RESEARCH ARTICLE

Evaluation of Insulin Loaded Microspheres for Oral Delivery

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ABSTRACT

Microsphere-based colon-specific medication delivery devices should improve bioactive chemical administration and residence periods. In the first step, insulin microspheres were made using Eudragit RL 100 and L-100 by quasi-emulsion solvent diffusion. Microspheres were made since prior research showed that colon tissue macrophages could take up drug carrier systems with a molecular weight of 956 m or less. The uptake process allows accurate medication delivery to the specified site. Microspheres' longer residence time than conventional drug delivery methods may allow dosage reduction and therapeutic efficacy. Because microspheres are permeable, they may be compacted and used to make stronger tablets. Thus, the CPDRS1 formulation performs well, enabling insulin delivery via an anti-diabetic microsphere. Drug-polymer ratio affects microsphere size and form. Variations in emulsifying agent amounts affect microsphere sizes and manufacturing yield. Using appropriate polymer and emulsification agent concentrations improves insulin-loaded Eudrajit L microsphere (Eudrajit RL) formulation and manufacturing yield.

Keywords: Evaluation, Insulin, Oral Delivery, Microspheres.

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INTRODUCTION

Numerous pharmacological delivery techniques are now accessible for the management of diabetes. While the regular use of injections may elicit concern among parents, the constant utilization of the drug often offers as substantiation for its efficacious therapeutic outcomes. The current research endeavor set out to investigate this issue and offer a possible solution. The hypothesis was posited that the use of colon-specific microspheres as carriers for medication delivery might enhance the efficacy of identifying bioactive compounds and extend their duration of action. The degradation of insulin occurs rapidly in stomach as a result of presence of proteolytic enzymes and acidic conditions. Advancement of the "Insulin tablet" has hitherto faced two notable obstacles: the absence of a dedicated peptide carrier mechanism inside the gastric environment and the intricacies linked to the process of digestion. The investigation of insulin encapsulation in microspheres is now underway as a possible strategy to bypass the activity of these enzymes and traverse the intestinal barrier. It is crucial to acknowledge, however, that these inquiries are now in their early phases.[1,2]

Currently, Provalis is engaged in the development of an oral drug mostly comprised of insulin. The methodology entails the integration of insulin into the aqueous phase of an oil-and-water microemulsion, while cholesterol, lecithin, and non-esterified fatty acids are suspended within the oil phase. Medicine polymer conjugate is synthesized by chemical conjugation of insulin with low molecular weight polymers inside the Nobex oral insulin system. Currently, the study is at the phase II level in the United States of America. There have been recent reports suggesting that a team of chemical engineers affiliated with Purdue University in the United States has successfully created a polymer that shows promise in improving the delivery of insulin inside the stomach environment. The insulin molecule is entrapped inside the polymer's acidic environment by adopting a small spherical configuration. The insulin-releasing polymer experiences a period of expansion lasting thirty minutes upon exposure to the alkaline conditions inside the colon. The absorption rate and amount of insulin are still unclear, despite the shown efficacy of the tablet in canines and rodents. Furthermore, a significant proportion of 85% is wasted. The purpose of this research is to create and evaluate microsphere-based tablet formulations that are optimal for colon-targeted distribution.[3-5]

During first stage of insulin microsphere manufacturing, the quasi-emulsion solvent diffusion technique was used Eudragit RL 100 and Eudragit L100. The primary motivation for the advancement of microspheres is to enhance the ability of macrophages in colon tissue to effectively uptake drug carrier systems by reducing their size to 200 µm. This enables the precise and focused delivery of drugs to their designated sites. In contrast to contemporary methodologies for drug

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administration, microspheres exhibit an extended duration of presence, hence possibly facilitating a decrease in dose and augmenting therapeutic effectiveness.[6] Furthermore, the generation of these particles was impacted by the matrix-like arrangement of the microspheres and their ability to be compacted into tablets possessing remarkable mechanical robustness. Subsequently, the process of direct compression was used to produce microsphere core tablets, which were then subjected to compression with a blend of pectin and hydroxypropyl methylcellulose (HPMC). The choice of the research issue was based on the process by which colonic bacteria in the colon break down pectin. The experimental findings indicated that adding HPMC to tablet coating led to an enhancement in mechanical strength and strengthened the structural integrity of the coating in the jejunum of the gastrointestinal system.[7]

