

A Review on Estimation of Etoricoxib and Paracetamol in Pharmaceutical Dosage Form

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INTRODUCTION

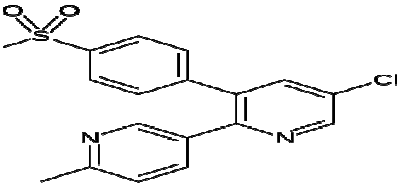
Non-Steroidal anti-inflammatory drugs deals with complains of pain. It works pharmacologically to inhibit the prostaglandin and be able to reduce pain, fever with inflammation and that is accompanied by other pain disorders. The use of NSAIDs is very effective for reducing pain symptomatically, most widely prescribed and are the first choice in the treatment of inflammatory pain. There are various types of NSAIDs that are known, such as aspirin, paracetamol, ibuprofen, mefenamic acid, indomethacin, diclofenac, piroxicam and nimesulide. From various kinds of NSAIDs, each has advantages and disadvantages that are seen in the therapeutic effect and the side effects caused. Therapeutic effects related to the mechanism of action of this preparation. The use of NSAIDs in children really needs attention. Nonsteroidal anti-inflammatory drugs (NSAIDs) are among the most frequently prescribed drugs worldwide and are used for relief of inflammatory, chronic (e.g., rheumatoid arthritis, osteoarthritis, and gout), and acute (e.g., headache, postoperative pain, and orthopedic fractures) pain conditions [1]. NSAIDs formulations are also available as over-the-counter pharmaceutical preparations. The anti-inflammatory activity of NSAIDs and most of their

other pharmacological effects are related to the inhibition of the conversion of arachidonic acid to prostaglandins, which are mediators of the inflammatory process. NSAIDs are potent inhibitors of cyclooxygenase in vitro and in vivo, thereby decreasing the synthesis of prostaglandins, prostacyclin, and thromboxane products. The growing demand for NSAIDs stimulates higher level of quality control of these therapeutic substances and preparations. Hence, there is need to develop new analytical methods for qualitative and quantitative analysis of NSAIDs and their combination drugs.

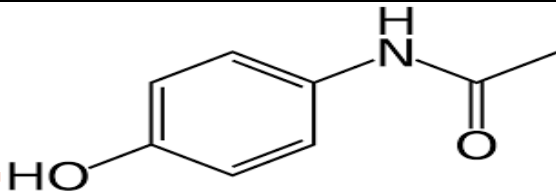
Etoricoxib [1], (5-chloro-2-(6-methyl pyridine-3-yl)-3-(4-methylsulfonyl phenyl) pyridine), is a relatively new non-steroidal anti-inflammatory drug with high selectivity in cyclooxygenase-2-inhibitory activity. It is indicated to relieve the signs and symptoms of osteoarthritis, ankylosing spondylitis and acute gouty arthritis.

Paracetamol is an acetanilide derivative chemically 4-hydroxy acetanilide having analgesic, antipyretic and weak antiinflammatory action^{1,2} and also administered in the management of more severe pains in advanced cancers³.

Drug profile:
Etoricoxib

Structure	
Chemical name	5-Chloro-6 methyl-3
Molecular formula	C ₁₈ H ₁₅ ClN ₂ O ₂ S
Molecular weight:	361.9 g/mol
Appearance	White
Category	NSAID
Melting point:	140.68 °C
Solubility	Soluble

Paracetamol

Structure	
Chemical name	N-(4-Hydroxyphenyl)acetamide
Molecular formula	C ₈ H ₉ NO ₂
Molecular weight:	151.16 g/mol
Appearance	COLOURLESS CRYSTALS OR CRYSTALLINE POWDER
Category	Analgesics and Antipyretics
Melting point:	169 °C (336 °F)
Solubility	Soluble

Etoricoxib:

Mechanism of action:

Etoricoxib works by blocking the effect of a natural chemical called cyclo-oxygenase-2 (COX-2) enzyme. This enzyme helps to make other chemicals, called prostaglandins, in the body. Some prostaglandins are produced at sites of injury or damage, and cause pain and inflammation. By blocking the effect of COX-2 enzymes, fewer prostaglandins are produced, which means pain and inflammation are eased.

Etoricoxib is indicated for the treatment of rheumatoid arthritis, psoriatic arthritis, osteoarthritis, ankylosing spondylitis, chronic low back pain, acute pain, and gout. Approved indications differ by country. In the U.K., it is also "used for the short term treatment of moderate pain after dental surgery" of adults.^[2]

A Cochrane review assessed the benefits of single-dose Etoricoxib in reduction of acute post-operative pain in adults.^[3] Single-dose oral Etoricoxib provides four times more pain relief post-operatively than placebo, with equivalent levels of adverse events.^[3] Etoricoxib given at a dose of 120 mg is as effective as or even better than other analgesics that are commonly used.

Paracetamol:

Mechanism of action:

Paracetamol has a central analgesic effect that is mediated through activation of descending serotonergic pathways. Debate exists about its primary site of action, which may be inhibition of prostaglandin (PG) synthesis or through an active metabolite influencing cannabinoid receptors. Prostaglandin H (2) synthetize (PGHS) is the enzyme responsible for metabolism of arachidonic acid to the unstable PGH (2). The two major forms of this enzyme are the constitutive PGHS-1 and the inducible PGHS-2. PGHS comprises of two sites: a cyclooxygenase (COX) site and a peroxidase (POX) site. The conversion of arachidonic acid to PGG (2) is dependent on a tyrosine-385 radical at the COX site. Formation of a ferryl protoporphyrin IX radical caution from the reducing agent Fe(3+) at the POX site is essential for conversion of tyrosine-385 to its radical form. Paracetamol acts as a reducing substrate on the POX site and lessens availability of the ferryl protoporphyrin IX radical caution.

