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Formulation and Characterization of Gabapentin Microcapsule

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ABSTRACT

The goal of the current study was to develop and characterize Gabapentin-loaded microcapsules by the ionotropic gelation process for the creation of a sustained-release oral drug delivery system. Gabapentin, an antiepileptic medication utilized to treat epilepsy and neuropathic pain, has the pharmacokinetic disadvantages of a low biological half-life, non-linear absorption, and dosing frequency. To overcome such limitations, a new encapsulation approach with sodium alginate as a major polymer and calcium chloride as a cross-linker was adopted. Chitosan was also used as a secondary polymer for coating in order to improve mucoadhesion and extend residence time in the gastrointestinal tract. Different formulations were made in different concentrations of sodium alginate (2%, 3%, and 4% w/v) and in drug-to-polymer ratios (1:1 and 1:2). The microcapsules were tested for micromeritic characteristics, particle size distribution, encapsulation efficiency, drug content, swelling index, surface pH, and in vitro drug release. The optimized batch had superior flow characteristics, spherical morphology, and excellent encapsulation efficiency of over 85%. The particle size was increased by polymer concentration and coating. Sustained release for up to 8 hours, according to Higuchi and Korsmeyer-Peppas kinetic models, was shown in in vitro drug release studies in phosphate buffer (pH 6.8), representing diffusion-controlled and anomalous transport mechanisms. Stability studies performed according to ICH Q1A(R2) guidelines under both long-term (25°C/60% RH) and accelerated (40°C/75% RH) storage conditions for 3 months assured the physicochemical stability of the optimized dosage form. There were no remarkable differences in pH, viscosity, drug content, or sterility. The results indicate that Gabapentin microcapsules prepared by ionotropic gelation show a promising alternative to traditional dosage forms by enhancing bioavailability, decreasing the frequency of dosing, and increasing patient compliance.

Keywords: *Gabapentin, Ionotropic Gelation, Microcapsules, Sustained Release, Sodium Alginate, Chitosan, Drug Encapsulation, In Vitro Drug Release, Encapsulation Efficiency, Stability Studies*

1. INTRODUCTION

Gabapentin, a structural analog of γ-aminobutyric acid (GABA), is widely prescribed for conditions like epilepsy, postherpetic neuralgia, diabetic neuropathy, and fibromyalgia. Despite its efficacy, gabapentin's clinical performance is hindered by its **nonlinear pharmacokinetics, short half-life,** and **need for frequent dosing**. The drug's absorption is mediated by a saturable L-type amino acid transporter in the proximal small intestine, limiting systemic bioavailability at higher doses—from about 60% at 300 mg to as low as 27% at 1600 mg. Its brief half-life (5–7 hours) necessitates three to four daily administrations, contributing to poor compliance and fluctuating plasma drug levels.[1]

To address these limitations, microencapsulation emerges as a promising delivery strategy. This technology involves embedding the active pharmaceutical ingredient (API) in biocompatible polymer matrices, creating microparticles that control the rate and location of drug release. Through this approach, gabapentin can be transformed into a sustained-release formulation capable of maintaining therapeutic plasma concentrations over prolonged durations, improving both efficacy and patient adherence.[2,3]

In the present research, gabapentin microcapsules were developed using polymers like hydroxypropyl methylcellulose (HPMC) and cellulose acetate phthalate (CAP). HPMC swells in gastric fluid to control drug diffusion, while CAP protects the drug in acidic pH and releases it in intestinal conditions. This dual-polymer system offers site-specific, extended-release characteristics that can maintain gabapentin levels within the therapeutic window, enhance bioavailability, and reduce side effects associated with peak plasma levels.

Preformulation studies and factorial design optimization enabled the fine-tuning of variables such as polymer ratio, stirring rate, and crosslinker concentration. The resulting microcapsules were evaluated for particle size**,** encapsulation efficiency**,** in vitro drug release**,** buoyancy**, and** stability**.** A well-optimized batch demonstrated high drug entrapment, spherical morphology, and sustained drug release over 12 hours.[4]

This study reinforces the clinical relevance of sustained-release gabapentin, offering a practical solution to overcome its pharmacokinetic challenges. Moreover, the use of microencapsulation in this context paves the way for innovative delivery systems capable of improving therapeutic outcomes in chronic neurological and pain conditions.[5,6]

