ISSN 2349-7203

IJPPR
INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH
An official Publication of Human Journals

HUMAN

Human Journals
Research Article
May 2016 Vol.:6, Issue:2

Development and *In Vitro* Characterization of Canagliflozin Sustained Release Matrix Tablets

IJPPR
INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH
An official Publication of Human Journals
ISSN 2349-7203
HUMAN

Srinivas Martha[*1], Gulle.Srikanth babu[2], J.devilal[3], Shravan Kumar Nanumala[4]

1Assistant professor, Department of pharmaceutics, Joginpally BR Pharmacy College, Yenkapally village, moinabad mandal, Hyderabad, ranga reddy district, Telangana, India- 500075

2Department of pharmaceutics, Joginpally BR Pharmacy College, Yenkapally village, moinabad mandal, Hyderabad, ranga reddy district, Telangana, India- 500075

3Associate professor, Department of pharmaceutical analysis, Bhaskar Pharmacy College, Yenkapally village, moinabad mandal, Hyderabad, ranga reddy district, Telangana, India- 500075

4Assistant professor, Department of pharmacology, Joginpally BR Pharmacy College, Yenkapally village, moinabad man reddy district, Telangana, Indiadal, Hyderabad, ranga, India - 500075

Submission: 7 May 2016
Accepted: 12 May 2016
Published: 25 May 2016

www.ijppr.humanjournals.com

Keywords: Sustained release, Polymer, Matrix tablet, Direct compression, Polymethyl methacrylate

ABSTRACT

Sustained release matrix tablet is formulated mainly by direct compression method by dispersion of solid particle within a porous matrix formed by using different polymers like Polymethyl methacrylate (PMMA), Polyglycolic acid, HPMC etc. The matrix controls the release rate of drug. Release retardants like HPMC can aid in sustained release and thus they form core excipient of the formulation. The method involves the direct compression of blend of drug, retardant material and additives to formulate a tablet in which the drug is embedded in a matrix core of the retardant, alternatively, granulation can be carried out prior to compression. The matrices used may be of hydrophilic, hydrophobic, mineral, or biodegradable types. The drug release rate can be studied by *in-vitro* dissolution studies. Thus, sustained release matrix tablets can assure better patient compliance through reduction in total dose and dosage regimen, which can be of great help to treat chronic diseases.

INTRODUCTION

Pharmaceutical products designed for oral delivery are mainly conventional drug delivery systems, which are designed for immediate release of drug for rapid or immediate absorption.

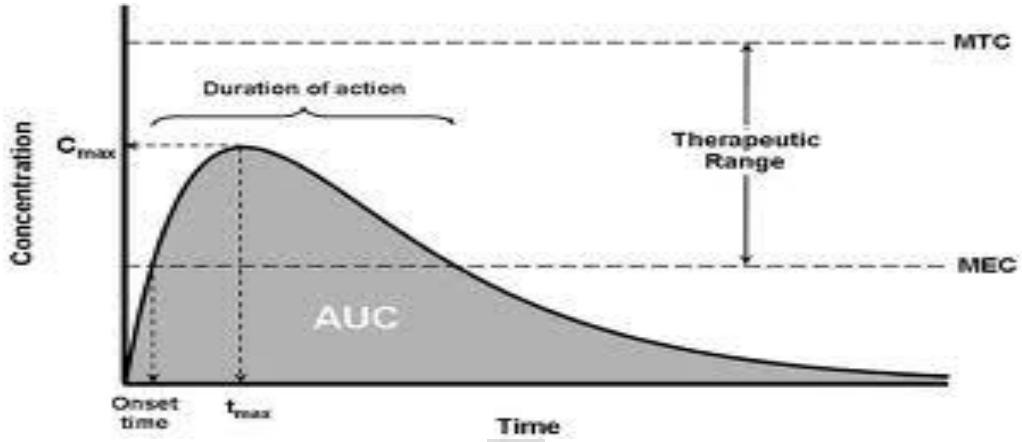

Figure: 1. A hypothetical plasma concentration-time profile from conventional multiple dosing and single doses of sustained and controlled delivery

Formulations (MSC = maximum safe concentration, MEC = minimum effective concentration).

As can be seen in the graph (Figure1), administration of the conventional dosage form by extravascular route does not maintain the drug level in blood for an extended period of time. The short duration of action is due to the inability of the conventional dosage form to control temporal delivery.

- The conventional dosage forms like solution; suspension, capsules, tablets and suppository etc. have some limitations such as:
- Drugs with short half-life require frequent administration, which increases chances of missing the dose of drug leading to poor patient compliance.
- A typical peak-valley plasma concentration-time profile is obtained which makes attainment of steady state condition difficult. The unavoidable fluctuations in the drug concentration may lead to under medication or over medication as the steady state concentration values fall or rise beyond the therapeutic range.
- The fluctuating drug levels may lead to precipitation of adverse effects especially of a drug with small therapeutic index, whenever overdosing occurs.

In order to overcome these limitations, Modified drug delivery systems are preferred for such therapy because they offer better patient compliance, reduce dose and side effects, and increase the safety margin for high-potency drugs.

The term modified-release drug product is used to describe products that alter the timing and/or the rate of release of the drug substance. A modified-release dosage form is defined as "one for which the drug release characteristics of time course and/or location are chosen to accomplish therapeutic or convenience objectives not offered by conventional dosage forms such as solutions, ointments, or promptly dissolving dosage forms as presently recognized".

Modified Release Systems

Modified release systems may be conveniently divided into 4 categories.

- Sustained release
- Controlled release
- Prolonged release
- Delayed release
- Site specific release

Sustained Release Systems:

Sustained release systems include any drug delivery system that achieves slow release of drug over an extended period of time. If the system is successful in maintaining constant drug levels in the blood or target tissue, it is considered as a *controlled release system*. If it is unsuccessful at this but nevertheless extends the duration of action over that achieved by conventional delivery, it is considered as a prolonged release system. Controlled release systems not only prolong the duration of action but also result in predictable and reproducible drug release kinetics.

A sustained release product may be formulated to contain an immediately available dose to provide an immediate action. This is followed by a more gradual and continuous release of subsequent doses to maintain the plasma concentration of the drug over an extended period of time.

