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Next-Generation Nanoemulsion Gels: Bridging Nanotechnology and Herbal Medicine

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Abstract

These gels work particularly well for applying medication on the skin and through it, as they help dissolve drugs better, allow them to penetrate the skin more effectively, and make it easier for patients to use them. Nanoemulsions are stable mixtures made up of oil, water, surfactants, and co-surfactants, with small droplets that usually measure between 20 and 200 nanometers. When these Nanoemulsions are mixed into a gel using ingredients like Carbopol 940, HPMC, or xanthan gum, the resulting Nanoemulgel becomes thicker, stays on the skin longer, and feels less greasy. These qualities lead to better treatment results. The tiny size of the droplets creates a wide surface area, allowing for improved contact with the skin and helping medicines to pass through the outer layer of the skin more easily. Both water-loving and fat-loving medications can be successfully mixed depending on how well they dissolve. The inclusion of surfactants and co-surfactants helps to break down the skin's fat layers, making it easier for substances to penetrate. Nanoemulgels have shown good effectiveness in delivering medicines for inflammation, fungal infections, bacterial infections, acne, and cancer treatment, among other uses. Physicochemical analysis, which involves checking things like pH, thickness, how easily a product spreads, how consistent the drug amount is, and how it releases in laboratory tests, is important for assessing the quality of a formulation. Franz diffusion cells are often utilized for studying how substances are released, and stability tests conducted according to ICH guidelines help confirm that the product remains effective over time.

Because of their beneficial traits and versatility, Nanoemulsion gels are becoming a popular choice for both targeted and overall drug delivery, addressing the challenges faced by traditional topical products.

Keywords: Herbal Nanoemulgel, Topical Drug Delivery, Skin Penetration Enhancement, Bioavailability Enhancement, Controlled Drug Release.

Introduction

In the past few decades, the field of nanotechnology has greatly changed different areas, including healthcare, beauty products, and medicine. One of the many products created using nanotechnology is Nano emulsions, which have gained a lot of attention because of their special physical and chemical features, like tiny droplet size, larger surface area, and better ability to dissolve drugs that do not mix well with water. A Nanoemulsion gel is a creative mix that combines Nanoemulsions within a gel structure, giving two main benefits: better efficiency in delivering drugs and easier application for patients. This new way to deliver medication has created new possibilities for applying treatments on the skin, through the skin, and even throughout the body. A Nano emulsion is described as a stable mixture of two liquids that usually do not mix well, like oil and water, which is kept stable by a suitable surfactant or co-surfactant, with droplet sizes that usually range from 20 to 200 nanometers[1]. These mixtures can be either oil in water or water in oil, depending on what is on the outside and the type of medicine that needs to be delivered. Because of their tiny size and strong surface energy, Nano emulsions can improve how drugs pass through biological barriers, raise how much of the drug is available in the body, and provide delivery that is controlled or directed[2].However, even with these encouraging qualities, traditional liquid Nano emulsions face some problems, including low thickness, inadequate staying power at the application area (particularly for skin and transdermal uses), and possible weakness under physical strain or over extended storage time. To address these issues, scientists have created Nanoemulsion gels, which are made by blending the Nanoemulsion into a gel structure using thickening substances such as carbomers, xanthan gum, or hydroxypropyl methylcellulose (HPMC)[3]. This mix gives nice flow characteristics and leads to better application uniformity, easier spreading, and longer-lasting contact on the skin or mucous membranes. From a medicine viewpoint, Nano emulsion gels have shown great promise for delivering different types of treatment substances, such as pain relievers, antifungal medications, antimicrobial agents, anti-inflammatory medicines, and cancer treatments. The improved penetration and absorption offered by the tiny droplets, along with the sticking and protective qualities of the gel, help ensure that the medicine goes deeper and stays in the tissues longer[4].For instance, gels made with Nano emulsion that contain diclofenac have demonstrated better ability to reduce inflammation compared to standard products, as they allow the medicine to penetrate the skin more effectively and release the drug over a longer period[5]. In the beauty industry, Nanoemulsion gels are being used more and more to deliver active substances such as vitamins, antioxidants, and moisturizing agents. The tiny droplets allow these ingredients to go deeper into the skin, improving how well the cosmetic products work. Additionally, the gel structure improves the feel of the products, offering a smooth and calming effect when applied, which is very important for products aimed at consumers[6].Despite their many benefits, Nanoemulsion gels also face some difficulties. A significant problem is their thermodynamic instability, which can result in phase separation, merging of droplets, or Ostwald ripening as time goes by. Although Nano emulsions show kinetic stability, they do not achieve true thermodynamic balance. It is crucial to carefully choose surfactants, optimize droplet size, and adjust pH to maintain stability. Additionally, the long-term safety and possible harmful effects of tiny particles, particularly with regular use, are still subjects of ongoing research [7].

