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EFFECT OF VARIOUS SUPERDISINTEGRANTS ON IMMEDIATE RELEASE FORMULATIONS OF SGLT2 INHIBITOR CANAGLIFLOZIN

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ABSTRACT

Globally 285 million people and 80 million in India going to get affected in the year 2030 with Type II diabetes. India has become world capital of diabetes. Recently, few novels anti diabetic drugs emerging which belongs to sodium glucose transporter -2 inhibitors (SGLT2). These SGLT2 inhibitors prevent the reabsorption of glucose into blood by the kidney. The present study was under taken to evaluate the effect of various super disintegrants on immediate release of SGLT2 inhibitor Canagliflozin containing formulations. In the present study, total 12 formulations were developed various super disintegrants like Sodium starch glycolate, cross caremellose sodium, pregelatinized starch and Kyron T-314 were used in varying concentration and tablets were prepared by direct compression technique. All the prepared formulations subjected for pre compression and post compression parameters, disintegration time, dispersion, wetting time profiles and in-vitro dissolution profiles. Results revealed that formulation containing 6% Kyron T-314 (CIR12) was found to be the best amongst all other having 99.10% of drug release in 30 minutes. The optimized formulation IR12 (6% Kyron T-314) also showed satisfactory drug content (99.10%), disintegration time of 20 seconds and stability studies were satisfactory.

KEYWORDS: *Canagliflozin, Superdisintegrants, Wetting Time, Type II Diabetes*

INTRODUCTION

For the control of diabetes mellitus, Canagliflozin and Dapagliflozin are a new antidiabetic agents that belongs to the class of sodium glucose transporter 2 (SGLT-2) inhibitors. By decreasing renal glucose absorption, these agents target hyperglycemia independent of insulin secretion or insulin sensitivity.[1] This unique mechanism of action differentiates them from existing antidiabetic agents currently on the market. It has been hypothesized that SGLT-2 inhibitors can be effectively and safely combined with other agents, including insulin, and incretin-based therapies. They can be used either as monotherapy, or in dual- or triple-agent combinations

When there is increase in the blood sugar level that is caused due to type two diabetes a patient should be given dose of SGLT-2 inhibitors and Metformin Hydrochloride in combination. SGLT-2 inhibitors inhibits subtype 2 of the sodium-glucose transport proteins (SGLT2) which are responsible for at least 90% of the glucose reabsorption in the kidney.[2] Blocking this transporter mechanism causes blood glucose to be eliminated through the urine. When the combination of Metformin Hydrochloride and SGLT-2 inhibitor given simultaneously it will give better pharmacological effect and it will help to the patient against high blood sugar level.[3]

CHARACTERIZATION OF PURE DRUGS

Organoleptic properties

Table 1: Color Description of Pure Drugs

Drug Name	Color
Canagliflozin	White to off white powder

Table 2: Odor and Taste Description of Pure Drugs

Drug Name	Odor	Taste
Canagliflozin	Sweet smell	sweet or metallic taste

Table 3(a): Solubility Study of Canagliflozin

Solvent	Canagliflozin
Water	Sparingly Soluble
Ethanol	Soluble
DMSO	Soluble
DMF	Soluble
METHANOL	Soluble
0.1N HCl	Soluble
Acetate buffer pH 4.5	Soluble
Phosphate buffer pH 6.8	Soluble

Table 3(b): Solubility Study of Canagliflozin

Flow Parameter	Canagliflozin
Bulk density (gm/ml)	0.56
Tapped density(gm/ml)	0.84
Carr's index (%)	27.54
Hausner's ratio	1.33
Angle of repose(^{0})	27.34

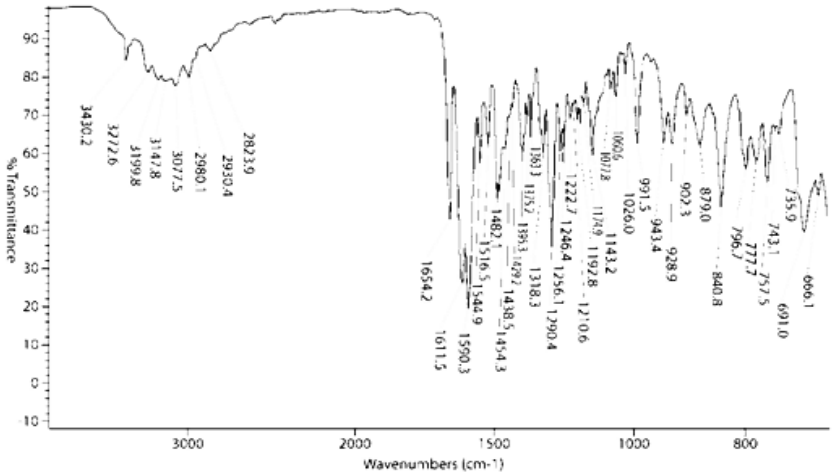

Figure 1: FTIR Spectrum of Canagliflozin (PURE).

