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Research Article

Formulation and Evaluation of Microspheres of Ramipril

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Abstract

Background: Ramipril an antihypertensive medicine has a 28 percent oral bioavailability and is promptly eliminated from the body through the kidneys. When Ramipril is administered as an immediate dosage form, it has also been linked to a wide range of side effects, including hypotension, an increase in potassium level, and angioedema. The present study was therefore conducted in an effort to reduce the drug's negative effects and boost its bioavailability.

Objectives: In the current work, ramipril microspheres are created and evaluated utilizing the solvent evaporation method and natural or synthetic polymers. Use natural polymers like ramipril, sodium hydroxide, potassium dihydrogen orthophosphate, dichloromethane (DCM), and synthetic polymers like ethyl cellulose, eudragit RL100, etc.

Methods: A solvent evaporation technique was used to create the microsphere, and polymers like EudragitRL100 and ethyl cellulose were used. Particle size analysis, percent entrapment efficiency, Differential scanning calorimetry (DSC), Drug encapsulation efficiency (DEE), FTIR spectroscopy, in vitro release research, and stability study were all performed on the produced formulations.

Results: The results were observed to be within the normative ranges. The FT-IR analysis of the formulations indicated there was no interaction between Ramipril and other excipients. The range of entrapment efficiency was found to be between 68.7 and 94.08%. The drug release investigation was conducted in gastrointestinal fluid (SGF) for 12 hours and demonstrated the largest quantity of drug release in a regulated and sustained manner over a prolonged length of time. The size of the microsphere was in the range of 25.7 to 49.2 m. According to the DSC study, molecules of drugs are uniformly dispersed in an amorphous state.

Conclusion: The designed formulation was discovered to be stable and it provides a potential system for the controlled and sustained distribution of ramipril.

Keywords: Ramipril, EudragitRL100, Ethylcellulose, Potassium dihydrogen orthophosphate, Solvent evaporation method.

INTRODUCTION:

The four basic pathways of drug transport and modification in the body absorption, distribution, metabolism, and elimination, determine a medicine's therapeutic effectiveness. Insufficient drug concentration caused by poor absorption, quick metabolism and elimination, poor drug solubility, and excessive plasma levels brought on by uncertain bioavailability are all examples of therapeutic failure. The creation of an appropriate medication colloidal carrier system is a viable solution to these issues. Microspheres are a colloidal carrier system that, in comparison to other colloidal carrier systems, has a lot of benefits and few drawbacks. Due to their biodegradable, biocompatible, and low-toxic qualities, microspheres have attracted attention as carriers for the manufacture of a wide range of poorly water-soluble medicines. [1]

Treatment for hypertensive diseases has included the use of the powerful antihypertensive drug ramipril. Absolute bioavailability is between 28 and 35 percent, and the medication is extremely lipophilic (log p octanol/water) and poorly water-soluble [2]. The most beneficial and preferred method of drug administration for the foundational course is oral drug administration. Recently, the pharmaceutical industry has adopted an oral controlled medication delivery method to manage better therapeutic preferences. Recurring dosing of the medication is necessary to accomplish the therapeutic impact since drugs that are quickly removed from the systemic circulation and have a short half-life are easily retained from the gastrointestinal tract. Setting up a continuous regulated discharge protocol that dignifiedly releases the drug into the gastrointestinal tract is necessary to prevent this [3-6].

As a prodrug, ramipril is transformed into the active metabolite ramipril by liver esterase catalysts. Normally, the kidneys eliminate ramiprilat. Ramiprilat's unexpected half-life can be prolonged by failing organs such the heart, liver, and kidneys. Under the brand names Cardiac, Zigpril, and Zorem, ramipril is advertised in India. A single dose of Ramipril between 2.5 and 20 mg results in a 4-hour ACE activity inhibition of around 60 to 80 percent, with a typical range of 40 to 60 percent [7-9].

Drug Profile

Ramipril

Structure:[10]

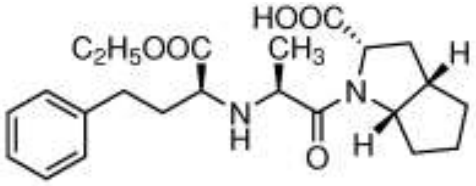

Fig.1: Ramipril

Systematic (IUPAC) name:(2*S*, 3aS, 6aS)-1-[(*S*)-2-{[(2*S*)-1-(ethoxycarbonyl)-3-phenylpropyl] amino] propanoyl] octahydrocyclopenta[*b*]pyrrole-2-carboxylic acid.

Angiotensin converting enzyme (ACE) inhibitors like ramipril are used to treat congestive heart failure and high blood pressure, respectively. ACE inhibitors ease the muscles surrounding small arteries by blocking an enzyme (arterioles). The arterioles widen, facilitating easier blood flow. Blood pressure falls as a result. [11]

Physicochemical properties [12]

Molecular formula : $C_{23}H_{32}N_2O$

Molecular weight : Average: 461.5106

Monoisotopic : 416.231122144

Superclass : Organic acid and derivatives

Class : Carboxylic acid and Derivatives

Subclass : Amino acids, Peptides and Analogues

Classification : This compound belongs to the peptides.

