Formulation and Evaluation of Enalapril Maltae sustain release tablet

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Abstract:

The present study focuses on the formulate and evaluate of sustained release (SR) matrix tablets of Enalapril Maleate, an angiotensin-converting enzyme (ACE) inhibitor to treat hypertension and cardiovascular disorders. The objective was to develop a sustained-release oral dosage form that prolongs drug release, improves therapeutic efficacy, enhances patient compliance, and minimizes dosing frequency.

To achieve this, a combination of natural polymers—Locust Bean Gum (LBG) and Tamarind Seed Powder (TSP)—along with the synthetic polymer Eudragit RL-100 was employed. The prepared formulations to comprehensive pre-compression and post-compression evaluations, including bulk density (BD), tapped density (TD), angle of repose, friability test, Carr's index, Hausner's ratio, and drug content uniformity.

Among all formulations (F1–F6), Formulation F3 demonstrated optimal performance, showing sustained drug release of up to 85.4% over 12 hours, with acceptable mechanical and physical properties. FTIR studies confirmed the absence of any drug-excipient interaction.

This research confirms that a suitable combination of synthetic polymers and natural polymer can successfully modulate drug release, providing an effective, stable, and patient-friendly sustained-release delivery system for Enalapril Maleate. The advance formulations holds potential for improving therapeutic management with chronic cardiovascular diseases.

Introduction:

Sustained Release Tablet:

A sophisticated type of medication delivery mechanism, sustained-release (SR) tablets are made to release the (API) gradually and under control. By keeping therapeutic drug

concentrations in the bloodstream for a longer amount of time, these formulations hope to minimize side effects linked to peak plasma drug levels, increase patient compliance, and decrease the frequency of administration.(1)

Traditional immediate-release tablets release the medication quickly, and in order to maintain therapeutic efficacy, several doses must frequently be taken daily. This frequent dose schedule, however, could cause variations in medication concentration, which could lead to hazardous or subtherapeutic consequences. By guaranteeing a constant and uninterrupted medication release, enhancing pharmacokinetics, and enhancing therapeutic results, sustained-release tablets overcome these difficulties.(2)

A number of biological and physicochemical concepts form the foundation of the sustained-release medication delivery idea. These formulations control medication absorption and dissolution like- coatings, polymers, matrix systems, and other technologies. Depend upon formulation design, may entail osmosis, diffusion, dissolution, the drug mechanism or a mix of these mechanisms.(3)

Advantages:

- Increased Patient Compliance: Sustained-release tablets improve patient adherence to prescribed prescription regimens by lowering administration, especially for chronic disease for long-term therapy.
- Reduced Side Effects: By avoiding abrupt increases in drug concentration, these formulations lessen negative effects associated with dosage.
- Steady Drug Levels: Sustained-release tablets maximize therapeutic efficacy and reduce variations by preserving steady plasma drug levels.
- Lower Dosing Frequency: Patients gain from taking fewer doses each day, which is particularly helpful for drugs with brief half-lives.
- Reduced Gastric Irritation: High dosages of some medications may result in gastrointestinal distress. By releasing the medication gradually, sustained-release formulations reduce local irritation.
- Economic Benefits: By lowering hospital stays, problems, and the need for extra prescription drugs, sustained-release formulations can save overall healthcare costs, despite their potential higher initial costs. (4)(5)

Challenges:

Despite their numerous advantages, sustained-release tablets present certain formulation and regulatory challenges:

• Complex Manufacturing Processes: Advanced methods are needed to provide consistent release kinetics and homogenous medication distribution.

• Variability in Drug Absorption: Drug bioavailability may be impacted by variations in stomach pH, motility, and enzyme activity.

• Dose Dumping: If a formulation error occurs, the drug may leak quickly and become hazardous.

• Problems with Cost and Stability: Expensive excipients and extensive stability testing are necessary for certain sustained-release formulations. (9)

A major development in pharmaceutical science, sustained-release tablets provide better treatment efficacy, patient adherence, and general health advantages. A thorough understanding of drug characteristics, excipients, and release processes is necessary for the development of these formulations. Newer and more advanced sustained-release systems are anticipated to improve the accuracy and efficacy of medicine therapy as drug delivery research advances.(10)

Enalapril maleate:

