**"Current Trends in Analytical and Bioanalytical Methods for Etodolac: A Review**

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**Abstract**

Etodolac belongs to a class of nonsteroidal anti-inflammatory drug (NSAID). Its therapeutic effect is due to inhibition of prostaglandin synthesis. The development of analytical techniques and the many approaches now in use for etodolac estimate, whether in bulk or pharmaceutical dose form, are the main focus of the current study. Analytical procedures are crucial for determining compositions because they allow us to obtain both qualitative and quantitative data using state-of-the-art analytical equipment. Chromatographic, electrochemical, spectroscopic, and other methods can be used to analyze it. These methods aid in comprehending important process factors and reducing the detrimental influence they have on accuracy and precision. The development of analytical methods is required to meet regulatory requirements and maintain high standards for the quality of commercial products. In response to the reference, regulatory bodies in a number of nations have developed guidelines and procedures for approving, authenticating, and registering.

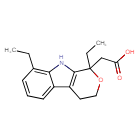
**Keywords -** Etodolac, UV- Visible Spectrophotometer, HPLC, HPTLC, bioanalytical method.

**Introduction**

Etodolac is an NSAID that belongs to the pyranocarboxylic acid class. It is an organic heterotricyclic molecule and a monocarboxylic acid. It inhibits prostaglandin synthesis and cyclooxygenase 2 inhibitor. It is used to treat the symptoms of osteoarthritis and rheumatoid arthritis. It functions as an antipyretic, non-narcotic analgesic, and non-steroidal anti-inflammatory medication. It comes in extended release, immediate release tablets and capsules. The S-form of etodolac enantiomers is biologically active.(1)

**Physicochemical properties**

Etodolac is white, crystalline substance. It is soluble in alcohols, chloroform, dimethyl sulfoxide, and aqueous polyethylene glycol but insoluble in water. Its molecular weight is 287.35 g/mol. Its melting point is 145-148 ºC. Its pKa is 4.65. (2)



**Figure 1. Chemical structure of Etodolac.**

**Pharmacokinetic**

The systemic bioavailability of etodolac in tablet or capsule form is at least 80%, according to mass balance tests. More than 99 percent is protein bound, mostly to albumin. Its half-life is six to eight hours. The liver metabolizes etodolac substantially. The main excretion pathway for etodolac and its metabolites is the kidneys (72%).(3)

**Pharmacodynamic**

Etodolac has analgesic and antipyretic qualities and is an anti-inflammatory drug. It is used to manage acute pain and treat rheumatoid arthritis and osteoarthritis. Etodolac works therapeutically by preventing the production of prostaglandins that cause fever, discomfort, oedema, and inflammation. As a racemate, etodolac is administered. It has been demonstrated that the R-form is inactive and the S-form is active, similar to other NSAIDs.(4)

**Mechanism of action**

Etodolac's anti-inflammatory effects, like those of other NSAIDs, are caused by suppression of the cyclooxygenase (COX) enzyme. As a result, fewer peripheral prostaglandins that mediate inflammation are synthesized. Etodolac blocks the entry of arachidonic acid, the substrate of the COX enzyme, by attaching itself to the top part of the active site. Etodolac is now recognized to be more selective for COX-2 than COX-1, despite the fact that it was once believed to be a non-selective COX inhibitor. By acting centrally on the hypothalamus, antipyresis can cause peripheral dilatation, elevated cutaneous blood flow, and consequent heat loss.(5)

**Need of analytical method development**

Analytical technique development culminates in official test procedures. Quality control labs therefore employed these methods to analyse the efficacy, safety, purity, performance, and identification of pharmaceutical products. For regulatory agencies, production-related analytical methods are extremely important. To get the medicine approved by regulatory bodies, the applicant must show that they have complete control over the drug development process using recognized analytical methodologies [15]. Recent analytical guideline documents produced by the ICH include stability testing (Q1), analytical technique validation (Q2), contaminants in drug substances and products (Q3), and specifications for novel drug substances and products (Q6).(6)

**Analytical method development by UV-visible spectroscopy**

Under UV-visible spectroscopy is the study of interactions between matter and electromagnetic radiation in the UV-visible spectrum. The ultraviolet's (UV) wavelength range is 200–400 nm. The basis for this is the Beer-Lambert law, which states that the absorbance of a solution and the length of its journey are directly proportional. For a given path length, it can therefore be used to determine the absorber's concentration in a solution. The rate at which absorbance changes with concentration must be understood.(7)

