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A REVIEW ON MOUTH DISSOLVING FILM

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ABSTRACT

Mouth Dissolving Films (MDF) or Oral Thin Films (OTFs), offer a convenient way of dosingmedications, not only to special inhabitant's groups with swallowing difficulties such as Paediatrics and Geriatrics, but also to the general population. Fast dissolving drug delivery have been developed as an alternative to conventional dosage form as an oral means of drug delivery in case of chronic conditions. Present days fast dissolving films are preferred over conventional tablets and capsules for masking the taste of bitter drugs to increase the patient compliance. Mouth Dissolving Films consist of a very thin oral strip which dissolves in less than one minute when placed on the tongue. Dissolvable oral thin films are in the market since past few years in the form of breath strips and are widely accepted by consumers for delivering vitamins, vaccines and other drug products. Mouth Dissolving Films are the novel dosage forms that disintegrate and dissolve within the oral cavity. Intra-oral absorption permits rapid onset of action and helps by-pass first-pass effects, thereby reducing the unit dose required to produce desired therapeutic effect.

KEYWORDS: Fast Dissolving Oral Film, Oral Thin Films, Oral cavity, Mouth Dissolving Films.

INTRODUCTION

Oral route is most common and mostly applicable route of drug administration. Recent advances and developments in the technology have presented viable dosage alternatives from oral route for pediatrics, geriatric, bedridden, nauseous or noncompliant patients. Various bio adhesive mucosal dosage forms have been urbanized which includes adhesive tablets, gels, ointments, patches and more recently the use of polymeric films for buccal delivery, also known as mouth dissolving films. Mouth dissolving films, a new drug delivery system for the oral delivery of the drugs, was developed based on the technology of the transdermal drug delivery system. The delivery system consists of a very thin oral strip, which is simply placed on the patient's tongue or any or tissue, instantly wet by saliva the film rapidly hydrates and adheres onto the site of application. It then rapidly disintegrates and dissolves to release the medication for Oro mucosal absorption or with formula modifications, will maintain the quick-dissolving aspects allow for gastrointestinal absorption to be achieved when swallowed.In contrast to other existing, rapid dissolving dosage forms,which consist of lyophilizates, the rapid films can be produced with a manufacturing process that is competitive with the manufacturing costs of conventional. Pharmaceutical companies and consumers alike haveembraced oral thin films (OTFs) as a practical and accepted alternative to traditional OTC medicine forms such as liquids, tablets, and capsules. OTFs offer fast.

Mouth dissolving films (MDF): Oral route is the most preferred route for the delivery of thedrugs till date as it bears various advantages over the other route of drug administration, the particular class of patients which includes geriatric, paediatric and dysphasic patients associated with many medical conditions as they have difficulty in swallowing or chewing solid dosage forms. Many paediatric and geriatric patients are unwilling to take solid preparations due to fear of choking. That's way the MDF are very essential to used.

Definition of FDF: Fast dissolving films are most advance form of solid dosage form due toits flexibility. It improves efficacy of Active pharmaceutical ingredient (API) dissolving in the short duration oral cavity after the contact with less amount of saliva as compared to dissolving tablet.

Mechanism of absorption through saliva: There are two possible routes for drug absorption: the transcellular (intracellular, passing through the cell) and the paracellular (intercellular, passing around the cell) route. Another classification involves passage through non-polar (lipid elements) and polar (hydrophilic material through aqueous pores) routes.

The permeation mainly occurs by the par cellular route,

but the route taken depends on the physicochemical properties of the drug. Small molecules, predominantly lipophilic, are absorbed most rapidly, whereas large hydrophilic Molecules are generally poorly absorbed. Hydrophilic molecules take the paracellular route, compared to lipophilic molecules, which take the transcellular route. The permeability decreases as the molecule size increases. The 4 passages across the oral mucosa follows a first order simple diffusion process. Although passive diffusion is the main mechanism of drug absorption.

OBJECTIVES

This review tries to explain the obstacles which formulators usually face during formulation development of fast dissolving oral films. In addition to this, review also elaborates remedies to overcome these challenges which will help in formulation of poorly water soluble or bitter drug fast dissolving oral film. These remedies will enhance production of this dosage form in minimum time.

