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

FORMULATION AND EVALUATION OF BILAYER TABLETS OFMETFORMIN AND LINAGLIPTIN

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Abstract:

The present study was to establish Bi-layer tablets of Metformin HCl and Linagliptin of which Metformin HCl as sustained release (SR) and Linagliptin as immediate release (IR) layer. Different amounts of crospovidone were utilized as disintegrating agents when making bilayered tablets, and HPMC K100, gattigum, and sodium alginate were used as sustained release polymers. The manufactured bilayered tablets underwent evaluations for homogeneity of drug content, hardness, weight fluctuation, thickness, friability, and in-vitro dissolution investigations. The maximum drug release for Formulations F6 and L4 for SR and IR, respectively, was seen to be up to 99.84% and 99.85% within 12 hours and 30 minutes, respectively. F6 was put through drug release kinetics tests that included zero order, first order, the Higuchi matrix, and Peppas model equations. Formulation F6 was prepared as the best formulation for (SR) based on several assessment factors, while L4 for (IR) was further subjected to a stability study. The formula had high stability, and the values were within the acceptable range. Thus, it may be concluded that stable bilayered tablet dosage forms for metformin's prolonged release and linagliptin's quick release are both possible.

Keywords: *Anti-diabetic, Linagliptin, Metformin, Disintegrating agents, Immediate release layer, sustained release.*

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INTRODUCTION:

Diabetes mellitus, often simply referred to as diabetes, is a group of metabolic diseases in which a person has high blood sugar, either because the body does not produce enough insulin or because cells do not respond to the insulin that is produced [1]. Diabetes is one of the major causes of death and disability in the world. World Health Organization estimate for the number of people with diabetes worldwide, in 2000, is 171 million, which is likely to be at least 366 million by 2030. Non-insulin dependent (Type 2) diabetes mellitus is a heterogeneous disorder characterized by an underlying insufficiency of insulin. This insufficiency results from defective insulin utilization and can be corrected by administration of one or more of the currently available oral hypoglycemic agents [2,3].

Combination therapy have various advantages over monotherapy such as problem of dose-dependent side effects is minimized, a low dose combination of two different agents reduces the dose-related risk, the addition of one agent may counteract some deleterious effects of the other, using low dosage of two different agents minimize the clinical and metabolic effects that occur with maximal dosage of individual component of the combined tablet [3,4].

Metformin is an oral biguanidine first-line choice of drug. Metformin has an oral bioavailability of 50–60% under fasting conditions, and is absorbed slowly. The average elimination half-life in plasma is 6.2hours. Peak plasma concentrations (Cmax) are reached within 4 to 8 hours with extended-release formulations [4,5]. Linagliptin is in a class of medications called dipeptidyl peptidase-4 (DPP4) inhibitors. It works by increasing the amounts of certain natural substances that lower blood sugar when it is high. Linagliptin is not used to treat type 1 diabetes or diabetic ketoacidosis [6,7]

Materials and Methods

Materials

Metformin and Linagliptin was obtained from Hetero Pvt Ltd. Hyderabad. Hydroxy Propyl Methyl Cellulose K100, K15M was obtained from Research lab chem. Industries (Mumbai). Crospovidone, Magnesium Stearate, Sodium Alginate was obtained from SD Fine chemicals

Methods

Pre-formulation Studies

Preformulation is a stage of research and development where the formulation scientist characterizes the physical, chemical, and mechanical properties of new therapeutic ingredients in order to prepare stable, safe, and efficient dosage forms [8].

Organoleptic properties:

Solubility analysis

The pre-formulation parameter of solubility is crucial since it influences the drug's bioavailability and how well it dissolves. Metformin hydrochloride's solubility in ethanol, acetone, ether, and chloroform was assessed. Metformin hydrochloride was taken in excess and dissolved in various solvent-containing beakers to conduct solubility investigations [9].

Melting point

A little amount of metformin hydrochloride and linagliptin was obtained and placed in an equipment to test the melting point, and the result was compared to standards using the capillary method.

Loss on drying

Determined 1 g in an oven at 100°C to 105°C for three hours. The test material was thoroughly mixed and weighed. Make a determination using a shallow glass weighing bottle with a glass stopper that has been dried for 30 minutes in the same conditions. measured the empty bottle's weight (W1). Place the sample in the bottle, cover it, and precisely weigh the full bottle (W2) before using it [10].

