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Advancement in the therapeutic potential of drug candidates via oral films: a brief update

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ABSTRACT: Oral disintegrating films are unique patient-friendly miniature dosage forms that can get hydrated in saliva, disintegrate abruptly and release the drug that gets absorbed into systemic circulation via the oral mucosa. This distinct dosage form has captured the pharmaceutical market due to its therapeutic standpoint, especially in cases delivering drugs to psychic, un-cooperative, and ambulatory patients. This article provides an insight into oral films, their pros and cons, formulation aids, strategies, and challenges. We also address the unique properties, of these systems and polymers used and their properties. The review adds to case studies and also marketed formulations. We also address the unique properties of this system and polymers used and properties.

KEYWORDS: Fast dissolving film; Oral disintegrating film; Oro dispersible film; Mouth dissolving.

1.INTRODUCTION

The oral route has remained the foremost popular drug distribution system since it offers numerous advantages over other methods for administration, noninvasiveness, and patient compliance. However, drug delivery limitations via this route include premature metabolism, degradation of drugs, and the inconvenience of drug administration to geriatric, pediatric patients, and dysplasia conditions. Therefore, systems can still be improved to overcome the issues mentioned above [1].

Orally disintegrating systems (ODSs) were developed as an alternate to beat the above-said limitations, pointing to a quick release of the drug without the necessity for water absorption, further allowing drug absorption straight through the oral mucosa into circulation, bypassing hepatic metabolism. Orally dissolving medication must dissolve quickly within the mouth without requiring water for intake. The palatability of orally dissolving medication in the oral cavity is one of the most significant factors [2].

Among ODS, oral films are increasing their attention these days. Orally disintegrating films (ODFs) are popular due to their thinness and flexibility [3]. The film is applied to the tongue's top or bottom. It remains at the application location and promptly discharges the practical component for local absorption. Progress of oral film also allows for a market line expansion for various pharmaceuticals (e.g., neuroleptics, cardiovascular therapies, analgesics, histamines, anti-asthmatics, and erectile dysfunction medication [4].

When placed in the mouth, the thin polymer films break rapidly, releasing the embedded API, which can be ingested or absorbed through the oral mucosa. As of the novelty of this dosage form, there are no clear regulatory standards in place. The European Pharmacopoeia (Eu Ph) specifies that the films should have a sufficient mechanical force to allow for damage-free handling and quick disintegration of films. The disintegration behavior of the films is one of the essential quality aspects for achieving good patient compliance and acceptance of ODFs. The failure to disintegrate at a particular time can affect the entire properties of the film. According to published studies disintegration time 60 sec mandated by the European pharmacopoeia and 30sec time limit mandated by the FDA [5].

The additional benefits include the risk of choking, being comfortable to hold and administer or apply, flexibility, and ease to scale up and pack in, thus filling the gaps in oral quick disintegrating tablets. However, low drug loading in comparison to tablets is the drawback. The width of these films' ranges from 1-10 mm and an area of 1-20 cm^2. The films can hold up to 15 mg of therapeutic agents. When the film is wet, it gets

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hydrated, and due to the adhesiveness, the film retains in situ at the applying site. The pliability and strength are particular to assist in production operations, including rewinding, die-cutting, and packaging [6].

If local action is needed, ODFs can also be used as a local anesthetic for toothaches, cold sores, and mouth ulcers. This fast-acting drug delivery technology is ideal for pharmaceuticals exposed to much heat. As a result, adverse/side effects and costs are minimized [7].

Fast dissolving technology can be applied to some of the indications, such as;

- Pediatrics (Antitussives, Expectorants, Anti-asthmatic)
- Geriatrics is the study of older adults (Expectorants, Antiepileptic)
- Problems with the digestive system
- Vomiting (As a result of cytostatic treatment)
- Ache (Hemicrania)
- Central Nervous System (CNS) (Anti parkinsonism therapy) [4].

2. ADVANTAGES AND DISADVANTAGES OF ORAL FILMS [4,6].

Table 1: Advantages and disadvantages of oral films.

Advantage	Disadvantages
Improved oral absorption	Low drug loading capacity
Faster onset of action	Expensive packing
The first-pass impact can be reduced	Drugs that are unstable at the buccal pH can't be given
Improved bioavailability	ODFs not suitable for drugs for that irritate the mucosa
No chewing or swallowing	Only one dosage of drug with a modest dose need can be given
No water is needed,	Taste masking of medicament is required as bitter taste, which necessitates the use of a taste masking agent
Enhanced safety and efficacy	OFDFs are delicate and must be protected from water, hence they require specialised packaging
Improved patient compliance	Limited flavour masking option
Oral mucosa's high vascularity	Dose uniformity is a technical challenge
Consume at any place at any time	Low drug loading

3.ORAL FILMS CLASSIFICATION [8].

Table 2: Oral films classification.

Property/ Subtype	Flash release wafer	Wafers with a mucoadhesive layer that melts away	Sustained-release mucoadhesive
Part (cm^2)	2:8	2:7	2:4
Width µm	20:70	20:500	50:250
Shape	Film-single layer	Multilayer scheme soluble	Multilayer scheme
Excipients	A solvable, extremely hydrophilic polymer	Solvable, hydrophilic polymers	Low solvable polymer
Drug phase	Solid solution solid	Solid solution or suspended drug atoms	Suspension and solid solution
Application	Tongue (greater plate)	Buccal region	Gingival
Dissolution	Highest 60 sec	Disintegration in a few min, forming a gel	Highest 8-10hrs

4.COMPONENTS IN ORAL FILMS [8].