MATERIALS AND METHODOLOGY

Canagliflozin (Shanghai send pharmaceutical technology co, Ltd, China), lactose (SD fine chem.) Micro crystalline cellulose (MCC) PH 102 (Goyal chem) Sodium starch glycolate (SSG) (Amishi Drugs & Chemicals Private ltd), Crosscarmellose sodium (CCS) (Crest cellulose), pregelatinized starch (shreeji pharma), Kyron T-314 (Corel Pharma Chem), Iron oxide red (Durga ceramic) and all other chemicals and reagents are of analytical grade.

Drug Excipients Compatibility Studies

The Compatibility studies of Canagliflozin and with their various excipients were conducted for one month. The drugs with other excipients (on a 1:1 ratio) were subjected to storage at elevated temperature at 45°C/ 75% RH in stability chamber for one month. Results are as shown in table.4

Table 4: Canagliflozin with Excipients

Ingredients	Ratio	Physical description (initial)	Condition (40°C / 75%RH)			
			After one week	After two week	After three week	After four week
Canagliflozin + MCC	1:1	White powder	NCC	NCC	NCC	NCC
Canagliflozin + lactose	1:1	White powder	NCC	NCC	NCC	NCC
Canagliflozin + Kyron T-314	1:1	White powder	NCC	NCC	NCC	NCC
Canagliflozin +SSG	1:1	White powder	NCC	NCC	NCC	NCC
Canagliflozin +CCS	1:1	Cream to off White powder	NCC	NCC	NCC	NCC
Canagliflozin +Pregelatinized starch	1:1	white powder	NCC	NCC	NCC	NCC
Canagliflozin +talc	1:1	White powder	NCC	NCC	NCC	NCC
Canagliflozin +magnesium stearate	1:1	White powder	NCC	NCC	NCC	NCC
Canagliflozin + iron oxide Yellow	1:1	Yellow color powder	NCC	NCC	NCC	NCC

NCC-No Color Change

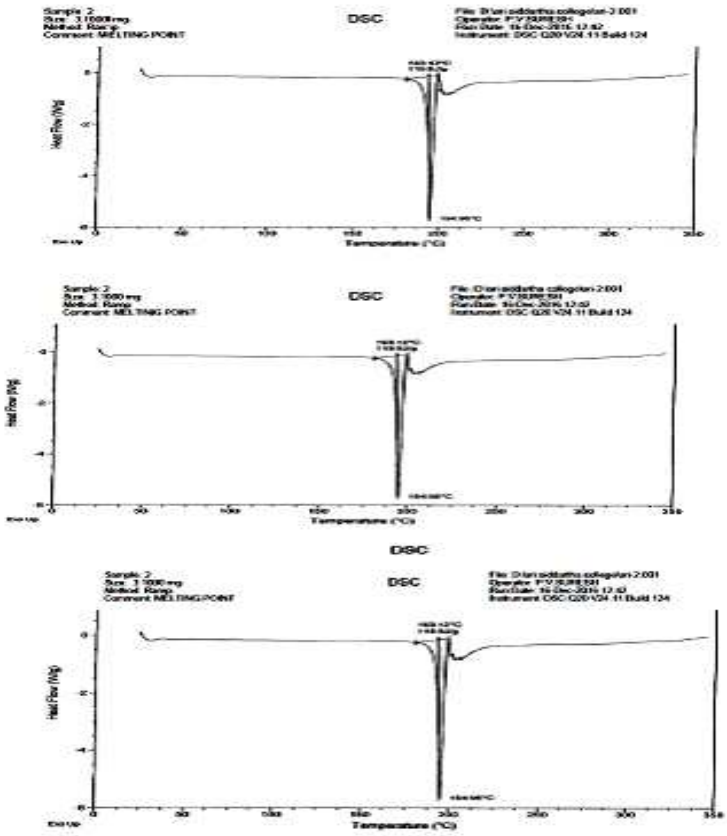

Figure 2: DSC Thermograms of Canagliflozin, Its Mixture with Other Excipients Before, and After (1C) Accelerated Stability Studies.

