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FLASH RELEASE ORAL FILM OF CANDESARTAN CILEXETIL FORMULATION *AND IN-VITRO* EVALUATION

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Keywords:

Candesartan Cilexetil, Flash release, Solvent casting method, oral film

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ABSTRACT: In the present study, to develop a novel flash release fast dissolving oral film of candesartan cilexetil to achieve rapid dissolution and further improve the bioavailability of the drug. Also, to resolve the swallowing problems in pediatrics, geriatric patients by rapid dissolution in saliva and improve the patient compliance. Fast dissolving flash release oral flim of candesartan cilexetil was formulated using HPMCE5, HPMCE15 and HPMCK15 as film-forming polymers. Glycerol, polyethylene glycol and propylene glycol were used as a plasticizer by solvent casting method and found to satisfy the mouth dissolving film and other film parameters. The formulated films of candesartan cilexetil were evaluated for parameters like thickness, weight variation, folding endurance, SEM, surface pH disintegration time, drug content, *in-vitro* dissolution studies and kinetics studies. The *in-vitro* disintegration time of the optimized batch F5 was found to be 56 ± 0.12 sec. The films exhibited satisfactory thickness and folding endurance. The optimized batch F5 (HPMCE15) showed a faster disintegrating time, showing 96.02 ± 0.49 drug release within 30 min. *The in-vitro* release profile of optimized formulation F5 followed a first-order kinetic model with non-fickian diffusion law.

INTRODUCTION: Oral delivery is the safest, most convenient and economical method of drug delivery. Mouth dissolving strips have attained great importance in the pharmaceutical industry due to their unique properties and advantages [1]. Fast dissolving drug delivery system gaining popularity and acceptance as new drug delivery.

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A system because they are easy to administer and leading to better patient compliance. Oral fast-dissolving dosage form consists of mouth dissolving tablets & fast dissolving films. Mouth dissolving tablets are associated with many problems like leaving residues in the mouth, which causes feeling of grittiness in mouth; there is a fear of choking and difficulty in swallowing tablets.

To beat the issues of mouth dissolving tablets, a new drug delivery system for the oral delivery of the drugs was investigated, known as Fast dissolving films/oral dispersible film/ mouth dissolving films / oral disintegrating film/ oral dissolving film [2, 3].

Fast dissolving flash release oral film was developed based on the technology of the transdermal patches for oral delivery of drugs. The delivery system consists of a thin film of the size of a postage stamp placed on the patient's tongue or mucosal tissue, where it instantly hydrates by absorbing saliva; the film then rapidly disintegrates and dissolves to release the drug for oral mucosal absorption. The availability of a larger surface area of the film leads to rapid disintegration in the oral cavity. It is retained at the application site and rapidly releases the active agent for local and/systemic absorption. Patients suffering from dysphasia, repeated emesis, motion sickness, mental disorder, pediatric and geriatric patients prefer this dosage form as they cannot swallow large quantities of water [4, 5]. The oral or buccal mucosa being highly vascularized, drugs can be absorbed directly and can enter the systemic circulation without undergoing first-pass hepatic metabolism. This advantage can be exploited in preparing products with improved oral bioavailability of molecules that undergo first-pass effect [6]. Candesartan cilexetil is an anti-hypertensive agent, angiotensin II receptor antagonist used to treat hypertension, congestive heart failure, and diabetic nephropathy. It has 15% oral bioavailability due to poor aqueous solubility that makes absorption and dissolution rate limited. This novel drug delivery system can also be beneficial for meeting the industry's current needs: improved solubility/stability, biological half-life, and bioavailability enhancement of drug [7].

MATERIAL AND METHOD: Candesartan cilexetil was obtained as a gift sample from Medopharm Pvt limited, Bangalore. HPMC E5, HPMC E15 and HPMC K15 were obtained from Swiss Garnier Genenexiaa Sciences, Sikkim. All other chemicals and ingredients were used for the study are of Analytical grade.

Drug Polymer Compatibility: Pure drug (Candesartan Cilexetil) and polymers were subjected to FTIR (Shimadzu, Japan) studies alone and in combinations. The pellets were placed in the sample holder for recording the IR spectra to study the interference of polymers with the drug [8]. The scanning range was 400-4000 $cm^{-1,}$ and the resolution was 4 cm^{-1}.

TABLE 1: COMPOSITION OF FLASH RELEASE ORAL FILM OF CANDESARTAN CILEXETIL (F1-F4)

INGREDIENTS	FORMULATION			
	F1	F2	F3	F4
Candesartan cilexetil (mg)	60	60	60	60
Hydroxyl propyl methyl cellulose E5 (mg)	350	400	450	500
Glycerol (mg)	125	125	125	125
Cross carmellose sodium (mg)	125	125	125	125
Mannitol (mg)	30	35	40	45
Citric acid (mg)	20	20	20	20
Amaranth (mg)	q.s	q.s	q.s	q.s
Vanilline (mg)	q.s	q.s	q.s	q.s
Water (ml)	14	14	14	14

TABLE 2: COMPOSITION OF FLASH RELEASE ORAL FILM OF CANDESARTAN CILEXETIL (F4-F8)

INGREDIENTS	FORMULATION			
	F5	F6	F7	F8
Candesartan cilexetil (mg)	60	60	60	60
Hydroxyl propyl methyl cellulose E15 (mg)	350	400	450	500
Poly ethylene glycol (mg)	125	125	125	125
Sodium starch glycollate (mg)	15	20	25	30
Sodium sacharin (mg)	30	35	40	45
Tartaric acid (mg)	20	20	20	20
Orange II (mg)	q.s	q.s	q.s	q.s
Lavander oil (ml)	q.s	q.s	q.s	q.s
Water (ml)	14	14	14	14

Formulation of Flash Release Oral Film: Candesartan Cilexetil flash release oral film was prepared by the Solvent casting method. The formulation composition of the different batches was Shown in **Tables 1, 2, 3.** First, the water-soluble polymers are dissolved in water at 100 rpm

at a magnetic stirrer, and all other excipients are dissolved in a suitable solvent separately. Then both the solutions are mixed thoroughly and stirred at 1000 rpm. The obtained solution is incorporated with drug dissolved in a suitable solvent. The entrapped air is removed by vacuum and cast into Petri plate and dried. The film was carefully removed from the petriplate, checked for imperfections and cut to the required size to deliver the equivalent dose per strip (2 × 2 cm^{-2} sizes). Film samples with imperfections were excluded from study [9].

