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Research

Formulation and Evaluation of Empagliflozin and Linagliptin Immediate Release Tablet

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Abstract

This study focuses on the development and assessment of immediate-release tablets with Empagliflozin and Lingagliptin for effective type 2 diabetes mellitus management. Using the wet granulation technique, tablets were made with Excipients like mannitol, microcrystalline cellulose, Crospovidone, and Crospovidone. The compatibility of drugs and Excipients was confirmed through FTIR analysis. The parameters for pre-compression and post-compression fell within acceptable limits, guaranteeing good flow properties and mechanical strength. Batch F6 demonstrated optimal results among all formulations, exhibiting acceptable hardness, friability of less than 1%, and uniform weight and drug content. Rapid drug release was demonstrated in in-vitro dissolution studies, with 98.96% of Empagliflozin and 99.32% of Linagliptin achieved within 30 minutes, adhering to first-order kinetics. Stability studies, carried out according to ICH guidelines, showed no significant changes in physical or chemical properties. The optimized formulation was shown to be stable and effective, making it appropriate for producing an immediate therapeutic response in diabetes management.

Keywords: Formulation,Evaluation, Empagliflozin, Linagliptin, Immediate Release tablet, Type-2 diabetes

INTRODUCTION:

For many years, oral medicine administration was considered a highly common method of delivering medications. Drug administration by looking into how different kinds of drugs and pharmacological ingredients are delivered. The acceptance of patient, oral medication has long been regarded as being quite natural, plain, easy,and safe.

Reasons for Usage and Development of Drug Empagliflozin and Linagliptin:

Primary objective -Empagliflozin and Linagliptin combined is to treat type 2 diabetic mellitus. When combined, their complementary mechanisms of action reduce the risk of hypoglycaemia, enhance blood glucose management, and offer additional benefits.

a. Purpose of Using Empagliflozin and LinagliptinManagement ofDiabetes MellitusType 2
Empagliflozin and Linagliptin are primarily utilized to decreaseincreased blood glucose levels intype 2 diabetes personswho cannot properlymaintain their blood sugar levels with diet and exercise alone.

b. Combination of Drugs Empagliflozin and Linagliptin

- Empagliflozin is an inhibitor of SGLT2. It reduces blood sugar by stopping glucose from being reabsorbed by the kidneys, which causes excess glucose to be excreted in the urine.(an insulin-independent process).
- One DPP-4 inhibitor is linagliptin. It functions by raising the levels of the incretin hormones GLP-1 and GIP, which raise insulin secretion and suppress glucagon release in a glucose-dependent manner.Together, they target different pathways in glucose regulation, offering better overall control than either drug alone.

c. Benefits of This Combination

- Improved fasting and postprandial blood glucose control
- Weight neutrality or loss (due to empagliflozin)
- Lowriskofhypoglycemia(becausebothactina glucose-dependent or insulin-independent manner)
- Convenient once-daily oral dosing

Additionally, Empagliflozin, which has been found to help patients with heart failure or chronic kidney disease, may offer cardiovascular and renal protection.

Materials and Methods:

Material used in the formulation of empagliflozin and Linagliptin tablets Active Pharmaceutical Ingredient(API)-MSNlabs Mannitol, Diluent, chemical Microcrystalline cellulose (AvicelPH102) Diluent FMCinternationalhealthand nutrition CrospovidoneXL Disintegrates Ashland Copovidone Binder Ashland Isopropylalcohol Solvent Emplura Microcrystalline cellulose (AvicelPH101) Diluent FMCinternationalhealth and nutrition CrospovidoneXL10, Disintegrates Ashland Magnesium Stearate Lubricant FMC international health and nutrition Opa dry yellow Colorant/coating material Color con Asia Pvt limited Purified water solvent NA

Equipment's used in manufacture of Empagliflozin and linagliptin

S.no	Equipment name	Stage
1	Weighing balance	In-process weighing
2	Analytical weighing balance	In process testing
3	Sifter with sieves(#20,#24#40 and #60 sieve)	Sifting
4	Octagonal Blender	blending
5	Rapid mixer granulator	Granulation
6	Quadraco mil	milling
7	Fluid bed dryer	drying
8	Tablet compression machine	Compression
9	Stirrer	Coating suspension preparation
10	Coating machine	Tablet coating

DRUGPROFILE: Empagliflozin:

- Generic Name: Empagliflozin
- Brand Name(s): Jardiance
- Drug Class: Inhibitor of sodium-glucose co-transporter 2 (SGLT2)
- Category of Therapy: Oral antidiabetic agent

Chemical and Physical Characteristics

- **Appearance: O**ff-white to White crystalline powder
- **Solubility:** Slightly soluble in water, freely soluble in methanol and ethanol
- **Melting Point:** 157–159°C
- **pKa:** Not ionizable; weakly acidic properties
- **Stability:** Stable in typical storage settings, but susceptible to strong acids and oxidizers

Mechanism of action: The sodium-glucose co-transporter 2, which is presentinThe selective inhibition of the proximal renal tubules of the kidneys by Empagliflozinn. Nearly 90% of the glucose that was filtered fromglomerular filtrate is reabsorbed into the bloodstream by SGLT2 under typical physiological conditions.

