Sys Rev Pharm 2023; 14(5): 356-358
A multifaceted review journal in the field of pharmacy
E-ISSN 0976-2779 P-ISSN 0975-8453 / DOI: 10.31858/0975-8453.14.5.356-358

Review Article

# Methods of Preparation and Characterization of Orodispersible Film: A Review

**Fitha TV*, K Selvaraju, NL Gowrisankar**
Department of Pharmaceutics, Prime College of Pharmacy, Kerala, India

*Article History:* *Submitted: 17.04.2023* *Accepted: 12.05.2023* *Published: 19.05.2023*

ABSTRACT
One of the latest dosage forms, Orodispersible Film (ODF), can be easily dissolved in the mouth without the need for water. One of the key components used to make Orodispersible Film is polymer. While making ODF, both organic and synthetic polymers are utilised. Additionally, other approaches are discussed for developing ODF. The focus of this review involves information regarding Orodispersible Film preparation and usage of natural and synthetic polymers as film formers for quick film disintegration in the buccal cavity. Additionally, it is regarded as an easy-to-take dose form since the saliva in the mouth causes the film to disintegrate quickly. Drug permeability can be increased by incorporating the permeation enhancer, which also increases bioavailability. One can also administer Orodispersible Film dosage form for directly treating the oral diseases. When compared to buccal gel and buccal tablets, ODF is more practical for daily consumption. ODF helps with patient compliance to some extent. The idea of Orodispersible Films is mostly beneficial for specific population like geriatrics and children. The most frequently utilised method for preparing ODF is solvent casting process in both the industrial and laboratory settings.

**Keywords:** Orodispersible Film (ODF), Polymers, Buccal delivery, Permeability, Solvent casting method

***Correspondence:** Fitha TV, Department of Pharmaceutics, Prime College of Pharmacy, Kerala, India, E-mail: fithamohdali97@gmail.com

## INTRODUCTION

Orodispersible Films (ODF) are innovative drug formulations that introduce a promising approach to pharmacotherapy. They represent single- or multi-layer polymer films that show sufficient stability but disintegrate easily. ODF are suitable for patients with swallowing difficulties such as elderly people, children, or patients with restricted transport in the gastrointestinal tract. Since ODFs may be accurately split by cutting them into distinct pieces (even up to 6 or 8 pieces), issues linked to tablet swallowing or excessive fluid intake are efficiently dealt with, and these groups may greatly benefit from the dosage flexibility that is inherent to ODFs (Musazzi UM, *et al*., 2020). There are currently a few industrially made ODFs available for adult usage. The majority of these ODFs are, however, less or not suited for the pediatric and elderly patient populations because to the set dose of these formulations. Additionally, many medications used in children or the elderly are not offered as ODFs. Therefore, further study in this area is warranted. ODFs can be utilized for oral delivery after the dissolved substance has been ingested. Yet they may also be approaching to receive a rapid onset of action because some of the active pharmaceutical ingredient directly absorbed through the oral or buccal mucosa (Sriganaranjan P and Leopold CS, 2020).

Numerous techniques have been investigated for the production of ODFs, including Hot Melt Extrusion (HME), spin coating, semisolid casting, solid dispersion extrusion, rolling, and solvent casting. Solvent casting is the ideal production process for small-scale pharmaceutical formulations. On a small scale, it may be carried out rather easily, and no expensive equipment is required. Every component, including plasticizer, medication, and polymers that make films, is suspended or dissolved in water before being cast and dried to form a film (Shipp L, *et al*., 2022).

So far, many film-forming polymers have been employed in the fabrication of ODFs. Good mucoadhesive qualities of the polymer are a crucial need. Polyacrylic acid, sodium Carboxymethylcellulose (sodium CMC), Hydroxypropylcellulose (HPC), Hydroxyethyl Cellulose (HEC), and hypromellose are examples of frequently used polymers (Hydroxypropyl Methylcellulose, HPMC). Natural polymers like chitosan, alginate, starch, or maltodextrin have also been employed in place of these semi-synthetic polymers. Pullulan and Lycoat are two more costly polymers with good film forming capabilities that have been used in industrial manufacturing. Taste-maskers, plasticizers (glycerol, propylene glycol, Polyethylene Glycol (PEG)), and solvents are other frequent excipients in ODFs (Pacheco MS, *et al*., 2021).