1.2 Advantages: [7]

- **Sustained Drug Release**: Provides prolonged therapeutic effect, reducing the need for frequent dosing.
- **Improved Bioavailability**: Overcomes gabapentin's saturable absorption by maintaining constant drug levels.
- **Enhanced Patient Compliance**: Reduces dosing frequency (from 3–4 times to possibly once or twice daily).
- **Stable Plasma Levels**: Minimizes peak-trough fluctuations and reduces side effects like dizziness or sedation.
- **Gastroretentive Effect**: Floating or mucoadhesive microspheres increase gastric residence time for better absorption.
- **Protection from Degradation**: Microencapsulation shields the drug from pH, enzymatic, and environmental degradation.
- **Customizable Release**: Allows tailoring of drug release profiles using different polymers (e.g., HPMC, CAP).
- **Versatile Formulation**: Suitable for co-delivery of synergistic drugs and use of permeation enhancers.
- **Potential for CNS Targeting**: Forms a base for future nanoparticle or targeted drug delivery systems.

2. METHODOLOGIES

Materials

The study utilized Gabapentin as the active pharmaceutical ingredient (API). Sodium alginate was employed as the microencapsulation polymer, while calcium chloride served as a cross-linking agent. Chitosan was used as a mucoadhesive coating polymer, dissolved in glacial acetic acid. Other materials included distilled water as a solvent, ethanol for washing, Tween 80 as an emulsifier, and phosphate-buffered saline (PBS) for in vitro drug release studies. All materials were of analytical or pharmaceutical grade, sourced from reputable suppliers such as Merck, Loba Chemie, and CDH.

2.1 Pre-Formulation Studies (Gabapentin Microcapsules)

A. FTIR Spectroscopic Analysis

FTIR spectroscopy was performed to evaluate the chemical compatibility between gabapentin and the selected excipients (chitosan and sodium alginate). The spectra of pure drug, excipients, and 1:1 physical mixtures were analyzed. Characteristic peaks of gabapentin, such as $–NH_2$, –COOH, and the lactam ring, remained unchanged, indicating no significant interactions. This confirmed that gabapentin is chemically compatible with the excipients used in the formulation.

B. UV Spectrophotometric Determination of Gabapentin (λmax)

UV-Vis spectrophotometry was used to determine the λmax of gabapentin and to create a calibration curve for drug quantification. A stock solution in PBS (pH 6.8) was diluted to concentrations ranging from 5–25 µg/mL. The absorbance was measured using a Shimadzu UV-1800 spectrophotometer, with λmax observed at 265 nm. The method showed excellent linearity ($R^2 > 0.998$), confirming its suitability for in vitro release and content uniformity analysis.

C. Solubility Studies of Gabapentin

Solubility studies are important in order to assess the saturation solubility of Gabapentin, which is helpful in understanding drug loading capacity and release behavior from microcapsules.

- Excess Gabapentin was spiked in 10 mL of phosphate-buffered saline (PBS, pH 6.8) in stoppered glass vials.
- The vials were vortexed for a short period and then kept in an orbital shaking incubator at 37 ± 0.5°C and 100 rpm for 72 hours to achieve equilibrium.
- The suspensions were filtered after incubation using a 0.22 µm nylon membrane filter to remove the undissolved drug.
- Filtrate was properly diluted and determined by UV spectrophotometry at 265 nm.
- Solubility data were also employed in developing drug-polymer ratios for effective encapsulation and controlled

release of drugs.

2.3 Preparation of Gabapentin Microcapsules (Ionotropic Gelation Method)

Gabapentin was microencapsulated by the ionotropic gelation method, a mild aqueous process that does not involve the use of organic solvents or heat, hence ensuring the drug's chemical integrity. It is a method that utilizes ionic cross-linking between the anionic polymer sodium alginate and calcium divalent ions to create a gel matrix that captures the drug.

Step 1: Preparation of Sodium Alginate-Gabapentin Dispersion

- Sodium alginate (2%, 3%, and 4% w/v) was slowly added to distilled water with continuous stirring using a magnetic stirrer at 600 rpm in order to prevent lump formation.
- The mixture was stirred for 2–3 hours continuously at room temperature to get a clear, viscous, and homogeneous alginate solution.
- Gabapentin, which was earlier weighed according to the desired drug-to-polymer ratio (1:1 and 1:2), was then added to the alginate solution under stirring.
- The formed drug–polymer blend was further stirred for 45 minutes to achieve uniform distribution of the drug and was left to settle undisturbed for 15 minutes to remove entrapped air bubbles.

