Journal of Pharmaceutical Research International

33(5): 49-60, 2021; Article no.JPRI.65615
ISSN: 2456-9119
(Past name: British Journal of Pharmaceutical Research, Past ISSN: 2231-2919, NLM ID: 101631759)

Design, Characterization and *In-vitro* Evaluation of Favipiravir Orodispersible Films

Kalyan Chakravarthy Yamali[1*], Madhu Gudipati[1] and Rama Rao Nadendla[1]

[1]Department of Pharmaceutics, Chalapathi Institute of Pharmaceutical Sciences (Autonomous), Lam, Guntur-522 034, Andhra Pradesh, India.

Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/JPRI/2021/v33i531180
Editor(s):
(1) Dr. Mohamed Fawzy Ramadan Hassanien, Zagazig University, Egypt.
(2) Dr. Jongwha Chang, University of Texas, USA.
Reviewers:
(1) K. B. Kishore Mohan, SRM University, India.
(2) Hasta Handayani Idrus, Universtas Muslim Indonesia, Indonesia.
(3) Alexis Mendoza-León, Universidad Central de Venezuela, Venezuela.
(4) Kuo-Chen Chou, Gordon Life Science Institute, USA.
Complete Peer review History: http://www.sdiarticle4.com/review-history/65615

Original Research Article

Received 20 December 2020
Accepted 25 February 2021
Published 01 March 2021

ABSTRACT

Introduction: Orodispersible films (ODF) is a thin strip that is mostly transparent, biodegradable and it has hydrophilic polymers that disintegrate and dissolves immediately when getting in contact with saliva. Different disintegrants play a crucial role in film properties such as organoleptic properties, film thickness, and in particular disintegration time of the film. The main reason for the development of oral films is for their prominent role in increased patient compliance among pediatrics and geriatrics by disintegrating faster, releasing the drug rapidly, without the need for water, and mostly decreasing the risk of choking.
Aim: To formulate orodispersible films of favipiravir and to study the effect of different superdisintegrants on various film properties.
Methods: The method used to prepare the film is the solvent casting method. In this method, the solution is prepared using polymer, drug, and superdisintegrants. This solution is casted on a film-forming apparatus using a spreader an instrument to obtain a thin film.
Results: The prepared oral films weights ranging from 148mg to 237mg based on the superdisintegrant concentration. The pH of the prepared films didn't vary significantly and percent

E-mail: madhugudipati7@gmail.com;

moisture absorption doesn't have significant variation. However, the texture varied from smooth to rough and transparent to translucent. Disintegration time is varying from 28 to 42 seconds. The optimum batch formulation gave 98% of drug release.

Keywords: Favipiravir; oral films; superdisintegrants; COVID-19.

1. INTRODUCTION

From past decades patient compliance is being improved from one formulation to other formulations. The main reason for developing orodispersible films is to improve patient compliance by not effecting the drug delivery to the body. For this approach, orodispersible films which are very thin, can be taken without water just by placing them on tongue [1]. Also, in many cases taste of the drug can be masked by taste-masking agents, just by incorporating them into oral films. Orodispersible films are commercially available since 1970s itself [2].

Orodispersible film is a thin strip that is mostly transparent, biodegradable and it has hydrophilic polymers that disintegrate and dissolves immediately when getting in contact with saliva [3]. Most of these films are useful for drug delivery in pediatric and geriatric patients. Using a conventional dosage form decreased patient compliance, for this reason, orodispersible tablets were first developed. Still, these tablets may disintegrate faster but there come several disadvantages such as less hardness, brittleness, and the risk of choking [4]. To avoid these disadvantages films were developed. To get films, commonly used polymers are hydroxypropyl cellulose (HPC), and hydroxypropyl methylcellulose (HPMC) using solvent casting technique [5]. This can be achieved by using Film Former apparatus (VJ INSTRUMENTS^{TM}). The obtained films are evaluated based on various, evaluation parameters such as thickness of the film, tensile strength, disintegrating time, folding endurance, moisture uptake analysis, *in-vitro* dissolution studies. The obtained or prepared film should pass all the evaluation parameters.