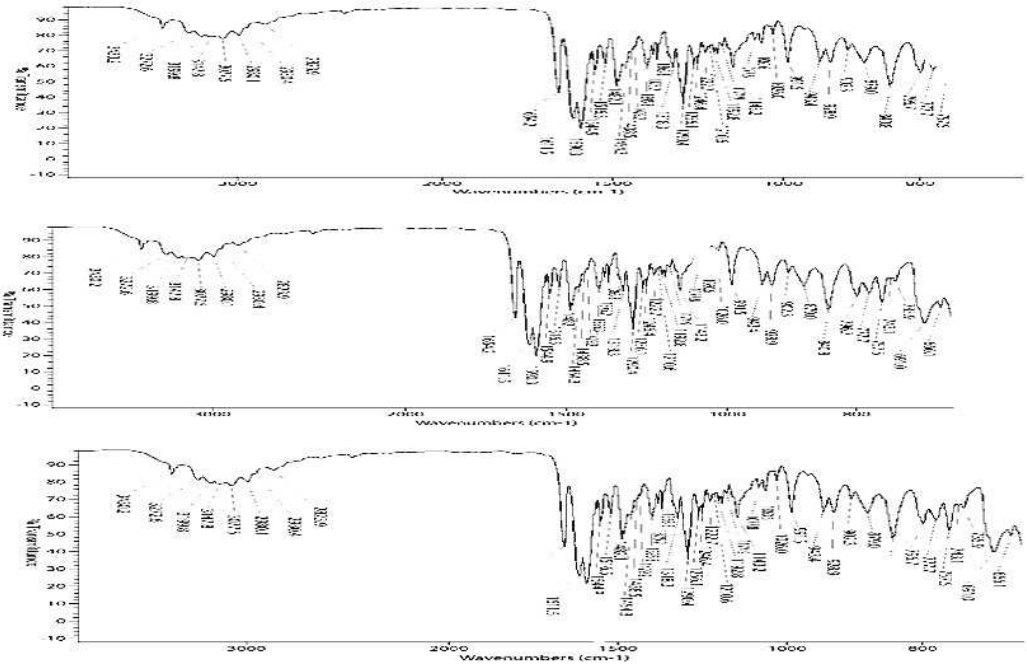

Figure 3: FTIR Spectrum of Canagliflozin, Its Mixture with Other Excipients Before and After Accelerated Stability Studies.

The DSC thermograms of pure Canagliflozin its physical mixture with other excipients (before and after of accelerated stability studies) are shown in Figure 2. Thermogram 1 exhibits a sharp endothermic peak at 190.12 Canagliflozin. When Canagliflozin was mixed with other excipients, Thermogram 2 and 3 still retained drug peak, which is the indication of Canagliflozin compatibility with other excipients used for the proposed formulation composition.

Similarly, FTIR spectrum of pure Canagliflozin exhibits the peak C=N stretching, C-N stretching, and C-H bending at 1590.3cm^{-1},1305.2cm^{-1} and 991.5cm^{-1}respectively when compared with reported reference spectrum of the drug. These distinctive drug peaks were present in FTIR spectrum of physical mixture of the drug with other excipients before the accelerated stability study and the optimized tablet after the accelerated stability study as well were shown in Fig.3

PROCEDURE FOR IMMEDIATE RELEASE TABLETS CONTAINING CANAGLIFLOZIN

Direct Compression Method

Various formulations were prepared using four different super disintegrating agents in different concentrations by direct compression method using MCC as filler. All the ingredients were passed through sieve #40 and were subjected for drying to remove moisture content at 40 to 45^{0}C. Weighed amount drug and excipients except magnesium stearate and talc were mixed properly by geometric addition method for 20 minutes manually.

Talc and magnesium stearate were then passed through sieve #80, mixed and blended well with the initial mixture. The mixed blend of drug and the excipients were compressed on 10 station rotary punching machine using 2 mm diameter round concave punch (force used: 58.5 kN)

