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CLINICAL AND PHARMACOLOGICAL COMPARISON BETWEEN ACECLOFENAC AND DICLOFENAC: WHICH NSAID IS BETTER?

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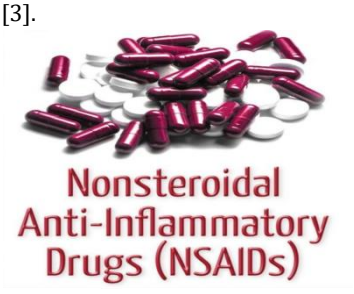
Abstract
Aceclofenac and Diclofenac are both non-steroidal anti-inflammatory drugs (NSAIDs) commonly Used to treat pain and inflammation, especially in conditions like arthritis. Both drugs work by blocking the action of cyclooxygenase (COX) enzymes, which produce substances that cause pain and swelling in the body. However, Aceclofenac is a derivative of Diclofenac and shows some Differences in terms of clinical effectiveness and tolerability. Aceclofenac is often considered a better option for long-term treatment due to its better gastrointestinal safety profile. It causes fewer side effects like stomach pain, nausea, vomiting, and Ulcers when compared to Diclofenac. This makes Aceclofenac more suitable for patients who are at Risk of gastrointestinal issues. Additionally, studies suggest Aceclofenac provides similar or even Greater pain relief than Diclofenac, with fewer complications. In terms of pharmacokinetics; both drugs are effective but differ slightly in their half-life (T½), dose, Elimination rate, and bioavailability. Aceclofenac has a half-life of about 4 hours and is usually given in a dose of 100 mg twice daily. Diclofenac has a shorter half-life and may need more frequent Dosing. In conclusion; both Aceclofenac and Diclofenac are effective NSAIDs. The choice between them Depends on the patient's condition, medical history, and tolerance to side effects. Aceclofenac is generally preferred for its better efficacy and lower gastrointestinal side effects, especially in long term use.

Keywords: Aceclofenac, Diclofenac, osteoarthritis, Safety, Meta analysis.

INTRODUCTION

NSAIDs (Non-Steroidal Anti-Inflammatory Drugs) are medicines that help to reduce pain, swelling, and fever. They are commonly used for many health problems, including osteoarthritis, where people often feel pain and stiffness in their joints. While NSAIDs work well for pain, they can also cause serious stomach problems. These include: Erosion (small injuries to the stomach lining),Ulcers (painful sores inside the stomach),And in serious cases, holes in the stomach or bleeding, which can be life-threatening(1).To solve this problem, scientists developed a newer type of NSAID called COX-2 inhibitors.These medicines are special because:They block the COX-2 enzyme, which causes pain and inflammation.But they do not block COX-1 much, which protects the stomach lining [2].This means COX-2 inhibitors cause fewer stomach problems than older NSAIDs.Many studies have shown that people who take COX-2 inhibitors have a lower risk of ulcers and bleeding.However, there is one concern:Some research studies found that COX-2 inhibitors might increase the risk of heart problems, like heart attacks or strokes.Three large studies and a combined review of many trials found this possible risk. So, doctors must be careful when giving these medicines, especially to people who already have heart issues [3].



Osteoarthritis (OA) is a long-term joint disease that causes pain and makes it hard to move. It mostly affects older adults. The exact cause of OA is still not fully known.It usually starts slowly, and the pain or stiffness can get worse over time [4]. Some people may feel more pain than others, even if their joint damage looks the same in an X-ray. Doctors cannot fully cure OA, but they can help manage the pain and make daily life easier. One of the most common treatments is using medicines called NSAIDs (nonsteroidal anti-inflammatory drugs). These medicines reduce pain and swelling, and they have been used for a long time to treat joint problems like OA [5].

