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Review Article

AN OVERVIEW ON ORAL THIN FILMS–METHODOLOGY, CHARACTERIZATION AND CURRENT APPROACH

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ABSTRACT

The pharmaceutical sector is looking for new ways to deliver drugs, and one such way is through thin films. It has been said that thin films offer an alternative to traditional dosage forms. They offer rapid, local, or systemic effects and are a very flexible platform. Furthermore, patients with dysphagia, elderly, paediatrics, or bedridden patients, as well as those who have difficulty accessing water, can easily utilize these systems on their own. There are several ways to administer these drug delivery systems, including transdermally, ocularly, buccally, sublingually, and orally.

One of the most creative and patient-focused novel drug delivery systems is Orodispersible Thin Films (OTF). Numerous pharmaceutical companies and academic experts worldwide are currently investigating the potential of these films for delivering drugs derived from both synthetic and natural sources. The beauty of this special drug delivery method is that, as we can see from the subjects' consumption of conventional dosage forms (tablets, capsules), they don't require water to be consumed. Furthermore, these delivery methods do a great job of encouraging patient compliance in general, especially in the case of both older and pediatric patients.

This review shows a detailed review of oral thin film its applications and method of preparation; mainly focus of this research is thin film introduction to researchers and last 10 y of research on thin film with drugs and polymers used in research.

Keywords: Oral thin film, Fast release, Solvent casting, Disintegration, Saliva, etc

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INTRODUCTION

The oral route is the most preferred route for the delivery of drugs to date as it bears various advantages over the other routes of drug administration, but oral drug delivery systems still need some advancements to be made because of their drawbacks related to particular classes of patients which include geriatric, pediatric and dysphasic patients associated with many medical Conditions as they have difficulty in swallowing or chewing solid dosage forms. Many pediatric and geriatric patients are unwilling to take solid preparations due to fear of choking. Even with fast-dissolving tablets, there is a fear of choking due to the tablet-type appearance. One study showed that 26% of 1576 patients experienced difficulty in swallowing tablets [1]. The most common complaint was tablet size, followed by surface form and taste. The problem of swallowing tablets was more evident in geriatric and pediatric patients, as well as traveling patients who may not have ready access to water. So, fast-dissolving drug-delivery systems came into existence in the late 1970s as an alternative to tablets, capsules, and syrups for pediatric and geriatric patients who experience difficulties in swallowing traditional oral solid dosage forms [2, 3]. These systems consist of solid dosage forms that disintegrate and dissolve quickly in the oral cavity without the administration of water. Research and development in the oral drug delivery segment has led to the transition of dosage forms from simple conventional tablets or capsules to modified release tablets or capsules to oral disintegrating tablets (ODT) to wafers to the recent development of oral fast dissolving films (OFDFs). Amongst the plethora of avenues explored for rapid drug-releasing products, oral strip technology is gaining much attention [4].

The film is an ideal intraoral fast-dissolving drug delivery system, which satisfies the unmet needs of the market, is easy to handle and administer, maintains a simple and convenient packaging, alleviates unpleasant taste, and is straightforward to manufacture [5]. The film is placed on the top or the floor of the tongue. It is retained at the site of application and rapidly releases the active agent for local and/or systemic absorption. Oral fast-dissolving film (FDF) is one such novel approach to increase consumer acceptance by rapid dissolution and self-administration without water or chewing. The need for non-invasive delivery systems continues due to patients' poor acceptance and compliance with existing delivery regimes, limited market size for drug companies and drug uses, coupled with high cost of disease management [6, 7].

Numerous pharmaceutical preparations are administered as liquids, tablets, granules, and powders. A tablet design is typically given to patients in a form that allows them to chew or swallow a specific dosage of medication. However, swallowing or chewing solid dosage forms can be challenging for patients, especially those who are elderly or young [8]. Because of their fear of asphyxiation, many elderly and children are unwilling to take those solid dosage forms. To address this need, oral dissolving tablets, or ODTs, have been developed. Short dissolution/disintegration times do not, however, eliminate the risk of asphyxiation and the nervousness of swallowing the solid form of medication (tablet, capsule) for some patient populations. In these circumstances, oral thin film (OTF) drug delivery systems are a better option [9, 10].

Approximately one-third of the population, primarily the geriatric and pediatric populations, has swallowing difficulties, resulting in poor compliance with oral tablet drug therapy, which leads to reduced overall therapy effectiveness [11]. A new oral fast-dissolving dosage form such as the fast-dissolving tablet or fast-dissolving film, has been developed, which offers the combined advantages of ease of dosing and convenience of dosing in the absence of water or fluid. Most of the existing fast-dissolving drug delivery systems are in the form of solid tablets and are designed to dissolve/disintegrate in the patient's mouth within a few seconds or minutes without the need to drink or chew. However, the fear of taking solid tablets and the risk of choking for certain patient populations still exist despite their short disintegration/dissolution times [12]. The film overcomes the danger/fear of choking1. The development of a fast-dissolving film also provides an opportunity

for a line extension in the marketplace; a wide range of drugs (e. g., neuroleptics, cardiovascular drugs, analgesics, antihistamines, anti-asthmatic and drugs for erectile dysfunction) can be considered candidates for this dosage form [13].

Fig. 1: Oral thin film pictorial form [14]

Oral cavity

The mucus produced by the 40–50 cell layer of the oral tissue epithelium is composed of proteins and carbohydrates. The mucosal thickness varies between 100 and 200 µm at the base of the mouth, the tongue, and the gums. Mucus, a small gel-like fluid secreted by the submucosal layer, is composed of 90%–99% water, 1%–5% water-insoluble glycoprotein, and other components like proteins, enzymes, electrolytes, and nucleic acids [15, 16]. In contrast, saliva and parotid are secreted by lobules within the salivary glands from the salivary duct in the vicinity of the sublingual canals and submandibular teeth. Most frequently, small salivary glands are located on the mucosa of the cheeks and lips. About 1-2 ml of saliva is secreted in total in a minute [17-20].

The mucus, water, the enzymes lysozyme and amylase, mineral salts, immunoglobulins, and blood clotting factors make up saliva [21]. Saliva and mucin function as barriers for the oral mucosa as well. There are two distinct regions in the mucosal epithelial structure: the lipophilic space between cells and the lipophilic membrane of the stratified epithelium and the more hydrophilic region. In terms of substance permeability, the oral mucosa can withstand conditions that the intestinal mucosa and the epidermis cannot [22]. The buccal mucosa is thought to have 4–4000 times greater permeability than the skin. There are two primary drug absorption pathways provided by the mucosal epithelium: the transcellular (intercellular) and paracellular (intercellular) pathways (fig.). While more hydrophilic molecules can enter the intercellular space due to their polarity, particles with a high partition coefficient can more easily pass through the lipophilic structure that makes up cell membranes. The drug's absorption depends on whether it is hydrophilic, hydrophobic, or amphiphilic [23, 24].

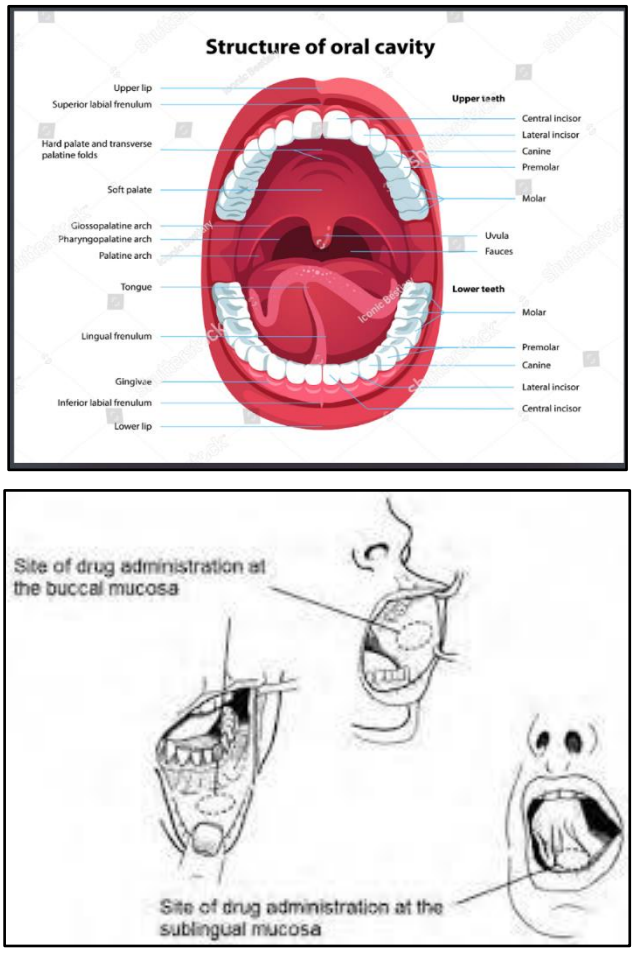

Fig. 2: Structure of oral cavity [17-20]