Table 5: Direct Compression Method

Ingredients (mg)	BATCH NO											
	CIR1	CIR2	CIR3	CIR4	CIR5	CIR6	CIR7	CIR8	CIR9	CIR10	CIR11	CIR12
Canagliflozin	50.0	50.0	50.0	50.0	50.0	50.0	50.0	50.0	50.0	50.0	50.0	50.0
Lactose	20.0	20.0	20.0	20.0	20.0	20.0	20.0	20.0	20.0	20.0	20.0	20.0
MCC pH 102	71.0	69.0	67.0	73.0	72.0	71.0	69.0	64.0	59.0	72.0	70.0	68.0
SSG	3.0	5.0	7.0	-	-	-	-	-	-	-	-	-
CCS	-	-	-	1.0	2.0	3.0	-	-	-	-	-	-
Pregelatinized starch	-	-	-	-	-	-	5.0	10.0	15.0	-	-	-
Kyron T-314	-	-	-	-	-	-	-	-	-	2.0	4.0	6.0
Talc	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0
Magnesium stearate	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0
Iron oxide yellow	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0
Total (mg)	150.0	150.0	150.0	150.0	150.0	150.0	150.0	150.0	150.0	150.0	150.0	150.0

Precompression Studies[4]

Powder Blend Properties

Bulk Density and Tapped Density

The bulk density is ratio of the powder to volume it occupies. It is expressed as g/cc^3.bulk density is imparted in determining the size of the container needed for handling and processing. An accurately weighed quantity of the each of prepared formulations blend (w) was carefully poured into the graduated cylinder and the volume (V_o) was measured, and then the graduated cylinder was closed with lid, set into the density determination apparatus. The density apparatus was set for 500 taps and after that, the volume (V_f) was measured and continued operation till the two consecutive readings were equal

The bulk density, and tapped density were calculated using the following formulae:

Bulk density (B.D) = W/V_o

Tapped density (T.D) =W/V_f

W = weight of the powder,

V_O = initial volume,

V_f= final volume.

Angle of Repose

This is the maximum angle possible between the height of file of blend powder and horizontal plane. The frictional forces in the lose powder can be measured by angle of repose. The tangent of angle of repose is equal to the co efficient friction (θ) between the particles. Hence the rougher and more irregular the surface of particles the greater will be angle of repose.

Tan θ = h/r

Where

H = height of the pile, R = radius of the pile

Table 6: Standard Values of Angle of Repose

S. NO.	Flowability	Angle of repose (θ)
1	Excellent	<25
2	Good	25-30
3	Passable*	30-40
4	Poor	37-45
5	Very poor	>45

* Adding glidant for improving flow

Hausner's Ratio

Hausner's ratio was determined by following equation,

Hausner's ratio=Tappedbulkdensity/ Bulkdensity

A Hausner's ratio less than 1.25 indicates good flow while greater than 1.5 indicates poor flow.

Carr's Compressibility Index[5]

It is a simple index that can be determined on small quantities of powder.

The Compressibility Index is measure of the propensity of a powder to be compressed as described above. As such it is measure of the powder's ability to settle, and it permit an assessment of the relative importance of interparticulate interactions. In a free-flowing powder, such interactions are less significant, and the bulk and tapped densities will be closer in value. For poorer flowing materials, there are frequently greater interparticle interactions, and a greater difference between the bulk and tapped densities will be observed. These differences are reflected in the Compressibility Index. In theory, the less compressible a material the more flowable it is. The compressibility indices of the powder blends was determined using following formula,

Compressibility Index = 100(V0 - VF)/V0

V0 is unsettled apparent volume

VF is final tapped volume

Table 7: Standard Values of Carr's Index

S. NO.	Carr's index	Type of flow
1	5-15	Excellent
2	12-16	Good
3	18-21	Fair to passable
4	23-35	Poor*
5	33-38	Very poor*
6	>40	Extremely poor*

* May be Improved by Glidant

EVALUATION OF IMMEDIATE RELEASE LAYER OF CANAGLIFLOZIN

Weight Variation

Twenty tablets were weighed collectively and individually. Average weight was calculated and based on the obtained weights % weight variation was calculated using the formula,

$$\% \text{ Weight Variation} = \frac{\text{Average weight} - \text{Individual weight}}{\text{Average weight}} \times 100$$

Specifications of Weight Variation

Table 8: Weight Variation

S.NO	Average Weight of Tablets (mg)	Maximum Percent Deviation Allowed (%)
1.	80 mg or less	10
2.	More than 60mg but less than 250 mg	7.5
3.	250 mg or more	5

Hardness

Hardness of the tablet was tested by placing the tablet longitudinally in between the two plungers of the Monsanto tablet hardness tester and the obtained hardness was mentioned in terms of kg/sq.cm. Limits for Hardness are 4-6kg/sq.cm.