This effect can be reduced in the presence of hydro peroxide-generating lipoxxygenase enzymes within the cell (peroxide tone) or by swamping the POX site with substrate such as PGG(2). Peroxide tone and swamping explain lack of peripheral analgesic effect, platelet effect, and anti-inflammatory effect by paracetamol. Alternatively, paracetamol effects may be mediated by an active metabolite (p-aminophenol). P-Aminophenol is conjugated with arachidonic acid by fatty acid amide hydrolase to form AM404. AM404 exerts effect through cannabinoid receptors. It may also work through PGHS, particularly in areas of the brain with high concentrations of fatty acid amide hydrolase.

METHODOLOGY:

HPLC Methods:

High-performance liquid chromatography is a simple and sensitive technique used for the quantitative estimation of chemicals, drugs, biological products. In HPLC, the separation is mainly achieved through partition and adsorption phenomenon. If the drug or any compound having more affinity towards the mobile phase will elute faster than the substances which have an affinity towards the stationary phase. There are two types of separation carried out based on the column type normal phase and reverse-phase in the normal phase the column is polar, and the mobile phase is non-polar, in the reverse phase, the column is nonpolar, and the mobile

Sr. No.	Drugs	Method	Chromatographic conditions	Author
1.	Etoricoxib & Paracetamol	RP-HPLC	Stationary phase: Column: ODS C8-3 Colum, 5 μ . Mobile phase: Methanol: Phosphate Buffer: acetonitrile(40:20:40) Wavelength: 285 nm Flow rate : 1.0ml/min Temp: Ambient	S.R. Pattan
2.	Etoricoxib & Paracetamol	RP-HPLC	Stationary phase: C18 (250 \times 4.6) column Mobile Phase: Acetonitrile: Methanol: Water (60:15:25)wavelength: 236 nm Flow rate: 1.0 ml/min Temperature: Ambient	Krishna. R. Gupta
3.	Etoricoxib & Paracetamol	RP-HPLC	Stationary phase: C18 X – TERRA Column (150X3.5mm)5 μ . Mobile phase: buffer: acetonitrile (60:40) Wavelength: Flow rate: Temperature: Ambient	K. G.Baheti
4.	Etoricoxib	RP-HPLC	Stationary phase: ODS,C18 (250X4.6nm)5 μ . Mobile phase: acetonitrile: Potassium: Phosphate Buffer(40:50:20)Wavelength: Flow rate: 1.2ml/min, Etoricoxib Temperature: 30 $^{\circ}$ C	Shrinivasu Topalli
5.	Etoricoxib & Thiocolchico side	RP-HPLC	Stationary phase: ODS C18column, (250 x4.6) mm 5 μ Mobile phase: phosphate buffer: methanol,(30:70) Wavelength:255nm , Flow rate: 1.2ml/min Temperature:	Suresh kumar
6.	paracetamol	RP-HPLC	Stationary phase: C18 column Mobile phase:orthophosphoric acid: phosphate buffer (pH 6.8 \pm 0.2) and acetonitrile: water 70:30 v/v Wavelength: 207nm. Flow rate:1ml/minTemperature:28 $^{\circ}$ C	G.K. soujanya
7.	ETC and PARA	RP-HPLC	Stationary phase: C18(250mm*4.6mm,5m) Mobile phase: Orthophosphoric acid buffer: methanol: acetonitrile in the ration 50:30:20 v/vWavelength:241nm Flow rate:1.0ml/min Temperature: 40oC	A.Shrinivas
8.	ETC	RPHPLC Assay	Stationary phase: Hyper ODS C18 (4.5 x 250 nm Mobile phase:methanol HPLC GRADE Wavelength:233 nm Flow rate: 1 ml/min	Manju sasidharan
9.	ETC	Single Rapid phase HPLC method	Stationary phase C18 column, 5um Mobile phase: methanol : phosphate buffer (70:30) Wavelength: 215nm Flow rate: 0.5 ml/min Temp: Ambient	Muhammad Alzweiri

10.	Paracetamol	HPLC	Stationary phase C18 column, 5µm 4.6 x 250) Mobile phase –acetonitrile: Para: water(25:75)v/vFlow Rate: 1ml/min	T.A .phazna Devil
11.	ETC	-HPLC	Stationary phase: C18column (250 mm × 4.6 mm, 5µm) Mobile phase: methanol Wavelength:233nm Flow rate:1 ml/min Temp: Ambient	Gangane P.S.
12.	ETC and PARA	HPLC	Stationary phase: C18 column (250mm × 4.6mm, 5µm) Mobile phase: Acetonitrile and 0.05 M potassium hydrogen phosphate buffer pH 4 (65:35 v/v) Wavelength:220 nm Flow rate: 1 .0ml/min Temp: Ambient	Maitereyi
13.	PARA And Thrice	stability indicating RP-HPLC	Stationary phase: C18 column (250x3.2 mm) 5µmMobile phase: :Buffer: Acetonitrile: : triethylamine (50:30;20v/v)Wavelength: 275nmFlow rate: : 1.ml per min	RamzyaElba gary

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