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Formulation and Evaluation of Candesartan Cilexetil Matrix Tablets

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ABSTRACT

Candesartan cilexetil is an antihypertensive drug effective for the treatment of hypertension and heart failure. The main goal is to formulate and evaluate the sustained release matrix tablets of candesartan cilexetil using different polymers like hydrophilic and hydrophobic. Different formulations were prepared by direct compression method using various release retarding polymers like carbopol 934P, HPMC K15M, sod.CMC. Water soluble surfactant SLS was employed for enhancing the solubility of candesartan cilexetil. Drug-excipients compatibility was carried out by FTIR. Different formulations were evaluated for hardness, thickness, friability, drug content and *in vitro* drug release. The results were found to be satisfactory in terms of physico-chemical parameters. The F10 formulation was found to display highest drug release of drug. Mathematical analysis of the release kinetics was carried out to determine the mechanism of drug release. *In vitro* release data was fitted into various models to ascertain the kinetic of drug release.

Keywords: Sustained release matrix tablets, HPMCK 15M, carbopol 934P, sodium CMC, SLS, Direct compression, Candesartan cilexetil.

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INTRODUCTION

Hypertension is a most common risk factor for cardiovascular risk problems. The percent prevalence of pre-hypertension and newly diagnosed hypertension in India was found to be 42 and 15 respectively by the end of the year 2012. Candesartan cilexetil[1] is a prodrug which is rapidly converted to its active metabolite (candesartan) during its absorption in the gastrointestinal tract. Candesartan is an angiotensin-receptor blocker. It lowers blood pressure and may be used alone or with other agents to treat hypertension. Candesartan may also be used to treat isolated systolic hypertension, diabetic neuropathy. The dose ranges from 8mg to 32mg once or twice daily. It shows poor bioavailability (15-40%) due to extensive first pass metabolism. Long term treatment may require frequent administrations of the drug which is difficult due to toxicity effects such as hepatic and renal impairment. Traditional drug delivery system has been characterized by the immediate release and repeated dosing of the drug which may lead to the risk of dose fluctuation. This arises the need of the formulation with modified release[2].

Sustained Release Drug Delivery Systems:

These are the drug delivery systems that are designed to achieve a prolonged therapeutic effect by continuously releasing medication over an extended period of time after administration of single dose of drug. Furthermore, the possibility of repeating successful drugs, coupled with the increasing expense in bringing new drug entities to market, has been instrumental in generating interest in sustained-release dosage forms[3]. In recent years, sustained release dosage forms continuous to draw attention in the field of research for improved patient compliance and decreased incidence of adverse drug reaction[4]**.** The drug release from the dosage form depends on the type of the polymer in which it is embedded and the quantity of the drug contained. Sustained release dosage forms can smooth fluctuating drug levels which better controls patient illness or symptoms.

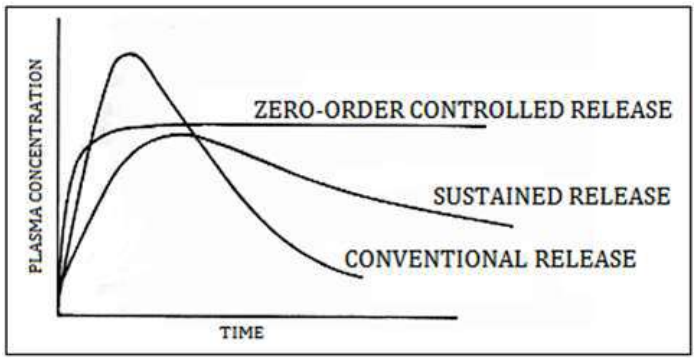

Figure 1: Plasma drug concentration profile of conventional release, sustained release and zero order release.

Hence in the present study an attempt was made to formulate sustained release matrix tablets of candesartan cilexetil using retardant polymers like carbopol 934P, HPMC K-15M, sodium carboxy methyl cellulose (sod. CMC). However, developing oral sustained release tablets for water-insoluble drugs has always been a challenge which was overcomed by incorporating water soluble surfactant like SLS (Sodium Lauryl Sulphate) in the prescribed limits into the formulation which acted as a solubilizer. Release pattern of candesartan cilexetil was evaluated and the drug release data were plotted using various kinetic equations.

