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REVIEW ARTICLE

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TAZAROTENE IN NANOGEL FORMULATION A STRATEGIC ENHANCEMENT IN TOPICAL RETINOID DRUG DELIVERY

Ashutosh Rajput *, Jitender Malik, Gyan Singh

Research Scholar, Faculty of Pharmacy, PK University, Thanra - 473665, Madhya Pradesh, India.

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Correspondence should be addressed to
Ashutosh Rajput,
Research Scholar,
Faculty of Pharmacy, PK University,
Thanra - 473665, Madhya Pradesh,
India.

Email- ashutoshrajput1989@gmail.com

ABSTRACT: Tazarotene, a potent retinoid, is commonly used for treating acne, psoriasis, and signs of aging. However, challenges such as poor skin penetration, irritation, and instability limit its effectiveness. Nanogels—self-assembling, stimuli-responsive delivery platforms—emerge as a revolutionary solution in overcoming these challenges. By responding to external stimuli, nanogels provide precise, controlled, and sustained release of Tazarotene directly at the target site, improving its therapeutic potential. This review investigates recent advancements in nanotechnology for enhancing Tazarotene delivery. The role of AI-driven drug design is explored, where computational simulations aid in optimizing nanogel carriers for maximum drug loading, controlled release, and targeted delivery. Further, we examine multi-functional nanogels capable of responding to diverse environmental triggers such as pH, temperature, and light, enabling dynamic drug release. The integration of digital health technologies, including wearable biosensors for real-time monitoring, is also discussed to personalize and adjust treatment according to individual patient needs. Tazarotene-loaded nanogels significantly enhance bioavailability, dermal penetration, and sustained release compared to traditional formulations. These systems minimize irritation, improve stability, and increase drug efficacy by ensuring deeper skin penetration. The combination of smart polymers and AI-assisted optimization ensures precision in drug delivery, promoting effective, personalized treatment regimens for dermatological conditions. Nanogels for Tazarotene delivery represent the next generation of precision dermatology, merging AI, smart polymers, and personalized medicine to offer a patient-centric, adaptive, and effective solution for skin disorders. This approach marks a significant step toward individualized, future-proofed dermatological therapies.

Keywords: Tazarotene, Nanogels, Smart drug delivery, Stimuli-responsive, Personalized medicine

1. INTRODUCTION

Tazarotene is the third generation of retinoid which has been an essential part of fighting acne vulgaris, psoriasis and the visible effects of ageing on the skin including hyperpigmentation and skin lines. It is an essential therapeutic agent because it can regulate skin cell turnover and decrease inflammation [1]. Tazarotene has great promise but its own limitations such as insufficient dermal penetration, photo instability and skin irritation at higher doses frequently act as bottlenecks. These downsides lead to suboptimal therapy outcomes and lack of patient adherence to prescribed regimens [2]. Traditional topical Tazarotene creams and gels do not absorb well and such cream and gels do not retain the concentration in the skin that is required for therapeutic effect. However, side effects worsen because of the need for higher dosages, which puts the safety and the efficacy of the treatment for the long term at risk [3].

Drugs can be distributed in a new way using nanogel technology, which has become state of the art response to these problems. Self-assembling hydrogel networks (nanogels) on nanoscale, an unique way to overcome skin permeability obstacle. These networks can encapsulate Tazarotene [4]. Because of their extraordinarily tailored and dynamic release of the medication that is dependent on environmental factors such as pH, temperature, and light, their responsiveness to environmental factors ensures accurate targeting and extended therapeutic efficacy. In its turn, Tazarotene becomes much more stable and bioavailable in Nanogels, making them an ideal dermatological therapy. It could spark a revolution in skin care treatments, making them more effective, decreasing irritation, and enabling patient adaptive, drug delivery [5].

2. Nanogels as Drug Delivery Systems

Hydrogel particles made nano size (nanogels), able to encapsulate medications, make the drugs more stable, increase bioavailability, as well as allowing their target delivery. These systems have a distinctive structure and response qualities that render them superior to more traditional forms [6]. Usually, Nanogel are active components (e.g., Tazarotene) contained in hydrophilic polymer networks, which allows them to have a lot of water entrapped. Because they are nanoscale in size, and composed of polymeric material, the combination of these properties allows for deep tissue penetration, even controlled release and fewer adverse effects [7].

