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UV SPECTROPHOTOMETRIC METHOD FOR SIMULTANEOUS ESTIMATION OF DICLOFENAC SALT AND EPERISONE HYDROCHLORIDE IN BULK AND CAPSULE DOSAGE FORM

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Keywords:

UV Spectrophotometry, Simultaneous Estimation, Diclofenac Sodium, Eperisone Hydrochloride, Acetate Buffer

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ABSTRACT: The present paper describes a new, simple, accurate, environmentally friendly, economic spectrophotometric method for simultaneous estimation of Diclofenac salt and Eperisone HCl in bulk and Capsule Dosage Form. Acetate buffer pH5.5 was used as solvent. The wavelength selected for analysis is 276nm & 261.20nm for estimation of Diclofenac Salt and Eperisone HCl respectively. Beers law was obeyed in the range of 10-50µg/ml and 5-25µg/ml with correlation coefficient of0.999 and 0.998 respectively. Detection limit and quantification limit were found to be 0.6031g/ml and 1.87g/ml for Diclofenac sodium and 0.208g/ml and 0.6302g/ml for Eperisone hydrochloride respectively. The developed method was found to be simple, accurate, precise and reproducible. Assay results were found to be 99.20% and 101.13% for Eperisone hydrochloride and Diclofenac sodium respectively. The value of relative standard deviation and percentage recovery was found to be satisfactory. The obtained results proved the method can be used for routine analysis of Diclofenac sodium and Eperisone Hydrochloride in capsule dosage form. The method where tested and validated as per ICH guidelines.

INTRODUCTION: The combination of Eperisone Hydrochloride (EPS) and Diclofenac sodium(DIC), available in sustained release capsule dosage form, is used in the treatment of acute musculoskeletal spasm associated with low back pain. The combination of these two drugs having (EPS) 150 mg and (DIC) 100 mg is approved by Central Drugs Standard Control Organization in India in the year 2012 [1]. Diclofenac sodium is phenyl acetic acid derivative and chemically Sodium salt of 2-[{2, 6-dichlorophenyl} amino] benzene acetic acid sodium salt (**Fig.1**) [4].

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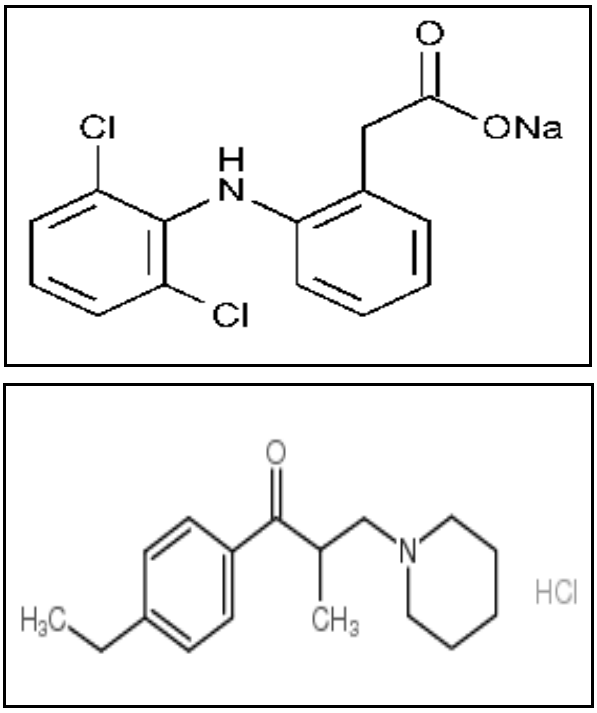
It is having anti-inflammatory, analgesic and antipyretic activities in both animals and human beings. It is often used to treat chronic pain associated with cancer. Diclofenac sodium is official in Indian Pharmacopoeia, British Pharmacopoeia, and United States Pharmacopoeia. The literature survey revealed that various analytical methods involving UV spectrophotometry, HPTLC, HPLC have been reported for estimation of DIC and EPS alone or in combination with other drugs [2, 5].

Eperisone hydrochloride is chemically 1-(4-ethylphenyl)-2-methyl-3-piperidin-1-yl-propan-1-one (**Fig.1**) [10]. EPS having both skeletal muscle relaxant and vasodilator activity because of its action within the central nervous system and on vascular smooth muscle and demonstrate variety of pharmacological effect such as cervical spondylitis,

low back pain and headache. EPS is also anti-spasmodic activity with relatively low incidence of central depression compared with other antispasmodic drug. Many methods like RP-HPLC, HPLC-MS, GC-MS, NMR, UV, IR analytical techniques and electrospray ionization method are reported for the estimation of Eperisone hydrochloride. Hence an attempt has been made to develop simple, sensitive, rapid, precise, economical and accurate UV method to analyze the drugs smoothly [11, 14].