## LITERATURE REVIEW

### *Solvent casting methods*

Solvent casting is the most widely used method for the preparation of ODF. It is also the first one investigated in laboratory settings. The production process is based on three steps: Preparation of a homogenous slurry mixture of components, obtaining a dried laminate by solvent casting and die cutting. In the first step active pharmaceutical ingredient and excipients are dispersed in an appropriate solvent. Then formed slurries were casted and dried in a specific thickness which assures the uniformity of drug content. Solvent casting can be also be adapted to the production of small batches of ODF and multi-layer films intended to administer fixed drug combinations. Active Pharmaceutical Ingredient (API) with physicochemical incompatibility can be loaded at different strengths in different film layers in the same preparation. The simplest method of ODF preparation is mainly based on the use of petri plate or a proper slab, in which a predetermined amount of drug loaded polymeric slurries were casted and dried at suitable temperature (Shahzad Y, *et al*., 2020).

### *Electrospinning*

Another solvent-based approach being investigated to create ODF with a very porous interior structure is electrospinning. The fundamental setup of an electrospinning machine is a metallic needle through which the formulation is pumped and charged, however other electrospinning machines have different configurations. In order to produce electrospun ODF, Poly Vinyl Pyrrolidone (PVP), gelatin, and poloxamers are among the most researched materials. These polymers are appropriate for loading both API and dietary supplements, and they also improve the drug's apparent solubility (Visser JC, *et al*., 2015). Poloxamers provide increased wettability in addition to molecular dispersion, and PVP stabilises a supersaturated solution by creating hydrogen bonds with the other component, which increases the apparent solubility. The spinning of melted components was studied instead of employing a solvent and polymer-based dispersion by using a complicated spironolactone-hydroxypropyl-cyclodextrin model system. In addition, the combination of electrospinning and inkjet printing was suggested as a viable alternative to the solvent-casting of multi-lamina in order to construct a fixed-dose combination (Sinha S, *et al*., 2021).

### *Hot-Melt Extrusion (HME)*

The viability of extrusion technologies has been examined in order to prevent the usage of solvent(s) in the manufacturing of ODF. Hot-Melt Extrusion (HME) in particular may be utilized for both continuous production and the creation of various dosage forms. HME typically comprises of a device that melts a mixture before extruding it through a die. In the case of making films, the extrudate is stretched variably during the manufacture of the reel, and this is regulated not only by the die dimension but also by the geometry and rotational rate of the calendar. The extrusion device may be screw-or ram-based. The melt materials are compressed by a ram in a heated barrel and forced through a die in the first arrangement (Elbl J, *et al*., 2020).

Despite the potential benefits of this approach, the HME application to ODF preparation is restricted to a small number of examples because the polymers used to prepare ODF (such as polysaccharides) are typically heat sensitive and/or have high values for their glass transition temperatures, which are difficult to adjust by adding a plasticizer. In fact, adding a lot of plasticizer might make ODF excessively sticky or ductile (Klingmann V, *et al*., 2020). Our research team demonstrated in 2008 how screw-extrusion technique may be used to produce maltodextrin ODF. Using an experiment design, Low and colleagues looked at how medications and excipients with various physicochemical and technical qualities affected the functionality of ODF manufactured of hydropropyl cellulose. Additionally, they demonstrated that the presence of may modify the disintegration and dissolution characteristics. Compared to other solvent-based preparation methods, HME enables improved preservation of the physicochemical stability of APIs that are water-sensitive. The number of API that could be processed with this method was however constrained by the higher operating temperatures (Sheikh FA, *et al*., 2021).

### *Printing technologies*

Pharmaceutical printing refers to two distinct deposition models, both of which may produce ODF. A layer-by-layer process in 3D printing allows for printing in the Z direction as well as the X and Y directions, creating a 3D dosage form. 2D printing necessitates the use of an edible carrier (or "substrate") that would contain or sorb the deposited ink in a digitally determined pattern. The majority of the procedures described in the literature, however, seem more appropriate for the creation of tiny or very small batches, despite efforts to switch from a discontinuous to continuous printing process. The importance of mechanical characteristics in the formulation of the quality attributes is further constrained since the ODF are created using a prepared film or immediately formed with the necessary surface and shape (Guo X, *et al*., 2020).

### *2D printing*

**Inkjet printing:** Inkjet printing process is widely understood. The API is either solved or suspended in "ink," and the ink is printed on an edible surface. The production process is finished and the ODF is prepared for usage once the ink has dried. Although loading doses are relatively modest compared to other procedures, this approach works best for patients who need minimal dosages, such as youngsters, and API with a narrow therapeutic index or high potency (Morath B, *et al*., 2022).

The printer technology and the mechanism for producing drops have an impact on ink formulation. There are two types of printing: Continuous-Jetting Printing (CJP) and Drop-On-Demand (DOD) printing. The ink droplets may be produced constantly or on demand. The corresponding print heads in each scenario may have a single nozzle or many nozzles. However, the mechanical characteristics of the film might alter following loading. In order to maintain a stable medication formulation, this barrier can be removed by coating the film after production (Cupone IE, *et al*., 2022).