**Table no.1 Analytical method development using UV - spectrophotometer**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **S. No.** | **Sample / Dosage form** | **Method / Instrument model** | **Solvent / Solution** | **Wavelength (nm)** | **References** |
| **1.** | Tablet | UV-Visible double beam spectrophotometer by Shimadzu Corporation (Japan),  Model UV-1800 | Methanol: Water  (60:40) | 280 | (8) |
| **2.** | Tablet and bulk | Thermospectronic double-beam UV  spectrophotometer (HEλIOSβ) | Methanol | 277 | (9) |
| **3.** | Bulk | Elico SL-159, UV-Visible  spectrophotometer | Methanol and water (1:9V/V) | 279.5 | (10) |
| **4.** | Tablet | UV-Visible double beam spectrophotometer by ANALYTICAL  Model UV-2310 (Tech comp) | Phosphate buffer pH 7.4 | 223.5 | (11) |
| **5.** | Tablet and bulk | UV-Visible  Spectrophotometer (UV 1800) ELICO SL-159 | Methanol and water  (70:30) | 226 | (12) |

**Analytical method development by HPLC**

Among the most widely used separation techniques, high performance liquid chromatography (HPLC) is one of the most well-established analytical processes. It has been used in labs worldwide for more than 40 years for evaluations of food and the environment, clinical chemistry, pharmaceutical sciences, synthetic chemistry, etc. The stationary phase in this method could be either a liquid or a solid phase. HPLC can be used to separate a combination's constituent parts by employing a liquid mobile phase. When the stationary phase is housed within a column and the liquid mobile phase is mechanically pumped through the column, the process is known as "high-performance liquid chromatography" (HPLC). The column is a vital component in HPLC systems. A good silica and bonding process will result in a reproducible and symmetrical peak, which is necessary for accurate certification. Commonly used RP columns include Cyno (USP L18), Phenyl (USP L11), C18 (USP L1), and C8 (USPPL8).(13)

**Table 2. Analytical method development by HPLC**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **S.No.** | **Sample** | **Stationary phase/column** | **Mobile phase** | **Wavelength (nm)** | **Flow rate (ml/min)** | **RT (min)** | **Reference** |
| **1.** | Tablet | BDS 250mm x 4.6 mm, 5µ particle size | Methanol: Phosphate Buffer (85:15) | 232 | 0.6 | 2.777 | (14) |
| **2.** | Tablet | C18  column (4.5mm x 250 mm, 5μm) | Methanol: Acetonitrile: Water  20:60:20 (v/v/v) | 274 | 1.0 | 7.86 | (15) |
| **3.** | Tablet | C18  column | Acetonitrile: Methanol (60:40 v/v) | 226 | 1.0 | - | (16) |
| **4.** | Tablet and bulk | C18 (250 × 4.6 mm, 5µm particle size) column | Acetonitrile and di-potassium hydrogen phosphate buffer (pH 6.4; 25 mM) (60:40 %v/v) | 280 | 1.0 | 11.5 | (17) |
| **5.** | Tablet | C18(250 x 4.6 mm, 5 µm) | Methanol: Buffer (60:40) | 254 | 1.0 | 3.942 | (18) |
| **6.** | Tablet | C8 analytical column (250 mm x  4.6 mm, 5 um) | Acetonitrile-water  (80:20, v/v) | 272 | 1.0 | 4.21 | (19) |
| **7.** | Tablet | C18, (250 mm x 4.5 mm) | AcetonitriLe: water (50:50) pH 5.8 | 232 | 1.0 | 1.932 | (20) |
| **8.** | Tablet | C18,  150 X 4.6 mm, 5 μm | Acetate buffer and acetonitrile  (55:45% v/v) | 221 | 1.0 | 3.1 | (21) |

**Analytical method development by HPTLC**

It is a powerful analytical method that is effective for both qualitative and quantitative applications. Separation may result from partitioning, adsorption, or both, depending on the variety of adsorbents used on the plates and the development solvent system. HPTLC fundamentals include a number of aspects, including principle, theory, instrumentation, implementation, optimization, validation, automation, qualitative and quantitative analysis.(22)

**Table 3. Analytical method development by HPTLC**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **S.No.** | **Sample** | **Stationary Phase/ Column** | **Mobile phase** | **Wavelength (nm)** | **Reference** |
| **1.** | Tablet | Silica gel aluminum plates, 20 × 10 cm with a layer of 60 F254 | Ethyl acetate, methanol, and glacial acetic acid (8.5:1.5:0.25, by v/v) | 276 | (23) |
| **2.** | Tablet | Silica gel aluminum plates, 20 cm × 10 cm precoated plates with 250 mm layer of 60 F254 | Toluene–ethyl acetate–ethanol (6:1.5:2.5, v/v/v) | 260 | (24) |

