

Formulation and Evaluation of Thermoresponsive Injectable hydrogel of Curcumin for Rheumatoid Arthritis

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ABSTRACT

Rheumatoid arthritis (RA) is a chronic inflammatory disorder associated with persistent joint inflammation and progressive tissue damage. Curcumin possesses promising anti-inflammatory activity; however, its poor aqueous solubility and limited bioavailability restrict its therapeutic application. The present study aimed to develop and evaluate a thermoresponsive injectable hydrogel for localized and sustained delivery of curcumin in RA. The hydrogel was prepared using chitosan, β -glycerophosphate, hyaluronic acid, and Pluronic F127 by the cold method. Different formulations were developed and evaluated for physical appearance, pH, spreadability, viscosity, gelation temperature, gelation time, syringeability, swelling behavior, drug content, and in-vitro drug release. The optimized formulation F4 exhibited a suitable pH (6.89 ± 0.02), gelation temperature ($34.2 \pm 0.2^\circ\text{C}$), gelation time (4.3 ± 0.2 min), viscosity (1986 ± 20 cP), good syringeability, and swelling index of $176 \pm 5\%$. The drug content was found to be $98.3 \pm 0.8\%$. In-vitro release studies demonstrated sustained curcumin release, with 93.7% cumulative drug release after 24 h. The release data showed the best fit with the first-order kinetic model ($R^2 = 0.9998$). Furthermore, the optimized formulation showed no significant changes in appearance, pH, drug content, gelation temperature, or syringeability during stability evaluation. Overall, the developed thermoresponsive injectable hydrogel demonstrated suitable physicochemical characteristics and sustained drug-release behavior, suggesting its potential as a localized delivery system for curcumin in rheumatoid arthritis.

Keywords: Curcumin; Rheumatoid arthritis; Thermoresponsive hydrogel; Injectable hydrogel; Chitosan; Pluronic F127; β -Glycerophosphate;

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INTRODUCTION

Rheumatoid arthritis (RA) is a chronic inflammatory autoimmune disorder primarily affecting the synovial joints and characterized by persistent inflammation, cartilage degradation, and progressive bone damage [1]. The disease can significantly impair joint function and quality of life. Although conventional therapies such as non-steroidal anti-inflammatory drugs, corticosteroids, disease-modifying antirheumatic drugs, and biological agents are widely used, their long-term administration may cause systemic adverse effects and may not provide sustained drug availability at the affected site [2]. Curcumin, a naturally occurring polyphenolic compound obtained from *Curcuma longa*, possesses promising anti-inflammatory and antioxidant properties and has been investigated as a potential therapeutic candidate for inflammatory disorders including RA [3]. However, its poor aqueous solubility, limited bioavailability, and rapid elimination restrict its therapeutic application.

Therefore, an appropriate drug-delivery system is required to improve its local retention and provide

sustained drug release. Thermoresponsive injectable hydrogels offer a promising approach for localized drug delivery. These systems can remain flowable during administration and undergo sol-to-gel transition at physiological temperature, thereby improving site retention and enabling prolonged drug release [4]. In the present study, a curcumin-loaded thermoresponsive injectable hydrogel was developed using chitosan, β -glycerophosphate, hyaluronic acid, and Pluronic F127. The developed formulations were evaluated for their physicochemical properties, gelation behavior, syringeability, swelling, drug content, in-vitro drug release, release kinetics, and stability to identify an optimized system for potential localized and sustained delivery of curcumin in rheumatoid arthritis.

2. Materials and methods

2.1 Materials

Curcumin was procured from Genome

Pharmaceuticals Pvt. Ltd., while β -glycerophosphate and hyaluronic acid were obtained from Molychem Pvt. Ltd. Pluronic F127 and chitosan were purchased from SRL Chem Pvt. Ltd. Acetic acid was also procured from Molychem Pvt. Ltd. All materials and chemicals used in the formulation and evaluation were of suitable analytical/pharmaceutical grade and were used as received without further purification.

2.2 Experimental study

Preformulation is the essential initial step in drug development, involving the study of the drug candidate's physical, chemical, and mechanical properties [5]. The Preformulation studies carried out in this project include several parameters.

2.2.1 Organoleptic properties

The organoleptic properties of curcumin were observed and recorded.

2.2.2 Melting point

Curcumin's melting point was measured and noted using the capillary technique and a digital melting point equipment.

2.2.3 FTIR spectroscopy

The identification of characteristic functional groups and confirmation of the chemical nature of the curcumin sample were performed using FTIR. The drug was finely ground with IR-grade potassium bromide and prepared as a pellet using a hydraulic press at 5.5 metric tons of pressure for analysis. The prepared pellet was then loaded into the sample chamber of the FTIR, and the spectrum was obtained in the range of 4000–450 cm^{-1} . The distinctive absorbance peaks of the functional groups obtained in the experiment were compared and analyzed with the reported reference values (B.P., 2009).

2.2.4 Solubility study

Solubility study of curcumin using standard IP methods. To select appropriate dispersible media for drug discharge for testing, its solubility profile in various solvents was examined. Briefly, a portion of the drug was separately mixed with organic solvents such as distilled water, 7.2 pH PBS, 7.4 pH PBS, Phosphate buffer 6.8, ethanol, methanol, acetone, and chloroform. These mixtures were then reciprocally shaken at 37°C for 5 minutes to assess drug dissolution.

2.2.5 UV-Visible spectroscopy

2.2.5.1 Determination of Absorption Maxima (λ_{max}) of curcumin

The Labindia UV 3000+ UV instrument was utilized to analyze the maximum absorption wavelength and purity of curcumin. The drug was quantitatively

analyzed using UV–visible spectroscopy. A standard solution of Cr was formulated by using Methanol: Phosphate Buffer pH 6.8 (30:70 v/v). The maximum absorption wavelength (λ_{max}) of curcumin was determined by scanning the solution in a 1 cm quartz cuvette using with the wavelength range 200–800 nm [6].