A common angiotensin-converting enzyme (ACE) inhibitor, enalapril maleate is essential for treating a number of cardiovascular and renal diseases, chief among them hypertension (high blood pressure), heart failure, and diabetic nephropathy. It is a prodrug taken orally that the body transforms into enalaprilat, its active form(11). Enalapril maleate functions as ACE inhibitor by preventing angiotensin I from becoming angiotensin II, a potent vasoconstrictor that raises (bp) and promotes the release of aldosterone. This inhibition makes it a useful medication for the long-term treatment of cardiovascular disorders because it causes vasodilation (blood vessel expansion), lower water and salt retention, and a lighter heart strain.(12)

Heart failure and hypertension are two of the most prevalent and important public health issues in the world. Serious side effects include heart attack, heart failure, and end-stage kidney

disease (ESKD) can result from untreated high blood pressure. Because they can control blood pressure, prevent cardiac remodeling, and increase long-term survival in patients with heart disease, ACE inhibitors, such as enalapril maleate, are regarded as a cornerstone medication for managing these disorders.(13)

Pharmacological Action of the Drug:

Enalapril maleate primarily acts by inhibiting the renin-angiotensin-aldosterone system (RAAS). The RAAS is essential for controlling the body's fluid balance and blood pressure. Blood volume and blood pressure are further increased by angiotensin II's stimulation of the release of aldosterone, a hormone that encourages the kidneys to retain water and salt.(8)(11) By blocking ACE, enalapril maleate prevents the formation of angiotensin II, leading to the following effects:

1. Decreased Aldosterone Secretion: This lowers blood volume and blood pressure by reducing water and sodium retention.
2. Decrease in Cardiac Workload: Enalapril maleate is very helpful in heart failure since it lowers due to decreased blood volume and vascular resistance.
3. Kidney Protection: Enalapril maleate slows the progression of kidney disease, especially in diabetic patients, by reducing glomerular pressure. (14)

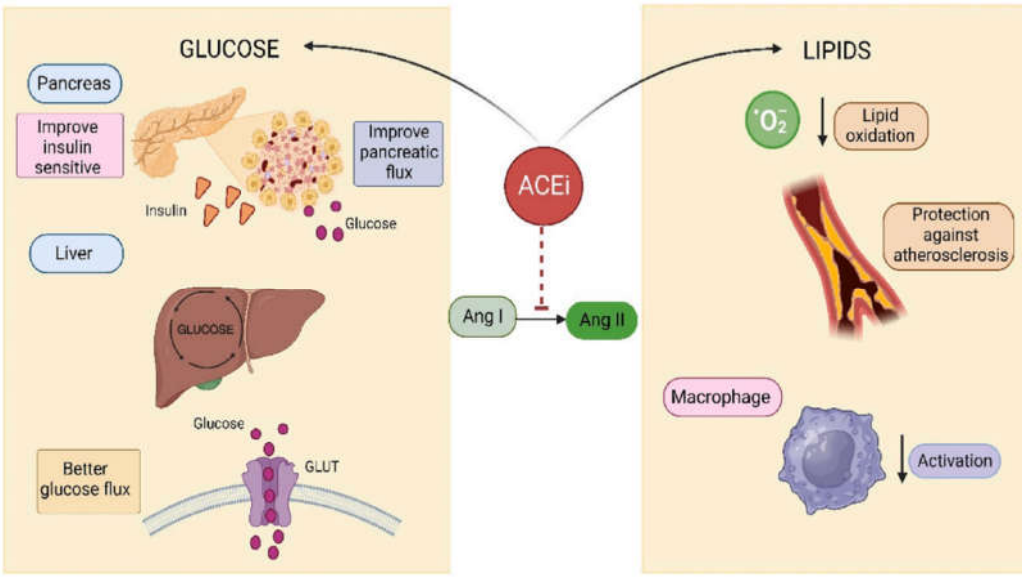

Figure: ACE Mechanism
(15)

The medication's therapeutic effects are caused by enalapril maleate, which is absorbed in the gastrointestinal system and transformed into enalaprilat by hepatic metabolism after oral administration. With a half-life of roughly 11 hours and a peak plasma concentration that

happens 3–4 hours after administration, enalaprilat once or twice daily. Since the kidneys are the responsible for excretion, people with renal impairment must modify their dosage.

Therapeutic Effect of the Drug:

The following are important therapeutic indications:

1.Hypertension (high blood pressure) As a first-line treatment for hypertension, enalapril maleate can be taken antihypertension medications such calcium channel blockers or diuretics. It helps avoid consequences like heart attacks, strokes, and renal damage by reducing blood pressure.