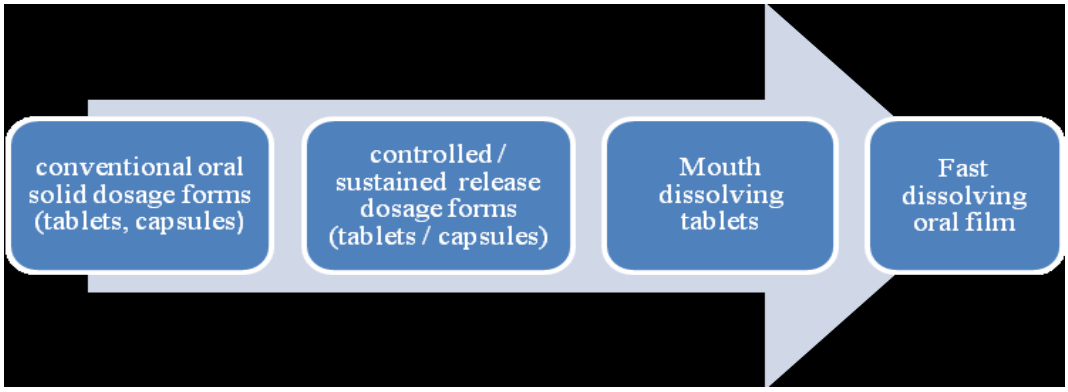


Figure 1: Flow Chart for the Development of Fast Dissolving Oral Film.

Requirement of drug candidate into film formulation: A large number of drugs can be formulated into mouth dissolving films. The main requirement of drug to be used in oral filmis its lipophilic nature. Lipophilic drug is highly permeable which is quickly absorbed in the oral mucosa. So, BCS class I (high solubility, high permeability) or BCS class II (low solubility, high permeability) drugs can be used in oral film due to their high permeable nature. Following is some of drug categories to be used for treatment of paediatrics and geriatrics populations in oral film formulation.

Paediatrics (antitussives, expectorants, antiemetic & anti-asthmatic): Paediatrics populations are very delicate as compared to younger and geriatrics population. Dosage form administered to paediatrics should be taste masked. Because, they are fond of sweet taste and refuse to take bitter or obnoxious drug in. In case of oral film, chocking problem does not appear which may appear in tablet dosage form. Because, film is chewed in oral cavity instead of swallowing and paediatrics like to take chewing gums and chocolates. So, film dosage form is the best for paediatrics.

Geriatrics (antiepileptic, expectorants, antiparkinsonism therapy, antimigraine) Geriatrics populations are generally suffered from many disorders like epilepsy, cough, Parkinsonism and migraine. Tablet and capsule are difficult to swallow for them in case of dysphasic conditions. So, oral film is the best alternative dosage form for geriatrics in thesedisorders.

Table 1: List of drugs used in formulation of oral film.

Sr. No.	Category of drugs	Examples
1	Anti-Emetics	Ondansetron, granisetron, palonosetron,dronabinol, aprepitant, ramosetron, metopimazine, nabilone, tropisetron, metoclopramide, prochlorperazine, trimethobenzamide, dimenhydrinate, prochlorperazine and dolasetron.
2	Selective serotonin reuptake inhibitors	Fluoxetine, sertraline, paroxetine, fluvoxamine, citalopram and alaproclate
3	5HT3 antagonists	Alosetron, ondansetron, granisetron, palonosetron, ramosetron and tropisetron.
4	Anti-migraines	Almotriptan, dihydroergotamine mesylate, eletriptan, rovatriptan, naratriptan, rizatriptan,sumatriptan and zolmitriptan.
5	Anti-epileptics	Carbamazepine, clonazepam, diazepam, divalproex sodium, fosphenyloin, gabapentin, lamotrigine, levetiracetam, oxcarbazepine, phenyloin, pregabalin, primidone, tiagabine,topiramate, valproate sodium, vigabatrin and zonisamide.
6	Dopamine D1 and D2	Amisulpride, bromperidol, cabergoline, domperidone, fenoldopam,

	antagonists	haloperidol, metoclopramide, metopimazine, pergolide mesylate, prochlorperazine, quetiapine, ropinirole hydrochloride, sulpiride, tiapride and zotepine.
7	Statins	Atorvastatin, cerivastatin, fluvastatin, lovastatin, pitavastatin, pravastatin, rosuvastatin andsimvastatin.
8	Nootropics	Almitrine dimesylate and raubasine, cevimelinehydrochloride, codergocrine mesylate, donepezil, galantamine, ginkgo biloba extract (EGb 761), memantine, nicergoline, piracetam.

