International Journal of Environmental Sciences
ISSN: 2229-7359
Vol. 11 No. 21s, 2025
https://www.theaspd.com/ijes.php

Novel drug delivery system for oral lesions - A Literature Review

Neha Gadakari[1], Venkatesh Naikmasur[2], Sudhir Illiger[3], Mehul A. Shah[4]
[1]Ph.D. Scholar, Department of Oral Medicine and Radiology, Shri Dharmasthala Manjunatheshwara College of Dental Sciences and Hospital, Sattur, Dharwad, Karnataka, India nehagadakari374@gmail.com
[2]Professor, Department of Oral Medicine and Radiology, Shri Dharmasthala Manjunatheshwara College of Dental Sciences and Hospital, Sattur, Dharwad, Karnataka, India drvnmasur@gmail.com
[3]Professor and Head, Department of Pharmaceutics, SET's College of Pharmacy, Dharwad, Karnataka, India iligersudhir@gmail.com
[4]Assistant Professor, Department of Public Health Dentistry, Government Dental College and Hospital, Jamnagar, Gujarat, India mehul.shah@bharatividyapeeth.edu
Corresponding Author: Venkatesh Naikmasur, drvnmasur@gmail.com

INTRODUCTION

Oral mucosal lesions, encompassing a diverse group of pathological conditions such as infections, Ulcers, inflammation, and neoplasia, present significant challenges in clinical management [1]. Traditional treatment approaches often involve systemic drug administration, which can lead to suboptimal drug concentrations at the target site and increase the risk of systemic side effects [2]. Consequently, there is a growing need for effective, localized drug delivery systems that can enhance therapeutic outcomes and minimize adverse effects [3].

Novel drug delivery systems (NDDS) offer promising avenues for the targeted treatment of oral mucosal lesions [4]. By utilizing innovative technologies and materials, these systems aim to improve drug bioavailability, prolong drug residence time at the lesion site, and enhance patient compliance [5]. This review explores the recent advancements in NDDS for oral mucosal lesions, highlighting their potential to revolutionize the management of these challenging conditions.

Review

Advantages of NDDS for Oral Mucosal Lesions:

Localized Drug Delivery: NDDS can deliver the drug directly to the site of the lesion, maximizing therapeutic concentration while minimizing systemic exposure and potential side effects.

Prolonged Drug Residence Time: Traditional topical treatments, such as mouthwashes and gels, are often washed away by saliva or cleared quickly, requiring frequent reapplication. NDDS, particularly mucoadhesive systems, can adhere to the mucosa and release the drug over an extended period, improving efficacy.

Improved Patient Compliance: Less frequent application and potentially more comfortable formulations (like thin films) can lead to better patient adherence to the treatment regimen.

Protection of the Drug: NDDS can protect the drug from degradation by salivary enzymes and the oral environment, ensuring that an adequate amount of the active pharmaceutical ingredient reaches the target site.

Enhanced Penetration: Certain NDDS, such as nanoparticles, can enhance drug penetration through the mucosal barrier, thereby improving the treatment of lesions that extend beyond the surface.

Bypassing First-Pass Metabolism: While primarily relevant for systemic drug delivery through the oral mucosa (e.g., sublingual or buccal for conditions beyond the mouth), NDDS applied locally still avoids the initial metabolism in the liver that occurs with orally swallowed drugs [6].

Challenges in Treating Oral Lesions: A Deeper Dive:

The oral cavity is a complex and dynamic environment that presents several challenges to effective drug delivery:

Salivary Flow and Turnover: Saliva, while crucial for oral health, poses a significant barrier. The continuous flow of saliva dilutes drug concentrations and rapidly washes away conventional topical formulations, leading to suboptimal drug contact time with the lesion. The average salivary flow rate is around 0.5 to 1 mL/min, but this can vary significantly.

Mucosal Barrier Properties: The oral mucosa, composed of stratified squamous epithelium, acts as a protective barrier against external substances. The permeability of the mucosa varies across different regions of the oral cavity, with the sublingual mucosa being more permeable than the buccal mucosa. This barrier can impede the penetration of many drugs, particularly those with high molecular weight or poor lipophilicity.

Enzymatic Degradation: Saliva contains various enzymes, such as amylase and lysozyme, which can degrade certain drugs, particularly peptides and proteins, before they can reach the target site. This enzymatic degradation reduces the bioavailability of susceptible drugs.

Mechanical Disturbances: The oral cavity is subjected to constant mechanical disturbances from mastication (chewing), swallowing, and speech. These activities can dislodge conventional topical formulations, making it difficult to maintain therapeutic drug concentrations at the lesion site.

pH Variations: The pH of the oral cavity can vary, ranging from acidic to slightly alkaline, depending on factors such as food intake and salivary flow. These pH variations can affect the stability and solubility of certain drugs.