2.2.5.2 Calibration of curcumin

A standard calibration curve of curcumin was developed using Methanol: Phosphate Buffer pH 6.8 (30:70 v/v) as solvent system. Initially, 10 mg of curcumin was weighed and moved into a 10 mL flask, then mixed and adjusted to volume with the prepared solvent mixture to obtain a primary stock solution of 1000 $\mu\text{g/mL}$. Subsequently, 1 mL of this solution was further diluted to 10 mL using the same solvent system to prepare a secondary stock solution containing 100 $\mu\text{g/mL}$. Different aliquots of the secondary stock solution (0.2–1.6 mL) were then moved into separate 10 mL flasks and appropriately diluted to yield concentrations ranging from 2–16 $\mu\text{g/mL}$. The absorbance of each prepared dilution was recorded at the maximum wavelength of approximately 425 nm using Methanol: PBS pH 6.8 (30:70 v/v) as the blank solution. Finally, a calibration graph was constructed by plotting curcumin concentration against absorbance values.

2.3 Formulation of curcumin injectable hydrogel

The injectable thermosensitive curcumin hydrogel formulations were prepared by cold method using chitosan, β -glycerophosphate (β -GP), hyaluronic acid, and Pluronic F127. Chitosan was liquefied in 1% v/v acetic acid under magnetic stirring at 800 rpm for 5–6 h to obtain a clear, homogeneous solution, which was then stored at 4°C overnight. β -GP, hyaluronic acid, and Pluronic F127 were prepared separately in cold distilled water under continuous stirring and maintained at 4°C. Curcumin was dissolved in a small quantity of methanol and sonicated for 10–15 min to obtain a uniform solution. The hyaluronic acid and Pluronic F127 solutions were slowly added to the chitosan solution under constant mixing, and adjust the temp below 10°C using an ice bath. Subsequently, the curcumin solution and the cold β -GP solution were added dropwise while stirring continuously to obtain a homogeneous injectable hydrogel. The final volume was adjusted to 20 mL with distilled water and formulations were stored in amber-colored glass containers at 4°C. The prepared formulations remained liquid at room temp at 37°C (**Table 1**).

Table 1: Composition of curcumin injectable hydrogel.

Ingredients	F1 (Blank)	F2	F3	F4	F5
Chitosan (2% w/v) (gm)	0.40	0.40	0.40	0.40	0.40
β -Glycerophosphate (5% w/v) (gm)	1.00	1.00 g	1.00	1.00	1.00
Hyaluronic acid (0.5% w/v) (gm)	—	0.10	0.10	0.10	0.10
Pluronic F127	—	—	2.0 g (10%)	3.0 g (15%)	3.6 g (18%)

Curcumin	—	0.05 g	0.10 g	0.15 g	0.20 g
Acetic acid (1% v/v)	q.s.	q.s.	q.s.	q.s.	q.s.
Distilled water	Up to 20 mL	Up to 20 mL	Up to 20 mL	Up to 20 mL	Up to 20 mL

2.4 Evaluation of curcumin injectable hydrogel

2.4.1 Physical Evaluation

The prepared curcumin injectable hydrogel was subjected to visual inspection to evaluate its physical characteristics, including appearance, clarity, consistency, occlusiveness, washability, and other organoleptic properties [7].

2.4.2 Determination of pH

The pH of the developed curcumin injectable hydrogel was analyzed by a calibrated digital pH meter. Triplicates were measured for all measurements and the mean value was recorded [8].

2.4.3 Spreadability

One gram of the produced formulation was placed between two square glass plates (20 × 20 cm²) to determine the spreadability of the prepared curcumin injectable hydrogel. After gently placing Precise (500 g) on top of the upper plate, the spread gel's diameter was measured five minutes later [9]. The spreadability was considered using the following equation:

$$S = \frac{M \times L}{T}$$

Where S means Spreadability, M means the Weight applied to the upper plate, L indicates the Length of the glass plate in centimetres, and T refers to the Time needed for separation in seconds.

2.4.4 Viscosity

The prepared formulation viscosity was determined using Brookfield viscometer at different rotational speeds. The analysis were conducted at room temp and at physiological temperature (37°C) to evaluate flow behavior and thermosensitive characteristics [9].

2.4.5 Gelation Temperature

The hydrogel compositions' gelation temperature was ascertained using the test tube inversion method. A test tube containing about 2 mL of the produced solution was heated progressively in a water bath while the temperature was constantly monitored. Gelation temperature was defined as the temperature at which the preparation stopped flowing when the test tube was inverted.

2.4.6 Gelation Time

The prepared hydrogel formulation was placed in a water bath maintained at 37°C. The time required for complete sol-to-gel transition without flow upon tilting was recorded as gelation time.

2.4.7 Syringeability Study

The syringeability of the hydrogel formulations was evaluated by filling them into a 5 mL disposable syringe fitted with a 22–24-gauge needle. The ease of extrusion through the needle was observed

manually at room temperature.

2.4.8 Swelling Study

The swelling performance of the prepared hydrogel preparations was assessed by immersing accurately weighed gel samples PBS (PBS, pH 7.4) at 37 ± 0.5°C. At prearranged breaks, the swollen gels were detached, surface moisture was blotted, and the samples were weighed. The SI was calculated using the increase in weight relative to the original wt of the hydrogel. All analysis were performed in thrice and conveyed as mean ± SD.

