REVIEW ARTICLE

Revolutionizing Dermatology with Precision Delivery of Tazarotene *via* Nanogel Systems

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ABSTRACT

The field of dermatology is being revolutionized with the introduction of precision delivery strategies, especially nanogels, which are improving the therapeutic potential of dermatological interventions. The present review has been compiled to elaborate on the remarkable potential of nanogel systems in targeting tazarotene, a retinoid that is deeply and widely utilized for treating several skin ailments such as acne, psoriasis, and photoaging. Given their outstanding priority, nano gels have attracted significant attention due to their distinct extent characteristics, including high biocompatibility, governed discharge properties as well and fast skin penetration contributed to improving formulation contrast of the traditional method. In this review, we summarize the various mechanisms of how nanogels enhance tazarotene solubility, stability and bioavailability, finally achieving better therapeutic effects with lower side effects. The article also delves into the latest nanogel manufacturing methods and what they mean for potential dermatologic treatments of the future. Leveraging the power of nanogel-based delivery routes ensures more efficient, targeted treatments; these innovative nano-delivery vehicles will enable a revolution in dermatological practice.

Keywords: Nanogel systems, Tazarotene delivery, Precision dermatology, Controlled release, Skin penetration enhancement.

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INTRODUCTION

In the past few decades, knowledge of skin physiology and pathology has led to dramatic changes in dermatological treatments.[1] Traditional methods include using topical formulations, oral usage of drugs and phototherapy to treat a variety of skin conditions. However, the conventional therapies used to date have repeatedly confronted problems with subtherapeutic drug concentrations at bound sites, systemic adverse effects, and inconsistent patient compliance.[2] In this regard, the demand for better approaches to therapy and the development of ingenious delivery systems that would improve therapeutic effects but reduce complications were also examined.[3]

In recent years, precision delivery systems have offered a possible alternative to the issue. Moreover, such systems are developed to administer the drug at a site of action in order to increase therapeutic efficacy and minimize systemic exposure.[4] Precision delivery systems provide a considerable advantage over conventional techniques by successfully ensuring the controlled, sustained release of an active pharmaceutical ingredient (API). Advanced delivery systems are very beneficial in dermatology due to the barrier function of the skin that generally yields difficulty when attempting drug penetration, as mentioned above. cmSystem was employed in this context too.[5]

Tazarotene is a representative third-generation retinoid that has been utilized in dermatology for the treatment of acne, psoriasis and photoaging. Due to its effectiveness in regulating cellular differentiation, proliferation and inflammation, it has become a key component of dermatological therapy. Despite these benefits, the clinical use of tazarotene is limited by its skin-irritating effect and requirements for dosages(nonatomice thelessользов)). An endeavor for future research is to improve the delivery of tazarotene and, at the same time, decrease its side effects.[6]

The above study indicates that nanogel systems are an effective and promising approach in drug delivery, especially for dermatological purposes.[7] Nanogels are 3D nanosized networks that can entrap active agents and release them in a controlled manner. Given their unique characteristics, such as

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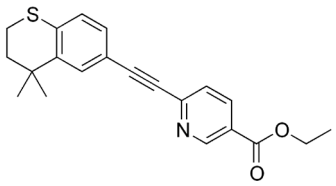

Figure 1: Structure of tazarotene

high biocompatibility, tunable mechanical strength and great skin penetration, they are appropriate carriers for tazarotene. This result suggested that the use of the nanogel technology, it is expected to solve tazarotene poor solubility and stability in water with a view to achieving sufficient bioavailability. [8]

This review will address the breakthrough that nanogel platforms have for dermatological tazarotene delivery. Herein, we will address how nanogels work towards improving the bioavailability of drug molecules, the methods used to manufacture them and lastly, deliberating on clinical applications. In this review, we provide an exhaustive analysis of the current landscape and the potential nanogel-based precision delivery systems that will revolutionize dermatological therapy by rendering them more efficacious and convenient for patients. [9]

