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Review Article

Fast dissolving oral thin films: an innovative herbal drug delivery system

Senthamarai Rajagopalan, Dinesh Rajendhiran*, Ismail Abdulrahim Mohamed, Shakila Banu Sherbudeen

Department of Pharmcognosy, Periyar College of Pharmaceuticals Sciences, Tiruchirappalli, Tamil Nadu, India

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***Correspondence:**
Dr. Dinesh Rajendhiran,
E-mail: dineshvkp1806@gmail.com

ABSTRACT

Fast-dissolving drug delivery systems were first developed as an alternative to common dosage forms in the late 1970s. The oral thin film is an innovative drug administration approach based on transdermal patch technology. These systems consist of solid dosage forms that dissolve and disintegrate quickly in the mouth without the need for water. Oral thin films (OTFs) and oral disintegrating tablets (ODTs) are two types of fast-acting pharmaceutical delivery methods. ODTs are "A solid dosage form containing medicinal substances, which disintegrates rapidly, usually within a matter of seconds, when placed upon the tongue." As a result, OTFs hydrate fast before dissolving or disintegrating, allowing the medicine to be absorbed locally and systemically. This method provides a solid platform for extending the patient lives of existing products while also developing new ones without infringing on patients. Fast- dissolving oral thin films are being used for sublingual and gastro retentive administration methods in addition to the buccal technique. This review focusses on the composition of various types of polymers, both natural and synthetic, as well as manufacturing processes, packaging materials, and OTF evaluation tests.

Keywords: Fast dissolving drug delivery systems, Oral Thin Films, Oral Disintegrating Tablets, Polymers, Sublingual

INTRODUCTION

In recent years, herbal therapy has received a global reputation and has grown more incorporated into the mainstream healthcare system. Herbal medicine is utilized by people of all genders, socioeconomic classes and races in both industrialized and developing nations. This increase in consumption and patronage has been attributed to several factors, including low cost, widespread acceptance as a natural medication with minimal toxicity and effectiveness in a range of difficult ailments, and flexibility in accessibility, preparation, and application.[1] Herbal drugs, which are widely used in both developed and developing countries for therapeutic purposes due to their low oral absorption are complex chemical mixtures derived from plants that have limited efficiency.[2] The oral route is now the most prevalent way of administering drugs due to its numerous benefits over other routes of administration.[3] However, oral drug delivery systems still need to be improved due to limitations specific to a certain patient population, which includes children, geriatric, and dysphasic individuals who have a range of medical issues and have trouble swallowing or digesting solid dose forms.[4]Many elderly and child patients hesitate to take solid pills out of fear of choking. Tablet size was the most commonly expressed anxiety, followed by surface shape and flavour.[5] The difficulty in consuming pills was more prevalent in elderly and young patients, as well as those who were travelling and may not have had ready accessibility to water.[6] In the late 1970s, fast-dissolving films were developed using super disintegrants and hydrophilic ingredients that had excellent bioavailability, quick action, and high patient compliance as an alternative to traditional dosage forms for pediatric and geriatric

patients who have difficulty swallowing traditional oral solid dosage forms. Many FDTs are prepared using the expensive lyophilization method, which can make them delicate and friable, as well as difficult to handle, transport, and store.[7] The dimensions and thickness of fast-dissolving films bear a striking resemblance to those of an ultra-thin postage stamp band. The formulation of these films involves a combination of polymers, plasticizers, saliva-stimulating chemicals, tastes, preservatives, sweeteners, and colors. Upon simple application to the patient's tongue or any other oral mucosal tissue, fast- dissolving films quickly hydrate and adhere to the application site after being moistened by saliva. In the field of pharmaceuticals, oral-dissolving thin films are gaining popularity due to their notable oral absorption and clinical benefits. These ultra-thin dosage forms dissolve in the oral cavity when they come into contact with saliva, offering precise dosage without requiring chewing or drinking. Moreover, their pre-gastric absorption enhances the drug's effectiveness, resulting in better bioavailability compared to conventional tablets. For suppressing coughs, fast-dissolving poly herbal films are a reliable, convenient, and effective option.[8]

