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Review on Oral Dispersible Film

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ABSTRACT: Oral dispersible film are gaining popularity and acceptance as new DDS to ensure safety, efficacy, compliance and patient acceptability. This delivery system helps to achieve drug response by local and systemic action through different routes. ODF can be taken without water, is easy to administer has rapid onset of action and can surmount first pass metabolism. This novel approach of preparing of dispersible film (odf) Provide benefits to pediatric geriatric and bed ridden patient. Most frequently used technique to develop ODF is the solvent casting into this method using film forming polymers which have a fast-disintegrating time, improved drug dissolution and better drug contents. Evaluation of prepared ODFs done by considering parameter is such as film thickness folding endurance disintegration time surface ph, weight variation, in-vitro dissolution test content uniformity and FTIR.

KEYWORDS: Oral dispersible film, solvent casting method, evaluation techniques, patient acceptability, film forming polymers, local and systemic action Rapid onset of action, surmount first pass metabolism**.**

I. INTRODUCTION OF ORAL DISPERSIBLE FILMS

The oral mucosal epithelium is a multi-cell layer (40–50 cells thick) and is made up of proteins and carbohydrates. Mucus is a gel-like fluid released from the mucosal epithelium, having 90–99% water content, the remaining components being (water-insoluble) glycoproteins, nucleic acids, electrolytes, and enzymes.

The mucosal epithelium layer consists of two areas—a hydrophilic area and a lipophilic area. The oral mucosa has a higher permeability as compared to the intestine and epidermis and has around 4–4000 times more penetrationpower than the skin.

[1] The mucosal epithelium layer has two absorption routes for drugs—the transcellular and paracellular paths. The amphiphilic, hydrophilic, or hydrophobic nature determines the absorption capacity of drugs. Hydrophilic drug penetration is facilitated by the polar nature of the intercellular space, while lipophilic structure facilitates drug molecules with a high partition coefficient.

[2] Conventional tablets are easily broken down and require substantial packaging for handling, storage, and transportation, while oral films are flexible, easy to handle, and can be stored for longer use.

[3] The oral mucosa has greater power of penetration because of more blood vessels and the thin membrane structure—properties that provide good bioavailability. The higher the permeation, the higher the systemic bioavailability of drug contents, with avoidance of the first pass effect. Generally, ODFs are flexible and consist of athin polymer layer, made with or without the use of plasticizers. By using this novel drug delivery system (film technology), the side effects of drugs are reduced, metabolism of drugs is increased, absorption is improved, and, most significantly, the bioavailability of drugs is increased. ODFs provide rapid dissolution, appropriate drug loading capacities, and improve the stability of drug formulations. Furthermore, they are non-toxic, biocompatible, and biodegradable.

[4] ODFs have been developed for a wide range of drugs providing local action or systemic action. For local action, ODFs are used for toothaches, local anaesthetic, cold sores, and oral ulcers.

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Fig no. 1 Oral Dispersible Film

II. MERITS AND DEMERITS OF ORAL DISPERSIBLE FILM

[5] ODFs have many advantages over conventional dosage forms because they do not require any drinking of fluid for intake regardless of condition. They are stable, efficacious, have improved absorption, and higher bioavailability because of no first pass effect. ODFs have higher patient compliance because geriatric, paediatric, and paralyzed patients can easily take them without water and without choking problems. ODF technology helps to incorporate drugs at low doses as well as drugs that are incompatible with the gastrointestinal tract, and bioavailability problems are easily resolved. They provide quick effects in emergency conditions, such as asthmatic attack, migraine attack, angina attack, and in intraoral diseases. The development process of ODFs is easy and can be completed within a few days.

[6] Oral Dispersible Films have disadvantages because they require special equipment for packaging, and storage. This technology is not appropriate for drugs that are not ionized at oral pH or drugs that require large doses. ODFs are hygroscopic and therefore susceptible to deterioration, which makes them difficult to protect. Drugs that are absorbed by active diffusion cannot be incorporated into ODFs. They have fast dissolution and disintegration processes and so dose termination cannot be like that of tablets.

III. CLASSIFICATION OF ORAL DISPERSIBLE FILMS

ODFs are generally classified into three classes: type 1, according to dissolution; type 2, according to layering; and type 3, according to the nature of the API.

