ORIGINAL ARTICLE

INTERNATIONAL JOURNAL OF CLINICAL PHARMACOKINETICS AND MEDICAL SCIENCES
Published by Pharma Springs Publication Journal Home Page: https://pharmasprings.com/ijcpms/

Formulation and Evaluation of Mucoadhesive Beads of Dexamethasone

Naga Roopini B*[1], Pradeep Kumar M[2]

[1]Department of Pharmaceutics, Vasavi Institute of Pharmaceutical Sciences, Vasavi Nagar, Peddapalli (V), Sidhout (M), YSR Kadapa-516 247, Andhra Pradesh, India
[2]Department of Pharmaceutical Technology Vasavi Institute of Pharmaceutical Sciences, Vasavi Nagar, Peddapalli (V), Sidhout (M), YSR Kadapa-516 247, Andhra Pradesh, India

Article History:

Received on: 15 Jul 2023
Revised on: 07 Aug 2023
Accepted on: 08 Aug 2023

Keywords:

Mucoadhesive beads, bio adhesion, Dexamethasone

ABSTRACT

The goal of the current study was to formulate and evaluate mucoadhesive Dexamethasone beads to significantly lengthen the duration of the drug's stay in the GI system to treat Crohn's disease. Dexamethasone is a corticosteroid that acts as an anti-rheumatic and anti-inflammatory. To decrease the dosage frequency Dexamethasone adhesive beads were formulated for Intimate contact with the underlying absorption surface is made possible by a prolonged stay at the location, which enhances the drug's therapeutic effectiveness. In the current study, calcium chloride and aluminium chloride were utilised as cross-linking agents to create Dexamethasone mucoadhesive beads employing adhesive polymers like sodium alginate, HPMC, and Eudragit L-100. The prepared beads' entrapment efficiencies ranged from 57.15 to 99.16%. Regarding entrapment effectiveness, particle size, surface properties, and in-vitro drug release experiments, the impact of bioadhesive polymers and cross-linking ions was assessed. The MPS-7 delayed the drug's release for 12 hours, which may be related to the cross-linking agent aluminium chloride. According to drug release kinetics, all of the formulations were more linear concerning zero order (r2=0.99) than concerning first order (r2=0.751 to 0.828). Super Case 2 Transport was discovered to be the precise release mechanism.

*Corresponding Author

Name: Naga Roopini B
Phone: +91 7901238892
Email: rupabn95@gmail.com

eISSN: 2583-116X

DOI: https://doi.org/10.26452/ijcpms.v3i2.504

Production and Hosted by

Pharmasprings.com

INTRODUCTION

The science of regulated drug delivery is developing quickly. Polymeric materials' traditional prosthetic function in medical devices is being complemented by cutting-edge pharmacological and pharmaceutical uses. There is a lot of ambiguity on what should be referred to as "controlled" drug delivery in the scientific literature due to their field's relative youth [1]. Although this phrase is now widely used in the literature, it is frequently misconstrued. "Controlled" drug delivery specifically refers to the fine control of the rate at which a specific drug dosage is released from a delivery system (ideally in a constant or nearly constant manner over a long period) instead of the necessity for frequent, repeated administration, whether by mouth or parentally [2]. Zero-order kinetics, wherein the rate does not vary by concentration, is the theory that describes drug release rates that are constant throughout a fixed protracted period. To maintain the proper therapeutically effective drug concentration levels in the blood, oral tablets and the majority of parenteral populations (other than continuous i.v. infusions) release drugs at an initial rapid rate, followed by a steady decline thereafter more

or less in the first order manner, in which the rate is directly proportional to the concentration [3, 4]. Controlled drug delivery means, that the rate of disposition of the active substance for absorption and the rate of availability at the actual site of action is controlled [5, 6].

