ISSN 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES

Available online at: http://www.iajps.com *Research Article*

FORMULATION AND EVALUATION OF METFORMIN IMMIDIATE RELEASE TABLET

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ABSTRACT:

Formulate immediate release tablets of metformin to achieve rapid dissolution, absorption and further improving the bioavailability of the drug. Immediate release tablets and Films of Metformin were designed with a view to enhance the patient compliance and provide a quick onset of action. Metformin Immediate release Tablets were prepared by direct compression method using crosspovidone, croscarmellose sodium, sodium starch glycolate and combinations of CP+CCS, and CP + SSG as super disintegrants Formulations F13, F14, 15 and F16 which contained increasing concentrations of combination of CP + CCS have recorded drug release 94.5%, 96.52%, 99.87% and 96.38% respectively, at the end of 25 to 30 min. Formulations F17, F18, F19 and F20 which contained increasing concentrations of combination of CP + SSG have recorded drug release 88.56%, 92.5%, 95.48% and 94.51respectivel, at the end of 30 min.

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INTRODUCTION:

Immediate release drug delivery system is also conventional type of drug delivery system and it is defined as Immediate release of special rate controlling features such as special coatings and other techniques. These preparations are primarily intended to achieve faster onset of action for drugs such as analgesics, antipyretics, and coronary vasodilators[1,2].Other advantages include enhanced oral bioavailability through transmucosal delivery and pregastric absorption, convenience in drug administration to dysphasic patients, especially the elderly and bedridden, and new business opportunities[3]. Conventional IR formulations include fast disintegrating tablets and granules that use effervescent mixtures, such as sodium carbonate (or sodium bicarbonate) and citric acid (or tartaric acid), and super disintegrants, such as sodium starch glycolate, crosscarmellose sodium, and crospovidone. Current technologies in fast-dispersing dosage forms include modified tableting systems, floss or Shear form technology, which employs application of centrifugal force and controlled temperature, and freeze-drying. In another aspect of the invention a formulation as described herein with a compound of formula (I), or an acid addition salt thereof, releases drug under pH conditions such as pH=1 to 3, especially at, or about, pH=1. Thus, formulations of the invention may release at least 70% (preferably 80%) of active ingredient within 4 hours, such as within 3 hours, preferably 2 hours, more preferably within 1.5 hours, and especially within an hour (such as within 30 minutes), of administration, whether this be oral or parenteral[4,5,6].

Metformin's mechanisms of action differ from other classes of oral antihyperglycemic agents[7]. Metformin decreases blood glucose levels by decreasing hepatic glucose production, decreasing intestinal absorption of glucose, and improving insulin sensitivity by increasing peripheral glucose uptake and utilization. These effects are mediated by the initial activation by metformin of AMP-activated protein kinase (AMPK), a liver enzyme that plays an important role in insulin signaling, whole body energy balance, and the metabolism of glucose and fats. Activation of AMPK is required for metformin's inhibitory effect on the production of glucose by liver cells.

Using various disintegrants like Crosspovidone, Croscarmellose sodium, Sodium starch glycolate tablets were prepared along with other additives. Direct compression method was used for the preparation of tablets[8,9].

MATERIALS AND METHODS:

Metformin , Crosspovidone, Croscarmellose sodium, Sodium starch glycolate, Avicel PH 102 were gift samples from Hetero Drugs, Hyderabad.

Preparation of Metformin Immediate Release Tablets:

Metformin Immediate release tablets were prepared using direct compressiontechnique. Direct compression technique is a convenient method but the excipients used in this method are costlier when compared to the excipients used in the wet granulation technique.

Different formulations of Metformin Immediate release tablets were designed to be prepared by direct compression technique using three super disintegrants, (Crosspovidone, Croscarmellose sodium and Sodium starch glycolate). Super disintegrant is varied with 4 different concentrations, (i.e., 3, 6, 9, 12% respectively) keeping all other ingredients constant, there are assigned with formulations codes shown in Table-1and 2.

Table 1: Formula of Metformin Immediate release tablets prepared by direct compression method with various super disintegrants

Ingredients	Super disintegrants concentration (%) of Crosspovidone/ Croscarmellose Sodium/ Sodium Starch Glycolate			
	3%	6%	9%	12%
Metformin	500	500	500	500
Superdisintegrants	18	36	54	72
Avicel PH 102	59	41	23	5
Pearlitol SD200	10	10	10	10
Sodium saccharin	10	10	10	10
Orange flavor	2	2	2	2
Sodium stearyl fumerate	0.5	0.5	0.5	0.5
Talc	0.5	0.5	0.5	0.5
Total weight (mg)	600	600	600	600

