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REVIEW

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Advances in oral dissolving film research in the food field

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Abstract

Oral dissolving film (ODF) emerges as a novel active substance delivery system, offering portability, safety, and compliance. ODF presents superior gastrointestinal absorption compared to conventional food products, making it ideal for providing nutrition and medication support to vulnerable populations such as children, the elderly, and individuals with dysphagia. With promising applications in pharmaceuticals and especially food industry, ODFs offer a highly absorbable method for delivering nutritious and healthy foods. This review underscores the potential of orally dissolving films in active substance delivery, outlining their advantages over traditional oral delivery methods and their current market status. Additionally, the review discusses the formulation procedure, production methods, and quality evaluation methods for film dosage forms of ODFs. Lastly, it examines the limitations of ODFs and speculates on their future trends in the food industry. This study serves as a valuable reference for the development and utilization of orally dissolving films in the food sector.

Keywords Oral dissolving film, Formulation process, Preparation method, Evaluation criteria

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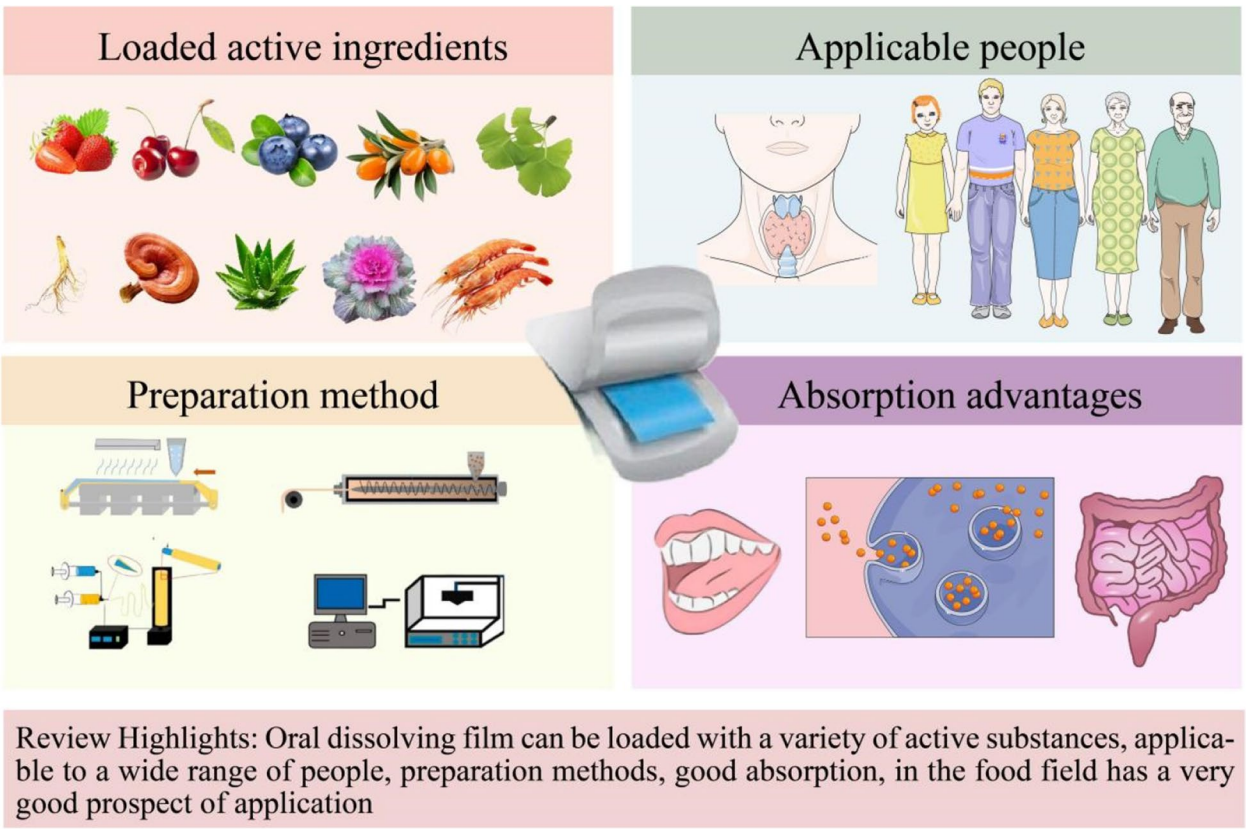
Graphical Abstract



Introduction

Traditional oral preparations like tablets, capsules, and liquids have drawbacks such as inconvenience in carrying, difficulty swallowing, and limitations for elderly individuals, children, those prone to nausea, or those under anesthesia (He et al., 2021). Hence, there is a need for safer and more convenient delivery systems (Fernandes, 2023; Lou et al., 2023). Oral dissolving film (ODF) emerges as a novel method for delivering active substances orally. It is portable, exhibits good safety and compliance features, and demonstrates significant potential for delivering active substances orally. Particularly for conditions such as Parkinson's disease, stroke, muscular disorders, and esophageal disorders, characterized by severe swallowing difficulties, ODF offers therapeutic active substances and essential micronutrients needed by the body (McIntosh, 2023). ODFs are also recognized in the United States Pharmacopeia (USP32-NF27) as thin sheets inserted into the mouth, potentially containing one or more layers of active substances. According to the 11th Edition of the European Pharmacopoeia, an ODF is a formulation designed for oral drug delivery. The Chinese Pharmacopoeia defines a film formulation as a film-like preparation created by processing a drug with a suitable film-forming material for oral or mucosal administration. Consequently, ODF is gaining increasing attention as a safe and effective new method of oral delivery. In the realm of food, ODFs function as effective carriers capable of delivering active ingredients, thereby enhancing the bioavailability of these components. They overcome barriers related to difficult absorption and low utilization of active ingredients, emerging as visible options for nutritional and healthcare products.

This paper examines the research trends concerning ODF, focusing on its advantages over traditional oral delivery, current market status, formulation process, preparation methods, and limitations. We conducted searches on the Web of Science, PubMed, and Scopus databases using keywords such as oral film, oral dissolution film, preparation method, development method, and detection method. We selected literature from the past decade, differentiating between research articles and

review articles. Subsequently, we focused on the formulation process of oral instant film, preparation methods, and applications in the food industry based on the content of the selected readings. In contrast to prior studies, this paper primarily evaluates the current market landscape, assesses the impact of formulation processes on membrane agent performance, and explores new preparation methods to further advance the development of ODF. It anticipates future research directions in the health food sector concerning ODF.

Differences between ODF and traditional active delivery

ODF, as a novel delivery method, offers advantages not found in other dosage forms. Compared to traditional oral routes, some active ingredients face limitations in human absorption due to various drawbacks such as low bioavailability, slow onset of action, poor solubility and permeability, intolerance to the acidic and enzymatic environment of the gastrointestinal tract, and susceptibility to hepatic first-pass effect (Karki et al., 2016). ODF facilitates rapid penetration and absorption of active ingredients without harming normal tissues while also shielding them from degradation in the acidic and enzymatic digestive environment. In terms of public acceptance, ODF outshines other oral preparations due to its portability and dosing flexibility afforded by packaging. It enjoys widespread acceptance for its ease of administration and dosage flexibility. Compared to traditional oral dosage forms, ODF is more readily absorbed in the oral cavity and suits a broader demographic, including the elderly, children, infants, individuals with swallowing difficulties, and the general populace.

The emergence of ODF as a new membrane agent that increases active ingredient absorption through its concentration flexibility has been widely studied in the pharmaceutical field, and for food-active ingredients, dietary supplements have been increasingly studied. The emergence of ODF as a novel membrane agent, enhancing active ingredient absorption through its concentration flexibility, has been extensively studied in the pharmaceutical field. Additionally, there is a growing body of research focusing on food-active ingredients and dietary supplements. Studies have investigated ODF loaded with natural active substances such as curcumin (Silvestre et al., 2023), micronutrients (Cupone et al., 2023), and apigenin (Takashima et al., 2022) to enhance their bioavailability in the human body. Furthermore, there is a rising interest in exploring other food ingredients for loading into ODF (Yuan et al., 2022). Numerous studies have conclusively demonstrated that ODF enjoys wide acceptance among various demographic groups due to its ease of administration, potentially leading to improved adherence to various active components (Abdelhakim et al., 2020; Laffleur & Keckeis, 2020). While ODF is not a new delivery technology, its easy absorption and portability make it promising for developing beneficial health and wellness products. This potential could significantly impact the future of the food industry (Bala et al., 2013; Garcia et al., 2018, 2020; Musazzi et al., 2019).

ODF current market situation

Initially, films were primarily utilized as oral fresheners loaded with active ingredients such as vitamins. For instance, in 2001, Pfizer developed an oral film tablet, Listerine, as an oral freshener. Subsequently, Prestige Brands introduced ODF, the first drug utilizing benzocaine and menthol to treat a sore throat. Another company followed suit, introducing ODF containing herbal saponin to address constipation (Preis, 2015). The FDA approved the first drug formulation of ODF, Zuplenz (ondansetron), in 2010, with suboxone (buprenorphine hydrochloride and naloxone) being the second FDA-approved drug. Gradually, ODF gained traction in the pharmaceutical field. However, during the early stages of market adoption, the standardization of the film was unclear, and challenges such as imperfect testing standards for vertebrae and drug load limitations arose. In recent years, with improved research on the quality of standard vertebrae in the film, ODF has transitioned from initial use in fresh dose products to clinical research (Cilurzo et al., 2018). Due to their convenient and effective delivery of active ingredients, ODFs have garnered significant attention from research institutions. While related products are available in the Chinese market, their exploration in the food industry remains limited. Various products, such as new melatonin ODFs (Musazzi et al., 2019), ODFs for protein delivery (Tian et al., 2018), and other healthcare-oriented ODFs, continue to be developed, expanding the market for film agents' applications (Table 1). However, the preparation of ODFs loaded with bioactives is currently widely studied in food processing. The application of ODFs in food aims to deliver dietary supplements or natural bioactive compounds to the body, including anti-inflammatory and antioxidant natural active ingredients from herbs (Bodini et al., 2020), the widely available but underutilized dietary polyphenol quercetin (Lai et al., 2015), the essential nutrient vitamin C (Cheng et al., 2024), and soy protein for bone health (Kaur & Santhiya, 2022). However, the selection of active ingredients requires caution as some are not yet approved for food use, potentially increasing costs, and ODFs may only maintain the bioactivity of the active ingredient for a brief period, posing limitations in functional food processing.