2.1 Definition and Basic Structure of Nanogels

Nanogels are networks of three-dimensional cross-linked polymers that are usually between twenty and two hundred nanometre in diameter. They are made of natural or synthetic polymers which can be made to have some properties, such as the capacity to respond to changes in light, temperature or pH. The basic building block of nanogel is to encapsulate the active pharmaceutical ingredient (API) such as Tazarotene inside the hydrophilic polymer matrix. This allows for a controlled release of the drug over time in order to prevent the drug from degrading and to maximise therapeutic effects of the drug [8].

2.2 Mechanism of Action in Topical Delivery

Topical drug delivery using nanogels is effective for slow release of chemical contained inside the nanogel as these nanogels could cross the epidermis. Applied to the skin, the nanogels stick to the surface and move into the skin through diffusion and hydration of the outermost layer of the skin through the stratum corneum [9]. Having such small size means they can penetrate further into the skin than its naturally bestowed defences would allow, thus enabling delivery of drugs to specific layers of skin. Additionally, the nanogels can be engineered to react with certain stimuli such as pH, temperature or enzymatic activity. Thus, Tazarotene is released only when needed, without being associated with side effects, and thereby achieving the optimal efficacy [10].

2.3 Advantages of Nanogels Over Conventional Gels and Other Nanosystems

The traditional gels as well as other nanosystems have many advantages over the nanogels (Fig. 1). Compared to typical gels, nanogels have increased penetration and are therefore suitable for deeper administration of drugs and improved bioavailability as their bad skin penetration and fast drug release. They can release medications in a controlled way allowing it to minimize the discomfort while maximizing therapeutic effectiveness [11]. As compared to other nanosystems such as liposomes or solid lipid nanoparticles, nanogels possess aspects of stability, biocompatibility, and ease of modification that make them a good choice for cutaneous applications (Table 1). Besides their versatility and the fact that they find a large application in dermatological therapy, they have the ability to encapsulate hydrophobic as well as hydrophilic medications [12].

Table 1: Comparison between Gel, Nanoemulsion, and Nanogel Formulations [13]

Property	*Gel*	*Nanoemulsion*	*Nanogel*
Size	Micron-sized (1-100 microns)	50-1000 nm	Nanoscale (20-200 nm)
Drug Encapsulation	Limited to surface loading	High drug loading	High drug loading and encapsulation
Skin Penetration	Limited penetration	Enhanced penetration	Deep skin penetration
Stability	Often unstable, especially in light	Generally stable, but sensitive to heat and pH	Excellent stability, less sensitive
Release Profile	Rapid release, short duration	Fast release, limited control	Controlled, sustained release
Viscosity	High viscosity, thick consistency	Low viscosity, fluidic consistency	Medium viscosity, adaptable
Irritation Potential	Moderate (depending on formulation)	Low irritation	Minimal irritation (due to slow release)
Formulation Complexity	Simple formulation process	Requires complex preparation	Moderately complex formulation
Targeted Delivery	No targeted delivery	Limited targeting capability	Highly targeted delivery (via nanoscale size)
Biocompatibility	Good (depending on ingredients)	Good (with biocompatible surfactants)	Excellent, highly biocompatible
Cost of Production	Low cost	Moderate cost	High cost due to complex design
Application in Dermatology	Commonly used for surface-level treatments	Used for topical and transdermal applications	Ideal for targeted and sustained drug release in dermatology

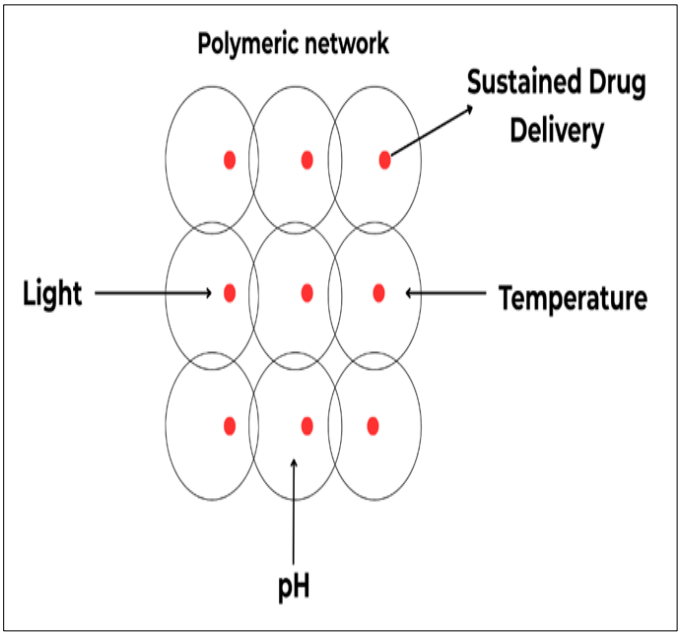

Fig. 1: Schematic illustration of nanogel network structure [14]

3. Tazarotene Nanogel Formulations

Tazarotene nanogel formulations have been very popular because they have the ability to increase drug's therapeutic index and reduce side effects. These formulations centre on optimizing parameters, selecting appropriate excipients, and incorporating the drug, in order to obtain the regulation release of Tazarotene that is safe for the skin [15].