**Bioanalytical method development**

Evaluation and interpretation of bioequivalence, PK, and toxicokinetic studies are greatly aided by bioanalysis, which is used to quantify medicines and their metabolites in biological fluids. For pre-clinical and/or biopharmaceutics and clinical pharmacology studies to be effective, sensitive and selective analytical techniques for the quantitative assessment of medications and their metabolites are essential.(25)

**Table 4. Bioanalytical method development**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **S.No.** | **Method** | **Sample** | **Stationary phase/ column** | **Mobile phase** | **Wavelength (nm)** | **Flow rate (ml/min)** | **RT (min)** | **Reference** |
| **1.** | UV- spectrophotometry | Tablet and human urine | - | Methanol | 223 | - | - | (26) |
| **2.** | HPLC | Bulk and rat plasma | C18 column (3.5 µm, 75 mm × 4.6 mm) | Phosphate  buffer (pH-4): acetonitrile (45: 55, v/v) | 254 | 0.8 | 4.4 | (27) |
| **3.** | HPLC | Tablet and human plasma | ODS-80TM 4.6 × 150 mm 5 µm | Phosphate buffer (pH 3.5) and methanol  (85:15 h/h) | 259 | 1.0 | 6.4 | (28) |

**Conclusion**

The primary focus of this study has been on the numerous analytical and bioanalytical techniques used to estimate the amount of etodolac in different medications and in the pharmaceuticals' bulk form. There are several dosage formulations that contain etodolac in combination. UV spectrophotometry, LC, HPLC, HPTLC, RP-HPLC, TLC, and other hyphenated procedures are among the analytical and bioanalytical techniques that the researchers have worked to create. Among the hyphenated techniques are LC-APCI/MS/MS, HPLC-MS/MS, and LC-MS/MS. Every analytical technique created is very accurate, reproducible, sensitive, automated, and has a better sample throughput. The purpose of the literature review is to gather data on various analytical instrumental techniques. Such information would be useful in creating a new analytical technique.

**Competing interest**

The author reported no conflict of interest in this article.

**Reference**

1. Suyama H, Kawamoto M, Gaus S, Yuge O. Effect of etodolac, a COX-2 inhibitor, on neuropathic pain in a rat model. Brain Res. 2004;1010(1–2):144–50.

2. Shah KP, Gumbhir-Shah K, Brittain HG. Etodolac. Anal Profiles Drug Subst Excipients. 2002;29(C):105–47.

3. Sánchez-Luquez K, Reis Silveira AM, Sánchez-Vinces S, Rosini Silva AA, Barreto J, Lemos de Brito RBS, et al. Etodolac Single Dose Metabolic Profile Elucidation: Pharmacokinetics and Adverse Events in Healthy Volunteers. Pharmaceuticals. 2025;18(1):1–17.

4. de Miranda Silva C, Rocha A, Tozatto E, da Silva LM, Donadi EA, Dalla Costa T, et al. Development of an Enantioselective and Biomarker-Informed Translational Population Pharmacokinetic/Pharmacodynamic Model for Etodolac. AAPS J. 2017;19(6):1814–25.

5. Publishers KA. E T O D O L A C IN THE M A N A G E M E N T OF PAIN : A CLINICAL REVIEW OF A M U L T I P U R P O S E ANALGESIC. 1997;139–52.

6. P. Ravisankar\*1, 2, S. Gowthami1 GDR. A Review on Analytical Method Devlopment. Indian J Res Pharm Biotechnol. 2014;2(3):1183–95.

7. Singh D, Chauhan V, Chaudhar S, Kaushik A. a Review on Instrumentation and Validation Method of Uv-Visible Spectroscopy and Hplc for the Analysis of Drugs. Int Res J Pharm. 2021;12(3):14–21.

8. Jadav Alpa V, Gohel Bhavika A, Sondagar Mital M, Patel Bhavna A, Parmar Shraddha J. Method development and validation for the simultaneous estimation of paracetamol and etodolac by Derivative UV spectroscopic method. Int J PharmTech Res. 2013;5(3):1155–60.

9. Pinar Demirci I, Alptug A, Yucel K, Atakan T. Quantitative determination of Etodolac by UV spectrophtometric method in bulk drug and commercial formulations. Int J Pharm Sci Res. 2013;4(8):2927–32.

10. Kokane PA, Bhairav BA, Saudagar RB. UV Spectrophotometric Method Development and Validation of Benazepril Hydrochloride. Asian J Res Chem. 2016;9(8):369.

11. Thankappan S, Ashok P, Bhavika S, Kinjal V, Dolita S. Simultaneous Estimation of Etodolac and Thiocolchicoside by UV Spectrophotometric Method in Tablet Formulation. Int J Pharm Innov. 2012;2(2):192–200.

