Development And Evaluation Of Sustained – Release Empagliflozin Matrix Tablets Using HYdroxypropyl Methylcellulose And Guar Gum

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***Abstract*—The present research work focuses on the development and evaluation of sustained- release matrix tablets of empagliflozin using hydroxypropyl methylcellulose (HPMC) and guar gum as releaseretarding polymers. Empagliflozin is an oral antidiabetic drug used in the management of type 2 diabetics mellitus. Conventional dosage forms require frequent administration and may produce fluctuations in plasma drug concentration. Sustained-release formulations are designed to maintain therapeutic drug levels for an extended period, improve patient compliance, and reduce dosing frequency. In this study, matrix tablets of empagliflozin were prepared by the direct compression method using varying concentrations of HPMC and guar gum. The prepared formulations were evaluated for precompression parameters such as angle of repose, bulk density, cars index, and Hausner ratio to determine the flow properties of the powder blend. Post-compression evaluation included thickness, hardness, friability, weight variation, drug content uniformity, and in-vitro dissolution studies. The dissolution studies were carried out using suitable dissolution media to assess the sustained-release behavior of the formulations. The results indicated that polymer concentration significantly affected the drug release profile. Formulations containing a combination of HPMC and guar gum showed controlled and prolonged drug release over an extended period. Stability studies demonstrated that the optimized formulation remained stable under specified storage conditions. The study concluded that sustained-release matrix tablets of empagliflozin can be successfully formulated using HPMC and guar gum, providing effective controlled drug release and improved therapeutic efficacy for the treatment of diabetes mellitus.**

***Index Terms*—Introduction, objective, Role of polymer, methodology, Preformulation studies, evaluation of tablets, invitro drug release study, drug relese kinetics, key findings, stability studies, conclusion.**

I. INTRODUCTION

Empagliflozin is an oral glucose-lowering drug that was approved and came into clinical use in 2014. It belongs to the sodium-glucose cotransporter 2 (SGLT2) inhibitor group. medications introduced for the treatment of the type 2 diabetes mellitus (T2DM). SGLT2 is the main transporter responsible for the reabsorption of glucose from the glomerular filtrate and represents a novel target in the treatment of T2DM.By potently blocking glucose reabsorption in the proximal tubule, it increases urinary glucose excretion. Among the currently used or tested SGLT2 inhibitors, empagliflozin has the highest selectivity for SGLT2 over sodium–glucose cotransporter 1 (SGLT1) (2500-fold).

Chemically, empagliflozin belongs to C-glucosides , which determines the greater metabolic stability of the drug compared to O-glucoside derivatives. In the case of the Oglucoside derivatives, hydrolysis by intestinal enzymes occurs, resulting in low absorption. C-glucoside derivatives have a favorable pharmacokinetic and pharmacodynamic profile. They only need to be used once daily. Moreover, renal or hepatic impairment does not significantly affect the concentration of the drug (or its metabolites) in the body. Empagliflozin tablets are widely prescribed not only for glycemic control but also for their additional benefits in reducing the risk of cardiovascular diseases, heart failure, and slowing the progression of chronic kidney disease (CKD) in diabetic and non-diabetic patients. The drug is typically administered once daily and is available in different strengths such as 10 mg and 25mg tablets. It may be used alone or in combination with other antidiabetic agents like metformin, insulin, or DPP-4 inhibitors. of the drug

from the tablet matrix. It provides uniform drug release, good compressibility, and stability. Guar gum is a natural polysaccharide obtained from the Form a pharmaceutical formulation perspective, empagliflozin tablets are commonly prepared using direct compression or wet granulation techniques, with excipients such as diluents, binders, disintegrants, and lubricants to ensure proper drug release, stability, and patient compliance.

Sustained release (SR) tablets are pharmaceutical dosage forms designed to release the drug slowly over an extended period of time in order to maintain therapeutic drug concentration in the body for a prolonged duration. SR formulations help to reduce dosing frequency, minimize fluctuations in plasma drug levels, improve patient compliance, and decrease side effects associated with conventional immediate-release dosage forms.

Hydrophilic matrix systems are widely used in the development of sustained-release formulations because they can control drug release over an extended period, improve patient compliance, and maintain therapeutic drug levels. Among the various hydrophilic polymers, Hydroxypropyl Methylcellulose (HPMC) and guar gum are commonly employed due to their excellent swelling, gel-forming, and drug-retarding properties.

