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Formulation and evaluation of hydrocortisone micro beads

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Abstract

The current study aimed to develop hydrocortisone mucoadhesive microbeads to prolong the drug's action in the gastrointestinal system, targeting Crohn's disease treatment. Hydrocortisone, known for its anti-inflammatory and anti-rheumatic effects, was utilized in bead form to enhance therapeutic efficacy, extend residence time, and reduce dosage frequency. Using sodium alginate, HPMC, and Eudragit L-100 as adhesive polymers, and calcium chloride and aluminium chloride as cross-linking agents, the study crafted microbeads with an entrapment efficiency between 57.23% and 91.69%. Evaluations focused on in vitro drug release, particle size, surface characteristics, entrapment efficiency, and the role of cross-linking ions. Of the formulations, HCS-8 (with sodium alginate and Eudragit L-100 using aluminium chloride as the gelling solution) and HCS-2 showed optimal drug release profiles. Notably, HCS-8 achieved a 12-hour drug release delay, attributed to aluminium chloride's cross-linking action. Drug release kinetics revealed a zero-order linearity (R2=0.99), suggesting super case 2 transport as the primary release mechanism.

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INTRODUCTION

Microbeads have a diameter ranging from 0.5 to 1000 µm and are almost spherical in shape. The distributed drug particles in solid or crystalline form within the solid and free-flowing particulate carriers provide multiple release profiles or a sustained release of treatment with different active agents without significant side effects. Furthermore, the microbeads continue to function normally under physiological settings and can integrate medications to deliver high concentrations locally, guaranteeing that therapeutic quantities are achieved at the target site as well as minimising negative effects by maintaining low systemic concentration. A variety of polymers, including cationic polymers like chitosan, anionic polymers like sodium alginate, and binding components like gelatin, chondroitin sulphate, and avidin, are combined in a preset ratio to create the microbeads. A typical method for creating controlled release dosage forms is microencapsulation. A method for producing polymeric gel beads using a controlled release formulation of various medicinal ingredients. The medicine is coated or encapsulated in the centre of the beads, which are distinct spherical

microcapsules that function as a solid substrate. Drugs can be distributed more uniformly throughout the gastrointestinal tract and have sustained-release qualities due to the beads. Moreover, medicines packed in beads now have improved bioavailability. The use of alginate beads as a controlled release carrier has been the subject of numerous studies that have been published.

In cosmetics and personal hygiene products including toothpaste, body scrubs, as well as face wash, microbeads—minuscule plastic microspheres—are employed as exfoliating agents. The natural exfoliating ingredients pumice, oats, and walnut husks are substituted with these beads. Our lakes, rivers, and ocean are filled with these little particles that wastewater treatment systems are unable to filter out. What's worse is that these microplastics may act as microscopic chemical and toxin transfer stations.

Table 1 Various formulations of micro beads drug delivery system were made as given in table

S.No	Ingredients	HCS-1	HCS-2	HCS-3	HCS-4	HCS-5	HCS-6	HCS-7	HCS-8
1	Hydrocortisone (g)	1	1	1	1	1	1	1	1
2	Sodium alginate (g)	2	3	2	3	2	3	2	3
3	Eudragit L-100 (g)	1	1	-	-	1	1	-	-
4	HPMC K15 (g)	-	-	1	1	-	-	1	1
5	Calcium chloride %w/v	3	3	3	3	-	-	-	-
6	Aluminium chloride %w/v	-	-	-	-	3	3	3	3

MATERIALS AND METHODS

The gift sample Hydrocortisone is from Drug india and polymer mixtures such as Sodium alginate (Himedia), Hydroxyl propyl methyl cellulose (paxmy), Eudragit L-100 (Fischer scientific), Calcium chloride (Microfine chemical), and luminium chloride (Drugs india).

METHODOLOGY

Method of preparation

Preparation of Micro beads

The Ionotropic External Gelation process was utilised to create micro beads. Here, distilled water was used to dissolve sodium alginate, HPMC, and Eudragit L-100 in a 1:0.5 and 2:0.5 ratio with stirring. This solution was mixed with the medication, and after 15 minutes, the drug suspension was added to the mixture that contained varying percentages of CaCl2 and AlCl3. Using a needle-equipped syringe, the drug suspension was gradually added to this mixture. Following two rounds of deionized water washing, the resultant beads were filtered through Whatman paper filters and dried for 48 hours at 450C. A dosage of eight milligrammes of dried beads was placed into the capsules.

EVALUATION

Determining the organoleptic characteristics of hydrocortisone:

Organoleptic qualities are typically difficult to quantify because there are no standard laboratory tests as well as the process requires experts with extensive experience. This study evaluated the following organoleptic properties: physical appearance, odour, as well as taste. Amorphous, hygroscopic, and in the form of white powder. For these samples of Hydrocortisone powder was investigated and evaluated using the natural senses (e.g., eyes, nose, as well as mouth).

