WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
Coden USA: WJPRAP Impact Factor 8.453
Volume 15, Issue 2, 233-246. Review Article ISSN 2277–7105

ACECLOFENAC - LOADED NOVEL DRUG DELIVERY SYSTEM FOR ENHANCED ANTI-INFLAMMATORY ACTIVITY

Mr. S. Pragadheeshwaran[1]*, Mr. M. Praveen Kumar[2], Mr. P. Prakash[1], Mr. R. Thirumalai[1], Mr. S. Hari Prasanna[1], Mr. C. Jothimanivannan[3]

[1]Students, SS Institute of Pharmacy, Sankari, Salem, 637301.

[2]Assistant Professor, Department of Pharmacology, SS Institute of Pharmacy, Sankari, Salem, 37301.

[3]Professor and Principal, SS Institute of Pharmacy, Sankari, Salem, 637301.

Article Received on 15 Dec. 2025,
Article Revised on 05 Jan. 2026,
Article Published on 16 Jan. 2026

https://doi.org/10.5281/zenodo.18256497

***Corresponding Author**

Mr. S. Pragadheeshwaran

Students, SS Institute of Pharmacy, Sankari, Salem, 637301.

How to cite this Article: Mr. S. Pragadheeshwaran[1]*, Mr. M. Praveen Kumar[2], Mr. P. Prakash[1], Mr. R. Thirumalai[1], Mr. S. Hari Prasanna[1], Mr. C. Jothimanivannan[3]. (2026) ACECLOFENAC - LOADED NOVEL DRUG DELIVERY SYSTEM FOR ENHANCED ANTI-INFLAMMATORY ACTIVITY. World Journal of Pharmaceutical Research, 15(2), 233–246.

ABSTRACT

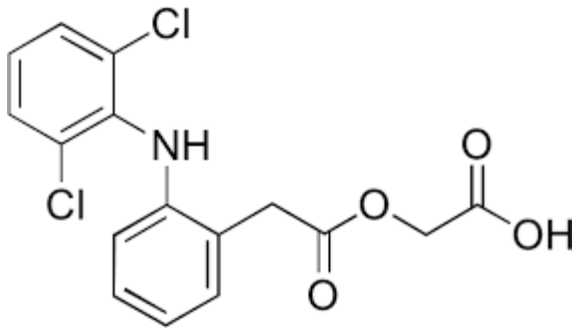
Aceclofenac is a non-steroidal anti-inflammatory drug (NSAID) commonly used for the treatment of pain and inflammation in musculoskeletal disorders. It belongs to the phenylacetic acid class of NSAIDs and exhibits both analgesic and anti-inflammatory properties. The drug acts mainly by inhibiting cyclooxygenase enzymes, resulting in decreased prostaglandin synthesis. Aceclofenac is widely prescribed in conditions such as osteoarthritis, rheumatoid arthritis, ankylosing spondylitis, and low back pain. Several clinical studies have demonstrated its effectiveness in reducing pain and improving joint gastrointestinal tolerability profile. The incidence of adverse effects such as gastric irritation and ulceration is relatively lower. This makes it suitable for long-term use in chronic inflammatory function. Compared to other conventional NSAIDs, aceclofenac shows comparable or superior therapeutic efficacy. An important advantage of aceclofenac is its favorable conditions. Aceclofenac is rapidly absorbed after oral administration and shows good bioavailability. It is extensively metabolized in the liver and excreted mainly through urine. The drug is generally well tolerated when used at recommended doses. However, caution is advised in patients with hepatic, renal, or cardiovascular disorders. Overall, aceclofenac represents an effective and safe NSAID option

for managing pain and inflammation.

KEYWORDS: Aceclofenac; Non-steroidal anti-inflammatory drugs (NSAIDs); Analgesic activity; Anti-inflammatory activity; Cyclooxygenase inhibition; Musculoskeletal disorders; Gastrointestinal tolerability; Osteoarthritis; Rheumatoid arthritis; Pharmacokinetics.

