International Journal of Pharmaceutical Research and Applications
Volume 10, Issue 4 July-Aug 2025, pp: 300-304 www.ijprajournal.com ISSN: 2456-4494

Novel Gel Techniques for Meloxicam Transdermal Administration as Topical Gel: A Systematic Review

Deepak Kumar Pandey[1], Dr. Jai Narayan Mishra[2], Ashutosh Kushwaha[3], Dhaneshwar Kumar Vishwakarma[4]
[1,2,3,4]*Kailash Institute of Pharmacy & Management, Gorakhpur, Gida, U.P.*

Date of Submission: 15-07-2025 Date of Acceptance: 25-07-2025

ABSTRACT
A potential non-steroidal anti-inflammatory medication (NSAID) for the prevention and treatment of both acute and chronic pain is meloxicam. Meloxicam has limited therapeutic application because of its weak water solubility. Furthermore, it is challenging to develop a suitable NSAID-based delivery system that can pass through the skin barrier for transdermal treatments due to the skin's impermeability. Developed as transdermal drug delivery systems, hydrophilic/hydrophobic gels can significantly enhance other drug administration methods (such oral or intravenous) while preventing or reducing negative effects. This study's main goal was to highlight several gel formulations with improved qualities that may be applied to the long-term administration of meloxicam in a minimally invasive way.

Keywords: NSAID, Anti-inflammatory, Non-steroidal, Meloxican, Transdermal, Topical

I. INTRODUCTION

The pharmaceutical industry has shown a lot of interest in transdermal drug delivery systems because of its potential advantages over more conventional techniques like injection or oral delivery. Small molecules and lipophilic medications can pass through the skin, whereas hydrophilic medications or polymer chains cannot [1,2]. The stratum corneum, which is the outermost layer of the epidermis, can significantly restrict the diffusion of drugs over the skin. In order to lessen discomfort and hasten the healing of wounds, regenerative medicine looks at the possibilities of overcoming skin resistance. One of the main causes of pain and tissue damage is ignoring inflammation. Using non-steroidal anti-inflammatory medicines (NSAIDs) is one way to get beyond these obstacles. When taken as directed, medicine can greatly improve quality of life and reduce suffering [3-5].

One of the substances in the enolic acid class of nonsteroidal anti-inflammatory drugs (NSAIDs) that preferentially inhibits the cyclooxygenase-2 isoform (COX-2) over the cyclooxygenase-1 isoform is meloxicam (MX). Effective analgesic, antipyretic, and anti-inflammatory qualities make MX stand out. With a minimal therapeutic effective dose (less than that of most NSAIDs) and few adverse effects, MX is an active principle of pharmacological interest [6]. Despite MX's extremely low water solubility, a lot of work has been done to integrate it into suitable matrices because of its analgesic and anti-inflammatory properties. For both humaN and veterinary applications, several types of gels appear to be appropriate ways to load and distribute this active principle [7].

Physicochemical properties:

Meloxicam (MX), an active ingredient with the structural formula C14H13N3O4S2 and IUPAC nomenclature, is a member of the oxicam class. 5-methyl-2-thiazolin 4-hydroxy-2-methyl-N-Three-carboxamide-1,1-dioxide -2H-1,2-benzothiazian [8]. Different tautomer forms of MX exist, depending on the solvent's polarity and pH levels.For instance, the anionic form predominates at neutral pH. While non-polar solvents result in enolic forms of MX, polar solvents typically promote the development of the zwitterion form. However, the creation of the cationic structure is favored by the acidic pH [9-11].

