Yemen Journal of Medicine

https://yemenjmed.com

Article information

DOI: 10.63475/yjm.v4i2.0201

Article history:
Received: 01 September 2025
Accepted: 21 September 2025
Published: 23 September 2025

Correspondence to:
Syed Faizan Syed Nizamuddin
Email: syed22996@gmail.com
ORCID: 0009-0006-8339-1896

How to cite this article
Nizamuddin SFS. Orodispersible and mucoadhesive buccal films: Advances, formulation challenges, and future perspectives in oromucosal drug delivery. Yemen J Med.2025;4(2):294-302

Review Article

Orodispersible and Mucoadhesive Buccal Films: Advances, Formulation Challenges, and Future Perspectives in Oromucosal Drug Delivery

Syed Faizan Syed Nizamuddin[1]

1 Professor, Vidyabharti College of Pharmacy, Amravati, Maharashtra, India

ABSTRACT

Mucosal systems such as orally disintegrating films (ODFs) and mucoadhesive buccal films (MBFs) have gained attention and become a potential alternative to the conventional oral drug delivery systems, especially for patients who are geriatric or pediatric or those having difficulty in swallowing or drugs with extensive first-pass metabolism. Such films provide benefits, including a quick onset of action, increased bioavailability, and patient compliance. Successful development entails meticulous optimization of ingredients such as film-forming polymers, plasticizers, surfactants, taste maskers, and material selection for the corresponding manufacturing process, including solvent casting, hot-melt extrusion, 3D printing, and electrospinning. Limitations remain, with challenges including low drug loading capacity, no unified evaluation standard, stability problems, and regulatory vagueness of the liposome carrier. Emerging trends signal the promise of nanocarrier-based films, solid dispersions, and stimuli-responsive systems to circumvent these barriers. Personalization technologies, specifically 3D printing and natural and biodegradable polymers, are expected to broaden the clinical use of oromucosal films. This article provides an overview of the current state of development, along with formulation and manufacturing considerations of ODFs and MBFs, the role of which is significant in addressing translational and regulatory hurdles.

Key words: Orodispersible films, mucoadhesive buccal films, oromucosal drug delivery, patient compliance, bioavailability, dysphagia

INTRODUCTION

The oral route of drug administration in conventional dosage forms can be problematic for patients, and it may not result in the expected therapeutic benefits. Limitations such as poor pharmacokinetic parameters, hydrolysis in the acidic gastric environment, and first-pass metabolism in the liver can significantly erode the activity of a drug. [1] These limitations are especially problematic for certain populations of patients, including pediatric, geriatric, and mentally ill patients, and patients who cannot swallow or who feel nauseated. [2] For the aforementioned patients, new oromucosal drug delivery systems were formulated to potentially alleviate some of the problems associated with conventional dosage forms. [1,3] Specifically, orally disintegrating films (ODFs) and mucoadhesive buccal films (MBFs) have emerged as new drug delivery systems with several advantages. [4,5] The oral cavity is a favorable tissue absorption area; due to its rich vasculature and relatively low enzymatic activity, it allows systemic absorption of the drug with no hepatic first-pass metabolism to subsequently improve the bioavailability of the drug and therapeutic effect. [1,3] ODFs are ultra-thin films that disperse in saliva within minutes and can be taken without water, offering convenience to patients who have challenges and cannot swallow tablets or capsules. [6,7] MBFs are films that adhere to the mucosal surface of the oral cavity, allowing drug residence time, in

addition to sustained release of the drug and drug-mucosal membrane interactions. [1,3] The properties of oromucosal films are beneficial for drugs with requirements for rapid onset of action, enhanced absorption, or increased patient experience, and include agents such as cytisine for smoking cessation, [1] telmisartan for antihypertensive, [2] vitamin D3 for supplementation, [6] and various agents for pain, migraine, diabetes, and opioid or nicotine dependence. [3] Recent studies also continue to demonstrate the utility of these dosage forms. ODFs have the advantage of enhancing patient compliance by disintegrating quickly and ease of administration, especially for pediatric and geriatric patients, as shown in the literature. [4,6,7] It has been documented that MBFs are believed to act as controlled drug delivery mimics, leading to enhanced drug permeation and maintaining drug release to achieve better therapeutic effectiveness. [3,5] In addition, the potential to increase bioavailability, circumvent first-pass metabolism, and broaden applicability for various therapeutic classes by being versatile and patient-friendly drug carriers further validates their use as a drug delivery system platform. [2,3,6]