2.4.9 Drug content

Accurately weighed quantity of hydrogel equivalent to 10 mg of curcumin was liquefied in Methanol: PBS pH 6.8 (30:70 v/v) with continuous stirring. The mixture was sieved and suitably diluted. By using UV photometer absorbance was measured at 424 nm and assay of drug was determined [10].

2.4.10 In-vitro drug release study

In vitro drug release testing was carried out to assess and optimize the formulation of optimized curcumin injectable hydrogel. A diffusion cell with a 0.4 µm dialysis film was used for the study. Before testing, the membrane was hydrated with PBS (pH 7.4) for an entire day. The donor compartment contained approximately 1 g of the curcumin injectable hydrogel, while the receptor compartment was filled with 13.3 mL of phosphate buffer (pH 7.4). The setup was maintained at 37 ± 1°C, with a magnetic stirrer at 400 rpm to ensure proper mixing. The experiment ran for twelve hours. Samples were periodically taken from the receptor side and swapped with renewed buffer to keep sink environments. The quantity of drug discharge was measured using a validated UV method at 424 nm. [10].

2.4.11 In-vitro drug release kinetics studies

Zero-Order Kinetic Model

A drug release system where the release rate remains constant independent of the drug concentration in the formulation is described by the zero-order kinetic model. Controlled-release delivery devices that exhibit a consistent release pattern over time are frequently utilised.

First-Order Kinetic Model

Drug release behaviour is explained by the first-order kinetic model, in which the amount of drug left in the dose form directly correlates with the release rate. The equation representing first-order kinetics is given below:

Higuchi Model

The Higuchi model explains drug release in matrix systems, where diffusion through the polymer matrix is the main controlling factor. In this model, the slope of the graph corresponds to the Higuchi release constant.

Korsmeyer–Peppas Model

The Korsmeyer–Peppas model is widely employed to analyze drug release from polymeric systems exhibiting anomalous or non-Fickian diffusion behavior. This model helps in identifying the mechanism governing drug release from the formulation.

2.5 Stability studies

The optimized hydrogel formulation was stored at refrigerated temperature (4°C) and room temperature for a specified period. The formulations were evaluated periodically for changes in physical appearance, pH, gelation behavior, and drug content.

3. RESULT AND DISCUSSION

3.1 Preformulation Studies

3.1.1 Organoleptic Properties

The organoleptic properties of curcumin were evaluated by visual and sensory examination. Curcumin was observed as a bright yellow colored powder with a characteristic odor and slightly bitter taste. The drug appeared fine, smooth, and

crystalline, with no visible impurities. The organoleptic characteristics confirmed the purity and identification of curcumin used for formulation development.

3.1.2 Melting point analysis

The curcumin melting point was analyzed by digital melting point apparatus. The examination was done in triplicate, and the average melting point was 183 °C. The observed value was in close agreement with the reported pharmacopeial range of 175-183.5 °C (USP), indicating the drug sample's purity and identity.

3.1.3 Solubility study

The solubility study of curcumin was performed using standard IP methods in various solvents to determine suitable media for formulation and drug-release studies. Excess amount of curcumin was added separately into various solvents and shaken reciprocally at 37°C for 5 min. The solubility of curcumin was then observed visually and recorded (Table 2).

Table 2: Solubility Profile of Curcumin.

S. No.	Solvents	Solubility (mg/mL)
1	Distilled water	0.0006 ± 0.0001
2	Phosphate buffer (pH 6.8)	0.012 ± 0.002
3	Phosphate buffer (pH 7.2)	0.015 ± 0.002
4	Phosphate buffer (pH 7.4)	0.018 ± 0.003
5	Ethanol	8.42 ± 0.21
6	Methanol	12.68 ± 0.34
7	Acetone	10.54 ± 0.26
8	Chloroform	7.83 ± 0.19

3.1.4 FT-IR spectrum of chlorhexidine

Curcumin's FTIR spectrum showed distinctive peaks that matched its chemical structure and functional groups. The stretching vibrations of hydroxyl (O–H) groups were identified as the cause of a wide absorption band seen in the 3200–3500 cm⁻¹ region. The curcumin structure's carbonyl (C=O) and olefinic (C=C) groups' overlapping stretching vibrations were suggested by the strong signal at 1628 cm⁻¹. The aromatic C=C stretching vibration was observed around 1427 cm⁻¹, while a strong intense band at 1512 cm⁻¹ corresponded to mixed vibrational modes involving carbonyl stretching, aromatic ring vibrations, and bending vibrations associated with keto–enol tautomeric

forms of curcumin. These characteristic peaks confirmed the structural integrity and purity of curcumin.

3.1.5 Preparation of Calibration Curve and Identification of λ_{max}

The UV absorption spectrum of curcumin was examined to identify its λ_{max}. The drug showed peak absorbance at 424 nm, aligning with the experimental data. The wavelength of curcumin 424 nm was chosen for all further analytical measurements. A UV-visible spectrophotometer measured the absorbance of standard curcumin solutions at concentrations of 2-14 µg/mL at 424 nm. The calibration curve demonstrated a direct linear relationship between drug concentration and

absorbance. The regression coefficient (R^2) value of 0.9967 indicated excellent linearity of the developed

analytical method (**Fig. 1**).