Need for preparing fast-dissolving oral thin films

Individuals with central nervous system disorders, paediatric patients, the elderly, bedridden individuals, and those who experience nausea often find it challenging to consume solid medications, causing them to avoid taking their prescribed drugs out of fear of choking. Even oral disintegrating tablets (ODTs) pose a risk of asphyxia. However, a novel OTF when placed on the tongue's tip or floor, saliva quickly moistens the thin film, allowing for rapid hydration and subsequent disintegration to release the medication. Unlike ODTs, which can be brittle and break during handling and transport, oral thin-film drug delivery technologies dissolve quickly, offering a promising solution for patients who struggle with swallowing or chewing solid medication.[9]

MECHANISM OF ACTION

The drug delivery system can use the tongue or any other mucosal tissue in the mouth. The film is quickly moistened by saliva and then breaks down, releasing the drug for oral mucosal absorption. This is due to the use of hydrophilic polymer and other excipients.[10]

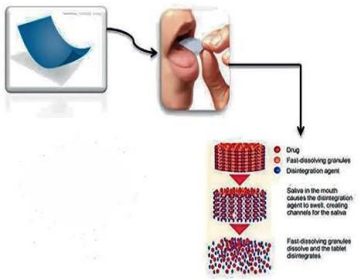

Figure 1: Mechanism of action.

IDEAL FEATURES OF ORAL THIN FILMS

The drug should be good taste. The drug should dissolve easily in saliva and be highly moisture-resistant. The drug should have the right amount of tension resistance. The drug should be ionized in the pH of the oral cavity. The drug should be able to permeate the oral mucosa and medications11 should be able to act quickly.

Table 1: Differences between OTFs and ODFs.

S. no.	OTFs	ODTs
1.	Oral thin films	Oral/disintegrating tablets
2.	More dissolving because of the surface area's Greater size	Less dissolving because of lower Surface area
3.	When compared to ODTs, it is more resilient.	When compared to OTFs, it is less resilient.
4.	There is high patient compliance.	There is low patient compliance
5.	It might have a small dose	It might have a high dose[12,13]
6.	There is no asphyxia risk.	The fear of asphyxiation is present.

FORMULATION OF ORAL THIN FILMS

The quickly dissolving poly herbal oral thin films were prepared by any of the following suitable methods i.e. solvent casting method; semisolid casting method; hot melt extrusion; semi-dispersion extrusion method; roller method; drying of films.

Solvent casting method

The solvent casting method is the preferred method for formulating fast-dissolving oral thin films. In this method, the drug and other excipients are dissolved in a suitable solvent after the water-soluble ingredients have been dissolved to form a clear viscous solution. The two solutions are then combined swirled and dried in a Petri dish. This method is mostly used in pharmaceutical industries.

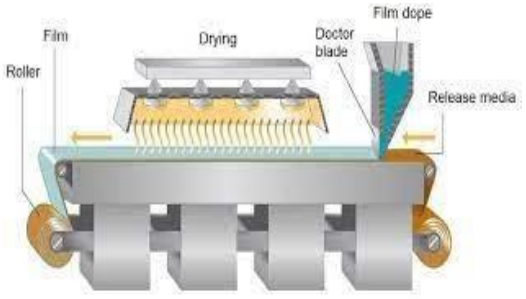

Figure 2: Solvent casting method.

