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Fabrication And Characterization of 3D Printed Fast Dissolving Oral Films of Ivabradine Hydrochloride

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Abstract

Three-dimensional (3D) printing technology is gaining significance due to its wide applications, rapid prototyping and customization. Fast-Dissolving Oral Films (FDOFs) provide an alternative approach to increase consumer acceptance by advantage of rapid disintegration and dissolution and administration without water. Combination of fused deposition modelling with preparation of the FDOFs seems to be extra advantageous in terms of pharmaceutical parameters. Ivabradine Hydrochloride was selected for formulating FDOF which is an Anti-Anginal drug. The aim of the present study is to fabricate filament extruder and 3D printed fast dissolving oral films by FDM technique and to check the influence of disintegrant on disintegration time and drug release kinetics. For FDM 3D printing technique the polymers were converted into filaments by using extrusion process. The drug loaded filaments were prepared by using hydrophilic polymers viz. PVA and HPC SL along with Sodium Starch Glycollate as Super-disintegrants and Polyethylene Glycol 400 as plasticizer and the drug. The drug loaded filaments were introduced into 3D printer and FDOF were printed at 185°C (HPC SL) and 195°C (PVA). Preformulation studies and compatibility studies (DSC, FT-IR) were done. The films were evaluated for physicochemical parameters and mechanical strength. All the formulations exhibited more than 90% of drug release within 15 minutes. The optimized formulation, P3 was selected as it showed lowest disintegration time of 42.33 ± 1.15 sec and faster dissolution rate of 99.22% with a release time of 8 minutes. The morphology of the films was studied by SEM analysis.

Keywords

Ivabradine HCl, 3D printing, Fast Dissolving Oral film, HPC.

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INTRODUCTION

Three-dimensional printing (3DP) is the leading-edge technology with the potential to vary the means by which the drug products are designed, produced and prescribed. 3D printing also known as additive manufacturing by developing the 3D model, owing to the layer-by-layer manner of manufacturing of a component. Such technology can greatly benefit areas wherein dose individualization or patient specific dose is required and also prototyping due to effortless customization. As such this technology would merge the worlds of imagination and reality significantly. There are several 3DP technologies, but Fused Deposition Modelling (FDM) is the most extensively researched 3DP technique among pharmaceuticals.

Fast Dissolving Oral Films (FDOF) are thin drug loaded polymeric films for oral use when placed on or under the tongue or in the buccal cavity, dissolves rapidly upon contact with saliva within seconds to few minutes without the need of water. Upon hydration, it adheres to the oral or buccal cavity, disintegrates and dissolves thereby releasing drugs for oro-mucosal absorption thus increasing the efficacy of the drug. FDOF have proved advantageous in improving patient compliance in dysphagia patients and also when a rapid onset of action is needed.

Formulation of oral films involves the complex application of aesthetic and performance characteristics such as taste masking, fast dissolving, physical appearance, pleasant taste, stability etc. Ivabradine was Introduced in European Medicines license in 2005 and a "pure" heart rate lowering agent is used in the management of stable angina. It acts by blockade of cardiac pacemaker (sino-atrial) cell "f" channels which are "funny" cation channels that open during early part of slow diastolic (Phase 4) depolarisation. Selective blockade of If current by Ivabradine results in heart rate reduction which further decreases cardiac oxygen demand and prolongation of diastole tends to improve perfusion i.e oxygen supply. It is well absorbed orally and 40% bioavailable due to first pass metabolism, metabolised by CYP3A4 and excreted in urine with a t½ of 2 h. It is BCS class I drugs owing good solubility and permeability.

RESEARCH METHOD

Fabrication of Drug Loaded Filaments: 3D Printed FDOF's of Ivabradine HCl were fabricated by Fused Deposition Modeling technique involving 2 steps procedure viz fabrication of drug loaded filaments and fabrication of FDOF by 3D printing process. Polymers used were HPC and PVA possessing hydrophilicity, HME property and suitable for the formulation of oral dosage forms. The composition of FDOF is illustrated in Table No. 1.

Table No. 1: Composition of each 3D Printed Fast Dissolving Oral Film

Formulation Code	Ivabradine HCl (%w/w)	HPC SL (%w/w)	PVA PE-05JPS (%w/w)	SSG (%w/w)	PEG 400 (%w/w)
P1	5	90	-	-	5
P2	5	88.5	-	4	2.5
P3	5	84.5	-	8	2.5
P4	5	-	87.5	-	7.5
P5	5	-	86	4	5
P6	5	-	82	8	5

Procedure:

a. Drug and excipients were accurately weighed and transferred into a mortar.
b. Contents were ground to form fine powder by using mortar and pestle.
c. The powder was then transferred into a clean, dry beaker and required quantity of plasticizer was added and closed properly. The powder was mixed for 20 minutes on a magnetic stirrer to obtain a uniform mixture.
d. The temperature of the extrusion barrel was set at 180°C for HPC SL and 190°C for PVA and was allowed to thermally equilibrate for 15 min.
e. The speed of the screw was programmed at 30RPM and nozzle with a diameter of 1.6 mm was fitted to the barrel.
f. The contents were charged into the hopper of single screw filament extruder and extrusion process was carried out.
g. The hot soft extruded filament was cooled and solidified by blowing air.
h. The filaments diameter was measured every 50-100 mm using digital vernier calliper to ensure uniformity of the filament.
i. The extrudate filaments were packed in air-tight plastic bags to avoid any moisture absorption before 3D printing of FDOF was performed.

