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FORMULATION AND EVALUATION OF DICLOFENAC SODIUM GEL USING NATURAL POLYMER XANTHAN GUM

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Abstract:

This research focused on developing a Diclofenac Sodium topical gel using Xanthan Gum as the gelling polymer. Multiple formulations were prepared by varying polymer concentration, and one optimized batch was selected based on overall performance. The prepared gel showed good physical properties, uniformity, and consistent release behavior. Stability testing confirmed that the optimized formulation remained intact and usable during the study period. When compared with a marketed product, the developed gel showed acceptable and comparable characteristics. Overall, the study successfully produced a stable, effective Diclofenac Sodium gel suitable for further development and practical use.

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INTRODUCTION:

Drug delivery refers to the process of transporting a therapeutic substance within the body in a controlled manner to achieve the desired pharmacological response safely and effectively. Traditionally, the oral route has been favored due to its convenience, but it often presents limitations such as low bioavailability, gastrointestinal degradation, and extensive first-pass metabolism, all of which reduce the concentration of the active drug reaching its target site. Parenteral routes like injections provide direct delivery but are painful, inconvenient, and less suitable for long-term therapy. To address these limitations, alternative delivery routes such as buccal, nasal, ocular, vaginal, rectal, pulmonary, transdermal, and topical systems have been explored. Among them, topical delivery has gained significant prominence because it is non-invasive, easy to use, and capable of delivering drugs directly to affected areas, especially in conditions involving local pain, inflammation, or skin infections.[1,2]

The skin, the largest organ of the human body, acts as a protective barrier against physical, chemical, and microbial threats while regulating temperature, hydration, and sensory perception. Its layered structure determines the extent of drug absorption, making a clear understanding of skin anatomy and physiology essential for designing effective topical formulations.[3,4]

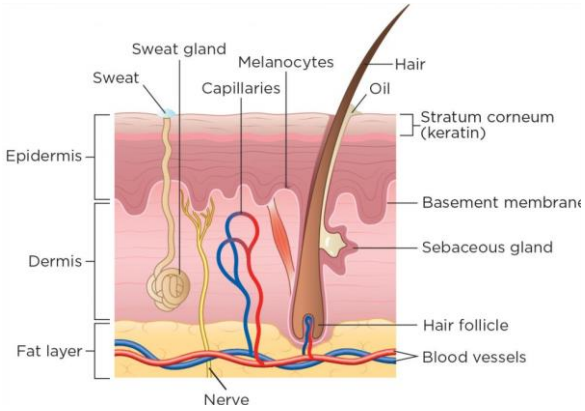


Figure 1: Cross-section of human skin showing the epidermis, dermis, and subcutaneous tissue.

Human skin is organized into three major layers—epidermis, dermis, and subcutaneous tissue—each contributing to protection, support, and drug absorption.[5–6] The epidermis, composed mainly of keratinocytes, provides the primary barrier to permeation, while the stratum corneum, with its brick-and-mortar structure, strongly restricts hydrophilic and large molecules unless hydrated.[7–11] Beneath this, the dermis supplies vascular networks that aid drug distribution once the epidermal barrier is crossed.[12–13] The hypodermis, rich in adipose tissue, can serve as a reservoir for lipophilic drugs.[14–15] Skin physiology—barrier function, hydration, metabolism, and sensory responses—directly influences drug uptake.[16–17] Understanding these features is essential for designing effective topical formulations that align with skin structure.[18–20]

Topical drug delivery relies on drug diffusion through transcellular, intercellular, or appendageal pathways, influenced by solubility, lipophilicity, vehicle, and skin condition.[21–22] It offers localized action, avoids first-pass metabolism, and minimizes systemic toxicity, though limited permeation and irritation remain challenges.[23–25]

Gels serve as ideal topical carriers due to their semi-solid network, smooth texture, and ability to uniformly disperse drugs.[26] Hydrogels provide high hydration and biocompatibility, while organogels offer stability for lipophilic drugs.[27–37] Emulgels combine advantages of gels and emulsions, enhancing penetration and patient acceptability, though requiring careful optimization.[37–40]

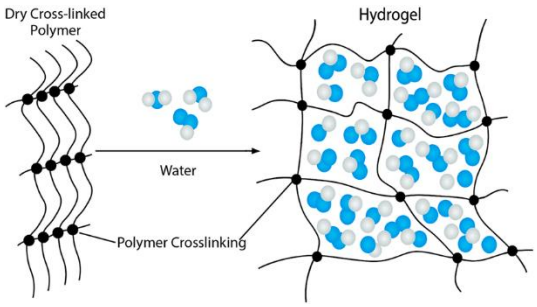


Figure 2: Representation of gel microstructure showing the three-dimensional polymeric network entrapping water molecules within its cross-links

Advantages of Gel-Based Formulations

Gels allow uniform drug distribution and typically follow diffusion-controlled release, where the drug diffuses through the hydrated polymer matrix at a predictable rate.[41] They are simple to manufacture, require fewer excipients, exhibit good physical stability, and can accommodate both hydrophilic and lipophilic drugs depending on the polymer used.[42]

Role of Polymers in Gel Formulation

Polymers determine a gel's viscosity, mechanical strength, spreadability, and drug diffusion rate. They may be synthetic, semi-synthetic, or natural. Natural polymers like xanthan gum are favored for their biocompatibility, biodegradability, non-toxicity, and ability to form stable gels at low concentrations.[43]

Mechanism and Limitations of Gels

After application, solvent evaporation increases drug concentration at the skin surface, generating a diffusion gradient that drives permeation into the stratum corneum. Release rate depends on polymer type, concentration, and matrix structure.[44] However, gels may face issues like microbial

contamination, syneresis, or phase separation, necessitating proper polymer selection and preservative use.[45]

Limitations of Oral NSAIDs

Oral NSAIDs such as diclofenac or ibuprofen undergo gastrointestinal degradation and hepatic metabolism, reducing bioavailability and increasing organ toxicity.[46] A major drawback is gastrointestinal irritation caused by COX-1 inhibition, which decreases protective prostaglandins and predisposes to ulcers and mucosal injury.[47]