Distributed the sample to a depth of approximately 5 mm by gently shaking it side to side. positioned the loaded bottle in the drying room. Before weighing, dry the sample at the prescribed temperature in a desiccator. A bottle scale (W3) was used. The difference between successive weights should not less than 0.3%.

$$\% \text{ LOD} = \frac{(W_2 - W_3)}{(W_2 - W_1)} \times 100$$

Where,

W_1 = Weight of empty weighing bottle

W_2 = Weight of weighing bottle + sample

W_3 = Weight of weighing bottle + dried sample

Angle of repose: Angle of repose, which is determined by friction, cohesion, and the shapes of the particles, is the maximum angle of a stable slope. The angle of repose, also known as the internal angle between the pile's surface and the horizontal surface, is influenced by the raw material's density, surface area, and coefficient of friction [11].

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

Where,

h = height of heap,

r = radius of heap,

Θ = angle of repose.

Bulk density:

The mass of the powder divided by the bulk volume is known as bulk density. A sample of 5 grammes of

powder was weighed, transferred to a measuring cylinder, and its volume was measured [12]. Calculation of the beginning volume. Bulk density was calculated using the formula.

Bulk density = Bulk mass / Bulk volume

Tapped density:

Tapped density is achieved by mechanically tapping a measuring cylindercontaining a powder sample.

At intervals of 2 seconds, the measuring cylinder's powder was tapped at a height of 2.5 cm for a predetermined number of times. At intervals of two seconds, the graduated cylinder's powder was tapped at a height of 2.5 cm for a predetermined number of times [13]. The final volume occupied by the sample was noted and tapped density was calculated by using the formula:

Tapped density = $\frac{m}{v_f}$

Where, m = initial weight of material in gm,

V_f = volume of material after tapping.

Measurement of powder compressibility

Based on the apparent bulk and the tapped density, the percentage compressibility of bulk was determined by the following formula [14].

Compressibility index: = $100\ \frac{(V_0-V_f)}{V_0}$

Where,

V_f = final tapped volume,

V_o = initial

Hausner Ratio*:* $= \frac{V_0}{V_f}$

Where,

V_f = final tapped volume,

V_o = initial un tapped volume.

Drug excipient compatibility study

Metformin dosage forms, infrared spectra of the physical mixing of the polymers individually, and the mixture of drug and polymer were examined prior to the invention of linagliptin [15].

Formulation

Table 1: Formulation of Immediate release tablet

S.No.	Ingredients	L1	L2	L3	L4
1	Linagliptin	2.5	2.5	2.5	2.5
2	Cros povidone	0	2	4	6
3	Mannitol	q.s	q.s	q.s	q.s
4	PVP K 90	3	3	3	3
5	Magnesiumstearate	4	4	4	4

Table 2: Formulation of bilayer tablet

S.NO	Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
IR release granules (LG4)										
1	Linagliptin	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5
2	Cros povidone	6	6	6	6	6	6	6	6	6
3	Mannitol	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s
4	PVP K 90	3	3	3	3	3	3	3	3	3
5	Magnesiumstearat	4	4	4	4	4	4	4	4	4
SR release granules										
6	Metformin	250	250	250	250	250	250	250	250	250
7	HPMC K100M	67	90	113	---	---	---	---	---	---
8	Guar gum	---	---	---	67	90	113	---	---	---
9	Sodium alginate	---	---	---	---	---	---	67	90	113
10	MCC	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s
11	Aerosil	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5
12	Mg.Stearate	11.5	11.5	11.5	11.5	11.5	11.5	11.5	11.5	11.5
	Total weight(mg)	500	500	500	500	500	500	500	500	500

Preparation of Bilayer tablets

Preparation of Immediate release layer:

The immediate release layer includes a consistent mixture of linagliptin cros povidone, MCC that has been weighted, shifted through a 40# filter, and thoroughly mixed with a PVP K-90 binder solution to create a moist mass. Later, the wet mixture was dried after being put through a 20# filter. Magnesium stearate was utilized to lubricate the final granules, and the thoroughly combined powder served as the top layer [16].

Preparation of Sustained release layer:

Direct compression was used to prepare all Formulations. Approximately five minutes were spent completely blending metformin and excipients after sieving them via a no. 40 sieve. Magnesium stearate that had already been through sieve 60 was used to lubricate this mixer for two minutes [17]. The lubricated granules were then made into tablets by compression.

Preparation of Bilayer tablet:

Fast release layer and different sustained release layer formulations were combined to prepare bilayer tablets [18]. The die containing the originally crushed matrix tablet on the multi station punching machine employing flat punches, with the hardness of 6.5 kg/cm2, was then lifted, and the mix of powder for instant release layer was put into the die.

Evaluation of Bilayer Tablets:

Appearance:

Visual identification of the bilayer tablets was done by examining the color difference.

Thickness:

A calibrated dial caliper was used to measure thickness. Five tablets of the mixture were chosen at random, and each tablet's thickness was measured [19].

Hardness:

Monsanto's hardness tester was used to measure hardness. Three tablets from each batch were examined.