MATERIALS AND METHOD

Candesartan cilexetil was obtained as a gift sample from Smilax laboratory, Hyderabad. Hydroxy propyl methyl cellulose (K 15M) was obtained from Colorcon Asia Pvt. Ltd, Goa. SLS and carbopol 934P were obtained from Indian Drugs, Hyderabad. Avicel pH 101, Magnesium stearate, Sodium hydroxide, Potassium dihydrogen phosphate were procured from Hetero lab, Hyderabad. All other chemicals and reagents used in the study were of analytical grade.

METHODS

Drug-polymer compatibility studies

FTIR spectroscopy was employed to ascertain the compatibility between candesartan cilexetil and the selected polymers. The FTIR analysis of the sample was also carried out for qualitative compound identification. The spectrum obtained for drug-polymer was compared with pure candesartan cilexetil spectra.

Pre-compression Parameters[5]

Bulk Density (Db)

It is the ratio of total mass of powder to the bulk volume of powder. It was measured by pouring the weight powder (passed through standard sieve # 20) into a measuring cylinder and initial weight was noted. This initial volume is called the bulk volume. From this the bulk density is calculated according to the formula mentioned below. It is expressed in g/ml and is given by

$$\mathbf{Db = M/ Vb}$$

Where, M is the mass of powder, Vb is the bulk volume of the powder.

Tapped Density (Dt)

It is the ratio of total mass of the powder to the tapped volume of the powder. Volume was measured by tapping the powder in apparatus. Tapping was continued until the difference between successive volumes is less than 2% (in a bulk density apparatus). It is expressed in g/ml and is given by:

$$Dt = M / Vt$$

Where, M is the mass of powder, Vt is the tapped volume of the powder.

Angle of Repose (θ)

The friction forces in a loose powder can be measured by the angle of repose (q). It is an indicative of the flow properties of the powder. It is defined as maximum angle possible between the surface of the pile of powder and the horizontal plane.

$$\tan(\theta) = h / r$$

$$\theta = \tan^{-1}(h / r)$$

Where, θ is the angle of repose. h is the height in cm and r is the radius in cm.

Carr's index (or) % compressibility:

It indicates powder flow properties. It is expressed in percentage and is given by

$$I = \frac{Dt - Db}{Dt} \times 100$$

Where, D_t is the tapped density of the powder and D_b is the bulk density of the powder.

Hausner's ratio:

Hausner's ratio is an indirect index of ease of powder flow. It is calculated by the following formula.

$$\text{Hausner ratio} = \frac{Dt}{Db}$$

Where, D_t is the tapped density and Db is the bulk density.

Formulation development

Candesartan cilexetil tablets were manufactured by direct compression in all the formulations using retardant polymers like carbopol 934P, HPMC K-15M, sodium carboxy methyl cellulose (sod.CMC). Development of the formulation in the present was mainly based on the type and concentration of polymers. Ten formulations were made with varying types and concentration of polymers selected with incorporation of SLS[6]. The ingredients depicted in Table below (except magnesium stearate and talc) were passed through sieve # 60, mixed homogenously and co-grinded in a mortar and pestle. Finally magnesium stearate was passed through sieve # 60, mixed and blended with initial mixture. Then it is mixed for 5 min. The mixed blend of drug and excipients was compressed into tablet to produce convex faced tablets of 250 mg using 8 mm round punches on multipunch tablet compression machine.

Table 1: Formulation chart

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
Candesartan cilexetil	32	32	32	32	32	32	32	32	32	32
Carbopol 934P	32	64	-	-	-	-	-	-	-	-
HPMC K-15M	-	-	32	64	-	-	32	64	-	-
SodiumCMC	-	-	-	-	32	64	-	-	32	64
SLS							2.5	2.5	2.5	2.5
MCC	183.5	151.5	183.5	151.5	183.5	151.5	181	149	181	149
Magnesium stearate	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5
Total(mg)	250	250	250	250	250	250	250	250	250	250

Post-compression parameters[5]:

Hardness:

Hardness or tablet crushing strength, the force required to break a tablet is expressed in kg/cm^2 was determined using Pfizer hardness tester.