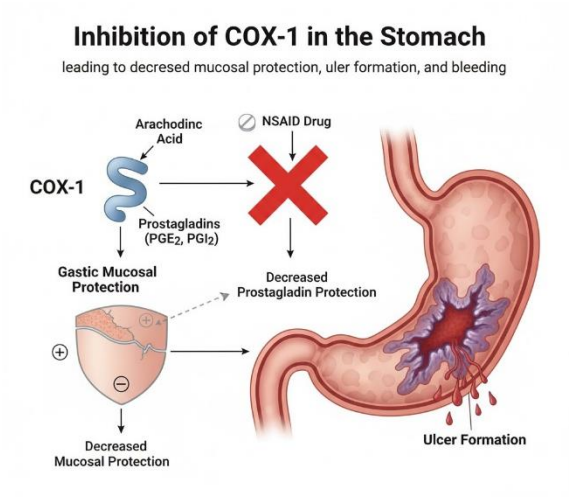


Figure 3: Illustration showing inhibition of COX-1 in the stomach leading to decreased mucosal protection, ulcer formation, and bleeding.

Hepatic First-Pass Metabolism and Reduced Bioavailability

Oral NSAIDs, particularly Diclofenac Sodium, undergo extensive hepatic first-pass metabolism, which significantly reduces the amount of active drug reaching systemic circulation. Only about half of the absorbed dose remains available in its active form, often requiring higher oral doses to achieve therapeutic plasma levels. This increases the overall systemic exposure and heightens the risk of adverse effects. In some individuals, continuous use may elevate liver enzymes and contribute to hepatotoxicity, especially with long-term therapy.[48]

Renal and Cardiovascular Effects

NSAIDs reduce prostaglandin synthesis that supports renal blood flow, leading to sodium retention, fluid overload, and potential renal impairment. Chronic use is associated with hypertension, edema, and increased risk of cardiovascular events such as myocardial infarction and stroke.[49]

Short Half-Life and Lack of Target Specificity

Diclofenac's short half-life of one to two hours necessitates frequent dosing, which may reduce patient compliance.[50] Additionally, oral delivery distributes the drug systemically, meaning only a small portion reaches the inflamed tissue while the remainder may cause unwanted systemic effects.

Need for Safer Alternatives

Due to these limitations, safer and more targeted approaches such as topical drug delivery systems have become essential. Topical gels minimize systemic exposure while delivering Diclofenac directly to the affected area, improving both safety and therapeutic efficiency.[51]

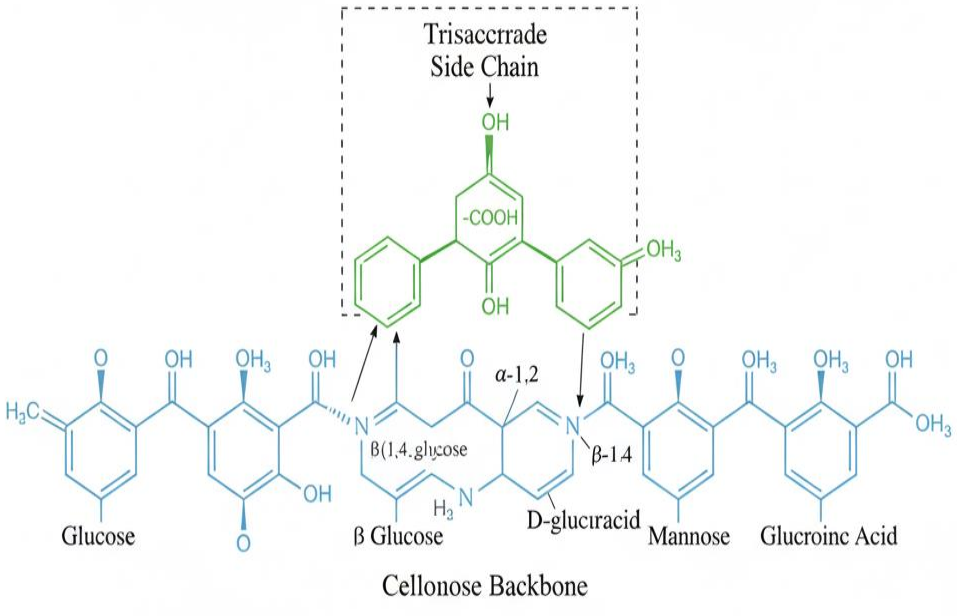


Figure 4: Structural representation of Xanthan gum molecule showing the cellulose backbone and side chains of mannose and glucuronic acid.

Physicochemical Properties and Applications of Xanthan Gum

Xanthan gum is an odorless, tasteless powder that dissolves easily in hot or cold water to form highly viscous solutions. Its viscosity remains stable across different temperatures and pH levels, and it exhibits shear-thinning behavior, allowing easy spreading and good retention on the skin.[60] In pharmaceutical formulations, it functions as a thickener, stabilizer, and controlled-release polymer.[62]

Mechanism of Diclofenac Sodium Gel

After application, Diclofenac diffuses from the gel matrix into the skin due to a concentration gradient. The hydrophilic base enhances solubilization, while polymers regulate controlled release. Penetration depends on molecular weight, lipophilicity, and enhancers. Diclofenac then accumulates in deeper tissues and synovial fluid, providing localized anti-inflammatory and analgesic effects.[63]

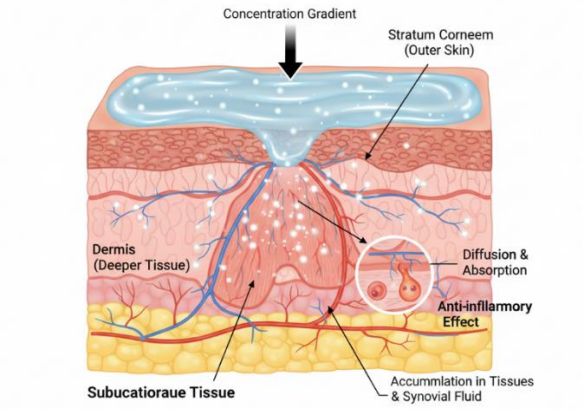


Figure 5: Diagrammatic representation of Diclofenac Sodium diffusion from the gel matrix through the stratum corneum and into the dermal tissues.