MATERIALS AND METHODS

Preparation of sodium alginate beads

Ionotropic external gelation was used to create alginate beads. In this procedure, distilled water was mixed with sodium alginate, HPMC, and Eudragit L-100 to dissolve them in a 1:0.5:2 ratio. The drug was added to this solution, and after 15 minutes of curing, the drug suspension was added to a solution that contained CaCl2 and Alcl3 at varying quantities. Using a syringe and needle, the drug suspension was dripped into this mixture. The collected beads were filtered using Whatman paper filters, twice rinsed in deionized water, and finally dried at 450°C for 48 hours. The dried beads were filled into the capsules with a dose equivalent to 8 mg.

Formulation and manufacture of Dexamethasone extended-release Beads

Evaluation of Mucoadhesive Beads

Determination of the organoleptic properties of Dexamethasone:

Since there are no established laboratory procedures for measuring organoleptic qualities, it is typically challenging and requires employees with extensive process knowledge. The physical look, odour, and taste of the organoleptic qualities were evaluated in this study. The natural senses (such as the eyes, nose, and mouth) were used to examine and evaluate these samples of Dexamethasone powder.

Pre-evaluation parameters

Drug-Excipient compatibility study: FT-IR spectroscopy

The Japanese FT-IR spectrometer Shimadzu 8400S was used to research FT-IR patterns. The samples were first finely pulverised and fully blended with potassium bromide, an infrared transparent matrix, at a ratio of 1:5 (Sample: KBr). The powders were compressed in a hydraulic press for five minutes at a pressure of five tonnes to create the KBr discs. The scans, which ranged in resolution from 4 cm-1 to 400 cm-1, were taken.

Angle of Repose

The sharpest angle of descent or dip of the slope relative to the horizontal plane, when material on the slope face is on the verge of sliding, is known as the angle of repose, or the critical angle of repose, of a granular material. This angle falls between 0° and 90°.

Angle of Repose (Θ) <25 –indicates excellent flow

Angle of Repose (Θ) >40 –indicates very poor flow

This is the greatest angle that can be formed between a powder pile's surface and the horizontal. A funnel was used to let 10 g of powder flow at a height of 4 cm from the base. The diameter of the base and pile height were measured, and the formula for calculating the angle of repose was used.

$\tan \theta = h/r$

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

Where, Θ = angle of repose, h = Height of the heap, r = Radius of the heap.

Bulk Density

The ratio between the mass of an untouched powder sample and its volume, including the contribution of the interparticulate void volume, is the bulk density of a powder.

The volume that was measured is referred to as the bulk volume, and the bulk density is determined using the formula below;

Bulk density = Weight of powder / Bulk volume

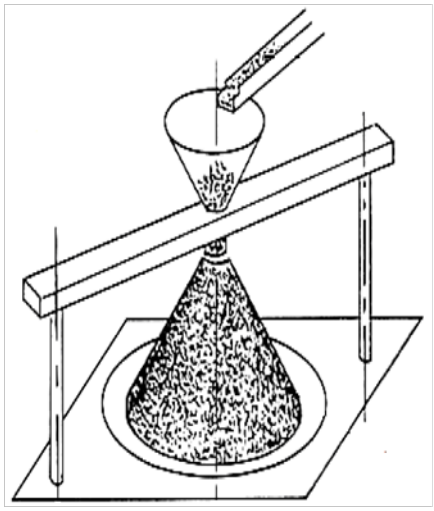

Figure 1: Funnel method for angle of repose

Tapped Density

The powder sample was contained in a container that was mechanically tapped to enhance the bulk density, which is known as the tapped density. The following formula is used to compute the tapped density.

Tapped density = Weight of powder / Tapped volume

Table 1: Various formulations of mucoadhesive drug delivery system were made as given in the table

Ingredients	MPS-1	MPS-2	MPS-3	MPS-4	MPS-5	MPS-6	MPS-7	MPS-8
Dexamethasone (gms)	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
Sodium alginate (gms)	2	3	2	3	2	3	2	3
Eudragit L-100 (gms)	1.0	1.0	-	-	1.0	1.0	-	-
HPMC K15 (gms)	-	-	1.0	1.0	-	-	1.0	1.0
Calcium chloride (% w/v)	3	3	3	3	-	-	-	-
Aluminium chloride (% w/v)	-	-	-	-	3	3	3	3