Table 1 Oral film products in China and international markets

District	Name of product	Effective ingredients	Standard	Year
China	Meperidine hydrochloride orally dissolved film	Meperidine hydrochloride	5 mg; 10 mg	2022
	Ondansetron orally dissolved film	Ondansetron	4 mg; 8 mg	2022
	Aripiprazole orally dissolved film	Aripiprazole	10 mg; 15 mg	2022
	Tadalafil orally dissolved film	Tadalafil	2.5 mg; 5 mg; 10 mg	2022
	Montelukast sodium orally dissolved film	Montelukast sodium	4 mg; 5 mg	2021
	Olanzapine oral dissolution film	Olanzapine	5 mg; 10 mg	2021
China Taiwan	Please orally soluble film	Sildenafil	100 mg	2021
	Caliberi Orodispersible Film	Tadalafil	5 mg; 20 mg	2020
FDA approval for marketing	Diazepam	Diazepam	5 mg; 7.5 mg; 10 mg, etc	2022
	Buprenorphine hydrochloride and naloxone hydrochloride	Buprenorphine Hydrochloride; naloxone hydrochloride	8 mg;12 mg	2022
	Igalmi	Dexmedetomidine hydrochloride	0.12 mg;0.18 mg	2022
	Buprenorphine hydrochloride	Buprenorphine hydrochloride	0.075 mg; 0.15 mg; 0.3 mg, etc	2021
	Kynmobi	Apomorphine hydrochloride	10 mg; 15 mg; 20 mg	2020
	Buprenorphine hydrochloride and naloxone hydrochloride	Buprenorphine Hydrochloride; naloxone hydrochloride	2 mg; 4 mg	2020
	Exservan	Riluzole	50 mg	2019
EU approval for marketing	Emylif	Riluzole	50 mg	2022
	Kynmobi	Apomorphine hydrochloride	30 mg	2022
	Isicort	Dexamethasone	4 mg; 6 mg; 8 mg	2021
	Setofilm 4/8 mg schmelzfilme	Ondansetron	4 mg; 8 mg	2019
PMDA approval for marketing	rusefi OD film 2.5 mg	Rousseffi	2.5 mg	2022
	Ondansetron OD film 4 mg「GFP」	Ondansetron	2 mg; 4 mg	2019
	Revactio OD film 20 mg	Sodium citrate	20 mg	2018
	Zolpidem tartrate OD film	Zolpidem tartrate	5 mg; 10 mg	2012
	Donepezil hydrochloride OD film	Donepezil hydrochloride	3 mg; 5 mg; 10 mg	2013

Oral dissolving film formulation process

ODF necessitates a suitable skeleton material to carry the bioactive substance and facilitate rapid dissolution within the oral cavity, such as in the buccal or sublingual mucosa (Illangakoon et al., 2014). Generally, ODF consists of active substances, film-forming materials, plasticizers, and flavor modifiers, all of which must be non-toxic, edible, and compliant with film agent requirements. Most film agents have compositions comprising 0–70% (W/W) active substances for primary loading, 30–70% film-forming materials, 0–20% plasticizers, 1–2% surfactants, 0–20% fillers, 0–2% (W/W) coloring agents, and appropriate quantities of release agents (Turković et al., 2022).

Film-forming materials

Film-forming materials represent the most crucial components of ODF, directly impacting the rate of active substance release and compatibility with the membrane agent (Salawi, 2022). These materials fall into two main categories: natural and synthetic or semisynthetic polymers. The first category includes natural materials like chitosan, sodium alginate, hyaluronic acid, starch, and gelatin (Pacheco et al., 2021). The second category comprises synthetic or semisynthetic polymers such as hydroxypropyl methylcellulose (HPMC), hydroxypropyl cellulose (HPC), polyvinyl alcohol (PVA), and polyethylene glycol (PEG) (He et al., 2021). Researchers often favor natural polymers over synthetic ones due to their perceived safety and consumer reassurance. However, membrane agents derived from natural polymers can be unstable. Therefore, recent studies tend to combine multiple natural polymers to enhance stability. For instance, Qin et al. (2019) utilized electrostatic spinning technology to produce chitosan/prulan polysaccharide composite nanofiber ODFs, resulting in improved thermal stability, good water solubility, and well-spun membrane agents. To further bolster stability and active ingredient release, some studies employ a combination of natural

and synthetic film-forming materials. Chen and Doyle (2022) developed oral films containing homogeneous drug nanoparticles embedded in a dry HPMC matrix, yielding highly effective oral films with adjustable release rates.

Plasticizers

Plasticizers are primarily utilized in film agents to enhance their toughness and prevent breakage or cracking. Common plasticizers, such as propylene glycol, polyethylene glycol, glycerol, and sorbitol, typically improve the mechanical characteristics of oral film agents. Variances in plasticizer usage and the type of film-forming material employed can influence the quality of the final product. Mazumder et al. (2017) investigated the impact of plasticizer-to-film-former ratio variables on ODF quality, revealing a sensitivity of dissolution rate to this ratio. This underscores the critical role of the plasticizer-to-film-former ratio in ODF manufacturing. Research has also explored the use of multiple plasticizers in combination to enhance film agent performance. Relevant tests have shown that employing different plasticizer blends yields more satisfactory improvements in film mechanical features. Shojaee et al. (2020) elucidated that polyvinyl alcohol (PVA)/chitosan blends and polyethylene glycol/glycerol exhibited synergistic plasticizing effects, enhancing blend compatibility and improving elongation at break. Such film agents boast favorable mechanical and morphological properties and hold promise for applications in the food industry.

Disintegrants

Disintegrants facilitate the rapid breakdown of tablets into fine particles in gastrointestinal fluid, allowing for swift dissolution, absorption, and effectiveness of functional components. They are commonly employed in tablets, capsules, and membranes to achieve the disintegration and release of active ingredients. Commonly used disintegrating agents include low-substituted hydroxypropyl cellulose and cross-linked sodium carboxymethyl cellulose. ODFs function within the oral cavity, requiring swift release of loaded active chemicals, necessitating the addition of a disintegrant. Excellent film agents typically disintegrate within approximately 30 s, with most falling within the range of 30 to 120 s. In a study by Alghaith et al. (2022), utilizing flibanserin as a fast-dissolving oral film agent and cross-linked povidone as a disintegrant, optimization of the formulation process yielded good physical and mechanical properties, achieving an optimized disintegration time of 30 s. This film agent bypasses the first-pass effect, offering fast-acting properties that enhance bioavailability, making it superior to traditional dosage forms. Some studies have highlighted the benefits of natural disintegrants, such as their non-toxic disintegration properties. Draksiene et al. (2021) utilized the natural polymer chitosan as a superdisintegrant in rapidly orally disintegrating meloxicam tablets, resulting in favorable mechanical and disintegration properties, as well as impressive dissolution rates. However, there is limited research on the incorporation of natural disintegrants in ODFs, likely due to their potential impact on film agent stability.

Sweeteners

The mouth is the most sensitive organ for taste in humans, and many filmic agents loaded with active ingredients or substances taste bitter. This necessitates the use of sweeteners to improve the taste of the film agent. However, ODFs are specifically designed for children or older adults with swallowing difficulties, making their taste requirements more significant than those of other dosage forms. Various types of sweeteners, both natural and synthetic, are employed in research. Sweeteners are particularly common in ODF products with health benefits. For example, erythritol was FDA-approved as a flavor modifier in Strative Pharmaceuticals' ondansetron ODF formulation Zuplenz in 2010. Abou-Taleb et al. (2022) screened three sweeteners (sorbitol, acesulfame K, and sucralose) to solubilize and mask the bitter taste of vardenafil loaded with biodegradable polymeric materials. Their findings indicated that while the solubilization capacity of the three sweeteners was comparable, ODFs based on sucralose or acesulfame K exhibited superior sweetness and palatability compared to those containing sorbitol.

Stabilizers and thickeners

Typically, oral film agents begin with the preparation of the first active ingredients and excipients in a solution or suspension. To maintain consistency in the active components or suspension, stabilizers or thickeners are necessary additives. Commonly utilized stabilizers and thickeners include pectin and cellulose derivatives. Additionally, some studies have incorporated cosolvents, such as Tween 80, to expedite solvent dissolution and active ingredient release.

Due to its characteristics, such as adhesion and disintegration in the oral cavity, ODF requires excipients to serve as a backbone alongside the active ingredient in its formulation. The film-forming material acts as the backbone, necessitating careful consideration of the stability of the film agent loaded with the active substance. The polymer used should be safe and non-toxic. Other additives, including disintegrants, plasticizers, and sweeteners, are also essential for achieving the desired quality performance and pleasant taste of ODF. Ensuring

compatibility between these excipients and the active ingredients is crucial, especially in food research. Interactions between active substances and these excipients can result in the loss of desirable active ingredients, as well as potential side effects and toxicity (He et al., 2021). When these necessary additives are combined, mouth-soluble films of consistent quality, good performance, and pleasant taste can be produced.

Preparation process

ODF consists of flat sheets that are inserted into the mouth. These sheets comprise very thin polymer strips containing an active ingredient designed to break down within seconds in the mouth, thus enhancing the efficacy of the active ingredients (Hoffmann et al., 2011; Jaiswal, 2014; Silva et al., 2015). Numerous studies have demonstrated the versatility of ODF for both food and pharmaceutical applications. For instance, Yu et al. (2022) utilized 3D printing to prepare curcumin-containing ODFs, customizing health and nutritional products. Heinemann et al. (2013) developed ODFs for delivering probiotics in the oral cavity, serving as a simple and innovative carrier for probiotic intake. Ockun et al. (2022) extracted ODFs from anthocyanin-rich Vaccinium myrtillus fruit extracts to improve anthocyanin bioavailability in the human body, enhancing nutritional value. Additionally, Saha et al. (2013) formulated a new probiotic oral film for treating/preventing oral diseases and serving as a biotherapy agent for oral health. Common techniques for preparing ODF include solvent casting, hot melt extrusion, electrostatic spinning, printing, and electrostatic spray deposition (Fig. 1).