Type 1 ODFs:

Type 1 ODFs are divided into three subclasses: fast, moderate, and slow. Films that dissolve within thirty seconds are termed fast-dissolving ODFs and have a thickness of around 50–150 m; films that dissolve within one to thirty minutes are known as moderately dissolving ODFs; and slow-dissolving ODFs can take more than thirty minutes to dissolve.

[7] Fast-dissolving films are used in emergency conditions, while slow/moderately dissolving films are used to prepare nicotine-based products, as they help to lessen or eradicate cravings in patients who have used tobacco regularly and become dependent.

Type 2 ODFs:

Type 2 ODFs are classified according to the number of layers they contain. Layers can be monolayers, bilayers, or multilayers. Monolayer oral films consist of an API, a film-forming polymer, and excipients, while bilayer or double layer films consist of one API layer and another taste-masking or permeation-enhancing layer. In multilayer films the API layer is sandwiched between two layers.

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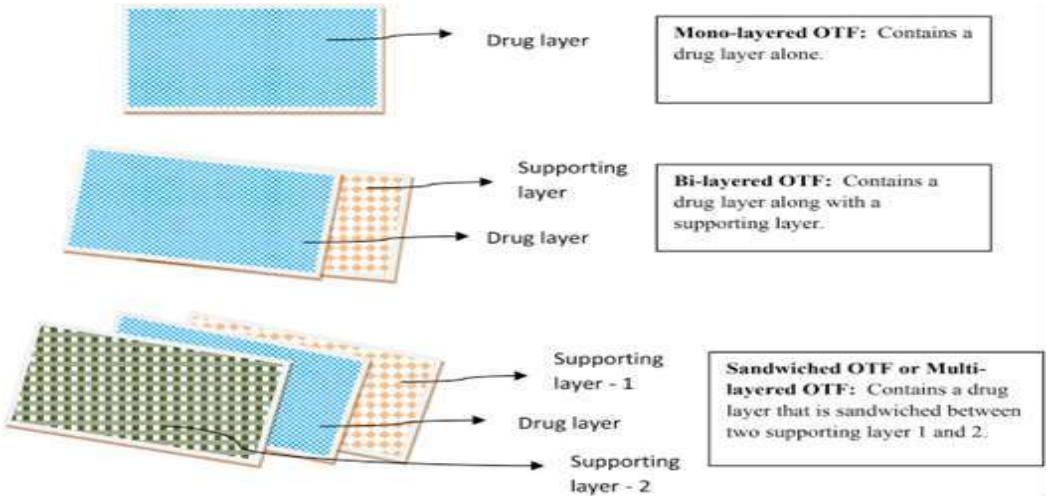

Fig no 2 layers of ODFs

Type 3 ODFs:

[8] Type 3 ODFs are further classified according to API source, which may be synthetic, e.g., sildenafil or natural (animal or plant), e.g., ginger and turmeric.

[9] Films prepared using minerals, vaccines, vitamins, or micronutrients constitute the other class of type 3 ODFs, e.g., vitamin D ODFs.

[10] All of these ODFs contain prescription drugs or over-the- counter drugs, while ODFs prepared from plant sources are difficult to fabricate.

IV. FORMULATION OF ORAL DISPERSIBLE FILMS

[11] ODFs must have a pleasant taste, be of appropriate size, and be packed in suitable packing material. To ensure all these properties, drugs and excipients must have good stability, the required solubility and permeability, and the dose of the incorporated drug must be small dose with a low molecular weight (MW). A good ODF can be formulated using the desired active compound, either an active nutraceutical or a pharmaceutical ingredient, and excipients (film formers, stabilizers, plasticizers, sweeteners, and thickeners).

Drugs: -

[12] Other than pharmaceutical ingredients films, ODFs have also been prepared using plant leaf extracts that have therapeutic activities, e.g., cannabinoids. The preparation methods for ODFs seems to be easy but there are two difficult issues, namely, the unpleasant tastes of drugs and dose uniformity.

[13] Taste masking can also be achieved by altering film composition (film-formers and drugs at a ratio of 9:1). Taste masking also helps to reduce drug load. However, by using obscuration methods, the taste masking of bitter drugs can be achieved easily. Another major problem in ODF formulation is drug agglomeration, which causes non-uniformity. Many companies have tried to resolve this issue in vain; to overcome it, they have made use of multilayer formulations. However, multilayer film formulation is expensive and time consuming.

