. Jeyabalan; N Kalra; G. Parveen; S. Choudhary, *Research and Reviews*: *Journal of Pharmaceutical Analysis*,**2012**, 1(1), 1-8.

[4] M. Alagar; D. Banji; K. Rao; D. Selva,*Asian Journal of Research in Chemistry*,**2015**, 3(3), 84 - 89.

[5] V. Sekar; S. Jayaseelan; E .Udhaya; N.Subash; M.Prakash; P.Perumal, **2010**, 2 (1), 168-171.

[6] S. Gandhi; S. Syed,*International Journal of Research in Pharmaceutical and Biomedical Sciences*,**2013**, 4(4),1090- 1094.

[7] S. Kesharwani; D. Kohali,*International Journal OfChemtech Research*,**2010**, 2(3), 1816-1822.
[8] M. Bhure; A. Hemke; K. Gupta, *J. Pharm. Sci. & Res.*, **2010**, 2(7), 426-432.
[9] S. Narade; S. Patil; S. Surve; D. Shete; Y. Pore, *J. Pharm. Sci. & Res.*,**2010**, 2(2), 137-142.
[10] S. Chitlange; G. Pawbake; A. Mulla; S. Wankhede,*Der PharmaChemica*, **2010**, 2(1), 335-341.
[11] S. Bhoir; S. Dhole; N. Kulkarni; P. Sangole; S. Thorat; D. Bhoite, *International Journal of Pharmacy and Pharmaceutical Sciences*, **2012**, 4(4),501-504
[12] S. Gandhi; S. Tapale;*AshEse Journal of Pharmacy*,**2016**,1(1), 1-8.
[13] S. Gandhi; A. Pahade; S. Tapale,*Pharm Analysis & Quality Assurance*, **2016**, 3(2), 1-5.