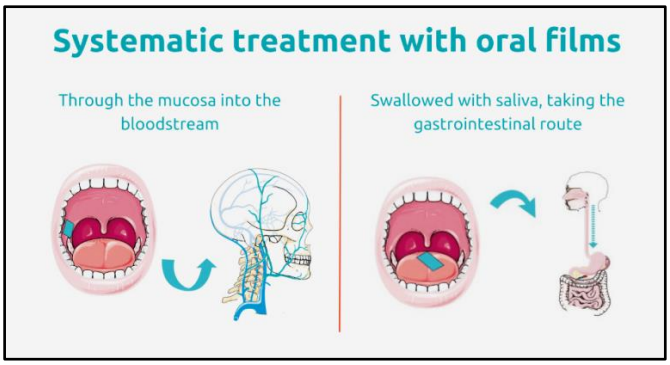

Fig. 3: Route of administration for OTF [23-25]

The ideal characteristics of the drug to be selected

The drug should have a pleasant taste. The therapeutic dose of the drug should not be greater than 40 mg [13]. The drug should have small molecular size and low molecular weight. The drug should have good solubility and stability in water as well as in saliva. It should be partially unionized at the pH of the oral cavity. The drug should exhibit low sensitivity to environmental conditions. It should have the ability to permeate oral mucosal tissue [13, 16, 17].

Advantages of oral thin films

Rapid onset of action with increased bioavailability due to bypassing the hepatic first-pass effect [18]. Convenient for pediatric, geriatric, and dysphasic patients having difficulty in swallowing. Rapid disintegrating and dissolution in the oral cavity due to the larger surface area of films. Reduce dose, enhances the efficacy and safety profile of the drug with reduced side effects. Beneficial in cases such as motion sickness, acute pain, sudden allergic attack, asthmatic attack, and coughing, where an ultra-rapid onset of action is required [19]. No need for water for administration. Flexible and portable, they provide ease of handling, transportation, and storage. Ease of administration to mentally ill, disabled, uncooperative patients and patients who are on reduced liquid intake plans or are nauseated [20]. Beneficial in cases such as motion sickness, acute pain, sudden allergic attack, asthmatic attack, and coughing, where an ultra-rapid onset of action is required. Stability for a longer duration of time since the drug remains in solid dosage form till it is consumed. Accuracy in dose as compared to liquid formulations. Pleasant mouthfeel, leaving negligible or no residue in the mouth after administration.

Disadvantages of oral thin films

High doses of 40-50 mg cannot be incorporated. Drugs which irritate the oral mucosa cannot be administered by this route [25]. Excessive bitter drugs are not feasible [26]. Dose uniformity is a technical challenge. They require special packaging for the product's stability and safety.

Ideal characteristics of drug for oral thin film

The therapeutic dose of the drug should not be greater than 40 mg. The drug should have a pleasant taste. The drug should have small molecular size and low molecular weight. It should be partially unionized at the pH of the oral cavity. The drug should have good solubility and stability in water as well as in saliva. It should have the ability to permeate oral mucosal tissue. The drug should exhibit low sensitivity to environmental conditions [28].

Types of Oral Thin Films

Flash Release. Mucoadhesive melt-away wafer. Mucoadhesive sustained-release wafers [29].

Table 1: General composition of the oral thin film

S. No.	Ingredient	Percentage amount %	Example
1	Drug (API)	1-30%	Anti-emetics, Anti-migraines, Dopamine D1 and D2 antagonists, Anti-epileptics, 5HT3 antagonists, Statins
2	Polymer	Up to 50%	HPMC E3, E5 and E15, and K-3, Methylcellulose A-3, A-6, and A-15, Pullulan, carboxymethylcellulose cekol 30, polyvinylpyrrolidone PVP K-90, pectin, gelatin, sodium, alginate, hydroxypropyl cellulose, polyvinyl alcohol, maltodextrins. [27]
3	Plasticizer	0-20%	Glycerin, PEG-400, 300, propylene glycol, malic acid, sorbitol, castor oil, triethyl citrate,
4	Surfactant (Solubility Enhancer)	q. s	Sodium lauryl sulfate, benzalkonium chloride, polysorbate, and poloxamer 407, etc.
5	Saliva stimulating agent	2-6%	Ascorbic acid, citric acid, lactic acid, tartaric acid, and malic acid [28].
6	Sweetening agent	3-6%	Natural (sucrose, mannitol, sorbitol, dextrose, glucose, liquid glucose, fructose, and isomaltose, etc.), synthetic (aspartame, saccharin, sucralose, acesulfame-K, cyclamate and neotame [29].
7	Flavoring agent	0-10%	Peppermint, cinnamon, clove, lemon, orange, vanilla, and chocolate, etc.
8	Colouring agent	q. s	Titanium oxide, silicon dioxide, and zinc dioxide, etc.
9	Stabilizer or thickening agent	0-5%	Carrageenan, xanthan gum, locust bean gum, and cellulose derivatives are commonly utilized in gums [30].

Table 2: Types of oral thin films

Properties	Flash release	Mucoadhesive melt-away wafers	Mucoadhesive sustained released wafers
Area (cm2)	2-8	2-7	2-4
Thickness (mm)	20-70 mm.	50—500 mm.	50-250 mm.
Structure	Single layer	Single or multilayer	Multilayer system
Excipients	Soluble hydrophilic polymers	Soluble hydrophilic polymers	Low/non-soluble polymers
Drug phase	Solid solution	Solid solution or suspended drug particle	Suspension and/or solid solution
Site of action	Systemic or local	Systemic or local	Systemic or local
Application	Tongue (upper palate)	Gingival or buccal region	Gingival (another region in the oral cavity)
Dissolution	60 s [30, 31].	In a few minutes forming gel	Maximum 8-10 h [30, 31].

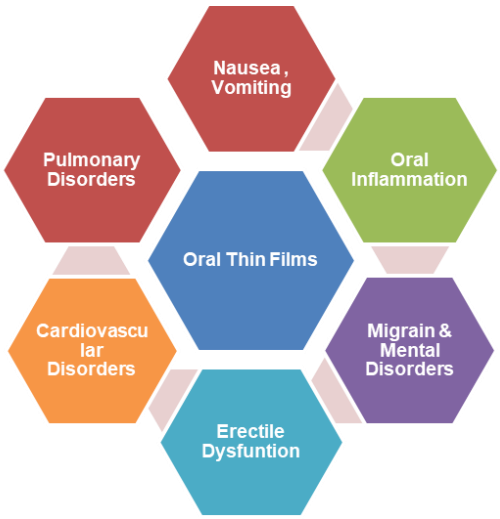

Fig. 4: Therapeutic applications of oral thin films [1-10, 30]

Methods of preparations

Solvent casting method

The most widely used technique for creating OTFs is solvent casting, which has low processing costs, straightforward application, and easy preparation [32]. To put it briefly, components that dissolve in water are made by combining them in a heated magnetic stirrer. To create a viscous solution, the medication and additional excipients are then added to this mixture. This method's solution is put into a petri dish, and the solvents are left to evaporate. These are stored for 20–25 or 24-48 h at room temperature or for a shorter time at 40–50 °C in the oven, according to the solvent system that was used. After the solvents evaporated, 15-20 mm diameter and 0.2–0.3 mm thick films were carefully removed from the petri dishes. [33]. They are cut into the appropriate size pieces based on the concentration of active ingredients they contain.1,7 Using gel-forming polymers, the semisolid gel mass is dried after being poured into appropriate molds in the solvent casting technique. After that, they are ready by being cut into the appropriate sizes [34, 35]. They have about 90%±used this technique for the formulation of OTF. The advantage of this method is to get film of uniform thickness and it is quite flexible. The cost of this method is also very low [36, 37].

