International Journal of Health Care and Biological Sciences

Research Article Open Access

Formulation development and invitro evaluation of captopril fast dissolving oral thin films by solvent casting method

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Article History

Received on: 22-11-2021
Revised On : 08-12-2021
Accepted on : 14-01-2022

***Keywords*:** Captopril, crospovidine, super disintegrants, solvent casting method

DOI:
https://doi.org/10.46795/ijhcbs.v3i1.261

Abstract

The present study formulation development of captopril oral thin films by using solvent casting method .the formulation contain the Crospovidone was found At 4% w/w of crospovidone with 3% PVA concentration level dispersion time of 7.23±0.151 sec highest release of more than 99.27% drug in 30 min. therefore the formulation contain shows the better formulation.

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Introduction

The oral route of administration continues to be most preferred route due to various advantages including ease of administration, avoidance of pain, versatility and most importantly patient compliance. His novel drug delivery system can also be beneficial for meeting the current needs of the industry are improved solubility/stability, biological half-life and bioavailability enhancement of drugs [2, 3]. Although oral disintegrating tablets have an advantage of administration without choking and fast disintegration; the disintegrated materials contained in them are insoluble and remain until swallowing. In such cases formulation of fast dissolving film will be advantageous [4, 5].

The film is manufactured as a large sheet and then cut into individual dosage units for packaging in a range of pharmaceutically acceptable formats [10]. Captopril is a potent, competitive inhibitor of angiotensin-converting enzyme (ACE), the enzyme responsible for the conversion of angiotensin I (ATI) to angiotensin II (ATII). ATII regulates blood pressure and is a key component of the renin-angiotensin-aldosterone system (RAAS). Captopril may be used in the treatment of hypertension.

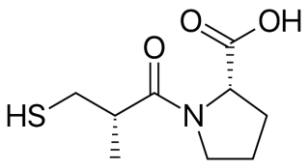

Figure 1: chemical structure of Captopril

Experimental work

Materials and methods

Captopril, Gelatin, P.V.A , HPMC, Crospovidone, Microcrystalline cellulose , PEG 400, Citric acid , Sucrose

, Trusil mixed flavour R.S.V purchased from matrix lab and all chemical purchased from Merck Pvt Ltd. All instruments used in the experiments were well calibrated.

Methodology

Calibration curve for captopril in 0.5% sodium lauryl sulphate (SLS) solution

Procedure

Preparation of Standard Stock Solution

100mg of Captopril was accurately weighed into 100 ml volumetric flask and dissolved in small quantity of 0.5% SLS solution. The volume was made up to 100 ml with the 0.5% SLS solution to get a concentration of (1000 µg/ml) SS-I. From this, 10 ml was withdrawn and diluted to 100 ml with 0.5% SLS solution to concentration of (100 µg/ml) SS-II.

Scanning of Drug

From stock solution (SS-II), 1 ml was withdrawn and the volume was made up to 10 ml with 0.5% SLS solution to get a concentration of 10 µg/ml. UV between the wavelengths 200-400 nm. It gave a peak at 205 nm and the same was selected as λ_{max} for Captopril.

Calibration Curve in 0.5% of SLS solution

From the standard stock solution (SS-II), 1, 2, 3, 4 and 5 ml were withdrawn and volume was made up to 10 ml with 0.5% SLS solution to give a concentration of 10, 20, 30, 40 and 50 µg/ml. Absorbance of these solutions was measured against a blank of 0.5% SLS solution at 205 nm for Captopril and the absorbance values are summarized in Table 3. Calibration curve was plotted, drug concentrations versus absorbance was given in the Fig. 4.

Drug-excipient compatibility studies by I.R

Infra-Red spectroscopy is one of the most powerful analytical techniques to identify functional groups of a drug and drug and excipient interaction

Differential scanning calorimetry (DSC)

Differential scanning calorimetry (DSC) was performed using Differential Scanning Calorimeter (METTLER). The instrument was calibrated using indium (1560C), Tin (232oC) and Zinc (419.5oC) as internal standards. Samples of 2-10 mg were placed in aluminium pans and sealed. The probes were heated from 0 to 300oC. Samples were heated in an open pan at a rate of 10oC min-1 under a nitrogen flow of 10K/min under nitrogen atmosphere.