International Journal of Pharmaceutical Research and Applications
Volume 10, Issue 4 July-Aug 2025, pp: 300-304 www.ijprajournal.com ISSN: 2456-4494

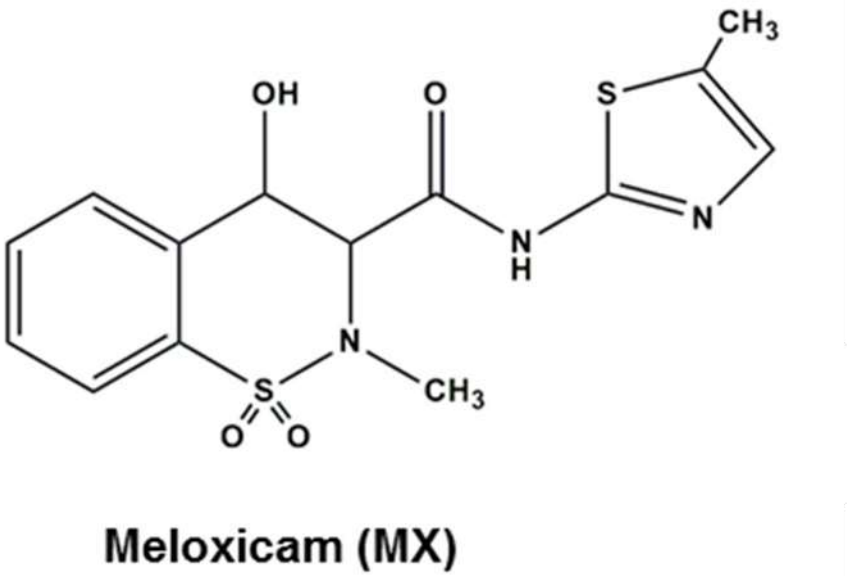

Figure 1: Chemical Structure of Meloxicam

MX has a minor solubility in liquid paraffin or propylene glycol (PG), but it is insoluble in water. Tween 20 and Span 20 are examples of surfactants that improve MX solubility.

MX increases the solubility of the active ingredient under administration circumstances by reacting with bases to produce salts. For instance, it produces sodium and ammonium salts when combined with sodium hydroxide or ammonia, respectively [12]. Since MX is difficult to dissolve in an aqueous or alcohol-based environment, an acidic pH is not ideal for its integration. Additionally, MX can be recrystallized from tetrahydrofuran in its enolic state. MX dissolves in an aqueous sodium hydroxide solution to produce the zwitterion structural form, but at low pH, the cationic structure is more prevalent [13].

Depending on how much of the active ingredient is reabsorbed from the gastrointestinal tract, unpleasant gastrointestinal responses can develop due to the solubility of NSAIDs and the ratio of ionized to non-ionized forms. The shift from the non-ionized to the ionized form is favored by a low pH, which reduces the solubility of the active ingredient [14].The solubility of MX in comparison to other NSAIDs, including piroxicam, diclofenac sodium, ibuprofen, and acetyl salicylic acid, was emphasized by the use of HPLC techniques. Even in an acidic environment, acetyl salicylic acid seems to be the most soluble NSAID, based on this representation. The majority of its molecules are in the non-ionized state, which might have adverse consequences and readily pass through the stomach membrane. In contrast, MX is the most difficult NSAID in its class to disintegrate [15].

Therapeutic efficiency:

NSAIDs' capacity to lower pain, fever, and inflammation accounts for their therapeutic effectiveness; they are recommended for rheumatoid arthritis, osteoarthritis, postoperative pain, osteochondrosis, and seronegative spondyloarthritis. MX works well for a wide range of ailments, particularly rheumatic, inflammatory, and bone disorders. MX is recommended to lessen chronic condition-related pain. This active ingredient can also be used to treat degenerative joint illnesses, where pain is the primary cause of discomfort, and a variety of inflammatory conditions. Furthermore, because it encourages the production of proteoglycans and is specifically used to treat related symptoms including pain and inflammation, MX is regarded as the preferred active ingredient in osteoarthritis [16].

Lower back pain syndrome is another sign of MX. However, the administration of NSAIDs is linked to negative gastrointestinal side effects, like gastropathy, which make patients less likely to stick to their treatment plan [17].

Comparing MX's gastrointestinal toxicity to that of other NSAIDs has been done. MX has substantially less gastrointestinal effects than naproxen, diclofenac, and piroxicam, according to multiple studies with over 5600 individuals. MX is

International Journal of Pharmaceutical Research and Applications
Volume 10, Issue 4 July-Aug 2025, pp: 300-304 www.ijprajournal.com ISSN: 2456-4494

linked to less side effects, including diarrhea, vomiting, nausea, dyspepsia, and abdominal discomfort, than diclofenac. Furthermore, compared to diclofenac, MX had a decreased rate of thromboembolic side effects [18].