Tazarotene: A Potent Dermatological Agent

Chemical structure and properties

Ethyl 6-[2-(4,4-dimethylthiochroman-6-yl)ethynyl]nicotinate is a synthetic third-generation polyaromatic Tazarotene retinoid chemically. The chemical structure consists of an aromatic ring in which naphthalene substituted a second phenyl. Meanwhile, the acetylenic bond provides it the potent activity and selectivity for its retinoic acid receptors (RARs). Tazarotene is a prodrug that undergoes rapid de-esterification to its active form, tazarotenic acid, upon topical application. The active form shows high binding affinity with its receptors, such as RAR-β and then to RAR-γ, which is more specifically expressed in the skin.[10]

Mechanism of action

Tazarotene exerts its therapeutic effects using a clear and specific mechanism of action based on retinoic acid receptors: [11]

- *Gene regulation*

Activation by tazarotenic acid of RARs in the nucleus regulates gene transcription through binding to retinoic acid response elements in DNA promoters. This process controls different cell functions which are importantly required for skin health. [12]

- *Cellular differentiation*

By inducing terminal differentiation of keratinocytes, tazarotene helps in normalizing the epidermal turnover. Hence, this is especially useful wherever there is abnormal keratinocyte hyperproliferation, like psoriasis. [13]

- *Proliferation inhibition*

Tazarotene inhibits the proliferation of keratinocytes, which in turn decreases the thickness of psoriatic plaques.[14]

- *Anti-inflammatory effects*

Tazarotene also modulates and inhibits the expression of several inflammatory cytokines like IL-6, IL-8, TNF-α, etc, in the skin, causing a decrease in inflammation and immune response. [15]

Clinical applications in acne, psoriasis, and photoaging

Dermatologic use of Tazarotene - In dermatology, tazarotene is frequently prescribed for the treatment of:

- *Acne*

Tazarotene Treatment of comedonal as well as inflammatory acne lesions. Our best evidence comes from studies showing that tazarotene 0.1% gel treats an important amount of acne lesions better than placebo and other treatments after just 4 weeks of treatment.[16]

- *Psoriasis*

Of the cutaneous diseases, clinical trials have shown the efficacy of tazarotene on psoriatic plaques. Tazarotene 0.05 and 0.1% creams applied once daily are both safe and effective with significant reductions in plaque elevation, scaling, and erythema. Data is lacking in pustular psoriasis. [17]

- *Photoaging*

Tazarotene results in an improvement in the visible signs of photoaging, including fine wrinkles. Mottled hyper-pigmentation and skin roughness a 24-week study defined meaningful changes in photodamage scores from baseline with tazarotene 0.1% cream.[18]

Drawbacks of traditional tazarotene administration

Though effective, tazarotene use in clinical practice is severely limited by several obstacles:

- *Skin irritation*

Tazarotene is associated with a high incidence of skin irritation manifested by erythema, dryness, desquamation and stinging. Patient compliance and discontinuation of therapy are most likely occurred due to these side effects. [19]

- *Photosensitivity*

The use of tazarotene increases the sensitivity of the skin to UV radiation, so it is necessary to apply sunscreens and take measures for photosensitization. [20]

- *Stability and solubility*

Due to chemical degradation and poor solubility in water, Tazarotene lacks stability and bioavailability, leading to reduced therapeutic efficacy. [21]

- *Controlled release*

Standard topical formulations are unable to facilitate an adequately controlled and sustained release of tazarotene, resulting in low drug concentrations at inappropriate times and intermittent erratic therapeutic effects. [22]

Nanogel Systems: An Overview

Nanogels are nanoscopic 3D constructs made of hydrophilic polymers crosslinked by a physical or chemical network.