4.1. Active pharmaceutical agents

Any pharmaceutically active agent belongs to antiulcer, antiasthmatics, antitussives, antihistaminic, antiepileptics, antianginal, expectorants, etc., well tolerated in the oral cavity, and the mucosa can be used active pharmacological agent (API). The dose limit of API should be (<20 milligrams/day). Other pharmacological class of drugs belongs to antiemetics, anxiolytics, cardiovascular agents, neuroleptics, antiallergics, antiepileptics, analgesics, sedatives, diuretics, hypnotics, anti-parkinsonism agents, erectile dysfunction drugs, anti-bacterial agents, expectorants, anti-Alzheimer, and antitussives can also be prepared as films.

Table 3: Components ın oral fılms.

Sl. No	Component	Volume% (w/w)
1.	Drug (API)	5-30
2.	Water solvable polymer	40-50
3.	Plasticizers	0-10
4.	Saliva stimulant	2-6
5.	Sweeting agent's surfactant	3-6
6.	Surfactant flavours	Q. S
7.	Flavour, colour, fillers	Q. S

The traits of a drug that should be selected are as follows:

- Pleasing flavor
- Small dosage, often <30mg
- Lower molecular weight and modest molecular weight
- An esthetically pleasing and also saliva and water-soluble
- To be slightly nonionized at the pH of the oral cavity
- Must be capable of penetrating oral mucosal tissue [9].

4.2. Water-soluble polymer

The water-soluble polymer gives the films quick disintegration, a pleasant mouthfeel, and mechanical qualities. Larger molecular weight polymers slow down the disintegrating time. HPMC E-3, Methylcellulose A-3, A-6 and A-15, Pullulan, Carboxymethyl- cellulosecekol 30, Polyvinylpyrrolidone PVP K-90, Sodium alginate, Polyvinyl alcohol, Pectin, Maltodextrins, Gelatin, Hydroxypropyl cellulose, and Eudragit-RD10 are some of the water-soluble polymers used as film formers. Polymerized rosin is another unique film-forming polymer [10].

4.2.1. The importance of polymer in oral films

Oro dispersible films remain a form of a polymeric matrix made of several polymers with typical physicochemical and operative characteristics. Depending on the kind or grade of polymer, numerous features can be regulated, including mucoadhesion, disintegration time, mechanical strength, drug loading capacity, elasticity, and handling capabilities are just a few of the variables to consider [11].

4.2.2. Polymers in preparation of oral films [12].

Table 4: polymer avaılable preparatıon of oral fılms.

Sl. No	Polymer	Examples
1	Natural polymer	Starch, Pectin, Pullulan Maltodextrins, sodium alginate, Gelatin, Polymerized rosin.
2	Synthetic	Sodium carboxymethylcellulose, Hydroxypropylmethylcellulose, Polyvinyl alcohol, Hydroxypropyl cellulose, Polyethylene oxide, Polyvinylpyrrolidone.

4.2.3. Characteristics of different polymers used in oral film manufacturing [13].

Table 5: characterıstıcs of dıfferent polymers used ın oral fılm manufacturıng.

Polymer used	Disintegration Time(sec)	Appearance	Film Forming Capacity
HPMC E-15 + PEG 400	120	Translucent	Good
HPMC E-15 + Glycerin	92	Translucent	Good
HPMC K4M	_	_	Very poor
HPMC E-15 + Pullulan	_	_	Poor
HPMC E-15 + PVA (Polyvinyl alcohol)	78	Translucent	Standard
HPMC E-15 + PVP (Polyvinyl pyrrolidone)	67	Translucent	Standard
HPMC E-15 + PVA (polyvinyl alcohol) + MCC (microcrystalline cellulose)	_	_	Poor
HPMC E-15 + MCC	42	Semi-Translucent	Improved
PVA (polyvinyl alcohol)	52	Translucent	Standard
PVA (polyvinyl alcohol) + PVP polyvinylpyrrolidone) + Glycerin	64	Translucent	Standard
PVA (polyvinyl alcohol) + PVP (polyvinylpyrrolidone)+ PEG 400	52	Translucent	Standard
PVP (polyvinylpyrrolidone)	_	_	Very poor
Pullulan + PVA (polyvinyl alcohol)	_	_	Very poor
Pullulan + Guar Gum + Xanthan Gum + Carrageenan	19	Translucent	Finest
Gelatin	_	_	Very poor
Eudragit RL_100	_	_	Very poor

4.3. Plasticizer

Plasticizers improve the mechanical properties of films, such as tensile strength and elongation). Plasticizers have different mechanical properties depending on their concentration. The most commonly used ones are glycerol, di-butyl phthalate, and another plasticizer, such as polyethylene glycol, also used in filmmaking [14].

4.4. Saliva stimulating agents

By enhancing saliva production, saliva stimulating chemicals assist in speeding up the disintegration of the strip that dissolves quickly. Preparation of digestive fluid stimulants includes, acids such as citric acid, tartaric acid, lactic acid, malic acid [15].