Excipients: -

[14] Out of all the excipients used in the formulation of ODFs, the film former plays an important role and is one of the key constituents. Maintaining the balance between disintegration times and the mechanical properties of ODFs, polymers, concentrations, and types is the main issue because the properties of polymers are affected by molecular weight.

[15] Pullulan, polyvinyl alcohol (PVA), and cellulose derivatives are the commonest polymers that are usedin the preparation of films.

[16] Some of the examples of mixtures of polymers used in ODFs are methacrylic acid and Hypromellose, croscarmellose and PVA and macrogol-PVA and povidone.

[17] A class of substances that help to provide

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flexibility in films are plasticizers, which aid the fabricationof films.

[18] In the literature, researchers have studied the impact of plasticizers on ODF preparation, and the selection of type and amount is an important consideration.

V. TECHNIQUES OF MANUFACTURING ORAL DISPERSIBLE FILMS

The manufacturing of ODFs is not an easy process and a number of techniques have been developed to manufacture them, such as the solvent casting method, the hot-melt extrusion method, the rolling method, semi-solid casting, and solid dispersion extrusion.

[19] Hot-melt extrusion and the solvent casting method are the commonest methods used by researchers and industries for the manufacture of films.

1. Solvent Casting Method:

Solvent casting is one of the oldest methods used for the preparation of ODFs. It is a hydrous method, and thermostable and thermolabile drugs in dosage form are prepared via this method.

[20] The solvent casting method is the best method for preparing heat- and light-sensitive active ingredients because lower temperatures are required by the volatile ingredients and for removing any solvent from the films. However, this method has some limitations, as during preparation, trace amounts of solvents can be left which hinder compendial compliance. Moreover, flammable solvents, such as methanol and ethanol, or volatile solvents require special protection to avoid fire.

2. Hot-Melt Extrusion Method:

The hot-melt extrusion method was used for the preparation of sustained release tablets and granules in transmucosal drug delivery systems and in transdermal drug delivery systems such as skin patches in the past. In this technique, one or more drugs can easily be extruded to achieve the desired dosage forms for delivering drugs. With this method, drugs and excipients are easily modified into film form for drug delivery instead of using the solvent casting method. In the hot-melt extruded method, films are created by the blending of the drug, film former, plasticizer, surfactants, and other required excipients in appropriate amounts for uniform mixing.

[21] After mixing, the extrude is fed into a hopper and conveyed to a heated barrel where homogeneous films are developed with thicknesses of less than 1 mm. In medical devices, drugs can be incorporated into catheters and biodegradable stents by hot-melt extrusion methods. These perspectives may increase innovation, research, and commercialization across research institutes, universities, pharmaceutical industries, and biotechnology industries.

3. Semi-Solid Casting:

[22] The semi-solid casting method is also used for the development of ODFs. In this method, water-soluble solutions and film forming polymers are prepared and then added to acid insoluble polymer solution. Plasticizers in the required ratios are added to the previously prepared solution with the aim of obtaining the required gel mass. Under controlled conditions, the prepared gel mass is cast in the form of films of 0.015–0.05-inch thickness.

4. Rolling Method:

ODFs can also be prepared via the rolling method, in which drug solutions are rolled on a drum. The drug is dissolved in distilled water or a mixture of alcohol and water. After rolling the premixed solutions on the roller, the thin film is dried and cut into the desired sizes.

[23] The premixed solution comprises the active ingredient, polar solvent, film forming polymer, and the required excipients are added in the tank. The solution with the intended dose is fed by a controlled valve pump to obtain the desired thickness.

5. 3D Printing:

[24] Researchers have developed ODFs using 3D printing techniques, and in the final step of production the resultant is formed by the solidification of powder material or semi-solid material or by liquid materials. In 3D printing methods, extrusion technologies with fused deposition are the commonest means of developing drug delivery systems.

[25] One example of this method is the fabrication of aripiprazole ODFs. Initially, aripiprazole filaments are prepared by hot-melt extrusion then mixed with PVA and moistened with ethanol before drying. The film filaments are prepared using an extruder. The blended powder is fed and extruded through the die at a constant

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speed. The film filament is then collected and further used to fabricate 3D-modeled ODFs. The fabricated ODFs have specific lengths, widths, and depths.