MATERIALS AND METHODS

Materials

All materials were provided by Astron Research Limited, Ahmedabad, India: human insulin (Abbott India Ltd), methacrylic acid copolymer (Eudrajit L 100 & Eudrajit RL 100), and polysorbate 20. Polyvinyl pyrrolidone and potassium dihydrogen phosphate were purchased from Astron Research Limited, which is situated close to Ahmedabad. All of the chemicals and reagents used were of analytical quality, and the solvents employed were of HPLC grade

Methods

Optimization of formulation

Biodegradable microspheres are made up of proteins or manmade polymers and have a particle size of less than 200 μm, which is a good particle size. Small, spherical particles with dimensions between one micrometer and one thousand micrometers are known as microspheres. There is a type of matter called microspheres, which are also sometimes called microparticles. When making microspheres, a broad variety of substances, both synthetic and natural, can be utilized.[8] Microsponges refer to polymeric delivery methods that are comprised of porous microspheres. These particles possess a sponge-like structure, characterized by their small size and spherical shape, together with a wide porous surface. Moreover, it is possible for them to augment stability, mitigate negative consequences, and positively alter the discharge of medicine. Microsponge technology provides a diverse method for administering medicine, owing to its several advantageous characteristics. Microsponge Systems are constructed using a small microsphere made of polymer material that has the potential to capture or hold a wide range of substances. Subsequently, the microspheres have the potential to be integrated into an already existing medium, such as a powder, emulsion, lotion, or liquid. In general, it is customary for the surface of the spheroid to be punctured in order to facilitate a continual departure of materials.[9] Microsponges, characterized by their porosity nature and composition of polymeric microspheres, are mostly used in topical applications. However, there has been a recent emergence of their utilization in oral administration as well. The main roles of microsponges include augmenting stability, minimizing the incidence of side effects, regulating drug release, and effectively delivering a low dose of a pharmaceutical active ingredient.[10]

Characterization of microspheres

- *Determination of encapsulation efficiency*

The efficiency of insulin microspheres in drug entrapment was assessed by the accurate measurement of 50 mg of microspheres, followed by complete pulverization using a glass mortar and pestle. After being suspended in a hydrochloric acid buffer solution with a pH of 1.2, the microspheres were left undisturbed for a duration of 24 hours. The spectrophotometric determination of insulin concentration in the filtrate was conducted at a wavelength of 276 nm using a UV after appropriate dilution was performed.[11,12]

- *Particle size analysis*

Our optical microscopes were fitted with ocular and stage micrometers, which allowed us to measure each microsphere precisely. Fifty microspheres' sizes were stochastically analyzed using an optical microscope. We were able to find the average microsphere particle size by dividing the total microsphere size by the total number of microspheres.[13]

- *Zeta potential*

Measurements of the Zeta potential were taken using the Malvern Zetasizer, a laser Doppler anemometry-based analyzer that can do multiple angle particle electrophoresis analysis (DTS Ver. 4.10, Malvern Instruments, Malvern, UK). The determination of the $ potential was carried out by using the Helmholtz-Smoluchowski formula and utilizing the electrophoretic mobility of the nanoparticles. The Zetasizer 4.1 application was used for all computational tasks.[14]

- *Scanning electron microscopy analysis*

The microsphere samples' surface morphology and form were examined using a scanning electron microscope (SEM). Clusters of microspheres were seen to be present on double-sided carbon dust. These microspheres were then affixed to a sample carrier consisting of nine metal segments using double adhesive tape. The sample carrier, which had a cylindrical form, had a diameter of 10 mm and a weight of 5 mm. AU-Pd (Gold Platinum) combination was subjected to sputter coating, resulting in a thickness of 50 nm. This process took place under a vacuum environment with a pressure of 9100 m torr. Images of samples were captured using a 5–15 kilovolt electron beam. The microscope pictures were obtained at a suitable magnification in order to accurately represent the surface topography.[15]

