An extensive Review of Mouth dissolving films combining anti-epileptic drugs

Sandip Kumar Tiwari[a], Mr. Vipul Singh[b], Prof. (Dr.) Sanjay Kumar Kushwaha[c*]

[a] Research Scholar Bhavdiya Institute of Pharmaceutical Sciences and Research, Ayodhya, Uttar Pradesh, 224126 India.
[b] Associate Professor Bhavdiya Institute of Pharmaceutical Sciences and Research, Ayodhya, Uttar Pradesh, 224126 India.
[C] Professor , Bhavdiya Institute of Pharmaceutical Sciences and Research, Ayodhya, Uttar Pradesh, 224126 India.*
India.

ABSTRACT-

Millions of people worldwide suffer with epilepsy, a persistent neurological illness marked by recurring seizures. Long-term medication is frequently needed for the treatment of epilepsy, which can be difficult for patients, particularly those who are elderly or young.

The oral route's high permeability, blood flow, and huge surface area make it one of the most crucial channels for both local and systemic drug administration. The most advanced oral forms are mouth dissolving films because they are less complicated and easier to use than other dosage forms like sublingual and oro-soluble tablets. In order to provide adults and adolescents who have trouble swallowing traditional oral solid dose forms with an alternative to capsules, syrups, and tablets, fast dissolving drug delivery systems were created quickly in the 1970s.

As a drug delivery method for antiepileptic medications (AEDs), mouth dissolving films (MDFs) have shown promise due to their quick start of action, simplicity of use, and increased patient compliance.

The article provides an overview of packaging, assessment criteria, formulation procedures, and several commercially available mouth dissolving film products.

Keywords: Epilepsy, Mouth dissolving film, solvent casting, fast disintegration.

INTRODUCTION-

Epilepsy is a chronic neurological disorder that affects approximately 50 million people worldwide, imposing a considerable burden on both quality of life and healthcare systems.[1,2] Effective management of epilepsy primarily depends on the regular and consistent administration of anti-epileptic drugs (AEDs). However, patient compliance can be challenging due to various factors, including the difficulty of swallowing conventional oral dosage forms and the associated side effects. To address these issues, mouth dissolving films (MDFs) have emerged as an innovative drug delivery system that offers several advantages over traditional dosage forms.

The condition requires continuous and often lifelong medication to control seizures and prevent their recurrence.[2] However, several challenges hinder effective treatment:

1**. Patient Compliance:** Compliance with medication regimens is crucial for preventing seizures and maintaining stability. Non-compliance can result from forgetfulness, side effects, or the inconvenience of taking multiple doses daily.[2]

2. Swallowing Difficulties: Many patients, especially pediatric and geriatric populations, have difficulty swallowing conventional tablets and capsules. This can lead to missed doses and suboptimal therapeutic outcomes.[2]

3. Immediate Need for Medication: In certain situations, such as acute seizures, there is an urgent need for medication with rapid onset of action. Conventional dosage forms may not provide the necessary speed for effective intervention.[3]

Oral route of drug administration is a most preferred route due to its ease of administration, non-invasiveness, adaptability, patient compliance and acceptability. Regarding oral route of drug administration, many substitutes have continuously been presented by using recent novel technologies for pediatrics, geriatrics, nauseous and non-compliance patients.

Bioadhesive mucosal dosage forms including adhesive tablets, gels and patches are outcomes of technological development. Among various dosage forms, the use of polymeric films for delivering medication into buccal cavity has developed great potential in recent area. Orally disintegrating films (ODFs), when placed on tongue, immediately hydrates by soaking saliva following disintegration and/or dissolution releasing active pharmaceutical agent from the dosage form. ODFs are kind of formulations which are commonly prepared using hydrophilic polymers enabling rapid dissolution upon contact with saliva.

Oral disintegrating tablets (ODTs) and oral disintegrating films (ODFs) are the typical examples of orally disintegrating drug delivery systems.

The administration of ODFs has numerous advantages and some of them are as follows:

- Easy transportation.
- Ease of swallowing for geriatrics and pediatrics.
- Convenient and accurate dosing.
- No need of water for administration.
- Convenient for dysphasic patients having difficulty in swallowing tablets and capsules.
- Rapid onset of action with increased bioavailability due to bypassing hepatic first pass effect and stability.

