IJCRT.ORG ISSN : 2320-2882

INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

"Simultaneous Estimation Of Paracetamol And Diclofenac Sodium In Marketed Drug By Using Uv Visible Spectroscopy"

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Abstract - The UV spectrophotometric analysis confirms that the developed method is simple, rapid, and precise for the simultaneous estimation of Paracetamol and Diclofenac Sodium in their combined marketed formulation. The Isosbestic point observed at 245 nm further validates the stoichiometric relationship and molar absorptivity consistency required for the Q-analysis and simultaneous equation approach. The results obtained are in close agreement with the label claim, indicating the minimal interference of excipients in the formulation. A percentage estimation of Paracetamol and Diclofenac Sodium in the tablet dosage form by Simultaneous Equation (Vierordt's) method was obtained at the wavelength 254 nm (For Paracetamol) and 236 nm (for Diclofenac Sodium) as 94.31% and 82.60% and the content of both drugs in mg is 306.5 mg and 41.3 mg. Total percent content of both drugs in tablet dosage form is 92.74% and a total drug concentration in mg is 347.8 mg, which shows accuracy in result. Paracetamol and Diclofenac Sodium in their combined dosage forms has been found to be simple, quick, accurate, the proposed UV spectrophotometric method for simultaneous estimation of, and cost-effective.

Key words - Simultaneous, Stoichiometric, Absorptivity, Spectrophotometric, Concentration.

Introduction - 1. Pharmaceutical Analysis: An Overview

Pharmaceutical analysis is a vital branch of pharmaceutical sciences that deals with the qualitative and quantitative determination of drugs and their formulations. It plays a significant role in ensuring the identity, purity, potency, and safety of pharmaceutical products. The increasing complexity of drug formulations, especially combination dosage forms, has led to the development of advanced analytical techniques for accurate and reliable estimation of multiple active pharmaceutical ingredients (APIs).

The quality control of pharmaceutical formulations requires validated analytical methods that comply with regulatory standards. These methods must be precise, accurate, reproducible, and capable of detecting even small variations in drug concentration. With the growing demand for multi-component drug therapy, the simultaneous estimation of drugs has become an essential part of pharmaceutical analysis. Such methods not only reduce analysis time but also minimize the use of reagents and solvents, making them cost-effective and environmentally friendly.

Introduction of Paracetamol

Paracetamol, also known as acetaminophen, is one of the most widely used over-the- counter (OTC) drugs for the treatment of pain and fever. Chemically, it is N-(4- hydroxyphenyl)acetamide and belongs to the class of para-aminophenol derivatives. It is a white crystalline powder that is slightly soluble in water and freely soluble in alcohol.

Paracetamol is extensively used due to its effectiveness and favorable safety profile. It is commonly indicated for the relief of mild to moderate pain such as headache, toothache, dysmenorrhea, and musculoskeletal pain, as well as for reducing fever. Unlike non-steroidal anti-inflammatory drugs (NSAIDs), Paracetamol exhibits minimal anti-inflammatory activity.

The mechanism of action of Paracetamol is primarily central. It inhibits the synthesis of prostaglandins in the brain by blocking the cyclooxygenase (COX) pathway, thereby reducing pain perception and regulating body temperature. It is also believed to act on serotonergic pathways and the endocannabinoid system, contributing to its analgesic effects.

One of the major advantages of Paracetamol is its minimal gastrointestinal irritation and lack of significant effect on platelet aggregation, making it safer than many NSAIDs. However, overdose or prolonged use can lead to hepatotoxicity, emphasizing the importance of accurate dosage and quality control in pharmaceutical formulations.

Introduction to Diclofenac Sodium

Diclofenac Sodium is a widely used non-steroidal anti-inflammatory drug (NSAID) that belongs to the phenylacetic acid group. It is chemically known as sodium [2-(2,6- dichloroanilino)phenyl]acetate and appears as a white to slightly yellow crystalline powder. Diclofenac Sodium exhibits potent anti-inflammatory, analgesic, and antipyretic properties. It is commonly prescribed for the treatment of inflammatory conditions such as rheumatoid arthritis, osteoarthritis, ankylosing spondylitis, and acute musculoskeletal injuries. It is also used in postoperative pain management and in conditions involving soft tissue inflammation.

The pharmacological action of Diclofenac Sodium is primarily due to the inhibition of cyclooxygenase enzymes (COX-1 and COX-2), which are responsible for the synthesis of prostaglandins. Prostaglandins play a key role in mediating inflammation, pain, and fever. By inhibiting their production, Diclofenac effectively reduces inflammation and associated symptoms.

Despite its therapeutic benefits, Diclofenac Sodium is associated with certain adverse effects, particularly gastrointestinal irritation, ulceration, and renal toxicity, especially with long-term use. Therefore, it is often combined with safer analgesics like Paracetamol to achieve a balanced therapeutic effect while minimizing side effects.

