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A Review on validated analytical methods for Aceclofenac

B. Thangabalan*, V. Hari, G. Swapna and D. Jothieswari
Sri Venkateswara College of Pharmacy, RVS Nagar, Chittoor-517127, A.P., India.

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ABSTRACT:
Aceclofenac is a nonsteroidal anti-inflammatory drug analog of diclofenac. It is used for the relief of pain and inflammation in rheumatoid arthritis, osteoarthritis and ankylosing spondylitis. The official method of analysis of Aceclofenac is potentiometric method. Several UV spectrophotometric, HPLC methods in pure form, pharmaceutical formulation and HPTLC methods have been reported to determine.This review provides an overview of various analytical techniques used for Aceclofenacdetermination both in a single preparation and in combination.

KEYWORDS: Aceclofenac, spectrophotometric, HPLC, HPTLC.

I. INTRODUCTION

Aceclofenac is an oral non-steroidal anti-inflammatory drug (NSAID) with anti-inflammatory and analgesic properties. Although there are some differences in the authorized indications between countries, aceclofenac is mainly recommended for the treatment of inflammatory and painful processes, such as low back pain, scapulohumeralperiarthritis, extraarticular rheumatism, odontalgia, and osteoarthritis, rheumatoid arthritis, and ankylosing spondylitis It was patented in 1983 and approved for medical use in 1992. Its formula is $C_{16}H_{13}C_{l2}NO_4$, Its molar mass is 354.1847 g/mol[1].

Aceclofenac is a phenylacetic acid derivative with anti-inflammatory and analgesic properties similar to those of diclofenac. The analgesic efficacy of aceclofenac 100mg is more prolonged than that of paracetamol (acetaminophen) 650mg. If the apparently improved gastrointestinal tolerability of aceclofenac compared with diclofenac is confirmed by wider clinical experience, aceclofenac will have the potential to become a preferred initial drug in an individualised NSAID regimen in patients with rheumatic disorders [2].

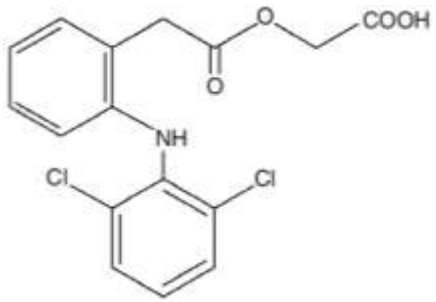

Fig. 1: Structure of Aceclofenac

ANALYTICAL METHODS

Spectrophotometry methods:

Two simple, precise and accurate visible spectrophotometric methods were developed for the estimation of Aceclofenac in bulk drug and in pharmaceutical formulations. The proposed methods were indirect and based on determination of aceclofenac after its reaction with either (p-dimethylaminocinnamaldehyde or 3-Methyl-2-benzothiazolinone hydrazine hydrochloride and measuring the chromogen at the λmax by 658 and 592, respectively. Beers law obeyed in the concentration range of 1-200 µg/ml for method A and 1-100 µg/ml for method B. The accuracy of the methods was determined by recovery studies. The methods showed good reproducibility and recovery with relative standard deviation (in %) less than 2. The methods were found to be simple, economical, accurate and reproducible and can be used for routine analysis of Aceclofenac in bulk drug and in pharmaceutical formulations[3].

A new sensitive, simple, rapid and precise method for simultaneous estimation of paracetamol and aceclofenac in combined tablet dosage form

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has been developed. The method is based on ratio derivative spectrophotometry. The amplitude in first derivative of the ratio spectra at 256 nm and 268 nm (minima) were selected to determine paracetamol and aceclofenac in combined formulation. The method showed good linearity, accuracy and reproducibility. Results of analysis were validated statistically and by recovery studies [4].

Three simple, accurate and economic methods; multicomponent, two wavelength and simultaneous equations using area under curve have been described for the simultaneous estimation of aceclofenac and paracetamol in tablet dosage form. Absorption maxima of aceclofenac and paracetamol in methanol diluted with glass double distilled water was found to be 274.5 nm and 244 nm, respectively. Beer's law was obeyed in the concentration range 2-20 mg/ml for aceclofenac and 5-40 mg/ml for paracetamol. The methods allow rapid analysis of binary pharmaceutical formulation with accuracy. Results of three methods were validated statistically and by recovery studies and were found to be satisfactory [5].

Simple, rapid, sensitive, precise and reproducible specific UV spectrophotometric method for the determination of Aceclofenac (ACE) and Tramadol (TRM) in bulk drug and pharmaceutical dosage form were developed and validated. A simple double beam UV spectrophotometric method has been developed and validated with different parameters such as linearity, precision, repeatability, limit of detection (LOD), Limit of Quantification (LOQ), accuracy as per ICH guidelines. UV-visible spectrophotometric method, measurement of absorption at maximum wavelength in 10 ml methanol and volume make with water solvent system as reference ACE and TRM were found to be at 203 nm and 241 nm respectively. The drug obeyed the Beer's law and showed good correlation. Beer's law was obeyed in concentration range 5 - 25 µg/ml for ACE and 2 - 10 µg/ml for TRM respectively with correlation coefficient was 0.999. The LOD and LOQ of ACE were found to be 4.7862 µg/ml and 14.50 µg/ml, TRM were found to be 2.0518 µg/ml and 6.2176 µg/ml, respectively. Percentage assay of ACE and TRM in tablets. The proposed method is simple, precise, accurate and reproducible can be used for routine analysis of ACE and TRM in bulk and tablet dosage form[6].

The present paper describes multicomponent UV spectrophotometric method for the determination of paracetamol, aceclofenac, and thiocolchicoside based on the fundamentals of green analytical chemistry. Major pharmaceutical companies and research laboratories encompass on green analytical methodologies for developing environmental friendly analytical methods. The present work is based on the principle of simultaneous equation involving additive of absorbances at the selected wavelengths. The linear range was established between 5–15 µg/mL for paracetamol, 1–5 µg/mL for aceclofenac, and 1–5 µg/mL thiocolchicoside. The greenness profile of the developed UV spectrophotometric technique was evaluated using National Environmental Methods Index, Analytical Eco-scale and AGREE metrics which proved the greenness of the method with respect to solvent, chemicals, energy consumed, and waste produced. The proposed method being simple, economical, and eco-friendly could be convenient substitutes for the use of hazardous chemicals in the routine investigation of the selected triple drug combination[7].