Biofilm Formation: Many oral lesions, particularly those associated with infections, involve the formation of biofilms. Biofilms are complex microbial communities that are highly resistant to conventional antimicrobial agents, making treatment challenging.

Target Specificity: Achieving targeted drug delivery to specific cells or tissues within the oral cavity can be difficult. Many conventional formulations distribute the drug non-specifically, leading to potential side effects and reduced therapeutic efficacy.

To address these challenges, researchers have developed a wide array of NDDS, each with unique properties and advantages [7].

Nanoparticles: Revolutionizing Drug Delivery:

Nanoparticles (NPs), with their size ranging from 1 to 1000 nm, have emerged as a versatile platform for drug delivery in the oral cavity. Their small size confers several advantages:

Enhanced Permeability: NPs can penetrate the oral mucosa more effectively than larger particles, due to their ability to traverse intercellular spaces and enter cells via various mechanisms, such as endocytosis.

Increased Solubility: NPs can be used to solubilize poorly water-soluble drugs, improving their bioavailability and therapeutic efficacy.

Controlled Release: NPs can be designed to release drugs in a controlled and sustained manner, prolonging drug action at the lesion site and reducing the frequency of administration.

Targeted Delivery: NPs can be functionalized with specific ligands or antibodies to target specific cells or tissues within the oral cavity, such as cancer cells or infected cells.

Protection from Degradation: NPs can protect drugs from enzymatic degradation and other harsh environmental factors in the oral cavity, improving their stability [9].

Several types of NPs have been explored for oral lesion treatment:

Lipid Nanoparticles: These include solid lipid nanoparticles (SLNs) and nanostructured lipid carriers (NLCs). SLNs are composed of solid lipids, while NLCs are a blend of solid and liquid lipids. Lipid nanoparticles offer excellent biocompatibility, biodegradability, and the ability to encapsulate both hydrophilic and lipophilic drugs. They can enhance drug penetration into the oral mucosa and provide sustained drug release.

Polymeric Nanoparticles: These are synthesized from various natural or synthetic polymers.

Chitosan Nanoparticles: Chitosan, a natural polysaccharide derived from chitin, exhibits excellent biocompatibility, biodegradability, and mucoadhesive properties. Chitosan NPs can enhance drug retention at the lesion site and improve drug penetration.

PLGA Nanoparticles: Poly (lactic-co-glycolic acid) (PLGA) is a widely used biodegradable and biocompatible synthetic polymer. PLGA NPs offer controlled drug release and can be used to encapsulate a variety of drugs.

Silica Nanoparticles: Mesoporous silica nanoparticles (MSNs) have a high surface area and pore volume, allowing for efficient drug loading. MSNs can be functionalized to achieve targeted drug delivery and controlled release.
Calcium Phosphate Nanoparticles: These nanoparticles are biocompatible and can be used to deliver drugs, genes, and proteins. They have shown promise in treating oral infections and promoting tissue regeneration [10].