HPMC is a semi-synthetic polymer that forms a viscous gel layer upon contact with gastrointestinal fluids, thereby controlling the diffusion seeds of Cyamopsis tetragonoloba. It is biodegradable, biocompatible, economical, and capable of sustaining drug release by swelling and forming a gel barrier.

Empagliflozin is a sodium-glucose co-transporter (SGLT-2) inhibitor that is a new class of oral hypoglycemic agent. Such inhibition of SGLT-2, it prevents the reabsorption of glucose from the glomerular filtration of a kidney. Since oral absorption of empagliflozin from a tablet is comparatively poor (takes almost 3 hours to get absorbed), hence an effort was made to enhance its absorption by formulating it as the fast dissolving tablet. The objective of the present work is to develop fast dissolving empagliflozin tablets and to study.

The effect of functionality differences of super disintegrants (Kollidon-CL, Ac-Di-Sol) on the tablet properties.3-5Tablets by direct compression techniques have a unique nature in the form of less time consumption, rapid production, and economy in operational management among the many methods of manufacturing techniques available.

Aim:

To develop and evaluate sustained-release matrix tablets of empagliflozin using hydrophilic polymers such as hydroxypropyl methylcellulose (HPMC) and guar gum in order to prolong drug release, improve therapeutic efficacy, and enhance patient compliance.

Objective:

1. To formulate sustained-release matrix tablets of empagliflozin using hydrophilic polymers such as Hydroxypropyl Methylcellulose (HPMC) and guar gum.
2. To evaluate the effect of different concentrations of HPMC and guar gum on the drug release profile of empagliflozin.
3. To prepare empagliflozin tablets by direct compression method and optimize the formulation for sustained drug release.
4. To study the pre-compression parameters of the powder blend such as angle of repose, bulk density, tapped density, Carr's index, and Hausner ratio.
5. To evaluate post-compression parameters of tablets including hardness, thickness, friability, weight variation, and drug content uniformity.
6. To perform in-vitro dissolution studies for determining the sustained release behavior of empagliflozin tablets.
7. To compare the release pattern of different formulations and identify the optimized formulation with desired sustained-release characteristics.
8. To analyze the drug release kinetics and mechanism of release from the matrix tablets.
9. To improve patient compliance by reducing dosing frequency through sustained drug delivery.
10. To develop a stable and effective sustained-release formulation of empagliflozin for the management of type-2 diabetes mellitus.

II. REVIEW OF LITERATURE:

Joanna forycka, Joanna hajdys, Julia krzeminska, Piotr wilczopolski, Magdalena wronka, ewrlina mlynarska, jacek rysz:review on empagliflozin a comprehensive review. Empagliflozin is an oral glucose-lowering drug that was approved and came into clinical use in

2014. It belongs to the sodium-glucose cotransporter 2 (SGLT2) inhibitor group —medications introduced for the treatment of the type 2 diabetes mellitus (T2DM). SGLT2 is the main transporter responsible for the reabsorption of glucose from the glomerular filtrate and represents a novel target in the treatment of T2DM. By potently blocking glucose reabsorption in the proximal tubule, it increases urinary glucose excretion. Among the currently used or tested SGLT2 inhibitors, empagliflozin has the highest selectivity for SGLT2 over sodium–glucose cotransporter 1 (SGLT1)

Dunumutla neetha sree, Dr. M. Sunitha Reddy, Dr. K. Anie vijetha: review on design and characterization of empagliflizin tablets. The aim of the present study is to formulate and evaluate Empagliflozin controlled release tablets. Method: Controlled release tablets are prepared using emulsification-solvent evaporation method involves dissolving the polymer and drug in an organic solvent, forming an emulsion by dispersing this solution in an aqueous phase containing an emulsifier and then evaporating the solvent to form Granules. These Granules are collected, washed and dried to obtain the final product, which is typically used for controlled or sustained release formulations Results:

Akanksha dwivedi, G. N.darwhekar: review design, optimization and evaluation of empagliflozin tablets

Empagliflozin is a sodium glucose co-transporter (SGLT-2) inhibitor that is the new class of oral hypoglycemic agent and indicated as an adjunct to exercise and diet to improve glycemic control in adult patients of type-2 diabetes (non-insulin-dependent diabetes). The SGLT-2 co-transporters are responsible for reabsorption of glucose from the glomerular filtrate of the kidney, so inhibition of SGLT-2 promotes excretion of blood glucose. Empagliflozin also contributes to reduced hyperglycemia and assists in weight loss and reduction of blood pressure.

