FORMULATION AND EVALUATION OF FAST MOUTH DISSOLVING FILM OF METOPRLOL SUCCINATE

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ABSTRACT

Mouth dissolving dosage forms are gaining popularity in recent time because of good patient compatibility, fast disintegration time, flexibility in transportation etc. In this research work Metoprolol Succinate is used to treat chronic hepatitis B. Metoprolol Succinate is an antiretroviral drug. Metoprolol Succinate is selected as model drug for the preparation of Mouth dissolving film (MDF). MDF was prepared by solvent casting method using HPMC E15 as film former and Glycerol & PEG-400 as plasticizers. MDF were evaluated for physical characteristics such as tensile strength, percentage elongation, drug content uniformity, surface pH, folding endurance, uniformity weight, and thickness and gave satisfactory result. The formulations were subjected to disintegration time, in vitro drug release test and stability study. The FTIR studies revealed that there was no physicochemical interaction between excipients and drug. The FTIR studies revealed that there was no physicochemical interaction between excipients and drug. A marked % drug release was exhibited by MDF of Metoprolol Succinate containing HPMC E15 as a polymer at 30 sec.

KEYWORDS: Metoprolol Succinate, Mouth-dissolving film, HPMC E15, PEG-400, Solvent Casting Method.

I. INTRODUCTION

Oral route is the most preferred route for the delivery of the drugs till date as it bears various advantages over the other route of drug administration, the particular class of patients which
includes geriatric, pediatric and dysphasic patients associated with many medical conditions as they have difficulty in swallowing or chewing solid dosage forms. Many pediatric and geriatric patients are unwilling to take solid preparations due to fear of choking. That’s why the MDF are very essential to use.

Mouth dissolving films (MDF)

Definition of FDF: Fast dissolving films are most advance form of solid dosage form due to its 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 paracellular 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 passage across the oral mucosa follows a first order simple diffusion process. Although passive diffusion is the main mechanism of drug absorption.

Criteria for fast dissolving film

Fast dissolving film should,

- Have a pleasant mouth feel.
- Not require water to swallow, but it should dissolve or disintegrate in the mouth in matter of seconds.
- Be compatible with taste masking
- Leave minimum or no residue in the mouth after oral administration.
- Exhibit low sensitivity to environmental conditions such as temperature and humidity.
- Allow the manufacture of the tablet using conventional processing and packaging equipment at low cost.
Advantages of mouth dissolving film

- Ease of administration to pediatric, geriatric, bedridden patients and psychiatric patients who refuse to swallow tablets
- Availability of larger surface area that leads to rapid disintegrating and dissolution in the oral cavity.
- Elegant film convenient dosing various sizes and shapes no water needed
- Unobstructed no risk of choking
- Mucoadhesion taste masking
- Fast disintegration enhanced stability
- Quick dissolving improved patient compliance
- Rapid release life cycle management

Classification mouth dissolving film

Mouth dissolving film is classified into three categories they are as follows,

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

II. LITURATURE REVIEW

Mital S. Panchal et al., (2012): prepared mouth dissolving films of Ropinirole Hydrochloride with the purpose of developing a dosage form for a very quick onset of action, which is very convenient for administration, without the problem of swallowing and using water. The films of Ropinirole Hydrochloride were prepared by using polymers such as pullulan and PEG 400 as plasticizer, by a solvent casting method.

Kaushal Patel et al., (2012): development of Telmisartan (TLM) is an angiotensin II receptor antagonist used in the treatment of hypertension. TLM mouth dissolving tablets were prepared using skimmed milk powder (SMP) and poloxamer-188 (PXM-188) as carriers and crosspovidone as super disintegrant.

Vijay kumar Ghorwade et al., (2011): prepared the montelukast sodium fast dissolving films were prepared by solvent casting method using HPMC as film base with different concentrations of superdisintegrants like microcrystalline cellulose and crospovidone using PEG 400 as plasticizer.
III. EXPERIMENTAL

**Methods for mouth dissolving film formulation**: One or combination of the following process can be used for manufacture the mouth dissolving film.

**Solvent casting method**: In solvent casting, method water-soluble polymers are dissolved in water and the drug along with other excipients is dissolved in suitable solvent then both the solutions are mixed and stirred and finally casted in to the Petri plate and dried in hot air oven for specific temperature.

**Preparation of dilutions for calibration curve**- Appropriate aliquots of the stock solutions of the drug was transferred to 10 ml volumetric flasks. The aliquots stock solutions were diluted serially with sufficient amount of Phosphate buffer (pH 6.8) to obtain the concentration range of 0-10 μg/ml.

**IV. RESULT AND DISCUSSION**

**Determination of λ_{max}** - The absorption maxima were determined by scanning 5 μg/ml solutions against the blank on UV-visible spectrophotometer between 200-400 nm ranges.
4.1 Infrared spectrum of API

![Infrared spectrum of Metoprolol Succinate](image1.png)

Figure 4.1: Observed IR spectra of Metoprolol Succinate.