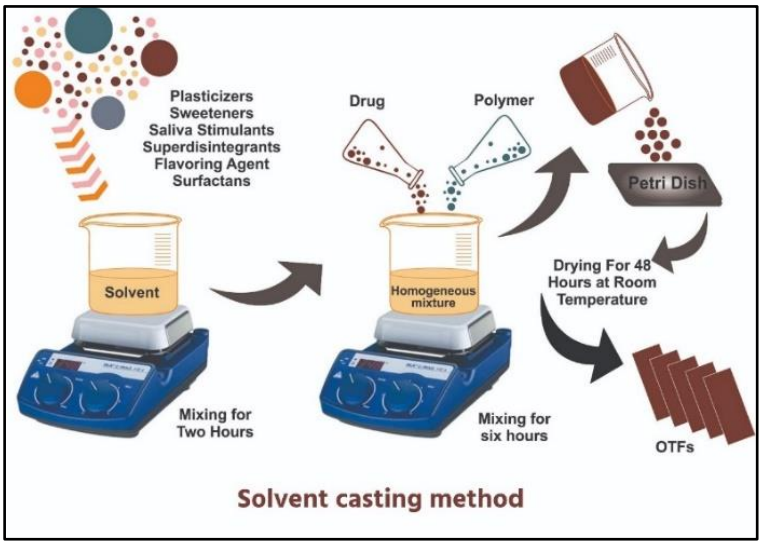

Fig. 5: Solvent casting method [38-42]

Hot-melt extrusion method

Transdermal delivery methods, sustained-release pills, and granules have all been produced using Hot Melt Extrusion. It takes its cues from the plastics manufacturing sector. To achieve desired drug-release profiles, oral film manufacturing components, including combinations of drugs, polymers, and plasticizers, are extruded into various end forms [42].

It is distinct due to the heat treatment and lack of solvent. After the API and additional excipients are combined in a dry condition, heat is delivered through the extruder's heaters to create a molten mass that is forced out of the orifice. After allowing the films to cool, the necessary size is cut from them. Hoffmann had discussed using this method in continuous-release oral films despite ongoing issues with the films' thickness and breakdown [43, 44]. The HME procedure has the following drawbacks: it works best with pharmaceuticals that are thermostable, and finding heat-resistant film-forming polymers might be challenging.

Solid dispersion method.

Solid dispersion refers to the dispersion of one or more solids (such as drugs or therapeutic actives) utilizing techniques like HME into another solid, the inert carrier (such as an amorphous hydrophilic polymer). To create a solution, the medicine is first dissolved in an appropriate liquid solvent. Subsequently, the solution is mixed into the polyol melt, such as polyethylene glycol, without eliminating the liquid solvent [45-48]. It's possible that the medicine or solvent of choice won't mix well with the melted polyethylene glycol. As it cools, a solid dispersion forms and the drug's immiscible components are forced through dies to produce the structure of the film. The drug's polymorphic form that precipitates in the solid dispersion may change depending on the type of liquid solvent utilized [49].

Rolling method

In the rolling process, film is created by first preparing the pre-mix, then adding the active ingredient, and then forming the film. The pre-mix batch is introduced to the main batch feed tank together with additional materials such as polar solvent, film-forming polymer, and API. The first metering pump and control valve then feed a predefined amount of the masterbatch [50]. Once the mixer is filled with the proper amount of medication, it is combined long enough to create a homogenized matrix. The second metering pump feeds a certain amount of matrix into the pan. The film thickness was measured by the metering roller. At last, the film is produced on the substrate and removed by the support roller. Controlled bottom drying is used to dry the wet material [51-53].

Evaluations of OTF

Organoleptic test

A fast-dissolving product (OTF) should have the following required organoleptic qualities: taste, flavour, and colour. The formulation should have appropriate organoleptic pleasant properties because it will dissolve in the oral cavity [55]. Patients find a formulation more agreeable when it is coloured, and when oral films are given to children, they should also be colourful. Therefore, the formulation's hue should be consistent and appealing. Visual inspection is one method of evaluating colour. The smell is the other organoleptic feature [56]. The taste that is incorporated into the recipe should give it a pleasant scent. The addition of a flavoring compound should disguise the smell of the polymer, medication, and any other excipient. Another crucial component that needs to be considered is taste [57-60].

Thickness

Digital Vernier Callipers that have been calibrated or a micrometer screw gauge are used to measure the thickness of the film [61]. The ideal range for film thickness is 5-200 µm. Assuring uniformity in the film's thickness is crucial since it directly affects the precision of the dosage distribution in the film. The thickness should be measured at five separate locations—four at the corners and one in the middle. [62] A minimum of five films from every formulation are measured at five separate places to determine the optimal thickness of buccal thin films, which is between 50 and 1000 µm.10 The results are reported as the mean along with the standard deviation ($\bar{x}$ and SS) [63].

Percent elongation

Strain is the result of an example of stretching when tension is applied to a film. The definition of strain is the difference between the original and starting lengths of the film experiment and the change in film length. The quantity of plasticizer employed in the film formulation has a quantitative relationship with percent elongation. The strip elongates more readily when the plasticizer content in the film is higher. It is ascertained using the subsequent formula: [64-66].

$$\% \text{ Elongation} = \frac{\text{Change in length}}{\text{Initial length}} \times 100.$$

Folding endurance

The films' folding endurance was ascertained by folding a small, 2 x 2 cm^2 strip repeatedly at the same location until it broke; the value of folding endurance was calculated as the number of times the film could be folded at the same location without breaking; the three readings average and standard deviation of all films were computed [67, 68].

Drug content uniformity

The uniformity of drug content can be ascertained using any standard testing method specified in a standard pharmacopeia for that specific API. By evaluating the API content in each strip, content consistency is ascertained. 85–115% is the limit of content uniformity [69, 70].

Swelling property

Tests for film swelling are conducted in a solution that resembles saliva. Every film sample is weighed before being inserted into a preweighed stainless steel wire mesh. The mesh that holds the film sample is immersed in a 15 ml medium within a plastic container. The weighing of the film has been raised at pre-arranged intervals until a consistent weight is noted. The values of the parameter wt-w0/w0, where wt. is the weight of the film at time t and w0 is the weight of the film at time zero, were used to calculate the degree of swelling [71].

Disintegration test

The amount of time (in seconds) that a film disperses when it comes into contact with water or saliva is known as the disintegration time. The thin film starts to break down or disperse at the disintegration moment. The physical characteristics of water-soluble films are mostly determined by the film's weight and thickness [72].

The disintegration periods of OTFs can also be ascertained using the disintegration test equipment listed in pharmacopeias. The disintegration duration of the film composition typically ranges from 5 to 30 seconds, and this phenomenon is dependent on the formulation content. When determining the disintegration times of films that degrade quickly, no formal guide is available [73].

***In vitro* dissolution test**

The quantity of drug material that dissolves under standard conditions of temperature, solvent concentration, and liquid/solid interface is known as the dissolution rate. Any of the pharmacopeia's conventional basket or paddle apparatuses can be used for dissolution testing. Because paddle-type dissolving devices can float above the dissolving liquid, it is challenging to conduct an oral film dissolving study with one. The maximum dosage of the medication and the sink conditions dictate the choice of dissolving media. Throughout the dissolving inquiry, the medium should be held at 37±0.5 ℃ and 50 rpm [72-75].

Contact angle

Goniometers are used to measure contact at room temperature. Put a droplet of purified water onto the dry film's surface. A digital camera was used to capture pictures of the water droplets within ten seconds after their deposition. On both sides of the descent, the contact angle was recorded and an average was determined [73].

Scanning electron microscopy

One beneficial method for examining the surface morphology of a film between several excipients and drugs is scanning electron microscopy. A film sample was obtained and put in a sample holder, and several photomicrographs were made at a ×1000 magnification employing tungsten filament as the electron source [76].

Stability testing

OTF has been held for 12 mo at controlled temperatures of 25 °C/60% RH and 40 °C/75%, under ICH requirements. OTF should have their morphological characteristics, material thickness, reduction in film thickness, tensile qualities, water content, and dissolving behaviours thoroughly inspected before being stored [75, 77].