2. Failure of the Heart (conjestive) (CHF) can be effectively treated with enalapril maleate because it improves cardiac output, lessens the load on heart, and stops the disease from getting worse.

3.Chronic Kidney Disease (CKD) and Diabetic Nephropathy Diabetic nephropathy is the result of kidney damage brought on by high blood sugar levels in diabetic people. By lowering glomerular pressure and proteinuria (excess protein in urine), enalapril maleate helps to protect kidney function and slows the progression of kidney disease.

4. Treatment for Myocardial Infarction (Heart Attack) Patients recuperating from a heart attack are frequently offered enalapril maleate to stop additional cardiac re-modeling and lower their likelihood of experiencing another cardiovascular catastrophe. (17)

Advantages:

• Effective Blood Pressure Control: By blocking the RAAS system, enalapril maleate helps maintain stable and controlled blood pressure levels.

• Cardioprotective Effects: Reduces the strain on the heart, preventing complications in heart failure and post-myocardial infarction patients.

• Kidney Protection: Slows the progression of chronic kidney disease, especially in diabetic patients.

• Well-Tolerated in Most Patients: With proper dosage adjustments, enalapril maleate is generally well tolerated, making it suitable for long-term therapy.(18)(19)

Objective

Objectives:

1.Formulation of sustained release Enalapril Maleate for hypertension.

S.No	Equipment Required	Company
1	Sieves	Manikarn Test Seives
2	Rotary punching machine	Fluidpack
3	Dissolution apparatus(USP-2)	Veego
4	Friabillator	Roche friabillator
5	Hardness tester	Monsanto
6	XRD	EVO18
7	FTIR	Thermoscientific
8	UV-VIS Spectroscopy	Shimadzu1900i
9	Hotairoven	Thermolifesciences
10	Vernier Calliper	Mitutoyo

2.To study pre-formulation Parameters.

3.To study the (PCP) post compression parameters of the SR Drug.

Material and Methods

Apparatus Required:

Chemical required

Formulation of Enalapril Maleate:

S.NO	CHEMICALREQUIRED	SUPPLIER
1	Enalapril maleate	YarrowChem
2	EudragitRL-100	Central Drug House Pvt.Ltd.
3	Locust bean gum	Pioneer ChemicalCo.
4	Microcrystalline cellulose	Central Drug House Pvt. Ltd.
5	Tamarind seed powder	Sisco Research LaboratoriesPvt. Ltd.
6	PVP	Pioneer ChemicalCo.
7	Disodium hydrogen phosphate	Central Drug House Pvt. Ltd.
8	Potassium dihydrogen phosphate	Central Drug House Pvt. Ltd.
9	Distilled water	-

The

Enalapril Maleate sustained-release tablets were formulated using a combination of natural and synthetic polymers to achieve prolonged drug release. The ingredients roles in drug release modulation, tablet integrity, and patient acceptability.

Composition of the Tablet (per 100 tablets):

Ingredient	Quantity (g)	Function
Enalapril Maleate	10 g	Active pharmaceutical ingredient
Eudragit RL-100	5 g	Sustained release modifier (synthetic polymer)
Tamarind Seed Polysaccharide (TSP)	15 g	Natural polymer for controlled release
Locust Bean Gum (LBG)	10 g	Natural polymer, binder, gel-former
Microcrystalline Cellulose (MCC)	20 g	Diluent, improves compressibility
Polyvinylpyrrolidone (PVP K30)	5 g	Binder and disintegrant
Talc	2 g	Glidant (enhances flow)
Magnesium Stearate	1 g	Lubricant (prevents sticking)
Purified Water	q.s.	Solvent (evaporates during drying)

Method of Preparation

Sifting and Mixing

All solid ingredients, including Enalapril Maleate, Eudragit RL-100, TSP, LBG, MCC, and PVP, were weighed accurately and passed through sieve number 44 to ensure uniform particle size. The powders mixed using a mortar and pestle or a dry mixer for homogeneity.

Binder Preparation and Wet Granulation

A binder solution was prepared by dissolving Locust Bean Gum in purified water under constant stirring. The binder solution was added dropwise to the powder blend and mixing to form a cohesive wet mass. The wet mass was passed through the sieve number 12 to form uniform granules.

Drying

The granules were dried in oven at 60°C for half an hour until a consistent moisture-free state was achieved.

Lubrication

The dried granules blended with Talc and Magnesium Stearate for 5-7 minutes to enhance flow and prevent sticking during compression.

Compression

The granules are compressed into tablets using a tablet punching machine fitted with appropriate punches to produce tablets of the desired size and weight.

