Current Journal of Applied Science and Technology

40(15): 54-60, 2021; Article no.CJAST.70043
ISSN: 2457-1024
(Past name: British Journal of Applied Science & Technology, Past ISSN: 2231-0843, NLM ID: 101664541)

Formulation and Evaluation of Captopril Mouth Dissolving Film

V. T. Iswariya[1*], P. Deepika[1] and Sowjanya Battu[1]

[1]Department of pharmaceutics CMR College of pharmacy, Hyderabad, Telangana, India.

Authors' contributions

This work was carried out in collaboration among all authors. Author VTI designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors PD and SB managed the analyses of the study and managed the literature searches. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/CJAST/2021/v40i1531414
Editor(s):
(1) Dr. A. A. Hanafi-Bojd, Tehran University of Medical Sciences, Iran.
Reviewers:
(1) Naveen Dhingra, Mody University of Science and Technology, India.
(2) Rajendra Kumar Jadi, Anurag University, India.
(3) Amal Ajaweed Sulaiman, Baghdad College for Medical Sciences, Iraq.
Complete Peer review History: http://www.sdiarticle4.com/review-history/70043

Original Research Article

Received 18 April 2021
Accepted 28 June 2021
Published 05 July 2021

ABSTRACT

The goal of this research is to develop captopril mouth dissolving films and evaluate the impact of various formulation factors on the physical and mechanical properties of the films, as well as drug release behaviour. In different grades, hydroxypropyl methyl cellulose (HPMC E15 and K4M) was employed as the film forming polymer. Formulation disintegration times were determined to be in the range of (52 2.5 to 125.6 2.02 s). Formula F2 had the fastest disintegration time in vitro (52 2.5 s) and was determined to be acceptable for film production with ideal physicochemical qualities, faster disintegration, and optimal in vitro release. It may be concluded that the solvent casting approach can be used to make captopril mouth dissolving films with a higher dissolution rate and greater patient compliance.

Keywords: Captopril; HPMC; disintegration time; mechanical properties; mouth dissolving film.

1. INTRODUCTION

The oral route of administration has always been preferred over the other routes of administration namely, parenteral, topical, rectal and vaginal by the medical practitioners, manufacturers due to patient acceptance [1,2]. Ease of administration, convenience and cost effectiveness has been

**Corresponding author: E-mail: iswariyapharma@gmail.com;*

the reason behind the popularity of this route among the patient population [3]. The oral cavity has unique environment that offers its potential as a site for drug delivery [4]. There has been a lot of advancement in the oral solid drug delivery system, from conventional dosage forms such as tablets and capsules to modified release dosage forms and recently the fast dissolving dosage forms . The limitation of difficulty in swallowing oral solid dosage forms has been the reason for the evolution of mouth dissolving drug delivery system.

The Mouth dissolving films are thin and elegant in appearance which Can be available in various shapes and sizes [5] in the market. They can be taken without water so beneficial while travelling as Disintegrates dissolves in mouth when placed on tongue so no risk of choking takes place .its the most Convenient and accurate dose can be administered in comparison to liquid orals. These can be used for site specific local action [6] in the oral cavity.

The drawback of these films is that high dose of the drug cannot be incorporated into the film [7] and Taste masking [8] is essential if the drug is having a bitter taste. Packaging needs special care and equipments [9]. The technical challenges in manufacture of films include achieving uniformity of dose and in thickness of mouth dissolving film while casting of the film [10].

The aim of the present research is to enhance the patient compliance with desired therapeutic response.

2. MATERIALS REQUIRED

Captopril was purchased from Sun pharma, major excipient HPMC E_{15}, HPMC K_4M was also purchased from sun pharma, propylene glycol, carbopol, SSG and citric acid used were of analytical grade only.

3. METHODS EMPLOYED

3.1 Preformulation Studies for Captopril

3.1.1 Solubility

The solubility of a drug may be expressed in number of ways. The U.S. pharmacopoeia and national formularies list the solubility of the drugs as the number of milli litres of solvent in which 1 gram of solute will dissolve.

For substance whose solubility is not definitely known, the values are described in the pharmaceutical compendia by the use of certain general terms. One gm of Captopril was dispersed in the solvent and based on the following table solubility was determined. The solubility of the drug was determined in water, ethanol, methylene chloride, methanol, chloroform and acetone [11].

