Formulation and In-Vitro Evaluation of a Thermoreversible Mucoadhesive Liquid Suppository of Diclofenac Sodium

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ABSTRACT

Conventional rectal suppositories can present limitations related to administration, retention, and patient acceptability. Thermoreversible liquid suppositories are administered as liquids and form gels at physiological temperature, potentially improving retention and controlling drug release. This study developed and evaluated a poloxamer-based mucoadhesive liquid suppository containing diclofenac sodium prepared by a cold method using Poloxamer 407 (P407), Poloxamer 188 (P188), and mucoadhesive polymers—sodium alginate, hydroxypropyl methylcellulose (HPMC), or Carbopol 934. P407/P188 combinations were screened, followed by preparation of 18 formulations (FM1–FM18). Preformulation assessment included organoleptic examination, melting point, UV spectrophotometry, FT-IR, and solubility testing. Formulations were evaluated for gelation temperature, gel strength, gelation time, mucoadhesive force, pH, drug content, and in-vitro drug release using a modified Franz diffusion cell. The reported optimized formulation, FM7, contained P407/P188/sodium alginate at 20/8/1% w/v. It had a gelation temperature of 37.4 ± 0.2 °C, gel strength of 47.96 ± 1.03 (reported as a penetration-time/strength measure in the source), gelation time of 1.11 ± 0.02 min, mucoadhesive force of 10.54 ± 0.20 (as reported), and drug content of 99.39%. Cumulative in-vitro drug release was 92.84 ± 0.65% at 360 min. The source reports a Korsmeyer–Peppas release exponent of 0.2529; the interpretation of this value requires verification against the original calculation and model-fitting data. The findings support the feasibility of a thermoreversible, mucoadhesive diclofenac sodium liquid suppository prepared by the cold method. FM7 showed gelation near physiological temperature and sustained in-vitro release over six hours.

KEYWORDS

Diclofenac sodium, thermoreversible gel, liquid suppository, Poloxamer 407, Poloxamer 188, mucoadhesion, rectal drug delivery

1. INTRODUCTION

Conventional drug delivery systems often produce fluctuations in plasma drug concentrations due to variations in drug absorption, distribution, metabolism, and elimination. These fluctuations may necessitate frequent administration and can affect patient compliance and therapeutic outcomes.

Controlled drug delivery systems (CDDS) have therefore been developed to regulate the rate, duration, and, where appropriate, site of drug release. The primary objective of these systems is to maintain drug concentrations within the desired therapeutic range for an extended period while minimizing fluctuations between peak and trough concentrations. Depending on their design, controlled drug delivery systems may also facilitate localized drug delivery, thereby improving drug availability at the intended site of action and potentially reducing unwanted systemic exposure[1].

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The major advantages of controlled drug delivery systems include prolonged drug action, reduced dosing frequency, improved patient compliance, maintenance of therapeutic drug concentrations, and reduced fluctuations in plasma levels. By limiting excessive peak concentrations, these systems may also reduce concentration-related adverse effects and improve therapeutic outcomes. Furthermore, controlled

drug delivery can be beneficial in the management of chronic conditions, including hypertension, diabetes, and chronic pain, where prolonged and consistent therapeutic activity is desirable[2,3].

Inflammation is a protective biological response initiated by the body in response to tissue injury, infection, harmful stimuli, or disease. It involves a coordinated series of vascular and cellular events intended to eliminate the causative agent, remove damaged tissue, and initiate repair. The inflammatory response commonly involves vasodilation, increased vascular permeability, and the migration of leukocytes to the affected tissue. Acute inflammation is typically short-lived and may resolve following the elimination of the initiating stimulus. In contrast, chronic inflammation persists over an extended period and may contribute to tissue damage, fibrosis, and disease progression. Persistent inflammatory processes have been associated with several pathological conditions, including rheumatoid arthritis, atherosclerosis, obesity, diabetes, and certain neurodegenerative disorders. Appropriate anti-inflammatory therapy is therefore important for controlling inflammatory symptoms, limiting tissue damage, and improving patient outcomes[4,5,6].

Rectal drug delivery represents an alternative route for both local and systemic drug administration. It is particularly useful when oral administration is difficult or impractical, such as in infants, children, patients experiencing nausea and vomiting, and individuals who are unable to swallow conventional dosage forms. Depending on the drug and formulation, rectal administration may provide an alternative to oral therapy and may partially avoid hepatic first-pass metabolism. Rectal drug delivery offers several potential advantages, including ease of administration in selected patient populations, avoidance of the need for swallowing, and the possibility of localized drug action[7,8,9].