This work introduces three eco-friendly UV spectrophotometric methods for the simultaneous estimation of Paracetamol, Aceclofenac and Eperisone Hydrochloride in pharmaceutical tablet formulation. The procedures employed were simultaneous equation method and multivariate chemometric methods with phosphate buffer pH 7.80 as diluent. The simultaneous equation method encompasses absorbance measurement at three different wavelengths (λmax of the drugs). It exhibits linearity between 12–18 µg/mL for paracetamol, 3.69–5.53 µg/mL for Aceclofenac, and 2.76–4.15 µg/mLEperisone hydrochloride. The results obtained for accuracy and precision by the simultaneous equation method were within the permissible limits. Principal component regression and partial least squares were the tools used for chemometric methods. The calibration set and prediction set were constructed, and the UV spectra were recorded in zero order mode, further subjected to chemometric analysis. The % recoveries obtained for Paracetamol, Aceclofenac, and Eperisone Hydrochloride by chemometric techniques showed good accuracy, and the results obtained for analytical figures of merit were acceptable. Statistical comparison of the assay results obtained for the proposed methods showed no significant difference found among the methods using one way analysis of variance. Greenness evaluation tools revealed the greenness profile of the proposed methods and found them to be ecofriendly. The described methods were

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appropriate for routine quality control laboratories, facilitating eco-friendly, fast, and cost effective determination of Paracetamol, Aceclofenac, and Eperisone Hydrochloride in Acemyoset P tablets[8].

Three simple, specific, reproducible methods have been developed and validated for the simultaneous estimation of Aceclofenac and Diacerein in pharmaceutical formulation by UV-Spectrophotometric methods viz; Method I, Absorbance Correction method, Method II, Simultaneous Equation method and Method III, Absorbance Ratio method. For development of Method I, wavelengths selected were 277.0 nm λmax for ACE and 341.5 nm λmax for DIA. For method II, wavelengths selected were 256.5 nm and 277.0 nm for estimation of DIA and ACE respectively, while for Method III, 277.0 nm λmax for ACE and 267.5 nm an isoabsorptive point of ACE and DIA. The two drugs follow Beer-Lambert's law over the concentration range of 10-50 µg/mL for ACE and 5-25 µg/mL for DIA for all three methods. The percent recovery of the drugs was found to be nearly 100 % representing the accuracy of the all three methods. Validation of the proposed methods was carried out for its accuracy, precision, specificity and ruggedness according to ICH guidelines. The proposed methods can be successfully applied in routine work for the determination of ACE and DIA in combined dosage form[9].

Aceclofenac is a non steroidal anti-inflammatory drug and paracetamol is an analgesic and antipyretic drug. Simple, precise, rapid and selective simultaneous equation and Q- analysis UV spectrophotometric methods have been developed for the simultaneous determination of aceclofenac and paracetamol from combined tablet dosage forms. The methods involve solving of simultaneous equations and Q-value analysis based on measurement absorptivity at 274nm, 267.5nm and 245 nm respectively. The method shows good linearity, accuracy and reproducibility. Results of analysis validated statistically and by recovery studies[10].

The aim of the study was to develop UV-spectrophotometric and RP-HPLC methods for the simultaneous analysis of paracetamol and aceclofenac in marketed tablets. The methods were validated in terms of linearity, accuracy (% Recovery), precision (inter day, intraday and reproducibility) and robustness. Both the methods were linear (R^2 = 0.997-0.999 for UV method and 0.999 for RP-HPLC method) and accurate (% recovery was 99.19% - 100.14%).

The method was also found precise (% RSD< 2%) and robust. Potency of three marketed brands was determined by both the methods and no statistically significant difference was noticed between the potency obtained by two methods by paired t -test at 5% significance level. Paracetamol released from marketed products was found to comply compendia specification but inter brand variation in case of aceclofenac release was observed by ANOVA (Sig. 0.000). Any one of the validated methods can be used for the analysis of paracetamol and aceclofenac tablets[11].

In present research work a new simple, specific, precise, accurate, robust and economical UV-Spectrophotometric method for simultaneous estimation of Aceclofenac and Pantoprazole in bulk and tablets dosage form using hydrotropic solvent was developed and validated. In the present work mixture of 0.1 M sodium bicarbonate solution and 0.1 M urea solution was used as a hydrotropic solvent to increase the solubility of poorly water soluble Aceclofenac. The analytical wavelengths for Aceclofenac and Pantoprazole are 273nm and 293nm respectively. The developed method was validated as per ICH guidelines in terms of linearity and range, specificity, accuracy, precision, sensitivity and ruggedness. Linearity was obtained in the concentration range of 5-40µg/ml for Aceclofenac and 2-16µg/ml for Pantoprazole with correlation coefficient 0.9998 for both drugs. The % RSD for intraday precision and inter-day precision of Aceclofenac was found to be 0.84 and 1.23 respectively. An intra-day precision and interday precision of Pantoprazole was found to be 1.49 and 1.40 respectively. In both cases values were within the acceptance limit of less than 2%. The mean percent recovery for

Aceclofenac and Pantoprazole were found to be 98.10% to 99.54 % and 98.66 to 101.33 % respectively. Based on the results obtained the proposed method can be regarded as simple, precise, accurate, reliable, cost-effective and can be used for routine quality control of Aceclofenac and Pantoprazole in bulk and its tablet dosage forms[12].