MATERIALS AND METHODS

Table: 1. List of Materials

S.NO	Ingredients	Company Name
1	Canagliflozin	Natco chemicals, Hyderabad
2	Eudragit RS 100	Colorcon Asia Pvt. limited, India
3	Carbopol	Colorcon Asia Pvt. limited, India
4	Lactose	Loba chemie Pvt. Ltd, Mumbai
5	MCC	Krystal colloid Ltd,Mumbai
6	Talc	Loba chemie Pvt. Ltd, Mumbai
7	Xanthan gum	Krystal colloid Ltd,Mumbai Mumbai
8	Magnesium stearate	Loba chemie Pvt. Ltd, Mumbai

Excipients for Formulation:

Table: 2. Selected Excipients for formulation

SI.NO	EXCIPIENTS	FUNCTION
1	Eudragit RS 100	Release rate retardant
2	Xanthan gum	Release rate retardant
3	Carbopol	Release rate retardant
4	Lactose monohydrate	Diluent
5	Microcrystalline cellulose	Diluent
6	Talc	Glidant
7	Magnesium stearate	Lubricant

Canagliflozin Matrix Tablets Preparation:

All the matrix tablets, each containing 250mg of Canagliflozin, were prepared by direct compression method and some of the formulations were prepared by using Eudragit RS100, Xanthan gum and Carbopol to study the effect of Polymer on the drug release. Canagliflozin and polymers such as Eudragit RS100, Xanthan gum and Carbopol were accurately weighed, geometrically mixed and passed through #40 mesh and then diluents such as lactose and

microcrystalline cellulose were accurately weighed and passed through #40 mesh. Both mixtures were mixed for 5 minutes as a dry mixing. Then, the lubricant magnesium stearate was passed through #60 mesh added to the mixture and mixed for 2 minutes. Then finally talc was added to free flow of granules. Then the mixtures were compressed into tablets using 8 station rotary compressed machines with punch size 9mm.

Method:

Direct Compression:

The sustained release matrix tablets of Canagliflozin were prepared through direct compression method (without granules making step). Various steps (Sieving, Dry mixing, Lubrication & Compression) involved in the tablet production by direct compression method were orchestrated below:

Sieving:

Canagliflozin and polymers such as Eudragit RS100, Xanthan gum and Carbopol were accurately weighed, geometrically mixed and passed through #40 mesh and then diluents such as lactose and microcrystalline cellulose and binder were accurately weighed and passed through #40 mesh.

Dry Mixing:

All the ingredients (Including the active ingredient) were taken in poly bag and mixed for 5mins to ensure uniform mixing of the ingredients with the drug.

Lubrication:

Then Magnesium Stearate was mixed with the powder mixture in a poly bag for 5mins to get a uniform blend.

Compression:

Finally, the powder mixture was compressed into tablets using tablet compression machine at the weight of 300mg each.

Table: 3. Composition of Different formulations from F1 to F9

INGREDIENTS (mg/tab)	F1	F2	F3	F4	F5	F6	F7	F8	F9
Canagliflozin	100	100	100	100	100	100	100	100	100
Xanthan gum	50	75	100	-	-	-	-	-	-
Carbopol	-	-	-	50	75	100	-	-	-
Eudragit RS100	-	-	-	-	-	-	50	75	100
Lactose	72	59.5	47	72	59.5	47	72	59.5	47
M.C.C.	72	59,5	47	72	59.5	47	72	59.5	47
Talc	3	3	3	3	3	3	3	3	3
Magnesium stearate	3	3	3	3	3	3	3	3	3
Total {mg}	300	300	300	300	300	300	300	300	300

Evaluation of Precompression Blend:

a) Angle of repose:

The angle of repose of powder was determined by the funnel-method. The accurately weighed granules were taken in a funnel. The height of the funnel was adjusted in such a manner that the tip of the funnel just touched the apex of the heap of the powder. The granules were allowed to flow through the funnel freely onto the surface.

The diameter of the powder cone measured and angle of repose was calculated using the following equation [69]

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

Where h and r are the height and radius of the powder cone, θ is the angle of repose.

Table: 4. Angle of repose

Angle of repose(θ)	**Flow property**
25-30	Excellent
31-35	Good
36-40	Fair
41-45	Passable
46-55	Poor
56-65	Very poor
>66	Very very poor

b) Determination of Bulk Density and Tapped Density:

An accurately weighed quantity of the powder (W) was carefully poured into the graduated cylinder and volume (V_0) was measured. Then the graduated cylinder was closed with lid and set into the tap density tester (USP). The density apparatus was set for 100 tabs and after that the volume (V_f) was measured and continued operation till the two consecutive readings were equal. [70]

The bulk density and the tapped density were calculated using the following formula

$$\text{Bulk density} = W/V_0$$

$$\text{Tapped density} = W/V_f$$

Where,

W= Weight of the powder

V_0 = Initial volume,

V_f = final volume

c) Compressibility Index (Carr's Index):

Carr's index (CI) is an important measure that can be obtained from the bulk and tapped densities. In theory, the less compressible a material the more flowable it is

$$CI = (TD-BD) \times 100/TD$$

Where,

TD is the tapped density

BD is the bulk density

Table: 5. Carr's Index Values

Carr's Index	Properties
5-12	Free flowing
13-16	Good
18-21	Fair
23-35	Poor
33-38	Very poor
>40	Extremely poor

d) Hausner's Ratio:

It is the ratio of tapped density and bulk density. Hausner found that this ratio was related to interparticle friction and as such, could be used to predict powder flow properties [70]. Generally, a value less than 1.25 indicates good flow properties, which is equivalent to 20% of Carr's index.

Hausner's ratio= TD/BD.

Evaluation of Canagliflozin Matrix Tablets:

The prepared matrix tablets were evaluated for the following parameters:

a. Thickness

b. Hardness

c. Friability

d. Weight variation

e. Assay

a) Thickness:

Twenty tablets from the representative sample were randomly taken and individual tablet thickness was measured by using digital vernier calipers. Average thickness was calculated.

b) Hardness:

Tablet hardness was measured by using Monsanto hardness tester. From each batch, six tablets were measured for the hardness and average of six values was noted.

c) Friability Test:

From each batch, ten tablets were accurately weighed and placed in the friability test apparatus (Roche friabilator). Apparatus was operated at 25rpm for 4 minutes and tablets were observed while rotating. The tablets were then taken after 100 rotations, dedusted and reweighed. The friability was calculated as the percentage weight loss.