Special features of mouth dissolving films

1. Mouth dissolving films are thin elegant film.
2. Films are available in various sizes and shapes.
3. Film shows an excellent mucoadhesion. So, film is not detached from mouth cavity while administration.
4. It shows fast disintegration within 1 minute.
5. Drug is rapidly released from dosage form due to its fast disintegration and gives quickonset of action.

Criteria for fast dissolving film

Fast dissolving film should,

1. Have a pleasant mouth feel.
2. Not require water to swallow, but it should dissolve or disintegrate in the mouth in matterof seconds.
3. Be compatible with taste masking
4. Leave minimum or no residue in the mouth after oral administration.
5. Exhibit low sensitivity to environmental conditions such as temperature and humidity.
6. Allow the manufacture of the tablet using conventional processing and packagingequipment at low cost.

Classification mouth dissolving film

Mouth dissolving film is **classified in to three categories** they are as follows,

- Flash release,
- Mucoadhesive melt-away wafer
- Mucoadhesive sustained-release wafers

Advantages of mouth dissolving film

1. Water is not needed for administration of oral film. Film uses saliva in oral cavity fordisintegration and dissolution.
2. Risk of chocking never appears after administration of film.
3. Dosage form improves patient compliance.
4. It shows rapid disintegrating and dissolution in oral cavity.
5. Flexible and portable nature provides ease in transportation, handling and storage.
6. Film avoids first pass metabolism due to pre-gastric absorption.
7. It reduces side effects associated with drug.
8. Film dosage form is generally useful for patient suffering from diseases like motion sickness, repeated emesis and mental disorder
9. It is appropriate to all age group
10. Appropriate for patients who are ill or uncooperative
11. Films remain stable for longer time as it is a solid dosage form until its administration The drug absorbed directly from film formulation into the blood, so it avoids undergoing first-pass hepatic metabolism which seen in conventional dosage forms
12. Rapid disintegration of film gives quick onset of action; thus, it enriches safety and efficacy profile of active pharmaceutical ingredient (API)
13. Pain-free self-administration is possible

Disadvantages of Mouth Dissolving Film

1. Drug(s) which requires to take in high doses cannot be incorporated into films.
2. Maintaining dosage uniformity is challenging task for the films.
3. Moisture sensitivity.
4. Require special packaging.
5. API's which are unstable at pH of the saliva cannot be designed in the form of film.
6. AAPI's which can cause irritation of the oral mucosa cannot be administered.

Ideal Characteristics for Mdf's

The ideal characteristics of MDFs are as follows.

1. It should be thin, flexible, and easy to handle.
2. The films should be transportable, not sticky and keep a plane form without rolling up.
3. It should be easy to administer.
4. The film should offer agreeable taste and a satisfying mouth-feel.
5. The disintegration time should be as rapid as possible.
6. Film surface should be smooth and uniform.
7. It should remain physically and chemically stable during its shelf life.
8. It should be cost effective and ease of commercial production.
9. It should have low sensitivity to environmental/atmospheric conditions such as humidityand temp.
10. Size of a unit film should not be too bulky that it will affect the patient's compliance.

Table 1: Relationship Between MDF and ODT.

MDF	ODT
Greater durable than ODT	A lesser durable as compared with MDF
Larger surface area gives better dissolutionas this is thin film suitable for drugs which need low dose	Lesser dissolution due to less surface area as this is tablet high dose can be incorporated
Patient compliance for film is more	Patient compliance is less than films

MDF: Mouth dissolving film, ODT: Orally disintegrating tablet

Table 2: General composition of MDF.

Ingredients	Concentration percentage
API (drug)	01–25
Plasticizer	00-20
Flavouring agents	02-10
Sweetening agents	03-06
Hydrophilic polymer/film former	40-50
Saliva stimulating agent	02-06
Colour	01
Surface active agent	Quality sufficient

API: Active pharmaceutical ingredient

The ideal characteristics of an API to be selected in MDF

1. Taste of API - pleasant.
2. The API dose - up to 40 mg.
3. The molecular weight of API preferably smaller.
4. API should be stable in the fluid present in mouth.
5. It API should be moderately unionized in oral cavity fluid.
6. Permeability through mucosal tissue

Hydrophilic polymer/film formers

Properties of polymer play a significant role in disintegration time of film. Several frequentlyused water-soluble polymers/film formers are hydroxypropyl methylcellulose, methylcellulose, pullulan, carboxymethyl cellulose, polyvinyl pyrrolidone, etc. An example of novel film former is polymerized rosin.

