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Development And Characterization Of Floating Microspheres Of Losartan Potassium

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ABSTRACT

Objectives: The objectives of this study to formulate the floating microspheres of Losartan Potassium in order to achieve a better dissolution rate which would further help in enhancing oral bioavailability.

Materials method: Preparation of Floating Microspheres by Emulsification solvent diffusion techniques, Evaluation of various properties of floating microspheres.

Result and discussion: Emulsification solvent diffusion technology was built and tested using Glycerolmonstearate, Ethanol, and Chloromethane polymers. Losartan potassium microparticles. LP1 to LP9 were partitioned. FT-IR was used to investigate the drug-excipient interaction. The functional group region of the pure drug spectrum showed waves 615.29cm^{-1}, 754.17cm^{-1}, 1095.57cm^{-1}, 1205.01cm^{-1}, 1498.69cm^{-1}, 1618.28cm^{-1},1676.14cm^{-1}, 3415.93cm^{-1}. The spectral peak for functional group stretching vibrations is 615.29 cm^{-1} (OH, CH, CH_3, CH_2OH). In the spectrum of Losartan microparticles, there are no interactions between the medicine and its excipients. Some formulations have limited yields due to microsphere loss after washing.

Conclusion: The polymer-to-drug ratio also affects particle size and drug release pattern. LP2 and LP9 have higher drug entrapment efficiency than LP1 to LP9. LP9 loaded 96% faster than F8. It produced large percentages, with LP9 yielding 96%. The flow properties of LP1–LP9 were measured. Carr's index and angle of repose measurements revealed no flow quality issues. 96.89 percent of the formulations showed progressive and sustained in vitro drug release over 8 hours. Losartan potassium microparticles were assessed for stability at 40°C, 2°C, and 75% RH. The drug's solubility and colour did not change in an in vitro drug release test.

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Keywords: Losartan potassium, Floating microspheres, Drug release, Emulsification solvent diffusion technique (ESDT).

INTRODUCTION

Dosage forms can be kept in the stomach for a longer period of time using a variety of methods. Floatation systems, high density systems, mucoadhesive systems, magnetic systems, unfoldable, extendible or swellable systems, and superporous hydrogel systems have all been utilised to keep dosage forms in the stomach so that the gastric residence time (GRT) might be lengthened. Dosage forms can be improved through floating drug delivery systems (FDDS) or hydrodynamically balanced systems (HBS), among other ways[1]. There are systems with a single unit and systems with numerous units. Because the single unit floating systems feature an all-or-nothing emptying mechanism, the gastrointestinal transit time might vary greatly. Gastroretentive drug delivery system (GRDDS) can remain in the gastric region for several hours and hence significantly prolong the gastric residence time of drugs. Prolonged gastric retention improves bioavailability, reduces drug waste, and improves solubility of drugs that are less soluble in a high pH environment that have narrow therapeutic window, by this way they prolong dosing interval. It has applications also for local drug delivery to the stomach and proximal small intestines[2]. With microspheres (e.g., multiple unit particle dosage forms), on the other hand, there is less fluctuation in absorption and less danger of local irritation because they move uniformly through the digestive tract (GIT) to avoid the vagaries of gastric emptying and give a customizable release. Microspheres with a lower density than gastrointestinal fluids have recently been used[3]. To create the floating microspheres, emulsion solvent diffusion evaporation techniques were used using a variety of different polymer mixtures. Microspheres are solid, nearly spherical particles ranging in diameter from 1 to 1000 nm in diameter, with a core of drug and a totally outside layer of polymers as a coating material, which can be described as a microsphere. Biodegradable synthetic polymer and modified natural products, such as starches, gums, proteins, fats, and waxes, make up these materials, which are polymeric or waxy in nature. An effective antihypertensive medication, losartan potassium undergoes hepatic first-pass metabolism before reaching the bloodstream[4-6]. Maintaining plasma drug concentrations requires a three- to four-hour half-life (t1/2) of 1.5-2 hours. Controlled drug release is therefore required. If you want to increase therapeutic efficacy, reduce dosage frequency, and enhance half-life and bioavailability then an alternative delivery mechanism is needed[7]. Because of this, a fresh formulation must be developed that releases the medicine over a longer period of time. As a result, floating microspheres containing losartan potassium could be a promising treatment option for hypertension. This work used emulsification solvent diffusion to create microspheres. Losartan potassium microparticles were generated by mixing Eudragit RS and RL 100 with ethanol and dichloromethane[8]. Then the polymer solution got losartan potassium. Sodium lauryl sulphate (0.1%) was added to the liquid drop by drop while stirring. After 30 minutes of 900 rpm swirling, the organic solvent had evaporated. Solvent evaporation transformed the dispersed drug and polymer into microparticles that may be used in drug delivery[9]. A filtration process dried the microparticles for 24 hours at room temperature after four to five washes with distilled water. The drug-loaded microparticles were made in nine batches utilising polymers with varied ratios and formulation codes LP1 through LP9.