Note: No tablet should stick to the walls of the apparatus. If so, brush the walls with talcum powder. There should be no capping also.

% Friability was calculated as follows

$$\%F = \frac{W_1 - W_2}{W_1} \times 100$$

Where,

W_1 = Initial weight of the 20 tablets.

W_2 = Final weight of the 20 tablets after testing.

Friability values below 0.8% are generally acceptable.

d) Weight Variation Test:

To study weight variation individual weights (W_I) of 20 tablets from each formulation were noted using electronic balance. Their average weight (W_A) was calculated. Percent weight variation was calculated as follows. Average weights of the tablets were calculated.

$$\% \text{ weight variation} = (W_A - W_I) \times 100 / W_A$$

According to IP 1996, out of twenty tablets ±5 % variation can be allowed for not more than two tablets.

According to USP 2004, ±5% weight variation can be allowed for not more than two tablets out of twenty tablets.

e) Assay:

Five tablets were weighed and triturated, from that transfer an accurately weighed portion of the powder equivalent to about 250mg of Canagliflozin to a 100ml volumetric flask containing buffer solution and then concentration is measured at λ_{max} i.e. 244nm.

***In-Vitro* Dissolution Studies**

The *in-vitro* dissolution studies were performed using the USP-II (Paddle) dissolution apparatus at 50 rpm. The dissolution medium consisted of 900ml of phosphate buffer pH 6.8, maintained at 37±0.5^{o}C. An aliquot (5ml) was withdrawn at specific time intervals and drug content was determined by UV-visible spectrometer at 244nm.

Dissolution Test Parameters for Matrix Tablets:

Medium : 900ml of 6.8 pH phosphate buffer solution.
rpm : 50
Time : 2, 4, 8, 16, 20, 24 hours
Apparatus : Paddle
λ_{max} : 244nm
Temperature : 37^{0} C ± 0.5^{0}C

RESULTS AND DISCUSSION

Standard Curve of canagliflozin:

The absorbance was measured with a UV spectrophotometer at 304nm against phosphate buffer solution of pH of 6.8. The absorbance so obtained was tabulated as in Table 6. Calibration curve was plotted and shown in Figure 2.

Table: 6. Spectrophotometric data for the estimation of Canagliflozin

SL. NO	Concentration (µg/ml)	Absorbance(244nm)
1	0	0
2	2	0.091
3	4	0.178
4	6	0.254
5	8	0.343
6	10	0.428

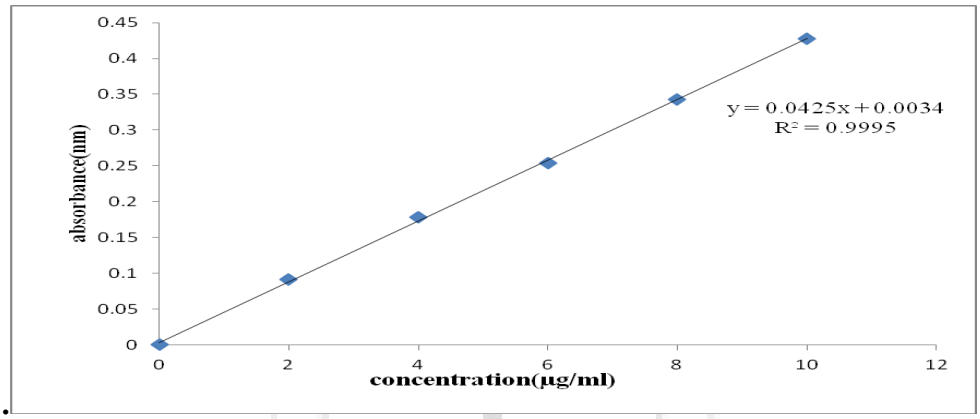

Figure: 2. Standard curve of Canagliflozin in pH 6.8 phosphate buffer solution

Discussion:

Development of calibration curve:

Calibration curve of the pure drug Canagliflozin was prepared in the concentration range of 2 to 10µg/ml at the wavelength of 244nm. The calibration curve showed good linearity and regression coefficient was 0.999 (r^2).

Compatibility Study by Using FTIR Spectroscopy:

FTIR:

The possible interaction between the Canagliflozin and the polymers such as xanthan gum, Carbopol and Eudragit RS 100 was studied by IR spectroscopy. The IR spectra for Canagliflozin, Xanthan gum, Carbopol and Eudragit RS 100 and its physical mixtures are shown in figures 3 to 6.

