

# Novel Approaches in Headache Management: Beyond Traditional NSAIDs with Indomethacin and Innovative Drug Delivery

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**Background:** Headache disorders such as hemicrania continua (HC) and paroxysmal hemicrania (PH) pose unique treatment challenges, as they are unresponsive to most NSAIDs. Indomethacin is highly effective in treating these conditions, positioning it as the cornerstone of their management. However, the limitations of traditional NSAID therapies, such as gastrointestinal side effects, have spurred interest in novel drug delivery systems to enhance therapeutic outcomes.

**Objective:** This study investigates indomethacin's role in managing HC and PH, while exploring cutting-edge drug delivery technologies, particularly solid lipid nanoparticles and polymeric nanoparticles. The focus is on improving indomethacin's pharmacokinetics, minimizing side effects, and increasing precision in targeting headache-related pathways.

**Methods:** A systematic review of clinical and experimental studies from the past decade was conducted. Key areas of investigation include indomethacin's pharmacodynamic properties, its mechanisms in headache disorders, and the potential of nanoparticle-based systems to enhance its bioavailability and therapeutic effect.

**Results:** Indomethacin not only inhibits COX enzymes but also impacts neurovascular processes critical to the pathophysiology of HC and PH. Emerging research on nanotechnology-based delivery, particularly through solid lipid and polymeric nanoparticles, shows promise in reducing systemic adverse effects and providing more efficient CNS targeting of indomethacin, which could improve its efficacy in headache management.

**Conclusion:** While indomethacin remains a critical treatment for indomethacin-responsive headaches, integrating nanotechnology-based delivery methods such as solid lipid and polymeric nanoparticles could further enhance its therapeutic profile. These innovations hold the potential to reduce side effects and optimize drug delivery in the central nervous system, expanding indomethacin's role in managing headache disorders.