3.1.2 Determination of pH

pH of the drug solution was tested by using previously calibrated pH meter. 6.8 % w/v solution of Captopril was prepared using as a solvent and sonicated for30 minutes. The glass electrode of the pH meter was immersed in the prepared solution and the pH of the solution was recorded [12].

3.1.3 Moisture content

The moisture content was determined using Sartorius moisture determining apparatus. 50 mg of the pure Captopril was transferred to an aluminium plate and the moisture content was determined at 105^0C.

3.1.4 Melting point

Melting point of the drug was determined by using Scientek digital melting point apparatus.

3.1.5 Drug polymer compatibility studies

Study was carried out using FT-IR spectrometer (Shimazdu).FT-IR Spectra of Captopril and polymers with Captopril were obtained. The spectrum was studied for specific peaks of drug and polymer. The spectra are shown in Figs. 2 and 3.

3.1.6 General method for the preparation of oral thin films (OTF)

The current preferred manufacturing process for making this film is solvent casting method [13]. Water-soluble polymers are completely soaked in water over night and dispersed to form a homogeneous viscous dispersion using a homogenizer. The active ingredient (if water insoluble) was dissolved in alcohol and to this propylene glycol was added. This solution was added to the polymeric dispersion with stirring. Other ingredients such as sweeteners etc were added by dissolving in small quantity of water

and were added to the dispersion. The resulting bubble free dispersion was poured onto glass moulds and was kept in oven. Dried film was then cut into desired shape and size for the intended use. The formulae of the different films were given below.

3.2 Formulation of Mouth Dissolving Film

Following processes are generally used to manufacture the mouth dissolving film: hot melt extrusion, solid dispersion extrusion, rolling, semisolid casting and solvent coating. The current preferred manufacturing process for making this film is solvent casting method. Water-soluble polymers are completely dissolved in a mixing tank to form a homogeneous viscous solution. Other ingredients, including active ingredient are dissolved in a small portion of aqueous solvent using a high shear processor. The active mixture is then added to the viscous colloidal solution to form a homogeneous viscous solution. This viscous solution is degassed under vacuum. The resulting bubble free solutions poured on to glass mould and were kept in oven. Dried film is then cut into the desired shape and size for the intended application [14].

3.3 Analytical Methods

There were many analytical methods that were used to determine the concentration of Captopril in pharmaceutical preparations such as spectrophotometric methods, HPLC methods etc.

In this project spectrophotometric technique (as per USFDA) was used to determine the concentration of Captopril in the prepared formulation (i.e. UV visible spectrophotometry).

3.3.1 Procedure for calibration of captopril

3.3.1.1 Preparation of standard solution

50 mg of Captopril was accurately weighed and was transferred into 1000 ml volumetric flask. The drug was dissolved in a little quantity of 28.8 gm of disodium hydrogen phosphate and 11.54 gm of potassium dihydrogen phosphate (Stock A, 1mg/ml).

3.3.1.2 *Scanning*

From the prepared stock 10 µg/ ml solution was prepared and was scanned in the UV range of 200 – 400 nm and the absorption maxima (λ max) was found to 203 nm for further analysis.

3.3.1.3 Drug – excipient compatibility study

Study was carried out using FTIR (BRUKER) where the spectra of the films were taken with and without the drug. The specific peaks of drug and the polymers were studied for the interactions.

4. RESULTS AND DISCUSSION

In preformulation studies, it was found that, the λmax of Captopril by UV spectroscopic method was found at 203 nm in 0.01N HCL and phosphate buffer pH 7.4. Captopril was found to be freely soluble in water, ethanol, methanol, phosphate buffer solution (PBS) pH 7.4 and 0.01N HCL. The results are given in Table 2. The Captopril inclusion complexes were characterized by FTIR spectroscopy for drug interaction with HPMC.Captopril contains number of –CH peaks at 1450 cm-1 1700 cm-1. These peaks were unaltered when the inclusion complex were mixed with different excipients used in the formulation. Thus, indicating that the mixture prepared was physical in nature. The IR spectrum is shown in Fig. 3.

The surface PH of all formulations were found to be in the range of 6.02 ± 0.153 to 6.79 ± 100 which is in the official range of salivary pH.

All the films are free from the moisture uptake and there is no evidence of moisture attack in the prepared films.

4.1 Weight Variation of the Films

Mouth dissolving films were prepared by casting method.Five Films each of one square inch were cut at five different places from casted films and weight variation was measured. Weight variation varies from 89.28 ± 0.5450 to 96.78 ± 0.1021 mg. The results of weight variations are shown in the Table 2.