MATERIALS AND METHOD

Table 1 : Various batches of floating microspheres are created.

S.NO	API ingredients	Batch formulation								
		LP1	**LP2**	**LP3**	**LP4**	**LP5**	**LP6**	**LP7**	**LP8**	**LP9**
1.	Losartan potassium	0.6 g	0.6 g	0. 6g	0.6 g	0.6 g	0.6g	0.6 g	0.6 g	0.6 g
2.	Glycerolmonostearate	0.6 g	0.5 g	0.2 g	0.2g	0.4g	-	3 g	-	2 g
3.	Eudragit RL 100	-	-	-	-	-	-	-	3 g	3 g
4.	Eudragit RS 100	-	-	-	-	-	-	0.6 g	-	-
5.	Ethanol	20 ml	20 ml	20 ml	20 ml	20 ml	20 ml	20 ml	20 ml	20 ml
6.	Dichloromethane	20 ml	20 ml	20 ml	20 ml	20 ml	20 ml	20 ml	20 ml	20 ml
7.	Sodium lauryl sulphate (0.1%)	100/ ml	100/ ml	100/ ml	100/ ml	100/ ml	100/ ml	100/ ml	100/ ml	100 / ml

Developing a stock solution

To obtain a concentration of 100 g/ml, phosphate - buffered pH 7.4 was used to dissolve and dilute 10 mg of a precisely weighed medication.

Process of preparing a test solution

We found quantities of 5, 10, 15, 20, 25, and 30 g/ml in phosphate buffer dilute stocks. The UV systronics-2202 spectrophotometer was used to measure absorbance at 360 nm. On a standard curve, the X-axis showed concentration and the Y-axis showed absorbance.

Analysis of Losartan Potassium Microparticles

Determined using a UV spectrophotometer (systronics-2202) 50 mg drug-loaded microspheres extracted in 50 ml chloroform were measured at 360nm.

$$EE\% = \frac{\text{actual drug loading}}{\text{theoretical drug loading}} \times 100\%$$

Buoyancy Test:

Study used a USP dissolution equipment to dissolve microparticles (0.3g) (type II). A 100 RPM paddle fragmented material for eight hours. Microparticles were collected from the air and the seabed. It was dried and weighed. the mass of flapping microparticles divided by the total mass of flapping microparticles.

$$\text{Buoyancy Equation : } m = \frac{m'\left(1-\frac{d_a}{d_w}\right)}{\left(1-\frac{d_a}{d}\right)}$$

Analysis of particle morphology and size

The particle size was measured optically. A calibrated optical microscope examined the particle size of about 100 samples. SEM was used to determine the microsphere's surface shape (SEM). After being set in individual stabs, the microparticles were sputter coated with gold-palladium.

Swell index:

Swell ability indexes were determined using pH 1.2 and phosphate buffer pH 7.4 at 37.5 0.5°C for 8 hours. In the experiment, drug-loaded microcapsules were removed, filtered, and weighed at intervals of one hour in several test tubes.

$$\text{Swelling index} = \frac{W_s - W_d}{W_d}$$

Micromeritic Characteristics

Angle of Repose

A microsphere flow study was carried out using this technique. The angle of repose of several formulations was measured using a fixed funnel standing method.

Table 2: Angle of repose and flow characteristics

Angle of repose	Flow Properties
<25	Greater
25-30	good
30-40	Poor
>40	Very poor

Two different densities: the bulk density and the tapping density

We used a graduated 10 ml cylinder to determine out the bulk and tapped sample densities. 100 mechanical taps of the sample measured the tap volume and bulk density.

