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Formulation and Evaluation of Mouth Dissolving Film containing Enalapril

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Abstract

The prime objective of the work was to formulate mouth dissolving films containing Enalapril to achieve its maximum concentration with a very short time and also to ease the administration of the medicament through oral route. All the formulations exhibited instant drug release, quick disintegration and optimum mechanical strength. The formulations also did not exhibit either much loss or uptake for moisture as observed from the studies. The amount of drug loaded in the films initially increased with increasing the polymer ratio but decreased in EMDF4 and EMDF5 suggesting that the higher swelling of the polymers was detrimental for uptake of the hydrophobic drug by the polymer matrix. Formulation EMDF3 exhibited the higher drug content (96.3±6.13). All the formulations were found to disintegrate in less than 40 seconds thereby paving the road for quick release of Enalapril from the films. The formulations EMDF 1, EMDF2 and EMDF3 were able to release 95, 94 and 96% drug respectively at the end of 10 minutes whereas EMDF4 and EMDF5 were able to release 92 and 88% respectively.

Keywords

Enalapril, mouth dissolving, release, film, solvent casting.

Introduction

One of the major problems coupled with the use of conventional oral dosage forms is the time required for the onset of action, which is usually at least half an hour in case of the conventional dosage forms and higher in the controlled and sustained release dosage forms.[1] Difficulty in swallowing (dysphagia) of medicine is a universal problem with all age groups, especially the elderly and children, owing to the physiological changes associated with these groups. Other categories of people that experience problems in using conventional oral dosage forms include the mentally ill, and patients suffering from nausea, vomiting, motion sickness and sudden episodes of allergic attack or coughing. It is estimated that about 35-50% of the population is affected by the problem of swallowing the medication.[2]

These problems led to the development of a novel type of solid oral dosage form called as mouth dissolving films (MDFs). These delivery systems either dissolve or disintegrate in the mouth rapidly, without requiring any water to aid in the swallowing of the medication.[3,4]

Upon ingestion, the saliva provides the necessary conditions to rapidly disperse/ dissolve the MDF. The saliva containing the dissolved medicament is absorbed from the mouth, pharynx and esophagus. The bioavailability of drugs is significantly increased in these case as compared to those observed from conventional dosage forms such as tablets and capsules.[5]

Enalapril is Anti-hypertensive agent used for all grades of essential and renovascular hypertension, and peripheral vascular resistance without causing an increase in heart rate.It has good solubility in aqueous media &its intravenous bioavailability is 40%. Its terminal half-life is 11-14 h.[6] For better bioavailability drug should release fast from formulation to media, hence the present study was undertaken with an objective to formulate mouth dissolving films (MDFs) of enalapril with the intention of providing quicker onset of action of the medication.

Material and Methods

Enalapril was obtained as generous gift from Intas Pharmaceuticals, Ahmedabad, Guar Gum, Sucrose, sodium starch glycolate and citric acid were procured from Oxford Lab Fine Chemicals, Mumbai.

Preformulation Studies[7]

The preformulation studies were carried out in the terms of tests of identification like physical appearance, melting point and FTIR spectroscopy. It also includes solubility profile of drug in various solvent systems, determination of partition coefficient and quantitative estimation of drug.

Calibration curve of Enalapril[8]

A UV spectrophotometric method was used in the present study for the estimation of Enalapril for the samples. Calibration curve was constructed in the concentration range 10-600 µg/mL. 100 mg drug was dissolved in 10 mL 0.1N NaOH and the volume was made up to 100 mL with the buffer solution (pH 6.8). This stock solution was used to prepare working standards 10, 20, 30, 40, 50 and 100 µg/mL concentration. The absorbance was measured for these aliquots by UV visible spectrophotometer at 226 nm and calibration curves were plotted.

Preparation of Enalapril MDFs[9,10]

Solvent casting method has been the most widely used methods to fabricate smooth films. The MDFs of Enalapril were prepared using the solvent casting method. Aqueous solution of the polymer was prepared by dissolving guar gum in 5 mL of distilled water and kept aside to remove any trapped air bubbles. The drug was dissolved in very small quantity of suitable solvent and dissolved in the polymer solution. All the other components of the film like plasticizer, sweetener, saliva secreting agent etc were dissolved separately in distilled water. The excipient solution was mixed with continuous stirring to the polymer solution and stirred at 1000 rpm for 10 minutes. The obtained mixture was casted on petriplates as a film and dried in hot air oven at 50°C for 24h. After 24 h the films were carefully removed from the petriplates and observed for any imperfections. The films were wrapped in butter paper or aluminum foils and stored in desiccator until further use. The composition of the MDFs are presented in Table 1.