**Flexographic printing:** Flexographic printing, an offset, rotary printing method, has been described as an alternative printing technology to Inkjet printing. Labels and boxes for packing are commonly printed using this method. An anilox roller receives the ink through a fountain roll. Extra ink is taken off with a doctor's blade. After that, the ink is transferred to a plate cylinder and subsequently to an unrolled ODF. For successful printing, pressure is produced by the imprint cylinder (Gupta S, *et al*., 2020).

### *Different kind of polymers*

**Polymers:** All formulas are built on polymers, and there are several different materials accessible. These have to be non-toxic, non-irritating, and impurity-free. The ideal listing for them would be GRAS (Generally Regarded as Safe). Natural or artificial polymers can be used alone or in combination to produce various films with various qualities. Numerous combination qualities have been discussed in the literature, and there are countless others (Salawi A, 2022).

**Natural polymers:** To create ODF, many natural polymers have been tried. The most promising polymer was starch since it is inexpensive and widely accessible. Pure starch films, however, are fragile. Additionally, the readily available edible paper has been utilized as a substrate for inkjet printing, however this caused the film's disintegration to take longer. The creation of starch derivatives was prompted by the difficulties of dissolving starch in water (Scarpa M, *et al*., 2017).

Hydrolyzed starches, like maltodextrin, a combination of polymers made up of d-glucose units, are examples of modified starches that have adequate film-forming properties. Pullulan is another modified starch. It is made up of maltotriose units and d-glucose units, which are produced during the fermentation of the yeast *Aureobasidium pullulans*. Although it is pricey, it is soluble in both hot and cold water and produces smooth, stable films (Krampe R, *et al*., 2016). Because of this, it is combined with other polymers to save costs, and 50 to 80 percent of pullulan may be substituted by starch without losing the necessary pullulan characteristics. Okra biopolymer, *Moringa* gum, chitosan, hyaluronic acid, sodium alginate, pectin, gelatin, trehalose, and other natural polymers have also been identified (Zaki RM, *et al*., 2023).

**Semi synthetic polymers:** Widespread use of cellulose and (semi)synthetic derivatives is made while producing ODF. Hydroxypropyl Methylcellulose (HPMC), Hydroxypropyl Cellulose (HPC), Hydroxymethyl Cellulose (HMC), and Carboxymethyl Cellulose (CMC) are examples of common forming agents. One of the most popular is HPMC (Liu J, *et al*., 2023). There are several grades of this partially O-methylated and O-(2-hydroxypropylated) cellulose. The amount of substituent groups and molecular weight of these variations affect the film characteristics differently. To improve HPMC's film-forming capabilities, additional polymers are occasionally added to the mixture (Tam CH, *et al*., 2021).

**Synthetic polymers:** Copolymers with Polyvinyl Alcohol (PVA) are frequently employed while making ODF. A synthetic polymer known as PVA is created by partially or completely hydrolyzing polyvinyl acetate. PVA is a substance that is frequently used for fused deposition modelling and film-forming. There are several PVA copolymers available, such as Kollicoat® IR's Polyethylene Glycol-Polyvinyl Alcohol (PEG-PVA) graft copolymer. It is made up of 25% PEG units and 75% PVA units. Unlike PVA, which can only be fully dissolved in hot water, this copolymer is freely soluble in water, which provides benefits for the production process. The absence of extra plasticizers is another advantage of Kollicoat® IR (Suryawanshi D, *et al*., 2021).

**Other synthetic polymer:** Different molecular weights of Poly Vinyl Pyrrolidone (PVP), a polymer having linear 1-vinyl-2-pyrrolidinone groups, are available. It can be used independently or in conjunction with other polymers for making films. The adequate solubility of PVP in both water and organic solvents is a benefit (Limpongsa E and Jaipakdee N, 2020).

## DISCUSSION AND CONCLUSION

The ideal ODF is physically stable, thin, flexible, and simple to administer. A quick disintegration is preferable for the patients' comfort. The mechanical characteristics of ODFs will be impacted by residual water and plasticizers. The mechanical characteristics and appearance of ODFs may be affected by the quick solvent evaporation or the inclusion of APIs. Therefore, the features of ODFs will depend on the kind and quantity of various film forming polymers, plasticizers, solvents, and APIs as well as the manufacturing process circumstances.