4.2 Infrared spectra of HPMC E15.

![Infrared spectra of HPMC E15](image2.png)

Figure 4.2: Observed IR spectra of HPMC E15.
4.3 Standard calibration curve

Standard calibration curve of Metoprolol Succinate.

![Calibration Curve of Inosine Standard Solutions](image)

\[ y = 10793x + 0.0345 \]
\[ R^2 = 0.99578 \]

**Figure 4.3:** Standard calibration curve of Metoprolol Succinate in water.

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Concentration (µg/ml)</th>
<th>Absorbance</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>2</td>
<td>20</td>
<td>0.123</td>
</tr>
<tr>
<td>3</td>
<td>40</td>
<td>0.233</td>
</tr>
<tr>
<td>4</td>
<td>60</td>
<td>0.367</td>
</tr>
<tr>
<td>5</td>
<td>80</td>
<td>0.467</td>
</tr>
<tr>
<td>6</td>
<td>100</td>
<td>0.615</td>
</tr>
</tbody>
</table>

4.4 Standard calibration curve of Metoprolol Succinate in phosphate buffer (pH 6.8)

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Concentration (µg/ml)</th>
<th>Absorbance</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>2</td>
<td>20</td>
<td>0.113</td>
</tr>
<tr>
<td>3</td>
<td>40</td>
<td>0.202</td>
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<tr>
<td>4</td>
<td>60</td>
<td>0.298</td>
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<tr>
<td>5</td>
<td>80</td>
<td>0.389</td>
</tr>
<tr>
<td>6</td>
<td>100</td>
<td>0.489</td>
</tr>
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</table>
Figure 4.4: Standard calibration curve of Metoprolol Succinate in Phosphate Buffer (pH 6.8)

Table 2 Preparation of drug free placebo batches

<table>
<thead>
<tr>
<th>Components (mg)</th>
<th>M11</th>
<th>M12</th>
<th>M13</th>
<th>M14</th>
<th>M15</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metoprolol Succinate</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>HPMC E15</td>
<td>150</td>
<td>200</td>
<td>250</td>
<td>300</td>
<td>350</td>
</tr>
<tr>
<td>Glycerol</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>Sorbitol</td>
<td>*</td>
<td>*</td>
<td>20</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>Sucrose</td>
<td>*</td>
<td>20</td>
<td>*</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>Mannitol</td>
<td>20</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>Citric acid</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>20</td>
<td>10</td>
</tr>
<tr>
<td>SLS</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Flavor</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Colour</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>Water (ml)</td>
<td>20</td>
<td>20</td>
<td>20</td>
<td>20</td>
<td>20</td>
</tr>
</tbody>
</table>

Optimization of drug loaded Fast mouth dissolving films. :-

- Formulation M15 showed good physical properties, acceptable taste and good mechanical properties.
- Formulation M14 was found to be acidic taste in nature because of higher amount of anhydrous citric acid and showed poor mechanical properties as compared to M15.
- M11 and M12 were not acceptable because of poor taste masking properties of mannitol and sucrose.
- Hence for formulation M15 was optimized.
Table: Final formulation of FDF containing Metoprolol Succinate.

<table>
<thead>
<tr>
<th>Ingredients</th>
<th>Batch (M15)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metoprolol Succinate</td>
<td>100 mg</td>
</tr>
<tr>
<td>Glycerol</td>
<td>100 mg</td>
</tr>
<tr>
<td>HPMC</td>
<td>31 mg</td>
</tr>
<tr>
<td>Anhydrous citric acid</td>
<td>10 mg</td>
</tr>
<tr>
<td>SLS</td>
<td>1 mg</td>
</tr>
<tr>
<td>Flavor</td>
<td>5 mg</td>
</tr>
<tr>
<td>Water</td>
<td>20 ml</td>
</tr>
</tbody>
</table>

Figure 4.5: Picture of fast mouth dissolving film (batch M15),

V. CONCLUSION

The oral mucosa being highly vascularized, drug can be absorbed directly and can enter the systemic circulation without undergoing first-pass metabolism. This advantage can be exploited in preparing products with improved oral bioavailability of molecules that undergo first-pass metabolism. Thus, oral mucosa is attractive site for drug delivery. The objective of this research work to explore oral drug delivery route by formulating Fast mouth dissolving film for improved bioavailability and faster onset of action of METOPROLOL SUCCINATE in chronic hepatitis B. in present study, formulating Fast mouth dissolving film of METOPROLOL SUCCINATE were successfully developed which offers a suitable and practical approach in serving desired objective of fast disintegration and dissolution characteristics with increased bioavailability by the administration through oral route. Films were formulated using HPMC E15 and PVP K30 as film forming polymer, glycerol and PEG400 as plasticizer. Optimization of polymer and plasticizer was done on the preliminary trials conducted. Preformulation study of drug and excipients was conducted using FTIR spectrophotometer. No drug-excipients interaction was observed. Optimized formulation batch M15 containing 350mg HPMC E15 polymer, glycerol as plasticizer, sucrose as
sweetening agent and other excipients casted on glass petriplate using water as solvent. The batch M15 was evaluated based on parameters like tensile strength, in vitro disintegration time and in vitro dissolution in acceptable range.

VI. REFERENCE


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