New simple, precise, rapid and reproducible UV-spectrophotometric method has been developed for the estimation of Drotaverine Hydrochloride and Aceclofenac in both bulk and tablet formulation. Drotaverine and Aceclofenac in combined tablet formulation were estimated by using the multicomponent mode at 307 nm for

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Drotaverine and 276 nm for Aceclofenac in their solution in ethanol: distilled water in the ratio of 50:50 (v/v %), With correlation coefficient of 0.999 for the both the drugs. The Beer's law obeyed the concentration range of 4-40 µg/mL for Drotaverine and 5-40 µg/mL for Aceclofenac. Mean recovery of 99.54% for Drotaverine and 98.23% for Aceclofenac signifies the accuracy of the method. This method was validated with respect to linearity, accuracy (recovery), precision, Limit of detection (LOD) and limit of quantification (LOQ) as per ICH guidelines and successfully applied for the estimation of Drotaverine Hydrochloride and Aceclofenac in commercially available tablet dosage form[13].

A simple, economical, precise and accurate method for simultaneous determination of Drotaverine (DRT) and Aceclofenac (ACE) in combined dosage form has been developed. The first method is Ratio Derivative spectroscopy method (Method A) in which ratio derivative amplitudes were measured at selected wavelengths. Second method is Area under Curve Spectrophotometry (Method B). The amplitudes at 330.13 nm and 228.06 nm in the Ratio derivative spectra were selected to determine DRT and ACE, respectively and wavelength ranges 299-305 nm and 270-277 nm were selected to determine DRT and ACE, respectively by AUC method in methanol, distilled water. Beer's law is obeyed in the concentration ranges of 4-20 µg mL^{-1} and 5-25 µg mL^{-1} for DRT and ACE, respectively in method A while 4-24 µg mL^{-1} and 5-30 µg mL^{-1} by DRT and ACE, respectively in method B. The % assay for commercial formulation was found to be in the range 99.48 – 100.01 % for DRT and 99.52 – 99.89 % for ACE by the proposed methods. Recovery was found in the range 99.18-100.10 for DRT and 99.52 – 101.09% for ACE by ratio derivative spectroscopic method and 99.82 – 101.12% for DRT and 99.73-101.09% for ACE by AUC method for both the Formulations. The results of analysis have been validated statistically and recovery studies confirmed the accuracy and of the proposed methods which were carried out by following ICH guidelines[14].

A simple, rapid and extraction free spectroscopic method was developed and validated for simultaneous estimation of aceclofenac and pregabalin in tablet dosage form. The method was validated as per ICH guidelines and profitably used for the quantitative analysis of commercially available tablet. The both the drugs are separated based upon the solubility, in which the aceclofenac was insoluble in water and whereas pregabalin is soluble in water. The method was validated with respect to linearity, robustness, precision and accuracy and was favorably applied for the simultaneous Estimation of aceclofenac and pregabalin from the combined dosage formulation. The % amount for both the drugs was found to be within limits in the tablet dosage form for selected method. The calibration curve was linear over all the concentration range of 10 - 50µg/ml with wavelength of 276 nm for aeclofenac and 50 - 500µg/ml for pregabalin with the wavelength of 406 nm. The LOD was found to be 0.50µg/ml for aceclofenac and 0.6µg/ml for pregabalin and LOQ was found to be 2µg/ml for aceclofenac and 4µg/ml for pregabalin indicated good sensitivity for developed method. Aceclofenac and pregabalin was assayed a simple, sensitive and precise UV - Spectroscopic method. The developed method was validated according to the ICH guidelines. The method can be used for routine quality control experiments for simultaneous estimation of aceclofeanc and pregabalin in their pharmaceutical dosage form[15].

The present work reveled that UV Spectrophotometric method was developed for the quantitative determination of Aceclofenac in bulk drug and pharmaceutical dosage forms and has an absorption maximum at 273 nm in distilled water. The Beer's law was obeyed over the concentration range of 5-40 µg/ml. The correlation coefficient was found to be 0.999 and it has showed good linearity, reproducibility, precision in this concentration range. The % recovery values were found to be within 99.23%showed that the method was accurate. The LOD and LOQ were found to be 0.461073 µg /ml and 1.39719µg/ml respectively[16].

Two simple spectrophotometric methods have been developed for simultaneous estimation of Drotaverine hydrochloride and Aceclofenac from tablet dosage form. Method I is an Absorbance correction method in which absorbance is measured at two wavelengths, 360 nm at which Aceclofenac has no absorbance and 276 nm at which both the drugs have considerable absorbance. Method II is First order derivative method which involves two zero crossing points, 249 nm (for measurement of Drotaverine hydrochloride) and 306.5 nm (for measurement of Aceclofenac). Both the methods were found linear between the range of 10-40µg/ml for Aceclofenac and 8-32 µg/ml for Drotaverine hydrochloride. The accuracy and precision were determined and found

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to comply with ICH guidelines. Both the methods showed good reproducibility and recovery with % RSD in the desired range. The methods were found to be rapid, specific, precise and accurate and can be successfully applied for the routine analysis of Drotaverine hydrochloride and Aceclofenac in their combined tablet dosage form[17].

Three UV spectrophotometric methods for the simultaneous determination of Diacerein (DIA), andaceclofenac (ACE) in tablets were developed in the present work. Method I is simultaneous equation method, wavelength selected are 258.5 nm (λmax of Diacerein) and 274 nm (λmax of aceclofenac). Method II involves multicomponent mode of analysis, wavelength selected are 258.5 nm (λmax of Diacerein) and 274 nm (λmax of aceclofenac). Method III is area under curve method, wavelength range selected are 263.5-253.5 nm for Diacerein and 279-269 nm for aceclofenac respectively. All the methods were found linear between 2-14 µg/ml for Diacerein and 4-28 µg/ml for aceclofenac. The accuracy and precision of the methods were determined and validated stastically which showed no significant difference between the results obtained by the three methods. The proposed methods are simple, accurate and can be used for its intended purpose[18].