A List of some marketed products available as fast dissolving film-

Product	Manufacturer	API	Use
Listerine	Pfizer	Cool mint	Mouth fresheners
Triaminic	Novartis	Dextromethorphan HBr	Cough suppressants
Suppress®	InnoZen®, Inc	Menthol	Mouth fresheners
Chloraseptic	Prestige	Benzocaine Menthol	Local anesthetic
Gas-X	Novartis	Simethicone	Anti Flatuating
Theraflu	Novartis	Dextromethorphan HBr	Anti allergic
Setofilm	BioalliancePharma	Ondansetron	Prevention of Nausea and Vomiting
Zuplenz(R)	MonoSol Rx	Ondansetron	Prevention of Nausea and Vomiting
Donepezil Rapid film	Labtec	Donepezil	Alzheimer's disease
Sudafed PE	Wolters Kluwer Health Inc.	Phenyleprine	Relieving Congestion
Klonopin Wafer	Solvay Pharmaceuticals	Clonazepam	Treatment of anxiety

SPECIAL FEATURES OF MOUTH DISSOLVING FILMS

1. Thin elegant film
2. Unconstructive
3. Available in various size and shapes
4. Fast disintegration
5. Rapid release
6. Give a pleasant mouth feel.
7. Have an acceptable taste.
8. Should not leave residues in mouth.

DISADVANTAGES

1. Dose uniformity is a technical challenge.
2. Hygroscopic in nature.
3. High doses cannot be incorporated

Anti-Epileptic Drugs in Mouth Dissolving Films-

The incorporation of anti-epileptic drugs (AEDs) into mouth dissolving films (MDFs) has garnered significant attention due to the potential benefits in epilepsy management. MDFs can improve bioavailability, provide rapid onset of action, and enhance patient compliance. Clinical studies have demonstrated the efficacy of MDFs in improving seizure control and patient compliance. For instance, a study on lamotrigine MDFs showed a significant reduction in seizure frequency and improved patient satisfaction compared to conventional tablets. Similarly, levetiracetam MDFs have been well-received in pediatric populations, providing an effective and convenient treatment option.

Lamotrigine

Lamotrigine is a widely used AED for the treatment of partial and generalized seizures. Incorporating lamotrigine into MDFs can significantly improve its bioavailability and provide a rapid onset of action, which is critical for managing seizures effectively.

Parvez et al. (2021) demonstrated that lamotrigine-loaded MDFs showed enhanced dissolution rates compared to conventional oral tablets, leading to quicker absorption and onset of action.

Levetiracetam

Levetiracetam is a broad-spectrum AED effective for various types of epilepsy. MDFs containing levetiracetam offer a convenient and patient-friendly alternative to traditional oral tablets and solutions, particularly for pediatric and geriatric patients.

Singh et al. (2020) developed levetiracetam MDFs using the solvent casting method. The films exhibited rapid disintegration within 30 seconds and showed comparable bioavailability to oral solutions, making them suitable for patients who have difficulty swallowing tablets.

Clonazepam

Clonazepam, a benzodiazepine, is used for the management of acute seizures. Incorporating clonazepam into MDFs can provide quick relief due to the rapid absorption through the oral mucosa.

Bansal et al. (2019) formulated clonazepam MDFs using HPMC and PEG as film-forming polymers. The MDFs demonstrated rapid disintegration and absorption, with a significantly faster onset of action compared to conventional tablets, making them ideal for acute seizure management.

Valproic Acid

Valproic acid is a broad-spectrum AED used for various types of epilepsy. MDFs containing valproic acid can potentially reduce gastrointestinal side effects and improve patient compliance by offering a more palatable and easyto-administer dosage form.

Reddy et al. (2021) formulated valproic acid MDFs and evaluated their in vitro and in vivo performance. The MDFs showed rapid disintegration and dissolution, leading to improved bioavailability and reduced gastrointestinal irritation compared to conventional oral tablets.