Thermoreversible mucoadhesive liquid suppositories have emerged as a potential alternative to conventional solid suppositories. These formulations are designed to remain liquid at or below room temperature, facilitating administration, and subsequently undergo gelation at physiological temperature after rectal administration. The resulting gel may improve retention at the administration site, reduce leakage, and prolong contact between the formulation and the rectal mucosa. Their performance depends on formulation characteristics such as gelation temperature, gel strength, mucoadhesive properties, and drug-release behaviour[9-15].

Poloxamers are frequently investigated as thermoresponsive components in these formulations. They are non-ionic triblock copolymers composed of polyoxyethylene and polyoxypropylene segments arranged in a polyoxyethylene–polyoxypropylene–polyoxyethylene (PEO–PPO–PEO) structure. Their aqueous solutions can exhibit temperature-dependent gelation under appropriate concentration and formulation conditions. This property enables the development of systems that are readily administered as liquids but form semisolid gels upon exposure to physiological temperatures. The gelation behaviour of poloxamer-based formulations can be influenced by polymer concentration, the combination of different poloxamers, the presence of other excipients, pH, and ionic strength.

Diclofenac sodium is a non-steroidal anti-inflammatory drug widely used for the management of pain and inflammatory conditions, including musculoskeletal and rheumatic disorders. Its relatively short elimination half-life and limited aqueous solubility present formulation challenges when prolonged drug availability is desired. Oral administration may also be associated with gastrointestinal adverse effects, which has encouraged the investigation of alternative delivery systems.

A poloxamer-based thermoreversible mucoadhesive liquid suppository containing diclofenac sodium may provide a suitable approach for rectal administration. The formulation can be designed to remain sufficiently fluid during administration and undergo gelation at physiological temperature, potentially improving retention at the rectal site. Depending on the final formulation and its experimentally established properties, this approach may facilitate controlled drug release and provide an alternative to conventional solid suppositories. However, improved bioavailability, prolonged therapeutic activity, and reduced gastrointestinal adverse effects must be established experimentally rather than assumed solely from the dosage form.

Conventional solid suppositories may present limitations related to insertion, patient acceptability, and retention at the administration site. In contrast, thermoreversible liquid suppositories offer the possibility of easier administration and in situ gel formation, potentially improving formulation retention and drug-

release performance. The combination of poloxamers with suitable mucoadhesive excipients may help achieve the desired balance between fluidity during administration and gel strength after administration. These characteristics are particularly relevant to the development of rectal formulations intended to provide prolonged drug release.

The present study was therefore designed to formulate and evaluate a poloxamer-based thermoreversible mucoadhesive liquid suppository containing diclofenac sodium. The study focuses on the physicochemical characteristics of the formulation, including its gelation behaviour, gel strength, mucoadhesive properties, drug-release characteristics, and stability. The investigation aims to identify a formulation with suitable handling and administration properties, adequate retention potential, and controlled drug-release behaviour for rectal delivery of diclofenac sodium. The findings may contribute to the development of an alternative rectal dosage form for the management of inflammatory conditions.

2. MATERIALS AND METHODS

Diclofenac sodium was purchased from BLD Pharma, Telangana. Poloxamer 407, Poloxamer 188 wasreceived as gift sample from BASF India Limited, Navi Mumbai. Carbopol 934 was gift from Ases Chemical Works, Jodhpur, Rajasthan. All other chemicals and reagents used were of analytical grade.

2.1 Preformulation studies

The drug was examined for organoleptic properties and melting point. UV scanning was used to determine the wavelength of maximum absorbance, and a calibration curve was prepared over 10–20 µg/mL. FT-IR spectroscopy was used to examine the drug and excipients individually and in combination. Solubility was assessed in selected aqueous and non-aqueous solvents[16-21].

2.2 Formulation Development

Liquid suppositories were prepared by the cold method. Poloxamer 407 and Poloxamer 188 were added gradually to distilled water under continuous stirring, and the mixtures were refrigerated overnight at approximately 4 °C to obtain clear solutions. Diclofenac sodium and the selected mucoadhesive polymer were then incorporated. Initial screening examined P407/P188 combinations reported as 25/6, 20/8, and 20/10% w/v. The selected combinations were used to prepare 18 formulations (FM1–FM18) containing sodium alginate, Carbopol 934, or HPMC at 1 or 1.5% w/v[21,22].