By blocking SGLT2, empagliflozin decreases the kidneys' reabsorption of glucose and encourages **glucosurea**, i.e., the excretion of excess glucose through urine. This mechanism lowers **glucose concentrationsin plasma**in an manner that isinsulin-independent .Empagliflozin thereby aidsin improving glycemic control and reducing blood glucose levels in people with type 2 diabetes mellitus (T2DM).

Additionally, empagliflozin may lead to **weight loss**, **lower blood pressure**, and **cardiovascular risk reduction** due to its osmotic diuretic effect and modest calorie loss.

Linagliptin:

- Generic Name: Linagliptin
- Brand Name(s): Tradjenta®, Trajenta®
- Class of Drug: Inhibitor of Dipeptidyl Peptidase-4 (DPP-4)
- Category of Therapy: Oral antidiabetic agent

Chemical Information: Molecular Formula and Weight $C_{25}H_{28}N_8O_2$ and 472.54 g/mol, Molecular Weight: 472.54 g/mol

Physical information: Appearance: Crystalline powder that varies between white to pale yellow.Solubility: moderately soluble in water, free y soluble in methanol and ethanolMelting Point: Approx131–136°C**Stability:**Stable in typical storage settings, but susceptible to moisture and light.

Mechanism of Action of API's:The oral antidiabetic medication linagliptinbelongs todipeptidyl peptidase-4 (DPP-4) inhibitor class. Incretin hormones such as glucagon-like peptide-1 (GLP-1) and glucose-dependent insulin tropic polypeptide (GIP) are broken down by an enzyme known as DPP-4.Linagliptin prolongs activity of endogenous incretion hormonesby blocking the DPP-4 enzyme. Therefore, it suppresses the release of glucagon from α-cells and enhances the pancreatic β-cells' release of glucose-dependent insulin**,** the CombinedEffectWhen used in combination, empagliflozin and linagliptin offer **a** complementary mechanism of action. Empagliflozin lowers glucose independently of insulin by promoting renal glucose excretion, Linagliptin, on the other hand, reduces glucagon release and elevates insulin secretion that is dependent on glucose. For treatment of diabetes, this dual mechanismuseful since it offers a low chance of hypoglycemia and an efficient glycemic control method.

METHODOLOGY:

PRE-FORMULATIONSTUIDES:

Foremost in methodical creation of tablets for novel medication or chemical entity is called preformulation. It entails a thorough examination of the active ingredients in pharmaceuticals (API) properties, bothseparately and in combination with Excipients. Preformulation aims to collect the necessary information to guarantee that the formulation is stable, safe, efficient, and profitable to produce.

FORMULATIONOFEMPAGLIFLOZINANDLINAGLIPTINTABLET

PREPARATION OFCORETABLET:

Empagliflozin and Linagliptin was prepared by wet granulation.**Weighing:**The required quantities of all ingredients were accurately weighed as per the formulation.**Co-sifting:**Empagliflozin, linagliptin, and mannitol were co-sifted using a #20 sieve. Crospovidone (Polyplasdone XL-10) and microcrystalline cellulose were separated and sieved using the same sieve.All the sifted materials were then co-sifted once again using sieve no. 20 to ensure uniform particle size distribution.

Dry mixing:

The final blend of sifted materials was transferred to aRapid Mixer Granulator (RMG). Operated the impeller at a low speed and with the chopper off, mixing was done forfifteen minutes.

Binder Preparation:

Isopropyl alcohol was transferred into a mixing vessel equipped with a stirrer. After that, copovidone was added gradually while being stirred continuously until a transparent solution was achieved.

Wet Granulation:

A peristaltic pump was used to add the binder solution while keeping the chopper off and the impeller running slowly. To aid in the development of granules, the wet mass was further kneaded under the same circumstances.

Drying:

In order to reach the desired loss on drying (LOD), the wet granulated mass was placed into the fluid bed drier and dried for ten minutes while being periodically raked.