3.1 Commonly Used Polymers and Excipients

The formulation decisions related to the polymers and excipients significantly affect the effectiveness of Tazarotene loaded nanogel. Polymers like chitosan, polyvinyl alcohol (PVA), carbopol and poloxamers are usually biocompatible, biodegradable and form stable hydrogel matrices [16]. It may also use natural polymers, like alginate or gelatin, as the calming effects and lower skin irritant characteristics. In order to improve solubility, permeability and stability of the drug in the gel system, stabilisers, surfactants (such as Tween 80) and penetration enhancers (like oleic acid, Transcutol®) are added [17].

3.2 Methods of Drug Incorporation into Nanogels

Nanogels are loaded with Tazarotene using different methods. The most common techniques are nanoprecipitation, solvent evaporation, coacervation, and emulsion polymerisation. These methods have their purpose in trying to enclose the medicine in such a way that it retains as much of its chemical composition as possible. Chemical conjugation and physical entrapment of the drug in the polymeric network can be formulated strategies. Consistent particle size and nanoscale dispersion is not guaranteed, and high energy techniques such as ultrasound or high shear homogenisation are often used [18].

3.3 Optimizing Nanogel Formulation Parameters

Optimisation of the efficient and secure delivery of Tazarotene by the nanogel is required. Errors should be considered, such as pH, zeta potential, particle size, and viscosity (Fig. 2). When used topically, there is one thing that is paramount, namely, to keep the product at skin acceptable pH (5.5) and suitable viscosity to avoid any discomfort to the patient and make application simple. Finally, permeation tests and drug release kinetics are further employed to optimally formulate the formulation for best performance [19]. Efficiently optimising these parameters are the targets of which researchers are now using advanced techniques such as AI based predictive modelling and Design of Experiments (DoE). These methods alleviate the trial-and error burden and shortens the formulation time [20].

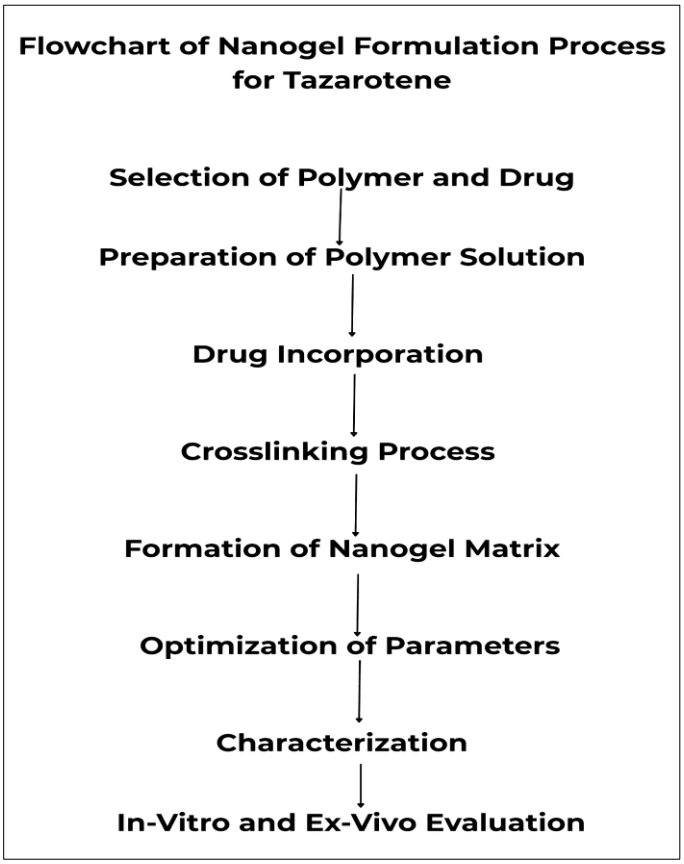

Fig. 2: Flowchart of nanogel formulation process for Tazarotene [21]

4. Characterization and Evaluation Parameters

4.1 Physical Properties: Appearance, Viscosity, and pH

Preliminary measures of formulation stability and patient acceptability are the physical properties of Tazarotene nanogels. The majority of people have a look for a gel with a smooth texture encompassing translucent to opaque. Viscosity is key though, because without it the nanogel would be too easy to apply, destroying its structural integrity. Because the pH ideally should be between 5.0 and 6.0, it is important to use it in order to avoid cutaneous irritation especially in the case of sensitive skin or skin prone to acne [22].