357 participants participated in a long-term research in which they received 15 mg of MX daily for 18 months. Thus, in terms of effectiveness and tolerance, MX was contrasted with other NSAIDs. Skin, respiratory, musculoskeletal, and gastrointestinal problems were the most frequent side effects. Additionally, MX is less likely to cause gastrointestinal adverse effects than naproxen. In general, people tolerate it better. Additionally, individuals with comorbidities such as hepatic cirrhosis, congestive heart failure, nephrosis, etc., as well as those with pre-existing gastrointestinal disorders, should not use NSAIDs. NSAID use increases the risk of acute renal failure in the last group of patients. However, there was no correlation between the deterioration of renal function and the administration of MX at the highest permitted doses [19-21].

Meloxicam and Other Active Substances' Synergistic Effects:

To increasethe anti-inflammatory impact, lessen unpleasant responses, or enhance formulations and other therapeutic properties, the interaction of MX with other active ingredients was studied. Therefore, in order to increase the range of action or lessen particular symptoms in particular diseases, MX can be mixed with other active substances, such as antibiotics, anesthetics, antiseptics, and more. Additionally, to increase MX's anti-inflammatory properties or lower the dosage, it can be coupled with other plant-based medicinal compounds. Thus, the minimal effective concentration of MX is used to limit undesirable responses. Conversely, plant active ingredients, such as essential oils, can work as a phytocomplex [22].

They can increase the bioavailability of the active ingredient at the site of action by acting through particular therapeutic characteristics. Consequently, it is possible to view essential oils as MX enhancers, which improve the therapeutic impact by facilitating epithelial crossing. Eucalyptus essential oil (Eucalyptus globulus) is one instance of this. Eucalyptol (1,8-cineole), the active ingredient, has been shown to have analgesic and anti-inflammatory effects. Eucalyptol improved therapeutic efficacy and bioavailability. Cimetidine and antacids do not alter the pharmacokinetic profile of MX. Furthermore, MX had no effect on the pharmacokinetics of other medications taken at the same time, including methotrexate, digoxin, or furosemide. Because NSAIDs can intensify the effects of this active ingredient, warfarin should be administered cautiously when taken with MX [23].

Gel compositions using meloxicam as an active ingredient

Because of its physicochemical nature, MX can be used in topical preparations. Therefore, characteristics like low molecular weight (354.1 g), high efficacy at low doses, ease of crossing the lipid skin layer, and absence of skin toxicity make MX suitable for skin administration [24]. However, NSAIDs administered locally have the benefit of avoiding hepatic metabolism and reducing adverse effects on the gastrointestinal tract. When addressing illnesses that call for localized anti-inflammatory actions, MX may be a viable treatment alternative. Because of MX's unique insolubility in an aqueous environment, incorporating it into various gels becomes difficult. The way the drug molecules interact with the vehicle affects the MX release profile.The release rate, skin permeability, and gel viscosity all affect how well active molecules are absorbed via the skin [25].

Drugs with low water solubility can be delivered utilizing in situ gelling systems that contain active ingredients. Below the lower critical solution temperature (LCST), these systems behaved like liquids; at LCST, micelles with a hydrophilic core and a hydrophobic shell developed. The hydrophobic interactions cause a dramatic sol–gel transition as the temperature and polymer concentration rise [26]. The primary obstacle to MX's integration into delivery vehicles is its poor solubility in aquatic environments. Numerous attempts have been focused on appropriate methods to enhance MX transdermal administration and encourage local analgesia while reducing adverse effects [27].