Carr's index

Equation was used to calculate the microparticle Carr's index (CI) or compressibility index (CI).

$$\text{Carr's index (\%)} = \frac{\text{Bulk density} - \text{Tapped density}}{\text{Tapped density}} \times 100$$

Table 3: Relation between % Compressibility and Flowability Ratio of Hausner

% Compressibility Ratio	Flowability Ratio
5-15	Excellent
12-16	Good
18-21	Fair-passable
23-35	Poor
33-38	Very poor
>40	Very very poor

In-vitro dissolution investigation of Losartan potassium

The drug was removed from the microsphere using USPXXIV's rotating basket process. 100 mg of drug-equivalent microparticles were dropped into a rotating basket while the liquid was held at 37°C and spun at 750 rpm. Every hour, a new 10 ml aliquot replaced the old. A UV spectrophotometer estimated drug dosage based on absorbance at 360 nm[11-13].

Infrared spectroscopy using the Fourier transfor

Fig 1: FT-IR Spectra of Losartan potassium

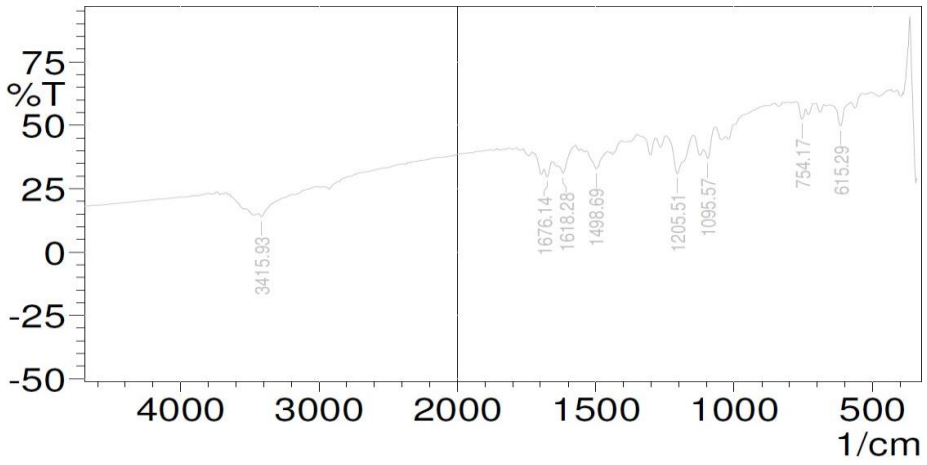


Table 4: FT-IR Spectra of Losartan potassium

S.NO.	PEAK	INTENSITY	CORR. INTENSITY	BASE (H)	BASE (L)	AREA	CORR. AREA
1.	615.19	50.817	9.674	660.02	588.60	19.12	2.53
2.	758.17	51.431	6.03	787.31	750.63	10.301	1.591
3.	1094.57	35.847	7.637	121.6	1166.67	17.671	2.138
4.	1203.51	31.924	16.079	126.764	1247.68	42.16	8.375
5.	1492.69	33.868	7.310	1635.54	1569.76	30.07	3.344
6.	1611.28	32.189	6.01	1735.44	1671.98	29.03	2.12
7.	1674.14	30.693	5.094	1785.69	1758.79	14.424	1.827
8.	340.93	14.933	2.843	3537.95	3288.36	180.438	3.766

Table 5: Losartan Potassium Standard Calibration Curve in a Phosphite Buffer at pH 7.4

Standard graph for Losartan potassium

SNO.	Conc µg/ml	Absobanced
1.	0	0
2.	5	0.072
3.	10	0.141
4.	15	0.222
5.	20	0.275
6.	25	0.350
7.	30	0.422