Raghvendra K Gunda, JNS kumar, ABS Prasad, Bodepudi Sandhya, gajja bhargavi,KNVL padmaja, sriram Praveen department of pharmaceutics development and characterization of SR tablets

Empagliflozin is a sodium-glucose co-transporter (SGLT-2) inhibitor that is a new class of oral hypoglycemic agent.Such inhibition of SGLT-2, it prevents the reabsorption of glucose from the glomerular filtration of a kidney. Since oral absorption of empagliflozin from a tablet is comparatively poor (takes almost 3 hours to get absorbed), hence an effort was made to enhance its absorption by formulating it as the tablet.

Omeed Sizar, Vivek podder, talati: review on empagliflozin. Empagliflozin is an antidiabetic agent used in adult patients with type 2 diabetes mellitus. It was FDA-approved in 2014. Empagliflozin can be used as a single agent or as a combination agent with other antidiabetic products. Combination products include empagliflozin and linagliptin and empagliflozin in combination with metformin. These newer agents can be more expensive for patients, thus impeding the clinician's ability to prescribe them based on patient financial considerations. However, the American Diabetes Association (ADA) is calling for agents with proven mortality reduction for use as second-line therapy after metformin. Such agents include empagliflozin and liraglutide. The primary treatment for diabetes is lifestyle management and exercise, followed by metformin use. Per Standards of Medical Care in Diabetes, if the A1c is greater than 9%, then combination therapy with metformin is recommended.

Tushar madaan, Abul kalam najmi review on:sodium glucose co trasporter inhibitors. Empagliflozin (Trade name: Jardiance) was the last SGLT2 inhibitor to be approved by the US FDA. It was approved in May 2014 by the European Medicines Agency and in August 2014 by the US FDA. Jardiance was developed by Boehringer Ingelheim and Eli Lilly & Company (Anon, 2014i; Anon, 2014j; EPAR, 2014). The recommended dose of empagliflozin is 10 mg once daily which may be increased to 25 mg once daily with or without food (Anon).

We were unable to find an absolute bioavailability of empagliflozin in humans.

III. PHYSICOCHEMICAL PROPERTIES

Empagliflozin is a white to off-white crystalline powder with a molecular formula of C23H27CIO7 and a molecular weight of 450.9 g/mol. The drug exhibits low aqueous solubility and belongs to biopharmaceutics classification system (BCS) Class 2, characterized by low solubility and high permeability. These properties necessitate formulation trategies that improve dissolution behaviour and prolong drug release.

Table No 1:Absorption characteristics

Parameter	Value	Relevance to dosage form
Oral bioavailability	~75 – 78%	Suitable for oral tablets
Time to peak plasma concentration (T max)	1.5 – 2.0 h	Rapid absorption favors matrix control
Absorption site	Upper GI tract	Sustained – release feasible
Effect of food	Minimal	Flexible dosing

Table No 2:Distribution characteristics

Parameter	Value	Significance
Plasma protein binding	~86 – 90%	Prolongs systemic presence
Main binding protein	Albumin	Predictable pharmacokinetics
Volume of distribution (vd)	~73 L	Extensive tissue distribution

Table No 3: Metabolism

Parameter	Details
Primary metabolic pathway	Glucuronidation
Enzymes involved	UGT2B7, UGT1A3, UGT1A8, UGT1A9
CYP450 involvement	Minimal
Active metabolites	None (metabolites inactive)

IV. ROLE OF POLYMER

Polymers play an important role in the development and evaluation of empagliflozin tablets, especially in sustained-release (SR) or controlled-release formulations. They help to control drug release, improve tablet stability, enhance patient compliance, and maintain therapeutic drug levels for a longer duration.

Empagliflozin is an oral antidiabetic drug used in the treatment of type 2 diabetes mellitus. To improve therapeutic efficacy and reduce dosing frequency, sustained-release matrix tablets are developed using hydrophilic polymers such as Hydroxypropyl Methylcellulose (HPMC) and natural polymers like guar gum.