II. CONCLUSION:

One active ingredient with great promise as an analgesic and anti-inflammatory medication is meloxicam. Over time, a number of drug delivery gels were created to include this hydrophobic medication, increase the duration of MX release, and decrease the frequency of administration, all of which improved patient safety and compliance. Significant research has also been

International Journal of Pharmaceutical Research and Applications
Volume 10, Issue 4 July-Aug 2025, pp: 300-304 www.ijprajournal.com ISSN: 2456-4494

done to improve MX's skin penetration, and several drug carriers for transdermal MX delivery have been created, including liposomes, semi-solid gels, nanostructures, and gels based on β-cyclodextrin.

REFERENCES:

[1]. Drosopoulou, K.; Kosheleva, R.I.; Ofrydopoulou, A.; Tsoupras, A.; Mitropoulos, A. Topical and transdermal delivery of nonsteroidal anti-inflammatory drugs (NSAIDs) for inflammation and pain: Current trends and future directions in delivery systems. Processes **2025**, 13, 907.

[2]. Shah, A.W.A.; Li, X.; Yuan, H.; Shen, H.; Quan, S.; Pan, G.; Ishfaq, M.; Shah, A.U.; Xie, H.; Shao, J. Innovative transdermal drug delivery systems: Benefits, challenges, and emerging application. BMEMat **2025**, e70001.

[3]. Zheng, P.; Wei, Y.; Cao, K.; Xu, C.; Yu, S.; Liu, Y.; Li, M.; Zhang, C.; Wang, T. Sustained-release microspheric gel of meloxicam: Preparation, evaluation in vitro and in vivo. Biomed. Microdevices **2025**, 27, 23.

[4]. Yang, J.; Zhao, Q.; Lu, B.; Lv, Y.; Jiang, W.; Chen, X.; Zhang, S.; Zhao, W.; Jiang, L.; Zhang, J. Injectable thermosensitive hydrogel based on hyaluronic acid and poloxamer for sustained bupivacaine release and prolonged analgesia. Int. J. Biol. Macromol. **2025**, 309, 142845.

[5]. Li, X.Y.; Cai, J.; Duan, X.M.; Zhang, Y.M.; Cui, M.; Wang, S.G.; An, X.; Wang, H.F. Injectable polyamide-amine dendrimer-crosslinked meloxicam-containing poly-γ-glutamic acid hydrogel for prevention of postoperative tissue adhesion through inhibiting inflammatory responses and balancing the fibrinolytic system. J. Colloid Interface Sci. **2024**, 670, 486–498.

[6]. El-Badry, M.; Fetih, G.; Fathalla, D.; Shakeel, F. Transdermal delivery of meloxicam using niosomal hydrogels: In vitro and pharmacodynamic evaluation. Pharm. Dev. Technol. **2015**, 20, 820–826.

[7]. Fetih, G. Meloxicam formulations for transdermal delivery: Hydrogels versus organogels. J. Drug Deliv. Sci. Technol. **2010**, 20, 451–456.

[8]. Beetge, E.; du Plessis, J.; Muller, D.G.; Goosen, C.; van Rensburg, F.J. The influence of the physicochemical characteristics and pharmacokinetic properties of selected NSAIDs on their transdermal absorption. Int. J. Pharm. **2000**, 193, 261–264.

[9]. Luger, P.; Daneck, K.; Engel, W.; Trummlitz, G.; Wagner, K. Structure and physicochemical properties of meloxicam, a new NSAID. Eur. J. Pharm. Sci. **1996**, 4, 175–187.

[10]. Yang, Z.; Liu, L.; Sheng, L.; Wang, H.; Li, C.; Lin, X.; Yang, P. Design of an injectable sustained release in-situ forming depot of meloxicam for pain relief. J. Drug Deliv. Technol. **2024**, 93, 105460.

[11]. Maheshwari, R.; Sharma, M.; Chidrawar, V.R. Development of engineered transferosomal gel containing meloxicam for the treatment of osteoarthritis. Ann. Pharm. Fr. **2024**, 82, 830–839.

[12]. Chen, J.; Gao, Y. Strategies for meloxicam delivery to and across the skin: A review. Drug Deliv. **2016**, 23, 3146–3156.

[13]. Rehman, K.; Zulfakar, M.H. Recent advances in gel technologies for topical and transdermal drug delivery. Drug Dev. Ind. Pharm. **2013**, 40, 433–440.