Description : These are compound containing on amide derived from two or more amino carboxylic acid molecules by formation of a covalent bond from the carbonyl carbon of one to the nitrogen atom of another.

Melting point : 109^0C

Solubility : Ramipril is springy soluble in water, soluble in Glacial acetic acid and Methanol.

Pharmacodynamics:

Benazepril, fosinopril, and quinapril are ACE inhibitors, as is ramipril. It is an inactive prodrug that the liver and kidneys, which serve as the primary sites of activation, transform into ramiprilat. By counteracting the effects of RAAS, ramiprilat lowers blood pressure. The RAAS is a homeostatic system that controls the balance of electrolytes, water, and hemodynamics. The granular cells of the juxtaglomerular apparatus in the kidneys release rennin when the sympathetic nervous system is stimulated or when renal blood pressure or blood flow is decreased. Rennin breaks down circulating angiotensinogen in the bloodstream to create ATI, which ACE then breaks down to create ATII. Multiple pathways are used by ATII to raise blood pressure.

Mechanism of action:

ACE comes in two different isoforms. the testicular isoform, which has a reduced molecular mass and is assumed to be involved in sperm maturation and binding of sperm to the oviduct epithelium, and the somatic isoform, which exists as a glycoprotein made up of a single polypeptide chain of 1277 amino acids. N and C, two functionally active domains of somatic ACE, are produced by tandem gene duplication. Despite the significant degree of sequence similarity between the two domains, they have different physiological functions. The N-domain is important for hematopoietic stem cell differentiation and proliferation, whereas the Codomain is primarily engaged in blood pressure control. Although ACE inhibitors bind to and block the activity of both domains, they are significantly more effective against the Codomain and have a far higher affinity for it. As mentioned in the pharmacology section above, ramiprilat, the primary active metabolite of ramipril, competes with ATI for binding ACE and decreases ATII levels in the body by reducing ATII's pressor effects. Blood pressure drops as a result. Ramipril also increases plasma rennin activity, which is likely brought about by a reduction in the ATII-mediated feedback control of renin release and/or the baroreceptor-mediated stimulation of reflex mechanisms.

Absorption:

Absorption has reached at least a 50%–60% level. Food slows down GI tract absorption without changing absorption itself. Ramipril's absolute bioavailabilities were 28 percent lower when administered orally versus intravenously.

Protein binding: Protein binding of Ramipril is 73%.

Metabolism:

Ramipril is metabolised to a maximum of 75% in the liver. Via liver esterase enzymes, 25% of hepatic metabolism results in the active metabolites ramiprilat. Ramipril is completely converted to ramiprilat in the kidneys. The inactive glucuronides of ramipril and ramiprilat are other metabolites.

Half-life : 2 to 4 hrs

Mode of excretion : Renal

Bioavailability : 60%

Dose : Oral-1.25mg - 10mg/ day

The dicarboxylate-containing ACE inhibitors (enalapril, perindopril, lisinopril, ramipril, trandolapril, quinapril, benazepril, and cilazapril) make up the second and largest class [13]. The goal of the current work is to create and evaluate a Ramipril microsphere using the solvent evaporation method and natural or synthetic polymers.

MATERIALS AND METHODS:

Chemicals and reagents:

Ramipril was a kind gift sample provided by Parth Web Solution Pvt Ltd in Pune, while Eudragit E 100 was a gift sample provided by Loba Chem Pvt Ltd. From Himedia lab Pvt Ltd. in Mumbai, ethyl cellulose Dichloromethane from Ozone International Pvt Ltd. in Mumbai. All other chemicals used were of analytical grade and were acquired from Central Drug House in New Delhi, along with sodium hydroxide and potassium dihydrogen orthophosphate from Mumbai.

All the reagents and materials used in formulation and evaluation are listed below.

Table 1: List of materials used for experiments

Sl. No.	Chemicals	Supplier/Manufacturer
1	Ramipril	Parth web solution Pvt ltd, Pune
2	Ethylcellulose	Himedia lab Pvt Ltd. Mumbai
3	Eudragit RL 100	Loba chem. Pvt Ltd. Mumbai
4	Sodium hydroxide (NaOH) pallets	Central drug house-New Delhi
5	Potassium dihydrogen orthophosphate	Central drug house-New Delhi
6	Dichloromethane (DCM)	Ozone International Pvt Ltd. Mumbai
7	Distilled water (H2O)	BLDEA's SSM College of Pharmacy Vijayapura

Equipment's:

All the materials used in formulation, evaluation and other equipments are listed below.

Table 2: List of equipment used for experiments

Instruments/equipment's	Make and model
Mechanical stirrer (overhead stirrer)	Remi equipment Mumbai
UV-Visible spectrophotometer	Shimadzu-1700, Shimadzu Corporation, Japan.
Digital balance	Orion automation system, & Shimadzu.
Dissolution apparatus (USP) TDT 08L	Electro lab, Mumbai.
FTIR spectrophotometer	Shimadzu 8400 S, Japan.
Scanning electron microscopy (SEM)	JEOL Model JSM – 6390LV Kyoto Japan.
Differential scanning calorimetry (DSC)	DSC-60, Shimadzu corporation, Japan.
X-ray diffraction (XRD)	Bruker AXS D8 Advance
Hot air oven	Oswald, JRFC-7/A Mumbai.