The present work aimed to develop and validate spectrophotometric methods for simultaneous estimation of rabeprazole sodium and aceclofenac in a pure and capsule dosage form. Method 1 is based on solving a simultaneous equation. Absorbances of rabeprazole sodium and aceclofenac were measured at their respective absorbance maximas (λ_{max}) of 283 and 276 nm. Method 2 is the Q-analysis or absorption ratio method. Absorbances were measured at 256 nm (isosbestic point) and 276 nm (λ_{max} of aceclofenac). Methods are validated according to ICH guidelines. A linearity range for rabeprazole sodium and aceclofenac is 10–60 µg/ml at respective selected wavelengths. The coefficient of correlation for rabeprazole at 283 nm and for aceclofenac at 276 nm is 0.9981 and 0.9997, respectively. A percentage estimation of rabeprazole sodium and aceclofenac from the capsule dosage form by method 1 is 100.22 and 99.96 and by method 2 is 99.99 and 100.05, respectively, with a standard deviation less than 2. The proposed methods are simple, rapid, and validated and can be used successfully for routine simultaneous estimation of rabeprazole sodium and aceclofenac in a pure and capsule dosage form[19].

The ratio difference spectrophotmetric method is employed for the simultaneous estimation of Paracetamol and Aceclofenac in tablet dosage form. For the estimation of Paracetamol wavelengths 245nm and 270nm were chosen as λ1 and λ2 and for the estimation of Aceclofenac wavelengths 214nm and 242nm were chosen as λ1 and λ2.The drug obeys Beer's law in concentration range of 3-40µg/ml and 3-10µg/ml for Paracetamol and Aceclofenac respectively. Limit of Detection for Paracetamol and Aceclofenac were found to be 0.1449µg/ml and 0.156µg/ml respectively. The method was validated with other ICH validation parameters also like precision and accuracy. The result shows that the method can be used for routine quality control analysis of the tablet formulations containing Paracetamol and Aceclofenac. The proposed method is simple yet rapid, accurate and cost effective [20].

The present work aimed to develop and validate spectrophotometric methods for simultaneous estimation of rabeprazole sodium and aceclofenac in a pure and capsule dosage form. A simple, sensitive, spectrophotometric method in UV region has been developed for the simultaneous estimation of Rabeprazole sodium and Aceclofenac in bulk and semi dosage form (Capsule). Standard solution of Rabeprazole sodium shows maximum absorbance at 283 nm and Aceclofenac shows maximum absorbance at 276 nm. Beer's Lamberts law is obeyed in concentration range 10-60 µg/ml for Rabeprazole with regression, slope and intercept of 0.991, 0.0918 and 0 respectively while for, Beer's Aceclofenac Lambert law is obeyed in concentration range 10-60 µg/ml with regression, slope and intercept having 0.9984, 0.2069 and 0.0253 respectively. Method was validated for linearity, range, accuracy, precision, recovery studies and interference study of mixture. All these parameters showed the adaptability of the method for the quality control analysis of the drug in bulk and in combination formulations[21].

An accurate and precise UV spectrophotometric method was developed for the simultaneous determination of Diacerein (DIA) and Aceclofenac (ACF) from combined solid dosage form. The absorbance maxima at 257nm and 274 nm were selected for the determination of Diacerein and Aceclofenac respectively. UV-Spectroscopy was carried out with a solvent system composition of Methanol: Phosphate buffer pH-6.8 in the ratio of (25:75). The method was linear over the concentration range of 1-10mcg/ml and 2-

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18mcg/ml for both drugs of Diacerein and Aceclofenac with a correlation coefficient of 0.999. The percentage label claim was found to be 99.03±0.87% and 101.05±0.85% for Diacerein and Aceclofenac respectively. The method was showed good reproducibility, recovery studies and successfully applied for the determination of different brands of pharmaceutical formulations [22].

The present study deals with UV spectrophotometric method development and validation for estimation of Tizanidine and Aceclofenac tablet dosage form by Viedort's method and first order UV derivative spectrophotometry. The Vierodt's method involves measurement of absorbance at λmax of Tizaridine and Aceclofenac at 282 nm respectively. The linearity of Tizanidine and Aceclofenac was found to be in the range of 1-10 µg/ml respectively. The % recovery of Tizanidine and Aceclofenac was found out to be 99.2% and 99.69%s respectively. First order CV derivativespectrophotonmetry (D1 method). The zero crossing method was chosen as Tizanidine could he easily analyzed without any interference from Aceclofenac and vice-versa. Tizanidine was determined by measurement of its D1 amplitude at the zero crossing point of Aceclofenac at (270nm), While Aceclofenac was determined by measurement of its D1 amplitude at zero crossing point of Tizanidine at (318 nm) The proposed method was validated as per ICH guidelines[23].

Two simple, precise and accurate visible spectrophotometric methods were developedfor the estimation of Aceclofenac in bulk drug and in pharmaceutical formulations. Theproposed methods were indirect and based on determination of aceclofenac after itsreaction with either (p-dimethylaminocinnamaldehyde or 3-Methyl-2-benzothiazolinonehydrazine hydrochloride and measuring the chromogen at the λmax by 658 and 592,respectively. Beers law obeyed in the concentration range of 1-200 µg/ml for method Aand 1-100 µg/ml for method B. The accuracy of the methods was determined by recoverystudies. The methods showed good reproducibility and recovery with relative standarddeviation (in %) less than 2. The methods were found to be simple, economical, accurateand reproducible and can be used [24].

A simple, precise, rapid and selective simultaneous equation and Q-analysis UV spectrophotometric method has been developed for the simultaneous determination of aceclofenac and paracetamol from combined tablet dosage form. The method involves solving of simultaneous equation value analysis based on measurement of absorptivity at 276, 249 and 270 nm, respectively. Linearity lies between 2-25 mcg/ mL for aceclofenc and 1-30 mcg/mL for paracetomol. Results of analysis for both the method were validated statistically and by recovery studies [25].