Figure 2: Losartan potassium standard graph

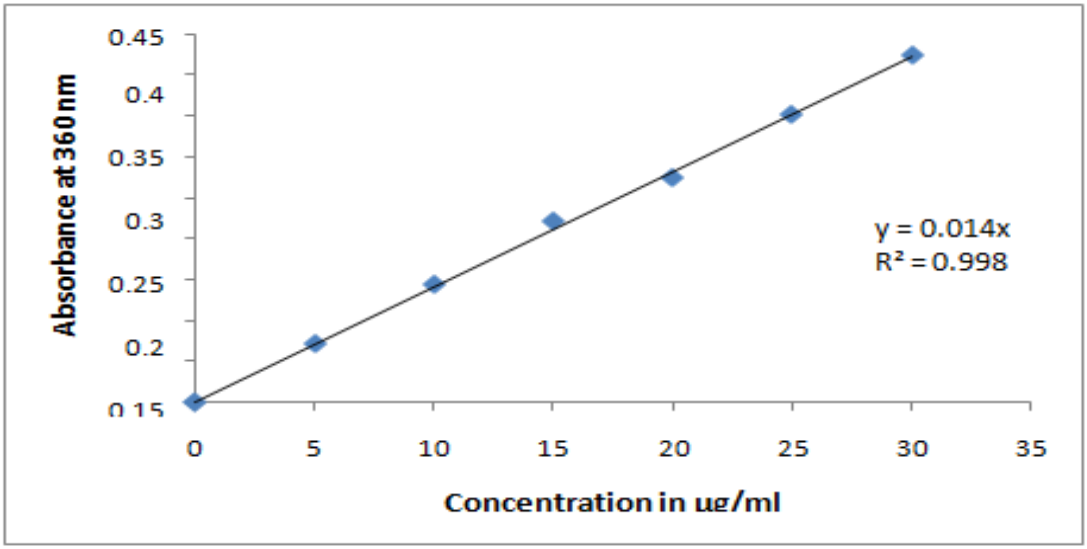


Table 6: Microparticles of Losartan potassium: Yield %

S.NO	FORMULATION BATCH	YEILD %
1.	LP1	44
2.	LP2	94
3.	LP3	52
4.	LP4	64
5.	LP5	71
6.	LP6	74
7.	LP7	76
8.	LP8	81
9.	LP9	95

Figure 3: % yield of Losartan Potassium Microparticles

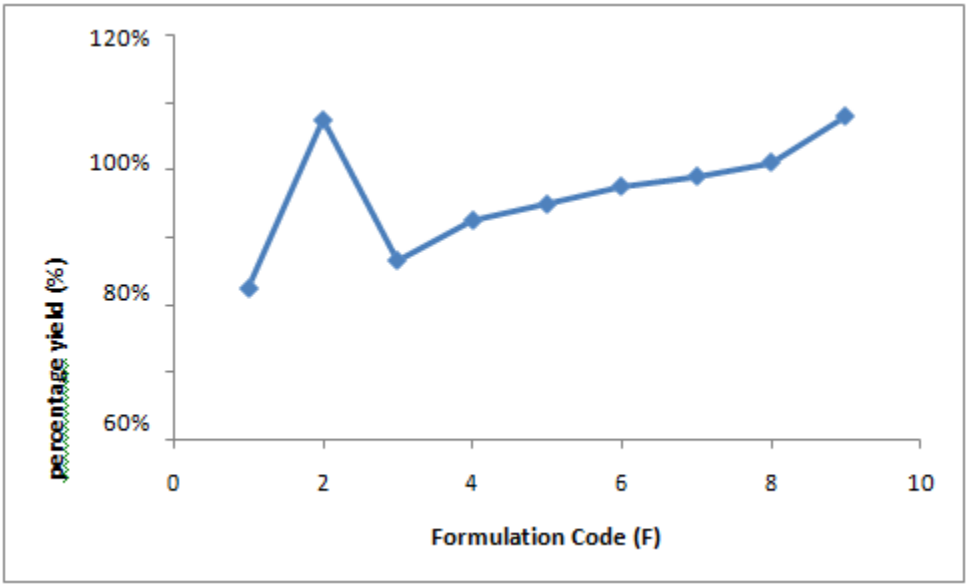


Table 7: Property of Losartan potassium Microparticles in the Field of Micromeritics