Fabrication of FDOF by 3D Printing:

a. FDOF'S were printed by using FDM Flashforge Finder 3D Printer (Zhejiang Flashforge3D technology Co.
b. China).
c. Three dimensional digital templates of the films were designed in AutoCAD 2019 software (Autodesk Inc. USA).
d. The digital film models were designed by cube modification with dimensions of 20 mm length and 20 mm width and 0.2 mm height. The 3D models were exported as stereolithography files in. stl format.
e. 3D printing slicing software Flashprint 2019 (Zhejiang Flashforge3D Technology Co. China)

was used to export the 3D design in the 3D printer by converting. stl format files into. gcode format that are readable by the 3D printer software.

f. The printer extrusion parameters were set at 100% infill, shells (n=3) and 0.2 mm of layer height.
g. Extruder nozzle with a diameter of 0.2 mm was fixed to printer head and the extruder temperature was set at 185°C and 195°C for HPC SL and PVA drug loaded filaments respectively.
h. The travelling speed was programmed at 30 mm/s for HPC SL and 50 mm/s for PVA.
i. The slicing software displayed the quantity of drug loaded filament to be used for 3D printing the required quantity of films by feeding in the necessary attributes of the filaments.

RESULTS AND DISCUSSION:

Standardization of Ivabradine Hydrochloride:

1.Determination of λ_{max} of Ivabradine Hydrochloride.

A solution of 10 µg/ml of Ivabradine HCl was prepared in Phosphate buffer pH 6.8. This solution was scanned in the UV range of 200- 400 nm. The wavelength of maximum absorbance (λmax) of pure drug Ivabradine HCl was observed to be 286 nm (Figure No. 1).

2. Preparation of Calibration curve of Ivabradine in Phosphate buffer pH 6.8.

Standard Calibration curve of Ivabradine HCl was drawn by plotting absorbance obtained at 286 nm v/s concentrations (µg/ml). The Standard calibration plot for the same along with equation of line and regression coefficient are shown in Figure No. 2.

Compatibility studies

1. FT-IR Spectroscopy Analysis:

FT-IR spectra of pure drug Ivabradine HCl and physical mixture of drug with individual excipients are shown in Figure Nos. 3 -5. Evaluation of IR spectrum of pure Ivabradine and spectra of physical mixture of drug and excipients indicated that there was no significant interaction between the drug and excipients. Hence, it can be concluded that the drug is compatible with the excipients.

2. Differential Scanning Calorimetry (DSC) analysis:

Calorimetric evaluation of Ivabradine HCl and the drug in combination with the individual polymers were carried out to ascertain the purity of the drug and the compatibility of drug with the individual polymer. The DSC thermogram of pure Ivabradine exhibited its characteristic endothermic peak at 199.20°C.

The thermograms of the pure drug when compared with that of the physical mixtures of Ivabradine with HPC SL and PVA displayed endothermic peak at 192.16°C and 192.91°C, thus indicated that there is no significant interaction of Ivabradine with the polymers. DSC Thermogram of drug and its physical mixture are shown in Figure Nos. 6-8.

Formulation of 3D printed FDOF by FDM

Ivabradine HCl Fast Dissolving Oral Films were fabricated by Fused Deposition Modeling technique. Here, the fabrication of films involves two steps:

i. Fabrication of drug loaded filaments

ii. Fabrication of Oral films by 3D printing six different formulations with varying amounts of excipients were formulated and tested.

The formulations prepared are shown in Table No. 1.

i. Fabrication of Drug loaded filaments

Selection of Polymers

High melting point polymers were chosen which had melting point/ softening temperature close to the melting point of the drug in order to achieve uniform solid dispersion. This also contributed to the prevention of thermal degradation of drugs and excipients and avoiding poor dispersion of drug in the filament.

Polymers not only act as carriers of the drug but also contribute to the mechanical strength of filament necessary during the printing process. The motive was to compare two hydrophilic polymers such as HPC SL and Polyvinyl alcohol (PVA) since many researchers have worked on 3D printing using PVA by FDM technique.

Hydrophilic Polymers such as Polyvinyl alcohol (PVA) and Hydroxypropyl cellulose (HPC-SL) showed exceptional extrusion properties and film forming properties. Both these polymers possessed identical melting point/softening temperatures, low viscosity and minimal resistance during extrusion.

Drug

The amount of drug to be loaded in the film was determined by the dose considerations of Ivabradine HCl in a unit film and the average dimensions of filament and film. Ivabradine HCl possesses outstanding aqueous solubility and the dose of drug per film (5 mg) was far lesser than the practical solubility of the drug (>100 mg/mL). Therefore, it can be ascertained that dose will be fully solubilised in minimum amount of oral saliva in significantly less time.