HPLC Methods:

A simple, selective, rapid, precise and economical reverse phase high-pressure liquid chromatographic method has been developed for the simultaneous estimation of Paracetamol, Aceclofenac and Thiocolchicoside from pharmaceutical formulation. The method was carried out on a HiQSil C18 (250 mm × 4.6 mm, 5.0 µ) from Japan, with a mobile phase consisting of acetonitrile: water (30: 70, v/v) at flow rate of 1.0 ml/min. Detection was carried out at 263 nm. This method has been applied to formulation without interference of excipients of formulation. The linear regression analysis data for the calibration plots showed a good linear relationship over the concentration range of 50-175 µg/mL for Paracetamol, 10-35 µg/mL for Aceclofenac and 0.40-1.4 µg/mL for Thiocolchicoside respectively. The mean values of the correlation coefficient, slope and intercept were 0.9959 ± 0.98, 11389 ± 1.02 and 7020 ± 0.86 for Paracetamol and 0.9975 ± 0.64, 15521 ± 0.32 and 16800 ± 0.86 for Aceclofenac and 0.9984 ± 0.73, 13144 ± 0.74 and 357.9 ± 1.11 for Thiocolchicoside respectively. The method was validated for precision, robustness and recovery. The limit of detection (LOD) and limit of quantitation (LOQ) was 0.25 µg/mL and 0.50 µg/mL for Paracetamol, 1 µg/mL and 2 µg/mL for Aceclofenac and 0.24 µg/mL and 0.4 µg/mL for Thiocolchicoside respectively. Statistical analysis showed that the method is repeatable and selective for the estimation of Paracetamol, Aceclofenac and Thiocolchicoside[26].

Aceclofenac and Pregabalin in combination significantly reduce pain as compared to individual drug in chronic low back pain. A selective, sensitive, accurate, and precise, high performance liquid chromatographic method withUVdetector analysis ofAceclofenac and Pregabalin was investigated.Good chromatographic separation was achieved using anODS-BP hypersil C18 column (250mm× 4.6 mm, i.d., 5 μm) and a mobile phase consisting of 0.05Mphosphate buffer (KH_2PO_4) (pH 6.0) :methanol (60 : 40, v/v) at a flow rate 1 mL/min. The ultraviolet detector was

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set at wavelength 218 nm. Retention time for Aceclofenac and Pregabalin was found to be 3.220 and 5.910 min, respectively. Rectilinear relationship with good regression coefficients 0.999 and 0.999 was found over the concentration ranges of 5–25 μg/mL and 3.75–18.75 μg/mL for ACF and PGB, respectively, with detection limits 0.64 and 0.35 μg/mL and quantitation limits 1.95 and 1.06 μg/mL.The mean percentage recoveries were in the range of 98.45–100.08 and 99.69–100.48 for ACF and PGB, respectively.The developed method was successfully applied to the analysis of the drugs in their commercial tablets[27].

A rapid and sensitive RP-HPLC method with UV detection and UV spectrophotometric method for routine Pharmaceutical quality control of aceclofenac, paracetamol and tizanidine in tablets formulation was developed. Chromatography was performed by using Phenomenex-Luna C18 (250 x 4.6 mm, 5µ) with a mobile phase containing Methanol: Water (90:10v/v), flow rate 1mL/min, wavelength at 256 nm. Linearity observed over the concentration range between 5-30µg/mL, 10-60µg/mL and 2-12µg/mL for aceclofenac, paracetamol and tizanidinerespectively.The UV spectrophotometric method was performed at 277, 248 and 323 nm by derivative spectrophotometry with simultaneous equation method. The entire three drugs obey Beer's law in the concentration range between 5-30 µg/mL, 2-16 µg/mL and 2-30 µg/mL respectively. The proposed methods were simple, rapid, precise, accurate and sensitive and can be used for routine quality control in pharmaceuticals[28].

A simple, rapid, and precise Reverse Phase HPLC method has been developed for determination of Rabeprazole Sodium (RBP sodium) and Aceclofenac (ACE) in combined Dosage form. The RP-HPLC method carried out on Hypersil BDS C18 (150 mm x 4.6 mm, 5µm) as stationary phase by using mobile phase consisting of 0.02M Phosphate buffer (pH 6with orthophosphoric acid) : acetonitrile (67:33). Mobile phase was maintained at a flow rate 1.0 ml/min. The UV detector was operated at 280nm. Retention time was found to be 4.3min for RBP Sodium and 5.9 min for Aceclofenac. The specificity studies shows that the analyte peaks were well resolved from the intermediates. Developed method was found to be linear over the range of 100-300µg/ml and 10-30µg/ml for Aceclofenac and Rabeprazole Sodium respectively; the correlation coefficient was found to be 0.9995 and 0.9995 for Aceclofenac and Rabeprazole Sodium. The precision study showed that the percentage relative standard deviation was within the range of acceptable limits, and the mean recovery was found to be 100.45 % and 99.63 % for Aceclofenac and Rabeprazole Sodium respectively. Statistical analysis proves that the method is reproducible & selective for the estimation of said drug, as the method could effectively separate the drug from its degradation product[29].

The purpose of the study is to develop and validate method for assay of Aceclofenac in tablet dosage forms using ultra violet spectrophotometry (UV) and high performance liquid chromatography (HPLC) techniques. A method was developed and validated for analysis of Aceclofenac using UV technique with methanol and phosphate buffer 7.4 as solvent. The HPLC analysis was conducted using two mobile phases, that is, "A" as Acetonitrile: Methanol (80:20 v/v) and "B" as Acetonitrile: methanol: NH_3 solution (225:50:1 v/v/v). The method was used for assay determination for tablets dosage forms and results were found to be in compliance with official standards. Validation studies were also carried out for both methods. Linearity, LOD, single point calibration, precision and accuracy and % RSD were calculated. Aceclofenac standard was analysed with UV Spectrophotometer in the concentration ranges f 0.5-50 and 0.4-50 mg/L for each solvent and results showed good linearity with R^2 = 0.9998 and 0.9999. The method was also specific that verifies the absence of interference at the λmax of Aceclofenac. UV analysis was precise with % RSD falling within 2% and LOD as 0.5 and 0.4 mg/L for methanol and PBS 7.4, respectively. The tablets of three brands showed assay percentages within specified limits in methanol (109.33, 103.90 and 105.61%) and PBS 7.4 (108.70, 100.69 and 106.60%). In HPLC analysis, mobile phase 'B' showed more sharp peaks with lesser HETP and Tf compared to mobile phase 'A'. The method was checked for reliability and efficiency for assay and some of the parameters like height efficiency to theoretical plates (HETP), tailing factor, peak heights, peak widths along with validation studies (Linearity range 0.1-50 mg/L, specificity, precision, and limit of detection and single point calibration). The more basic mobile phase B using NH_3 solution produced more sharp peaks as compared to less basic mobile phase A[30].