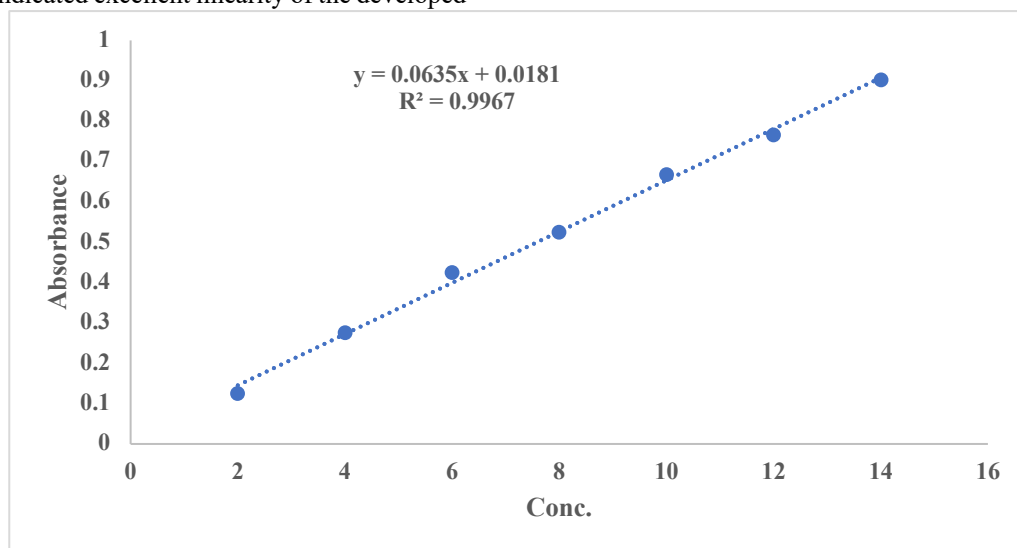


Fig. 1: Linearity curve of curcumin

3.2 Results of Thermosensitive Curcumin Hydrogel

3.2.1 Physical Appearance

The colour, homogeneity, clarity, and phase separation of the manufactured injectable hydrogel

formulations were visually assessed. Every formulation had a smooth look and no discernible particles. At ambient temperature, the formulations stayed liquid, but at physiological temperature, they changed into gel (**Table 3**).

Table 3: Physical Appearance of Injectable Curcumin Hydrogel Formulations

Formulation	Color	Appearance	Homogeneity	Phase Separation
F1	Transparent	Smooth liquid	Homogeneous	Absent
F2	Light yellow	Smooth liquid	Homogeneous	Absent
F3	Yellow	Slightly viscous	Homogeneous	Absent
F4	Deep yellow	Viscous liquid	Homogeneous	Absent
F5	Dark yellow	Highly viscous	Homogeneous	Absent

3.2.2 pH Determination

The pH of formulations F1, F2, F3, F4, and F5 was found to be 6.71 ± 0.03 , 6.76 ± 0.05 , 6.82 ± 0.04 , 6.89 ± 0.02 , and 6.95 ± 0.04 , respectively (**Fig. 2**). A slight increase in pH was observed as polymer

concentration and Pluronic F127 content increased. Among all formulations, F4 showed optimum pH close to physiological condition, suggesting better compatibility and reduced chances of irritation at the site of administration.

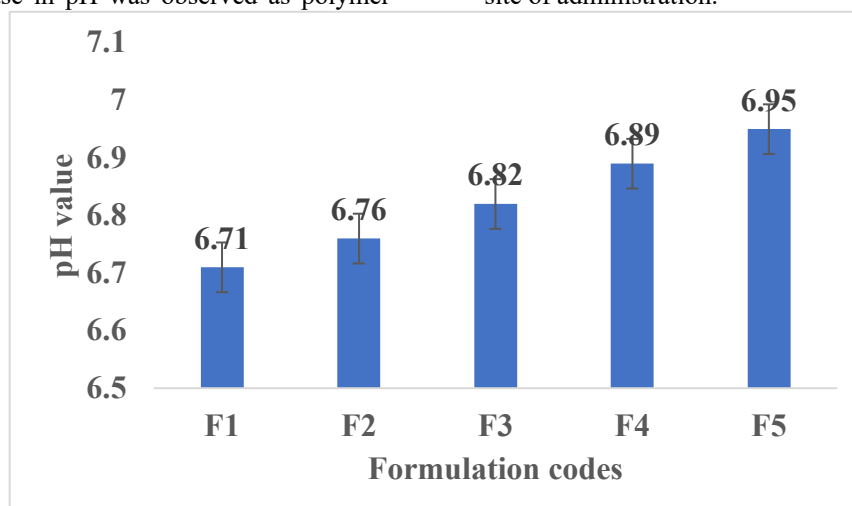


Fig. 2: Graph of pH of Injectable Curcumin Hydrogel Formulations (F1-F5).

3.2.3 Spreadability Study

The prepared hydrogel formulations showed satisfactory spreadability due to their semisolid

consistency. The spreadability of formulations F1, F2, F3, F4, and F5 was found to be 12.8 ± 0.4 , 11.9 ± 0.3 , 10.8 ± 0.3 , 9.7 ± 0.2 , and 8.9 ± 0.2 g·cm/s, respectively (**Fig. 3**). A gradual decrease in spreadability was observed as polymer and Pluronic

F127 concentrations increased, due to increased formulation viscosity. Formulation F4 exhibited suitable spreadability along with optimum consistency and gel strength. These results indicated that the developed hydrogel formulations possessed satisfactory application and handling characteristics.

