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Formulation Development and Evaluation of Fast Dissolving Oral Film of Midodrine Hydrochloride

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ABSTRACT

Oral fast dissolving midodrine hydrochloride films prepared by solvent casting method, PEG 400 was the selected plasticizers, incorporating superdisintegrants such as croscarmellose sodium (CCS) and sodium starch glycolate (SSG) to achieve the goal. Drug content, weight variability, film thickness, disintegration time, endurance, percentage of moisture content, and *in vitro* dissolution tests were analyzed for the prepared films. In all formulations, the tensile strength value was found from 0.965±0.045 and 1.256±0.032 and the folding capacity was over 100. The assay values ranged from 97.98±0.25 to 99.89±0.36 percent for all formulations. The disintegration time was ranging between 55±9 to 120±6 sec, the minimum time for disintegration was found in formulation F5 (55±9). The prepared F5 formulation shows greater release of the drug (99.25±0.41 percent) within 15 min relative to other formulations. As the drug having low solubility, fast disintegration may leads to more drug availability for dissolution, resulting in faster absorption in systemic circulation increased systemic availability of drug leads to quick onset of action which is prerequisite for hypertension.

Keywords: Midodrine hydrochloride, Fast dissolving films, Solvent casting method, Superdisintegrants.

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INTRODUCTION

The rapidly dissolving dosage forms are referred by various names by researchers like quick disintegrating, orally disintegrating, mouth dissolve or melt in mouth dosage forms[1,2,3]. Rapidly dissolving or quick dissolving dosage forms have acquired great importance in the pharmaceutical industry due to their unique properties and advantages[1,4]. These dosage forms possess certain specific advantages like no need of water for disintegration, accurate dosing, rapid onset of action, ease of transportability, ease of handling, pleasant taste and improved patient compliance. United States Food and Drug Administration (USFDA) defined the fast dissolving oral thin films as a thin, flexible, non-friable polymeric film strip containing one or more dispersed/dissolved active pharmaceutical ingredients, which is intended to be placed on the tongue for rapid *in vitro* disintegration or dissolution in the saliva prior to swallowing for delivery into the gastrointestinal tract [5]. They undergo disintegration in the salivary fluids of the oral cavity within a minute, where they release the active pharmaceutical ingredient. The major amount of the active pharmaceutical ingredient is swallowed orally with the saliva where subsequent absorption takes place in the gastrointestinal tract[3,4]. Midodrine Hydrochloride is an Antihypotensive/Vasopressor agent. Its chemical name is 2-amino N-[2-(2,5-dimethoxyphenyl)-2-hydroxy-ethyl]-acetamide. Melting Point is 200 to 203°C.pKa value is 7.8 (0.3% aqueous solution). pH is 3.5 to 5.5(5% aqueous solution). It is also used in the treatment of Cirrhosis and Hepato renal syndrome. Marketed brands are Bramox, Gutron, Amatine[6]. The developed formulation was simple, easy to prepare and economical with great applicability and also giving faster *in vitro* drug dissolution rate as compared to the commercially available immediate release tablets.

MATERIALS AND METHODS

Materials

Midodrine Hydrochloride was obtained as a gift sample from pharmaceutical company. HPMC was procured from Qualikems fine chem. Pvt Ltd Vadodhara. PEG400, sodium starch glycolate, croscarmellose sodium was obtained from S.D fine chemicals limited, Mumbai. Citric acid, ethanol was

obtained from Loba Chemical Pvt Ltd (Mumbai, India). Hydrochloric acid, KH_2PO_4, NaOH was obtained from S. D. Fine Chem. Ltd., Mumbai. All other chemical were purchased from Hi Media, Mumbai. Double distilled water was prepared freshly and used whenever required. All the chemicals used in this work were of analytical grade.

Formulation development of oral film

Solvent casting technique

Drug Midodrine hydrochloride was manufactured using solvent casting method, containing fast dissolving films. The optimized quantity of HPMC was dissolved in 5ml of water and continuously stirring for 1 hour, the optimized quantity of Plasticizer and drug was dissolved in 95 percent ethanol and then applied to the polymer solution, the optimized quantity of drug was dissolved in 2ml of water and placed on sonication for proper dispersion. Polymeric solution was stirred for 30 min using magnetic stirrer and was kept in undisturbed condition till the entrapped air bubbles were removed. The aqueous solution was casted in a glass moulds having 2.5 x 2.5 cm x 12 films area and was dried at controlled room temperature (25°-30°C, 45 %RH) as well as at increased temperature (microwave oven). The film took approximately 48 hr to dry at controlled room temperature. The dried film was carefully removed from the glass plates and was cut into size required for testing. The films were stored in air tight plastic bags till further use. The compositions of the formulations were shown in table 1 and prepared formulation shown in figure 1&2.