TABLE 3: COMPOSITION OF FLASH RELEASE ORAL FILM OF CANDESARTAN CILEXETIL (F9-F12)

INGREDIENTS	FORMULATION			
	F9	F10	F11	F12
Candesartan cilexetil (mg)	60	60	60	60
Hydroxyl propyl methyl cellulose KI5 (mg)	350	400	450	500
Propylene glycol (mg)	125	125	125	125
Cross povidone (mg)	15	20	25	30
sucrose (mg)	30	35	40	45
Citric acid (mg)	20	20	20	20
Indigo carmine (mg)	q.s	q.s	q.s	q.s
Peppermint oil (ml)	q.s	q.s	q.s	q.s
Water (ml)	14	14	14	14

TABLE 4: CALIBRATION OF CANDESARTAN CILEXETIL USING PHOSPHATE BUFFER PH 6.8

S. no	CONCENTRATION (µg/ml)	ABSORBANCE AT255 nm ± SD
1	0	0
2	5	0.132 ±0.0047
3	10	0.280 ±0.0038
4	15	0.443 ±0.0044
5	20	0.579 ±0.0450
6	25	0.733 ±0.0560
7	30	0.860 ±0.0490
8	35	1.024 ±0.0642
9	40	1.156 ±0.0683
10	45	1.315 ±0.0805
11	50	1.452 ±0.0962

Evaluation of Flash Release Oral Film:

Surface Morphology: Properties such as homogeneity, transparency, and surface of the oral films were evaluated by scanning electron microscopy (SEM Tescan, Europe [10].

Film Thickness: The film thickness of the film was measured by vernier Caliper (Linker, Mumbai) at a different location (center and four corners) and meant ± S.D calculated. This is crucial to determine the film thickness uniformity as this is directly correlated to the dose accuracy in film [11].

TABLE 5: FTIR SPECTRUM INTERPRETATION OF CANDESARTAN CIEXETIL AND POLYMER

Functional group assignment	Standard wave number (cm^{-1})	Test wave number (cm^{-1}) of API	Test wave number (cm^{-1}) ofExcipients		
			HPMC E5	HPMC E15	HPMC K15
N-H stretching	2000-3600	3666.85	3490.31	2934.79	3454.62
C-H stretching	2700-3300	2992.66	2982.05	2826.77	3293.56
N-H bending	1500-1700	1612.54	1620.26	1653.05	1604.83
COOH stretching	1500-1760	1709.95	1620.26	1634.73	1604.83
Alkanes(bending)	1340-1470	1416.76	1388.79	1446.66	-
C-N stretching	1180- 1360	1386.86	1328.03	1311.64	1317.43
O-H bending	1200-1400	1315.50	1365.65	1366.61	1288.49
C-F stretching	1100-1250	1207.48	-	1150.58	-
N-H rocking	700-900	-	885.36	852.56	895.96
Monosub benzene ring (rocking)	730-770	-	-	667.39	-
C-O stretching	1050-1300	1291.39	1014.59	1188.19	1288.49

Weigh Variation of Films: Average Weight is studied by individually weighing five randomly selected films and calculating the average weight. The average weight should not deviate significantly from the average weight [12].

Average weight of films = weight of 5 films/5

Folding Endurance: The flexibility of the film is measured quantitatively in terms of what is known as folding endurance. The folding endurance of the film was determined by repeatedly folding a small strip of the film at the place till it broke.

The number of times the film can be folded without breaking gives The folding endurance value. This test was performed on five films of each formulation and mean ± S.D was calculated [13].

TABLE 6: FTIR SPECTRUM INTERPRETATION OF CANDESARTAN CIEXETIL AND POLYMER MIXTURE

Functional group assignment	Standard wave number (cm^{-1})	Test wave number (cm^{-1}) of API	Test wave number (cm^{-1}) of Mixtures		
			Drug + HPMCE5	Drug + HPMCE15	Drug + HPMCK15
N-H stretching	2000-3600	3666.85	3114.18	2918.40	3261.74
C-H stretching	2700-3300	2992.66	3063.06	2848.96	3053.42
N-H bending	1500-1700	1612.54	1509.05	1693.19	1663.66
COOH stretching	1500-1760	1709.95	1612.33	1702.24	1733.10
Alkanes(bending)	1340-1470	1416.76	1409.05	1467.88	1436.05
C-N stretching	1180- 1360	1386.86	1246.06	1309.71	1229.66
O-H bending	1200-1400	1315.50	1409.05	1274.03	1330.93
C-F stretching	1100-1250	1207.48	1113.93	1187.23	1177.58
N-H rocking	700-900	-	884.93	892.11	830.00
Mono sub benzene ring (rocking)	730-770	-	-	-	-
C-O stretching	1050-1300	1291.39	1246.06	1294.28	1163.42

Drug Content Uniformity: The films were tested for drug content uniformity by UV - visible spectrophotometric method. Films of the required size (2 cm × 2 cm) were cut at three different places from the casted film. Each cut film was placed in 100 ml volumetric flask and was dissolved using methanol and set aside for 2 h. From this stock solution, 1 ml was pipette out and transferred into a 10 ml volumetric flask and the volume was made to the mark with methanol. The absorbance of the resulting solution was measured at 255 nm against blank using UV visible spectrophotometer. The percentage drug content was determined using the standard graph [14].