Pharmacological Activity in Local Tissues

Diclofenac Sodium acts locally by inhibiting COX-1 and COX-2 enzymes within inflamed tissues. This inhibition suppresses prostaglandin synthesis, reducing mediators responsible for pain, swelling, and inflammation. By lowering prostaglandin levels, Diclofenac decreases vascular permeability and prevents sensitization of nociceptors, providing effective localized relief.[64]

Advantages of the Gel Mechanism

Topical gel application delivers Diclofenac directly to the inflamed site, ensuring high local concentrations with minimal systemic absorption. The xanthan-based polymer matrix enables sustained release, prolonging therapeutic action while reducing dosing frequency. Additionally, the water-rich gel base hydrates the skin, enhances permeation, and produces a soothing cooling effect that further alleviates discomfort and inflammation.

Diclofenac Sodium: Chemistry and Pharmacological Profile

Chemical Nature and Description

Diclofenac Sodium is a widely used nonsteroidal anti-inflammatory drug belonging to the arylacetic acid class. It is the sodium salt of 2-[(2,6-dichlorophenyl)amino]benzeneacetic acid. The compound appears as a white to slightly yellow crystalline powder with a bitter taste and faint odor. It has a molecular weight of 318.13 g/mol and a molecular formula of C14H10Cl2NNaO2.]

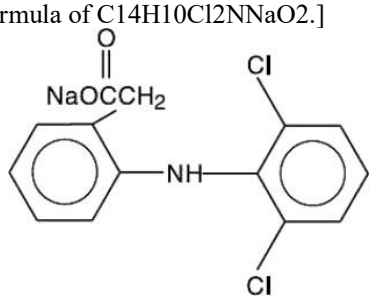


Figure 6: Chemical structure of Diclofenac Sodium showing dichlorophenyl group linked to acetic acid moiety.

It is freely soluble in methanol, sparingly soluble in ethanol, and slightly soluble in water. This low water solubility limits its permeability in aqueous environments, which makes the use of a suitable polymer matrix necessary for effective topical delivery.

Mechanism of Action

Diclofenac acts by inhibiting cyclooxygenase enzymes (COX-1 and COX-2), which convert arachidonic acid into prostaglandins, prostacyclins, and thromboxanes. These compounds are responsible for inflammation, pain, and fever. By blocking their synthesis, Diclofenac reduces the inflammatory response and provides analgesic and antipyretic effects.[91]

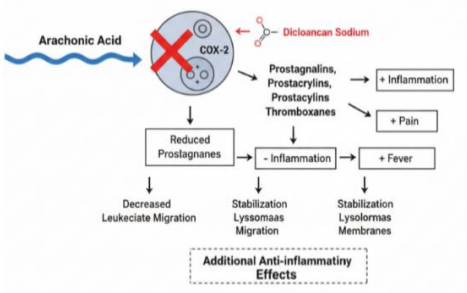


Figure 7: Mechanism of action of Diclofenac Sodium showing inhibition of COX enzymes and reduced prostaglandin synthesis.

Additional Anti-inflammatory Actions

Apart from COX inhibition, Diclofenac reduces leukocyte migration, stabilizes lysosomal membranes, and inhibits the lipoxygenase pathway, further enhancing its anti-inflammatory activity.[92]

Absorption
It is rapidly absorbed orally, but extensive first-pass metabolism limits systemic availability to about fifty percent.

Distribution
Diclofenac binds over 99% to plasma proteins and accumulates in synovial fluid.

Metabolism
It is metabolized mainly by CYP2C9 into hydroxylated and glucuronidated metabolites.[93]

Excretion
Eliminated via urine (≈60%) and bile (≈35%) with a 1–2 hour half-life.

Pharmacodynamics
It acts peripherally and centrally, reducing nociceptor sensitivity and modulating pain pathways.

MATERIALS AND METHODS:

MATERIALS

Table 1: Materials Used in the Formulation of Diclofenac Sodium Gel

Sr. No.	Material	Category	Grade	Function in Formulation
1	Diclofenac Sodium	(API)	Analytical grade	Anti-inflammatory and analgesic agent
2	Xanthan Gum	Natural polymer	Pharmaceutical grade	Gelling agent, viscosity enhancer, release modifier
3	Carbopol 934	Synthetic polymer (reference batch only)	Pharmaceutical grade	Gelling agent for comparison batch
4	Distilled Water	Solvent	Laboratory grade	Vehicle for polymer hydration and gel base
5	Methanol	Solvent (analytical)	Analytical grade	Used for drug content and UV analysis
6	Ethanol (95%)	Solvent	Laboratory grade	Used for dissolving preservatives
7	Methylparaben	Preservative	Pharmaceutical grade	Antimicrobial preservative
8	Propylparaben	Preservative	Pharmaceutical grade	Enhances preservative efficiency
9	Glycerin	Humectant	Pharmaceutical grade	Improves moisture retention and spreadability
10	Propylene Glycol	Cosolvent / Penetration enhancer	Pharmaceutical grade	Improves drug solubility and skin permeation
11	Triethanolamine (TEA)	pH Adjusting Agent	Laboratory grade	Adjusts gel pH to skin-compatible range
12	Marketed Diclofenac Gel	Reference Product	Commercial standard	Used for comparative evaluation

Pre-formulation Studies – Organoleptic Evaluation
Organoleptic evaluation of Diclofenac Sodium was performed by observing a small sample on a clean watch glass. The drug appeared as a white to off-white crystalline powder with a fine texture and no coarse particles. It was essentially odourless with a slight characteristic smell, and a minimal taste check confirmed its typical bitter taste.[104]

Table 2: Organoleptic Evaluation of Diclofenac Sodium

Parameter	Ideal Expected Observation
Colour	White to off-white crystalline powder
Odour	Odourless / Very faint characteristic smell
Appearance	Fine crystalline or amorphous powder
Taste	Bitter

Melting Point Determination
The melting point was determined using the capillary method to confirm drug purity. I filled a thin glass capillary tube with a small amount of Diclofenac Sodium and carefully sealed one end. The capillary was placed in a melting point apparatus and the temperature was increased gradually. I closely watched the powder as it heated. At around 283°C, the drug began to soften, and by 285°C, it completely liquefied. The narrow melting range indicated that the drug sample was pure and free from impurities.[105]