Granule sifting and sizing:

The granules were milled using a co-mill and sifted using a #24 mesh sizesieve to achieve aparticle size uniformly

Pre -Lubrication and lubrication materialsSifting:

Microcrystalline cellulose and crospovidoneXL were passed through a fortymesh sieve, whilesiftedmagnesium stearateusing a #60 mesh size sieve to ensureto produce uniform particle size before

blending.

Pre-Lubrication and Lubrication:

After being dried and ground, the granules were put into an octagonal blender and run at 4 rotations per minutesfor 10 minutes. The pre-sifted magnesium stearate was added, and blending process was maintained for five more minutes at the same speed.

Compression:

Round, concave punches measuring 4.5 mm were used to compress the powder mixture into tablets.

Coating of core tablet:Preparation of Film coating suspension:

Purified water was agitated in the solution preparation tank until a visible vortex formed. Opadry Yellow was gradually added into the vortex to prevent lump formation, followed by continuous stirring for approximately 45 minutes to ensure a uniform dispersion.

Ingredients (mg/unit)	Formulation							
	F1	F2	F3	F4	F5	F6	F7	F8
Empagliflozin	10.000	10.000	10.000	10.000	10.000	10.000	10.000	10.000
Linagliptin	5.000	5.000	5.000	5.000	5.000	5.000	5.000	5.000
Mannitol	11.700	11.400	12.000	11.200	11.000	10.800	10.600	10.300
Microcrystalline cellulose	4.400	4.200	4.550	4.000	3.800	3.600	3.400	3.200
CrospovidoneXL-10	1.000	1.500	0.440	2.000	2.250	2.500	2.750	3.000
Copovidone	0.440	0.440	0.440	0.440	0.440	0.440	0.440	0.440
Isopropyl alcohol	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s
Microcrystalline cellulose	3.530	3.530	3.530	3.530	3.530	3.530	3.530	3.530
CrospovidoneXL	1.250	1.250	1.250	1.250	1.250	1.250	1.250	1.250
Magnesium stearate	0.290	0.290	0.290	0.290	0.290	0.290	0.290	0.290
Opadry yellow	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000
Purified water	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s

Formulation Trail Batches of Empagliflozin and Linagliptin tablets

PRE- COMPRESSION PARAMETERSEVALUATION: 1 Bulk Density 2.Tapping Volume 3. Carr's Indices 4.Hausner's Ratio 5. Angle of Repose

POST COMPRESSION PARAMETERS: Weight Variation:Thickness,Hardness:friability, Disintegration testFriability:

DRUG RELEASE KINETICS:

Several kinetic models that are used to examine data on in vitro release data.Zero-Order Kinetic Model, First Order Kinetic Model

Examination of Stability:

Accelerated stability has been attained by adhering to the ICH criteria. A high-density polyethylene container containing the optimized Formulation CF6 was sealed and kept at 40 degrees Celsius ± 2 degrees Celsius and 75 degrees Celsius ± 5% humidity. Materials are subjected to chemical content studies and in vitro dissolving study at one, two, and three month intervals.

RESULT AND DISCUSSION

PRE FORMULATION STUDIES:

Analytical Technique for Measuring Linagliptin and Empagifloxin, Spectrum of Empagliflozinfor determination of λ max by UV visiblespectrophotometer. Empagliflozin and Linagliptinwas prepared at different concentrations in pH 6.0, 7.2, and 0.1NHCl solutions and analysed by observed across the two and four hundred nanometre wavelength UV range.

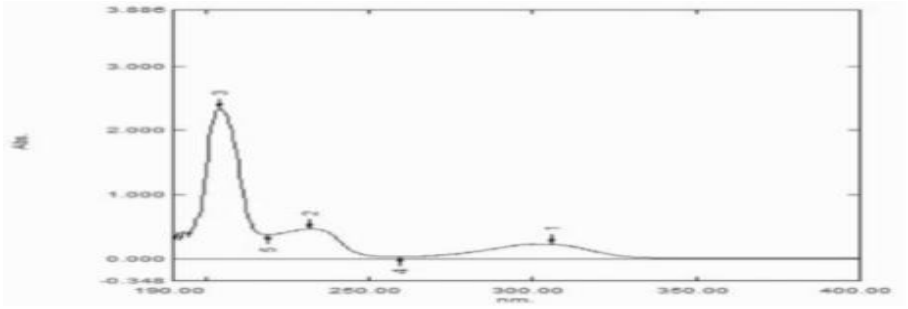


Figure 1: Empagliflozin's absorption maximum was discovered to be 232 nm.