4.5. Flavouring agent

Flavoring agents come in several forms, including artificial flavor oils, oleoresins, and extracts from several portions of plants, including fruits and leaves. Tastemakers are available in several forms, used alone or in conjunction with other flavors and essential oils. Menthol solvable extracts, sweet solid mint, spearmint, peppermint, wintergreen, sour fruit, cinnamon, clove citrus, orange, or sweet flavor vanillin, are some of the flavors that can be used in flavoring and taste making. Moreover, flavors such as raspberry, cherry, and pineapple are also popular. The kind and strength of the flavour determine how much is required to cover the taste [9].

4.6. Sweetening agents

Sweeteners, such as fructose, dextrose, liquid glucose, glucose, sucrose, and isomaltose, become critical components of nutraceuticals and medications that dissolve in the mouth. Fructose is an excellent sweetener and sweeter than mannitol and sorbitol because polyhydric alcohols like mannitol, sorbitol, and isomaltose have a pleasing mouth-filling and freezing effect; in combination with other sweeteners produce better sweetening action. Polyhydric alcohols are less carcinogenic and have no after, taste effect, which is crucial in formulating oral preparations [14].

4.7. Coloring agents

FD&C-approved coloring compounds (with concentration levels ≤ 1%w/w) are used to orally produce quick-dissolving films such as titanium dioxide [1].

4.8. Surfactants

Using surfactants as a solubilizing and wetting agent in the formulation also allows the film to dissolve in seconds, and the effective ingredient discharges quickly. Sodium lauryl sulfate is one of the most regularly utilized sulfate, benzalkonium chloride, tweens, and other chemicals among this category is poloxamer 407 [14].

5.METHODS OF PREPARATION

5.1. Solvent casting method

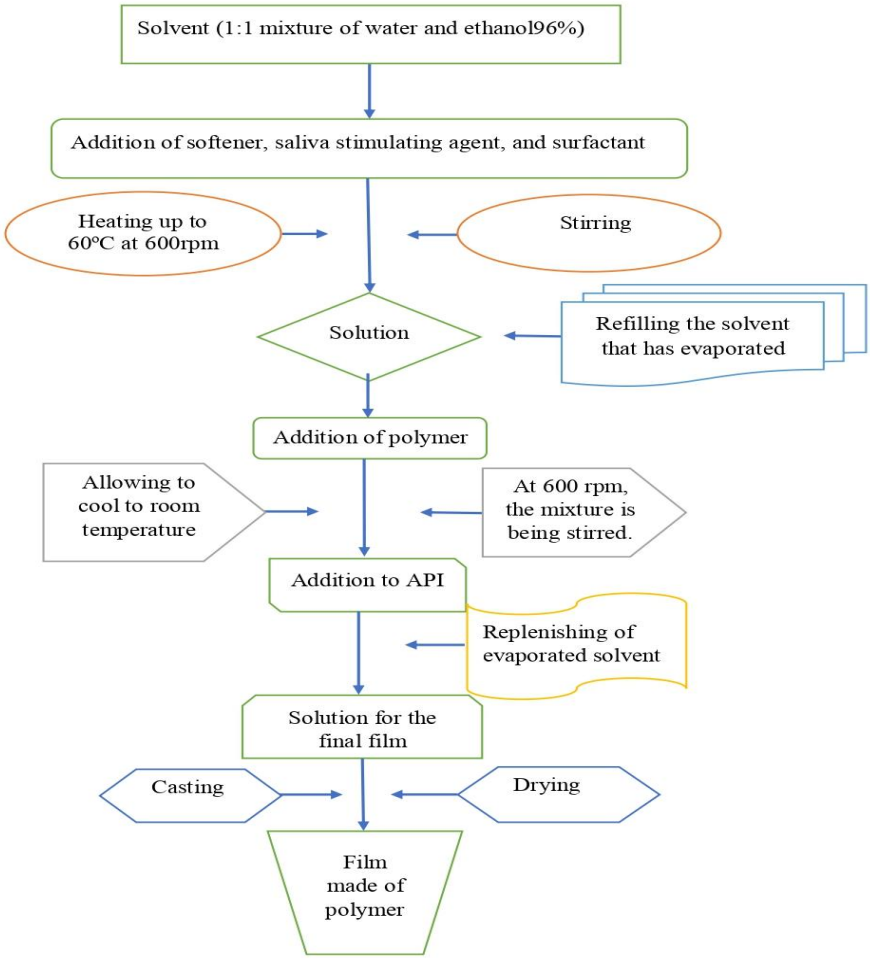

Figure 1: Solvent casting method [13].

5.2. Semisolid casting

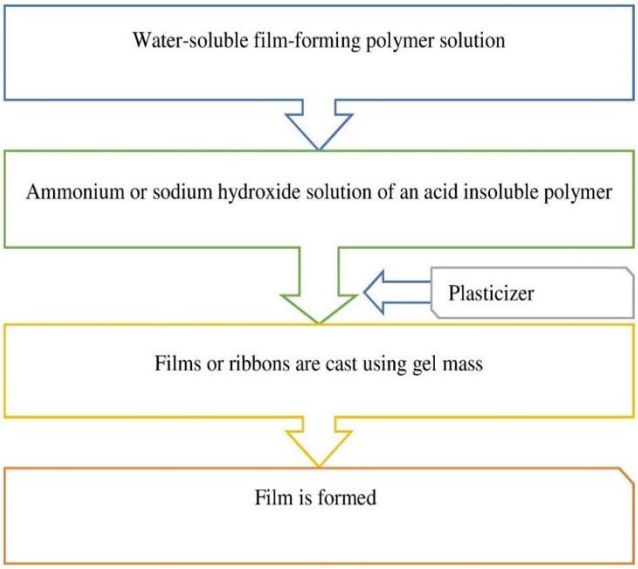

Figure 2: Semisolid casting [16].

