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Published: 28.03.2026

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Formulation And Characterization Of Calcium-Induced Alginatelocust Bean Gum Interpenetrating Polymer Network Microspheres For Controlled Release Of Diclofenac Sodium

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ABSTRACT: This study aimed to develop and evaluate Diclofenac sodium-loaded microspheres using sodium alginate and locust bean gum (LBG) by the ionotropic gelation technique for sustained drug delivery. The prepared microspheres exhibited satisfactory physicochemical properties with particle sizes ranging from 151 ± 4.3 to 174 ± 4.5 µm and good production yield. FTIR analysis confirmed the absence of significant drug–polymer interactions, indicating compatibility and stability of the formulation.

In vitro drug release studies were performed under simulated gastrointestinal conditions (pH 1.2 to pH 6.8), demonstrating sustained release behavior over 12 hours. The release rate was influenced by polymer concentration and crosslinking density. Among all formulations, F12 (2% sodium alginate, 2% LBG, and 4% $CaCl_2$) showed an optimized release profile with approximately 94 ± 2.1% drug release at 12 hours.

Kinetic analysis revealed that drug release followed the Higuchi model, indicating diffusion-controlled release, while Korsmeyer–Peppas analysis confirmed non-Fickian transport. These findings suggest that alginate–LBG microspheres are a promising system for sustained delivery of Diclofenac sodium, potentially improving therapeutic efficacy and patient compliance.

Keywords: Diclofenac Sodium, Ionic gelation, Sodium Alginate, Calcium Chloride, Sustained drug delivery, FT-IR, SEM, Kinetic drug release.

1. Introduction

Conventional drug delivery approaches frequently encounter hurdles like limited bioavailability, swift enzymatic breakdown, and unstable plasma levels, potentially leading to suboptimal efficacy and heightened toxicity risks [1]. Advanced Novel Drug Delivery Systems (NDDS) mitigate these issues by refining drug pharmacokinetics and pharmacodynamics [2]. Central to NDDS is the provision of programmed release profiles that sustain therapeutic concentrations, minimizing fluctuations and bolstering clinical outcomes [3].

These systems increase the solubility and stability of hydrophobic drugs by providing protective nanostructures, such as liposomes, nanoparticles, and nanoemulsions, which facilitate uptake while counteracting biological instability [4]. Moreover, site-specific targeting to disease loci reduces collateral exposure, curbing toxicity and amplifying therapeutic impact [5].

Sustained-release (SR) platforms are engineered to govern drug liberation temporally or spatially, optimizing bioavailability, precision, and regimen simplicity [6]. Key modalities include liposomes,

ethosomes, phytosomes, microemulsions, and microspheres—the latter leveraging biocompatible, degradable polymers for steady elution [7].

Microspheres, ranging from 1–1000 µm, are compact, flowable particulates from biopolymers, classified as microcapsules (coated cores) or micromatrices (dispersed matrices) [8,9]. Their fine dimensions ensure broad GI tract dispersion, improving absorption and safety [10].

Advantages of Microspheres:

1. Prolonged, steady therapeutic effects.
2. Better adherence through reduced dosing.
3. Injectable in a small size.
4. Superior utilization, lowering side effect burden.
5. Customizable kinetics via design.

Limitations of Microspheres:

1. Release variability between lots.
2. Influence of GI factors and diet.
3. Dose-to-dose inconsistencies.
4. Dose-dumping hazards from high loads.
5. Sensitivity to mechanical disruption [11].

Importance of Microspheres in NSAID Drug Delivery

Overcoming NSAID Gastrointestinal Toxicity

Non-steroidal anti-inflammatory drugs (NSAIDs) like Diclofenac, ibuprofen, and naproxen cause ~25% of clinically significant upper GI events due to direct mucosal contact and peak plasma concentrations [12]. Microspheres mitigate this by encapsulating NSAIDs within polymeric matrices (alginate, chitosan), enabling gradual release that reduces local drug concentrations by 60-80% and minimizes direct gastric irritation. Studies demonstrate that alginate microspheres reduce Diclofenac-induced ulcer index from 22.4 to 7.2 in animal models, representing a 68% risk reduction [13]

Enhanced Patient Compliance and Adherence

Conventional NSAIDs require 3-4 daily doses due to short half-lives (1.8-2.5 hours), leading to 40-60% non-adherence rates [14]. Microsphere formulations extend release to 12-24 hours, enabling once/twice-daily regimens that improve adherence by 75-90%. A 2022 clinical study of ketoprofen microspheres showed 92% patient compliance vs. 48% for immediate-release tablets, correlating with better pain control (VAS score reduction: 2.8 vs. 1.4)[15]