2.3 Evaluation Of Gel

2.3.1 Physical Examination

The formulations were visually evaluated for color, clarity, and the presence of particulate matter. Briefly, a 5 mL sample was transferred into a clean, dry, transparent glass test tube and inspected visually against both black and white backgrounds. Any observed color changes, clarity level, or visible particles were observed[23].

2.3.2 Measurement Of Gelation Temperature

Gelation temperatures were evaluated using the tube-tilting method. Ten milliliters of the formulation were transferred into a test tube and placed in a 4°C water bath. The temperature was progressively raised, and the sample was monitored every 1–2 minutes. The temperature at which the solution failed to flow upon a 90° tilt of the tube was defined as the gelation temperature. The assay was conducted up to 60°C, with all samples analyzed in triplicate[21].

2.3.3 Measurement Of Gel Strength

A 50 g sample was gelled in a 100 mL graduated cylinder at 37 ± 1 °C for 30 minutes. A 35 g measuring apparatus was placed on the gel surface, and the time required for the device to sink 5 cm was recorded. If penetration exceeded 5 minutes, supplementary weights were added, and the minimum total load needed to move the device 5 cm through the gel was reported[21].

2.3.4 Gelation Time
Gelation time was evaluated by incubating 10 g of the formulation in a thermostatically controlled water bath at 37 °C. The time taken for the liquid mixture to undergo sol-to-gel transition was recorded using a stopwatch, and the mean gelation time was determined from triplicate measurements[24].

2.3.5 Measurement Of Mucoadhesive Power
Mucoadhesive strength was determined via a modified tissue-detachment method. Briefly, excised rectal tissue was mounted on two glass vials with mucosal surfaces exposed (d = 2 cm) and equilibrated at 37 °C for 10 min. A 0.15 g gel sample was placed between the two opposing mucosal surfaces. Water was added incrementally to a collection vessel attached to a modified balance pan until detachment occurred. The mucoadhesive force was calculated using the equation m x g = A
Where, m : weight added to the balance (gm), g : acceleration of gravity, A : area of the tissue exposed ($\pi r2$). Tissue samples were replaced between runs, and measurements were conducted in triplicate[20-22].

2.3.6 pH Of Sol-Gel Suppository
Formulation pH was measured using a calibrated digital pH meter. Standard phosphate buffer (pH 7.4) was used for instrument calibration prior to analyzing the liquid suppository samples[22].

2.3.7 Drug Content Estimation
For drug content analysis and spectral scanning, a 1 mL aliquot of the formulation was transferred into a 100 mL volumetric flask and dissolved in phosphate buffer (pH 7.4). After 10 minutes of sonication, the solution was diluted to volume and agitated for 2 hours. The mixture was then filtered through a 0.45 µm nylon membrane filter. Spectral scanning was performed over a wavelength range of 200–600 nm on a Shimadzu UV-Visible spectrophotometer using phosphate buffer (pH 7.4) as the blank. The drug concentration in the formulation was quantified using the standard calibration curve equation[21,24].

2.3.8 In-Vitro Drug Release From Liquid Suppository
In vitro drug release of diclofenac sodium from the sol–gel formulations was monitored across a nylon membrane using a modified Franz diffusion apparatus. The receptor cell contained phosphate buffer (pH 7.4) kept at 37 ± 0.5 °C under constant magnetic agitation. One gram of gel was loaded into the donor compartment. Samples (1 mL) were drawn from the receptor cell at set time points and replaced with fresh buffer to ensure sink conditions. Diclofenac sodium content was measured spectrophotometrically at 273.6 nm[21,24].

2.3.9 Drug Release Kinetics
To investigate the kinetics and mechanism of drug release, various mathematical models—including zero-order, first-order, Higuchi, and Korsmeyer–Peppas models—were fitted to the *in vitro* release data [53]. To characterize the release mechanism, the Korsmeyer–Peppas power law equation was applied $Mt/M\infty = ktn$, where fractional solute release is represented by Mt, $M\infty$ = Drug release period after an indefinite amount of time, T is the ejection time, and k is the drug release mechanism constant.