5.3. Hot melt extrusion

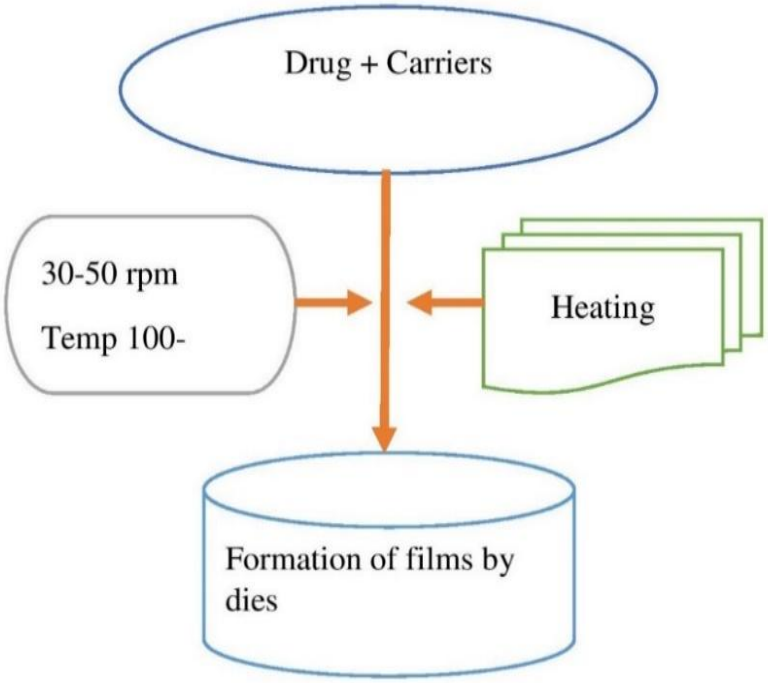

Figure 3: Hot melt extrusion [17].

5.4. Solid dispersion extrusion

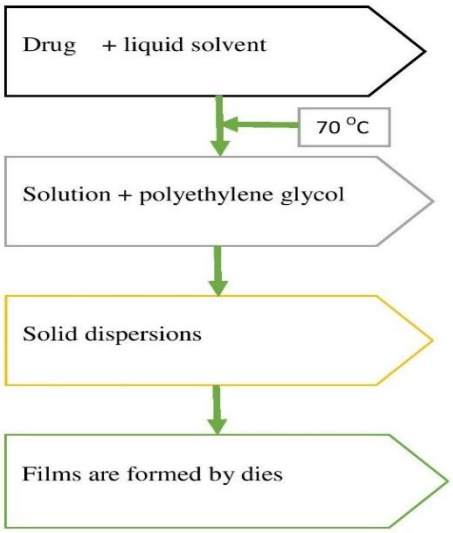

Figure 4: Solid dispersion extrusion [13].

5.5. Rolling method

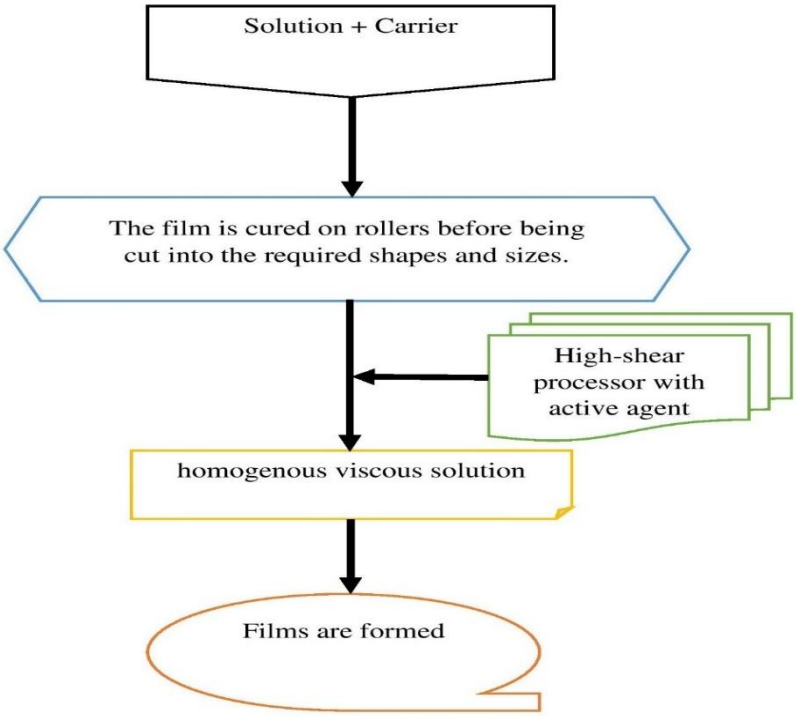

Figure 5 : Rolling method [18].