Table 1. Formulation of captopril mouth dissolving film

INGREDIENT	F1	F2	F3	F4	F5	F6	F7	F8	F9
Drug	10 mg	10 mg	10 mg	10 mg	10 mg	10 mg	10 mg	10 mg	10 mg
HPMC E15	80 mg	85mg	90mg	-	-	-	-	-	-
HPMC K4M	-	-	-	80 mg	85 mg	90 mg	-	-	-
Carbopol	-	-	-	-	-	-	80 mg	85 mg	90 mg
PVA	5 mg	5 mg	5 mg	5 mg	5 mg	5 mg	5 mg	5 mg	5 mg
Propylene Glycol	15 mg	15 mg	15 mg	15 mg	15 mg	15 mg	15 mg	15 mg	15 mg
Sodium Starch Glycolate	20 mg	20 mg	20 mg	20 mg	20 mg	20 mg	20 mg	20 mg	20 mg
Aspartame	5 mg	5 mg	5 mg	5 mg	5 mg	5 mg	5 mg	5 mg	5 mg
Citric Acid	5 mg	5 mg	5 mg	5 mg	5 mg	5 mg	5 mg	5 mg	5 mg

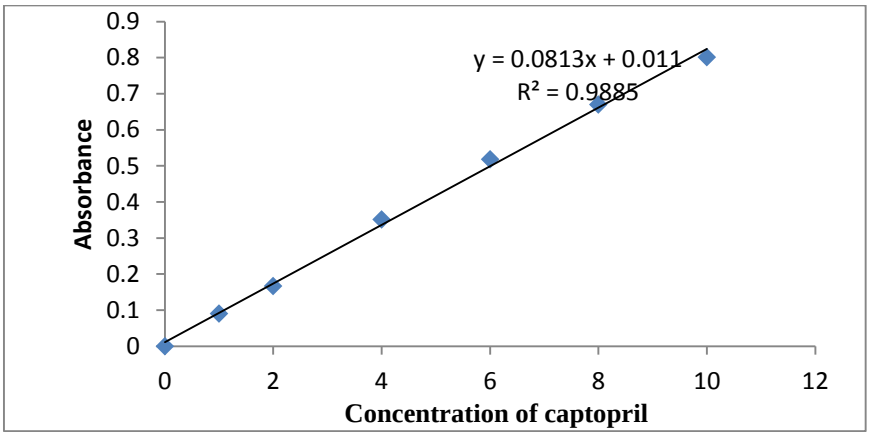

Fig. 1. Standard graph of captopril

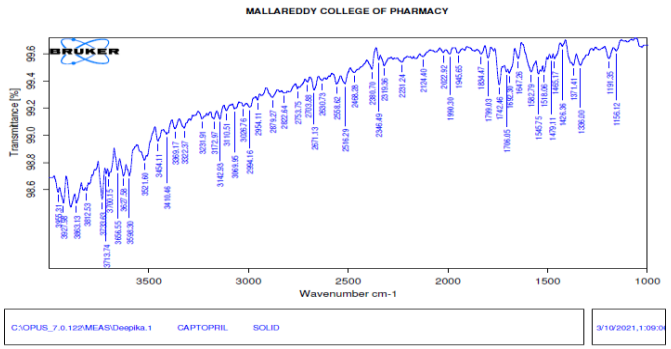

Fig. 2. FTIR spectrum of pure captopril

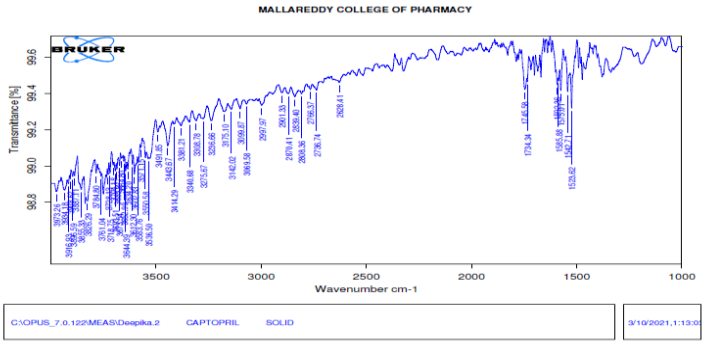

Fig. 3. FTIR spectrum of captopril film

Table 2. Solubility profile of captopril

solvents	solubility
Distilled Water	+++
Methanol	++
Ethanol	++
0.01 N HCL	++

4.2 Thickness of the Film

The thickness of the drug loaded films were measured with the help of screw gauge by combining of five films of film F1 to F9 formulations, as it was difficult to measure the thickness of the single film, thickness varies from 0.313± 0.0358 to 0.373 ± 0.0183 mm. The results were reported in the Table 2.

