



Mefenamic Acid: Pharmacological Profile, Clinical Applications, and Emerging Therapeutic Perspectives with Special Reference to Dysmenorrhoea

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Received: February 20, 2026; **Published:** February 27, 2026

Abstract

Mefenamic acid (MFA) is an anthranilic acid derivative belonging to the fenamate class of non-steroidal anti-inflammatory drugs (NSAIDs). It is widely used for the management of mild to moderate pain, particularly in dysmenorrhoea. Despite its long-standing clinical use, its physicochemical limitations, short half-life, and emerging therapeutic applications warrant renewed attention. This review summarizes the pharmacological characteristics, mechanism of action, pharmacokinetics, clinical indications, contraindications, and recent randomized controlled trials (RCTs) evaluating its role in dysmenorrhoea. Additionally, emerging evidence regarding its neurological and adjunctive oncological applications is discussed. While mefenamic acid remains an effective therapeutic agent, its adverse effect profile and formulation challenges must be carefully considered.

Introduction

Mefenamic acid is a non-steroidal anti-inflammatory drug (NSAID) derived from anthranilic acid (fenamate group). Chemically known as 2-[(2,3-dimethylphenyl)amino] benzoic acid, it was introduced into clinical practice in the 1960s. It is primarily indicated for mild to moderate pain and has gained particular importance in the treatment of primary dysmenorrhoea.¹

Mefenamic acid is a highly lipophilic compound that is rapidly absorbed from the gastrointestinal tract and widely distributed in tissue fluids. It crosses the blood-brain barrier and interacts with molecular targets in the cerebral cortex and hippocampus. However, its extremely low aqueous solubility (<1 mg/mL) presents significant formulation challenges, limiting its biopharmaceutical performance and necessitating repeated dosing due to its short half-life.

Recent research has expanded interest in mefenamic acid beyond analgesia, exploring its potential neuroprotective and antiparasitic effects, as well as its possible adjunctive role in certain malignancies.^{2,3}

Physicochemical and Pharmacokinetic Characteristics⁴

Characteristic	Description
Molecular Formula	C ₁₅ H ₁₅ NO ₂
Molecular Weight	241.28 g/mol
Chemical Name	2-[(2,3-dimethylphenyl)amino] benzoic acid
Volume of Distribution	1.06 L/kg
Protein Binding	~90%
Half-life	~2 hours
Solubility	0.0137 mg/mL
Melting Point	230–231°C
Appearance	White to off-white powder

The drug's short biological half-life (~2 hours) necessitates multiple daily dosing to maintain therapeutic plasma concentrations. It is traditionally available in tablet, capsule, and suspension forms.



Mechanism of Action⁵

Mefenamic acid exerts its pharmacological effect primarily through inhibition of cyclooxygenase (COX-1 and COX-2) enzymes, thereby suppressing prostaglandin synthesis.

COX-1 Inhibition

COX-1 is constitutively expressed in tissues including the stomach and kidneys. It regulates protective gastric mucosal function and platelet aggregation. Inhibition may contribute to gastrointestinal adverse effects.

COX-2 Inhibition

COX-2 is primarily inducible and expressed at sites of inflammation. Inhibition reduces the synthesis of pro-inflammatory prostaglandins, leading to decreased inflammation and pain.

By reducing prostaglandin production, mefenamic acid alleviates uterine hypercontractility and ischemia associated with primary dysmenorrhoea.

Clinical Indications^{6,7}

Mefenamic acid is indicated in:

- Mild to moderate acute pain
- Dysmenorrhoea
- Musculoskeletal and arthritic pain
- Headache and dental pain
- Menorrhagia associated with ovulatory dysfunctional uterine bleeding

It reduces menstrual blood loss and alleviates uterine cramping by decreasing prostaglandin levels.

Emerging literature suggests potential roles in:

- Schistosomiasis treatment
- Depressive symptom modulation in animal models
- Cognitive impairment disorders
- Adjunctive therapy in castration-resistant prostate cancer
- However, these applications require further clinical validation.

Contraindications and Safety Considerations^{8,9}

Mefenamic acid should be avoided in patients with:

- History of gastrointestinal bleeding
- Inflammatory bowel disease
- Aspirin-sensitive asthma
- Hemorrhagic disorders
- Dengue fever or other thrombocytopenic states
- Concurrent anticoagulant therapy

NSAIDs may not be recommended for fever management post-vaccination in young children.

Notably, some comparative studies suggest a relatively higher association of central nervous system adverse effects, including convulsions, compared to certain other NSAIDs.

Randomized Controlled Trials in Dysmenorrhoea^{10,11}

1. Mefenamic Acid vs Peppermint Extract

A double-blind crossover study involving 127 female students with primary dysmenorrhoea compared mefenamic acid with peppermint extract. Both interventions significantly reduced pain severity and duration. Mefenamic acid showed greater reduction in menstrual bleeding, whereas peppermint was associated with fewer gastrointestinal side effects. Analgesic rescue medication use was lower in the mefenamic acid group.

2. Mefenamic Acid vs Exercise

In a randomized clinical trial of 122 students with moderate to severe dysmenorrhoea, participants were assigned to either structured abdominal-pelvic exercises or mefenamic acid (250 mg every 8 hours). Pain intensity was assessed using a visual analog scale over two menstrual cycles. Both interventions were effective, highlighting exercise as a potential non-pharmacological alternative.

3. Mefenamic Acid vs Chamomile^{12,13}

In a randomized study of 200 female students with primary dysmenorrhoea, participants received either mefenamic acid (250 mg) or chamomile (500 mg) three times daily for two consecutive cycles. Chamomile demonstrated comparable reductions in pain severity and menstrual bleeding, suggesting potential herbal alternatives in selected patients.

Formulation Challenges and Future Perspectives

The extremely low water solubility of mefenamic acid limits its dissolution rate and bioavailability. Advances in formulation strategies—including solid dispersions, nanoformulations, and lipid-based delivery systems—may enhance its therapeutic performance.

Additionally, further research is warranted to:

- Clarify its neurological effects
- Investigate long-term safety
- Explore potential oncological and antiparasitic applications
- Develop sustained-release formulations to overcome short half-life limitations

Conclusion

Mefenamic acid remains a well-established NSAID with proven efficacy in dysmenorrhoea and other pain conditions. Its mechanism of action through COX inhibition underpins its analgesic and anti-inflammatory properties. Despite its benefits, gastrointestinal, hematological, and neurological adverse effects necessitate cautious use. Emerging evidence suggests broader therapeutic potential, although robust clinical trials are required. Improved drug delivery strategies may further optimize its clinical utility.

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