BATCH CODE	ANGLE OF REPOSE	BULK DENSITY	TAPPED DENSITY	CARR'S INDEX	HAUSNER'S RATIO
LP1	20.41±0.20	0.74±0.64	0.81±0.73	10.2±0.84	1.05±0.55
LP2	26.80±0.80	0.56±0.042	0.42±0.012	9.52±0.024	1.078±0.22
LP3	20.65±0.36	0.73±0.62	0.86±0.72	7.73±0.23	1.14±0.031
LP4	19.64±0.20	0.65±0.30	0.65±0.36	10.1±0.82	1.17±0.066
LP5	19.10±0.20	0.72±0.46	0.66±0.32	10.05±0.51	1.16±0.052
LP6	28.49±0.21	0.62±0.068	0.722±0.058	12.67±0.040	1.10±0.023
LP7	32.01±0.63	0.64±0.52	0.769±0.074	16.65±0.069	1.15±0.068
LP8	25.62±0.05	0.53±0.32	0.58±0.012	10.13±0.42	1.12±0.015
LP9	24.93±0.32	0.40±0.013	0.54±0.014	9.12±0.011	1.122±0.062

Table 8: In-Vitro Buoyancy (percentage) Studies

Batch code	Percentage of buoyancy
LP1	87.4
LP2	96.1
LP3	88.9
LP4	83.6
LP5	88.4
LP6	88.1
LP7	89.3
LP8	91.22
LP9	97.01

Fig 4: In vitro Buoyancy (percentage) Studies

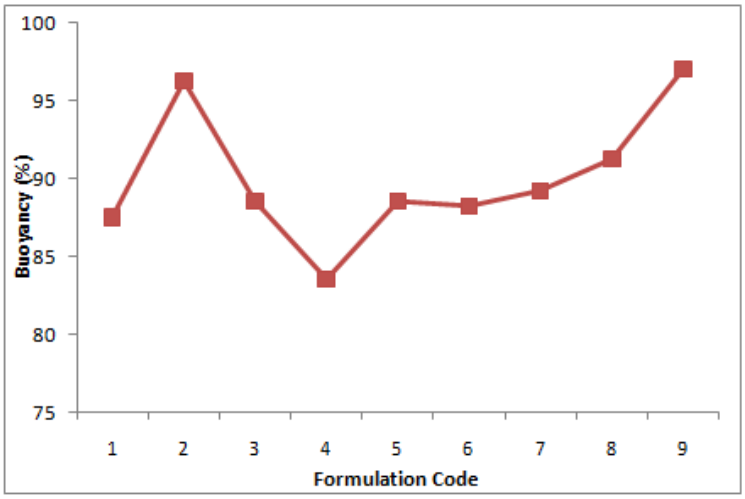
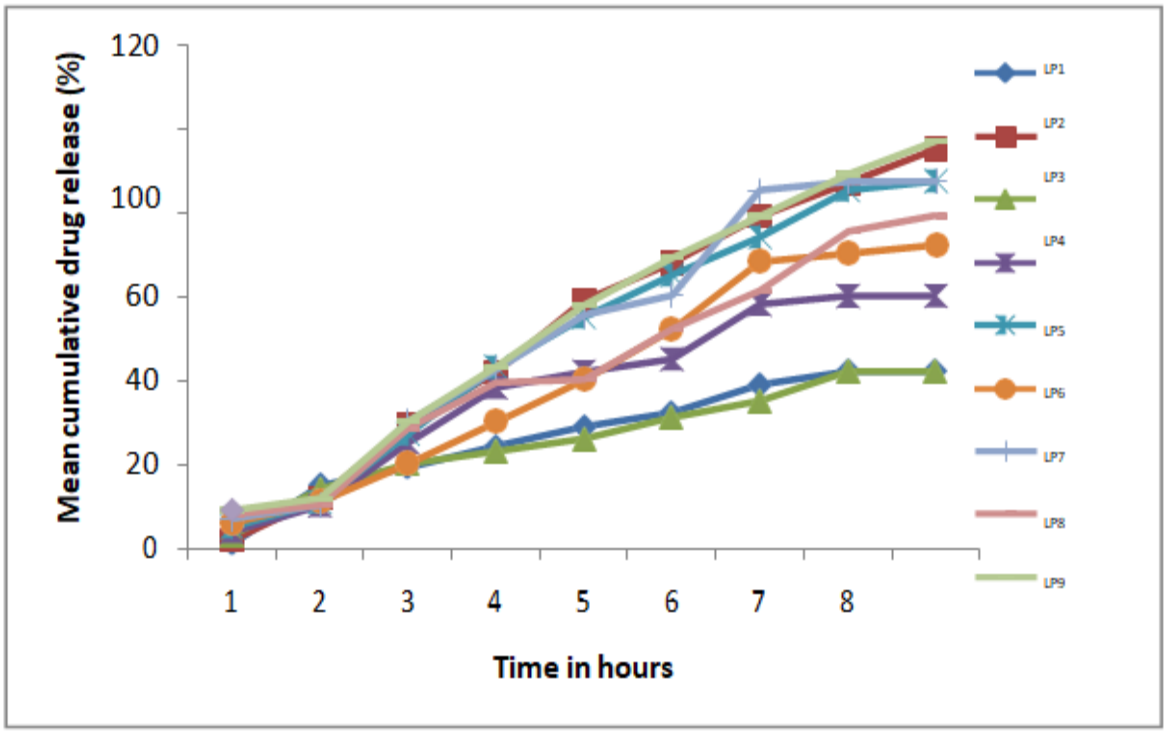