Friability:

Twenty tablets were weighed and put in the Roche friabilator, which was circulated for 4 minutes at a speed of 25 rpm [20]. The tablets were once more weighed after revolutions. The percentage friability was measured using formula,

$$\% F = \{1-(W_t/W)\} \times 100$$

Where, % F = Friability in percentage

W = Initial weight of tablets

W_t = Weight of tablets after revolution

Weight variation

From each batch, ten tablets were selected at random and weighed one by one. Calculations were made for the average weight and standard deviation of 20 pills. If there are just two tablets in the batch that depart from the average weight, the batch passes the weight variation test [21].

***In-vitro* dissolution studies for IR**

The tablets were broken down using a paddle on a USP dissolving type II device. The hydration mechanism held the tablet to the paddle. A dissolution vessel was filled with 900 ml of pH 1.2 buffers (0.1N HCL) as the dissolution media, and the temperature of the medium was set to 37 0.50 C. The paddle's rotational speed was set to 100 rpm [22]. At predefined intervals of up to 90 minutes, 1 ml of the sample was removed, and the same volume of fresh medium was substituted. The removed samples were diluted to 10 ml with 0.1N HCL, filtered, and then examined using 0.1N HCL as a blank for UV spectrophotometer analysis at 241 nm. Calculated was the cumulative drug release percentage.

***In-vitro* dissolution studies for SR:**

The tablets were broken down using a paddle on a USP dissolving type II device. The hydration mechanism held the tablet to the paddle. A dissolving vessel was filled with 900 ml of pH 6.8 buffer as the dissolution medium, and the temperature of the liquid was set to 37 0.50 C. The paddle's rotational speed was set to 50 rpm. At regular intervals up to 12 hours, 5 ml of the sample were removed, and the same volume of fresh medium was substituted [23]. The samples that were withdrawn were examined using a UV spectrophotometer at 232 nm and 0.1N HCL as a blank. Percentage cumulative drug release was calculated.

Data analysis:

The data were fitted into the PSP-DISSO - v2 software's Zero order, First order, Higuchi matrix, Peppas, and Hixson Crowell models in order to analyse the mechanism of release and release rate kinetics of the dosage form. The best-fit model was decided upon using the r-value [24].

Zero order kinetics

The following equation can be used to model drug dissolution from pharmaceutical dosage forms that do not disaggregate and release the medication gradually, provided that the area does not change and no equilibrium conditions are attained,

$$Q_t = Q_o + K_o t$$

Where Q_t = amount of drug dissolved in time t.

Q_o = initial amount of the drug in the solution and

K_o = zero order release constant.

First order kinetics:
To study the first order release rate kinetics, the release rate data were fittedto the following equation,

$$\text{Log } Q_t = \log Q_o + K_1 t/2.303$$

Where Q_t is the amount of drug released in time t, Q_o is the initial amount of drug in the solution and K_1 is the first order release constant.

Higuchi model:
Higuchi develop a number of theoretical models to analyze how pharmaceuticals that are incorporated into semisolids or solid matrices but are only weakly soluble in water or other solvents escape. Drug particles dispersed in a homogeneous matrix acting as the diffusion medium were given mathematical formulas.

Q

$$t = K_H \cdot t^{1/2}$$

Where Q_t = amount of drug released in time t,
K_H = Higuchi dissolution constant.

Korsmeyer and Peppas release model:
To study this model the release rate data are fitted to the following equation,

$$Mt / M_\infty = K \cdot t^n$$

Where Mt / M_∞ is the fraction of drug release, K is the release constant, t is the release time and n is the diffusional coefficient for the drug release that is dependent on the shape of the matrix dosage form.

Stability studies of the optimized formulation:
In the current investigation, stability tests for a particular formulation were performed at 40 0C and 75% RH for a predetermined time period up to 3 months. The tablets were placed in aluminium container that had a polyethylene coating inside for stability testing [25]. These sample containers were put in a desiccator with a 75% relative humidity setting.

Evaluation of samples
Appearance: At intervals of one month to three months, the samples were examined for any changes in colour.

Hardness:
At intervals ranging from one month to three months, the samples were evaluated for hardness.

Drug content: At intervals of between one month and three months, the samples were examined for drug content.
Drug release: Drug release tests were performed on the samples every month or every three months.

RESULTS AND DISCUSSION:

Preformulation Study
Solubility analysis:
Metformin was discovered to be easily soluble in water and only marginally soluble in ethanol. However, it was nearly insoluble in acetone, ether, and chloroform.
Linagliptin was found to be soluble in water

Melting point
Metformin melting point was found to be 224. 5°C using the capillary method. Comparing the melting point to USP requirements revealed that the medication is pure. The melting point of Linagliptin was found to be 203°C using the capillary technique. The drug's melting point in comparison to USP criteria demonstrated its purity.