Table 2: Post formulation studies of dexamethasone mucoadhesive beads

Formulations	Bulk density (g/ml)	Tapped density (g/ml)	Haussner's ratio (%)	Carr'sindex (%)	Angle of repose(0)
MPS-1	0.716	0.741	1.035	3.39	21.81
MPS-2	0.850	0.868	1.023	2.05	18.78
MPS-3	0.789	0.809	1.024	2.6	20.31
MPS-4	0.822	0.885	1.071	7.15	18.27
MPS-5	0.584	0.609	1.044	4.09	22.28
MPS-6	0.566	0.634	1.13	10.76	24.71
MPS-7	0.629	0.669	1.07	5.89	19.30
MPS-8	0.629	0.666	1.08	5.56	27.03

Table 3: Evaluation tests

Formulations	Percentage yield (%)	Drug entrapment efficiency (%)	Swelling index (%)
MPS-1	78.8	57.15	57
MPS-2	98.4	76.23	63
MPS-3	88.8	65.37	53
MPS-4	84.5	71.46	58
MPS-5	77.2	77.39	43
MPS-6	91.4	99.16	35
MPS-7	72.5	83.45	21
MPS-8	98.8	91.83	22

Table 4: Microscopical Studies

Formulations	Particle Size (mm)
MPS-1	0.198
MPS-2	0.288
MPS-3	0.279
MPS-4	0.325
MPS-5	0.299
MPS-6	0.323
MPS-7	0.316
MPS-8	0.399

Table 5: FT-IR Interpretations of pure drug and Excipients

Functional Group	Dexamethasone		Sodium alginate		HPMC		Eudragit L 100	
	Observed	Obtained	Observed	Obtained	Observed	Obtained	Observed	Obtained
=C–H bend (Alkenes)	1000–650	965.19	1500–1400	1419.15	1000–650	965.19	1300–1150	1159.72
C–H bend (Alkanes)	1470–1450	1451.46	3000–2850	2888.13	1470–1450	1451.46	1300–1150	1159.72
C–N stretch (Aliphatic amines)	1250–1020	1159.95	1250–1020	1028.13	1250–1020	1159.95	1500–1400	1423.87
C=O stretch (Aldehydes)	1740–1720	1727.60	1500–1400	1419.15	1740–1720	1727.60	1320–1000	1017.78

Table 6: FT-IR Interpretation data for Mixture

Frequency (cm-1) observed	Obtained	Bond	Functional group
1250–1020	1071.45	C–N stretch	Aliphatic amines
1300–1150	1114.22	C–H wag (–CH 2X)	Alkyl halides
1650–1580	1650.05	N–H bend	1° amines
1760–1690	1707.18	C=O stretch	carboxylic acids

Figure 2: Lab India dissolution apparatus (DS-8000)