TABLE 9 : Losartan potassium Microsphere Absolute Cumulative Percent Drug Release in-Vitro Dissolution Profile (percent)

Time (hr)	LP1	LP2	LP3	LP4	LP5	LP6	LP7	LP8	LP9
1	14.81	11.93	14.02	10.19	10.93	11.63	10.14	10.26	11.84
2	19.22	29.86	20.02	25.13	27.21	20.03	30.12	28.51	30.10
3	24.26	42.00	23.01	38.22	43.03	30.04	42.44	39.45	43.11
4	28.95	59.05	26.05	42.03	55.08	40.06	55.48	40.13	57.88
5	32.29	68.03	31.08	45.05	65.03	52.03	60.17	52.19	69.11
6	38.92	79.08	35.04	58.04	74.05	68.13	85.14	61.28	78.96
7	42.03	87.03	42.05	60.01	85.24	70.12	87.16	75.33	89.01
8	42.06	95.04	42.06	60.06	87.44	72.17	87.29	79.15	96.82

Fig 5: Losartan potassium Microparticle Mean Cumulative Percentage Drug Release (percent)



RESULT AND DISCUSSION

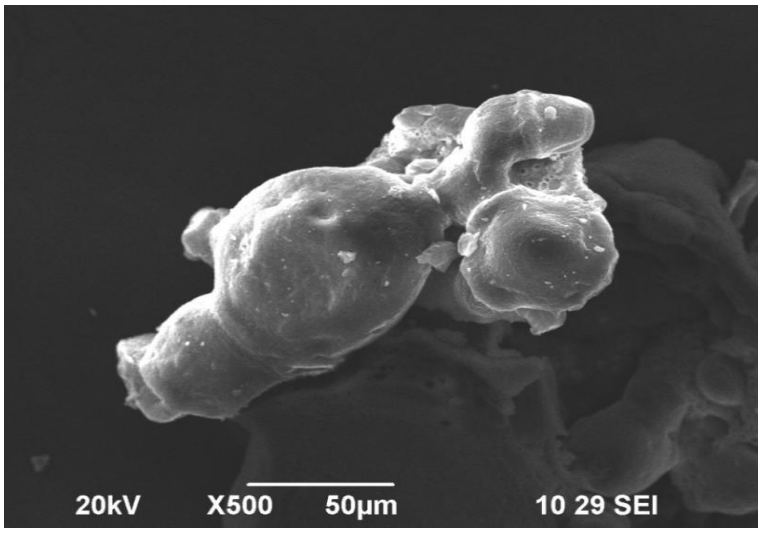
Emulsification solvent diffusion technology was built and tested using Glycerolmonstearate, Ethanol, and Chloromethane polymers. Losartan potassium microparticles. LP1 to LP9 were partitioned. These polymers were selected for their biocompatibility, high stability, and ease of production. This technology was used to manufacture emulsion solvent diffusion microspheres because they are easy to make and maintain medication effects. This approach produced spherical, distinct, and flowable microspheres. Particle size, SEM morphology, swelling index (%), drug content (%), Drug Entrapment efficiency (%), buoyancy experiments, in-vitro release, and stability studies were all evaluated for micromeritic properties. An infrared FT-IR analysis was utilised to assess drug-polymer incompatibility and full physical adsorption on the polymer matrix. Figure 1 depicts one of the IR finds. The potassium salt of losartan was visible. The polymer and drug-loaded Microspheres, as well as the physical combination, displayed the identical peaks. During testing, the functional peaks of the drug, polymer, physical mixing of the drug and polymer, or drug-loaded microspheres did not vary considerably. FT-IR was used to investigate the drug-excipient interaction. The functional group region of the pure drug spectrum showed waves 615.29cm^{-1}, 754.17cm^{-1}, 1095.57cm^{-1}, 1205.01cm^{-1}, 1498.69cm^{-1}, 1618.28cm^{-1},1676.14cm^{-1}, 3415.93cm^{-1}. The spectral peak for functional group stretching vibrations is 615.29 cm^{-1} (OH, CH, CH3, CH2OH). In the spectrum of Losartan microparticles, there are no interactions between the medicine and its excipients. Some formulations have limited