Friability:

Friability of the tablets was determined using Roche friabilator revolving at 25 rpm and dropping the tablets at a height of 6 inch in each revolution. Pre-weighed sample of tablets was placed in the friabilator and were subjected to 100 revolutions and reweighed. The friability (F %) is determined by the formula.

$$F\% = \left(1 - \frac{Wo}{W}\right) X100$$

Where,

W_0 is initial weight of the tablets before the test.

W is the weight of the tablets after test.

Weight variation test:

As per IP, twenty tablets were taken and weighed individually and collectively using digital balance. The average weight of each tablet was calculated. The percent deviation is verified with the prescribed IP limits.

Procedure for calibration of Candesartan cilexetil in phosphate buffer (6.8):

Candesartan cilexetil (100 mg) was weighed accurately into 100 ml volumetric flask and dissolved in ethanol to get a concentration of 1000 µg/ml. From this 10 ml was withdrawn and diluted to 100 ml in phosphate buffer pH 6.8 to get concentration of 100 µg/ml. From the stock solution, appropriate aliquots were pipetted into different volumetric flasks and volume was made up to mark with phosphate buffer (pH6.8) solution, so to get concentration of 10-50 µg/ml.

Procedure for determination of drug content[7]:

Ten tablets were selected randomly and average weight was calculated. Tablets were crushed in a motor and accurately weighed amount of tablet powder was taken from the crushed blend. Then the samples were transferred to 100 ml volumetric flask and diluted with phosphate buffer (pH 6.8) solution. The contents were shaken periodically and kept for 2 hrs for solvation of drug completely. The mixture was filtered using whatman filter paper. From this resulted solution 1 ml was taken and diluted with 100ml of phosphate buffer and absorbance was measured at 255 nm using phosphate buffer as a blank. The drug content in each tablet was calculated using standard calibration curve of Candesartan cilexetil.

Procedure for determination of in vitro drug release[8]:

In vitro drug release of the tablets was carried out using USP – type II dissolution apparatus (paddle type). The dissolution media, 900 ml of phosphate buffer (pH6.8) solution, was placed into dissolution flask maintaining the temperature of 37±0.5º and rpm of 50. One tablet was placed in each flask of dissolution apparatus. The apparatus was allowed to run. Samples measuring 5 ml were withdrawn after every 1 hr interval. Samples were filtered through 10 µm whatman filter paper. The fresh dissolution medium was replaced every time to maintain sink conditions. The collected samples were analyzed at 255 nm using 6.8 pH buffer media as blank. The cumulative drug release was calculated. The released data obtained was fitted into Higuchi mathematical model[9,10]. Higuchi's model: Plot of percent drug release versus square root of time.

RESULTS AND DISCUSSION

Drug Polymer Interaction Studies

The FTIR spectra of pure candesartan cilexetil and physical mixture are shown in Figure 2 and Figure 3 respectively. Candesartan cilexetil exhibits peak due to hydroxyl (2800-2850 cm-1), ketone (1700- 1750 cm-1), carbonyl (1200-1250 cm-1), O substitution (700-750 cm-1) and aromatic CH (2850-2950 cm-1) group as depicted in Table 2. It was observed that there were no changes in their main peaks in the FTIR spectra of physical mixture of drug and polymers. Hence, it was concluded that no physical or chemical interactions of candesartan cilexetil with selected polymers.

Table 2: Interpretation of pure Candesartan cilexetil.

Functional group	Range	Presence of peak
Hydroxyl group	2800 – 2850 cm^{-1}	Present
Ketone group	1700 – 1750 cm^{-1}	Present
Carbonyl group	1200 – 1250 cm^{-1}	Present
O- substitution	700 – 750 cm^{-1}	Present
Aromatic C-H	2850-2950 cm^{-1}	Present

