(Research Article)

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Simultaneous Spectrophotometric Estimation of Aceclofenac and Drotaverine Hydrochloride in Tablet Dosage Form

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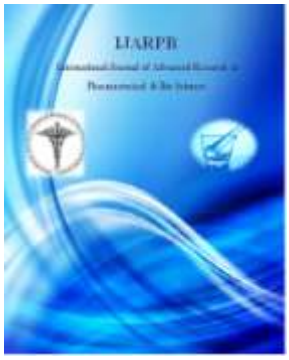

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ABSTRACT

Two simple, accurate and precise UV methods were developed for the estimation of Aceclofenac (ACF) and Drotaverine Hydrochloride (DRT) in Tablet dosage form. Both the drugs are used against the muscle spasm. Method A Area under Curve Spectrophotometry. The wavelength range selected for Quantitation are 266 -288nm for Aceclofenac and 222-232 nm for Drotaverine Hydrochloride. Method B is Multicomponent mode method. Wavelength selected were 277.0 nm (λ_{max} of ACF) and 228.0 nm (λ_{max} of DRT) for the analysis. Wavelengths were successfully applied for the simultaneous determination of both the drugs in commercial tablet preparation. The results of the analysis have been validated statistically and by recovery studies.

KEYWORDS: Aceclofenac, Drotaverine Hydrochloride, UV-Spectrophotometry, Area under curve, Multicomponent mode method.

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INTRODUCTION

Aceclofenac [ACF] (fig 1A) is a non steroidal anti-inflammatory drug with good analgesic and anti-rheumatic properties. Chemically it is [[[2-[(2, 6-Dichlorophenyl) amino]phenyl] acetyl] oxy] acetic acid. It is used in various pain conditions like rheumatoid arthritis, osteoarthritis and ankylosing spondylatis. [1, 2] It is official in Indian Pharmacopoeia[3].Drotaverine hydrochloride [DRT] (fig1B), 1-[(3, 4-diethoxyphenyl) ethylene]-6, 7-diethoxy-1, 2, 3, 4-tetra hydroisoquinolene is an analogue of papaverine[3]. It acts as an antispasmodic agent by inhibiting phosphodiesterase IV enzyme, specific for smooth muscle spasm and pain, used to reduce excessive labor pain[4]. Drotaverine hydrochloride is official in Polish Pharmacopoeia[5].Both the drugs are marketed as combined tablet dosage formulation in the Ratio is 100:80mg ACF: DRT. A few UVSpectrophotometric[6, 7] and HPLC[8-9] methods have be reported individually or in combination with other drugs for estimation of Drotaverine hydrochloride. Literature Survey revealed that a number of methods have been reported for estimation of both the drugs individually and in combination of other drugs, but not a single method is reported for the estimation of both the drugs simultaneously. Present work describes two precise, accurate, and reproducible methods for simultaneous estimation of ACF and DRT in tablet formulation. The proposed methods were validated as per the International Conference on Harmonization (ICH) guidelines

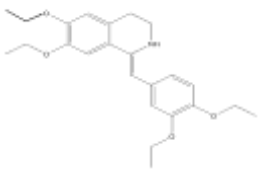

Fig 1A ACF

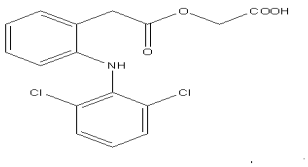

Fig 1B DRT

MATERIAL AND METHODS:

Instruments: [10]

UV-Visible Spectrophotometer (Double Beam)
Make: SHIMADZU
Model: model UV-1800
Spectral Bandwidth: 1nm wavelength accuracy of ± 0.3 nm and 1.0 cm matched quartz cells was used for analytical method development

Materials:

Standard gift sample of Aceclofenac and Drotaverine Hydrochloride were provided by Biocon Ltd., Bangalore. Combined dose Tablet (Drotin-A, 100 mg Aceclofenac and 80mg Drotaverine Hydrochloride; manufactured by Martine and Harris Laboratories Ltd.), were purchased from local market for analysis.

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Solvent used: Methanol is used as solvent.

Stock solution: Stock solution of both the drugs100mcg/ml is prepared by dissolving 10mg each drug in100ml volumetric flask and the volume is made up by methanol.