Scanning Electron Microscopy (SEM)

Morphology of the prepared film was observed under a scanning electron microscope (SEM) (Model QUANTA-200 FEI Neither land). The samples were attached to the slab surfaces with double-sided adhesive tapes and the scanning electron photomicrograph was taken at 1000X magnification.

Formulation of fast dissolving films of captopril

Table 01: Formulation details of Captopril Fast dissolving Oral thin films

Formulation	Captopril (mg)	Gelatin (%w/v)	PVA (%w/v)	HPMC (%w/v)	Crospovide (%w/w of polymer)	MCC (%w/w of polymer)	Sucrose (%w/w of polymer)	Citric acid (%w/w of polymer)	Trusil flavour (%w/w) of polymer	Poly Ethylene Glycol (% (w/w) of Polymer
F 1	50	4.5	--	--	2.0	--	4.0	4.0	8.0	30
F2	50	4.5	--	--	4.0	--	4.0	4.0	8.0	30
F3	50	4.5	--	--	6.0	--	4.0	4.0	8.0	30
F4	50	4.5	--	--	--	5	4.0	4.0	8.0	30
F5	50	4.5	--	--	--	10	4.0	4.0	8.0	30
F6	50	4.5	--	--	--	15	4.0	4.0	8.0	30
F7	50	--	3.5	--	2.0	--	4.0	4.0	8.0	30
F8	50	--	3.5	--	4.0	--	4.0	4.0	8.0	30
F9	50	--	3.5	--	6.0	--	4.0	4.0	8.0	30
F10	50	--	3.5	--	--	5	4.0	4.0	8.0	30
F11	50	--	3.5	--	--	10	4.0	4.0	8.0	30

F12	50	--	3.5	--	--	15	4.0	4.0	8.0	30
F13	50	--	--	5.0	2.0	--	4.0	4.0	8.0	30
F14	50	--	--	5.0	4.0	--	4.0	4.0	8.0	30
F15	50	--	--	5.0	6.0	--	4.0	4.0	8.0	30
F16	50	--	--	5.0	--	5	4.0	4.0	8.0	30
F17	50	--	--	5.0	--	10	4.0	4.0	8.0	30
F18	50	--	--	5.0	--	15	4.0	4.0	8.0	30

Evaluation of fast dissolving oral thin films

The Captopril fast films were evaluated for the following properties:

a) Physical appearance and surface texture
b) Weight uniformity
c) Thickness uniformity
d) Folding endurance
e) Surface pH
f) In vitro disintegration time
g) Drug content uniformity
h) In vitro drug release

Drug content uniformity study of films

The films were tested for drug content uniformity by UV-Spectrophotometric method. Films of 2 cm diameter were cut from three different places from the casted films. Each patch was placed in 100 ml volumetric flask and dissolved in 0.5 % SLS solution and 0.2 ml is taken and diluted with water up to 10 ml. The absorbance of the solution was measured at 205 nm using UV/visible spectrophotometer (Shimadzu UV-1700). The percentage drug content was determined using the standard graph and the same procedure was repeated for three films.

In vitro Dissolution Study

In vitro dissolution of Captopril mouth dissolving films was studied in USP XXIV dissolution test apparatus 900ml 0.5% SLS solution was used as dissolution medium. The stirrer was adjusted to rotate at 50rpm. The temperature of dissolution medium was maintained at 37±0.5ºC throughout the experiment. One film was used in each test. Samples of dissolution medium (5ml) were withdrawn means of syringe fitted with pre-filter at known intervals of time and analysed for drug release by measuring the absorbance at 205nm. The volume withdrawn at each time interval was replaced with fresh quantity of dissolution medium. Cumulative percent Captopril released was calculated and plotted against time

Data Analysis (Curve fitting analysis)

To analyse the mechanism of the drug release rate kinetics of the dosage form, the data obtained were plotted as:

1. Cumulative percentage drug released Vs time (In-Vitro drug release plots)
2. Log cumulative percentage drug remaining Vs Time (First order plots)

Results and Discussion

Standard Calibration Curve of Captopril In 0.5% W/V Sodium Lauryl Sulphate.