Loss on Drying:

Table 3: Observations for loss on drying

	Test	Loss on Drying	Observation
Metformin	Loss on Drying	Not more than 0.5%	0.41%
Linagliptin	Loss on Drying	Not more than 0.5%	0.43%

Angle of repose

Table 4: Angle of Repose

Material	Angle of repose
Metformin	27°32’
Linagliptin	27°54’

The results showed that the raw material has good flow characteristics.

Flow properties

Table 5: Flow properties of drugs

Material	Bulk Density	TappedDensity	Carr's index	Hausner Ratio
Metformin	0.320	0.409	10.98	1.20
Linagliptin	0.368	0.418	10.76	1.09

Drug excipient compatibility study

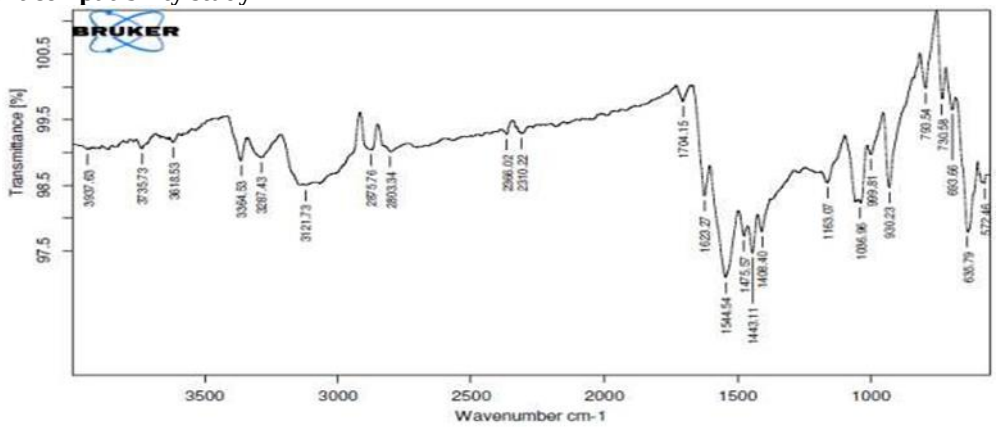

Fig 1: FTIR Spectra of Metformin

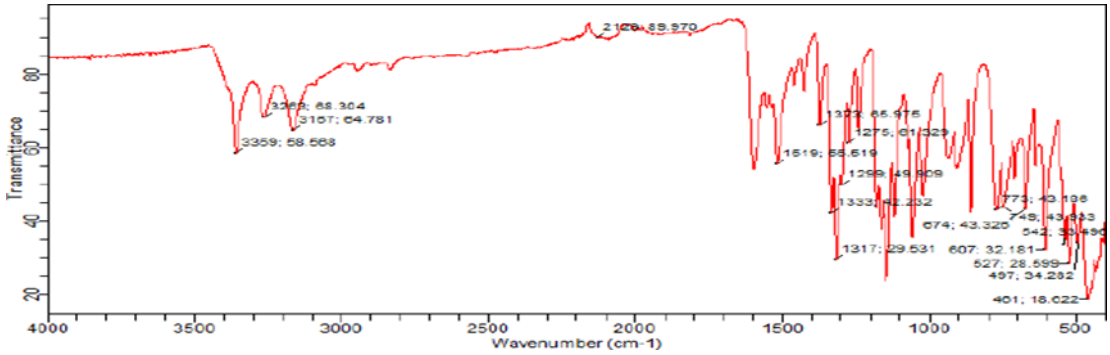

Fig 2: FTIR Spectra of Metformin best formulation

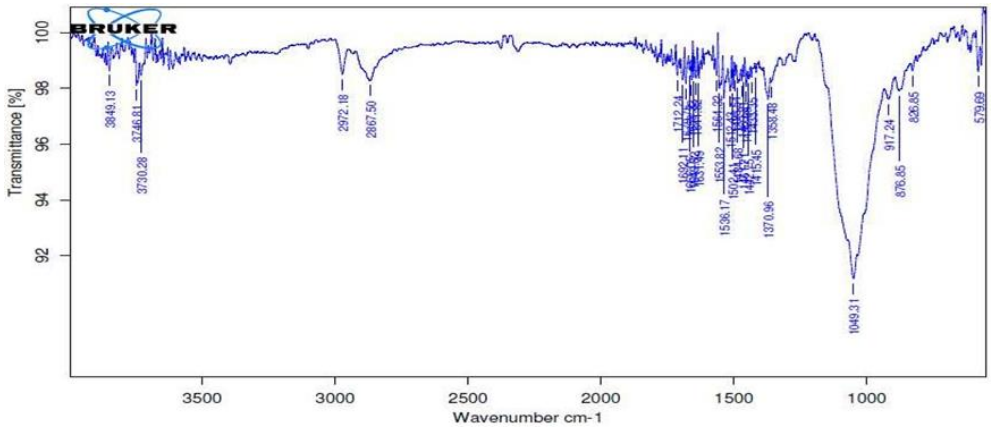

Fig 3: FTIR spectra of Linagliptin

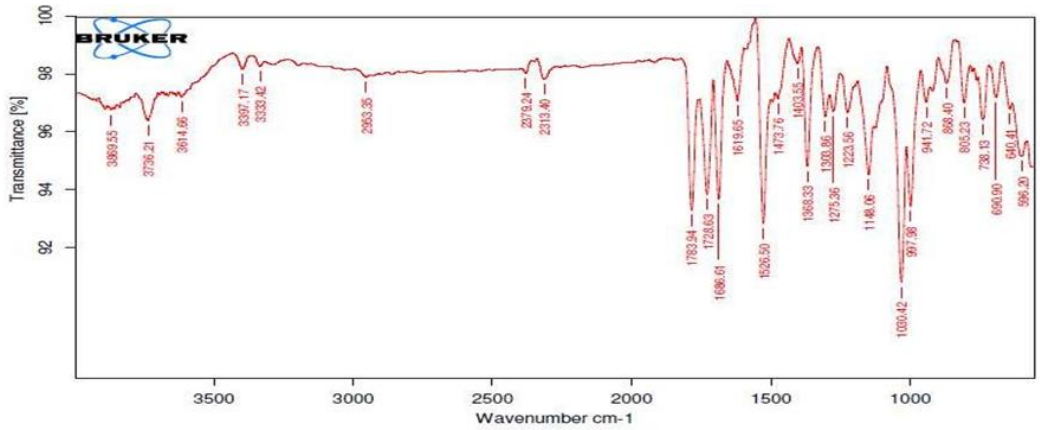

Fig 4: FTIR spectra of Linagliptin best formulation

Formulation of bilayer tablet:

Table 6. Precompression parameters for all formulations of IR (Linagliptin)

Code	Angle Repose ±SD	Bulk Densi (g/ml)±SD	Tapped Densi (g/ml)±SD	Carr's Inde (%)±SD	Hausner's ratio±SD
L_1	27°48'±0.42	0.368±0.022	0.418±0.018	10.92±0.22	1.09±0.018