INTRODUCTION

Nonsteroidal anti-inflammatory drugs (NSAIDs) constitute a diverse class of organic acidic compounds widely employed for their analgesic, antipyretic, anti-inflammatory, and antiplatelet properties. These agents exert their therapeutic effects primarily through the inhibition of cyclooxygenase (COX) enzymes, which play a central role in the inflammatory cascade. Suppression of COX activity results in reduced synthesis of pro-inflammatory prostaglandins and cytokines, thereby alleviating pain, inflammation, and fever via both central and peripheral mechanisms. Despite their clinical effectiveness, prolonged use of NSAIDs is frequently associated with gastrointestinal (GI) adverse effects, which often restrict long-term therapy. Gastrointestinal toxicity remains a major limitation in the widespread clinical application of conventional NSAIDs. To overcome these limitations, selective COX-2 inhibitors were developed to maintain therapeutic efficacy while minimizing GI complications. Aceclofenac (AC) is a potent and relatively selective COX-2 inhibitor that is extensively used in the management of rheumatoid arthritis, osteoarthritis, ankylosing spondylitis, and various painful inflammatory conditions. The drug exhibits significant analgesic, antipyretic, and anti-inflammatory activity. Aceclofenac was developed in Spain by Grau and co-workers in 1991 with the objective of improving gastrointestinal safety. Several studies have demonstrated that aceclofenac possesses superior gastric tolerability compared to many traditional NSAIDs. Experimental and clinical observations indicate that the ulcerogenic potential of aceclofenac is markedly lower than that of commonly used NSAIDs such as naproxen, diclofenac, and indomethacin. Structurally, aceclofenac shares similarities with diclofenac; however, its therapeutic index has been reported to be significantly higher, suggesting an improved safety margin. Although aceclofenac exhibits comparable anti-inflammatory efficacy to other NSAIDs, its enhanced tolerability and better patient compliance may offer important clinical and economic advantages in long-term inflammatory disease management.



ACECLOFENAC

Analytical and physicochemical consideration

Aceclofenac (CAS No. 89796-99-6) appears as a white to off-white crystalline powder**.** It is practically insoluble in water**,** while exhibiting high solubility in acetone and moderate solubility in alcohol**.** When dissolved in methanol, aceclofenac displays a characteristic UV absorption maximum at approximately 275 nm**,** which is commonly utilized for its spectrophotometric analysis. Chemically, aceclofenac is classified as a phenylacetic acid derivative and is designated as [2-{(2,6-dichlorophenyl)amino} phenylacetoxyacetic acid]**.** The molecular formula of aceclofenac is $C_{16}H_{13}Cl_2NO_4$**,** with a molecular weight of 354.18 g/mol**.** As a weakly acidic compound (pKa ~4–5)**,** its solubility is strongly influenced by the pH of the surrounding medium. Aceclofenac demonstrates enhanced solubility under alkaline conditions**,** whereas its solubility is comparatively lower in water and acidic environments. Variations in solubility across different dissolution media have been reported and are summarized in Table 1. From a pharmaceutical processing perspective, aceclofenac exhibits poor flowability and compression properties**,** which can pose challenges during solid dosage form development. Consequently, formulation strategies are often required to improve its manufacturability. A wide range of analytical techniques have been reported for the quantitative determination of aceclofenac**.** These include titrimetric, voltammetric, densitometric, colorimetric, spectrophotometric, spectrofluorometric, and polarographic methods**.** Advanced instrumental techniques such as high-performance liquid chromatography (HPLC), capillary electrophoresis, and mass spectrometry have also been extensively employed due to their sensitivity and specificity. Additionally, several validated analytical methods have been developed for the simultaneous estimation of aceclofenac in combination formulations containing other active pharmaceutical ingredients. Stability studies indicate that aceclofenac remains stable in plasma at room temperature for a minimum duration of six hours**,** supporting its suitability for bioanalytical and pharmacokinetic investigations.