6. EVALUATİON

6.1. Mechanical properties

6.1.1. Thickness

Micrometer screw gauges or calibrated digital vernier determine the film thickness. The film thickness should be in the 5-200m range. The film's thickness at five distinct points (four bends and one within the middle) is checked, and consistency within the thickness of the film is critical since it has directly associated with the precision of dose distribution within the film [19].

6.1.2. Dryness test/Tack tests

Set-to-touch, tack-free, dust-free, dry-hard, dry print-free, dry-to-recoat, dry-through, and dry-to-touch are the eight phases of the film drying process. Although the majority of these studies are intended to evaluate dry films, they will be severely altered to evaluate pharmaceuticals. Screw refers to the tenacity with which a strip sticks to an adjunct that has been kept in interaction with it. There is a range of instruments presented for this analysis [20].

6.1.3. Tensile strength

A 2*2cm^2 film strip with no air bubbles is clamped between two clips 3 cm apart. Double-sided secure cardboard to the clamp's surface keeps the film from being sliced by the clamp's groves. Throughout measurements, drag the strips at the bottom clamp by applying load to the pan until the film split [21].

$$\text{T strength g/of} = \frac{force\ at\ break}{initial\ cross{-}sectional\ area\ of\ the\ film\ (mm2)}$$

6.1.4. Percent Elongation

The extent of stretching determines the percent elongation of the strip, which is computed using the following formula [22].

$$\text{Breaking elongation (\%)} = \frac{increase\ in\ length\ at\ breaking\ point\ (mm) \times 100\%}{Original\ length\ (mm)}$$

6.1.5. Young's Modulus

The young's modulus, also known as the elastic modulus, measures the strip toughness. It relates realistic stress to strain in an elastic deformation area [10].

$$\text{Young's modulus} = \frac{Slope \times 100}{strip\ thickness \times cross{-}head\ speed}$$

6.1.6. Tear resistance

Tear resistance is obtained by subjecting it to a consistent distortion rate. Newton's force calculates the amount of strength essential to strip the film. The larger a stress-strain curve's area, the greater the stress-strain curve, the stronger the film, and the more energy a single fragment can sustain. The force to induce tearing in inches per minute(in)/min measures Newton's force. The maximum stress or force that tear resistance of the specimen is a Newtonian value (pounds-force). The most typical loading rate is 51min [23].

6.1.7. Organoleptic test

The organoleptic test measures the ability to break down fast in the buccal cavity and its retetion potential of its organoletic peroperties duting its stay in the product must have the required sweetness, and taste attributes that appeal to a larger audience. Particular measure human taste panels are required to analyze the product's psychophysical assessment. In-vitro treatments employing specially developed palate instruments and drug release using improved pharmacopoeia methods are known. These equipment and processes for in-vitro taste evaluation are right for tall-through-out palate testing of buccal pharmaceutical preparations. The electronic tongue dimension has been used in experiments to differentiate between different stages of sweetening in the taste-masking formulation [24].

6.1.8. Folding Endurance

The film's folding endurance is experimented with by bending it repeatedly within the same spot until the strip breaks, and the number gives the folding endurance value. This property can identify the film's brittleness [24].

6.2. Swelling test

The prepared film's swelling index, S_w, was calculated using the equation:

$$W = \frac{Ws - Wd}{Wd} \times 100$$

The masses of the completely hydrated and dry films are represented by W_s and W_d, respectively [25].

6.3. Surface pH test

The test film is placed in a petri dish and soaked in 0.5ml distilled water for about 30 seconds. The pH meter's conductor is allowed to be in touch with the surface of the film pH is recorded simultaneously [26].

6.4. Contact angle

A goniometer measures the contact angle at room temperature. A droplet of distilled water is added from the dried film's top. A digital camera captures the pictures of the water drop within 10 seconds of its deposition. Angle is measured using Image J 1.28v software from the national institutes of health (NIH, USA). A minimum of five measurements, each at a distinct film location. The contact angles of two edges of the droplet are measured and averaged [25].

6.5. Transparency

A basic UV spectrophotometer can be used to check the transparency of the films. Cut the film samples into rectangles and set them on the spectrophotometer's interior side. At 284nm, determine the transmittance of films. The films transparency was determined as:
Transparency = (logT600)/b = -€c, where T 284 is the transmittance at 284nm, B is the film thickness (mm) and C is the concentration [27].

6.6. Assay/ content uniformity

The films are sliced (area of 2.25cm^2), placed in a 100ml volumetric flask, dissolved in methanol, and diluted suitably. The solution's absorbance was measured at 228nm [28].

6.7. Disintegration test

The disintegration time of each film was measured by placing a patch area of 6.2 cm^2 containing 4mg of the drug in a petri-dish containing 2ml of distilled water and the time taken for the film to complete breakdown was noted [29].

6.8. In-vitro dissolution test

The USP apparatus is utilized in vitro dissolution test (paddle with a sinker). The dissolution test is performed at 37°C±0.5°C in 900ml 0.1 N HCL with a stirring speed of 75 rpm. Dose administration requires a specific film size. The area used is (2*2 cm^2). Dissolution aliquot of 5 ml of the media is collected at 1,2, 5-, 10- and 15-minutes intervals, 15 minutes under sink conditions. The samples are run through filter membrane filters with a 0.45 m pore size, and the concentration of the drug is determined using UV-Visible spectroscopy [30].