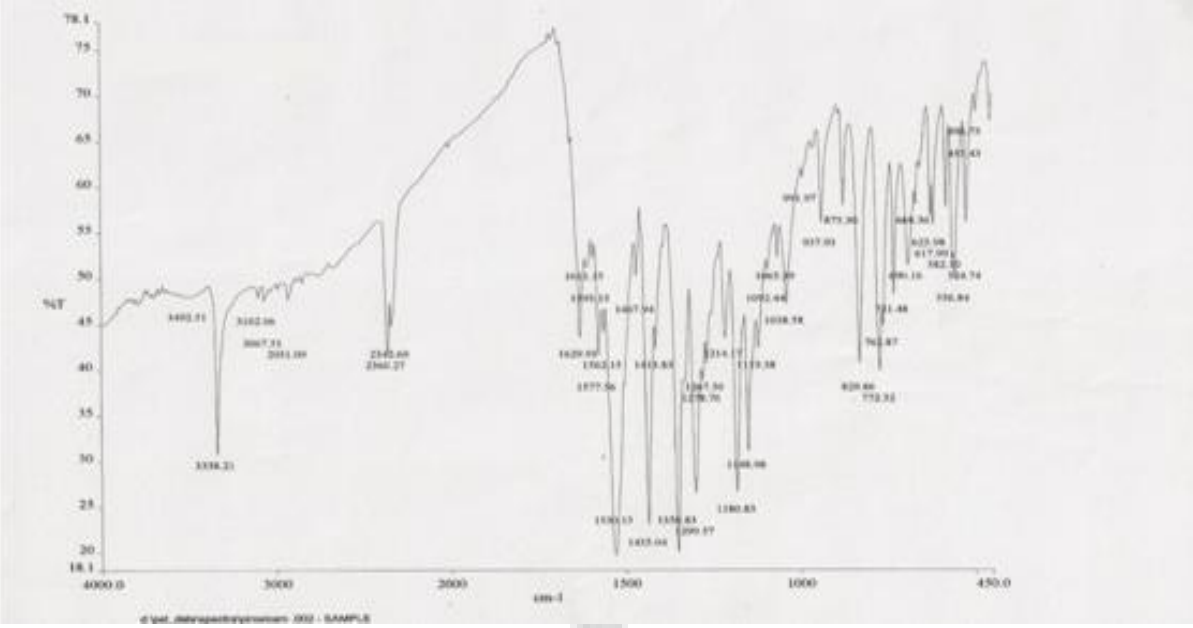

Figure: 3. IR Spectra of Canagliflozin pure drug

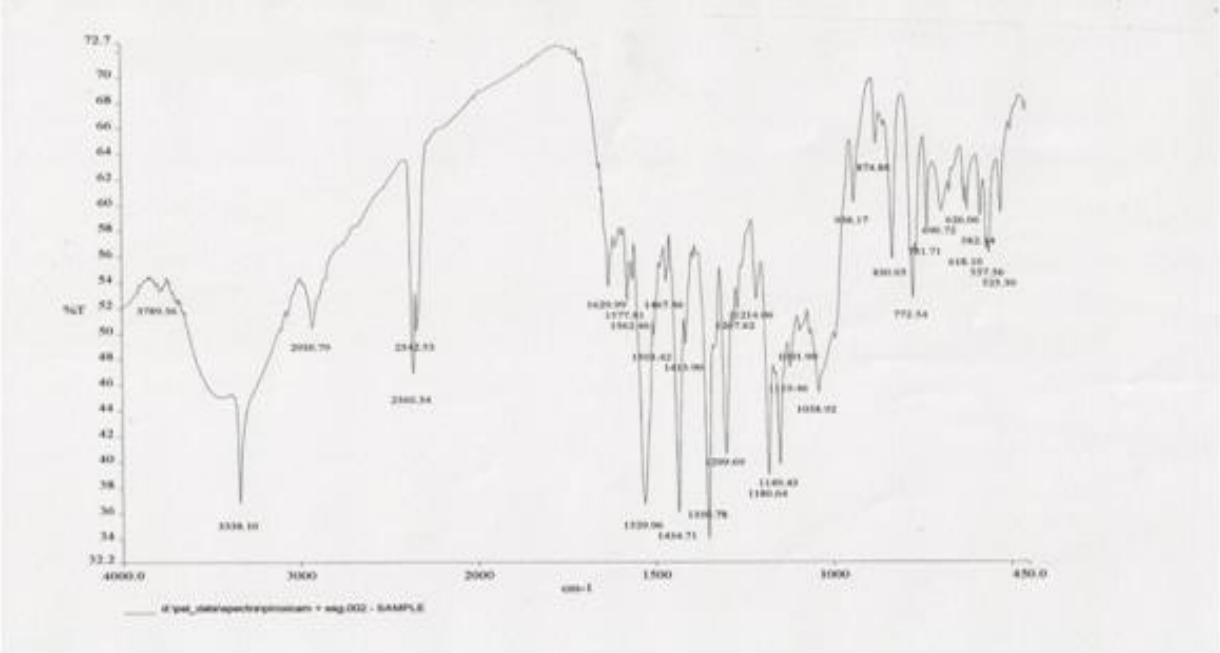

Figure: 4. IR spectra of Canagliflozin with Xanthan gum

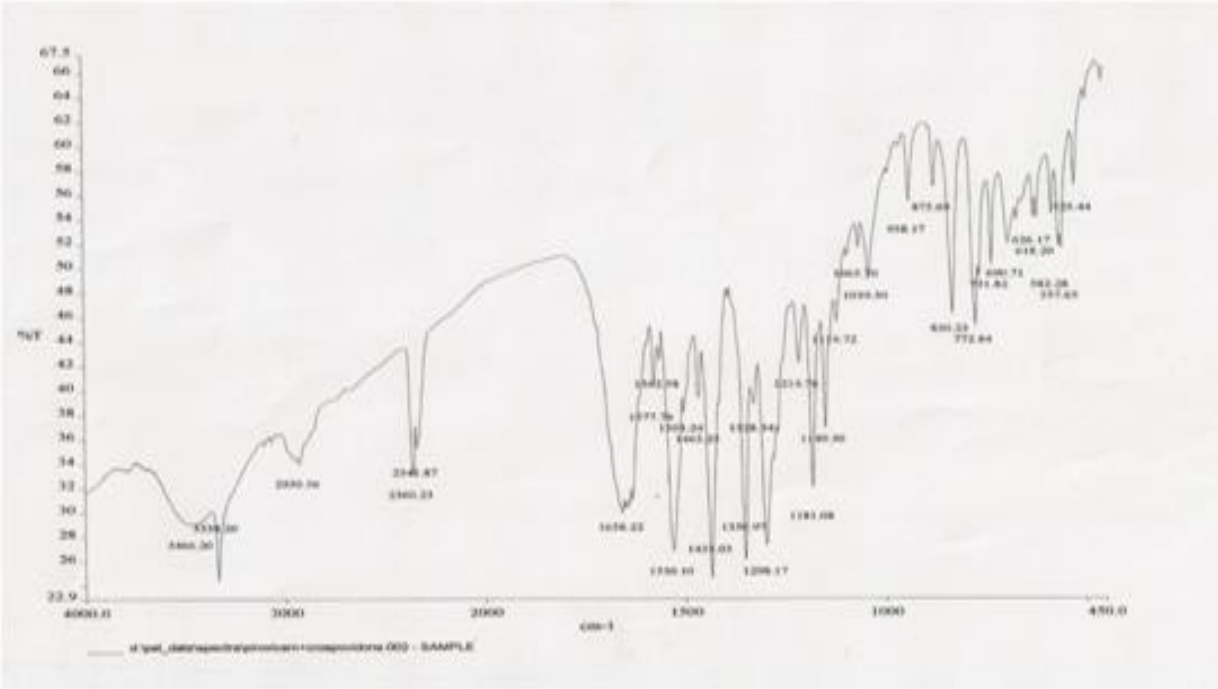

Figure: 5. IR spectra of Canagliflozin with carbopol

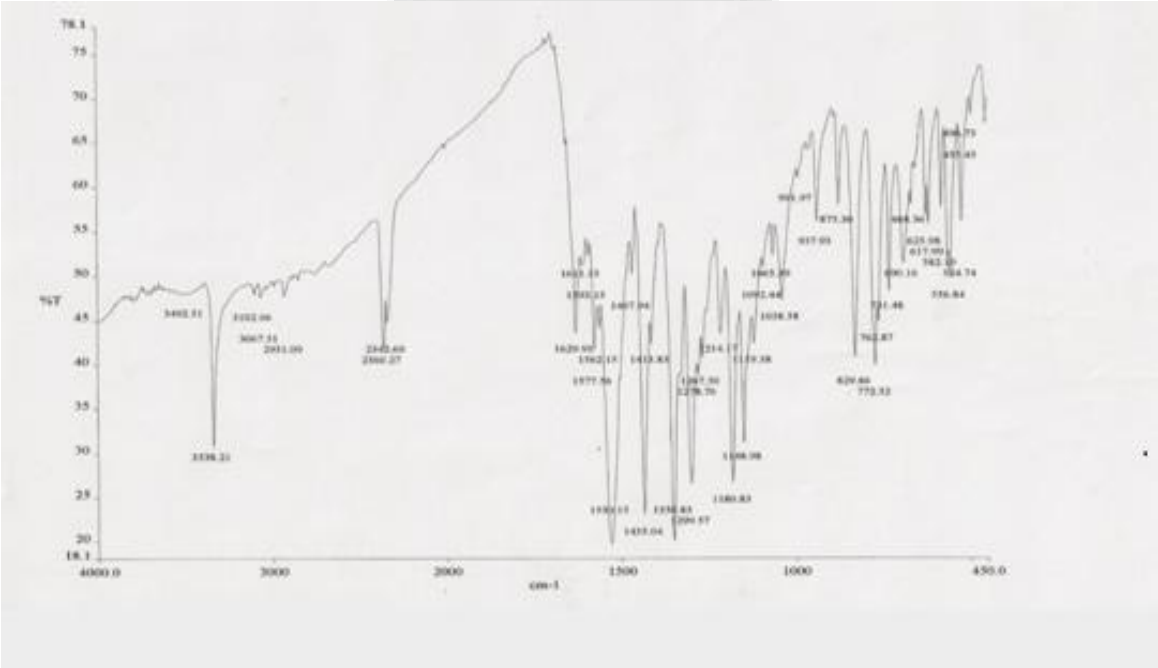

Figure: 6. IR spectra of Canagliflozin with Eudragit RS100

Table: 7. Peaks observed in FTIR spectra's

Peak	Canagliflozin pure drug	Canagliflozin and Xanthan gum	Canagliflozin and Carbopol	Canagliflozin and Eudragit RS 100
C-O Str (1Alcohol)	1051.73 cm^{-1}	1051.47 cm^{-1}	1051.76 cm^{-1}	1047.84 cm^{-1}
C-O Str in C-O-C	1113.94 cm^{-1}	1113.01 cm^{-1}	1114.00 cm^{-1}	1112.32 cm^{-1}
C-O Str in C=C-O-C	1242.15 cm^{-1}	1242.90 cm^{-1}	1242.15 cm^{-1}	1242.56 cm^{-1}
C-O Str in COOH	1615.62 cm^{-1}	1617.08 cm^{-1}	1616.13 cm^{-1}	1619.87 cm^{-1}
C-H Str	2924.41 cm^{-1}	2926.04 cm^{-1}	2924.55 cm^{-1}	2932.04 cm^{-1}
C=C Ring Str	1561.94 cm^{-1}	1561.33 cm^{-1}	1562.61 cm^{-1}	1559.58 cm^{-1}
N-C Str	3431.37 cm^{-1}	3431.13 cm^{-1}	3414.76 cm^{-1}	3418.11 cm^{-1}