Table 2: Formulation codes of MIR Tablets

Disintegrant used	Concentration (%)	Formulation code
Crosspovidone	3	**F1**
	6	**F2**
	9	**F3**
	12	**F4**
Croscarmellose sodium	3	**F5**
	6	**F6**
	9	**F7**
	12	**F8**
Sodium starch glycolate	3	**F9**
	6	**F10**
	9	**F11**
	12	**F12**
Crosspovidone + crosscarmellose sodium	6 (3:3)	**F13**
	8 (4:4)	**F14**
	10 (5:5)	**F15**
	12 (6:6)	**F16**
Crosspovidone + sodium starch glycolate	**6 (3:3)**	**F17**
	8 (4:4)	**F18**
	10 (5:5)	**F19**
	12 (6:6)	**F20**

Charecterization of MIR Tablets:

FTIR studies:

FTIR spectra of IR spectrum of pure Metformin, croscarmellose sodium, crosspovidone, sodium starch glycolate and combination thereof were recorded on Perkin Elmer spectrophotometer. The scans were evaluated for presence of principal peaks of drug, shifting and masking of drug peaks due to presence of polymer.

Pre Compressional Parameters of Pioglitazone Blend:

Angle of Repose

While there is some variation in the qualitative description of powder flow using the angle of repose, much of the pharmaceutical literature appears to be consistent with the classification by Carr'sin the table below. There are examples in the literature of formulations with an angle of repose in the range of 40-50^o that manufactured satisfactorily. When the angle of repose exceeds 50^o, the flow is rarely acceptable for manufacturing purposes.

The angle of repose (θ) was calculated using the following formula.

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

Bulk Density and Tapped Density

Bulk density is the ratio between a given mass of powder or granules and its bulk volume. Tapped density is the ratio between a given mass of powder or granules and the constant or fixed volume of the powder or granules after tapping. An accurately weighed quantity of powder (W) (which was previously passed through sieve no. 40) was carefully transferred into 250 ml measuring cylinder and initial volume (V_o) was measured. The cylinder is then allowed to tap on to a wooden surface from the height of 2.5 cm at 2-second intervals. The tapping was continued until no further change in volume (until a constant volume) was obtained (V_f). The bulk density and tapped density are calculated by using the following formula.

Bulk Density $= W/V_o$

Tapped Density $= W/V_f$

Compressibility Index

In recent years, the compressibility index and the closely related Hausner's ratio have become the simple, fast, and popular methods of predicting powder flow characteristics. The compressibility index has been proposed as an indirect measure of bulk density, size and shape, surface area, moisture content, and cohesiveness of materials, because all of these can influence the observed compressibility index. The compressibility index determined by measuring both the bulk volume and tapped volume of a powder.

Basic methods for the determination of compressibility Index

While there are some variations in the method of determining the compressibility index the basic procedure is to measure the unsettled apparent volume, (V_0), and the final tapped volume, (V_f), of the powder after tapping the material until no further volume changes occur. The compressibility index and the Hausner's ratio are calculated as follows:

$$\text{Compressibility Index} = \left(\frac{V_0 - V_f}{V_0}\right) x100$$

Post Compressional Parameters:

Weight variation test

20 tablets were randomly selected from each formulation and their average weight was calculated using digital balance. Individual weight of each tablet was also calculated using the same and compared with the

average weight. Thee Mean ± S.D. were noted. The tablets meet USP specifications if no more than 2 tablets outside the percentage limit and if no tablet differs by more than 2 times the percentage limit.

Thickness

Randomly 10 tablets were taken from each formulation and their thickness was measured using a digital screw gauge. The individual tablet was placed between two anvils of the screw guage and sliding knob was rotated until the tablet was tightly fitted. The digital reading displayed was noted. The Mean ± S.D. were noted. The tablet thickness should be controlled within a ± 5% variation of standard value.

Hardness

The tablet hardness of different formulations was measured using the Monsanto hardness tester. The tester consists of a barrel containing a compressible spring held between two plungers. The lower plunger was placed in contact with the tablet, and a zero was taken. The upper plunger was then forced against the spring by turning a threaded bolt until the tablet fractures. As the spring is compressed, a pointer rides along a gauge in the barrel to indicate the force. The force of fracture is recorded, and the zero force reading is deducted from it. Generally, a minimum hardness of 4 kg is considered acceptable for uncoated tablets. The hardness for Immediate release tablets should be preferably 1-3 kg.

Friability

This test is performed using a laboratory friability tester known as Roche Friabilator. 10 tablets were weighed and placed in a plastic chambered friabilator attached to a motor, which revolves at a speed of 25 rpm, dropping the tablets from a distance of 6 inches with each revolution. The tablets were subjected to 100 revolutions for 4 minutes. After the process, these tablets were dedusted and reweighed. Percentage loss of tablet weight was calculated.

% Friability =

Where,

W1 = Initial weight of the 20 tablets before testing.

W2 = Final weight of the 20 tablets after testing.

Friability values below 1% are generally acceptable.

