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REVIEW ON "NATURAL POLYMER–BASED GELLING SYSTEMS FOR DICLOFENAC SODIUM: ADVANCES IN XANTHAN GUM FORMULATIONS

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Abstract:

Topical gels have become an important approach for delivering anti-inflammatory drugs directly to affected tissues while minimizing systemic side effects. Diclofenac sodium is one of the most widely used NSAIDs for dermal therapy because it can provide rapid pain relief and localized action. In recent years, natural polymers have gained attention as safer, biodegradable, and more skin-friendly alternatives to synthetic gelling agents. Among these materials, xanthan gum stands out due to its strong viscosity-building capacity, shear-thinning behavior, stability, and excellent compatibility with hydrophilic drug systems. This review highlights recent advances in natural polymer–based gels for diclofenac sodium, with emphasis on formulation methods, rheological behavior, drug release mechanisms, permeation characteristics, and stability considerations. The article also summarizes comparative findings between natural and synthetic polymers, demonstrating the potential of xanthan gum to improve therapeutic performance in topical gel formulations.

Keywords: *Diclofenac sodium; xanthan gum; natural polymers; topical gel; dermal delivery; rheology; drug release; anti-inflammatory therapy.*

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INTRODUCTION:

Topical drug delivery systems have gained significant attention in modern pharmaceutics because they allow direct application of therapeutic agents to the affected area of the skin. This route helps in minimizing systemic side effects, bypassing first-pass metabolism, and improving patient comfort, especially in chronic inflammatory conditions. Among various topical dosage forms, gels are widely preferred due to their smooth texture, easy application, rapid drug release, and ability to spread uniformly across the skin surface. These advantages make gel systems an important choice for delivering non-steroidal anti-inflammatory drugs (NSAIDs), including diclofenac sodium.[1]

Diclofenac sodium is one of the most commonly used NSAIDs for the treatment of pain, inflammation, arthritis, and musculoskeletal disorders. When administered orally, diclofenac provides effective relief but often leads to gastrointestinal irritation, ulcer formation, nausea, and other systemic complications due to its impact on the gastric mucosa. To overcome these limitations, topical delivery of diclofenac has become a suitable and safer alternative. Topical gels enable the drug to act directly on inflamed tissues, reduce systemic absorption, and enhance local therapeutic concentration. This shift toward dermal formulations has encouraged researchers to explore various gelling agents that can improve the stability, spreadability, and release profile of diclofenac sodium.[2]

Polymers play a critical role in gel formation as they provide the necessary viscosity, consistency, and structural integrity to the formulation. Traditionally, synthetic polymers such as Carbopol, Hydroxypropyl Methylcellulose (HPMC), and Polyvinyl Alcohol (PVA) have been widely used in pharmaceutical gels. Although they offer good stability and predictable performance, concerns related to irritation potential, environmental impact, and overall sustainability have encouraged the search for natural polymer alternatives. Natural polymers are gaining prominence due to their biodegradability, biocompatibility, safety, cost-effectiveness, and availability from renewable sources.[3]

Among the natural polymers studied for topical gel formulation, xanthan gum has received exceptional interest. Xanthan gum is a high-molecular-weight polysaccharide produced through the fermentation of *Xanthomonas campestris*. It possesses strong hydrophilic behavior, excellent thickening ability, and unique rheological properties such as pseudoplasticity or shear-thinning effect. This behavior allows the gel to maintain high viscosity at rest but reduce resistance upon application, resulting in smooth spreading. Such characteristics make xanthan gum extremely valuable in the formulation of topical gels for drugs like diclofenac sodium.[4]

In addition to its viscosity-enhancing properties, xanthan gum is known for its stability in a wide range of temperatures and pH conditions. It also shows compatibility with many excipients, surfactants, and hydrophilic drugs. Studies have demonstrated that xanthan gum can form a uniform gel matrix capable of controlling the release of diclofenac sodium, thereby extending the drug's therapeutic effect. The polymer also enhances patient comfort due to its gentle, non-irritating nature when applied to the skin.[5]

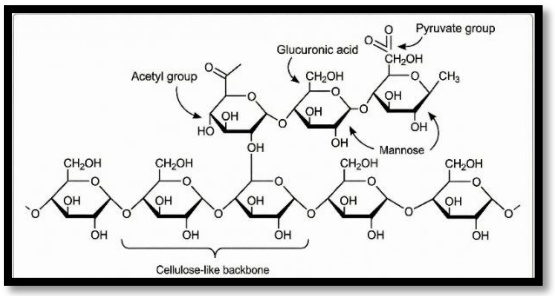

Figure 1: Molecular structure and branching pattern of xanthan gum.