Table 1: Selection and Optimization of Film Forming Agents

Name of ingredients (mg) (mg for 12 strips)	F1	F2	F3	F4	F5	F6
API	60	60	60	60	60	60
HPMC	250	300	350	400	450	500
Glycerin	-	-	-	-	-	-
PEG-400	100	100	100	100	100	100
SSG	100	200	300	-	-	-
CCS	-	-	-	100	200	300
Aspartame	5	5	5	5	5	5
Citric acid	50	50	50	50	50	50
DM water qs to (ml)	-	-	-	-	-	-

Dose calculations

- Width of the plate = 5cm
- Length of the plate = 12cm
- No. of 2.5 x 2.5 cm^2 films present whole plate = 12
- Each film contains 20mg of drug.
- 12 no. of films contains mg of drug? = 5×12 = 60mg
- The amount of drug added in each plate was approximately equal to 60mg.

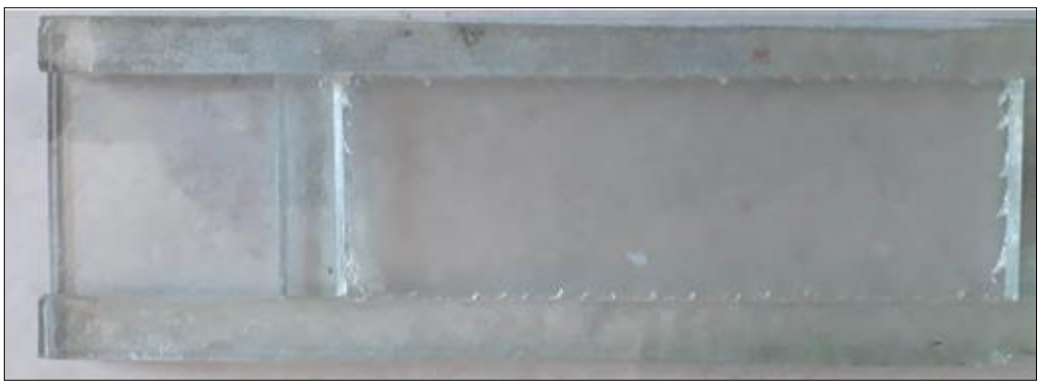

Figure 1: Preperation of fast dissolving oral films

Figure 2: Prepared fast dissolving oral film

Evaluation

The formulations were evaluated by the following tests[7-10].

Thickness

Randomly 10 films were selected and thickness was measured using vernier calliper at three different places.

Weight variation

For each formulation, three randomly selected patches were used. For weight variation test, 10 films from each batch were weighed individually by digital electronic balance and the average weight was calculated.

Folding endurance

This was determined by repeatedly folding one film at the same place until it broke. The number of times the film could be folded at the same place without breaking cracking gave the value of folding endurance.

Percentage of moisture content

The films were weighed individually and kept in desiccators containing activated silica at room temperature for 24 hrs. Individual films were weighed repeatedly until they showed a constant weight. The percentage of moisture content was calculated as the difference between initial and final weight with respect to final weight.

Drug content analysis

The patches (n = 3) of specified area were taken into a 10 ml volumetric flask and dissolved in methanol and volume was made up with 10 ml methanol. Subsequent dilutions were made and analyzed by UV spectrophotometer at 272nm.

Disintegrating time

The most important criteria of present work are to that dosage form should be dissolved within few seconds. The incorporation of super disintegrating agent to minimizes the disintegrating time. Three super disintegrating agent were selected for this work. The film of (2.5*2.5cm^2) size (unit dose) was placed on a petridish containing 10 ml of distilled water. The time required for the film to break was noted as cursive *in vitro* disintegration time Figure 3.

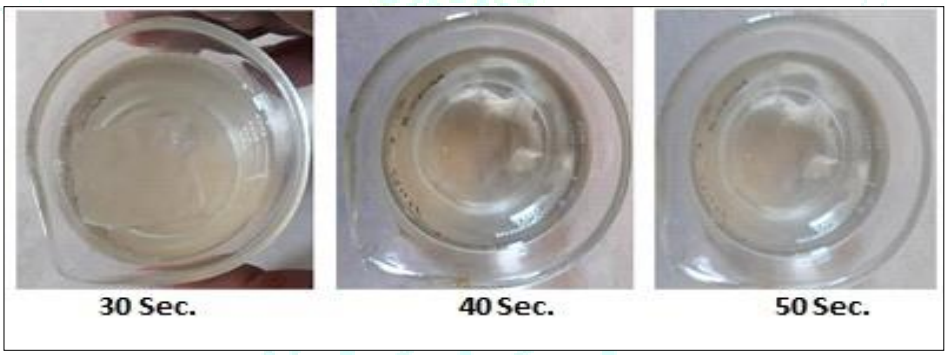

Figure 3: Determination of disintegrating time

In vitro dissolution study

The *in vitro* dissolution test was performed using the USPXXX dissolution apparatus II (Paddle with sinker). The dissolution studies were carried out at 37±0.5°C; with stirring speed of 50 rpm in 900 ml phosphate buffer (pH 6.8). Film size required for dose delivery (2.5×2.5 cm^2) was used. Five ml aliquot of dissolution media was collected at time intervals of 1, 2, 5, 10 and 15 minutes and replaced with equal volumes of phosphate buffer (pH 6.8). The collected samples were filtered through 0.45 µm membrane filter and the concentration of the dissolved Midodrine hydrochloride was determined using UV-Visible spectrophotometer at 272 nm. The results were presented as an average of three such concentrations.