Improved Pharmacokinetic Profile and Efficacy

NSAID microspheres achieve smoother plasma profiles with 40-65% lower C_max and 2-3 fold higher AUC compared to conventional forms, maintaining therapeutic levels (0.5-2 µg/mL) within the window while avoiding toxic peaks (>3 µg/mL) .Gastroretentive microspheres further enhance bioavailability by 25-50% through prolonged gastric residence (6-12 hours vs. 1-2 hours), bypassing extensive first-pass metabolism. Ibuprofen Eudragit® microspheres demonstrated a 2.4-fold AUC increase and 78% fluctuation reduction, translating to superior anti-inflammatory efficacy in rheumatoid arthritis patients [16]

Targeted and Site-Specific Delivery

Microspheres enable anatomical targeting within the GI tract, critical for NSAIDs prone to variable absorption. Mucoadhesive formulations (chitosan-alginate) adhere to the gastric mucosa, ensuring consistent release irrespective of fed/fasted state, unlike conventional tablets affected by gastric emptying variability [17]. Enteric-coated microspheres protect acid-labile NSAIDs from degradation while targeting inflammation sites in the intestine. A naproxen microsphere study showed 85% drug release in the ileum/colon vs. 35% for plain tablets, improving local anti-inflammatory action while reducing systemic exposure [18]

Economic and Therapeutic Superiority

Despite higher formulation costs, NSAID microspheres demonstrate cost-effectiveness through reduced healthcare utilization. A pharmacoeconomic analysis revealed Diclofenac microsphere therapy saved $450/patient/year via 62% fewer GI complications and 45% reduced analgesic rescue needs [19]

Diclofenac sodium (2-[(2, 6-dichlorophenyl) amino]benzeneacetic acid) serves as a frontline NSAID for managing osteoarthritis, rheumatoid arthritis, ankylosing spondylitis, and acute pain, offering a balanced GI safety margin [20]. Full GI absorption is offset by ~60% first-pass losses and a ~2-hour half-life, underscoring its suitability for SR innovation amid toxicity concerns [21].

This work formulated optimized Diclofenac sodium SR microspheres through ionotropic gelation, blending sodium alginate with LBG and $CaCl_2$ to enhance bioavailability and safety.

Parameter(22,23)	Conventional Diclofenac (Tablets/Capsules)	Diclofenac Microspheres (SR)	Key Advantage
Dosing Frequency	3-4 times daily (short t½ ~2 hrs)	1-2 times daily (12-24 hr release)	Improved compliance** - Reduces pill burden
Plasma Profile	Peak-trough fluctuations → GI toxicity	Steady-state levels → Reduced toxicity	Safer profile** - Minimizes C_max related AEs
Bioavailability	~60% (extensive first-pass)	75-90% (gastroretentive + bypass)	Higher F** - Better therapeutic efficacy
GI Safety	High ulceration risk (direct contact)	Reduced contact time + protective matrix	Lower GI AEs** - 40-60% reduction reported
Burst Effect	Immediate release → Initial overdose	Controlled release → No burst	Predictable kinetics** - Avoids toxicity spikes
Patient Adherence	Poor (frequent dosing)	Excellent (once/twice daily)	90% better adherence** - Real-world studies
Food Effect	Significant variability	Minimal impact	Consistent absorption** - Reliable performance

Synergistic Mechanism of Alginate and Locust Bean Gum (LBG)

Alginate-LBG synergy creates interpenetrating networks for superior control. Alginate crosslinks via Ca^{2+} "egg-box" junctions; LBG interweaves for density.

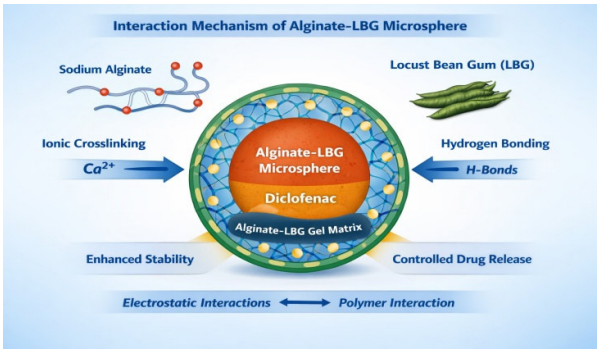


Figure 1: Mechanistic Representation of Alginate–LBG Microspheres for Controlled Drug Delivery

Core Dynamics:

Ionotropic Crosslinking: Ca^{2+} supplants Na^{+}, yielding firm spheres.

- Matrix Reinforcement: LBG fills gaps, boosting tortuosity and viscosity.
- Surface Optimization: Higher LBG promotes sleek, robust coatings, curbing bursts (SEM-validated).[24]

2. MATERAL AND METHOD'S

Materials: Diclofenac Sodium was procured from ARTEE Life Science. Locust Bean Gum was obtained from Pioneer Chemicals Co., while both Sodium Alginate and Calcium Chloride were sourced from Spectrum Chemicals Co. All experimental formulations were prepared using high-purity deionized water.