L_2	25°68'±0.18	0.391±0.018	0.442±0.022	11.08±0.08	1.08±0.042
L_3	24°28'±0.32	0.358±0.028	0.418±0.042	13.06±0.34	1.08±0.028
L_4	26°36'±0.18	0.382±0.020	0.442±0.018	13.48±0.26	1.2±0.05

Table 7: Precompression parameters for all formulations of SR (Metformin)tablets

Code	Angle of Repose ±SD	Bulk Density (g/ml) ±SD	Tapped Density (g/ml) ±SD	Carr's Index.(%)±SD	Hausner'sratio±SD
F_1	27°28'±0.18	0.322±0.028	0.408±0.042	11.05±0.22	1.09±0.009
F_2	25°12'±0.32	0.362±0.032	0.428±0.022	13.26±0.08	1.10±0.030
F_3	28°26'±0.08	0.368±0.024	0.408±0.028	10.38±0.28	1.08±0.020
F_4	27°48'±0.42	0.368±0.024	0.418±0.016	10.52±0.22	1.08±0.018
F_5	25°58'±0.18	0.378±0.018	0.428±0.022	11.80±0.08	1.08±0.042
F_6	24°52'±0.32	0.356±0.028	0.418±0.030	13.58±0.30	1.2±0.028
F_7	26°38'±0.32	0.368±0.021	0.442±0.032	13.12±0.08	1.08±0.024
F_8	25°58'±0.18	0.372±0.008	0.418±0.016	10.28±0.18	1.08±0.030
F_9	23°32'±0.18	0.382±0.008	0.442±0.020	13.52±0.24	1.08±0.028

Physicochemical evaluation:
The manufactured tablets were initially evaluated for their hardness, thickness, weight fluctuation as a percentage, friability, and medicine content. The parameters of the formulations evaluated were all within permissible limits.