Table 3: Oral thin film formulations research done by some listed researchers in the last 5-7 y

Drug name	Disease	Preparation methods	References
Pregabalin and Methylcobalamine	Pain originating in the central nervous system	Solvent Pouring Method	(Ozakar, Emrah, *et al.,* 2023) [78]
Captopril	Hypertension, or elevated blood pressure	Solvent casting method	(Abdelkader, Hamdy, *et al.* 2023) [79]
Cytisine	Nicotine addiction	Solvent casting method	(De Caro, Viviana, *et al.*, 2023) [80]
Zolmitriptan	Migraine	Solvent casting method	(Prajapati, Vipul D., *et al.* 2018) [81]
Ketamine	Anesthesia, pain relief, and treatment of depression.	Randomized crossover design.	(Simons, Pieter, *et al.*,2022) [82]
Cholecalciferol	Vitamin D deficiency	Solvent casting method	(Bartlett, Allison L., *et al.* 2023) [83]
Meclizine hydrochloride	Motion sickness	Solvent casting method	(Zhao, Yuan, *et al.*,2015) [84]
Donepezil	Alzheimer disease	Melt condensation method	(Anji Reddy, Keshireddy, 2019) [85]
Enrofloxacin	Urinary tract, respiratory, and skin infections	Solvent casting method	(Kumar, G. Prem, *et al.* 2014) [86]
Escitalopram	Anxiety disorder	Solvent casting method	(Mushtaque, Madiha, *et al.*, 2020) [87]
Diclofenac sodium	NSAID, Pain, Inflammation	Solvent casting method	(Khadra, Ibrahim, *et al.*, 2019) [88]

Drug name	Disease	Preparation methods	References
Verapamil	Antianginal, antiarrhythmic, and antihypertensive	Solvent casting method	(Kunte, S., and P. Tandale, 2010) [89]
Levocetirizine dihydrochloride	perennial allergic rhinitis.	Solvent casting method	(Prabhu, Prabhakara, *et al.*, 2011) [90]
Probiotic bacteria	*Candida* spp. infections	Solvent casting method	(Lordello, Virgínia Barreto, *et al.* 2021) [91]
Amphotericin B	Oropharyngeal Candidiasis	Solvent casting method	(Serrano, Dolores R., *et al.* 2019) [92]
Esomeprazole	Peptic Ulcer	Solvent casting method	(T, Balakrishna, *et al.* 2018) [93]
Gabapentin	Anticonvulsant, Neuropathic pain	Solvent casting method	(Bhusnure O. G* *et al.* 2018) [94]
Clonazepam	Anticonvulsants used for several types of seizures, photosensitive epilepsy	Solvent casting method	(G. Arjun *et al.* 2022) [95]
Diazepam	Seizure emergencies, including acute repetitive seizures	Solvent casting method	(Ms, Ali, and Vijendar C 2016) [96, 97]
Metoprolol Tartrate	β1-adrenoreceptor antagonist widely used in the treatment of essential hypertension and other cardiac disorders	Solvent casting method	(Allam, Ayat, and Gihan Fetih 2016) [98]
Sildenafil Citrate	Erectile dysfunction	Solvent casting method	(Hosny, Khaled Mohamed, *et al.* 2016) [99]
Acetaminophen	Analgesic, Antipyretic	Solvent casting method	(Al-Nemrawi, Nusaiba K., *et al.* 2016) [100]
Montelukast Sodium	Anti-allergic,	Solvent casting method	(Barbosa, Jessica Silva, *et al.* 2016) [101]
Spironolactone	Treatment of hyperaldosteronism, management of hypertension	Solvent casting method	(Shamma, Rehab, and Nermeen Elkasabgy. 2016) [102]
Diclofenac	NSAID, Analgesic	Solvent casting method	(Khadra, Ibrahim, *et al.* 2019) [103]
Rizatriptan	To Treat Migraine	Solvent casting method	(Nair, Anroop B., *et al.* 2021) [104]
Chitosan Microparticle Bioactive Peptide	Treat Hypertension	Microparticle, solvent casting method	(Batista, Patrícia, *et al.* 2019) [105]
Usnea barbata (L.), dry acetone extract (F-UBA)	Oral squamous cell carcinoma (OSCC)	Solid dispersion extrusion	(Popovici, Violeta, *et al.* 2022) [106]
Cytisine	Used as A powerful anti-smoking compound	Solvent casting method	(De Caro, Viviana, *et al.* 2022) [107]
Mirtazapine	Used as Antidepressant	Solvent casting method	(Kumar, Sanjay, *et al.* 2020) [108]
Atenolol	Adrenergic β 1-antagonist, treats hypertension, angina pectoris, arrhythmias, and myocardial infarction	Solvent casting method	(P, Sanjay, *et al.* 2018) [109]
Tenofovir	The vaginal administration of the antiviral Tenofovir	Solvent casting method	(Martín-Illana, Araceli, *et al.* 2022) [110]
3,3-Diindolylmethane	Melanoma topical treatment	Nanocapsule, solvent casting method	(Reolon, Jéssica Brandão, *et al.* 2023) [111]
Buprenorphine Hydrochloride	Treatment of moderate to severe pain as well as chronic pain	Microemulsion, Solvent casting method	(Mundhey, D., *et al.* 2020) [112]
Donepezil hydrochloride	Alzheimer's disease	Solvent casting method	(Lakshmi, P. K., *et al.* 2014) [113]
Nifedipine	Hypertension by decreasing heart rate and myocardial contractility.	Solvent casting method	(Venkateswarlu, Kambham, *et al.* 2017) [114]
Bufotenine	Treat brain disorders	Solvent casting method	(K, Venkateswarlu. 2016) [115]
Zolpidem	To treat insomnia.	Solvent casting method	(Rani, T. Neelima. 2017) [116]
Lansoprazole	Treatment of gastric acid disorders	Solvent casting method	(Sk. Haneesha, *et al.* 2018) [117]
Loratadine	Treatment of allergies such as urticaria, allergic rhinitis, sneezing, running nose, itching, and watering eyes.	Solvent casting method	(Linku Abraham 2018) [118]
Tofacitinib Citrate	Rheumatoid arthritis in adult patients, Ulcerative colitis, Psoriatic arthritis. Janus kinases (jaks)	Solvent casting method	(Raykar, Meghana, 2023) [119]
Cefixime trihydrate	Antibacterial agent, used as Antibiotic	Freeze drying method	(Khan, Qurrat-ul-ain, *et al.* 2020) [120]
Trazodone HCl	Used as Antidepressant	Solvent casting method	(Sahu, Rahul Kumar, *et al.* 2019) [121]
Ramipril	Used as an anti-hypertensive drug and is an ACE inhibitor	Solvent casting method	(Nirmala, Puttaswamy. 2020) [122]
Ergotamine Tartrate and Caffeine Anhydrous	5-HT1 receptor agonist is an Antimigraine drug.	Solvent casting method	(Jelvehgari, Mitra, *et al.* 2015) [123]
Tramadol HCL	Opioid analgesic binding to specific opioid receptors.	Solvent casting method	(Murthy AV, Ayalasomayajula LU 2018) [124]
Etoricoxib	Analgesic	Solvent casting method	(Md. Reyad-ul-ferdous *et al.*, 2015) [125]
Furosemide	Dysphagia	Solvent casting method	(Adrover, Alessandra, *et al.*,2018) [126]
Ondansetron hydrochloride	Antiemetic, treatment of nauseous and vomiting	Solvent casting method	(Kumria, Rachna, *et al.*2013) [127]
Domperidone	Treatment of nauseous and vomiting	Solvent casting method	(Zayed, Gamal M., *et al.* 2020) [128]

CONCLUSION

OTFs are a more promising and advantageous administration method because of their improved therapeutic impact, responsiveness, and patient compliance. They have the potential to revive breath. Because oral films have a greater response than tablet formulations, many companies are now creating oral films instead. This type of technology has been investigated and has a lot of potential.

OTF dosage forms have demonstrated significant potential as a novel substitute for conventional dosage forms. This is attributed to their ease of administration for pediatrics, geriatric, and non-cooperative patients, as well as their cost-effective manufacture and convenient handling, storage, and transportation, including the potential to incorporate different medication ingredients, such as chemical medications, vaccinations, probiotics, and herbal extracts. Additionally, ODF is becoming more and more well-liked as a delivery system for treating conditions including oral inflammation, cardiovascular illness, pain management, nausea and vomiting, mental or emotional disorders, erectile dysfunction, pulmonary diseases, and more. When a quick onset impact is necessary and, in an emergency, it is one of the most significant dosage forms for oral administration that can be used. Thus, it can be said that OTFs with great patient compliance and numerous benefits have novel, forward-thinking prospects.