Assay

20 tablets were randomly selected, weighed and finely powdered; powder equivalent to one tablet was added to 100ml of pH 6.8 phosphate buffer in a conical flask. Conical flasks were placed on a rotary shaker overnight. An aliquote of solution was centrifuged and supernatant was filtered through a 0.22µ filter. Absorbance of the resulted supernatant solution was measured using U.V Visible spectrophotometer at a wavelength of 232nm against pH 6.8 phosphate buffer as blank. Concentrations were calculated with the help of standard graph and total amount present in the formulation was calculated.

Wetting time and Water absorption ratio (R)

Five circular tissue papers were placed in a petri dish with a 10-cm diameter. Ten milliliters of water containing eosin, a water-soluble dye, was added to the petri dish. The dye solution is used to identify the complete wetting of the tablet surface. A tablet was carefully placed on the surface of tissue paper in the petri dish at room temperature. The time required for water to reach the upper surface of the tablets and completely wet them was noted as the wetting time. To check for reproducibility, the measurements were carried out in replicates (n=6). The wetting time was recorded using a stopwatch.

The weight of the tablet before keeping in the petri dish was noted (W_b) using Shimadzu digital balance. The wetted tablet from the petri dish was taken and reweighed (W_a) using the same. The Water absorption ratio, R, was determined according to the following equation:

$R = 100 (Wa - W_b) / W_b$

Where $W_b$and$W_a$are the weight before and after water absorption respectively.

Disintegration Time

Disintegration time was also measured using a modified disintegration method (n=6). For this purpose, a Petri dish (10 cm diameter) was filled with 10 ml of water. The tablet was carefully put in the center of the Petri dish and the time for the tablet to completely disintegrate into fine particles was noted using a stop watch.

Dissolution Study

Dissolution test was carried out using USP rotating paddle method (apparatus 2). The stirring rate was 50 rpm. 6.8 pH phosphate buffer was used as dissolution medium (900ml) and was maintained at 37 ± 1^0C. Samples of 5ml were withdrawn at pre – determined intervals (2, 4, 6, 8, 10, 15, 20, 25, 30 min), filtered and replaced with 5ml of fresh dissolution medium. The collected samples were suitably dilutedwith dissolution fluid, where ever necessary and were analyzed for the Metformin at 232 nm by using UV spectrophotometer. Each dissolution study was performed for three times and mean values were taken.

RESULTS AND DISCUSSIONS:

Drug and excipients compatibility:

The Fourier transform infrared spectroscopy studies were carried out for pure drug along with excipients. The results are summarized in figure 1.The above peaks are considered as characteristic peaks of Metformin. These peaks were not affected and prominently observed in IR spectra of drug and excipients. This indicates there is no interaction between drug and excipients.

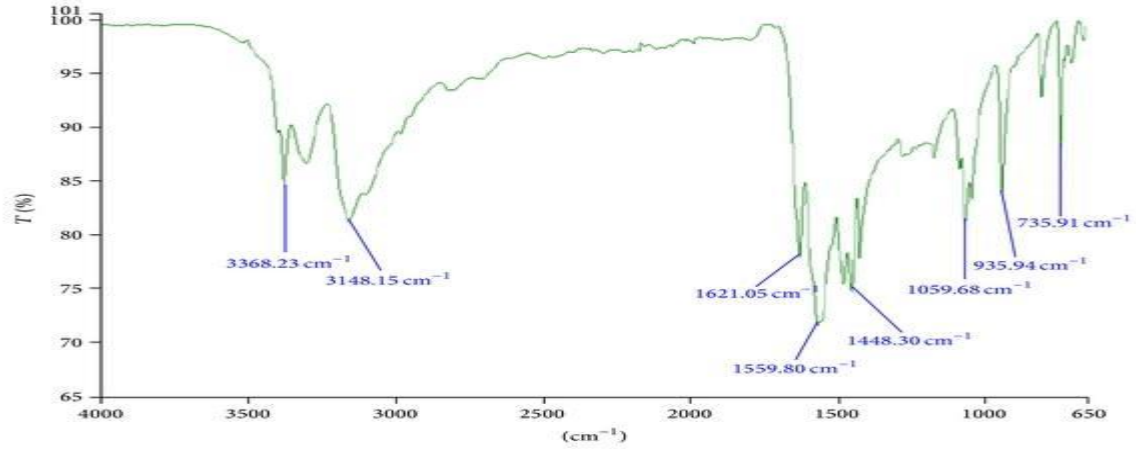

Figure 1 FTIR spectra of Metformin and excipients

Pre Compressional Parameters:

The pre-compression parameters like bulk density, tapped density, Carr's index and hausner's ratio have been performed. These were found to be good for all the formulations but the formulation F4,F8 and F15 are found to be focused specially. Results were given in the table-3 that describes all the values of all the formulated batches.