VI. CHARACTERIZATION AND EVALUATION

[26] The characterization and evaluation of prepared ODFs is important, and numerous methods, such as organoleptic, disintegration time, dissolution, surface pH visual inspection, moisture content, swelling index, mechanical properties, transparency, contact angle, and content uniformity tests, have been developed to assess prepared ODFs according to desired aims and objectives.

1. Organoleptic Evaluation:

[27] Organoleptic evaluation is an in vivo and in vitro taste evaluation method, and special, controlled human taste panels are used to conduct them. In in vivo evaluation, human volunteers are involved in the taste evaluation, and in vitro taste evaluation of films is performed using electronic taste sensing systems.

2. Surface Morphology:

[28] Surface morphology or visual inspection of ODFs gives evidence regarding transparency, homogeneity, and colour.

[29] For this, light microscopy (LM) and scanning electron microscopy (SEM) have been used. SEM performance, due to advancement and uniform surfaces with an absence of pores, can be used to determine the high quality of ODFs. Films of 1 cm2 were placed on the stage of a microscope over a glass slide and the structure of film was observed at the micro-level, while SEM observed film structure more deeply.

3. Disintegration Time:

[30] In pharmacopoeias, numerous disintegration apparatuses are listed for use in the determination of film disintegration times (DTs). DT is a function of film composition because DT varies with formulations. Typically, ODFs disintegrate within 5–30 s. To date, no official pharmacopeial guidelines have been made available for determining the DTs of ODFs.

[31] There are two methods for determining the DTs of ODF formulations by Petri dish method and slide frame methods, but mostly investigators use the Petri dish method.

4. In Vitro Dissolution Test:

For in vitro dissolution testing, two official paddle and basket apparatuses have been used to determine film dissolution time. During the dissolution testing, sink conditions must be maintained. Occasionally, during dissolution, film floats over the medium and testing became difficult.

[32] This problem occurs mostly with a paddle apparatus; therefore, the basket apparatus method is preferred. In the context of a study, the media used in both apparatuses were phosphate-buffered solution of pH 6.8, 0.1 N HCL, purified water, gastric fluids, and intestinal fluids. Six aliquots of 5 mL were drawn after every minute and then at 8, 10, 12, 16, 20, and 30 min. The drawn samples were analyzed using a UV spectrophotometer.

5. Swelling Properties:

[33] Swelling properties of ODFs are determined because polymers are used for making films hydrophilic in nature.

[34] Simulated saliva solution has been used to augment the swelling profile of films. The swelling of filmswas evaluated with the percentage of hydration. For this, firstly, films were weighed (W1) and immersed in simulated salivary fluid for a pre-set time. After that time, the samples were taken out, excess water was removed from the surfaces, and they were again weighed (W2). The percent hydration was calculated using the followingformula: formal……

$$\text{Hydration (\%)} = \frac{W2 - W1 \times 100}{W1}$$

[35] To calculate the degree of swelling, the initial film weight (Wi) was noted and then the film was placed on a wire mesh and dipped into medium. The film weight was noted till no more increase in weight was observed after regular time intervals (Wf). The degree of swelling was calculated using the following formula:

$$\text{Degree of swelling} = \frac{Wf - Wi}{Wi}$$

6. Surface pH:

[36] The surface pH of the buccal cavity is in the range of 5.5 to 7.4. ODFs are designed to quickly dissolve in the oral cavity after placement on the tongue, so ODF pH levels must be in the

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range of buccal cavity pH, as formulations having alkaline or very acidic pHs cause mucosal irritation. Randomly, films were selected for determining surface ph. The pH of dry film cannot be determined, so, first, film state was altered to measure pH by dissolving the films in 2 mL of distilled water. The electrode of the pH meter was placed on the surface of the solution and the reading was noted after 10 min to allow the stabilization of the pH value.

7. Mechanical Properties:

[37] Mechanical properties of ODFs were calculated on the basis of results obtained for surface thickness, percent elongation, young's modulus, tear resistance folding endurance, and tensile strength.