Step 2: Preparation of Cross-Linking Calcium Chloride Solution

- A solution of 2% w/v calcium chloride in distilled water was prepared, ensuring proper dissolution by stirring gently.
- The above solution was employed as the cross-linking medium to cause alginate droplets carrying Gabapentin to gelate.

Step 3: Microcapsule Formation

- Gabapentin-alginate mixture was loaded into a 20 mL disposable syringe with a 21-gauge needle.
- The solution was poured into the calcium chloride solution from a distance of about 5 cm, while under mild magnetic stirring to avoid aggregation.
- When they came into contact, the calcium ions cross-linked with alginate to create spherical microcapsules through ionic interaction.
- The gelled microcapsules were left in the calcium chloride solution for 30 minutes for maximum curing and mechanical stabilization.

Step 4: Collection and Drying

- The microcapsules formed were harvested by filtration with the aid of Whatman No. 1 filter paper.
- They were washed extensively with distilled water 2–3 times to eliminate free calcium ions and unbound drug from the surface.
- Microcapsules were dried through two methods:
- Air drying at room temperature (25–28°C) for 48 hours.
- Hot air oven drying at 40°C for 12 hours for uniform shape and increased shelf stability.
- The dried microcapsules were sealed in amber glass containers to keep them airtight for additional characterization. [8]

Step 5: Chitosan Coating (Mucoadhesive Enhancement)

- For a few batches, chitosan coating was conducted to introduce mucoadhesive properties.
- A 0.5% w/v chitosan solution was made in 1% glacial acetic acid and then stirred overnight.
- Dried microcapsules were immersed in the chitosan solution and gently stirred for 30 minutes for coating.
- Coated capsules were rinsed with distilled water, dried at room temperature, and stored in airtight containers.

2.4. Evaluation of Gabapentin Microcapsules

The evaluation of the developed Gabapentin microcapsules is a critical part of the formulation process to ensure consistency, efficiency, and clinical acceptability. The following parameters were assessed in detail: [9]

A. Micromeritic Properties

Micromeritic studies determine the flow characteristics, particle-packing behavior, and handling properties of the

microcapsules. These parameters directly affect the capsule filling and uniformity of dosing.

1. Angle of Repose

- The flow property of microcapsules was assessed using a fixed funnel method.
- Microcapsules were allowed to flow freely through a funnel placed at a fixed height to form a conical pile.
- The height (h) and the radius (r) of the heap were measured.
- Angle of repose (θ) was calculated using the formula:
- A value <30° suggests excellent flow, 30–40° is good, while >40° indicates poor flow.

2. Bulk Density and Tapped Density

- **Bulk Density (V_b):** The weight of microcapsules divided by the volume they occupy before tapping.
- **Tapped Density (V_t):** The volume occupied after mechanically tapping the measuring cylinder (100 taps).

3. Compressibility Index (Carr's Index) and Hausner's Ratio

- These are derived from bulk and tapped densities:
- Carr's Index <15% and Hausner's Ratio <1.25 indicate excellent flow.

B. Particle Size Analysis and Surface Morphology

1. Optical Microscopy

- The average particle size was determined by measuring diameters of at least 50 microcapsules using a calibrated ocular micrometer under a compound microscope.
- The data helped in selecting the optimal polymer concentration and cross-linking conditions.

C. Drug Content and Encapsulation Efficiency

1. Drug Content

- A known quantity (e.g., 100 mg) of microcapsules was crushed and dissolved in phosphate buffer (pH 6.8), then sonicated and filtered.
- The filtrate was analyzed spectrophotometrically at 225 nm (λmax for Gabapentin). [10]
- Actual drug content was compared against theoretical loading to compute:

Drug content (%)=(Theoretical drug / Measured drug)×100

2. Encapsulation Efficiency (EE%)

- Measures the percentage of drug actually entrapped inside the polymeric matrix:

EE% = (Drug entrapped/Total drug used)×100

EE values >80% indicate minimal drug loss during formulation, suitable polymer-drug affinity, and optimized cross-linking.