Table 1 Composition of MDF of Enalapril

S.No	Formulation	EMD F1	EMD F2	EMD F3	EMD F4	EMD F5
1	Enalapril (mg)	19.635	19.635	19.635	19.635	19.635
2	Guar gum (mg)	100	150	200	250	300
3	Poly ethylene glycol (mg)	0.4	0.4	0.4	0.4	0.4
4	Sodium starch glycolate (mg)	10	10	10	10	10
5	Citric acid (mg)	5	5	5	5	5
6	Sucrose (mg)	5	5	5	5	5
7	Vanillin (mg)	5	5	5	5	5
8	Water (mL)	8	8	8	8	8

Evaluation of MDFs[11,12]

Weight variation

The films were subjected to mass variation by individually weighing randomly selected films. These determinations were carried out for each formulation.

Thickness

The thickness of each film was measured by using Vernier calliper at different positions of the film and the average thickness was calculated.

Folding endurance

Folding endurance was determined by repeatedly folding one patch from the same place till it broke. The number of times the film could be folded from the same place without breaking/ cracking gave the value of folding endurance.

Drug content test

The films were dissolved in 100mL of phosphate buffer pH 6.8 enriched with 1% sodium lauryl sulfate. After complete dissolution of the film, the amount of Enalapril was estimated using UV spectrophotometry by measuring the absorbance at 226 nm.

Moisture Content

Films of 4 cm^2 area were cut out and weighed accurately and stored in desiccators containing fused anhydrous calcium chloride. After 24 h the films were removed and weighed again. The percent moisture content of the film was calculated by the following formula

% Moisture content = (Initial weight – Final weight)/Initial weight x 100

Moisture uptake

The pre-weighed films were exposed to relative humidity of 84% at 28°C for three days using a saturated solution of sodium chloride. After 3 days the films were removed from the desiccators and weighed. The moisture absorbed by the films was calculated using the following formula

% Moisture uptake = (Final weight – Initial weight)/Initial weight x 100

In-Vitro Disintegration time

In order to determine the disintegration time, the films were placed on glass petriplates containing 10 mL of distilled water. The time required for breaking of the film was recorded as the *in vitro* disintegration time of the film.

In-Vitro Dissolution Study

A film of 4 cm^2 was placed in a glass petriplate and 25 mL of dissolution medium (phosphate buffer pH 6.8) was added to it. The solution was stirred at 100 rpm throughout the study. Aliquouts of 2.5 mL were withdrawn and the medium was replenished with equal volume of fresh buffer at regular intervals of 1, 2, 3, 4, 5 and 10 minutes. The collected samples were filtered and the concentration of Enalapril in each sample was estimated by measuring its absorbance at 226 nm using UV spectrophotometer.

Results and Discussion

Preformulation Studies

Preformulation studies were carried out for Enalapril for determination of its physical and chemical properties and also to confirm the specifications of the sample. The melting point was determined using open capillary method and was found to be 141-143°C. The partition coefficient study was performed and the log P value was found to be 1.1. It was observed from the results that Beer-Lamberts law was obeyed over the analyzed concentration range of 10-60 µg/mL with regression value of 0.9998 signifying and providing statistical evidence that the calibration curve can be used for analysis of Enalapril in the formulations (Figure 1).

