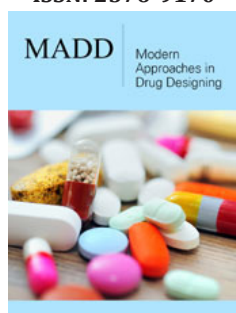


Mucoadhesive Polymer Films for Local and Systemic Drug Delivery via the Oral Mucosa

Vladislav Sepp*, Nadezhda Kondratyeva, Konstantin Bakulin and Sandji Ubushaev

Institute of Pharmacy and Medicinal Chemistry, Pirogov Russian National Research Medical University, Russia

ISSN: 2576-9170



Abstract

This mini-review examines the main trends in the development of oromucosal film as an oral drug delivery system for topical and systemic therapy. Based on published research data for the period 2022-2025, the main development trends of this dosage form are analysed. The review considers target nosologies and active ingredients used by researchers, as well as technologies and composition of structure-forming components of oromucoadhesive films.

Keywords: Oromucosal films; Buccal drug delivery; Drug delivery system

Introduction

Drug delivery systems that take advantage of the increased permeability of the oral mucosa have been known for quite some time. The clear advantages of this route of administration include enhanced bioavailability, rapid onset of therapeutic effect, and convenience for the patient. Initially, these were orally disintegrating tablets designed to dissolve in the sublingual area. Over the past 20 years, the number of dosage forms that release active substances in the oral cavity has increased significantly. Various types of polymeric films containing active pharmaceutical ingredients are gaining increasing relevance. The development of these dosage forms is progressing along two main directions: films intended for rapid disintegration and/or dissolution in the oral cavity, and films that adhere to the surface of the oral mucosa (commonly referred to in scientific literature as mucoadhesive buccal, oromucosal, or bioadhesive films). Researchers often group these two fundamentally different dosage forms together and fail to distinguish between them. However, films intended for rapid dissolution (Orodispersible Films, ODFs) release active substances into the oral cavity under the action of saliva. As a result, pharmacologically active compounds are partially absorbed through the oral mucosa and partially swallowed, entering the stomach. Often, it is impossible to determine the exact proportion of these two pathways, which may lead to inaccuracies in dosing due to significant differences in the bioavailability of substances absorbed through the oral mucosa versus those absorbed via the gastrointestinal tract after first-pass hepatic metabolism. Oromucosal films (Mucoadhesive Buccal Films, MBFs), on the other hand, release active substances almost entirely through the oral mucosa, thereby delivering it more accurately and efficiently into the systemic circulation while bypassing first-pass hepatic metabolism. Consequently, MBFs are significantly better suited for the systemic delivery of drugs requiring precise dosing.

The purpose of this mini-review is to examine the main directions in the development of mucoadhesive oral films as a promising drug delivery system. Given that several fairly comprehensive reviews on this topic have been published in previous years, and considering the chosen mini-review format, the search and analysis of data were limited to the period from 2022 to 2025. This review discusses the target diseases, the active pharmaceutical ingredients used by researchers, the technologies and composition of the structural components of mucoadhesive films.

***Corresponding author:** Vladislav Sepp, Institute of Pharmacy and Medicinal Chemistry, Pirogov Russian National Research Medical University, Russia

Submission: June 12, 2025

Published: July 07, 2025

Volume 4 - Issue 4

How to cite this article: Vladislav Sepp*, Nadezhda Kondratyeva, Konstantin Bakulin and Sandji Ubushaev. Mucoadhesive Polymer Films for Local and Systemic Drug Delivery via the Oral Mucosa. Mod Appro Drug Des. 4(4). MADD. 000594. 2025. DOI: [10.31031/MADD.2025.04.000594](https://doi.org/10.31031/MADD.2025.04.000594)

Copyright@ Vladislav Sepp, This article is distributed under the terms of the Creative Commons Attribution 4.0 International License, which permits unrestricted use and redistribution provided that the original author and source are credited.

Nosologies and Active Pharmaceutical Ingredients

In previous years, oromucosal films have been tested and used for the treatment of various conditions, including pain and inflammation (immediate relief), central nervous system disorders (as these films are easy for caregivers to administer and promote better compliance), cardiovascular diseases (fast onset of therapeutic effect), and cancer (enhanced safety and efficacy due to direct systemic absorption and ability to bypass the first-pass metabolism) [1,2]. Oromucosal films containing plant extracts or naturally purified substances derived from plants are also widely represented among the developments.