3. RESULTS AND DISCUSSION

3.1 Preformulation
Diclofenac sodium had a reported melting point of 282.67 ± 1.53 °C. The UV absorption maximum was reported at 273.6 nm. A calibration curve over 10–20 µg/mL in phosphate buffer (pH 7.4) gave a reported correlation coefficient of 0.9925. FT-IR analysis showed characteristic bands and the source reports no new peaks in the combined drug–excipient spectrum, which was interpreted as indicating no detectable incompatibility under the conditions tested. The drug was reported to be soluble in methanol, chloroform, and phosphate buffer (pH 7.4), while showing limited solubility in water and 0.1 N hydrochloric acid.

3.2 Optimization Of Poloxamer Concentration

Twenty batches were formulated by varying Poloxamer 407 and Poloxamer 188 concentrations. Formulations **F12** (6/25% w/v), **F15** (8/20% w/v), and **F19** (10/20% w/v) demonstrated gelation temperatures within the physiological rectal and colonic temperature range (Table 1).

Table 1. Result Obtained for combination of poloxamers Gelation temperature (% w/v)

Formulations	Poloxamer 188	Poloxamer 407	Gelation temperature (°C)
F1	2	15	Liquid more than 60°C
F2	2	18	48.3 ± 0.2
F3	2	20	41.9 ± 0.2
F4	2	25	40.4 ± 0.5
F5	4	15	Liquid more than 60°C
F6	4	18	43.2 ± 0.5
F7	4	20	39.7 ± 0.2
F8	4	25	38.8 ± 0.1
F9	6	15	48.6 ± 0.8
F10	6	18	41.4 ± 0.3
F11	6	20	39.7 ± 0.6
F12	**6**	**25**	**37.8 ± 0.1**
F13	8	15	45.7 ± 0.2
F14	8	18	41.5 ± 0.3
F15	**8**	**20**	**37.7 ± 0.6**
F16	8	25	34.6 ± 0.1
F17	10	15	46.2 ± 0.5
F18	10	18	39.4 ± 0.2
F19	**10**	**20**	**37.5 ± 0.2**
F20	10	25	34.7 ± 0.8

3.3 Optimization Of Mucoadhesive Polymer

Formulations exhibiting an optimal gelation temperature of 37±1^{0}C (**F12**, **F15**, and **F19**; Table 3.14) were selected to optimize the mucoadhesive polymer concentration. Inclusion of sodium alginate, Carbopol, and HPMC at various concentrations resulted in 18 optimized mucoadhesive formulations (**FM1–FM18**; Tables 2, 3 and 4).

Table 2. Formulation F12 P407/P188 (25/6 %w/v)

Formulation Code	Mucoadhesive Polymers	Mucoadhesive Polymers Concentration (%w/v)
FM1	Sodium Alginate	1
FM2	Sodium Alginate	1.5
FM3	Carbopol	1
FM4	Carbopol	1.5
FM5	HPMC	1
FM6	HPMC	1.5

Table 3. Formulation F15 P407/P188 (20/8 %w/v)

Formulation Code	Mucoadhesive Polymers	Mucoadhesive Polymers Concentration (%w/v)
FM7	Sodium Alginate	1
FM8	Sodium Alginate	1.5
FM9	Carbopol	1
FM10	Carbopol	1.5
FM11	HPMC	1
FM12	HPMC	1.5

Table 4. Formulation F19 P407/P188 (20/10 %w/v)

Formulation Code	Mucoadhesive Polymers	Mucoadhesive Polymers Concentration (%w/v)
FM13	Sodium Alginate	1
FM14	Sodium Alginate	1.5
FM15	Carbopol	1
FM16	Carbopol	1.5
FM17	HPMC	1
FM18	HPMC	1.5

Physical Examination

To assess visual appearance and clarity, 5ml of the formulation was placed in a clean, dry glass vial and inspected against black and white backgrounds. The preparation was clear, homogeneous, and free of visible particulate matter or color change, showing no physical alterations.(Figure 1(a) and 1(b))

Figure 1(a). Suppository in liquid state, Figure 1(b). Suppository in gel state

3.4 Measurement Of Gelation Temperature

The gelation temperature of formulations **FM1–FM18** was evaluated following polymer addition. Formulations **FM1, FM5, FM7, FM12, and FM13** demonstrated optimal gelation behavior (Tables 5,6 and 7).