8. Young's Modulus:

[38] Young's modulus reflects the extent of film elasticity or stiffness. It specifies resistance to deformation films and can be determined by drawing a graph between the stress–strain curves and the slopes showing young's moduli. The higher the slope, the higher the tensile modulus, and vice versa.

$$\text{Young's modulus} = \frac{\text{Slope x 100}}{\text{Film thickness x Speed}}$$

[39] For this test, first dissolve the ODF of size 1 cm2 in 100 mL buffer solution. From that solution, take aliquots of 2 mL and dilute with buffer solution up to 10 mL. The diluted sample is then to be checked with a UV– Visible spectrophotometer by setting the absorbance according to the active ingredient used. The absorbance value helps to estimate the amount of drug in the film to check drug content uniformity.

VII. PACKAGING OF FILMS

[40] Packaging of films is important to maintain stability during storage and retain the mechanical properties of ODF formulations. Packaging material acts as a barrier to provide protection from light, heat, oxygen, and moisture. Commercially available packaging materials for the storage of films include foil paper, aluminium pouches, plastic pouches, and blister packs. However, none of them is effective in providing stability in the storage of film products.

[41] Commercially, different sizes of ODFs and simple films are available on the market of size 1 2cm2, 2 2cm2, and 32cm2.

[42] The packing of ODFs is economical, safe, and easy, though time-consuming; it also provides ease in handing, and films of any size and dimensions can be packed in pouches.

[43] The multiple film packaging system is an automated and computer-driven process for ease of use and to increase patient compliance.

VIII. CONCLUSION

In conclusion it shows that develop process of ODFs is easy and can completed within few days. They ensure safety, efficacy as well as patient compliance. ODFs does not require water to intake. ODFs are stable, have improved absorption and having high bioavailability. As a rapid dissolving film in oral cavity, it avoids the first pass effect ODFs techniques helps to administer drugs at low doses. It protected from gastric diseases such as peptic ulcer, GERD, etc. It provides rapid effect in emergency condition such as hypertension, angina pectoris, etc. Film technology future of looks forward for delivering drugs by any route to overcome issues related with conventional dosage forms.

REFERENCES

1) Siddiqui, M.; Garg, G.; Sharma, P.K. A short review on "A novel approach in oral fast dissolving drug delivery system and their patents". Adv. Biol. Res. 2011, 5, 291–303.
2) Chan, R. Oral thin films–realms of possibility. ON drug Delivery Mag. 2016, 69, 12–17.
3) Mahboob, M.B.H.; Riaz, T.; Jamshaid, M.; Bashir, I.; Zulfiqar, S. Oral films: A comprehensive review. Int. Curr. Pharm. J. 2016, 5, 111–117. [Cross Ref]
4) Hussain, W.; Kushwaha, P.; Rahman, A.; Akhtar, J. Development and evaluation of fast dissolving film for oral-buccal drug delivery of chlorpromazine. Indian J. Pharm. Educ. Res. 2017, 51, S539–S547. [Cross Ref]
5) Kumar, V.D.; Sharma, I.; Sharma, V. A comprehensive review on fast dissolving tablet technology. J. Appl. Pharm. Sci. 2011, 1, 50–58.
6) Karki, S.; Kim, H.; Na, S.-J.; Shin, D.; Jo, K.; Lee, J. Thin films as an emerging platform for drug delivery. Asian J. Pharm.

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Volume 8, Issue 1 Jan-Feb 2023, pp: 1270-1277 www.ijprajournal.com ISSN: 2249-7781