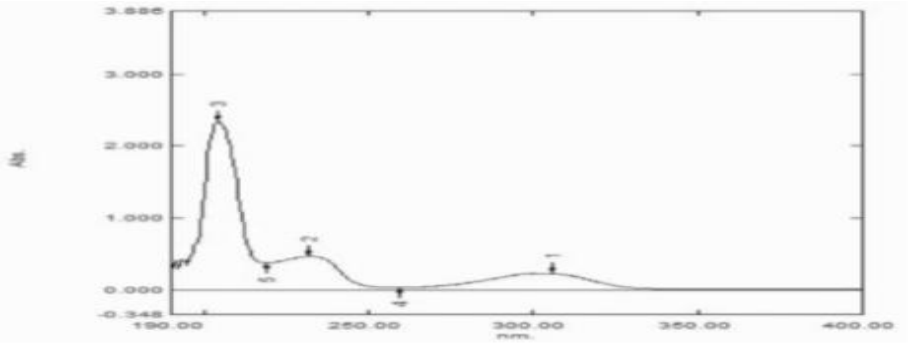


Figure 2: Linagliptin's absorption maximum was discovered to be 296 nm.

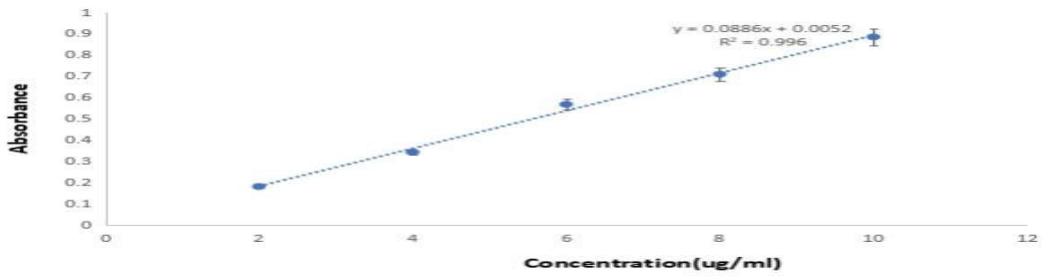
Scanning using spectrophotometry of Empaglifolzin and Linagliptinin 0.1NHydrochloric acid solution: Ten, eight, six, four, and two µg/ml levels have been created and scanned in a UV spectrophotometer.Approximately 232 nm acrossempagliflozin'sMaximum Absorbency, and 296nm linagliptin absorbency was optimized.Consequently , 232 and 296 nanometers have been chosen as empagliflozin and linagliptinlambda maximumrespectivley

Standard curve of Empagliflozin and Linagliptin in 0.1N HCl

Concentration	Absorbance (nm) Empagliflozin	Absorbance (nm) Linagliptin
2	0.182± 0.013	0.104 ± 0.008
4	0.352 ± 0.025	0.198 ± 0.012
6	0.567 ± 0.032	0.312 ±0.015
8	0.709 ± 0.036	0.422 ± 0.018
10	0.884 ± 0.041	0.531 ± 0.20

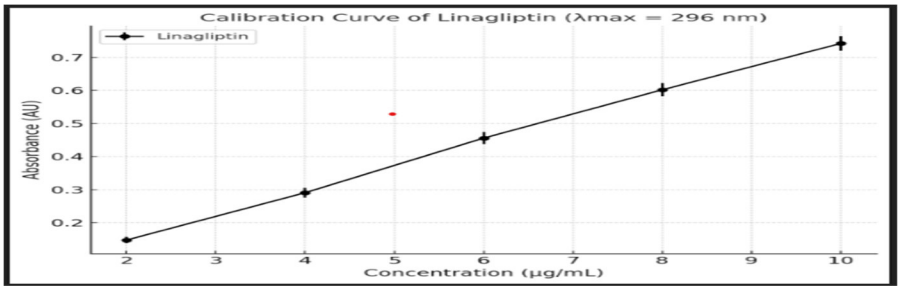
Every result is given as mean ± standard deviation, with n = 3.