These structures can enclose active ingredients (APIs) in their network that may provide a controlled setting for the delivery of drugs. The size of nanogels typically falls between 20 to 200 nm, thus perfect for applications demanding deep tissue distribution or skin application improvement. [23]

Types of Nanogels

Polymeric nanogels

Prepared through synthetic polymers, i.e., polyethylene glycol, polyacrylamide, etc, or natural such as chitosan and alginate. The nano gels can be tailor-made for different drug release profiles and biocompatibility. [24]

Hydrogel nanogels

High water content and are similar to a gel, thus they can be applied topically or transdermally. [25]

Responsive nanogels

Designed to respond toward specific stimuli, including pH, temperature and enzymatic emission, for providing better control over drug release at the targeted site. [26]

Multifunctional nanogels

These have been developed with the ability to perform various functions simultaneously, including targeting of specific cells or tissues, image contrast and drug deliverance. [27]

Physicochemical Properties

Nanogels present an array of physicochemical properties which contribute to their importance for drug delivery. Nanogels possess:

Size and surface area

The small size (20–200 nm) as well as high surface area, provides efficient drug loading capacity, which can penetrate deep tissue. The large surface area to volume ratio enhances the interaction with biological tissues. [28]

Porosity

The high porosity of nanogels enables the encapsulation of a large amount of drug, making it have greater load capacity than other delivery systems. [29]

Biocompatibility

Nanogels, when prepared from biocompatible materials that are biodegradable due to lesser toxicity risk and reduced possibility of adverse effects, become safe for long-term use. [30]

Swelling behavior

Nanogels could swell and de-swell through the environmental or stimuli-responsive mechanisms such as pH, and temperature, so that could provide well-controlled drug release.[31]

Surface functionalization

Nanogels may also be functionalized on their surface with ligands, antibodies, or other targeting moieties, which would improve the specificity of drug delivery to a certain cell type or tissue and enhance efficacy while reducing side effects. [32]

Benefits of Using Nanogels in Drug Delivery

Considering that nanogels show several advantages over conventional drug delivery systems, these offer great potential in targeted and controlled-release chemical applications:

Enhanced drug stability

The use of nanogels protects the drugs included in them from degradation by environmental factors, such as light or heat and other molecules like enzymes. [33]

Improved solubility

The use of nanogel enhances the drug delivery efficacy of nonpolar drugs, allowing previous hydrophobics to be introduced into aqueous environments and increasing available blood levels.[34]

Controlled release

Preparation of nanogels allows to control and sustains the drug delivery, leading to an extended therapeutic effect at a minimum frequency of dosing.[35]

Targeted delivery

Nanogels can be functionalized to specifically target distinct cells or tissue which results in maximizing the action of the drug at the particular tumor and minimizing the destruction of healthy tissues due to side effects. [36]

Reduced side effects

Since nanogel can deliver the drug at the desired site and restrict systemic exposure, it helps reduce the occurrence of side effects.[37]

Increased patient compliance

That's because, by lowering the frequency of dosing and minimizing side effects, decreased patient compliance was less likely to occur. [38]

Comparison with Other Delivery Systems

Nanogels provide many unique advantages compared to various other drug delivery systems, liposomes, microemulsions and conventional hydrogels.[39] The differences are summarized in the table below:

Biocompatibility and safety

Both Nanogels and traditional hydrogels have specific biocompatibility that can reduce their toxicity, which is very important due to the materials' safe for human beings. Hence, due to the above properties nanogels are favorable in dermatological and transdermal therapy. [41]

Controlled release

It provides better control over drug release than used liposomes and microemulsions. The drug released is known to maintain a continuous therapeutic effect, which eliminates the possibility of repeated administration. [42]

Skin penetration

The nanoscale size and increased permeability of nanogels allow increased skin penetration compared to larger particles

Table 1: Comparison of nanogels with other drug delivery systems[40]

Delivery system	*Biocompatibility*	*Controlled release*	*Skin penetration*	*Stability*	*Drug loading capacity*	*Ease of preparation*	*Scalability*	*Cost*
Nanogels	High	Excellent	Enhanced	High	High	Moderate to Complex	Moderate	Moderate to High
Liposomes	Moderate	Good	Moderate	Moderate	Moderate	Moderate to Complex	Low to Moderate	High
Microemulsions	Moderate	Good	Moderate	Moderate	Moderate	Moderate	High	Moderate
Traditional hydrogels	High	Good	Low	High	Moderate	Simple	High	Low

in traditional hydrogels. Information, this makes the nanogels more suitable for topical and transdermal drug delivery. [43]