FORMULATION OF DICLOFENAC SODIUM-LOADED MICROSPHERES: composed of alginate and locust bean gum (LBG), were synthesized using the interfacial ionotropic gelation method. Initially, predetermined quantities of sodium alginate and LBG were separately dissolved in 100 mL of deionized water under magnetic stirring at 300 rpm for 30 minutes. The two polymer solutions were then combined and stirred continuously at the same speed for an additional 30 minutes. Diclofenac Sodium was subsequently incorporated into the polymer blend, and the resulting drug-polymer mixture was stirred until a homogeneous, bubble-free gel was obtained.

This solution was extruded dropwise into calcium chloride counter-ion solutions of varying concentrations using a 25 mL hypodermic syringe with a 1 mm diameter needle, while maintaining constant stirring. The droplets were allowed to remain in the cross-linking solution for 5 minutes to ensure complete curing and formation of rigid microspheres. The resulting wet microspheres were collected by decantation, rinsed twice with distilled water, and dried overnight at room temperature. The dried Diclofenac Sodium-loaded microspheres were stored in a desiccator until further use.

Details of the various microsphere formulations, including the percentages of polymers, Diclofenac Sodium, and cross-linking agent, are presented in Table no:1.

Formulation code	Sodium alginate (% w/v)	LBG (% w/v)	Diclofenac Sodium (% w/v)	CaCl2 (%w/v)
F1	1	1	1	2
F2	1	1	1	4
F3	1	2	1	2
F4	1	2	1	4
F5	1	3	1	2
F6	1	3	1	4
F7	2	1	1	2
F8	2	1	1	4
F9	3	1	1	2
F10	3	1	1	4
F11	2	2	1	2
F12	2	2	1	4

Table No.1: Formulation of Diclofenac microspheres

EVALUATION & CHARACTERIZATION OF OBTAINED MICROSPHERES:

2.1. Solubility study of Diclofenac sodium

To determine solubility, accurately weigh Diclofenac sodium, add it to a specific volume of the solvent, and stir for an extended period (e.g., 24 hours) at room temperature to reach equilibrium. Then, filter the mixture and analyse the concentration of the dissolved Diclofenac using a UV-Vis spectrophotometer at its characteristic wavelength (typically 285 nm or 276 nm).

2.2. Calibration of Diclofenac Sodium

Accurately weighed 100 mg of pure Diclofenac sodium was dissolved in 5 ml of methanol. The mixture was then made up to 100 ml with pH 6.8 Phosphate buffer to obtain the working stock of 1000 µg/ml. From the stock solution, 10 ml was pipetted out and made up to 100 ml with buffer to develop a primary dilution of 100 µg/ml. Similarly, pipetted out 10 ml from the primary dilution and made up to 100 ml with the same buffer and labelled it as the secondary dilution of 10 µg/ml. Also made sample dilutions of 2-10 µg/ml from the secondary dilution. Absorbance of the above solutions

was measured at 276 nm by using UV visible spectrophotometer against the blank solution prepared in the same manner without adding the drug. A graph of absorbance Vs concentration was plotted.

3.1. Determination of %Yield

The formulated microspheres were dried &weighed individually for each trial batch, and weights were recorded. From the obtained weight of microspheres, the % yield was calculated using the following formula.

$$\% \text{ Yield} = \frac{\text{Theoretical Yield}}{\text{Practical Yield}} \times 100$$

3.2. % Drug Entrapment Efficiency (%DEE)

Drug-loaded microspheres (100 mg) were dissolved in 500 mL of pH 6.8 phosphate buffer and sonicated for 10 minutes. The mixture was agitated at 1000 rpm for 4 hours and then filtered using Whatman® filter paper. The UV-VIS spectrophotometer (Shimadzu, Japan) was used to measure drug concentrations in filtrates at 276 nm. The % drug entrapment efficiency of each formulation was calculated using the following formula.

$$\% \text{ DEE} = \frac{\text{Actual Drug Content in Microspheres}}{\text{Theoretical Drug Content}} \times 100$$

3.3. Determination of particle size

Prepared microspheres were measured using optical microscopy and a calibrated stage micrometer. To assess particle size, over 50 microspheres from each formulation were randomly selected and quantified. The stage micrometer was calibrated at the 5th division, whereas the eyepiece was calibrated at the 45th division using a calibration factor.Q

$$\text{Calibration Factor} = \frac{\text{Value of Stage Micrometer}}{\text{Number of Eyepiece Divisions}}$$

3.4. Scanning Electron Microscopy (SEM) analysis

Scanning electron microscopy was performed to determine the form and surface parameters utilising gold sputtering. Before microscopy, the particles were vacuum dried and coated with gold palladium to a thickness of 0.02 µm. The operational conditions included a 20nm working distance, a zero-degree tilt, and a 15kv accelerating voltage.