A. Roles of Polymers in Empagliflozin Tablets

1. Control of Drug Release

Polymers regulate the release of empagliflozin from the tablet matrix.

- Hydrophilic polymers absorb water and form a gel layer.
- The gel barrier slows drug diffusion and prolongs release.
- Helps maintain plasma drug concentration for extended periods.

Example:

- HPMC
- Guar gum

2. formation of matrix system

Polymers form the matrix structure of sustained-release tablets.

Drug particles are embedded in the polymer network.

- Drug release occurs gradually through diffusion and erosion mechanisms.

3. Improvement of tablet integrity polymers improve mechanical strength and prevent tablet breakage.

- Increase hardness
- Reduce friability
- Maintain shape during dissolution

4. Enhancement of Patient Compliance

Sustained-release formulations reduce dosing frequency.

- Once-daily dosing improves convenience
- Better adherence to diabetes therapy

5. Modification of Swelling and Erosion

Hydrophilic polymers swell in gastrointestinal fluids.

- Swelling controls penetration of dissolution medium
- Polymer erosion determines release rate

6. Improvement of Drug Stability

Polymers protect the drug from environmental factors such as moisture and oxidation.

- Increase shelf life
- Improve formulation stability

7. Bioavailability Enhancement

Certain polymers improve wetting and dissolution of poorly soluble drugs.

- Enhance uniform drug release
- Improve absorption profile

V. MATERIAL AND METHODS

A. Materials

Empagliflozin was obtained as a gift sample from a reputed pharmaceutical company.

Hydroxypropyl Methylcellulose (HPMC) and Guar Gum were used as release-retarding polymers. Microcrystalline cellulose (MCC) was used as a diluent. Magnesium stearate and talc were used as lubricants and glidants ,respectively. All other chemicals and reagents used were of analytical grade.

B. Methodology

1. preformulation studies:

Preformulation studies of empagliflozin were carried out to evaluate its physicochemical properties such as solubility, melting point, and compatibility with polymers.

Preformulation studies are the initial investigation carried out before formulation development to determine the physical, chemical, and mechanical properties of a drug. these studies help in designing a stable, safe, and effective dosage form.

Drug-polymer compatibility study

Compatibility between empagliflozin and polymers (HPMC and Guar Gum) was studied using fourier transform infrared spectroscopy (FTIR). The spectra of pure drug and physical mixtures were compared to identify any possible interaction.

Drug-polymer compatibility study is an important preformulation study carried out to determine the interaction between the drug and polymers used in formulation development. It ensures that the selected polymers do not produce any chemical or physical changes in the drug during formulation and storage.

2. Formulation of sustained release tablets

Sustained release tablets of empagliflozin were prepared by the Direct compression method.

a) Weighing and sieving: Accurately weighed quantities of empagliflozin, HPMC, guar gum, and MCC were passed through a 60 sieve to ensure uniform particle size distribution.
b) Mixing: The sieved ingredients were blended thoroughly in a tumbling blender to achieve a uniform powder mixture. Correct blending ensured uniform drug distribution and minimized content variability. Mixing time:- 10 -15 minutes

Fig no 1: mixing

c) Lubrication: Magnesium stearate and talc were added at the final stage and mixed gently for 2-3 minutes to prevent over-lubrication, which can adversely affect tablet hardness and dissolution.
d) Compression: The final blend was compressed into tablets using a rotary tablet compression machine fitted with appropriate punches. Tablet weight was maintained at 500 mg for all formulations. After tablet compression dry a tablet in hot air oven at 30°c.

Fig No 2: Direct compretion machine

Fig No 3: Hot air oven

Table 4: composition of different empagliflozin sustained-release tablets

Ingredient (mg/tablet)	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
Empagliflozi n	0.25g	0.25g	0.25g	0.25g	0.25g	0.25g	0.25g	0.25g	0.25g	0.25g
HPMC	0.5g	0.75g	1.2g	1.5g	1.8g	0.5g	0.75g	1.2g	1.5g	1.8g
Guar Gum	1.5g	1.25g	1.2g	0.9g	0.6g	2.4g	2.1g	1.5g	1.25g	1.2g
MCC	2.6g	2.6g	2.6g	2.6g	2.6g	2.52g	2.52g	2.52g	2.52g	2.52g
Magnesium Stearate	0.1g	0.1g	0.1g	0.1g	0.1g	0.1g	0.1g	0.1g	0.1g	0.1g
Talc	0.05g	0.05g	0.05g	0.05g	0.05g	0.05g	0.05g	0.05g	0.05g	0.05g
Total Weight (mg)	500mg	500mg	500mg	500mg	500mg	500mg	500mg	500mg	500mg	500mg