The objective of present research is to develop a simple, sensitive, linear, precise and accurate RP-HPLC and UVSpectrophotometric

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method for simultaneous estimation of Cyclobenzaprine hydrochloride and Aceclofenac in bulk and tablet formulation as developed and validated. UV-Spectrophotometric method Calibration plot were linear R^2 =0.9996 over the concentration range 1-5µg/ml for Cyclobenzaprine hydrochloride, R^2= 0.9995 for the Aceclofenac 13-65µg/ml. And Chromatographic conditions used are stationary phase Inertsil ODS column (250 × 4.6 mm ~5µ) (5µm particle size) the mobile phase Methanol: 10mm KH_2PO_4 Buffer (pH-3) (70:30) and flow rate was maintained 0.9ml/min, detection wavelength was 220nm. The retention times were 4.7min and 2.9 min for Cyclobenzaprine hydrochloride and Aceclofenac respectively. Calibration plot were linear R^2 = 0.9996 over the concentration range 3-15µg/ml for Cyclobenzaprine hydrochloride, R^2 = 0.9994 for the Aceclofenac 40-200µg/ml. No interference from any component of pharmaceutical dosage form was observed. The proposed method has been validated as per ICH guidelines, validation studies revealed that method id specific, rapid, reliable and reproducible. The developed method successfully employed for routine quality control analysis in the combined pharmaceutical dosage form[31].

A simple, precise, accurate, and validated reverse phase HPLC method has been developed for the simultaneous estimation of aceclofenac and paracetamol in tablet by reverse phase C-18 column (Intersile 4.6 mm×25 cm, 10 µm) using acetonitrile: 50 mM NaH_2PO_4 in a ratio of 65:35 (pH adjusted to 3.0 with orthophosphoric acid) as a mobile phase at a flow rate of 1.5 ml/min and detection at 276 nm. The retention time for aceclofenac and paracetamol was found to be 1.58 and 4.01 min respectively, and recoveries from tablet were between 99 and 101%. The method can be used for estimation of combination of these drugs in tablets[32].

A reverse phase liquid chromatographic method for estimation of Aceclofenac in bulk drug and tablet dosage form was developed and validated. The chromatographic conditions to achieve the highest performance parameters using octylsilyl column with guard filter were optimized. The separation was carried out using a mobile phase containing 10 mM Phosphate Buffer, pH 2.1 and methanol (30:70% v/v) pumped at a flow rate of 1.0 mL/min with detection at 272 nm. The method was shown to be linear in 19.8–148.5 µg/ mL concentration range (regression coefficient of 0.999). The limit of detection (LOD) and limit of quantification (LOQ) was found to be 0.0692 µg/mL and 0.2076 µg/mL, respectively. The accuracy of the method was assessed by adding fixed amount of pre-analyzed sample to different standard solutions (80%, 100%, and 120% of the tested concentration) in triplicate. The percentage mean recoveries were 97.91% to 100.39% with %RSD values of 0.64–0.79. The method was found to be precise with %RSD value of 1.13 and 1.60 for intraday and interday precision study, respectively. The method specificity and robustness were also established. New and sensitive HPLC method for estimation of Aceclofenac has been developed, in respect to the reviewed analytical methods[33].

A simple, precise and accurate reversed-phase liquid chromatographic method has been developed for the simultaneous estimation of aceclofenac (ACF), paracetamol (PCM) and tramadol hydrochloride (TRM) in pharmaceutical dosage form. The chromatographic separation was achieved on a HiQ-Sil™ HS C18 column (250×4.6 mm i.d., 5 µm particle size), kromatek analytical column at ambient temperature. The mobile phase consisted of 40: 60 (v/v); phosphate buffer (pH 6.0): methanol. The flow rate was set to 1.0 mL/min and UV detection was carried out at 270 nm. The retention time (t(R)) for ACF, PCM and TRM were found to be 14.567 ± 0.02, 3.133 ± 0.01 and 7.858 ± 0.02 min, respectively. The validation of the proposed method was carried out for linearity, precision, robustness, limit of detection, limit of quantitation, specificity, accuracy and system suitability. The linear dynamic ranges were from 40-160 µg/mL for ACF, 130-520 µg/mL for PCM and 15-60 µg/mL for TRM. The developed method can be used for routine quality control analysis of titled drugs in pharmaceutical dosage form[34].

A simple, rapid, and precise reversed-phase liquid chromatographic method is developed for simultaneous determination of paracetamol, aceclofenac, and chlorzoxazone in their ternary mixtures of commercial pharmaceutical preparation. This method uses a Zorbax SB C18, 250 x 4.6 mm, 5 microm analytical column. Mobile phase is acetonitrile and buffer (40:60, v/v), buffer containing 50 mMorthophosporic acid; pH of the buffer is adjusted to 6 with 10% w/v sodium hydroxide solution. The instrumental settings are at a flow rate of 1 mL/min; the column temperature is 25 degrees C, and detector wavelength is 270 nm. The sample concentrations are measured on weight basis to avoid the internal standard. The method is validated and shown to be linear. The correlation coefficients for paracetamol, aceclofenac, and

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chlorzoxazone are 0.9981, 0.9990, and 0.9986, respectively. The recovery values for paracetamol, aceclofenac, and chlorzoxazone ranged from 100.7-101.4%, 100.4-101.0%, and 100.5-101.3%, respectively. The relative standard deviation for six replicates is always less than 2%. This HPLC method is successfully applied to the simultaneous quantitative analysis of the title drugs in tablets and can be applied for assay and dissolution test of tablets for the estimation of paracetamol, aceclofenac, and chlorozoxazone in their commercial samples[35].