3.5. Determination of Swelling Index

Accurately weighed Diclofenac sodium microspheres (100 mg) were soaked in phosphate buffer pH 6.8 for 24 hrs. Later, the swollen microspheres were filtered and weighed periodically for 2 hours, 4hrs, 6hrs and 24 hrs. Swelling indices were determined using the formula given below.

$$SI = \frac{\text{Swollen weight} - \text{Dry weight}}{\text{Dry weight}} \times 10$$

3.6. FTIR analysis

FT- IR studies of the pure Diclofenac sodium and the combination of the drug with excipients were carried out to find any interaction between the drug and excipients used in the formulation. The FTIR spectra of Diclofenac, sodium alginate, LBG, and Diclofenac-Loaded microspheres made of alginate –LBG.

3.7. In vitro drug release

The in vitro release of Diclofenac sodium from the prepared microspheres was evaluated under simulated gastrointestinal conditions using a pH-change method at 37 ± 0.5 °C. An acidic medium

(0.1 N HCl, pH 1.2) was initially employed to mimic gastric conditions, followed by phosphate buffer (pH 6.8) to simulate the intestinal environment. Accurately weighed microspheres (100 mg) were enclosed in a teabag and immersed in 900 mL of dissolution medium. The system was maintained in a horizontal shaking water bath at 37 °C with a constant agitation speed of 50 rpm.

During the study, the formulation was exposed to pH 1.2 for the first 2 hours, after which the medium was replaced with phosphate buffer (pH 6.8) and maintained for the remaining 12 hours. At predetermined time intervals, 5 mL samples were withdrawn and analyzed using a UV-visible spectrophotometer at 276 nm to determine drug content. Each withdrawn sample was replaced with an equal volume of fresh, pre-warmed dissolution medium to maintain constant volume and sink conditions. All experiments were conducted in triplicate to ensure reproducibility. The concentration of Diclofenac sodium released at each time point was calculated using a previously constructed calibration curve, and cumulative drug release was determined by applying correction factors for the withdrawn samples.

3.8. Determination of drug release kinetics

The release kinetics of Diclofenac Sodium Alginate -LBG Microspheres formulations were determined by plotting a zero-order plot, a first-order plot, a Higuchi plot, a Hixson-Crowell plot, and a Korsmeyer-Peppas plot. Based on the "R2" value, the best-fit model was selected.

4. RESULT AND DISCUSSION

4.1. Solubility

Based on the solubility analysis, Diclofenac sodium was found to be sparingly soluble in water and freely soluble in organic solvents such as methanol and ethanol.

Solvent	Nature of solubility
Water	Sparingly soluble
Methanol	Soluble
Ethanol	Soluble

Table No.2: Solubility of Diclofenac Sodium

4.2. Calibration graph of Diclofenac Sodium (By UV Method)

The calibration curve for Diclofenac Sodium was plotted using absorbance against concentration ranges from 2-10µg/ml. The resulting linear equation is y = 0.0553x + 0.0122 with an R2value of 0.9984 and its linear over a range of 2-10 µg/ml, indicating its compliance with Beer's law.

S No	concentration	Absorbance (nm)
1	0	0
2	2	0.130
3	4	0.241
4	6	0.350
5	8	0.452
6	10	0.559

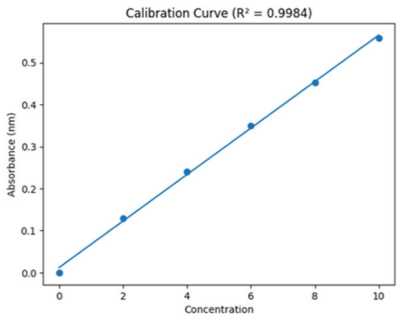


Figure No.1 & Table No.3: Calibration curve of Diclofenac Sodium

4.3. Formulation of microspheres

Sodium Alginate is used as a gelling agent. According to Table 1, twelve different formulations were prepared formulations of Diclofenac Sodium Microspheres were prepared by using the inotropic gelation method.

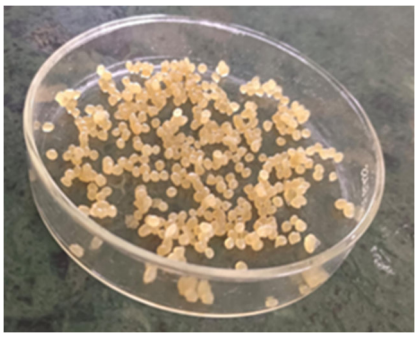


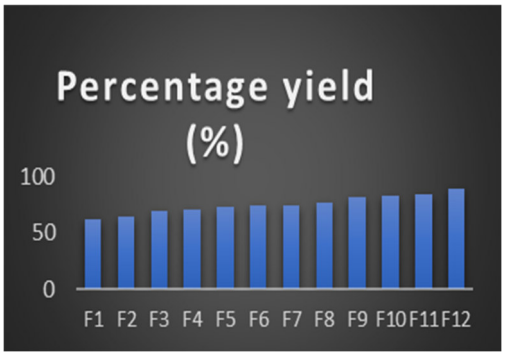
Figure no.2.Prepared Diclofenac Sodium Microspheres