[14]. Karateev, A.E.; Uspensky, Y.P.; Pakhomova, I.G.; Nasonov, E.L. Brief history of NSAIDs. Sci. Pract. Rheumatol. **2012**, 50, 101–116.

[15]. Slei, P.; Püschner, H. Intramuscular tolerance of meloxicam compared to piroxicam and diclofenac in rabbits. Scand. J. Rheumatol. **1994**, 98, 109.

[16]. Ghozlan, P.R.; Bernhardt, M.; Velicitat, P.; Bluhmki, E. Tolerability of multiple administration of intramuscular meloxicam: A comparison with intramuscular piroxicam in patients with rheumatoid arthritis or osteoarthritis. Br. J. Rheumatol. **1996**, 35 (Suppl. S1), 51–55.

[17]. Plugariu, I.A.; Gradinaru, L.M.; Avadanei, M.; Rosca, I.; Nita, L.E.; Maxim, C.; Bercea, M. Thermosensitive polyurethane-based hydrogels as potential vehicles for meloxicam delivery. Pharmaceuticals **2023**, 16, 1510.

[18]. Gao, D.; Zhao, Y.; Liu, J.; Chu, R.; Wang, J.; Bian, W.; Liu, X.; Lu, W.; He, J. Bupivacaine multivesicular

liposomes/meloxicam nanocrystals in a thermosensitive gel adapted to the "microenvironment" for long-term analgesia. Eur. J. Pharm. Biopharm. **2025**, 207, 114630.

[19]. Shehata, T.M.; Elnahas, H.M.; Elsewedy, H.S. Development, characterization and optimization of the anti-inflammatory influence of meloxicam loaded into a eucalyptus oil-based nanoemulgel. Gels **2022**, 8, 262.

[20]. Usama, A.; Fetih, G.; El-Faham, T. Performance of meloxicam niosomal gel formulations for transdermal drug delivery. Br. J. Pharm. Res. **2016**, 12, 1–14.

[21]. Kovacevic, Z.; Mugoša, S.; Lalic-Popovic, M.; Tešin, N.; Marić, D.; Todorović, N.; Božić, F. Veterinary compounding: The impact of different gelling agents on the rheological characteristics and release kinetics from meloxicam oral gels in the treatment of cats. Vet. Arch. **2024**, 93, 695–708.

[22]. De la Puente, R.; Diez, R.; Diez, M.J.; Fernandez, N.; Sahagun, A.M.; Rodriguez, J.M.; Garcia, J.J.; Lopez, C. Pharmacokinetics of meloxicam in different animal species: A comprehensive review. Vet. Sci. **2024**, 11, 519.

[23]. Tsai, R.-S.; Carrupl, P.-A.; Tayar, N.-E.; Giroud, Y.; Andrade, P.; Testa, B.; Breé, F.; Tillement, J.-P. Physicochemical and structural properties of non-steroidal anti-inflammatory oxicams. Helv. Chim. Acta **1993**, 76, 842–854.

[24]. Mwangi, A.N.; Njogu, P.M.; Maru, S.M.; Njuguna, N.M.; Njaria, P.M.; Kiriiri, G.K.; Mathenge, A.W. Meloxicam emulgels for topical management of rheumatism: Formulation development, in vitro and in vivo characterization. Saudi Pharm. J. **2021**, 29, 351–360.

[25]. Price, A.H.; Fletcher, M. Mechanism of NSAID induced gastroenteropathy. Drugs **1990**, 40 (Suppl. S5), 1–11.

[26]. Del Tacca, M.; Colucci, R.; Fornai, M.; Blandizzi, C. Efficacy and tolerability of meloxicam, a COX-2 preferential nonsteroidal anti-inflammatory drug. Clin. Drug Investig. **2002**, 22, 799–818.

[27]. Zaychenko, G.; Liapunov, O.M.; Bezugla, O.P. The place of meloxicam in the series of modern non-steroidal anti-inflammatory drugs. News Pharm. **2016**, 2, 69–76.