N-H deformation	1385.80 cm^{-1}	1387.39 cm^{-1}	1385.74 cm^{-1}	1392.37 cm^{-1}
Disubstituted benzene	809.90 cm^{-1}	809.96 cm^{-1}	809.95 cm^{-1}	808.73 cm^{-1}

Discussion:

The results revealed no considerable changes in the IR peaks of Canagliflozin, when mixed with excipients compared to pure Canagliflozin, these observations indicated the compatibility of Xanthan gum, Carbopol and Eudragit RS 100 with Canagliflozin. The FTIR studies revealed that there is no interaction between drug and polymers.

Table: 8. Physical evaluation of Pre-compression Blend

Formulation	Bulk density (g/cc)	Tapped density (g/cc)	Hausner ratio	Compressibility index (%)	Angle of repose (ɵ)
F1	0.49±0.04	0.57±0.02	1.17±0.03	14.04±0.04	27.40±0.05
F2	0.48±0.06	0.55±0.03	1.14±0.02	12.72±0.02	26.06±0.02
F3	0.46±0.01	0.53±0.01	1.15±0.05	13.20±0.04	24.38±0.01
F4	0.43±0.02	0.49±0.02	1.14±0.04	12.24±0.03	23.72±0.06
F5	0.41±0.02	0.47±0.03	1.13±0.01	12.76±0.05	21.94±0.03
F6	0.45±0.03	0.48±0.05	1.12±0.05	11.36±0.02	20.48±0.04
F7	0.51±0.05	0.57±0.03	1.18±0.01	13.85±0.06	24.54±0.04
F8	0.55±0.01	0.56±0.02	1.15±0.03	13.11±0.03	25.74±0.02
F9	0.48±0.06	0.55±0.03	1.14±0.02	12.72±0.02	26.06±0.02