Physiochemical Assay:

Pre-formulation Parameters:

1. Organoleptic Properties

The organoleptic characteristics of Enalapril Maleate were analyzed to assess its physical traits. The drug checked its appearance, color, and odor. These attributes were recorded to confirm its identity and ensure that the drug complies with standard specifications.(37)

2. Determination of λmax and Calibration Curve Preparation

To determine the wavelength of maximum absorbance (λmax) and create a calibration curve for Enalapril Maleate:

- In a volumetric flask, 10 mg medication was soluble in 100 ml of ethanol to create a stock solution with a concentration of 100 µg/ml.
- 10 µg/ml working solution, 1 ml of this solution was moved to a 10 ml volumetric flask and diluted with distilled water.
- To create additional dilutions, 1 ml, 2, 3, 4, 5, and 6 ml of solition and diluted with 10

ml of dm water. The final concentrations obtained from them 10, 20, 30, 40, 50, and 60 µg/ml, in that order.

• A UV-visible spectroscopy to measure each solution's absorbance at 223 nm, to be determine the λmax.

3. Melting Point Determination

The melting point of Enalapril Maleate was measured using the capillary tube method. A small quantity of the drug was filled into a capillary , then attached to a thermometer. This assembly was preheated bath, and the temperature increased. The onset and completion temperatures of melting were noted. This test helps confirm the purity and identification the drug. (39)

1.**Solubility Analysis**

To assess solubility, limited amount of Enalapril Maleate was add 10 ml of solvent and shaken using a rotary flask shaker set at 70–80 RPM for 3 hours. The solution was then filtered, appropriately diluted, the absorbance was calculated at 223 nm. The procedure was perform in triplicate to ensure accuracy and reproducibility of results. Solubility helps determine the drug's behavior in different media and guides formulation design.(40)

1.**FTIR Analysis**

FTIR analysis to identify potential chemical between the active drug and formulation excipients:

- A sample of the pure drug was merge with potassium bromide (KBr) using a mortar and pestle to form a fine powder.
- The powder was transferred into a die and compressed using a hydraulic press to form a transparent pellet.
- The KBr was scanned in an FTIR spectrometer over a wavelength range of the 4000–400 cm^{-1}.
- The resulting of spectrum was analyzed for peaks, confirming the drug's identity and assessing any interactions with excipients,(38)

Evaluation Parameter:

a. **Pre-Compression Parameter:**

1. **Bulk Density:**Bulk density is defined as weight per unit volume. The bulk density, denoted as gm/cm3. Mostly, the size distribution, shape, and stickiness of the particles that make up a powder dictate its bulk density. Bulk density play a vital role in determining the size of containers needed for the handling, shipping, and storage of mixes and raw materials. It is also essential for equipment that blends sizes. A 10 g powder mixture was sieved and then placed to a dry 20 ml cylinder without compression. The powder was gradually leveled without compacting.. (41)**The formula was used to bulk density:**

Bulk Density = M / Vo
Where M = weight of the sample, Vo = apparent volume of powder

2. **Tapped Density:**

Following the procedures described density measurement, the sample was tapped using a mechanical tapped density tester the generates 100 drops per minute. The tapped volume, V, was then closest graded unit after this

Tap = M / V
Where Tap= Tapped Density, M = Weight of sample, V= Tapped volume of powder

procedure until the discrepancy between succeeding measurements was nlt2%.(42)

3. **Angle of Repose :**To calculate the frictional force in a loose powder. It is the greatest angle that can exist between the powder pile's surface and the horizontal plane. When more powder is added, until the gravitational force and friction of particles are equal. The angle of repose is measured using the fixed funnel technique. A graph paper was set on a level horizontal surface, and a funnel was fastened a specified height (h). The gently pushed the conical pile's peak just touched the funnel's tip. The conical pile's base's radius (r) was measured:

Tan θ = h / r Tan θ = Angle of repose
h = Height of the cone, r = Radius of the cone base

Angle of Repose	Nature of Flow
<25	Excellent
25-30	Good
30-40	Passable
>40	Very Poor

Table: Angle of Repose

Powder Compressibility

A powder's tendency to compress is gauged by the Compressibility Index, often known as Carr's Index. It gauges how significant interparticulate interactions are. Interactions are less important in a free-flowing powder. A larger disparity between the tapped density and bulk densities will be seen for materials with worse flow are usually more interparticle interactions. The Compressibility Index reflects these variations.(43)

Formula to calculate Powder Compressibility

Carr's Index = [(tap - b)/tap] × 100
Where b = Bulk Density, Tap = Tapped Density

Carr's Index	Properties
5-15	Excellent
12-16	Good
18-21	Fair to Passable
2-35	Poor
33-38	Very Poor
>40	Very Very Poor

Carr's compressibility index was measured using a typical tapping technique was measured using a stationary funnel approach to evaluate the flow properties of powder (i.e., a mixture of powders prior to compression).

