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ORALLY DISINTEGRATING FILM: AN INNOVATIVE AND EASY APPROACH

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ABSTRACT

Orally disintegrating film (ODF) is a novel and simple method for delivering therapeutically or medicinally active chemical substances to the body(s). The major goals of orally disintegrating films (ODFs) are to improve drug's bioavailability, permeability, and time to action, as well as enhance patient compliance. The process of making films is identical to that of making a transdermal patch. When a film is placed in the mouth, salivary fluid causes it to disintegrate quickly, releasing the medication(s). The medication(s) will subsequently be absorbed into the bloodstream, revealing therapeutic effect. This overview covers the pros and demerits of ODF formulations, as well as formulation aspects, technologies involved in making ODF formulations, and evaluation tests conducted for the same, as well as packing and storage. Orally disintegrating film formulations are a unique dosage form designed to enhance drug delivery, therapeutic action, and patient compliance.

Keywords *– Orally disintegrating film, Permeability, Bioavailability, Polymer, Solvent Casting, Extrusion.*

1. INTRODUCTION

Because it has distinct advantages over the other routes of administration, the oral route is the most preferred method of drug delivery [1]. Though it has various benefits, it also has certain disadvantages, including those associated with unconscious patients, geriatrics, children, and patients with a variety of health issues, such as difficulty swallowing or digesting solid dose forms [2]. Because of tablet size, chewing, surface form, and flavor, the majority of pediatric and geriatric patients are afraid of taking solid dosage forms. Fast dissolving drug delivery was devised in the 1970s in response to the mentioned difficulties. It is used as a substitute for tablets, capsules, and syrups in children and the elderly who have trouble ingesting oral solid dose forms [3]. This kind of solid dosage form dissolves and disintegrates without the use of water in the oral cavity [4]. Oral drug delivery technology has progressed from traditional dose forms through modified release dosage forms, oral disintegrating tablets, and now orally disintegrating films (ODF). Because most ODTs are brittle and fragile, they require special packaging for storage and shipping. The films, on the other hand, are flexible; they are not as fragile as ODTs, and they are easier to transport, handle, and store [5]. Oral fast disintegrating films are a new dosage type in the oral drug delivery system [6]. It was founded on the concept of transdermal films. When placed on the tongue or oral cavity, an orally disintegrating film or strip uses a water dissolving polymer that allows the dosage form to immediately hydrate by saliva, attach to mucosa, and disintegrate within a few seconds, dissolve and release

medication for Oro mucosal absorption. Because of its thin membrane and numerous veins, the sublingual mucosa is relatively permeable [7]. Because of the strong blood flow, drugs are absorbed quickly and have immediate bioavailability. A wide sheet of oral film or strips is made and then cut into smaller dose units for packaging [8]. Oral film is a type of local anesthetic used in the mouth to treat toothaches, oral ulcers, cold sores, and teething [9]. Cough syrups, antiasthmatics, antihistaminics, erectile dysfunction drugs, sore throat, digestive disturbances, nausea, pain, and CNS drugs are all examples of drugs that can be included. Other uses include making caffeine strips, multivitamins, sleeping aids, and snoring aids, among others.

2. MERITS

The following are some of the advantages of oral films over other oral dose forms:

- Simple to administer
- Oral films are less brittle than ODTS and are more flexible, compliant, and less brittle.
- Storage and transportation are simple.
- OTFs have been widely adopted by pharmaceutical companies and customers as a viable alternative to traditional OTC dosage forms such as tablets and capsules. [10]
- Oral films, from a commercial viewpoint, offer additional business opportunities such as product differentiation, promotion, and so on [11].
- Because it is in solid dose forms until it is consumed, it has a higher bioavailability and stability.
- This does not require the use of water and may be used at any time and in any location.
- Therapeutic action is more.

3. DEMERITS

- Incorporating a higher dose is challenging.
- The amount of drug that can be incorporated is limited.
- Drug penetration enhancement is more.
- Dose uniformity is difficult to attain.
- Techniques such as iontophoresis cannot be used to improve bioavailability and penetration for medications that are poorly absorbed. Because they have the potential to harm the oral mucosa [12].

4. IDEAL CHARACTERISTICS OF DRUGS TO BE SELECTED TO ORAL DISPERSIBLE FILMS:

- It is preferable to use drugs that have a pleasing flavour.
- Drugs with a low dose of up to 40mg can be included.
- It should be able to pass through the oral mucosa.
- At oral cavity pH, it should be unionized.
- Drugs with a low molecular weight are preferred.
- In water and saliva, it should be stable and soluble [13].