Tablet formulations

- *Preparation of colon specific tablet formulations*

Core tablets were produced using the process of direct compaction, utilizing magnesium stearate, Na-CMC, and

microspheres having a dosage of 40 mg of insulin. The tablet components underwent compression using an 8-station tablet press (Kambert Machinery, D-8) after being weighed, mixed, and squeezed for 15 minutes using 12 mm round flat inserts. The tables provided in this study provide the compositions of the primary tablets of the medication, which include eudragit RL-100 and eudragit L-100. Table 1 displays the formulation of the primary tablets including eudragit RL-100, while Table 2 presents the formulation of the primary tablets containing eudragit L-100. During the compression coating process, the tablet's external layer consisted of a 200 mg combination of pectin and hydroxypropyl methylcellulose (HPMC) in an 80:20 ratios. After the incorporation of 50% of the coating material, the core tablet was placed near the geometric center of the die cavity. Subsequently, the residual coating material was integrated. The process of encircling the central tablet with flat tools measuring 16 mm in diameter was achieved by the use of the same tableting technique.[16]

Evaluation of core and coated tablets

- *Weight variation*

To perform the weight variation test, 20 tablets were weighed both singly and in a group. The mean weight was then calculated, and the weight of each tablet was compared to that value.[17]

- *Thickness*

The measurement of tablet thickness was conducted with vernier calipers. In order to achieve the intended objective, the thickness of ten tablets was measured separately.

- *Hardness*

The hardness of the tablet was assessed using a Monsanto hardness tester. The testing apparatus comprises a cylindrical container housing a spring with compressible properties, which is secured in place by two pistons. The bottom plunger is brought into contact with the tablet, and an initial measurement is recorded as zero.[18]

RESULT AND DISCUSSION

Characterization of Microspheres

Quasi-emulsion solvent diffusion technique was selected as an approach for the production of microspheres because of its ease of execution and capacity to provide reliable outcomes. In addition, one of the advantages is the capability to protect against the potentially disastrous consequences of solvent poisoning. Drug and polymer were mixed together in a number of different proportions to produce the various microsphere formulations, including 5:1, 4:1, 3.33:1, and 2.86:1. In each of the formulations, amounts of polymer (200 mg), dichloromethane (5 mL), and PVA (0.5% w/v) were kept at same level throughout the whole process. In order to create the microsphere formulations, a mechanical stirrer was used for 8 hours at a speed of 500 rpm for the Eudragit RL-100-based microspheres and 1000 rpm for the Eudragit L-100-based microspheres. Microspheres of various formulations, denoted by the numbers SP1, SP2, SP3, and SP4, were created by mixing the medication Eudragit RL-100 in varying proportions, namely 5:1, 4:1, 3.33:1, and 2.86:1, respectively. In addition, formulations of PS1, PS2, PS3, and PS4 were created by using ratios of Eudragit L100: medication that were 5:1, 4:1, 3.33:1, and 2.86:1, respectively. In the study, the researchers looked at how the properties of microspheres were affected by a number of variables, including the ratio of medicine to polymer, the velocity of stirring, the volume of the internal phase, and the amount of emulsifying agent (Table 3).

Table 1: Core tablet composition for eudragit RL100-based microspheres

Core tablet formulation codes	*Microspheres formulations (mg) in Each*				*Na-CMC (mg)*	*Magnesium stearate (mg)*
	SP1	*SP2*	*SP3*	*SP4*		
CPDRS1	60.0	-	-	-	32	8
CPDRS2	-	55.0	-	-	87	8
CPDRS3	-	-	50.0	-	102	8
CPDRS4	-	-	-	50.0	112	8

50 tablets for each formulation

Table 2: Core tablet composition for eudragit L 100-based microspheres

Core tablet formulation codes	*Microspheres formulations (mg) in each*				*Na-CMC (mg)*	*Magnesium stearate (mg)*
	PS1	*PS2*	*PS3*	*PS4*		
CPDS1	65.0	-	-	-	37	8
CPDS2	-	60.0	-	-	82	8
CPDS3	-	-	55.0	-	102	8
CPDS4	-	-	-	50.0	117	8

No. of tablets: 50 for each formulation.

Percentage yield

Practical yield and percentage yield were determined after the manufacture of microspheres (Table 4). The observed percentage yield ranged from 80.14 to 92.85%.

Carr's index, angle of repose and Hausner's ratio

The investigation of flow characteristics of microspheres was conducted by using established standard methodologies (Table 5). The experiments were conducted in triplicate, with a sample size of three (n = 3).