Table 8: Range for value of preliminary characterization of formulations

Parameters	Range
Hardness (kg/cm^2)	6.34-7.52
Thickness (mm)	2.2-3.4
% Friability	0.5-0.66
Drug content (%)	95.09 - 101.14

***In-vitro* dissolution studies**

Table 9: Cumulative percent drug release of linagliptin tablets

S.No.	Time in minutes	L1	L2	L3	L4
1.	05	16.42±0.414	15.32±0.412	26.38±0.518	33.82±0.518
2.	10	33.82±0.518	37.84±0.618	42.12±0.418	56.42±0.332
3.	15	47.36±0.444	52.42±0.422	61.7±0.408	77.18±0.306
4.	20	56.42±0.335	62.18±0.252	72.12±0.316	90.32±0.418
5.	30	65.92±0.518	77.15±0.322	80.88±0.352	99.82±0.618
6.	40	67.72±0.488	79.18±0.308	90.08±0.130	---
7.	50	76.58±0.492	83.62±0.432	97.56±0.252	---
8.	60	80.90±0.388	94.72±0.332	---	---
9.	75	92.09±0.429	98.28±0.421	---	---
10	90	99.65±0.248	---	---	---

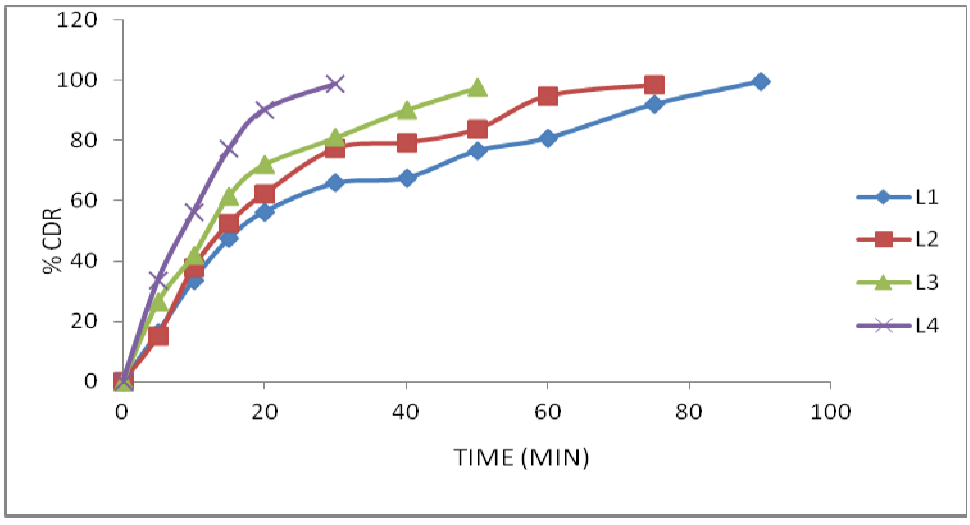

Fig 5: Cumulative percent drug release versus time plots of linagliptin tablets

Table 10: Evaluation parameters bilayer formulations.

Formulationcode	Mean Hardne Kg/cm2	Thickness(mm	Friability % w/w	Average Weight(mg)	Mean drug content %±SD	
					Linagliptin	Metformin
F1	6.42	3.0	0.59	995.8	97.96±0.88	99.52±0.18
F2	7.38	2.9	0.56	998.98	96.36±1.38	99.52±1.58
F3	7.2	3.3	0.49	1001.1	96.12±0.88	96.12±0.18
F4	7.48	2.9	0.58	998.90	99.06±0.08	99.05±0.78
F5	7.18	3.1	0.49	998.9	101.0±1.22	100.0±1.08
F6	7.4	2.6	0.50	998.7	96.02±0.65	96.02±0.55
F7	7.4	2.9	0.58	999.2	96.0±2.04	98.65±1.36
F8	7.4	2.9	0.65	1000.2	99.2±0.88	99.25±0.65
F9	7.2	2.1	0.58	999.2	100.08±1.36	98.96±1.88

Evaluation parameter

Table 11: Evaluation parameters of SR formulations

Formulationcode	Mean Hardne Kg/cm2	Thickness(mm	Friability % w/w	Average weig (mg)	Mean dr Content %±SD
F1	6.32	3.08	0.59	297.9	96.92±1.15
F2	6.28	2.78	0.65	299.8	99.02±0.88
F3	6.36	2.18	0.62	299.8	100.2±1.36
F4	6.48	3.02	0.61	298.8	98.04±0.88
F5	6.0	3.58	0.55	298.9	97.45±1.36
F6	6.35	3.38	0.56	300.2	97.04±0.88
F7	6.48	2.75	0.62	300.1	99.12±0.22
F8	6.25	3.3	0.51	298.8	99.98±1.2
F9	6.35	2.9	0.51	299.9	96.98±0.65