A simple, sensitive and precise RP-HPLC method was developed for the determination of aceclofenac in tablet dosage form. The RP-HPLC separation was achieved on hypersil C18 column (250 mm, 4.6 mm, 5µm) using mobile phase water: acetonitrile (55:45 v/v) at flow rate of 1 ml/min at ambient temperature. Quantification was achieved with photodiode array detection at 277 nm over the concentration range of 1- 10 µm/ml. The method was validated statistically and applied successfully for the determination of aceclofenac[36].

A new simple precise, accurate and selective RP-HPLC method was developed for the simultaneous estimation of Paracetamol and Aceclofenac in their mixed formulation by separating Diclofenac. All the three drugs were separated on Kromasil C18 (150x4.6, 5µ) with reverse phase elution of the mobile phase compose of 0.05M potassium dihydrogen phosphate and Acetonitrile in the ratio 40:60 v/v at a flow rate of 1.0mL/min. The detection was made at 275nm. The retention times were 2.36 min for Paracetamol, 3.23 min for Aceclofeanc and 6.38 min for Diclofenac. The linearity ranges for paracetamol and aceclofenac were 16.25 to 48.75 and 5 to 15 mcg/ml respectively with correlation coefficients 0.999 and 1.0. The proposed method statistically validated with respect to system suitability, specificity, linearity, range, precision, accuracy, robustness and ruggedness. The method was accurate, linear, precise, specific, selective and rapid found to be suitable for the quantitative estimation of Paracetamol and Aceclofenac by separating Diclofenac[37].

A simple, accurate and precise RP-HPLC method was developed for the estimation of Aceclofenac and Rabeprazole Sodium in the bulk and marketed formulation. The method was performed by using the mobile phase containing Methnol, Water and Acetonitrile (60:30:10 v/v), pH- 6.14 was found to be most suitable for RP-HPLC as it showed sharp peak with symmetry and significant reproducible retention time for Aceclofenac (4.549 min) along with Rabeprazole Sodium (6.048 min). From the results of system suitability parameters, it was observed that the peak was sharp and symmetrical with satisfactory capacity factor and column efficiency. From the developed methods, percent content of Aceclofenac and Rabeprazole Sodium was found to be 99.97%, 99.91% and 99.94% 99.6%, 99.8% and 94.45% respectively by RP-HPLC. The method was validated by parameters like accuracy, precision, specificity, linearity, ruggedness and robustness. The results indicated that, the method is simple, accurate, precise, rugged. The method described enables to the quantification of Aceclofenac and Rabeprazole Sodium. The advantages lie in the simplicity of sample preparation and the low costs of reagents used. The proposed HPLC conditions ensure sufficient resolution and the precise quantification of the compounds. Results from statistical analysis of the experimental results were indicative of satisfactory precision and reproducibility. Hence, this HPLC method can be used for routine drug analysis[38].

A simple, precise and accurate reversed-phase liquid chromatographic method has been developed for the simultaneous estimation of aceclofenac (ACF), paracetamol (PCM) and tramadol hydrochloride (TRM) in pharmaceutical dosage form. The chromatographic separation was achieved on a HiQ-Sil™ HS C18 column (250×4.6 mm i.d., 5 µm particle size), kromatek analytical column at ambient temperature. The mobile phase consisted of 40: 60 (v/v); phosphate buffer (pH 6.0): methanol. The flow rate was set to 1.0 mL min^{-1} and UV detection was carried out at 270 nm. The retention time (t_R) for ACF, PCM and TRM were found to be 14.567 ± 0.02, 3.133 ± 0.01 and 7.858 ± 0.02 min, respectively. The validation of the proposed method was carried out for linearity, precision, robustness, limit of detection, limit of quantitation, speci city, accuracy and system suitability. The linear dynamic ranges were from 40–160 µg mL^{-1} for ACF, 130–520 µg mL^{-1} for PCM and 15–60 µg mL^{-1} for TRM. The developed method can be used for routine quality control analysis of titled drugs in pharmaceutical dosage form[39].

A simple, rapid and selective HPLC method has been developed for quantitation of aceclofenac and paracetamol from bulk drug and pharmaceutical formulations using a mobile phase consisting mixture of methanol and water (70:30 v/v) at the flow rate of 1mL/min. An ODS C-18

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(Intersile 25 cm x 4.6 mm, 10 µm.) column was used as stationary phase. The retention time of aceclofenac and paracetamol were 1.8 min. and 2.7 min. respectively. Linearity was observed in the concentration range of 2-50 µg/mL for aceclofenac and 5-50 µg/mL for paracetamol. Percent recoveries obtained for aceclofenac and paracetamol were 100.6 and 100.7 respectively. The proposed method is precise, accurate, selective and rapid for the simultaneous determination of aceclofenac and paracetamol [40].

A reverse phase high performance liquid chromatographic method (HPLC) has been developed for the simultaneous estimation of aceclofenac (ACE), paracetamol (PARA) and chlorzoxazone (CHZ), in the pharmaceutical formulation using RP-C8 column. The mobile phase (Acetonitrile and Double distilled water) was pumped at a flow rate of 1 ml/min in the ratio of 60:40 and the eluents were monitored at 230.0 nm. Linearity was obtained in the concentration range of 1-60 µg/ml for ACE, 1-50 µg/ml for PARA and CHZ. The accuracy of the method was found to be 98-102% and RSD was found to be less than 2% indicating high degree of accuracy and precision of the proposed HPLC method. Due to its simplicity, rapidness, high precision and accuracy, the proposed HPLC method may be used for determining aceclofenac, chlorzoxazone and paracetamol in bulk drug samples or in pharmaceutical dosage form [41].

A new RP- HPLC method was developed and validated for the estimation of aceclofenac and thiocolchicoside in their tablet dosage form. The chromatographic separation was carried out by using Agilent Zorbax column (150 × 4.6mm, 5µm). The mobile phase containing the combination of methanol and 0.1% ortho phosphoric acid of 75:25 (v/v) ratios. In this method the flow rate used is 1 min/ml for the separation at the detection wavelength of 275 nm. The proposed method was validated according to the ICH guidelines. The method was linear (R2 > 0.99), precise (RSD < 2.0%), accurate, simple, sensitive and robust. This method can be successfully used for the routine pharmaceutical analysis [42].