Solvent casting

Solvent casting has become the most practical and widely utilized method for their preparation. In this process, film-forming substances, active ingredients, and other edible excipients are dissolved or dispersed in water and stirred at high speed. This action helps to discharge air bubbles from the liquid, which is then spread in a mold or directly coated into a film. Finally, the film is cut and packed according to specifications and opened before use (Fig. 2). Prajapati et al. (2018) utilized the solvent casting method to formulate oral films of zolmitriptan with purulan polysaccharide, optimizing their properties and ensuring stable zolmitriptan preparation. Similarly, Shah et al. (2022) employed the solvent casting method to design and develop an oral membrane containing zolmitriptan with excellent properties for the treatment of migraines.

The solvent casting method is simple, versatile, and suitable for industrial manufacturing. However, strict regulation of production parameters is essential throughout the process. Additionally, this method requires the use of a significant amount of volatile organic solvents, which can lead to solvent residue and safety concerns. Furthermore, the final products may exhibit issues such

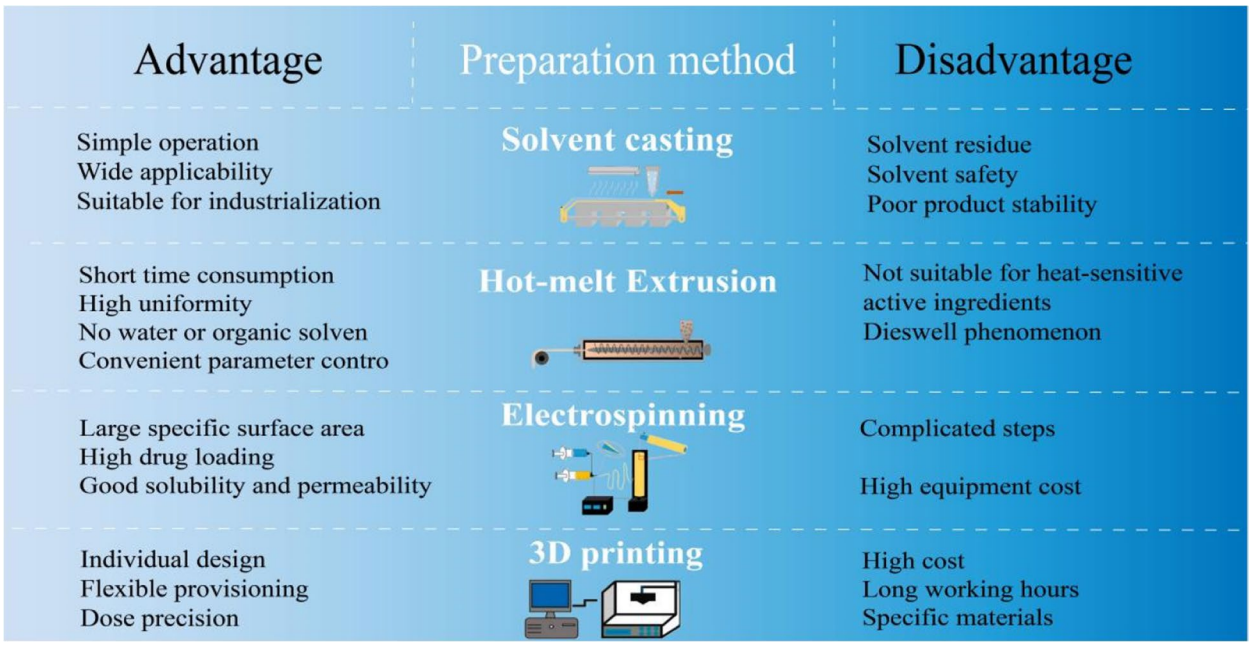


Fig. 1 Comparative chart of advantages and disadvantages of oral dissolving film preparation methods. (Pant et al., 2019) Copyright 2019 Pharmaceutics., (Elkanayati et al., 2022) Copyright 2022 Elsevier B.V

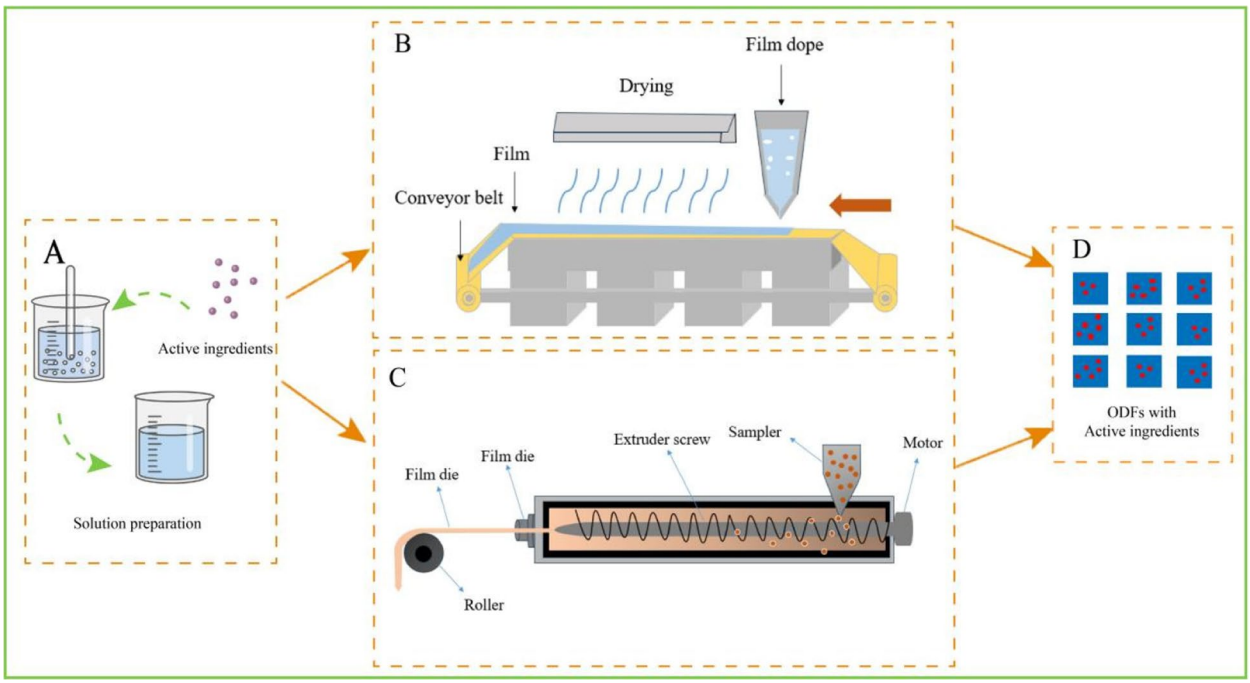


Fig. 2 **A** Preparation of solutions containing active ingredients. **B** Diagram of the solvent pouring method. **C** Diagram of the hot melt extrusion method. **D** Preparation of orosol films with active ingredients

as a rough film surface, variable film agent thickness, and poor product stability (Ferlak et al., 2023).

Hot-melt extrusion method

Hot-melt extrusion (HME) is essentially a method for shaping thin films from a molten mixture of raw materials and excipients. During the preparation process, the active ingredients, film-forming material, and other excipients are mixed and heated to their melting point to create a homogeneous molten mixture. This mixture is then forced through a perforated die with external pressure to form the desired film. Finally, the film is chopped, chilled, and packed to produce the final product (Fig. 2). Cho et al. (2020) utilized hot melt extrusion combined with 3D printing to prepare ODF from olanzapine. The results demonstrated that this technique enables the rapid preparation of personalized films with stable properties and a fast dissolution rate. Similarly, Speer et al. (2018) developed an oral film containing anhydrous theophylline as the model ingredient and polyacrylic resin as the matrix-forming agent using solvent calendering combined with hot melt extrusion. This film exhibited rapid disintegration and prolonged release of the active ingredient. HME is increasingly employed in industry as a solvent-free continuous process that offers improved content uniformity (Jani & Patel, 2015).

HME is a brief and efficient manufacturing process that eliminates the need for water or organic solvents, as well as heating and drying. Additionally, active ingredients and excipients are uniformly dispersed in the molten state, resulting in a film with excellent content homogeneity. This method offers straightforward parameter control throughout manufacturing and minimizes waste of raw materials and excipients. However, the HME method requires precise formulation and has limitations regarding the compatibility of certain active ingredients, particularly heat-sensitive ones. The melting process can affect the stability of the API, as well as the taste and stability of the polymers, making it unsuitable for temperature-sensitive bioactive molecules. Another challenge associated with HME is the phenomenon of off-die swelling, also known as the balas effect, which can significantly diminish film properties.

Electrostatic spinning

Electrostatic spinning, also known as electrospinning, is a common technique used for preparing nanofibers. When subjected to an electric field, droplets of the polymer solution can transition from spheres to cones and then further extend into nanoscale filaments. As the potential of electrostatic spinning has been explored, it has found widespread use in recent years for producing oral films loaded with active substances (Fig. 3).