Table 5. Formulation F12 P407/P188 (25/6 %w/v)

Formulation Code	Mucoadhesive Polymers	Mucoadhesive Polymers Concentration (%w/v)	Gelation Temperature (°C)
FM1	Sodium Alginate	1	**37.3 ± 0.3**
FM2	Sodium Alginate	1.5	36.4 ± 0.3
FM3	Carbopol	1	36.2 ± 0.7
FM4	Carbopol	1.5	35.8 ± 0.4
FM5	HPMC	1	**37.2 ± 0.2**
FM6	HPMC	1.5	36.5 ± 0.6

Table 6. Formulation F15 P407/P188 (20/8 %w/v)

Formulation Code	Mucoadhesive Polymers	Mucoadhesive Polymers Concentration (%w/v)	Gelation Temperature (°C)
FM7	Sodium Alginate	1	**37.2 ± 0.3**
FM8	Sodium Alginate	1.5	35.6 ± 0.5
FM9	Carbopol	1	36.2 ± 0.9
FM10	Carbopol	1.5	33.6 ± 0.5
FM11	HPMC	1	39.1 ± 0.6
FM12	HPMC	1.5	**37.8 ± 0.9**

Table 7. Formulation F19 P407/P188 (20/10 %w/v)

Formulation Code	Mucoadhesive Polymers	Mucoadhesive Polymers Concentration (%w/v)	Gelation Temperature (°C)
FM13	Sodium Alginate	1	**37.1 ± 0.4**
FM14	Sodium Alginate	1.5	35.9 ± 0.2
FM15	Carbopol	1	34.3 ± 0.9
FM16	Carbopol	1.5	34.8 ± 0.5
FM17	HPMC	1	38.7 ± 0.1
FM18	HPMC	1.5	39.5 ± 0.2

3.5 Measurement Of Gel Strength

Gel strength was determined by measuring the minimum load required to achieve a penetration depth of 5cm into the gel. Penetration times were maintained within 10-50s to prevent rectal leakage (<10s) and facilitate ease of administration (>50s). Increasing the concentrations of poloxamers and mucoadhesive polymers resulted in a concentration-dependent increase in gel strength. (Tables 8,9 and 10)

Table 8. Formulation F12 P407/P188 (25/6 %w/v)

Formulation Code	Mucoadhesive Polymers	Mucoadhesive Polymers Concentration (%w/v)	Gel Strength (g)
FM1	Sodium Alginate	1	**46.84± 1.51**
FM2	Sodium Alginate	1.5	31.16± 2.07
FM3	Carbopol	1	76.53± 1.76
FM4	Carbopol	1.5	73.82± 1.35
FM5	HPMC	1	**45.26 ± 1.67**
FM6	HPMC	1.5	35.46 ±1.48

Table 9. Formulation F15 P407/P188 (20/8 %w/v)

Formulation Code	Mucoadhesive Polymers	Mucoadhesive Polymers Concentration (%w/v)	Gel Strength (g)
FM7	Sodium Alginate	1	**47.69± 1.05**
FM8	Sodium Alginate	1.5	42.81± 1.73
FM9	Carbopol	1	82.46± 1.36
FM10	Carbopol	1.5	70.13± 1.90
FM11	HPMC	1	51.97± 2.98
FM12	HPMC	1.5	**46.52± 1.23**

Table 10. Formulation F19 P407/P188 (20/10 %w/v)

Formulation Code	Mucoadhesive Polymers	Mucoadhesive Polymers Concentration (%w/v)	Gel Strength (g)
FM13	Sodium Alginate	1	**46.84 ± 1.28**
FM14	Sodium Alginate	1.5	38.25± 1.29
FM15	Carbopol	1	64.80± 1.24
FM16	Carbopol	1.5	62.45± 1.25
FM17	HPMC	1	74.56 ± 1.27
FM18	HPMC	1.5	69.66 ±1.84

3.6 Gelation Time

Gelation time was directly dependent on poloxamer concentration. Statistical evaluation via one-way ANOVA followed by the Newman–Keuls multiple comparison post-hoc test revealed significant differences among all formulations ($P < 0.0001$). Among the tested batches, **FM1, FM5, FM7, FM12, and FM13** demonstrated optimal gelation times suitable for rectal administration. (Tables 11,12 and 13)

Table 11. Formulation F12 P407/P188 (25/6 %w/v)

Formulation Code	Mucoadhesive Polymers	Mucoadhesive Polymers Concentration (%w/v)	Gelation time (minutes)
FM1	Sodium Alginate	1	**1.25 ± 0.10**
FM2	Sodium Alginate	1.5	0.64± 0.26
FM3	Carbopol	1	3.86±0.42
FM4	Carbopol	1.5	4.88± 0.58
FM5	HPMC	1	**1.32± 0.11**
FM6	HPMC	1.5	0.39±0.23