3. Evalution of precompression parameters:-

Precompression parameters are evaluated before tablet compression to determine the flow properties and compressibility of the powder blend. These studies help ensure uniform die filling, proper tablet weight, and good tablet quality.

The prepared powder blends were evaluated for:

A. Angle of repose

The angle of repose for powder blends used in empagliflozin tablets generally ranges between 20 and 30 , indicating excellent to good flow properties, which is ideal for direct compression methods.

The angle of repose was calculated by measuring the diameter and height of powder cone and putting the values to the following equation.

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

Where h = height of the cone.

R = radius of the cone.

–Polymer Compatibility

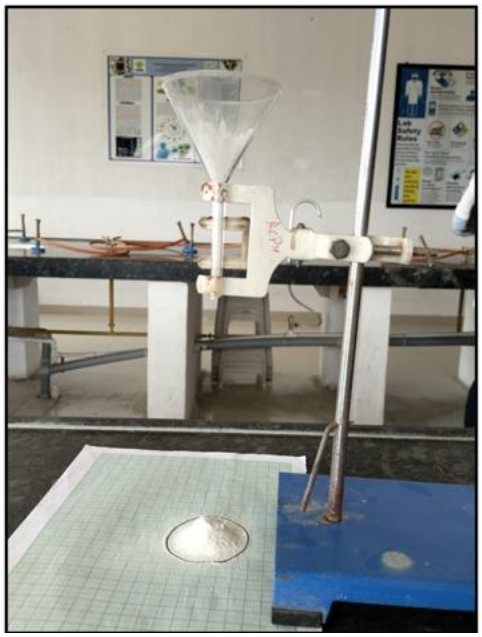

Fig No 4: angle of repose

B. Bulk density

Bulk density is the ratio of the mass of powder to its bulk volume before tapping. It indicates the packing ability and flow property of the powder blend used for tablet formulation.

This was calculated by using the formula:

Bulk density = weight of the sample/bulk volume of the powder

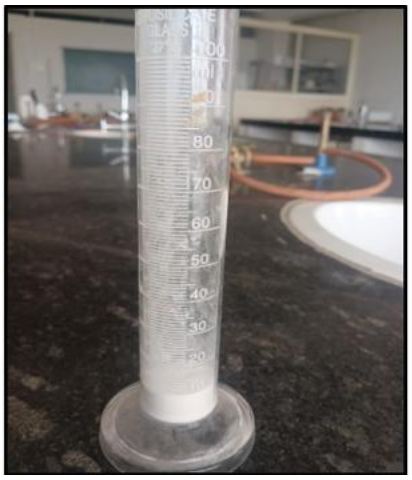

Fig no 5: Bulk density

C. Tapped density

Tapped density is the ratio of the mass of powder to the volume occupied after mechanical tapping. It is an important pre-compression parameter used to evaluate the flow properties and compressibility of powder blends during formulation of empagliflozin tablets.

Tapped density was calculated by using the following formula:

Tapped density = weight of the sample/tapped volume of powder

Fig no 6:Tapped density

D. Carr's index
Carr's index of the powder blend was determined by using the formula:
Carr's index (%) I = [(v0 –vt)÷v0] ×100
Where, v0 = tapped density of powder,
Vt =bulk density of powder

E. Hausner's ratio
It was calculated by following formula:
Hausner's ratio = tapped density / bulk density

VI. EVALUTION OF POST COMPRESSION PARAMETER:

1. Hardness

It was carried out with the help of Monsanto tablet hardness
tester.

- it does not break during packaging or transport,
- it releases the medicine properly,
- and it is still easy for patients to swallow.

Hardness test
A hardness test measures the force needed to break a tablet using a hardness tester machine.
Common units:
kg/cm²
Newtons (N)
Why hardness matters
Too hard → tablet may not dissolve properly.
Too soft → tablet may crumble or break easily.