Selection of Plasticizer

Two plasticizers namely Polyethylene Glycol (PEG 400) and Propylene Glycol (PG) were tested during blank trials. PG produced filaments with significantly lower mechanical strength and as compared to that of PEG infused filaments and fumes were generated

during extrusion process on account of extrusion temperature being close to the boiling point of PG whereas PEG has a higher boiling point. The PG + polymer filament stretched exorbitantly under its own weight after extruding out leading to poor filament structure and characterised by irregular shape making it unfit for printing stage. PEG produced less lustrous filaments but were characterised by good mechanical properties such as rigidity and flexibility. During extrusion of HPC filaments, the concentration of plasticizer added was lower than that of PVA owing to its low viscosity and also depression in Glass transition temperature. The concentration of plasticizer above 6% produced HPC filaments of springy nature and less rigid.

Super-disintegrant

They played a crucial role in the formulation of FDOF's as they aided in disintegration of the film at a faster rate. This subsequently resulted in the faster dissolution of the film due to increased effective surface area.

Characterisation of Ivabradine HCl Fast Dissolving Films

General Appearance: All the formulations of fast dissolving films were fabricated into definite sizes of dimensions 20 mm in length and 20 mm in breadth. All the films appeared off white to light yellow, semitranslucent to opaque. The films were flexible, smooth in texture and devoid of any odour or visible deformities.

Weight Variation: The results of the weight variation tests are shown in Table No. 3. The results obtained can be correlated to the type and amount of polymer and concentration of disintegrant and plasticizer. Data was recorded in triplicate and analysed for mean and standard deviation.

Thickness: The observed thickness of films was found to be approximately constant and can be correlated to the formulation parameters and die swell effect. Results indicated are acceptable for oral administration.

The resulting thickness of the formulated films is presented in Table No. 4.

Folding Endurance: The results obtained can be correlated with the amount and the type of polymer and also the concentration of plasticizer used for the formulation. The results of the folding endurance are shown in Table No 5. The measurements were recorded in triplicate.

Tensile Strength: The results of the tensile strength are given in the Table No. 6 and data was recorded in triplicates and calculated for mean and standard deviation. The results revealed moderate values of tensile strength for the films and showed a correlation among the different formulation depending on the type of the polymer employed and the amount of plasticizer used in each formulation.

Percent Elongation: The results of the percent elongation are presented in Table No. 7. The measurements were taken in triplicate, and the mean and standard deviation was calculated.

Drug Content Uniformity: The percent drug content ranges from 91.31% to 96.04 % and all found to be within acceptable limits. The results obtained for drug content uniformity are shown in Table No.8.

Surface pH: The pH values ranged from 6.08 ± 0.02 to 6.86 ± 0.0964. All the formulations presented nearly neutral pH which indicated safe for oral administration. The measurements were taken in triplicate, and the mean and standard deviation was determined. The surface pH results are tabulated in Table No. 9.

Percent Moisture Loss: The results of percent moisture loss are shown in Table No. 10, and measurements were taken in triplicate wherein the mean and standard deviation was calculated for the same. The percent moisture loss values ranged from 0.42% ± 0.1074 to 0.82% ± 0.1964.

Percent Moisture Content: The results of the percent moisture content are shown in the Table No. 11. The moisture content in the films can be predicted due to the presence of hygroscopic material and alcohol groups and also indicate the stability of the films. The moisture content values range from 4.76 ± 0.6474 to 5.73 ± 0.5924

In-vitro disintegration test: The results obtained when compared showed variation in their disintegration time due to the amount of disintegrants and the concentration of polymer used in the formulation. Formulation P1 and P4 showed longer disintegration time due to the absence of disintegrants. The results of the in vitro disintegration test are shown in the Table No. 12 and ranges from 42.33 ± 1. 1547 sec to 176.33 ± 2.5166 sec.

Table No. 2: Filament diameter

Formulation Code	Filament Diameter (Mean ± S.D.) (mm)
P1	1.66 ± 0.06
P2	1.70 ± 0.05
P3	1.72 ± 0.03
P4	1.65 ± 0.05
P5	1.72 ± 0.02
P6	1.71± 0.04

Table No. 3: Weight variation (Mean ± S.D, n=3)

Formulation Code	Film 1 (mg)	Film 2 (mg)	Film 3 (mg)	Mean ± S.D. (mg)
P1	89.1	88.3	88.9	88.7 ± 0.4163
P2	96.0	95.8	94.5	95.4 ± 0.8145
P3	91.6	93.4	94.7	93.2 ± 1.5567
P4	103.9	102.7	102.7	103.1± 0.6928
P5	105.3	105.7	106.8	105.9 ± 0.7767
P6	107.7	107.9	107.6	107.7± 0.1528

Table No. 4: Thickness (Mean ± S.D, n=3)

Formulation Code	Film 1 (mm)	Film 2 (mm)	Film 3 (mm)	Mean ± S.D. (mm)
P1	0.22	0.22	0.21	0.2167 ± 0.0058
P2	0.20	0.21	0.20	0.2033 ± 0.0058
P3	0.20	0.20	0.21	0.2033 ± 0.0058
P4	0.20	0.22	0.21	0.21 ± 0.01
P5	0.21	0.20	0.21	0.2067 ± 0.0058
P6	0.21	0.20	0.20	0.2033 ± 0.0058

Table No. 5: Folding Endurance (Mean ± S.D, n=3)

Formulation Code	Film 1	Film 2	Film 3	Mean ± S.D.
P1	33	35	32	33.33 ±1.528
P2	32	31	32	31.67 ± 0.577
P3	29	32	31	30.67 ± 1.528
P4	36	37	34	35.67 ± 1.528
P5	36	32	35	34.33 ± 2.082
P6	32	34	35	33.67 ± 1.52