Surface pH Study: The fast-dissolving strip's surface pH was determined to investigate the possibility of any side effects *in-vivo*. As an acidic or alkaline pH may cause irritation to the oral mucosa, it was determined to keep the surface pH as close to neutral as possible.

A combined pH electrode was used for this purpose. Oral strip was slightly wet with the help of water and kept for 30 sec. The pH was measured by bringing the electrode in contact with the surface of the oral film and allowing equilibrating for 1 min. This study was performed on three films of each formulation, and mean ± S.D was calculated [15].

TABLE 7: FTIR SPECTRUM INTERPRETATION OF CANDESARTAN CIEXETIL ORAL FILM FINAL PRODUCT

Functional group assignment	Standard wave number(cm^{-1})	Test wave number(cm^{-1}) of API	Test wave number (cm^{-1}) of Final product
N-H stretching	2000-3600	3666.85	2979.16
C-H stretching	2700-3300	2992.66	2940.58
N-H bending	1500-1700	1612.54	1611.58
COOH stretching	1500-1760	1709.95	1573.00
Alkanes(bending)	1340-1470	1416.76	1401.33
C-N stretching	1180- 1360	1386.86	1267.27
O-H bending	1200-1400	1315.50	1304.89
C-F stretching	1100-1250	1207.48	1176.62
N-H rocking	700-900	-	-
Mono sub benzene ring (rocking)	730-770	-	-
C-O stretching	1050-1300	1291.39	1245.09

In-vitro **Disintegration Studies:** Disintegration time indicates the disintegration characteristics and dissolution characteristics of the film. As per the dimensions (3×2 cm) required for dose delivery, the film was placed on a stainless steel wire mesh placed in a petridish containing 10 ml phosphate buffer pH 6. The time required for the film to break was noted as in vitro disintegration time. This test was performed on six films of each formulation, and mean ± S.D calculated [16].

TABLE 8: CHARACTERISTICS OF CANDESARTAN CIEXETIL ORAL FILMS

Formulation code	Film thickness (µm)	Weight variation (mg)	Folding Endurance
F1	61 ± 2.0	31.1 ± 0.78	94 ± 1.1
F2	79 ± 1.8	36.6 ± 0.84	86 ± 1.5
F3	99 ± 2.5	41.0 ± 0.61	93 ± 2.2
F4	91 ± 2.0	42.1 ± 0.66	102 ± 1.7
F5	78 ± 1.8	37.3 ± 0.73	108 ± 1.3
F6	79 ± 2.9	38.0 ± 0.63	124 ± 1.9
F7	85 ± 2.2	38.8 ± 0.80	111 ± 2.3
F8	110 ± 3.3	40.3 ± 0.82	102 ± 2.2
F9	51 ± 1.5	24.4 ± 0.59	53 ± 1.7
F10	71 ± 2.1	31.8 ± 0.77	56 ± 1.3
F11	98 ± 2.8	38.6 ± 0.63	62 ± 1.3
F12	54 ±2.6	43.4 ± 0.91	61 ± 1.1

TABLE 9: CHARACTERISTICS OF CANDESARTAN CIEXETIL ORAL FILMS

Formulation code	Surface pH	Disintegration Time (sec)	Content Uniformity (%)
F1	6.14 ± 0.05	67 ± 0.16	90.75 ± 1.13
F2	6.25 ± 0.10	71 ± 0.09	99.00 ± 0.97
F3	6.35 ± 0.09	90 ± 0.12	89.50 ± 0.82
F4	6.50 ± 0.05	113 ± 0.16	91.50 ± 1.19
F5	6.85 ± 0.07	56 ± 0.12	103.25±0.95
F6	6.75 ± 0.12	84 ± 0.11	96.50 ± 0.71
F7	6.65 ± 0.17	99 ± 0.13	98.00 ± 1.27
F8	6.82 ± 0.09	93 ± 0.17	105.25±1.20
F9	6.71 ± 0.07	121 ± 0.14	90.25 ± 0.93
F10	6.94 ± 0.12	76 ± 0.10	105.00±1.59
F11	6.38 ± 0.10	136 ± 0.17	87.00 ± 1.76
F12	6.57 ± 0.16	158 ± 0.14	93.00 ± 1.67

TABLE 10: *IN-VITRO* CUMULATIVE % DRUG RELEASE OF CANDESARTAN CILEXETIL ORAL FILMS

Time (min)	F1	F2	F3	F4	F5	F6
0	0	0	0	0	0	0
2	58.2	64.9	58.6	55.50	68.2	51.09
5	61.5	67.82	63.17	61.19	71.41	57
10	66.65	73.18	67.81	65.38	76.35	64.89
15	71.24	83.00	73.73	73.14	82.07	70.25
20	75.52	86.78	78.16	78.76	92.29	79.39
30	83.44	91.78	82.95	87.09	96.02	87.32

TABLE 11: *IN-VITRO* CUMULATIVE % DRUG RELEASE OF CANDESARTAN CILEXETIL ORAL FILMS

Time (min)	F7	F8	F9	F10	F11	F12
0	0	0	0	0	0	0
2	56.63	58.3	54.3	57.5	51.5	52.5
5	66.00	63.86	59.56	63.33	55.68	57.61
10	69.33	70.92	63.91	66.19	60.75	62.82
15	73.8	77.62	69.44	74.86	67.1	67.72
20	81.61	83.34	74.26	83.12	73.28	72.73
30	87.49	93.35	76.57	90.24	78.86	76.97

***In-vitro* Dissolution Test:** A dissolution test of films was performed using (400 ml) phosphate buffer pH6.8 with USP dissolution apparatus I (Lab India, Mumbai).