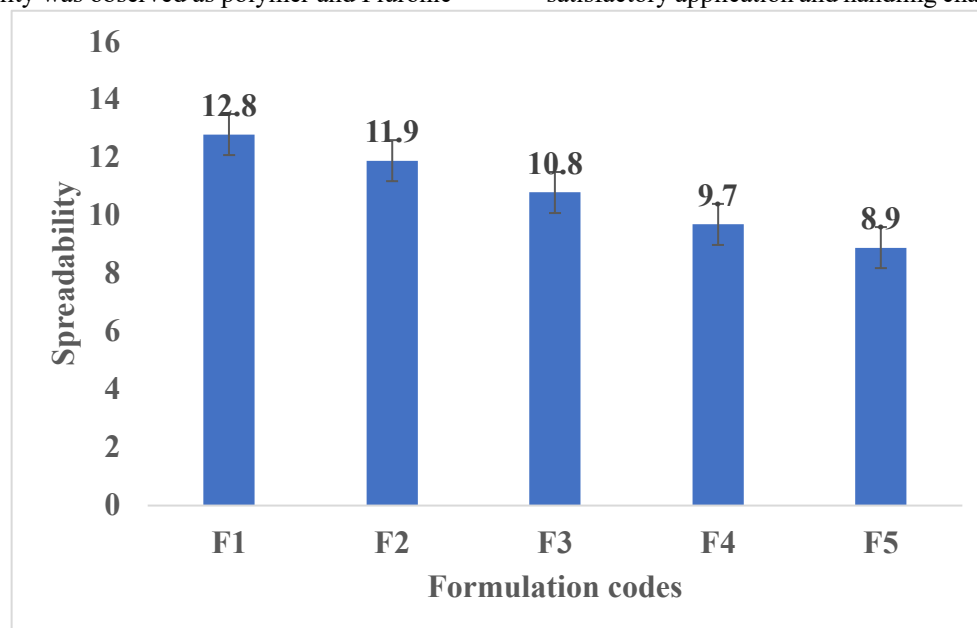


Fig. 3: Graph of spreadability of Injectable Curcumin Hydrogel Formulations (F1-F5).

3.2.4 Gelation Temperature

The gelation temperature of formulations F1, F2, F3, F4 and F5 was found to be $39.4 \pm 0.5^\circ\text{C}$, $37.8 \pm 0.4^\circ\text{C}$, $35.9 \pm 0.3^\circ\text{C}$, $34.2 \pm 0.2^\circ\text{C}$, and $32.8 \pm 0.4^\circ\text{C}$, respectively (**Fig. 5.7**). A gradual decrease in gelation temperature was observed as polymer and

Pluronic F127 concentrations increased. Among all formulations, F4 exhibited an optimum gelation temperature near physiological condition, indicating suitable thermosensitive and injectable characteristics. The results confirmed the successful formation of in situ thermogelling hydrogel system for sustained rheumatoid arthritis therapy.

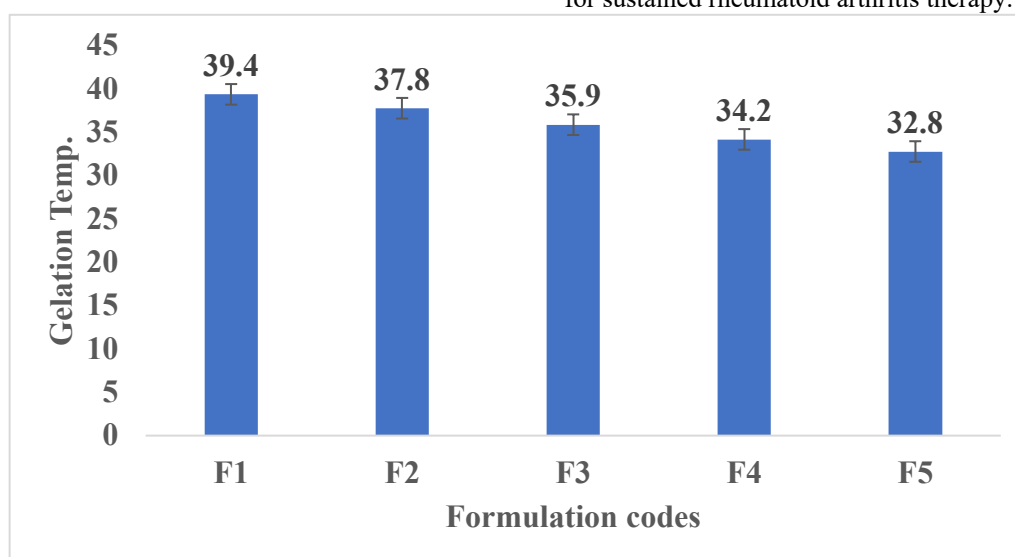


Fig. 5.7: Graph of Gelation temperature of Injectable Curcumin Hydrogel Formulations (F1-F5).

3.2.5 Gelation Time

The gelation times of formulations F1, F2, F3, F4, and F5 were 8.4 ± 0.4 , 7.2 ± 0.3 , 5.8 ± 0.2 , 4.3 ± 0.2 , and 3.7 ± 0.1 min, respectively (**Fig. 4**). A decrease in gelation time was observed with increasing

concentration of polymers and Pluronic F127. Formulation F4 exhibited an appropriate gelation time, indicating rapid in situ gel formation at physiological temperature while maintaining adequate injectability. These findings confirmed the

efficient thermosensitive behavior of the developed injectable hydrogel system.