Ideal properties of hydrophilic polymers

- Polymer should be not irritant to oral mucosa, inert, and non-toxic.
- Should not delay or extend the disintegration time of film.
- Polymer should possess good mechanical properties.
- Polymer should be affordable

Plasticizer

It avoids breakability of films. It should have compatibility with other ingredients. Some excipients are such as polyethylene glycol, phthalate, citrate derivatives, and castor oil.

Sweetening agents

Artificial or natural sweetening agents can be used in MDFs. Examples of some sweeteningagents are sucrose, fructose, aspartame, sorbitol, acesulfame-K, and sucralose, etc.

Saliva stimulating agent

These are useful to enhance the saliva creation in the mouth that gives quick disintegration. The examples of used acids are such as tartaric, lactic, malic, ascorbic, and citric.

Flavouring agents

Commonly used flavours are vanilla, coffee, cocoa, chocolate, citrus, etc.

Colouring agents

Colouring agent like titanium dioxide is used in making films.

Surfactants

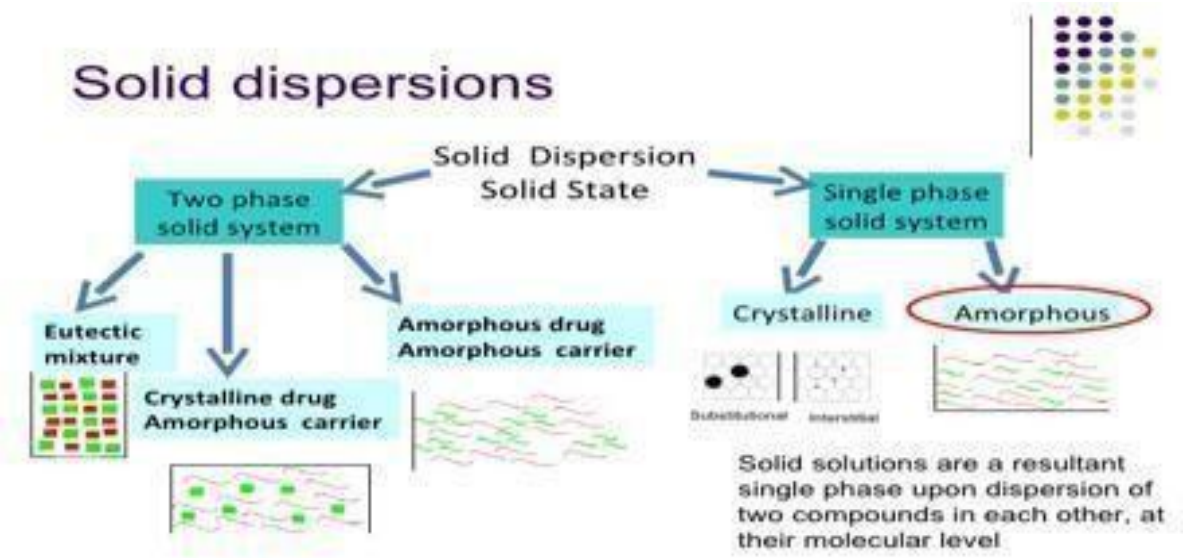
They act as wetting, dispersing, or solubilizing agents, few examples are poloxamer, sodium lauryl sulphate, and tweens.

METHODS USED IN PREPARATION OF MDF

Anyone of the following or a combination of one or more methods can be followed for makingfilm formulation.