FTIR analysis

FTIR spectra were obtained to evaluate the chemical interactions or alterations that took place during the creation of the microsphere. The physical characteristics of the medicine and its formulations with Eudragit RL-100, L-100, SP1-SP4, and PS1-PS4 were recorded and subjected to analysis, along with FTIR spectra of the medication. FTIR spectra of insulin exhibited a discernible stretching band associated with the carbonyl (C=O) functional group at a wavenumber of 1718.45 cm^{-1}, which is consistent with values published in the literature. The FTIR spectra of the two separate microsphere formulations,

Table 3: Characterization of microspheres

Formulation Code	*Evaluation Parameters*				
	Angle of Repose (θ)	*Poured density (gm/cm3)*	*Tapped Density (gm/cm3)*	*Carr's Index (%)*	*Hausners Ratio*
SP1	24.49 ± 1.30	0.48 ± 0.01	0.53 ± 0.01	6.60 ± 0.86	1.06 ± 0.47
SP2	19.46 ± 2.16	0.45 ± 0.08	0.52 ± 0.05	13.46 ± 0.01	1.15 ± 0.33
SP3	25.05 ± 1.97	0.40 ± 0.01	0.41 ± 0.01	2.39 ± 0.05	1.02 ± 0.11
SP4	21.12 ± 1.14	0.38 ± 0.01	0.41 ± 0.01	5.00 ± 0.01	1.07 ± 0.16
PS1	21.41 ± 2.10	0.40 ± 0.01	0.42 ± 0.04	4.68 ± 0.05	1.05 ± 0.06
PS2	18.81 ± 3.15	0.39 ± 0.01	0.41 ± 0.01	4.97 ± 0.09	1.05 ± 0.07
PS3	14.14 ± 1.12	0.35 ± 0.01	0.38 ± 0.01	7.89 ± 0.01	1.08 ± 0.04
PS4	17.12 ± 2.23	0.35 ± 0.01	0.38 ± 0.01	7.90 ± 0.28	1.08 ± 0.11

Mean ± S.D. (n = 3)

Table 4: %yield

Formulation	*Theoretical yield (g)*	*Practical yield (g)*	*% yield (%)*
F1	2.1	1.950	92.85
F2	1.6	1.447	90.43
F3	1.1	1.057	96.09
F4	0.850	0.797	93.76
F5	0.600	0.576	96
F6	0.350	0.280	80.14

Table 5: Standard values of angle of repose, Carr's index and Hausner's ratio

Angle of Repose	*Carr's Index*	*Hausner's Ratio*	*Type of Flow (Inference)*
< 20	5–15	-----	Excellent
20–30	12–16	< 1.25	Good
30–40	18–21	----	Passable
----	23–35	>1.25	Poor
----	33–38	1.25-1.50	Very poor
>40	>40		Extremely poor

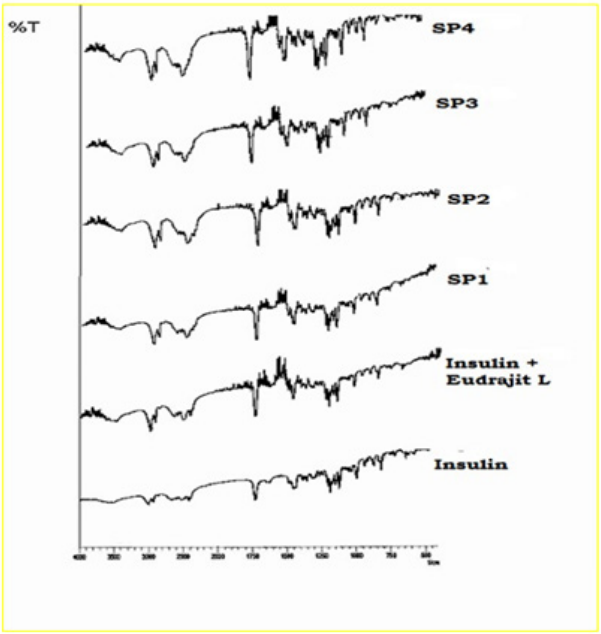

Figure 1: FTIR spectra of insulin, physical mixture of drug & eudragit RL-100, and microsphere formulations SP1–SP4

namely PS1-PS4 and SP1-SP4, displayed unique peaks corresponding to the respective drugs. The findings of this study revealed that there were no observable chemical modifications or interactions that took place throughout the process of microsphere creation. Drug and all excipients included in the formulation of microspheres demonstrated compatibility.[19] To evaluate the chemical interactions or alterations that took place during the development of the microsphere, FTIR spectra were obtained. FTIR spectra of medications, as well as their physical interactions with various polymers and different formulations of the microspheres, were recorded using a Shimadzu Model 8400 FTIR spectrometer. These recordings were made on a potassium bromide disc. FTIR spectra of several formulations of Microspheres are shown in Figures 1 and 2.