Favipiravir is a modified pyrazine analog discovered by Toyama Chemical Co., Japan. The colour of favipiravir is a pale yellow to white. It is soluble in water and freely soluble in ethanol. The oral bioavailability of favipiravir is 97.6%. It is a broad-spectrum antiviral which is already approved for new and re-emerging pandemic influenza. It was initially used against influenza [6]. COVID-19 virus lifecycle depends on RpRp (RNA-dependent RNA polymerase) and nsp12 protein which lies in the core of the virus. Favipiravir inhibits this RdRp, nsp12 protein of RNA viruses, helps in the termination of COVID-19 virus [7]. The side effects associated with the drug such as nausea and increased gas in digestive system can be controlled by orodispersible film formulation. Favipiravir is contraindicated in pregnancy as it is having potential embryotoxicity. Favipiravir is also excreted in human breast milk; hence it is also contraindicated in childbearing women [8].

COVID-19 which is originated in Wuhan, China in 2019 and was declared a pandemic by WHO on March 12^{th,} 2020 [9]. The virus which is causing influenza in patients was identified to be Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-Cov-2). The constant research is going on repurposing of drugs such as hydroxychloroquine, remdesivir, lopinavir, ritonavir, and some drugs that previously existing against COVID-19 treatment. The previously existing drug favipiravir is showing effectiveness in SARS-CoV and MERS (Middle East Respiratory Syndrome) which are having similarities in the genome sequence of SARS-CoV-2. Hence, favipiravir is studied for its effectiveness in the treatment of SARS-CoV-2 [10]. The dosage for adults is varying from 600-800mg, whereas in children 100mg to 200mg, still data on favipiravir use in children is very limited, extensive clinical trails are needed to recommend the use of favipiravir in children in COVID-19 situation [11]. In present research, each of the films are loaded with 100mg of drug. So, two films can be given as a single dose or one film based on severity of the disease. The present study involves the study of drug release from oral film, and compatibility of drug with excipients involved in the preparation of oral films. These films help in the faster release of drug when compared to conventional tablets.

2. MATERIALS AND METHODS

Favipiravir was received as a gift sample from Biophore Pvt Ltd, Hyderabad. Hydroxypropyl methylcellulose E50 LV (LobaChemiePvt.Ltd, Mumbai) is used as a film former. Sodium starch glycollate (LobaChemiePvt Ltd, Mumbai), microcrystalline cellulose (LobaChemie Pvt Ltd,

Mumbai), crospovidone (FMC Biopolymer) were used as superdisintegrants. Propylene glycol (Qualigens fine chemicals) was used as a plasticizer. Aspartame as a sweetener. Distilled water as a solvent.

Various equipment used in the preparation of oral films are electronic balance, Ax 200 (Shimadzu corporation), magnetic stirrer 5MLH DX (Remi Japan), film former (VJ instruments, Mumbai), pH meter (Elico Ltd Hyderabad), Glassware (Borosil), dissolution apparatus (Lab India Disso 8000), weighing balance (SHIMADZU ELB 300).

2.1 Method Used

Oral film was prepared by the solvent casting method. In a beaker distilled water (solvent) of the required amount is taken. Using a magnetic bead, the water was stirred, to this HPMC E50 LV (polymer) of required quantity was added. This solution named as solution A. Drug is separately mixed in solvent water named as solution B. Solution B was mixed with solution A slowly until uniformly mixed. To this mixture of solutions different super disintegrants as mentioned in formulation F1 – F9 (Table 1) were added based on formulation requirements. After obtaining a homogenous solution, PEG was added as a plasticizer. Aspartame is added as a sweetener and mixed using a magnetic stirrer (5 MLH Remi). The obtained solution was kept aside for about 15 minutes to make it bubble-free, and spread using a spreader on a film former apparatus. The temperature was set to 40°C. After drying we get a thin layer of film which is then removed and evaluate.

The following (Table 1) formulations were based on polymers which are having different properties. HPMC E50 is having a good film-forming property, optimized concentration for film-forming capacity was found to be 5% w/v by trial and error method. Sodium starch glycollate has a good swelling capability 700% of its original size, disintegrates film when gets contact with water. Microcrystalline cellulose on the other hand having a good contact angle with water helpful in quick disintegration and release of the drug. Crospovidone absorbs water via capillary action which helps in faster disintegration of prepared films. Propylene glycol is imparting an important property of film for the elegant look, elasticity, and folding endurance property. The last 3 formulas in (Table 1) are optimized based on selected superdisintegrants and their combinations.