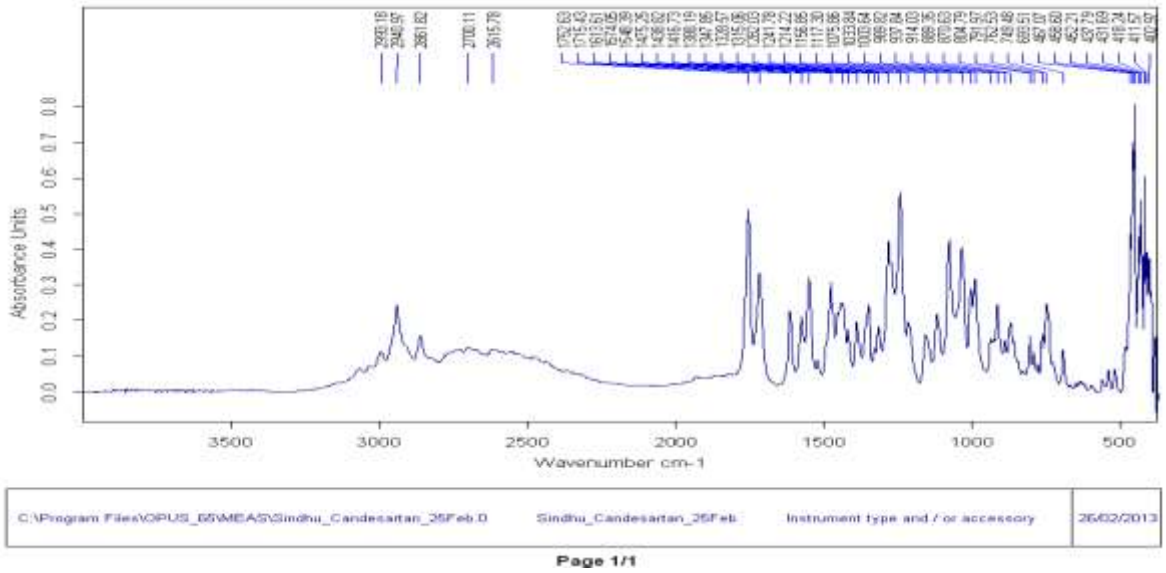

Figure 2-IR spectra of pure candesartan cilexetil

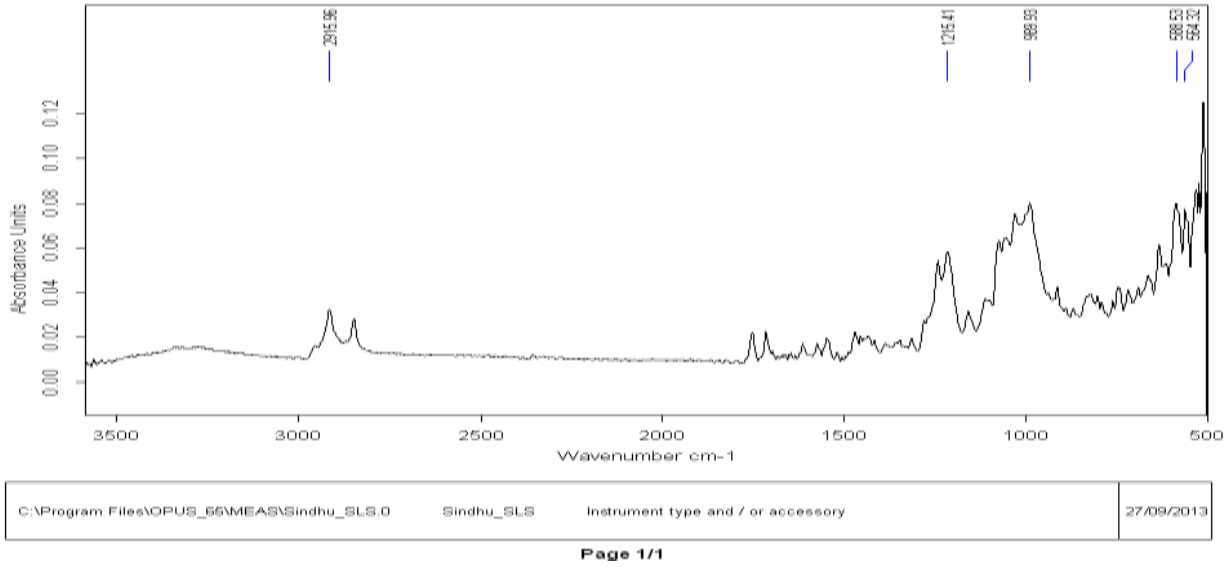

Figure 3- IR spectra of physical mixture

Pre compression parameters

The powdered blend was evaluated for angle of repose, bulk density, tapped density, compressibility index and Hausner's ratio and the results are shown in table 3

- The angle of repose varied from 24.26º to 31.02º.
- The bulk density of the powder blend was found to be in the range of 0.451 to 0.668 gm/ml and the tapped density ranged from 0.525 to 0.754 gm/ml.
- The compressibility indexes were in the range of 11.36 to 14.36% and in all the cases the Hausner's ratio was found to be less than 1.2.