Rationale for Combination Therapy

The combination of Paracetamol and Diclofenac Sodium is widely used in clinical practice due to its synergistic therapeutic effects. While Paracetamol acts centrally to relieve pain and reduce fever, Diclofenac Sodium exerts peripheral anti-inflammatory action. This complementary mechanism enhances overall analgesic efficacy and provides faster and more effective relief from pain and inflammation.

The advantages of this combination include:

- Enhanced analgesic and anti-inflammatory effect
- Reduced dose requirement of individual drugs
- Improved patient compliance
- Faster onset of action
- Broader therapeutic coverage

Such combinations are commonly formulated as tablets, capsules, and suspensions. Due to their widespread use, it is essential to develop reliable analytical methods for their simultaneous estimation to ensure quality and regulatory compliance.

Introduction to UV Visible spectroscopy

UV-Visible spectroscopy is one of the most widely used analytical techniques in pharmaceutical analysis. It is based on the absorption of electromagnetic radiation in the ultraviolet (200–400 nm) and visible (400–800 nm) regions by molecules. This absorption results in electronic transitions from lower energy levels to higher energy levels.

The fundamental principle governing UV-Visible spectroscopy is Beer–Lambert's law, which states that the absorbance of a solution is directly proportional to the concentration of the absorbing species and the path length of the cell. Mathematically, it is expressed as:

$$A=\varepsilon bc$$

Where:

A = Absorbance

ε = Molar absorptivity

b = Path length

c = Concentration

UV-Visible spectroscopy offers several advantages:

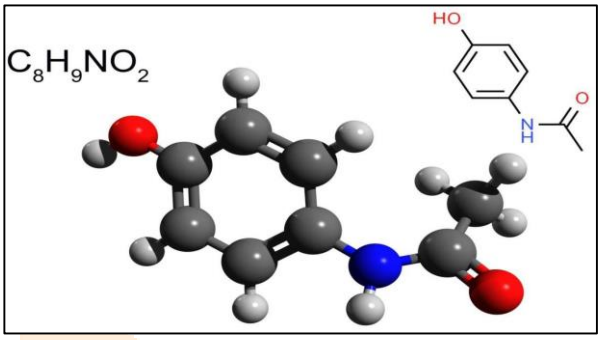
- Simplicity and ease of operation
- Rapid analysis
- High sensitivity and accuracy
- Cost-effectiveness
- Minimal sample preparation

DRUG PROFILE

1. Paracetamol-

Paracetamol also called acetaminophen, is one of the commonly used non-opioid analgesics and antipyretics. It is generally used for pain relief and fever. Because it has an excellent safety profile and no gastrointestinal side effects, it is one of the most commonly used over-the-counter drugs.

Structure of Drug:



Paracetamol (acetaminophen)

Structural Features:

- Aromatic benzene ring
- Para-substituted hydroxyl group (–OH)
- Amide linkage (–$NHCOCH_3$)
- IUPAC Name:- N-(4-hydroxyphenyl) acetamide

Chemistry:-

- Molecular Formula: $C_8H_9NO_2$
- Molecular Weight: 151.16 g/mol
- Category: Para-aminophenol derivative
- Physical State: White crystalline solid
- Melting Point: 168–172°C
  Solubility: Slightly soluble in water, freely soluble in alcohol

Chemical Properties:

Paracetamol is a weak acid that is stable in normal conditions but can degrade at oxidative conditions. The presence of hydroxyl and amide groups is responsible for its pharmacological activity. It is slightly soluble in water and has a melting point of 168°F. It is stable

Pharmacodynamics

Paracetamol has analgesic and antipyretic effects. It has very little anti-inflammatory action compared to NSAIDs. Its action is central thus, it is used for conditions where inflammation is of little concern.

Mechanism of Action

Paracetamol blocks the synthesis of prostaglandins in the central nervous system through the inhibition of cyclooxygenases, especially COX-2. It also influences serotonergic systems and may modulate endogenous cannabinoid systems.

Uses

- Fever (antipyretic)
- Headache
- Toothache
- Dysmenorrhea
- Musculoskeletal pain
- Cold and flu

Pharmacokinetics

Absorption: Rapid and almost complete from gastrointestinal tract
Bioavailability: 70–90%
Distribution: Uniformly distributed; crosses blood-brain barrier
Protein Binding: Low (10–25%)

Metabolism: Liver (glucuronidation and sulfation) Toxic Metabolite: NAPQI (detoxified by glutathione)
Elimination: Urine
Half-life: 2–3 hours

Side Effects

- Hepatotoxicity (dose-dependent)
- Nausea and vomiting
- Skin reactions (rare)
- Hypersensitivity reactions