Studies published between 2022 and 2025 continue to follow the trend of focusing on the aforementioned nosologies, as well as the widespread use of natural components. Among the most recent research, notable developments include anticancer agents (primarily for oral squamous cell carcinoma) and antimicrobial formulations based on ethanol and acetone extracts of *Usnea barbata* [3,4]. These studies have demonstrated promising results. Publications focused on the development of mucoadhesive films for dental applications, incorporating CO₂ clove extract and essential oils of lavender and grapefruit as active ingredients are also noteworthy [5]. Of particular interest is research on mucoadhesive oral films with optimized contents of Olive Leaf Extract (OLE) and microencapsulated Thyme Essential Oil (TEO), which have proven antioxidant and antimicrobial activities [6]. An example of the development of a film based on a novel active pharmaceutical ingredient previously not used in this dosage form is the creation of an oromucosal film containing a new biocompatible Substance-Solubilized Eggshell Membrane (SESM), which has demonstrated effects on cell proliferation and the expression of inflammation marker genes [7]. More traditional developments among recent publications include chitosan-based wound-healing films [8], as well as the investigation of a local dosage form using chitosan loaded with cisplatin for the treatment of oral squamous cell carcinoma [9]. Another example of an anticancer formulation using an oromucosal drug delivery system was proposed in a recent publication dated 2023. In this study, native κ -Carrageenan (κ -CA) was thiolated with phosphorus pentasulfide in sulfolane [10]. This formulation demonstrated promising levels of specific anticancer activity. Among oromucosal films containing synthetic and biotechnological active pharmaceutical ingredients, studies published in recent years highlight the development of bilayer mucoadhesive buccal films loaded with Triamcinolone Acetonide (TA) for the treatment of recurrent aphthous stomatitis [11]. The study published in 2022 focuses on the design of peroral films containing betamethasone for the treatment of oral diseases [12].

Particular attention should be given to studies focused on the development of oromucosal films containing active pharmaceutical ingredients with systemic action. By releasing active components directly into the systemic circulation, such delivery systems fully leverage the advantages of the transbuccal route of administration. A notable number of studies have explored vaccination methods using oromucosal films. For example, a microparticulate Zika

virus vaccine administered via the buccal route using thin films was investigated [13]. Research on oromucosal vaccines for the prevention and treatment of Coronavirus disease-19 (COVID-19) is ongoing [14,15]. Other examples of oromucosal films with resorptive active pharmaceutical ingredients include the development of a therapeutic formulation for the treatment of Childhood Disintegrative Disorder (CDD) containing ganaxolone [16], as well as a study focused on the development of an oromucosal formulation containing the anti-tobacco agent cytosine [17].

Thus, the directions of modern research in the field of oromucosal films logically continue the trends of the past years, in addition, there is an expansion of the list of nosologies and, accordingly, the active substances that are included in the composition of oromucosal films. Compared to previous years, researchers pay a little more attention to oromucosal films of resorptive action.

Technology of production and composition of films

There are rather few publications that focus on materials and technologies for the production of oromucosal films. In the vast majority of cases, researchers are limited to the method of casting on a substrate. In the case of obtaining multilayer films, the method of step-by-step casting with solidification of the previous layer is used. Among the used structure-forming materials in the publications of recent years, cellulose derivatives such as hypromellose and hydroxypropylcellulose traditionally prevail, and polyvinyl alcohol, polyvinylpyrrolidone, polyethylene glycol are also frequently mentioned. Ethylcellulose is often used as a substrate. These are so-called first-generation polymers [18]. The second generation includes thiolated polymers, which can extend the residence time of the therapeutic agent at the application site and allow controlled release.

Typical polymers used as mucoadhesive components are gelatin, chitosan, pullulan, sodium carboxymethylcellulose, hydroxypropylcellulose and sodium hyaluronate. Various natural polysaccharides exhibit mucoadhesive properties such as psyllium and some rice varieties with high amylose content [2].

The mucoadhesive properties of commonly used polymers such as chitosan can be enhanced by thiolation.

Among other materials used for the production of oromucosal films in the studies of recent years we can mention quite a wide use of natural and semi-synthetic materials, such as gum [6,16], as well as carrageenan [19] and thiolated carrageenan [10]. Alginate polymer-based films are quite often mentioned in studies [5,6]. Traditionally, glycerol and polyethylene glycol 400 are mainly used as plasticisers.

In addition to the traditional method of casting on a substrate, modern studies also encounter descriptions of other methods of producing oromucosal films: hot melt extrusion method, semi-solid casting production method, pressing method, and solid dispersion solution extrusion method [18] of particular note is the research appearing in recent years using modern, innovative

technological approaches to obtain oromucosal films, such as 2D and 3D printing, electrospraying and electrospinning [20]. Thus, the list of structure-forming agents and technological methods for the production of oromucosal films has been steadily increasing in recent years. This confirms the promising nature of this dosage form and the legitimate interest in it on the part of researchers and manufacturers.

Conclusion

The interest in the development of oral delivery systems has maintained an increasing trend over the period 2022-2025. Oromucosal films as one of the most promising delivery systems for topical and resorptive active substances have also often become the subject of researchers attention. The directions of development with natural active components, as well as methods of vaccination and correction of metabolic disorders with the use of oromucosal films remain in demand. The technology of film production is improving; in addition to classical methods, 2D and 3D printing methods are increasingly being used.