Table 3- Precompression parameters results

Parameters Formulation	Bulk Density (gm/ml)	Tapped Density (gm/ml)	Hausner's Ratio	Compressibility Index (%)	Angle of Repose(^{o})
F1	0.451	0.525	1.164	14.09	29.98
F2	0.465	0.543	1.167	14.36	31.71
F3	0.471	0.534	1.133	11.86	28.82
F4	0.481	0.544	1.130	11.58	24.26
F5	0.613	0.701	1.143	12.55	25.45
F6	0.634	0.728	1.148	12.91	27.76
F7	0.594	0.685	1.153	13.28	25.02
F8	0.569	0.651	1.162	13.97	26.57
F9	0.608	0.688	1.131	11.62	29.49
F10	0.668	0.754	1.129	11.36	27.15

Post compression parameters:

Candesartan cilexetil tablets were prepared by direct compression method. The tablets were evaluated for weight variation, hardness, friability, drug content and dissolution. The results of physicochemical evaluation of prepared tablets are shown in the table 4.

- The hardness was in the range of 4.0 to 5.5 kg/cm^2 and in all the cases the friability was less than 1%.
- The drug content of all the formulations was found to be in the range of 94.54% to 101.12%.

Table 4- Post compression parameters

Parameters Formulations	Weight variation (%)	Friability (%)	Hardness* (kg/cm^2)
F1	1.35	0.315	5.3
F2	1.65	0.321	5.5
F3	1.03	0.336	4.0
F4	1.54	0.367	4.2
F5	1.76	0.345	4.5
F6	1.43	0.540	4.0
F7	1.14	0.539	4.8
F8	1.89	0.628	5.1
F9	1.97	0.589	4.0
F10	1.38	0.608	4.5

Calibration curve data:

The calibration curve of Candesartan cilexetil was prepared in phosphate buffer (pH 6.8). The plot of different concentrations of Candesartan cilexetil versus absorbance was found to be linear in the concentration range of 10-50 µg/ml at 255 nm. The absorbance at different concentrations was shown in Table 5. The data of standard curve were linearly regressed. The slope and correlation

coefficient values were found to be 0.021 and 0.999 respectively. The calibration curve was shown in Figure 4.

Table 5- Calibration curve data of Candesartan cilexetil

S.no	Concentration µg/ml	Absorbance
1	0	0
2	10	0.195
3	20	0.417
4	30	0.654
5	40	0.859
6	50	1.05

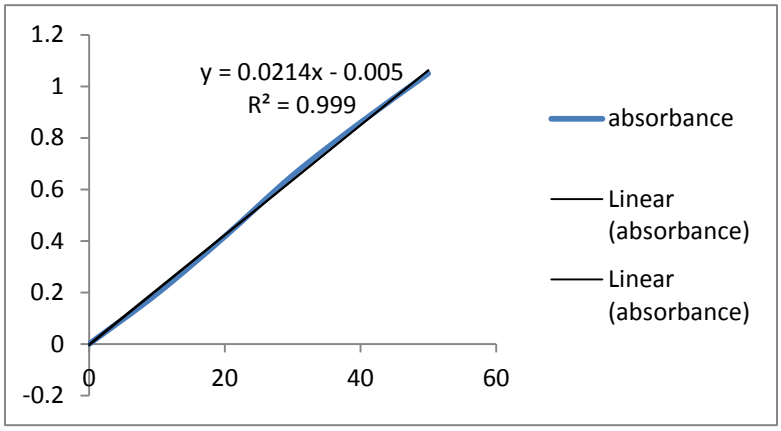

Figure 4- Calibration curve of Candesartan cilexetil at 255 nm.