Table No. 6: Tensile strength (Mean ± S.D, n=3)

Formulation Code	Film 1 (Kg/mm^2)	Film 2 (Kg/mm^2)	Film 3 (Kg/mm^2)	Mean ± S.D. (Kg/mm^2)
P1	0.408	0.449	0.496	0.451 ± 0.0438
P2	0.655	0.680	0.696	0.677 ± 0.0207
P3	0.628	0.643	0.661	0.644 ± 0.0165
P4	0.705	0.738	0.763	0.735 ± 0.0291
P5	0.846	0.820	0.861	0.842 ± 0.210
P6	0.805	0.825	0.846	0.825 ± 0.0203

Table No. 7: Percent Elongation (Mean ± S.D, n=3)

Formulation Code	Film 1 (%)	Film 2 (%)	Film 3 (%)	Mean ± S.D. (%)
P1	22.87	22.61	25.34	23.61 ± 1.5020
P2	14.25	14.51	15.09	14.62 ± 0.4293
P3	16.14	16.72	16.02	16.30 ± 0.3764
P4	13.63	12.67	12.20	12.83 ± 0.7279
P5	10.00	09.66	09.25	09.63 ± 0.3735
P6	11.01	11.05	10.44	10.83 ± 0.3418

Table No. 8: Drug content uniformity (Mean ± S.D, n=3)

Formulation Code	Film 1 (mg)	Film 2 (mg)	Film 3 (mg)	Mean ± S.D.	% Drug Content (%)
P1	4.8452	4.5226	4.3290	4.5656 ± 0.2607	91.31
P2	4.5871	4.7806	4.8452	4.7376 ± 0.1343	94.75
P3	4.7806	4.6516	4.9742	4.8022± 0.1624	96.04
P4	4.2000	4.7161	4.8452	4.5871 ± 0.3414	91.74
P5	4.6516	4.8452	4.7806	4.7591 ± 0.0986	95.18
P6	4.5226	4.5871	4.7161	4.6086 ± 0.0986	92.17

Table No. 9: Surface pH (Mean ± S.D, n=3)

Formulation Code	Film 1	Film 2	Film 3	Mean ± S.D.
P1	6.42	6.34	6.37	6.38 ± 0.0404
P2	6.07	6.06	6.10	6.08 ± 0.0208
P3	6.22	6.23	6.25	6.23 ± 0.0152
P4	6.82	6.97	6.79	6.86 ± 0.0964
P5	6.71	6.69	6.74	6.71 ± 0.0251
P6	6.56	6.67	6.69	6.64 ± 0.07

Table No. 10: Percent moisture loss (Mean ± S.D, n=3)

Formulation Code	Film 1 (%)	Film 2 (%)	Film 3 (%)	Mean ± S.D. (%)
P1	0.73	0.42	0.85	0.67 ± 0.2181
P2	0.42	0.32	0.53	0.42 ± 0.1074
P3	0.52	0.41	0.42	0.45 ± 0.0593
P4	0.67	0.76	1.04	0.82 ± 0.1964
P5	0.38	0.57	0.37	0.44 ± 0.11
P6	0.37	0.46	0.56	0.46 ± 0.0929

Table No.11: Percent moisture content (Mean ± S.D, n=3)

Formulation Code	Film 1 (%)	Film 2 (%)	Film 3 (%)	Mean ± S.D. (%)
P1	6.27	5.10	5.82	5.73 ± 0.5924
P2	5.64	5.26	4.77	5.22 ± 0.4335
P3	5.13	5.50	5.17	5.26 ± 0.2032
P4	5.25	4.55	5.79	5.20 ± 0.6234
P5	5.13	5.30	5.99	5.47 ± 0.4579
P6	4.09	5.38	4.38	4.76 ± 0.6474

Table No. 12: In vitro disintegration (Mean ± S.D, n=3)

Formulation Code	Film 1 (sec)	Film 2 (sec)	Film 3 (sec)	Mean ± S.D. (sec)
P1	152	156	155	154.33 ± 2.0817
P2	65	62	64	63.67 ± 1.5275
P3	41	43	43	42.33 ± 1.1547
P4	174	179	176	176.33 ± 2.5166
P5	76	80	77	77.67 ± 2.0817
P6	54	52	51	52.33± 1.5275

Table No. 13: Values of Regression Coefficient and Kinetics for all Formulations

Formulation Code	Zero Order		First Order		Higuchi Plot		Peppa's plot	
	R^2	K	R^2	K	R^2	K	R^2	n
P1	0.937	6.615	0.957	-0.087	0.948	27.46	0.964	0.687
P2	0.781	6.786	0.949	-0.156	0.955	27.85	0.971	0.338
P3	0.731	10.483	0.983	-0.251	0.935	35.354	0.952	0.309
P4	0.950	6.138	0.961	-0.071	0.965	25.518	0.975	0.691
P5	0.840	7.390	0.933	-0.152	0.966	29.417	0.911	0.502
P6	0.790	8.257	0.953	-0.196	0.957	30.57	0.972	0.313

***In-vitro* dissolution test:** Drug dissolution profiles for the formulations were obtained with a USP-I apparatus (basket type) using phosphate buffer pH 6.8 as the dissolution medium. The test was run for 15 min. The in vitro release profiles indicated that all the formulations released more than 90% of drug within 15 min. This could be attributed to high aqueous solubility of Ivabradine HCl belonging to BCS Class I and also hydrophilic nature of polymers used. However, the formulations containing super-disintegrant showed almost complete release in 8-12 min with P3 formulation exhibiting maximum release in shortest duration i.e 99.22% drug release within 8 min. The type of polymer used also influenced the duration for complete drug release that can be attributed to the difference in their hydrophilicity. The formulations containing SSG decreased duration to attain maximum release with increasing concentration. Hence, it is apparent that the presence of superdisintegrant influenced the fast release of the drug from the film.