7.CHALLENGES IN THE FORMULATION OF ORAL FILMS

According to technology catalysts, the market for Oro-dispersible film preparation drug products was priced at $ 500 million in 2007 and is predicted to increase to $ 2 billion. Due to the patient's nonreference for tablets and capsules, an oral film is now a market option. However, Oro- dispersible film knowledge is still in its infancy, soon becoming the treatment of choice for patients. Since 2003, there have been over 80 oral film brands in North America. However, the market has remained small in comparison to oral dissolving tablets.

Over-the-counter films are available for pain relief and motion sickness prevention in the United States. Three powerful nations have approved oral prescription films: the United States, the European Union, and Japan. The FDA-permitted films develop the ability to surpass other pharmaceutical dose formats. The worth of the oral film business looks to be skyrocketing. Much knowledge is available today in preparing, expanding, and estimating oral fast dissolving (ODF) and film. Though, in developing such dosage forms, the formulator has significant obstacles. There is a need to overcome such issues, which may aid in overall preparation and growth. Patient compliance is a prime requirement in any therapy, so film preparation should be prioritized in formulation and development [31].

8.CASE STUDIES ON ORAL FILMS

Table 6: Case studies on oral films.

Author	Drug / category	Polymers	Purpose/ observatıons
Manar Adnan Tamer, Shaimaa Nazar ABD-AL Hammid, Balqis Ahmed	Bromocriptine Mesylate / antidiabetic	Hydroxypropyl methylcellulose, polyvinyl alcohol (PVA), pectin and gelatin,	Solubility enhancement, Improvement of oral bioavailability, shorter disintegration time, rapid drug action *In vitro* drug release profile showed a drug release of 86.8 % in 2 min and the disintegration time of 9.2±0.1 seconds [32].
Rajni Balaa, Shailesh Sharmab, IKGPTU	Aprepitant / Antiemetics	Pullulan and PEG 400.	Enhancement of maximum therapeutic efficacy, increased bioavailability and maximum stability, the *in vitro* dissolution rate of 88.87 % disintegration time 20 s assures the increased bioavailability [33].
Gamal M. Zayed, Saleh Abd-El Rasoul, Mohamed A. Ibrahim, Mohammed S. Saddik, Doaa H. Alshora	Domperidone / Antiemetics	Polyvinylpyrrolidone (PVP K-90)	Solubility enhancement, improve oral bioavailability via pharmacokinetics analysis / About 40% was released in the first five minutes. *In vivo* pharmacokinetics analysis indicated a higher maximum plasma concentration (Cmax) and a shorter time to reach Cmax (t_{max}) [34].
Sujith S. Nair, Roopitha Padmanabhan, and Sreena K.	Prochlorperazine maleate / Antipsychotic	HPMC E15, glycerol and propylene glycol, tween 80, mannitol, citric acid, and sodium starch glycolate.	Enhancement of drug dissolution, rapid disintegration and good patient compliance *In vitro* disintegration time was 25.67±0.57s and *in vitro* drug release is 94.59 % at the end of 10 minutes [35].
Alka Tomar, Kiran Sharma, Nitesh S Chauhan, Ashu Mittal, Umakant Bajaj	Dicyclomine / anticholinergic	HPMC (hydroxypropylmethylcellulose), PVA (polyvinylalcohol), Eudragid RL-100	A faster disintegration, dissolution with improved bioavailability dissolution About 94.14 % drug release in 5 min, first-order drug kinetic pattern [25].
D.V.R.N.Bhikshapathi, V. Durga Madhuri1, V.V.Rajesham1, R. Suthakaran	Naratriptan hydrochloride / Antimigraine	HPMC (E3 and E6), Propylene glycol, PEG-400	Rapid disintegration, higher dissolution better patient compliance the *in vitro* disintegration time was 10 sec, and *in vitro* dissolution of 98.23% of the drug within 6 min was observed [36].

Pavani. S and goutham. P	Atenolol / Anti hypertension.	HPMC E15	The quick onset of action with higher patient compliance. About 99.89 % of the drug was released in 20 min with a disintegration time of 15.3 sec [7].
Venkateshwarlu k	Bufotenin	HPMC E5, E15, K15, Microcrystalline Cellulose (MCC), Polyvinyl Alcohol (PVA), and Glycerol	Rapid dissolution, Rapid onset of action, with additional improvement in bioavailability. / *In vitro* dissolution is 98.9 ± 0.63 % [22].
Verena Garsuch and JorgBreitreutz	Caffeine and Caffeine citrate	Carboxymethyl cellulose, Hydroxypropyl methylcellulose	Comparative investigation of film-forming agents were used for the preparation of films, thus hydroxypropyl methyl cellulose was most suitable film-forming agents for drug-free [38].
Bhyan Bhupinder, Jangra Sarita	Rizatriptan Benzoate / Anti-migraine	Hydroxypropyl methylcellulose (HPMC E 15), maltodextrin, sodium starch glycolate, Glycerol, mannitol, aspartame, and sodium lauryl sulphate	Rapid onset of action and better therapeutic benefits / About 90% drug release within 7 min was observed the observed DT time of 25-50 sec. About 61% *ex-vivo* drug permeation within16 min. The film exhibited an excellent under storage conditions of 40^0 C±5^0C att75%±5% RH [21].