Hausner ratios were determined by

Hausner ratio = Dt/Db,

Compressibility Index (%) = [(Dt-Db) × 100]/Dt

b. Evaluation of Post Compression Parameters:

The physicochemical properties of the suggested formulation tablets, including weight variation, hardness, thickness, and drug contents, were examined.(44)

Weight Variation Test

Twenty pills were ingested, and using a digital weighing scale and collectively to examine the weight fluctuation. From the total weight, the average weight of a single pill was calculated. The consistency of drug content could be satisfactorily ascertained using the weight fluctuations test.

None of the individual and the average of weight by more than twice the percentage, and no two diverge.(45)

The percent deviation was calculated using the formula

% Deviation = (Individual weight - Average weight / Average weight) × 100

Average weight (mg) (I.P)	Average weight of tablet (U.S.P)	Maximum percentage difference allowed
Less than 80	Less than 130	10
80-250	130-324	7.5
More than 250	More than 324	5

Table: specifications for tablet weight variation

Hardness: The force required to shatter the tablet across its circumference the tablet's hardness. The tablet's hardness determines how resistant it is to chipping, abrasion, or fracture during transformation and handling prior to use. Monsanto is a hardness tester was used to measure the hardness of three tablets for each formulation. The average was then computed and displayed with deviation..(46)

Thickness: One crucial factor in recreating look is tablet thickness. One crucial factor in recreating look is tablet thickness. Core and coated tablet average thickness is computed and displayed with deviation.(47)

Friability: By following the steps, the friability was ascertained using the Roche friabilator. The friabilator was filled with pre-weighed pills. For four minutes, the tablets are spun 100 times at 25 rpm. The tablets is reweighed at the conclusion of the test; a decrease in weight indicates friability.(46)

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$$\% \text{ Friability} = [(W1-W2)/W] \times 100$$

Where W1 = Initial weight of three tablets, W2 = Weight of the three tablets after testing

Dissolution Test

Tablets an **in-vitro dissolution study** using **(paddle method)** under controlled conditions. The study at **37°C ± 0.5°C**, with a **paddle rotation speed of 50 revolutions per minute (rpm)**. A total of **900 ml of dissolution** was maintained the test. The procedure was structured into the following phases:

- **Phase 0 (Initial Setup):** Calibration and preparation of the UV-Visible spectrophotometer, and pre-equilibration of the dissolution apparatus with the specified temperature and volume. This phase ensured the system was stabilized and ready for accurate data collection.
- **Phase 1 (Acidic Phase - Simulated Gastric Fluid):** For the **first two hours**, **simulated stomach juice (simulated gastric fluid)** was used as the dissolution medium. This phase mimicked the gastric environment to evaluate drug release in acidic conditions.
- **Phase 2 (Buffer Phase - Simulated Intestinal Fluid):** After two hours, the medium was replaced with a **phosphate buffer** to simulate intestinal conditions for the **remaining duration** of the study.

- **Phase 3 (Sampling and Analysis):** Samples were withdrawn at **entirely distinct predetermined intervals** during both phases. The sample was analyzed used by a **UV-Visible spectrophotometer at 238 nm**. The **amount and percentage of drug dissolved** on the absorbance readings.