The dissolution data were analysed using mathematical models to determine the drug release kinetics. The data of the plots was subjected to linear regression analysis. The models that best fits the data were evaluated by correlation coefficient (R2). The R2 values of zero order and first order plots were compared and it was noticed that R2 values of first order plots were close to 1 with highest correlation coefficient value of 0.983 and relatively higher than the zero order plots. This signifies that all the formulations followed first order kinetics.

Further, the data was treated to Higuchi equation, the correlation coefficient values of all the formulation obtained were found to be close to 1 with highest R2 value of 0.966 indicating that all formulations exhibited diffusion mechanism in drug release. Similarly, the drug release data was subjected to Peppa's model to understand the type of diffusion process and the 'n' value was derived. In most of the formulations "n" value was ≤0.5 thus concluding that the drug release follows Fickian diffusion type.

From the data obtained from all the models, it was deduced that the drug release through the film formulation is diffusion controlled following first order kinetics with Fickian diffusion mechanism.

Figure No. 1: UV-Spectra of Ivabradine HCl in Phosphate buffer pH 6.8

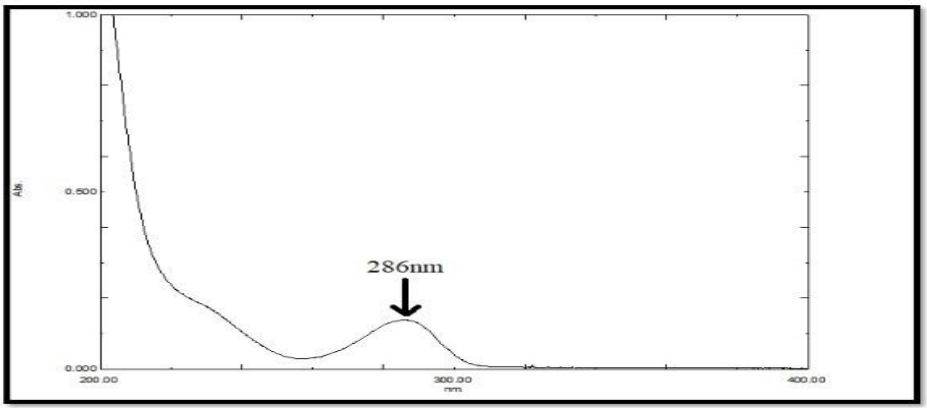


Figure No. 2: Standard calibration curve of Ivabradine HCl in Phosphate buffer pH 6.8