9.ORAL FILMS MARKETED PRODUCTS [39].

Table 7: Oral films marketed products.

Types of Products	Ingredients	Application
Energy Boosters	Extract green tea, caffeine, and guarana	The product keeps a high level of energy
Detoxification Strip	Green tea extract contains a lot of polyphenols and antioxidants.	Wound healing, blood sugar regulation, body temperature, and a healthy digestive system wound healing properties
Male Vitality Stripe Ale	Siberian ginseng extract, maca root extract, and herbs that enhance libido, cinnamon flavor	Aphrodisiac
Appetite-Suppressant	Garcinia Cambogia, focus vesiculous and guarana extract,	Cambogia suppresses appetite, allowing you to eat less.
Vitamins and Food Supplements	Minerals, Various vitamins, and supplements	It's helpful for folks who don't enjoy popping pills or taking soluble vitamins.
Breath Freshener Strip, (Antibacterial Strip)	Antibacterial agent and contain mint flavor-cetyl pyridinium chloride	Mouth freshener
Saliva Promoting Strips	a variety of tastes, fruit acid extracts	Used to treat xerostomia which is caused by other drugs.
Donepezilrapid film	Donepezil hydrochloride 5 mg and 10mg	Medication for Alzheimer's dementia ranges from mild to moderately severe.
Paladins (Bioenvelop) smoking cessation	Nicotine	Helps people quit smoke
Adults and children's multivitamin	B12, B6, C; D3 for kids, D3 for adults	Multivitamin supplement

Food Supplements	Caffeine, Vinpocetine Melatonin, Mentholomega, Protein, Benzocaine, Hoodie	Nutraceuticals
Natural products	Guarana, Ginseng	Appetite reducer, Aphrodisiac
Chloraseptic® relief strips	Corn starch, erythritol, FD&C red 40, hydroxypropyl methylcellulose, BHT, menthol, malic acid, monoammonium glycyrrhizinate, cherry flavors, sucralose, polyethylene oxide	Minor discomfort, soreness, sore mouth, and painful throat, on occasion

REFERENCE:

[1] Reddy usha kiran, Reddy sunil kumar, Katta M, Thyagaraju K. a Detailed Review on Fast Dissolving Oral Films. IAJPR. 2018; 8(06): 1351–1326.

[2] Desu PK, Brahmaiah B, Nagalakshmi A, Neelima K, Nama S, Baburao C. An overview on rapid dissolving films. Asian J Pharm Clin Res. 2013; 3(1): 15-23.

[3] Takeuchi Y, Usui R, Ikezaki H, Tahara K, Takeuchi H. An advanced technique using an electronic taste-sensing system to evaluate the bitterness of orally disintegrating films and the evaluation of model films. Int J Pharm X. 2017; 531(1): 179-190. [CrossRef]

[4] Reddy usha kiran, Reddy sunil kumar, Katta M, Thyagaraju K. a Detailed Review on Fast Dissolving Oral Films. IAJPR. 2018; 8(06): 1351–1326.

[5] Speer I, Steiner D, Thabet Y, Breitkreutz J, Kwade A. Comparative study on disintegration methods for oral film preparations. Eur J Pharm Biopharm. 2018; 132(9): 50-61. [CrossRef]

[6] Desu PK, Brahmaiah B, Nagalakshmi A, Neelima k, Nama S, Baburao C. An overview on rapid dissolving films. Asian J Pharm Clin Res. 2013; 3(1): 15-23.

[7] And PS, Goutham P. Formulation Development and Evaluation of Taste Masked Oral Disintegrating Films of Atenolol. Innov Int J Med Pharm Sci. 2017; 2(2): 2–4. [CrossRef]

[8] Bhattarai M, Gupta AK. Fast Dissolving Oral Films: A Novel Trend to Oral Drug Delivery System. Sunsari Tech Coll J. 2016; 2(1): 58–68. [CrossRef]

[9] Ghodake PP, Karande KM, Osmani RA, Bhosale RR, Harkare BR, Kale BB. Mouth Dissolving Films : Innovative Vehicle for Oral Drug Delivery. Int J Pharma Clin Res. 2013; 2(10): 41–47.

[10] Arya A, Chandra A, Sharma V, Pathak K. Fast dissolving oral films: An innovative drug delivery system and dosage form. Int J Chemtech Res. 2010; 2(1): 576–583.

[11] Borges AF, Silva C, Coelho JF, Simões S. Oral films: Current status and future perspectives: I - Galenical development and quality attributes. J Control Release. 2015; 206: 1-19. [CrossRef]

[12] Nagar P, Chauhan I, Yasir M. Insights into Polymers: Film Formers in Mouth Dissolving Films. Drug Invent Today. 2011; 3(12): 280–289.

[13] Mahboob MBH, Riaz T, Jamshaid M, Bashir I, Zulfiqar S. Oral Films: A Comprehensive Review. Int J Curr Pharm Res. 2016; 5(12): 111–117. [CrossRef]

[14] Siddiqui MDN, Garg G, Sharma PK. A Short Review on " A Novel Approach in Oral Fast Dissolving Drug Delivery System and Their Patents " Conventional oral solid dosage forms (tablets , capsules) Modified release tablets/capsules Fast action oral solid dosage form (fast dissolving tablet. Adv Biol Res (Rennes). 2011; 5(6): 291–303.