Table 12. Formulation F15 P407/P188 (20/8 %w/v)

Formulation Code	Mucoadhesive Polymers	Mucoadhesive Polymers Concentration (%w/v)	Gelation time (minutes)
FM7	Sodium Alginate	1	**1.12± 0.03**
FM8	Sodium Alginate	1.5	0.58± 0.12
FM9	Carbopol	1	2.26±0.16
FM10	Carbopol	1.5	2.41± 0.24
FM11	HPMC	1	**1.19± 0.05**
FM12	HPMC	1.5	0.66±0.30

Table 13. Formulation F19 P407/P188 (20/10 %w/v)

Formulation Code	Mucoadhesive Polymers	Mucoadhesive Polymers Concentration (%w/v)	Gelation time (minutes)
FM13	Sodium Alginate	1	**1.31± 0.11**
FM14	Sodium Alginate	1.5	0.61± 0.34
FM15	Carbopol	1	2.51±0.46
FM16	Carbopol	1.5	2.69± 0.59
FM17	HPMC	1	2.45± 0.11
FM18	HPMC	1.5	2.32±0.45

3.7 Measurement Of Mucoadhesive Force

Mucoadhesive force is a critical physicochemical property for *in situ* gelling rectal formulations, as sufficient adhesion prevents the formulation from migrating to the upper rectum and undergoing first-pass hepatic clearance. The addition of mucoadhesive polymers significantly enhanced the mucoadhesive strength of the liquid suppositories in a concentration-dependent manner. In contrast, Poloxamer 188 (P-188) exerted a less pronounced effect on mucoadhesion than the primary mucoadhesive polymers. High-molecular-weight polymers played a key role in improving bioadhesion, predominantly through chain entanglement and van der Waals interactions. Among all evaluated batches, formulations **FM1, FM5, FM7, FM12, and FM13** demonstrated optimal mucoadhesive strength and appropriate gel strength required for effective rectal administration. (Tables 14,15 and 16)

Table 14. Formulation F12 P407/P188 (25/6 %w/v)

Formulation Code	Mucoadhesive Polymers	Mucoadhesive Polymers Concentration (%w/v)	Mucoadhesive force (dyne/cm^2)*100
FM1	Sodium Alginate	1	**10.39 ± 0.10**
FM2	Sodium Alginate	1.5	13.75± 1.11
FM3	Carbopol	1	15.83± 0.86
FM4	Carbopol	1.5	17.72± 1.63
FM5	HPMC	1	**10.24± 0.30**
FM6	HPMC	1.5	14.78± 0.43

Table 15. Formulation F15 P407/P188 (20/8 %w/v)

Formulation Code	Mucoadhesive Polymers	Mucoadhesive Polymers Concentration (%w/v)	Mucoadhesive force (dyne/cm^2)*100
FM7	Sodium Alginate	1	**10.55± 0.20**
FM8	Sodium Alginate	1.5	14.14± 1.34
FM9	Carbopol	1	18.23± 1.12
FM10	Carbopol	1.5	18.38± 1.47
FM11	HPMC	1	06.84 ±0.51
FM12	HPMC	1.5	**10.63± 0.20**

Table 16. Formulation F19 P407/P188 (20/10 %w/v)

Formulation Code	Mucoadhesive Polymers	Mucoadhesive Polymers Concentration (%w/v)	Mucoadhesive force (dyne/cm^2)*100
FM13	Sodium Alginate	1	**09.69 ± 0.30**
FM14	Sodium Alginate	1.5	12.33± 1.31
FM15	Carbopol	1	18.76± 0.45
FM16	Carbopol	1.5	22.52± 0.71
FM17	HPMC	1	13.46 ± 0.28
FM18	HPMC	1.5	17.88± 0.34

3.8 pH Of Sol-Gel Suppository

The pH of formulations FM1 through FM18 was determined using a digital pH meter, with all values found to be suitable for rectal delivery. (Tables 17,18 and 19)

Table 17. Formulation F12 P407/P188 (25/6 %w/v)

Formulation Code	Mucoadhesive Polymers	Mucoadhesive Polymers Concentration (%w/v)	pH
FM1	Sodium Alginate	1	7.22± 0.3
FM2	Sodium Alginate	1.5	7.46 ± 0.2
FM3	Carbopol	1	7.82 ± 0.4
FM4	Carbopol	1.5	7.19 ± 0.5
FM5	HPMC	1	6.96 ± 0.3
FM6	HPMC	1.5	7.18 ± 0.3