Empagliflozin Calibration line in 0.1N Hydrochloricsolution



Empagliflozin standard calibration curve in 0.1N HCl solution

Linagliptin Calibration line in 0.1N Hydrochloric solution



Standard calibration curve of Linagliptin in 0.1N HCl solution

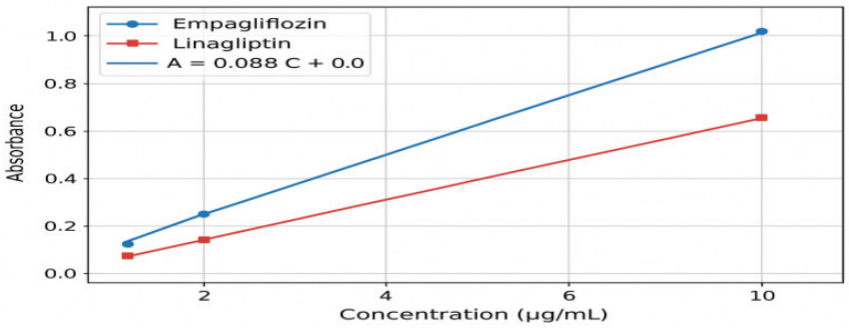
Empagliflozin and Linagliptin

spectrophotometric scanning in pH 6.0 phosphate buffer: A UV spectrophotometer's ability to Quantities of ten, eight,six,four , twomicrogram per milliliterhad been created and scanned. The highest absorbance of empagliflozin and linagliptin was observed at 232 and 296 nm, respectively.Thus, in pH 6.0 phosphate, 301 nm was selected as the λmax for empagliflozin and 401 nm as the λmax for linagliptin.

Standard curve of active ingredientsin pH 6.0 phosphate buffer

Concentration	Absorbance (nm) Empagliflozin -Drug 1	Absorbance (nm) Linagliptin Drug -2
2	0.182 ±0.013	0.148 ±0.010
4	0.342 ±0.025	0291 ±0.015
6	0.567 ±0.032	0.045 ±0.018
8	0.709 ±0.036	0.602 ±0.020
10	0.884 ±0.017	0.742 ±0.022

Every result is given as mean ± standard deviation, with n = 3. Empagliflozin calibration line in pH 6.0 buffer phosphate



Empagliflozin's standard calibration curve in phosphate buffer with a pH of 6.0

Spectrophotometric scanning of empagliflozin and linagliptin in buffered phosphate at a pH of 7.2:

In a UV spectrophotometer, samples with concentrations of two, four, six, eight, and ten µg/ml were scanned. Empagliflozin had its greatest absorption at 301 nanometers.Therefore, the measured empagliflozin lambda of maximum is 301 nanometer. Linagliptin's highest absorbance was observed at 365 nanometers. As a result, the measured lambda of max is 365 nanometer

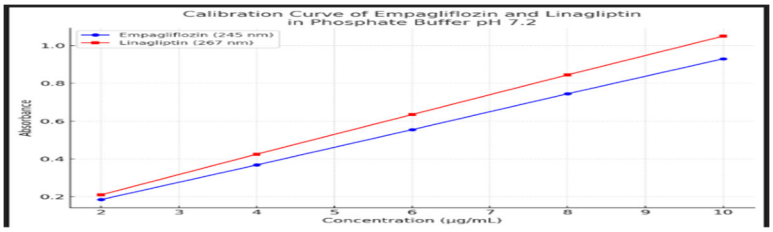
Standard Curve of Empagliflozin and Linagliptin in pH 7.2 Phosphate buffer

Concentration	Absorbance (nm) Empagliflozin	Absorbance (nm) Linagliptin
2	0.185 ± 0.010	0.210 ± 0.012
4	0.368 ± 0.015	0.425 ± 0.015
6	0.555 ± 0.018	0.635 ± 0.020
8	0.745 ± 0.020	0.845 ± 0.022

10	0.930 ± 0.022	1.085 ± 0.025

Every result is given as mean ± standard deviation, with n = 3.

Empagliflozincalibration line in buffer phosphate at 7.2 pH



Calibration curve for standard empagliflozin and linagliptin in 7.2 pH buffer The phosphate

DRUG EXCIPIENT COMPATIBILITY STUDIES:

No noteworthy drug-excipient interactions have been found in studies on the compatibility of drug excipients.

Drug and excipient compatibility studies ofEmpagliflozin:

Interpretation of FTIR Spectra of Empagliflozin and linagliptinpure drug +all excipients

Functional Group	Empagliflozin pure Drug (cm-1)	Linagliptin pure drug (cm-1)	Empagliflozin and Linagliptin + all excipients (cm-1)
C-O-C	1100.0	1150.1	1150.1
C-H	2900.2	2950.2	2902.2
C=C	1600.5	1620.3	1620.4
C-H	1450.0	900.2	1450.0

The pronounced, characteristic peaks in pure empagliflozin's spectrumwere identified at1100.0 , 2900.2 , 1600.5 and1450.0 cm-1. andlinagliptinwere identified at 1150.1,2950.2,1620.3 and 900.2cm-1.These peaks are also clearly visible in the physical sample's FTIR spectra. combinations where the final formula includes other excipients in addition to medications It was discovered that both medications were compatible with the excipients chosen for the formulation.