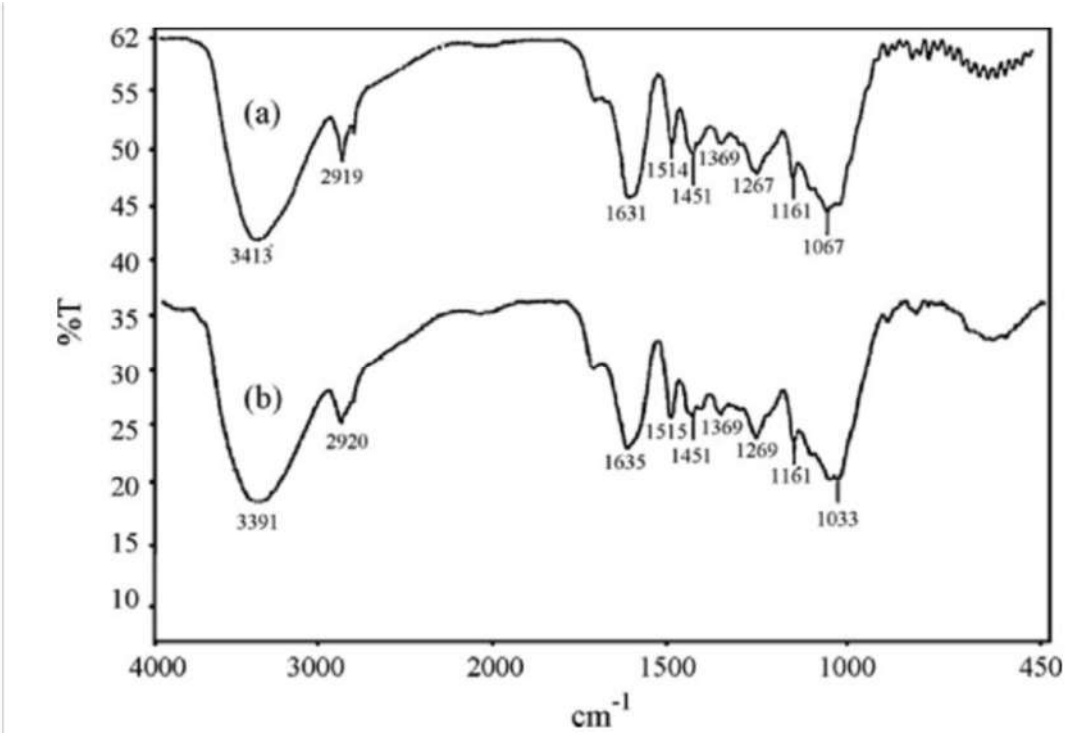
Results:

Organoleptic Properties	Colour: Off White Odor: Odourless Appearance: Crystalline powder
Solubility	Water: Practically insoluble Ethanol: Slightly soluble Methanol: Soluble Chloroform: Freely soluble Acetone: Soluble pH 7.4 Buffer: Slightly soluble
Melting Point	120-160°C

WAVELENGTH:

Wavelength (nm)	Absorbance of drug	Absorbance of Standard
200nm	**0.102**	**0.23**
220nm	**0.254**	**0.32**
240nm	**0.412**	**0.39**
260nm	**0.645**	**0.44**
280nm	**0.823**	**0.812**
300nm	**0.787**	**0.6**
320nm	**0.645**	**0.543**
340nm	**0.456**	**0.521**
360nm	**0.435**	**0.321**
380nm	**0.324**	**0.231**
400nm	**0.312**	**0.1**

FTIR



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Analysis:

x axis – wavenumber **y axis- Transmission** **FTIR OF PURE DRUG** **FTIR OF DRUG WITH NATURAL POLYMER**

Bulk Density

Bulk density of the formulation F1 To F6

Formulation	Bulk density
F1	0.55 ± 0.011
F2	0.54 ± 0.02
F3	0.56 ± 0.014
F4	0.54 ± 0.024
F5	0.53 ± 0.021
F6	0.53 ± 0.012

Tapped Density

Tapped density of the formulation F1 To F6

Formulation	Tapped density
F1	0.62 ± 0.016
F2	0.62 ± 0.021
F3	0.64 ± 0.016
F4	0.63 ± 0.014
F5	0.67 ± 0.033
F6	0.64 ± 0.024

Angle of Repose

The formulation is F1 To F6

Formulation	Angle of Repose
F1	23.45 ± 0.14
F2	19.65 ± 0.21
F3	22.35 ± 0.24
F4	20.69 ± 0.18
F5	20.82 ± 0.32
F6	20.72 ± 0.23

Carr's Index

Formulation	Carr's Index (%)
F1	0.62 ± 0.016
F2	0.62 ± 0.021
F3	0.64 ± 0.016
F4	0.63 ± 0.014
F5	0.67 ± 0.033
F6	0.64 ± 0.024

Hausner's Ratio

Hausner's Ratio of the formulation F1 To F6

Formulation	Hausner's Ratio
f1	0.25 ± 0.021
f2	0.16 ± 0.018
f3	0.18 ± 0.016
f4	0.11 ± 0.025
f5	0.22 ± 0.021
f6	0.18 ± 0.024