Calculating Hydrocortisone's Solubility

For therapeutic efficacy, all medications, regardless of the mode of administration, must have at least a minimal level of water solubility. Dissolution is the process by which molecules or ions move from a solid state into a liquid one. The Noyes-Whitney formula describes it.

$$dC / dt = DA (C_s - C) / h$$

where A is the surface area of the particle in interface with the gastrointestinal (GIT) fluids, D is the diffusion coefficient of the drug in solution, as well as dC / dt is the rate of drug particle dissolution. Using gravimetric analysis, the amount of solute in the saturated solution sample was ascertained. The following equation was used to determine the solubility.

$$\text{Solubility} = \frac{Weight\ of\ initial\ powder - weight\ of\ dried\ residue}{Volume\ of\ Solvent} \times 100$$

Pre Evaluation

Parameters

Drug-Excipient compatibility study:

FT-IR spectroscopy

The Japan FT-IR spectrometer Shimadzu 8400S was used to examine FT-IR patterns. Before the samples were completely mixed at a ratio of 1:5 (Sample: KBr) with an infrared transparent matrix, they were ground into powder. The KBr discs were made by compressing the powders for five minutes at a pressure of five minutes in a hydraulic press. The scans were obtained at 4 cm-1 resolution, ranging from 4000 to 400 cm-1.

Angle of Repose

The angle of repose of a granular material, or its critical angle of repose, is the sharpest angle at which the slope dips or descends in relation to the horizontal plane when the material on the slope face is about to slip. Angles between 0° and 90° make up this range.

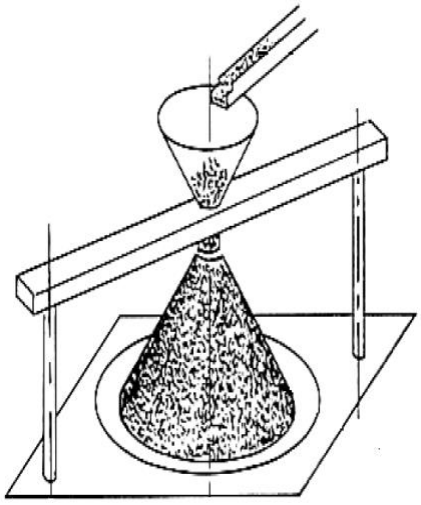

Figure 1 Funnel method for angle of repose

Table 2 Standard limits of angle of repose

S.No	Angle Of Repose (θ)	Type of Flow
1	<25	Excellent
2	25-30	Good
3	30-40	Passable
4	>40	Very poor

The angle that can be formed between a powder pile's surface and the horizontal plane is at its highest here. A funnel set 4 cm above the base was used to let 10 g of powder escape. The formula was used to compute the angle of repose based on measurements of the pile's height and base's diameter.

$$\tan \theta = h/r$$

$$\theta = \tan^{-1} h/r$$

Bulk Density

An untapped powder sample's bulk density is determined by dividing its mass by volume, which includes the interparticulate void volume. With the following formula, the bulk density is calculated and the volume measured is referred to as the bulk volume.

$$\text{Bulk density} = \frac{\text{Weight of powder}}{\text{Bulk volume}}$$

Tapped Density

The higher bulk density that results from mechanically tapping a container holding the powder sample is known as the "tapped density." Here is the formula for calculating the tapped density:

$$\text{Tapped density} = \frac{\text{Weight of powder}}{\text{Tapped volume}}$$

Carr's Index (Compressibility Index)

Table 3 Standard limits of compressibility/Carr's index

S.No	Carr's Index	Type of Flow
1	5-15	Excellent
2	12-18	Good
3	18-23	Fair to passable
4	23-35	Poor
5	35-38	Very poor
6	>38	Extremely poor

It is one of the most essential parameters used to describe the properties of powders and granules.

It can be determined by using the following equation:

$$\text{Carr's Index} = \frac{Tapped\ density - Bulk\ density}{Tapped\ density} \times 100$$

Hausner's Ratio

Determining the flow characteristics of powders and granules requires knowledge of Hausner's ratio, an essential property. Here is the formula that can be used to find this.

$$\text{Hausner's ratio} = \frac{\text{Tapped density}}{\text{Bulk density}}$$

HR<1.25 denotes a favourable flow attribute

HR>1.25 denotes a poor quality of flow

Post evaluation parameters

Drug Content

After drying, the beads were weighed, and the process yield and required yield were computed (-22/+44 sieve fraction). To determine drug concentration, in 100 millilitres of water, 100 mg of beads were triturated as well as dissolved. At 242 nm, the solution was spectrophotometrically analysed.

Drug loading

Dissolving 25 mg of muco adhesive beads in 100 mL of water allowed researchers to calculate the drug loading. Spectrophotometric analysis was performed at 242 nm using 45 µm filter paper to filter the prepared solution. The Formulary calculations were used to determine the medication loading.

$$\textbf{\% drug loading} = \frac{\textbf{Amount of drug in beads}}{\textbf{Amount of beads}} \textbf{ X } 100$$

Percentage encapsulation efficiency

The following formula was used to get the percentage encapsulation efficiency:

$$\textbf{Percentage encapsulation efficiency} = \frac{\textbf{AQ}}{\textbf{TQ}} \times 100$$

Microscopical characteristics of beads

A motic microscope was used to assess the particle size of 50 hydrocortisone muco adhesive beads. The mean size of the particles was computed.

SEM of beads

Using a scanning electron microscope, the morphological characterisation of the Hydrocortisone microbeads was accomplished (Model Jeol JSM-5200). Razor-sharpened bead slices were used to acquire cross-sectional views. Prior to microscopy, the samples were coated with gold-palladium to a thickness of 200 Aº. The working conditions were 20 KV for the accelerating voltage. Images were captured between 7000 and 12000 times magnification.