Estimation of Ramipril

A spectrophotometric method based on the measurement of absorbance at 210 nm of UV region in pH 7.4. Phosphate buffer of pH 7.4 were used for the estimation of ramipril.

Preparation of standard curve of Ramipril in phosphate buffer pH 7.4.

In a 100 ml volumetric flask, 100 mg of Ramipril was precisely weighed, dissolved in 40 ml of methanol, and the volume was increased to 100 ml by adding phosphate buffer, pH 7.4. This primary stock solution has a 1000 ug/ml concentration. From this initial stock solution, 10 ml was pipette out and placed in a volumetric flask with a capacity of 100 ml. This volume was then filled with phosphate buffer pH 7.4 at a concentration of 100 g/ml (Second stock solution). Aliquots of the second stock solution (10, 20, 30, 40, and 50 ml) that equated to 10 to 50 g were pipette out into a series of 100 ml volumetric flasks, and the volume was then topped up with phosphate buffer pH 7.4 to reach 100 ml. Using a UV-visible double beam spectrophotometer, the absorbance of these solutions was measured at 210 nm using phosphate buffer pH 7.4 as the reference. The concentration in g/ml was then plotted on the X-axis and the absorbance on the Y-axis to create a calibration curve.

Preparation of Ramipril microspheres by solvent evaporation method.

The liquid manufacturing vehicle phase is where this process is carried out. The liquid manufacturing vehicle phase and the volatile solvent used to spread the microcapsule coating are incompatible. In the coating polymer solution, a core substance that will be microencapsulated is dissolved or disseminated. To create the proper size microcapsule, the core material combination is disseminated in the liquid manufacturing vehicle phase with agitation. When the polymer of the core material is dispersed in the polymer solution, the combination is then heated if necessary to evaporate the solvent. The polymer shrinks around the core. Matrix-type microcapsules are created if the core material is dissolved in the coated polymer solution. The primary components could either be water-soluble or water-insoluble. When a solvent is evaporated, an emulsion is created between a polymer solution and an immiscible continuous, whether it is aqueous or not.

Table 3: Formulation of Microsphere of Ramipril

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
Ramipril	4mg	4mg	4mg	4mg	4mg	4mg	4mg	4mg	2mg
Ethyl cellulose	800mg	1gm	1.2gm	-	-	-	400mg	600mg	800mg
Eudragit RL 100	-	-	-	800mg	1gm	1.2gm	400mg	600mg	800mg
Polyvinyl alcohol	5%	5%	5%	5%	5%	5%	5%	5%	5%
Dichloromethane & Methanol (1:1)	20ml	20ml	20ml	20ml	20ml	20ml	20ml	20ml	20ml

1) Determination of mean particle size:

Approximately 100 microspheres were randomly chosen for the optical microscopy particle size study, and their sizes were calculated using a conventional micrometre scale attached to an optical microscope.

2) Differential scanning calorimetry (DSC)

Microspheres infused with the pure medication Ramipril underwent a DSC examination. Under nitrogen flow of 25 ml/min, the thermal analysis was carried out by recording thermograms for 5–15 mg samples heated at a rate of 10 K/min from 200–3000C. Prior to the test, the samples were placed within sealed aluminium crucibles with perforated lids. As a guide, an empty aluminium crucible was employed.

3) FTIR analysis

Compatibility is one of the criteria for choosing an appropriate excipient or carrier for a pharmaceutical formulation. Therefore, a study was conducted in the current work to assess any potential drug-polymer interactions. The pellets were made using KBr at a high compaction pressure, with a sample to KBr ratio of 1:1000. The prepared pellets were analysed, and spectra between 4000 and 400 cm-1 were recorded.

4) Drug encapsulation efficiency (DEE)

50 mg of microspheres that were precisely weighed were taken for analysis. By periodically crushing the microspheres, extracting them with aliquots of 7.4 pH phosphate buffer, and gently heating them, we were able to assess how much medication was entrapped. The volume was made up with 7.4 pH phosphate buffer after the extract was transferred to a 100 ml volumetric flask. Filtering the solution allowed for the measurement of absorbance at 210 nm using the proper blank. The formula below was used to determine how much medication was trapped in the microspheres.

$$\text{DEE} = \frac{\text{Amount of drug actually present} \times 100}{\text{Theoretical drug load expected}}$$

5) In-vitro drug release studies

The in-vitro release rate of ramipril microspheres was tested for 12 hours with a dissolution device (Electro lab TDT 08L, India) that contained 900 ml of pH 7.4 phosphate buffer solution until the completion of the study (12 hours), was kept at 37°C, and had a 100 rpm agitation speed. For the investigation, 50 mg of microspheres that were precisely weighed through a 12-hour disintegration process. The 5 ml aliquots were removed at intervals of 0, 1, 1.5, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 and 12 hours and replaced with an equal volume of brand-new, prewarmed dissolving medium. Shimadzu-1700 spectrophotometer was used to perform a spectrophotometric analysis of the samples after the appropriate dilution at a maximum wavelength of 210 nm. When fitting the release data.The following mathematical models were fitted to the release data in order to determine which model best fit the resulting release profile.