ABBREVIATIONS

Oral Thin Films (OTF), Oral Dispersible Tablets (ODT).

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AUTHORS CONTRIBUTIONS

All the authors have contributed equally.

CONFLICTS OF INTERESTS

The authors declare no conflicts of interest.

REFERENCES

1. Karki S, Kim H, Na SJ, Shin D, Jo K, Lee J. Thin films as an emerging platform for drug delivery. Asian J Pharm Sci. 2016 Oct;11(5):559-74. doi: 10.1016/j.ajps.2016.05.004.
2. Sevinc Ozakar R, Ozakar E. Current overview of oral thin films. Turk J Pharm Sci. 2021;18(1):111-21. doi: 10.4274/tjps.galenos.2020.76390, PMID 33634686.
3. Oral thin-films from design to delivery: a pharmaceutical viewpoint. Biointerface Res Appl Chem. 2022 Mar 30;13(2):177. doi: 10.33263/BRIAC132.177/wp-content/uploads/2022/03/BRIAC132.177.pdf.
4. Yuan C, Sha H, Cui B. Orally disintegrating film: a new approach to nutritional supplementation. Food Bioprocess Technol. 2022;15(12):2629-45. doi: org/10.1007/s11947-022-02835-y.
5. Scarpa M, Stegemann S, Hsiao WK, Pichler H, Gaisford S, Bresciani M. Orodispersible films: towards drug delivery in special populations. Int J Pharm. 2017;523(1):327-35. doi: 10.1016/j.ijpharm.2017.03.018, PMID 28302515.
6. Palezi SC, Fernandes SS, Martins VG. Oral disintegration films: applications and production methods. J Food Sci Technol. 2023;60(10):2539-48. doi: 10.1007/s13197-022-05589-9, PMID 37599841.
7. Jacob S, Boddu SHS, Bhandare R, Ahmad SS, Nair AB. Orodispersible films: current innovations and emerging trends. Pharmaceutics. 2023;15(12):2753. doi: 10.3390/pharmaceutics15122753, PMID 38140094.
8. 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;178:504-13. doi: 10.1016/j.ijbiomac.2021.02.180, PMID 33647337.
9. Sanap DP, Mhatre US, Sheth RR. Oral thin films: a multi-faceted drug delivery system. IJPSRR. 2022 Jan. 15;72(1). doi: 10.47583/ijpsrr.2022.v72i01.013.
10. Gupta MS, Kumar TP, Gowda DV. Orodispersible thin film: a new patient-centered innovation. J Drug Deliv Sci Technol. 2020 Oct;59:101843. doi: 10.1016/j.jddst.2020.101843.
11. Tiwari RR, Umashankar DMS, ND. Recent update on oral films: a bench to market potential. Int J App Pharm. 2018;10:27. doi: 10.22159/ijap.2018v10i6.28725.
12. Borges AF, Silva C, Coelho JFJ, Simoes S. Oral films: current status and future perspectives. J Control Release. 2015;206:1-19. doi: 10.1016/j.jconrel.2015.03.006.
13. Surendran, Saritha, Joshua, Julie, Hari R, Jyothish, Fithal. Fast dissolving oral thin films: an effective dosage form for quick releases. International Journal of Pharmaceutical Sciences Review and Research. 2016;38:280-9.
14. B Sontakke, Patil S, Daswadkar DS. A comprehensive review: natural polymers used for fast dissolving mouth film. IJPSRR 2020;65(2):14-21. doi: 10.47583/ijpsrr.2020.v65i02.003.
15. Famuyide A, Massoud TF, Moonis G. Oral cavity and salivary glands anatomy. Neuroimaging Clin N Am. 2022 Nov;32(4):777-90. doi: 10.1016/j.nic.2022.07.021, PMID 36244723.
16. Zhang Y, Wang X, Li H, Ni C, Du Z, Yan F. Human oral microbiota and its modulation for oral health. Biomed Pharmacother. 2018 Mar;99:883-93. doi: 10.1016/j.biopha.2018.01.146, PMID 29710488.
17. Zhang Y, Jiang R, Lei L, Yang Y, Hu T. Drug delivery systems for oral disease applications. J Appl Oral Sci. 2022 Mar 9;30:e20210349. doi: 10.1590/1678-7757-2021-0349, PMID 35262595, PMCID PMC8908861.
18. Madani M, Berardi T, Stoopler ET. Anatomic and examination considerations of the oral cavity. Med Clin North Am. 2014 Nov;98(6):1225-38. doi: 10.1016/j.mcna.2014.08.001, PMID 25443674.
19. Yates CB, Phillips CD. Oral cavity and oropharynx. Curr Probl Diagn Radiol. 2001 Mar-Apr;30(2):38-59. doi: 10.1067/mdr.2001.113657, PMID 11300548.
20. Mukherji SK, Castillo M. Normal cross-sectional anatomy of the nasopharynx, oropharynx, and oral cavity. Neuroimaging Clin N Am. 1998 Feb;8(1):211-8. PMID 9449761.
21. Hermans R, Lenz M. Imaging of the oropharynx and oral cavity. Part I: Normal anatomy. Eur Radiol. 1996;6(3):362-8. doi: 10.1007/BF00180613, PMID 8798007.
22. Stutley J, Cooke J, Parsons C. Normal CT anatomy of the tongue, floor of mouth and oropharynx. Clin Radiol. 1989 May;40(3):248-53. doi: 10.1016/s0009-9260(89)80184-9, PMID 2752681.
23. Sigal R. Oral cavity, oropharynx, and salivary glands. Neuroimaging Clin N Am. 1996 May;6(2):379-400. PMID 8726912.
24. Weissman JL. Imaging of the salivary glands. Semin Ultrasound CT MR. 1995 Dec;16(6):546-68. doi: 10.1016/s0887-2171(06)80025-9, PMID 8747417.
25. Dostalova M, Rabiskova M. Mucoadhesive oral tablets-a modern dosage form with controlled drug release [Mucoadhesive oral tablets-a modern dosage form with controlled drug release]. Ceska Slov Farm. 2000 Mar;49(2):55-61. PMID 10953444.
26. De Mohac LM, Caruana R, Cavallaro G, Giammona G, Licciardi M. Spray-drying, solvent-casting and freeze-drying techniques: a comparative study on their suitability for the enhancement of drug dissolution rates. Pharm Res. 2020;37(3):57. doi: 10.1007/s11095-020-2778-1, PMID 32076880.
27. Orlu M, Ranmal SR, Sheng Y, Tuleu C, Seddon P. Acceptability of orodispersible films for delivery of medicines to infants and preschool children. Drug Deliv. 2017;24:1243-8. doi: 10.1080/10717544.2017.1370512, PMID 28856931.
28. Maske Rahul Rohidas, Mahajan Vijay Rajaram, Bhalerao Sakshi Bhagwan. Polymers used in mouth dissolving film: a review. World J Adv Res Rev. 2022;16:378-89. doi: 10.30574/wjarr.2022.16.3.1318.
29. Bala R, Pawar P, Khanna S, Arora S. Orally dissolving strips: a new approach to oral drug delivery system. Int J Pharm Investig. 2013;3(2):67-76. doi: 10.4103/2230-973X.114897, PMID 24015378.
30. Waugh J, Goa Karen L. Escitalopram: a review of its use in the management of major depressive and anxiety disorders. CNS Drugs. 2003;17(5):343-62. doi: 10.2165/00023210-200317050-00004, PMID 12665392.
31. Musazzi UM, Khalid GM, Selmin F, Minghetti P, Cilurzo F. Trends in the production methods of orodispersible films. Int J Pharm. 2020;576(Feb.):118963. doi: 10.1016/j.ijpharm.2019.118963, PMID 31857185.
32. He M, Zhu L, Yang N, Li H, Yang Q. Recent advances of oral film as a platform for drug delivery. Int J Pharm. 2021;604:120759. doi: 10.1016/j.ijpharm.2021.120759, PMID 34098053.
33. Culpepper L. Escitalopram: a new SSRI for the treatment of depression in primary care. Prim Care Companion J Clin Psychiatry. 2002;4(6):209-14. doi: 10.4088/pcc.v04n0601, PMID 15014711.
34. Wang G, You X, Wang X, Xu X, Bai L, Xie J. Safety and effectiveness of escitalopram in an 8-week open study in Chinese patients with depression and anxiety. Neuropsychiatr Dis Treat. 2018;14:2087-97. doi: 10.2147/NDT.S164673, PMID 30147321.
35. Waugh J, Goa Karen L. Escitalopram: a review of its use in the management of major depressive and anxiety disorders. CNS Drugs. 2003;17(5):343-62. doi: 10.2165/00023210-200317050-00004, PMID 12665392.
36. Drago E, Campardelli R, Lagazzo A, Firpo G, Perego P. Improvement of natural polymeric films properties by blend formulation for sustainable active food packaging. Polymers. 2023;15:2231. doi: 10.3390/polym15092231, PMID 37177377.
37. Dahl DK, Whitesell AN, Sharma Huynh P, Maturavongsadit P, Janusziewicz R, Fox RJ. A mucoadhesive bio dissolvable thin film for localized and rapid delivery of lidocaine for the treatment of vestibulodynia. Int J Pharm. 2022;612:121288. doi: 10.1016/j.ijpharm.2021.121288, PMID 34800616.
38. Abd El Azim H, Nafee N, Ramadan A, Khalafallah N. Liposomal buccal mucoadhesive film for improved delivery and permeation of water-soluble vitamins. Int J Pharm. 2015;488:78-85. doi: 10.1016/j.ijpharm.2015.04.052, PMID 25899288.
39. Joshi R, Akram W, Chauhan R, Garud N. Thin films: a promising approach for drug delivery system. Intech Open; 2022. doi: 10.5772/intechopen.103793.