Swelling studies

The swelling properties of beads were examined. Only batches with good drug content and more than 50% entrapment efficiency were chosen. Weighing the sample from the drug-loaded beads, we put it in the wire basket of the USP dissolving equipment II. Predefined intervals were used to periodically remove and weigh the beads. Next, using the following formula, the swelling ratio was determined:

$$\textbf{Swelling ratio} = \frac{\textbf{weight of wet beads}}{\textbf{weight of dried beads}}$$

In-vitro dissolution studies

Using a USP Type II dissolution equipment with 900 cc of phosphate buffer (pH 7.2) kept at 37±0.50C and agitated at 50 rpm, the dissolution of Hydrocortisone muco sticky beads was investigated. Periodically, samples were taken and changed out with new dissolving media. With the aid of a UV spectrophotometer (UV-1700, Pharmaspace, Shimadzu), the drugs included in these samples were examined. For the release study, only batches with good drug content as well as drug entrapment efficiency greater than 50% were chosen.

Table 4 Dissolution equipment parameters for in vitro drug release studies of hydrocortisone microbeads

Dissolution medium	7.2 pH buffer
Dissolution medium volume (ml)	900ml
Bath temperature(0c)	37±0.5^{0}c
Speed of paddle (rpm)	50
Sampling intervals (min)	60min
Sample withdrawn volume (ml)	5ml
Sample replaced (ml)	5ml
Wave length (nm)	242nm

Figure 2 Lab India dissolution apparatus (DS-8000)

Mathematical modeling of drug release profile

A number of kinetic models, including the Higuchi, First, Zero, as well as Korsemayer-Peppas models, were fitted to the total quantity of hydrocortisone released from the manufactured tablets at various time intervals in order to characterise the drug release mechanism.

Zero order kinetics

It explains the mechanism by which the rate of drug release is unaffected by concentration.

$Q_{ts} = Q_0 + K_0 t$

In vitro drug release study data were displayed as cumulative drug release vs. time to analyse the release kinetics.

First order kinetics

It explains how drugs are released from systems where the rate of release is dependent on concentration.

$\text{Log } Q_t = \text{Log } Q_0 + K_1 t/2.303$

Plotting the data received as a log cumulative proportion of medicine remaining vs time.

Higuchi model

It explains how the square root of time determines the proportion of drug release from a matrix.

$Mt/M\alpha = K_H t^{1/2}$

Plotting the data was done as a cumulative proportion of drug release against the square root of time.

Korsemeyer-Peppas model (Power law)

The potent law effectively characterises the release of drug from slabs, cylinders, as well as spheres by stating that the relationship between the fractional drug release and the release time is exponential.

$Mt/M\alpha = Kt^n$

$\text{Log } [Mt/M\alpha] = \text{Log } K + n \log t$

Researchers were able to analyse the release kinetics by plotting data from in vitro drug release trials as log cumulative % drug release vs. log time.

Table 5 Diffusional exponent "n" as well as diffusional release mechanism from swellable controlled release systems with varying geometric configurations

Slab	Cylinder	Sphere	Drug release mechanism
0.5	0.45	0.43	Fickian diffusion
0.5-1.0	0.45-0.89	0.43-0.85	Anomalous transport (Non-Fickian)
1.0	0.89	0.85s	Zero order
1.0	0.89	0.85	Case 2 transport
1.0	1.0	1.0	Super case 2 transport

RESULTS AND DISCUSSION

Table 6 Pre-formulation studies for Hydrocortisone

Testing	Hydrocortisone
Organoleptic properties	Amorphous, hygroscopic, and in the form of white powder
Solubility	Water-soluble: approximately 500 mg/mL. comparable solubility in methanol and ethanol; limited solubility in chloroform
Bulk density	0.48gm/cm^3
Tapped density	0.62gm/cm^3
Compressibility index	22.5 %
Hausner's ratio	1.29
Angle of repose	$26^0.5^1$

Density and flow properties:

Table 6 lists the outcomes of pre- and post-compression metrics such as bulk density, tapped density, carr's index, as well as porosity.

Table 7 Post formulation studies Hydrocortisone Micro beads

Formulations	Bulk density(g/ml)	Tapped density(g/ml)	Haussner's ratio (%)	Carr's index(%)	Angle of repose(⁰)
HCS-1	0.722	0.738	1.036	4.63	22.79
HCS-2	0.838	0.872	1.044	1.12	17.68
HCS-3	0.779	0.812	1.044	2.56	21.32
HCS-4	0.876	0.879	1.073	8.18	18.28
HCS-5	0.622	0.599	1.054	4.12	21.18
HCS-6	0.555	0.629	1.22	9.81	25.68
HCS-7	0.632	0.671	1.07	4.79	20.32
HCS-8	0.644	0.668	1.08	6.52	27.04

Table 8 Post Evaluation tests

Formulations	Percentage yield (%)	Drug entrapment efficiency (%)	Swelling index(%)
HCS-1	76.8	57.23	57
HCS-2	99.4	74.15	61
HCS-3	88.7	63.25	50
HCS-4	81.5	69.28	58
HCS-5	77.2	77.35	44
HCS-6	91.2	98.28	32
HCS-7	70.5	81.48	24
HCS-8	99.5	91.69	21

Comparing the beads to pure hydrocortisone, the results show that the beads' flow characteristic has increased. A decrease in particle cohesiveness could be the cause of the increased flow property.