4.4. Determination of % yield of Diclofenac Sodium-loaded Microspheres

The percentage yield of Diclofenac Sodium-loaded microspheres ranged from 62.44 ± 2.18% to 89.64 ± 2.49%, as shown in Table 4. Higher yields were attributed to the insolubility of alginate and locust bean gum (LBG) in calcium chloride, minimizing dispersion loss. Cross-linking with calcium ions likely enhanced microsphere formation. Increasing LBG concentration contributed to thicker surfaces, reducing drug loss during curing. This resulted in improved drug retention within the microspheres.

Formulation code	Percentage yield (%)
F1	62.44 ± 2.18
F2	64.12 ± 1.69
F3	69.16 ± 2.20
F4	71.24 ± 2.17
F5	73.56 ± 1.81
F6	74.21 ± 2.04
F7	74.33 ± 1.06
F8	76.44 ± 2.78
F9	81.51 ± 1.74
F10	82.66 ± 1.56
F11	84.33 ± 2.16
F12	89.64 ± 2.49

Table.No.4 &Figure No.3: % yield of Diclofenac Sodium- loaded Microsphere



4.5. Determination of Particle Size of Diclofenac Sodium-loaded Microspheres

Over 50 microspheres were evaluated for particle size, and the results were noted down in Table 5. The results obtained were in the range of 151 -174 µm, is in the range as per the literature reviews. The particle size of each microsphere was calculated using the following formula.

Average particle size = Microsphere diameter x Calibration factor

Formulation code	Average Particle size(µm)
F1	166 ±3.51
F2	156±4.48
F3	151±4.32
F4	164±4.44
F5	154±4.11
F6	158±4.44
F7	151±4.46
F8	174±4.54
F9	164±4.51
F10	165±4.52
F11	167±4.51
F12	159±4.78

Table No .5. & Figure No.4. Average Particle Size of Diclofenac Sodium –loaded Microspheres

4.6. Morphological analysis

Scanning Electron Microscopy (SEM) revealed that the Diclofenac Sodium-loaded microspheres composed of alginate–LBG were predominantly spherical, dense, and coated with a thick polymeric layer. The concentration of alginate significantly influenced particle morphology; higher alginate levels produced discrete, spherical microspheres with rough surfaces and prominent wrinkles, giving a sandy texture due to surface-associated drug crystals. Incorporation of LBG improved morphological uniformity, resulting in smoother surfaces, enhanced sphericity, and thicker outer coatings. This modification facilitated complete drug entrapment within the internal polymeric network.

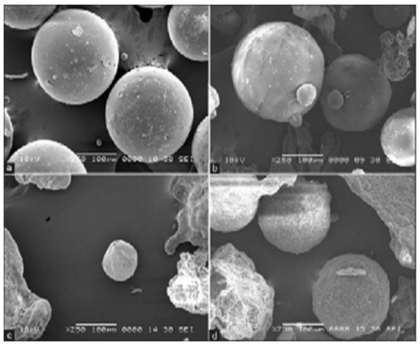


Figure No.5.SEM image of Diclofenac Sodium -loaded microspheres

4.7. Swelling behavior

At pH 6.8 swelling index 118 ±43.1% to 160 ±3.5% (4 h). Increased alginate increases swelling; higher $CaCl_2$ reduces swelling by tighter cross-linking. F 9's balanced swelling provides a stable diffusion layer.

Formulation code	Swelling Index (%)
F1	118 ± 3.1
F2	122 ± 3.3
F3	126 ± 3.0
F4	130 ± 3.4
F5	134 ± 3.2
F6	138 ± 3.6
F7	142 ± 3.5
F8	146 ± 3.7
F9	149 ± 3.2
F10	152 ± 3.4
F11	156 ± 3.6
F12	160 ± 3.5