PRE-COMPRESSION PARAMETER EVALUATION:

Empaglifozin and linagliptin immediate-release tablet granules were made using the wet granulation technique. Carr's index, Hausner's ratio, bulk density, tapped density, and angle of reposewere assessed for each batch of mixtures, as mentioned inthe table

All results are expressed as mean ± standard deviation, n = 3

Table 10: Lubricated blend parameters of formulation F1-F8

Formulation	Bulk Density (gm/ml)	Tapped Density (gm/ml)	Carr's Index (%)	Hausners's Ratio	Angle of Repose
F1	0.44 ± 0.01	0.55 ±0.01	20.0 ± 0.08	1.25 ± 0.02	32.0 ± 0.3
F2	0.46 ± 0.01	0.56 ±0.01	17.9 ± 0.7	1.22 ±0.02	31.0 ± 0.5
F3	0.45 ± 0.01	0.57 ±0.01	21.1 ±0.9	1.27 ± 0.03	33.0 ± 0.5
F4	0.47 ± 0.01	0.58 ±0.01	18.9 ± 0.8	1.23 ± 0.02	30.5 ± 0.5
F5	0.49 ± 0.01	0.61 ± 0.01	19.7 ± 0.7	1.24 ± 0.02	29.5 ± 0.5
F6	0.50 ± 0.01	0.57 ± 0.01	12.3 ± 0.3	1.14 ± 0.02	25.0± 0.4
F7	0.42 ± 0.01	0.53 ± 0.01	20.8 ± 0.9	1.26 ± 0.03	34.0 ± 0.7
F8	0.40 ± 0.01	0.52 ± 0.01	23.1 ± 1.0	1.30 ±0.03	35.0 ± 0.8

Every result is given as mean ± standard deviation, with n = 3.

It is discovered that the bulk density varies between 0.40 and 0.50 gm/cm3. The tapped density ranged from 0.52 to 0.61 gm/ml.The formulations compressibility index values ofF1, F2, F3 ,F4, F5, F7,and F8 are

20.0,17.9, 21.1, 18.9, 19.7, 12.3, 20.8 and23.1 , each, demonstrating the feature of fair flow, while F6 of value 12.3 showing the excellent powder flow, Hausners ratioabove ~1.25 (F3, F7, F8) showsmoderate flow problems, which can impact uniform die fill and potentially cause variability in tablet weight and dissolution.

The findings showed that the angle of repose for each formulation ranged from 29° to 33°.F6 showingbest flow and compressibility: lowest Carr's index, lowest Hausner ratio,lowest angle of repose.

POST COMPRESSION PARAMETERS:

A range of evaluation tests were conducted on the uncoated tablets of different formulations to determine variations in weight, thickness, hardness, and friability.

Empagiflozin and linagliptin core tablets evaluation of formulations F1-F8

Formulations	Weight Variation(mg)	Thickness(mm)	Hardness (Kg/cm2)	Friability
F1	36.42 ± 0.28	2.38 ± 0.04	3.12 ± 0.14	0.48
F2	36.29 ± 0.32	2.36 ± 0.05	3.25 ± 0.16	0.46
F3	36.35 ± 0.34	2.40 ± 0.06	3.18 ± 0.12	0.44
F4	36.41 ± 0.31	2.42 ± 0.05	3.28 ± 0.15	0.43
F5	36.61 ± 0.26	2.45 ± 0.04	3.35 ± 0.15	0.42
F6	36.49 ± 0.07	2.41 ± 0.02	3.35 ± 0.11	0.36
F7	36.28 ± 0.29	2.39 ± 0.05	3.42 ± 0.05	0.45
F8	36.32 ± 0.33	2.7 ± 0.06	3.20 ± 0.13	0.47

Every result is given as mean ± standard deviation, with n = 3.Because the weight variation percentage was within pharmaceutical standards at ±5% of the average weight, the pills passed the weight variation test.

The F6 batch exhibits the lowest standard deviation (±0.07), indicating excellent uniformity and superior manufacturing consistency.

The tablets' diameters ranged from 2.0 to 2.6 millimeters. This is because the high and low punches are altered throughout the compression process. The hardness values of each batch vary, ranging from 3.12 to 3.4 kilogram/square centimeter. The friability of the tablets was found to be within 1%. The friability test has been passed by each of the sample formulations shown above.