Stability

Nanogels provide a highly stable milieu for the drugs enclosed in them, which creates no chance of any chemical degrading methods occurring inside the nanosensor particles and also promises that there will be continuous drug release. [44]

Drug loading capacity

The nanogels may load even the comparatively larger quantity of drugs as a result of their porous structure and greater surface area exposure, allowing for more significant therapeutic activity compared to other delivery systems. [45]

Mechanisms of Nanogel-Enhanced Delivery

The mechanisms underlying the enhanced delivery of various therapeutic agents by nanogel systems, including those incorporated into dermatological formulations, revolve around several factors:

Solubility and Stability Improvement

Nanogels are also capable of encapsulating hydrophobic drugs inside their hydrophilic matrix, which can enhance these drugs' solubility in aqueous media. This envelope also isolates drugs from loss of activity, oxidation damage and enzymatic degradation, which in turn allow them to be more stable and have a longer life. [46]

Controlled and Sustained Release Profiles

Nanogels have crosslinked structures that can provide control over the drug release kinetics. Modulation of polymer composition, crosslinking density and environmental triggers have enabled nanogels with controlled release profiles varying from sustained to pulsatile or triggered, which can maintain therapeutic dose for an extended period. [47]

Enhanced Skin Penetration and Retention

The nanoscale dimensions of nanogels allow them to more easily enter the stratum corneum, which is the top layer of skin. The flexibility and deformability of nanogels allow them to move around in the intercellular spaces and follicular pores, which is very useful for deeper penetration into both the epidermis and dermis. Once inside the skin, nanogels can bind to the tissue leading to retention of drugs in it and enhancing concentration gradients. [48]

Biocompatibility and Safety

Nanogels are usually made of safe biocompatible polymers like polyethylene glycol, polyvinyl alcohol, or a natural base-like combination of polysaccharides, which reduce the exposure to possible immunogenicity, cytotoxicity and inflammation. They have a soft and flexible structure so that they do not there is less chance of tissue damage or irritation when used to the skin, making them well tolerated by the skin and effective for long-term treatment.[49]

Figure 2 demonstrates the mechanism through which nanogel systems help to penetrate skin.[50] It shows the interaction of nanogels with corneum lucidium and then penetration through intercellular, hair follicular pores and hair shines. The nanogels release the encapsulated drug payload within layers of skin to exert its pharmacological action. Furthermore, the aforementioned image brings to light whether various factors, including prodrug configuration and pH influence their interaction with the skin barrier and, therefore, drug delivery behavior that is vital for effective treatment. Finally, it may be used to show that other factors including nanogel size, surface charge, and surface modification, govern this interaction.[51]

Fabrication Techniques of Nanogels

Different fabrication methods synthesize nanogels and approaches that are tailored to desired properties and functions for drug delivery applications as in the case of tazarotene encapsulated nanogels.[52] There are a number of techniques used in the making of nanogels. Some of them are as follows

Synthesis Methods

Emulsion polymerization

This makes use of monomers in an emulsified systemic phase featuring surfactants and mutual stabilizers. Then, the emulsion droplets act as a template for polymerizing nanogels within them up to around one micron in diameter considerably smaller than aggregates achievable by other means. Emulsion polymerization enables precise size and morphological control, making it widely used for producing hydrophobic nanogels. [53]

Click chemistry

Click chemistry or examples such as azide-alkyne cycloaddition, is used to make nanogels that have high crosslinking density control and functionalization. The high efficiency, selectivity

and biocompatibility of click chemistry make it suitable for preparing multiple-function nanogels equipped with various targeting groups or responsive properties. [54]