SEARCH STRATEGY

A systematic literature review was completed in PubMed, Elsevier, Taylor & Francis, and MDPI databases to identify literature on mouth dissolving films, orally disintegrating films (ODFs), buccal films (BFs), orally thin films, fast dissolving films, drug delivery systems, enhancing bioavailability or drug release, formulation, evaluation, manufacturing techniques, stability studies, incorporation with patient compliance, and regulatory requirements, as well as emerging drug delivery technologies available in English from inception to July 2025. The search employed combinations of keywords and Boolean operators for methodology. Additionally, articles identified through examining reference lists from identified studies were also considered.

Emphasizing original research papers, systematic reviews, and meta-analyses related to their stability studies and formulations associated with ODF and BF systems were included.

FORMULATION CONSIDERATION

The successful development of ODFs depends on the careful selection and optimization of various components and manufacturing processes. The main formulation considerations are given below.

Active pharmaceutical ingredient (API)

ODFs can contain a variety of APIs, both soluble and poorly soluble, with varying therapeutic effects (e.g., antitussive, anti-epileptic, anti-asthmatic, anti-emetic, and antihypertensive medications). [8–10] Low-dose APIs are typically favored for use in ODFs. [10] A significant constraint in ODFs is the relatively modest and restricted amount of medicine that can be employed–API levels in the final formulation typically range from 1% to 25% w/w. [9–11] Drug candidates must have acceptable buccal mucosal penetration, great taste masking, and water resistance. Polymorphism, particle size, and hygroscopicity are important physical-chemical characteristics that affect how the API performs in ODF formulations. Furthermore, the medication's pH should be similar to that of saliva. [2,9–11,13].

Film-forming polymers (hydrophilic polymers)

The polymers form the physical structure and matrix of the film; they are one of the most important factors affecting the film's mechanical strength, disintegration, and dissolution. [2,9,10,12] Typically, these polymers are hydrophilic, enabling hydration and dissolution when they are placed in saliva. [9,10] Some common examples are hydroxypropyl methylcellulose (HPMC), pullulan, polyvinyl alcohol (PVA), carboxymethyl cellulose (CMC), sodium alginate, starch, and gelatin. [9,10,12] The concentration of the polymer is an important consideration and is usually around 45% w/w of dry film. The concentration of the polymer used can be raised to increase the helpful qualities to be achieved. [2,9] For example, if a relatively high concentration of HPMC is used, stability and mechanical strength increase [9,10] while also most likely causing an increased disintegration time. [9,12,13] Furthermore, these polymers must be safe, nontoxic, non-irritant, and affordable, as well as have the appropriate shelf life, ease of application, tensile strength, and film thickness, as these attributes have a significant impact on ODF performance. Oral films typically have a thickness of 50 to 1000 µm (0.05–1.0 mm), which is crucial for accurate dosing, mechanical strength, and disintegration. [9–12]

Plasticizers

They are incorporated to enhance some mechanical parameters, such as tensile strength and percent elongation, to improve film processability, spreadability, and flexibility in a film dosage form. [9,10] These excipients work by lowering the glass transition temperature of polymers. [9,10] Common examples are polyethylene glycol (PEG), propylene glycol (PG), glycerin, diethyl phthalate, and triethyl citrate. [2,9,10] The concentration of plastic amide typically ranges between 0% and 20% w/w. [9] Concentration should be carefully optimized because higher concentrations can cause tacky films or stability issues. After all, it can impair moisture resistance. [10]

Surfactant

Surfactants are dispersing, wettability, and solubilizing agents that are important in allowing quick film disintegration and drug release. Examples are benzalkonium chloride, tweens, sodium lauryl sulphate, and poloxamer 407. [9,10]

Taste masking agents (flavors and sweeteners)

These agents are important for patient acceptance and adherence, especially for medications that have an unpleasant taste or bitterness. [9,10] Sweetening agents can be either natural (e.g., glucose, fructose, or sucrose) or synthetic (e.g., sucralose, acesulfame-K, or aspartame). [9,10]

Flavors

Flavors (e.g., mint, fruit essences, etc.) are used to further improve organoleptic properties; however, patients experience differences in preference based on age group. [10]

Saliva-stimulating agents

These agents, generally acidic, will stimulate the production of saliva in the buccal cavity, which facilitates ODF disintegration.