Procedure

Method A - Area under Curve Spectrophotometry

In this method, the stock solution of both the drugs100mcg/ml is prepared by dissolving 10mg each drug in100ml volumetric flask and the volume is makeup by methanol, by appropriate dilution of standard stock solutions of both the drugs to 20mcg/ml dilution respectively is scanned in the spectrum mode from 400nm to 200 nm. The absorption spectra thus obtained is selected for analysis, from the overlain spectra of both the drugs (fig.1),

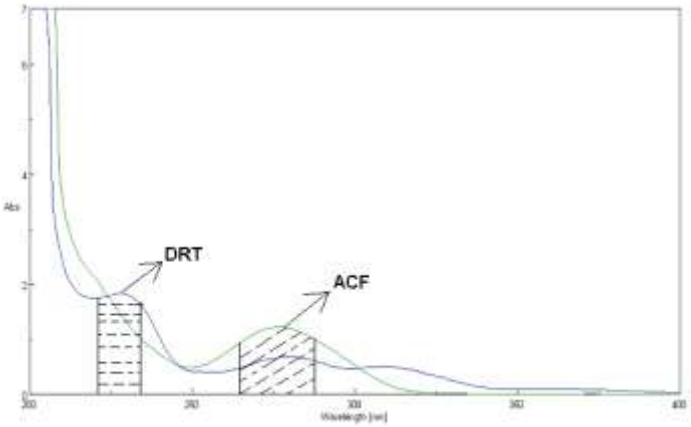

Fig-1: Overlain spectra of ACF and DRT for method A and B

wavelength range selected for Quantitation were from 266-288 nm and 222-232 nm for Aceclofenac and Drotaverine Hydrochloride

$C_{acf} = Q0 – Q_{drt}/ Q_{acf} – Q_{drt} X A / a_{acf}$ ---------- (1)

$C_{drt} = Q0 – Q_{acf}/ Q_{drt}– Q_{acf} X A / a_{drt}$ ---------- (2)

. Where $AUC_{222-232}$ and $AUC_{266-288}$ are the area under curves of solution at wavelength range between 222 – 232 nm (DRT) and 266– 288 nm (ACF) respectively

Method B - Multicomponent mode method.

By appropriate dilutions of standard drug solutions with Methanol containing 8 mcg/ml DRT and 10mcg/ml ACF were prepared separately, each solutions and their mixture were scanned between 400nm to 200nm and the overlain spectra of two drugs were recorded from the wavelength which could be utilized for simultaneous analysis of two drugs using the Multicomponent mode . Wavelength selected for Quantitation are277 nm and 228.0 nm for Aceclofenac and Drotaverine Hydrochloride
Which are the λ_{max} of both the drugs.

Application of the proposed method for the determination of ACF and DRT in Tablets

For the estimation of drugs in the commercial formulations, Twenty Tablets were weighed and average weight was calculated. The tablets were crushed to obtain fine powder. Tablet powder equivalent to 80mg of DRT and 100mg of ACF was weighed and transferred to 100ml volumetric flask and volume made up to the mark with methanol and ultrasonicated for 30 min. the solution was then filtered through Whatman filter Paper No. 41. This tablet solution was further diluted to obtain10mcg/ml for ACF and and 8mcg/ml for DRT In The mixed sample solutions were analyzed to obtain spectras and the AUC is recording using wavelength range from 222 – 232nm for DRT and 266 – 288nm for ACF were noted. The concentration of ACF and DRT were

calculated from the equation. At each level of the amount of three determinations were performed and results obtained.

VALIDATION [11]

The methods were validated with respect to linearity, accuracy and precision.

Linearity: The linearity of measurement was evaluated by analyzing different concentration of standard solution of ACF and DRT For both the methods, the Beer- Lamberts concentration range was found to be 2-12mcg/ml for ACF and DRT, Both.