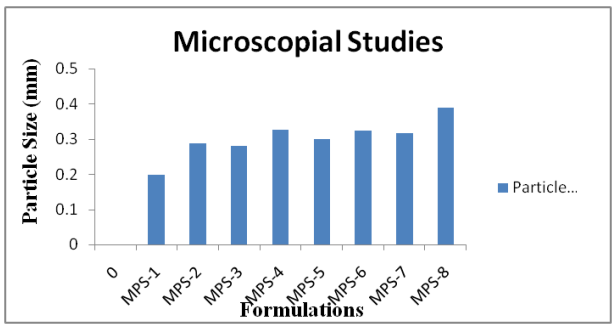

Figure 3: Microscopical studies

Table 7: In-vitro drug release data for Dexamethasone Mucoadhesive beads

Sl.no	Medium	Time	MPS-1	MPS-2	MPS-3	MPS-4	MPS-5	MPS-6	MPS-7	MPS-8
1		1	9.8	9.6	9.4	9.8	9.3	8.3	9.4	8.3
2		2	21.5	18.8	24.7	20.4	15.9	20.3	17.4	21.5
3		3	28.3	25.9	39.4	28.3	22.5	25.9	25.7	29.7
4		4	39.6	36.9	45.5	36.4	31.9	33.4	39.5	34.7
5		5	49.8	47.9	53.6	42.8	43.5	46.9	47.8	42.9
6	7.2 phosphate buffer	6	53.5	59.8	69.7	56.8	56.9	54.7	57.4	59.4
7		7	66.2	67.6	74.4	63.3	65.8	61.3	63.6	69.3
8		8	78.8	74.5	85.3	75.7	73.4	66.5	68.5	75.9
9		9	86.7	85.7	99.0	84.8	86.5	76.8	88.9	81.6
10		10	98.5	88.4	-	97.6	93.6	80.4	96.5	93.7
11		11	-	99.7	-	-	99.3	92.5	-	96.9
12		12	-	-	-	-	-	98.9	-	-

Table 8: Parameters and determination coefficients of release profile from Dexamethasone mucoadhesive beads

Formulation code	Correlation Coefficient values (r2)				Diffusion Exponent value (n)
	Zero Order	First order	Higuchi	Korsemayer-Peppas	
MPS-1	0.997	0.778	0.906	0.992	0.098
MPS-2	0.996	0.775	0.922	0.996	1.415
MPS-3	0.993	0.751	0.929	0.992	0.967
MPS-4	0.993	0.753	0.904	0.809	1.425
MPS-5	0.994	0.820	0.898	0.849	1.434
MPS-6	0.994	0.753	0.943	0.992	0.971
MPS-7	0.990	0.764	0.895	0.991	1.03
MPS-8	0.993	0.828	0.919	0.991	1.016

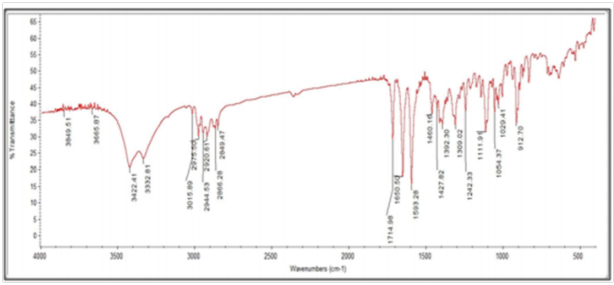

Figure 4: IR Spectrum of Dexamethasone

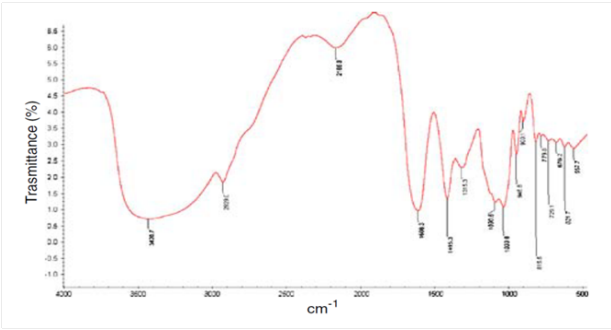

Figure 5: IR Spectrum of sodium alginate

Carr's Index (Compressibility Index)

One of the most crucial factors in determining the nature of powders and granules is this. The following equation can be used to compute it.

Carr's Index (5-15): indicates excellent flow

Carr's Index (12-18): indicates good flow

Carr's Index >38: indicates extremely poor flow

Carr's index = Tapped density - Bulk density / Tapped density X 100

Table 9: Stability studies In-vitro dissolution profile of MPS–7

S.NO	Medium	Time	% drug release of MPS-7		
			Batch-1 (25°C/60%RH)	Batch-2 (40°C/70%RH)	Batch-3 (60°C/80%RH)
1		1	8.5	9.3	10.5
2		2	19.5	22.4	19.4
3		3	23.9	29.8	28.6
4		4	30.4	34.4	40.3
5	7.4 Phosphate buffer	5	45.4	50.5	49.8
6		6	52.2	59.8	63.3
7		7	60.3	65.4	67.7
8		8	64.6	71.2	79.8
9		9	74.9	77.9	80.9
10		10	84.3	89.8	90.2
11		11	90.3	97.4	97.6
12		12	97.8		