Friability

The friability of the tablets was determined by Roche Friabilator in which the tablets were subjected to the combined effect of abrasions and shock in a plastic chamber revolving at 25rpm and dropping the tablets at a height of 6 inches in each revolution. Pre weighed sample of 10 tablets were placed in the Friabilator and allowed to rotate for 100 revolutions. Later the tablets were degusted and the tablets were reweighed.

Percent friability is given by the formula

$\%F = (1-W/W0) \times 100$

Where, W0 is the weight of the tablets before the test

W is the weight of the tablets after the test

Limits for friability are % friability should not be more than 1%.

Thickness

The thickness of the tablets was determined using a Vernier caliper. Tablets from each formulation were used and average values were calculated.

Disintegration Time of Immediate Layer

Single dosage unit was placed in each of the six tubes of the basket and added a disk. Operate the apparatus using water as the immersion fluid, maintained at 37 ± 2^{o}C. Time was noted when disintegration completed for all prepared samples.

Dispersion Time of Immediate Layer

Dispersion time test was performed by placing 6 tablets in 100 mL of water and stir gently until completely dispersed. A smooth dispersion was obtained which passed through a sieve screen with a nominal mesh aperture of 710 mm (22#).

Wetting Time of Immediate Layer

Wetting time was performed by pouring the die solution into the petridish. The four folded tissue paper was placed upon the die solution. The sample was put above the tissue paper and noted down the time required to wet the tablet completely.

Dissolution Studies for Immediate Layer of Canagliflozin

In-vitro dissolution tests of all prepared formulations were carried out using USP apparatus type II (ELECROLAB TDT 08 T, Bombay). The dissolution medium consisted of 1000mL of acetate buffer 4.5 maintained at 37 ± 0.5^0C and stirred at 60 rpm. Samples (10 mL) were withdrawn at predetermined time intervals of 5, 10, 15, 20 and 30 min. Equal amount fresh dissolution medium, maintained at same temperature, was replaced immediately, and withdraw sample was analyzed by HPLC under optimized chromatographic conditions . Percentage drug release was computed from prepared standard curve. The release study was conducted in the triplicate and mean values were plotted.

Instrument Waters HPLC system controlled with software Empower 2, fitted with a Photo Diode Array detector and a gradient run was used for resolving the drug. The column used for the separation of the drug was BDS column and the column temperature was maintained at the ambient temperature. Preparation of mobile phase

A mixture of Acetonitrile and Ortho phosphoric acid was used as the mobile phase. The optimized method consists of the mobile phase in the ratio of 55:45v/v. Methanol (HPLC grade) was used for dissolving the drug and further dilutions were made using water (HPLC grade).

Chromatographic Conditions

Table 9: Chromatographic Conditions

Mobile Phase	Acetonitrile: Orthophosphoric Acid (55:45)
Column	BDS
Flow rate	1.0ml/min
Column temperature	Room temperature(20-25^0 C)
Sample temperature	Room temperature(20-25^0 C)
Wave length	203nm
Run time	10 min

RESULTS AND DISCUSSION

The present study of Canagliflozin immediate release tablets were developed with a view to deliver the drug immediately. The formulation development work was initiated with direct compression method and a total of 12 formulations (CIR1-CIR12) were prepared. The formulated tablets were evaluated for various pre compression parameters and post compression parameters like thickness, hardness, weight variation, and friability, and disintegration test, dispersion, wetting time, drug content uniformity and in vitro release studies. The formulation CIR12 showed satisfactory physical parameters, and it was found to be stable among other formulations.

Flow Property of Prepared Formulations Blend

Table 10: Pre-Compression Parameters

Batch no	Bulk density (gm/cm^3)	Tapped density (gm/cm^3)	Angle of Repose (θ)	Carr's Index(%)	Hausner's ratio
CIR1	0.53±0.02	0.63±0.01	21.2±1.3	25.2±1.4	1.28±0.1
CIR2	0.56±0.01	0.69±0.03	24.3±1.6	24.5±1.3	1.24±0.2
CIR3	0.56±0.02	0.69±0.01	26.0±1.3	19.8±1.7	1.25±0.1
CIR4	0.57±0.03	0.64±0.02	24.2±1.2	20.3±1.6	1.28±0.2
CIR5	0.57±0.02	0.71±0.02	27.2±1.6	21.2±1.2	1.30±0.2
CIR6	0.56±0.01	0.71±0.03	26.4±1.6	24.5±1.7	1.22±0.2
CIR7	0.56±0.02	0.70±0.01	27.0±1.8	18.6±1.6	1.25±0.2
CIR8	0.55±0.03	0.72±0.03	26.5±2.1	17.3±1.8	1.23±0.3

