ASIAN JOURNAL OF PHARMACEUTICAL AND CLINICAL RESEARCH

INNOVARE ACADEMIC SCIENCES
Knowledge to Innovation

Vol 11, Special issue 4, 2018

Online - 2455-3891
Print - 0974-2441

Review Article

AN OVERVIEW ON MOUTH DISSOLVING FILM

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Received: 10 October 2018, Revised and Accepted: 11 December 2018

ABSTRACT

Context: Mouth dissolving film (MDF) is an innovative approach for systemic delivery of therapeutically/ medicinally active drug substance(s).

Objective: The main objectives of Oral mouth dissolving films is to provide better bioavailability of drug, to have improved permeability, quick onset of action as well as improve patient compliance

Method: Preparation of films is similar to that of transdermal patch. Film when placed in mouth it get dissolve rapidly due to salivary fluid then it releases medicament(s), It will get absorbed within blood to show therapeutic action.

Results: This overview provides information about formulation, technologies used in making mouth dissolving film formulations and evaluation tests carried out for the same.

Conclusion: Mouth dissolving film formulations are innovative dosage form to improve the drug delivery, onset of action as well as improve patient compliance

Keywords: Mouth dissolving film, Permeability, Bioavailability, Salivary fluid.

 DOI: http://dx.doi.org/10.22159/ajpcr.2018.v11s4.31712

INTRODUCTION

The mouth dissolving film (MDF) can be used for delivering a drug systemically to achieve the therapeutic or pharmacological effect. MDF formulations have improved systemic bioavailability as it escapes first pass effect [1,2]. Drug(s) which is to be delivered systemically, oral mucosa is a discerning site. This may be due to existence large surface area of the film which facilitates better absorption, pain avoidance also film can easily be swallowed without aqua [3]. New developments in technology have offered alternatives for oral dosage forms [4].

Orodispersible dosage forms have further advantages in patients who suffering from dysphagia (difficulty in swallowing), geriatric, and pediatric and also patients who undertaking anticancer therapy. Some available formulations like tablet, mouth dissolving films which are when placed in mouth they releases drug instantaneously with rapid onset of action [5-7].

IDEAL CHARACTERISTICS FOR MDF'S

The ideal characteristics of MDFs are as follows [8-10]:

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

ADVANTAGES OF MDF'S

Advantages are as follows [8-11]:

- It can be taken without water
- It disintegrate/dissolve quickly in mouth
- Flexible and light in weight
- It is appropriate to all age group
- Appropriate for patients who are ill or uncooperative
- 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
- Rapid disintegration of film gives quick onset of action; thus, it enriches safety and efficacy profile of active pharmaceutical ingredient (API)
- Pain-free self-administration is possible.

DISADVANTAGES OF MDFS

Disadvantages are as follows [7-11]:

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

Relationship among MDF and orally disintegrating tablet is shown in Table 1.

COMPOSITION OF MDF

The ingredients used in the formulation of MDF with its concentration are as shown in Table 2 [12].

API (drug)

The API from various classes that can be formulated into MDFs some examples areantiemetic, neuroleptics, antihypertensive, analgesics,

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 dissolution as this is thin film	Lesser dissolution due to less surface area as this is tablet
Suitable for drugs which need low dose	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
Flavoring agents	02–10
Sweetening agents	03–06
Hydrophilic polymer/film former	40–50
Saliva stimulating agent	02–06
Color	01
Surface active agent	Quantity sufficient

API: Active pharmaceutical ingredient

anxiolytics, diuretics, antitussives, antialzheimers, and parkinsonism agents [13-16].

The ideal characteristics of an API to be selected in MDF

- Taste of API - pleasant.
- The API dose - up to 40 mg.
- The molecular weight of API preferably smaller.
- API should be stable in the fluid present in mouth.
- It API should be moderately unionized in oral cavity fluid.
- Permeability through mucosal tissue [17-21].

Hydrophilic polymer/film formers

Properties of polymer play a significant role in disintegration time of film. Several frequently used water-soluble polymers/film formers are hydroxypropylmethylcellulose, methylcellulose, pullulan, carboxymethyl cellulose, polyvinyl pyrrolidone, etc. An example of novel film former is polymerized rosin [22,23].

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 [23].

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 [24].

Sweetening agents

Artificial or natural sweetening agents can be used in MDFs. Examples of some sweetening agents are sucrose, fructose, aspartame, sorbitol, acesulfame-K, and sucralose, etc.[25].

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 [26].

Flavoring agents

Commonly used flavors are vanilla, coffee, cocoa, chocolate, citrus, etc., [27].