The solid casting method

A newly formulated water-soluble polymer is capable of producing films when combined with an acid-insoluble polymer solution, like cellulose acetate butyrate or phthalate, to create a gel mass. An ideal gel mass can be achieved by adding the right amount of plasticizer. With specialized heat-controlled drums, the gel mass can be shaped into ribbons or films, ranging from 0.015 to 0.05 inches in thickness. For the best outcome, it is recommended to maintain a 1:4 ratio between the acid-insoluble polymer and the film-forming polymer.[16]

Hot melt extrusion method

The drug is initially combined with solid carriers using the hot melt extrusion process. Then, dried granular material is added to the extruder, and the granules in the barrel are processed for approximately 3 to 5 minutes at a screw speed of 15 rpm. The optimal processing temperatures for zones 1, 2, 3, and 4 are 800°C, 1150°C, 1000°C, and 650°C, respectively. Subsequently, the extrudate (T= 650°C) is forced into a cylindrical calendar to produce a film. The use of hot melt extrusion has specific advantages. Reduced number of operation units, improved consistency of content, a procedure without water.[17,18]

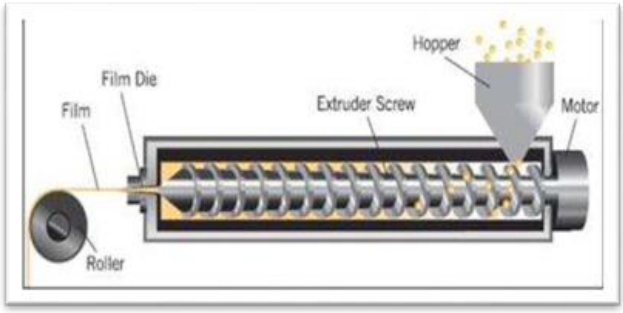

Figure 3: Hot melt extrusion method.

Solid dispersion extrusion method

This approach prepares solid dispersions by first extruding immiscible components with the medication. Dies are used to mold the solid dispersions into films finally.

Roller method

This film is produced using a specialized process that involves creating a pre-mix and then adding an active ingredient to form the final product. To make the pre-mix, various components such as a polar solvent, a film-forming polymer, and the drug to be emitted are combined. This pre-mix is then added to a master batch feed tank. The first and second mixers can receive the pre-mix through a first metering pump and control valve. Once the desired consistency is reached, the necessary amount of medicine is added to the mixture. The drug is mixed with the master batch premix to create a uniform matrix. Next, a predetermined volume of the homogenous matrix is supplied to the pan using the second metering pump. The film is ultimately created on the substrate and it is removed using the support roller. Finally, controlled bottom drying is used to dry the wet film.[19]

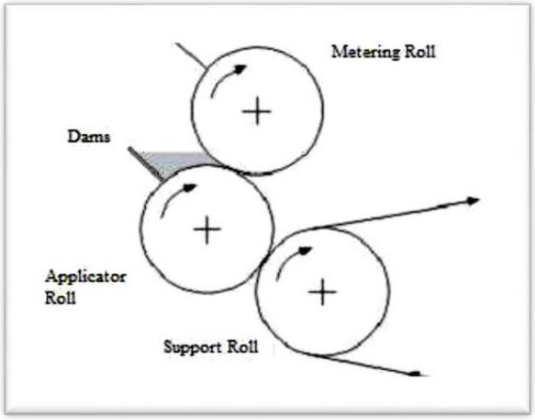

Figure 4: Roller Method.

Film drying process

The drying process plays a crucial role in maintaining a low internal temperature of films. Even when the film surfaces are exposed to heat-sensitive APIs, the temperature within the film remains lower than the temperature at which API degradation occurs. This temperature difference effectively prevents API deterioration. Typically, films dry in less than ten minutes, and after 10 minutes of drying at 80°C, the temperature differential between the environment and the film matrix is around 5°C. This temperature differential influences the films composition and can be maintained by drying the films at high air temperatures without causing API deterioration.

As the volatile liquid evaporates, uniform heat dispersion occurs across the film, and the desired distribution of elements is maintained throughout the film, resulting in a viscoelastic solid. Even with small amounts of remaining water, the film can be further dried without losing its intended heterogeneity.[20] Even usually the solvent is entirely removed resulting in a final film that is less than 6% water.