Contraindications

- Severe hepatic impairment
- Chronic alcoholism
- Hypersensitivity

Drug Interactions

Alcohol → Increased liver toxicity Warfarin → Increased anticoagulant effect Rifampicin → Reduced effectiveness Phenytoin → Increased toxicity risk

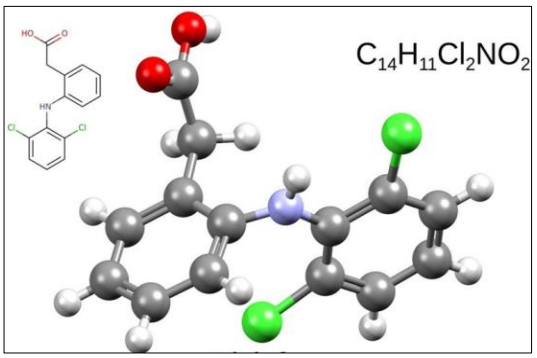
Brand Names

- Crocin
- Calpol
- Tylenol
- Panadol

Diclofenac Sodium

Diclofenac Sodium is a highly effective non-steroidal anti-inflammatory drug (NSAID) used to treat pain, inflammation, and fever. Diclofenac Sodium is commonly used to treat chronic inflammatory conditions and to manage acute pain.

Structure of drug -



Diclofenac

Chemistry

Molecular Formula: $C_{14}H_{10}Cl_2NNaO_2$

Molecular Weight: 318.13 g/mol

Category: Phenylacetic acid derivative

Physical State: White to light yellow crystalline powder

Melting Point: ~283°C

Solubility: Slightly soluble in water, soluble in organic solvents

Chemical Properties:

Diclofenac Sodium is a weak acid salt, which demonstrates satisfactory stability under usual storage conditions. The presence of halogen atoms improves the lipophilicity and potency of the compound.

Pharmacodynamics

Diclofenac possesses anti-inflammatory, analgesic, and antipyretic activity. Diclofenac is more potent in reducing inflammation compared to other NSAIDs.

Mechanism of Action

Diclofenac inhibits cyclooxygenase enzymes (COX-1 and COX-2), leading to decreased synthesis of prostaglandins, which are mediators of inflammation, pain, and fever.

Uses

- Rheumatoid arthritis
- Osteoarthritis
- Ankylosing spondylitis
- Acute musculoskeletal pain
- Postoperative pain
- Dysmenorrhea

Pharmacokinetics

Absorption: Rapid and complete after oral administration Bioavailability: ~50% (first-pass metabolism)
Distribution: Highly protein bound (>99%) Metabolism: Liver (CYP2C9 enzyme)
Elimination: Urine and bile
Half-life: 1–2 hours

Side Effects

- Gastric irritation
- Peptic ulcer
- Nausea and vomiting
- Renal impairment
- Cardiovascular risk (long-term use)

Contraindications

- Peptic ulcer disease
- Severe renal or hepatic impairment
- Hypersensitivity to NSAIDs
- Asthma (NSAID-induced)

Drug Interactions

Anticoagulants → Increased bleeding risk
Diuretics → Reduced effect
ACE inhibitors → Reduced antihypertensive effect Other NSAIDs → Increased toxicity

Brand Names

- Voveran
- Voltaren
- Dicloran
- Cataflam

Sodium in Tablet Combination of Paracetamol and Diclofenac Form

The combination of Paracetamol and Diclofenac Sodium is commonly formulated in a tablet dosage form for the effective management of pain and inflammation. This combination is commonly used in a clinical setting for its enhanced efficacy.

Composition of Tablet

A typical combination tablet contains:

1. Paracetamol: 325 mg
2. Diclofenac Sodium: 50 mg

Along with suitable pharmaceutical excipients such as:

- Binders (e.g., starch)
- Fillers (e.g., lactose)
- Disintegrants
- Lubricants (e.g., magnesium stearate)

Rationale of Combination

The combination is designed to provide a dual mechanism of action:

- Paracetamol acts centrally to relieve pain and reduce fever.
- Diclofenac Sodium acts peripherally to reduce inflammation.

Advantages:

- Enhanced analgesic effect
- Faster onset of action
- Reduced individual drug dose
- Improved patient compliance

Mechanism of Combined Action

Paracetamol: It inhibits the synthesis of prostaglandins in the central nervous system Diclofenac Sodium: It inhibits the cyclooxygenases (COX-1 and COX-2) and hence the inflammation is reduced. Together, they provide better pain relief than single-drug therapy.