Table 02: Calibration data of Captoprilin 0.5% w/v Sodium lauryl sulphate at λ max 205 nm

SL. No.	Concentration (μg/ml)	Absorbance*
1	0	0
2	10	0.181
3	20	0.375
4	30	0.653
5	40	0.755
6	50	0.946

*Each reading is an average of three determinations

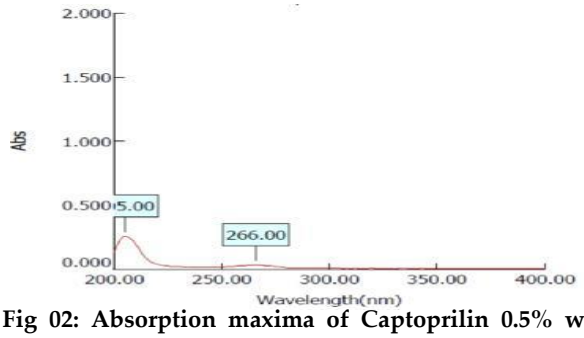

Fig 02: Absorption maxima of Captoprilin 0.5% w/v Sodium lauryl sulphate

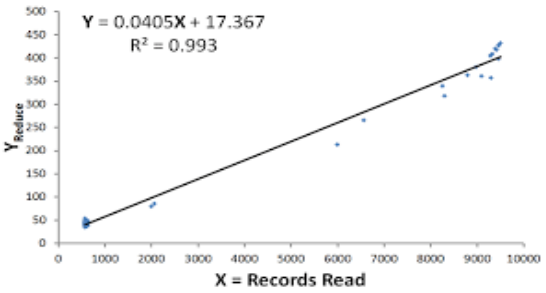

Fig 03: The linear regression analysis for standard curve in 0.5% w/v SLS solution

Differential Scanning Calorimetry

The DSC thermogram of Captoprilexhibited an endothermic peak at 67.54^{0}C corresponding to its melting point. Other excepitents does not show profound shift in peaks which indicates compatibility. The DSC thermogram of the individual drug and drug with Gelatin, PVA and HPMC were shown in fig 04,05.