Evaluation of Post Compression Parameters:

Weight Variation

Weight variation in the tablet formation from F1 to F6

Formulation	Average weight
f1	99.6 ± 0.54
f2	98.75 ± 0.45
f3	101.67 ± 0.23
f4	96.40 ± 0.64
f5	102.56 ± 0.34
f6	99.67 ± 0.54

Hardness

Hardness of the tablet of F1 to F6 formulations

Formulation	Hardness
f1	5.4 ± 0.43
f2	5.5 ± 0.64
f3	5.3 ± 0.43
f4	5.6 ± 0.64
f5	5.3 ± 0.34
f6	6.0 ± 0.65

Thickness

Thickness of the tablet of F1 to F6 formulations

Formulation	Thickness
f1	2.41 ± 0.11
f2	2.45 ± 0.09
f3	2.43 ± 0.32
f4	2.35 ± 0.31
f5	2.54 ± 0.12
f6	2.60 ± 0.21

Friability

Friability of the tablet of F1 to F6 formulations

Formulation	Friability (%)
f1	0.16 ± 0.35
f2	0.18 ± 0.54
f3	0.17 ± 0.34
f4	0.25 ± 0.46
f5	0.22 ± 0.75
f6	0.3 ± 0.36

Dissolution Test

Dissolution of the tablet of F1 to F9 formulations

Time(h)	F1	F2	F3	F4	F5	F6
1	9.7± 0.11	10.5±0.53	10.5±0.12	18.5±0.11	15.5±0.43	10.2±0.22
2	15.6±0.13	15.8±0.34	15.8±0.43	24.6±0.45	21.6±0.21	18.6±0.65
4	25.5±0.23	26.9±0.24	26.9±0.53	35.6±0.23	30.5±0.53	26.12±0.12
6	38.9±0.22	49.8±0.64	49.8±0.34	41.7±0.54	39.5±0.87	38.7±0.23
8	51.2±0.12	70.2±0.45	70.2±0.53	60.7±0.21	51.8±0.13	50.7±0.45
12	68.6±0.32	85.4±0.63	85.4±0.23	78.9±0.74	70.9±0.43	64.4±0.21

Discussion

The current study focused on sustained release tablets of Enalapril Maleate using a combination of natural polymers (Locust Bean Gum and Tamarind Seed Powder) and synthetic polymers (Eudragit RL-100, PVP). The intention was to optimize the release profile of Enalapril, enhance patient compliance, and minimize dosing frequency in the management of chronic conditions such as hypertension and heart failure.

Pre compression Evaluation

The **pre-compression parameters** like bd, td, angle of repose, Carr's index, and Hausner's ratio provided insight into the flow properties of the granules:

- **Angle of repose values** (F1 to F6) were below 25°, indicating **excellent to good flow properties**, crucial for uniform tablet compression.
- **Carr's index** and **Hausner's ratio** were within acceptable ranges (<15% and <1.25 respectively), further confirming the **compressibility and flowability** of the granules.

These parameters are indicative of a robust pre-formulation blend suitable for direct compression or wet granulation methods.

Post Compression Evaluation

All six formulations (F1–F6) were evaluated for drug content:

- **Weight variation** values remained within pharmacopoeial limits, ensuring uniform dosage.

- **Tablet hardness** ranged from 5.3 to 6.0 kg/cm², demonstrating mechanical integrity suitable for packaging and transport.
- **Friability values** were <1% in all formulations, confirming sufficient resistance to abrasion.
- The **thickness** of tablets remained consistent, indicating precise and controlled compression during tablet formation.

  The physical properties of the formulated tablets met standard criteria for sustained-release dosage forms.

Dissolution and drug Profile

The **in-vitro dissolution studies** revealed that:

- Formulations F2 and F3 exhibited superior **controlled drug release**, with up to **85.4% release at 12 hours**, closely mimicking a sustained release profile.
- F1, F5, and F6 showed moderate release rates, while **F4 displayed faster release** in initial hours, possibly due to polymer concentration or differences in polymer swelling behavior.

Formulation **F3**, containing a balanced combination of **Eudragit RL-100 and natural polymers**, emerged as the **optimum batch**, providing a desirable extended-release profile while maintaining mechanical strength and stability.

FTIR Compatibilty Test

FTIR spectra confirmed the absence of **incompatibility or significant chemical interaction** between Enalapril Maleate and the excipients used. Characteristic peaks remained intact in the formulation, validating the stability of the active ingredient throughout the manufacturing process.