Uses of Combination Tablet

- Musculoskeletal pain
- Arthritis
- Postoperative pain
- Dental pain
- Back pain
- Inflammatory conditions

Pharmacokinetic Considerations:

- Both drugs are well absorbed orally
- Paracetamol acts quickly (short half-life)
- Diclofenac provides prolonged anti-inflammatory action
- No significant pharmacokinetic interaction when used in recommended doses

Side Effects

- Gastric irritation (due to Diclofenac)
- Hepatotoxicity (Paracetamol overdose)
- Nausea, vomiting
- Rare allergic reactions

Contraindications

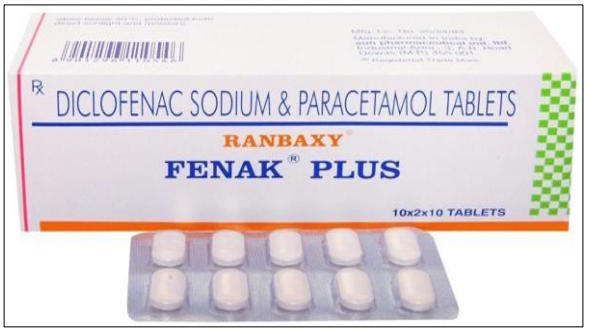
- Severe liver disease
- Peptic ulcer
- Hypersensitivity to NSAIDs
- Severe renal impairment

Drug Interactions

Alcohol → Increased liver toxicity Anticoagulants → Increased bleeding risk Other NSAIDs → Increased side effects

Brand Names of Combination:

- Diclocet
- Dicom-P
- Diaclo-M
- Paindep-D
- D-Fec



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EXPERIMENTAL WORK

The composition of pharmaceutical preparation in tablet form is-

1. Paracetamol
2. Diclofenac sodium

The method for analysis of quantitative estimation (Quality Control) begins with a study of physiochemical properties of drug substances.

Study of Solubility

- Combination of Paracetamol and Diclofenac sodium is showing high solubility in methanol and Sodium Hydroxide and poorly soluble in water.

Materials and Methods

- UV Spectrophotometer: Shimadzu 1800 double beam UV-Visible Spectrophotometer with 1cm matched quartz cells.
- Digital balance: Shinko vibra analytical balance.
- The other chemicals and glass wares were used of analytical grade from market and college.

Standard Stock Solution Preparation:

- Standard stock solution of drug was prepared by dissolving 10mg of drug in 95% of methanol solution in volumetric flask.
- Then take 1ml of prepared solution in other flask and make volume up to 10ml with 95% of methanol, the concentration of solution is 100µg/ml.
- Standard Serial Dilution Preparation:
- Std.–1: Take 1 ml of stock Solution (100µg/ml) in 10 ml of 95% of methanol solution (10µg/ml).

Sample Stock Solution Preparation:

- Sample Stock Solution of Paracetamol and Diclofenac sodium was prepared by Crushing 20 Tablets of marketed Drug into fine powder and then dissolved 10mg of powdered drug in 10 ml of 95% of methanol solution (1000µg/ml).
- Then take 1ml of prepared solution in other flask and make volume up to 10ml with 95% of methanol, the concentration of solution is 100µg/ml.

Standard Serial Dilution Preparation:

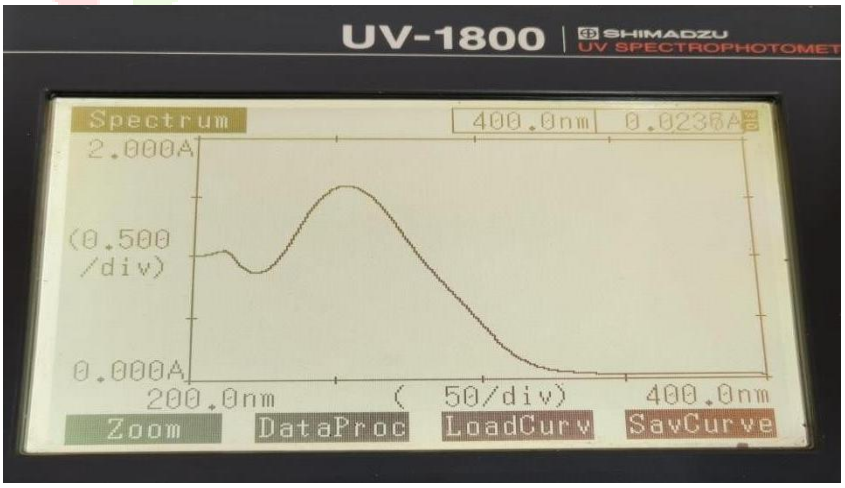
- Std.–1: Take 1 ml of stock Solution (100µg/ml) in 10 ml of 95% of methanol solution (10µg/ml).
- Sample Stock Solution Preparation:

- Sample Stock Solution of Paracetamol and Diclofenac Sodium was prepared by Crushing 20 Tablets of marketed Drug into fine powder and then dissolved 10mg of powdered drug in 10 ml of 95% of methanol solution (1000µg/ml).
- Then take 1ml of prepared solution in other flask and make volume up to 10ml with 95% of methanol, the concentration of solution is 100µg/ml.
- Sample Serial dilution Preparation:
- Take 1 ml of stock Solution (100 µg/ml) in 10 ml of 95% of methanol solution(10µg/ml).