The dissolution medium was kept at 37 ± 0.5 °C and stirred at 50 rpm for 30 min. The drug release was analyzed spectro-photometrically at λ_{max} 255 nm using an ultraviolet (UV) spectrophotometer (Shimadzu, Japan) by using a calibration. The film was placed into each vessel and the test (5ml) sample was withdrawn at a particular time interval (2, 5, 10, 15, 20 and 30 min) and replaced with fresh dissolution media.

This test was performed on six films of each formulation and mean ± S.D was calculated [17, 18].

Kinetic Modeling of Drug Release: To analyze the mechanism for the release and release rate kinetics of Candesartan cilexetil, the data obtained were fitted to various kinetic equations such as zero-order, the first order, Higuchi matrix and Korsmeyer- Peppas equation.

The regression coefficient values were calculated. In this, by comparing the regression coefficient values obtained, the best fit model was selected [19].

RESULTS AND DISCUSSION:

Determination of λ_{max}: The absorption maximum (λ_{max} 255 nm) of Candesartan cilexetil was estimated by scanning the drug solution (50 µg/ml) between 400-200 nm regions on UV spectro-photometer. The obtained spectrum showed that the absorption maximum (λ_{max}) was 255 nm for the Cand. cilexetil. Also, absorption maximum showed that the drug sample was authenticated in **Fig. 1.**

TABLE 12: KINETIC ANALYSIS OF *IN-VITRO* DRUG RELEASE DATA OF CANDESARTAN CILEXETIL ORAL FILMS

Formulation code	Zero-order R^2	First-order R^2	Higuchi model R^2	Korsmeyer- Peppas equation		Hixsoncrowel R^2
				R^2	N	
F1	0.5302	0.7849	0.7694	0.5497	0.9504	0.6986
F2	0.5297	0.8612	0.7789	0.5508	0.9775	0.7543
F3	0.5145	0.7679	0.7636	0.5494	0.9545	0.6772
F4	0.5951	0.8697	0.8280	0.5680	0.9694	0.7681
F5	0.5301	0.9055	0.7743	0.5475	0.9832	0.8016
F6	0.6491	0.9058	0.8687	0.5851	0.9789	0.8339
F7	0.5597	0.8491	0.8057	0.5631	0.9721	0.7512
F8	0.6077	0.9188	0.8057	0.5709	0.9858	0.8395
F9	0.5064	0.7048	0.7650	0.5516	0.9421	0.6356
F10	0.6030	0.8958	0.8310	0.5681	0.9771	0.8124
F11	0.5839	0.8063	0.8213	0.5679	0.9501	0.7334
F12	0.5351	0.7434	0.7871	0.5579	0.9432	0.6717

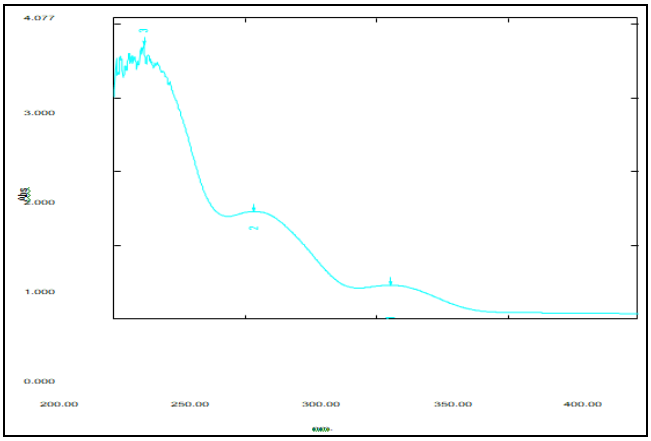


FIG. 1: ABSORPTION MAXIMUM (Λ_{MAX}) OF DRUG SAMPLE

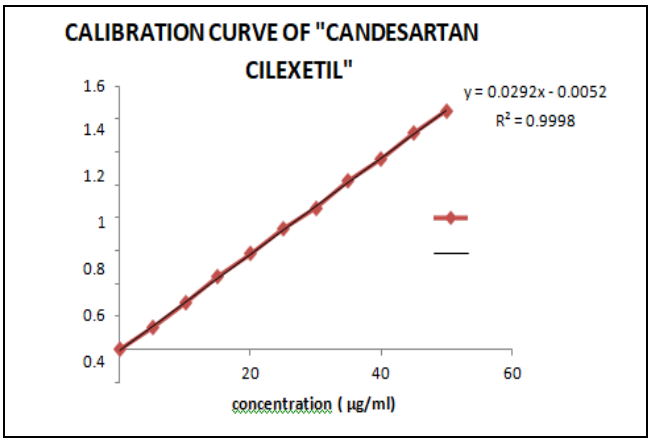


FIG. 2: STANDARD CURVE OF DRUG IN PHOSPHATE BUFFER PH 6.8

Calibration Curve of Candesartan Cilexetil: The Standard Calibration curves of Candesartan cilexetil was prepared using phosphate buffer pH 6.8. The absorbance was measured at λ_{max} of 255 nm. The correlation coefficient was found to be 0.9998. Candesartan cilexetil obeys the beer's law within the concentration range of (10-50 µg/ml). The calibration plot of Candesartan cilexetil in phosphate buffer pH 6.8 was shown in **Table 4** and **Fig. 2.**

Compatability Studies (Fourier Transform Infrared Spectroscopic (FT-IR): Drug polymer interaction was checked by comparing the IR spectra of pure drug **Fig. 3.** and the physical mixture of the drug with the excipients used **Fig. 5, 10.** and optimized/final formulation **Fig. 4.** The results found no possible interactions between drugs and polymers used in the study were shown in **Table 5, 7.**