Dissolution Medium	Solubility	Temperature	Reference
Purified water	75.59 µg/mL	37 °C	12
0.1N HCl	15.24 µg/mL	37 °C	12
Phosphate buffer (pH 6.8)	10.58 mg/mL	37 °C	12
Water	0.018 g/100mL	Room Temperature	13
Buffer solution (pH 7.4)	0.065 g/100 mL	Room Temperature	13
Buffer solution (pH 8.0)	0.069 g/100mL	Room Temperature	13
Buffer solution (pH 9.0)	0.075 g/100mL	Room Temperature	13
Water	0.053 mg/mL	Room Temperature	14
0.1N HCl	0.013 mg/mL	Room Temperature	14
Water	58.67 µg/mL	37 °C	15
Normal HCl	21.93 µg/mL	37 °C	15
Buffer solution (pH 4.5)	995 µg/mL	37 °C	15
Buffer solution (pH 6.8)	1538.7 µg/mL	37 °C	15
Water	55.46 µg/mL	37 °C	16
Buffer solution (pH 1.2)	11.77 µg/mL	37 °C	16
Buffer solution (pH 6.8)	4962 µg/mL	37 °C	16
Water	0.076 mg/mL	37 °C	17
0.2N HCl	0.018 mg/mL	37 °C	17
Buffer solution(pH4)	6.79 mg/ mL	37 °C	17

DOSAGE AND ADMINISTRATION

In adults with arthritic conditions or experiencing moderate to severe pain, the standard oral dose of aceclofenac is 100 mg taken twice daily. This non-steroidal anti- inflammatory drug is absorbed rapidly and has a short elimination half-life of approximately 4 hours**,** which necessitates frequent dosing to maintain therapeutic plasma levels. Because of this pharmacokinetic profile, aceclofenac is a strong candidate for sustained-release formulations**,** which can provide more consistent systemic exposure and potentially smoother analgesic effects compared to immediate-release preparations. Aceclofenac is contraindicated in individuals with current or recurrent peptic ulceration or gastrointestinal bleeding, significant renal dysfunction, or hypersensitivity to aceclofenac or other NSAIDs. Use in pregnancy and lactation is generally not recommended due to potential risk, and alternative analgesic strategies should be considered for these populations.

PHARMACOKINETIC AND PHARMACODYNAMIC PROPERTIES

Aceclofenac is efficiently absorbed from the gastrointestinal tract following oral administration and predominantly circulates in plasma as the unchanged drug. After a single 100 mg dose, the highest plasma levels are generally observed within approximately 1.25 to 3 hours**,** with peak concentrations in the range consistent with previous clinical measurements. The drug exhibits a moderate volume of distribution (~25 L) and is extensively bound to

plasma proteins (>99%), which limits its free fraction in circulation. Food intake does not significantly affect the overall extent of aceclofenac absorption, although it can slow the rate at which peak levels are reached, prolonging the time to maximum concentration. Pharmacokinetic profiling indicates that aceclofenac demonstrates linear increases in Cmax and AUC with escalating doses within the therapeutic range, and elderly patients do not show clinically significant alterations in these parameters that would necessitate routine age-related dose adjustments. Once absorbed, aceclofenac undergoes substantial hepatic metabolism**,** primarily to 4′-hydroxyaceclofenac**,** which is the principal circulating metabolite in humans. Other minor metabolic products include derivatives such as diclofenac and various hydroxy-metabolites, which together represent a smaller fraction of the administered dose. The involvement of CYP2C9-mediated pathways has been implicated in these biotransformations. The drug's elimination is mainly via the renal route**,** with roughly 70–80 % of an administered dose excreted in urine as glucuronide and hydroxylated metabolites, and roughly 20 % recovered in feces**.** The plasma elimination half-life of aceclofenac is approximately 4 hours, a profile that supports twice-daily dosing while minimizing accumulation during regular therapeutic use. While preclinical species such as rodents metabolize aceclofenac extensively to diclofenac and related compounds, humans retain a greater proportion of the parent molecule in systemic circulation, reflecting important interspecies differences in metabolic pathways. Clinically, aceclofenac is widely used as an effective analgesic and anti-inflammatory agent in various musculoskeletal disorders, including osteoarthritis, rheumatoid arthritis, and ankylosing spondylitis, and has also been utilized for relief of other acute pain conditions. It inhibits the cyclooxygenase (COX) pathway, reducing prostaglandin E2 synthesis, and its pharmacodynamic actions extend to suppression of pro-inflammatory cytokines (e.g., IL-1β, IL-6, TNF) and modulation of inflammatory cellular interactions. Some evidence also suggests a favorable effect on glycosaminoglycan synthesis**,** which may contribute to its therapeutic efficacy in degenerative joint conditions. Compared with some traditional NSAIDs, aceclofenac has been associated with lower incidence of gastrointestinal adverse events in comparative studies, likely related in part to its COX-2 preferential activity and improved GI tolerance**.**

DOSAGE FORMS AND PHARMACEUTICAL FORMULATIONS OF ACECLOFENAC

Aceclofenac is available in a range of dosage forms designed to meet different therapeutic needs, improve patient compliance, and optimize drug release profiles.