Coloring agents

Coloring agent like titanium dioxide is used in making films [28].

Surfactants

They act as wetting, dispersing, or solubilizing agents, few examples are poloxamer, sodium lauryl sulfate, and tweens [29].

METHODS USED IN PREPARATION OF MDF

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

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 Petri plate then allow it to dry for some period and cut the film into the appropriate size [30,31].

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 uniformity [32].

Semisolid casting method

If films formulation contains some acid insoluble polymers, then this technique is appropriate [27]. 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 [33,34].

Rolling method

API containing suspension or solution is taken on a carrier and allowed to move onto it. Then keep to drying for some period and finally cut in appropriate dimensions [35].

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 [35].

PACKING AND STORAGE OF MDF

Blister card can be used as a packaging system for films. Single/unit packaging system is required. Widely used packaging- aluminum pouch, stored in a dry place [36].

EVALUATION PARAMETERS

The film produced by anyone of the above manufacturing method, then, they are subjected to evaluation. Evaluation is very crucial step to maintain inter- and intra-batch uniformity between films. Various evaluation parameters are as follows:

1. Organoleptic evaluation - prepared films are analyzed for its properties [37].
2. Morphology study - the scanning electron microscopic at fixed magnification is used to check morphology of prepared film [38].
3. Thickness - the film thickness is measured by micrometer or screw gauge [39,40].
4. Weight variation test - the average weights are determined by weighing each film, and then, the average weight of the films is subtracted from the individual film weight [41].
5. Texture and physical appearance - texture is checked by simple touch and appearance to be determined simply with visual infection of films [42].
6. Folding endurance - the film again and again folded at same point until get breaks. F. endurance value is considered as number of times

it is folded without breaking [42].

7. Tensile strength (TS) - it is calculated by Kumar *et al.* [43].

TS=Load applied at failure×100/film thickness×width of film.

8. Drug content uniformity - the assay method described in pharmacopeia is followed. It is determined by measuring the drug content in the individual film [43].
9. Surface pH - the prepared formulation is taken in a glass plate for 30 s containing water. The pH was noted after bringing the electrode of the pH meter in contact with the surface of the formulation and allowing equilibration for 1 min. The average of three determinations for each formulation was done [44].
10. Moisture content - The amount of moisture present in the film affects the brittleness and friability of films. The amount of moisture present in the film can be determined using Karl Fischer titration method, or by weighing method, a specific size of pre-weighed film is heated to 100–120°C until it attains constant weight and the difference in weight gives the amount of moisture present in the film. Moisture content can be calculated by following formula: % Moisture content = [(Initial weight-Final weight)×100/initial weight] [44].
11. Disintegration time - disintegration time of MDFs carried out using U.S.P. disintegration apparatus. The disintegration time should be about 30 s or less for mouth dissolving strips. Disintegration time will vary depending on the formulation ingredients but typically the disintegration range from 5 to 30 s. Although there is no official guidance available for mouth disintegrating films [45].
12. *In vitro* drug release - it is carried out by USP XXIII Type II apparatus in phosphate buffer pH 6.8 in 500 ml media and 0.1N HCl 500 ml media at the temperature is 37±0.5°C, and the rotation speed should be 50 rpm. The samples are withdrawn at various time intervals and should analyze spectrophotometrically [45].
13. Percentage elongation - it is percentage ratio of the rise in length to the original length [46].
14. Young's modulus (YM) - [46].

YM = (Force at corresponding strain/cross section area)×1/(corresponding strain)

15. Stability studies - it is to be conducted as per the International Conference on Harmonization guidelines [46].

CONCLUSIONS

The MDF formulations are one of the innovative approaches in the pharmacy field in future it may become one of the promising dosage forms for treatment of disease or disorders. These novel formulations have improved and better patient compliance as well as acceptance, with enhanced safety and effectiveness than conventional formulations. MDF is having numerous advantages and leading to improved therapeutic response. At present, these formulations are available only for the management of some diseases so reflecting their importance likely other diseases can be managed by making film formulations using suitable API.

ACKNOWLEDGMENT

The authors are gratified to Vels Institute of Sciences, Technology, and Advanced Studies, Chennai, and HSBPVT's Parikrama Group of Institutions, Kashti, for providing required facilities for doing this review work. We are thankful to Prof. Amol Khedkar, Principal, PDIPS Kashti for providing a necessary facility for work. We are grateful to Dr. Pratibhatai Babanrao Pachpute Madam, President of HSBPVT's Parikrama Group of Institutions, Kashti, for constant encouragement and valuable support received from her.

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