Sci. 2016, 11, 559–574. [Cross Ref]
7) Kumar, V.D.; Sharma, I.; Sharma, V. A comprehensive review on fast dissolving tablet technology. J. Appl. Pharm. Sci. 2011, 1, 50–58.
8) Gupta, M.S.; Kumar, T.P. The potential of ODFs as carriers for drugs/vaccines against COVID-19. Drug Dev. Ind. Pharm. 2020, 47, 179–188. [Cross Ref] [PubMed]
9) Radicioni, M.; Castiglioni, C.; Giori, A.; Cupone, I.; Frangione, V.; Rovati, S. Bioequivalence study of a new sildenafil 100 mg oral dispersible film compared to the conventional film-coated 100 mg tablet administered to healthy male volunteers. Drug Des. Dev. Ther. 2017, 11, 1183. [Cross Ref] [PubMed]
10) Gopi, S.; Amalraj, A.; Kalarikkal, N.; Zhang, J.; Thomas, S.; Guo, Q. Preparation and characterization of nanocomposite films based on gum arabic, maltodextrin and polyethylene glycol reinforced with turmeric nanofiber isolated from turmeric spent. Mater. Sci. Eng. C 2019, 97, 723–729. [Cross Ref] [PubMed]
11) Gupta, M.S.; Kumar, T.P. The potential of ODFs as carriers for drugs/vaccines against COVID- 19. Drug Dev. Ind. Pharm. 2020, 47, 179–188. [Cross Ref] [PubMed]
12) Siddique, W.; Sarfraz, R.; Zaman, M.; Butt, M.; Hayat, Z.; Gul, M.; Gul, M.; Asghar, F. Impact of polymer and plasticizer on mechanical properties of film: A quality by design approach. Lat. Am. J. Pharm. 2021, 40, 3002–3008.
13) Allen, E.; Davidson, R.; LaRosa, T.; Reid, D. Oral Dissolvable Film That Includes Plant Extract. Google Patent 10,307,397, 4 June 2019.
14) Horstmann, M.; Laux, W.; Hungerbach, S. Rapidly Disintegrating Sheet-Like Presentations of Multiple Dosage Units. Google Patent 5,629,003, 13 May 1997.
15) Garsuch, V.; Breitkreutz, J. Comparative investigations on different polymers for the preparation of fast-dissolving oral films. J. Pharm. Pharmacol. 2010, 62, 539–545. [Cross Ref]
16) Boateng, J.S.; Matthews, K.H.; Auffret, A.D.; Humphrey, M.J.; Stevens, H.N.; Eccleston, G.M. In vitro drug release studies of polymeric freeze-dried wafers and solvent-cast films using paracetamol as a model soluble drug. Int. J. Pharm. 2009, 378, 66–72. [Cross Ref]
17) Sharma, R.; Parikh, R.; Gohel, M.; Soniwala, M. Development of taste masked film of valdecoxib for oral use. Indian J. Pharm. Sci. 2007, 69, 320. [Cross Ref]
18) Kulkarni, A.; Deokule, H.; Mane, M.; Ghadge, D. Exploration of different polymers for use in the formulation of oral fast dissolving strips. J. Curr. Pharm. Res. 2010, 2, 33–35
19) Cao, N.; Yang, X.; Fu, Y. Effects of various plasticizers on mechanical and water vapor barrier properties of gelatin films. Food Hydrocoll. 2009, 23, 729–735. [Cross Ref]
20) Mishra, R.; Amin, A. Manufacturing techniques of orally dissolving films. Pharm. Technol. 2011, 35, 70–73.
21) Melegari, C. Study of Different Technologies for Film Coating of Drug Layered Pellets Using Ethyl cellulose as Functional Polymer; Università di Bologna: Bologna, Italy, 2016.
22) Tumuluri, V.S.; Kemper, M.S.; Lewis, I.R.; Prodduturi, S.; Majumdar, S.; Avery, B.A.; Repka, M.A. Off-line and on-line measurements of drug-loaded hot-melt extruded films using Raman spectroscopy. Int. J. Pharm. 2008, 357, 77–84. [Cross Ref]
23) Arya, A.; Chandra, A.; Sharma, V.; Pathak, K. Fast dissolving oral films: An innovative drug delivery system and dosage form. Int. J. Chem Tech Res. 2010, 2, 576–583.
24) Yang, R.K.; Fuisz, R.C.; Myers, G.L.; Fuisz, J.M. Thin Film with Non-Self-Aggregating Uniform Heterogeneity and Drug Delivery Systems Made Therefrom. Google Patent 7,425,292, 16 September 2008. Pharmaceuticals 2022, 15, 844
25) Annaji, M.; Ramesh, S.; Poudel, I.; Govindarajulu, M.; Arnold, R.D.; Dhanasekaran, M.; Babu, R.J. Application of extrusion-based 3D printed dosage forms in the treatment of chronic diseases. J. Pharm. Sci. 2020, 109, 3551–3568. [Cross Ref] [PubMed]
26) Łyszczarz, E.; Brniak, W.; Szafraniec-Szczęsny, J.; Majka, T.M.; Majda, D.; Zych, M.; Pielichowski, K.; Jachowicz, R. The impact of the preparation method on the properties of oral dispersible films with aripiprazole: Electrospinning vs. casting and 3D printing methods. Pharmaceutics 2021, 13, 1122. [Cross Ref]
27) Chaudhary, H.; Gauri, S.; Rathee, P.;