- ✓ Zero order and first order release kinetics.
- ✓ Higuchi model.
- ✓ Korsmeyer-Peppas model.

RESULTS AND DISCUSSION:

Ramipril microspheres were created using the solvent evaporation process from ethyl cellulose and edragit RL100 under different drug loading conditions. For several physicochemical tests, including particle size, drug entrapment effectiveness, and in-vitro drug release behaviours, the produced microsphere were assessed. A preliminary investigation on the formulation of the microsphere revealed that for a microsphere to have the desired characteristics, a ratio of EudragitRL100/ethyl cellulose of greater than 1:1 and stirring rates of 500–1000 rpm should be utilised.

Using optical microscopy and a standard micrometre, the microsphere's size was measured and documented in table 5. The microspheres ranged in size from 25.7 to 49.2 m, on average. The size of the microsphere increased along with the concentration of crosslinking of the polymers, and it also shrank with an increase in stirring rate. The results of the prepared microsphere's drug entrapment efficiency (DEE) are given in table 5. The drug entrapment efficiency was observed to range from 94.08 to 68.07 percent; the DEE fell as microsphere crosslinking concentration rose.

Table 4: Spectrophotometric data for estimation of ramipril in phosphate buffer pH 7.4

Sl. No	Concentration (mcg/ml)	Absorbance
1.	0	0
2.	1	0.029
3.	2	0.057
4.	3	0.092
5.	4	0.126
6.	5	0.142

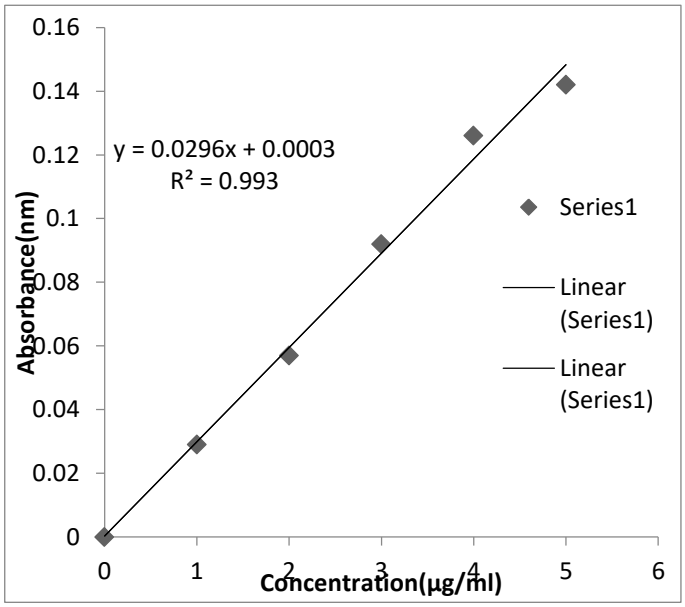

Fig-2: Standard Calibration Curve of Ramipril in Phosphate Buffer pH in 7.4 (210nm)

Table 5: Average size and drug entrapment efficiency (DEE) ramipril dried microspheres.

Microspheres	Average size (µm)	DEE (%)
F1	34.5 ± 8.58	94.08%
F2	28.6 ± 6.31	91.40%
F3	25.7 ± 5.14	86.90%
F4	47.4 ± 7.87	80.60%
F5	44.9 ± 5.67	80.02%
F6	46.25 ± 6.62	74.50%
F7	43.2 ± 7.93	69.60%
F8	49.2± 8.3	74.70%
F9	47.4±7.87	68.70%