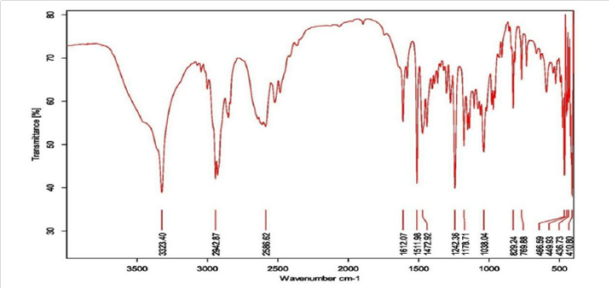

Figure 6: IR Spectrum of HPMC

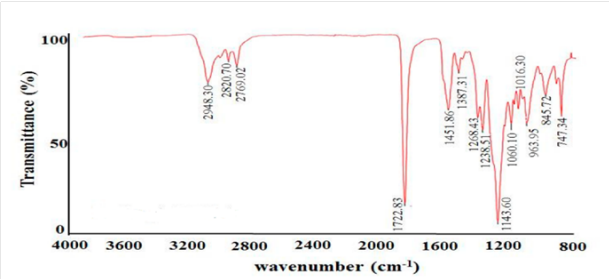

Figure 7: IR Spectrum of Eudragit L 100

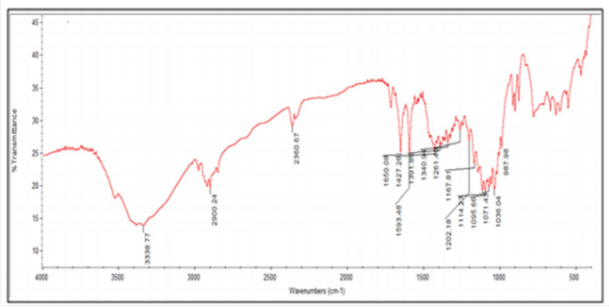

Figure 8: IR Spectrum of Dexamethasone + sodium alginate+ HPMC+ EUDRAGIT L 100

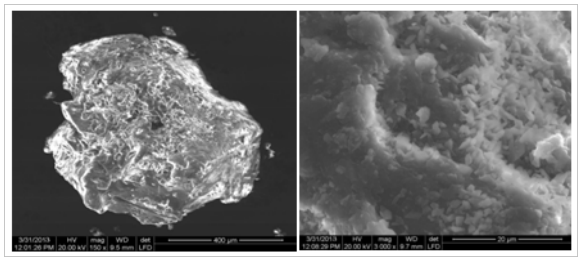

Figure 9: SEM Analysis of Dexamethasone mucoadhesive beads byusing calcium chloride as a gallant solution (MPS-2)

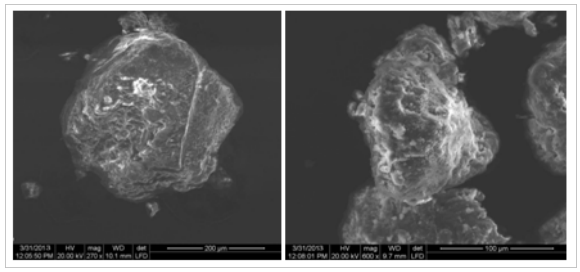

Figure 10: SEM Analysis of Dexamethasone mucoadhesive beads byusing aluminium chloride as gallant solution (MPS-6)

Hausner's Ratio

Hausner's ratio is a crucial factor in figuring out how well powders and granules flow. This can be determined using the formula below.

Hausner's ratio = Tapped density / Bulk density

HR<1.25-indicates good flow property

HR>1.25-indicates poor flow property

Post evaluation parameters

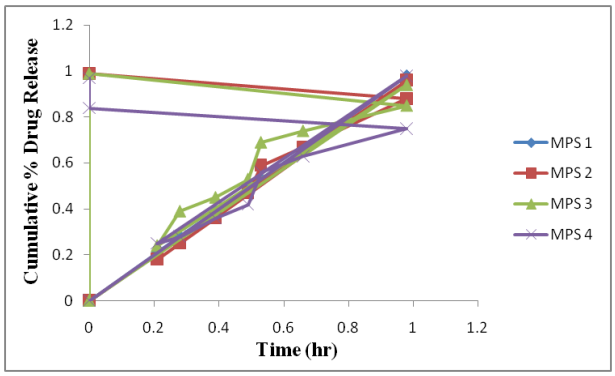

Figure 11: Cumulative % drug release data for MPS-1, MPS-2, MPS-3, MPS-4 formulations