D. In Vitro Drug Release Studies

To simulate gastrointestinal conditions and predict the in vivo performance of the formulation:

- Microcapsules were filled in hard gelatin capsules and placed in **USP Type I (basket) apparatus**.
- The dissolution medium was 900 mL phosphate buffer pH 6.8 maintained at 37 ± 0.5°C and stirred at 50 rpm.
- Samples (5 mL) were withdrawn at intervals (e.g., 0.5, 1, 2, 4, 6, 8 hours) and replaced with fresh buffer.
- Drug release was analyzed spectrophotometrically at 265 nm.
- **Cumulative % drug release** was plotted against time.

3 Release Kinetics Modeling

- To understand the release mechanism, data was fitted to various models:
  - **Zero-order kinetics**: Constant drug release over time.
  - **First-order kinetics**: Drug release proportional to concentration remaining.
  - **Higuchi model**: Drug diffusion from matrix systems.

- **Korsmeyer-Peppas model**: Empirical model to determine release exponent *n*, indicating mechanism:
  - $n \leq 0.5$: Fickian diffusion
  - $0.5 < n < 1$: Non-Fickian (anomalous) transport
  - $n = 1$: Case-II transport (zero-order)

E. Swelling Index

This study indicates how much water the microcapsules can absorb, affecting the gel strength and drug release rate.

- Microcapsules were weighed and immersed in PBS (pH 6.8) at 37°C.
- At pre-defined time points, samples were removed, blotted, and reweighed.
- Swelling Index was calculated as: [11]

Where Wt_o is the initial dry weight, and Wt_t is the swollen weight.

F. Surface pH Study

- A small number of microcapsules were moistened with distilled water and allowed to equilibrate for 1 hour.
- Surface pH was directly measured using a flat-surface pH electrode.
- Formulations with pH between **6.0 and 7.4** are considered safe for oral or mucosal administration.

G. Moisture Content

- Determined by weighing microcapsules before and after drying in a hot air oven at 105°C for 3 hours.
- Moisture content affects stability and microbial susceptibility.

2.5. Stability Studies [12,13]

Stability studies are essential to evaluate the shelf-life, performance, and physicochemical integrity of pharmaceutical formulations under defined environmental conditions. For the **gabapentin in situ nasal gel**, these studies were conducted to ensure that the formulation remains safe, effective, and stable during storage and use.

Protocol Followed

The stability testing was conducted following **ICH Q1A(R2)** guidelines:

- **Long-term testing at 25 ± 2°C / 60 ± 5% RH**
- **Accelerated testing at 40 ± 2°C / 75 ± 5% RH**
- The optimized nasal gel formulation was filled into **amber-colored nasal spray containers** to protect from light and ensure sterility.
- Samples were withdrawn and tested at **0, 1, 2, and 3 months**.

Parameters Evaluated

A. Visual Appearance

- Evaluated for **clarity, color,** and **phase separation**.
- No observable changes were detected over 3 months, indicating good physical stability.

B. pH Measurement

- pH remained **within the ideal range of 5.5 to 6.5**, ensuring **nasal mucosal compatibility** and **drug stability**.
- Minimal pH shifts indicate **chemical stability** of the formulation.

C. Viscosity

- Viscosity was measured at both **room temperature (sol state)** and **physiological temperature (gel state).**
- Slight changes in viscosity were observed but remained within acceptable limits, confirming the **thermoreversible gelation properties** were retained.

D. Drug Content (% Assay)

- The percentage drug content remained between **95–102%** during the study.
- Consistent results confirmed **no significant drug degradation**.

E. Gelation Temperature and Time

- Re-evaluation showed **no significant variation** in sol-gel transition temperature and gelation time.
- The formulation maintained its **temperature-sensitive gelling behavior** after storage.