All values are mean ± S.D, n=3

Physical Evaluation of Pre-compression Blend

a. Bulk Density:

It is the ratio between a given mass of powder and its bulk volume. The bulk densities of the powder blends of all the formulations ranged from 0.41 to 0.55gm/cc.

b. Tapped Density:

Tapped density is the ratio between weight of the sample powder taken and the tapped volume. The Tapped densities of the powder blends of all the formulations ranged from 0.47 to 0.59gm/c.

c. Hausner's Ratio:

Hausner's ratio is the ratio of tapped density and bulk density. Hausner's ratio is an indirect index of ease of powder flow. The Hausner's ratio values ranged from 1.12 to 1.18. Evaluated values of Hausner's ratio obtained were less than 1.25 indicating good flow. It means that the powder flow properties were within the pharmacopoeial limits.

d. % Compressibility or Carr's index:

It indicates powder flow properties. The Carr's index was within the pharmacopoeial specifications and the values ranged from 11.36 to 14.04%. 12-16 Carr's index value indicates good flow, 18-21 Carr's index value indicates fair.

e. Angle of Repose:

It is defined as maximum angle possible between the surface of the pile of powder and the horizontal plane. The angle of repose of the powder blends of all the formulations were determined and the values ranged from 20.48^0 to 27.40^0 and it was observed to within the pharmacopoeial limits. The results of angle of repose (< 25) indicate excellent flow properties of granules, and it was observed to be within the pharmacopoeial limits.

Table: 9. Physical evaluation of matrix tablets

Formula Code	Hardness (kg/cm^2)	Thickness (mm)	Weight Variation (mg)	Friability (%)	Assay (%)
F1	4.4±0.15	4.12±0.17	2977.2±0.13	0.18±0.15	97.98±0.13
F2	4.2±0.11	4.25±0.15	298.3±0.12	0.22±0.16	100.15±0.12
F3	4.6±0.13	4.21±0.12	297.5±0.15	0.20±0.12	99.12±0.15
F4	4.1±0.15	4.42±0.15	302.9±0.14	0.19±0.17	99.53±0.14
F5	4.3±0.12	4.10±0.13	300.3±0.11	0.16±0.11	100.24±0.12
F6	4.7±0.13	4.37±0.15	297.8±0.13	0.14±0.12	98.57±0.11
F7	4.8±0.13	4.14±0.12	299.2±0.13	0.21±0.14	99.28±0.14
F8	4.9±0.12	4.13±0.11	302.2±0.11	0.17±0.15	99.15±0.13
F9	4.6±0.11	4.01±0.16	300.1±0.15	0.11±0.13	100.04±0.02

Where,

***All values are mean ± S.D, n=20.**

Evaluation of Formulated Matrix Tablets

a. Hardness:

The hardness of all the formulations ranged from 4.1 to 5.1 kg/cm^2. The pharmacopoeial limit for hardness is 3-5 kg/cm^2. Hence, all the formulations passed the test for hardness.

b. Thickness:

The thickness of all the formulations was between 4.12 to 4.42 mm which was according to the pharmacopoeial specifications.

c. Weight variation:

The weight variation test was performed and the weights of the tablets were between 297.5 to 302.2mg. The pharmacopoeial specification for weight variation limit is ±5. Hence, all the formulations passed the weight variation test and the % weight variation was within the pharmacopoeial specifications.

d. Friability (F):

Friability of the tablets was determined by using Roche friabilator. The friability of all the formulations was determined, and the values were in the range from 0.11 to 0.22%. Friability values below 1% were an indication of good mechanical resistance of the tablets. Hence, all the formulations were within the pharmacopoeial limits.

e. Assay:

The percentage drug content of all the tablets was found to be in the range of 97.98 to 100.24%. This was within the acceptable limits. The preparation complies with the test if each individual content is 85 to 115% of the average content. Hence, all the formulations were passed the test and the values are within the pharmacopoeial limits.

In-Vitro Drug Release Studies

The *in-vitro* dissolution studies were performed using the USP-II (Paddle) dissolution apparatus at 50rpm. The dissolution medium consisted of 900ml of phosphate buffer pH 6.8, maintained at 37±0.5^{o}C. An aliquot (5ml) was withdrawn at specific time intervals and drug content was determined by UV-visible spectrometer at 244nm.

Table: 10. *In-vitro* drug Release data of Canagliflozin from formulations F1 to F9 and Marketed product

Time in hrs	0	2	4	8	16	20	24
%Drug release in F1	0	9.5±1.6	22.5±1.1	32.2±1.3	40.10±2.2	64.05±1.4	70.05±1.4
%Drug release in F2	0	10.70±0.2	24.62±1.3	34.5±1.2	40.18±2.0	69.31±2.2	72.31±2.2
%Drug release in F3	0	11.31±0.9	26.81±1.6	36.8±1.7	44.31±2.3	72.84±1.5	74.81±1.5
%Drug release in F4	0	11.40±1.1	33.91±1.7	37.7±1.8	44.38±1.3	74.96±2.6	77.96±2.6
%Drug release in F5	0	13.51±1.4	28.0±0.8	38.6±1.9	46.94±1.9	76.35±2.4	79.35±2.4
%Drug release in F6	0	17.3±1.9	39.1±2.4	44.1±2.0	72.4±1.6	78.1±1.1	85.1±1.1
%Drug release in F7	0	19.2±0.2	41.8±1.9	46.3±2.2	77.5±2.1	80.3±0.5	90.21±0.5
%Drug release in F8	0	18.4±2.5	42.3±1.4	45.8±1.8	63.7±0.7	82.5±1.7	86.7±1.7
%Drug release in F9	0	17.9±1.2	38.1±1.4	44.1±2.4	70.4±1.9	76.1±1.2	83.1±1.6
%Drug release in marketed product.	0	13.3	33.8	45.8	51.5	75.09	88.02