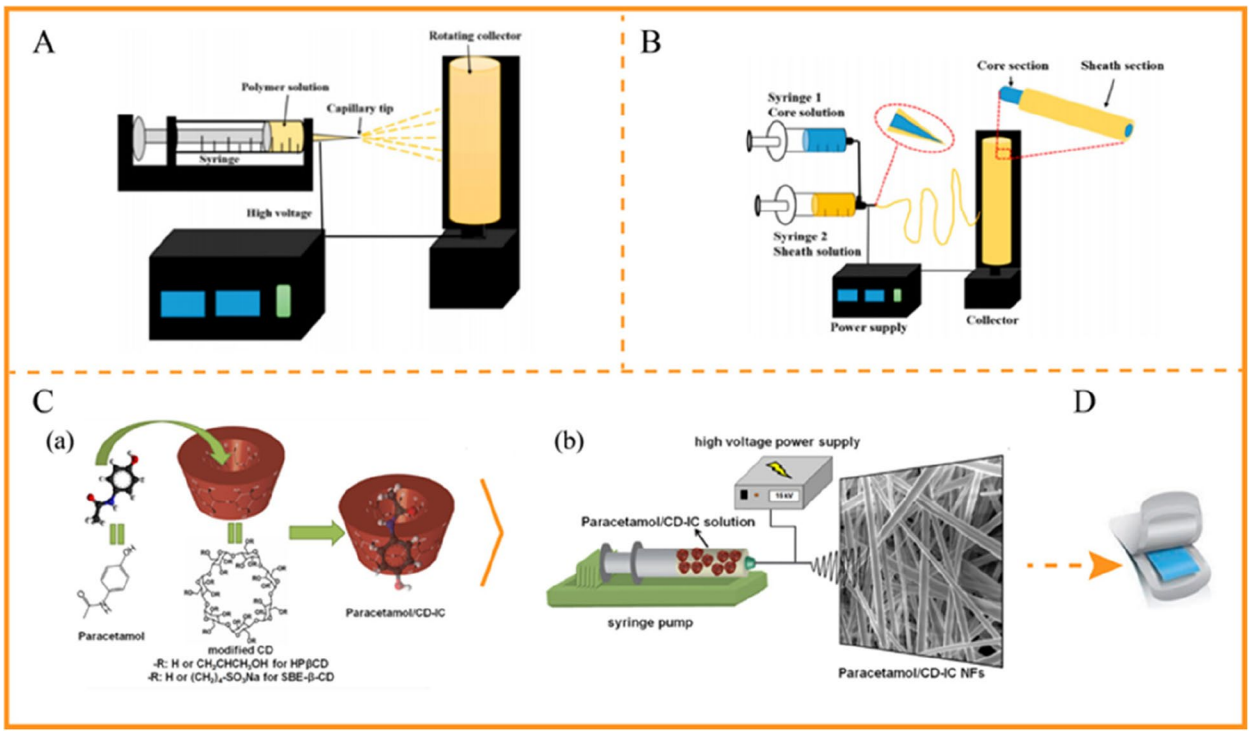


Fig. 3 **A** Schematic diagram of the electrostatic spinning method equipment. (Pant et al., 2019) Copyright 2019 Pharmaceutics, **B** Diagram of the coaxial electrostatic spinning equipment. (Pant et al., 2019) Copyright 2019 Pharmaceutics, **C** Preparation of polyvinylpyrrolidone fibres loaded with paracetamol (PCM) and caffeine (CAF) by electrostatic spinning technique. (Yildiz & Uyar, 2019) Copyright © 2019 Elsevier B.V., **D** An oral dissolving film. (Cupone et al., 2023) Copyright 2022 Pharmaceutics

Illangakoon et al. (2014) prepared polyvinylpyrrolidone fibers loaded with paracetamol (PCM) and caffeine (CAF) using electrostatic spinning. They investigated these fibers as potential ODFs, resulting in a film agent with a high loading capacity for active ingredients, good resistance to folding, excellent solubility, and ease of swallowing. Similarly, Song et al. (2019) selected the poorly soluble medication piroxicam (PX) as an API. PX microcrystals were produced through antisolvent precipitation and then incorporated into ODFs using electrostatic spinning. By combining micronization and electrostatic spinning processes, poorly stable components can be formulated into high-quality ODFs.

The substantial specific surface area of membrane agents prepared by electrostatic spinning enhances the loading capacity of active ingredients, improves their solubility and permeability, and facilitates excellent sustained release. However, the electrostatic spinning method requires complex and costly equipment, as well as multiple phases in the preparation process. These factors significantly hinder its industrialization and commercialization in the food and biomedical fields.

Printing method

Printing technology, a computer-aided design (CAD) process, involves stacking printed materials layer by layer to create a product with the desired form. This approach enables continuous one-step manufacturing and allows for the individual design of multiple active ingredients at different doses (Çöl et al., 2023; Wang et al., 2022) (Fig. 4). Due to its characteristics, 3D printing is also referred to as additive manufacturing and holds significant potential for food production, rapid administration of active ingredients, and personalized treatment (Dong et al., 2022; Mirazimi et al., 2022). Currently, 3D printing is utilized in the preparation of oral dissolving film agents through various techniques such as fused deposition modeling (FDM) (Jamróz et al., 2017), 3D inkjet printing (Edinger et al., 2018) and semisolid extrusion 3D printing (Panraksa et al., 2021). Elbl et al. (2023) employed a novel semisolid extrusion 3D printing method to produce multilayer ODFs with added porogenic agents, resulting in membranes with favorable disintegration times and multilayer structures that enhance the loading of active ingredients. This

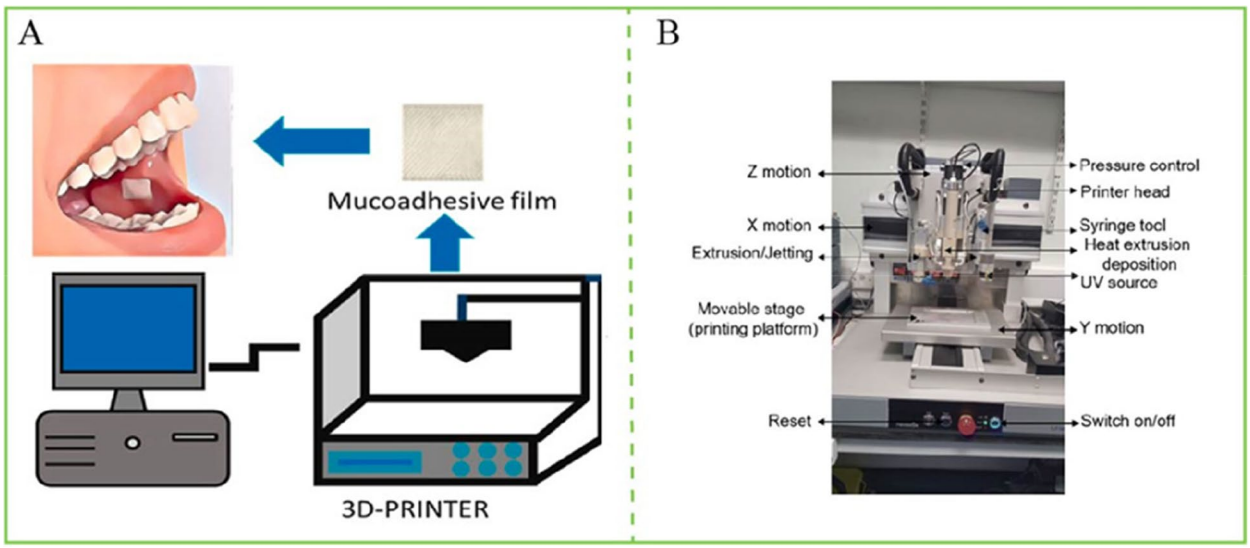


Fig. 4 **A** Schematic diagram of the 3D printing method for the preparation of orolithic films. (Elkanayati et al., 2022) Copyright 2022 Elsevier B.V., **B** Diagram of the 3D printing method equipment. (Khaled et al., 2018) Copyright 2018 AAPS PharmSciTech

discovery holds significant potential for applications in the pharmaceutical and food industries.

Compared to the solvent casting method, 3D printing offers more options for personalization in terms of the size, geometry, and internal structure of the printed object. This allows for greater flexibility in selecting and formulating the dose of active ingredients and improves the solubility of the prepared film agent (Jamróz et al., 2017). However, 3D printing techniques are expensive, time-consuming, and unsuitable for large-scale production. Additionally, they require specific printing materials, and certain printing methods have limitations. For example, FDM 3DP printing at high temperatures (> 120 °C) may lead to active ingredient degradation and relatively low resolution.

Solvent casting remains the classical method for preparing ODFs, commonly used in industrial production today. However, numerous new techniques are emerging and developing, including hot melt extrusion, electrostatic spinning, and printing methods. The choice of preparation method for ODFs depends on the properties of the loaded active substance and the stability of the film agent itself. HME offers uniformity and safety without the need for organic solvents but is unsuitable for heat-sensitive ingredients and is highly restrictive in its prescription requirements. 3D printing provides flexibility in form and taste, allowing optimization of the formulation process at any time and enabling increased content of the active ingredient, enhancing marketability. Electrostatic spinning encases the loaded active substance in a fiber core, improving bioavailability, while the fine fiber composition of the film agent features many tiny voids, enabling rapid release of the ODFs. These methods have gained increasing attention as emerging technologies. In the food industry, solvent casting remains popular due to its suitability for industrial production, though it suffers from unstable quality of the membrane active ingredient. Combining these methods with other emerging technologies not only overcomes the limitations of traditional solvent casting but also enhances ODF performance, including the preparation of multilayered oral membranes for slow release of the drug, resulting in more desirable ODFs. Particularly noteworthy is the increasing recognition of the flexibility and customization benefits of 3D printing. However, the manuscript lacks crucial information regarding methods for loading or incorporating micronutrients into the ODFs, as well as details on storage and shelf life.

Film evaluation

ODF products, primarily drugs or food items, have specific quality and stability requirements in the market. Currently, most ODF products available are medications and nutritional supplements, necessitating stringent quality and stability standards. However, as film agent products continue to evolve, there is a lack of clear quality evaluation standards tailored to ODF characteristics and international film preparation standards. Presently, market evaluation of film agents primarily focuses on appearance, solubility, active ingredient content, and mechanical properties.

Apparent properties

The visible characteristics of the film include its color, morphology, and flavor. These properties serve as fundamental test criteria for the film and offer the most visible indicators of ODF quality. Asatiani et al. (2023) utilized two types of hydroxypropylmethylcellulose as substrates for ODFs prepared via electrostatic spinning and observed that the resulting films were brittle. Their study highlighted how minor discrepancies in different polymers can significantly influence the crucial properties of electrostatically spun orally disintegrating films. Liu et al. (2018) developed palatable donepezil ODFs to aid in swallowing and investigated the taste-masking effect of cyclodextrin through dynamic processes and in vivo absorption of active ingredients. They used hydroxypropyl-β-cyclodextrin to encapsulate and mask the active ingredients. Based on these findings, the improved film is more easily ingested and yields results comparable to those of the donepezil hydrochloride film.