[15] Chaturvedi A, Srivastava P, Yadav S, Bansal M, Garg G, Kumar Sharma P. Fast Dissolving Films: A Review. Curr Drug Deliv. 2011; 8(4): 373–380. [CrossRef]

[16] Apurva G, Rushikesh J, Mrunal S. Oral thin film technology - current challenges and future scope. Int J Adv Res Eng Appl Sci. 2018; 7(2): 1–14.

[17] Pimparade MB, Vo A, Maurya AS, Bae J, Morott JT, Feng X, et al. Development and evaluation of an oral fast disintegrating anti-allergic film using hot-melt extrusion technology. Eur J Pharm Biopharm. 2017; 119(06): 81–90. [CrossRef]

[18] Ketul P, Patel KR, Patel MR, Patel NM. Fast Dissolving Films: a Novel Approach To Oral Drug Delivery. Int Res J Pharm. 2011; 2(12): 69–74.

[19] 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. [CrossRef]

[20] Dixit RP, Puthli SP. Oral strip technology: Overview and future potential. J Control Release. 2009; 139(2): 94–107. [CrossRef]

[21] Tomar A, Sharma K, Chauhan NS, Mittal A, Bajaj U. Formulation and Evaluation of Fast Dissolving Oral Film of Dicyclomine as a potential route of Buccal Delivery. IJDDR. 2012; 4(2): 408–417.

[22] 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(1): 183-189.

[23] Chonkar AD, Bhagawati ST, Udupa N. An Overview of Fast Dissolving Oral Films. Asian J Pharm Technol. 2015; 5(3): 129-137. [CrossRef]

[24] Ghose S. Development of Fast Dissolving Films of Timolol Maleate : Role of Hydrophillic Polyme. Int J Pharm Clin Res Sch. 2016; 5(1): 671–677.

[25] Bettini R, Romani AA, Morganti MM, Borghetti AF. Physicochemical and cell adhesion properties of chitosan films prepared from sugar and phosphate-containing solutions. Eur J Pharm Biopharm. 2008; 68(1): 74–81. [CrossRef]

[26] Prabhu SC, Parsekar SD, Shetty A, Monteiro SS, Azharuddin M, Shabaraya AR. A review on fast dissolving sublingual films for systemic drug delivery. Int J Pharm Chem Sci. 2014; 3(2): 501-511.

[27] Sumi S, Alam MN, Chowdury MI, Mazumdar MM, Chowdhury S, Alam SA. Effective development and evaluation of oral thin film of etoricoxib. World J Pharm Res. 2015; 4: 257-272.

[28] Kanekar R, Dandagi PM, Gadad AP. Formulation and evaluation of fast dissolving oral films of prochlorperazine maleate. Indian Drugs. 2015; 52(12): 23–33.

[29] Talekar SD, Haware RV, Dave RH. Evaluation of self-nanoemulsifying drug delivery systems using multivariate methods to optimize permeability of captopril oral films. Eur J Pharm Sci. 2019; 130: 215-224. [CrossRef]

[30] Kathpalia H, Sule B, Gupte ; Harsha Kathpalia A. Development and Evaluation of Orally Disintegrating Film of Tramadol Hydrochloride. Asian J Biomed Pharm Sci. 2013; 3(24): 27–32.

[31] Jadhav YG, Galgatte UC, Chaudhari PD. Challenges in formulation development of fast dissolving oral films. IAJ PR. 2013; 3(8): 1746–1751.

[32] Tamer MA, Abd-Al Hammid SN, Ahmed B. Formulation and in vitro evaluation of bromocriptine mesylate as fast dissolving oral film. IJABPT. 2018; 10(1): 7–20.

[33] Bala R, Sharma S. Formulation optimization and evaluation of fast dissolving film of aprepitant by using design of experiment. Bull Fac Pharmacy, Cairo Univ. 2018; 56(2): 159–168.

[34] Zayed GM, Rasoul SA, 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): 266-273. [CrossRef]

[35] Shukla AK, Shende S, Jain V. Formulation, Development and Evaluation of Fast Dissolving Oral Film of Levosulpiride. Asian J Pharm Educ Res. 2021; 10(2): 1–7.

[36] Bhikshapathi DVRN, Madhuri VD, Rajesham V V, Suthakaran R. Preparation and Evaluation of Fast Dissolving Oral Film Containing Naratriptan HCl. Am J Pharmtech Res. 2014; 4(03): 799–812.

[37] Venkateswarlu K. Preparation and evaluation of fast dissolving buccal thin films of bufotenin. Journal of In Silico & In Vitro Pharmacology. 2016; 2(4): 12.

[38] Garsuch V, Breitkreutz J. Comparative investigations on different polymers for the preparation of fast-dissolving oral films. J Pharm Pharmacol. 2010; 62(4): 539-545. [CrossRef]

[39] Panda BP, Dey NS, Rao ME. Development of innovative orally fast disintegrating film dosage forms: a review. IJPSN. 2012; 5(2): 1666-1674.