Table 12: *In-vitro* drug release data of metformin SR tablets metformin

Time(hrs)	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
0.5	8	6.5	4	7	5	4	7	5	3
1	50.28	35.22	22.24	32.22	24.70	14.54	35.22	22.18	14.10
2	70.92	65.32	39.88	50.92	38.50	20.36	52.24	47.65	21.42
4	81.72	74.64	57.58	69.92	51.86	30.88	73.84	72.48	35.84
6	99.76	86.62	69.65	88.42	72.24	49.35	90.15	88.18	52.15
8		98.92	85.78	99.88	86.56	64.30	100.08	99.9	88.24
10			97.6		99.88	87.58			98.88
12						99.92			

***In-vitro* drug release profile:**

In-vitro drug release studies were performed on the dissolving test apparatus USP XXIII with paddles in 900ml of 0.1N HCL. The results of these release investigations revealed that the formulations L4 for immediate release and F6, which was deemed to be the best formulation, were released in the order listed below: the Higuchi mechanism, zero order release.

Table 13: *In-vitro* drug release data of bilayer tablets of linagliptin (IR) best & metformin (SR)

		F1		F2		F3		F4		F5		F6		F7		F8		F9
TIME (HRS	L4 IR	F1	L4 IR	F2	L4 IR	F3	L4 IR	F4	L4 IR	F5	L4 IR	F6	L4 IR	F7	L4 IR	F8	L4 IR	F9
0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
0.5	99.908		99.08	6.4	99.924		98.887		99.725		99.624		99.907		99.425		99.853	
1		50.40		35.22		22.08		32.25		24.75		14.72		35.2		22.30		14.12
2		70.90		65.30		39.88		50.90		38.50		20.50		52.20		47.60		21.42
4		81.72		74.48		57.72		69.9		51.89		30.86		73.85		72.45		35.85
6		99.90		86.48		69.65		88.45		72.24		49.22		90.2		88.35		52.1
8				98.92		85.92		99.88		86.55		64.30		100.2		99.75		88.20
10						97.4				99.88		87.5						98.88
12												99.9						