40. Gala RP, Morales JO, McConville JT. Preface to advances in thin film technologies in drug delivery. Int J Pharm. 2019;571(v):118687. doi: 10.1016/j.ijpharm.2019.118687, PMID 31518633.
41. Kathpalia H, Gupte A. An introduction to fast dissolving oral thin film drug delivery systems: a review. Curr Drug Deliv. 2013;10(6):667-84. doi: 10.2174/15672018100613112515024 9, PMID 24274635.
42. Yir Erong B, Bayor MT, Ayensu I, Gbedema SY, Boateng JS. Oral thin films as a remedy for noncompliance in pediatric and geriatric patients. Ther Deliv. 2019;10:443-64. doi: 10.4155/tde-2019-0032, PMID 31264527.
43. Singh PN, Byram PK, Das L, Chakravorty N. Natural polymer-based thin film strategies for skin regeneration in lieu of regenerative dentistry. Tissue Eng Part C Methods. 2023;29(6):242-56. doi: 10.1089/ten.TEC.2023.0070, PMID 37171125.
44. Nyamweya N, Hoag SW. Assessment of polymer-polymer interactions in blends of HPMC and film-forming polymers by modulated temperature differential scanning calorimetry. Pharm Res. 2000;17(5):625-31. doi: 10.1023/Aa:1007585403781, PMID 10888317.
45. Sheikh FA, Aamir MN, Haseeb MT, Abbas Bukhari SN, Farid Ul Haq M, Akhtar N. Design, physico-chemical assessment and pharmacokinetics of a non-toxic orodispersible film for potential application in musculoskeletal disorder. J Drug Deliv Sci Technol. 2021;65:102726. doi: 10.1016/j.jddst.2021.102726.
46. 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. doi: 10.1016/j.jsps.2015.02.024, PMID 27752225.
47. Kaufmann C. 'Overview: oral films and their administration routes. *AdhexPharma*, AdhexPharma; 2023. Available from: www.adhexpharma.com/blog/overview-oral-films-and-their-administration-routes.
48. Bhyan B. Orally fast dissolving films: innovations in formulation and technology. Int J Pharm Sci Rev Res. 2011;9(2):9-15.
49. Kathpalia H, Gupte Aasavari. An introduction to fast dissolving oral thin film drug delivery systems: a review. Curr Drug Deliv. 2013;10:667-84. doi: 10.2174/15672018100613112515024 9
50. Joshi R, Akram W, Chauhan R, Garud N. Thin films: a promising approach for drug delivery system. Drug carriers. Intech Open; 2022.
51. Kaur P, Garg Rajeev. Oral dissolving film: present and future aspects. J Drug Delivery Ther. 2018;8:373-7. doi: 10.22270/jddt.v8i6.2050.
52. Himani Singla M, Prabhakar PK, Sharma A, Meghwal M. Edible and oral thin films: formulation, properties, functions, and application in food packaging and pharmaceutical industry; 2022. p. 411-32. doi: 10.1007/978-981-16-2383-7_21.
53. Chaturvedi A, Srivastava P, Yadav S, Bansal M, Garg G, Sharma PK. Fast dissolving films: a review. Curr Drug Deliv. 2011 Jul;8(4):373-80. doi: 10.2174/156720111795768022, PMID 21453260.
54. Barbosa JS, Almeida Paz FA, Braga SS. Montelukast medicines of today and tomorrow: from molecular pharmaceutics to technological formulations. Drug Deliv. 2016;23:3257-65. doi: 10.3109/10717544.2016.1170247, PMID 27011101.
55. Shamma R, Elkasabgy N. Design of freeze-dried soluplus/polyvinyl alcohol-based film for the oral delivery of an insoluble drug for pediatric use. Drug Deliv. 2016;23:489-99. doi: 10.3109/10717544.2014.921944, PMID 24892631.
56. Formulation and evaluation of lansoprazole oral thin films. J Pharm Neg Results. 2023;14:455-67. doi: 10.47750/pnr.2023.14.02.58.
57. Formulation and evaluation of esomeprazole oral thin films. J Pharm Neg Results. 2023;14:442-54. doi: 10.47750/pnr.2023.14.02.57.
58. Nair AB, Shah J, Jacob S, Al-Dhubiab BE, Patel V, Sreeharsha N. Development of mucoadhesive buccal film for rizatriptan: *in vitro* and *in vivo* evaluation. Pharmaceutics. 2021;13(5):728. doi: 10.3390/pharmaceutics13050728, PMID 34063402.
59. Gupta MS, Kumar TP, Gowda DV. Thin films orodispersible: a new patient-centered innovation. J Drug Deliv Sci Technol. 2020;59. doi: 10.1016/j.jddst.2020.101843.
60. Koland M, Sandeep VP, Charyulu NR. Fast dissolving sublingual films of ondansetron hydrochloride: effect of additives on *in vitro* drug release and mucosal permeation. J Young Pharm. 2010;2:216-22. doi: 10.4103/0975-1483.66790, PMID 21042474.
61. Alipour S, Akbari S, Ahmadi F. Development and *in vitro* evaluation of fast-dissolving oral films of ondansetron hydrochloride. Trends Pharm Sci. 2015;1:25.
62. Giordani B, Abruzzo A, Prata C, Nicoletta FP, Dalena F, Cerchiara T. Ondansetron buccal administration for paediatric use: a comparison between films and wafers. Int J Pharm. 2020;580:119228. doi: 10.1016/j.ijpharm.2020.119228, PMID 32184180.
63. Can AS, Erdal MS, Gungor S, Ozsoy Y. Optimization and characterization of chitosan films for transdermal delivery of ondansetron. Molecules. 2013;18:5455-71. doi: 10.3390/molecules18055455, PMID 23666010.
64. Joshi P, Patel H, Patel V, Panchal R. Formulation development and evaluation of mouth dissolving film of domperidone. J Pharm Bioallied Sci. 2012;4(5)Suppl 1:S108-9. doi: 10.4103/0975-7406.94159, PMID 23066181.
65. Md S, Kumar S, Doddayya H. Fabrication and evaluation of mouth-dissolving films of domperidone. Int J Curr Pharm Sci. 2023:36-43. doi: 10.22159/ijcpr.2023v15i2.2088.
66. Bhyan B, Bhatt DC, Jangra S. Pharmacokinetic study in humans and *in vitro* evaluation of bioenhanced bilayer sublingual films for the management of acute migraine. Int J App Pharm. 2023;15(3):190-9. doi: 10.22159/ijap.2023v15i3.46684.
67. Priya NS, Molly BA, Nori LP "Fabrication and characterization of fast dissolving films of eclipta prostrate leaves extract to treat mouth ulcers." SSM Int J Appl Pharm. 2021;13(5):263-71. 10.22159/ijap.2021v13i5.4159.
68. Khan FB, Kilor V, Sapkal N, Dule P. Formulation development of mouth dissolving printed film of ketorolac and *in vitro* evaluation. Int J App Pharm. 2022;14(5):128-36. doi: 10.22159/ijap.2022v14i5.45350.
69. Farooqui P, Gude Rajashree. Formulation development and optimisation of fast dissolving buccal films loaded glimepiride solid dispersion with enhanced dissolution profile using central composite design. Int J Pharm Pharm Sci. 2023;15(6):35-54. doi: 10.22159/ijpps.2023v15i6.47992.
70. Haju SS, Yadav Sheela. Formulation and evaluation of cilnidipine mucoadhesive buccal film by solvent casting technique for the treatment of hypertension. Int J Pharm Pharm Sci. 2021;13(9):34-43. doi: 10.22159/ijpps.2021v13i9.42641.
71. Zucchi A, Costantini E, Scroppo FI, Silvani M, Kopa Z, Illiano E. The first-generation phosphodiesterase 5 inhibitors and their pharmacokinetic issue. Andrology. 2019 Nov;7(6):804-17. doi: 10.1111/andr.12683, PMID 31350821, PMCID PMC6790582.
72. Alaei S, Omidian H. Mucoadhesion and mechanical assessment of oral films. Eur J Pharm Sci. 2021 Apr 1;159:105727. doi: 10.1016/j.ejps.2021.105727, PMID 33484813.
73. Fonseca Santos B, Chorilli M. An overview of polymeric dosage forms in buccal drug delivery: state of the art, design of formulations and their *in vivo* performance evaluation. Mater Sci Eng C Mater Biol Appl. 2018 May 1;86:129-43. doi: 10.1016/j.msec.2017.12.022, PMID 29525088.
74. Walicova V, Gajdziok J. Oral films as perspective dosage form [Oral films as perspective dosage form]. Ceska Slov Farm. 2016;65(1):15-21. PMID 27118500.
75. Morales JO, McConville JT. Manufacture and characterization of mucoadhesive buccal films. Eur J Pharm Biopharm. 2011 Feb;77(2):187-99. doi: 10.1016/j.ejpb.2010.11.023, PMID 21130875.
76. Palezi SC, Fernandes SS, Martins VG. Oral disintegration films: applications and production methods. J Food Sci Technol. 2023 Oct;60(10):2539-48. doi: 10.1007/s13197-022-05589-9, PMID 37599841, PMCID PMC10439052.
77. Ozakar E, Sevinc Ozakar R, Yılmaz B. Preparation, characterization, and evaluation of cytotoxicity of fast dissolving hydrogel based oral thin films containing pregabalin and methylcobalamin. Gels. 2023;9:147. doi: 10.3390/gels9020147, PMID 36826317.
78. Abdelkader H, Abdel Aleem JA, Mousa HS, Elgendy MO, Al Fatease A, Abou Taleb HA. Captopril polyvinyl alcohol/sodium