1. **Conventional Oral Dosage Forms**

- **Immediate-Release Tablets:** The most widely used form is the standard immediate-release tablet, typically containing 100 mg of aceclofenac. These are formulated for rapid dissolution and systemic absorption following oral administration and are suitable for general pain and inflammation management.
- **Fast-Disintegrating / Mouth-Dissolving Tablets:** Specially formulated tablets that rapidly disintegrate in the mouth without the need for water have been developed to enhance convenience and onset of action, particularly useful for patients with difficulty swallowing conventional tablets. Such formulations use super-disintegrants and direct compression techniques to achieve rapid disintegration and release.

2. **Modified and Controlled Release Oral Systems**

- **Sustained-Release (SR) Matrix Tablets:** To reduce dosing frequency and provide more consistent plasma drug levels, sustained-release matrix tablets have been developed. These typically incorporate hydrophilic polymers such as hydroxypropyl methylcellulose (HPMC), natural gums (e.g., guar or xanthan gum), polyethylene oxides (PEO), or proprietary retarding polymers (e.g., Kollidon SR) to control drug diffusion and release over extended periods (e.g., 12–24 h).
- **Bilayer and Dual-Release Tablets:** Advanced designs such as bilayer tablets combine an immediate-release layer with a sustained-release layer to achieve a rapid onset followed by prolonged effect. Such formulations utilize combinations of polymers (e.g., HPMC and hydroxypropyl cellulose) to tailor release kinetics.
- **Floating and Gastric-Retention Tablets:** Innovative matrix tablets that remain buoyant in the stomach have been investigated to prolong gastric residence time and enhance absorption for improved bioavailability. These use polymers like HPMC K15 to achieve sustained release while floating.

3. **Novel and Specialized Delivery Systems**

- **Mucoadhesive Buccal Tablets:** Buccal adhesive formulations have been explored as a route to bypass first-pass metabolism and allow controlled drug release directly through the oral mucosa. Polymers such as carbopol enhance adhesion and extend residence time at the absorption site.
- **Mucoadhesive Microspheres and Microcarriers:** Research has also investigated microsphere systems that adhere to mucosal surfaces to facilitate controlled and

prolonged drug release, potentially improving therapeutic efficiency in certain applications.

4. Fixed-Dose Combination Formulations: Aceclofenac is also available in combination with other therapeutic agents (e.g., muscle relaxants like thiocolchicoside) in sustained-release capsules. These combination products integrate aceclofenac and a second active ingredient in a sustained-release pellet form within a hard gelatin capsule to address multi-symptom conditions (e.g., musculoskeletal pain with spasms).

FORMULATION CONSIDERATIONS

Pharmaceutical development of aceclofenac dosage forms involves careful selection of excipients and polymers to achieve the desired release profile. Common excipients include:

- **Matrix-forming polymers:** such as HPMC, PEO, xanthan and guar gums for sustained or controlled
- **Coating and release-modulating polymers:** including Eudragit grades in press-coated and delayed-release systems.
- release.
- **Disintegrants:** like croscarmellose sodium for fast-disintegrating tablets.
- **Direct compression aids:** such as microcrystalline cellulose and lactose for immediate release formulations.

The choice and proportion of these excipients influence mechanical strength, dissolution behavior, and in vitro/in vivo performance of the final product.