Evaluation test for oral dissolving thin films morphological and organoleptic characteristics

The colour, homogeneity, transparency, odour, and texture, taste, flavour of the oral thin films are examined as visible and sensitive.[21,22]

Thickness test

The film's thickness indicates the drugs precise dosage. The micrometer screw gauge or calibrated digital Vernier

calipers are used to measure it at five distinct critical places. The mean value obtained from these measurements is used to determine the ultimate thickness of the film. The ideal range for the film's thickness is 5 to 200 µm.[23,24]

Dryness test

The film drying process has been divided into eight stages: dry to touch, dry hard, dry through (dry to handle), dry to recoat, dust-free, tack free (surface dry), and dry print-free. While paint films are the primary application for these tests the majority of the studies can be carefully modified to assess pharmaceutical oral fast dissolving film. The specifics of evaluating these characteristics in depth are outside the purview of this review and can be found elsewhere. The strip's tenacity to stick to an accessory a piece of paper after being pressed into contact with it is known as its tack. For this investigation, instruments are also accessible.[25]

Folding endurance

One film is folded repeatedly in the same spot until it breaks to assess the films folding endurance. The folding durability of a film is measured by counting how many times it can be folded in one location without breaking.

Content uniformity

By spectrophotometrically assessing the API concentration in each of the 20 films the content homogeneity is ascertained. The ideal range for content homogeneity is 85-115% while the ideal relative standard deviation is no more than 6%.[26]

Scanning electron microscopy

Scanning electron microscopy is a crucial technique for studying the surface morphology of the layer between excipients and drugs. The process involves using a tungsten filament as an electron source to capture images of a film sample, which is placed in a sample holder and photographed at a magnification of 1000x.[27]

Differential scanning calorimetry

The Distinctive Scanner is a tool that determines the compatibility of medicine with other ingredients through the use of calorimetry. Additionally, Differential Scanning Calorimetry can be performed on both the drug and other components in the formulation. To carry out the analysis, 5mg film samples are cut, sealed in aluminum pans, and exposed to a nitrogen environment at a flow rate of 25ml/min. Temperatures ranging from 0°C to 200°C are used with a heating rate of 10°C/min.[28]

Surface of pH

To begin the process, first dissolve 2% w/v agar in a warmed isotonic solution with the desired characteristics while continuously stirring. Next, transfer the solution to a petri dish and allow it to gel at room temperature. Once the agar plate has formed, place the films on the surface and let them swell for two hours. To measure the surface pH, simply place a pH paper on the swelling film.

Weight variation

After cutting 1x1cm^2 films from each formulation the weight variability of each is determined by weighing each one separately on a sensitive scale.[29]

Tensile strength

The absolute tensile force supplied to a thin-film specimen before it breaks is its tensile strength. By dividing the applied force by the films cross-sectional area30 and multiplying the result by 100 it can be found.

Percentage tensile strength = (Load at Failure/Film Thickness×Film Width) ×100

Disintegration test

The time it takes for a film to break down or disperse when it comes into contact with water or saliva is referred to as the disintegration time, and it's measured in seconds. This moment marks the point at which the thin film begins to break down or disperse. The characteristics of water- soluble films are largely determined by their weight and thickness. The disintegration periods of OFDFs can be determined using the disintegration test equipment listed in pharmacopeias. The disintegration time of film compositions usually lasts between 5 to 30 seconds, and this duration depends on the formulation content. In cases where films degrade quickly, there is no formal guide available to determine their disintegration times.[31,32]

Dissolution test

Dissolution testing is a vital process that determines the amount of drug material that dissolves within a specific time frame, under standardized conditions. This evaluation is typically conducted using paddle or basket apparatuses. However, conducting an oral film dissolution investigation using paddle-type dissolving apparatuses can be challenging, as they may float above the dissolution media.

The dissolving medium used is determined by sink conditions and the maximum drug dosage. During the investigation, it is essential to maintain the medium's temperature at 37±0.5℃ and set its rotational speed to 50 for accurate results.