Table 10: Contd.,

CIR9	0.57±0.03	0.69±0.02	27.2±2.0	20.3±1.5	1.28±0.2
CIR10	0.53±0.04	0.63±0.01	26.8±1.4	15.8±0.03	1.08±0.03
CIR11	0.52±0.01	0.68±0.03	27.3±1.7	23.5±0.03	1.28±0.04
CIR12	0.51±0.04	0.62±0.05	23.4±2.1	16.6±0.09	1.18±0.07

All Values are Expressed as mean ± standard deviation, n=3

The formulation of tablets were done by direct compression technique because the flow properties of powder blend have good flow as shown in table 10. The values of angle of repose have found in the range of 21-27° (good powder flow). Hausner's ratio and Carr's index have in the range of 1.08-1.30 and 15-25 respectively. Hence the prepared powdered blend of batch no CIR12 has good flow property rather than other batches.

Post Compression Study Data

Table 11(a): Post Compression Study Data of Prepared Formulations

Batch no	Average wt (mg) n=20	Thickness(mm)n=10	Hardness(kg/cm^2) n=6	Friability(%) n=10
CIR1	149.2±1.1	2.50 ± 0.06	4.0± 0.4	0.494
CIR2	149.8±1.6	2.52 ± 0.02	4.0± 0.3	0.487
CIR3	150.3±1.5	2.56 ± 0.04	4.2± 0.1	0.528
CIR4	149.7±1.8	2.52 ± 0.03	4.2± 0.5	0.574
CIR5	149.9±1.9	2.52 ± 0.02	4.0± 0.2	0.631
CIR6	149.2±1.8	2.58 ± 0.02	4.1± 0.4	0.597
CIR7	151.2±2.1	2.59 ± 0.04	4.1± 0.6	0.631
CIR8	150.5±1.8	2.52 ± 0.02	4.1± 0.2	0.624
CIR9	150.3±1.5	2.58 ± 0.06	4.2± 0.3	0.428
CIR10	149.8±1.8	2.52 ± 0.02	4.2± 0.2	0.517
CIR11	150.1±1.9	2.58 ± 0.04	4.1± 0.3	0.535
CIR12	149.2±1.4	2.56 ± 0.02	4.0± 0.1	0.482

All Values are Expressed as mean ± standard deviation, n=3

Table 11(b)

Batch no	Disintegration time (sec)n=6	Dispersion time (sec) n=6	Wetting time (sec) n=6	Drug content (%)
CIR1	34±2	128±06	114±7	99.05±0.28
CIR2	47±2	84±8	89±4	98.47±0.14
CIR3	30±1	82±6	72±3	99.28±0.17
CIR4	38±2	152±5	126±8	99.65±0.22
CIR5	42±1	97±6	98±8	100.05±0.37
CIR6	39±1	69±7	84±6	99.47±0.29
CIR7	72±4	153±7	135±6	98.28±0.18
CIR8	38±3	122±4	120±4	98.12±0.11
CIR9	36±2	64±3	83±5	101.08±0.10
CIR10	42±3	54±3	39±6	101.93±0.16
CIR11	37±3	42±2	34±4	99.34±0.24
CIR12	28±2	29±2	31±5	99.02±0.17

All Values are Expressed as mean ± standard deviation, n=3

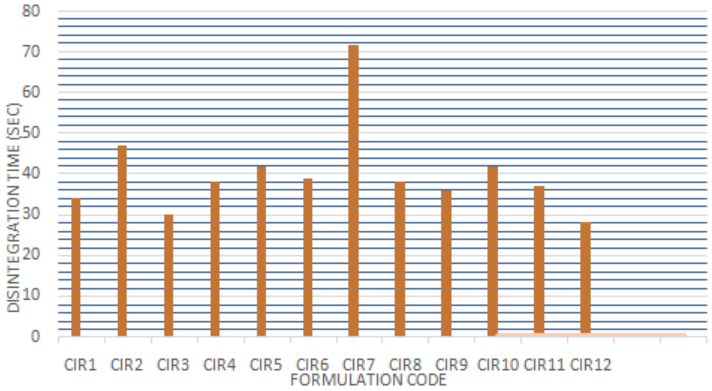

Figure 4: Disintegration Time Profile of Prepared Formulations.