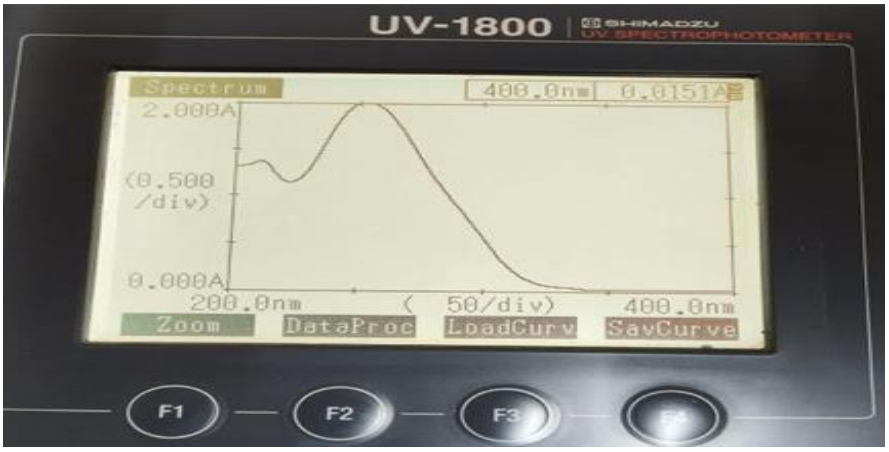
UV–Visible Spectrometry data of Standard and Sample Solutions

- The quantitative estimation of Paracetamol and Diclofenac sodium was performed using a UV–Visible spectrophotometer, which measures the amount of light absorbed by the drug at a specific wavelength. The instrument was first switched on and allowed to warm up, and calibration was performed using methanol as the blank to eliminate any interference from the solvent.
- Standard solutions of Paracetamol and diclofenac sodium were prepared by appropriate dilutions of the stock solution to cover the required concentration range. The absorbance of each standard solution was measured at λmax ≈ 254nmand λmax ≈ 236nm.
- For the sample solutions, aliquots of the filtered and diluted tablet solution were prepared to match the concentration range of the calibration standards. The absorbance was measured at the same wavelength (254 nm and 236 nm), and the concentration of Paracetamol and Diclofenac sodium in the sample was calculated.
- The absorbance ratio method of analysis is based on the absorbance at two selected wavelengths; one is an isosbestic point and the other being the wavelength of maximum absorption of one of the two components. From overlain spectra wavelength 245.9 nm (isosbestic point) and 254 nm (λmax of Paracetamol) are selected for the formation of Q absorbance equation.
- The absorptivity values determined for Paracetamol are 0.23 (ax1), 0.15 (ax2) and for Diclofenac sodium are 0.10(ay1), 0.25 (ay2) at 254nm and 236 nm, respectively. These values are average of three estimations. The absorbances andabsorptivity at these wavelengths were substituted in equations to obtain the concentration of drugs.
- The overlain spectra of Paracetamol and Diclofenac sodium at 245.9 nm which is isosbestic point or an iso-absorptive point.