## REFERENCES

1. Musazzi UM, Khalid GM, Selmin F, Minghetti P, Cilurzo F. Trends in the production methods of orodispersible films. Int J Pharm. 2020; 576: 118963.
2. Sriganaranjan P, Leopold CS. Effect of pullulan as additive to the synthetic polymeric coating blend Eudragit® NM-L55 on the properties of the resulting films. J Pharm Sci. 2020; 109(7): 2166-2172.
3. Shipp L, Liu F, Kerai-Varsani L, Okwuosa TC. Buccal films: A review of therapeutic opportunities, formulations and relevant evaluation approaches. J Control Release. 2022; 352: 1071-1092.
4. Pacheco MS, Barbieri D, da Silva CF, de Moraes MA. A review on orally disintegrating films (ODFs) made from natural polymers such as pullulan, maltodextrin, starch, and others. Int J Biol Macromol. 2021; 178: 504-513.
5. Shahzad Y, Maqbool M, Hussain T, Yousaf AM, Khan IU, Mahmood T, *et al*. Natural and semisynthetic polymers blended orodispersible films of citalopram. Nat Prod Res. 2020; 34(1): 16-25.
6. Visser JC, Woerdenbag HJ, Crediet S, Gerrits E, Lesschen MA, Hinrichs WL, *et al*. Orodispersible films in individualized pharmacotherapy: The development of a formulation for pharmacy preparations. Int J Pharm. 2015; 478(1): 155-163.
7. Sinha S, Garg V, Singh RP, Dutt R. Chitosan-alginate core-shell-corona shaped nanoparticles of dimethyl fumarate in orodispersible film to improve bioavailability in treatment of multiple sclerosis: Preparation, characterization and biodistribution in rats. J Drug Deliv Sci Technol. 2021; 64: 102645.
8. Elbl J, Gajdziok J, Kolarczyk J. 3D printing of multilayered orodispersible films with in-process drying. Int J Pharm. 2020; 575: 118883.
9. Klingmann V, Pohly CE, Meissner T, Mayatepek E, Möltner A, Flunkert K, *et al*. Acceptability of an orodispersible film compared to syrup in neonates and infants: A randomized controlled trial. Eur J Pharm Biopharm. 2020; 151: 239-245.
10. Sheikh FA, Aamir MN, Haseeb MT, Bukhari SN, ul Haq MF, Akhtar N. Design, physico-chemical assessment and pharmacokinetics of a non-toxic orodispersible film for potential application in musculo-skeletal disorder. J Drug Deliv Sci Technol. 2021; 65: 102726.
11. Guo X, Cun D, Wan F, Bera H, Song Q, Tian X, *et al*. Comparative assessment of *in vitro/in vivo* performances of orodispersible electrospun and casting films containing rizatriptan benzoate. Eur J Pharm Biopharm. 2020; 154: 283-289.
12. Morath B, Sauer S, Zaradzki M, Wagner AH. Orodispersible films-recent developments and new applications in drug delivery and therapy. Biochem Pharmacol. 2022: 115036.
13. Cupone IE, Sansone A, Marra F, Giori AM, Jannini EA. Orodispersible Film (ODF) platform based on maltodextrin for therapeutical applications. Pharmaceutics. 2022; 14(10): 2011.
14. Gupta S, Kumar TP, Gowda DV. Patent perspective on orodispersible films. Recent Pat Drug Deliv Formul. 2020; 14(2): 88-97.
15. Salawi A. An insight into preparatory methods and characterization of orodispersible film-A review. Pharmaceuticals. 2022; 15(7): 844.
16. Scarpa M, Stegemann S, Hsiao WK, Pichler H, Gaisford S, Bresciani M, *et al*. Orodispersible films: Towards drug delivery in special populations. Int J Pharm. 2017; 523(1): 327-335.
17. Krampe R, Visser JC, Frijlink HW, Breitkreutz J, Woerdenbag HJ, Preis M. Oromucosal film preparations: Points to consider for patient centricity and manufacturing processes. Expert Opin Drug Deliv. 2016; 13(4): 493-506.
18. Zaki RM, Alfadhel M, Seshadri VD, Albagami F, Alrobaian M, Tawati SM, *et al*. Fabrication and characterization of orodispersible films loaded with solid dispersion to enhance Rosuvastatin calcium bioavailability. Saudi Pharm J. 2023; 31(1): 135-146.
19. Liu J, Zhang Y, Li H, Liu C, Quan P, Fang L. The role of hydrophilic/hydrophobic group ratio of polyvinyl alcohol on the miscibility of amlodipine in orodispersible films: From molecular mechanism study to product attributes. Int J Pharm. 2023; 630: 122383.
20. Tam CH, Alexander M, Belton P, Qi S. Drop-on-demand printing of personalised orodispersible films fabricated by precision micro-dispensing. Int J Pharm. 2021; 610: 121279.
21. Suryawanshi D, Wavhule P, Shinde U, Kamble M, Amin P. Development, optimization and *in-vivo* evaluation of cyanocobalamin loaded orodispersible films using hot-melt extrusion technology: A quality by design (QbD) approach. J Drug Deliv Sci Technol. 2021; 63: 102559.
22. Limpongsa E, Jaipakdee N. Physical modification of Thai rice starch and its application as orodispersible film former. Carbohydr Polym. 2020; 239: 116206.