4.2 Particle Size, Zeta Potential, and Drug Content

Nanogels are made up of very small particles, which are usually twenty to two hundred nanometres in size. When the particles are smaller the Tazarotene is released more slowly and more deeply into the skin as the surface area increases. The zeta potential can be calculated and indicates the surface charge on the particles to predict the colloidal stability of the formulation. Because the repulsive forces prevent aggregation when the value of the value is greater than ±30 mV, it is considered stable. Accurate dosing and consistent therapeutic efficacy across batches are ensured by quantification of drug content [23].

4.3 Entrapment Efficiency and Spreadability Studies

The definition of drug entrapment efficiency is the percentage of the drug present in the nanogel matrix. Hence, it is highly desirable because it makes possible the controlled release of drugs, decreases waste, and also increases shelf life. The spreadability of the nanogel is another important metric to keep in mind, denoting its ease in the application on the skin. A formulation that disperses well will impoved the treatment adherence, uniform drug application as well as patient comfort [24].

5. *In-Vitro* and *Ex-Vivo* Study Findings

5.1 Drug Release Behavior and Kinetics

Tazarotene-loaded nanogels usually exhibit a biphasic pattern in *in vitro* drug release tests, with an early burst followed by continuous release over time. Diffusion through the polymeric matrix and regulated degradation of the nanogel structure drive this dual-phase kinetic behaviour. A precise and predictable release mechanism is indicated by the majority of research that conform to Higuchi, Korsmeyer-Peppas, or zero-order models. Reduced dosage frequency and side effects are additional benefits of the regulated kinetics, which significantly improve therapeutic efficiency (Table 2) [25].

5.2 Permeation Studies Using Franz Diffusion Cells

Nanogel systems outperform traditional formulations in *ex vivo* permeation investigations utilising Franz diffusion cells on pig or human cadaver skin. With improved skin adherence and longer residence time on the stratum corneum, the nano-sized particles are able to penetrate deeper into the dermis. The

nanogels' hydrophilic-lipophilic balance guarantees appropriate flow, leading to increased cumulative drug penetration and enhanced local bioavailability [26].

5.3 Comparative Study: Nanogel *vs.* Conventional Tazarotene Gel

Scientific investigations have shown that Tazarotene formulations based on nanogels have superior therapeutic efficacy. Groups treated with nanogel had markedly better medication retention in epidermal layers, better spreadability, and lower scores for redness and irritation, according to studies. Additionally, compared to conventional gels, nanogels have improved entrapment efficiency and stability, making them a more acceptable and effective treatment option for patients [27].

Table 2: Summary of *in-vitro* and *ex-vivo* study outcomes [28]

S. No.	*Study Parameter*	*Observation/Outcome*
1	Drug release pattern	Biphasic release: initial burst followed by sustained release
2	Release kinetics	Follows Higuchi and Korsmeyer-Peppas models
3	Cumulative drug release (%)	80–95% over 24 hours in optimized nanogel formulations
4	Permeation through skin	Enhanced permeation compared to conventional gels (2–3× improvement)
5	Retention in skin layers	Higher epidermal and dermal retention in nanogels
6	Skin irritation index	Significantly lower in nanogels vs. traditional Tazarotene gels
7	Flux rate (µg/cm²/h)	Increased flux rate observed in nanogel formulations
8	Spreadability	Improved spreadability due to softer, flexible nanostructure
9	Viscosity influence	Medium viscosity found optimal for sustained release and application
10	Zeta potential effect	Stable formulations with zeta potential values between -20 to -35 mV
11	Drug loading and entrapment efficiency	High entrapment efficiency (up to 85%) with suitable polymers
12	Comparative efficacy	Nanogels showed superior clinical efficacy in psoriasis and acne models

6. Therapeutic Advantages of Nanogel-Based Tazarotene

6.1 Enhanced Skin Penetration and Bioavailability

The high surface area-to-volume ratio and nanoscale size of nanogels greatly improve the skin penetration of Tazarotene in formulations based on these materials. These characteristics make it easier for nanogels to pass through the stratum corneum than for regular gels to do so. Plus, the hydrophilic matrix of these cells allows drugs to diffuse deeper into the dermal and epidermal layers, where they are more effective. With this method of targeted delivery, Tazarotene is more bioavailable locally, meaning it reaches its therapeutic peak at the site of action with less systemic exposure [29].