ORAL CONTROLLED RELEASE SYSTEM

Oral controlled-release drug delivery systems (CRDDS) are designed to release therapeutic agents at a predetermined rate, prolonging drug action and maintaining optimal plasma concentrations over extended periods**.** This approach aims to enhance patient compliance, reduce dosing frequency, and minimize fluctuations in plasma drug levels, which can lead to improved therapeutic outcomes. Conventional immediate-release formulations often result in rapid absorption followed by a sharp decline in drug levels**,** necessitating frequent administration to maintain efficacy. In contrast, CRDDS utilize physicochemical and biological mechanisms to modulate drug release, including diffusion, dissolution, osmosis, and biodegradation, thereby providing a sustained and predictable pharmacokinetic profile**.** Several strategies have been developed for oral controlled release, including matrix systems,

reservoir systems, osmotic pumps, and multiparticulate dosage forms**.** Matrix systems involve embedding the drug within a polymeric network, allowing gradual release through diffusion or erosion. Reservoir systems, on the other hand, encapsulate the active drug in a polymeric coat, controlling release by membrane permeability. Osmotic systems leverage osmotic pressure gradients to achieve zero-order release kinetics, while multiparticulate systems (e.g., pellets or granules) provide uniform distribution in the gastrointestinal tract and reduce the risk of dose dumping. Oral CRDDS are particularly beneficial for drugs with short half-lives, narrow therapeutic windows, or significant first-pass metabolism, as they can maintain steady-state plasma concentrations while reducing adverse effects. Despite their advantages, the design of CRDDS must consider physiological factors such as gastric emptying time, pH variability, and intestinal motility, which can influence drug release and absorption. Overall, oral controlled-release systems represent a critical advancement in pharmaceutical technology, offering the potential for enhanced efficacy, reduced side effects, and improved patient adherence in chronic therapies. Aceclofenac is a nonsteroidal anti-inflammatory drug commonly used to manage pain and inflammation in conditions such as osteoarthritis and rheumatoid arthritis. Conventional immediate-release formulations require frequent dosing, which can lead to fluctuations in plasma drug levels and increase the risk of gastrointestinal side effects. Oral controlled-release (CR) drug delivery systems have been developed to overcome these limitations by providing a sustained and predictable release of aceclofenac over an extended period. These systems, which may include matrix-based, reservoir-based, osmotic, or multiparticulate designs, utilize polymers such as hydroxypropyl methylcellulose, ethylcellulose, and pH-sensitive coatings to regulate the drug release. By maintaining therapeutic drug concentrations for longer durations, CR formulations reduce dosing frequency, minimize adverse effects, and improve patient compliance, offering a more convenient and effective approach for long-term management of chronic inflammatory conditions.

TOPICAL DELIVERY SYSTEM

Topical delivery systems for aceclofenac have emerged as an effective alternative to oral administration, particularly for managing localized pain and inflammation associated with conditions such as osteoarthritis, rheumatoid arthritis, musculoskeletal injuries, and soft tissue inflammation. Unlike oral formulations, topical systems deliver the drug directly to the affected area, allowing it to penetrate through the skin layers and reach underlying tissues while minimizing systemic absorption and thereby reducing the risk of gastrointestinal side effects commonly associated with NSAIDs. Various dosage forms are available, including gels, creams, ointments, lotions, and transdermal patches, each designed to optimize drug release and absorption. Advanced formulations often incorporate penetration enhancers**,** such as ethanol or propylene glycol, or nanocarrier systems like liposomes, niosomes, microemulsions, and solid lipid nanoparticles, which improve skin permeation, provide sustained release, and enhance therapeutic efficacy. The drug's efficacy in topical form depends on factors such as drug concentration, the type of base or vehicle used, and the physicochemical properties of aceclofenac itself. Topical delivery also allows for targeted therapy, where higher local drug concentrations can be achieved at the site of inflammation without increasing systemic exposure, which is particularly advantageous in chronic conditions that require long-term treatment. Overall, topical aceclofenac formulations combine effectiveness, safety, and patient convenience, making them a valuable option in the management of localized inflammatory and painful conditions.

CONCLUSION

Aceclofenac is an effective and safe nonsteroidal anti-inflammatory drug widely used to relieve pain and inflammation in musculoskeletal disorders such as osteoarthritis, rheumatoid arthritis, and ankylosing spondylitis. Its pharmacological properties, including good oral absorption and favorable tolerability, make it suitable for both immediate- and controlled-release oral formulations. Controlled-release systems help maintain consistent drug levels, reduce dosing frequency, and improve patient adherence, while topical delivery systems

provide localized treatment with minimal systemic side effects. Innovations in formulation techniques, including polymer-based matrices, nanocarriers, and penetration enhancers, have enhanced the drug's therapeutic performance and safety profile. Overall, aceclofenac's versatility in various dosage forms supports its role as a reliable option for managing chronic pain and inflammation effectively.