The values are average of three determinations. ± indicates SD values

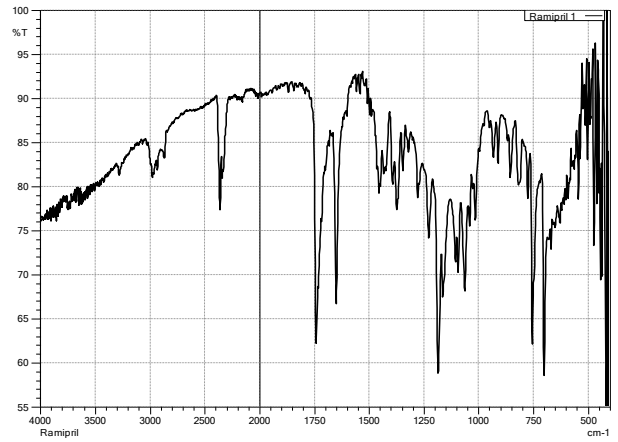

Fig. 3: FTIR spectra of pure drug(A) Ramipril

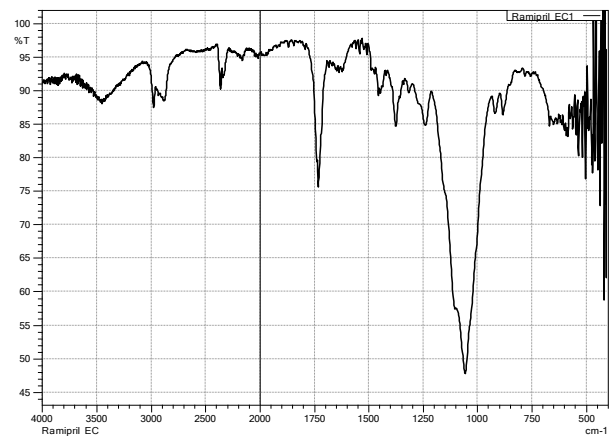

Fig.4: FTIR spectra of pure drug (B) ramipril, ethyl cellulose

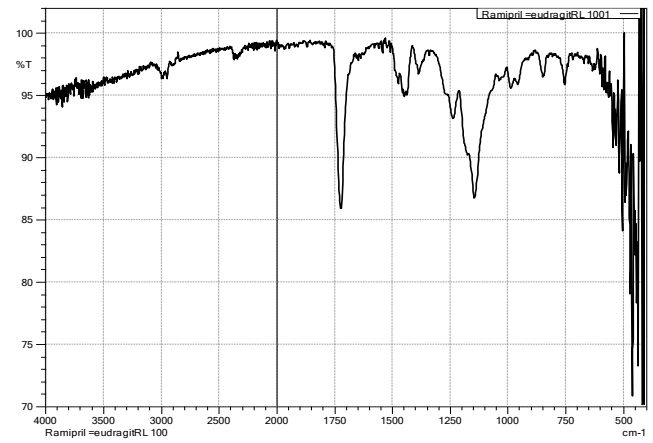

Fig-5: FTIR spectra of pure drug (C) Ramiprileudragit RL100

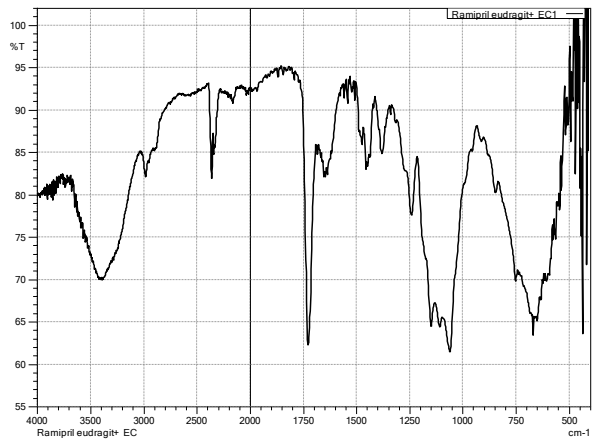

Fig-6: FTIR spectra of pure drug (D) ramipril, ethyl cellulose and eudragit RL100

FTIR spectroscopy was used to examine the drug-polymer interaction for a particular drug combination with chitosan and xanthan gum. Figure 2 shows the obtained FTIR spectra. Ramipril has a large peak at a wavelength of 2936 cm-1, which corresponds to the -CH stretchings for the -CH2 and -CH3 groups. Stretching of C=C is shown by the broad hump seen at 1437 cm-1. Strong absorption peaks at 1720 cm-1 and 1651 cm-1 correspond to -C=O groups, which are indicative of ketone. Alkyl amines have a significant absorption peak at 1022 cm-1 that is related to their C-N. The same ramipril-related characteristics peaks were observed with very minor variations when the drug was combined with ethyl cellulose and EudragitRL100, indicating that there was no drug-polymer interaction and that the drug is stable in the formulations. Drug-loaded microspheres displayed an endothermic peak at 81 and 820C in the DSC study, whereas plain ramipril, microspheres, and drug-loaded microspheres displayed an endothermic peak at 1180C. The endothermic peak of the pure drug ramipril at 114°C and 126°C was caused by the drug melting, however the drug was uniformly spread in an amorphous condition in the microspheres.

Table 6: In-vitro release of Ramipril from F1, F2 and F3 microspheres in intestine fluids.

S.No	Time (hrs)	Square root of time (hrs)	Log Time (hrs)	F1		F2		F3	
				% Drug released	Log % drug released	% Drug released	Log % drug released	% Drug released	Log % drug released
1	0.0	0.000	0.000	0	0	0	0	0	0
2	0.5	0.707	0.301	9.87	0.99	9.97	0.99	9.11	0.95
3	1.0	1.000	0.000	18.78	1.27	16.62	1.22	16.25	1.21
4	1.5	1.225	0.176	25.36	1.40	24.35	1.38	25.72	1.41
5	2.0	1.414	0.301	34.58	1.53	32.71	1.51	31.76	1.50
6	3.0	1.732	0.477	41.65	1.61	39.12	1.59	38.90	1.58
7	4.0	2.000	0.602	47.03	1.67	45.08	1.65	44.40	1.64
8	5.0	2.236	0.698	54.52	1.73	52.96	1.72	51.96	1.71
9	6.0	2.449	0.778	61.86	1.79	60.78	1.78	55.88	1.74
10	7.0	2.646	0.845	66.72	1.82	64.57	1.81	59.50	1.77
11	8.0	2.828	0.903	70.23	1.84	69.66	1.84	63.79	1.80
12	10	3.102	1.000	74.46	1.87	71.18	1.85	67.58	1.82
13	12	3.464	1.079	78.87	1.89	75.32	1.87	73.42	1.86

Table 7: In-vitro release of Ramipril from F4, F5 and F6 microspheres in intestine fluids.