Impact of Polymers on Drug Release

- The **natural polymers** (LBG and TSP) demonstrated high swelling and gel-forming capacities, contributing significantly to **controlled diffusion and erosion-based release**.
- **Eudragit RL-100**, a hydrophobic polymer, helped **retard drug release**, especially in the intestinal pH range, contributing to the sustained-release nature of the formulation.
- The combination of **hydrophilic and hydrophobic polymers** allowed for modulation of the release kinetics, reducing the chances of dose dumping while promoting steady plasma concentration.

Conclusion

The aim of formulating and evaluating sustained release (SR) matrix tablets of Enalapril Maleate using both natural polymers (Locust Bean Gum and Tamarind Seed Powder) and a synthetic polymer (Eudragit RL-100), to enhance the therapeutic potential of the drug in managing chronic cardiovascular conditions such as hypertension and heart failure. Enalapril

Maleate, an ACE inhibitor, has proven clinical benefits in reducing blood pressure, protecting kidney function, and improving heart function. However, its short half-life and relatively frequent dosing requirement present challenges in long-term patient adherence. The development of a sustained-release system is therefore crucial to prolonged duration while minimizing side effects and improving compliance.

The formulation strategy employed in this research was based on the integration of natural and synthetic polymers to synergistically control the drug release rate. The pre-formulation studies—including organoleptic properties, solubility, FTIR analysis, and melting point—confirmed the purity and compatibility of Enalapril Maleate with the selected excipients. FTIR spectroscopy verified the absence of chemical interactions between the drug and the polymers, ensuring the stability and safety of the formulation.

Pre-compression parameters are indicated good flow and properties of granules. These consistent tablet weight, uniformity, and compressibility. All formulations (F1 to F6) displayed acceptable flow characteristics, which supported smooth manufacturing processes.

Post-compression parameters, including weight variation, tablet hardness, thickness, and friability, complied with IP/USP standards. This confirms that the tablets possessed sufficient mechanical strength to withstand handling, transport, and packaging without breaking or chipping. Among all formulations, Formulation F3 emerged as the most promising based on its optimal balance of mechanical strength and sustained drug release.

The in-vitro dissolution study demonstrated that Formulation F3 provided a consistent and extended drug release over a 12-hour period, with a cumulative release of 85.4%. The drug release profile followed a controlled pattern, likely governed by a combination of diffusion and erosion mechanisms, which aligns with the theory of non-Fickian transport described in the Korsmeyer-Peppas model. The natural polymers contributed significantly to swelling and gel formation, facilitating slow drug diffusion, while Eudragit RL-100 enhanced the retarding effect and helped modulate the release rate further.

From a formulation science perspective, (LBG) and Tamarind Seed Powder (TSP) offers a cost-effective, biocompatible, and eco-friendly alternative to synthetic agents, without compromising delivery system. Allowed fine-tuning of the drug release profile, making the overall formulation both stable and therapeutically effective.

The feasibility of developing a sustained-release oral delivery system for Enalapril Maleate but also highlights the critical role of polymer selection and optimization in achieving desired release kinetics. The results suggest that incorporating natural polymers with synthetic agents can significantly improve SR systems.

Future Prospect

The successful development of this sustained-release formulation has important clinical and economic implications. By reducing dosing frequency, the formulation is expected to improve patient adherence, particularly in populations requiring long-term antihypertensive therapy. Moreover, sustained plasma levels could potentially reduce the incidence of side effects such as hypotension, cough, and fluctuations in blood pressure, thereby improving patient outcomes and quality of life.

Looking ahead, the formulation can be further optimized by incorporating bioenhancers or permeability modulators, considering Enalapril Maleate's BCS Class III characteristics (high solubility, low permeability). In-vivo studies and pharmacokinetic evaluations will be essential to correlate the in-vitro findings with clinical performance. Moreover should be conducted to ensure long-term shelf life.

Additionally, exploring mucoadhesive or gastroretentive systems, particularly for drugs absorbed in the upper GIT like Enalapril, could further improve bioavailability. 3D printing technologies or nanoparticle incorporation to increase the customization and efficiency of sustained-release profiles.

conclusion, demonstrates that a rational combination of natural and synthetic polymers in appropriate ratios can successfully achieve a stable, efficient, and reproducible sustained-release matrix tablet of Enalapril Maleate. This formulation holds promising potential in providing cost-effective, patient-compliant therapy for cardiovascular diseases, contributing positively to public health and pharmaceutical innovation.

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