4.3 Tensile Strength of the Films

The film of 3 inch X 10 mm was taken for the studies. From the results it is clear that when the concentration of the polymer increases, the tensile strength of the film also increases. The formulation F III shows the maximum tensile strength, percentage elongation and folding endurance. Presence of glycerine as a plasticizer imparts the flexibility to the polymers. Tensile strength measures the ability of the film to withstand rupture. The formulation F2 shows the maximum value of tensile strength 1.513± 0.0465, percentage elongation 23.85± 0.6234 and folding endurance was 183 (no. of folds) as shown in the Table 2. This might be due to the formation of strong hydrogen bonds between polymer and plasticizer there by imparting flexibility to withstand rupture. Tensile strength of the films was recorded in the Table 2.

4.4 Percentage Elongation of the Films:

The film of 3 X 10 mm was taken for the studies. Percentage elongation was found to increase with increase in concentration of polymer in the film. Data are reported in the Table 2.

4.5 Folding Endurance of the Films

The folding endurance was me assured manually. A strip of film 4 square cm was cut and subjected for the folding endurance studies until it broke at the same place. Folding endurance increases with increase in polymer concentration. The number of times the film fold until it broke was reported in the Table 2.

4.6 Disintegration Time

Disintegration time of the film was done by using tablet disintegration test apparatus. A size of one square inch film was subjected for this study. Mouth dissolving time and disintegration time of the films were found to be increased with increase in the concentration of the polymer. The formulation F2 shows 52 Sec (disintegration time) and 45 Sec (mouth dissolving time) as shown in the Table 2.

4.7 Mouth Dissolving Time

The mouth dissolving time was determined by using beaker containing 6.8-pH phosphate buffer. A size of one square inch film was subjected for this study. The mouth dissolving time of the film was reported in the Table 2.

4.8 Drug Content Uniformity of Films

The prepared film formulations were analyzed for drug content and it was observed that all the formulation found to contain almost uniform quantity of drug as per content uniformity studies indicating reproducible technique. F2 formulation shows 99 percent of drug content. The data is reported in the Table 2.

4.9 *Invitro* Dissolution Studies

Dissolution profiles of the mouth dissolving films containing Captopril formulations were compared with pure drug. No significant differences were observed from Invitro dissolution studies for the film FI to F9 and pure drug due to film instantly get wet by dissolution medium and disintegrate. Percentage of drug release at different time intervals are shown in the Table 3. And F2 formulation showed the best percentage of dug release in 25 min i.e. 85.99 % and 98.90 at 30 minutes.

Table 3. Evaluation of oral thin film (mouth dissolving films) for various parameters

FC	Average weight of the 1 inch square film in mg	Elongation at break (%)	Average thickness in mm	Tensile strength in kgs	Folding Endurance	Disintegration time in Sec	Drug content in mg
F1	92.42± 0.4020	25.73± 0.9415	0.309± 0.0003	1.216± 0.0541	92.13± 6.0147	56.1±1.112	97.00±1.732
F2	96.78± 0.1021	23.85± 0.6234	0.383± 0.0163	1.513± 0.046	102.0± 10.1421	52 ± 2.528	99.00± 1.528
F3	93.28± 0.5450	26.32± 0.5128	0.313± 0.0358	1.321± 0.1210	154.13± 5.0242	125.6± 2.024	95.00±3.000
F4	94.54± 0.3118	30.74± 0.8742	0.335± 0.0128	1.246± 0.0745	124.3± 10.2813	96.0± 3.001	95.00±3.000
F5	96.42± 0.4070	22.73± 0.9335	0.356± 0.0163	1.187± 0.0524	91.34± 6.0157	55.6±1.134	94.00±1.732
F6	90.18± 0.2241	25.85± 0.6744	0.373± 0.0183	1.391± 0.044	105.1± 106.148	91 ± 2.514	96.00± 1.528
F7	89.28± 0.5450	24.52± 0.5228	0.343± 0.7148	1.316± 0.1021	161.33± 5.0352	120.6± 2.004	94.00±3.000
F8	93.14± 0.3138	27.74± 0.8112	0.325± 0.0148	1.324± 0.0748	180.1± 10.213	96.0± 3.120	96.00±3.000
F9	94.44± 0.3618	31.75± 0.8252	0.315± 0.0208	1.472± 0.0714	178.3± 10.233	92.0± 3.230	98.00±3.000