3. EVALUATION

3.1 Preparation of Standard Graph of Favipiravir

10 mg of favipiravir was dissolved in 10ml of water using a cyclo mixer. This solution is referred to as a standard solution. From the standard solution, 10 µg/ml stock solution was made and scanned in the range of 200 to 400 nm using a UV-VIS spectrophotometer. The obtained peak wavelength is selected as λ_{max}. The obtained spectrum is 235 nm. Different stock solutions of 3,6,9,12, and 15 µg/ml were prepared and observed for their linearity. The standard curve was plotted.

3.2 Thickness

10 films were selected randomly and thickness was measured using screw gauge (20×1/100). The four corners of each film and the center of the film thickness is measured and average thickness of each films is calculated [12].

3.3 Physical Appearance and Texture Analysis

By visually inspecting the film some parameters were measured by feel and touching the film [13].

3.4 Weight Variation

10 films were randomly selected for every formulation made. The average weights of films were calculated [14].

3.5 Content Uniformity

The formulated films were cut into required size (3×4 cm^2) and taken in a 100ml volumetric flask containing 6.8 pH phosphate buffer [15]. The solution was sonicated for 20 minutes and an aliquot of solution was filtered through a 0.22-micron filter and UV absorbance was measured at 235 nm against blank. Using a standard graph, the concentration of solution was measured.

Table 1. Formulation of favipiravir orodispersible tablets

S. No	Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
1	Favipiravir (mg)	200	200	200	200	200	200	200	200	200	200	200	200
2	HPMC E50 (%w/v)	5	5	5	5	5	5	5	5	5	5	5	5
3	Sodium Starch Glycollate (%w/v)	2	4	6	-	-	-	-	-	-	2	-	2
4	Microcrystalline cellulose (%w/v)	-	-	-	2	3	4	-	-	-	-	2	2
5	Crospovidone (%w/v)	-	-	-	-	-	-	1	2	3	1	1	-
6	Propylene glycol (ml)	2	2	2	2	2	2	2	2	2	2	2	2
7	Aspartame (mg)	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25
8	Water (ml)	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s

3.6 Folding Endurance [16]

Folding endurance of films are measured to know the withstanding capability of films at the time of packing. The procedure involved is repeatedly folding a small strip of the film till it was broken. The number of times the film folds without any breaks gives the folding endurance value of the film.

3.7 Surface pH of the Film

The surface pH may be measured to avoid possible irritation to the mouth by the acidic or basic nature of the film. The surface pH of the prepared films was measured using a pH meter. The film was taken along with 1 ml of distilled water. Kept at room temperature for 1 hour [17].

3.8 Percent Moisture Loss, Absorption [18]

3 films of different formulations are taken and weighed, and placed in a desiccator containing calcium carbonate for 72 h. After 72 h the patches are weighed and taken as final weight. The moisture loss was calculated using the formula given below.

$$\text{percent moisture loss} = \frac{\text{initial weight} - \text{final weight}}{\text{initial weight}} \times 100$$

Moisture uptake of the oral film was determined by exposing the film at 75% relative humidity for 72 h and the percent moisture uptake was calculated using the below formula

$$\text{percent moisture uptake} = \frac{\text{final weight} - \text{initial weight}}{\text{final weight}} \times 100$$

3.9 *In vitro* Disintegration

The film was cut into 3×4 cm^2 as a unit dose. This film was placed on a petri dish containing 10 ml of distilled water [13]. The time required for a film to disintegrate is noted. The results are varying from 28 to 43 seconds depends upon the concentration of polymer used, the detailed result is given in (Table 3).

3.10 *In vitro* Dissolution

Drug release from the prepared oral films was studied using dissolution test apparatus. The desired formulations were placed in the vessels containing 900ml of 6.8 pH phosphate buffer. USP type 1 basket type apparatus was used. Samples were collected at regular intervals for 15 minutes. The percent (%) of drug released or dissolved was calculated. 3 films of every formulation were taken individually and the mean is calculated.

4. RESULTS AND DISCUSSION

4.1 Drug Excipient Compatibility [19]

Analysis of pure drug and excipients physical mixture was done using FTIR pellet press method using Potassium Bromide. And obtained graphs were observed for their spectra wavelengths.

Drug-excipient compatibility studies carried out using FTIR.

In (Fig. 1) favipiravir API pellet was made and scanned in FTIR from 400-4000cm^{-1} the principle stretching peaks found, C=O stretching around 1670.54cm^{-1}, C-F stretching around 1264.43 cm^{-1}, C-OH stretching around 1184.99 cm^{-1}, N-H stretching around 3610 cm^{-1}.