5. ODF FORMULATION COMPONENT

a) Active pharmaceutical ingredients

b) Strip forming polymers

c) Plasticizers

d) Sweetening agents

e) Saliva stimulating agents

f) Flavoring agents

g) Coloring agents

a) Active Pharmaceutical Ingredients

Orally disintegrating films can be used to include and distribute a variety of active medicinal substances. The medication is present in ODFs in amounts ranging from 5 to 30% w/w [14]. Multivitamins were added at up to 10% w/w of dry film weight [15]. Small molecular weight active ingredients are frequently preferred in oral disintegrating films. The active medicinal components are micronized for improved solubility and homogeneity, as well as improved film texture [16]. The bitter taste of most active pharmaceutical ingredients makes the formulation more unpleasant, and patients reject it. To hide the bitter taste of active pharmaceutical substances, they are combined with sweetening excipients in a procedure known as obscuration.

b) Film forming polymer

This is a crucial component of ODFs. To acquire the needed film qualities for the development of oral film to prevent damage during handling and transit, polymers can be employed alone or in combination [17]. Because strip forming polymer is a key ingredient of ODFs, at least 45 percent w/w of polymers should be present [18]. In general, 60-65% water soluble polymer is suitable for the production of ODFs with desirable qualities [19]. For improved absorption, the ODFs must be water soluble and dissolve in the saliva. To make ODFs, the polymer must be water soluble, have a low molecular weight, and have a high film forming ability. Non-toxic and non-irritant polymers should be used. It should have high wetting and spreading properties as well as good shear and tensile strengths e.g. polyvinyl pyrolidine [13]. Natural and synthetic polymers have been utilized in the development of ODF formulations in recent years (Table 1).

Table 1: Most commonly used natural and synthetic polymers in ODFs.

Types of polymer	Example
Natural	Starch, polymerized rosin, pullulan, sodium alginate, Pectin, gelatin, and maltodextrins
Synthetic	Polyvinyl alcohol, hydroxy propyl methyl cellulose, sodium carboxy methyl cellulose, polyvinyl pyrrolidone, and hydroxy propyl cellulose

c) Plasticizers

In general, adding plasticizer to formulations improves mechanical qualities like as tensile strength and percent elongation. The type of plasticizer to use is determined by its compatibility with the polymer and the solvent [20]. Plasticizer concentrations typically vary from 0% to 20% w/w. PEG, glycerol, diethyl phthalate, triethyl citrate, tributyl citrate, and other plasticizers are common examples [21].

d) Sweetening Agents

Sweetening agents are made to dissolve or disintegrate in the mouth. In the preparation of ODFs, both artificial and natural sweeteners are used (Table 2).

Table 2: Examples of some commonly used sweetening agents in ODFs.

Sweetening agents	Example
Natural	Glucose, fructose, dextrose, sucrose, and isomaltose
Artificial	Acesulfame-K, sucralose, and neotame

Neotame and Alitame are 2000–8000 times sweeter than sucrose. In comparison to sorbitol and mannitol, fructose has a higher sweetening power [22]. When oral disintegrating films of donepezil were tested for taste, aftertaste, and tongue feel, sucralose was found to be 600–1000 times sweeter than sucrose. When compared to sucrose, aspartame and saccharin sodium are expected to be 200 and 300–500 times sweeter, respectively. Sweeteners and flavors are also said to have a slight effect on film flexibility [23].

e) Saliva Stimulating Agent

Saliva stimulating agents are used to increase the rate of saliva production. Salivary stimulants include acids like citric acid, malic acid, lactic acid, ascorbic acid, and tartaric acid. These agents make about 2-6 percent of the strip's weight in w/w. Sweeteners are also utilized to stimulate saliva [24].

f) Coloring Agents

These are also significant elements for improving the formulation's look. It is used up to 1%w/w. eg: titanium dioxide.

g) Flavoring agents

The flavors chosen are determined by the people's age, taste, and preferences. Fruit punch, raspberry, and other flavours are popular among younger people, whereas senior patients prefer orange, lemon, and mint flavours. The flavour is chosen based on the type of drug candidate. Flavors are added to oral film preparations at a rate of nearly 10% w/w. To increase the flavour strength, cooling agents might be used [25].