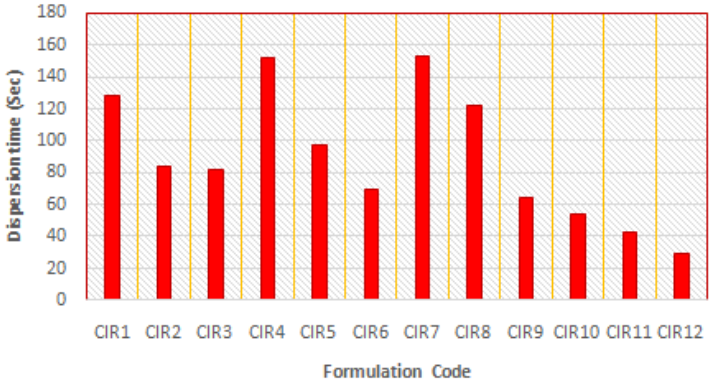

Figure 5: Dispersion Time Profile of Prepared Formulations.

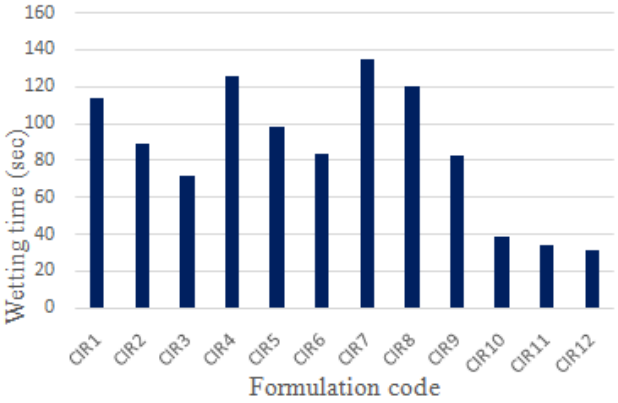

Figure 6: Wetting Time Profile of Prepared Formulations.

Figure 7: Wetting Times Images of Optimized Formulation CIR12.

All the 12 formulations were evaluated for pharmaco technical parameters like weight variation, hardness, thickness and friability. Average weight of the tablet did not deviate more than 7.5% which confirmed IP specification. Friability of all the formulations was below 1% which also confirmed specification. In preliminary study, CIR1-CIR3 batches were SSG (3-7%) was used as super-disintegrating agent. Hardness, friability, disintegration time, dispersion time and wetting time for preliminary batches CIR1 to CIR3 were found between 4.0-4.2 kg/cm^2, 0.482-0.52%, 30-47 sec, 82-128 sec, 72-114 sec respectively. Very less disintegration time obtained in batch IR3 was due to high concentration of super-disintegrating agent (SSG) in formulation. For IR4-IR6 batches where CCS (1-3%) was used as super-disintegrating agent. CIR4-CIR6 batches were CCS (1-3%) was used as super-disintegrating agent. Hardness, friability, disintegration time, dispersion time and wetting time for preliminary batches CIR4 to CIR6 were found between 4.0-4.2 kg/cm^2, 0.57-0.63%, 38-42sec, 69-152 sec, 84-126 sec respectively. CIR4 formulation shows more disintegration time compared to CIR5 and CIR6 due to presence of less concentration of Superdisintegrant. CIR7-CIR9 batches were Pregelatinized starch (5-15%) was used as super-disintegrating agent. Hardness, friability, disintegration time, dispersion time and wetting time for preliminary batches CIR7 to CIR9 were found between 4.1-4.2 kg/cm^2, 0.42-0.63%, 36-72 sec, 64-153 sec, 83-135 sec respectively. CIR7 formulation shows more disintegration time compared to all other formulations this may be Pregelatinized starch alone is not sufficient enough to provide desired disintegrant effect. CIR10-CIR12 batch where Kyron T-314 (2-6%) was used as super-disintegrating agent. Hardness, disintegration time, wetting time and friability for preliminary batches CIR10 to CIR12 were found between 4.0-4.2 kg/cm^2, 0.48-0.51%, 28-42 sec, 29-54sec and 31-39 sec respectively. Very less disintegration time obtained in batch CIR12 was due to high concentration of super-disintegrating agent (Kyron T-314) in formulation. CIR12 batch had given the best results with the disintegration time of 28 sec, friability of 0.482%, hardness of 4.0 kg/cm^2 with 99.02% as drug content.