Table 3: Melting Point of Diclofenac Sodium

Parameter	Ideal Value
Melting Point	283–285°C

Solubility Study

Solubility studies were performed by adding excess Diclofenac Sodium to different solvents and shaking for 24 hours. The drug showed slight solubility in water, free solubility in methanol, sparing solubility in ethanol, and moderate solubility in phosphate buffer pH 7.4. It dissolved in propylene glycol but remained insoluble in chloroform.[106]

Table 4: Solubility Profile of Diclofenac Sodium

Solvent	Ideal Solubility
Distilled Water	Slightly soluble (5–10 mg/mL)
Methanol	Freely soluble
Ethanol	Sparingly soluble
Phosphate Buffer pH 7.4	Moderately soluble (25–35 mg/mL)
Propylene Glycol	Soluble
Chloroform	Practically insoluble

Determination of λmax

To determine the maximum wavelength of absorption (λmax), I prepared a dilute solution of Diclofenac Sodium in methanol and scanned it between 200–400 nm using a UV–Visible spectrophotometer. The spectrum showed a sharp peak at 276 nm, which is the characteristic λmax of Diclofenac Sodium. This wavelength was used for all subsequent UV estimations. The λmax obtained matched the reported literature values, confirming the identity and purity of the API.[107]

Table 5: λmax of Diclofenac Sodium

Parameter	Ideal Value
λmax in Methanol	276 nm

Calibration Curve of Diclofenac Sodium

To prepare the calibration curve, I prepared a stock solution of Diclofenac Sodium in methanol and then made serial dilutions (2–10 µg/mL). Each solution was scanned at 276 nm and absorbance values were recorded. I plotted the absorbance against concentration and obtained a straight-line graph. The linearity was excellent with an R^2 value close to 0.999, indicating high accuracy.[108]

Table 6: Calibration Curve Data of Diclofenac Sodium

Concentration (µg/mL)	Absorbance (Ideal)
2	0.145
4	0.287
6	0.432
8	0.578
10	0.721

pH Measurement of Drug Solution

A 1% w/v aqueous solution of Diclofenac Sodium was prepared and its pH was measured using a calibrated digital pH meter. The electrode was first rinsed with distilled water and gently dipped in the solution. The reading stabilized at 7.4–8.0, showing the slightly alkaline nature of Diclofenac Sodium due to its sodium salt form. This information was important for choosing a compatible polymer and adjusting the final gel pH within physiological range.[109]

Table 7: pH of Diclofenac Sodium Solution

Solution	Ideal pH Range
1% w/v Drug Solution	7.4 – 8.0

Drug–Polymer Compatibility (FTIR Study)

To check the compatibility of Diclofenac Sodium with Xanthan Gum, I performed FTIR analysis. I recorded the FTIR spectra of pure Diclofenac Sodium, pure Xanthan Gum, and the physical mixture (1:1 ratio). For each sample, a small quantity was mixed with dry KBr, compressed into a transparent pellet, and scanned between 4000–400 cm^{-1}. The characteristic peaks of Diclofenac Sodium such as N–H stretch (3310–3330 cm^{-1}), C=O stretching of carboxylate (1550–1570 cm^{-1}), C–Cl stretch (760–780 cm^{-1}) and aromatic C=C peaks (1450–1600 cm^{-1}) were all present in the mixture without significant shifting or disappearance.

This indicated that no chemical interaction occurred between Diclofenac Sodium and Xanthan Gum, confirming their compatibility.[110]

Table 8: FTIR Peak Result

Functional Group	Ideal Peak Range (cm^{-1})	Presence in Mixture
N–H Stretch	3310–3330	Present (No shift)
C=O (Carboxylate)	1550–1570	Present (No major change)

C–Cl Stretch	760–780	Present (Stable)
Aromatic C=C	1450–1600	Unchanged
C–O Stretch	1240–1280	Unchanged

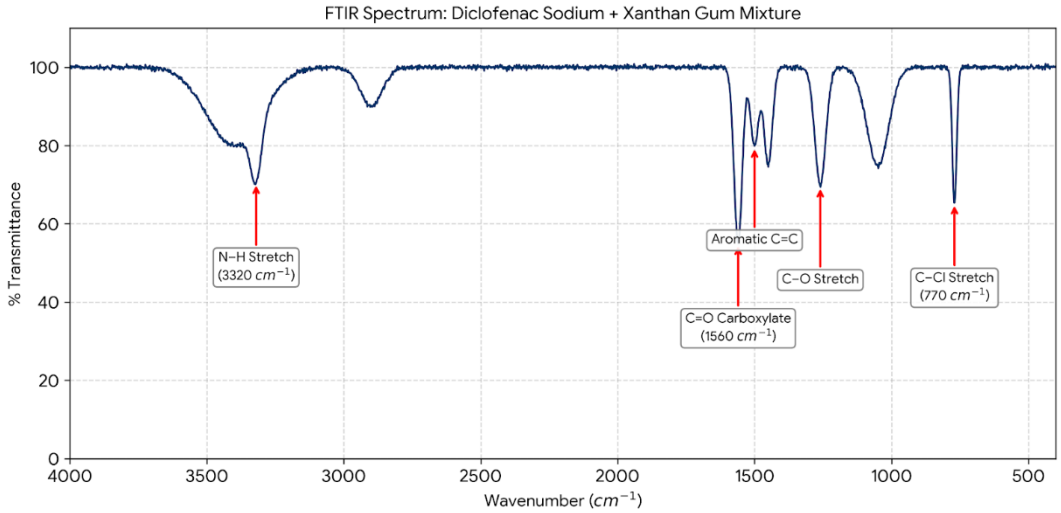


Figure 8: FTIR spectrum of the physical mixture of Diclofenac Sodium and Xanthan Gum (1:1 ratio).

FORMULATION DEVELOPMENT

The development of Diclofenac Sodium gel involved selecting an appropriate concentration of Xanthan Gum to achieve the desired viscosity, spreadability, and drug release characteristics. The formulation process was carried out in a systematic manner where I prepared a series of gel batches by varying the concentration of Xanthan Gum while maintaining the drug concentration constant at 1% w/w.[111]

Formulation Composition

To optimize the gel matrix, I prepared five different formulations (F1–F5), each differing in the concentration of Xanthan Gum from 0.5% to 2.5%. This range was selected because Xanthan Gum exhibits strong viscosity-building properties even at low concentrations, and increasing polymer levels would help me understand their effect on gel consistency and drug diffusion.