Examples are citric acid, malic acid, tartaric acid, and ascorbic acid. [9,10]

Coloring agents

Pigments (e.g., titanium dioxide and a variety of FD&C colors) can be used for aesthetics. [9,10] Concentrations should be kept to under 1% w/w. [10]

Permeation enhancers

Permeation enhancers are utilized in mucoadhesive films to promote drug permeation across the buccal and sublingual mucosa to facilitate the opportunities for systemic absorption. Examples of permeation enhancers include dextran sulfonated, cyclodextrin, and menthol. [10] The effect of disintegration agents can be complex and, in some cases, contradictory, as studies have shown that disintegration time can sometimes be increased or not affected at all instead of decreased. [11] At high concentrations of super disintegrants, gelling can occur, which can further delay disintegration. [13]

METHODS OF PREPARATION

The development of orally disintegrating films (ODFs) and BFs, especially those made with cellulose ethers (CEs), can be done using several different methods that have their own merits and constraints. The most prevalent methods of ODFs and BFs include solvent casting, hot-melt extrusion (HME), printing technologies (3D and inkjet printing [IJP]), and electrospinning methods. [14–17]

Solvent casting method

The solvent casting method (**Figure 1**) is one of the main techniques to make films that can dissolve in the mouth or are mucoadhesive. A main reason for its broader utilization stems from the fact that it is a relatively simple and cheap technique. In this method, you would dissolve a film-forming water-soluble polymer such as HPMC, methylcellulose, or hydroxyethyl cellulose in a suitable solvent and add the API with the goal of obtaining a homogeneous slurry. The coordinates are de-aerated and cast onto a release liner to dry into a drug-loaded polymer film. Among those variations from the process parameters that might affect the final product quality are the type of polymer, the grade of polymer, plasticizer concentration (e.g., glycerin, PG, PEG 400), the solvent selected, and the characteristics of the API: solubility, drug load, and taste. Above all, mixing and the efficacy of de-foaming are very important, for if the API is unable to be properly dispersed, agglomeration of the API may occur, which can lead to process insufficiencies and structural defects. The casting properties (i.e., viscosity, casting rate, and liner properties) dictate the film thickness, morphology, and content uniformity. The factors that impart the most important impact on the final product characteristics (i.e., less brittle, tacky, and stability) are the drying temperature and time, as well as the residual moisture level. While cutting, packaging, and storage conditions are crucial for dose accuracy, mechanical stability, and protection from environmental damage, solvent-cast films are uniform in thickness and display good mechanical and flexible properties, but may undergo solvent release, leading to embrittlement, and organic solvent use poses environmental and health concerns. [14–17]

Hot-melt extrusion (HME)

HME, using no organic solvents, is an alternative to solvent casting. HME (**Figure 2**) relies upon feeding a mixture of polymers, drugs, and excipients to an extruder, whereby it is exposed to elevated shear and temperature to generate a uniform melt. [14,15] The fluidized material is subsequently cast onto a target surface to create a smooth film, before being cut to the appropriate film size. Hydroxypropyl cellulose (HPC) is a CE that is commonly used in HME, as it provides lower viscosity and temperatures when compared to other grades. [14] HME can also facilitate poorly soluble drugs to become a solid dispersion or solid solution form and is effective for creating slow-release films. However, HME is not appropriate for heat-sensitive APIs, and it can cause the recrystallisation of drugs upon temperature decrease. [14,15]