Dissolution and active ingredient loading

Dissolution is the rate and degree of dissolution of bioactive ingredients from a solid formulation, such as a tablet, in a prescribed solvent. Dissolution is an important indicator for the quality control of tablets, and insoluble bioactive ingredients should generally be checked for dissolution. This is also a characteristic test item for oral film-based agents. There is still no acknowledged technique for detecting ODF dissolution, and a method for determining common formulations is often utilized. ODF is primarily distinguished by oral absorption, and standard formulation dissolution techniques are not physiologically relevant to ODF. Krampe et al. (2016) proposed a new method for determining ODF dissolution by simulating human oral saliva. The dissolution effect of ODF was observed by simulating the flow or mechanical force of human oral saliva, demonstrating that the conditions in the oral cavity differ significantly from those in pharmacopoeia tests on the dissolution effect of ODF. The small size of the film limits the ODF; therefore, the active ingredient loading capacity is generally 5–30% of the overall film dosage of the active ingredient. The greater the active-component loading, the weaker and less robust the film. Vuddanda et al. (2017) prepared orally administered polymeric films loaded with tadalafil (TDF) nanocrystals to study the effect of active ingredient loading on their physical, mechanical, and dissolution properties and demonstrated that the active ingredient properties of the films varied with the amount of active ingredient loading.

Mechanical properties

The mechanical properties of the film agent, including the folding resistance, elongation at break, tensile strength, and coefficient of elasticity, were evaluated. The folding resistance represents the brittleness of the film, which is the number of folds that break or show obvious increases after folding at the same position; the lower the number, the more brittle is the film agent. The tensile strength, or strength limit, is the maximum force used to pull the ODF agent off. Baranauskaite et al. (2022) prepared an ODF containing ginseng root extract, and the mechanical characteristics, disintegration, tensile strength, and elongation at fracture of the ODF were determined. The results showed that the resulting film was good. The results showed that the ODF had good mechanical properties and rapid release characteristics, and the incorporation of the active substance promoted a decrease in tensile strength and an increase in elongation.

Formulation stability studies

Stability studies are an important part of API or formulation quality control studies. The stability of the designed and developed film agent is an important indicator for determining whether the film agent qualifies after prescription optimization and property evaluation. It examines the sensitivity of the formulation to light, moisture, heat, oxidation, and the main degradation products and pathways and accordingly determines the choice of suitable packaging materials. DCruz et al. (2021) Formulation of lacidipine-loaded span-lastic ODFs. Stability studies performed after 3 months showed no changes in the physical appearance, mechanical properties, or bioavailability of lacidipine. Heinemann et al. (2013) developed an oral dissolving film (ODF) for the oral administration of probiotics and showed that less than 15% of the probiotics were lost during storage, and that the probiotics had high viability during 90 days of storage. The normal shelf life of ODFs is generally 3–6 months, whereas some pharmaceutical films have a shelf life of up to 12 months (Australian Public Assessment Report).

In vivo pharmacokinetic evaluation

One of the advantages of orally dissolving films is that bioactive ingredients are absorbed more rapidly and have better bioavailability. Bioactive ingredients are rapidly absorbed into the blood circulation via the oral cavity, avoiding the initial metabolism of the liver. Its bioavailability is higher than that of traditional oral tablets and capsules. Ma et al. (2020) developed a novel sublingual orally dispersible film loaded with everolimus (EVR). Pharmacokinetic studies demonstrated that loading a sublingual orally dispersible film significantly increased

the oral bioavailability of EVR. The Aldawsari and Badr-Eldin (2020) optimized ODF formulation enhanced the pharmacokinetic properties of dapoxetine hydrochloride and improved patient compliance. The bioavailability of other micronutrients and active substances is also affected by orally dissolving films. Liu et al. (2017) prepared an oral fast-dissolving film containing luteolin nanocrystals with a blood concentration twice that of the oral solution, which improved the low oral bioavailability of luteolin. Radicioni et al. (2022) compared the bioavailability of an orally disintegrating film of vitamin D3 with that of a commercially available oral vitamin D3 formulation in healthy subjects. The results showed that its bioavailability was slightly greater than that of the oral solution administered under the same conditions.

Examination of clinical experimental studies

Oral dissolving films, as a novel mode of active ingredient delivery for delivering active substances, need to be evaluated for clinical utility, in general for their safety, and efficacy in the human body. Nishigaki et al. (2012) developed an ODF containing dexamethasone as an antiemetic for clinical practice, and the results proved that its efficacy was not significantly different from that of tablets and that its oral acceptability was better than that of tablets. Elshafeey and El-Dahmy (2021) prepared an oral immediate-release film of a paroxetine (PX) nanosuspension for depression and anxiety, and an ODF loaded with a PX nanosuspension was clinically evaluated in healthy human volunteers for its ability to successfully enhance the bioavailability of PX. Seinfeld et al. (2020) developed a diazepam buccal film for the treatment of patients with epileptic seizures and evaluated the safety, tolerability, and availability of self- or caregiver-administered diazepam buccal film in an outpatient setting, demonstrating that DBF is easy to administer, safe, and well tolerated in adult, adolescent, and pediatric epilepsy patients experiencing seizure emergencies.

Although ODF is a reliable oral active ingredient, there are currently no established international regulations for ODF. The current research suggests that ODF quality assessment should follow a systematic approach to product development: Pharmaceutical Quality Design. This approach is a systematic development process that starts with predefined objectives and focuses on understanding and testing products and processes based on sound science and quality risk management. It includes relevant product definitions, target product quality profiles (TPQPs) and critical quality attributes (CQAs), material characterization and critical process parameters (CMAs and CPPs), design of experiments (DoEs) to define the design space, and the creation and implementation of a product control strategy based on TPQPs and CQAs (Gupta et al., 2021). Therefore, it is necessary to develop more technical procedures to analyze and ensure the quality of ODF. For example, the recommended conditions for investigating the disintegration and dissolution fail to accurately reflect the natural conditions of the oral cavity, including the volume of the dissolution medium. This is a concerning issue, as proper analysis is crucial for ensuring safe and effective ingredients. Therefore (Turković et al., 2022), more refined testing requirements need to be established to make them marketable to a larger audience.

Future and outlook

Presently, the market is still dominated by traditional food products; however, in recent years, the food industry has become more inclined toward diversification, functionalization, and precise nutrition (Sun & Liu, 2023). As a novel delivery method, ODF have excellent potential for rapid food development because of their rapid impact, improved bioavailability, increased safety benefits, and ability to bypass the first-pass effect. Currently, ODF have proven to have great potential for application in the food industry. It is an excellent carrier platform for many active ingredients such as probiotics, vitamins, melatonin, proteins, and functional extracts (Yuan et al., 2022). However, ODF still has certain disadvantages (Fig. 5): (1) The active ingredient loading capacity is not high. Because they are unable to encapsulate sufficient active ingredients due to their shortcomings, they cannot achieve the required efficacy for indications with low activity or high-dose requirements. Krull et al. (2017) showed that the brittleness of a film increased as the drug load increased, affecting the mechanical properties of the film and leading to a decrease in film stability. The solubility of active ingredients and loading capacity of active ingredients can be increased by stacking layers of films or by combining them with other new dosage form preparation techniques, such as solid dispersions, inclusions, microspheres, or nanoparticles (Sabatelle et al., 2022; Xu et al., 2017). (2) The film agent exhibits stability problems. The backbone of the film is mainly a polymer, which is prone to moisture absorption; therefore, the packaging material must achieve a moisture barrier effect, and the ratio of film-forming materials must be adjusted to optimize the process to reduce the moisture absorption effect. Gupta and Kumar (2020) demonstrated that a residual moisture content of 3–6% is considered an acceptable limit. Tian et al. (2018) have demonstrated that ODFs must be carefully packaged and stored to protect them from moisture, atmospheric oxygen, and sunlight. (3) The combination of the two ingredients is challenging; there are many differences in the disintegration rate and disintegration time between

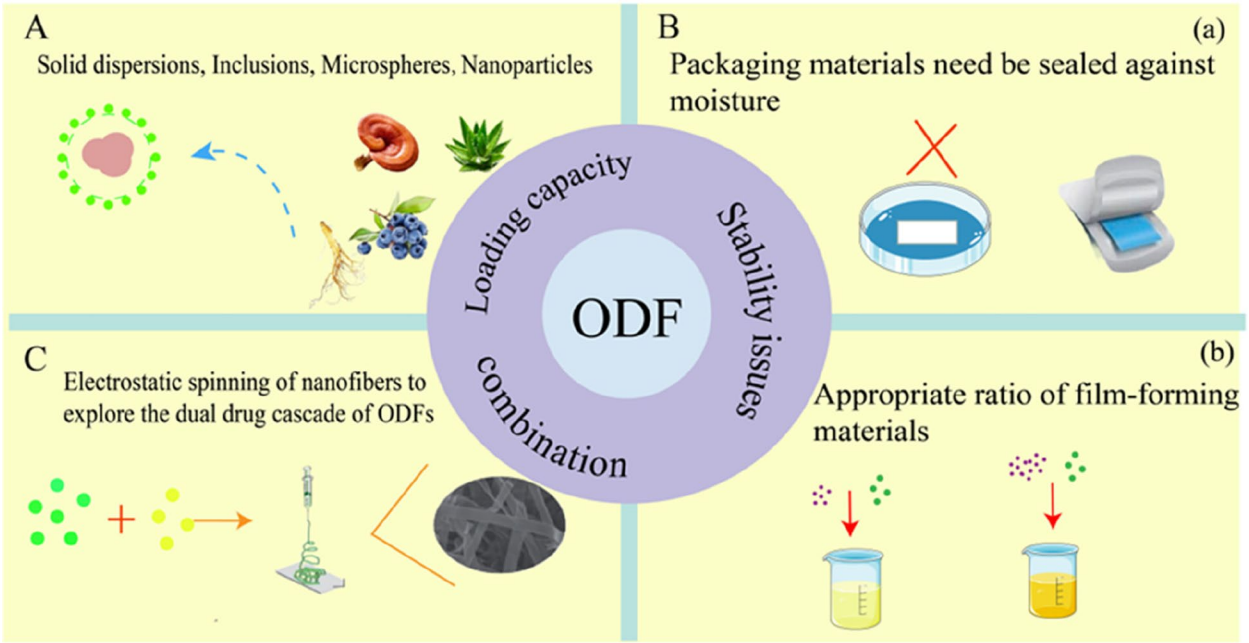


Fig. 5 Challenges and solutions for oral dissolving film. **A** Low loading of active ingredients can be achieved by using encapsulated carriers such as nanoparticles. **B** Poor stability of film agent. (Cupone et al., 2023) Copyright 2022 Pharmaceutics, (a) Packaging material. (b) Proportion of film-forming. **C** Coupling of two components by electrostatic spinning. (Montolio et al., 2017) Copyright 2017 Royal Society of Chemistry