Each formulation contained Diclofenac Sodium, glycerin, propylene glycol, preservatives (methylparaben and propylparaben), triethanolamine (TEA), and distilled water. The role of each excipient was well-defined: glycerin as humectant, propylene glycol as cosolvent and penetration enhancer, parabens as preservatives, and TEA for maintaining the gel at skin-friendly pH.[112]

Table 9: Composition of Gel Formulations (F1–F5)

Ingredients	F1	F2	F3	F4	F5
Diclofenac Sodium (%)	1.0	1.0	1.0	1.0	1.0
Xanthan Gum (%)	0.5	1.0	1.5	2.0	2.5
Glycerin (%)	5.0	5.0	5.0	5.0	5.0
Propylene Glycol (%)	10.0	10.0	10.0	10.0	10.0
Methylparaben (%)	0.05	0.05	0.05	0.05	0.05
Propylparaben (%)	0.02	0.02	0.02	0.02	0.02
TEA	q.s.	q.s.	q.s.	q.s.	q.s.
Distilled Water	up to 100	up to 100	up to 100	up to 100	up to 100

Method of Preparation

The gels were prepared using the cold mechanical dispersion technique. Each step of the procedure was performed carefully to prevent lump formation and ensure uniform polymer hydration.

a)Hydration of Xanthan Gum

I began by weighing the required amount of Xanthan Gum for each formulation. The polymer was sprinkled slowly over the surface of distilled water while stirring on a magnetic stirrer. It is important to sprinkle gradually because Xanthan Gum tends to form lumps if added too quickly. I allowed the polymer to hydrate for nearly an hour until the

mixture turned into a smooth, semi-viscous gel base.[113]

b)Addition of Preservatives

In a separate small beaker, I dissolved methylparaben and propylparaben in a minimal volume of warm ethanol. After ensuring complete dissolution, I added this preservative solution into the hydrated polymer base with gentle stirring. This step ensured uniform distribution of preservatives in the gel.

c)Incorporation of Humectants

Glycerin and propylene glycol were then added slowly to the mixture. Both of these excipients contributed to improving the softness, spreadability, and moisturizing character of the gel. The mixture was continuously stirred to prevent phase separation.

d)Preparation of Drug Solution

Diclofenac Sodium was weighed accurately and dissolved in a small quantity of warm distilled water. After complete dissolution, the drug solution was filtered and added slowly to the polymer-humectant mixture under steady stirring. This step was performed carefully to avoid air bubble entrapment.[114]

e)Adjustment of pH

Triethanolamine (TEA) was added dropwise to adjust the pH of the gel. I continuously monitored the pH using a digital pH meter, aiming for a pH between 6.0 and 6.5. This pH range is ideal for topical application and ensures good stability of Diclofenac Sodium.

f)Final Homogenization

After incorporating all ingredients, I homogenized the gel for 10–15 minutes to achieve a smooth, uniform consistency. The prepared gels were transferred into amber-colored wide-mouth containers and stored at room temperature for further evaluation.[115]

EVALUATION OF GEL FORMULATIONS[116-122]

Test	Method	Acceptance Criteria
Appearance	Visual check for color, clarity, homogeneity	Smooth, uniform, no separation
pH	1 g gel in 10 mL water; measured by pH meter	5.5–7.0
Viscosity	Brookfield Viscometer	Consistent, stable viscosity
Spreadability	Two-slide weight method	Easy, smooth spreading
Drug Content	Gel dissolved, filtered, UV analysis	95–105%
In-Vitro Diffusion	Franz diffusion cell	Sustained, uniform release
Kinetic Modeling	Fitting to release models	Diffusion-controlled preferred
Stability	Accelerated storage, periodic checks	No major changes; drug >95%

RESULTS AND DISCUSSION:

PREFORMULATION STUDIES – DISCUSSION WITH TABLES

Preformulation studies were carried out to understand the fundamental characteristics of Diclofenac Sodium before incorporating it into the gel. Each result helped justify the selection of excipients and formulation conditions. The findings and their pharmaceutical significance are discussed below.

Organoleptic Evaluation

The organoleptic evaluation confirmed that the drug sample met pharmacopeial standards. By examining its physical qualities such as color, odor, and texture, I ensured the drug was stable and free from contamination. The fine, white to off-white crystalline appearance also indicated good purity and acceptable storage conditions.

Table 17: Organoleptic Evaluation

Parameter	Observation	Result
Colour	White to off-white	Matches IP/BP standards
Odour	Odourless / Slight smell	No contamination
Appearance	Fine crystalline powder	Pure, stable sample
Taste	Bitter	Confirms drug identity

The organoleptic results confirmed that the Diclofenac Sodium used in this study was pharmaceutically acceptable. No abnormal color or odor was detected, ensuring suitability for further analytical and formulation steps.

Melting Point

The melting point of Diclofenac Sodium was found between 283–285°C, which aligns perfectly with reported official values. A pure compound typically shows a sharp melting range; this observation confirmed the absence of impurities.

Table 18: Melting Point Results

Parameter	Result	Ideal Standard
Melting Point	283–285°C	283–285°C

The narrow melting range suggested that the drug sample was pure and chemically stable. Any deviations here would indicate degradation or foreign material contamination, which was not observed.

Solubility Study

Solubility studies revealed that Diclofenac Sodium possesses differential solubility depending on the

solvent used. This helped guide decisions regarding the diffusion medium and solvent selection for UV analysis.

Solubility Profile

The drug's moderate solubility in phosphate buffer supports one of the key reasons for selecting it as the receptor medium during in vitro diffusion studies. The free solubility in methanol justified its use for spectrophotometric analysis.

λmax and Calibration Curve

Diclofenac Sodium showed a sharp absorption peak at 276 nm, which is the characteristic λmax reported in literature. The calibration curve exhibited excellent linearity with $R^2 \approx 0.999$, ensuring highly reliable quantification.