Table 3: Pre Compressional Parameters of Metformin Immediate release tablets

Formulation	Bulk density (g/cc)	Tapped density (g/cc)	Hausner ratio	Compressibilty index (%)	Angle of repose (ɵ)
F1	0.435	0.522	1.20	16.66	32.67
F2	0.429	0.518	1.20	17.18	29.08
F3	0.430	0.524	1.21	17.93	31.78
F4	0.432	0.528	1.22	18.18	30.64
F5	0.428	0.518	1.21	17.37	30.36
F6	0.420	0.510	1.21	17.64	31.05
F7	0.416	0.509	1.22	18.27	32.54
F8	0.417	0.515	1.23	19.02	29.67
F9	0.425	0.515	1.21	17.47	31.85
F10	0.421	0.509	1.20	17.28	29.56
F11	0.419	0.515	1.22	18.64	30.17
F12	0.415	0.512	1.23	18.94	32.08
F13	0.420	0.520	1.23	19.23	29.67
F14	0.423	0.512	1.21	17.38	29.54
F15	0.435	0.520	1.20	16.34	31.76
F16	0.422	0.512	1.21	17.57	32.04
F17	0.425	0.523	1.23	18.73	30.56
F18	0.434	0.526	1.21	17.49	31.23
F19	0.426	0.512	1.20	16.79	29.52
F20	0.420	0.519	1.23	19.07	29.32

Post Compressional Parameters:

In all formulations, tablet weight and thickness were within mean ±7.5% and mean ±5% respectively. The weight variation in all the twenty formulations was found to be 78.5 mg to 80.4 mg, which was in pharmacopoeial limits. The thickness varies between 3.84 to 3.92 mm. Friability values were less than 1% in all cases. Hardness of all the tablets was maintained at 2.9 to 3.19 kg for all the formulations as mentioned before. Assay was performed and percent drug content of all the tablets were found to be between 97.75% and 99.36% of Metformin, which was within the acceptable limits.

Wetting time was determined for all the formulations. The values lie between 11.16±0.75 to 57.33±0.81. The variability in wetting time for different formulations may be due to the changes in the compaction which cannot be controlled during tablet preparation and the type of the disintegrant affected the wetting of the tablets. On comparing the superdisintegrants the formulations containing crosspovidone + croscarmellose sodium and crosspovidone + sodium starch glycolate take less wetting time than the other formulatios containing single superdisintegrants.

Water absorption ratio ranged from 56.59 % – 67.54 %. Crosspovidone and croscarmellose sodium perform their disintegrating action by wicking through capillary action and fibrous structure, respectively with minimum gelling. The relative ability of the various disintegrants to wick water into the tablets was studied. After contact with water the tablets containing sodium starch glycolate swelled, the outer edge appeared gel like. Tablets containing crosspovidone quickly wicks water and were hydrated, but were soft as compared with tablets prepared with crosscarmellose sodium and sodium starch glycolate. The center of the tablets with sodium starch glycolate and croscarmellose sodium remained dry and hard.

Disintegration time is considered to be important criteria in selecting the best immediate release Tablet formulation. The *in vitro* disintegration time for all the twenty formulations varied from 17.66±0.51 to 171.83±1.16 seconds. The rapid disintegration was seen in the formulations containing crosspovidone and formulations containing combination of superdisintegrants (CP + CCS, CP + SSG). This is due to rapid uptake of the water from the medium, swelling and burst effect. It is also noticed that as the disintegrant concentration was increased from 9 to 12% the time taken for disintegration was reduced. The disintegration time of formulation (F15) containing 5% CP + 5% CCS was found to be lower (17.66±0.51) and was selected as the best immediate release Tablet formulation among all the 20 formulations shown in tables 4 and 5.

Table 4: Tabletting characteristics of Metformin Immediate release tablets

Formulation	Weight (mg)	Drug content (%)	Hardness (kg/cm^2)	Friability (%)	Thickness (mm)
F1	79.9±0.70	98.96±0.47	3.05±0.13	0.48	3.84±0.032
F2	79.52±0.85	99±0.65	3.10±0.15	0.53	3.85±0.028
F3	78.9±0.52	99.11±0.52	2.95±0.08	0.44	3.86±0.024
F4	80.2±1.17	99.15±0.60	2.95±0.10	0.57	3.86±0.051
F5	79.0±0.49	99.2±0.4	3.08±0.12	0.43	3.88±0.048
F6	78.8±0.58	98.85±0.58	3.11±0.14	0.56	3.90±0.052
F7	79.3±0.54	99.31±0.24	2.92±0.08	0.53	3.92±0.038
F8	80.4±1.0	98.96±0.28	3.0±0.09	0.45	3.91±0.042
F9	79.6±0.95	99.3±0.38	2.9±0.07	0.6	3.90±0.040
F10	79.2±0.97	99.36±0.29	3.05±0.08	0.49	3.89±0.042
F11	79.4±0.86	98.75±0.40	3.05±0.09	0.53	3.89±0.034
F12	78.5±0.42	99.21±0.38	2.93±0.08	0.58	3.87±0.031
F13	80.3±1.18	98.56±0.49	3.19±0.05	0.47	3.86±0.034
F14	79.3±0.53	98.61±0.60	3.16±0.04	0.52	3.86±0.023
F15	80.1±0.75	98.98±0.56	3.10±0.10	0.63	3.87±0.044
F16	80.3±0.86	99.03±0.58	3.05±0.09	0.58	3.89±0.051
F17	79.1±0.84	97.75±0.69	3.15±0.04	0.58	3.85±0.029
F18	78.8±0.56	98.76±0.56	2.92±0.08	0.53	3.88±0.046
F19	79.6±0.60	99.08±0.29	3.00±0.09	0.51	3.86±0.025
F20	80.0±0.75	98.86±0.39	3.12±0.12	0.55	3.84±0.034