Table 6- Drug content

Formulations	Drug content (%)
F1	100.2
F2	98.81
F3	97.42
F4	100.14
F5	94.54
F6	99.12
F7	96.74
F8	101.12
F9	98.96
F10	99.28

Table 7: *In vitro* drug release profile of Candesartan cilexetil for formulations F1 to F10

Time (hrs)	Cumulative % of drug release									
	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
0.5	0.22	0.08	1.98	1.54	3.23	3.01	38.36	35.53	22.01	18.34
1	0.31	0.15	4.03	2.51	6.75	4.98	40.01	42.83	28.78	23.28
2	0.54	0.29	11.46	7.83	7.94	5.04	46.76	47.41	34.82	27.61
3	0.56	0.38	14.60	10.64	9.21	6.98	58.04	55.84	39.67	32.42

4	0.64	0.45	17.87	13.45	12.68	10.13	69.73	61.26	43.58	38.76
5	0.83	0.59	23.05	18.76	16.99	15.65	74.28	66.03	47.31	43.97
6	1.16	0.76	25.25	22.32	23.56	19.99	82.56	78.48	56.52	49.45
7	1.44	0.98	28.99	26.07	27.87	24.41	90.41	86.24	61.83	54.89
8	1.57	1.11	31.17	28.42	30.43	28.92	95.92	93.64	68.37	62.83
9	1.81	1.33	33.92	29.77	33.12	31.43	99.83	96.98	76.24	71.30
10	1.96	1.61	35.76	30.49	36.23	33.47		99.74	87.96	79.82
11	2.01	1.83	36.53	32.69	38.94	35.76			99.13	87.17
12	2.15	1.99	39.14	33.04	40.32	37.93				99.94

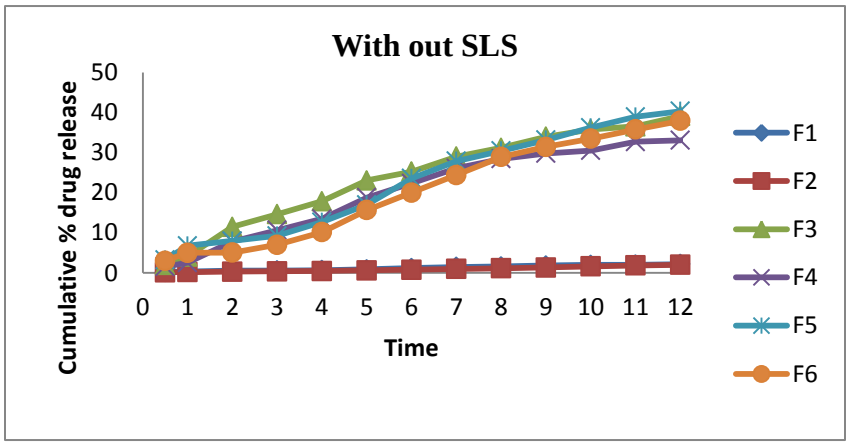

Figure 5-*In vitro* drug release profile of Candesartan cilexetil for formulation without SLS (F1-F6).

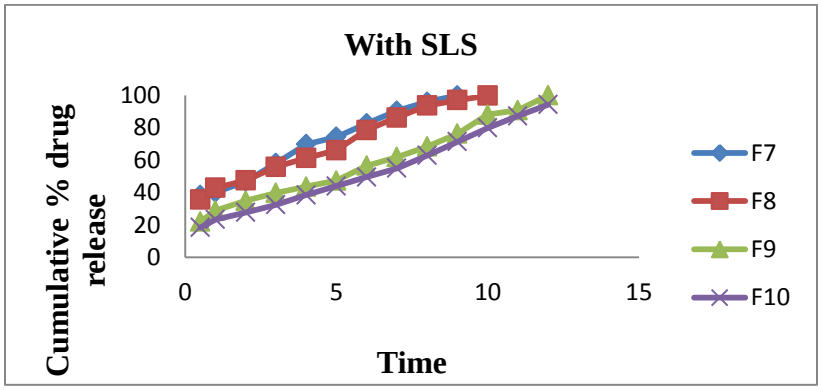

Figure 6-*In vitro* drug release profile of Candesartan cilexetil for formulations with SLS (F7-F10).