Drug content

Between 81 and 87.35% weight by weight of the substance was detected (Table 6 and Figure 3).

Table 6: Drug content

Formulation	*Drug content (%) w/w*
F_1	81.76
F_2	85.75
F_3	87
F_4	83.20
F_5	87.35
F_6	82.84

Entrapment efficiency

Ten milligrams of insulin microspheres were introduced into a volumetric flask. An amount of acetonitrile was introduced into the volumetric flask and agitated using a vortex mixer to facilitate the dissolution of the microspheres. Acetonitrile was used to further dilute the solution to about 80% of its total volume, followed by sonication for a duration of 15 minutes.

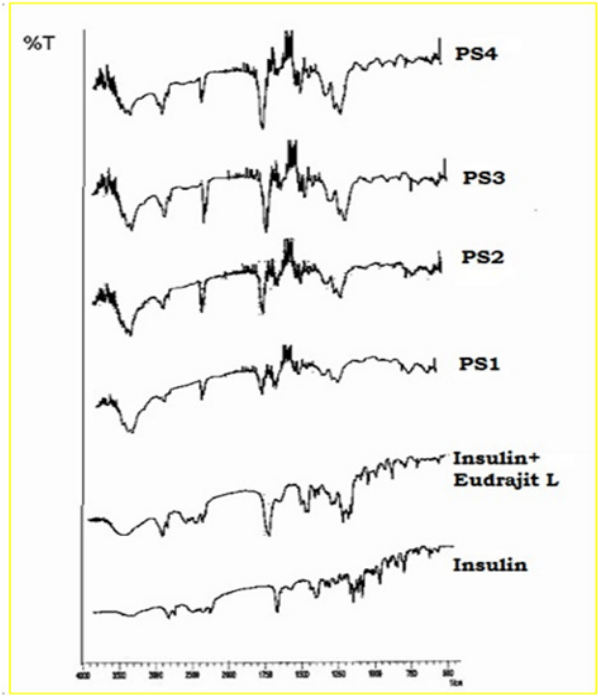

Figure 2: FTIR spectra of insulin, physical mixture of drug & eudragit L-100, and microsphere formulations PS1–PS4

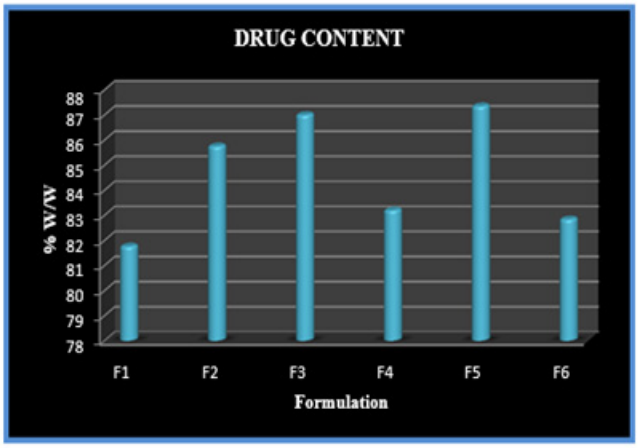

Figure 3: Drug content

The later fraction of the volume was comprised of acetonitrile. If deemed essential, the specimen underwent filtration using a syringe filter made of polyvinylidene fluoride with a pore size of 0.45 mm. Subsequently, it was diluted with acetonitrile to achieve a concentration falling within the limits of the standard curve before being subjected to high-performance liquid chromatography (HPLC) analysis.[20] The drug loading percentages were determined using triplicate sets, and the average value together with the standard deviation (SD) was reported as the outcome. The data pertaining to the entrapment effectiveness of microspheres is shown in Table 7 and Figure 4.

All microspheres had an entrapment efficiency percentage between 81 and 87.5%. F5 is the formulation with the best entrapment efficiency.