ADVANTAGES OF ORAL DISSOLVING THIN FILMS

Advantages of oral dissolving thin films are reducing the possibility of choking; prevent first-pass metabolism and offer a faster start of action at reduced dosages; transportable, no water required, cost affordable; a large surface area facilitates quick dissolution and disintegration within the oral cavity; dose accuracy and ease of administering film to patients with dysphagia, repetitive emesis, motion sickness, and mental illnesses; it has many uses in the pharmaceutical industry, including Rx prescriptions and over-the-counter (OTC) drugs for the treatment of pain, colds, erectile dysfunction, gastroesophageal reflux illness, sleep problems, and dietary supplements.[35] It gives a more precise dosage than liquids. It provides better chemical stability. It provides for both product differentiation and market expansion. Its development and launch can be completed in 12 to 16 months, which improves the product development life cycle time.[36]

CONCLUSION

Oral thin films that dissolve quickly are becoming the preferred product type for many pharmaceutical products, replacing traditional tablets. These films offer the same benefits as tablets, such as accurate dosing and simple application, but with the added advantage of faster absorption and more discreet use. They are particularly useful in emergencies where quick action is required, and they can be taken by people of all ages. Additionally, this innovative drug delivery system provides a solid foundation for extending the lives of existing medications and developing new ones without compromising patient safety. Ongoing research is exploring even more possibilities for this technology, including the use of multilayer films with incompatible active medicinal components.

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REFERENCES

1. Choudhary N, Sekhon BS. An overview of advances in the standardization of herbal drugs. J Pharm Edu Res. 2011;2(2):55.
2. Ackerknecht EH. Therapeutics: from the primitives to the twentieth century, New York, HafnerPress. 1973;526.
3. Habib W, Pritchard JF, Bozigian HP, Gooding AE, Griffin RH, Mitchell R, et al. Fast-dissolve drug delivery system. Crit Rev Ther Drug Carrier Syst. 2000;17:61-72.
4. Liang CA, Chen HL. Fast dissolving intraoral drug delivery systems. Expert Opin Ther Patents. 2001;11:981-6.
5. Anderson O, Zweidorff OK, Hjelde T, Rodland EA, Problems when swallowing tablets. TidsskrNorLaegeforen.1995;115:947-9.
6. Standing JF, Tuleu C. Paediatric formulations-getting to the heart of the problem. International Journal of Pharmaceutics. 2005;300:56-66.
7. Parmar D, Patel U. Orally Fast Dissolving Film as Dominant Dosage for Quick Releases. Int J Pharm Res BioSci. 2012;1(3):24-41.
8. Zhang H, Zhang J, Streisand JB. Oral Mucosal Drug Delivery: Clinical Pharmacokinetics and Therapeutic Applications. Clin Pharmacokinetics. 2002;41:661-80.
9. Reddy MR. A Review an Introduction to Fast Dissolving Oral Thin Film Drug Delivery Systems. J Pharm Sci Res. 2020;12(7):925-40.
10. Rekka MS, Sultana SS, Mahathi K, Parveen P, Prathima B, Seethadevi A. Novel Oral drug delivery system: Fast dissolving buccal films. Am J Pharm Health Res. 2014;2:17-41.
11. Saini P, Kumar A, Sharma P, Visht S. Fast disintegrating oral films: A recent trend of drug delivery. Int J Drug Dev Res. 2012;4:80-94.
12. Malke S, Shidhaye S, Desai J, Kadam V. Oral films: Patient compliant dosage form for pediatrics. Internet J Ped Neonatology. 2009;11:1-7.
13. Niyaz USH, Elango K. Oral fast dissolving films: An innovative drug delivery system. World J Pharm Pharm Sci. 2018;7:881-907.
14. Nehal S, Garima G, Pramod KS. A novel approach in oral fast dissolving drug delivery system and their patents. Advan Biol Res. 2011;5:291-303.
15. Pandya K, Patel KR, Patel MR, Patel NM. Fast dissolving films: a novel approach to oral drug delivery. Asian J Pharm Sci Technology. 2013;3:25-31.
16. Rathi V, Senthil V, Kammili L, Hans R. A brief review on oral film technology. Int J Res Ayu Pharm. 2011;2(4):1138-47.
17. Arya A, Chandra A. Fast Dissolving Oral Films: An Innovative Drug Delivery System and Dosage Form. Int J ChemTech Res. 2010;10:576-83.
18. Cilruzo F, Cupone EI. Fast dissolving films made of maltodextrins. Eur J Pharm Biopharm. 2008;70:895-900.
19. Bhyan B, Jangra S, Kaur M, Singh H. Orally fast dissolving films. Innovations in formulation and technology. Int J Pharm Sci Rev Res. 2011;9(2):50-7.
20. Patel R, Shardul N, Patel J, Baria A. Formulation development and evaluation of mouth melting film of Ondansetron. Arch Pharm Sci Res. 2009;1(2):212-7.
21. Murthy AV, Ayalasomayajula LU, Earle RR, Jyotsna P. Formulation and Evaluation of Tramadol Hydrochloride Oral Thin Films. Int J Pharm Sci. 2018;9:1692-8.
22. Chinnala KM, Vodithala S. Formulation and evaluation of fast disintegrating oral thin films of