In (Fig. 2) spectra of drug with HPMC E50 shows no interaction with drug peaks when compared to standard graph of pure drug favipiravir. (Figs. 3, 4, 5) which is a mixture of drug and superdisintegrants (SSG, MCC, CPV) also shows similar spectra in stretching, indicating there is no incompatibility with API used.

4.2 Standard Calibration Graph

From the standard spectrum (Fig. 6) we can observe that the maximum wavelength is 235nm. The standard spectrum is considered important to know at what wavelength favipiravir API is giving the highest peak. From (Fig. 6) we can observe two peaks with different wavelengths and absorbance. At 360nm the obtained absorbance is 0.642 and at 235 it is 0.680. So, all the obtained stock solutions were scanned using UV-Spectrophotometer to get standard calibration (Graph 1).

From (Graph 1) we can observe that the regression obtained is 0.9997 which is having good linearity. The graph was ploted using excel, concentration (µg/ml) vs absorbance.

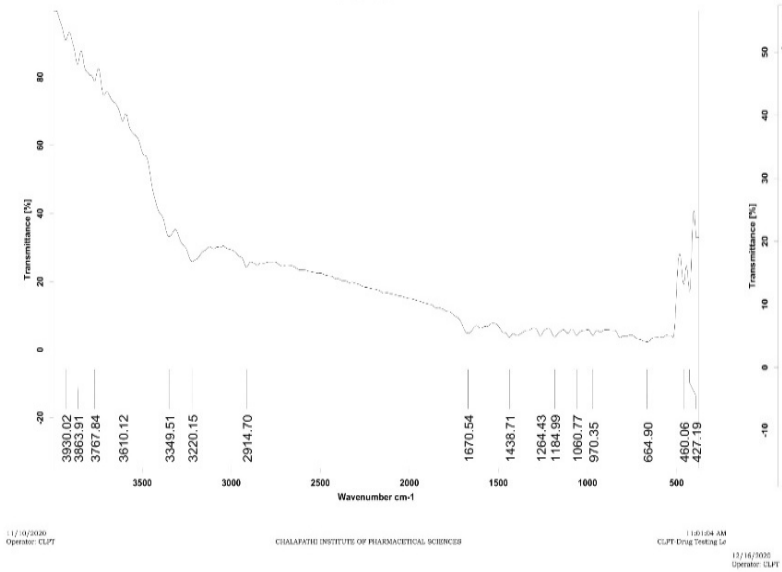


Fig. 1. FTIR spectra of pure drug favipiravir

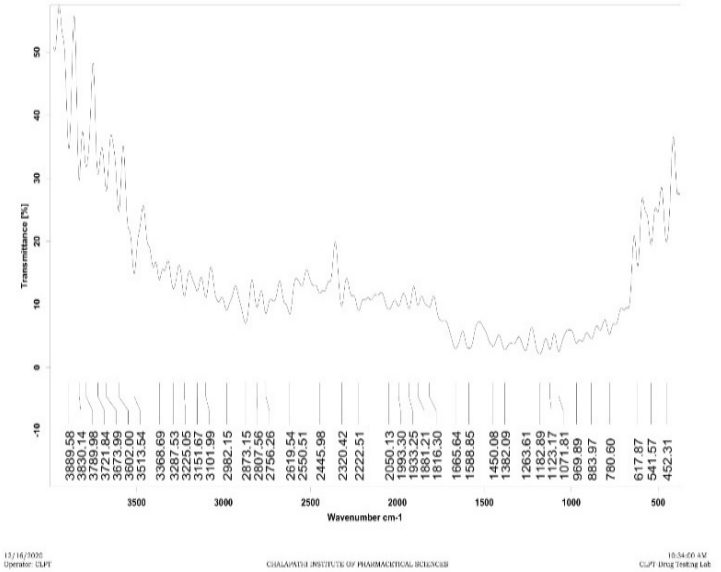


Fig. 2. FTIR spectra of mixture favipiravir and HPMC E50

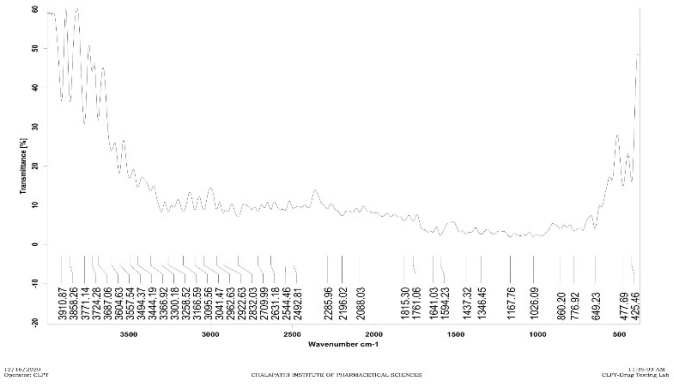


Fig. 3. FTIR spectra of mixture favipiravir and SSG

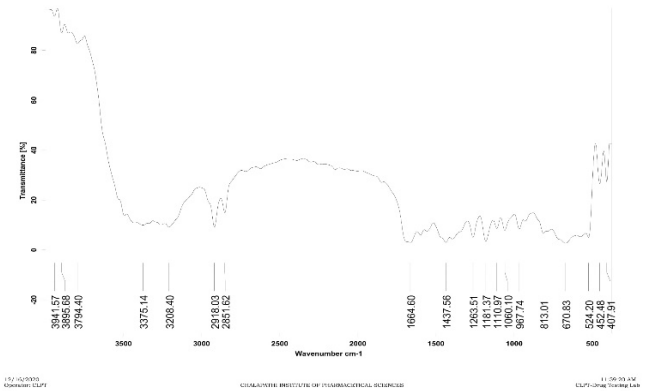


Fig. 4. FTIR spectra of mixture favipiravir and MCC

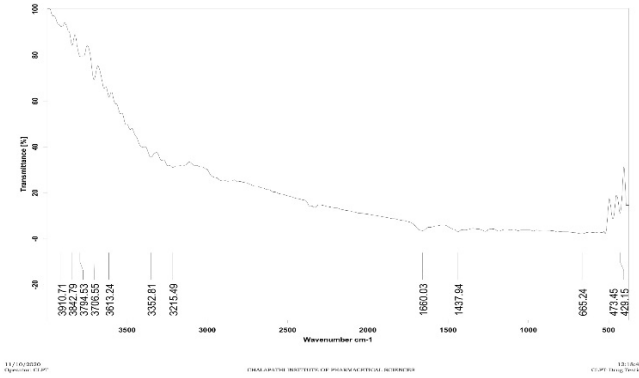


Fig. 5. FTIR spectra of mixture favipiravir and CPV

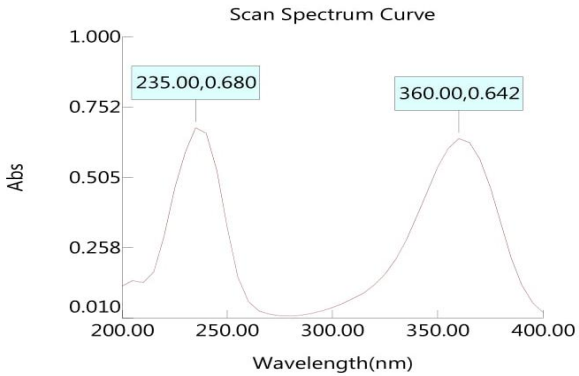
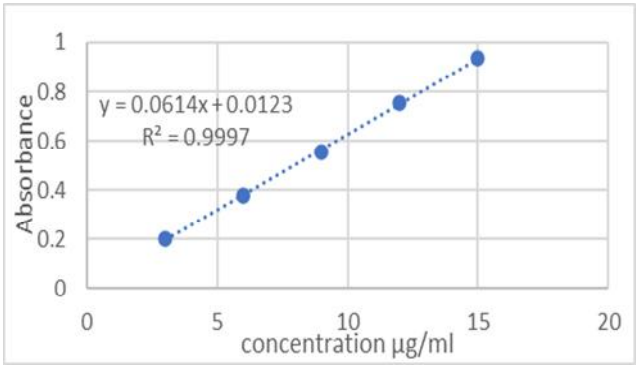