Table 5: Tabletting characteristics of Metformin Immediate release tablets

Formulation	Wetting time (sec)	*In vitro* dispersion time (sec)	Disintegration time (sec)	Water absorption ratio (%)
F1	24.83±0.98	221.33±1.03	116.5±1.37	58.45
F2	21.16±0.75	180.5±1.04	95.16±0.75	59.25
F3	14.66±0.51	75±0.89	56.50±1.64	58.9
F4	**11.66±0.51**	**54±0.63**	**27.83±1.16**	**60.65**
F5	57.33±0.81	244.5±1.04	168.83±1.94	59.88
F6	22.33±1.36	215.5±0.54	98±0.63	61.48
F7	28±1.09	177.83±1.16	73.16±1.47	59.55
F8	19.66±0.81	126.66±0.81	36.66±1.21	60.01
F9	37.33±0.81	259.83±1.47	171.83±1.16	64.37
F10	28.33±0.81	225.33±0.81	153±0.89	67.54
F11	26.66±0.81	186.83±0.75	81.5±1.04	65.50
F12	36.83±1.16	154.5±0.83	42.66±1.75	65.89
F13	19.33±0.51	91.66±1.21	82.5±1.04	59.49
F14	14.33±0.51	49.33±1.03	46±0.89	56.59
F15	**11.16±0.75**	**30.66±0.81**	**17.66±0.51**	**57.08**
F16	12.5±0.54	35.16±0.75	20.33±0.81	58.72
F17	19.1±0.75	96.83±0.40	86.16±0.75	57.95
F18	14.83±0.75	54.16±1.72	47.5±1.04	60
F19	11.5±0.54	46.66±0.81	23.66±0.51	61.50
F20	13±0.89	43.83±0.75	20.83±1.16	58.24

In-Vitro Dissolution Studies:

In *vitro* dissolution studies of the prepared immediate release Tablets was performed in pH 6.8 phosphate buffer using USP dissolution apparatus type 2. The dissolution rate was found to increase linearly with increasing concentration of superdisintegrant. Formulations F1, F2, F3 and F4 which contained increasing concentrations of crosspovidone have recorded drug release 95.78%, 96.85%, 97.96 and 98.99% respectively within 20 to 30 min. Formulations F5, F6, F7 and F8 which contained increasing concentrations of croscarmellose sodium have recorded drug release 89.53%, 92.36%, 94.46% and 95.43% respectively, at the end of 30 min. Formulations F9, F10, F11 and F12 which contained increasing concentrations of sodium starch glycolate have recorded drug release 85.4%, 88.45%, 90.4% and 92.38% respectively, at the end of 30 min.

Formulations F13, F14, 15 and F16 which contained increasing concentrations of combination of CP + CCS have recorded drug release 94.5%, 96.52%, 99.87% and 96.38% respectively, at the end of 25 to 30 min. Formulations F17, F18, F19 and F20 which contained increasing concentrations of combination of CP + SSG have recorded drug release 88.56%, 92.5%, 95.48% and 94.51respectivel, at the end of 30 min results were shown in tables 6 and 7, figures 2-6.

Table 6: Cumulative percent Metformin released from Immediate release tablets containing varying concentrations of different superdisintegrants

Cumulative percent (±S.D.) drug released						
Time (min)	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**
2	27.35±0.28	22.35±0.52	20.46±0.25	28.31±0.23	18.35±0.34	15.43±0.30
4	40.33±0.28	34.36±0.28	29.28±0.19	41.33±0.24	25.5±0.28	23.43±0.32
6	55.46±0.31	45.31±0.27	42.35±0.25	59.33±0.26	37.36±0.25	37.36±0.26
8	69.46±0.27	62.35±0.25	61.31±0.23	73.48±0.34	57.41±0.23	54.38±0.26
10	74.38±0.27	75.48±0.30	76.4±0.36	85.38±0.34	64.55±0.28	67.38±0.37
15	83.35±0.20	87.4±0.31	82.53±0.30	98.6±0.29	72.48±0.35	75.46±0.26
20	94.45±0.30	96.31±0.29	97.31±0.20	98.89±0.32	80.45±0.28	82.31±0.23
25	94.89±0.24	96.57±0.28	97.76±0.28	98.95±0.24	86.5±0.26	87.48±0.24
30	95.78±0.27	96.85±0.32	97.96±0.25	98.99±0.23	89.53±0.19	92.36±0.25
Cumulative percent (±S.D.) drug released						
Time (min)	**F7**	**F8**	**F9**	**F10**	**F11**	**F12**
2	22.33±0.25	14.38±0.31	19.33±0.20	23.43±0.16	18.48±0.33	19.4±0.32
4	33.36±0.31	22.1±0.59	28.36±0.32	35.31±0.27	27.18±0.18	27.41±0.26
6	45.46±0.26	36.43±0.30	36.45±0.25	47.36±0.29	34.43±0.23	35.28±0.29
8	62.43±0.23	55.46±0.30	49.43±0.26	53.5±0.34	45.61±0.17	52.43±0.26
10	70.28±0.20	62.46±0.25	55.48±0.26	64.45±0.30	52.41±0.36	65.41±0.33
15	78.41±0.26	75.58±0.27	68.46±0.32	72.6±0.27	61.25±0.55	78.45±0.35
20	86.28±0.24	80.4±0.26	74.58±0.27	78.41±0.14	70.46±0.21	84.51±0.24
25	90.28±0.17	83.48±0.30	78.43±0.27	83.45±0.28	75.41±0.24	88.36±0.18
30	94.46±0.25	95.43±0.19	85.4±0.22	88.45±0.18	90.4±0.33	92.38±0.19