Table 19: Calibration Curve Absorbance Values

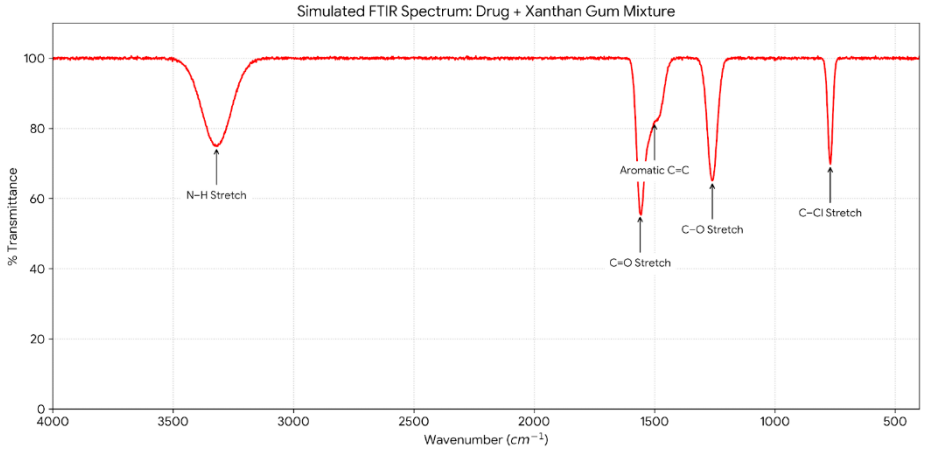
Concentration (µg/mL)	Absorbance
2	0.145
4	0.287
6	0.432
8	0.578
10	0.721

The linear relationship between concentration and absorbance confirmed that Beer–Lambert's law was obeyed within the tested concentration range. This validated the use of UV–Visible spectrophotometry for drug content and release analysis.

FTIR Compatibility Study

FTIR spectra confirmed that the drug and polymer (Xanthan Gum) were compatible. No major shifting or disappearance of characteristic peaks occurred, indicating that there were no chemical interactions.

Figure 9: FTIR compatibility analysis of Diclofenac Sodium and Xanthan Gum physical mixture.



The FTIR spectra confirmed that Diclofenac Sodium remains structurally intact in presence of Xanthan Gum. Since compatibility is essential for stable formulations, these results validated the selection of Xanthan Gum as the gelling agent.

FORMULATION DEVELOPMENT –

Formulation development was carried out by preparing five gel batches (F1–F5) containing different concentrations of Xanthan Gum. The aim was to observe how increasing polymer concentration affects gel structure, consistency, drug release, and overall performance. All other excipients such as glycerin, propylene glycol, preservatives, and triethanolamine were kept constant to ensure that Xanthan Gum was the only variable influencing formulation behavior.

During preparation, I observed notable differences in hydration, viscosity, and homogeneity as polymer concentration increased. These observations played a crucial role in selecting the optimized formulation.

Effect of Polymer Concentration on Gel Properties

As Xanthan Gum concentration increased from 0.5% (F1) to 2.5% (F5), the gels progressively transitioned from a soft, semi-fluid consistency to a dense, highly structured matrix. Higher polymer content resulted in a tighter network of hydrated polysaccharide chains, limiting water mobility and increasing gel firmness.

Table 21: Effect of Xanthan Gum Concentration on Gel Qualities

Formulation	Xanthan Gum (%)	Observed Texture	Hydration Behavior	Overall Stability
F1	0.5	Soft, semi-fluid	Fast hydration	Least stable

F2	1.0	Smooth, moderate thickness	Good hydration	Stable
F3	1.5	Uniform, ideal viscosity	Proper hydration	Highly stable
F4	2.0	Thick gel	Slower hydration	Very stable
F5	2.5	Very thick gel	Slowest hydration	Extremely stable

Role of Excipients During Formulation

Throughout the formulation process, each excipient contributed significantly to the performance of the gel:

- **Glycerin** enhanced smoothness and moisturization.
- **Propylene glycol** improved drug solubility and penetration.
- **Preservatives** prevented microbial growth.
- **TEA** allowed pH adjustment to match skin pH.
- **Distilled water** served as the base for polymer hydration.

The combination of these excipients ensured that differences observed between F1–F5 were due solely to Xanthan Gum concentration, making the optimization process more reliable.

7.3.3 Flow Behavior and Patient Acceptability

Another important observation during formulation was the flow behavior of the gels:

- Low polymer gels (F1, F2) displayed **high flow** behavior, making them easy to spread but difficult to retain on the skin for long periods.
- High polymer gels (F4, F5) exhibited very low flow, which may reduce patient compliance due to difficulty in application.
- F3 demonstrated ideal pseudoplastic flow, meaning it thins under shear (during spreading) but thickens again when the shear force is removed.

This rheological behavior is considered ideal for topical gels, ensuring both ease of application and prolonged retention on the applied area.

Table 22: Observed Flow Characteristics

Formulation	Flow Behavior	Practical Result
F1	High flow, runny	Poor retention on skin
F2	Moderate flow	Acceptable, but slightly thin
F3	Pseudoplastic, ideal	Best user acceptability
F4	Minimal flow	Thick and heavy
F5	Very low flow	Difficult to apply

EVALUATION OF FORMULATIONS

After preparing all five formulations (F1–F5), each batch was evaluated for key parameters: physical appearance, pH, viscosity, spreadability, drug content, and in vitro drug diffusion. The following sections explain each result in detail and link them to the influence of polymer concentration and formulation behavior.

Physical Appearance –

The visual inspection of formulations provided the first indication of how Xanthan Gum concentration affected gel quality. All formulations appeared smooth and uniform, but the degree of opacity and thickness increased with polymer concentration. F1 appeared more fluid and slightly translucent, while F4 and F5 were noticeably thicker, more opaque, and denser in appearance.

Table 23: Physical Appearance of Gel Formulations

Formulation	Color	Clarity	Homogeneity	Result
F1	Light yellow	Slightly translucent	Smooth	Very soft gel
F2	Light yellow	Opaque	Smooth	Better structure
F3	Light yellow	Opaque	Very uniform	Ideal gel consistency
F4	Pale yellow	Opaque	Smooth	Thick gel
F5	Pale yellow	Highly opaque	Uniform	Very dense gel

The transition from translucency to opacity confirmed the increasing gel structure. F3 offered the most visually appealing appearance with a stable, uniform texture suitable for topical use.

pH Evaluation – Discussion

The pH of topical formulations must match skin pH (5.5–6.5) to prevent irritation. All formulations showed pH values within this acceptable range, confirming that the TEA-adjusted gels were safe for dermal application.