different ODFs, and it is difficult to achieve optimal pharmacokinetic properties simultaneously. However, the study of two-acting ingredient conjugation using electrostatically spun nanofibers could potentially explore the two-component conjugation of ODFs. Illangakoon et al. (2014) successfully prepared oral films loaded with both paracetamol (PCM) and caffeine (CAF) using electrostatic spinning. (4) Owing to the lack of strict quality control standards as a new method of delivering active substances, some ODF quality development currently follows the quality of drugs by design (QbD). Gupta et al. (2021) provided a brief overview of Quality by Design (QbD) principles in ODF development. There are no strict requirements for the quality control of system specifications, such as dissolution conditions, disintegration time, and microbial contamination limitations for membrane dosage forms.

Therefore, there is a need to develop improved ODF quality testing requirements to ensure the effectiveness and safety of ODF as active substance delivery system.

Despite the limitations of ODFs, they have received increasing international attention because of their unique characteristics of rapid active ingredient absorption, high bioavailability, ease of use, and ability to avoid the first-pass effect of active ingredients in the gastrointestinal tract and liver, and have shown good prospects for application in both pharmaceutical and food fields. The application of ODFs in combination with other new dosage forms has recently become a popular research topic, particularly for proteins and peptides (food-active molecules with large spaces), which are excellent delivery systems (Castro et al., 2018). For example, in combination with nanotechnology, nanoparticles or nanocomplexes are encapsulated in oral films and dispersed uniformly or non-uniformly in the film matrix, which not only enhances the bioadhesive properties of the film but also improves the solubility and permeability of active ingredients and promotes the absorption of active ingredients to improve bioavailability. As highly absorbable and fast-delivering effective carriers of ODFs, in addition to loading drugs and bioactive ingredients to treat or improve human chronic degenerative diseases, inflammation, and other conditions, they can also deliver microorganisms and probiotics to improve human intestinal health and can be used as biological agents for the development of vaccines and oral vaccines as a novel route of administration.

Summary

In summary, ODFs offer significant advantages including rapid absorption, high safety compliance, increased bioavailability, and avoidance of first-pass effects in the gastrointestinal tract and liver. This novel mode of delivering active substances has garnered widespread attention and become a research focus in recent years, leading to the development of numerous active ingredients as

fast-dissolving film agents, with some progress made in ODF formulation processes. While current innovative preparation techniques have demonstrated promising results in terms of active ingredient loading, solubility, and stability, further enhancements are necessary to achieve shorter processing times and higher yields. Despite significant advancements in ODF formulation and production, challenges persist, such as limited active ingredient loading capacity and poor stability. Recent research has focused on combining ODF with other emerging dosage forms to enhance its efficacy. This article provides an overview of the current state of ODF processing in the food industry, highlighting current challenges and potential solutions. It is hoped that future research in food processing will overcome limitations in preparation methods, loading compositions, and membrane agent stability.

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Authors' contributions
Yue Li contributed to writing – original draft, Min Zhao contributed to editing and supervision, MingYue Zhao contributed to grammar, Jinlong Tian contributed to conceptualization, and writing – review and editing.

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Competing interests
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References

Abdelhakim, H. E., Williams, G. R., Craig, D. Q. M., Orlu, M., & Tuleu, C. (2020). Human mouthfeel panel investigating the acceptability of electrospun and solvent cast orodispersible films. *International Journal of Pharmaceutics, 585*, 119532. https://doi.org/10.1016/j.ijpharm.2020.119532

Abou-Taleb, H. A., Mustafa, W. W., Makram, T. S., Abdelaty, L. N., Salem, H., & Abdelkader, H. (2022). Vardenafil oral dispersible films (ODFs) with advanced dissolution, palatability, and bioavailability. *Pharmaceutics, 14*(3), 517. https://doi.org/10.3390/pharmaceutics14030517

Aldawsari, H. M., & Badr-Eldin, S. M. (2020). Enhanced pharmacokinetic performance of dapoxetine hydrochloride via the formulation of instantly-dissolving buccal films with acidic pH modifier and hydrophilic cyclodextrin: Factorial analysis, in vitro and in vivo assessment. *Journal of Advanced Research, 24*, 281–290. https://doi.org/10.1016/j.jare.2020.04.019

Alghaith, A. F., Mahrous, G. M., Shazly, G. A., Zidan, D. E. Z., Alhamed, A. S., Alqinyah, M., Almutairi, M. M., & Syed, S. A. (2022). The optimization and evaluation of flibanserin fast-dissolving oral films. *Polymers, 14*(20), 4298. https://doi.org/10.3390/polym14204298

Asatiani, N., Filipová, B., Pechočiaková, M., & Kluk, A. (2023). Electrospun HPMC/PEO-blend orodispersible films: How slight batch differences affect the crucial mechanical properties. *Cellulose, 30*, 4527–4541. https://doi.org/10.1007/s10570-023-05137-4

Australian Public Assessment Report for Buprenorphine/Naloxone, Suboxone sublingual film. https://www.tga.gov.au/sites/default/files/auspar-suboxone.pdf. Accessed 15 Dec 2020.

Bala, R., Pawar, P., Khanna, S., & Arora, S. (2013). Orally dissolving strips: A new approach to oral drug delivery system. *International Journal of Pharmaceutical Investigation, 3*(2), 67–76. https://doi.org/10.4103/2230-973X.114897

Baranauskaite, J., Ockun, M. A., Uner, B., Gungor, B., Duman, G., Tas, C., & Yesilada, E. (2022). Development and In vitro characterization of pullulan fast dissolving films loaded with Panax ginseng extract, antioxidant properties and cytotoxic efficiency on lung and breast cancer cell lines. *Journal of Drug Delivery Science and Technology, 76*, 103701. https://doi.org/10.1016/j.jddst.2022.103701

Bodini, R. B., Pugine, S. M. P., de Melo, M. P., & de Carvalho, R. A. (2020). Antioxidant and anti-inflammatory properties of orally disintegrating films based on starch and hydroxypropyl methylcellulose incorporated with Cordia verbenacea (erva baleeira) extract. *International Journal of Biological Macromolecules, 159*, 714–724. https://doi.org/10.1016/j.ijbiomac.2020.05.075

Castro, P. M., Baptista, P., Madureira, A. R., Sarmento, B., & Pintado, M. E. (2018). Combination of PLGA nanoparticles with mucoadhesive guar-gum films for buccal delivery of antihypertensive peptide. *International Journal of Pharmaceutics, 547*(1–2), 593–601. https://doi.org/10.1016/j.ijpharm.2018.05.051

Chen, L. H., & Doyle, P. S. (2022). Thermogelling hydroxypropyl methylcellulose nanoemulsions as templates to formulate poorly water-soluble drugs into oral thin films containing drug nanoparticles. *Chemistry of Materials, 34*(11), 5194–5205. https://doi.org/10.1021/acs.chemmater.2c00801

Cheng, E., Geng, Z., Xiang, L., Zhao, X., Xiang, A., & Tian, H. (2024). Development of vitamin C-loaded electrospun nanofibers of mixture of polysaccharides of pullulan/xanthan gum for fast dissolving oral film applications. *Materials, 17*(4), 861. https://doi.org/10.3390/ma17040861

Cho, H. W., Baek, S. H., Lee, B. J., & Jin, H. E. (2020). Orodispersible polymer films with the poorly water-soluble drug, olanzapine: Hot-Melt pneumatic extrusion for single-process 3D printing. *Pharmaceutics, 12*(8), 692. https://doi.org/10.3390/pharmaceutics12080692

Cilurzo, F., Musazzi, U. M., Franzé, S., Selmin, F., & Minghetti, P. (2018). Orodispersible dosage forms: Biopharmaceutical improvements and regulatory requirements. *Drug Discovery Today, 23*(2), 251–259. https://doi.org/10.1016/j.drudis.2017.10.003

Çöl, B. G., İmre, M., & Yıkmış, S. (2023). Virtual reality and augmented reality technologies in gastronomy: A review. *Efood*. https://doi.org/10.1002/efd2.84

Cupone, I. E., Roselli, G., Marra, F., Riva, M., Angeletti, S., Dugo, L., Spoto, S., Fogolari, M., & Giori, A. M. (2023). Orodispersible film based on maltodextrin: A convenient and suitable method for iron supplementation. *Pharmaceutics, 15*(6), 1575. https://doi.org/10.3390/pharmaceutics14102011

DCruz, C. E. M., Bhide, P. J., Kumar, L., & Shirodkar, R. K. (2021). Novel nano spanlastic carrier system for buccal delivery of lacidipine. *Journal of Drug Delivery Science and Technology, 68*, 103061. https://doi.org/10.1016/j.jddst.2021.103061

Dong, M., Ge, C., & Qingyu, Y. (2022). Effects of different colloids on the 3d printing properties of potato starch-based materials. *Journal of Food Science and Technology, 40*(1), 44–52. https://doi.org/10.12301/spxb202100851

Draksiene, G., Venclovaite, B., Pudziuvelyte, L., Ivanauskas, L., Marksa, M., & Bernatoniene, J. (2021). Natural polymer chitosan as super disintegrant in fast orally disintegrating meloxicam tablets: Formulation and Evaluation. *Pharmaceutics, 13*(6), 879. https://doi.org/10.3390/pharmaceutics13060879