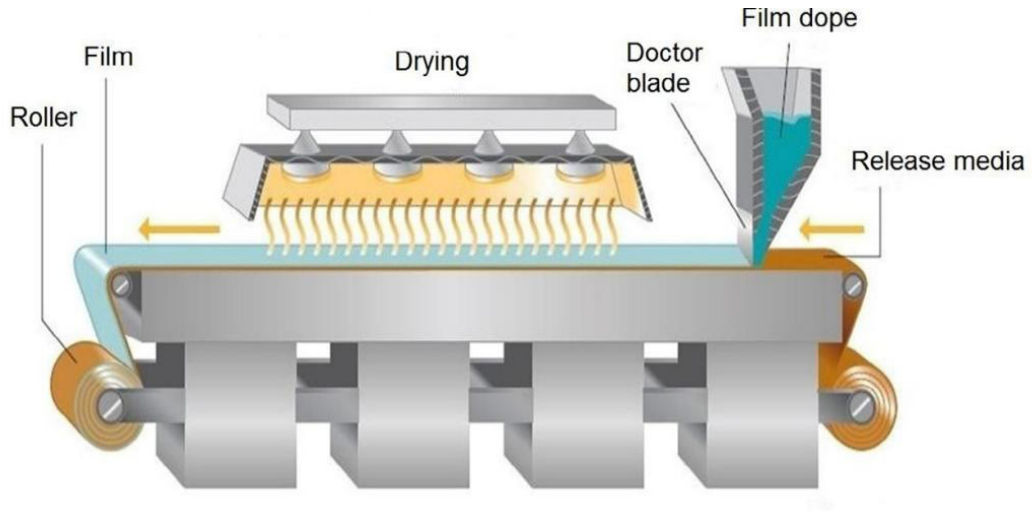

Figure 1: Commercially available solvent casting system for the preparation of films. [15]

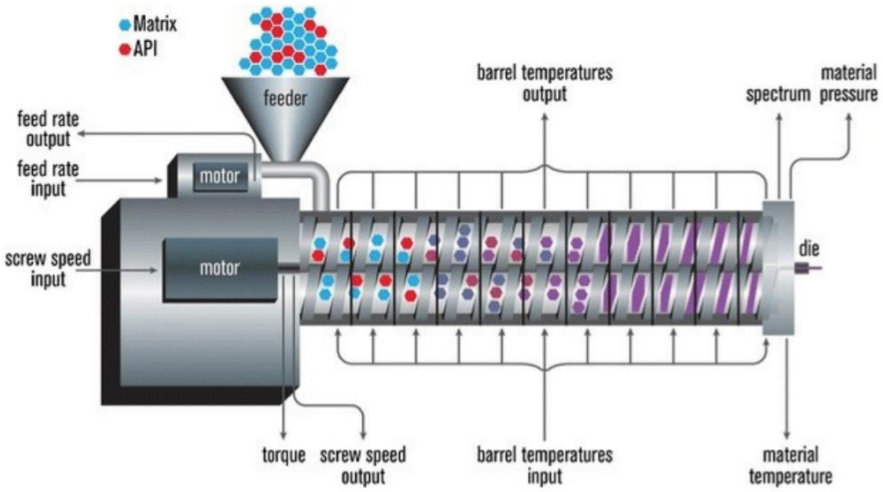

Figure 2: Hot melt extrusion equipment. [10]

3D printing technologies (3DP)

3DP offers a new method for manufacturing polymeric thin films, including the ability to create customized and personalized medicine. [14,15,18–20]

Inkjet printing (IJP)

IJP, or ink deposition printing, is an up-and-coming technology that can be used to produce buccal and/or ODFs with high efficiency, high precision, and repeatable accuracy through the micro-deposition of drug-loaded solutions onto blank substrates. [21] Either continuous inkjet or drop-on-demand printing modes can be used; the drop-on-demand mode ejects droplets only when you want/need them, allowing ink waste to be minimized and ejection accuracy maximized. [22,23] Different kinds of hydrophilic cellulose polymers, such as HPMC, HPC, and carboxymethyl cellulose sodium (CMC-Na), are commonly used as film-forming excipients. IJP is designed for formulations needing low doses and personalized medicine, because it relies heavily on the rheological properties of the printing ink for its uniformity. Further, additional layers of drug can be printed to tailor release properties, improve stability, or suppress drug crystallization. [24] Although IJP has the advantages of precision and versatility, it is currently less suited for commercial use on a high-volume basis system because of scalability and robustness, mostly in the overall process. [22,23]

Flexographic printing

Flexographic printing represents a new method for producing drug-loaded films designed for the high-output packaging and labelling sector, to make drug-loaded films continuously online, roll-to-roll, with high output. Flexographic printing is scalable, economic, and appropriate for patient-specific and/or low-dose formulations and allows for multi-layering of films to modify release characteristics. The quality of the film about the accuracy of the intended dose is determined by the ink flow properties, as well as the relief plate design and printing pressure. Disadvantages include crystallization of the drug upon drying, limitations with inks that are highly viscous, and limitations of substrates to achieve even deposition. [19,25]

Fused deposition modelling (FDM)