Entrapment efficiency:

Table 7 presents the findings of the gradual increase in the entrapment efficiency with a rise in the concentration of sodium alginate. The formulations that were crosslinked with Al3+ exhibited higher incorporation efficiencies overall. This could be attributed to the production of bigger beads in these formulations, which trap a higher concentration of medication.

Morphology and particle size:

It was discovered that the morphology of the different formulations of Micro beads was spherical and distinct. In figure 3, the dried Microbes' SEM pictures are displayed. When calcium chloride was used as a gellant solution, it was discovered that the Micro beads' surface was rough. A higher medication concentration that is unevenly distributed throughout alginate matrices could be the cause. Similar to how the surface of the beads prepared with calcium chloride gellent solution was discovered to be smoother than that of the beads prepared with aluminium chloride gellent solution. This can be the result of hydrocortisone's increased incorporation efficiency.

Table 9 Microscopical Studies

Formulations	Particle Size (mm)
HCS-1	0.198
HCS-2	0.283
HCS-3	0.276
HCS-4	0.324
HCS-5	0.298
HCS-6	0.322
HCS-7	0.315
HCS-8	0.387

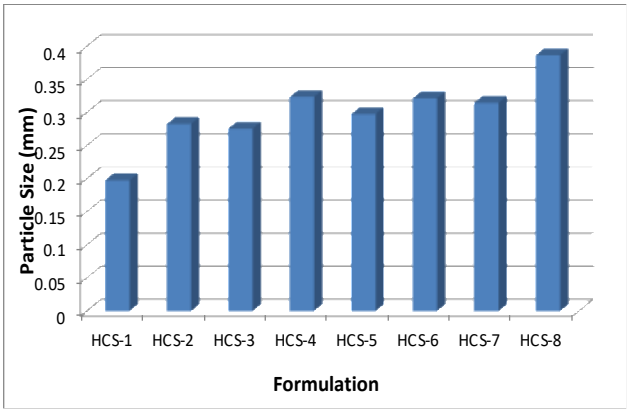

Figure 3 Microscopical studies

Drug- Excipient Compatibility studies (FT-IR):

Using infrared spectroscopy, the drug-polymer interaction was investigated. Using Perkin Elmer-883 IR spectroscopy, the IR spectra were recorded between 500 and 3100 cm-1 for pure hydrocortisone, 1020 to 3500 cm-1 for pure alginate, 650 to 3000 cm-1 for pure HPMC, 1000 to 3500 cm-1 for pure EUDRAGIT L 100, and 500 to 1760 cm-1 for a mixture of hydrocortisone and sodium alginate, HPMC, and Eudragit L 100 in KBr pellets. Based on the characteristic peaks, it was determined from the data that there is no incompatibility between the hydrocortisone as well as other excipients. The corresponding peaks were listed in Table 9.