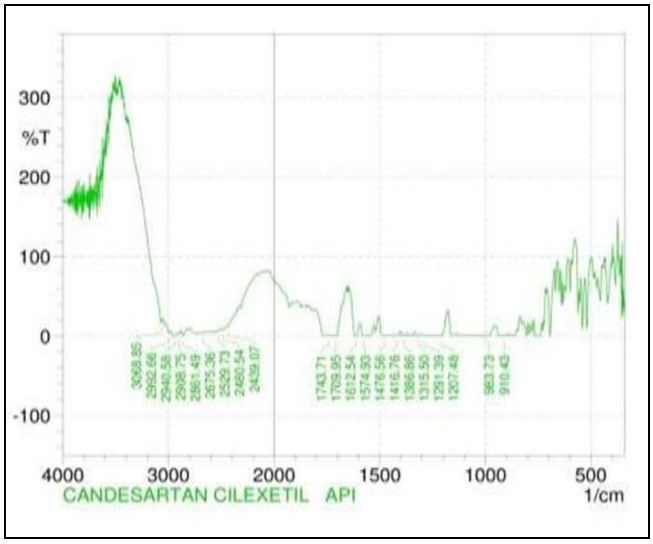


FIG. 3: FTIR SPECTRUM OF CANDESARTAN CILEXETIL

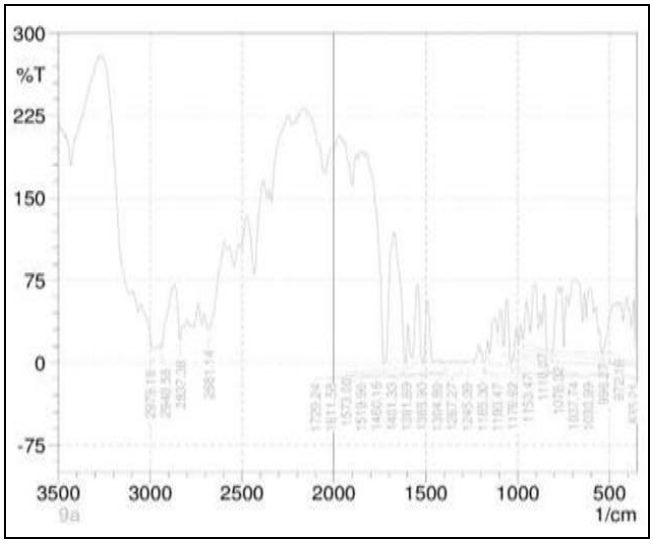


FIG. 4: FTIR SPECTRUM OF ORAL FILM OF FINAL PRODUCT

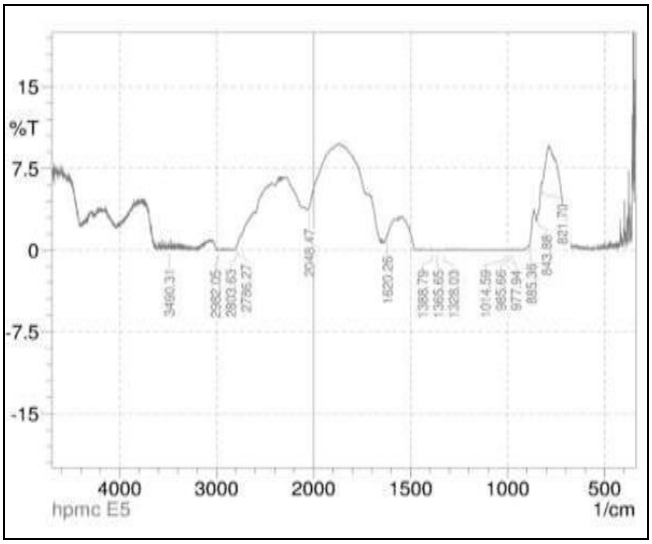


FIG. 5: FTIR SPECTRUM OF HPMCE5

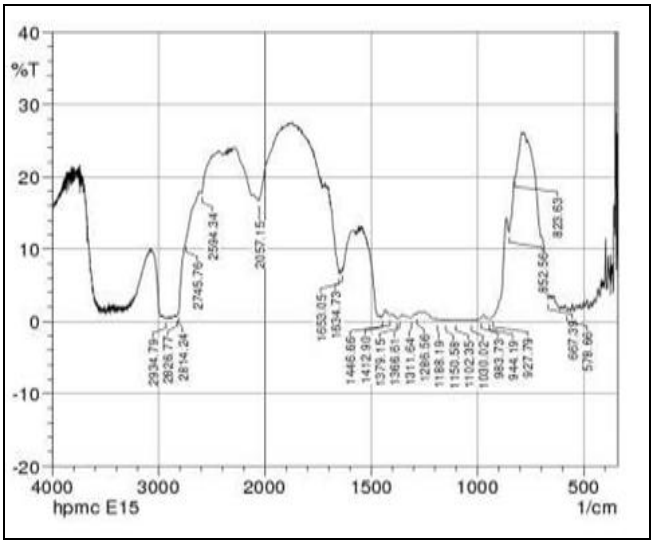


FIG. 6: FTIR SPECTRUM OF HPMCE15