Table 7: Entrapment efficiency

Formulation	*Entrapment efficiency (%)*
F_1	81
F_2	86.25
F_3	87
F_4	83.25
F_5	87.5
F_6	82

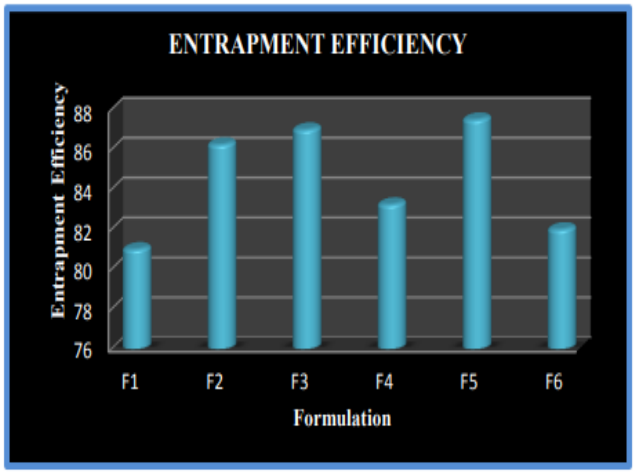

Figure 4: Entrapment efficiency

Differential scanning calorimetric analysis

Differential scanning calorimetric (DSC) is a technique that may be used to investigate possible interactions between pharmaceutical chemicals and other compounds present in microspheres. Additionally, DSC can provide valuable insights into the physical characteristics of medications themselves. A thermal examination was performed using DSC on various medications, physical mixtures of drugs with different polymers, and formulations of microspheres. The Shimadzu DSC-60 Thermal Analyzer was used for this purpose.[21] Two samples, each weighing two mg, were enclosed in metal canisters and fastened securely. Every specimen underwent a temperature rise of 20°C every minute, starting at 40 and to 430°C. DSC thermograms of different compositions of microspheres are shown in Figures 5 and 6.

DSC studies were conducted to determine lack of any chemical interactions between a drug and other components inside microspheres. The Thermograms clearly showed distinct endothermic peaks for medications, such as insulin, which provided as an indicator of the crystalline melting point of the molecule. DSC curve displays the thermal behavior of the physical combination, consisting of PS1-PS4 and SP1-SP4. The distinctive peaks of the substance were detected. The findings of the study suggest that there is potential for the coexistence of drugs and polymers. Furthermore, it may be inferred that the medicinal chemicals included in the microspheres remained unaltered despite the methods used during their manufacture.[22]

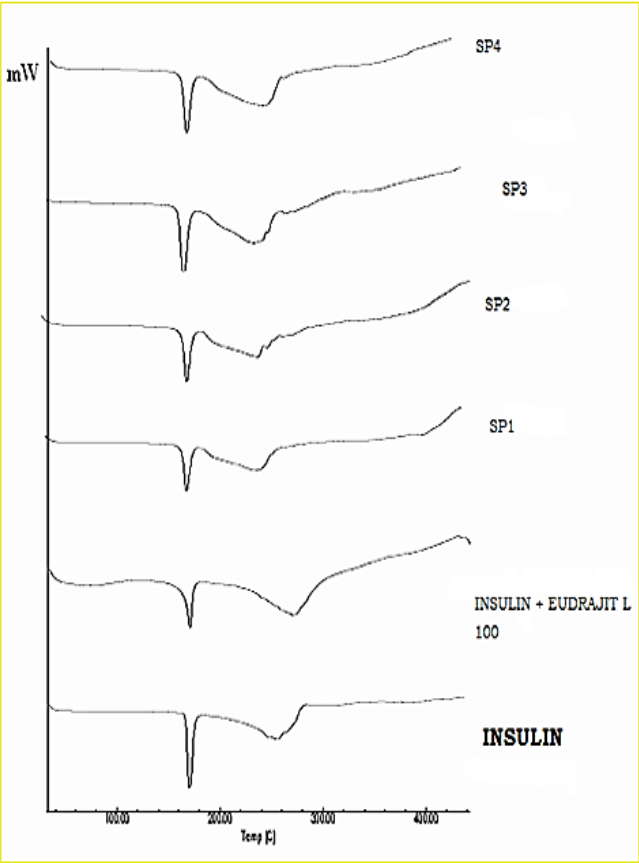

Figure 5: DSC of insulin, physical mixture of drug & eudragit RL-100, and microsphere formulations SP1–SP4