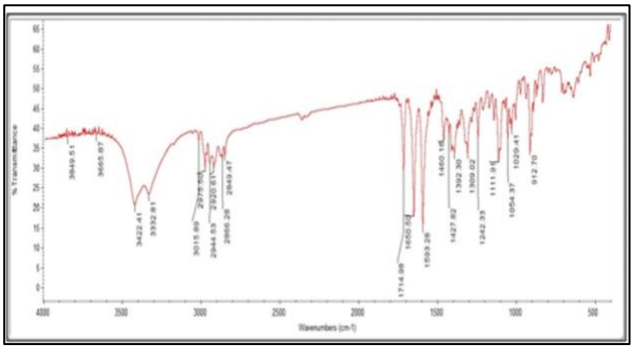

Figure 4 IR Spectrum of Hydrocortisone

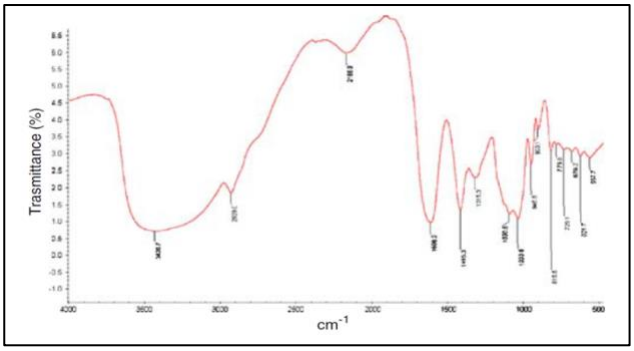

Figure 5 IR Spectrum of sodium alginate

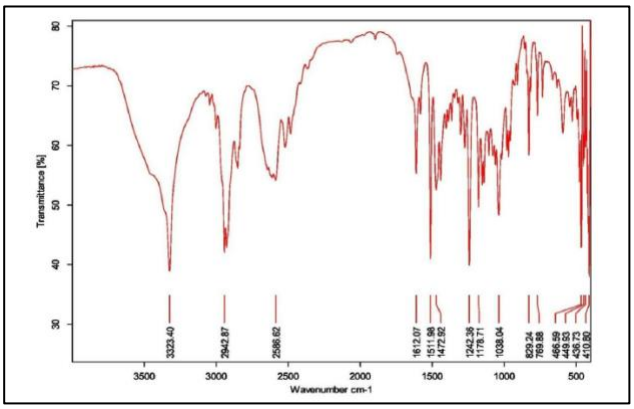

Figure 6 IR Spectrum of HPMC

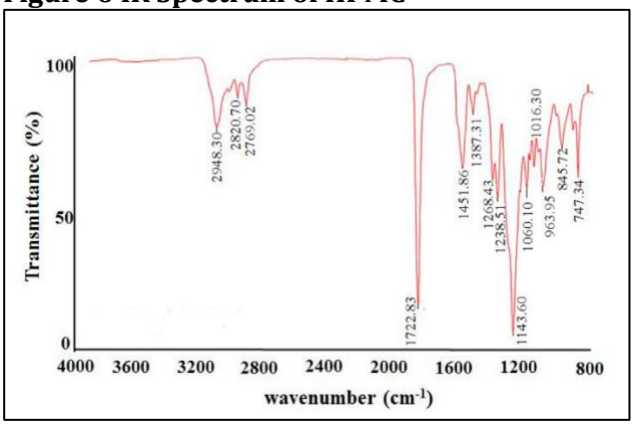

Figure 7 IR Spectrum of Eudragit L 100

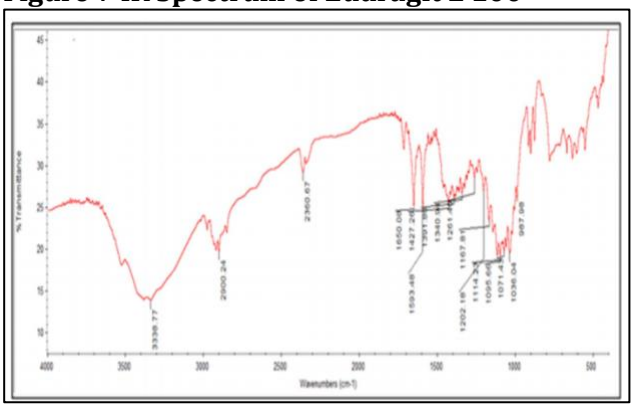

Figure 8 IR Spectrum of Hydrocortisone + sodium alginate+ HPMC+ Eudragit L 100

Table 10 FTIR interpretation data of drug and excipients

Functional Group	Hydrocortisone (drug)	Sodium alginate	HPMC	Eudragit L 100	Mixture of compound
C=O (Aldehydes)	1714	1419.15	1727.60	1017.78	1707.18
C-N stretch (Aliphatic amines)	1242	1028.13	1159.95	1622.17	1071.45
–C=C- (Aromatics)	1593	1419.15	965.19	1423.87	1114.22
C–H stretch (Alkanes)	1650	2888.13	2953.67	3059.72	3307.18

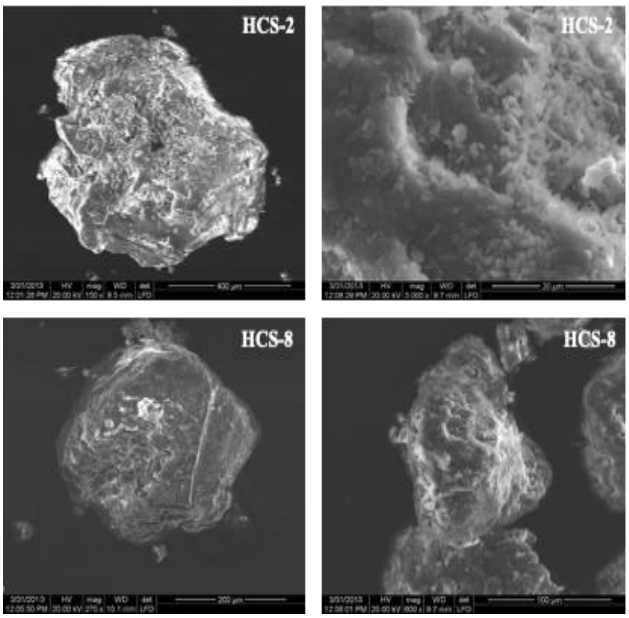

Figure 9 SEM Analysis of Hydrocortisone Micro beads by using calcium chloride and alluminium chloride as gellant solution (HCS-2 and HCS-8)

***In-vitro* dissolution:**

The effects of polymers on hydrocortisone were investigated using gellant solutions containing calcium chloride (2%w/v) and aluminium chloride (2%w/v) in addition to different amounts of sodium alginate (1%, 2% w/v), 0.5% HPMC, and 0.5% Eudragit L 100). Figure 10-13 and Table 10 displayed the release profiles for various formulations. As the concentration of sodium alginate in the gellant solution containing aluminium chloride increased, the release was found to have been delayed.