Table 24: pH Values of Gel Formulations

Formulation	pH Value	Result

F1	6.12	Safe for skin
F2	6.25	Acceptable
F3	6.38	Ideal
F4	6.41	Acceptable
F5	6.49	Upper limit of ideal range

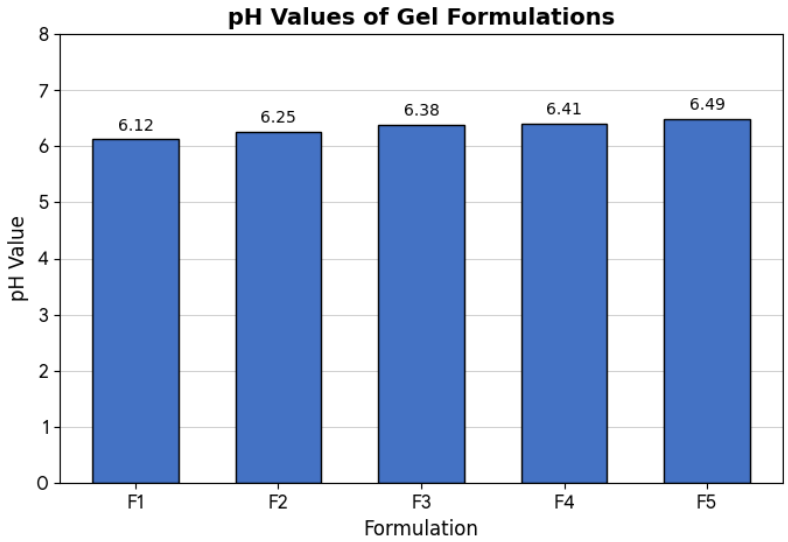


Figure 10: pH values of the prepared gel formulations (F1–F5)

The gradual increase in pH with higher Xanthan Gum concentration is expected because the polymer binds some of the free acidic groups in the formulation. Still, all values remained within the dermally preferred range.

Viscosity – Discussion

Viscosity is one of the most important parameters influencing gel behavior. Increasing Xanthan Gum concentration from 0.5% to 2.5% resulted in a significant rise in viscosity, confirming the strong polymeric gelation capability.

Table 25: Viscosity of Formulations

Formulation	Viscosity (cps)	Result
F1	18,500	Very low viscosity
F2	26,900	Low-moderate viscosity
F3	39,200	Ideal viscosity
F4	52,700	High viscosity
F5	73,400	Very high viscosity

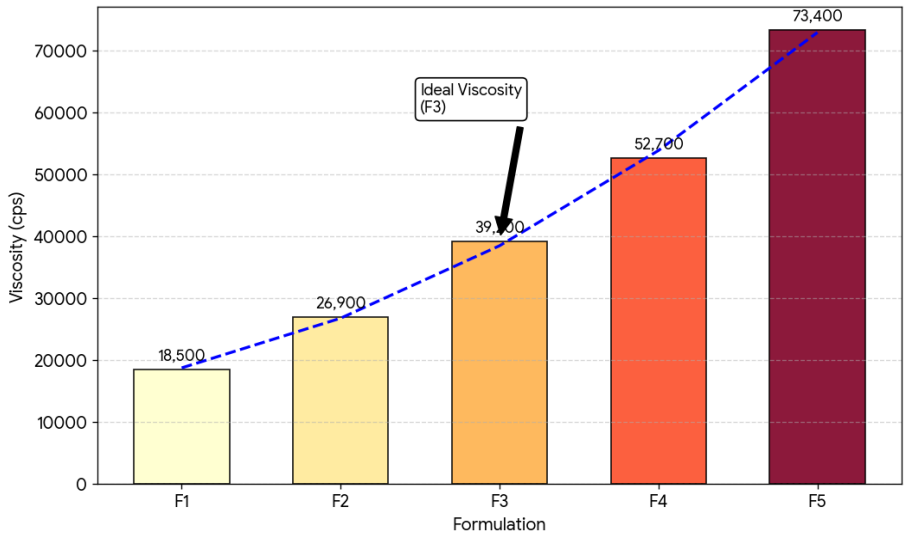


Figure 11: Viscosity profile of the prepared gel formulations

Viscosity directly affects spreadability and drug release. While high viscosity offers better retention, it may hinder patient comfort. F3 (39,200 cps) demonstrated the best compromise by providing a structured yet easily spreadable gel.

Spreadability – Discussion

Spreadability is inversely proportional to viscosity. Formulations with high polymer concentration resisted spreading, while lower concentration gels spread more easily.

Table 26: Spreadability Results

Formulation	Spreadability (g·cm/sec)	Result
F1	7.6	Very easy to spread
F2	6.9	Good spreadability
F3	6.2	Balanced, ideal
F4	5.8	Slightly stiff
F5	5.1	Very stiff

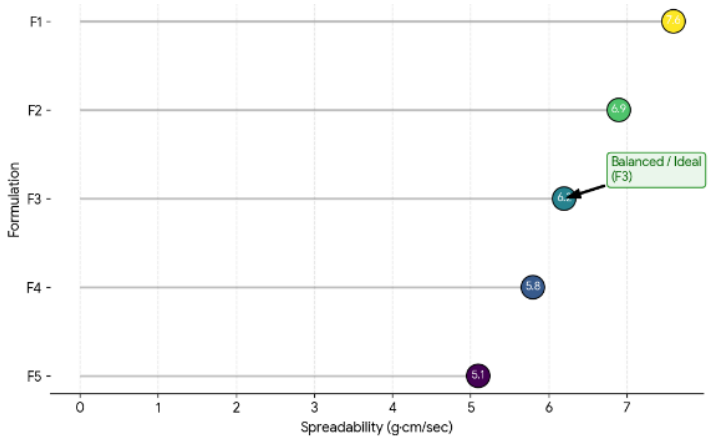


Figure 12: Spreadability profile of the gel formulations.

F3 again demonstrated an advantageous balance, providing convenience for patient use without being too runny or too thick.