S.No	Time (hrs)	Square root of time (hrs)	Log Time (hrs)	F4		F5		F6	
				% drug released	Log % drug released	% drug released	Log % drug released	% drug released	Log % drug released
1	0.0	0.000	0.000	0	0	0	0	0	0
2	0.5	0.707	0.301	15.03	1.17	16.35	1.21	16.06	1.20
3	1.0	1.000	0.000	19.84	1.29	20.95	1.32	21.23	1.32
4	1.5	1.225	0.176	24.09	1.38	25.66	1.40	26.68	1.42
5	2.0	1.414	0.301	29.96	1.47	28.03	1.44	31.31	1.49
6	3.0	1.732	0.477	34.05	1.53	33.36	1.52	34.36	1.53
7	4.0	2.000	0.602	38.86	1.58	33.74	1.59	37.65	1.57
8	5.0	2.236	0.698	45.67	1.65	45.65	1.65	41.56	1.61
9	6.0	2.449	0.778	50.06	1.69	51.83	1.71	47.63	1.67
10	7.0	2.646	0.845	55.82	1.74	56.69	1.75	54.92	1.73
11	8.0	2.828	0.903	61.56	1.78	63.36	1.80	61.71	1.79
12	10	3.102	1.000	66.36	1.82	68.76	1.83	69.72	1.84
13	12	3.464	1.079	69.93	1.84	73.89	1.86	74.92	1.87

Table 8: In-vitro release of Ramipril from F7.F8.F9 microspheres in intestine fluids.

Sl.No	Time (hrs)	Square root of time (hrs)	Log Time (hrs)	F7		F8		F9	
				% Drug released	Log % Drug released	% Drug released	Log % drug released	% Drug released	Log % drug released
1	0.0	0.000	0.000	0	0	0	0	0	0
2	0.5	0.707	0.301	17.75	1.24	18.02	1.25	17.07	1.23
3	1.0	1.000	0.000	21.62	1.33	23.09	1.36	21.20	1.32
4	1.5	1.225	0.176	26.53	1.42	29.60	1.47	25.96	1.41
5	2.0	1.414	0.301	29.90	1.47	36.50	1.56	29.08	1.46
6	3.0	1.732	0.477	34.56	1.53	43.69	1.64	34.60	1.53
7	4.0	2.000	0.602	39.83	1.60	51.36	1.71	39.52	1.59
8	5.0	2.236	0.698	44.06	1.64	55.64	1.74	44.60	1.64
9	6.0	2.449	0.778	49.50	1.69	59.72	1.77	48.79	1.68
10	7.0	2.646	0.845	56.80	1.75	64.83	1.81	55.93	1.74
11	8.0	2.828	0.903	61.26	1.78	69.03	1.83	59.90	1.77
12	10	3.102	1.000	69.96	1.84	73.43	1.86	65.72	1.81
13	12	3.464	1.079	76.30	1.88	78.56	1.89	71.05	1.85

Table 9: Kinetic values of Ramipril release.

Microspheres	Zero order Equation		First Order Equation		Higuchi Equation		Korsemeyer's Equation	
	N	R	N	R	N	R	N	R
F1	14.33	0.896	64.76	0.306	3.272	0.986	1.028	0.593
F2	14.53	0.891	65.50	0.271	3.549	0.981	1.012	0.602
F3	14.53	0.892	65.65	0.235	2.529	0.987	1.002	0.597
F4	14.43	0.925	65.61	0.190	0.746	0.994	1.056	0.510
F5	13.70	0.941	66.33	0.218	1.635	0.981	1.070	0.499
F6	14.19	0.943	65.83	0.209	0.786	0.982	1.073	0.488
F7	14.66	0.946	65.36	0.220	0.585	0.989	1.086	0.480
F8	19.29	0.882	63.88	0.962	1.722	0.993	1.131	0.474
F9	15.15	0.929	65.20	0.182	0.363	0.995	1.080	0.476

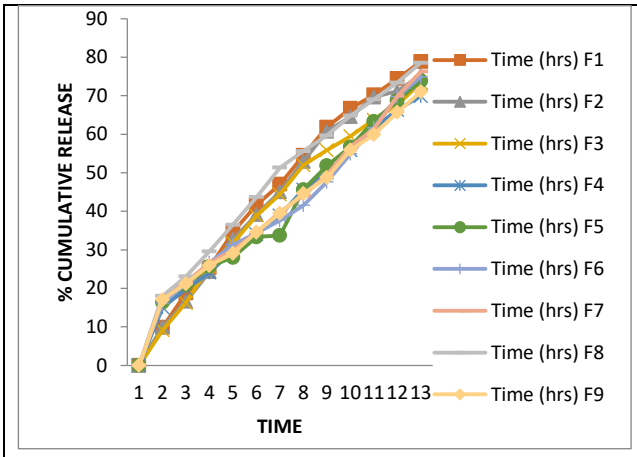

Fig-7:(A) Cumulative % Drug Released Vs Time Plots (Zero Order) of Formulations F1 to F9