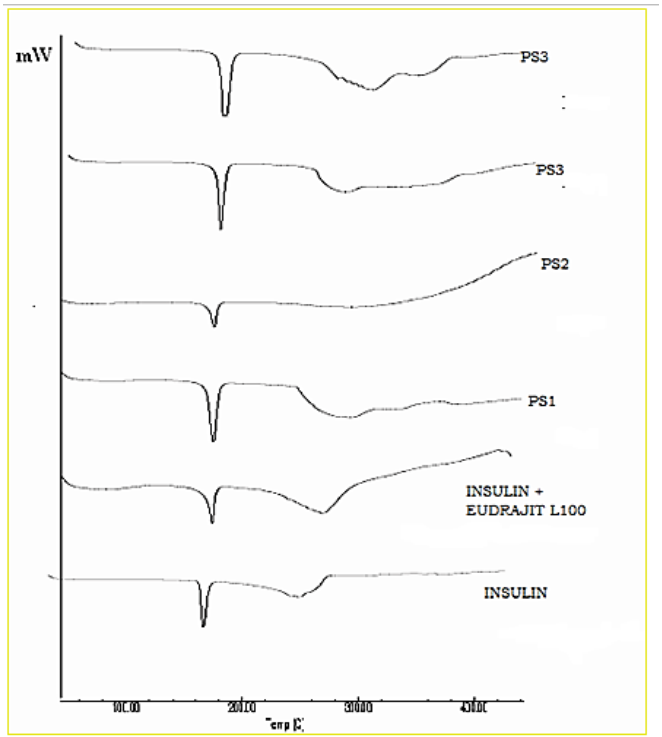

Figure 6: DSC of Insulin, physical mixture of drug & Eudragit L-100, and Microsphere formulations PS1–PS4

Evaluation of Flow Properties

Table 8 contains flow properties related to developed insulin microspheres.

Table 8: Flow properties of insulin microspheres

Formulation	Bulk density (g/mL)	Tapped density (g/mL)	Angle of repose (°)	Compressibility index (%)	Hausner's ratio
F1	0.6 ± 0.154	0.75 ± 1.125	26.46 ± 3.3894	20 ± 1.25	1.25 ± 0.1857
F2	0.625 ± 2.15	0.714 ± 1.84	26.83 ± 0.3412	12.46 ± 2.01	1.142 ± 0.2103
F3	0.7 ± 1.267	0.8 ± 2.54	24.61 ± 1.456	12.5 ± 1.01	1.142 ± 0.9577
F4	0.627 ± 0.145	0.718 ± 0.115	28.82 ± 1.270	12.47 ± 1.78	1.143 ± 0.1245
F5	0.7 ± 2.12	0.777 ± 0.255	26.2 ± 2.8202	9.09 ± 1.23	1.11 ± 0.2134
F6	0.71 ± 0.850	0.83 ± 1.12	25.54 ± 2.3810	12.36 ± 0.9997	1.141 ± 0.3988

Table 9: Characterization of core tablets

Core Tablets	*Evaluation parameters*				
	Average Weight mg ± SD (n = 20)	*Average Thickness mm ± SD (n = 10)*	*Hardness Kg/cm^2 ± SD (n = 5)*	*Friability % ± SD (n = 10)*	*Drug Content % ± SD (n = 5) Insulin*
CPDRS1	452.21 ± 0.13	2.8 ± 0.2	4.8 ± 0.2	0.24 ± 0.06	101.17 ± 0.15
CPDRS2	439.84 ± 0.12	2.7 ± 0.4	4.2 ± 0.2	0.38 ± 0.10	102.29 ± 0.35
CPDRS3	437.61 ± 0.19	2.6 ± 0.1	4.4 ± 0.1	0.47 ± 0.13	99.96 ± 0.25
CPDRS4	469.84 ± 0.25	3.1 ± 0.2	4.5 ± 0.2	0.49 ± 0.07	98.34 ± 0.20
CPDS1	448.68 ± 0.41	2.8 ± 0.4	4.8 ± 0.3	0.43 ± 0.17	96.45 ± 0.45
CPDS2	457.16 ± 0.19	2.9 ± 0.1	4.1 ± 0.2	0.47 ± 0.12	97.44 ± 0.23
CPDS3	461.21 ± 0.32	2.4 ± 0.3	4.6 ± 0.3	0.79 ± 0.15	98.20 ± 0.39
CPDS4	442.21 ± 0.73	2.8 ± 0.2	4.4 ± 0.5	0.23. ± 0.11	97.98 ± 0.18