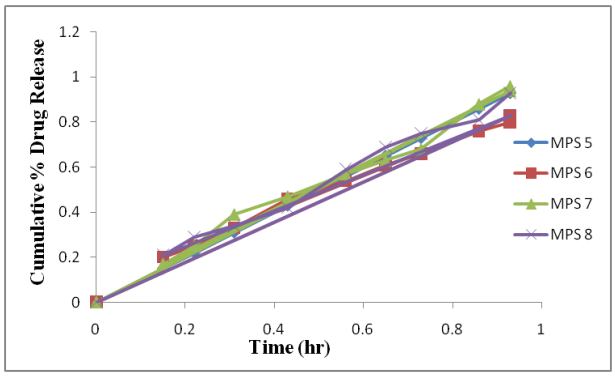

Figure 12: Cumulative % drug release data for MPS-5, MPS-6, MPS-7, MPS-8 formulations

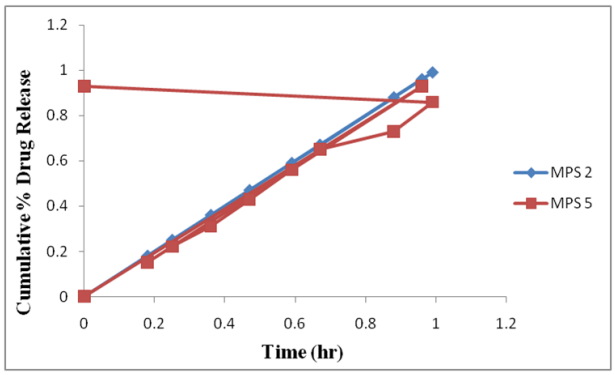

Figure 13: Cumulative % drug release data for MPS-2, MPS-5 formulations

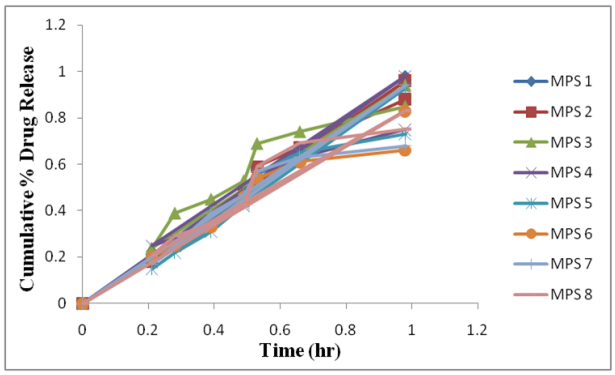

Figure 14: Cumulative % drug release data for MPS formulations

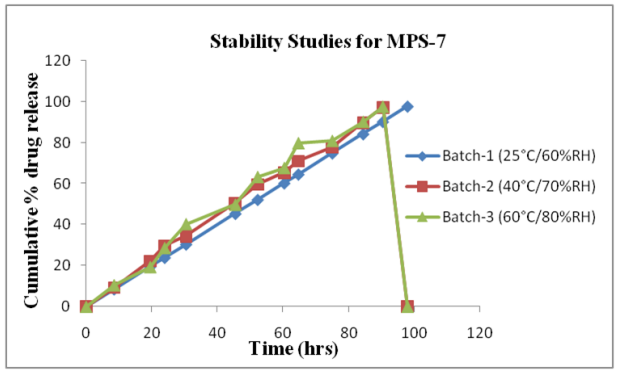

Figure 15: Stability studies for MPS-7

Drug Content

After drying, beads were weighed, and the target yield (-22/+44 sieve fraction) and process yield were computed. 100 mg of beads were triturated and dissolved in 100 mL of water to determine the drug content. At 242 nm, the solution underwent spectrophotometric analysis.