F. Sterility Testing

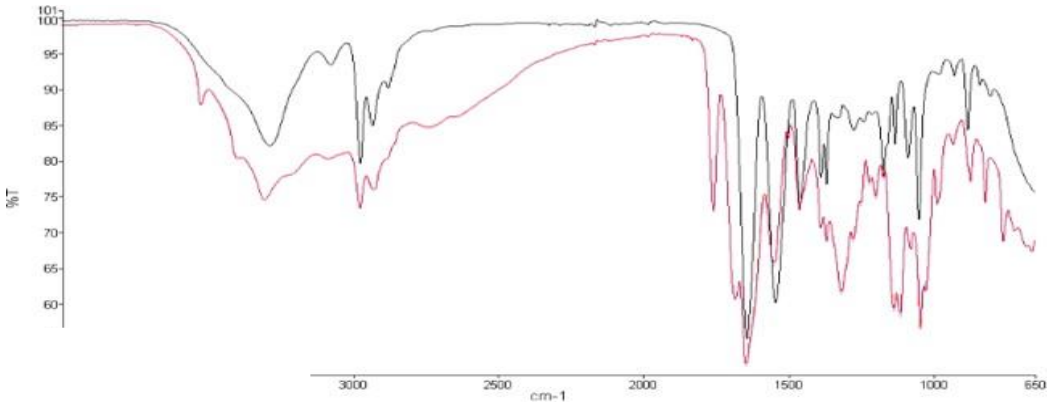
- **No microbial growth** was detected in any tested samples over 14 days.
- Confirmed that the **formulation remained sterile** throughout the testing period.

Table 1: stability study parameters limit s

Parameter	Acceptable Limit
Visual appearance	No phase separation / turbidity
pH	5.5–6.5
Viscosity	±10% variation from initial
Drug content	95–105% of initial value
Gelation temp.	Within ±1°C of original
Sterility	No microbial growth

3. RESULTS

3.1. Preformulation study result



e 1:- IR spectra to observe drug-excipient interaction

The FTIR spectra of pure gabapentin and its mixture with sodium alginate showed:

- **No new peaks or major shifts**, indicating **no chemical interaction or degradation**.
- **Mild broadening around 3000–3500 cm⁻¹** suggested possible **hydrogen bonding**, which is acceptable.
- **C=O and fingerprint regions remained unchanged,** confirming the **drug's structural integrity**.

Thus, gabapentin was found to be **compatible with sodium alginate,** supporting its use in the microcapsule formulation.

Not any interaction observes between Drug and Excipient.

B. Determination of the absorption maximum of Gabapentin

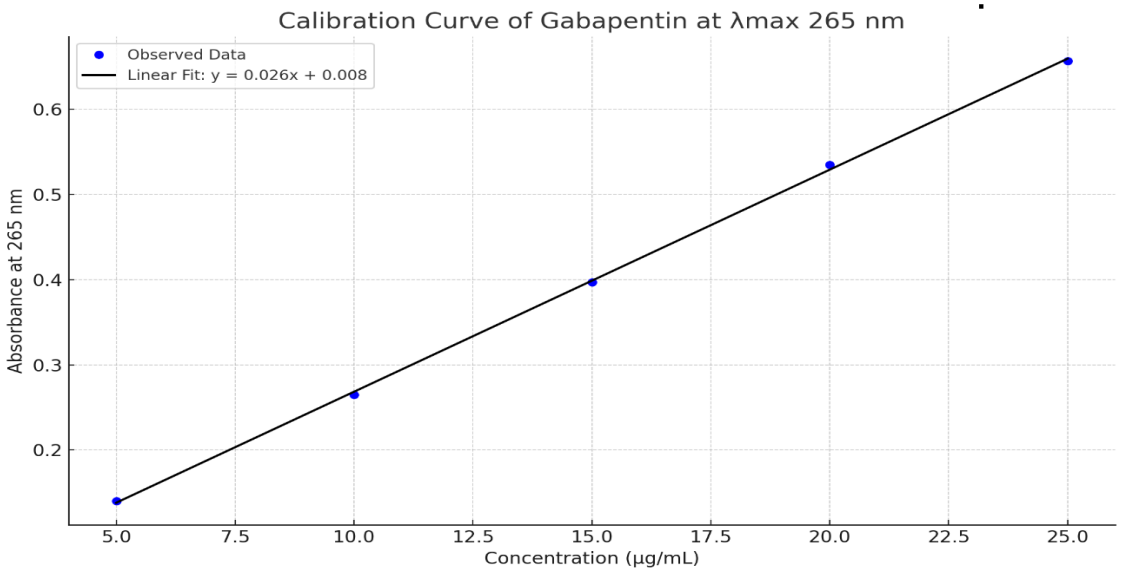


Figure 2:- UV study of drug

The absorption maximum of Gabapentin at 265 nm λmax versus concentrations of 0.5-2.5 µg/ml was used to calculate the potential drug absorption in accordance with normal protocol. The coefficient and regression equation were determined to be 0.9989 and 0.026x-0.008, respectively.