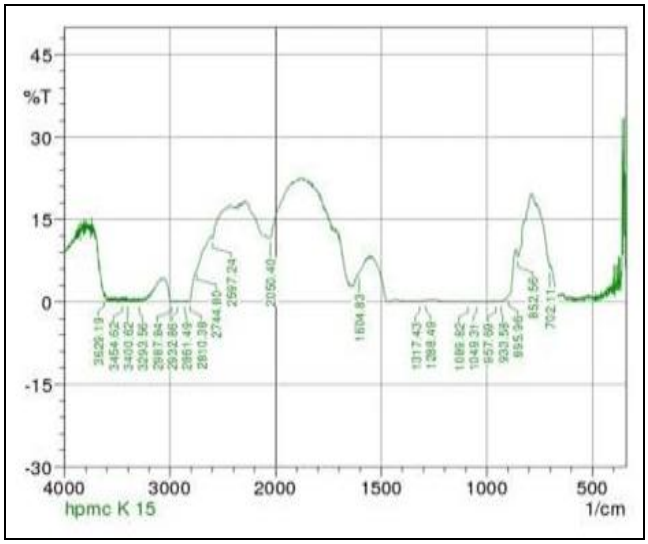


FIG.7: FTIR SPECTRUM OF HPMCK15

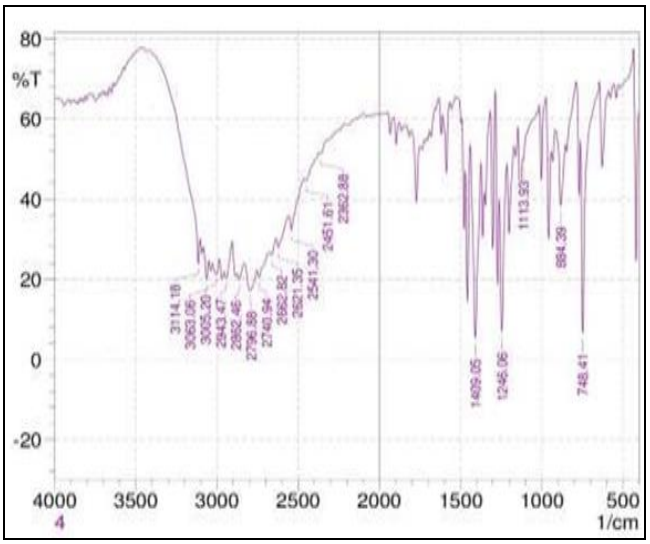


FIG. 8: FTIR SPECTRUM OF CANDESARAN DRUG + HPMCE5

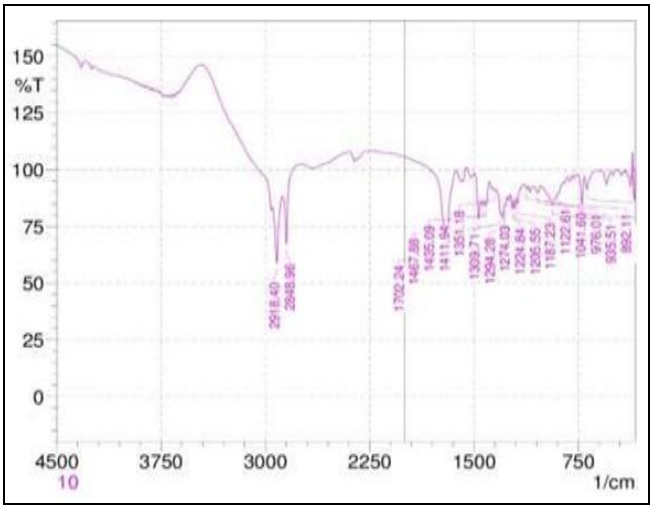


FIG. 9: FTIR SPECTRUM OF CANDESARTAN DRUG + HPMCE15

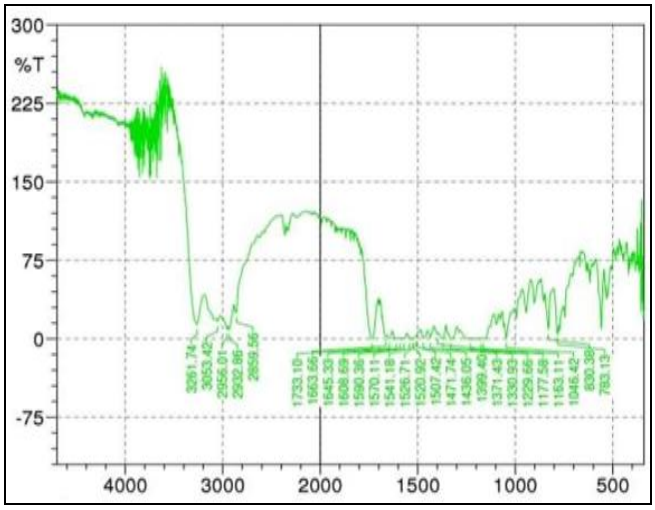
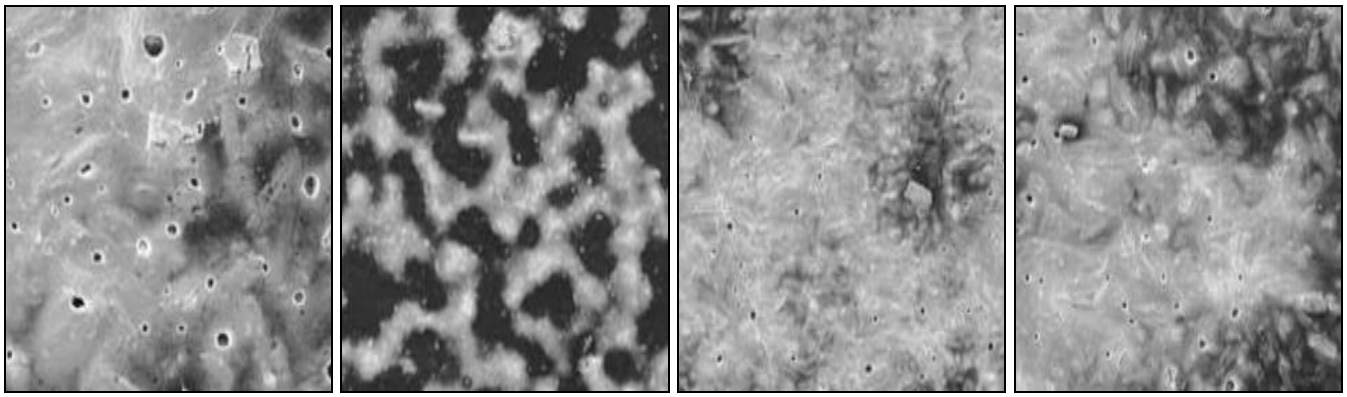