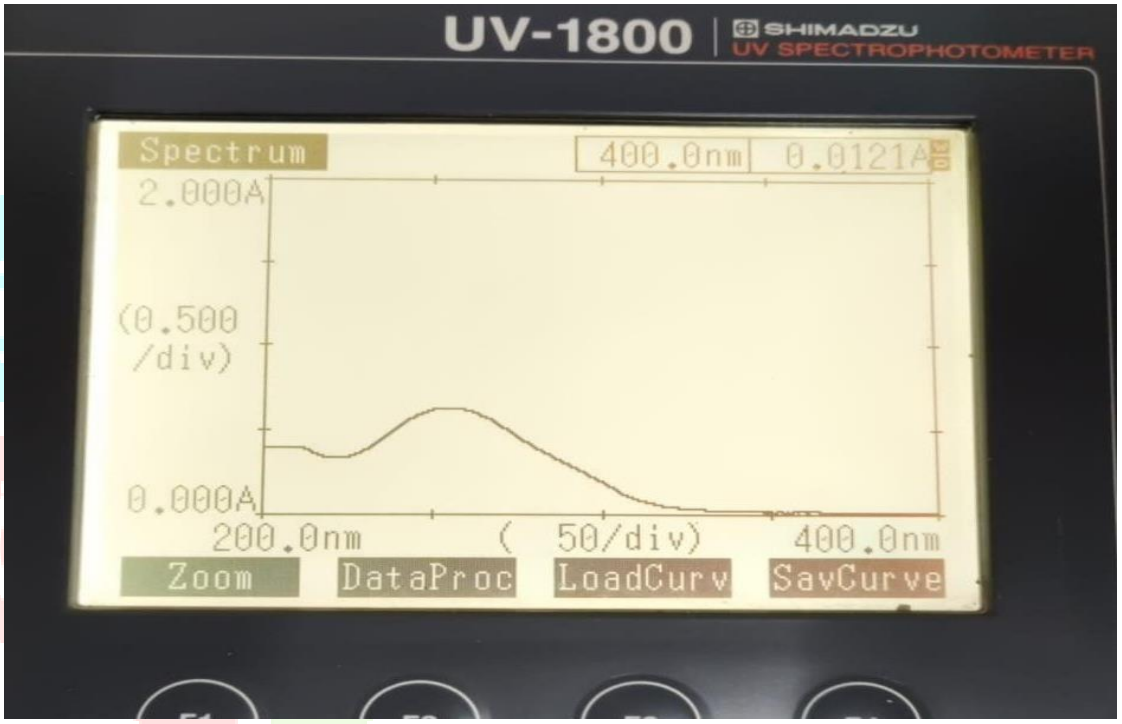
Absorbance of paracetamol at λ 1



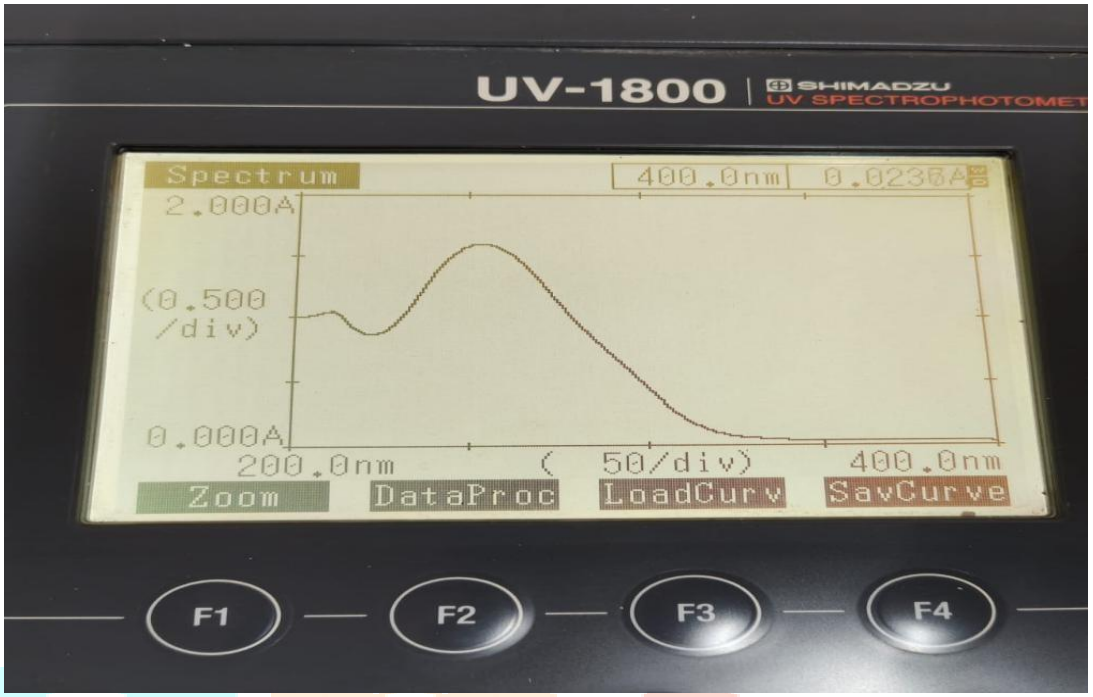
Absorbance of Paracetamol at λ2



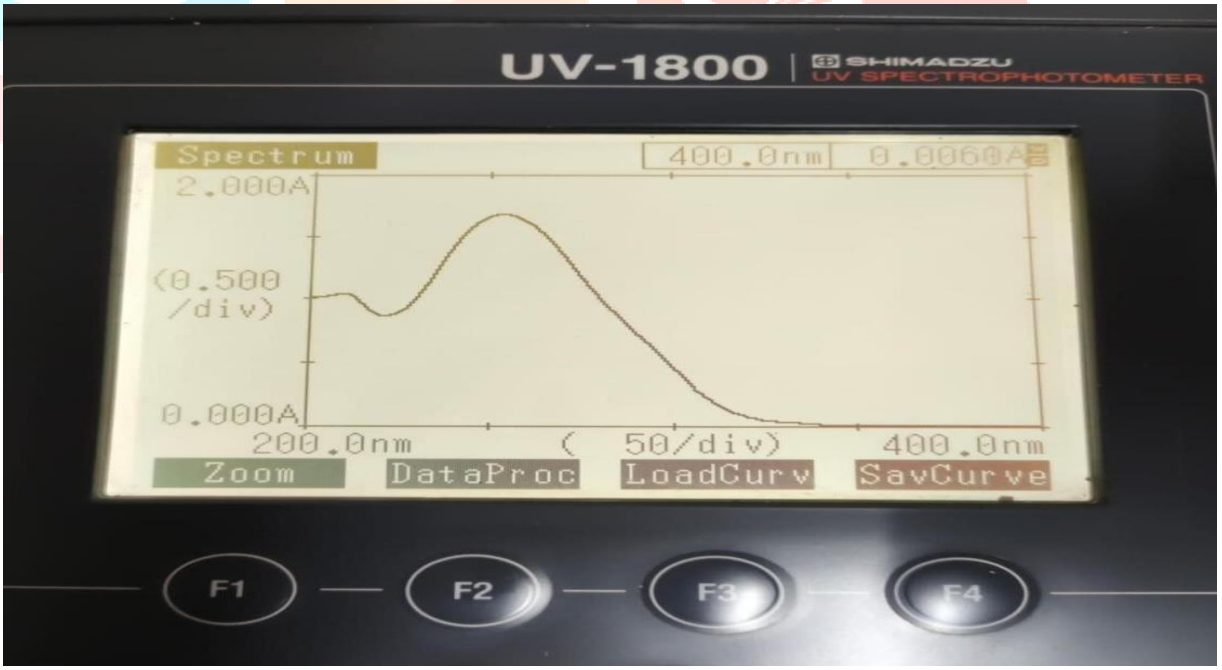
Absorbance of Diclofenac sodium at λ1



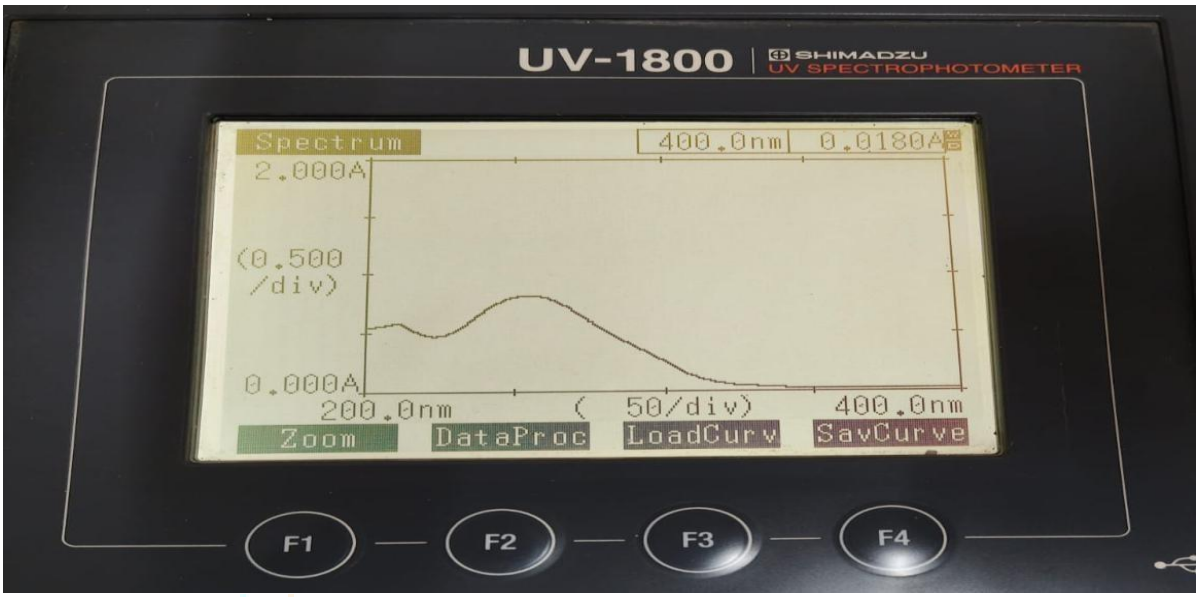
Absorbance of diclofenac sodium at λ2



Absorbance of mixture at λ1



Absorbance of mixture at λ2



S.no	Drugs	Absorbance	
		λ1 = 254nm (Isosbestic Point)	λ2 = 236nm
1.	Paracetamol	0.20	0.15
2.	Diclofenac Sodium	0.10	0.25
3.	Mixture	0.70	0.60

CALCULATION

Powder weight calculations

Label claim of tablet = 325mg Paracetamol

Label claim of tablet = 50mg Diclofenac Sodium

Wt. of tablets = 12382gm Sample / 14186gm Standard Avg. wt. of each tablet = 619.1gm Sample / 709.3 Standard