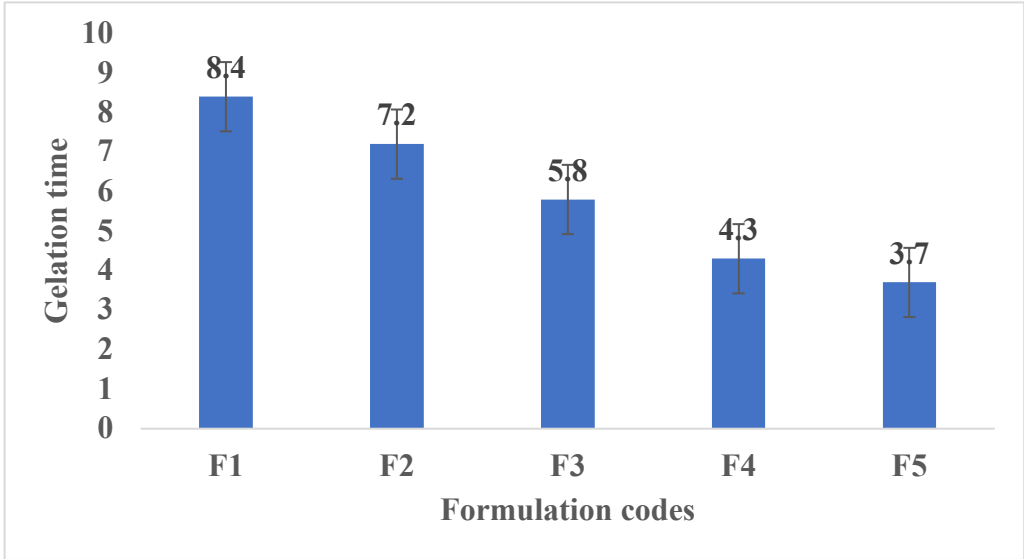


Fig. 4: Graph of Gelation time of Injectable Curcumin Hydrogel Formulations (F1-F5).

3.2.6 Syringeability Study

All formulations were evaluated for syringeability using disposable syringes fitted with 22–24-gauge

needles. Formulations F1–F4 showed good syringeability, while F5 exhibited comparatively higher resistance due to increased viscosity (Table 4).

Table 4: Syringeability of Injectable Curcumin Hydrogel Formulations

Formulation	Syringeability
F1	Excellent
F2	Excellent
F3	Good
F4	Good
F5	Moderate

3.2.7 Viscosity Study

The viscosity of formulations F1, F2, F3, F4, and F5 was found to be 892 ± 12 cP, 1084 ± 15 cP, 1527 ± 18 cP, 1986 ± 20 cP, and 2478 ± 24 cP, respectively (Fig. 5). An increase in viscosity was observed as the concentration of polymers and Pluronic F127 in

the formulations increased. Formulation F4 exhibited optimal viscosity, providing suitable flow behavior, good injectability, and gel strength. The results indicated the successful formation of a stable thermosensitive hydrogel network suitable for sustained drug delivery.

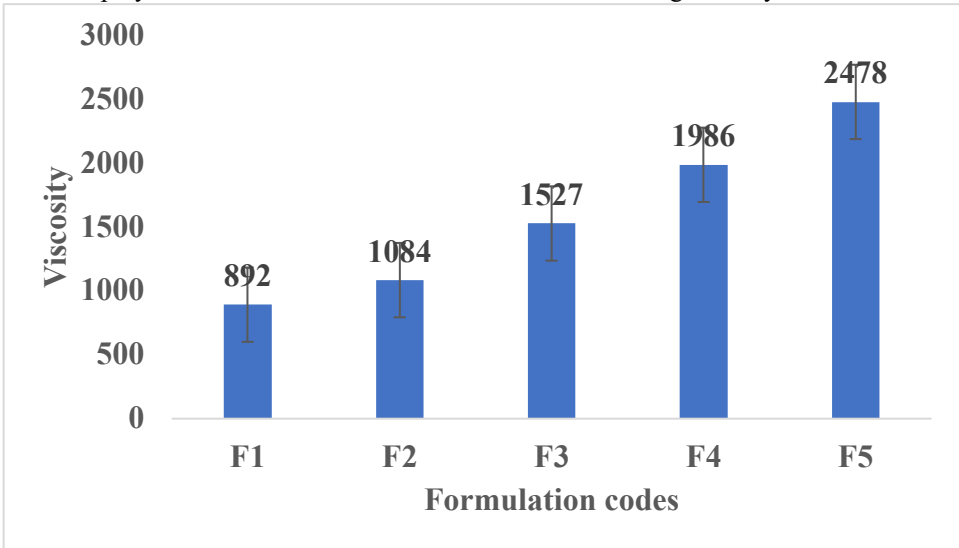


Fig. 5: Graph of viscosity of Injectable Curcumin Hydrogel Formulations (F1-F5).

The swelling index of formulations F1, F2, F3, F4,

3.2.8 Swelling Study

and F5 was found to be $118 \pm 4\%$, $136 \pm 5\%$, $154 \pm 6\%$, $176 \pm 5\%$, and $192 \pm 7\%$, respectively (**Fig. 6**). The swelling capacity increased gradually with increase in polymer concentration and Pluronic F127 content due to enhanced water absorption ability of the hydrogel network. Formulation F4

exhibited optimum swelling behavior, which may contribute to sustained drug release and improved retention at the site of administration. The results confirmed the hydrophilic and porous nature of the developed thermosensitive hydrogel formulations.

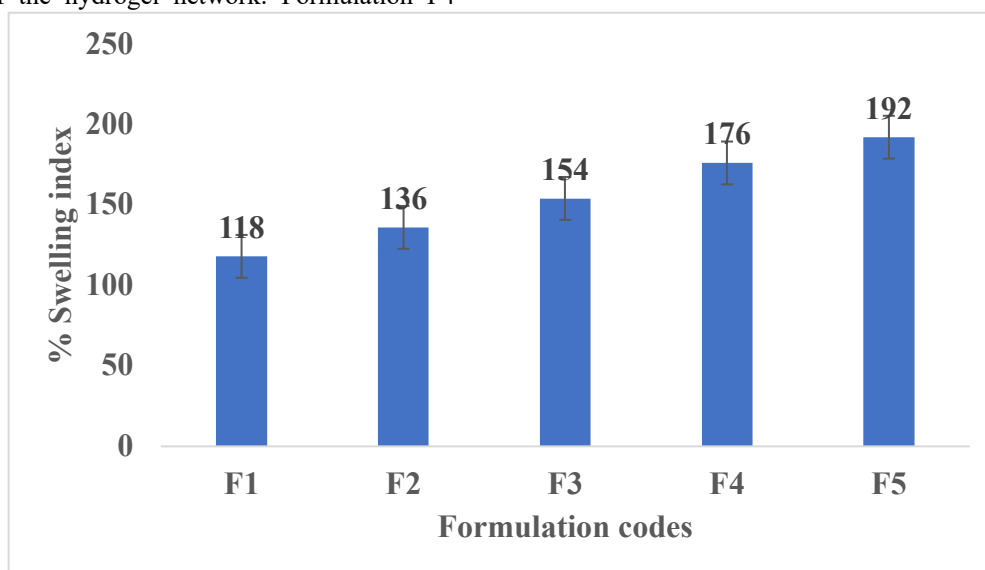


Fig. 6: Graph of swelling index of Injectable Curcumin Hydrogel Formulations (F1-F5).