FIG. 10: FTIR SPECTRUM OF CANDESARTAN DRUG + HPMCK15



A 2 KK **B 250 KK** **C 500 KK** **D 1000 KK**

FIG. 11: SEM IMAGES OF FLASH RELEASE ORAL FILM OF OPTIMIZED FORMULATION F5

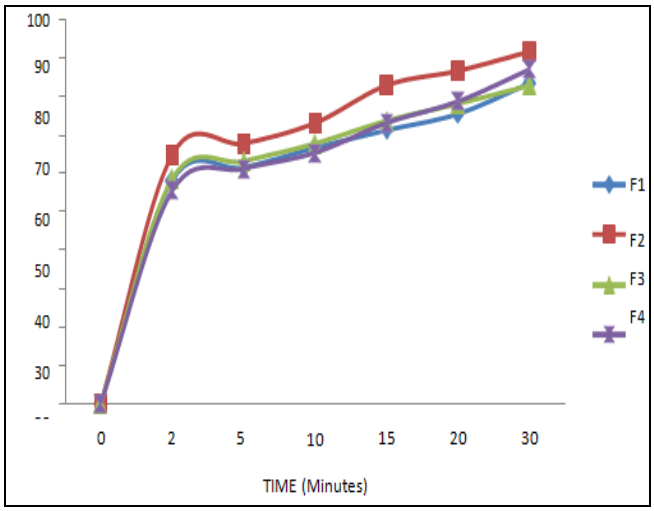


FIG. 12: *IN-VITRO* CUMULATIVE % OF CANDESARTAN CILEXETIL ORAL FILMS

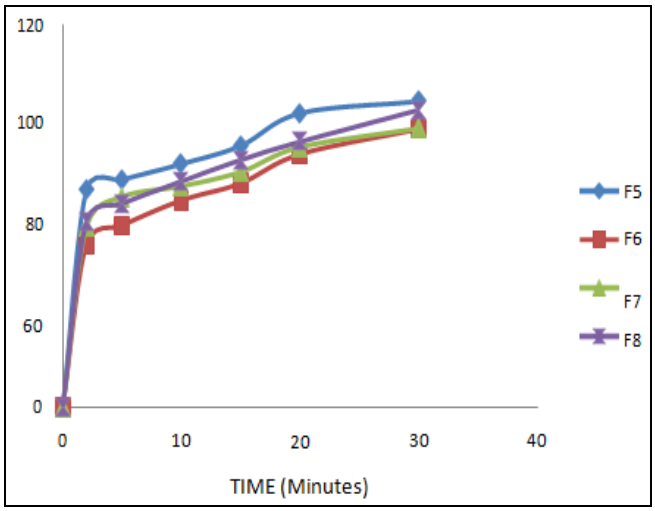


FIG. 13: *IN-VITRO* CUMULATIVE % OF CANDESARTAN CILEXETIL ORAL FILMS

Surface Morphology: Properties such as homogeneity, transparency, and surface of the oral films were evaluated by scanning electron microscopy with a magnification of 1K × to 1000K × was shown in **Fig. 11.**

Film Thickness: The film thickness of the film was measured by vernier calliper with and the average thickness of the film was given in **Table 8.** Hence the thickness was varied in the range of 51-110 µm.

Weight Variation of Films: The weight variations for the different formulation was calculated and the results were shown in **Table 8.**

Folding Endurance: Folding endurance of the film was determined by repeatedly folding a small strip of the film at the place till it broke. Folding endurance was found to be highest for F6 films (124 ± 1.9) and lowest for F9 films (53 ± 1.7). The optimum film exhibited good physical and mechanical properties are shown in **Table 8.**

Drug Content Uniformity: All the films were found to contain an almost uniform quantity of the drug, as per content uniformity studies indicating reproducibility of the technique. In case three, 2 × 2 films were cut an average drug content was calculated. The drug dispersed in the range of 87.00 ± 1.76 to 105.25 ± 1.20 was shown in **Table 9.** Thus, the preparation met the criteria of IP content uniformity (85-110%).

Surface pH Study: The pH of the film was measured and found to be between 6.14-6.98 for all the formulations. The results were presented in **Table 9.**