Kumar, V. Development and optimization of fast dissolving Oro-dispersible films of granisetron HCl using Box–Behnken statistical design. Bull. Fac. Pharm. Cairo Univ. 2013, 51, 193–201. [Cross Ref]

28) Pein, M.; Eckert, C.; Preis, M.; Breitkreutz, J. Taste Sensing System αAstree as Analytical Tool— Performance Qualification Using Caffeine Citrate as Model Substance. In Proceedings of the 8th Pharmaceutics & Biopharmaceutics World Meeting, Istanbul, Turkey, 19–22 March 2012.
29) Raju, S.; Reddy, P.S.; Kumar, V.A.; Deepthi, A.; Reddy, K.S.; Reddy, P.M. Flash release oral films of metoclopramide hydrochloride for paediatric use: Formulation and in-vitro evaluation. J. Chem. Pharm. Res. 2011, 3, 636–646.
30) Zaman, M. Formulation and Evaluation of Tizanidine-Meloxicam Mucoadhesive Buccal Films by Central Composite Rotatable Design and Their Pharmacokinetic Studies; Bahauddin Zakariya University Multan: Multan, Pakistan, 2018.
31) 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, 9–15.
32) Zaman, M.; Murtaza, H. Development and validation of RP-HPLC method for simultaneous estimation of tizanidine HCl and meloxicam in bilayer mucoadhesive buccal films. Acta Pol. Pharm. Drug Res. 2018, 75, 851–859. [Cross Ref]
33) Anwar, S.; Zaman, M.; Raja, M.A.G.; Mahmood, A.; Amjad, M.W. Rosuvastatin, Perindopril and Ezetimibe loaded instant release buccal films: Development and in vitro characterization. J. Appl. Biomed. 2020, 18, 115–125. [Cross Ref]
34) Peh, K.K.; Wong, C.F. Polymeric films as vehicle for buccal delivery: Swelling, mechanical, and bio adhesive properties. J. Pharm. Pharm. Sci. 1999, 2, 53–61.
35) Baranowski, P.; Karolewicz, B.; Gajda, M.; Pluta, J. Ophthalmic drug dosage forms: Characterisation and research methods. Sci. World J. 2014, 2014, 861904. [Cross Ref]
36) Irfan, M.; Rabel, S.; Bukhtar, Q.; Qadir, M.I.; Jabeen, F.; Khan, A. Orally disintegrating films: A modern expansion in drug delivery system. Saudi Pharm. J. 2016, 24, 537–546. [Cross Ref]
37) Kunte, S.; Tandale, P. Fast dissolving strips: A novel approach for the delivery of verapamil. J. Pharm. Bioallied Sci. 2010, 2, 325. [Cross Ref]
38) Preis, M.; Knop, K.; Breitkreutz, J. Mechanical strength test for oral dispersible and buccal films. Int. J. Pharm. 2014, 461, 22–29. [Cross Ref] [PubMed]
39) Wuzhu, Y.; Shifeng, W.; Jun, L.; Zhufeng, Y. Determination of reduced Young's modulus of thin films using indentation test. Acta Metall. Sin. 2009, 22, 468–480. [Cross Ref]
40) Siqueira, W.L., Jr.; Nicolau, J. Stimulated whole saliva components in children with Down syndrome. Spec. Care Dent. 2002, 22, 226–230. [Cross Ref] [PubMed]
41) Amin, P.M.; Gangurde, A.; Alai, P. Oral film technology: Challenges and future scope for pharmaceutical industry. Int. J. Pharm. Pharm. Res. 2015, 3, 184–203.
42) Sharma, D.; Kaur, D.; Verma, S.; Singh, D.; Singh, M.; Singh, G.; Garg, R. Fast dissolving oral films technology: A recent trend for an innovative oral drug delivery system. Int. J. Drug Deliv.2015, 7, 60–75
43) Dixit, R.P.; Puthli, S.P. Oral strip technology: Overview and future potential. J. Control. Release 2009, 139, 94–107. [Cross Ref] [PubMed]