Drug loading

By dissolving 25 mg of adhesive beads in 100 mL of water, the drug loading was ascertained. A 45 m filter paper was used to filter the produced solution before it was spectrophotometrically measured at 242 nm. A formula was used to compute the medication loading;

% drug loading = (Amount of drug in beads/Amount of beads) × 100

Percentage encapsulation efficiency

Percentage encapsulation efficiency was calculated using the following formula,

Percentage encapsulation efficiency= AQ / TQ × 100

Where AQ denotes the actual amount of drug present in the beads and TQ denotes the estimated amount of drug present in the beads.

Microscopical characteristics of beads

Dexamethasone many adhesive beads were tested for particle size using a motif microscope on 50 beads. The typical particle size was determined.

SEM of beads

Dexamethasone alginate beads' morphology was examined using a scanning electron microscope (Model Jeol JSM-5200). Using a razor blade, cross-sectional views of the bead were produced. Before microscopy, the samples were coated with gold-palladium to a 200 Ao thickness. The working settings were a 20 KV accelerating voltage. Photos were shot at magnifications between 7000x and 12000x.

Swelling studies

The features of swelling in beads were investigated. Only batches with good drug content and greater than 50% entrapment efficiency were chosen. Drug-loaded bead samples were removed, weighed, and put into the wire basket of the USP dissolving device II. The bead basket was placed in a beaker that contained 100 ml of phosphate buffer (pH 7.2) kept at 370C. The beads were periodically taken out and weighed at predetermined intervals. The swelling ratio was then determined using the formula below:

Swelling ratio = weight of wet beads/weight of dried beads

In-vitro dissolution studies

Utilising a USP Type II dissolving equipment with 900 ccs of phosphate buffer (pH 7.2) kept at 37°C and agitated at 50 rpm, the dissolution of Dexamethasone many sticky beads was investigated. Periodically, samples were taken, and the dissolving media was changed. With the aid of a UV spectrophotometer (UV-1700, Pharmaspace, Shimadzu), these samples were examined for the presence of drugs. Only batches with good drug content and drug entrapment efficiency of more than 50% were chosen for the release study.

Mathematical modelling for drug release profile

To describe the process of drug release, the cumulative amount of dexamethasone released from the formed tablets at various time intervals was fitted into several kinetic models, including zero-order kinetics, first-order kinetics, the Higuchi model, and the korsemayer-peppas model.

Zero-order kinetics

It indicates of a system where the medication release rate is unrelated to the drug's concentration.

$Q_{ts} = Q_0 + K_0\ t$

First order kinetics

It discusses how drugs are released from systems where the rate of release is influenced by concentration.

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

Higuchi model

It states that the percentage of drug release from a matrix is inversely related to time.

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

Korsemeyer-Peppas model (Power law)

The effective law accurately explains the release of drugs from slabs, cylinders, and spheres and states that the fractional amount of drug release is exponentially related to the release time.

$Mt/M\alpha = Kt^n$

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

RESULTS AND DISCUSSION

Density and flow properties:

Table 2 lists the results of pre-and post-compression parameters such as bulk density, tapped density, carr's index, and porosity. According to the findings, beads' flow properties are now better than those of pure dexamethasone. The decrease in cohesiveness between the particles may be the cause of the increased flow property.

Entrapment efficiency:

The Entrapment efficiency raised gradually as sodium alginate concentration was raised; the findings are shown in Table 3. The formulations cross-linked with Al3+ often had higher incorporation efficiencies, which could be explained by the production of larger beads with these formulations, which can hold more medication.

Drug- Excipient Compatibility studies (FT-IR):

Using infrared spectroscopy, the drug-polymer interaction was investigated. Using a Perkin Elmer-883 IR spectrometer, the IR spectra for pure Dexamethasone, pure alginate, pure HPMC, pure EUDRAGIT L 100, and a mixture of Dexamethasone and sodium alginate, HPMC, and Eudragit L 100 in KBr pellets were measured between 500 and 3100 cm-1. By looking at the typical peaks, it was concluded from the data that there is no incompatibility between the Dexamethasone and other excipients. The distinctive peaks (Tables 4, 5 and 6).