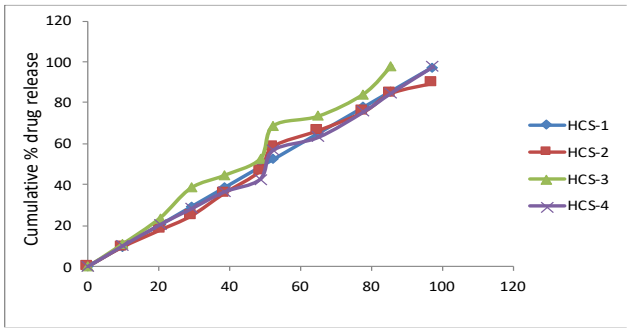

Figure 10 Cumulative % drug release data from HCS-1 to HCS-4 formulations

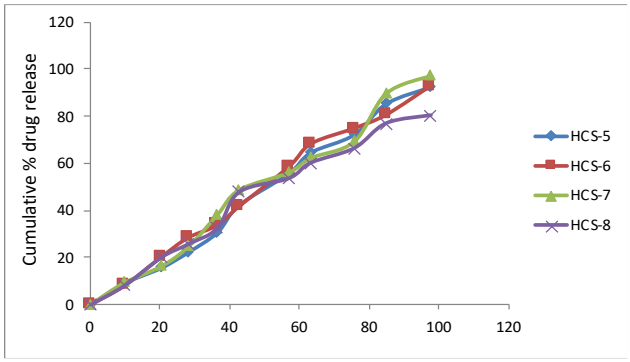

Figure 11 Cumulative % drug release data from HCS-5 to HCS-8 formulations

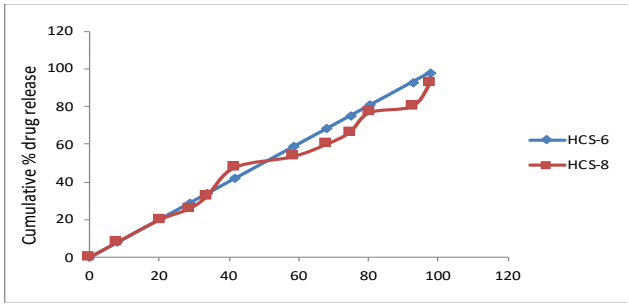

Figure 12 Cumulative % drug release data of HCS-6 and HCS-8 formulations

Table 11 In-vitro drug release data for Hydrocortisone Micro beads

Time (Hrs)	HCS-1	HCS-2	HCS-3	HCS-4	HCS-5	HCS-6	HCS-7	HCS-8
1	9.7	9.5	10.8	9.9	9.2	8.2	9.5	8.2
2	20.4	17.9	23.7	20.5	15.8	20.4	16.5	20.2
3	29.2	24.8	38.4	28.2	22.4	28.6	24.8	25.8
4	38.5	35.8	44.5	36.5	30.8	33.8	38.4	32.5
5	48.7	46.8	52.6	42.7	42.4	41.8	48.9	47.8
6	52.4	58.7	68.7	56.9	55.8	58.5	56.3	53.6
7	65.1	66.5	73.4	63.2	64.7	68.2	62.5	60.2
8	77.9	75.6	84.3	75.6	72.3	74.8	69.4	66.4
9	85.6	84.6	98.0	84.7	85.4	80.5	89.8	76.9
10	97.4	89.5	-	97.5	92.5	92.8	97.4	80.3
11	-	98.6	-	-	98.2	97.8	-	92.4
12	-	-	-	-	-	-	-	98.8