Edinger, M., Bar-Shalom, D., Sandler, N., Rantanen, J., & Genina, N. (2018). QR encoded smart oral dosage forms by inkjet printing. *International Journal of Pharmaceutics, 536*(1), 138–145. https://doi.org/10.1016/j.ijpharm.2017.11.052

Elbl, J., Veselý, M., Blaháčková, D., Ondruš, J., Kulich, P., Mašková, E., Mašek, J., & Gajdziok, J. (2023). Development of 3D printed multi-layered orodispersible films with porous structure applicable as a substrate for inkjet printing. *Pharmaceutics, 15*(2), 714. https://doi.org/10.3390/pharmaceutics15020714

Elkanayati, R. M., Chambliss, W. G., Omari, S., Almutairi, M., Repka, M. A., & Ashour, E. A. (2022). Mucoadhesive buccal films for treatment of xerostomia prepared by coupling HME and 3D printing technologies. *Journal of Drug Delivery Science and Technology, 75*, 103660. https://doi.org/10.1016/j.jddst.2022.103660

Elshafeey, A. H., & El-Dahmy, R. M. (2021). Formulation and development of oral fast-dissolving films loaded with nanosuspension to augment paroxetine bioavailability: In vitro characterization, ex vivo permeation, and pharmacokinetic evaluation in healthy human volunteers. *Pharmaceutics, 13*, 1869. https://doi.org/10.3390/pharmaceutics13111869

Ferlak, J., Guzenda, W., & Osmałek, T. (2023). Orodispersible films-current state of the art, limitations, advances and future perspectives. *Pharmaceutics, 15*(2), 361. https://doi.org/10.3390/pharmaceutics15020361

Fernandes, A. I. (2023). Polymers enhancing bioavailability in drug delivery, 2nd edition. *Pharmaceutics, 15*(11), 2604. https://doi.org/10.3390/pharmaceutics15112604

Garcia, V. A. D., Borges, J. G., Maciel, V. B. V., Mazalli, M. R., Lapa-Guimaraes, J. D., Vanin, F. M., & de Carvalho, R. A. (2018). Gelatin/starch orally disintegrating films as a promising system for vitamin C delivery. *Food Hydrocolloids, 79*, 127–135. https://doi.org/10.1016/j.foodhyd.2017.12.027

Garcia, V. A. D., Borges, J. G., Osiro, D., Vanin, F. M., & de Carvalho, R. A. (2020). Orally disintegrating films based on gelatin and pregelatinized starch: Ew carriers of active compounds from acerola. *Food Hydrocolloids, 101*, 105518. https://doi.org/10.1016/j.foodhyd.2019.105518

Gupta, M. S., & Kumar, T. P. (2020). Characterization of orodispersible films: An overview of methods and introduction to a new disintegration test apparatus using LDR - LED ensors. *Journal of Pharmaceutical Sciences, 109*(10), 2925–2942. https://doi.org/10.1016/j.xphs.2020.06.012

Gupta, M. S., Kumar, T. P., Gowda, D. V., & Rosenholm, J. M. (2021). Orodispersible films: Conception to quality by design. *Advanced Drug Delivery Reviews, 178*, 113983. https://doi.org/10.1016/j.addr.2021.113983

He, M., Zhu, L., Yang, N., Li, H., & Yang, Q. (2021). Recent advances of oral film as platform for drug delivery. *International Journal of Pharmaceutics, 604*(1), 120759. https://doi.org/10.1016/j.ijpharm.2021.120759

Heinemann, R. J. B., Carvalho, R. A., & Favaro-Trindade, C. S. (2013). Orally disintegrating film (ODF) for delivery of probiotics in the oral cavity — Development of a novel product for oral health. *Innovative Food Science and Emerging Technologies, 19*, 227–232. https://doi.org/10.1016/j.ifset.2013.04.009

Hoffmann, E. M., Breitenbach, A., & Breitkreutz, J. (2011). Advances in orodispersible film for drug delivery. *Expert Opinion on Drug Delivery, 8*(3), 299–316. https://doi.org/10.1517/17425247.2011.553217

Illangakoon, U. E., Gill, H., Shearman, G. C., Parhizkar, M., Mahalingam, S., Chatterton, N. P., & Williams, G. R. (2014). Fast dissolving paracetamol/caffeine nanofibers prepared by electrospinning. *International Journal of Pharmaceutics, 477*(1), 369–379. https://doi.org/10.1016/j.ijpharm.2014.10.036

Jaiswal, H. (2014). Oral strip technology: A review. *Indian Journal of Pharmaceutical and Biological Research*, *2*(2). https://doi.org/10.30750/ijpbr.2.2.20

Jamróz, W., Kurek, M., Łyszczarz, E., Szafraniec, J., Knapik-Kowalczuk, J., Syrek, K., Paluch, M., & Jachowicz, R. (2017). 3D printed orodispersible films with aripiprazole. *International Journal of Pharmaceutics, 533*(2), 413–420. https://doi.org/10.1016/j.ijpharm.2017.05.052

Jani, R., & Patel, D. (2015). Hot melt extrusion: N industrially feasible approach for casting orodispersible film. *Asian Journal of Pharmaceutical Sciences, 10*(4), 292. https://doi.org/10.1016/J.AJPS.2015.03.002

Karki, S., Kim, H., Na, S., Shin, D., Jo, K., & Lee, J. (2016). Thin films as an emerging platform for drug delivery. *Asian Journal of Pharmaceutical Sciences, 11*, 559–574. https://doi.org/10.1016/j.ajps.2016.05.004

Kaur, M., & Santhiya, D. (2022). Fabrication of soy film with in-situ mineralized bioactive glass as a functional food for bone health. *Food Bioscience*, *47*, 101767. https://doi.org/10.1016/j.fbio.2022.101767

Khaled, S. A., Alexander, M. R., Irvine, D. J., Wildman, R. D., Wallace, M. J., Sharpe, S., Yoo, J., & Roberts, C. J. (2018). Extrusion 3D printing of paracetamol tablets from a single formulation with tunable release profiles through control of tablet geometry. *An Official Journal of the American Association of Pharmaceutical Scientists, 19*(8), 3403–3413. https://doi.org/10.1208/s12249-018-1107-z

Krampe, R., Sieber, D., Pein-Hackelbusch, M., & Breitkreutz, J. (2016). A new biorelevant dissolution method for orodispersible films. *European Journal of Pharmaceutics & Biopharmaceutics, 98*, 20–25. https://doi.org/10.1016/j.ejpb.2015.10.012

Krull, S. M., Moreno, J., Li, M., Bilgili, E., & Davé, R. N. (2017). Critical material attributes (CMAs) of strip films loaded with poorly water-soluble drug nanoparticles: III. Impact of drug nanoparticle loading. *International Journal of Pharmaceutics*, *523(1)*, 33–41. https://doi.org/10.1016/j.ijpharm.2017.03.023

Laffleur, F., & Keckeis, V. (2020). Advances in drug delivery systems: Ork in progress still needed? *International Journal of Pharmaceutics, 590*, 119912. https://doi.org/10.1016/j.ijpharm.2020.119912

Lai, F., Franceschini, I., Corrias, F., Sala, M. C., Cilurzo, F., Sinico, C., & Pini, E. (2015). Maltodextrin fast dissolving films for quercetin nanocrystal delivery. A feasibility study. *Carbohydrate Polymers, 121*, 217–223. https://doi.org/10.1016/j.carbpol.2014.11.070

Liu, C., Chang, D., Zhang, X., Sui, H., Kong, Y., Zhu, R., & Wang, W. (2017). Oral fast-dissolving films containing lutein nanocrystals for improved bioavailability: Ormulation development, in vitro and in vivo evaluation. *An Official Journal of the American Association of Pharmaceutical Scientists, 18*(8), 2957–2964. https://doi.org/10.1208/s12249-017-0777-2

Liu, T., Wan, X., Luo, Z., Liu, C., Quan, P., Cun, D., & Fang, L. (2018). A donepezil/cyclodextrin complexation orodispersible film: Effect of cyclodextrin on taste-masking based on dynamic process and in vivo drug absorption. *Asian Journal of Pharmaceutical Sciences, 14*(2), 183–192. https://doi.org/10.1016/j.ajps.2018.05.001

Lou, J., Duan, H., Qin, Q., Teng, Z., Gan, F., Zhou, X., & Zhou, X. (2023). Advances in oral drug delivery systems: Challenges and opportunities. *Pharmaceutics, 15*(2), 484. https://doi.org/10.3390/pharmaceutics15020484

Ma, Y., Guan, R., Gao, S., Song, W., Liu, Y., Yang, Y., & Liu, H. (2020). Designing orodispersible films containing everolimus for enhanced compliance and bioavailability. *Expert Opinion on Drug Delivery, 17*(10), 1499–1508. https://doi.org/10.1080/17425247.2020.1828342

Mazumder, S., Pavurala, N., Manda, P., Xu, X., Cruz, C. N., & Krishnaiah, Y. S. R. (2017). Quality by Design approach for studying the impact of formulation and process variables on product quality of oral disintegrating films. *International Journal of Pharmaceutics, 527*(1–2), 151–160. https://doi.org/10.1016/j.ijpharm.2017.05.048

McIntosh, E. (2023). Dysphagia. *Home Healthcare Now, 41*(1), 36–41. https://doi.org/10.1097/NHH.0000000000001134

Mirazimi, F., Saldo, J., Sepulcre, F., Gràcia, A., & Pujola, M. (2022). Enriched puree potato with soy protein for dysphagia patients by using 3D Printing. *Food Frontiers, 3*(4), 706–715. https://doi.org/10.1002/fft2.149

Montolio, S., Abarca, G., Porcar, R., Dupont, J., Burguete, M. I., García-Verdugo, E., & Santiago, V. L. (2017). Hierarchically structured polymeric ionic liquids and polyvinylpyrrolidone mat-fibers fabricated by electrospinning. *Journal of Materials Chemistry A, 5*(20), 9733–9744. https://doi.org/10.1039/C7TA02447A