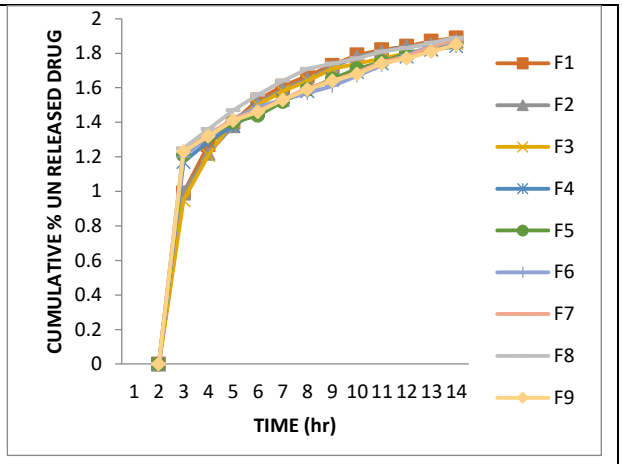

Fig-8: (B) Log cumulative % un released drug Vs time plots (first order) of formulation F1 to F9

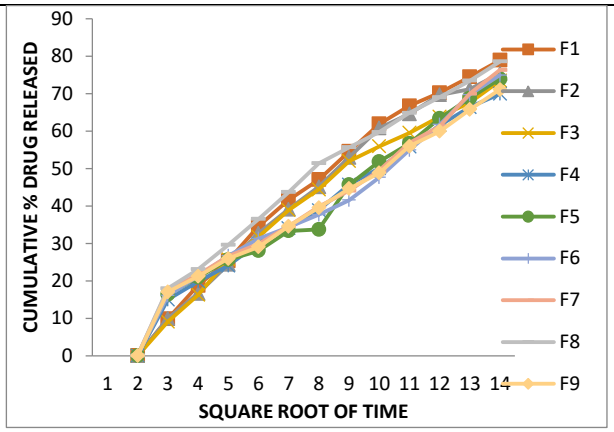

Fig-9: (C) Cumulative % drug released Vs square root of time (higuchi plots) of formulations F1 to F9

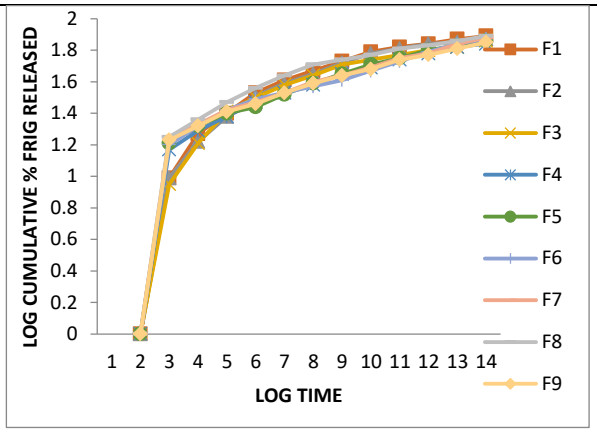

Fig-10: (D) Log cumulative % drug released Vs log time (peppas plots) of formulations F1 to F9

The dissolution rate test apparatus in phosphate buffer was used to conduct the in-vitro drug release investigation (pH 7.4). Ramipril's dissolution characteristics are shown in Figures 7, 8, 9, and 10. Data are shown in Tables 6, Tables 7, and Table 8. For formulations F1, F2, F3, F4, F5, F6, F7, F8, and F9, respectively, 78.87, 75.32, 73.42, 69.93, 73.89, 74.92, 76.30, and 78.56 percent of the medication was released. The results showed that the drug release increased as the concentration of ethyl cellulose increased, decreased as the concentration of EudragitRL100 increased, and increased as the initial drug loading increased. On the other hand, the drug release decreased as the concentration of ethyl cellulose and EudragitRL100 increased. We observed that stirring time and speed had an impact on the amount of drug released; when the stirring speed was increased from 500 rpm to 800 rpm, the amount of drug released rose, whereas the amount of drug released reduced as the stirring duration was increased.