Diclofenac: 2-[2-(2,6-dichloroanilino)phenyl]acetic acid

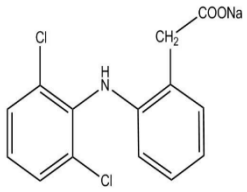


Fig 01: Chemical Structure of Diclofenac

Effectiveness of Diclofenac After Taking by MouthIn 2017, Costa and his team studied how well different medicines work for treating pain caused by osteoarthritis [6].They searched through a medical database (Cochrane Central Register of Controlled Trials) and looked at research papers from January 1980 to February 2015. They only included studies with at least 100 patients. In total, they reviewed 8,973 papers covering 58,451 patients [7].They compared how well pain medicines like paracetamol and various NSAIDs (such as naproxen, ibuprofen, diclofenac, celecoxib, lumiracoxib, rofecoxib, and etoricoxib) worked. These drugs were compared with each other and also with a placebo (a dummy pill) [8].The researchers found that diclofenac at a dose of 150 mg per day was the most effective in reducing pain and improving movement problems caused by osteoarthritis. It worked better than other common NSAIDs like ibuprofen, naproxen, and celecoxib even when those drugs were given at their highest safe doses [9]. Etoricoxib (60 mg per day) was found to be equally good as diclofenac in reducing pain, but it was not clear if it helped improve movement and disability as well as diclofenac [10].The researchers also said that while diclofenac is effective, doctors should carefully consider its safety risks and decide the dose for each patient based on their health condition [11]. Diclofenac is a pain-relieving medicine. Instead of taking it as a tablet or injection, it can also be used by applying it directly to the skin (called topical use). This method is helpful because it works on the painful area without sending a lot of the drug into the whole body. When taken as a tablet or injection, diclofenac can sometimes cause side effects like stomach ulcers, heart problems, or kidney issues. But when it's applied to the skin, these problems are much less likely to happen [12].Only about 10 to 15 out of 100 people get mild side effects from using diclofenac on the skin. These side effects are usually just some redness, itching, or a small rash where the cream or gel was applied. Most people tolerate it well, which is why it's often used for long-term pain problems like arthritis [13]. Applying medicine to the skin is also very easy and doesn't hurt-no need to swallow pills or get injections. That makes it more comfortable and convenient for many patients. However, how well the medicine goes through the skin can change from person to person. This depends on: What the drug is made of (its size, oiliness, and electric charge), What type of cream or gel is used to carry the medicine, How it is applied (how much, how often, how it's rubbed in),And what condition the skin is in (dry, oily, healthy, damaged, etc.).Because of these reasons, the amount of diclofenac that actually reaches inside the body through the skin can be different for each person [14].

Aceclofenac:2-[2-[2-(2,6-Dichlorophenyl)amino]phenyl]acetoxy]acetic acid

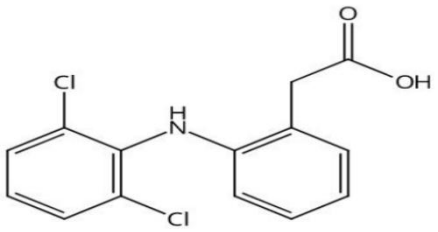


Fig 02: Chemical Structure of Aceclofenac

Taking aceclofenac (100 mg per day) helped reduce pain and improve movement a little more than diclofenac (150 mg per day) and acetaminophen (300mg per day) [15]. But this result is based on only a few studies, so we need to be careful when trusting it [16]. We couldn't compare different doses or how long the treatment was used because there wasn't enough information [17].In some studies where patients didn't know what medicine they were getting (called blinding), aceclofenac seemed to work better for pain [18]. This might be because people felt better just because they thought they were getting good treatment – this is called performance bias [19]. However, whether people knew which medicine they got didn't seem to change the results for improving movement [20]. We also saw that aceclofenac gave some pain and movement improvement in smaller studies. This matches older research, which says small studies in osteoarthritis often show better treatment results [21]. Out of 9 studies that looked at how well diclofenac and aceclofenac work and how safe they are, 5 were done on patients with osteoarthritis, 1 on rheumatoid arthritis, 1 on general muscle and bone problems, 1 on lower back pain, and 1 on pain after a tooth was taken out [22]. In one study by Anand R. Kanaki and team, patients with osteoarthritis aged between 40 and 60 years took part. There were 57 men and 70 women in the study. They were divided into two groups: one group took aceclofenac 100 mg twice a day, and the other took diclofenac 75 mg twice a day, both after meals. Doctors checked the patients after 1, 2, and 3 months using different methods like: WOMAC score (used