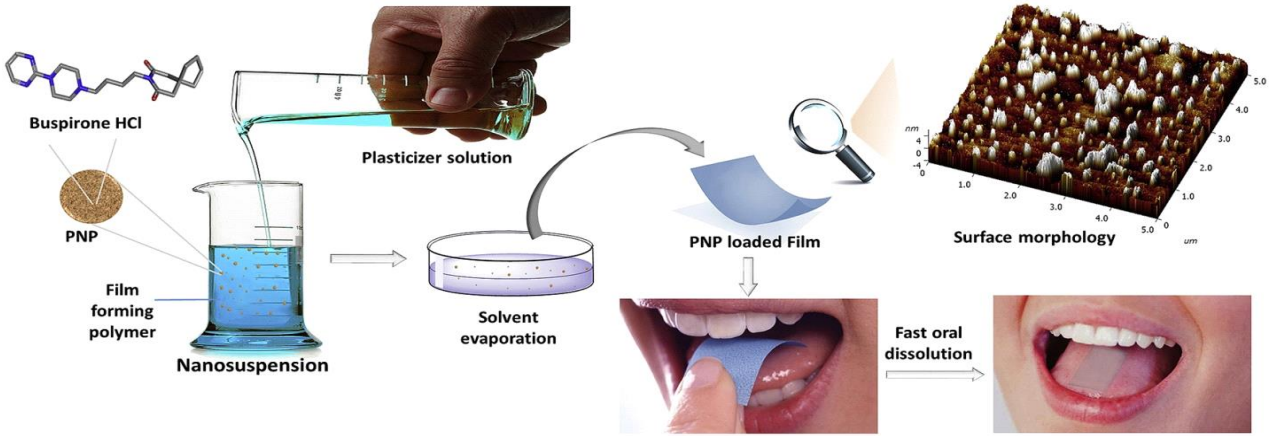
COMPOSITION OF MOUTH DISSOLVING FILM-

Ingredient	Amount	Uses (Example)
Drug	**5-30 %w/w**	**All drug with low dose**
Water soluble polymer	45% w/w	Film forming capability (HPMC E3, E5, E6, E15, K3, Methyl cellulose A3, A6, A15, Pullulan, Polyvinyl pyrollidon K-90, Pectin, gelatin, Sodium alginate, Hydroxy propyl cellulose, Polyvinylalcohol, Maltodextrin)
Plastisizers	0-20 %w/w	Increases the flexibility and reduces the brittleness of film (Glycerol, Polyethylene gycol, Dibutylpthallate,triethyl citrate)
Surfactant	q.s.	They are used as solubilizing and wetting agents making the film to dissolve rapidly within seconds(Tween 80,Sodium lauryl sulphate,benzalkonium chloride)
Sweetning agent	3-6 %w/w	Increasing the palatability of the film (Aspartame, Saccharin,Cyclamate,Alitame and Neotame, Acesulfame-K)
Saliva stimulating agent	2-6 %w/w	Increases the saliva stimulation for faster dissolution of film (Citric acid, Malic acid)
Colors, Flavours	should not exceed 1% w/w	Pigments like titanium dioxide, silicon dioxide are used as prominent coloring agents.Fruity flavors like cocoa, chocolate and fruit essence like apple, raspberry and cherry are most widely used. Essential oils like eucalyptol and thymol.

2. FORMULATION ASPECTS FOR MOUTH DISSOLVING FILMS:

Active Pharmaceutical Ingredient: Various classes of drugs can be incorporated into ODFs e.g., anti-histamine, anti-diarrheal, anti-depressants, vasodilators, anti-asthmatic, anti-emetic, etc. Dimenhydrinate can also be incorporated into ODFs for taste masking.

Common examples of drugs incorporated into ODFs are salbutamol sulfate, rizatriptan benzoate, verapamil ondansetron, dexamethasone, rofecoxib, cetirizine, pilocarpine, tianeptine sodium, indomethacin, etc.



Film Forming Polymer:

A variety of polymers are available for preparation of films of which pullulan, gelatin and hypromellose are most commonly used. Examples of watersoluble polymers include: Pullulan, Gelatin, guar gum, xanthan gum, Hydroxyl propyl methyl cellulose (HPMC), Modified starches, PVPK30, PVA etc. HPMC E3/E5/E6/E15.

Plastisizers:

In general, mechanical properties such as tensile strength and percent elongation are improved by adding plasticizer to the formulations. The concentration of plasticizer usually ranges from 0% to 20% w/w. Common examples of plasticizers are PEG, glycerol, diethyl phthalate, triethyl citrate, tributyl citrate, etc.

Sweetening Agent:

Sweeteners have become an important part of the food products as well as pharmaceutical products intended to be disintegrated or dissolved in the oral cavity. Natural sweeteners as well as artificial sweeteners are used to improve the palatability of the mouth dissolving formulations.

Saliva Stimulating Agent:

Salivary stimulants are generally acidic in nature stimulating the production of saliva in buccal cavity, consequently, promoting the disintegrating of ODFs. Some commonly used saliva stimulating agents are citric acid, malic acid, tartaric acid, ascorbic acid and lactic acid.

Surfactant:

Surfactants are used as solubilizing or wetting or dispersing agents as a result that the film gets dissolved within seconds and release active agent immediately. Surfactants also improve the solubility of poorly soluble drugs in fast dissolving buccal films. E.g.: Polaxamer 407, sodium lauryl sulfate, benzalkonium chloride, benzthonium chloride, tweens and spans etc.

Flavor:

Flavors are needed to mask the bitter or nauseating taste of incorporated drug. Amount of flavor depends upon its nature and strength. Any US-FDA approved flavor can be used such as sweet, sour or mint flavor one of the research work verified that mint, licorice and

sucralose mixture flavors appropriately mask the bitter taste of diclofenac sodium. Electronic tongues are used to discriminate the effect of various taste masking agents (TMAs)

Colouring Agent:

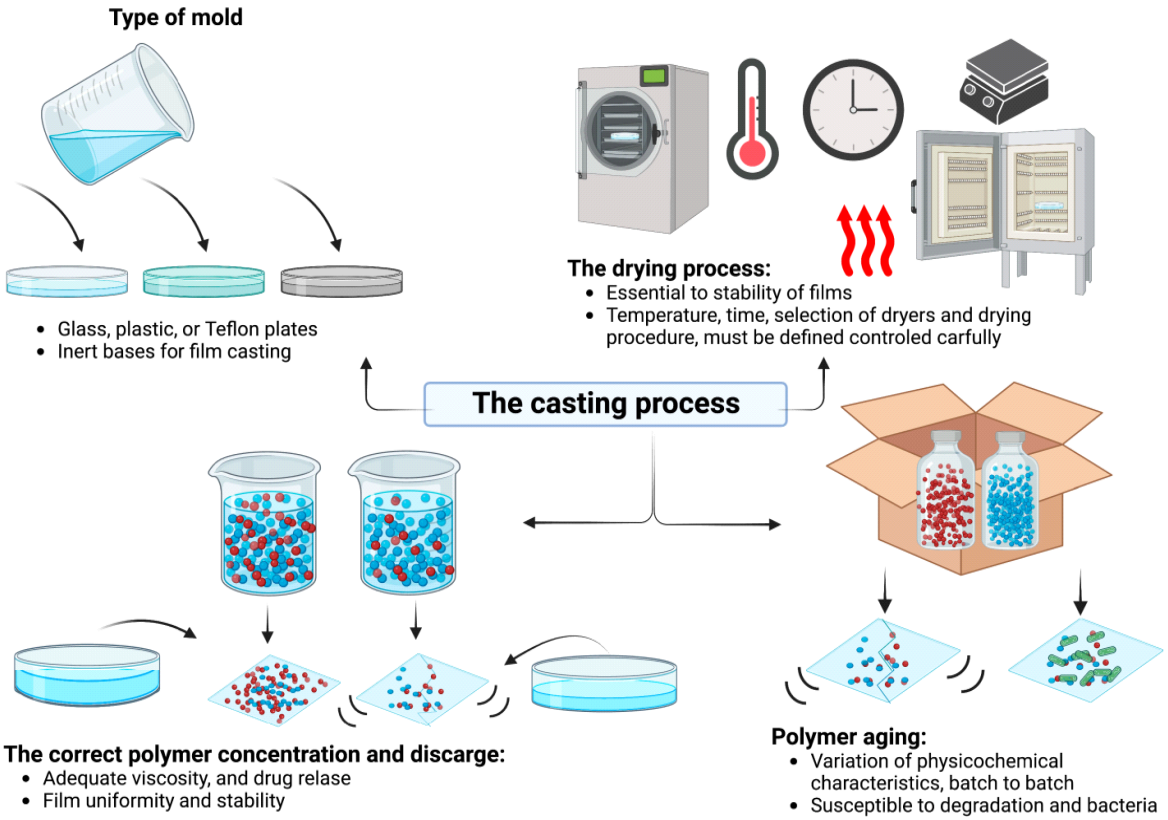
Pigments such as titanium dioxide or FD&C approved coloring agents are incorporated (not exceeding concentration levels of 1%w/w) in oral strips when some of the formulation ingredients or drugs are present in insoluble or suspension form[5] .

3. METHOD OF PREPARATION OF FAST DISSOLVING FILM:

One or a combination of the following processes can be used to manufacture the Mouth dissolving film:

1. Solvent casting
2. Hot-melt extrusion
3. Semisolid casting
4. Solid dispersion extrusion
5. Rolling.

1. Solvent casting method

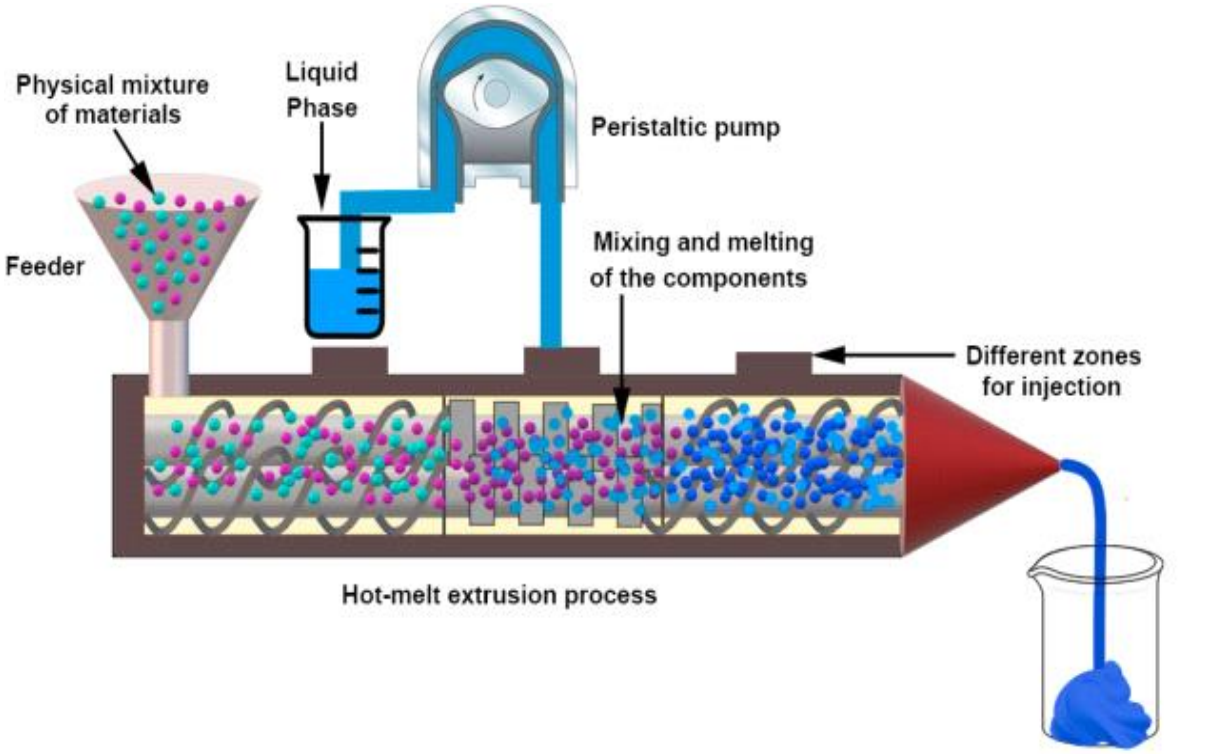


This is a very old method of film making. In this method the drug is dissolved or suspended in a solution containing polymers, plasticizers and other excipients which are dissolved in a volatile solvent such as ethanol or water.

Known as film dope, it is then poured into petri plates and passed through drying equipment such as ovens to remove all volatile solvents. The dried film is then cut into strips and packed in sealed weatherproof pouches. This method is suitable for films containing heat sensitive drug/API as the temperature required to remove the volatile solvent is comparatively lower than the hot melt extrusion method.

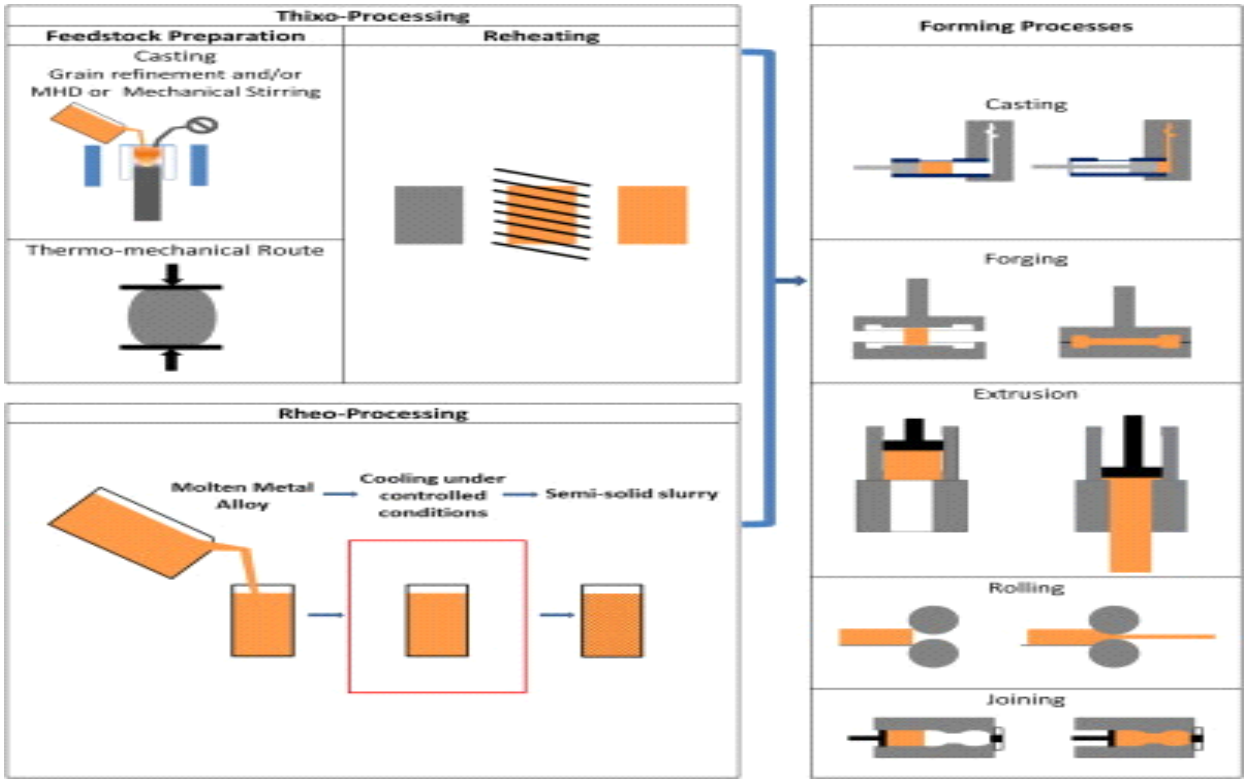
2. Hot-melt extrusion

This method involves forming the polymer into a film using a heating process. First, the drug- polymer mixture is filled into a hopper and conveyed, mixed and melted by an extruder. The mold shapes the melt into the desired shape. This method involves a lower temperature and a short residence time (< 2 min.) for the drug-polymer mixture. This method does not use organic solvents and can work continuously with minimal product wastage. Operating parameters canbe effectively controlled using this method.