Cinitapride hydrogen tartrate. Int J Curr Adv Res. 2017;6:4737-40.
23. Gowri R, Narayanan N, Revathy S, Prabhavathy P, Preethy MG, Rekha G. Melt in mouth films-an effective alternative drug delivery system. Int J Biol Pharm. 2013;4:645-50.
24. Rajini B, Pravin P, Sushil K, Sandeep A. Orally dissolving strips - a new approach to oral drug delivery system, Int J Pharm Investing. 2013;3:67-8.
25. Dixit RP, Puthli SP. Oral strip technology: Overview and future potential. J Control Rel. 2009;139:94-7.
26. Rajini B, Pravin P, Sushil K, Sandeep A. Orally dissolving strips-a new approach to oral drug delivery system, Int J Pharm Investing. 2013;(3):67-8.
27. Archana J, Vijaya V, Uma MR. Formulation and evaluation of oral thin films containing saxagliptin, IJJIPSR. 2014;2:2669-90.
28. Ammar HO, Ghorab M, El-Nahhas SA, Kamel R. Polymeric matrix system for prolonged delivery of Tramadol hydrochloride, Part I physicochemical evaluation. AAPS Pharm Sci Tech. 2009:10(1):7-20.
29. Jelvehgari M, Montazam SH, Soltani S, Mohammadi R, Azar K, Montazam SA. Fast-dissolving oral thin film drug delivery systems consist of ergotamine tartrate and caffeine anhydrous. Pharmaceutical Sciences. 2015;21:102-10.
30. Siddiqui MDN, Garg G, Sharma PK. A Novel Approach in Oral Fast Dissolving Drug Delivery System and Their Patents. Advan Biol Res. 2011;5:291-303.
31. Malke S, Shidhaye S, Desai J, Kadam V. Oral films: Patient compliant dosage form for pediatrics. Internet J Ped Neonatol. 2009;11:1-7.
32. Irfan M, Rabel S, Bukhtar Q, Qadir MI, Jabeen F, Khan A. Orally disintegrating films: A modern expansion in drug delivery system. Saudi Pharm J. 2016;24:537-46.
33. Dubson A, Shalev A. Electrospun dosage form and method of producing the same. WO2006106514 A3, 2007.
34. Sandeep S, Arun N, Monika HK, Fast Dissolving Films (FDF): Innovative drug delivery system, Pharmacologyonline. 2011;2:919-28.
35. Naziya K, Raghavendra R NG, Mahipal R, Overview on fast dissolving oral films. Int J Chem Pharm Sci. 1, 2013;1:63-75.
36. Dhere PM, Patwekar SL. Review on preparation and evaluation of oral disintegrating films. Int J Pharm Tech. 2011;3(4):1572-85.

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