alginate/gelatin-based oral dispersible films (ODFs) with modified release and advanced oral bioavailability for the treatment of pediatric hypertension. Pharmaceuticals (Basel). 2023;16:1323. doi: 10.3390/ph16091323, PMID 37765131.

79. De Caro V, Angellotti G, D'Agostino F, Di Prima G. Buccal thin films as potent permeation enhancers for cytisine transbuccal delivery. Membranes. 2022;12(11):1169. doi: 10.3390/membranes12111169, PMID 36422161.
80. Prajapati VD, Chaudhari AM, Gandhi AK, Maheriya P. Pullulan based oral thin film formulation of zolmitriptan: development and optimization using factorial design. Int J Biol Macromol. 2018;107(B):2075-85. doi: 10.1016/j.ijbiomac.2017.10.082, PMID 29074082.
81. Simons P, Olofsen E, Van Velzen M, Van Lemmen M, Mooren R, Van Dasselaar T. S-Ketamine oral thin film-part 1: population pharmacokinetics of s-ketamine, s-norketamine and s-hydroxynorketamine. Front Pain Res (Lausanne). 2022;3:946486. doi: 10.3389/fpain.2022.946486, PMID 35899184.
82. Bartlett AL, Zhang G, Wallace G, McLean S, Myers KC, Teusink Cross A. Optimized vitamin D repletion with oral thin film cholecalciferol in patients undergoing stem cell transplant. Blood Adv. 2023;7:4555-62. doi: 10.1182/bloodadvances.2023009855, PMID 37285801.
83. Zhao Y, Quan P, Fang L. Preparation of an oral thin film containing meclizine hydrochloride: *in vitro* and *in vivo* evaluation. Int J Pharm. 2015;496:314-22. doi: 10.1016/j.ijpharm.2015.10.008, PMID 26456247.
84. Anji Reddy K, Karpagam Subramanian. Hyperbranched cellulose polyester of oral thin film and nanofiber for rapid release of donepezil; preparation and *in vivo* evaluation. Int J Biol Macromol. 2019;124:871-87. doi: 10.1016/j.ijbiomac.2018.11.224, PMID 30496855.
85. Kumar GP, Phani AR, Prasad RG, Sanganal JS, Manali N, Gupta R. Polyvinylpyrrolidone oral films of enrofloxacin: film characterization and drug release. Int J Pharm. 2014;471(1-2):146-52. doi: 10.1016/j.ijpharm.2014.05.033, PMID 24858388.
86. Mushtaque M, Muhammad IN, Fareed Hassan SM, Ali A, Masood R. Development and pharmaceutical evaluation of oral fast dissolving thin film of escitalopram: a patient friendly dosage form. Pak J Pharm Sci. 2020;33:183-9. PMID 32122847.
87. Khadra I, Obeid MA, Dunn C, Watts S, Halbert G, Ford S. Characterisation and optimisation of diclofenac sodium orodispersible thin film formulation. Int J Pharm. 2019;561:43-6. doi: 10.1016/j.ijpharm.2019.01.064, PMID 30772459.
88. Kunte S, Tandale P. Fast dissolving strips: a novel approach for the delivery of verapamil. J Pharm Bioallied Sci. 2010;2(4):325-8. doi: 10.4103/0975-7406.72133, PMID 21180465.
89. Prabhu P, Malli R, Koland M, Vijaynarayana K, D'Souza U, Harish N. Formulation and evaluation of fast dissolving films of Levocitirizine di hydrochloride. Int J Pharm Investig. 2011;1(2):99-104. doi: 10.4103/2230-973X.82417, PMID 23071928.
90. Lordello VB, Meneguin AB, De Annunzio SR, Taranto MP, Chorilli M, Fontana CR. Orodispersible film loaded with enterococcus faecium CRL183 presents anti-candida albicans biofilm activity *in vitro*. Pharmaceutics. 2021;13:998. doi: 10.3390/pharmaceutics13070998, PMID 34209453.
91. Serrano Dolores R, Fernandez Garcia R, Mele M, Healy AM, Lalatsa A. Designing fast-dissolving orodispersible films of amphotericin B for oropharyngeal candidiasis. Pharmaceutics. 2019;11(8):369. doi: 10.3390/pharmaceutics11080369, PMID 31374879.
92. TB, SV, Tegk M, AR, Rlc S. Formulation and evaluation of esomeprazole fast dissolving buccal films. Asian J Pharm Clin Res. 2018;11(10). doi: 10.22159/ajpcr.2018.v11i10.27321.
93. Bhusnure OG. Formulation and evaluation of oral fast-dissolving film of gabapentin by Qbd approach. International Journal of Pharmacy and Biological Sciences. 2018;8(2):426-37.
94. Arjun G. Design and *in vitro* characterization of clonazepam oral thin films. J Pharmacreations. 2022;9(2):193-8.
95. Ms A, CV. Formulation and evaluation of fast-dissolving oral films of diazepam. J Pharmacovigil. 2016;4(3). doi: 10.4172/2329-6887.1000210.
96. Rogawski Michael A, Heller Allen H. Diazepam buccal film for the treatment of acute seizures. Epilepsy Behav. 2019;101(B):106537. doi: 10.1016/j.yebeh.2019.106537, PMID 31699662.
97. Allam A, Fetih Gihan. Sublingual fast-dissolving niosomal films for enhanced bioavailability and prolonged effect of metoprolol tartrate. Drug Des Devel Ther. 2016;10:2421-33. doi: 10.2147/DDDT.S113775, PMID 27536063.
98. Hosny KM, El-Say KM, Ahmed OA. Optimized sildenafil citrate fast orodissolvable film: a promising formula for overcoming the barriers hindering erectile dysfunction treatment. Drug Deliv. 2016;23:355-61. doi: 10.3109/10717544.2014.916763, PMID 24865296.
99. Al-Nemrawi Nusaiba K, Dave Rutesh H. Formulation and characterization of acetaminophen nanoparticles in orally disintegrating films. Drug Deliv. 2016;23:540-9. doi: 10.3109/10717544.2014.936987, PMID 25013958.
100. Barbosa JS, Almeida Paz FA, Braga SS. Montelukast medicines of today and tomorrow: from molecular pharmaceutics to technological formulations. Drug Deliv. 2016;23:3257-65. doi: 10.3109/10717544.2016.1170247, PMID 27011101.
101. Shamma R, Elkasabgy N. Design of freeze-dried soluplus/polyvinyl alcohol-based film for the oral delivery of an insoluble drug for pediatric use. Drug Deliv. 2016;23(2):489-99. doi: 10.3109/10717544.2014.921944, PMID 24892631.
102. Khadra I, Obeid MA, Dunn C, Watts S, Halbert G, Ford S. Characterisation and optimisation of diclofenac sodium orodispersible thin film formulation. Int J Pharm. 2019;561:43-6. doi: 10.1016/j.ijpharm.2019.01.064, PMID 30772459.
103. Nair AB, Shah J, Jacob S, Al-Dhubiab BE, Patel V, Sreeharsha N. Development of mucoadhesive buccal film for rizatriptan: *in vitro* and *in vivo* evaluation. Pharmaceutics. 2021;13(5):728. doi: 10.3390/pharmaceutics13050728, PMID 34063402.
104. Batista P, Castro P, Madureira AR, Sarmento B, Pintado M. Development and characterization of chitosan microparticles-in-films for buccal delivery of bioactive peptides. Pharmaceuticals (Basel). 2019;12:32. doi: 10.3390/ph12010032, PMID 30791572.
105. Popovici V, Matei E, Cozaru GC, Bucur L, Gird CE, Schroder V. *In vitro* anticancer activity of mucoadhesive oral films loaded with Usnea barbata (L.) F. H. Wigg Dry acetone extract, with potential applications in oral squamous cell carcinoma complementary therapy. Antioxidants (Basel). 2022;11(10):1934. doi: 10.3390/antiox11101934, PMID 36290658.
106. De Caro V, Angellotti G, D'Agostino F, Di Prima G. Buccal thin films as potent permeation enhancers for cytisine transbuccal delivery. Membranes. 2022;12(11):1169. doi: 10.3390/membranes12111169, PMID 36422161.
107. Kumar S, Gautam D, Talwan P. Formulation and evaluation of mirtazapine oral thin film. Int J Res Pharm Chem. 2020;10(1). doi: 10.33289/IJRPC.10.1.2020.10(7).
108. PS, N VG. Dv G, Sivadasu P. "Formulation and evaluation of oral disintegrating film of atenolol." Asian Journal of Pharmaceutical and Clinical Research. 2018;11(8):312. doi: 10.22159/ajpcr.2018.v11i8.26464.
109. Martin Illana A, Chinarro E, Cazorla Luna R, Notario Perez F, Veiga Ochoa MD, Rubio J. Optimized hydration dynamics in mucoadhesive xanthan-based trilayer vaginal films for the controlled release of tenofovir. Carbohydr Polym. 2022;278:118958. doi: 10.1016/j.carbpol.2021.118958, PMID 34973774.
110. Reolon Jessica B, Saccol CP, Osmari BF, Oliveira DB, Prado VC, Cabral FL. Karaya/gellan-gum-based bilayer films containing 3,3′-diindolylmethane-loaded nanocapsules: a promising alternative to melanoma topical treatment. Pharmaceutics. 2023;15(9):2234. doi: 10.3390/pharmaceutics15092234, PMID 37765203.
111. Mundhey D, Sapkal N, Daud A. Fabrication of an abuse deterrent and microemulsion-based sublingual film of buprenorphine hydrochloride for breakthrough pain management. Int J App Pharm. 2020;12(6):127-35. doi: 10.22159/ijap.2020v12i6.38877.
112. Lakshmi PK, Lavanya D, Ali MMH. Effect of synthetic super disintegrants and natural polymers in the preparation of