Table 7: Cumulative percent Metformin released from Immediate release tablets prepared by varying concentrations of combination of superdisintegrants

Cumulative percent (±S.D.) drug released				
Time (min)	**F13**	**F14**	**F15**	**F16**
2	17.41±0.26	26.21±0.17	25.43±0.29	21.4±0.24
4	25.43±0.25	32.38±0.21	37.41±0.31	31.43±0.33
6	37.43±0.33	45.31±0.27	51.36±0.28	40.25±0.18
8	53.45±0.26	60.25±0.15	68.35±0.31	64.45±0.28
10	66.43±0.24	75.31±0.29	77.35±0.28	71.53±0.26
15	78.45±0.24	87.48±0.24	89.4±0.2	79.46±0.22
20	83.45±0.24	89.31±0.17	93.38±0.24	84.53±0.25
25	85.35±0.25	96.52±0.19	99.87±0.18	89.55±0.16
30	94.5±0.21	------	------	96.38±0.24
Cumulative percent (±S.D.) drug released				
Time (min)	**F17**	**F18**	**F19**	**F20**
2	13.48±0.27	24.55±0.32	24.35±0.30	26.3±0.28
4	25.35±0.30	35.3±0.28	31.41±0.25	38.3±0.28
6	33.4±0.20	42.4±0.31	43.53±0.21	50.36±0.24
8	50.38±0.18	53.38±0.27	57.43±0.33	61.48±0.21
10	61.4±0.30	65.43±0.35	69.53±0.24	69.35±0.28
15	75.55±0.32	76.5±0.28	77.48±0.34	76.51±0.17
20	77.43±0.29	82.45±0.30	85.38±0.23	81.48±0.24
25	82.45±0.18	86.5±0.26	91.45±0.18	84.45±0.27
30	88.56±0.21	92.5±0.14	95.48±0.18	94.51±0.19

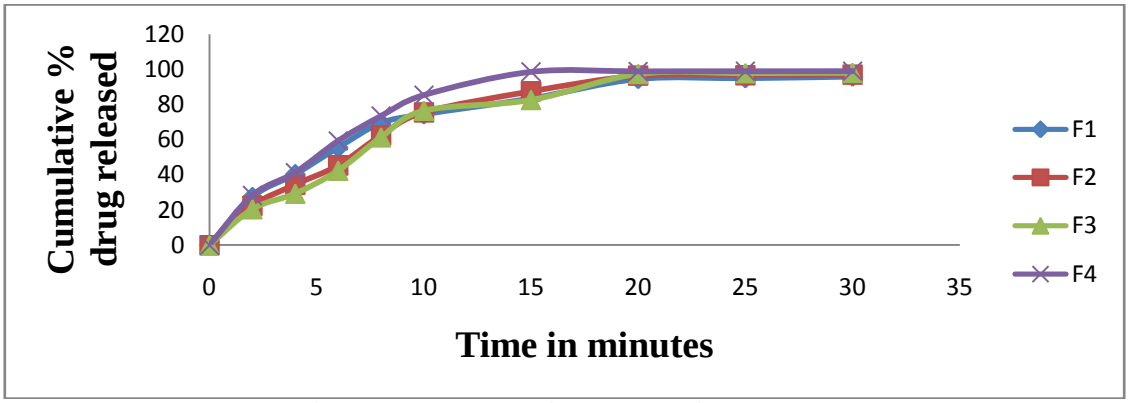

Figure 2: Graphical representation of Cumulative percent Metformin released from Immediate release tablets containing varying concentrations of crosspovidone.