to check pain and movement)Time to walk 100 feetPain level using a pain scale (VAS)Doctor's opinion using a rating scale (Likert scale)Joint pain check They also looked at any side effects the patients had. After 3 months, aceclofenac worked better and was easier on the body than diclofenac [23]. After surgery, especially bone or joint surgery, many patients feel pain. This is called postoperative pain, and it is a very common problem. To reduce this pain, doctors often use a group of medicines called NSAIDs (Non-Steroidal Anti-Inflammatory Drugs). These drugs are given by injection (parenteral route) and are a good choice because they help control pain well and usually have fewer side effects [24]. One such medicine is Aceclofenac. It belongs to a group of drugs called phenylacetic acid derivatives and is chemically related to another medicine called Diclofenac. The chemical name of Aceclofenac is long, but simply put; it is a type of painkiller [25]. When given as an injection, Aceclofenac is useful in relieving pain after surgery. It works by blocking an enzyme in the body called cyclo-oxygenase (COX). This enzyme helps produce prostaglandins, which are chemicals responsible for pain and inflammation. By stopping prostaglandins from forming, Aceclofenac helps reduce both pain and swelling [26]. Also, Aceclofenac can directly reduce the way pain signals are sent in the spinal cord, making the body feel less pain overall [27]. Osteoarthritis (OA) is a very common joint disease that lasts a long time and usually happens in older people. It mainly affects the joints we use for movement, like the knees and hips. These joints are called synovial joints [28]. OA doesn't usually start before the age of 40. But as people get older, it becomes more common. By the time someone reaches 75 years old, about 85 out of 100 people show signs of OA [29]. These signs can be seen through symptoms like joint pain and stiffness or in X-rays that show joint damage [30].After the age of 65, around 60% of men and 70% of women are affected by OA [31].In osteoarthritis, the smooth covering of the joint called cartilage slowly wears away [32]. This makes the bones rub against each other, which causes pain, swelling, and stiffness. The nearby bones also try toadjust by changing their shape, which can lead to more discomfort and difficulty moving [33].

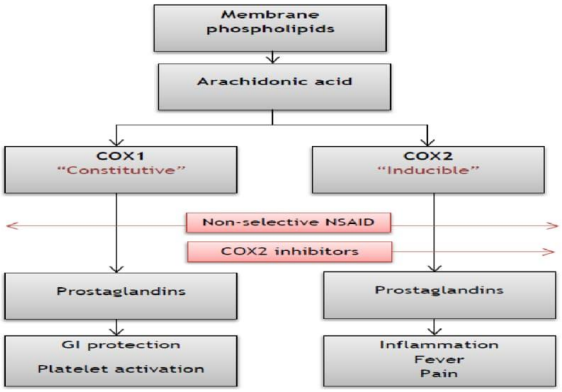
Mechanism of action: Target

Both drugs block an enzyme called Cyclooxygenase (COX).

Why Block COX?

COX enzymes help produce substances called prostaglandins, which cause pain, swelling, and inflammation.

Effect: By blocking COX, the drugs lower prostaglandin levels. This leads to less pain, less swelling, and reduced fever. Help produce substances called prostaglandins, which cause pain, swelling, and inflammation.



Pharmacokinetics of Diclofenac

Absorption - Rapidly absorbed; peak plasma concentration in 1–2 hours

Bioavailability - 50–60% (reduced due to first-pass metabolism in liver)

Protein Binding - 99% bound to plasma proteins (mainly albumin)

Distribution – Widely distributed; accumulates in inflamed tissues and synovial fluid

Metabolism - Liver metabolism via CYP2C9; forms inactive metabolites

Excretion - 65% excreted in urine (as metabolites); remainder in bile/feces

Elimination Half-life 1–2 hours

Pharmacokinetics of Aceclofenac

Absorption - Fast and almost complete (oral)

Bioavailability -100%

Protein Binding -99%

Metabolism In liver – converted to diclofenac

Elimination - Mainly urine; half-life -4 hours

Administration or dosage of diclofenac

Oral Diclofenac (Tablets/Capsules)

Form Typical Adult Dose Frequency Max Daily Dose

Immediate-Release Tablets	50 mg 2–3 times per day	150 mg/day
Extended-Release Tablets	75–100 mg Once daily or in 2 doses	150 mg/day
Diclofenac Potassium (fast)	50 mg 2–3 times per day	150 mg/day

Injectable Diclofenac (IM)

Form	Dose	Route	Use
Injection (75 mg/ml)	75 mg	Intramuscular	Acute pain, 1–2 times daily

Topical Diclofenac (Gel/Emulgel)

Form	Dose	Application
1% Gel	2–4 g per affected area	3–4 times daily
2% Gel	2 g per affected area	twice daily

Rectal Diclofenac (Suppositories)

Dose	Frequency	Use
50–100 mg	1–2 times daily	for patients unable to take oral

Administrationor dosage of Aceclofenac

Oral (PO)	Tablets (e.g., 100 mg)	most common form. Swallowed with water, preferably after food.
Topical	Gel or cream	Applied directly to the skin over painful areas. Used for localized pain.
Rectal	Suppository (less common)	Inserted into the rectum. Rare and not widely used.
Parenteral (Injection)	Not available	Aceclofenac is not available as an injection form.