Diclofenac sodium Eperisone hydrochloride

FIG. 1: CHEMICAL STRUCTURE OF EPERISONE HYDROCHLORIDE AND DICLOFENAC SODIUM [8, 9, 10]

MATERIALS AND METHODS:

Apparatus:

A shimadzu model 1800 (Japan) double beam UV/ Visible spectrophotometer with spectral width 2 nm, Wavelength accuracy of 0.5 nm and a pair of 1 cm matched quartz cell was used to measure absorbance of all the solution. Spectra where automatically obtained by UV probe system software. A shimadzu ATY-224 analytical balance (Philippines mfg. Inc.), an ultrasonic bath (Spectra lab UCB 40, Mumbai, India) was used in the study.

Reagents and Materials:

Diclofenac Sodium (DIC) bulk powder was kindly gifted by BAL Pharmaceutical Ltd., Bangalore, India. Eperisone Hydrochloride (EPS) bulk powder was kindly gifted by Sharon Bio-medicine Ltd., Raigad, Maharashtra, India, Sodium Acetate (AR Grade, Loba chemicals Ltd.), Rapisone-D SR Capsule (Abbott Healthcare Pvt. Ltd) purchased from local market Pune, India and Whatmann filter paper no. 41 were used in the study.

Preparation of Buffer Solution [8]:

Acetate buffer of pH 5.5 was prepared by weighed 5.48gm of sodium acetate dissolved in 900ml distilled water in 1000 ml volumetric flask. Add 10ml of 2N glacial acetic acid (0.6ml glacial acetic acid in 10 ml distilled water). The volume was made up with distilled water to get a final solution of pH 5.5.

Preparation of Standard Stock Solution:

An accurately weighed Standard DIC and EPS API powder (10 mg) were transfer to 100ml separate volumetric flasks and dissolved in acetate buffer pH 5.5 (50ml). The flask were sonicate for 15 min at 40°C to give clear solution and volume were made up to mark with Acetate buffer to give a solution containing 100 µg/ml of each DIC and EPS.

Simultaneous Equation Method:

The working standard solution of DIC 30 µg/ml and EPS 15 µg/ml were individually scanned in the range of 200-400nm to determine their λ_{max}. The λ_{max} of DIC (**Fig. 2**) and EPS (**Fig. 2**) were found to be 276 nm and 261.20 nm respectively.

The five standard solutions of DIC having concentration 10, 20, 30, 40, 50µg/ml were obtained by transferring 1, 2, 3, 4, 5 ml of standard stock solution to 10 ml volumetric flasks. Standard solutions of EPS in the concentration range of5, 10, 15, 20, 25µg/ml were obtained by transferring 0.5, 1, 1.5, 2.0, 2.5 ml of the stock solution to 10 ml volumetric flasks. The volume in each volumetric flask was made up with acetate buffer pH 5.5. The absorbance of these dilutions were measured at λ_{max} against acetate buffer as blank and absorptivity coefficients E(1%, 1cm) were calculated using Beer's Lambert law for each concentration. Calibration curves were plotted at each wavelength (**Fig.3**). Linear equations generated by calibration curves are as follows.