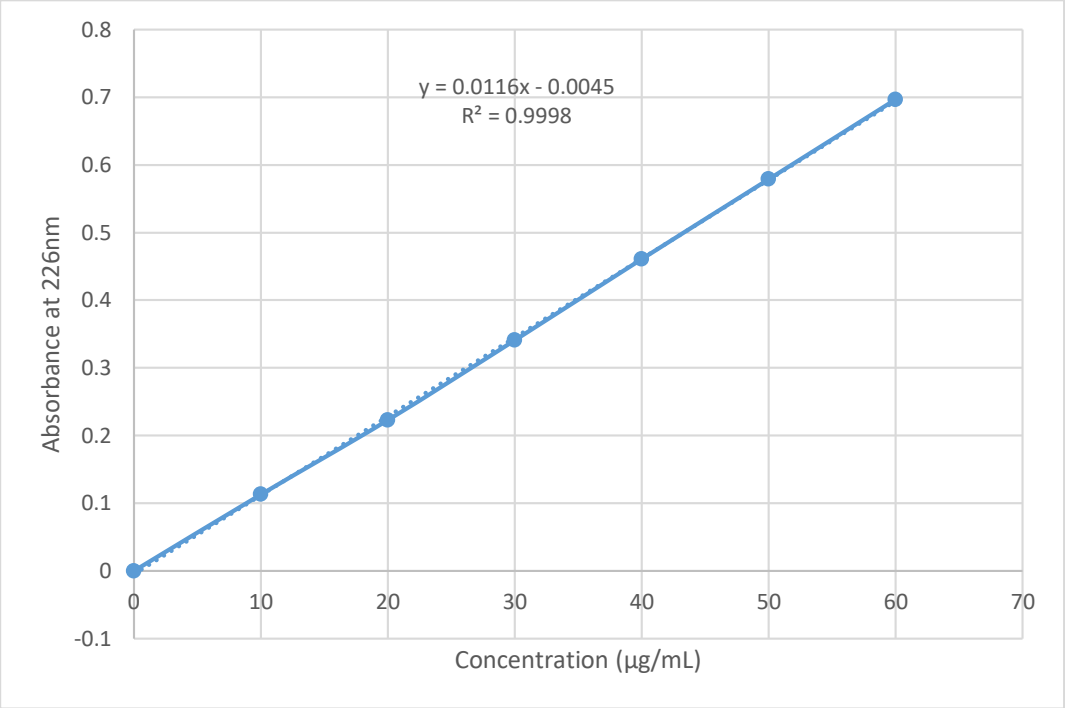

Figure 1 Standard Curve of Enalapril

Evaluation of MDFs

Physical Parameters of films

The evaluation of the different physical properties of the formulated films was performed as per the reported methodologies and the results obtained are reported in Table 2.

Table 2 Physiochemical Parameters of films

Formulation	Weight Variation (%)	Thickness (mm)	Folding Endurance	% Moisture loss	% Moisture uptake
EMDF1	1.985±0.103	0.52±0.06	8.23±1.15	6.7±1.27	3.8±1.20
EMDF2	1.783±0.278	0.55±0.02	8.54±1.51	7.2±0.88	3.2±1.35
EMDF3	1.663±0.385	0.63±0.05	12.55±1.51	5.7±1.25	4.6±0.86
EMDF4	1.746±0.130	0.68±0.03	15.22±1.14	6.3±1.74	5.8±0.94
EMDF5	1.687±0.212	0.72±0.07	11.55±1.14	6.7±1.44	5.8±0.78

Values are mean ± SD of 3 replicates

The thickness of the films was measured at five different locations to ensure the uniformity of the results. The weight variation was calculated as deviation from the average weight and is reported as the percentage weight variation obtained from 10 films.

The folding endurance and thickness were found to be related to the amount of the film forming polymer in the formulation except in EMDF5 where the folding endurance decreased contrastingly suggesting that a higher amount of polymer is unable to retain the moisture while formulating and hence exhibits a lower mechanical strength.

Drug content estimation in films

The evaluation of drug content in the prepared film formulations was performed as per the method reported by Velmurugan et al[56] and the amount of drug present in the formulations was calculated on the basis of absorbance of the sample at 226 nm in UV spectrophotometer. The results are reported in Table 3. The results show that all the formulations had drug content within the limit of 85-110% with the highest content in formulation EMDF3 (96.3 ± 6.13%). The amount of drug loaded in the films initially increased with increasing the polymer ratio but decreased in EMDF4 and EMDF5 suggesting that the higher swelling of the polymers was detrimental for uptake of the hydrophobic drug by the polymer matrix.

In vitro disintegration of MDFs

The in vitro disintegration of the films was performed using the petridish method in order to ascertain that the films will provide a rapid release of the Enalapril (Table 3). The disintegration time of all the formulations was less than 40 seconds showing that all the formulations were fast dissolving and will be able to release the drug in short span of time.

Table 3 Drug content in the MDFs

Formulation	Disintegration time (sec)	% Drug Content
EMDF1	37	87.2±5.81
EMDF2	35	91.6±6.22
EMDF3	38	96.3±6.13
EMDF4	36	88.4±5.45
EMDF5	37	90.1±6.21

***In vitro* release study**

All the formulations were found to disintegrate in less than 40 seconds thereby paving the road for quick release of Enalapril from the films. The ratio of polymer content was found to have no significant role in the disintegration time of the films. The results reveal that the formulations were able to release almost the entire amount of drug in around 10 minutes (Figure 2). The maximum amount of drug was released by EMDF3 (96%). This suggests that increasing the polymer concentration beyond an optimum value led to trapping of drug in the cross-linked matrix of the polymer.