Where,

***All values are mean ± % RS.D, n=6**

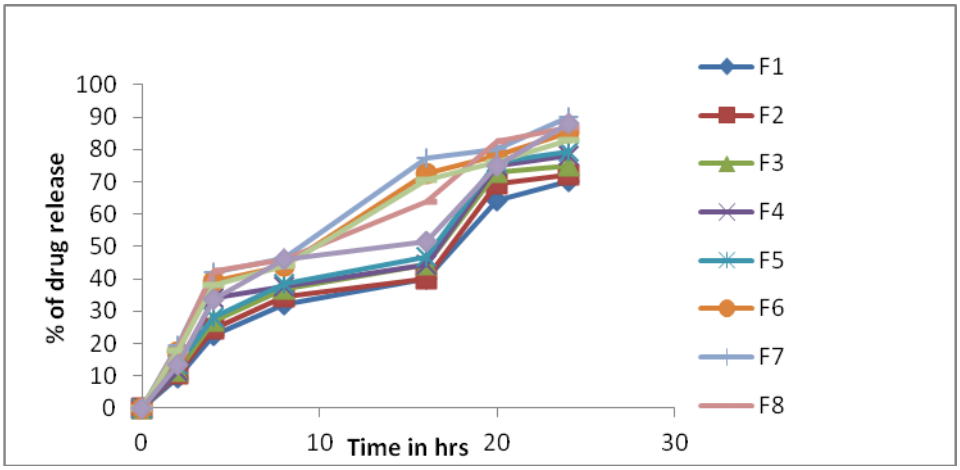

Figure: 7. *In-vitro* drug Release Profiles of Canagliflozin From F1 to F9 and Marketed product

Discussion:

The results of release studies of formulations F1 to F9 are shown in Table 10 and Figure 7. Here the matrix tablets were formulated using polymers such as Xanthan gum, Carbopol and Eudragit were used in different proportions and these tablets were done *in vitro* dissolution studies from F1 to F9. The release of drug depends not only on the nature of matrix but also upon the drug polymer ratio. As the percentage of polymer decreased, the kinetics of release increased. In above performed eight formulations F7 was best drug release.

Table: 11. *In-vitro* drug release data of Canagliflozin from optimized formulation F7 marketed product

Time in Hrs	0	2	4	8	16	20	24
%Drug release in F7	0	19.2	41.8	46.3	77.5	80.3	90.21
%Drug release in Marketed product.	0	13.3	33.8	45.8	51.5	75.09	88.02

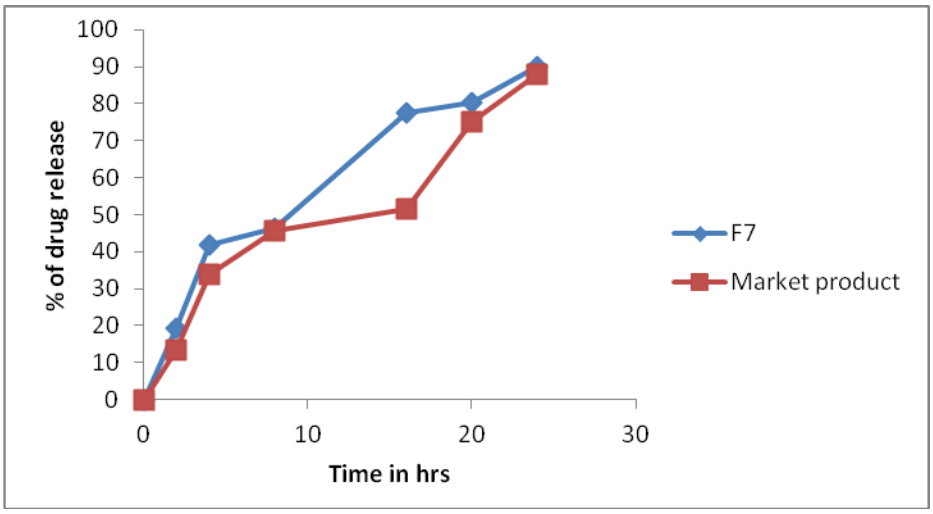

Figure: 8. Comparison of *in-vitro* drug release profiles of Canagliflozin from optimized formulation F7 and Marketed product.

Drug Release Kinetics

Table: 12. Dissolution Kinetics of optimized batch F7

Time	Square root	Log time	% drug released	log % drug released	% drug remaining	log % drug remaining
0	0		0		100	2
2	1.414214	0.30103	19.2	1.2833012	80.8	1.907411361
4	2	0.60206	41.8	1.6211763	58.2	1.764922985
8	2.828427	0.90309	46.3	1.665581	53.7	1.729974286
16	4	1.20412	77.5	1.8893017	22.5	1.352182518
20	4.472136	1.30103	80.3	1.9047155	19.7	1.294466226
24	4.898979	1.380211	90.21	1.9552547	9.79	0.990782692

Discussion:

Table 12 indicates the release kinetics of sustained release tablets of Canagliflozin. Dissolution data of the tablet of batch F7 were subjected to treatment with different kinetics equations, which showed that release patterns.