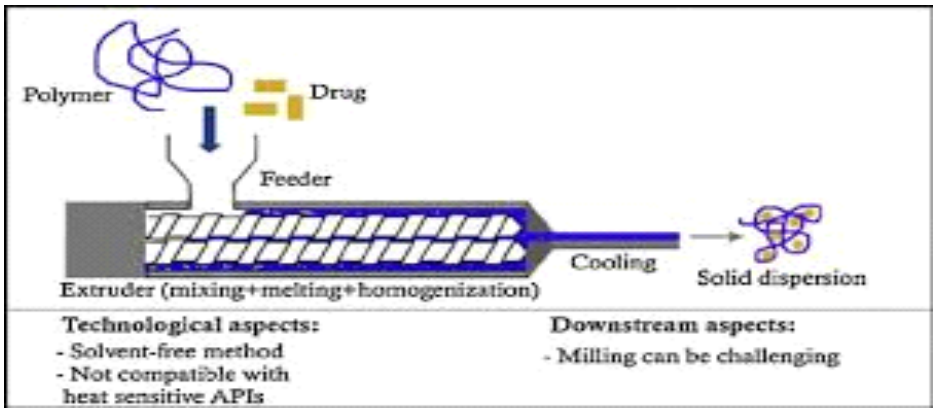
3. Semisolid Casting Method:

The semi-solid casting method is generally used when acid insoluble polymers are used. In this method, a solution of water-soluble film forming polymer is prepared, then this solution is poured into a solution of acid insoluble polymer, prepared in sodium or ammonium hydroxide. A plasticizer is then added to form a gel mass. The amount of plasticizer added affects the composition of the gel mass. The gel mass is then formed into a film or ribbon using heat controlled rollers/drums. The ratio of acid insoluble polymer to film forming polymer should be 1:4. Films made by this method have a thickness of about 0.015-0.05 inches.



4. Solid Dispersion Extrusion:

The term solid dispersion refers to the dispersion of active ingredients in a passive carrier in the solid state in the presence of an amorphous hydrophilic polymer. Initially, the drug is dissolved in a suitable liquid solvent and later this solution is added to a polyethylene glycol melt below 70C without removing the liquid solvent. And finally, the solids are dispersed and passed through dies to form a film.



5. Rolling Method:

According to this method, a premix is prepared, an active is added, and then a film is formed. Formulate premixes using polar solvents, film-forming polymers, and additional ingredients other than the drug. Fill the master batch feed tank with the premix. It was fed to the first mixer or to both the first and second mixers using a first metering pump and a control valve. Add the required amount of drug to the selected mixer. Combine the drug with the master batch premix to form a homogenous matrix.

The pan is then supplied with a predetermined quantity of homogeneous matrix using a second metering pump. Finally, the film is formed on the substrate and removed using a support roller. Then, using controlled down drying, the wet film is dried.

4. EVALUATION PARAMETERS:

1. Weight variation: Weight variation is calculated by individually weighing any five films from the formulation and then computing the average weight.

2. Thickness: The thickness of the films is calculated by selecting five films at random and then determining thickness of each film after calibration using a standard digital vernier calliper. The thickness of the film is measured at various critical points and average values are reported.

3. Folding endurance: Folding endurance is an important method for determining the mechanical properties of a film. This is determined by repeatedly folding the film at the same point until it breaks. Folding endurance values are calculated as the number of times they can be folded without breaking. The greater the folding the higher the endurance value, the higher the mechanical strength of the film.

4. Surface pH: The surface pH of the film is determined by soaking it in a petri dish with 10mlof distilled water and then measure it with a pH meter electrode by touching the surface of the film and recording the pH value.

5. Moisture absorption and moisture loss: The original weight of the film is first determinedand then the film is placed in a desiccators (including calcium carbonate) for three days to determine the moisture percentage. These films are removed and reweighed after three days and moisture loss is calculated using the formula:

% moisture loss = Initial weight – Final weight x 100 Initial weight

The percentage moisture absorption of the film is calculated by exposing it to room temperature for seven days at a relative humidity of 75% and then using the following method to calculate the moisture absorption:

% moisture uptake = Final weight – Initial weight x100 Initial weight

6. Disintegration time: Placing the film in a beaker containing 20 ml of distilled water is used to determine the disintegration time. The disintegration time is the time it takes for the film to dissolve completely.