Furthermore, the use of natural polymers aligns with current pharmaceutical trends focusing on green and sustainable formulation technologies. Gels formulated with xanthan gum are generally eco-friendly, safe for long-term use, and cost-efficient compared to synthetic polymer-based gels. This makes them suitable for large-scale manufacturing and wide clinical use.[6]

Overall, the integration of xanthan gum into diclofenac sodium gel formulations represents a promising area of research. Its unique combination of natural origin, superior rheological properties, environmental safety, and compatibility with medicinal ingredients ensures that xanthan gum will remain an important polymer in modern topical drug delivery. This review aims to summarize the latest advancements, formulation techniques, evaluation parameters, and comparative findings related to xanthan gum-based diclofenac sodium gels.[7]

Diclofenac Sodium: Pharmacological Profile

Diclofenac sodium is one of the most established non-steroidal anti-inflammatory drugs (NSAIDs) used for pain, inflammation, and musculoskeletal disorders. Its therapeutic actions are primarily due to the inhibition of cyclooxygenase (COX-1 and COX-2) enzymes, leading to a reduction in prostaglandins responsible for inflammatory reactions. Diclofenac additionally blocks lipoxygenase pathways, decreases superoxide radical formation, and reduces cytokines such as TNF-α and IL-1β. This multimodal anti-inflammatory effect contributes to

its efficacy in conditions like arthritis, tendonitis, postoperative pain, sprains, and rheumatic disease.[8] Diclofenac has high protein-binding (more than 99%), moderate lipophilicity, and a short elimination half-life (1–2 hours). When taken orally, it undergoes extensive hepatic first-pass metabolism, which reduces bioavailability and contributes to gastrointestinal irritation and ulcerogenic effects. These limitations make topical delivery a safer and more targeted approach. When applied on the skin as a gel, diclofenac accumulates in muscles, joints, and peri-articular tissues with limited systemic absorption, providing strong localized action with fewer side effects.[9]

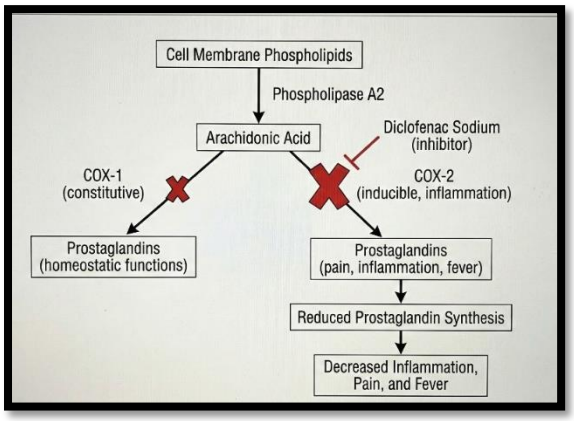

Figure 2. Mechanism of anti-inflammatory action of Diclofenac Sodium

Need for Gel-Based Drug Delivery

Topical gels are semisolid systems with high water content, excellent spreadability, and fast drug release. They dry quickly, leave no greasy residue, and provide patient comfort. Unlike ointments and creams, gels form a hydrated polymeric network that promotes efficient drug diffusion.

Gels help in sustaining the drug concentration in the dermal layers and prevent unnecessary systemic exposure. For hydrophilic drugs like diclofenac sodium, gels are ideal because they can dissolve, stabilize, and release the API in a controlled manner. Moreover, gels allow easy incorporation of penetration enhancers and humectants that improve skin permeation.