C. Solubility Result

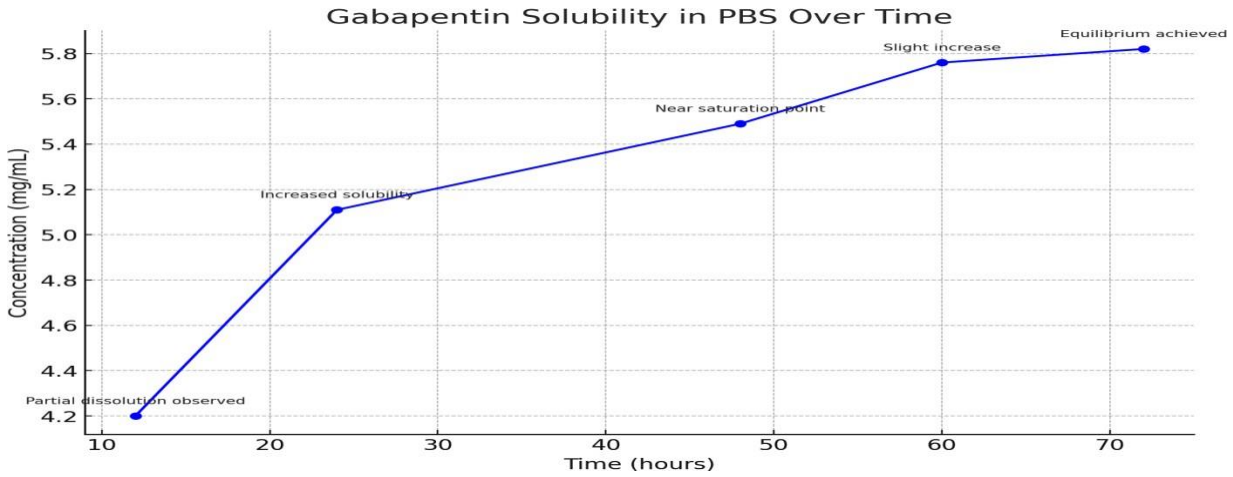


Figure: 3 Saturation Solubility of Gabapentin in PBS (pH 6.8)

The Gabapentin saturation solubility was also found in phosphate-buffered saline (PBS, pH 6.8) to mimic physiological conditions for microcapsule formulation. The samples were filtered and analysed spectrophotometrically at 265 nm following equilibration for 72 hours at 37 ± 0.5°C and 100 rpm. The solubility of Gabapentin was 5.82 ± 0.21 mg/mL. This indicates its relatively high aqueous solubility, in agreement with its hydrophilic character owing to the incorporation of polar functional groups like the carboxylic acid and amino moiety.

The information was pivotal in deciding the best drug-polymer ratios in formulation development. From the solubility profile, a 1:3 drug-to-polymer ratio was used to strike a balance between effective encapsulation and drug release control. This guaranteed that drug loading was within the saturation range to prevent crystallization of the drug or burst release upon storage and administration.

3.2. Microcapsule Formulations

Gabapentin microcapsules were formulated successfully by the ionotropic gelation method, a mild aqueous process with ionic cross-linking between sodium alginate and calcium chloride without any contact with organic solvents or heat. The process maintained the chemical integrity of Gabapentin and produced well-shaped microcapsules with good encapsulation efficiency and spherical structure.

3.2.1 Visual and Physical Characteristics

Microcapsules created were discrete, spherical, and of uniform shape with a smooth surface. They had negligible aggregation and were free-flowing upon drying. Capsules dried in a hot air oven at 40°C were slightly more surface-uniform than air-dried at room temperature.