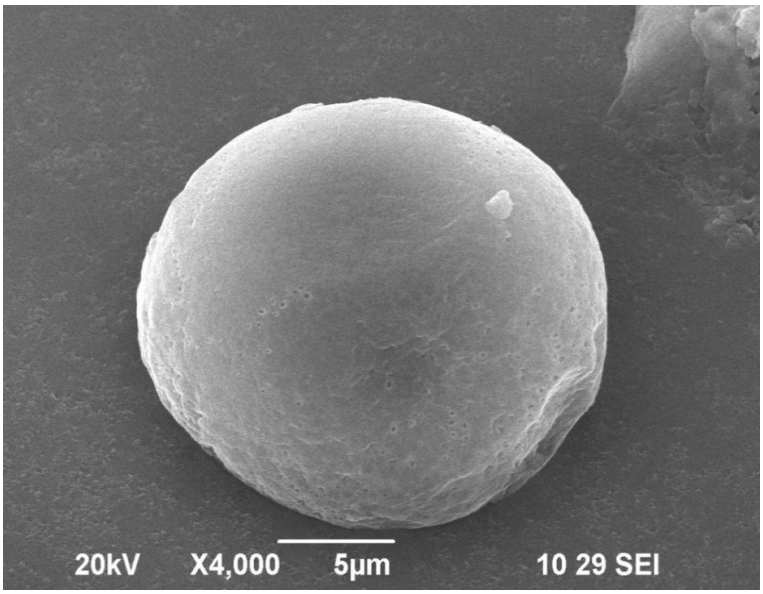
yields due to microsphere loss after washing. Table No.6 shows percentage yields from LP1 through LP9, with LP9 having the greatest percentage yield at 96%.

MORPHOLOGY

Figure 6 shows the surface and shape of Losartan potassium microspheres examined by SEM. The minuscule spheres are spherical and distinct in electron micrographs.

Fig 6 : Formulation F9 was analysed using SEM





DISSOLUTION STUDY

The cumulative percentage release of microspheres containing Losartan potassium was monitored over two and a half hours in a pH phosphate buffer at 7.4. The release rate was slowed by increasing polymer concentration and particle size. Because of its tiny particle size and low polymer concentration, LP9 formulation has a faster release rate than other formulations. All formulations had a sluggish, eight-hour medication release. After eight hours, all six subjects released 96.89 ounces of loaded medicine. Among the polymer/drug combinations tested, LP 9 showed the best sustained release and drug trapping. Figure 5 shows all formulations' in vitro profiles.

CONCLUSION

The polymer-to-drug ratio also affects particle size and drug release pattern. LP2 and LP9 have higher drug entrapment efficiency than LP1 to LP9. LP9 loaded 96% faster than F8. It produced large percentages, with LP9 yielding 96%. The flow properties of LP1–LP9 were measured. Carr's index and angle of repose measurements revealed no flow quality issues. 96.89 percent of the formulations showed progressive and sustained in vitro drug release over 8 hours. Losartan potassium microparticles were assessed for stability at 40°C, 2°C, and 75% RH. The drug's solubility and colour did not change in an in vitro drug release test.

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