donepezil hydrochloride fast disintegration films. Int Curr Pharm J. 2014;3(3):243-6. doi: 10.3329/icpj.v3i3.17892.
113. Venkateswarlu K, Babu CN, Triveni S, Kiran BSS. Preparation of transdermal films of nifedipine: ex-vivo and *in vitro* studies. Pharm Methods. 2017;8(2):144-8. doi: 10.5530/phm.2017.8.22.
114. KV. Preparation and evaluation of fast dissolving buccal thin films of bufotenin. J In Silico *In Vitro* Pharmacol. 2016;2(4). doi: 10.21767/2469-6692.100013.
115. Rani T Neelima. Formulation development and optimization of oral thin films of zolpidem tartarate. Medical Science and Healthcare Practice. 2017;1(1):26. doi: 10.22158/mshp.v1n1p26.
116. SK Haneesha, M Venkataramana, N Ramarao. Formulation and evaluation of lansoprazole-loaded enteric-coated microspheres. Int J Res Pharm Sci Tech 2020;1(4):124-30. doi: 10.33974/ijrpst.v1i4.201.
117. Abraham Linku. Formulation and evaluation of fast-dissolving oral film of anti-allergic drug. Asian J Pharm Res Dev. 2018;6(3):5-16. doi: 10.22270/ajprd.
118. Raykar M, Velraj Malarkodi. Design, development and evaluation of novel mouth dissolving film of tofacitinib citrate. Int J App Pharm. 2023 Jan;15(1):324-32. doi: 10.22159/ijap.2023v15i1.46064.
119. Khan QU, Siddique MI, Rasool F, Naeem M, Usman M, Zaman M. Development and characterization of orodispersible film containing cefixime trihydrate. Drug Dev Ind Pharm. 2020;46(12):2070-80. doi: 10.1080/03639045.2020.1843477, PMID 33112681.
120. Sahu RK, Jain S, Kapoor V, Gupta N. Formulation, development and evaluation of fast dissolving oral film of antidepressant drug. J Drug Delivery Ther. 2019;9(4-s):404-7. doi: 10.22270/jddt.v9i4-s.3346.
121. Nirmala P. Formulation and evaluation of fast dissolving oral films incorporated with ramipril and β-cyclodextrin complex. Int J Pharm Sci Drug Res. 2020:390-5. doi: 10.25004/IJPSDR.2020.120412.
122. 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. Pharm Sci. 2015;21(2):102-10. doi: 10.15171/PS.2015.24.
123. Murthy AV, Ayalasomayajula LU, Earle RR, Jyotsna P. Formulation and evaluation of tramadol hydrochloride oral thin films. Int J Pharm Sci Res. 2018;9(4):1692-8. doi: 10.13040/IJPSR.0975-8232.9(4).1692-98.
124. Md. Reyad-Ul-Ferdous. Effective development and evaluation of oral thin film of etoricoxib. World J Pharm Res. 2015;4(9):257-72.
125. Kumria R, Gupta V, Bansal S, Wadhwa J, Nair AB. Oral buccoadhesive films of ondansetron: development and evaluation. Int J Pharm Investig. 2013;3(2):112-8. doi: 10.4103/2230-973X.114894, PMID 24015383.
126. Zayed GM, Rasoul SAE, Ibrahim MA, Saddik MS, Alshora DH. *In vitro* and *in vivo* characterization of domperidone-loaded fast dissolving buccal films. Saudi Pharm J. 2020;28(3):266-73. doi: 10.1016/j.jsps.2020.01.005, PMID 32194327.
127. Adrover A, Varani G, Paolicelli P, Petralito S, Di Muzio L, Casadei MA. Experimental and modeling study of drug release from HPMC-based erodible oral thin films. Pharmaceutics. 2018;10(4):222. doi: 10.3390/pharmaceutics10040222, PMID 30423941.
128. Jacob S, Boddu SHS, Bhandare R, Ahmad SS, Nair AB. Orodispersible films: current innovations and emerging trends. Pharmaceutics. 2023;15(12):2753. doi: 10.3390/pharmaceutics15122753, PMID 38140094.