REFERENCES

1. Aronson JK. Non-steroidal anti-inflammatory drugs. Meyler's Side Effects of Drugs: The International Encyclopedia of Adverse Drugs Reactions and Interactions (15th edition), 2006; 2555-2582.
2. Legrand E. Aceclofenac in the management of inflammatory pain. Drug Evaluation, 2004; 5(6): 1347-1357.
3. Shavi GV, Nayak U, Averineni RK, Arumugam K, Meka SR, Nayanabhirama U, Sureshwar P. Multiparticulate drug delivery system of aceclofenac: development and in vitro studies. Drug Dev Ind Pharm., 2009; 35(2): 252-258.
4. Rao NGR, Kulkarni U, Deshmukh A, Suresh DK. Preparation and characterization of ionotropic cross-linked chitosan microparticles for controlled release of aceclofenac. Int J Pharm Sci Drug Res., 2010; 2(2): 107-111.
5. Brogden RN, Wiseman LR. Aceclofenac: A Review of its pharmacodynamic properties and therapeutic potential in the treatment of rheumatic disorders and in pain management. Drug Evaluation, 1996; 52(1): 113-124.
6. Aceclofenac. British Pharmacopoeia, 2004; 1: 36-38.
7. Chandrasekharan NV. Aceclofenac. XPharm: The comprehensive pharmacology reference, 2008; 1-5.
8. Grau M, Montero JL, Guasch J, Felipe A, Carrasco E, Julia S. The pharmacological profile of aceclofenac, a new nonsteroidal anti-inflammatory and analgesic drug. Drugs in Inflammation, 1991; 32: 125-129.
9. Chub LA. Nonaqueous liquid parenteral aceclofenac formulation. US patent 2009/0156670.2009 Jun18.
10. Aceclofenac. European Pharmacopoeia, 2008; 6.2: 3685-3686.
11. Sharma P. Aceclofenac as a potential threat to critically endangered vultures in India: a review. J Raptor Res., 2012; 46(3): 314–318, 315. doi:10.3356/JRR-11-66.1
12. World Health Organization. Chronic rheumatic conditions; 2020. Available from: https://www.who.int/chp/topics/rheumatic/en/.Accessed November 6, 2021.

13. Hoy D, Bain C, Williams G, et al. A systematic review of the global prevalence of low back pain. Arthritis Rheum, 2012; 64(6): 2028–2037. doi:10.1002/art.34347.
14. Cross M, Smith E, Hoy D, et al. The global burden of hip and knee osteoarthritis: estimates from the global burden of disease 2010 study. Ann Rheum Dis., 2014; 73(7): 1323–1330. doi:10.1136/annrheumdis-2013-204763.
15. Cross M, Smith E, Hoy D, et al. The global burden of rheumatoid arthritis: estimates from the global burden of disease 2010 study. Ann Rheum Dis., 2014; 73(7): 1316–1322. doi:10.1136/annrheumdis-2013-204627
16. Stolwijk C, van Onna M, Boonen A, van Tubergen A. Global pre-valence of spondyloarthritis: a systematic review and meta-regression analysis. Arthritis Care Res., 2016; 68(9): 1320–1331. doi:10.1002/acr.22831
17. Global Burden of Disease Study 2013 Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 301 acute and chronic diseases and injuries in 188 countries, 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013. Lancet, 2015; 386(9995): 743–800.
18. Dalys GBD, Collaborators H. Global, regional, and national disabil-ity-adjusted life-years (DALYs) for 333 diseases and injuries and healthy life expectancy (HALE) for 195 countries and territories,1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet, 2017; 390(10100): 1260–1344.
19. Pérez Busquier M, Calero E, Rodríguez M, et al. Comparison ofaceclofenac with piroxicam in the treatment of osteoarthritis. Clin Rheumatol, 1997; 16(2): 154–159. doi:10.1007/BF02247844.
20. Torri G, Vignati C, Agrifoglio E. Aceclofenac versus piroxicam in the management of osteoarthritis of the knee: a double-blind controlled study. Curr Ther Res Clin Exp., 1994; 55(5): 576–583.doi:10.1016/S0011-393X(05)80189-4
21. Batlle-Gualda E, Román Ivorra J, Martín-Mola E, et al. Aceclofenac vs paracetamol in the management of symptomatic osteoarthritis of the knee: a double-blind 6-week randomized controlled trial.Osteoarthritis Cartilage, 2007; 15(8): 900–908. doi:10.1016/j.joca.2007.02.008.
22. Paul S, Das N, Ghosh S. The effects of aceclofenac and nabumetone in osteoarthritis. JNMA J Nepal Med Assoc, 2009; 48(174): 121–125. doi:10.31729/jnma.226.
23. Ward DE, Veys EM, Bowdler JM, Roma J. Comparison of aceclofenac with diclofenac in the treatment of osteoarthritis. Clin Rheumatol, 1995; 14(6): 656–662. doi:10.1007/BF02207932.