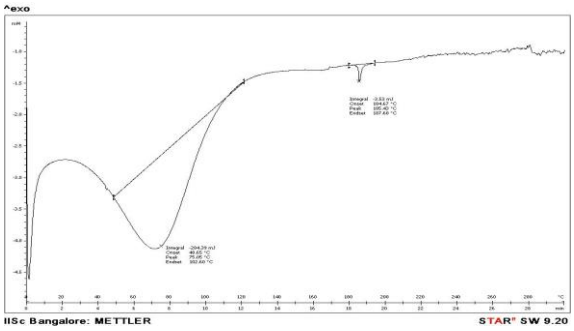

Figure 04: DSC of Drug + Gelatin

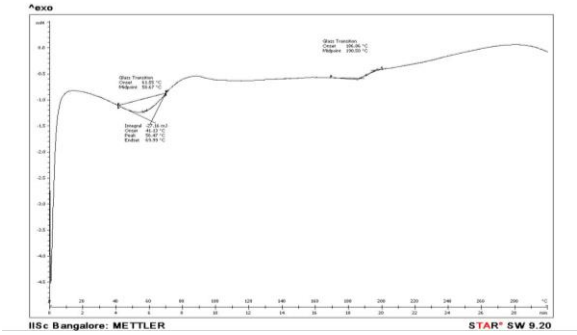

Fig 05: DSC of Drug + PVA

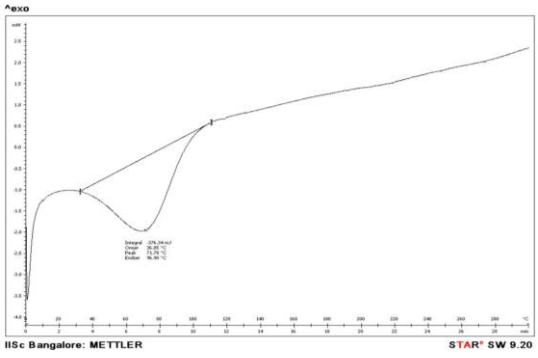

Fig 06: DSC of Drug + HPMC

Scanning Electron Microscopy

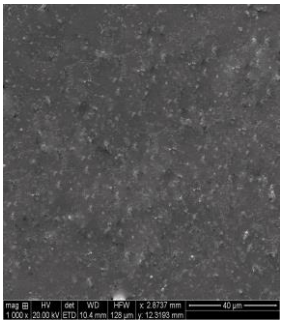

Fig 07: SEM of Drug + Gelatin

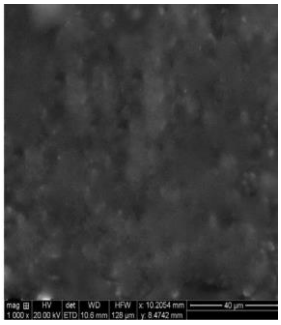

Fig 08: SEM of Drug + PVA

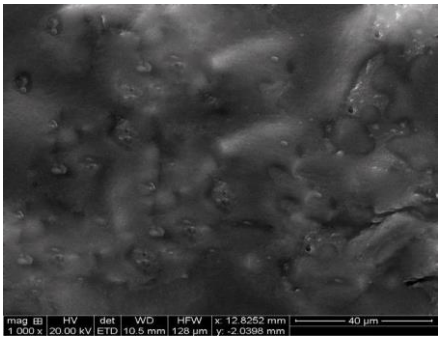

Fig 09: SEM of Drug + HPMC

Table 03: Evaluation of Fast Dissolving Films of Captopril

Formulation Code	Avg. Weight (mg) ± SD, n=3	Avg. Thickness (mm) ± SD, n=3	Avg. Folding Endurance ± SD, n=3
Fg	63.92±0.12	0.135 ± 0.010	272 ± 1.674
Fp	51.02±0.24	0.125 ± 0.005	265 ± 1.205
Fh	64.01±0.08	0.130 ± 0.010	275 ± 1.453
F1	65.21±0.28	0.140 ± 0.005	287 ± 2.340
F2	65.90±0.31	0.145 ± 0.010	289 ± 2.640
F3	67.04±0.21	0.150 ± 0.010	267 ± 1.000
F4	66.84±0.38	0.160 ± 0.015	271 ± 1.730
F5	68.21± 0.41	0.165 ± 0.005	274 ± 1.000
F6	72.12±0.11	0.170 ± 0.010	259 ± 3.310
F7	49.91±0.32	0.130 ± 0.020	266 ± 2.000
F8	51.22±0.23	0.130 ± 0.015	277 ± 3.460
F9	52.18±0.41	0.140 ± 0.015	260 ± 1.000
F10	51.11±0.22	0.145 ± 0.015	291 ± 2.000
F11	52.85±0.42	0.150 ± 0.010	293 ± 2.645
F12	54.92± 0.15	0.155 ± 0.005	274 ± 1.732
F13	65.21±0.54	0.145 ± 0.010	280 ± 2.645

F14	66.09±0.22	0.150 ± 0.015	283 ± 1.732
F15	66.97±0.10	0.150 ± 0.005	275 ± 3.000
F16	67.05±0.24	0.165 ± 0.020	281 ± 3.605
F17	68.90±0.33	0.170 ± 0.025	280 ± 2.645
F18	71.89±0.26	0.175 ± 0.015	282 ± 3.000

Drug content uniformity of films

Table 04: Evaluation of Fast Dissolving Films of Captopril.