2. Thickness

Thickness is usually measured using vernier caliper and Digital thickness tester
Average thickness of empagliflozin sustaine release tablet = 4.48 mm

3. weight variation

The weight variation test is a quality-control test used to check whether all tablets in a batch have a uniform weight. It helps ensure that each tablet contains approximately the correct amount of drug.
Procedure

- Select 5 tablets randomly.
- Weigh all tablets together.
- Calculate the average weight.
- Weigh each tablet individually.
- Compare individual weights with the average weight.

4. Disintegration test

The disintegration test determines how long a tablet takes to break into smaller particles in a liquid medium under specified conditions.

Apparatus Used
USP/IP Disintegration Test Apparatus
It contains:
Basket-rack assembly
Six glass tubes
Wire mesh at the bottom

Procedure

- Take 6 tablets.
- Place one tablet in each tube of the basket assembly.
- Add disc if required.
- Immerse basket in disintegration medium.
- Start the apparatus.
- Observe the tablets.
- Record the time when tablets disintegrate completely.

Disintegration within 15–30 minutes
Sustained-release (SR) tablets
For SR tablets: conventional disintegration limits may not apply,because they are designed for slow drug release.

Fig No7: disintegration apparatus

5. Friability Test
Apparatus: Roche friabilator
Rotation speed: 25 ± 1 rpm
Number of revolutions: 100 revolutions (about 4 minutes)
Sample quantity:
Since each tablet is 500 mg.
Procedure

- Dedust and accurately weigh the tablets (W1).
- Place tablets in the friabilator drum.
- Run at 25 rpm for 100 revolutions.
- Remove tablets, dedust again, and reweigh (W2).

Calculation
Acceptance Criteria
NMT (Not More Than) 1.0% weight loss
No tablet should be:
cracked
broken
chipped severely

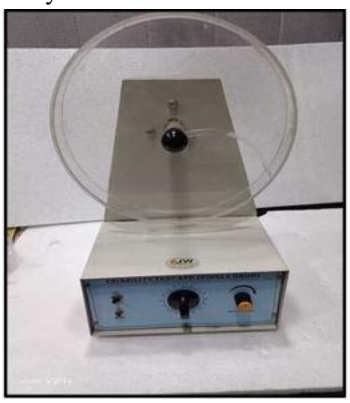
Fig No8: Roche friabilator

6. Dissolution test
For a sustained-release (SR) tablet of Empagliflozin, the dissolution test is typically designed to evaluate the controlled drug release profile over an extended period. There is no widely published official pharmacopeial monograph specifically for "empagliflozin SR tablets," so methods are generally developed and validated during formulation development based on ICH/USP guidance.

A commonly used dissolution approach for empagliflozin SR tablets is:
Typical Dissolution Method
Apparatus: USP Apparatus II (Paddle)
Dissolution Medium
Usually one of:
900 mL phosphate buffer pH 6.8 or 0.1 N HCl for initial stage followed by buffer change
Sometimes pH 1.2 → pH 6.8 sequential media for biorelevant profiling
Temperature: 37 ± 0.5°C
Paddle Speed: 50–75 rpm
Procedure

- Place one SR tablet into each dissolution vessel containing 900 mL medium.
- Maintain temperature at 37°C.
- Rotate paddles at selected rpm.
- Withdraw samples at predefined intervals.
- Filter samples.
- Replace equal volume with fresh medium.
- Analyze samples by UV/HPLC.
- Calculate cumulative % drug release

Fig No 9: Dissolution apparatus

B. In vitro drug release studies

In vitro dissolution studies were carried out using the USP Type 2 (paddle) dissolution apparatus. The dissolution medium consisted of 900 ml of simulated gastric fluid (PH 1.2) for the first 2 hours , followed by phosphate buffer (PH 6.8) for the remaining period. The temperature was maintained at 37 ± 0.5 °C and the paddle rotation speed was set at 50 rpm. Sample were withdrawn at predetermined time intervals and replaced with fresh dissolution medium. The sample were analyzed using a uv –visible spectrophotometer at the suitable wavelength.