FDM is a well-established 3D printing technique where a drug–polymer filament (typically prepared in a hot-melt extruder) is heated and extruded to create a 3D product in layers. [14] FDM can be used to print BFs containing HPC, using melt temperatures of 150°C to 230°C. [14, 23] FDM enables geometric control over the film, and dosing can be individualized to give custom drug release profiles. [14,23,24] FDM offers advantages in this dosage form development, but is limited to thermoplastic printer materials. [14]

Electrospinning

Electrospinning is a newly advanced nanotechnology-based technique that uses high-voltage electrostatic forces to create ultrafine nanofiber films from polymer solutions or melts. [14,26,27] The films have a high specific surface area and porous structure, which enhances drug-loading efficiency and permeability and enhances rapid drug release. [14,26,28] Therefore, electrospinning is suited for ODFs requiring rapid dissolution time and to enhance the solubility of poorly water-soluble drugs in the amorphous state. [14,29,30] The residual solvent found in the final electrospun fibers is also minimal and lends an advantage. [14,30] Although the prospect of using CE in electrospinning to create ODFs has potential, the application is relatively limited. While CEs are incorporated into ODFs, it is typically part of a blended formulation involving another carrier, such as PVA or polyvinylpyrrolidone. [14,30,31].

Limitations of 3D Printing

- The printability and uniformity of a film rely heavily on the rheological properties of the printing ink or slurry. [21,22]
- It is hard to scale up, and methods like IJP are not suitable for high-throughput manufacturing. [23,24]
- The use of FDM is confined only to thermoplastic polymers; thus, it is limited to the production of heat-sensitive drugs. [20,32]

- The reliance on synthetic polymers in electrospinning results in decreased scalability and acceptance by regulatory authorities. [33]
- Although multi-layered films provide release control, they still have the problem of increased manufacturing complexity and cost. [24,25]

EVALUATION

Physical properties

ODF film is assessed for the appearance of uniformity, color, transparency (**Figure 3**), smoothness, texture, and defect-free air bubbles, white patches, and insoluble particles. [34–37] If the drug loading of the ODF is above 10% (w/w), the films can appear opaque, and white patches signify drug precipitation. [35]

Size

ODF size can be referenced in terms of length, width, and thickness. A uniform thickness is required for the proper release and absorption. [6,34] ODFs are acceptable at 2 × 2 cm^2 with the films at a maximum thickness of 100 µm. [34] The thickness is typically measured via digital micrometer or vernier calipers at multiple locations. [34,35,38–40]

Weight uniformity

Weight uniformity refers to the variability of film weight representation across units in a batch. This is determined by calculating the deviation of an individual from the average weight. [34,36,39] Since the majority of ODFs studied typically have a weight variation of 100% ± 1.5%, if the weights are within those pre-described limits, it passes the weight uniformity test. [35]

Surface area

Surface area can influence the rate of disintegration as well as dissolution. Surface area is determined geometrically (length × width) for ODFs that are rectangular in dimension. [34]

Surface PH

The surface pH may be an indication of the irritation potential when the ODF, when released, comes in contact with the mucosa. A film is placed into distilled water, and a pH electrode is used to record when a steady reading is made. [34,35,37,39]

Moisture content (loss on drying)

Moisture content can influence stability, rate of disintegration, and mechanical strength of the film. Moisture is determined via thermogravimetric balance at 105°C until constant weight is observed. [34,37,39,40]

Tensile strength and elongation

Tensile strength is one of the key properties that define the stability of a film, such as being able to resist stretching or rupture under tension. [34,38] Usually, for such a test, films are cut into 10 × 50 mm strips or 2 cm diameter circles and fixed in a texture analyzer or tensile tester like the TAXT2i, Instron Model 1128, or LabThink auto stripping tester. [35,36,38,39] The sample is stretched slowly to the point of breakage, and the maximum force at break is recorded. TS is computed by dividing the maximum load at break by the cross-sectional area, while percent elongation represents the film's stretch before rupture. Mechanical properties such as tensile strength