3.2.9 Drug Content Determination

The drug content of formulations F2, F3, F4, and F5 was found to be $91.8 \pm 1.2\%$, $94.6 \pm 1.0\%$, $98.3 \pm 0.8\%$, and $96.9 \pm 1.1\%$, respectively (**Fig. 7**). The results demonstrated uniform distribution of curcumin within the hydrogel formulations. Among

all formulations, F4 exhibited the highest drug content, indicating better drug entrapment and greater homogeneity within the polymeric matrix. These findings confirmed the suitability of the developed injectable hydrogel system for effective curcumin delivery.

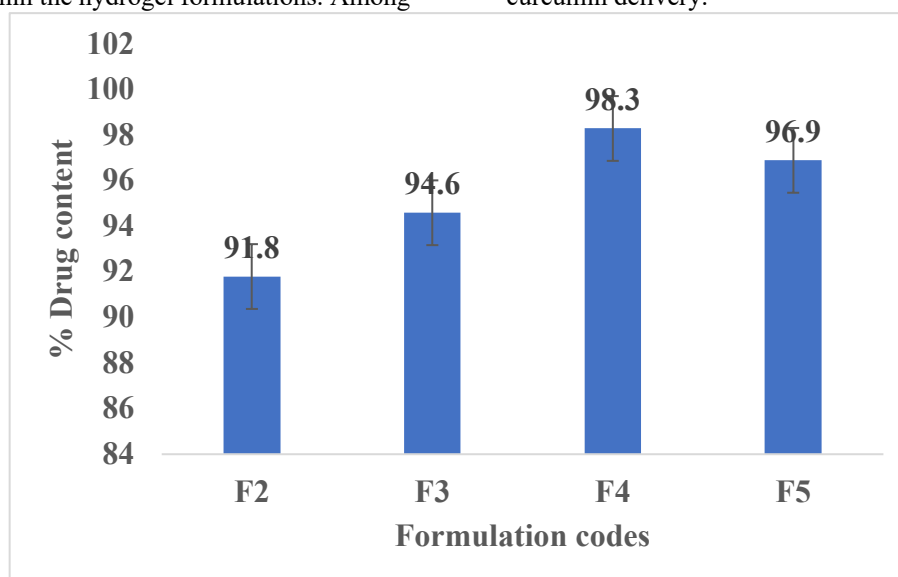


Fig. 7: Graph of Drug content of Injectable Curcumin Hydrogel Formulations (F2-F5).

3.2.10 *In-vitro* drug release study

The *in-vitro* drug-release study revealed sustained curcumin release from all hydrogel formulations over 24 h. Formulations F2, F3, F4, and F5 showed cumulative drug release of 98.2%, 95.8%, 93.7%, and 88.9%, respectively, at the end of 24 h (**Fig. 8**). A gradual decrease in drug release was observed as

polymer concentration increased, due to the formation of a denser hydrogel network. Formulation F4 exhibited controlled and prolonged drug release with 93.7% release at 24 h, indicating its suitability for sustained rheumatoid arthritis therapy.

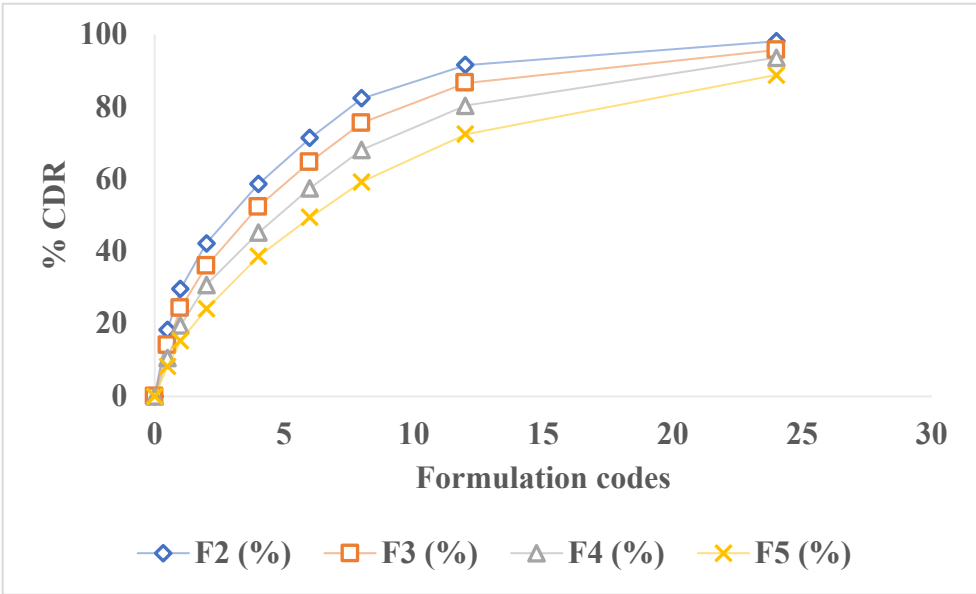


Fig. 8: In-vitro drug release of Injectable Curcumin Hydrogel Formulations (F2-F5).