Musazzi, U. M., Dolci, L. S., Albertini, B., Passerini, N., & Cilurzo, F. (2019). A new melatonin oral delivery platform based on orodispersible films containing solid lipid microparticles. *International Journal of Pharmaceutics, 559*, 280–288. https://doi.org/10.1016/j.ijpharm.2019.01.046

Nishigaki, M., Kawahara, K., Nawa, M., Futamura, M., Nishimura, M., Matsuura, K., Kitaichi, K., Kawaguchi, Y., Tsukioka, T., Yoshida, K., & Itoh, Y. (2012). Development of fast dissolving oral film containing dexamethasone as an antiemetic medication: Linical usefulness. *International Journal of Pharmaceutics, 424*(1–2), 12–17. https://doi.org/10.1016/j.ijpharm.2011.12.057

Ockun, M. A., Baranauskaite, J., Uner, B., Kan, Y., & Kırmızıbekmez, H. (2022). Preparation, characterization and evaluation of liposomal-freeze dried

anthocyanin-enriched Vaccinium arctostaphylos L. fruit extract incorporated into fast dissolving oral films. *Journal of Drug Delivery Science and Technology, 72*, 103428. https://doi.org/10.1016/j.jddst.2022.103428

Pacheco, M. S., Barbieri, D., da Silva, C. F., & de Moraes, M. A. (2021). A review on orally disintegrating films (ODFs) made from natural polymers such as pullulan, maltodextrin, starch, and others. *International Journal of Biological Macromolecules, 178*, 504–513. https://doi.org/10.1016/j.ijbiomac.2021.02.180

Panraksa, P., Qi, S., Udomsom, S., Tipduangta, P., Rachtanapun, P., Jantanasakulwong, K., & Jantrawut, P. (2021). Characterization of hydrophilic polymers as a syringe extrusion 3D printing material for orodispersible film. *Polymers, 13*(20), 3454. https://doi.org/10.3390/polym13203454

Pant, B., Park, M., and Park, S. J. (2019). Drug delivery applications of core-sheath nanofibers prepared by coaxial electrospinning: A review. Pharmaceutics, 11(7). doi: 10.3390/pharmaceutics11070305.

Prajapati, V. D., Chaudhari, A. M., Gandhi, A. K., & Maheriya, P. (2018). Pullulan based oral thin film formulation of zolmitriptan: Development and optimization using factorial design. *International journal of biological macromolecules, 107*(PtB), 2075–2085. https://doi.org/10.1016/j.ijbiomac.2017.10.082

Preis, M. (2015). Orally disintegrating films and mini-tablets-innovative dosage forms of choice for pediatric use. *An Official Journal of the American Association of Pharmaceutical Scientists, 16*(2), 234–241. https://doi.org/10.1208/s12249-015-0313-1

Qin, Z., Jia, X.-W., Liu, Q., Kong, B., & Wang, H. (2019). Fast dissolving oral films for drug delivery prepared from chitosan/pullulan electrospinning nanofibers. *International Journal of Biological Macromolecules, 137*, 224–231. https://doi.org/10.1016/j.ijbiomac.2019.06.224

Radicioni, M., Caverzasio, C., Rovati, S., Giori, A. M., Cupone, I., Marra, F., & Mautone, G. (2022). Comparative Bioavailability Study of a New Vitamin D3 Orodispersible Film Versus a Marketed Oral Solution in Healthy Volunteers. *Clinical Drug Investigation, 42*(2), 151–161. https://doi.org/10.1007/s40261-021-01113-7

Sabatelle, R. C., Liu, R., Hung, Y. P., Bressler, E., Neal, E. J., Martin, A., Ekladious, I., Grinstaff, M. W., & Colson, Y. L. (2022). Ultra-high drug loading improves nanoparticle efficacy against peritoneal mesothelioma. *Biomaterials, 285*, 121534. https://doi.org/10.1016/j.biomaterials.2022.121534

Saha, S., Tomaro-Duchesneau, C., Daoud, J. T., Tabrizian, M., & Prakash, S. (2013). Novel probiotic dissolvable carboxymethyl cellulose films as oral health biotherapeutics: In vitro preparation and characterization. *Expert Opinion on Drug Delivery, 10*(11), 1471–1482. https://doi.org/10.1517/17425247.2013.799135

Salawi, A. (2022). An insight into preparatory methods and characterization of orodispersible film—A review. *Pharmaceuticals, 15*(7), 844. https://doi.org/10.3390/ph15070844

Seinfeld, S., Gelfand, M. A., Heller, A. H., Buan, C., & Slatko, G. (2020). Safety and tolerability associated with chronic intermittent use of diazepam buccal film in adult, adolescent, and pediatric patients with epilepsy. *Epilepsia, 61*(11), 2426–2434. https://doi.org/10.1111/epi.16696

Shah, K. A., Gao, B., Kamal, R., Razzaq, A., Qi, S., Zhu, Q. N., Lina, S., Huang, L., Cremin, G., Iqbal, H., Menaa, F., & Cui, J. H. (2022). Development and characterizations of pullulan and maltodextrin-based oral fast-dissolving films employing a box-behnken experimental design. *Materials, 15*(10), 3591. https://doi.org/10.3390/ma15103591

Silva, B. M., Borges, A. F., Silva, C., Coelho, J. F., & Simões, S. (2015). Mucoadhesive oral films: The potential for unmet needs. *International Journal of Pharmaceutics, 494*(1), 537–551. https://doi.org/10.1016/j.ijpharm.2015.08.038

Silvestre, A. L. P., Dos Santos, A. M., de Oliveira, A. B., Ferrisse, T. M., Brighenti, F. L., Meneguin, A. B., & Chorilli, M. (2023). Evaluation of photodynamic therapy on nanoparticles and films loaded-nanoparticles based on chitosan/alginate for curcumin delivery in oral biofilms. *International Journal of Biological Macromolecules, 240*, 124489. https://doi.org/10.1016/j.ijbiomac.2023.124489

Shojaee Kang Sofla, M., Mortazavi, S., & Seyfi, J. (2020). Preparation and characterization of polyvinyl alcohol/chitosan blends plasticized and compatibilized by glycerol/polyethylene glycol. *Carbohydrate Polymers, 232*, 115784. https://doi.org/10.1016/j.carbpol.2019.115784

Song, Q., Guo, X., Sun, Y., & Yang, M. (2019). Anti-solvent precipitation method coupled electrospinning Process to produce poorly water-soluble drug-loaded orodispersible films. *An Official Journal of the American Association of Pharmaceutical Scientists, 20*(7), 273. https://doi.org/10.1208/s12249-019-1464-2

Speer, I., Preis, M., & Breitkreutz, J. (2018). Prolonged drug release properties for orodispersible films by combining hot-melt extrusion and solvent casting methods. *European Journal of Pharmaceutics and Biopharmaceutics, 129*, 66–73. https://doi.org/10.1016/j.ejpb.2018.05.023

Sun, B.G. & Liu, H. L. (2023). Current Situation of Health Food Industry and Transformation and Development of Food Industry. *Journal of Food Science and Technology*. *41*(02), 1–6. https://doi.org/10.12301/spxb202300126

Takashima, H., Tagami, T., Kato, S., Pae, H., Ozeki, T., & Shibuya, Y. (2022). Three-dimensional printing of an apigenin-loaded mucoadhesive film for tailored therapy to oral leukoplakia and the chemopreventive effect on a rat model of oral carcinogenesis. *Pharmaceutics, 14*(8), 1575. https://doi.org/10.3390/pharmaceutics14081575

Tian, Y., Visser, J. C., Klever, J. S., Woerdenbag, H. J., Frijlink, H. W., & Hinrichs, W. L. J. (2018). Orodispersible films based on blends of trehalose and pullulan for protein delivery. *European Journal of Pharmaceutics and Biopharmaceutics, 133*, 104–111. https://doi.org/10.1016/j.ejpb.2018.09.016

Turković, E., Vasiljević, I., Drašković, M., & Parojčić, J. (2022). Orodispersible films — Pharmaceutical development for improved performance: A review. *Journal of Drug Delivery Science and Technology, 75*, 103708. https://doi.org/10.1016/j.jddst.2022.103708

Vuddanda, P. R., Montenegro-Nicolini, M., Morales, J. O., & Velaga, S. (2017). Effect of surfactants and drug load on physico-mechanical and dissolution properties of nanocrystalline tadalafil-loaded oral films. *European Journal of Pharmaceutical Sciences, 109*, 372–380. https://doi.org/10.1016/j.ejps.2017.08.019

Wang, M., Li, D., Zang, Z., Sun, X., Tan, H., Si, X., Tian, J., Teng, W., Wang, J., Liang, Q., Bao, Y., Li, B., & Liu, R. (2022). 3D food printing: Pplications of plant-based materials in extrusion-based food printing. *Critical Reviews in Food Science and Nutrition, 62*(26), 7184–7198. https://doi.org/10.1080/10408398.2021.1911929

Xu, H., Zhang, L., Li, L., Liu, Y., Chao, Y., Liu, X., Jin, Z., Chen, Y., Tang, X., He, H., Kan, Q., & Cai, C. (2017). Membrane-loaded doxorubicin liposomes based on ion-pairing technology with high drug loading and PH-responsive property. *An Official Journal of the American Association of Pharmaceutical Scientists, 18*(6), 2120–2130. https://doi.org/10.1208/s12249-016-0693-x

Yildiz, Z. I., & Uyar, T. (2019). Fast-dissolving electrospun nanofibrous films of paracetamol/cyclodextrin inclusion complexes. *Applied Surface Science, 492*, 626–633. https://doi.org/10.1016/j.apsusc.2019.06.220

Yu, J. Y., Kim, H. W., & Park, H. J. (2022). Customized oral mucosal adhesive film-based functional-substance delivery system using embedded 3D printing method. *Food Hydrocolloids, 131*, 107762. https://doi.org/10.1016/j.foodhyd.2022.107762

Yuan, C., Sha, H., & Cui, B. (2022). Orally disintegrating film: A new approach to nutritional supplementation. *Food and Bioprocess Technology, 15*(12), 2629–2645. https://doi.org/10.1007/s11947-022-02835-y

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