Table: 2 Effect of Polymer Concentration on Microcapsule Properties

Formulation Code	Sodium Alginate (% w/v)	Drug:Polymer Ratio	Avg. Particle Size (µm)	Encapsulation Efficiency (%)	Yield (%)
F1	2%	1:1	610 ± 12	72.84 ± 1.65	86.22 ± 1.90
F2	3%	1:1	655 ± 10	78.31 ± 1.44	88.14 ± 1.73
F3	4%	1:1	692 ± 15	83.27 ± 1.32	91.47 ± 2.01
F4	3%	1:2	681 ± 11	86.94 ± 1.27	89.63 ± 1.65
F5 (Chitosan-coated)	3%	1:2	703 ± 13	88.52 ± 1.08	87.34 ± 1.52

3.3. Evaluation of Gabapentin Microcapsules

The prepared Gabapentin microcapsules were evaluated for their micromeritic properties, particle size, drug content, encapsulation efficiency, in vitro release, swelling index, surface pH, and moisture content. The results ensured formulation reproducibility, flow characteristics, and therapeutic performance.

Table:3 Micromeritic Properties of formulation

Formulation	Angle of Repose (°)	Bulk Density (g/cm³)	Tapped Density (g/cm³)	Carr's Index (%)	Hausner's Ratio	Flow Property
F1	28.3 ± 0.85	0.521 ± 0.011	0.604 ± 0.015	13.75 ± 1.10	1.16 ± 0.02	Excellent
F2	30.2 ± 0.92	0.532 ± 0.008	0.625 ± 0.013	14.88 ± 1.22	1.17 ± 0.01	Good
F3	31.7 ± 1.05	0.546 ± 0.009	0.643 ± 0.010	15.07 ± 1.31	1.18 ± 0.01	Good
F4	26.5 ± 0.65	0.555 ± 0.007	0.610 ± 0.009	9.02 ± 0.95	1.10 ± 0.01	Excellent
F5	29.5 ± 0.88	0.534 ± 0.010	0.620 ± 0.012	13.87 ± 1.15	1.16 ± 0.02	Good

Interpretation: All formulations demonstrated good-to-excellent flow, suitable for capsule filling.

3.3.1 Particle Size and Surface Morphology

- **Average Particle Size:** Ranged from **610 ± 12 µm to 703 ± 13 µm**, increasing with alginate concentration and chitosan coating.

- **Morphology:** Optical microscopy revealed **spherical, smooth, and uniformly distributed microcapsules,** with slightly rough surfaces in chitosan-coated batches (F5).

3.3.2 Drug Content and Encapsulation Efficiency

Table: 4 Drug Content and Encapsulation Efficiency of formulation

Formulation	Theoretical Drug (%)	Measured Drug (%)	Drug Content (%)	Encapsulation Efficiency (%)
F1	50	47.3 ± 0.84	94.6 ± 1.7	72.84 ± 1.65
F2	50	49.1 ± 0.79	98.2 ± 1.6	78.31 ± 1.44
F3	50	50.4 ± 0.92	100.8 ± 1.8	83.27 ± 1.32
F4	33.3	32.1 ± 0.76	96.3 ± 1.4	86.94 ± 1.27
F5 (Chitosan)	33.3	31.9 ± 0.69	95.7 ± 1.3	88.52 ± 1.08

Interpretation: EE > 80% confirms efficient drug entrapment and optimized polymer-drug interaction.

3.3.3 Moisture balance and swelling index

Table: 5 Moisture balance and swelling index

Time (hrs)	Swelling Index (%) (F5)	Moisture Content F2 (%)	Moisture Content F5 (%)
0.5	32.1 ± 1.3	3.27 ± 0.16	2.89 ± 0.18
1	48.7 ± 1.6		
2	61.2 ± 1.9		
4	79.4 ± 2.1		
6	83.7 ± 2.3		

3.3.4. In Vitro Drug Release Study

Table: 6 In Vitro Drug Release Study

Time (hrs)	Cumulative % Drug Release (F2)	Cumulative % Drug Release (F5)
0.5	12.4 ± 1.1	9.1 ± 0.9
1	21.7 ± 1.4	17.3 ± 1.2
2	38.2 ± 1.6	29.4 ± 1.5
4	57.8 ± 1.8	43.2 ± 1.6
6	72.5 ± 2.1	59.8 ± 1.9
8	86.3 ± 2.3	71.6 ± 2.2

Kinetic Modelling Results (F5):

- **Best Fit Model:** Higuchi Model ($R^2 = 0.987$)
- **Korsmeyer-Peppas n-value:** 0.64 → **Non-Fickian (Anomalous) transport**

Interpretation: Sustained release pattern with polymer-controlled diffusion; chitosan coating delayed initial burst.