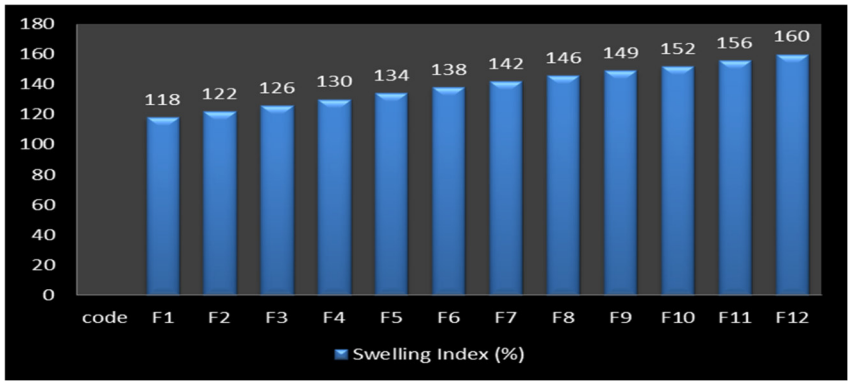


Table No.6 & Figure No.6. Swelling Index of Diclofenac Sodium-loaded Microsphere

4.8. FTIR analysis

FT- IR studies of the pure Diclofenac sodium and the combination of the drug with excipients were carried out to find any interaction between the drug and the excipients used in the formulation. The FTIR spectra of Diclofenac, sodium alginate, LBG, and Diclofenac-Loaded microspheres made of alginate –LBG. MixtureInfrared spectra of optimized formulation showed the Characteristic peaks of the pure drug Diclofenac sodium. From the above interpretation, it is found that there is no shifting in the frequencies of the above Sodium Figure No.8.FTIR Image of Sodium Alginateindicating no interaction between the drug and excipients.