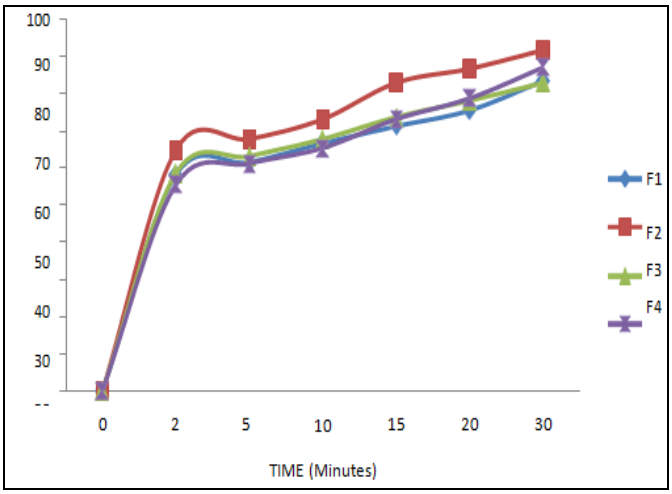
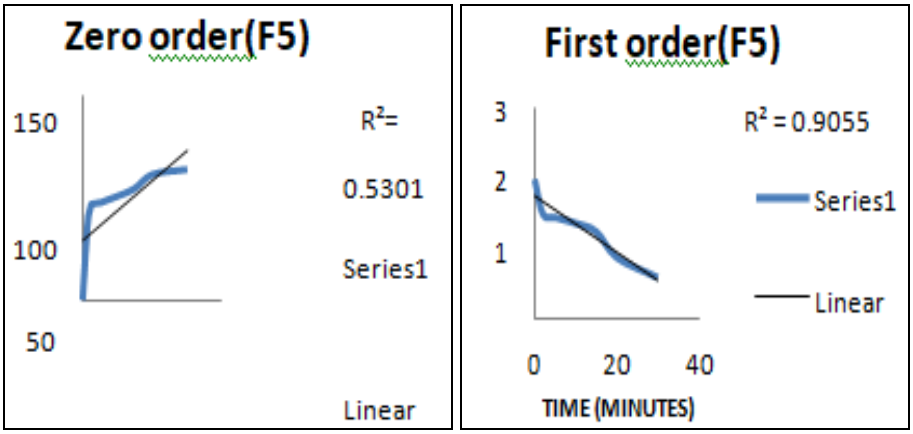


FIG. 14: *IN-VITRO* CUMULATIVE % DRUG RELEASE OF CANDESARTAN CILEXETIL ORAL FILMS

***In-vitro* Disintegration Studies:** The disintegration time of all the formulation were noted and shown in **Table 9.** Formulation F5 was found to give minimum disintegration time (56 ± 0.12) sec compared to other formulations.



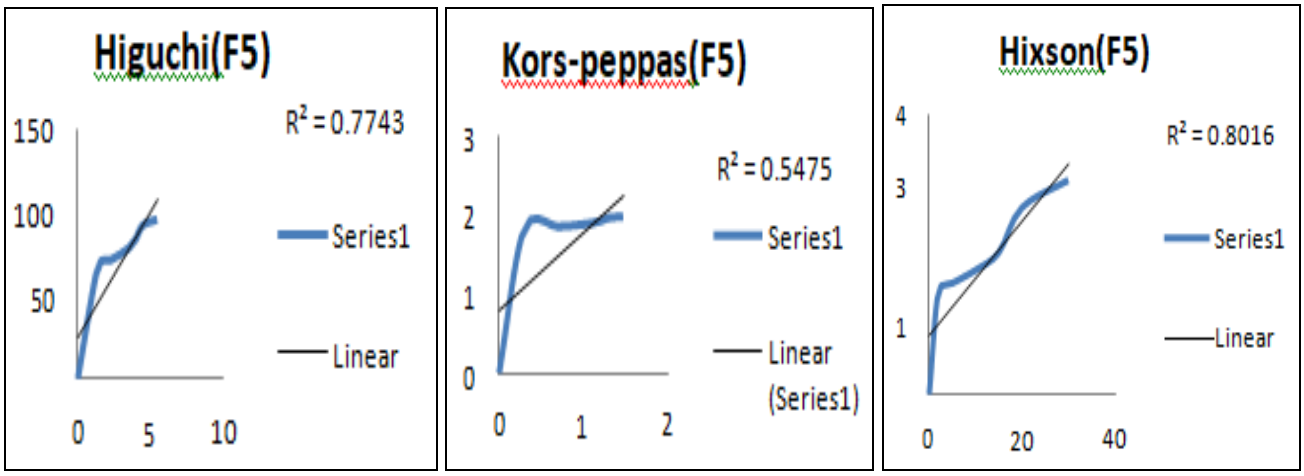


FIG. 15: RELEASE ORDER KINETICS OF OPTIMIZED FORMULATION F5

***In-vitro* Dissolution Test:** *In-vitro* dissolution and release studies of various formulations were performed using pH 6.8 phosphate buffer as dissolution medium and measuring drug concentration spectrophotometrically at 255 nm by using a calibration. The *in vitro* drug release profiles of formulations were given in **Table 10, 11,** and **Fig. 12, 14.** The drug release rate was very good with formulation (F5) containing HPMCE15 as a polymer.

Kinetic Modeling of Drug Release: In this study, the *in-vitro* drug release data were fitted to commonly employed release kinetic models, namely zero-order, first-order, Higuchi and Peppas models and Hixon-Crowell model to analyze drug release mechanism from the polymeric system as shown in **Table 12.** The highest regression coefficient (r^2) value of optimized formulation F5 was obtained 0.9832 (First order). The value of release exponent (n) was found to be greater than 0.5 that indicates non- Fickian diffusion (anomalous) based mechanism of drug release. Kinetics of drug release were shown in **Fig. 15.**

CONCLUSION: In the present investigation, an attempt was made to develop a flash release oral film of Candesartan cilexetil to achieve fast dissolution characteristics with improved bioavailability by the oral route.

Candesartan cilexetil flash release oral films were prepared by solvent casting method using HPMC E5, HPMC E15, HPMC K15 as a film-forming agent. Based on this physiochemical characterization, *in-vitro* drug release and drug release kinetics of candesartan cilexetil showed F5 formulation 96.02% at 30 min and followed the non-Fickian release mechanism.

From the results, it can be concluded that the fast dissolving oral film of candesartan cilexetil showed fast disintegration dissolution of drugs in salivary pH. Thus the prepared fast dissolving films of candesartan cilexetil could be a better alternative for achieving rapid oral bioavailability.

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