Formula:

$$\mathbf{Cx} = \frac{A_2\, ay_1 - A_1\, ay_2}{ax_2\, ay_1 - ax_1\, ay_2}$$

$$\mathbf{Cy} = \frac{A_1\, ax_2 - A_2\, ax_1}{ax_2\, ay_1 - ax_1\, ay_2}$$

Where,

C_x = Concentration of first drug (Paracetamol)

C_y = Concentration of second drug (Diclofenac)

A_1 = Absorbance of the mixture at λ_1

A_2 = Absorbance of the mixture at

$$\underset{\lambda 1}{\text{ax1}} = \text{Absorptivity of Paracetamol at } \lambda 1 = \frac{Absorbance\ of\ Paracetamol\ at}{Concentration\ of\ Paracetamol}$$

$$ax_1 = \frac{o.23}{10} = 0.23$$

$$\text{ax2} = \text{Absorptivity of Paracetamol at } \lambda 2 = \frac{Absorbance\ of\ Paracetamol\ at\ \lambda 2}{Concentration\ of\ Paracetamol}$$

$$ax_2 = \frac{0.15}{10} = 0.015$$

$$\text{ay1} = \text{Absorptivity of Diclofenac sodium at } \lambda 1 = \frac{Absorbance\ of\ Diclofenac\ sodium\ at\ \lambda 1}{Concentration\ of\ \ Diclofenac\ sodium}$$

$$ay_1 = \frac{0.10}{10} 0.010$$

$$\text{ay1} = \text{Absorptivity of Diclofenac sodium at } \lambda 1 = \frac{Absorbance\ of\ Diclofenac\ sodium\ at\ \lambda 1}{Concentration\ of\ \ Diclofenac\ sodium}$$

$$ay_2 = \frac{0.25}{10} = 0.025$$

By determining the concentration using the below formulas

$$C_x = \frac{A_2\, ay_1 - A_1\, ay_2}{ax_2\, ay_1 - ax_1\, ay_2}$$

$$= \frac{(0.60\times0.010)-(0.70\times0.025)}{(0.015\times0.010)-(0.020\times0.025)}$$

$$= \mathbf{31.42}\ ug/ml$$

$$CY = \frac{A_1\, ax_2 - A_2\, ax_1}{ax_2\, ay_1 - ax_1\, ay_2}$$

$$= \frac{(0.70\times0.015)-(0.60\times0.020)}{(0.015\times0.010)-(0.020\times0.025)}$$

$$= \frac{0.0105-0.012}{0.00015-0.0005}$$

$$= \mathbf{4.28}\ ug/ml$$

%*Content of* **both of the *drug*-**

$$\%Content\ of\ drug\ paracetamol = \frac{31.42}{325/10}\times100$$

$$= \mathbf{96.67\%}$$

Total paracetamol in mg = 314.17mg

$$\%Content\ of\ diclofenac\ sodium = 85.6\%$$

Total diclofenac in mg =42.8 mg

Total% content in Tablet

$$\text{Total \% content} = \frac{325\times96.67\%+50\times85.6\%}{375}$$

$$= \frac{314.17+42.8}{375}$$

Total % content = 356.97

Total % content = 95.19%

Result and Discussion

A percentage estimation of Paracetamol and Diclofenac Sodium in the tablet dosage form by

Simultaneous Equation (Vierordt's) method was obtained at the wavelength 254 nm (For Paracetamol) and 236 nm (for Diclofenac Sodium) as 94.67% and 85.60% and the content of both drugs in mg is 314.17 mg and 42.8 mg. Total percent content of both drugs in tablet dosage form is 95.19% and a total drug concentration in mg is 356.97 mg, which showsaccuracy in result.

The UV spectrophotometric analysis confirms that the developed method is simple, rapid, and precise for the simultaneous estimation of Paracetamol and Diclofenac Sodium in their combined marketed formulation. The Isosbestic point observed at 245.9 nm further validates the stoichiometric relationship and molar absorptivity consistency required for the Q-analysis and simultaneous equation approach.

Conclusion

The present work was undertaken to establish a simple, precise, and cost-effective analytical technique for the simultaneous estimation of Paracetamol and Diclofenac Sodium present in their tablet dosage form by using UV-Visible spectroscopy.

The proposed analytical technique for the simultaneous estimation of Paracetamol and Diclofenac Sodium is based on the measurement of absorbance of the drugs at selected wavelengths. Under the optimized experimental conditions, Paracetamol and Diclofenac Sodium showed maximum absorbance at 254 nm and 236 nm, respectively. The simultaneous equations technique was employed for the quantitative estimate of the drugs.

Calibration curves were constructed and found to be linear over the selected range of concentrations, conforming to Beer-Lambert’s law. The developed method was successfully used for analysis of formulations. The method was validated as per ICH guidelines, and parameters like accuracy, precision, and specificity were found to be within acceptable limits.

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