6. METHODS USED IN THE PREPARATION OF ODFs

For film formulation, any of the procedures listed below, or a combination of one or more, can be used.

a) Solvent Casting Method

This procedure can be used to generate films; the water-soluble ingredients are measured accurately and thoroughly mixed in a beaker to produce a transparent solution. Add precisely weighed API and other components to another beaker containing suitable solvent. After that, both beakers containing formulation ingredients are stirred together and then cast into the Petri plate, which is then allowed to dry for a length of time before being cut into the proper size [26,27].

b) Hot Melt Extrusion

Hot melt extrusion is a common process for producing granules, sustained-release tablets, and transdermal and transmucosal drug delivery systems. The method of processing film involves using heat to shape a polymer into a film. The extruder conveys, mixes, and melts the drug carrier mix that has been placed into the hopper. The melt is then die-shaped into the required film form [28].

c) Semisolid Casting Method

This approach is appropriate if the film composition incorporates acid insoluble polymers [29]. Cellulose acetate butyrate and cellulose acetate phthalate are two examples of such polymers. Film former and acid insol. polymer is typically employed in a ratio of 04:01 [30].

d) Solid Dispersion Extrusion

In this process, the medication is first dissolved in a suitable liquid solvent, and then mixed into a PEG melt at temperatures below 70°C. The chosen solvent or drug might not be miscible with PEG melt, and the polymorphic form of drug precipitated in solid dispersion could be influenced by the solvent [31].

e) Rolling Method

APIs in suspension or solution are placed on a carrier and allowed to move about on it. After that, let it cure for a while before cutting it into proper sizes [32].

f) Spray Technique

To make a clear solution, the drug ingredient, polymers, and other excipients are dissolved in a suitable solvent. This transparent solution is then sprayed onto a suitable surface, such as glass, non-siliconized Kraft paper polyethylene film, or Teflon sheet [33].

7. PACKING AND STORAGE OF ODFs

Blister cards can be used to package films. It's necessary to use a single-unit packaging system. Aluminum pouch, stored in a dry environment [34].

8. EVALUATION PARAMETERS

The film developed by any of the above mentioned manufacturing methods is then evaluated. To preserve inter and intra batch consistency between films, evaluation is a critical step. The following are some of the evaluation parameters:

1) Organoleptic evaluation - The attributes of prepared films are evaluated.[35].

2) Morphology study - The morphology of the sample is studied using scanning electron microscopy (SEM) at a specific magnification [36].

3) Thickness - At various stages, the thickness of the strip was measured with a micrometer screw gauge to ensure uniformity [37].

4) Weight variation test - The average weights are calculated by weighing each film individually, then subtracting the average weight of the films from the individual film weight [38].

5) Folding Endurance - It is calculated by folding the strip repeatedly in the same spot until the strip breaks. The folding endurance value is determined by how many times the film can be folded without breaking [39].

6) Tensile strength - It's the highest stress that can be given to a strip specimen at the point when it breaks [40]. It is determined using the following equation: applied load at rupture divided by strip cross-sectional area.

7) Drug content uniformity - The drug content is determined by any conventional test procedures indicated for the specific API. The API content of each film is calculated to evaluate content homogeneity. The consistency of the content is limited at 85-115 percent [41].

8) Surface pH - The pH value of a film is commonly determined by placing it in a petri dish, wetting it with distilled water, and then recording the pH by contacting the film surface with a pH meter electrode. The pH of the surface must be determined since an acidic or basic pH can irritate the oral mucosa [42].

9) Disintegration time - The time it took for ODFs to disintegrate was measured using a U.S.P. disintegration device. For ODFs, the disintegration time should be around 30 seconds or less. The time it takes for the chemicals in the formulation to disintegrate varies, but it usually takes between 5 and 30 seconds. Despite the fact that there is no official guidance for mouth dissolving films [43].

10) Dissolution test - Standard paddle or basket apparatus can be used for dissolution testing. The type of dissolution medium to use is determined by the sink's state and the active ingredient's high dose. When using a paddle device, dissolution tests can be problematic due to the strip's tendency to float on the dissolving media [44].

11) Percentage Elongation - When a strip sample is stressed, it stretches, which is referred to as strain. Strain is defined as the distortion of a strip divided by the sample's initial dimension. Strip elongation increases as plasticizer concentration rises [45].

12) Stability testing - ODFs were stored for a year at 25°C/60 % RH and 40°C/75 % RH, according to ICH recommendations. ODFs should be evaluated for morphological properties, mass thickness, film thickness reduction, tensile properties, and water content and dissolving behavior during storage [46].

9. CONCLUSION

The current review indicates that orally disintegrating films are one of the unique approaches in pharmaceutical sciences. These novel formulations have improved patient compliance and acceptance while also being safer and more effective than traditional formulations. The primary goal of developing ODFs was to address the difficulty in swallowing conventional oral dosage forms in pediatric, geriatric, and psychiatric patients with dysphagia. ODFs are now widely available for hypertension, acidity, allergy, pain, and other conditions, demonstrating their importance. The major advantages of such dosage forms include their administration without the use of water, which meets the need of the target population for convenience in drug administration while also bypassing hepatic metabolism, resulting in improved therapeutic response.