Aceclofenac – Uses

Aceclofenac is a nonsteroidal anti-inflammatory drug (NSAID) used mainly for:

Osteoarthritis – to reduce joint pain and stiffness

Rheumatoid arthritis – to control joint inflammation

Ankylosing spondylitis – to reduce spinal pain and stiffness

Musculoskeletal pain – like sprains, strains, or back pain

Dental pain – temporary relief of pain after tooth procedures

Diclofenac – Uses

Diclofenac is also an NSAID, and it has a broader range of uses:

Osteoarthritis, Rheumatoid arthritis, Ankylosing spondylitis

Postoperative pain – after surgery

Gout attacks – short-term relief from inflammation

Menstrual pain (dysmenorrhea) – common use in women

Back pain, sprains, and sports injuries

Migraine – certain forms of diclofenac (e.g., powder form)

Dental and ENT (ear, nose, throat) pain

Topical forms (gel/patch) – used for localized joint/muscle pain

Common Adverse Effects (Bothdrugs)

System Affected	Aceclofenac	Diclofenac
Gastrointestinal	Nausea, indigestion, abdominal pain, diarrhea, gastritis	Nausea, dyspepsia, ulcers, GI bleeding, perforation
Hepatic (Liver)	Mild liver enzyme elevations	Liver dysfunction, hepatitis, jaundice
Renal (Kidney)	Elevated serum creatinine (rare)	Renal impairment, nephrotic syndrome
Cardiovascular	Slight risk of hypertension, edema	Higher risk of stroke, myocardial infarction, edema
Skin	Rash, itching	Rash, Stevens-Johnson Syndrome (rare)
CNS (Brain)	Dizziness, headache	Headache, dizziness, drowsiness

Discussion

Diclofenac

Among traditional NSAIDs, diclofenac is one of the most widely prescribed due to its strong analgesic and anti-inflammatory effects. A large review (Costa et al., 2017) involving more than 58,000 patients reported that diclofenac at 150 mg/day was the most effective NSAID for reducing pain and improving function in osteoarthritis, even outperforming ibuprofen, naproxen, and celecoxib. Etoricoxib (a COX-2 inhibitor) was comparable in pain relief but less consistent in improving physical function.Diclofenac can be administered orally, intramuscularly, rectally, or topically. Topical diclofenac is particularly valuable because it provides localized pain relief with minimal systemic absorption, thus reducing the risk of gastrointestinal, renal, and cardiovascular adverse effects. However, systemic diclofenac use is associated with a higher risk of gastrointestinal bleeding, hepatotoxicity, and cardiovascular events, requiring caution in long-term therapy.

Aceclofenac, a phenylacetic acid derivative structurally related to diclofenac, was developed to improve tolerability. Clinical studies suggest that aceclofenac (100 mg twice daily) provides comparable or slightly superior pain relief and functional improvement in osteoarthritis compared to diclofenac, with a lower incidence of gastrointestinal side effects. In one comparative study, aceclofenac demonstrated better tolerability and efficacy after three months of treatment in OA patients. Pharmacologically, aceclofenac is rapidly absorbed with nearly 100% bioavailability and undergoes hepatic metabolism, partly converting to diclofenac. Its longer half-life (about 4 hours) allows twice-daily dosing, improving patient compliance. Beyond osteoarthritis, aceclofenac is also used in rheumatoid arthritis, ankylosing spondylitis, musculoskeletal pain, and dental pain. Unlike diclofenac, it is not widely available in injectable formulations, limiting its role in acute postoperative settings.

Conclusion

NSAIDs remain a cornerstone treatment for osteoarthritis (OA) and other painful conditions because they effectively reduce pain, stiffness, and inflammation. However, traditional NSAIDs like diclofenac carry significant risks of stomach ulcers, bleeding, and cardiovascular events, especially at higher doses or with long-term use.Newer COX-2 inhibitors were developed to reduce stomach side effects, but they may increase the risk of heart problems, so doctors must carefully weigh the benefits and risks for each patient.Comparisons show that diclofenac (150 mg/day) is one of the most effective NSAIDs for OA pain relief, while aceclofenac (100 mg/day) may offer slightly better tolerability and fewer gastrointestinal side effects, though evidence is based on fewer studies.Overall, the choice of drug depends on the patient's age, medical history (especially stomach, heart, liver, and kidney health), and treatment goals. NSAIDs should be used at the lowest effective dose for the shortest possible time, and topical forms are often safer for long-term use.

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Conflict of Interest

No Conflict of Interest

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Not Declared

Inform Consent and Ethical Statement

Not Applicable

Author Contribution

All authors are contributed equally.

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