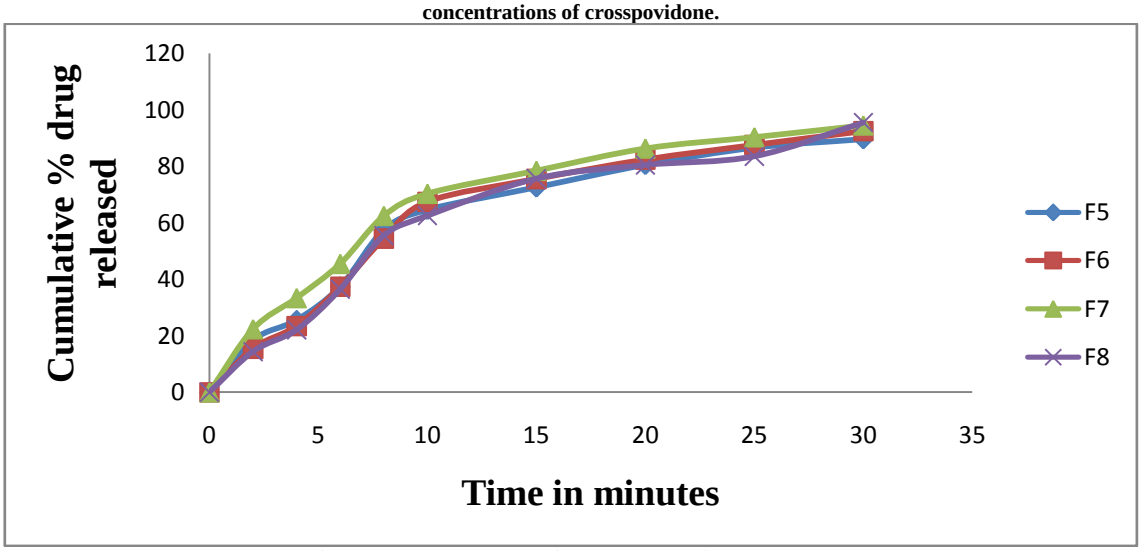

Figure 3: Graphical representation of Cumulative percent Metformin released from Immediate release tablets containing varying concentrations of croscarmellose sodium.

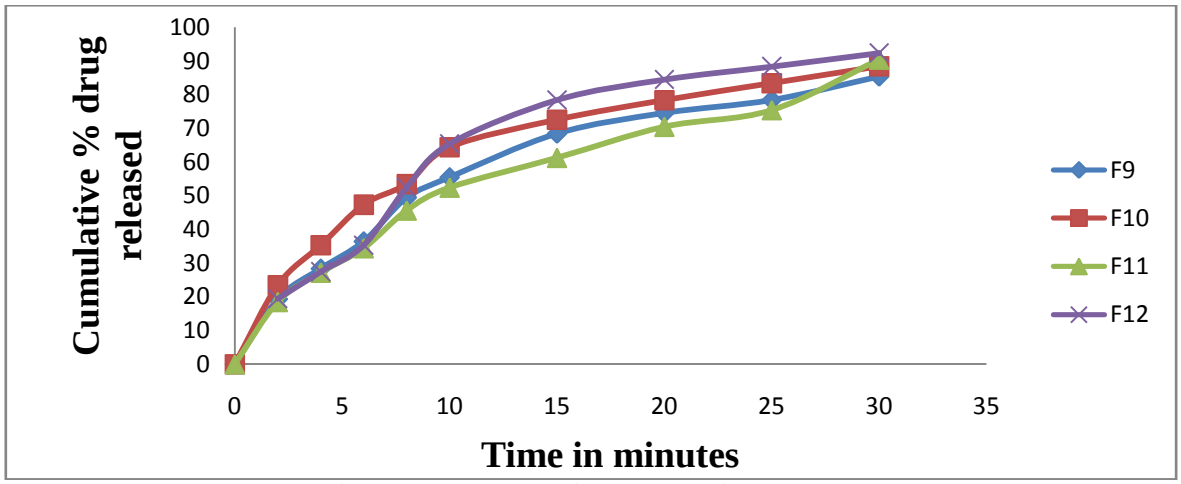

Figure 4: Graphical representation of Cumulative percent Metformin released from Immediate release tablets containing varying concentrations of sodium starch glycolate.