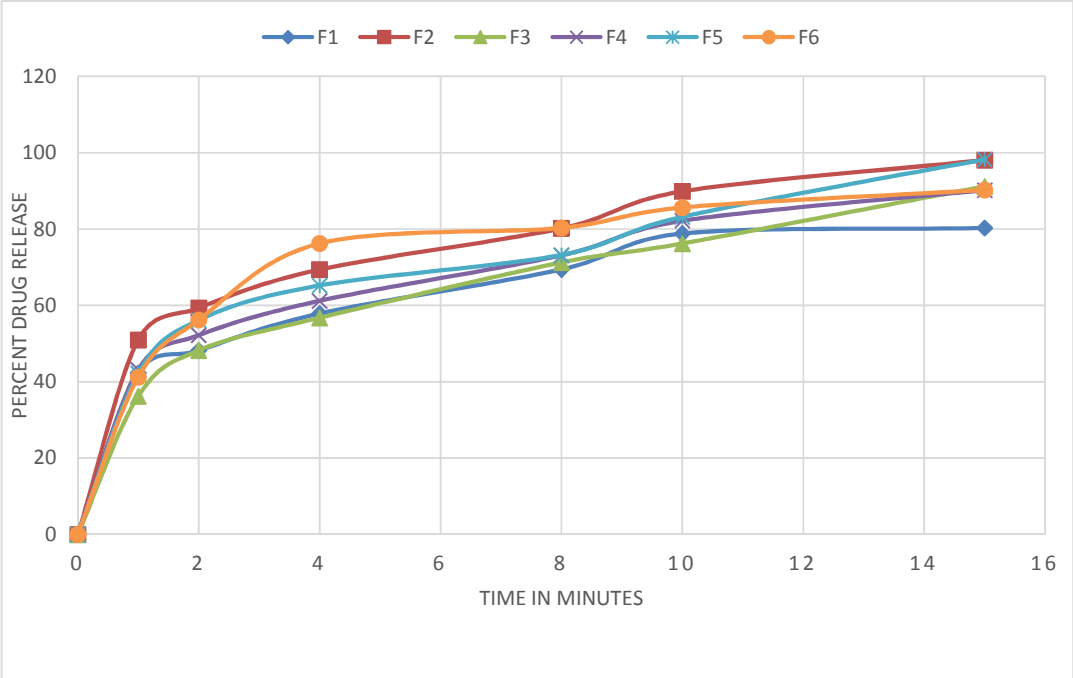
Fig. 6. UV spectrum standard graph of favipiravir



Graph 1. Standard calibration graph of favipiravir

Table 2. pH of different formulations

Formulation code	pH	Result
F1	6.81	Pass
F2	6.62	Pass
F3	6.83	Pass
F4	6.67	Pass
F5	6.62	Pass
F6	6.84	Pass
F7	6.65	Pass
F8	6.64	Pass
F9	6.62	Pass
F10	6.80	Pass
F11	6.71	Pass
F12	6.78	Pass



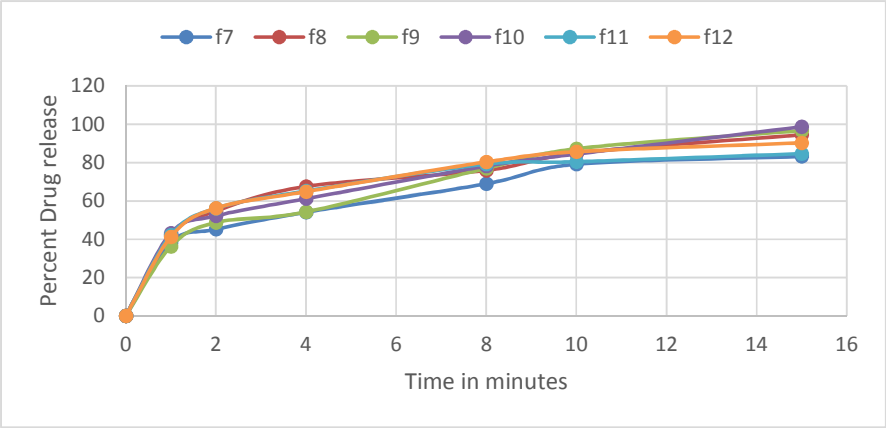
Graph 2. *In vitro* data of formulations f1-f6

Surface pH: All the prepared films have pH ranging from 6.6-6.8 which is similar to saliva pH in the mouth, it does not irritate. (Table 2) shows detailed information about the pH of different formulations. Explains that the disintegrants used don't have any significant effect on the pH of the prepared films.

From Table 3 we can observed that the thickness of the film increased with increased concentration of superdisintegrants, even though they didn't influence the disintegration time significantly. But due to patient acceptance importance, the physical appearance of the film is an important criterion, in which F5, F6, F11, and F12 having unfavourable results due to their organoleptic property. All films are having good moisture loss and absorption in acceptance criteria. Content uniformity of all the films was not affected by superdisintegrants but the folding endurance significantly affected by superdisintegrants F1, F4, F5, F6, and F8 has poor folding endurance. The disintegration time for the prepared films is around 30-40 seconds. But considering the film should disintegrate under 30 seconds as a key parameter, only F2 and F10 disintegrated under 30 seconds completely whereas the remaining formulations took 30-42 seconds.