Dissolution studies:

Studies on the final products' dissolution were conducted. Tablets were put into a dissolving media under the previously mentioned circumstances, and theAccording to the results, it was found that the release in the medium is Not less than 80%of the labelled amount of empagliflozin in 30 minutes and Not less than 80 % of the labelled amount of linagliptin in 30 minutes which is within the limits. A graph shows the cumulative % release of the medication over time for each formulation.

Empagliflozin in coated tablets of formulations F1–F8: in vitro drug release studies

Dissolution on Media	Time mins	% Cumulative drug release							
		F1	F2	F3	F4	F5	F6	F7	F8
pH 6.8 Phospahte buffer	5	58.32	58.25	65.02	68.05	69.08	88.89	88.47	89.58
	10	63.02	61.05	72.06	71.04	73.45	83.46	89.64	74.14
	15	70.85	73.45	63.84	81.03	78.87	85.58	93.58	68.46
	30	73.69	76.58	73.05	73.07	82.14	98.96	65.14	55.25

Invitro-drug release studies oflinagliptin in coated tablets offormulations F1-F8

Dissolution on Media	Time mins	% Cumulative drug release							
		F1	F2	F3	F4	F5	F6	F7	F8
pH 6.8 Phospahte buffer	5	67.85	59.12	64.48	68.92	70.14	88.32	87.95	90.06
	10	54.26	62.18	71.45	70.66	74.03	82.97	88.92	75.08
	15	71.42	74.08	64.52	80.46	79.35	86.04	94.26	69.12
	30	74.18	77.12	74.02	74.26	83.02	99.32	66.08	56.14

Eligibility requirements: at least 80% of the medication must be released into the phosphate buffer. Medication release in all compositions at 7.2 pH. It was found to vary throughout each production.

The percentage of drugs released from each coating manufacture is as follows:

- The formulation of F1 and F2's percentage of empagiflozin discharge at the conclusion of 30 minutes was determined to be 73.69 % and 76.58 % and linagiptin discharge is 74.18 % and 77.12 %
- Percentage of empagliflozin drug released for the formulations F3, F4, and F5 atthe end of 30 mins was found to be 76.58%, 73.05%, and 73.07% and for linagliptin was found to be 74.02 % , 74.26 % and 83.02
- After 30 mins, the % of empagliflozin released for the formulation F7 and f8 was foundto be 65.14% and 55.25% and for linagliptin 66.08 % and 56.14 %
- After 30 mins, the % of empagliflozinreleased for the formulation F6 was foundto be 98.96% and for linagliptin 99.32 %
- F6 was found to be the best-fit batch because it had the required medication release and flow characteristics.

Drug release kinetics:

Concepts such as zero order kinetics and initial-order kineticsare used to illustrate the kinetics of drug release parameters in graphs. The kinetic results follow first-order kinetics since the optimized formulation's correlation coefficient (R2) value is greater than the first-order release kinetics'.

Kinetics of Drug Release from Optimized Formulation

Time (mins)	Cumulative % Drug release Empagliflozin	Cumulative % Drug release- Linagliptin
5	88.89	88.32
10	83.46	82.97
15	85.58	86.04
30	98.96	99.32

Regression analysis data

Drug	Zero order	R2 (Zero order)	First order k 1 (min-1)	R2(First Order)	Kinetic model
Empagliflozin	0.843	0.985	0.099	0.998	Fisrt-Order
Linagliptin	0.840	0.984	0.101	0.998	First-Order

Stability studies:

As per ICH guidelines, samples used in stability study are samples which shown improved formulation of Empaglifozin and Linagliptin tablets were stored for a period of three months at 40±2ºc and 75±5% relative humidity. The test and drug release percentage have been established. Pre- and post-stability studies of the ideal batch revealed no significantchanges in the release pattern, pharmaceutical ingredients, or medication distribution percentage.

CONCLUSION:

The medications empagliflozin and linagliptin are used to treat diabetes mellitus.The present study set out to produce and evaluate Emapgliflozin and linagliptin immediate-release tablets using the wet granulation process. The nature of the API and its compatibility with excipients were investigated using the FT-IR approach.According to the findings, no interaction between the API and any of the selected excipients was found. The core tablets were made using different amounts of binders and disintegrants.Based on coating experiments, formulation CF6 demonstrated a medication release rate of 99.32% for linagliptin and 98.96% for empagliflozin after 30 minutes. Consequently, the optimum formulation was determined to be trial CF6. When compared to the initial results, stability tests conducted on the optimized coated formulation (F6) under accelerated storage conditions (40ºC/75% RH) revealed no impact on the assay and dissolution investigations.