3.2.11 *In-vitro* kinetic studies

The optimized Formulation (F4) of rate of release was calculated from graph slopes, and R^2 values were assessed. Release kinetics data [Table 5; Fig. 9

(A,B,C, and D)] showed that the first-order model had the maximum R^2 , shows the model fit and it is analyzed by making chart of time vs % of drug release giving an R^2 of 0.9998.

Table 5: Kinetic study of drug release of F4 optimized formulation.

Formulation	Zero Order model	First Order model	Higuchi's model	Peppas's model	Best model	fitted
Curcumin injectable hydrogel (F4)	0.9523	0.9998	0.998	0.9915	First order	(0.9998)

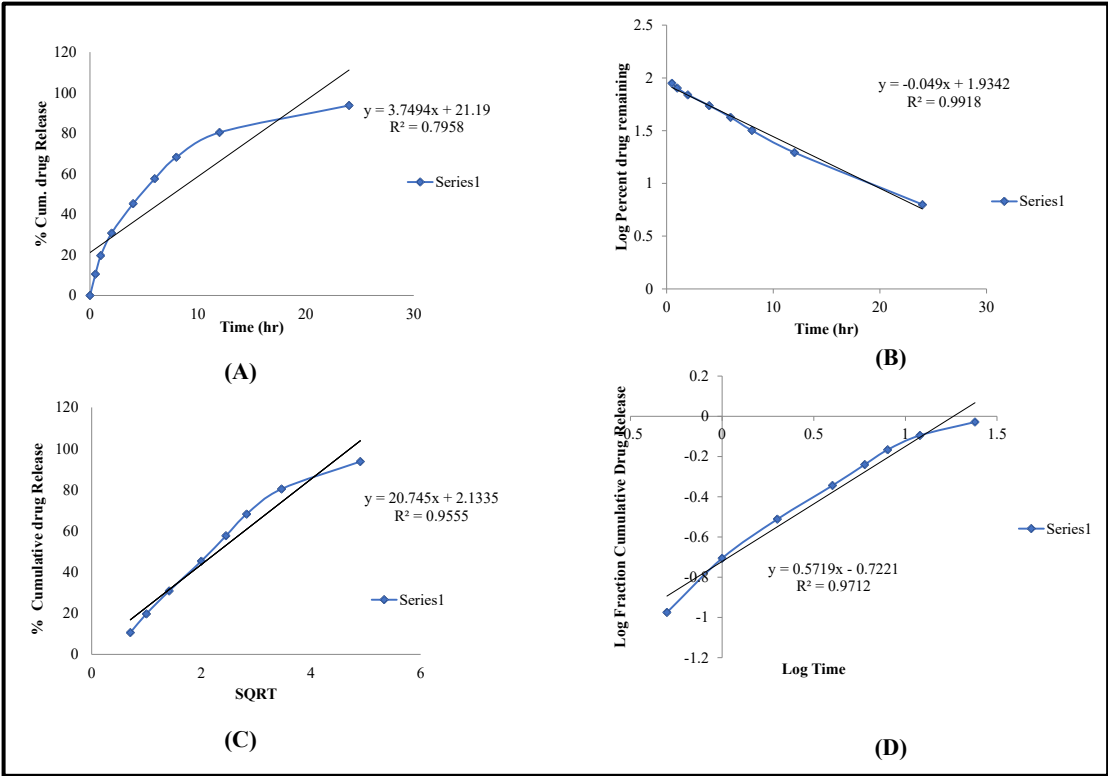


Fig. 9: (A) Zero order kinetic drug release, (B) First order kinetic drug release, (C) Higuchi plot of kinetic drug release, (D) Peppas's plot of kinetic drug release.

3.3 Stability Study

The optimized formulation remained stable during storage, with no significant changes in physical appearance, pH, or drug content (**Table 5.16**). **Table 5.16:** Stability Study of Optimized Formulation (F4)

Parameter	Initial	After 30 Days
Appearance	Smooth yellow gel	No significant change
pH	6.89 ± 0.02	6.84 ± 0.03
Drug content (%)	98.3 ± 0.8	97.5 ± 0.9
Gelation temperature (°C)	34.2 ± 0.2	34.6 ± 0.3
Syringeability	Good	Good

4. Conclusion

The present study successfully developed and evaluated a thermoresponsive injectable hydrogel for the localized and sustained delivery of curcumin, with the objective of exploring its potential application in rheumatoid arthritis. The hydrogel system was formulated using chitosan, β -glycerophosphate, hyaluronic acid, and Pluronic F127, which collectively provided suitable thermosensitive and injectable characteristics. Among the developed formulations, F4 demonstrated the most favorable overall performance, exhibiting an appropriate pH, satisfactory viscosity, good syringeability, suitable gelation temperature, rapid sol-to-gel transition, and adequate swelling behavior. The optimized formulation also showed high drug content (98.3 ± 0.8%), indicating uniform distribution of curcumin within the hydrogel matrix. In-vitro drug-release evaluation demonstrated prolonged curcumin release up to 24 h, with 93.7% cumulative drug release from F4, suggesting the ability of the hydrogel matrix to provide sustained drug availability. The release profile showed the best correlation with the first-order kinetic model. Furthermore, the optimized formulation maintained its physical appearance, pH, drug content, gelation temperature, and syringeability during the stability study, indicating satisfactory formulation stability. Overall, the developed thermoresponsive injectable hydrogel exhibited promising physicochemical and drug-release characteristics and may serve as a potential platform for localized and sustained curcumin delivery in rheumatoid arthritis. Further comprehensive in-vivo studies are required to establish its therapeutic efficacy and safety.

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