Formulation Code	Avg. Drug Content Uniformity (%) ± SD, n=3	Avg. In Vitro Disintegration (sec) ± SD, n=3	Avg. Surface pH ± SD, n=3
Fg	95.54 ± 0.205	72.21 ± 0.205	6.67± 0.154
Fp	96.52 ± 1.443	70.43 ± 0.165	6.89 ± 0.122
Fh	96.32 ± 1.657	73.54 ± 0.112	6.65 ± 0.111
F1	96.66 ± 0.925	14.33 ± 0.171	6.76 ± 0.153
F2	98.04 ± 1.539	9.10 ± 0.435	6.00 ± 0.100
F3	97.33 ± 0.369	11.50 ± 0.591	6.46 ± 0.115
F4	95.00 ± 1.056	18.76 ± 0.151	6.23 ± 0.152
F5	97.66 ± 1.396	12.86 ± 0.151	6.66 ± 0.152
F6	96.66 ± 1.396	14.10 ± 0.479	6.06 ± 0.153
F7	97.66 ± 1.545	12.00 ± 0.100	6.83 ± 0.057
F8	98.86 ± 1.175	7.23 ± 0.151	6.06 ± 0.152
F9	97.24 ± 1.001	11.93 ± 0.057	6.33 ± 0.152
F10	96.76 ± 0.350	15.41 ± 0.076	6.76 ± 0.152
F11	97.81 ± 0.902	10.26 ± 0.115	6.80 ± 0.100
F12	97.21 ± 1.791	12.02 ± 0.152	6.30 ± 0.173
F13	96.70 ± 0.540	14.05 ± 0.056	6.63 ± 0.152
F14	97.87 ± 1.002	10.60 ± 0.035	6.13 ± 0.152
F15	97.64 ± 1.963	11.09 ± 0.105	6.30 ± 0.100
F16	95.05 ± 0.355	20.75 ± 0.025	6.53 ± 0.321
F17	97.23 ± 0.880	13.25 ± 0.110	6.56 ± 0.057
F18	96.17 ± 2.403	15.92 ± 0.102	6.46 ± 0.057

Stability studies

Table 05: Stability data of F_2 formulation

Time in months	Formulation F2 stored at 40⁰c/ 75% RH		
	Physical appearance	In vitro Dispersion time	% Drug content
1	+++	9.20	98.00
2	+++	10.0	97.42
3	++	10.35	96.99

Table 06: Stability data of F8 formulation

Time in months	Formulation F8 stored at 40⁰c/ 75% RH		
	Physical appearance	In vitro Dispersion time	% Drug content
1	+++	7.33	98.40
2	+++	7.95	98.10
3	++	8.35	97.75
Time in months	**Formulation F14 stored at 40⁰c/ 75% RH**		
	Physical appearance	**In vitro Dispersion time**	**% Drug content**
1	+++	10.72	97.10
2	+++	10.94	96.67
3	++	11.10	95.99

Summary and Conclusion

The prepared film containing Captopril was clear and colourless. The scanning electron photo micrograph of the film at 1000 X magnification showed smooth surface with some little pores and without any scratches or transverse striations Formulated films gives satisfactorily result for various physio-chemical evaluation of films like physical appearance, and surface texture, weight uniformity, thickness uniformity, Folding endurance, Surface pH, Drug content uniformity, In vitro Disintegration time, In vitro drug release The low values of standard deviation for average weight and drug content weight and drug content uniformity within the batches prepared. Based on in vitro dispersion time, formulation F2 , F8 and F14 that is with 4% Crospovidone were approximately 7-10 s and the formulation F5 , F11 and F17 that is with 10% MCC were approximately 10-14 s.

which it was found to be promising dispersion time .It was observed from the results that, CP formulations showed maximum dissolution rate about 99.27% of drug release in 30 min. Whereas MCC showed dissolution rate about 97.42% of drug release in Short-term stability studies of promising formulation indicated that there is no significant change in drug content and in vitro dispersion time. Fast dissolving films of Captopril can be prepared by Solvent casting method using super disintegrants. Crospovidone was found. At 4% w/w of crospovidone with 3% PVA concentration level dispersion time of 7.23±0.151 sec highest release of more than 99.27% drug in 30 min.