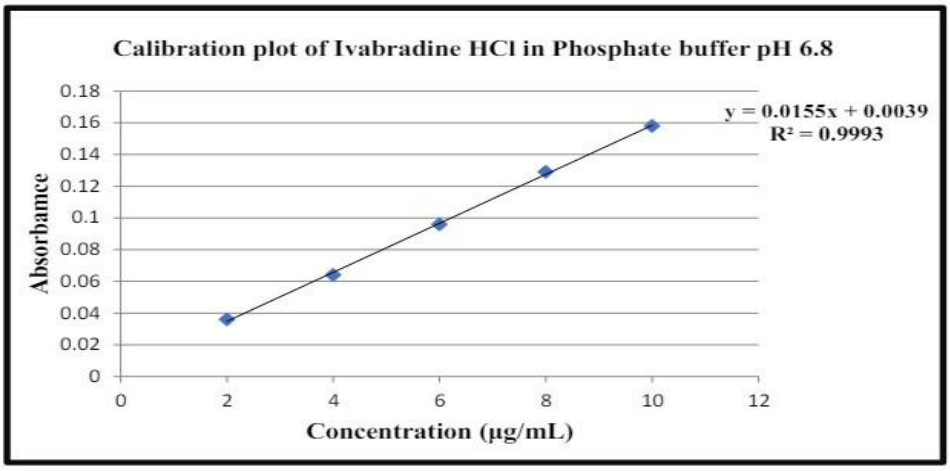


Figure No. 3: FT-IR Spectra of physical mixture of Ivabradine HCl & HPC SL

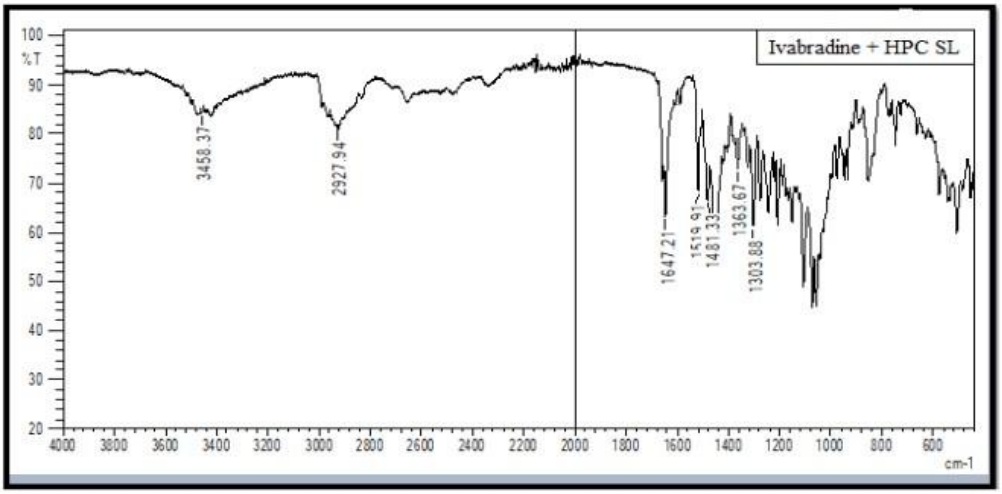


Figure No. 4: FT-IR Spectra of physical mixture of Ivabradine HCl & PVA

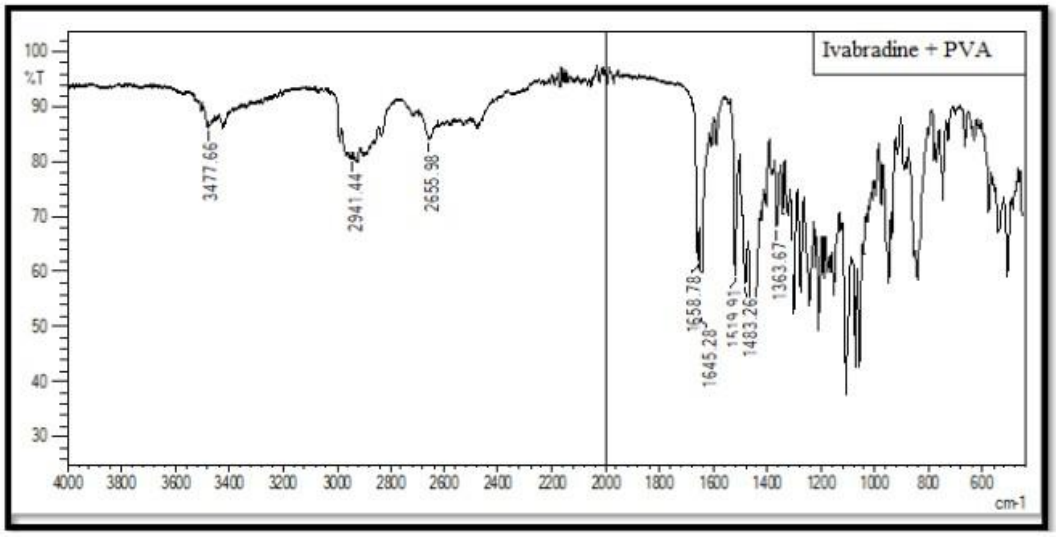


Figure No. 5: FT-IR Spectra of physical mixture of Ivabradine & SSG

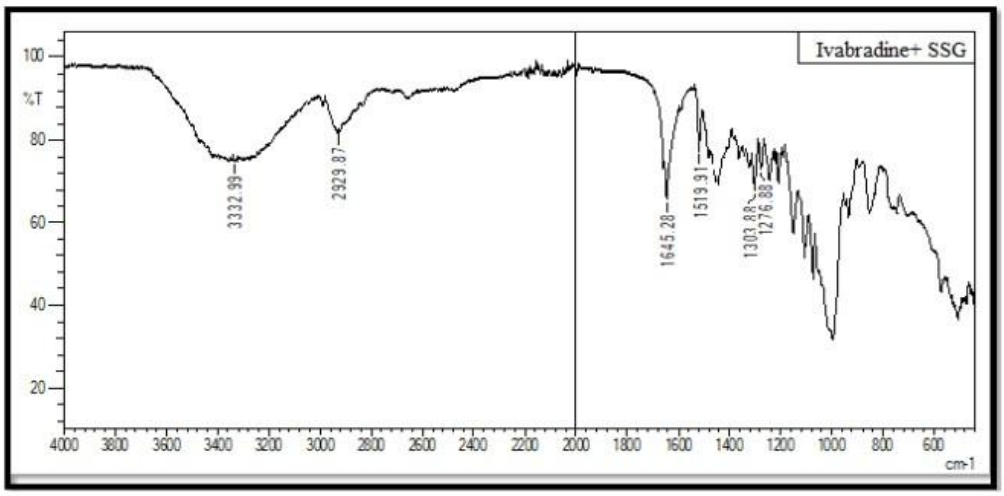


Figure No. 6: DSC thermogram of Ivabradine HCl

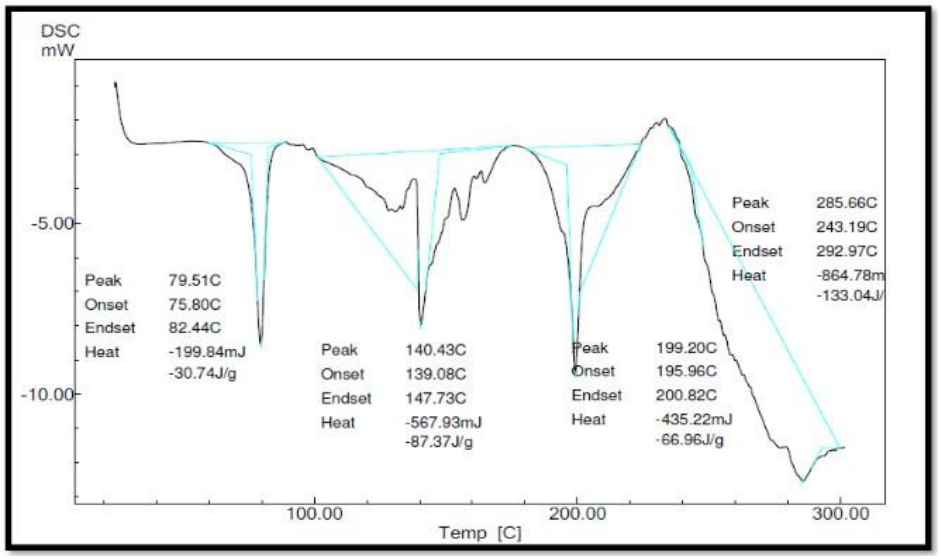


Figure No. 7: DSC thermogram of Ivabradine HCl + HPC SL

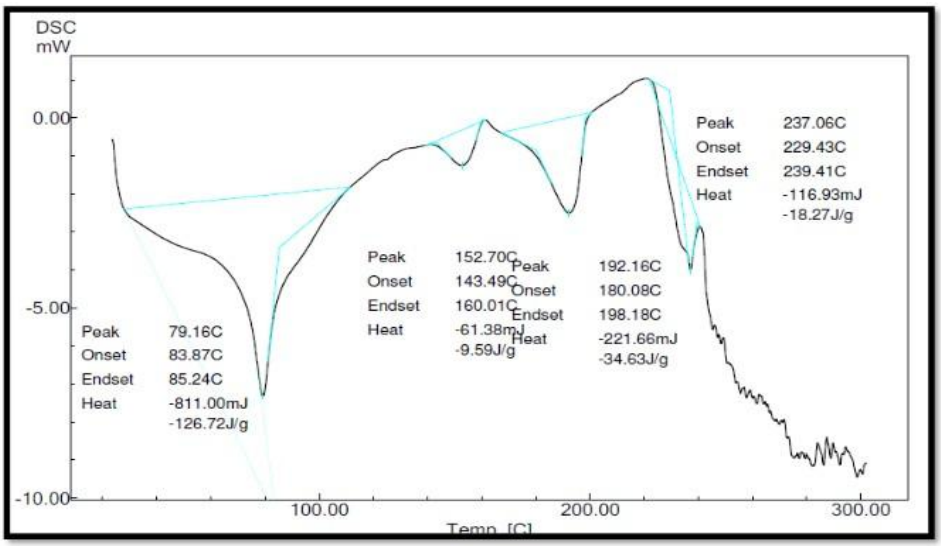


Figure No. 8: DSC thermogram of Ivabradine HCl + PVA

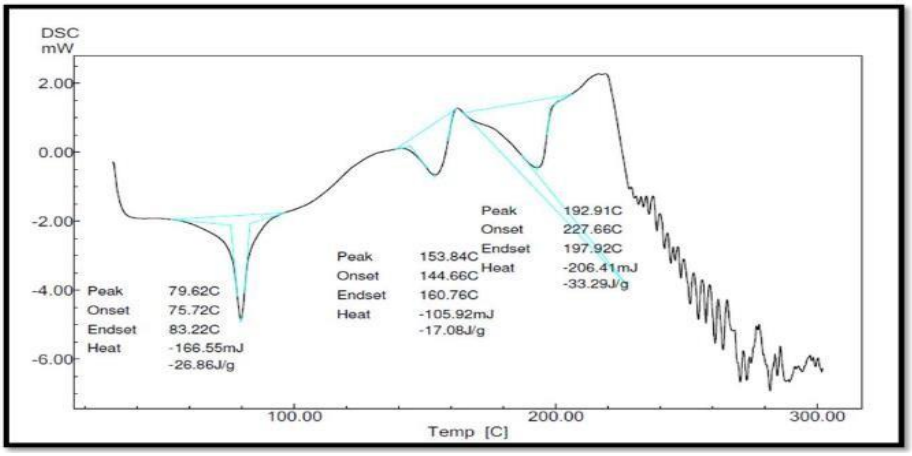


Figure No. 9: Ivabradine HCl Loaded Filaments

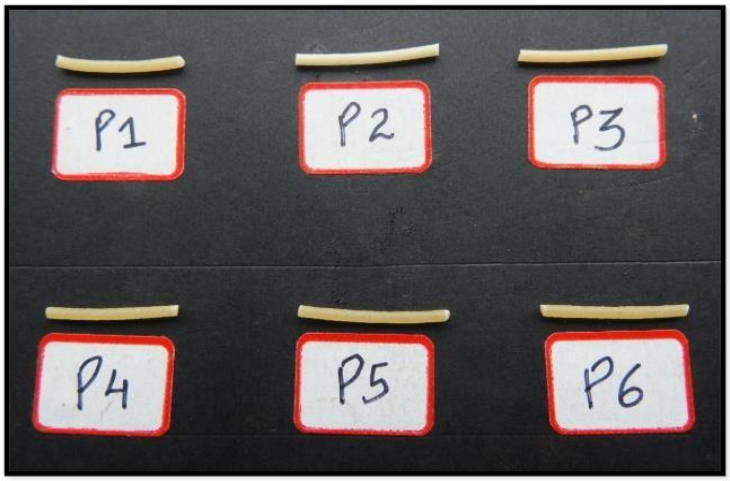


Figure No. 10: 3D Printed Fast Dissolving Oral Films of Ivabradine HCl

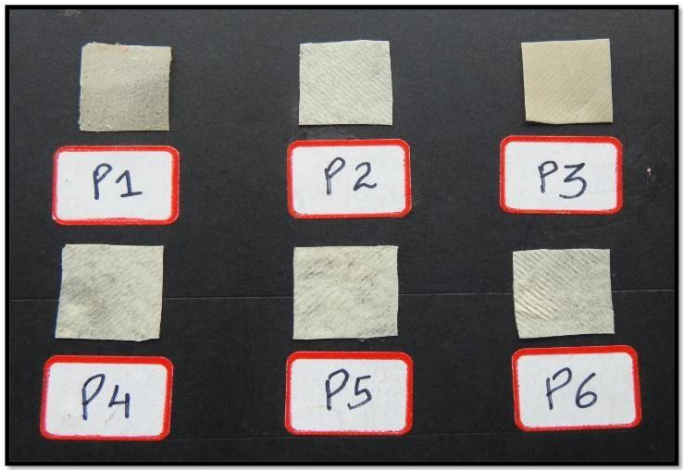
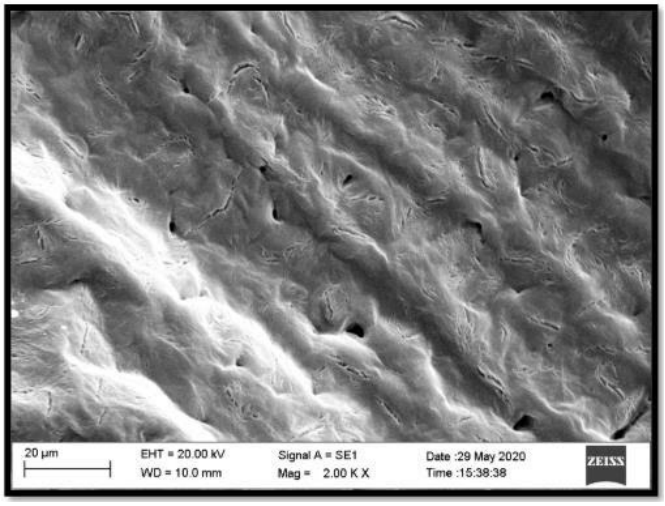


Figure No. 11: Scanning Electron Microscopy images of surface of optimized formulation P3 at 2000X magnification



CONCLUSION