Table 18. Formulation F15 P407/P188 (20/8 %w/v)

Formulation Code	Mucoadhesive Polymers	Mucoadhesive Polymers Concentration (%w/v)	pH
FM7	Sodium Alginate	1	6.87 ± 0.5
FM8	Sodium Alginate	1.5	6.72 ± 0.3
FM9	Carbopol	1	6.79 ± 0.6
FM10	Carbopol	1.5	7.09 ± 0.5
FM11	HPMC	1	7.32 ± 0.4
FM12	HPMC	1.5	7.06 ± 0.2

Table 19. Formulation F19 P407/P188 (20/10 %w/v)

Formulation Code	Mucoadhesive Polymers	Mucoadhesive Polymers Concentration (%w/v)	pH
FM13	Sodium Alginate	1	7.14 ± 0.5
FM14	Sodium Alginate	1.5	7.09 ± 0.7
FM15	Carbopol	1	6.98 ± 0.6
FM16	Carbopol	1.5	7.19 ± 0.3
FM17	HPMC	1	7.11 ± 0.7
FM18	HPMC	1.5	6.97 ± 0.9

3.9 Drug Content Estimation

The drug content of the various sol–gel suppositories was determined using UV–Visible spectroscopy at ƛ273.6 nm. Each formulation was dissolved in phosphate buffer (pH 7.4) and diluted appropriately to measure absorbance. The drug concentration was subsequently calculated using the standard calibration curve equation. The drug content across all sol–gel suppository formulations ranged between 94% and 99%.(Tables 20)

Table 20. Drug content determination obtained for different formulation

Formulation Code	Drug Content (%)	Formulation Code	Drug Content (%)
FM1	**98.89 ± 0.13**	FM10	95.23 ± 0.35
FM2	93.14± 0.26	FM11	96.76± 0.28
FM3	95.57±0.32	**FM12**	**97.02±0.09**
FM4	94.24± 0.46	**FM13**	**98.23± 0.65**
FM5	**98.96± 0.06**	FM14	94.37± 0.38
FM6	96.51± 0.22	FM15	95.76± 0.55
FM7	**99.39±0.11**	FM16	97.67±0.28
FM8	96.12± 0.18	FM17	96.32± 0.62
FM9	93.76± 0.62	FM18	95.18± 0.76

3.10 In-Vitro Drug Release From Liquid Suppository

In vitro release studies demonstrated that increasing the concentrations of Poloxamer 407 and Poloxamer 188 decreased the release rate of diclofenac sodium, attributable to increased micellar entanglement and reduced matrix porosity. Additionally, the drug release rate was modulated by the type and concentration of mucoadhesive polymer added. The release-retarding capacity followed the rank order of Sodium Alginate > HPMC > Carbopol, which strongly correlated with enhanced gel strength and a reduction in sol–gel transition temperature.(Figure 2 and 3)

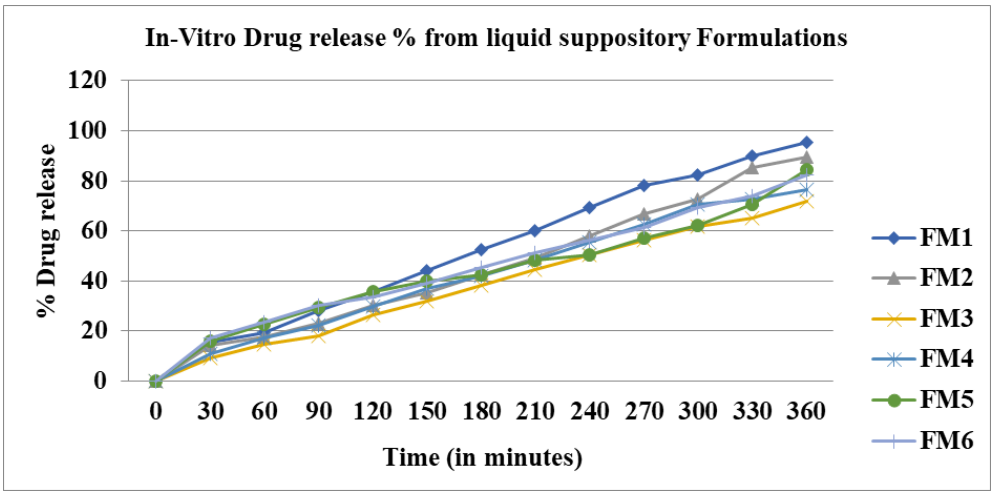

Figure 2. In-Vitro Drug release % from liquid suppository Formulations FM1 to FM6