RESULTS AND DISCUSSION

The general appearance, assay, weight variation and thickness of all the films were within acceptable limits table 2. The results for tensile strength, folding endurance, disintegrating time and % of moisture were shown in table 3. Tensile strength value of found between 0.965±0.045 to 1.256±0.032, and folding endurance was more than 100 in all formulations. The assay values of all the formulations were ranging from 97.98±0.25 to 99.89±0.36 %. The disintegration time was ranging between 55±9 to 120±6 sec, The Minimum disintegration time was found in formulation F5 (55±9). The optimized formulation F5 shows better drug release (99.25±0.41%) compared to other formulation within 15 min (Table 4). When the regression coefficient values of were compared, it was observed that 'r' values of first order was maximum i.e. 0.963 hence indicating drug release from formulations was found to follow zero order first order kinetics. The kinetic data of optimized formulation F5 was given in table 5. It was fallow first order drug release kinetics.

Table 2: Result of thickness, weight variation and % assay

Formulation code	Thickness in µm*	Weight mg*	% Assay*
F1	85±5	132±4	98.85±0.65
F2	89±6	135±6	97.78±0.74
F3	94±8	146±8	96.65±0.52
F4	98±9	155±6	98.12±0.63
F5	102±12	163±8	99.56±0.14
F6	105±10	173±7	96.56±0.23

*Average of three determinations (n=3)

Table 3: Result of disintegrating time, tensile strength &% of moisture content

Formulation code	Disintegrating* time (Sec.)	Tensile strength* in kg/cm²	Percentage of Moisture Content*
F1	120±6	0.965±0.045	1.25±0.36
F2	110±8	0.989±0.068	1.69±0.50
F3	89±7	0.988±0.095	1.78±0.25
F4	86±5	1.112±0.075	1.85±0.32
F5	55±9	1.256±0.032	0.98±0.14
F6	82±8	1.225±0.074	1.12±0.25

*Average of three determination (n=3)

Table 4: Results of *In-Vitro* release study of optimized formulation F5

S. No.	Time (Min.)	% CDR
1.	1	33.45±0.89
2.	2	49.65±0.65
3.	5	65.62±0.25
4.	10	88.45±0.36
5.	15	99.25±0.41

Table 5: Kinetics data of optimized formulation F5

Formulation	Regration Coefficient	Zero order	First order
F5	r^2	0.963	0.943

CONCLUSION

This is fast disintegrating oral film hence on the laboratory scale solvent casting technique was adopted for formulation of films. Different formulations (F1-F6) were prepared using varying amount of SSG and CCS. The prepared formulations were evaluated for thickness, weight uniformity, folding endurance, percentage of moisture content, drug content analysis, disintegrating time and *in vitro* dissolution study. Finally, it is concluded that the drug release from the fast dissolving film was increased by using the increased concentration of Superdisintegrant, thus assisting in faster disintegration in the buccal cavity. As the drug having low solubility, fast disintegration may leads to more drug availability for dissolution, resulting in faster absorption in systemic circulation increased systemic availability of drug may leads to quick onset of action which is prerequisite for hypertension.

REFERENCES

1. Liang AC, Chen LH. Fast-dissolving intraoral drug delivery systems. Exp Opin Ther Patents. 2001; 11:981–6.
2. Klancke J. Dissolution testing of orally disintegrating tablets. DissolutTechnol. 2003; 10:6–8.
3. Bhatt P, Patel D, Patel A, Patel A, Nagarsheth A. Oral Controlled Release Systems: Current Strategies and Challenges. In: Misra A, Shahiwala A, editors. Novel Drug Delivery Technologies: Innovative Strategies for Drug Re-positioning. Singapore: Springer Singapore; 2019. p. 73-120.
4. Borsadia S, O'Halloran D, Osborne JL. Quick dissolving films-A novel approach to drug delivery. Drug DelivTechnol. 2003; 3:63-6.
5. http:// www.access data. fda. gov/drugsatfda_docs/ nda/2015/022524orig1s000chemr.pdf.
6. Ananda K, Kavitha MP, Krishnakumar K. A review on the determination of Midodrine hydrochloride in bulk and marketed formulations by using different analytical techniques.2020; 7(14):260-266.
7. Yellanki SK, Jagtap S, Masareddy R. Dissofilm: a novel approach for delivery of phenobarbital; design and characterization. Journal of Young Pharmacists. 2011; 3(3):181–188.
8. Joshi P, Patel H, Patel V, Panchal R. Formulation development and evaluation of mouth dissolving film of domperidone. Journal of Pharmacy and Bioallied Sciences.2012; 4(5):108-109.
9. Janben EM, Schliephacke R, Breitenbach A, Breitkreutz J. Drug-printing by flexographic printing technology-a new manufacturing process for orodispersible films. International Journal of Pharmaceutics. 2013; 441(1-2):818–825.
10. Nafee NA, Boraie NA, Ismail FA, Mortada LM. Design and characterization of mucoadhesive buccal patches containing cetylpyridinium chloride. Acta Pharmaceutica. 2003; 53(3):199–212.