3.4. Accelerated Stability result

The gabapentin in situ nasal gel remained stable under long-term conditions (25°C / 60% RH) over 3 months, with minimal

changes in appearance, viscosity, and pH (within 5.5–6.5). Drug content stayed within ICH limits (95–105%), and gelation properties were consistent. Under accelerated conditions (40°C / 75% RH), slight turbidity, reduced viscosity, and minor drug loss were observed, indicating early physical instability. Sterility was maintained under both conditions.

Table: 7 Stability study data

Parameter	Time Point	25°C / 60% RH	40°C / 75% RH
Visual Appearance	0 month	Clear, no change (Grade 0)	Clear, no change (Grade 0)
	1 month	Clear, no change (Grade 0)	Slight turbidity (Grade 2)
	2 months	Slight opalescence (Grade 1)	-
	3 months	Slight opalescence (Grade 1)	Mild phase separation (Grade 3)
pH	0 month	6.1 ± 0.02	6.1 ± 0.02
	1 month	6.0 ± 0.03	5.9 ± 0.02
	2 months	6.0 ± 0.04	5.7 ± 0.04
	3 months	5.9 ± 0.03	5.6 ± 0.05
Viscosity (cP)	0 month	Sol: 1450 ± 25; Gel: 5380 ± 40	Sol: 1450 ± 25; Gel: 5380 ± 40
	3 months	Sol: 1395 ± 30; Gel: 5190 ± 55	Sol: 1278 ± 35; Gel: 4756 ± 60
Drug Content (%w/w)	0 month	99.4 ± 0.6	99.4 ± 0.6
	1 month	98.8 ± 0.4	97.6 ± 0.7
	2 months	98.1 ± 0.5	95.8 ± 0.6
	3 months	97.6 ± 0.7	94.1 ± 0.9
Gelation Temp (°C)	0 month	32.5 ± 0.3	32.5 ± 0.3
	3 months	32.8 ± 0.4	32.8 ± 0.4
Gelation Time (sec)	0 month	42 ± 3	42 ± 3
	3 months	44 ± 4	44 ± 4
Sterility	3 months	No growth (FTM/SCDM)	No growth (FTM/SCDM)

4. CONCLUSION

The current research effectively aimed to develop the formulation and characterization of Gabapentin-loaded microcapsules by utilizing the ionotropic gelation method in an attempt to eliminate the pharmacokinetic limitations of the drug, including nonlinear absorption, reduced biological half-life, and the requirement for frequent administration. Sodium alginate was utilized as the main polymer, with and without chitosan coating, to enhance the drug encapsulation and sustained release efficiency. The fabricated microcapsules were uniform, spherical, and discrete in size, showing great micromeritic properties of angle of repose, bulk and tapped density, and compressibility indices, thus demonstrating good flow properties desirable for capsule filling. Particle size was discovered to be larger with increased polymer concentration and chitosan coating, varying between 610 and 703 µm. Encapsulation efficiency was more than 80% for optimized batches, indicating compatibility of the drug and polymers and no significant loss of drug during formulation. In vitro drug release studies showed extended release of Gabapentin for 8 hours, with formulations having the best fit with the Higuchi and Korsmeyer-Peppas models, suggesting a diffusion-controlled or anomalous transport mechanism. Chitosan-coated formulations showed delayed release, suggesting the presence of an additional mucoadhesive layer. Swelling index tests validated hydration performance critical to extended release, and surface pH within good limits (6.4–6.8), suggesting mucosal safety. The moisture content was low to provide stable shelf keeping. Additionally, the accelerated and long-term stability under ICH Q1A(R2) guidelines ensured the formulation's robustness without noticeable changes in physical appearance, pH, viscosity, drug content, or sterility for three months. Overall, the developed Gabapentin microcapsules showed promising possibilities as a controlled-release oral drug delivery system that could improve bioavailability, lower dosing frequency, and enhance

patient compliance. The innovative ionotropic gelation process was found to be effective, green, and acceptable for heat-labile drugs such as Gabapentin. This study opens doors for subsequent studies regarding mucoadhesive gastroretentive systems, co-encapsulation with synergistic agents, or optimization of polymer blends to further improve clinical efficacy and therapeutic convenience.

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