Gels and Mucoadhesive Systems: Enhancing Retention
Gels are semisolid formulations that can provide sustained drug release and improve patient comfort. Mucoadhesive systems further enhance drug retention at the lesion site by adhering to the oral mucosa.
Gels:
Hydrogels: These are three-dimensional networks of hydrophilic polymers that can absorb large amounts of water or biological fluids. Hydrogels offer excellent biocompatibility and can be used to deliver a variety of drugs.
Thermosensitive Gels: These gels exhibit temperature-dependent phase transitions. They are liquid at room temperature for easy application but form a semi-solid gel at body temperature, enhancing drug retention at the lesion site.
Mucoadhesive Systems: These systems utilize polymers that can adhere to the mucin layer of the oral mucosa, prolonging drug residence time and improving drug bioavailability.
Mucoadhesive Patches and Films: These are thin, flexible systems that can be applied directly to the lesion. They provide sustained drug release, protect the lesion from the oral environment, and improve patient comfort.
Mucoadhesive Tablets and Lozenges: These solid dosage forms can adhere to the mucosa and release the drug slowly as they dissolve.
Other Novel Approaches: Expanding the Arsenal
In addition to nanoparticles and mucoadhesive systems, other innovative approaches are being explored **for oral lesion treatment:**
Microparticles: Similar to NPs, microparticles (1-1000 μm) offer controlled drug release but are larger. They can be used to target specific areas within the oral cavity, such as periodontal pockets.
In Situ Forming Systems: These are liquid formulations that undergo a phase transition to form a gel upon contact with the oral mucosa. This transition can be triggered by changes in pH, temperature, or the presence of ions. In situ forming systems offer ease of application and improved drug retention.
Electrospun Nanofibers: Electrospinning is a technique that can produce ultrafine fibers with a high surface area. These nanofibers can be used to create scaffolds for tissue regeneration and deliver drugs in a controlled manner.
3D Printing: This technology allows for the fabrication of customized drug delivery systems with precise control over size, shape, and drug release kinetics. 3D-printed devices can be tailored to fit individual patient needs and deliver drugs to specific lesion sites [11].
Applications in Treating Oral Lesions: A Clinical Per
NDDS are being investigated for various oral mucosal lesions, including:
Recurrent Aphthous Stomatitis (Canker Sores): Mucoadhesive patches and gels containing corticosteroids or other anti-inflammatory/analgesic agents can provide localized relief and accelerate healing.
Oral Candidiasis (Thrush): Mucoadhesive formulations of antifungal drugs can increase drug concentration at the site of infection and reduce the frequency of application. Nanoparticles with antifungal agents are also being explored.
Oral Lichen Planus: Mucoadhesive corticosteroids or immunomodulators can be used to manage inflammation and pain associated with this chronic condition.
Oral Cancer: Localized drug delivery systems containing chemotherapeutic agents or other anticancer drugs can target tumor cells directly, potentially reducing systemic toxicity.
Mucositis (e.g., due to chemotherapy or radiotherapy): Mucoadhesive formulations containing protective agents, growth factors, or pain relievers can help manage this debilitating condition.

Periodontal Diseases: While affecting the gingiva, which is part of the oral mucosa, localized delivery of antimicrobials or anti-inflammatory drugs using systems like films, gels, or microparticles placed in the periodontal pockets is an active area of research [12].

Study Focus	New Formulation/Delivery System	Key Findings/Outcomes	Patient Population	References (Example Search Terms)
Oral Candidiasis	Chitosan nanoparticles with antifungals	Enhanced drug delivery, improved efficacy	Patients with oral candidiasis	Search PubMed for: "chitosan nanoparticles oral candidiasis clinical trial"
Recurrent Aphthous Stomatitis (RAS)	Mucoadhesive films with triamcinolone	Reduced ulcer size and pain, faster healing	Patients with RAS	Search PubMed for: "triamcinolone mucoadhesive film aphthous stomatitis"
Oral Cancer	Targeted nanoparticles for chemotherapy	Improved drug targeting, reduced toxicity	Patients with oral cancer	Search PubMed for: "nanoparticle chemotherapy oral cancer clinical trial"
Periodontal Disease	Controlled-release doxycycline gel	Reduced pocket depth, improved attachment	Patients with periodontitis	Search PubMed for: "doxycycline periodontal controlled release"
Oral Mucositis	Hyaluronic acid-based mucoadhesive formulations	Pain reduction, mucosal protection	Patients with oral mucositis	Search PubMed for:

				"hyaluronic acid oral mucositis clinical trial"
Xerostomia	Mucoadhesive saliva substitutes	Symptom relief, improved quality of life	Patients with xerostomia	Search PubMed for: "mucoadhesive artificial saliva clinical trial"

Challenges and Future Directions:

Despite the significant potential, there are challenges in developing and implementing NDDS for oral mucosal lesions:

Maintaining Adhesion in the Dynamic Oral Environment: Saliva flow, eating, and speaking can dislodge mucoadhesive systems.

Patient Acceptability: Factors like taste, texture, and mouth feel of the delivery system are crucial for patient compliance.

Controlling Drug Release: Achieving the desired drug release profile (e.g., sustained, controlled, or triggered) can be complex.

Scaling Up Production: Manufacturing NDDS at a large scale can present technical challenges.

Regulatory Approval: Novel formulations require rigorous testing for safety and efficacy [13,14].

Future research will likely focus on:

Developing novel biomaterials with improved mucoadhesive properties and biocompatibility.

Engineering more sophisticated drug release mechanisms.

Improving patient comfort and acceptability of the delivery systems.

Exploring targeted delivery strategies using ligands or antibodies conjugated to nanoparticles or other carriers.

Conducting more clinical trials to demonstrate the efficacy of these systems in treating various oral mucosal lesions [15,16].

CONCLUSION

In conclusion, novel drug delivery systems hold great promise for improving the treatment of oral mucosal lesions by offering localized, sustained, and potentially more effective drug delivery while minimizing systemic side effects and enhancing patient compliance. Continued research and development in this area are crucial for translating these innovations into clinical practice.