Release kinetics and Mechanism studies

Table 7: Higuchi model release profile of Candesartan cilexetil tablets for formulations F1 to F10

Square root of Time	Cumulative % of Drug release F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
0	0	0	0	0	0	0	0	0	0	0
0.70710678	0.22	0.08	1.98	1.54	3.23	3.01	38.36	35.53	22.01	18.34
1	0.31	0.15	4.03	2.51	6.75	4.98	40.01	42.83	28.78	23.28

1.41421356	0.54	0.29	11.46	7.83	7.94	5.04	46.76	47.41	34.82	27.61
1.73205081	0.56	0.38	14.60	10.64	9.21	6.98	58.04	55.84	39.67	32.42
2	0.64	0.45	17.87	13.45	12.68	10.13	69.73	61.26	43.58	38.76
2.23606798	0.83	0.59	23.05	18.76	16.99	15.65	74.28	66.03	47.31	43.97
2.44948974	1.16	0.76	25.25	22.32	23.56	19.99	82.56	78.48	56.52	49.45
2.64575131	1.44	0.98	28.99	26.07	27.87	24.41	90.41	86.24	61.83	54.89
2.828427125	1.57	1.11	31.17	28.42	30.43	28.92	95.92	93.64	68.37	62.83
3.16227766	1.96	1.61	35.76	30.49	36.23	33.47		99.74	87.96	79.82
3.464101615	2.15	1.99	39.14	33.04	40.32	37.93				99.94

Table 8- Korsmeyer and Peppas model for Candesartan cilexetil tablets of formulations F1 to F10.

Log Time	Log cumulative % of Drug release									
	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
0	0	0	0	0	0	0	0	0	0	0
-0.301029996	-0.65	-1.09	0.29	0.18	0.50	0.47	1.58	1.51	1.34	1.26
0	-0.50	-0.82	0.60	0.40	0.82	0.69	1.60	1.63	1.45	1.36
0.301029996	-0.26	-0.53	1.05	0.89	0.90	0.70	1.67	1.67	1.54	1.44
0.477121255	-0.25	-0.42	1.16	1.02	0.96	0.84	1.76	1.74	1.59	1.51
0.602059991	-0.19	-0.34	1.25	1.12	1.10	1.0	1.84	1.78	1.63	1.58
0.698970004	-0.08	-0.22	1.36	1.27	1.23	1.19	1.87	1.82	1.67	1.64
0.77815125	0.06	-0.11	1.40	1.34	1.37	1.30	1.91	1.89	1.75	1.69
0.84509804	0.15	-0.009	1.46	1.41	1.44	1.38	1.95	1.93	1.79	1.73
0.903089987	0.19	0.04	1.49	1.45	1.48	1.46	1.98	1.97	1.83	1.79
1	0.29	0.20	1.55	1.48	1.55	1.52		1.99	1.94	1.90
1.079181246	0.33	0.29	1.59	1.51	1.60	1.57				1.97

FT-Infrared spectroscopy to find out the compatibility of drug with polymer:

This study was carried out to find out the possible interaction between the selected drug Candesartan cilexetil and the polymers carbopol 934P, HPMC K15M, sodium CMC and SLS. FT-IR of candesartan cilexetil showed the following characteristics peaks in the official range. Aromatic ring in the range of 2850-2950 cm^{-1}, carbonyl group 1200-1250 cm^{-1}, ketone group 1700-1750 cm^{-1}, o-substitution 700-750 cm^{-1} and hydroxyl group 2800-2850 cm^{-1}

Pre compression parameters:

The prepared Candesartan cilexetil tablet blends were evaluated for angle of repose, bulk density, tapped density and compressibility index. The bulk densities of the tablet blends were found to be in the range of 0.451 to 0.668 gm/ml and the tapped density ranged from 0.525 to 0.754 gm/ml. The flow characteristics of the tablets blend were assessed by determined their angle of repose. The values of compressibility indexes were in the range of (11.36 to 14.36%) and angle of repose varied from (24.26º to 31.02º) signifies reasonably good flow properties of the tablet blends for all

the formulations thus ensuring homogenous filling of dies. The Hausner's ratio of all formulation blends was found to be less than 1.2 indicates better flow properties.

Preparation of Candesartan cilexetil tablets:

Candesartan cilexetil tablets were prepared by direct compression method. Carbopol 934P, HPMC K15M, sodium CMC were used as retardant polymers and microcrystalline cellulose as a diluent. Sodium lauryl sulfate was used as a solubilizer. A total number of 10 formulations were made.