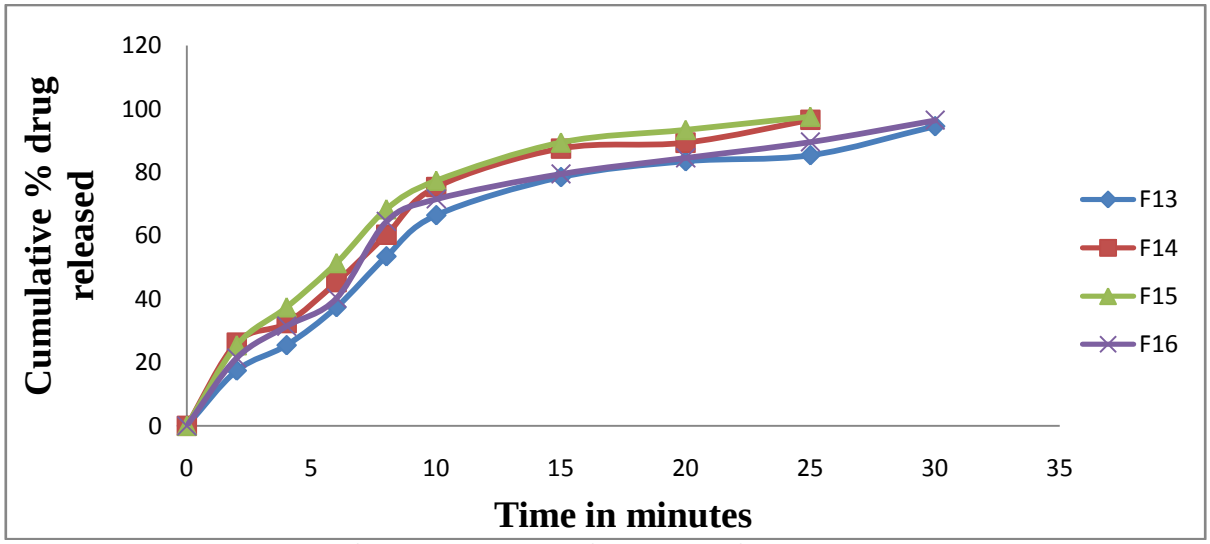

Figure 5: Graphical representation of Cumulative percent Metformin released from Immediate release tablets containing varying concentrations of CP + CCS

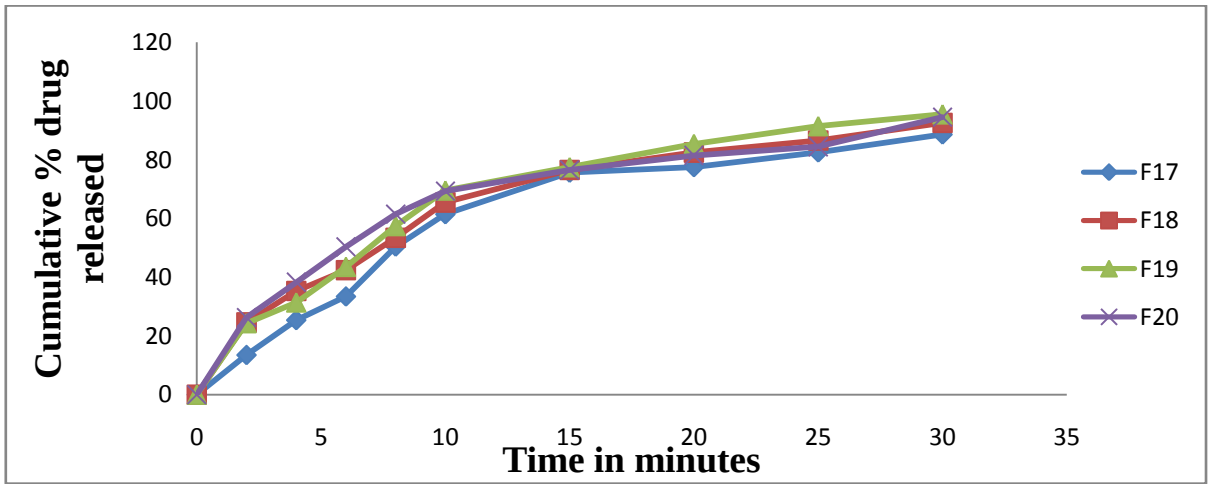

Figure 6: Graphical representation of Cumulative percent lisinopril released from Immediate release tablets containing varying concentrations of CP + SSG

CONCLUSION:

Immediate release tablets of Metformin were formulated with an aim to improve the versatility, patient compliance and accurate dosing. The formulations ere developed with an objective to use by the pediatric and geriatric patients. Metformin Immediate release Tablets were prepared by direct compression method using crosspovidone, croscarmellose sodium, sodium starch glycolate and combinations of CP+CCS, and CP + SSG as superdisintegrants exhibited good preformulation and tabletting properties.Of three superdisintegrants, the formulation contained combination of CP + CCS showed better performance in terms of disintegration time when compared to other formulations. Order of the superdisintegrant activity is as follows (CP + CCS) > (CP + SSG) > CP > CCS > SSG. The formulation F15 was found to be the best among the all twenty Metformin ODT formulations because it has exhibited faster disintegration time (17.66 sec) when compared to the other formualaions and it showed 99.87±0.18%drug release at the end of 25 min. Metformin Immediate release Films were prepared by solvent casting method using different grades of Hydroxy Propyl Methyl Cellulose like HPMC – E15, HPMC – 5cps, HPMC – 50cps.Based on disintegration and dissolution results it was concluded that the formulation F15 contained CP 5% + CCS 5% was the best formulation among the all other formulations.FTIR study showed no drug excipient interaction. The metallic taste of the drug was masked by Sodium saccharin, and Orange flavor.

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