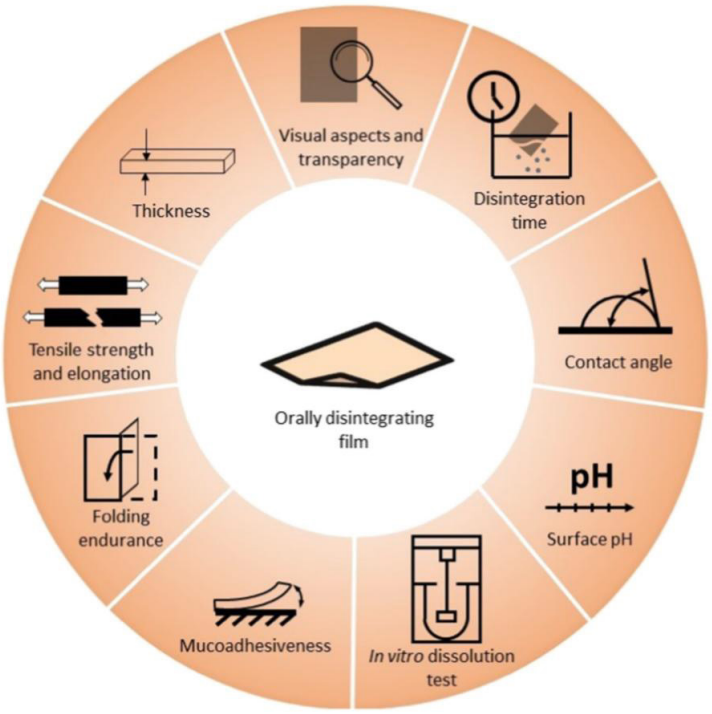

Figure 3: Characteristics of oral disintegrating/dispersible film. [17]

can be greatly altered by a multitude of factors, like polymer concentration, drug loading, plasticizer content, nanofillers, and film homogeneity, with higher polymer content usually resulting in a higher tensile strength, whereas higher drug loading or super-disintegrant content may lead to a decrease in it. [34–36,40]

Folding endurance

The number of times a film may be folded prior to breaking, which indicates flexibility and durability. A value greater than 16-fold [35] or a value nearer to 300-fold is indicative of good endurance. [34,39]

Mucoadhesive strength

This study evaluates the film's ability to remain adhered to the mucosa and measures how the film lowers the risk of swallowing or aspirating. Detachment forces are used to assess this feature. [34,36] Mucoadhesive polymers improve this property even more. [39]

Disintegration time

The disintegration test is used to measure the ability of ODFs that are designed to rapidly dissolve upon contact with a fluid, which is usually simulated salivary fluid. [34] Disintegration tests can be performed using various methods, such as the slide frame, immersion in a Petri dish, the drop method, the beaker method, and automated disintegration testers like the PharmaTest® PTZ AUTO EZ. [34–36,39,40] The typical test conditions are a temperature of 37 ± 0.5°C and the use of simulated saliva or distilled water as a medium. The thickness of the film is inversely proportional to the disintegration time, so that thinner films disintegrate faster, and in addition to that, the polymer type and concentration, the molecular weight, the additives (e.g., super-disintegrants, saliva stimulants, mucoadhesive polymers), drug loading, water sorption, and particle size of the embedded components all influence the rate of disintegration. [34,35,38–40] Even though there are no official guidelines for ODFs, disintegration times less than 180 seconds are generally regarded as acceptable when compared with reference values of USP and European Pharmacopoeia (Ph. Eur.) Limits for orodispersible tablets. [38–40] Thus, a thorough investigation of these mechanical and disintegration properties provides assurance of appropriate film performance as well as patient acceptance.

In vitro drug release

In vitro drug release may be assessed with either the US Pharmacopeia apparatus II, the US Pharmacopeia apparatus V, or using Franz diffusion cells, in simulated salivary fluids at 37°C. Calculated parameters may include dissolution efficiency, mean dissolution time, and similarity factors. [34–37,39,40]

In vivo performance

In vivo performance for oral film formulations is typically assessed through pharmacokinetic or pharmacodynamic studies done in both animals and humans. Pharmacokinetic or pharmacodynamic studies focus on the values of C_{max}, T_{max}, and area under the curve (AUC) or other pharmacokinetic values that would show the absorption window for the drug being studied. Often, pharmacokinetic references are made to conventional tablet formulations to signify how oral films may provide beneficial mechanisms, especially with the onset of action and bioavailability over tablet formulations. [34,35,37,39] Pharmacodynamic research would typically look for the therapeutic efficacy of the ODF formulations using animal models (e.g., pain, inflammation). Overall, these studies confirm the clinical relevance of oral films and substantiate their use as an alternative drug delivery system capable of increasing compliance and possible efficacy.