A simple, sensitive, precise, specific and accurate isocratic reversed phase-high performance liquid chromatography (RP-HPLC) method has been developed for the quantitative estimation of aceclofenac in pharmaceutical formulations. RP-HPLC method was developed by using WELCHROM C18 Column (4.6 X 250mm, 5µm), SHIMADZU LC-20AT prominence liquid chromatograph. The mobile phase consisting of phosphate buffer pH 6.8 and acetonitrile in the portion of 50:50 v/v. Isocratic elution at a flow rate of 0.5 mL/min was employed. The responses are measured at 278 nm using SHIMADZU SPD-20A prominence UV-Vis detector. The retention time for aceclofenac was 8.767 min. The method possesses linearity in the range of 2- 10µg/ml and correlation coefficient was 0.999. The % recovery was within the range between 99.91% and 101.26%. The accuracy and reliability of the proposed method was ascertained by evaluating various validation parameters like linearity, precision and specificity according to ICH guidelines. The percentage RSD for precision and accuracy of the method was found to be less than 2%. The proposed method was successfully employed for routine quality control analysis of aceclofenac in bulk samples and its pharmaceutical formulations [43].

A simple, rapid, and precise reversed-phase liquid chromatographic method is developed for simultaneous determination of paracetamol, aceclofenac, and chlorzoxazone in their ternary mixtures of commercial pharmaceutical preparation. This method uses a Zorbax SB C18, 250 x 4.6 mm, 5 µm analytical column. Mobile phase is acetonitrile and buffer (40:60, v/v), buffer containing 50mM orthophosporic acid; pH of the buffer is adjusted to 6 with 10% w/v sodium hydroxide solution. The instrumental settings are at a flow rate of 1 mL/min; the column temperature is 25°C, and detector wavelength is 270 nm. The sample concentrations are measured on weight basis to avoid the internal standard. The method is validated and shown to be linear. The correlation coefficients for paracetamol, aceclofenac, and chlorzoxazone are 0.9981, 0.9990, and 0.9986, respectively. The recovery values for paracetamol, aceclofenac, and chlorzoxazone ranged from 100.7–101.4%, 100.4–101.0%, and 100.5–101.3%, respectively. The relative standard deviation for six replicates is always less than 2%. This HPLC method is successfully applied to the simultaneous quantitative analysis of the title drugs in tablets and can be applied for assay and dissolution test of tablets for the estimation of paracetamol, aceclofenac, and chlorozoxazone in their commercial samples [44].

A simple, fast and precise reverse phase high performance liquid chromatographic method is developed for the simultaneous determination of aceclofenac, paracetamol and tizanidine. Chromatographic separation of the three drugs

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were performed on a hypersil C_{18} column (250 mm x 4.6 mm, 5 µm) as stationary phase with a mobile phase comprising of mix phosphate buffer pH 7.0: acetonitrile (40:60 v/v), at a flow rate of 0.7 mL min^{-1} and UV detection at 230 nm. The proposed method was validated for linearity, accuracy, precision, LOD, LOQ. Linearity, accuracy and precision were found to be acceptable over the ranges of 100-300 µg mL^{-1} for aceclofenac, 500-1500 µg mL^{-1} for paracetamol and 2-6 µg mL^{-1} for tizanidineHCl equivalent to tizanidine. It can be conveniently adopted for routine quality control analysis [45].

HPTLC Methods:

A simple, rapid, sensitive and highly precise High Performance Thin Layer Chromatographic

Method has been developed for the estimation of Paracetamol, Aceclofenac and Chlorzoxazone in tablets. HPTLC was performed on CAMAG LINOMAT IV, TLC Scanner Version 3.20, using toluene, ethyl acetate and glacial acetic acid (17.5:10:0.5 v/v) as mobile phase. The Chromatogram was developed in CAMAG twin trough glass containing mobile phase. The TLC plates were scanned at 271 nm in schimadzu dual wavelength scanner, and Rf value of Paracetamol, Aceclofenac and Chlorzoxazone was found to be 0.12, 0.29 and 0.72, respectively. The linearity of Paracetamol, Aceclofenac and Chlorzoxazone shows a correlation coefficient of 0.9995, 0.9991, and 0.9997, respectively. The proposed method was validated by determining sensitivity, accuracy, precision and system suitability parameters [46].

A simple, accurate, precise and reproducible high performance thin layer chromatographic method has been developed for the simultaneous estimation of paracetamol and aceclofenac in pharmaceutical dosage forms. It was performed on TLC plate precoated with silica gel 60F(254) as stationary phase using mobile phase comprising of toluene:isopropyl alcohol: ammonia (20:20:3, v/v/v) and the detection was carried out by UV detection at 254 nm showing R-f value of 4.8 for aceclofenac and 11.8 for paracetamol. The percentage estimation of labeled claims of aceclofenac and paracetamol from marketed tablet was found to be 99.84 and 99.72, respectively. The method was validated in terms of accuracy, precision, specificity and ruggedness. Linearity was observed between 60-140 mu g/mL for aceclofenac and 460540 mu g/mL for paracetamol. The recovery studies were carried out by adding known quantity of standard drugs in the pre-analysed test solution and percentage recovery calculated in each case. The percentage recovery studies for paracetamol and accelofenac were found within the range of 98.60-99.32%. The proposed method was found to be accurate, precise, simple and rapid could be used for routine analysis[47].

II. CONCLUSION:

There are many analytical methods have been used to determine accelofenac in bulk drug and in its pharmaceutical preparations at various levels. Spectrophotometry, high-performance liquid chromatography methods and high performance thin layer chromatographic methods are simple and easy to apply. However, the high performance liquid chromatographic analysis methods are often used in research because it can detect samples with lesser quantities. The HPLC methods can be applied in mixture of accelofenac with other drugs.

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