SEM Photographs

In-vitro dissolution:

Different concentrations of sodium alginate, including 1, 2% w/v, 0, 5% HPMC, and 0, 5% Eudragit L 100, have been used with calcium chloride (2% w/v) and aluminium chloride (2% w/v) as gellant solutions to evaluate the impact of polymers on dexamethasone. In Table 7 and Figures 11, 12, 13, 14 and 15, the release profiles for these formulations are displayed. The findings showed that the release had been delayed with an increase in the content of sodium alginate in the gellant solution of aluminium chloride.

In-vitro Drug Release Kinetics for Dexamethasone mucoadhesive Beads

To compare the profiles of all formulations, various model-dependent methods (Zero order, First order, dissolution Higuchi, and Korsemayer-Peppas plots) were used (Table 8). These models' findings

show that the "best fit model" for all mucoadhesive beads in capsules is zero order. This is a result of a previously established fact based on the model fitting R2 value. According to the findings, MPS-6 had a stronger release-delaying impact. Dexamethasone beads' Korsemayer-Peppas release exponent (n) values are more than 0.85, indicating Super Case 2 transport.

Stability Studies

The best MPS-7 was used for the stability tests because it is widely regarded as the best. Over the course of 12 weeks, the formulation's organoleptic characteristics and dissolving profile were examined. The outcomes showed that batch 3 (which is maintained at 60^0C/80% RH) had a modest alteration in the colour of the capsules and the gross nature of the beads. Both batch 1 (maintained at 25°C and 60% RH) and batch 2 (maintained at 40°C and 70% RH) did not alter. This could be brought on by a higher swelling ratio. Table 9 through 20 show the results in tabular form.

CONCLUSION

The study's findings led to the conclusion that the right formulation conditions are crucial for achieving high encapsulation efficiency and for managing the release of Dexamethasone from alginate beads. According to in-vitro dissolving trials, formulations made with higher concentrations of sodium alginate and HPMC released the medication more quickly than those made with higher concentrations of sodium alginate and Eudragit L-100. When compared to beads made with calcium chloride, which was used as the gallant solution, the beads made with aluminium chloride, which was used as the gallant solution, formed firmer beads. To create the most effective Dexamethasone formulations, further research must be conducted.

ACKNOWLEDGEMENT

I would like to thank to the management and principal sir from Vasavi Institute of Pharmaceutical Sciences, Vasavi Nagar, Peddapalli (Village), Sidhout(Mandal), Kadapa (Dist), for guiding and supporting us to complete this research work.

Conflict of Interest

The authors declare that there is no conflict of interest for this study.

Funding Support

The authors declare that they have no funding support for this study.

REFERENCES

[1] S Ganga. Mucosal Drug Delivery. *Pharmainfo.net*, (5), 2007.

[2] A J Kinloch. The science of adhesion. *J. Mater. Sci*, 15:2141–2166, 1980.

[3] R Khanna, S P Agarwal, and A Ahuja. Mucoadhesive buccal drug delivery: A potential alternative to conventional therapy. *Indian J Pharm Sci*, 60(1):1–11, 1998.

[4] Swetha Polagani, Narendra Kumar Reddy Kolli, Ganga Rao Battu, and Murali Krishna Kumar. Comparative Evaluation of in vitro Anti-Infammatory Activity of Selected Medicinal Plants from Andhra Pradesh. *International Journal of Research in Pharmaceutical Sciences*, 11(4):8231–8236, 2020.

[5] Flavia Carvalho et al. Mucoadhesive drug delivery systems. *Brazilian Journal of Pharmaceutical Sciences*, pages 46–46, 2010.

[6] J O Felipe et al. Mucoadhesion and the Gastrointestinal Tract. *Critical Reviews in Therapeutic Drug Carrier Systems*, 25:207–258, 2008.

Cite this article: Naga Roopini B, Pradeep Kumar M. Formulation and Evaluation of Mucoadhesive Beads of Dexamethasone. Int. J. of Clin. Pharm. Med. Sci. 2023; 3(2): 63-71.