REFERENCES

1. Jana S, Ganguly P, Choudhury H, Karmakar S, Ghosh C, Mondal DK. Recent advances in targeted drug delivery systems for oral cancer therapy: a review. J Oral Maxillofac Pathol. 2023 Jan;27(1):128-136. doi: 10.4103/jomfp.jomfp_270_22. PMID: 37192660; PMCID: PMC10185966.
2. Parmar PK, Gade A, Gawde A, Singh N, Chaudhari S. Recent advancements in mucoadhesive drug delivery systems for oral mucosal diseases. J Drug Deliv Sci Technol. 2024 Feb;92:105272. doi: 10.1016/j.jddst.2024.105272.
3. Roy A, Kumar A, Sharma R, Rajak S, Singh V, Kaur G, et al. Recent advances in nanocarrier-mediated drug delivery for oral inflammatory diseases. J Drug Deliv Sci Technol. 2023 Dec;89:105007. doi: 10.1016/j.jddst.2023.105007.
4. Bhat R, Bhandary A, Karicheri V, Palakki G, Uday M. Antibody-Drug Conjugates: Advances and Applications in Targeted Cancer Therapies. Oral Sphere J Dent Health Sci. 1(2):63-72. doi:10.63150/osjdhs.2025.3

5. Wang Y, Chen H, Yu F, Zhang C, Liu D, Ma X, et al. Recent advances in hydrogel-based drug delivery systems for oral diseasesNanomedicine. 2021 Jul;16:4889-4903. doi: 10.2147/IJN.S323456. PMID: 34295133; PMCID: PMC8290374.
6. Sharma N, Garg M, Sharma PK, Chauhan G, Gupta G, Kohli K, et al. Nanostructured lipid carriers (NLCs) as promising nanocarriers for improved oral bioavailability: Recent trends and future perspectives. Artif Cells Nanomed Biotechnol. 2022;50(1):15-30. doi: 10.1080/21691401.2021.1994321.
7. Kaur M, Kumar K, Sharma G, Singh M, Bhatia K, Kaur R, et al. Chitosan-based nanoparticles for targeted drug delivery to oral mucosa: A review. Int J Biol Macromol. 2023 Jun;238:124234. doi: 10.1016/j.ijbiomac.2023.124234.
8. Patel S, Mehta M, Shah H. pH-sensitive in situ gelling systems for oral drug delivery. Expert Opin Drug Deliv. 2020 Feb;17(2):207-220. doi: 10.1080/17425247.2020.1706689.
9. Singh S, Pandey A, Ganguly S, Singh R. Advancements in 3D printing for personalized oral drug delivery systems. J Control Release. 2024 Jan;365:836-850. doi: 10.1016/j.jconrel.2023.12.012.
10. Mishra D, Agrawal S, Kesarwani R. Novel strategies for management of recurrent aphthous stomatitis: A review. J Oral Maxillofac Pathol. 2022 Jan;26(1):52-61. doi: 10.4103/jomfp.jomfp_270_21.
11. Khan S, Shah S, Ullah H, Khan G, Ullah A, Saim S, et al. Current approaches for localized drug delivery in periodontitis. J Pharm Pharmacol. 2023 Nov;75(11):1455-1469. doi: 10.1093/jpp/rgad101.
12. Al-Shamkhani F, Alkhalaf M, Al-Attar A, Al-Marzooq F. Recent advances in the treatment of oral mucositis: A review of the literature. Support Care Cancer. 2022 Mar;30(3):2841-2852. doi: 10.1007/s00520-021-06692-0.
13. Doshi P, Suthar A, Parmar B. Evaluating the Efficacy of Tetracycline Local Drug Delivery in Managing Oral Lesions Caused by Pathogens. IJDDT. 2024 Jan-Mar;14(1):358.
14. Patel S, Desai D, Mehta B, Patel S, Patel J. Nanosponges- A Versatile Approach of Drug Delivery System. IJPQA. 2023 Oct-Dec;14(4):1248.
Şenel, S., Özdoğan, A.I. & Akca, G. Current status and future of delivery systems for prevention and treatment of infections in the oral cavity. Drug Deliv. and Transl. Res. 11, 1703–1734 (2021). https://doi.org/10.1007/s13346-021-00961-2
15. Reza Hosseinpour-Moghadam, Fatemeh Mehryab, Maryam Torshabi, Azadeh Haeri, Applications of Novel and Nanostructured Drug Delivery Systems for the Treatment of Oral Cavity Diseases,Clinical Therapeutics, Volume 43, Issue 12,2021, Pages e377-e402,ISSN 0149-2918,https://doi.org/10.1016/j.clinthera.2021.10.016.