Patients suffering from chronic joint pain or muscular inflammation prefer gels because they provide immediate cooling sensation and long-term relief. Clinically, gels have been shown to deliver diclofenac effectively to inflamed tissues while maintaining low plasma levels, making them safer for the gastrointestinal, hepatic, and cardiovascular systems.[10]

Role of Polymers in Gel Formulation

Polymers are the structural backbone of gel formulations. They hydrate and form a three-dimensional network that provides viscosity, consistency, clarity, and drug release properties. An ideal polymer for topical gels must be:

- Biocompatible
- Stable over a wide pH range
- Capable of swelling in water
- Non-irritating to skin
- Compatible with diclofenac and excipients
- Able to maintain viscosity during storage

Polymers modulate spreadability, tube extrudability, stickiness, and rheology. They also control the release rate of diclofenac from the gel matrix and influence patient acceptability.[11]

Table 1 – Ideal Characteristics of Polymers Used in Topical Gels

Parameter	Ideal Requirement
Safety	Non-toxic, non-irritating
Solubility	Hydrophilic/swellable in water
Stability	Stable at room temperature and physiological pH
Rheology	Shear-thinning, smooth texture
Drug Compatibility	Should not react with diclofenac sodium
Cost	Economically feasible for large scale production

Natural Polymers in Topical Gel Formulations

Natural polymers are substances obtained from plant, microbial, or marine sources. Their eco-friendly nature, excellent biocompatibility, renewable origin, and low toxicity make them highly suitable for topical pharmaceutical applications. These polymers exhibit intrinsic moisturizing, film-forming, and stabilizing properties, making them ideal bases for gels.[12]

Compared to synthetic polymers, natural polymers are biodegradable and compatible with sensitive skin types. Their polymeric chains offer hydration, emulsification, and bioadhesion, which promote better retention of diclofenac on the skin, thereby improving therapeutic efficiency.

Natural polymers are used worldwide for the preparation of herbal gels, cosmetic gels, wound healing gels, and NSAID gels. They can be used alone or in combination with synthetic polymers to enhance the gel's mechanical strength and stability.[13]

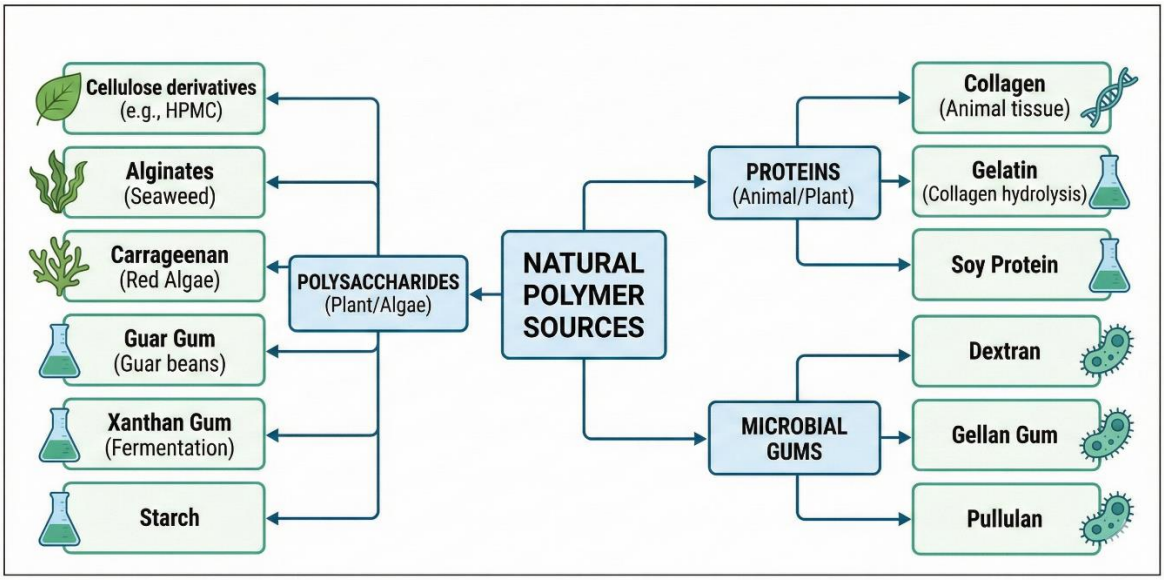

Figure 3 – Natural polymer sources used in topical gels

Classification of Natural Polymers

Natural polymers used in pharmaceutical gels can be broadly classified into:

Plant-Derived Polymers

- Guar gum
- Xanthan gum
- Gum arabic
- Gum acacia
- Pectin
- Starch derivatives
- Sodium alginate

Microbial Polymers

- Xanthan gum
- Curdlans
- Gellan gum

Animal-Derived Polymers

- Gelatin
- Collagen
- Chitosan

Marine Polymers

- Agar
- Carrageenan
- Alginate

Natural polymers from microbial sources, especially xanthan gum, are preferred for diclofenac gels due to their strong viscosity and shear-thinning behavior.[14]