Data shown in table.11 indicated there was no difference in results of weight variation, hardness and friability as well as in assay. The hardness of the tablets was found to be in the range of 4.1 to 4.2 kg/cm^2 whereas the percentage friability of all the formulations was found below 1% indicating that the friability was within the prescribed limits. The tablets were found to contain 99.28 to 101.05 % of the labelled amount of Canagliflozin indicating uniformity of drug content. The average percentage deviation of all tablet formulations was found to be within the limit, and hence all the formulation passed the test for uniformity as per official requirements. From the results of disintegration time, it was found that the tablets of batch CIR12 have minimum disintegration time i.e. 28±2 sec. whereas the batch CIR7 has maximum disintegration time 72±4 sec. From the results of dispersion time and wetting time, it was found that the tablets of batch CIR12 has minimum dispersion and wetting time i.e. 29±2 sec and 31±5 sec. respectively, whereas the batch CIR7 has maximum dispersion and wetting time 153±7 sec and 135±6 sec. respectively.

Table 12: *In-Vitro* Dissolution Profile of Preliminary Trial Formulations

Time (min)	Cumulative % Drug Release											
	CIR1	CIR2	CIR3	CIR4	CIR5	CIR6	CIR7	CIR8	CIR9	CIR10	CIR11	CIR12
5	54.48±0.61	59.36±0.30	62.77±0.33	55.65±0.51	58.12±0.55	59.71±0.51	50.24±0.11	54.37±0.51	56.35±0.35	45.87±0.53	51.66±0.29	59.24±0.57
10	86.24±0.51	89.54±0.49	91.2±0.53	75.3±0.29	80.18±0.26	82.46±0.29	78.54±0.29	82.76±0.21	84.77±0.26	78.82±0.46	84.44±0.46	91.56±0.43
15	96.15±0.42	96.62±0.51	97.35±0.41	95.56±0.34	94.21±0.31	93.42±0.37	95.67±0.35	94.24±0.33	93.53±0.19	98.85±0.36	96.25±0.25	97.15±0.22
20	97.51±0.53	97.62±0.51	98.35±0.41	96.98±0.22	96.02±0.31	95.42±0.37	96.67±0.45	95.24±0.44	96.53±0.53	98.85±0.22	97.25±0.54	98.07±0.28
30	-	-	-	-	-	-	-	-	-	-	-	99.1±0.51

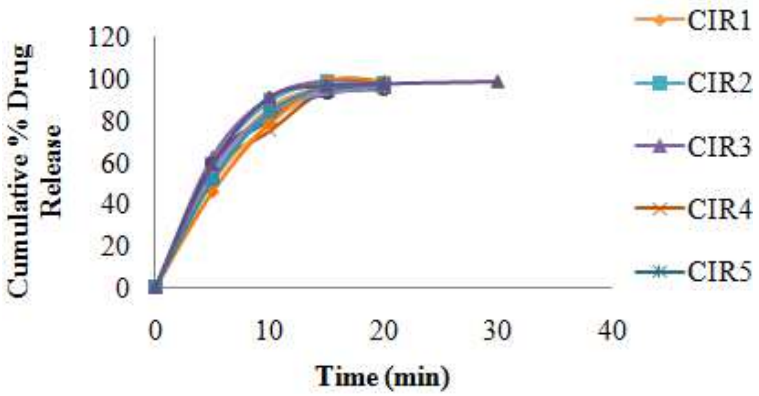

Figure 8: Dissolution Profile of Prepared Formulations.

The *in-vitro* dissolution study was carried out according the prescribed method. The results of drug release studies were shown in table.12. All the formulations released more than 90% of drug within 15 min. It was quiet good and confirmed the specification of immediate release dosage form. After 20 min of dissolution testing, only batch CIR12 released more than 99 % of drug than all other formulations Batches composed of SSG and Kyron T-314 in highest concentration indicates good super disintegranting effect thus the concentration of Super disintegrant and its nature plays an important role to release the drug. During the optimization of formulation it is observed that dissolution is highly dependent on the disintegrant and disintegration. For optimization, physical parameters were also considered along with *in-vitro* drug release. After considering all parameters on the basis of considerable disintegration time, good wetting time and the least concentration of disintegrating agent used, batch CIR12 containing 6% Kyron T-314 was optimized as immediate layer with 99.10% as drug release in 30 minutes.

CONCLUSIONS

From this study it can be concluded that the CIR12 batch containing 6% Kyron T-314 was found to be the best fit formulation, amongst 12 batches i.e.CIR1-CIR12, with the release rate of 99.10%. Further from this study it can be concluded that, 6% Kyron T-314 can further may used as super disintegrant for optimization of immediate release studies.

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