Empagliflozin sustain release tablet was analyzed for drug release study utilizing a lab- india usp type-2 tablet dissolution test apparatus and 900ml of PBS PH 6.8 buffer in accordance with the official method. Using a UV- visible spectrophotometer, sample' absorbance was measured at 222nm and the data was subjected to kinetic modelling.

C. Drug release kinetics

Drug release kinetic models are utilized to describe the release mechanism of drugs from pharmaceutical dosage forms. These models provide insights into the drug release behaviour and can help in formulating and optimizing drug delivery systems.

- Zero-order kinetics model

In contrast to the first-order model, the zero-order model suggests a constant rate of drug release over time. It implies a linear decrease in the amount of drug remaining to be released.

Mathematically, it is represented as dQ/dt = k0,where k0 is the zero order rate constant.

- First-order kinetic model

This model assumes that the rate of drug release is directly proportional to the amount of drug remaining to be released.

Mathematically, it is described as dQ/dt =k1 (Q? – Qt), where Q represents the amount of drug released at time t, Q? is the total amount of drug to be released, and k1 is the first-order rate constant.

- Higuchi's model

This model is based on Fickian diffusion principles and states that the release rate of a drug from a matrix system is directly proportional to the square root of time. It is represented as Q = kH * sqrt(t), where Q is the amount of drug released at time t, and kH is the Higuchi rate constant.

D. Korsmeyer-Peppas model

This model is based on the power law relationship between the cumulative drug release and time, Q = kt^n. Here, Q is the amount of drug released at time t, k is a constant, and n is the release exponent that indicates the mechanism of drug release (e.g., Fickian diffusion for n < 0 xss=removed> 1).

These kinetic models help in predicting the release behavior of drugs from dosage forms, enabling the design of effective drug delivery systems with controlled release properties.

VII. KEY FINDINGS

- Effective blood glucose control: Empagliflozin significantly reduces blood glucose levels in patients with type 2 diabetes mellitus by inhibiting sodium-glucose co-transporter-2 (SGLT2) in the kidneys.
- Reduction in HbA1c Levels: Regular use decreases HbA1c values, showing improved long-term glycemic control.
- Promotes Glucose Excretion: It increases urinary glucose excretion, which lowers plasma glucose concentration independently of insulin action. Effective Blood Glucose Control
- Weight Reduction: Patients often experience moderate body weight loss due to calorie loss through glucose excretion.
- Blood Pressure Lowering Effect: Empagliflozin may help reduce systolic and diastolic blood pressure because of mild diuretic activity.
- Cardiovascular Benefits: Clinical studies reported reduced risk of cardiovascular death and hospitalization in diabetic patients with cardiovascular disease.
- Renal Protective Effect: It slows progression of kidney disease and improves renal outcomes in diabetic patients.
- Sustained Release Matrix Tablets Improve Drug Release: In sustained-release formulations using polymers such as HPMC and guar gum, controlled drug release was observed for prolonged therapeutic action.
- Good Flow and Compression Properties: Precompression studies generally show acceptable bulk density, tapped density, Carr's index, Hausner ratio, and angle of repose for tablet manufacturing.

- Drug – polymer compatibility: FTIR and DSC studies usually indicate no significant interaction between empagliflozin and selected polymers/excipients.
- Acceptable tablet evaluation parameters: Prepared tablets commonly show acceptable hardness, friability, thickness, weight variation, and drug content uniformity.
- Improved Patient Compliance: sustained – release formulation reduce dosing frequency, enhancing patient convenience and adherence to therapy.

VIII. STABILITY STUDIES

stability studies play a crucial role in the pharmaceutical development process by providing valuable insights into the stability and shelf life of drug products. By subjecting samples to elevated temperatures and humidity levels for a defined period, these studies simulate harsh environmental conditions that the product may encounter during its lifecycle.

The accelerated conditions facilitate the rapid degradation of the product, allowing researchers to predict its long-term stability in a shorter time frame. Through the monitoring of parameters such as physical appearance, chemical composition, potency, and impurity levels, researchers can assess the product's stability and make informed decisions about its shelf life.