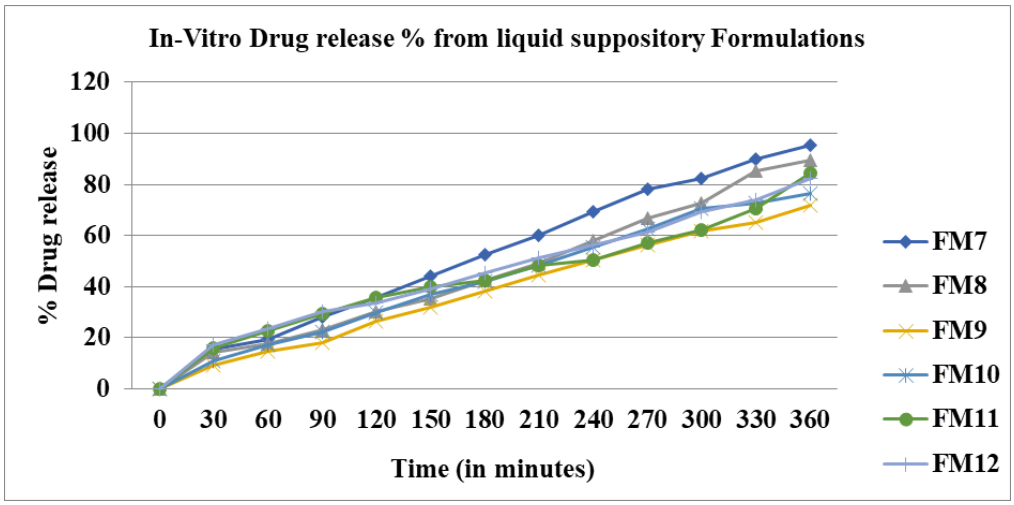

Figure 3. In-Vitro Drug release % from liquid suppository Formations FM7 to FM12

3.11 Release Kinetics Of The Optimized Formulation

Based on superior gelation temperature, gelation time, and mucoadhesive characteristics, batch **FM7** was selected as the optimized formulation for release kinetics analysis. The empirical data were fitted into zero-order, first-order, and Higuchi kinetic models. The mathematical model that yielded a correlation coefficient (R^2) nearest to unity was identified as the predominant drug release mechanism. Thus, it can be said that the optimized formula follows Zero order kinetics and Higuchi plots.(Table 21)

Table 21. Drug release kinetics of optimized Formulation FM7 by different kinetic models

Formulation	Zero order		First order		Higuchi		Korsmeyer-peppas	
	R^2	k	R^2	k	R^2	k	R^2	n
FM7	0.9793	7.1921	0.692	0.0084	0.9793	7.1921	0.692	0.2528

4. CONCLUSION

Diclofenac sodium mucoadhesive sol gel suppositories were made using the cold procedure. The impact of process parameters on gel strength, gelation length, gelation temperature, mucoadhesive force, and drug entrapment efficiency has also been clarified by such studies. Among the formulations evaluated, FM7, containing P407/P188/SA at concentrations of 20/8/1% w/v, respectively, was identified as the optimized formulation. It exhibited a gelation temperature of 37.2 ± 0.3°C, gel strength of 47.69 ± 1.05, gelation time of 1.12 ± 0.03, mucoadhesive force of 10.55 ± 0.20, and drug content of 99.39%. The formulation demonstrated 92.85 ± 0.64% in-vitro drug release at 360 minutes.The prolonged residence time and controlled-release profile of this system offer the potential to maintain therapeutic drug concentrations, thereby reducing administration frequency and minimizing dose-dependent side effects. Consequently, this rectal mucoadhesive sol–gel delivery system presents a promising approach for targeted local treatment of inflammatory conditions, ultimately improving patient compliance.The findings demonstrate the feasibility of a thermoreversible, mucoadhesive diclofenac sodium liquid suppository prepared by the cold method, showing suitable gelation and sustained release. Further studies are required to verify release-kinetic statistics, evaluate mucosal safety, and establish in-vivo performance prior to clinical translation.

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