References

1. Sinha S, Dutt R (2019) Oral soluble films: Attributes of the polymeric material and critical process parameters for designing good quality films. *Current Applied Polymer Science* 3(3):167-88.
2. Tian Y, Orlu M, Woerdenbag HJ, Scarpa M, Kiefer O, et al. (2019) Oromucosal films: From patient centricity to production by printing techniques. *Expert Opin Drug Deliv* 16(9): 981-93.
3. Popovici V, Matei E, Cozaru GC, Bucur L, Gird CE, et al. (2022) *In vitro* anticancer activity of mucoadhesive oral films loaded with usnea barbata (L.) F. H. wigg dry acetone extract, with potential applications in oral squamous cell carcinoma complementary therapy. *Antioxidants* 11(10): 1934.
4. Popovici V, Matei E, Cozaru GC, Bucur L, Gird CE, et al. (2022) Formulation and development of bioadhesive oral films containing usnea barbata (L.) F. H. wigg dry ethanol extract (F-UBE-HPC) with antimicrobial and anticancer properties for potential use in oral cancer complementary therapy. *Pharmaceutics* 14(9): 1808.
5. Maslii Y, Herbina N, Dene L, Ivanauskas L, Matulis G, et al. (2025) Mucoadhesive polymeric film with plant-based compounds for dental applications: Formulation, characterization and evaluation. *Pharm Dev Technol* 30(4): 505-520.
6. Goktas K, Yalcin D, Erdem C, Bicakci BT, Bayraktar O (2025) Optimization of mucoadhesive oral films containing olive leaf extract and microencapsulated thyme essential oil with potential antimicrobial activity. *Food Sci Nutr* 13(2): e4603.
7. Neduri K, Ailuno G, Zuccari G, Bassi AM, Vernazza S, et al. (2024) Development of a multilayer film including the soluble eggshell membrane fraction for the treatment of oral mucosa lesions. *Pharmaceutics* 16(10): 1342.
8. Gani A, Iskandar Z, Gani B, Diansari V (2025) Toxicity response of chitosan films on wound healing of oral mucosa epithelial cells, *in-vivo* and *in-silico* evaluation. *Research Journal of Pharmacy and Technology* 18(4): 1795-1804.
9. Goldberg M, Manzi A, Birdi A, Laporte B, Conway P, et al. (2022) A nanoengineered topical transmucosal cisplatin delivery system induces anti-tumor response in animal models and patients with oral cancer. *Nat Commun* 13(1): 4829.
10. Kali G, Fürst A, Efiana NA, Dizdarević A, Bernkop-Schnürch A (2023) Intraoral drug delivery: Highly thiolated κ-carrageenan as mucoadhesive excipient. *Pharmaceutics* 15(7): 1993.
11. Alhallak M, Karpukhina N, Patel M (2023) Triamcinolone acetonide release modelling from novel bilayer mucoadhesive films: An *in vitro* study. *Dent Mater* 39(6): 595-602.
12. Khaki S, Hadizadeh N, Rezaie SL (2022) Fabrication and characterization of betamethasone-loaded oral thin films as a novel drug delivery platform for oral lichen planus and recurrent mouth ulcers. *Journal of Ardebil University of Medical Sciences* 22(4): 393-408.
13. Shah S, Patel P, Ferguson A, Bagwe P, Kale A, et al. (2024) Buccal administration of a zika virus vaccine utilizing 3D-printed oral dissolving films in a mouse model. *Vaccines Basel* 12(7): 720.
14. Lee J, Khang D (2023) Mucosal delivery of nanovaccine strategy against COVID-19 and its variants. *Acta Pharm Sin B* 13(7): 2897-2925.
15. Hameed SA, Paul S, Dellosa GKY, Jaraquemada D, Bello MB (2022) Towards the future exploration of mucosal mRNA vaccines against emerging viral diseases; lessons from existing next-generation mucosal vaccine strategies. *NPJ Vaccines* 7(1): 71.
16. Pawar O, Godge R, Shinde G, Barde K, Vikhe A (2025) Design, development, and optimization of mucoadhesive buccal films of ganaxolone for enhanced bioavailability. *Journal of Applied Pharmaceutical Research* 13(2): 95-107.
17. De Caro V, Angellotti G, D'Agostino F, Di Prima G (2022) Buccal thin films as potent permeation enhancers for cytosine transbuccal delivery. *Membranes (Basel)* 12(11): 1169.
18. Kołodziejczyk M, Monika K, Justyna K, Małgorzata G, Michał NJ (2021) The formulation of mucoadhesive drug form for topical application in the oral cavity-application, manufacturing technology and testing methods. *Farmacja Polska* 77(10): 662-633.
19. Kristó K, Anahita S, Alharith AAH, Hala R, Krisztian P, et al. (2024) Study of the effect of temperature on the production of carrageenan-based buccal films and optimization of the process parameters. *Pharmaceutics (Basel)* 17(12): 1737.
20. Nair VV, Cabrera P, Ramírez-Lecaros C, Jara MO, Brayden DJ, et al. (2023) Buccal delivery of small molecules and biologics: Of mucoadhesive polymers, films, and nanoparticles-An update. *Int J Pharm* 636: 122789.