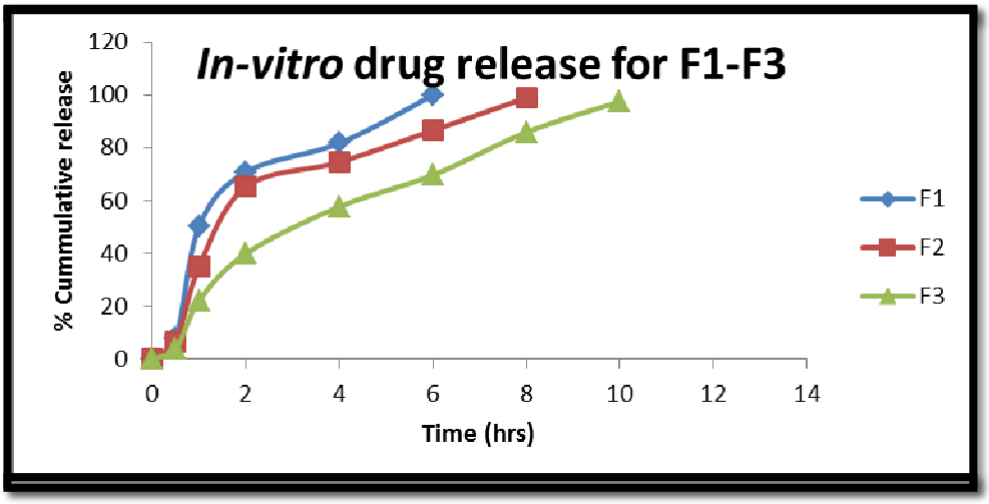

Fig 6: *In-vitro* drug release profile of bilayer tablets of batches F1 to F3

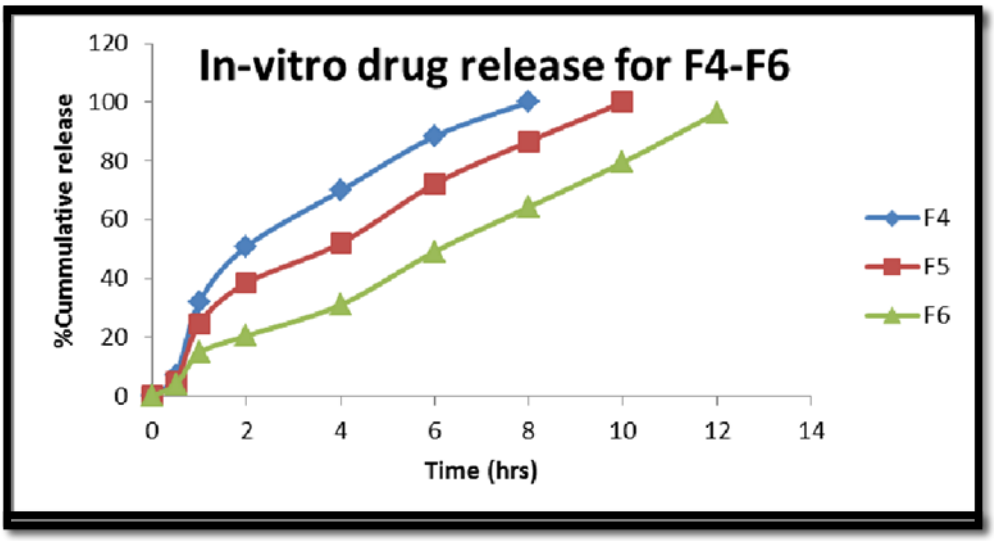

Fig 7: *In-vitro* drug release profile of bilayer tablets of batches F4 to F6.

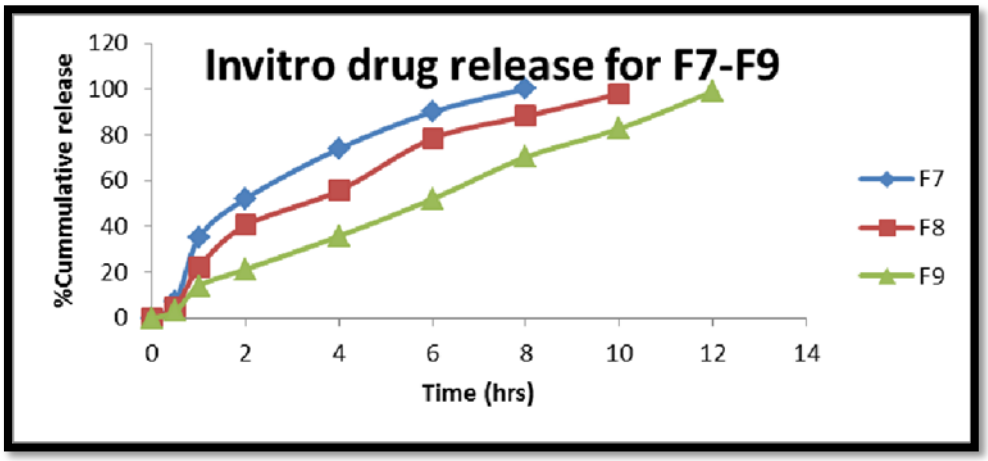

Fig 8: *In-vitro* drug release profile of Bilayer tablets of batches F7 to F9

L4 formulation for immediate release and F6 formulation for sustained release, both of which contain crospovidone, gatti gum, Mg Stearate, and talc, were chosen as the most optimal formulations out of all the available options.

Drug release kinetics of bilayer tablet

Table 14: Regression coefficients fit to different drug release kinetics models forbilayer tablets

Formulationcode Best	Zeroorder	Firstorder	Higuchi	Peppas
	r^2	r^2	r^2	r^2
L4 F6	0.9948	0.8270	0.942	0.7626

Stability studies of the optimized formulation:

Table 15: Stability Studies for Formulation F6

Time	Hardness (kg/cm^2)	Drug contentUniformity	% CDR
0 Month	6.3	99.18	97.88
1 Month	6.3	98.15	96.30
2 Month	6.2	99.48	95.72
3 Month	6.2	98.88	97.54

CONCLUSION:

Metformin completely absorbed in gastric pH but rapidly hydrolyzed in intestinal mucosa. Thus reducing its oral bioavailability. Therefore, by keeping the dosage form in the stomach for a longer amount of time, an effort was made to boost the oral bioavailability of metformin. These tablets were primarily created to shorten the lag time, but they may also boost the bioavailability of the medication by eliminating frequent dosing and, consequently, drug degradation in the intestine. Different amounts of crospovidone were utilised as disintegrating agents when making bilayered tablets, and HPMC K100, gattigum, and sodium alginate were used as sustained release polymers. Other excipients include mannitol, MCC, Mg stearate, and aerosol (a lubricant). Transform of Fourier There were no interactions between the drugs, polymers, or excipients, according to infrared spectroscopy. The manufactured bilayered tablets underwent evaluations for homogeneity of drug content, hardness, weight fluctuation, thickness, friability, and in-vitro dissolution investigations. The maximum drug release for Formulations F6 and L4 for SR and IR, respectively, was seen to be up to 99.84% and 99.85% within 12 hours and 30 minutes, respectively. F6 was put through drug release kinetics tests that included zero order, first order, the Higuchi matrix, and Peppas model equations. Formulation F6 was prepared as the best formulation for (SR) based on several assessment factors, while L4 for (IR) was further subjected to a stability study. The formula had high stability, and the values were within the acceptable range. Thus, it may be concluded that stable bilayered tablet dosage forms for metformin's prolonged release and linagliptin's quick release are both possible.

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