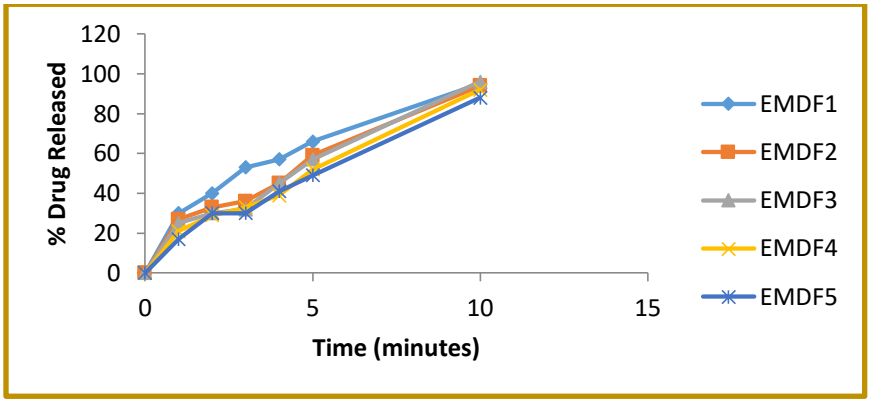

Figure 2 Release of enalapril from formulations

Conclusion

The objective of the present study was to formulate fast dissolving films of Enalapril for rapid release of the drug that would help in maintaining the blood pressure in the vessels. The study was able to justify the use of films for quickly releasing the drug using natural polymer guar gum as the matrix of the film and PEG-400 as the plasticizer. The release study of the drug from the film suggests that the film can be a good approach to improve the bioavailability of Enalapril and also improve the patient adherence to the prescribed regimen due to ease of administration of the films.

References

1. Dahiya M, Saha S, Shahiwala A. A Review on Mouth Dissolving Films. Curr Drug Del. 2009; 6: 469-476.
2. Patel AR, Prajapati DS, Raval JA. Fast dissolving films as a newer venture in fast dissolving formulations. Int J Drug Dev Res. 2010; 2(2): 232-246.
3. Gavaskar B, Kumar SV, Sharan G, Madhusudan Y. Overview on fast dissolving films. Int J Pharmacy Pharm Sci. 2010; 2(3), 29-33
4. Saini S, Nanda A, Monika Hooda M. Fast dissolving films (fdf) , innovative drug delivery system. Pharmacology online. 2011; 2: 919-928
5. Suresh B, Halloran D, James L. Quick dissolving films: A novel approach to drug Delivery. Drug Dev Tech. 2006; 1-7
6. Enalapril. Indian Pharmacopoeia, Vol 2, Ministry of Health and Family Welfare, Govt of India, 2007, pp 421-423.
7. Ahirwar P, Dhakar S, Dubey BK. Formulation Development and Evaluation of Fast Dissolving Oral Films of Nebivolol. Journal of Pharmacology and Biomedicine. 2018; 2(2): 164-170
8. Goel KK, Goel N, Gajbhiye A. Development of new UV spectrophotometric method for the estimation of enalapril maleate in bulk and tablet dosage form. The Asian Journal of Experimental Chemistry. 2008; 3(1-2): 92-93

9. Mashru R, Sutariya V, Sankalia M, and Parikh P. Development and Evaluation of Fast-Dissolving Film of Salbutamol Sulphate. Drug Dev Ind Pharm. 2005; 31, 25–34.
10. Ravi, Jain S. Formulation and evaluation of labetalol mouth dissolving tablets. Journal of Pharmacology and Biomedicine. 2021; 5(4): 398-407
11. Maheshwari KM, Devineni PK, Deekonda S, Shaik S, Uppala NP, Nalluri BN. Development and Evaluation of Mouth Dissolving Films of Amlodipine Besylate for Enhanced Therapeutic Efficacy. J Pharmaceut. 2014; http://dx.doi.org/10.1155/2014/520949
12. Bala R, Khanna S, Pawar P. Design Optimization and *In Vitro-In Vivo* Evaluation of Orally Dissolving Strips of Clobazam. J Drug Del. 2014; http://dx.doi.org/10.1155/2014/392783