Functionalization and Surface Modification

Nanogels can be functionalized and surface-modified to enhance stability, biocompatibility or targeting specificity:

Crosslinker modification

Both the type and concentration of crosslinker can be altered, which in turn enables full control over the mechanical strength, swelling behavior and responsiveness of nanogels. [55]

Surface PEGylation

Conjugation of polyethylene glycol (PEG) chains to the surface of nanogels with improved stability, reduced nonspecific binding to biomacromolecules and longer circulation time in vivo by preventing immune recognition and reto-endothelial system (RES) uptake. [56]

Encapsulation Techniques for Tazarotene

Tazarotene encapsulation in nanogels can be done with any of the following techniques for better loading and extended-release:

Co-dissolution and crosslinking

Drug is dissolved along with monomer solution before commencing the polymerization process, leading to entrapment of Tazarotene within the nanogel network during nanoparticle formation. After crosslinking, tazarotene gets encapsulated within the nanogel matrix. [57]

Post-loading encapsulation

In this type, as first, the nanogels were synthesized and then tazarotene was loaded in these nanogels after synthesis through mechanisms like diffusion, adsorption onto pre-formed NGLs, or physical entrapment within presynthesized NGLs. This technique enabled accurate control over drug loading and release kinetics. [58]

Scale-Up and Manufacturing Considerations

Upscaling nanogels production for commercial manufacturing is a concern and numerous process parameters, reproducibility/ design of the stored nanoparticles formulation into final drug product and economics will need to be addressed.

Process optimization

The parameters of monomer concentration, reaction temperature, agitation speed, or solvent composition must be optimized to maintain the appropriate particle size and morphology as well as drug loading within large-scale batches. [59]

Quality control

Strong procedures for quality control will be necessary to achieve consistency between batches and ensure the safety, effectiveness and compliance with regulatory standards of each final product. [60]

Table 2: Common nanogel fabrication techniques[62]

Fabrication technique	*Description*
Emulsion polymerization	Monomers dispersed in aqueous phase and polymerized within emulsion droplets
Click chemistry	Reaction between functional groups to form crosslinked nanogels
Inverse miniemulsion polymerization	Monomers dispersed in organic solvent with surfactants, leading to nanogel formation
Ionic gelation	Gelation of polyelectrolyte polymers in the presence of multivalent ions
Co-Dissolution and crosslinking	Tazarotene dissolved in monomer solution before polymerization
Post-loading encapsulation	Tazarotene loaded into pre-formed nanogels after synthesis

Cost-Efficiency

Choosing cost-effective raw materials, scaling up manufacturing, and using low-cost purification and sterilization methods represent the key to reducing costs while ensuring scalability. [61]

Clinical Implications and Outcomes

The nanogel mediated tazarotene delivery also promises a great potential to enhance the clinical performance in dermatological therapy so far.[63] Key clinical implications and outcomes of this innovative approach:

Preclinical and Clinical Studies on Nanogel-Based Tazarotene Delivery

There have been multiple preclinical and clinical investigations exploring the efficiency and toxicity of nanogel-mediated tazarotene delivery systems:

Preclinical studies

Animals studies have shown that nanogel formulations are more effective than conventional tazarotene drug delivery to the skin, as formulated. Studies have pointed out that nanogels exhibit better skin penetration drug release for a longer period and thereby improve the efficacy of the therapy. [64]

Clinical trials

Nanogel-based tazarotene delivery systems have undergone numerous clinical trials for the treatment of acne, psoriasis and photoaging, which have yielded fruitful results. These studies have demonstrated reductions in lesion counts, skin texture and tone improvement, along with greater patient satisfaction when compared to standard therapies. [65]

Efficacy Comparisons with Conventional Formulations

Comparative studies reveal that tazarotene conveyed *via* nanogels offers considerable advantages over conventional formulations:

Superior efficacy

It was discovered that nanogel formulations produced reductions in acne lesion counts that were significantly greater than those achieved by conventional creams, plaques of psoriasis improved to a greater extent, and photoaging signs cleared more quickly than their predecessors. [66]