7**. Drug content:** The amount of drug in the orally dissolving film is determined by continuously stirring the strip in 100 ml of water for 4 hours. After that, Whatman filter paper is used to filter the solution and drug content is evaluated using UV Spectro-photometer.

8. In-vitro drug release: The USP rotating paddle method is used to perform dissolution studies on films. Distilled water, 6.8 pH phosphate buffer (300 ml), 0.1 N HCl (900 ml) is commonly used as dissolution media. The release rate is determined at a temperature of 37±5ºC with a rotation speed of 50 rpm. The oral dissolving film is then added to the dissolution medium. Samples (2 ml) of dissolved drug are withdrawn at predetermined intervals i.e., every 30 seconds and replaced with fresh medium. The samples are then filtered and analyzed for drug release using a UV spectrophotometer.

Challenges and Future Directions –

Despite the advantages, there are challenges in the development and commercialization of MDFs:

1. Drug Loading and Stability: Ensuring adequate drug loading while maintaining film stability can be challenging, especially for drugs with poor solubility.
2. Taste Masking: Many AEDs have a bitter taste, necessitating effective taste-masking strategies to enhance patient acceptance.
3. Regulatory and Manufacturing Issues: Standardizing production processes and meeting regulatory requirements can be complex and time-consuming.

Future research should focus on optimizing formulation techniques, exploring novel polymers and excipients, and conducting large-scale clinical trials to establish the long-term efficacy and safety of MDFs loaded with AEDs. Additionally, advancements in 3D printing and nanotechnology hold promise for the personalized and targeted delivery of AEDs via MDFs.

CONCLUSION-

The current review demonstrates that one of the cutting-edge methods in the pharmaceutical sciences is the use of oral rapid dissolving films. Compared to conventional dose forms, they have higher safety and efficacy, better acceptability, and patient compliance with no choking risk. The primary motivation for the development of ODFs was to address the challenge that patients with dysphasia who are pediatric, geriatric, or psychiatric have while swallowing standard oral dose forms. Odds are now extensively accessible for conditions including hypertension, acidity, allergies, discomfort, etc., demonstrating their significance. The target population's need for ease in medication administration is satisfied by these dosage forms, which have two main advantages: they skip the hepatic metabolism and may be administered without the requirement for water, improving therapeutic response in the process.

The Review has indicated that MDFs containing clonazepam, levetiracetam, valproic acid, and lamotrigine are effective substitutes for traditional dose forms.

To completely demonstrate the therapeutic effects and optimize the formulations for general clinical usage, more investigation and clinical studies are necessary.

REFERENCES-

1. World Health Organization. (2022). Epilepsy. Retrieved from [WHO website] (https://www.who.int/newsroom/fact-sheets/detail/epilepsy).
2. Sander, J. W., &Shorvon, S. D. (1996). Epidemiology of the epilepsies. Journal of Neurology, Neurosurgery & Psychiatry, 61(5), 433-443.
3. Bala, R., Pawar, P., Khanna, S., Arora, S., 2013. Orally dissolving strips: A new approach to oral drug delivery system. Int. J. Pharm. Investig. 3, 67–73.
4. Chaudhary, H., Gauri, S., Rathee, P., Kumar, V., 2013. Development and optimization of fast dissolving oro-dispersible films of granisetron HCl using Box-Behnken statistical design. Bullet. Faculty Pharm. 51, 193–201.
5. Chauhan, I., Yasir, M., Nagar, P., 2012. Insights into polymers: film formers in mouth dissolving films. Drug Invent. Today 3, 56–73.