Stability study

Studies on accelerated stability typically take place at 40°C ± 2°C and 75% relative humidity (RH) ± 5% for 3 months. While the product is in this condition, critical quality attributes, including drug content, dissolution characteristics, and mechanical properties, will be assessed to assure the product's stability and performance (**Table 1**). [34,37,39,40]

GAPS AND LIMITATIONS

Absence of characterization standards

A frequent problem during the creation of ODFs has been the lack of standardized methods for assessing properties of these films, especially mucoadhesion and other quality features of CE-based buccal films. Characterization of the materials in these cases is often not standardized, so it is difficult to compare the properties of films made from different natural polymers directly. For example, no standards have been set for the film's mechanical properties and mucoadhesiveness, and there are criteria, however, stating that films must be strong, ductile, flexible, and mucoadhesive. At present, the Ph. Eur. does not provide any specific methods, requirements, or definitions for oromucosal films based on biologically relevant data. Although the Ph. Eur. 8th edition refers to oromucosal preparations, there are no tests for the disintegration of ODFs and enough guidance for mechanical strength so far, only indicating that films should have appropriate mechanical strength to resist handling without being damaged. Similar problems may be found, for example, at the point of residual moisture requirements. This lack of clearly defined guidance statements is a factor that makes it difficult to produce a product of good quality and, at the same time, to compare the different oral films. [5,8,13,15–17,23,41]

Evaluation of taste masking

There really is a very limited set of testing procedures that can capture the sensory parameters responsible for the behavior of the acceptability of ODFs as the main factor. Taste is a very important factor for patient acceptance and adherence, especially in the case of unpalatable drugs; nevertheless, masking taste effectively and evaluating it all along in a very reproducible manner is still very challenging. In addition, the production of a delicious, candy-like taste also implies the risk of drug abuse, particularly in the case of children. [5,19,24,42–44]

Drug loading capacity

One of the major restrictions of film dosage forms is the limitation of the area in which a high load of API can be put. Orally disintegrating films (ODFs), usually with the dimensions of 2 × 2 cm^2 and a maximum thickness of 100 µm, have a very

Table 1: Commercially available films. [14]

Brand name	Company	Indication	API
Libervant	Aquestive	Seizure	Diazepam
Voglibose OD films	Emergency Products Industry Co., Ltd	Postprandial hyperglycemia in diabetes	Voglibose
Zolpidem tartrate OD films	Emergency Products Industry Co., Ltd	Insomnia	Zolpidem tartrate
Donepezil hydrochloride OD films	Emergency Products Industry Co., Ltd	Alzheimer's disease	Donepezil hydrochloride
Viagra OD film	Joint Venture of Vitoris	Erectile dysfunction	Sildenafil citrate
Rizaport 5 mg schmelz film	Regintel Ltd	Migraine	Rizatriptan benzoate
Olanzaran	Ranbaxy Belgium N.V.	Schizophrenia	Olanzapine
Suboxone	Indivior Inc	Opioid drug addiction	Naloxone hydrochloride, buprenorphine hydrochloride
Exservan	Aquestive	Amyotrophic lateral sclerosis	Riluzole
Sympazan	Otter Pharms	Epilepsy	Clobazam
Igalmi	Bioxcel	Schizophrenia, bipolar disorder	Dexmedetomidine hydrochloride
Kynmobi	Sumitomo Pharma Am	Parkinson's disease	Apomorphine hydrochloride

small space available for the formulation, which limits their use only to the highly potent active ingredients. Although the substances can be combined to total up to 15 mg or 30% w/w of the film mass, the raising of the dose is always followed by some problems, such as the API recrystallisation, which leads to an increase in transparency and brittleness, or slow disintegration. Besides, very thick films are prone to not being thoroughly dried and may have a bad taste and a long disintegration time, while very thin films may lack drug load and toughness. [9–11,15,19,41–44]

Shelf life and stability

From a stability standpoint, shelf life, as well as isolation from the environment, particularly moisture, is the most vital issue that affects ODFs. ODFs are generally moisture-attracted, and this fact requires them to be handled very carefully in order to preserve them for a long time. Water present in films in large amounts can cause them to be sticky, facilitate microbial growth, and also lead to the degradation of the API. On the other hand, with the removal of the remaining solvent, the films will be more and more brittle during storage. Industry production stages, such as prolonged drying times or elevated drying temperatures, can still exert a negative influence on the stability of APIs and excipients. Packaging is a factor that contributes a lot to the stability of the product, as the correct packaging is necessary to keep the product in its original state, such as the drug dissolution rate. [5,15,16,19,43–45]