In the present study, development of FDOF's by FDM 3D printing involved the task of fabrication of filament extruder, drug loaded filament and dug loaded films. A working model of filament extruder was successfully designed, fabricated and qualified/optimized for manufacturing drug loaded filaments. The produced filaments possessed sufficient mechanical strength and diameter ranged from 1.65 ± 0.05 mm to 1.72 ± 0.04 mm suitable for 3D printing. The weight of the film formulations ranged from 88.7 ± 0.4163 mg to 107.7 ± 0.1528 mg depending upon the density of each formulation's filament. The printed films displayed almost consistent thickness for all the formulations in the range of 0.20 to 0.2167 mm ± 0.0058 mm which were designed to be 0.2 mm. The films containing HPC SL showed least tensile strength of 0.451 ± 0.0438 Kg/mm2 due to amount of plasticizer used. PVA containing films showed greater tensile strength of 0.842 ± 0.210 Kg/mm2 and moderate tensile strength was observed in other formulations.

The drug content uniformity of all formulations was uniform and in the acceptable limit ranging from 91.31% to 96.04 % and can be concluded that homogeneity occurred during hot melt extrusion and the drug did not undergo substantial thermal degradation. The values of surface pH obtained were close to neutral pH indicating no risk of irritation to oral mucosa. In vitro dissolution study, the %CDR of all formulation was witnessed to be more than 90% within 15 min owing to high aqueous solubility of drug and hydrophilic nature of film. Films without super-disintegrant showed less drug release i.e. 93.46% and 90.66% in 15 min. However, films containing SSG in varying quantities exhibited maximum drug release between 98.99% - 99.26% within 12 min with P3 formulation releasing 99.22% drug in short period of time of 8 min. Hence it is concluded that the concentration of SSG and also the type and amount of polymer used had a positive impact on the in vitro drug release. The in vitro dissolution data was further analysed with mathematical kinetic modelling in which it was observed that the drug release through the film formulation is diffusion controlled following first order kinetics with Fickian diffusion mechanism. All the formulation showed satisfactory results, however the **P3** formulation was selected as the optimised film formulation on the basis of in vitro disintegration time and in vitro drug release.

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