6.Desu, P.K., Brahmaiah, B., Nagalakshmi, A., Neelima, K., Nama, S., Baburao, C., 2013. An overview on rapid dissolving films. Asian J. Pharm. Res. 3, 15–23.
Dinge, A., Nagarsenker, M., 2008. Formulation and evaluation of fast dissolving films for delivery of triclosan to the oral cavity. AAPS Pharm. Sci. Tech. 9, 349–356.
Elmeshad1, A.N., Hagrasy, A.S.E., 2011. Characterization and optimization of orodispersiblemosapride film formulation. AAPS Pharm. Sci. Tech. 12, 1384–1392.
9.Goel H, Rai P, Rana V, Tiwary A. Orally Disintegrating Systems: Innovations in Formulation and Technology. Recent Patents on Drug Delivery & Formulation. 2008; 2(3):258-274.
10. Prabhu SC, Parsekar SD, Shetty A, Monteiro SS, Azharuddin M, Shabaraya AR. A Review on Fast Dissolving Sublingual Films for Systemic Drug Delivery. Int J Pharm Chem Sci. 2014; 3(2):501- 11.
11.Russo E, Selmin F, Baldassari S, Gennari C, Caviglioli G, Cilurzo F et al. A focus on mucoadhesive polymers and their application in buccal dosage forms. Journal of Drug Delivery Science and Technology. 2015;32:113-125.
12. Wening K Breitkreutz J. Oral drug delivery in personalized medicine: Unmet needs and novel approaches. Int J Pharm. 2011;404(1-2):1-9.
13. Hariharan M, Bogue A. Orally dissolving film strips (ODFS): the final evolution of orally dissolving dosage forms. Drug Deliv Technol. 2009 Feb;9(2):24-9.
14. Sakellariou P, Rowe R, White E. An evaluation of the interaction and plasticizing efficiency of the polyethylene glycols in ethyl cellulose and hydroxypropyl methylcellulose films using the torsional braid pendulum. IntJ Pharm. 1986; 31(1-2):55-64.
15. Patil PC, Shrivastava SK, Vaidehi S, Ashwini P. Oral Fast Dissolving drug delivery system: A modern approach for patient compliance. Int J Drug Regulatory Affairs. 2014 Jun 1; 2(2):49- 60.
16. Tatwashil Kshirsagar. Formulation & Evaluation of Fast Dissolving Oral Film. World Journal of Pharmaceutical Research.2021: 503-561.
17. Quazi Bilal. A Review on Mouth Dissolving Films. European Journal of Pharmaceutical and Medical Research. 2020: 232-238.
18. Vikrant K. Nikam. Most Promising Solid Dispersion Technique of Oral Dispersible Tablet. Beni-Suef University Journalof Basic and Applied Sciences. 2020: 9:62.
19. Kshitija P. Deshmukh. Formulation And Evaluation of Fast Dissolving Oral Films. World Journal of Pharmacy andPharmaceutical Sciences. 2020: 396-406.
20. Rajat Pawar. Formulation And Evaluation of Mouth Dissolving Film of Prochlorperazine Maleate. Journal Of DrugDelivery and Therapeutics. 2019: 110-115.
21. Pawar, R., Sharma, R., Sharma, P., &Darwhekar, G. A Review on Mouth Dissolving Film. Journal of Drug Delivery andTherapeutics. 2019: 206-210.
22. Verma Umakant, Rajput Rahul, Naik Jb. Development and Characterization of Fast Dissolving Film of Chitosan EmbeddedFamotidine Using 32 Full Factorial Design Approach. Science Direct. 2018: 408–414. 23. Sheoran Reena. Fast Dissolving Oral Films. A Review with Future Prospects. Ijppr. 2018: 15-32.
24. Jain A, Ahirwar H C, Tayal S, Mohanty P K. Fast Dissolving Oral Films. A Tabular Update. Journal Of Drug Delivery and Therapeutics. 2018: 10-19.

25. Sharma Pravin K, Sharma Pankaj K, Darwhekar Gajanan N, Shrivastava Birendra. Formulation And Evaluation of MouthDissolving Film of Tadalafil. Journal Of Drug Delivery and Therapeutics. 2017: 52-55. 26. Patel D M, Patel D J And Darji P J. Formulation and Evaluation of Fast-Dissolving Film of Cetirizine and Dextromethorphan. International Journal of Pharmaceutical Sciences and Nanotechnology. 2016: 3305-3311.
27. Mahboob Muhammad B H, Riaz Tehseen, Jamshaid Muhammad, Bashir Irfan and Zulfiqar Saqiba, Oral Films. AComprehensive Review. International Current Pharmaceutical Journal. 2016: 111-117.
28. Kumar R S, An Update on Fast Dissolving Films. World Journal of Pharmacy and Pharmaceutical Sciences. 2016: 466-486.
29. Prabhakara Prabhu. Formulation And Evaluation of Fast-Dissolving Films of Lisinopril. Egyptian Pharmaceutical Journal.2015: 56–64.
30. Vyas Himanshu D, Parmar Ghanshyam, Shah Nirmal, Chauhan Sachin, Seth A K. Formulation and Evaluation of FastDissolving Film of Methyl Cobalamin. An International Journal of Pharmaceutical Sciences. 2015: 50-68.
31. Bala R, Pawer P, Khanna S, Orally Dissolving Strip. A New Approach to Oral Drug Delivery System. Int J Pharma, 2013:67- 76.
32. Nalluri B.N. Development and Evaluation of Mouth Dissolving Film of Salbutamol Sulphate. J. Chem. Pharm.Res. 2013:53-60.
33. ShohinIe. Biowaiver Monographs for Immediate Release Solid Oral Dosage Forms Ketoprofen. J Pharma Sci. 2012: 3593-603.
34. Ashish P, Haroliya Ms, Pathan J K, Shruti S. Formulation of Mouth Dissolving Tablet. Int. J. Pharm. & Clinical Science2011: 1-8.
35. Prasanthi N.L. Design and Development of Sublingual Fast Dissolving Films For An Antiasthmatic Drug. Der Pharmacia Lettre, 2011: 382-395.