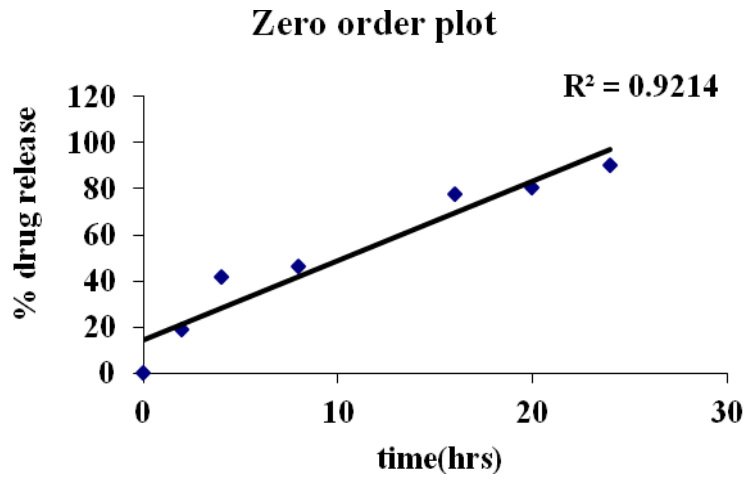

Figure: 9. Zero Order kinetics plot of optimized formulation F7

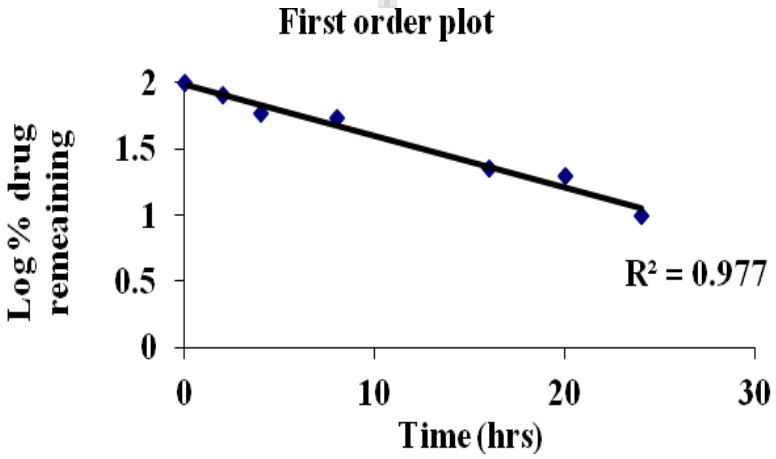

Figure: 10. First Order kinetics plot of optimized formulation F7

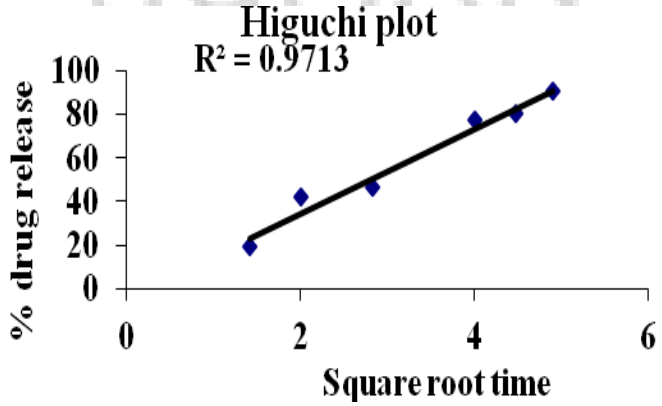

Figure: 11. Higuchi plot of optimized formulation F7

Discussion:

The drug release data obtained were extrapolated by Zero order, Higuchi, First order, Korsmeyer Peppa's to know the mechanism of drug release from the formulations. The release rate kinetic data for all the formulations was shown in Table 12. The release kinetics show that the release of drug followed First order release in all the formulations. As the drug release was best fitted in First order kinetics, indicating that the rate of drug release is concentration dependent

CONCLUSION

Canagliflozin was chosen as the model candidate for this study since it possesses nearly ideal characteristics that a drug must have in formulating a sustained drug delivery system.

- Among the hydrophilic matrix formers, the rate of drug release was in the following order Xanthan gum, Carbopol and Eudragit RS100.
- Optimized formulation F7 has successfully sustained the drug release for 24 hours and the drug release pattern was good.
- The results of the study demonstrate that hydrophilic polymer Eudragit RS100 can effectively control the extended release of Canagliflozin for 24 hrs.
- Direct compression is feasible for the development of once a day extended release tablet of Canagliflozin provided careful selection of optimum concentration of Eudragit RS100 is followed.
- It can be conclusively stated that development of extended release formulation of hydrophilic drugs does not necessitate the inclusion of the hydrophobic polymers to hydrophilic polymers and the desired extended release of hydrophilic drugs is also viable with hydrophilic polymer alone.
- The release kinetics show that the release of drug followed First order release in all the formulations and controlled by diffusion mechanism, Non-Fickian diffusion.

ACKNOWLEDGEMENT

We are sincerely thankful to Rainbow labs Pvt Ltd, Hyderabad for giving the opportunity to perform dissertation work and we would also like to thanks to our Joginpally B.R Pharmacy college management for encouraging us and providing all facilities to proceed with the work.

REFERENCES

1. Robinson,Controlled drug delivery system,2nd Edn,2005.
2. Vyas SP, Khar KR. Controlled Drug Delivery 1st Edn, Vallabh Prakashan, Delhi:2002:1-54.
3. Draganoiu E, Andheria M, Sakr A. Evaluation of the new polyvinyl acetate/povidone excipient for matrix sustained release dosage forms. Pharm Ind. 2001 ;(63):624–629.
4. Ian J. Hardy , Anne Windberg-Baarup , Claudia Neri ,Paul V. Byway , Steven W. Booth , Shaun Fitzpatrick . Modulation of drug release kinetics from hydroxypropyl methylcellulose matrix tablets using polyvinyl pyrrolidone. International Journal of Pharmaceutics 337 (2007) 246–253.
5. Manthena VS, Aditya M, Alka G, Sanjay G. Factors affecting mechanism and kinetics of drug release from matrix-based oral controlled drug delivery systems. Am J Drug Deliv. 2004; 2(1):43-57.
6. V.S. Varma.V.S.M, Kaushal.M.A, Garg.A,Factors effecting mechanism and
7. kinetics of drug release from matrix based oral controlled drug delivery systems Drug Delivery 2004, 2 (1), 43-5.
8. Stefanie C.Nigro, Daniel M.Riche , Michelle Pheng , William L .Baker Canagliflozin, a Novel SGLT2 Inhibitor for Treatment of Type 2 Diabetes Pharmacother October 2013 vol. 47 (10), 1301-1311.
9. Bhanja SB, Ellaiah P, Roy HK1, Samal BK1, Tiwari S2 and Murthy KVR3 Formulation and Evaluation of Perindopril Sublingual Tablets 2011; 1193-1198.
10. Balkrushna K. Patel, Paresh U. Patel Formulation and Evaluation of Controlled Release Floating Tablet of Perindopril 2012;393-403.
11. Varshosaz.J, Tavakoli.N, and Kheirolahi.F. Use of Hydrophilic Natural Gums in Formulation of Sustained-release Matrix Tablets of Tramadol Hydrochloride. AAPS Pharm Sci Tech 2006; 7(1);24.
12. Ghosh.S and Barik.B.B.Preparation and Evaluation of Aceclofenac Sustained Release Formulation and Comparison of Formulated and Marketed Product.IJMMS, September, 2009, Vol. 1 (9),375-382.