Table 10: Characterization of coated tablets

Coated tablets	*Evaluation parameters*			
	Average weight mg ± SD (n = 20)	*Average thickness mm ± SD (n = 10)*	*Hardness Kg/cm^2 ± SD (n = 5)*	*Friability % ± SD (n = 10)*
CPDRS1	652.26 ± 0.21	3.6 ± 0.3	6.2 ± 0.5	0.56 ± 0.22
CPDRS2	639.56 ± 0.10	3.4 ± 0.3	6.1 ± 0.3	0.78 ± 0.31
CPDRS3	636.67 ± 0.13	3.4 ± 0.2	5.9 ± 0.2	0.79 ± 0.24
CPDRS4	670.46 ± 0.35	3.6 ± 0.3	6.6 ± 0.3	0.73 ± 0.19
CPDS1	648.32 ± 0.31	3.8 ± 0.2	6.5 ± 0.3	0.53 ± 0.27
CPDS2	653.79 ± 0.24	3.6 ± 0.1	6.2 ± 0.1	0.72 ± 0.39
CPDS3	663.28 ± 0.29	3.7 ± 0.4	6.8 ± 0.1	0.41 ± 0.23
CPDS4	649.45 ± 0.14	3.49 ± 0.01	5.8 ± 0.4	0.78. ± 0.19

Evaluation of Core and Coated Tablets

The core tablets were produced via the direct compression method. The pills were composed of magnesium stearate, sodium carboxymethylcellulose (Na-CMC), and microspheres carrying insulin at dosages of 40 mg and 250 mg. The evaluation included drug content, thickness, weight fluctuation, hardness, and friability of the core tablets. The mean weight of the CPDRS1-CPDRS4 and CPDS1-CPDS4 core tablet formulations was found to range from 438 to 470 mg and 442 to 461 mg, respectively. Recorded fluctuations in weight did not surpass 5% and were consistent with the standards outlined in IP (1996). The observed range of hardness values (4.1–4.8 kg/cm^2) suggests that the material exhibited satisfactory mechanical strength. The study observed a range of 0.23 to 0.79% in the friability of the principal tablet formulations. The friability, which had a value below 1%, served as a sign of good mechanical resistance. The measured thickness exhibited a range between 2.76 and 3.01 mm. The tablets underwent compression and were thereafter coated with a mixture consisting of 80% pectin and 20% hydroxypropyl methylcellulose (HPMC) as an outer layer. Possible differences in thickness, hardness, friability, and weight were checked for in the coated tablet formulations. There was a 637 to 670 mg range for the coated tablet formulation CPDRS1–CPDRS4, and a 648 to 663 mg range for the CPDS1–CPDS4 formulation. The study's weight variation of less than 5% is in agreement with the standards stated by the pharmacopoeial guidelines. The observed hardness values, ranging from 5.8 to 6.8 kg/cm^2, suggest that the material has acceptable mechanical strength. The study observed a range of friability values, ranging from 0.41 to 0.79%, for the basic tablet formulations. The friability, which was shown to be less than 1%, served as a sign of good mechanical resistance. The observed thickness values exhibited a range of 3.40 to 3.67 mm (Tables 9 and 10).

CONCLUSION

Therefore, it can be concluded that the CPDRS1 formulation yields outstanding outcomes, facilitating the effective administration of insulin in the shape of an anti-diabetic microsphere. The present study investigates the impact of varying quantities of emulsifying agents on both the size of microspheres and the manufacturing yield. Additionally, the study examines the influence of drug-polymer ratio on microsphere size. Optimization of insulin-loaded Eudrajit L microspheres (Eudrajit RL) formulation and yield is achieved by the determination of the ideal concentrations of polymer and emulsification agent. Therefore, the oral insulin system offers numerous key benefits, including easy access to materials, straightforward preparation, efficient encapsulation, and continuous release of medicine over extended periods of time. The modified version of insulin exhibits many advantageous characteristics when compared to regular insulin. These include an extended half-life, lower likelihood of triggering an immune response in the gastrointestinal tract, enhanced absorption, decreased potential for stimulating cell division, equivalent effectiveness in terms of pharmacological action, preservation of a safe profile, and a greater ability to be cleared from the body as compared to regular insulin.

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