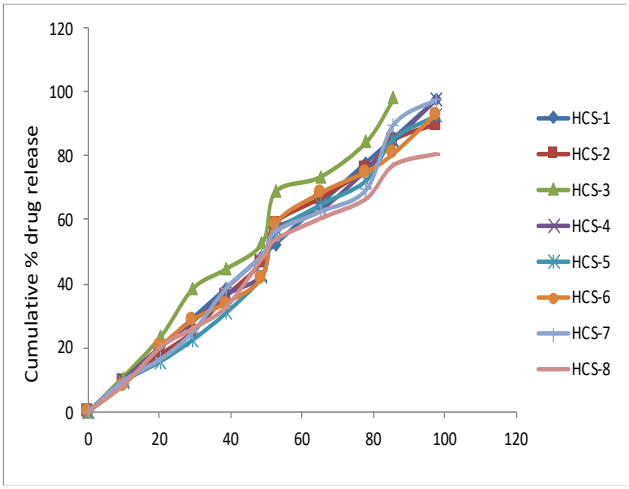

Figure 13 Cumulative % drug release data for HCS formulations

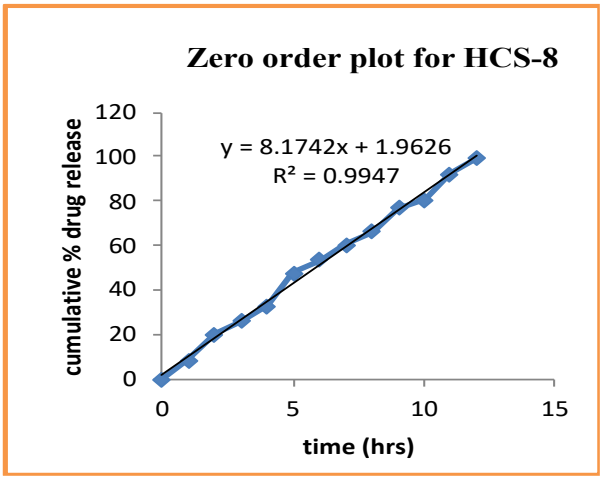

Figure 14 Zero order plot for HCS-8

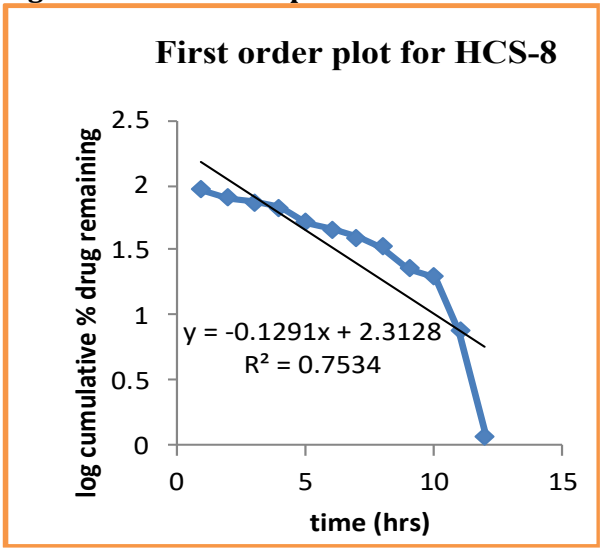

Figure 15 First order plot for HCS-8

IN-VITRO DRUG RELEASE KINETICS

For the purpose of comparing the dissolution profiles of all formulations (Tables 11 and 12) (fig. 14–17), several model-dependent techniques (Zero order, First order, Higuchi, and Korsemayer–Peppas plots) were used. These models' outputs show that the "best fit model" for every microbead poured into a capsule has a zero order. This is because the R2 value derived from model fitting has been shown to depend on this fact in the past. According to the data, HCS-8 had a stronger release-delaying impact. When the hydrocortisone bead Korsemayer-Peppas release exponent (n) value is more than 0.85, Super case 2 transport is indicated.

Table 12 In-vitro drug release kinetics data for formulation HCS-8

Zero order		First order		Higuchi's data		Korsemayer-Peppas data	
Time (h)	% CDR	Time (h)	% Log CD Remaining	SQRT of time	% CDR	Log time	% Log CDR
1	8.2	1	1.962	1.0	8.2	0	0.913
2	20.2	2	1.902	1.414	20.2	0.30	1.305
3	25.8	3	1.870	1.732	25.8	0.477	1.411
4	32.5	4	1.829	2.0	32.5	0.602	1.511
5	47.8	5	1.717	2.236	47.8	0.698	1.679
6	53.6	6	1.666	2.449	53.6	0.778	1.729
7	60.2	7	1.599	2.645	60.2	0.845	1.779
8	66.4	8	1.526	2.828	66.4	0.903	1.822
9	76.9	9	1.363	3.0	76.9	0.954	1.885
10	80.3	10	1.294	3.162	80.3	1.0	1.904
11	92.4	11	0.880	3.316	92.4	1.041	1.965
12	98.8	12	0.079	3.464	98.8	1.079	1.994

Table 13 The parameters and determination coefficients of the hydrocortisone microbead release profile

Formulation code	Correlation Coefficient values (R^2)				Diffusion Exponent value (n)
	Zero Order	First order	Higuchi	Korsemayer-peppas	
HCS-1	0.996	0.773	0.911	0.907	0.098
HCS-2	0.996	0.791	0.922	0.833	1.415
HCS-3	0.993	0.751	0.927	0.992	0.967
HCS-4	0.995	0.753	0.903	0.807	1.425
HCS-5	0.994	0.820	0.898	0.849	1.434
HCS-6	0.994	0.753	1.0	0.991	0.971
HCS-7	0.990	0.764	0.895	0.992	1.03
HCS-8	0.993	0.828	0.918	0.991	1.016

Table 14 Stability results of Hydrocortisone Micro beads in capsules (organoleptic properties)

(Batch -1) Week	Temperature and relative humidity (25°C/60%RH)		
	Size and shape of capsules	Gross nature of Beads	Colour of capsules
0	Regular '00	Smooth	Reddish brown
2	No change	Smooth	Reddish brown
4	No change	Smooth	Reddish brown
6	No change	Smooth	Reddish brown
8	No change	Smooth	Reddish brown
10	No change	Smooth	Reddish brown
12	No change	Smooth	Reddish brown

Table 15 Stability results of Hydrocortisone Micro beads in capsules (Batch-2)

(Batch -2) Week	Temperature and relative humidity (40°C/70%RH)		
	Size and shape of capsules	Gross nature of Beads	Colour of capsules
0	Regular '00	Smooth	Reddish brown
2	No change	Smooth	Reddish brown
4	No change	Smooth	Reddish brown
6	No change	Smooth	Reddish brown
8	No change	Smooth	Reddish brown
10	No change	Smooth	Reddish brown
12	No change	Smooth	Reddish brown

Table 16 Stability results of Hydrocortisone Micro beads in capsules (Batch-3)

(Batch -3) Week	Temperature and relative humidity (60°C/80%RH)		
	Size and shape of capsules	Gross nature of Beads	Colour of capsules
0	Regular '00	Smooth	Reddish brown
2	No change	Smooth	Reddish brown
4	No change	Smooth	Soft spot
6	No change	Smooth	Soft spot
8	No change	Sticky Beads	Discoloration
10	No change	Sticky Beads	Discoloration
12	No change	Sticky Beads	Discoloration