Faster Onset of Action

Nanogels may have the ability to act more rapidly with a shorter period of time passing before patients begin to see visible improvements in their skin condition than was required by traditional formulations. [67]

Safety and Tolerability Profiles

Nanogel-based delivery systems of tazarotene demonstrate favorable safety and tolerability profiles:

Reduced irritation

Nanogels are associated with less skin irritation than traditional formulations, including erythema, dryness and shedding. Release controlled by the device-based dispersed tazarotene results in a minimization of irritation irritation treatment which preserves its effectiveness. This is why the irritation of the skin can be reduced to a minimum and yet the medicine's effect will be undiminished.[68]

Decreased photosensitivity

Nanogel formulations may lower the chance of photosensitivity reactions associated with tazarotene use, drawing patient compliance and producing satisfaction. [69]

Patient Adherence and Satisfaction

Reported patient outcomes demonstrate notable adherence and satisfaction when using novel nanogel-based tazarotene delivery:

Improved compliance

Enhanced compliance stems from reduced side effects and better tolerability afforded by the nanogel formulation. This improved adherence leads to more favorable long-term management and control of disease.[70]

Enhanced satisfaction

The nanogel treatment prompts greater expression of satisfaction from those using it. Patients frequently cite enhancements in appearance and quality of skin texture coupled with an overall elevated quality of life in comparison to traditional options.[71,72]

Future Perspectives and Challenges

Nanogel technology could thus represent a paradigm-shifting trajectory in the growing arena of dermatological therapeutics capable of delivering therapeutic agents, including tazarotene, precisely and locally. Recent trends show that the future will include a constant growth in multifunctional and biodegradable nanogels, leading to personalized medication according to the patient's conditions. For nanogels to reach their full potential in dermatology, further regulatory and manufacturing hurdles must be addressed. Such challenges involve the development of standardized synthesis protocols and scale-up issues. Future avenues of research should take advantage of the potential capability for fabrication and varied properties of biomimetic and smart nanogel while conducting planned clinical trials that will answer questions about safety, efficacy and long-term results in wide-ranging populations.

The future of nanogel technology seems promising, and when it comes to personalized dermatological treatments, this is even more exciting. Tailored nanogels have enabled precisely dosed therapeutic payloads that minimize systemic side effects by means of tailored formulations. However, unlocking this potential requires navigating complex regulations and developing scalable manufacturing processes. For future research directions, one can shift toward blending nanogel or developing biomimetic and smart nanogels to improve biocompatibility muscle targeting ability with improved therapeutic efficacy. Furthermore, appropriately devised clinical trials are expected to provide compelling evidence for the safety and efficacy of nanogel-assisted dermatological interventions, abridging a new dimension for personalized skincare treatment according to patient wants and demands.

CONCLUSION

In conclusion, the application of nanogel systems to achieve an on-site delivery system for tazarotene in dermatology is a considerable breakthrough. By the fabrication and functionalization method, nanogels presented that solubility is improved, release profile controlled and ability for better skin penetration of tazarotene as compared to the counterpart, which resulting enhance clinical efficacy. These comparative studies clearly indicate the efficiency, safety, and potential of nanogel-based formulations as a revolution in dermatological therapy.

This review further ascertains that nanogel systems are most promising for future dermatology. Novel nanotechnology trends will enable us to develop personalized treatments based on what each unique patient requires. "Nanogels are a step to provide targeted delivery of therapeutics and minimize systemic side-effects and the use of medicine." In addition to that, their dynamic nature presents room for innovation in terms of disease management and skincare routine.

In conclusion, precision delivery systems such as nanogel technology signal a new era for dermatological therapeutics. Not only do these nanoparticles have benefits to conventional dermatological treatment, but they also allow targeted solutions to a wide range of skin conditions and patient bases. With further research and expanded clinical indications, the potential of precision delivery systems remains endless in dermatology practice, too, which may lead to favorable patient outcomes with improved quality of life.

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