REFERENCES

1. Irfan M, Rabel S, Bukhtar Q, Qadir MI, Jabeen F, Khan A. Orally disintegrating films: A modern expansion in drug delivery system. Saudi Pharmaceutical Journal. 2016 Sep 1;24(5):537-46.
2. Scarpa M, Stegemann S, Hsiao WK, Pichler H, Gaisford S, Bresciani M, Paudel A, Orlu M. Orodispersible films: Towards drug delivery in special populations. International journal of pharmaceutics. 2017 May 15;523(1):327-35.
3. Arya A, Chandra A, Sharma V, Pathak K. Fast dissolving oral films: an innovative drug delivery system and dosage form. International Journal of ChemTech Research. 2010 Jan;2(1):576-83.
4. Ali MS, Vijendar C, Kumar SD, Krishnaveni J. Formulation and evaluation of fast dissolving oral films of diazepam. J Pharmacovigilance. 2016 May 28;4(3):210.
5. Dixit RP, Puthli SP. Oral strip technology: overview and future potential. Journal of controlled release. 2009 Oct 15;139(2):94-107.
6. Jose J, Netto G. Role of solid lipid nanoparticles as photoprotective agents in cosmetics. Journal of cosmetic dermatology. 2019 Feb;18(1):315-21.
7. Barnhart SD, Sloboda MS. The future of dissolvable films. Drug Deliv Technol. 2007;7(8):34-7.
8. Desai PP, Date AA, Patravale VB. Overcoming poor oral bioavailability using nanoparticle formulations–opportunities and limitations. Drug Discovery Today: Technologies. 2012 Jun 1;9(2): e87-95.
9. Kumar VD, Sharma I, Sharma V. A comprehensive review on fast dissolving tablet technology. Journal of applied pharmaceutical science. 2011;1(05):50-8.
10. Frey P. Film strips and pharmaceuticals. Pharma. Mfg. & Packag. Sourcer. 2006:92-3.
11. Manivannan R. Oral disintegrating tablets: A future compaction. Drug Invention Today. 2009 Nov 1;1(1):61-5.
12. Joshua JM, Hari R, Jyothish FK, Surendran SA. Fast dissolving oral thin films: An effective dosage form for quick releases. Drugs. 2016; 11:12.
13. Pathare YS, Hastak VS, Bajaj AN. Polymers used for fast disintegrating oral films: a review. Int. J. Pharm. Sci. Rev. Res. 2013 Jul;21(1):169-78.