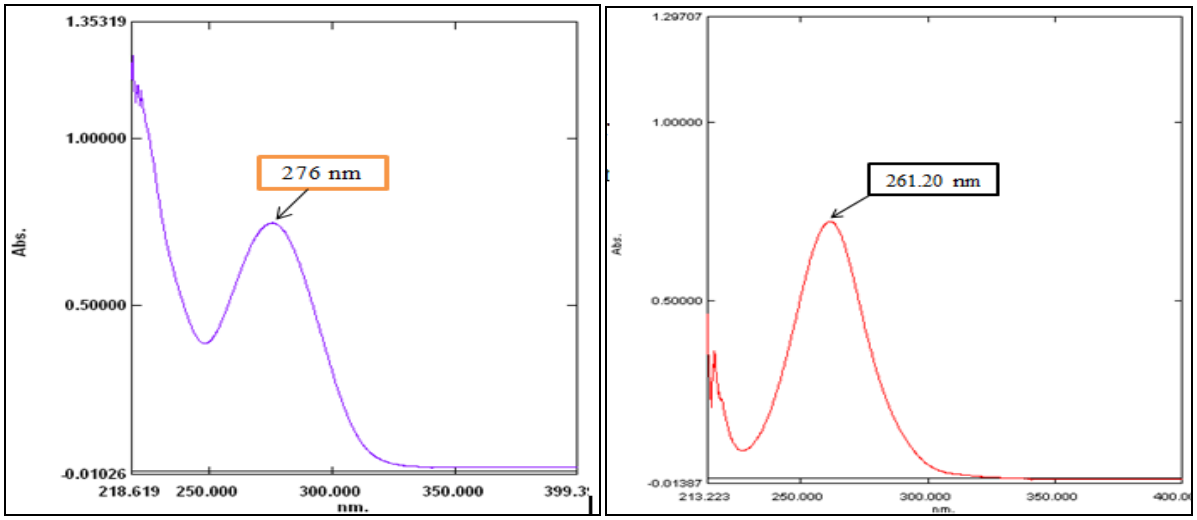


FIG. 2: DETERMINATION OF MAXIMUM WAVELENGTH OF EPERISONE HYDROCHLORIDE (261.20nm) AND DICLOFENAC SODIUM (276nm)

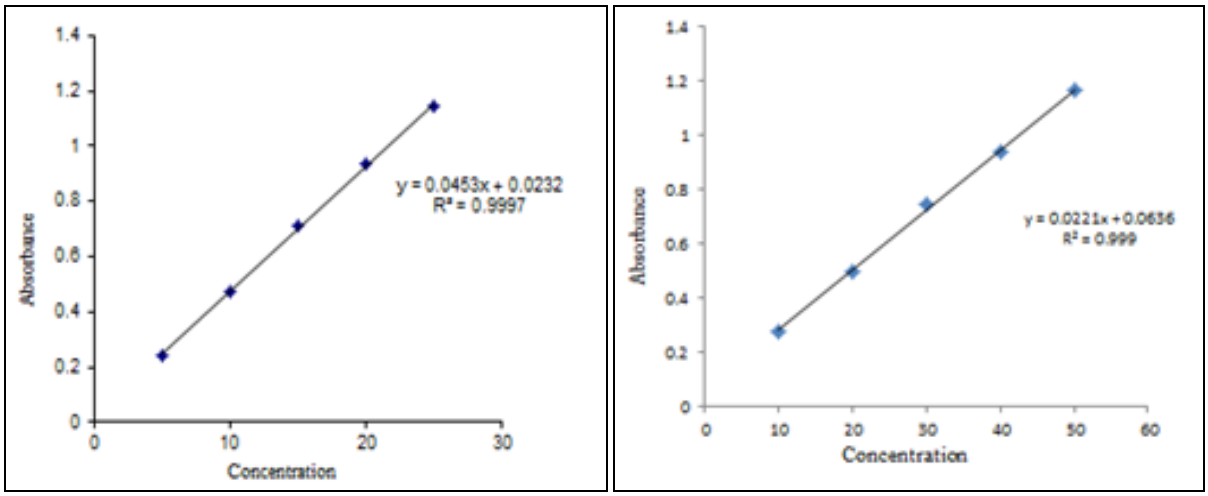


FIG. 3: CALIBRATION CURVE OF EPERISONE HYDROCHLORIDE (261.20nm) AND DICLOFENAC SODIUM (276nm)

Preparation and Analysis of Capsule Formulations:

To determine the content of DIC and EPS in sustained release capsules (Brand name: Rapisone-D SR, label claim: EPS 150mg and DIC 100mg), content of twenty capsules was weighed. The average weight was determined and contents were finely powdered using glass mortar pestle separately. An accurately weighed quantity of powder equivalent to 10 mg of DIC was transferred to 100ml volumetric flask and dissolved in acetate buffer pH 5.5, sonicated for 15 min at 40ºC and the volume was made to 100ml with the same solvent.

The solution was filter and was further diluted to get a final concentration of 20µg/ml of EPS and 15µg/ml DIC. The response of sample solution was measured at 261.20nm and 276nm of EPS and DIC (**Table 5**). As per Indian Pharmacopoeia Diclofenac tablet contains not less than 90.0 % and not more than 110.0 % of Diclofenac and as per Japanese Pharmacopoeia Eperisone dosage form contains not less than 90.0% and not more than 110.0% of Eperisone.