12. Biswal S, Mondal S, Mondal P. UV Spectrophotometric and Stability Indicating RP-HPLC Assay Methods for the Estimation of Etodolac in Bulk and Tablet Dosage Form. Int J Pharm Investig. 2019;9(2):53–8.

13. Gupta MK, Ghuge A, Parab M, Al-Refaei Y, Khandare A, Dand N, et al. A comparative review on High-Performance Liquid Chromatography (HPLC), Ultra Performance Liquid Chromatography (UPLC) & High-Performance Thin Layer Chromatography (HPTLC) with current updates. Curr Issues Pharm Med Sci. 2022;35(4):224–8.

14. Senapathi C, Somepalli A, Gopala N, Gona K, Priyanka S. A New RP-HPLC Method development and validation for Etodolac and Thiocolchicoside. Int J Multidiscip Res. 2024;6(3):1–20.

15. N. Sai Prudhvi\* MP and GAK. Method Development and Validation of Rp-Hplc for Simultaneous Estimation of Etodolac & Thiocolchicoside. World J Pharm Res. 2018;7(7):1321–30.

16. Gulabrao Bhamare V, Kamble RK. Determination of Etodolac By Rp-Hplc Method. Int Res J Pharm. 2020;11(9):25–30.

17. Goel H, Singla R, Chawla R, Sahoo U, Tiwary AK, Sinha VR. Facile validated HPLC method using photodiode array detector for the combined analysis of etodolac and 5-FU in bulk and tablet dosage form. Egypt J Chem. 2021;64(3):1601–14.

18. Syamala S. Development and validation of new RP-HPLC method for simultaneous estimation of drug Thiocolchicoside and Etodolac in tablet dosage form. Indian J Res Pharm Biotechnol. 2016;4(4):180–90.

19. Tugrul Cagri Akman | Yucel Kadioglu. Determination of Etodolac in Commercial Formulations by HPLC-UV Method. Int J Trend Sci Res Dev [Internet]. 2019;4(1):128–32. Available from: https://www.ijtsrd.com/papers/ijtsrd29452.pdf%0Ahttps://www.ijtsrd.com/pharmacy/analytical-chemistry/29452/determination-of-etodolac-in-commercial-formulations-by-hplc-uv-method/tugrul-cagri-akman

20. Siva Rama Krishna V, Belemkar S, Tiwari RN. RP-HPLC method development and validation of etodolac and paracetamol in tablet dosage form. Int J PharmTech Res. 2014;6(2):775–82.

21. Siddiraju S, Boga V. HPLC method development and validation for rapid estimation of Etodolac related impurity-H in pharmaceutical dosage form. Pharm Methods [Internet]. 2013;4(2):52–5. Available from: http://dx.doi.org/10.1016/j.phme.2013.12.002

22. Rashmin P, Mrunali P, Nitin D, Nidhi D, Bharat P. HPTLC method development and validation: Strategy to minimize methodological failures. J Food Drug Anal. 2012;20(4).

23. Rizk M, Ramzy E, Toubar S, Mahmoud AM, Helmy MI. Talanta Open Sustainable and smart multi-analyte HPTLC determination of tolperisone HCl together with three pain killers using smartphone camera as a detector : Comparative study with benchtop densitometry. Talanta Open [Internet]. 2025;11(December 2024):100415. Available from: https://doi.org/10.1016/j.talo.2025.100415

24. Patel MJ, Patel AN, Patel CN, Badmanaban R. A simple and sensitive HPTLC method for simultaneous analysis of tolperisone hydrochloride and etodolac in combined fixed-dose oral solid formulation. J Planar Chromatogr - Mod TLC. 2012;25(1):85–8.

25. Moein MM, El Beqqali A, Abdel-Rehim M. Bioanalytical method development and validation: Critical concepts and strategies. J Chromatogr B Anal Technol Biomed Life Sci [Internet]. 2017;1043:3–11. Available from: http://dx.doi.org/10.1016/j.jchromb.2016.09.028

26. Pandey R, Patil PO, Bari SB, Dhumal DM. Simultano odred{strok}ivanje etodolaka i tiokolčikozida u farmaceutskoj supstanci i tabletama. Chem Ind Chem Eng Q. 2014;20(1):9–17.

27. Abdelhameed AS, Afifi SA. A Validated HPLC-DAD Method for Simultaneous Determination of Etodolac and Pantoprazole in Rat Plasma. J Chem. 2014;2014.

28. Kucuk Tunca A, Sirin N. Quantity determination analysis of etodolac and thiocolchicoside combination with inverse phase-liquid chromatography method in human plasma. Sep Sci Plus. 2019;2(10):369–74.