References

1. Dixit R, Puthli S. Oral strip technology: Overview and future potential. J. Control Release 2009; 139: 94-107.
2. Arya A, Chandra A, Sharma V, Pathak K. Fast dissolving oral films: An Innovative Drug Delivery system and Dosage form. Int. J. Chem. Tech. Res. 2010:2: 576-83.
3. Mashru C, Sutariya V, Sankali M, Parikh P. Development and evaluation of fast-dissolving film of salbutamol sulphate. Drug Dev. Ind. Pharm. 2005; 31: 25-34.
4. Nishimura M, Matsuurab K, Tsukioka T, Yamashita H, Inagaki N, Sugiyama T, Itoh Y. *In vitro* and *in vivo* characteristics of prochlorperazine oral disintegrating film. International Journal of Pharmaceutics 2009 Oct 15; 398: 98–102.
5. Shimoda H, Taniguchi K, Nishimura M, Matsuura K, Tsukikoka T, Yamashita H, Hirano K, Yamamoto M, Kinosada Y, Itoh Y. Preparation of a fast dissolving oral thin film containing dexamethasone: A possible application to antiemesis during cancer chemotherapy. European Journal of Pharmaceutics and Biopharmaceutics. 2009 Aug 31.
6. Slowson M, Slowson, S. What to do when patients cannot swallow their medications. Pharm Times. 1985; 51: 90-96.
7. Doheny K. You really expect me to swallow those horse pills? Am Druggist. 1993; 208: 34-35.
8. Tora-Tora Gorahowski. Principles of Anatomy and Physiology, 7th Edition edited by Gerad J. Tora-Tora and Sandro Reynolds Gorahowski, published Harpet Collins College Publishers; 1992: 770-4.
9. Ross and Wilson. Anatomy and Physiology in Health and Illness, 9th Edition edited by Anne Waugh and Allison Goraw published by Churchill Livingstone Edinburgh; 2001: 289
10. *www.ondrugdelivery.com*
11. Vondrak B, Barnhart S. Dissolvable Films for Flexible Product Format in Drug Delivery, Pharmaceutical Technology Supplement. April 2008.
12. Frey P.Film Strips and Pharmaceuticals,. Pharma. Mfg. & Packag. Sourcer, winter, 2006: 92.93.
13. Zhang H, Zhang J, Streisand J.B. Oral mucosal drug delivery: clinical pharmaco- kinetics and therapeutic applications, Clin. Pharmacokinet.2002; 41 (9): 661-680.
14. Barnhart SD, Sloboda MS. The Future of Dissolvable Films. Drug Delivery Technol. 2007; 7 (8): 34-37.
15. Meathrel B, Moritz C. Dissolvable Films and Their Potential in IVDs. IVD Technol. 2007; 13 (9): 53-58.
16. Mishra R, Amin A. Quick API Delivery. Pharmaceutical Technology Europe: 1-5.
17. Marabathuni VJ, Dinesh P, Ravikumar R, Yamini P, Kiran PS, Hussain SP, Rao CM. Chitosan based sustained release mucoadhesive buccal patches containing amlodipine besylate (AMB). Asian Journal of Research in Pharmaceutical Science. 2017; 7(2):97-104.
18. Marabathuni VJ, Bhavani M, Lavanya M, Padmaja K, Madhavi N, Babu P, Rao CM. Formulation and evaluation of mouth dissolving Tablets of carbamazepine. Asian Journal of Pharmacy and Technology. 2017; 7(3):137-43.
19. Babu AK, Teja NB, Ramakrishna B, Kumar BB, Reddy GV. Formulation and evaluation of double walled microspheres loaded with pantoprazole. METHODS. 2011; 15:28.
20. Babu AK, Reddy VR, Reddy N, Vidyasagar J. Evaluating the post compression parameter of ibuprofen by using super disintegrants. An Int J Adv Pharm Sci. 2010; 1(2):247-53.
21. Aruna MS, Babu AK, Thadanki M, Gupta ME. Solid dispersions–an approach to enhance the dissolution rate of Irbesartan. IJRPC. 2011; 1(4):780-7.

22. Babu K, Ramana MV. Development and in vivo evaluation of gastro retentive floating tablets of antipsychotic drug risperidone. Int J Pharm Pharm Sci. 2016; 11:43-52.
23. Babu AK, Ramana MV. In Vitro and In Vivo Evaluation of Quetiapine Fumarate controlled gastroretentive floating drug delivery system.