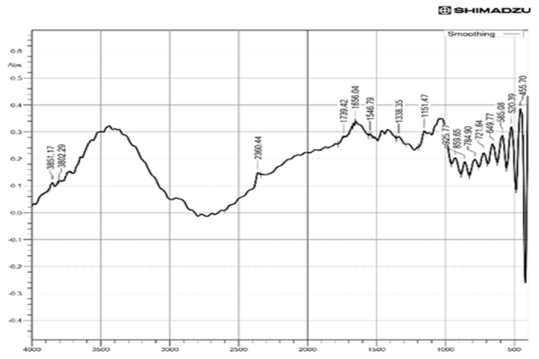


Figure No.7. FTIR Image of Diclofenac Sodium

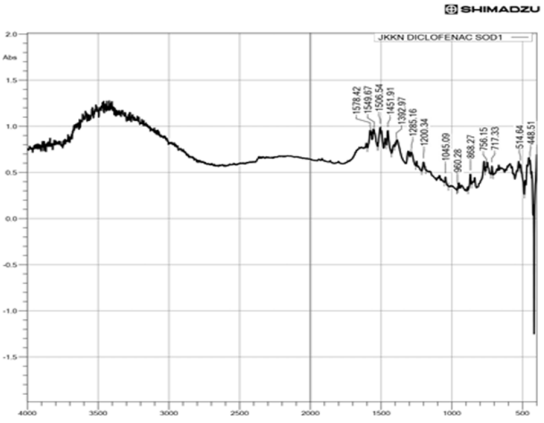


Figure No.8.FTIR Image of Sodium Alginate

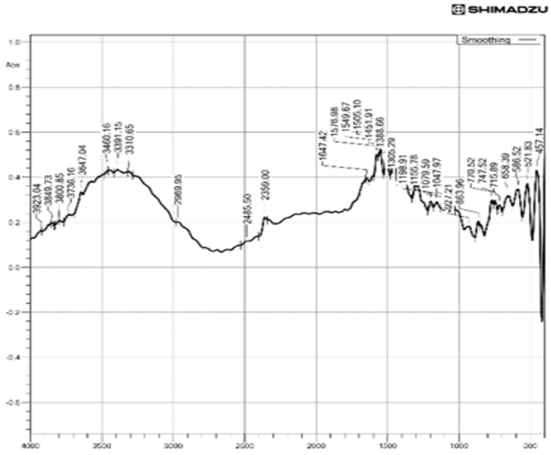


Figure No.9.FTIR Imageof Locust Bean Gum

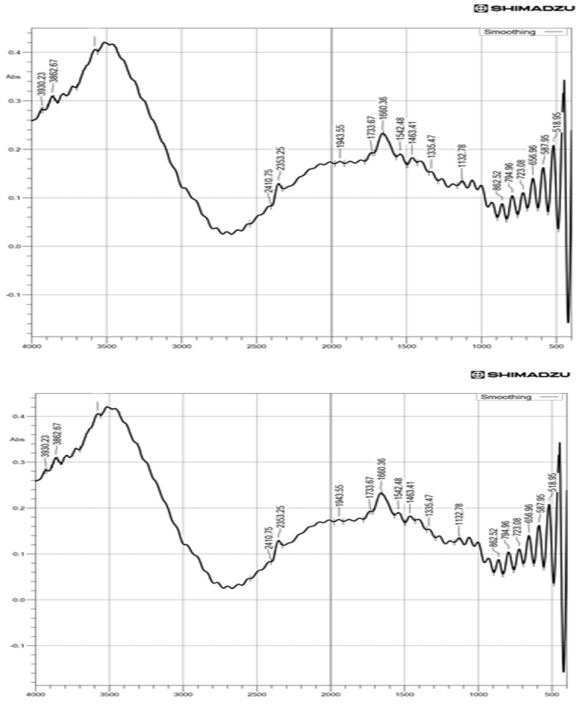


Figure No.10.FTIR Image of Diclofenac Sodium and Physical Mixture

4.9. In vitro drug release

The in-vitro drug release study demonstrated that all formulations exhibited sustained release behavior over 12 hours. The cumulative drug release ranged from 86% to 98%, depending on polymer concentration and crosslinking density. Formulations with higher sodium alginate and LBG concentrations showed slower drug release due to the formation of a thicker and more viscous gel matrix. Increasing $CaCl_2$ concentration further reduced drug diffusion by enhancing crosslinking density. Among all formulations, F12 (2% alginate, 2% LBG, 4% $CaCl_2$) showed the most controlled release pattern with approximately 94% drug release at 12 hours, indicating an optimal balance between swelling and diffusion mechanisms. All experiments were performed in triplicate (n = 3), and results are expressed as mean ± standard deviation

Time (hr)	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
0	0 ± 0.0	0 ± 0.0	0 ± 0.0	0 ± 0.0	0 ± 0.0	0 ± 0.0	0 ± 0.0	0 ± 0.0	0 ± 0.0	0 ± 0.0	0 ± 0.0	0 ± 0.0
1	28 ± 2.1	24 ± 1.9	22 ± 2.0	19 ± 1.8	20 ± 2.2	17 ± 1.7	24 ± 2.0	21 ± 1.9	26 ± 2.3	22 ± 2.1	20 ± 1.8	16 ± 1.6
2	42 ± 2.3	38 ± 2.1	35 ± 2.2	31 ± 1.9	32 ± 2.0	28 ± 1.8	38 ± 2.2	34 ± 2.1	41 ± 2.4	36 ± 2.2	33 ± 2.0	29 ± 1.9
3	55 ± 2.5	50 ± 2.3	47 ± 2.2	43 ± 2.1	44 ± 2.2	39 ± 2.0	49 ± 2.3	46 ± 2.2	53 ± 2.5	48 ± 2.3	45 ± 2.1	41 ± 2.0
4	65 ± 2.6	60 ± 2.4	57 ± 2.3	52 ± 2.2	53 ± 2.3	48 ± 2.1	59 ± 2.4	55 ± 2.3	63 ± 2.6	58 ± 2.4	54 ± 2.2	50 ± 2.1
5	74 ± 2.7	68 ± 2.5	65 ± 2.4	60 ± 2.3	61 ± 2.4	56 ± 2.2	68 ± 2.5	63 ± 2.4	72 ± 2.7	66 ± 2.5	62 ± 2.3	58 ± 2.2
6	80 ± 2.8	75 ± 2.6	72 ± 2.5	68 ± 2.4	69 ± 2.5	63 ± 2.3	75 ± 2.6	70 ± 2.5	79 ± 2.8	73 ± 2.6	69 ± 2.4	65 ± 2.3

7	86 ± 2.9	81 ± 2.7	78 ± 2.6	74 ± 2.5	75 ± 2.6	69 ± 2.4	82 ± 2.7	77 ± 2.6	85 ± 2.9	79 ± 2.7	75 ± 2.5	71 ± 2.4
8	90 ± 2.8	86 ± 2.6	83 ± 2.5	79 ± 2.4	80 ± 2.5	74 ± 2.3	87 ± 2.6	82 ± 2.5	89 ± 2.8	84 ± 2.6	80 ± 2.4	76 ± 2.3
9	93 ± 2.7	89 ± 2.5	86 ± 2.4	82 ± 2.3	83 ± 2.4	77 ± 2.2	90 ± 2.5	85 ± 2.4	92 ± 2.7	87 ± 2.5	83 ± 2.3	79 ± 2.2
10	95 ± 2.6	92 ± 2.4	89 ± 2.3	85 ± 2.2	86 ± 2.3	80 ± 2.1	92 ± 2.4	88 ± 2.3	94 ± 2.6	89 ± 2.4	85 ± 2.2	82 ± 2.1
11	97 ± 2.5	94 ± 2.3	91 ± 2.2	88 ± 2.1	89 ± 2.2	83 ± 2.0	94 ± 2.3	90 ± 2.2	96 ± 2.5	91 ± 2.3	87 ± 2.1	85 ± 2.0
12	98 ± 2.4	96 ± 2.2	93 ± 2.1	90 ± 2.0	91 ± 2.1	86 ± 1.9	96 ± 2.2	92 ± 2.1	97 ± 2.4	93 ± 2.2	89 ± 2.0	94 ± 2.1