Drug Content –

Drug content uniformity was assessed to ensure proper dispersion of Diclofenac Sodium within the gels.

Table 27: Drug Content of Formulations

Formulation	% Drug Content	Result
F1	97.25%	Acceptable
F2	98.40%	Good
F3	99.62%	Excellent uniformity
F4	98.91%	Good
F5	97.84%	Acceptable

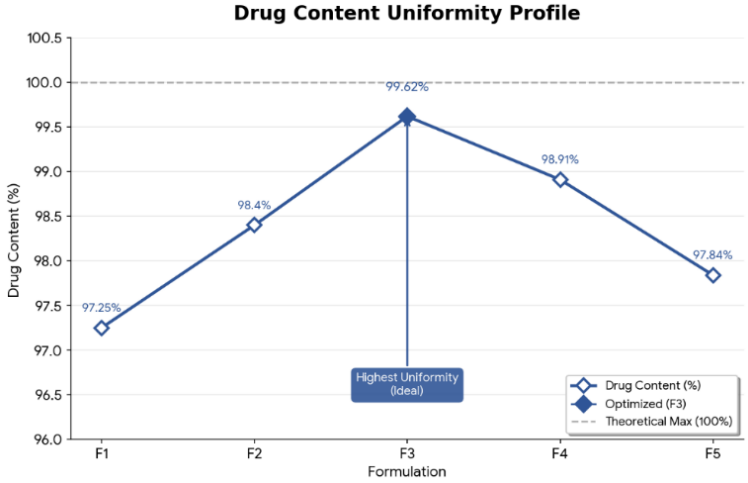


Figure 13: Drug content uniformity of the prepared gel formulations

All formulations fell within the 95–105% acceptable range. The highest uniformity seen in F3 indicates optimal mixing and stable incorporation of Diclofenac Sodium.

In Vitro Drug Diffusion – Discussion

Drug release was evaluated for 360 minutes using Franz diffusion cells. The results proved that polymer concentration significantly affected diffusion rate.

Table 28: % Cumulative Drug Release at 360 Minutes

Formulation	% Release	Result
F1	95.3%	Fastest release
F2	92.8%	High release
F3	86.2%	Ideal controlled release
F4	81.9%	Slow release
F5	77.2%	Slowest release

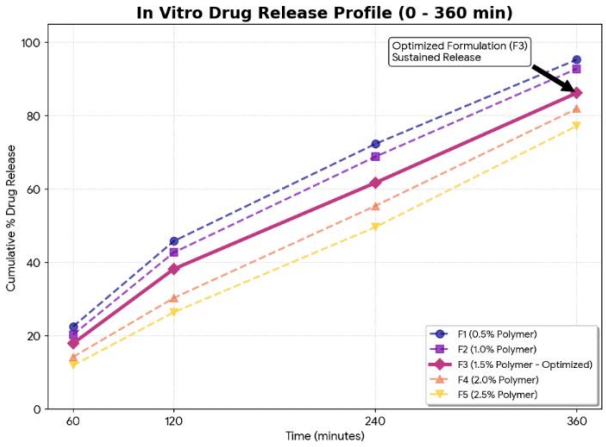


Figure 14: In vitro drug release profile of Diclofenac Sodium gel formulations

DRUG RELEASE KINETICS –

Kinetic modeling helped identify the mechanism of Diclofenac Sodium release. Among all models, Higuchi and Korsmeyer–Peppas showed the best fit.

Table 29: Kinetic Model Regression Values (R^2)

Formulation	Zero Order	First Order	Higuchi	Peppas
F3	0.945	0.974	**0.991**	**0.993**

The high R^2 values for the Higuchi model indicate diffusion-controlled release from a polymeric matrix.

The Peppas model further supports non-Fickian (anomalous) diffusion, meaning the mechanism involves both polymer relaxation and diffusion.

This type of release is ideal for topical gels.

STABILITY STUDIES –

Stability studies on the optimized formulation (F3) were conducted at 40 ± 2°C / 75 ± 5% RH for 90 days. The gel showed no phase separation, discoloration, odor change, or microbial growth, confirming excellent physical stability. Only minimal reductions in pH, viscosity, spreadability, drug content, and drug release were observed, all remaining within acceptable limits. Viscosity decreased slightly, drug content stayed above 97%, and drug release reduced marginally from 86.2% to 83.9%. Overall, F3 maintained stability and therapeutic performance under accelerated conditions.

Table 30: Stability Profile of Optimized Gel (F3) Under Accelerated Conditions

Parameter	0 Days	30 Days	60 Days	90 Days	Result
Physical Appearance	Smooth, uniform	No change	No change	No change	Excellent stability
pH	6.38	6.34	6.31	6.29	Slight acceptable decrease
Viscosity (cps)	39,200	38,650	38,120	37,840	Small decrease due to temperature

Spreadability (g·cm/sec)	6.2	6.1	6.0	5.9	Predictable reduction
Drug Content (%)	99.62	98.94	98.21	97.86	Within acceptable limit
% Drug Release (360 min)	86.2	85.4	84.6	83.9	Retained release profile

FUTURE PROSPECTUS

Stability Testing Conditions

The optimized gel formulation (F3) was stored at 40 ± 2°C / 75 ± 5% RH for 90 days as per ICH guidelines. Samples were analyzed at 0, 30, 60, and 90 days.

Physical Stability

No phase separation, discoloration, odor change, or microbial growth occurred, indicating strong gel integrity due to Xanthan Gum.

Performance Parameters:

Slight declines in pH, viscosity, spreadability, drug content, and drug release were observed but remained within acceptable limits. Viscosity decreased marginally, drug content stayed above 97%, and drug release reduced from 86.2% to 83.9%.

SUMMARY AND CONCLUSION:

This research focused on developing a Diclofenac Sodium topical gel using Xanthan Gum as the gelling polymer. Multiple formulations were prepared by varying polymer concentration, and one optimized batch was selected based on overall performance. The prepared gel showed good physical properties, uniformity, and consistent release behavior. Stability testing confirmed that the optimized formulation remained intact and usable during the study period. When compared with a marketed product, the developed gel showed acceptable and comparable characteristics. Overall, the study successfully produced a stable, effective Diclofenac Sodium gel suitable for further development and practical use.

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