REFERENCES:

1. **Ahmed Jishan Ali et al.** The goal of IR tablet formulation is to guarantee that the medication dissolves and disintegrates quickly in the gastrointestinal system. Jishan Ali Ahmed (IJPPR) asserts that the selection of excipients, particularly superdisintegrants, tablet production techniques, and drug solubility are important formulation characteristics. The mechanical strength and release properties of the tablet are significantly influenced by the choice of excipients, including binders, diluents, lubricants, and superdisintegrants.
2. According to **Patel et al. (2012),** Superdisintegrants that increase drug dissolving and speed up the disintegration process include sodium starch glycolate, crospovidone, and croscarmellose sodiumcan

speed up the disintegration process and improve drug dissolution. By assisting tablets in dissolving into smaller pieces when they come into touch with liquids, these agents facilitate quicker medication availability and absorption.

3. **Ratnaparkhi et al. (2012)**, Metformin HCl and Glibenclamide rapid release tablets were prepared with a variety of superdisintegrants. The study showed that sodium starch glycolate provided the fastest disintegration and highest drug release within the first 30 minutes of dissolution testing. This suggests that careful selection and optimization of disintegrant type and concentration is crucial for developing effective IR formulations.
4. **Das et al. (2013)** evaluated immediate release film-coated tablets of Quetiapine, where rapid disintegration and dissolution were achieved through optimization of excipients and coating materials. Their study highlighted the importance of film coating in improving tablet stability without compromising release behavior.
5. **Ahmed et al. (2013)**examined how various excipients affected the way Fexofenadine HCl IR tablets were made. The findings demonstrated that both the type and amount of disintegrant significantly affected the tablet's dissolution rate. Excipients not only aid in tablet formation but also influence pharmacokinetic behavior.
6. **Nyol and Gupta (2013)** further illustrated this in their work on Sitagliptin phosphate IR tablets. Their study concluded that the use of direct compression and optimized excipient ratios yielded tablets with excellent mechanical properties and rapid drug release.
7. Linagliptin was determined using an RP-HPLC method that was validated by Badugu et al. (2012), highlighting the technology's dependability in quality control procedures. Using a stability-indicating RP-HPLC approach, **Afzal et al.** (2018) concentrated onmeasurement of metformin and linagliptin intablet formulations, proving its robustness for combination therapy.
8. 8. **Madhusudhan et al.** created and verified an RP-HPLC method that offers a thorough analytical approach for the concurrentmeasurementlidagliptin and empagliflozintablets.Formulationand assessment onquetiapine instant release film-coated tablets were the main focus of **Das et al.** (2013), who emphasized the significance of coating in drug release patterns.
9. **Ratnaparkhi et al.** (2012) used various superdisintegrants to create and assess immediate release tablets of Glibenclamide and Metformin HCl, illustrating how excipient selection affects tablet performance.
10. **Ahmed et al.** (2013) investigated Fexofenadine HCl immediate release tablets, evaluating excipients for their influence on dissolution rates.
11. **Nyol and Gupta et.al** (2013) developed and assessed an immediate drug release tablet dosage form of Sitagliptin phosphate, highlighting formulation considerations for rapid drug release. Together, these trials advance our knowledge of and ability to produce quick release tablet formulations, guaranteeing both patient compliance and their effectiveness.
12. **Tejaswi Santosh Ubhe and PreetiGedamet. al**(2013) provided a brief overview on tablets and their types, discussing the factors influencing tablet design and formulation. This knowledge is essential for developing effective and patient-friendly oral dosage forms.
13. **Michel and Staskin et.a**l(2022) reviewed and challenged clinical study designs for evaluating the benefit/risk ratio of combination treatments over monotherapy, proposing that studies should report on percentages of responders.
14. **DunumutlaNeethaSree et al.** (2021) formulated Empagliflozin tablets using direct compression techniques, optimizing binder and Disintegrantoncentrations to ensure adequate tablet hardness and dissolution. Similar approaches can be adopted for Linagliptin.
15. **Ahmed et al. (2013)** emphasized the role of dissolution profiling in optimizing immediate release tablets, ensuring that the release of active ingredients meets therapeutic requirements.
16. In stability testing, guidelines outlined by the WHO (2009) and Kim Huynh-Ba (2008) highlight the importance of stress conditions (temperature, humidity, light) to evaluate the degradation behavior of APIs. These are crucial in ensuring that the combination tablet maintains efficacy over its intended shelf-life.