Table 4. Comparative evaluation of *invitro* dissolution profiles of mouth dissolving captopril films

Time in mins	F1	F2	F3	F4	F5	F6	F7	F8	F9
5	7.23	7.54	5.89	6.53	6.75	5.15	5.19	4.52	5.35
10	14.68	15.29	12.50	14.78	15.48	15.45	16.42	7.83	9.62
15	33.51	32.68	25.63	20.30	27.85	35.23	32.92	18.66	22.16
20	45.10	47.19	39.50	35.61	45.13	40.81	46.8	44.26	44.30
25	75.93	85.99	74.79	79.23	73.46	70.87	75.10	62.93	61.83
30	96.51	98.90	96.13	95.62	95.30	90.17	94.57	89.29	84.52

5. CONCLUSION

Fast dissolving films are the novel approach in oral drug delivery systems. It promises patient compliance especially in case of pediatrics and geriatrics patients. They can also be used when quick action is required. On the basis of obtained results, one can conclude that HPMC E15 and HPMC K4M are better for the formulation of oral film of captopril. The release of F2 formula show higher drug release, also F2 Show *in-vitro* disintegration time of 52 s. On the basis of data obtained from *in-vitro* dissolution that F2 is promising formulation suitable for the fast release of captopril for systemic use since they exhibited maximum drug release.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Bala R, Khanna S, Pawar P. Design optimization and in vitro-in vivo evaluation of orally dissolving strips of clobazam. J Drug Delivery. 2014;1:1-15.
2. Gurjeet Singh G, Singh A. Oral fast dissolving films: a new trend of drug delivery. International Journal of Universal Pharmacy and Biosciences. 2014;3(3):301-317.
3. Patil BS, Sonawane SJ, Kulkarni U, Hariprasanna RC. Formulation and in-vitro evaluation of captopril floating matrix tablets using HPMC 50cps. J Pharma Sci and Biosicentific Res. 2012;2(3):97-102.
4. Patil P, Shrivastava SK. Formulation, evaluation and optimization of fast dissolving oral film of selective antihypertensive drug. World J Pharm Pharm Sci. 2014;3(8):996-1060.
5. Kumar RK, Sulochana MM. Formulation and evaluation of fast dissolving films of lercanidipine hydrochloride. International Journal of Innovative Drug Discovery. 2014;4(1):46-53.
6. Abd-Alhammid SN, Saleeh HH. Formulation and evaluation of flurbiprofen oral film. Iraqi J Pharm Sci. 2014;23(1):53-9.
7. Khan S, Boateng JS, Mitchell J, Trivedi V. Formulation, characterisation and stabilisation of buccal films for paediatric drug delivery of omeprazole. AAPS Pharm Sci Tech. 2015;16(4):800–10.
8. Irfan M, Rabel S, Bukhtar Q, Qadir MI, Jabeen F, Khan A. Orally disintegrating films: A modern expansion in drug delivery system. Saudi Pharm J. 2016;24:537–46.
9. Dixit RP, Puthli SP. Oral strip technology: Overview and future potential. J Control Release. 2009;139:94–107.
10. Chen CC, White JL. Compatibilizing agents in polymer blends: Interfacial tension, phase morphology, and mechanical properties. Polym Eng Sci. 1993;33(14):923–30.
11. Alok Khunteta, Manish Kumar Gupta, Surendra Kumar Swarnka. Preformulation studies of rapid dissolving films containing granisetron hydrochloride. Journal of Drug Delivery and Therapeutics. 2019;9(4-A):511-515.
12. Madiha Mushtaque, Iyad Naeem Muhammad, Syed Muhammad Fareed Hassan. Development and pharmaceutical of oral fast dissolving thin film of escitalopram. Pakistan Journal of Pharmaceutical Sciences. 2020;33(1):183-189.
13. Abhibrata Roy, Madhavi Blr. Formulation development of oral fast-dissolving films of rupatadine fumarate in Asian journal of pharmaceutical and clinical research. 2020;13(11).
14. Hiraku Onishi, Osama Sakata. Preparation and evaluation of fast-dissolving films of etilefrine hydrochloride for practical buccal dosing. Pharmaceutical Development and Technology. 2021;26(5).

Peer-review history:
The peer review history for this paper can be accessed here:
http://www.sdiarticle4.com/review-history/70043