Post compression parameters:

The Candesartan cilexetil tablets were prepared by direct compression method and the results are shown in table. The tablets were evaluated for its weight variation, drug content, hardness, friability. Tablet hardness test is measure of the cohesiveness of tablets and it plays a vital role for drug release. It is one of the official methods for the determination of tablet strength. The other essential requirements of tablets are to have an acceptable friability to withstand shocks during packing and shifting. Hardness must be controlled to ensure that the product is firm enough to withstand handling without breaking or crumbling and not so hard that the disintegration time is unduly prolonged. The weight variation of the prepared tablet was found to be 1.03 – 1.97%. So it was predicted that all the tablets exhibited uniform weight with low standard deviation values within the acceptable variation as per IP. The friability of all the formulations was found to be less than 1.0 %, which indicates the tablet's ability to withstand abrasion in handling, packaging and shipment. The hardness of tablet was varied from 4.0 – 5.5 kg/cm^2, which have satisfactory strength to withstand with the applied mechanical shocks. The drug content of all the tablet formulations was determined spectrophotometrically at 255 nm. It varied from 94.54% – 101.12% per tablet, indicating uniformity of the drug content in the prepared tablets.

***In vitro* drug release studies:**

Dissolution testing has become a mandatory requirement for several oral dosage forms. Dissolution testing is an integral component in pharmaceutical research and development of solid dosage forms. *In-vitro* release of Candesartan cilexetil from the prepared sustained release matrix tablets was studied in phosphate buffer pH 6.8 for 12 hours. Initially the formulations with carbopol 934P were prepared and the results depicted that it did not show release from the tablets. This property attributed due to the water insoluble characteristic property of the drug and even the polymer carbopol 934P is hydrophobic. So this tightly bound matrix retarded the release of drug. So an attempt was made for the preparation of matrix tablets using water soluble polymers like HPMC K15M and sodium CMC. Even with these polymers there was no enough release. Incorporation of water soluble surfactant like SLS was the next attempt. The prescribed limit of

solubiliser was taken. The formulations with SLS showed satisfactory release as compared to others. Formulations F10 which contains sodium CMC with 1% SLS release was found to be 99.94% respectively after 12 hours. Sustained release was more pronounced in F10. Next the release data obtained were subjected for the kinetic treatment to know the type and order of drug release.

The obtained data from *in-vitro* drug release was fitted in Higuchi model and Korsmeyer-Peppa's model. Higuchi model is represented graphically as cumulative percentage drug release v/s square root time. Korsmeyer-Peppa's model is represented graphically as log cumulative percentage drug release v/s log time. The R^2 values for F1 to F10 were found to be 0.863, 0.759, 0.936, 0.899, 0.864, 0.820, 0.967, 0.959, 0.946 and 0.931 respectively after plotting the graphs. Correlation coefficient of the optimized formulation was closer to 1, so the release profile of the formulation was found to be in zero order. Korsmeyer-Peppa's model is widely used, when the release mechanism is not well known or more than one type of release could be involved. For non-fickian release, the value of n falls between 0.5 and 1.0; while in case of Fickian diffusion, n=0.5; for zero-order release (case II transport), n=1; and for super case II transport, n>1. According to 'n' value it is 2.03, so it follows super case II transport with zero order release.

CONCLUSION

From the above experiment, it was concluded that the sustained release matrix tablets were formulated using polymers like carbopol 934P, HPMC K15M and Sodium CMC. The method of direct compression utilizes minimum machinery and man power. From the economical point of view, it may be beneficial for the local pharmaceutical firms to adopt such simple technologies for the preparation of sustained release product. In subsequent studies, the prepared tablets were evaluated. Among all the formulations F10 showed a better drug release over 12 hours of time and it released over 99.94% of the drug out of 10 formulations with a sustained effect. Data of *in-vitro* drug release were fit into different equations and kinetic models to explain the release kinetics of candesartan cilexetil from the sustained release tablet. On experimental data it was concluded that sustained release matrix tablets of candesartan cilexetil would be an effective alternative approach for management of hypertension. Sodium CMC (1:2) along with SLS was proved to be the most promising dosage form for sustained release of candesartan cilexetil tablets. It also found to be that there was no interaction between the drug and polymer in all the formulations. Among all the formulations, the optimized formulation F10 fulfilled all the objectives.

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