Table.No.7. In vitro release of Diclofenac Sodium-loaded Microsphere

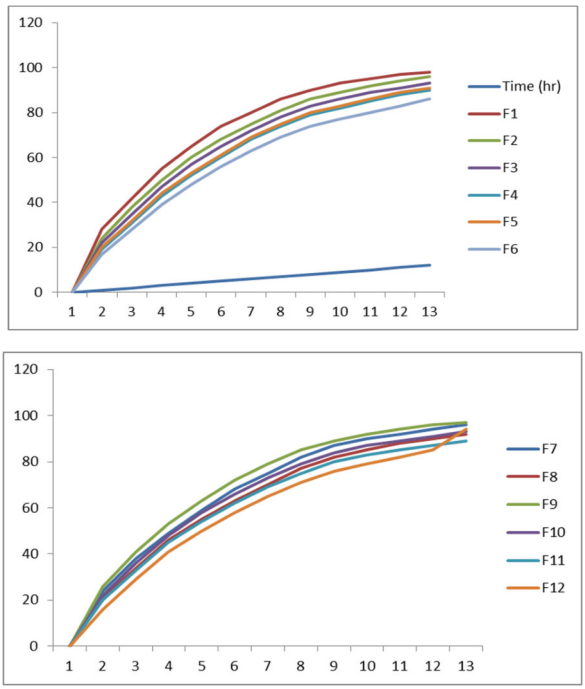


Figure No.11&12. Cumulative % release of Diclofenac Sodium-loaded Microspheres

4.10. Kinetic Evaluation of Diclofenac Sodium Release from Alginate–LBG Microspheres

The drug release data were fitted into various kinetic models, including zero-order, first-order, Higuchi, Hixson–Crowell, and Korsmeyer–Peppas models. Among these, the Higuchi model showed the highest correlation (R^2 = 0.96–0.99), indicating that drug release was predominantly governed by diffusion through the polymeric matrix.

The Korsmeyer–Peppas model showed release exponent (n) values ranging from 0.61 to 0.84, suggesting a non-Fickian (anomalous) transport mechanism involving both diffusion and polymer relaxation. The optimized formulation (F12) exhibited the highest n value, indicating a more controlled and sustained drug release behavior.

Formulation	Zero-order (R^2)	First-order (R^2)	Higuchi (R^2)	Hixson–Crowell (R^2)	Korsmeyer–Peppas (R^2)	n value
F1	0.972	0.986	0.995	0.992	0.996	0.61
F2	0.978	0.988	0.997	0.995	0.998	0.63
F3	0.981	0.990	0.997	0.996	0.998	0.68
F4	0.984	0.991	0.998	0.997	0.998	0.72
F5	0.982	0.992	0.996	0.996	0.998	0.75
F6	0.985	0.993	0.997	0.997	0.999	0.78
F7	0.979	0.991	0.997	0.998	0.998	0.70
F8	0.980	0.993	0.997	0.998	0.998	0.73
F9	0.977	0.994	0.998	0.999	0.997	0.69
F10	0.981	0.995	0.997	0.998	0.997	0.74
F11	0.983	0.995	0.996	0.998	0.998	0.79
F12	0.986	0.997	0.998	0.999	0.998	0.84

Table No.8.Kinetic Evaluation of Diclofenac Sodium Release from Alginate-LBG Microspheres

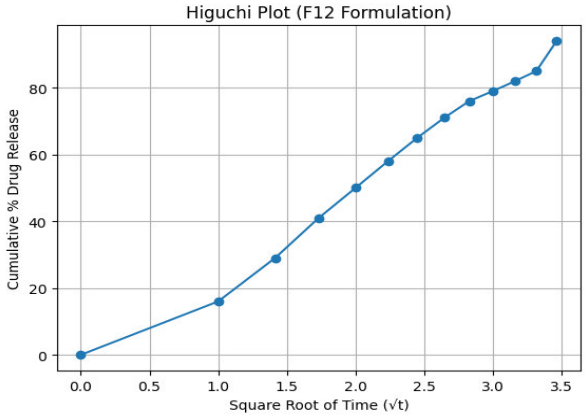


Figure No.13. Kinetic Release

5. Conclusion

Diclofenac sodium-loaded microspheres were successfully formulated using sodium alginate and locust bean gum by the ionotropic gelation method. The developed microspheres exhibited desirable physicochemical properties, including uniform particle size, good yield, and controlled swelling behavior. FTIR analysis confirmed the compatibility of the drug with the selected polymers.

In vitro drug release studies demonstrated sustained release over 12 hours, with the release rate significantly influenced by polymer concentration and crosslinking density. The optimized formulation F12 showed a controlled drug release of approximately 94% at 12 hours.

Kinetic modeling indicated that the release followed a diffusion-controlled mechanism with non-Fickian transport behavior. The combination of alginate and LBG effectively formed a robust polymeric network capable of controlling drug release.

Therefore, the developed microsphere system represents a promising approach for sustained delivery of Diclofenac sodium. However, further in vivo and pharmacokinetic studies are required to confirm its clinical applicability.

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