3D printing regulatory framework

The murky nature and ever-evolving regulations surrounding 3D-printed medical devices remain the primary cause of the slow uptake of 3D-printed medical devices, as there are no set standards or confirmed quality assurance or testing procedures. Though the US FDA gave the guidance on additive manufacturing for medical devices in 2017, this paper only sketches out the regulatory framework and the chemistry, manufacturing, and control (CMC) needs, but does not really refer to quality control, printer specification, or in-process and finished product testing parameters for product quality consistency. Variances of 3D printers produced by different companies with dissimilar technologies, software, hardware, printing speeds, and qualities have a significant impact on dosage form consistency; thus, products from different manufacturers could confuse consumers, especially if they are not experts in this technology. Hence, there is a need for a deeper understanding from regulatory agencies and collaboration among researchers, manufacturers, and regulators. [43]

Gap in translation

One of the primary reasons why conducting scientists perceive little use of CEs in the production of buccal films is that they are not used as a base in any commercial goods, resulting in a very small market share for published scientific articles. The scarcity of CE-based buccal films on the market could be attributed to the lack of both compendial and biorelevant evaluation methodologies required for effective in vitro characterization of the dosage forms. The need for additional research to identify novel materials and strategies for improving drug delivery to the oral mucosa is overwhelming. [41]

Thermal sensitivity

Generally, the production of drugs that are very sensitive to temperature changes, such as opioids, which go through high-temperature processes, is significantly limited. HME is indeed problematic for thermolabile drugs, as it requires melting drug-loaded mixtures at high temperatures (50–180°C, some even at 150–230°C). FDM 3D printing, which also includes heating the polymer filaments, works at high temperatures between

150 and 230°C. At such a high processing temperature, the risk for thermal degradation arises, which in turn compromises the stability and therapeutic efficacy of the formulation. Some methods try to fuse different techniques (e.g., FDM with IJP) to incorporate thermostable drugs, but even so, the high temperatures seriously limit these technologies. [5,8,19,32,43]

FUTURE PERSPECTIVE

Orodispersible buccal films and MBFs are novel drug delivery systems that have been developed to mitigate the inherent limitations of traditional oral dosage forms that otherwise compromise bioavailability, patient consent, and therapeutic efficacy. Advances in polymer, excipient, and manufacturing technology, such as solvent casting, HME, three-dimensional printing, and electrospinning, have led to the evolution of buccal films with custom-made properties. Nevertheless, the problems of poor drug loading, stability, lack of a global quality evaluation framework, and regulatory challenges strongly prohibit large-scale implementation. Recent advancements in hybrid nanocarrier films, stimuli-responsive systems, natural polymers, and designs with a greater focus on patients enable opportunities for new oromucosal films. Rigorous scientific investigation and development of established quality and standardization approaches will be central to enabling innovative approaches in bringing these promising products to market for the betterment of patient care.

CONCLUSIONS

Orodispersible buccal films and MBFs are novel drug delivery systems that have been developed to mitigate the inherent limitations of traditional oral dosage forms that otherwise compromise bioavailability, patient consent, and therapeutic efficacy. Advances in polymer, excipient, and manufacturing technology, such as solvent casting, HME, three-dimensional printing, and electrospinning, have led to the evolution of buccal films with custom-made properties. Nevertheless, the problems of poor drug loading, stability, lack of a global quality evaluation framework, and regulatory challenges strongly prohibit large-scale implementation. Recent advancements in hybrid nanocarrier films, stimuli-responsive systems, natural polymers, and designs with a greater focus on patients enable opportunities for new oromucosal films. Rigorous scientific investigation and development of established quality and standardization approaches will be central to enabling innovative approaches in bringing these promising products to market for the betterment of patient care.

ACKNOWLEDGMENTS

The author is deeply appreciative of the valuable assistance and motivation offered by his teacher and colleagues of Vidyabharti College of Pharmacy, Amravati, Maharashtra, India, for the preparation of this review.

SOURCE OF FUNDING

None.

CONFLICT OF INTEREST

None.

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