Table 3. Various evaluation tests of films (n=3)

Formulation code	Thickness (mm)	Physical appearance	Texture	Content uniformity (mg)	Weight variation	Percent moisture Loss (%)	Percent moisture absorption	Folding endurance	Disintegration time in seconds
F1	0.136±0.05	Transparent	Smooth	98.8±0.36	148.3±0.26	4.46±0.11	6.14±0.03	55±1	35±0.57
F2	0.172±0.06	Transparent	Smooth	100.13±0.9	199.9±0.7	4.6±0.1	6.24±0.02	98±4.72	30±1
F3	0.153±0.03	Transparent	Smooth	99.36±0.15	237.83±1.16	4.79±0.09	6.75±0.05	99±3.15	39±1.5
F4	0.198±0.025	Transparent	Smooth	98.3±0.26	151.23±0.35	4.98±0.1	6.67±0.04	56±2.21	34±0.46
F5	0.265±0.01	Translucent	Rough	100.73±0.72	181.42±0.57	5.26±0.075	6.59±0.08	62±2.41	35±1
F6	0.284±0.014	Translucent	Rough	99.4±0.3	200.3±0.242	5.33±0.17	6.47±0.05	67±2.36	42±0.35
F7	0.178±0.048	Transparent	Smooth	99.1±0.17	121.08±0.24	4.52±0.045	6.77±0.03	56±4.58	33±1
F8	0.284±0.029	Transparent	Smooth	99.26±0.2	151.096±0.46	4.7±0.06	6.67±0.03	65±6.21	34±1.56
F9	0.271±0.03	Transparent	Smooth	99.16±0.11	181.02±0.75	4.8±0.05	6.43±0.04	96±1	32±1.21
F10	0.231±0.05	Transparent	Smooth	98.3±0.26	188.06±0.77	4.69±0.08	7.67±0.04	101±1.57	28±1.37
F11	0.367±0.01	Translucent	Rough	100.8±0.6	180.87±0.56	4.75±0.03	7.19±0.02	98±0.57	37±1
F12	0.398±0.016	Translucent	Rough	99.38±0.36	200.44±0.49	4.81±0.02	7.29±0.07	99±0.46	33±0.57



Graph 3. *In vitro* data of formulations F7-F12

4.3 *In-vitro* Dissolution Studies

From (Graph 2) and (Graph 3) various formulations percent drug release with respect to time is given was plotted. It is observed that increased concentrations of superdisintegrants affected the release of the drug. At low and high concentrations of these superdisintegrants SSG, MCC the release of drug at 15 minutes is below 95%. But at medium concentrations the percent drug release is good observed in F2, F5, F8, F9, and F10. Formulations with CPV at all concentrations shown good drug release characteristics. F10, F11, F12 are formulated with a combination of superdisintegrants, the formulation with CPV and SSG in combination shows drug release 98% at 15 minutes.

5. CONCLUSION

The objective of the present investigation has been achieved by preparing orodispersible films of favipiravir 100mg usable to treat COVID-19. Believing in the future prospective favipiravir may be used for the treatment of other influenza virus strains. From various formulations, it is estimated that as the concentration of superdisintegrants increases the thickness is also increasing as we have seen in formulations F3, F6, F9. The formulations involved with microcrystalline cellulose gave a rough surface on the film however F4 shows at a low concentration giving smooth surface texture. Of all the formulations it is identified that formulations F2 and F10 are found to be good when compared to other formulations.

DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

ACKNOWLEDGEMENT

The author wish to appreciate Dr. Madhu Gudipati, Head of the Department of Pharmaceutics, Chalapathi Institute of Pharmaceutical Sciences (Autonomous) for the support during the research and Prof. Rama Rao Nadendla, Principal for his sacrifices in providing laboratory support services.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. MS A, CV. Formulation and evaluation of fast dissolving oral films of diazepam. J Pharmacovigil. 2016;4(3):1–6.
2. Takehisa Hanawa, Atsushi Watanabe, Takanori Tsuchiya, Rieko Ikoma, Masato Hidaka MS. New oral dosage form for elderly patients: Preparation and characterization of silk fibrion gel. Chem Pharm Bull. 1995;43(2):284–8.
3. Dixit RP, Puthli SP. Oral strip technology: Overview and future potential [Internet]. Journal of Controlled Release. Elsevier B.V. 2009;139:94–107.
   Available:http://dx.doi.org/10.1016/j.jconrel.2009.06.014
4. Bhyan B, Jangra S, Kaur M, Singh H. Orally fast dissolving films: Innovations in formulation and technology. International Journal of Pharmaceutical Sciences Review and Research. 2011;9:50–7.
5. Siddiqui MDN, Garg G, Sharma PK. A short review on “a novel approach in oral fast dissolving drug delivery system and their patents” conventional oral modified release fast action oral solid. Int J Pharm Sci Rev Res. 2011;5(6):291–303.
6. Joshi S, Parkar J, Ansari A, Vora A, Talwar D, Tiwaskar M, et al. Role of favipiravir in the treatment of COVID-19. Int J Infect Dis [Internet]. 2021;102:501–8.
   Available:https://doi.org/10.1016/j.ijid.2020.10.069
7. Furuta Y, Komeno T, Nakamura T. Favipiravir (T-705), a broad spectrum inhibitor of viral RNA polymerase [Internet]. Proceedings of the Japan Academy Series B: Physical and Biological Sciences. 2017; 93;449–63.
   Available:https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5713175/pdf/pjab-93-449

8. Nagata T, Lefor AK, Hasegawa M, Ishii M. Favipiravir: A new medication for the ebola virus disease pandemic. Disaster Med Public Health Prep. 2015;9(1):79–81.
9. Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y, et al. Early transmission dynamics in Wuhan, China, of Novel Coronavirus–Infected Pneumonia. N Engl J Med. 2020;382(13):1199–207.
10. Kaur RJ, Charan J, Dutta S, Sharma P, Bhardwaj P, Sharma P, et al. Favipiravir use in COVID-19: Analysis of suspected adverse drug events reported in the WHO database. Infect Drug Resist. 2020;13: 4427–38.
11. Gülhan B, Özkaya Parlakay A. Çocuklarda COVID-19 Tedavisi. Turkish J Pediatr Dis. 2020;9–14.
12. Kulkarini Parthasarathi Keshavarao, Dixit Mudit GK. Formulation and evaluation of mouth dissolving film containing rofecoxib. Int J Pharm. 2011;2(3):273–8.
13. Kanth NP, Prasad G, Kumar BV. Oral dissolving films of chlorpheniramine maleate. Int J Pharm Sci Res [Internet]. 2014;5(5):1859–73.
Available:http://www.wjpr.net/download/article/1404198266.pdf
14. Reyad-ul-Ferdous, Shahjahan DS. Effective development and evaluation of oral thin film of etoricoxib. World J Pharm Res. 2015;4(9):257–72.
15. Alam M, Tasneem F, Pathan MSI. Formulation and evaluation of swellable oral thin film of metoclopramide hydrochloride. Bangladesh Pharm J. 2015; 17(1):102–12.
16. Nishimura M, Matsuura K, Tsukioka T, Yamashita H, Inagaki N, Sugiyama T, et al. *In vitro* and *in vivo* characteristics of prochlorperazine oral disintegrating film. Int J Pharm. 2009;368(1–2):98–102.
17. Raza SN, Kar AH, Wani TU, Khan NA. Formulation and evaluation of mouth dissolving films of losartan potassium using 32 Factorial design. Int J Pharm Sci Res [Internet]. 2019;10(3):1402–11.
Available:http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L626825396%0Ahttp://dx.doi.org/10.13040/IJPSR.0975-8232.10(3).1402-11
18. Madhu Gudipati and Ramarao Nadendla. Formulation and Evaluation of biopolymers coated pellets of cyclophosphamide for colon drug delivery. Eur J Biom Pharm Sci. 2017;4(12):721-727.
ISSN: 2349-8870.
19. Sreekanth M, Gulshan M, Gupta EM, Rama Rao N. Design and evaluation of ORO - Flash release films of amlodipine besylate. Int J Pharm Sci Res [Internet]. 2014;5(6):2428–35.
Available:http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L373204609%0Ahttp://dx.doi.org/10.13040/IJPSR.0975-8232.5(6).2428-35

Peer-review history:
The peer review history for this paper can be accessed here:
http://www.sdiarticle4.com/review-history/65615