14. Kulkarni N, Kumar L, Sorg A, inventors; Warner Lambert Co LLC, assignee. Fast dissolving orally consumable films containing an antitussive and a mucosa coating agent. United States patent application US 10/423,735. 2003 Nov 6.
15. Ali S, Quadir A. High molecular weight povidone polymer-based films for fast dissolving drug delivery applications. Drug Delivery Technology. 2007;7(6):36-43.
16. Hariharan M. Orally dissolving film strips (ODFS): the final evolution of orally dissolving dosage forms. Drug Deliv. Tech.. 2009; 9:24-9.
17. Corniello C. Quick dissolving strips: from concept to commercialization. Drug Delivery Technology. 2006;6(2):68-71.
18. Fankhauser CE, Slominski G, Meyer S. Disintegrable oral films. Patent CA2640243 A. 2007 Nov 26;1.
19. Mahboob MB, Riaz T, Jamshaid M, Bashir I, Zulfiqar S. Oral films: A comprehensive review. International Current Pharmaceutical Journal. 2016 Nov 18;5(12):111-7.
20. Bala R, Pawar P, Khanna S, Arora S. Orally dissolving strips: A new approach to oral drug delivery system. International journal of pharmaceutical investigation. 2013 Apr;3(2):67.
21. Banker GS. Film coating theory and practice. Journal of pharmaceutical sciences. 1966 Jan;55(1):81-9.
22. Desu PK, Brahmaiah B, Nagalakshmi A, Neelima K, Nama S, Baburao C. An overview on rapid dissolving films. Asian J. Pharm. Res. 2013;3(1):15-23.
23. Liew KB, Tan YT, Peh KK. Characterization of oral disintegrating film containing donepezil for Alzheimer disease. Aaps Pharmscitech. 2012 Mar;13(1):134-42.
24. Patil PB, Shrivastava SK. Fast dissolving oral films: An innovative drug delivery system. Structure. 2012;20(70):50-0.
25. McGregor R, Homan H, Gravina S. Fast dissolving film delivery of nucleotides that inhibit the unpleasant taste of bitter tasting medications. WO Patent. 2004;19885.
26. Bhura N, Sanghvi K, Patel U, Parmar B, Patel D. A review on fast dissolving film. IJPRBS. 2012;1(3):66-89.
27. Juluru NS. Fast dissolving oral films: A review. IJAPBC. 2013 Jan;2(1):108-12.
28. Nagaraju T, Gowthami R, Rajashekar M, Sandeep S, Mallesham M, Sathish D, Shravan Kumar Y. Comprehensive review on oral disintegrating films. Current drug delivery. 2013 Feb 1;10(1):96-108.
29. Shimoda H, Taniguchi K, Nishimura M, Matsuura K, Tsukioka T, Yamashita H, Inagaki N, Hirano K, Yamamoto M, Kinosada Y, Itoh Y. Preparation of a fast dissolving oral thin film containing dexamethasone: a possible application to antiemesis during cancer chemotherapy. European Journal of Pharmaceutics and Biopharmaceutics. 2009 Nov 1;73(3):361-5.
30. Sharma R, Parikh RK, Gohel MC, Soniwala MM. Development of taste masked film of valdecoxib for oral use. Indian Journal of Pharmaceutical Sciences. 2007;69(2):320.
31. Ravindran CA. Pelagia research library. Der Pharmacia Sinica. 2011;2(4):218-40.
32. Prabhu SC, Parsekar SD, Shetty A, Monteiro SS, Azharuddin M, Shabaraya AR. A review on fast dissolving sublingual films for systemic drug delivery. Int J Pharm Chem Sci. 2014;3(2):501-11.
33. Panda BP, Dey NS, Rao ME. Development of innovative orally fast disintegrating film dosage forms: a review. International Journal of Pharmaceutical Sciences and Nanotechnology. 2012 Aug 31;5(2):1666-74.
34. Ghodake PP, Karande KM, Osmani RA, Bhosale RR, Harkare BR, Kale BB. Mouth dissolving films: Innovative vehicle for oral drug delivery. polymer. 2013; 9:20.
35. Anand V, Kataria M, Kukkar V, Saharan V, Choudhury PK. The latest trends in the taste assessment of pharmaceuticals. Drug Discovery Today. 2007 Mar 1;12(5-6):257-65.

36. Mashru RC, Sutariya VB, Sankalia MG, Parikh PP. Development and evaluation of fast-dissolving film of salbutamol sulphate. Drug development and industrial pharmacy. 2005 Jan 1;31(1):25-34.
37. Smriti T. Mouth dissolving films: a review. Int J Pharm Bio Sci. 2013 Jan; 4:899-908.
38. Nair AB, Kumria R, Harsha S, Attimarad M, Al-Dhubiab BE, Alhaider IA. In vitro techniques to evaluate buccal films. Journal of Controlled Release. 2013 Feb 28;166(1):10-21.
39. Shinde AJ, Garala KC, More HN. Development and characterization of transdermal therapeutics system of tramadol hydrochloride. Asian Journal of Pharmaceutics (AJP): Free full text articles from Asian J Pharm. 2014 Aug 25;2(4).
40. DE PK, DESU RK, BONTHAGARALA B, NAMA S, NAGALAKSHMI A. FORMULATION AND EVALUATION OF.
41. Pavankumar GV, Ramakrishna V, William GJ, Konde A. Formulation and evaluation of buccal films of salbutamol sulphate. Indian journal of pharmaceutical sciences. 2005;67(2):160.
42. Patel RS, Poddar SS. Development and characterization of mucoadhesive buccal patches of salbutamol sulphate. Current drug delivery. 2009 Jan 1;6(1):140-4.
43. Balamurugan K, KP J, Choudary PK, Balasubramaniam J. Systemic absorption of propranolol hydrochloride from buccoadhesive films. Indian journal of pharmaceutical sciences. 2001;63(6):473.
44. Nishimura M, Matsuura K, Tsukioka T, Yamashita H, Inagaki N, Sugiyama T, Itoh Y. In vitro and in vivo characteristics of prochlorperazine oral disintegrating film. International journal of pharmaceutics. 2009 Feb 23; 368(1-2):98-102.
45. Fulzele SV, Satturwar PM, Dorle AK. Polymerized rosin: novel film forming polymer for drug delivery. International journal of pharmaceutics. 2002 Dec 5;249(1-2):175-84.
46. Murray OJ, Dang W, Bergstrom D. Using an electronic tongue to optimize taste-masking in a lyophilized orally disintegrating tablet formulation-the electronic tongue technology provides a technically suitable and cost-effective. Pharmaceutical Technology. 2004; 23:42.