24. Kornasoff D, Frerick H, Bowdler J, Montull E. Aceclofenac is a well-tolerated alternative to naproxen in the treatment of osteoarthritis. Clin Rheumatol, 1997; 16(1): 32–38. doi:10.1007/BF02238760.
25. Pareek A, Chandanwale AS, Oak J, Jain UK, Kapoor S. Efficacy and safety of aceclofenac in the treatment of osteoarthritis: a randomized double-blind comparative clinical trial versus diclofenac - an Indian experience. Curr Med Res Opin, 2006; 22(5): 977–988. doi:10.1185/030079906X104722.
26. Patil P, Jaida J, Palani A, Rao K. A comparative study ofdiclofenac and aceclofenac in the treatment of osteoarthritispatients. J Drug Delivery Ther., 2012; 2(4). doi:10.22270/jddt.v22272i22274.22206
27. Sehgal A, Sehgal V, Singh R. Comparison of efficacy and tolerabilityof aceclofenac and diclofenac in osteoarthritis of knee joint. Int J Med Dental Sci., 2015; 4: 745. doi:10.19056/ijmdsjssmes/2015/v4i2/79789
28. Pareek A, Chandurkar N. Comparison of gastrointestinal safety andtolerability of aceclofenac with diclofenac: a multicenter, randomized, double-blind study in patients with knee osteoarthritis. Curr Med ResOpin., 2013; 29(7): 849–859. doi:10.1185/03007995.2013.795139
29. Patel PB, Patel TK. Efficacy and safety of aceclofenac in osteoar-thritis: a meta-analysis of randomized controlled trials. EurJ Rheumatol, 2017; 4(1): 11–18. doi:10.5152/eurjrheum.2017.160080
30. Batlle-Gualda E, Figueroa M, Ivorra J, Raber A. The efficacy andtolerability of aceclofenac in the treatment of patients with ankylosing spondylitis: a multicenter controlledclinical trial. AceclofenacIndomethacin Study Group. J Rheumatol, 1996; 23(7): 1200–1206.
31. Lee HS, Jeong CK, Choi SJ, Kim SB, Lee MH, KoGI, Sohn DH. Simultaneous determination ofaceclofenac and diclofenac in human plasma bynarrowbore HPLC using column-switching. JPharm Biomed Anal, 2000; 23: 775-781.
32. Godse VP, Deodhar MN, Bhosale AV, SonawaneRA, Sakpal PS, Borkar DD, Bafana YS. Reversephase HPLC method for determination ofaceclofenac and paracetamol in tablet dosageform. Asian J Research Chem., 2009; 2(1): 37-40.
33. Musmade P, Subramanian G, Srinivasan KK. High performance liquid chromatography andpharmacokinetics of aceclofenac in rats. AnalyticaChimica Acta., 2007; 585: 103-109.
34. Hınz B, Auge D, Rau T, Rietbrock S, BruneK, Werner U. Simultaneous determinationof aceclofenac and three of its metabolites inhuman plasma by high-performance

liquidchromatography. Biomed Chromatogr, 2003; 17: 268-275.