IX. RESULT AND DISCUSSION

The empagloflozin powder prepared for all formulations showed satisfactory flow properties there precompression evaluation parameter

Table No 5: Evaluation of precompression parameter of powder

Formulation code	Angle of repose	Bulk density (gm/ml)	Tapped density (gm/ml)	Carr's index (%)	Hausner's ratio
F1	30.40	0.51	0.57	10.52	1.117
F2	31.10	0.48	0.5	-46	1.04
F3	30.83	0.55	0.6	-91	1.09
F4	33.44	0.41	0.44	6.8	1.07
F5	28.52	0.59	0.61	3.27	1.03
F6	36.66	0.57	0.61	6.5	1.07
F7	32.10	0.58	0.61	4.9	1.05
F8	29.21	0.53	0.60	11.66	1.13
F9	30.20	0.59	0.64	7.8	1.08
F10	31.30	0.55	0.60	8.3	1.09

Post compression evaluation of matrix tablets

The prepared sustained release matrix tablets of empagliflozin were evaluated for physical parameters such as hardness, thickness, friability, weight variation, and drug content.

Table No 6: Evaluation table

No of Tablet	Tablet thickness	Hardness	Weight variation
1	4.4mm	6.1kg/cm^2	498mg
2.	4.5mm	6.3kg/cm^2	491mg
3.	4.6mm	6.2kg/cm^2	495mg
4.	4.5mm	6.4kg/cm^2	497mg
5.	4.4mm	6.1kg/cm^2	492mg
Average weight	4.48mm	6.28kg/cm^2	494.6mg

For a friability test of Empagliflozin Sustained Release Tablets 500 mg using 5 tablets, you generally record:
Initial weight of 5 tablets

- Final weight after friability testing
- % weight loss (friability)

Where:
W1 weight of tablets
W2=weight after test

Table No 7: friability evaluation parameter

Parameter	Reading
Number of tablet	5
Initial weight (1)	3.250g
Final weight (2)	3.238g
Weight loss	0.012g
Friability %	0.37%

Disintegration Test

Table No 8

Parameter	Observation
Product	Empagliflozin SR tablets 500 mg
Medium	Purified water/ specified medium
Temperature	37 °c
Number observed	5
Time observed	1 hour
Result	Tablet did not disintegrate completely
Conclusion	Pass

Swelling Index Study
The swelling behavior of matrix tablets increased with increasing concentration of HPMC and guar gum. Formulations containing higher polymer concentration showed greater swelling due to hydration and gel layer formation around the tablet surface.
HPMC produced a strong viscous gel barrier which controlled penetration of dissolution medium and reduced drug diffusion. Guar gum contributed to matrix swelling and viscosity enhancement. Combination of HPMC and guar gum exhibited synergistic swelling behavior, which effectively prolonged drug release.

Future Perspective

- Combination Therapies: Developing a bilayer tablet with an immediate-release layer (e.g., of metformin or sitagliptin) and a sustained-release empagliflozin matrix layer.
- Quality by Design (QbD): Utilizing software-assisted Design of Experiment (DoE) and response surface methodology to optimize polymer concentrations and predict critical quality attributes accurately.
- Chrono-pharmacological Delivery: Designing delivery systems programmed to release medication based on circadian rhythms to specifically manage fasting blood glucose levels.
- Nano-matrices & Modified Polysaccharides: Modifying guar gum chemically or combining it with novel synthetic polymers to achieve zero-order release kinematics without initial burst effects.
- Generic Affordability: As patents for empagliflozin have expired, formulating cost-effective, indigenous sustained-release generic alternatives expands access to advanced diabetes management.

X. CONCLUSION

The present study successfully developed and evaluated sustained release matrix tablets of empagliflozin using hydroxypropyl methylcellulose (HPMC) and guar gum as release-retarding polymers. The prepared formulations demonstrated satisfactory pre-compression and post-compression characteristics, including acceptable flow properties, hardness, thickness, friability, weight variation, and drug content uniformity.
The combination of HPMC and guar gum effectively controlled the release of empagliflozin over an extended period, indicating the suitability of hydrophilic matrix systems for sustained drug delivery. Among the prepared formulations, the optimized formulation showed a desirable drug release profile with prolonged release behavior, good tablet integrity, and satisfactory stability during storage conditions.
The study concludes that the use of HPMC and guar gum can successfully formulate sustained release empagliflozin matrix tablets, which may improve patient compliance by reducing dosing frequency and maintaining therapeutic drug levels for a longer duration. Therefore, this formulation approach represents a promising strategy for the oral sustained delivery of empagliflozin in the management of diabetes mellitus.

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