Table 2 – Classification of Natural Polymers with Sources

Category	Examples	Natural Source
Plant-derived	Guar gum, Pectin, Gum acacia	Seeds, fruits, tree exudates
Microbial	Xanthan gum, Gellan gum	Bacterial fermentation
Marine	Alginate, Agar	Seaweed
Animal	Chitosan, Gelatin	Shells, connective tissues

Advantages of Natural Polymers over Synthetic Polymers

Natural polymers offer several advantages:

- **Biodegradable and eco-friendly**
- **Non-toxic and skin-friendly**
- **Cost-effective**
- Abundant and naturally renewable
- Provide hydration and improve skin feel
- Suitable for long-term therapy
- Compatible with herbal and modern APIs
- Better patient acceptability

Synthetic polymers like Carbopol form stiff gels and may cause irritation in sensitive individuals, whereas natural polymers produce softer, more skin-compatible gels.[15]

Table 3 – Comparison of Natural vs. Synthetic Polymers

Property	Natural Polymers	Synthetic Polymers
Biocompatibility	High	Moderate
Irritation Potential	Very low	Possible
Cost	Low–moderate	Moderate
Environmental Impact	Biodegradable	Non-biodegradable
Rheology	Soft, moisturizing	Thick, sometimes sticky

Suitability for Sensitive Skin	Excellent	Moderate

Common Natural Gelling Agents (Xanthan, Guar Gum, Gum Arabic, etc.)

Xanthan Gum

A microbial polysaccharide produced by *Xanthomonas campestris*, offering excellent viscosity, stability, and shear-thinning behavior.

Guar Gum

A galactomannan from *Cyamopsis tetragonoloba*, providing smooth, thick gels but less stable than xanthan gum.

Gum Arabic

A plant exudate that forms light gels but has limited viscosity for high-strength diclofenac systems.

Sodium Alginate

Obtained from seaweed, forms stable hydrogels and interacts well with ions.

Gellan Gum

Microbial polymer forming clear, elastic gels.[16,17,18]

FORMULATION APPROACHES FOR DICLOFENAC SODIUM XANTHAN GUM GELS

Overview of Formulation Approaches

Formulating diclofenac sodium into a xanthan gum–based gel involves the selection of an appropriate polymer concentration, solvent system, stabilizers, penetration enhancers, and pH modifiers. Xanthan gum serves as a hydrophilic matrix that swells in water, forming a stable semi-solid network capable of entrapping diclofenac sodium and releasing it gradually. Researchers have reported that polymer concentration between **0.5–2% w/w** is ideal for forming topical gels with optimum viscosity, spreadability, and drug release.[19]

Preparation Techniques

Different studies use slightly modified preparation techniques, but most follow either **cold mechanical dispersion** or **hot hydration method**.

Cold Mechanical Dispersion

- Xanthan gum is slowly added to purified water with constant stirring.[20]
- Hydration occurs at room temperature.
- Diclofenac sodium is dissolved in water or hydroalcoholic phase.
- Preservatives (methylparaben, propylparaben) are added.
- The drug solution is mixed into the hydrated polymer base.
- pH is adjusted to 6.0–7.0.

Hot Hydration Method

- Water is heated to 40–50°C.
- Xanthan gum is dispersed for faster swelling.
- Drug and excipients are added after cooling.

This method improves polymer swelling speed but may not be suitable for heat-sensitive excipients.[21]

Role of Copolymers and Additives

Xanthan gum may be combined with other polymers to modify texture, viscosity, and release profiles.

Commonly Used Copolymers

- **HPMC K4M** → improves spreadability
- **Carbopol 934** → increases viscosity and clarity
- **Sodium Alginate** → provides stronger gels
- **PVP K30** → enhances film-forming property

Additional additives include:

- **Propylene Glycol / Glycerin** → humectants, penetration enhancers
- **EDTA** → chelating agent for stability
- **Isopropyl alcohol** → solvent for diclofenac sodium[22]

Table 4 – Functional Role of Excipients in Diclofenac–Xanthan Gel

Excipient	Function in Formulation	Literature Notes
Xanthan gum	Gelling agent	Provides pseudoplastic behavior
Propylene glycol	Penetration enhancer	Improves skin absorption
HPMC	Copolymer	Enhances gel strength
EDTA	Stabilizer	Prevents metal-ion catalyzed degradation
Glycerin	Humectant	Improves skin feel