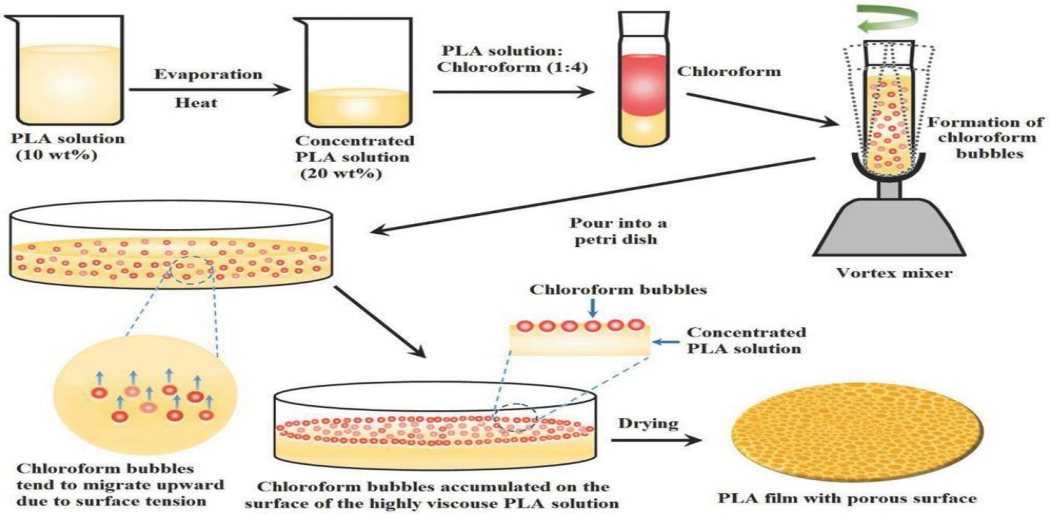
Solid dispersion extrusion

When some immiscible substances are extruded with API in this methodology is followed. Solid dispersions are prepared, and then these are designed into thin films using dies.



Solvent casting method

Films can be prepared using this method, the ingredients which are water-soluble are taken inaccurate quantity and are mixed well in beaker to make a clear solution. In other beaker containing suitable solvent add accurately weighed API and other ingredients. Then, both beakers containing formulation ingredients are mixed with stirring and finally cast into the Petriplate then allow it to dry for some period and cut the film into the appropriate size.



Semisolid casting method

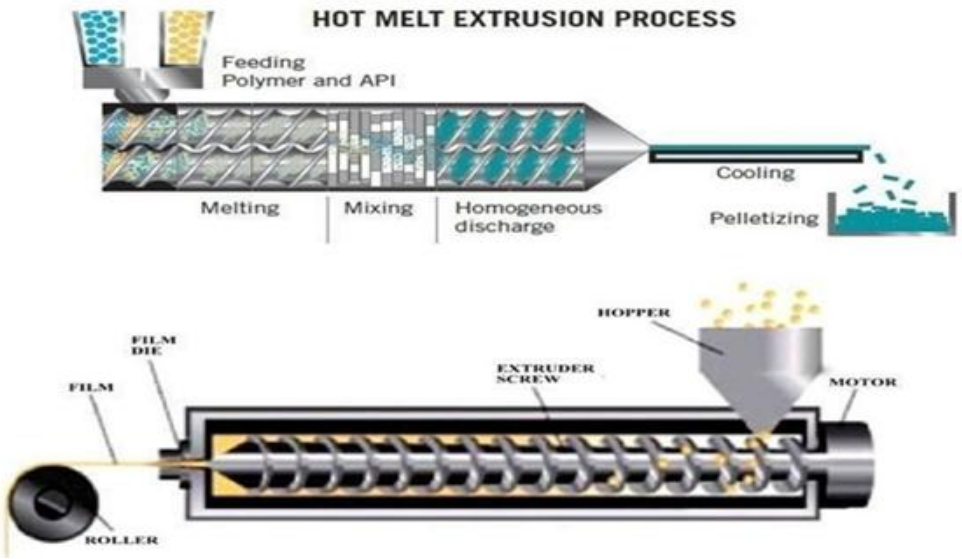
If films formulation contains some acid insoluble polymers, then this technique is appropriate. The examples of such polymers are cellulose acetate butyrate cellulose acetate phthalate. In general, film former and acid insol. polymer used in ratio of 04:01. uniformity.

Rolling method

API containing suspension or solution is taken on a carrier and allowed to move onto it. Thenkeep to drying for some period and finally cut in appropriate dimensions.

Hot melt extrusion

In this method, all substances required to make films are taken together into its solid powder form. Then, this mixture is melted using extruder which having heaters into it and the melt is shaped into film. It is then cooled, cut, and packaged. This method has some advantages over the other methods such as minimum product wastage and better content.



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