Table1: Spectral Characteristics and Linearity Data

Parameters	Method I		Method II	
	ACF	DRT	ACF	DRT
λ_{max}	271	228	271	246
Beer s low limit µg/ml	2-12	2-12	2-12	2-12
Slope(b)	18.2343	9.3744	18.1091	9.3905
Intercept(a)	0.0374	0.2139	0.0500	0.0.1441
coefficient Correlation	0.9998	0.9989	0.9999	0.9997
RegressionEqetion(y=a+bx)	0.054x	0.109x	0.054x	0.109x
LOD	0.006	0.075	0.009	0.1581
LOQ	0.020	0.228	0.276	0.4792

Precision: The reproducibility of proposed method was determined by performing tablet assay at different time intervals (morning, afternoon, and evening) on same day (Intra-day precision) and on three different days (Inter-day precision) Results of precision is expressed in %RSD. Result for precision was found to be 0.0664 (for ACF) and 0.0834(for DRT) in simultaneous equation method; 0.5567 (for ACF) and 0.5011(for DRT) in Q-Analysis method table 2.

Table 2: Analysis of Commercial Formulations (precision)

Method I				Method II	
S.NO		% Label Claim		% Label Claim	
		ACF	DRT	ACF	DRT
1		100.09	100.07	99	99.99
2		99.99	99.98	98.90	98.86

3		99.96	99.91	100.04	100.01
4		99.91	99.88	99.80	100.02
5		100.01	100.05	100.01	99.97
	Mean	99.99	99.97	99.55	99.97
	S.D	0.0664	0.0834	0.5565	0.5010
	%RSD	0.0665	0.0835	0.5567	0.5011
	± S.E	0.0296	0.0372	0.2549	0.224

n=5, S.D. = standard deviation, %R.S.D. = percentage standard deviation, S.E. = standard error

Accuracy (Recovery studies): To ascertain the accuracy of the proposed, methods, recovery studies were carried out by standard addition method at three different levels (80%, 100% and120%). Percent recoveries for ACF and DRT, by methods, were found in the range of 99.25% to 100.02% and perform recovery studies the % recovery was mention in table 3.

Table 3: Recovery Study

Method I								
Level of % Recovery	Amount present (mg/tab)		Amount of standard added (mg)		Total amount recovered (mg)		%Recovery	
	ACF	DRT	ACF	DRT	ACF	DRT	ACF	DRT
80	100	80	80	64	179.34	144.21	99.63	100.14
100	100	80	100	80	199.55	159.94	99.77	99.96
120	100	80	120	96	220.06	175.98	100.02	99.98

	ACF	DRT
Mean	99.80	100.02
SD	0.1975	0.0986
%RSD	0.1976	0.0986
SE	0.1140	0.0569

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Method II								
Level of % Recovery	Amount present (mg/tab) Amount of standard added (mg)				Total amount recovered (mg)		%Recovery	
	ACF	DRT			ACF	DRT	ACF	DRT
80	100	80	179.96	64	179.34	144.21	99.63	100.14
100	100	80	199.98	80	199.55	159.94	99.77	99.96
120	100	80	220.03	96	220.06	175.98	100.02	99.98

	ACF	DRT
Mean	99.25	99.50
SD	0.3	0.45
%RSD	0.1975	0.0986
S.E	0.1140	0.0569

*n=3 S.D. = standard deviation, %R.S.D. = percentage standard deviation, S.E. = standard error

RESULTS AND DISCUSSION

The methods discussed in the present work provide a convenient and accurate way for simultaneous analysis of ACF and DRT. In Area under curve, method wavelength range selected for Quantitation were 266.0 -288 nm for ACF and 222.0- 232nm for DRT. In both the methods linearity for detector response was observed in the concentration range of 2-12mcg/ml for ACF and DRT both. In method A, concentration of individual drug present in the mixture was determined against calibration curve in Quantitation mode .In method A, AUC values were calculated for both the drugs at selected wavelengths and substituted in equations for determining the concentration of ACF and DRT in tablet sample solution. Percent label claim for ACF and DRT in tablet analysis by both the methods was found in the range of 99.79% to 100.02%. Standard deviation and coefficient of variance for six determination of tablet sample, by both the methods was found to be less than $\pm$2.0 indicating precision of both the methods. Accuracy of both the methods was ascertained by recovery studies and the results are expressed as % recovery. Percent recovery for ACF and DRT by both the methods was found in the range of 99.25% to 100.02%, values of standard deviation and coefficient of variation - was satisfactorily low indicating the accuracy of both the methods. The result of analysis shows that the developed methods are accurate, precise, reproducible and economical and can be

employed for routine quality control analysis of or Aceclofenac and Drotaverine Hydrochloride in combined dose tablet formulation.

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