6.2 Reduced Skin Irritation and Better Retention

Common side effects of traditional Tazarotene formulations include reddening, dryness, and irritation of the skin. Nanogels' biocompatible and frequently biodegradable polymeric structure works as a buffer, reducing the likelihood of direct contact between the retinoid and delicate skin layers. An improvement in patient tolerability and a decrease in inflammatory reactions are the outcomes of this. Additionally, nanogels' sticky properties lengthen the skin's residence time, guaranteeing extended contact and improved drug retention in the targeted tissue [30].

6.3 Improved Patient Compliance and Targeted Delivery

Nanogel formulations are a good fit for dermatological patients because they provide sustained release, improved tolerability, and cosmetic appeal (non-greasy, clear texture). Treatment adherence improves as a result of the reduced application frequency and simplicity of application. Additionally, nanogels can be designed to respond to stimuli, allowing for targeted delivery to address particular skin problems. This could include pH- or temperature-sensitive release, for example. All things considered, Tazarotene based on nanogels is a promising new direction for retinoid treatment [31].

7. Challenges and Regulatory Perspectives

7.1 Stability and Shelf-Life Issues

Despite the therapeutic benefits, nanogels loaded with tazarotene encounter difficulties in terms of chemical and physical stability. It is unclear whether adding tazarotene to nanogels will entirely mitigate its sensitivity to light and oxidative destruction [32]. A decrease in entrapment efficiency, a shift in particle size, or phase separation might result from structural changes that nanogel matrices experience over time. A significant problem in medication formulation is maintaining the drug's bioactivity and release profile over an extended period of time while keeping it stable for storage [33].

7.2 Scale-Up and Manufacturing Concerns

A number of complicated obstacles must be overcome in order to bring nanogel compositions developed in the lab to a commercial manufacturing level. Achieving consistent medication loading, rheological characteristics, and particle size distribution during large-scale manufacture calls for repeatable and strong process control. Topical products have specific sterility and packaging requirements that can drive up production costs, in addition to the high cost of specialised polymers and equipment. Achieving commercial success requires optimising cost-efficiency without sacrificing quality [34].

7.3 Regulatory Framework for Nanogel Formulations

Drug delivery systems based on nanogels are still in the process of navigating the regulatory landscape. The one-of-a-kind characteristics and actions of nanosystems are not adequately addressed by conventional pharmacological standards [35]. When it comes to new excipients or delivery systems, regulatory bodies like the FDA and EMA need a mountain of data on physicochemical characterisation, safety, effectiveness, and toxicity. One obstacle to gaining regulatory approval for nanogels is the absence of standardised evaluation methodologies. Therefore, developers should think about

nanotoxicology and biodistribution studies as part of their product development process and communicate openly and early with regulatory agencies [36].

CONCLUSION

Tazarotene formulations based on nanogel have provided a game-changing method for retinoid drug delivery, which has altered the field of dermatological medicine. In comparison to traditional gels, these smart solutions are superior at overcoming important drawbacks such as skin irritation and poor stability through improved skin penetration, increased bioavailability, and provided prolonged, controlled release. Reducing systemic exposure and increasing therapeutic efficacy, the ability to specifically target the skin's deeper layers guarantees that Tazarotene functions where it is required most. Improving the therapeutic potential of Tazarotene and paving the way for a new age of dermatological therapies, nanogels effortlessly combine personalised medicine with cutting-edge nanotechnology.

Nanogels' novel characteristics provide obvious answers to persistent problems, such as formulation stability, increasing manufacturing volume, and understanding and complying with complicated regulatory environments. Tazarotene, a nanogel, has tremendous promise as an anti-aging and hyperpigmentation treatment, as well as a foundational component in skincare regimens for psoriasis and acne. Wearable biosensors that provide real-time monitoring in conjunction with AI-driven medication delivery systems has the potential to greatly enhance the personalisation and refinement of treatment, leading to unprecedented levels of precision and adaptability, as research progresses. Looking ahead, the key to a brighter future for Tazarotene therapy is not only removing the obstacles that stand in the way, but also developing a model that is adaptable to each patient's unique requirements. This will usher in a more intelligent and long-lasting strategy for skin health.

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CONFLICT OF INTEREST: Nil

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