35. Zinellu A, Carru C, Sotgia S, Porqueddu E, Enrico P, Deiana L. Separation of aceclofenacand diclofenac in human plasma by free zonecapillary electrophoresis using N- methyl-d-glucamine as an effective electrolyte additive. Eur J. Pharm Sci., 2005; 24(4): 375-380.
36. Kang W, Kim EY. Simultaneous determination ofaceclofenac and its three metabolites in plasmausing liquid chromatography-tandem massspectrometry. J Pharm Biomed Anal, 2008; 46(3): 587-591.
37. Dooley M, Spencer CM, Dunn CJ. Aceclofenac. Drugs., 2001; 61(9): 1351-1378.
38. Lakshmana PS, Shirwaikar AA, Shirwaikar A, Kumar A. Formulation and evaluation sustainedrelease microspheres of rosin containingaceclofenac. ARS Pharmaceutica, 2009; 50(2): 51-62.
39. Shivhare UD, Adhao ND, Bhusarı KP, MathurVB, Ambulkar DU. Formulation development, evaluation and validation of sustained releasetablets of aceclofenac. Int J Pharm Pharm Sci., 2009; 1(2): 74-80.
40. Bort R, Ponsoda X, Carrasco E, Gomez-LechonMJ, Castell JV. Comparative metabolism ofthe nonsteroidal anti-inflammatory drug, aceclofenac, in the rat, monkey and human. DrugMetab Dispos, 1996; 24(9): 969-975.
41. Bort R, Ponsoda X, Carrasco E, Gomez-LechonMJ, Castell JV. Metabolism of aceclofenac inhumans. Drug Metab Dispos, 1996; 24(8): 834-841.
42. Setty CM, Prasad DVK, Gupta VRM, Sa B. Development of fast dispersibleaceclofenac tablets: Effect of functionality ofsuperdisintegrants. Indian J Pharm Sci., 2008; 70(2): 180-185.
43. Akimoto H, Yamazaki R, Hashimoto S, Sato T, Ito A. 4'-Hydroxy aceclofenac suppresses the interleukin-1-induced production of promatrixmetalloproteinases and release of sulfated- glycosaminoglycans from rabbit articularchondrocytes. Eur J Pharm., 2000; 401: 429-436.
44. Yamazaki R, Kawai S, Mizushima Y, MatsuzakiT, Hashimoto S, Yokokura T, Ito A. A majormetabolite of aceclofenac, 4'-hydroxy aceclofenacsuppresses the production of interstitial pro-collagenase/proMMP-1 and pro-stromelysin-1/proMMP-3 by human rheumatoid synovial cells. Inflamm Res., 2000; 49: 133-138.
45. Chan WY, Fuchs F, Powell AM. Effects ofnaproxen sodium on menstrual prostaglandinsand primary dysmenorrhoea. Obstet Gynecol, 1983; 61: 285-291.
46. Letzel H, Megard Y, Lamarca R, Raber A, ForteaJ. The efficacy and safety of

aceclofenac versusplacebo and naproxen in women with primarydysmenorrhoea. Eur J Obstet Gynecol and Reproductive Biol., 2006; 129: 162-168.

47. Pareek A, Chandurkar NB, Patil RT, AgrawalSN, Uday RB, Tambe SG. Efficacy and safetyof aceclofenac and drotaverine fixed-dosecombination in the treatment of primarydysmenorrhoea: a double-blind, double-dummy, randomized comparative study with aceclofenac. Eur J Obstet Gynecol and Reproductive Biol., 2010; 152: 86-90.
48. Hinz B, Auge D, Werner U, Ramer R, Rietbrock S, Brune K. Aceclofenac spares cyclooxygenase 1 as aresult of limited but sustained biotransformationto diclofenac. Clin Pharmacol Ther., 2003; 74(3): 222-235.
49. Perez S, Osorio V, Barcelo D. Comparing thefate and occurrence of aceclofenac, diclofenacand their human metabolites: Conventionaltreatment, membrane bioreactor treatment. Presented in Water Scarcity and ManagementUnder Mediterranean Climate (WSMMC)Conference. Spain, 2008.
50. Yadav VB, Nighute AB, Yadav AV, Bhise SB. Aceclofenac size enlargement by non aqueousgranulation with improved solubility anddissolution. Arch Pharm Sci., 2009; 1(2): 115-122.