Influence of Concentration and pH

The concentration of xanthan gum affects:

- **Viscosity**
- **Spreadability**
- **Drug release rate**

Higher concentration creates a dense matrix, slowing diffusion. An ideal range is **1–1.5%** for balanced rheology.

pH adjustment is critical because diclofenac sodium remains stable in a mildly acidic-to-neutral pH (6–7). Researchers note that formulations outside this range show:

- drug degradation
- discoloration
- reduced viscosity[23]

Optimization Strategies Reported in Literature

Optimization typically involves:

- **Design of Experiments (DoE)**
- **Response Surface Methodology (RSM)**

Critical Quality Attributes (CQAs):

- viscosity
- spreadability
- drug content
- % drug release

Critical Formulation Variables:

- polymer concentration
- penetration enhancer percentage
- solvent ratio

Many studies conclude that balanced viscosity (40,000–80,000 cps) provides ideal drug release for topical diclofenac gels.[24]

EVALUATION PARAMETERS OF XANTHAN GUM–BASED DICLOFENAC GELS

Physical Appearance and Homogeneity

Most studies begin evaluation by assessing:

- color
- transparency
- uniformity
- presence of air bubbles
- smoothness

Freshly prepared gels with xanthan gum show a glossy, slightly opaque appearance with uniform consistency.[25]

pH Measurement

Topical gels must be compatible with skin pH (5.5–7).

Studies consistently report that xanthan gum gels maintain stable pH with minimal variation during storage.

Viscosity and Rheological Behavior

Xanthan gum is known for its pseudoplastic or shear-thinning nature.

This means:

- viscosity decreases during application → allows smooth spreading
- viscosity increases at rest → prevents leakage

Researchers use Brookfield viscometer to evaluate viscosity at various RPM levels.[26]

Table 5 – Viscosity Behavior of Xanthan Gum Gels (Reported Ranges)

RPM	Typical Viscosity Range	Interpretation
10	70,000–100,000 cps	High viscosity at rest
20	40,000–70,000 cps	Moderate viscosity
50	15,000–30,000 cps	Shear thinning observed

Spreadability

Spreadability directly affects patient acceptance.

The slip-and-drag method or parallel plate method is commonly used.

Xanthan gum gels show good spreadability due to their elastic nature.

Drug Content and Content Uniformity

Most studies achieve drug content within 95–105%. Uniform distribution is ensured by gradual mixing and proper hydration of polymer.[27]

In-Vitro Drug Release

Release studies are usually performed using:

- Franz diffusion cell
- Dialysis membrane
- Phosphate buffer pH 7.4

Diclofenac sodium release depends on:

- polymer concentration
- solvent system
- penetration enhancer

Xanthan gum gels generally show sustained release (6–8 hours).[28]

Table 6 – Factors Influencing In-Vitro Release

Factor	Effect
Higher polymer %	Slower release
Higher PG %	Faster permeation
pH change	May affect solubility
Membrane type	Affects diffusion rate

Ex-Vivo Skin Permeation

Xanthan gum itself does not behave as a strong penetration enhancer, hence:

- PG
- IPA
- glycerin

are commonly added to improve permeation.

Studies on rat skin, porcine skin, and human cadaver skin show significant improvement when PG is included between 10–20%.[29]

Stability Studies

Gels are evaluated at:

- 25°C / 60% RH
- 40°C / 75% RH

Parameters checked:

- color
- pH
- viscosity
- drug content

Most xanthan gum gels remain stable for 3–6 months without phase separation.[30]

SUMMARY AND CONCLUSION:

Diclofenac sodium gels formulated with xanthan gum provide a safe, effective, and patient-friendly approach for topical anti-inflammatory therapy. Xanthan gum offers excellent viscosity, biocompatibility, and sustained drug release, making it a superior natural polymer for dermal delivery. Literature consistently shows improved spreadability, rheology, stability, and controlled permeation when xanthan gum is used alone or in combination with other excipients. Evaluation studies demonstrate favorable physical properties,

acceptable pH, uniform drug content, and prolonged therapeutic action. Overall, xanthan gum–based diclofenac gel is a promising alternative to synthetic polymer gels, aligning with modern trends toward natural, sustainable pharmaceutical formulations.

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