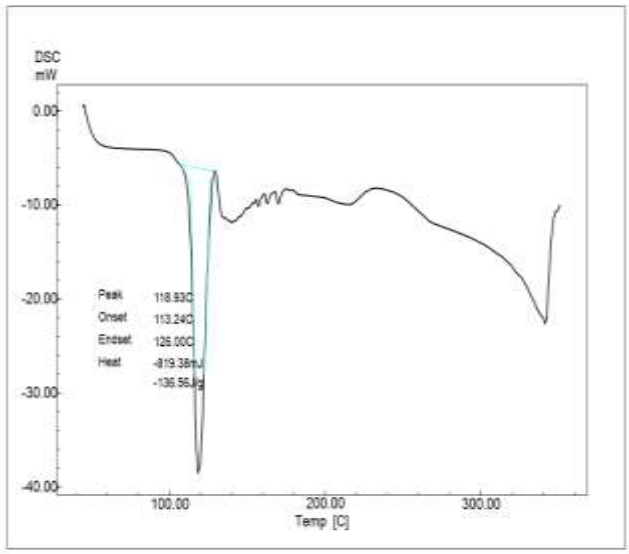

Fig-11: (A) DSC Thermograms of ramipril

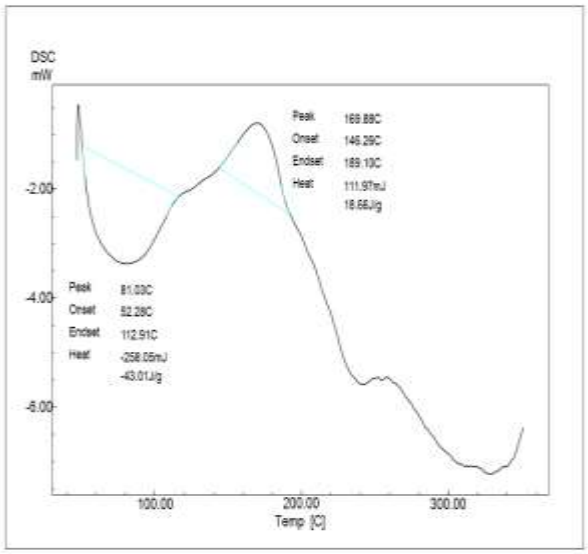

Fig-12: (B) DSC Ramipril, Ethyl cellulose

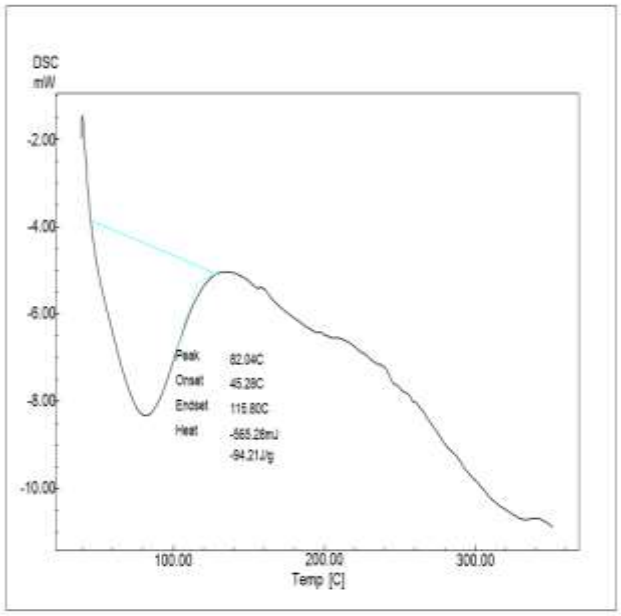

Fig-13: (C) DSC Ramiprileudragit RL100

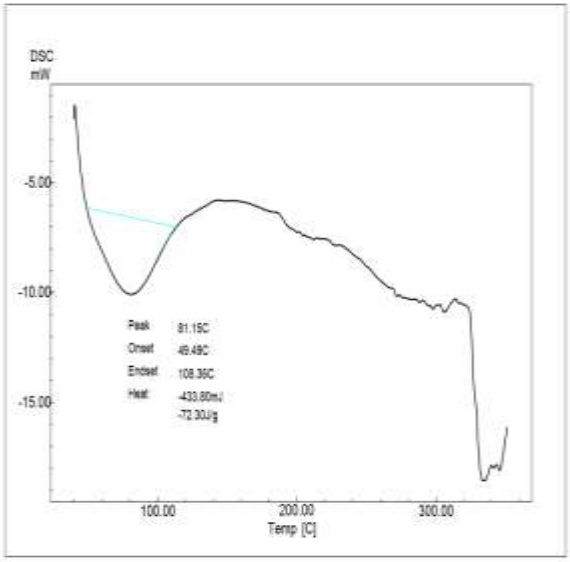

Fig-14: (D) DSC Ramipril, Ethyl cellulose and Eudragit RL100

The release data were fitted using the Higuchi, Korsemeyer, and zero order release equations, and the Peppas equation was used to determine the drug release mechanism. The values are displayed in Table-9.

CONCLUSION:

These results indicate that a biocompatible polymer such as EudragitRL100 and ethyl cellulose can be used to create an effective Ramipril microsphere with a high percentage of entrapment efficiency and a workable yield. The examination of particle size revealed that the particles had good flow characteristics and ranged in size from 25.7 to 49.2 m. Studies have produced encouraging results, and in-vitro release demonstrates that release from the microsphere is successfully delayed for more than 12 hours. Additionally, there is room for pharmacokinetic testing in experimental animals.

SUMMARY:

In the current work, an effort was undertaken to create and assess Ramipril microspheres using the solvent evaporation method from EudragitRL100 and ethyl cellulose. The produced microspheres were examined for particle size analysis, drug entrapment effectiveness, and in-vitro release after being characterized by FTIR and DSC. The smoothness of the produced microspheres' surfaces is substantially influenced by the polymer content. The microsphere's drug entrapment efficiency ranged from 94.02 to 68.07 percent, and its size ranged from 25.7 to 49.2µm. The in-vitro drug release demonstrated that the physiological condition of the stomach and intestines allowed for the maximal quantity of drug release. The DSC thermogram demonstrated that the formulation's medication is equally diffused at the molecular level. There is no interaction between the medication and polymer, according to the IR spectra. The non-Fickian conveyance of the drug release was followed by the drug release mechanism.

CONFLICT OF INTERESTS

The authors declare that no financial or commercial ties that might be viewed as creating a conflict of interest existed throughout the research.

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