Table 17 Stability studies In-vitro dissolution profile of HCS 8

S.NO	Medium	Time	% drug release of HCS 8		
			Batch-1 (25°C/60%RH)	Batch-2 (40°C/70%RH)	Batch-3 (60°C/80%RH)
1	7.4 Phosphate buffer	1	9.3	8.3	10.3
2		2	18.5	23.4	18.8
3		3	24.7	28.7	29.9
4		4	29.4	35.4	41.3
5		5	44.2	49.5	48.8
6		6	65.6	72.2	78.9
7		7	61.3	64.3	66.8
8		8	51.2	60.7	64.3
9		9	73.7	76.9	79.9
10		10	85.3	90.8	91.2
11		11	91.2	96.4	96.4
12		12	96.8	90.1	95.3

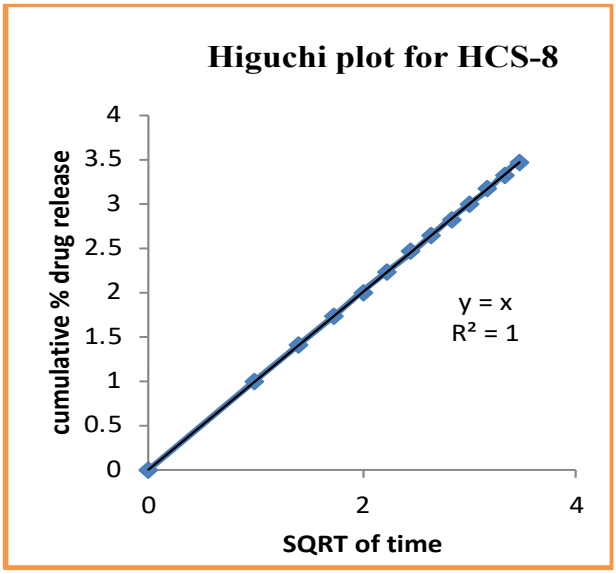

Figure 16 Higuchi plot for HCS-8

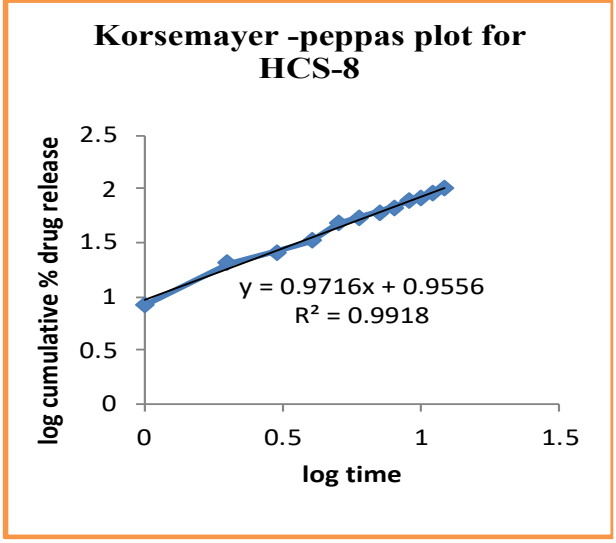

Figure 17 Korsemayer-Peppas plot for HCS-8

STABILITY STUDIES

The most advanced system, HCS-6, served as the subject of the stability testing. Throughout a 12-week period, the formulation's dissolving profile and organoleptic characteristics were examined. Based on the results, batch -3 (which is maintained at 600 °C and 80% relative humidity) had somewhat different capsule colour and less grainy beads. For batches -1, maintained at 250°C and 60% relative humidity, and -2, maintained at 400°C and 70% relative humidity, no alterations were determined. According to figure 18, batch -3, which is maintained at 600 degrees Celsius and 80% relative humidity, showed a faster percentage drug release after twelve weeks. where an elevated swelling ratio could be the cause of. Table 13-16 presents a tabulation of the outcomes.

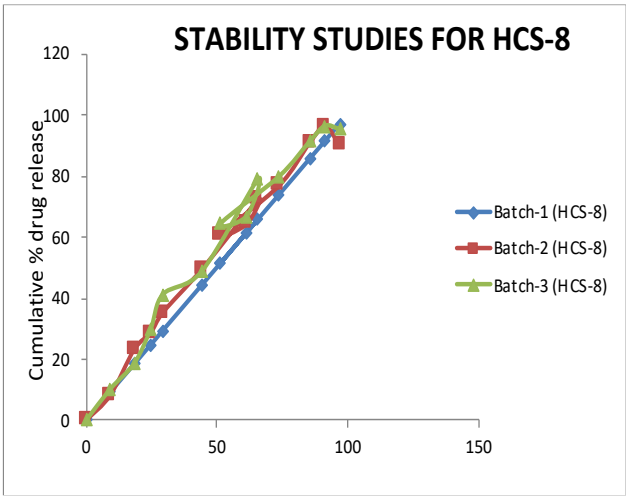

Figure 18 Stability studies for HCS-8

CONCLUSION

According to the research, using the right formulation conditions is crucial to achieving high encapsulation efficiency as well as managing hydrocortisone release from alginate beads. Studies on the dissolution of drugs in vitro revealed that formulations created with increasing concentrations of sodium alginate with HPMC released the medication more quickly than those prepared with increasing concentrations of sodium alginate with Eudragit L-100. Additionally, in comparison to beads manufactured using calcium chloride 2%w/v as a gellant solution, those made using aluminium chloride 2%w/v as a gellant solution formed tougher beads. Further research must be conducted in order to create the most effective hydrocortisone compositions.

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