RESULTS AND DISCUSSION:

Method validation:

The developed methods have been validated in terms of linearity, range, specificity, accuracy, precision, assay, LOD and LOQ as per ICH Q2(R1) guidelines (ICH, 2005).

Linearity:

As per ICH guidelines the linearity of an analytical procedure is its ability (within a given range) to obtain test results which are directly proportional to the concentration (amount) of analyte in the sample. Appropriate aliquots of DIC and EPS

standard stock solution were transferred to volumetric flask of 10ml capacity. The volume was adjusted to the mark with acetate buffer pH 5.5. All absorbance were measured at 276 nm and 261.20 nm respectively. Calibration curves were made by plotting average absorbance (n=5) versus concentrations for both drugs. Straight line equations were obtained from these calibration curves (**Table 1**). The linearity should not be less than 0.9888.

TABLE 1: LINEARITY PARAMETER OF EPERISONE HYDROCHLORIDE (261.20nm) AND DICLOFENAC SODIUM (276nm)

Parameter	Eperisone Hydrochloride	Diclofenac Sodium
Beer's law limit	5-25µg/ml	10-50µg/ml
Slope	0.0453	0.0442
Intercept	0.0232	-0.1576
Correlation coefficient (r^2)	0.999	0.9995

Precision:

Intra and inter-day precision was performed by measuring the absorbance of standard solution at three different times during the single day and on three subsequent days respectively. The percent relative standard deviation (%RSD) was calculated (**Table 2**) and (**Table 3**). The % RSD should not be more than 2%.

TABLE 2: INTRADAY PRECISION

Parameter	Eperisone Hydrochloride	Diclofenac Sodium
% RSD (n=3)	0.4141	0.4526
SD	0.0290	0.003

TABLE 3: INTERDAY PRECISION

Parameter	Eperisone Hydrochloride	Diclofenac Sodium
% RSD (n=3)	0.2644	0.2970
SD	0.001	0.001

Limit of Detection and Limit of Quantitation:

LOD and LOQ were calculated by the data obtained from the linearity studies. The slope of the linearity plot was determined. For each of the six replicate determinations, Y- intercept was calculated and the standard deviation of the Y-intercept was computed. From these values, the parameters Limit of Detection (LOD) and Limit of Quantitation (LOQ) were determined by using formulae LOD= 3.3 * S.D. of y intercept/slope and LOQ= 10 *S.D of y intercept/slope (**Table 4**). The %RSD should not be more than 2%.

Robustness:

To evaluate robustness of the method few parameters were purposely varied. The parameters were included variation of wavelength for DIC (276±2) and EPS (261.20±2). The average value of % RSD for determination of EPS and DIC less than 2 % revealed the robustness of the method (**Table 4).**

Accuracy (Recovery Studies):

Accuracy of the method was studied by recovery studies. The recovery studies were performed by applying the method to drug sample to which known amount of EPS corresponding to 80%, 100% and 120% of the label claim was added (standard addition method). The recovery was performed at three levels of the tablet and results were expressed as % RSD (it should not be more than 2%) (**Table 4**).

TABLE 4: RESULTS OF ACCURACY STUDY, LOD AND LOQ, ROBUSTNESS

Parameter	Eperisone HCl	Diclofenac Sodium
Accuracy(% recovery)	100.87 ± 0.213	100.64 ± 0.22
LOD	0.2082	0.603
LOQ	0.6302	1.87
Robustness	0.2201 ±0.001	0.267 ±0.001

TABLE 5: RESULTS OF ANALYSIS OF MARKETED FORMULATION

Sample no.	Label claim		Amount found (Based on Absorbance)		% assay (Based on amount found)	
	Eperisone hydrochloride mg/cap	Diclofenac sodium mg/cap	Eperisone hydrochloride mg/cap	Diclofenac sodium mg/cap	Eperisone hydrochloride mg/cap	Diclofenac sodium mg/cap
1	150	100	148.8	101.13	99.20	101.13

CONCLUSION: The result of our study indicates that the proposed UV spectroscopic method is simple, economic, rapid, precise and accurate. The developed UV spectroscopic method was found suitable for determination of DIC and EPS as bulk drug and in marketed solid dosage formulation without any interference from the excipients. Statistical analysis proves that, this method is repeatable and selective for the analysis of DIC and EPS. From the study it was also revealed that sodium acetate can be used as a hydrotropic agent for Diclofenac sodium. It can therefore be concluded that use of this method can save much time and money and it can be used in analytical laboratories with accuracy.

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