Characterization of Nanoemulsion Gels

Droplet size and the polydispersity index (PDI), assessed through dynamic light scattering (DLS), are important factors that indicate how consistent and stable nanoparticles are. The best Nano emulsion mixes usually show droplet sizes between 20 and 200 nm, which helps with better absorption by cells and longer-lasting presence in

the body. A PDI lower than 0. 3 suggests that the particles are uniform, which reduces clumping and improves consistency and prolonged storage life. These features are widely acknowledged standards in the study of drug delivery and Nano formulation[8,9,10].Zeta potential shows the charge on the surface of nanoparticles and is an important measure of how well they stay mixed. When the values reach ±30 mV or more, they create significant repulsion forces, which help stop the particles from clumping together and ensure they remain mixed over time. This standard is commonly used in Nanomedicine and colloidal science for creating stable Nano formulations that work reliably. The detailed review by Honary and Zahir explains that nanoparticles with zeta potential greater than ±30 mV are usually stable in water-based settings[11,12]. Rheological testing looks at how topical gels move when pressure is applied, showing that they become thinner (pseudoplastic) when stirred. This change decreases thickness when the gel is used, making it easier to spread, while it returns to its original thickness afterward, helping it stay on the skin better. These characteristics are important for the effective use of topical products, making sure they can be applied evenly and stay in place for a longer time at the treatment area[13]. Topical products need to have a pH level between 5. 0 and 6. 5 to align with how skin works and to avoid causing irritation. Testing how easily the product spreads is important to check how simple it is to apply, to guarantee even distribution of the medication, and to improve comfort and adherence for the user, all of which help make the product work better[14]. The consistency of drug content is usually checked with methods like UV spectroscopy or high-performance liquid chromatography (HPLC) to make sure dosages are precise and uniform. Tests for how quickly a drug is released in a lab, often done with Franz diffusion cells, measure the release speed and assist in forecasting how well topical products will work[15]. Stability testing at various temperature and moisture levels is important to detect alterations in look, texture, acidity, or separation of components. These assessments confirm that the product keeps its quality, effectiveness, and longevity while stored, meeting the legal requirements for pharmaceutical product creation[16].

Advantages of Nanoemulsion Gel[17]

- **Enhanced Drug Solubility and Bioavailability:**

Nano emulsions boost the dissolving ability of drugs that don't mix well with water, thereby improving how well the body can use them.

- **Improved Physical and Thermodynamic Stability:**

The tiny droplets and gel structure help prevent clumping and settling, making the system more stable.

- **Superior Skin Penetration and Controlled Release:**

Nano emulsion gels can go deeper into the skin and let the medicine be released steadily over a longer period.

- **Protection of Drugs from Degradation:**

Putting drugs inside Nano emulsion droplets shields them from breaking down due to water, air, or other damaging processes.

- **Better Patient Compliance:**

A non-greasy texture, easier spreading, and better appearance make it more likely for users to like and stick with the treatment.

- **Versatile Routes of Administration:**

Nanoemulgels can be used in various ways, including applying to the skin, through the skin, and in mucous membranes.

- **Reduced Surfactant Requirement and Ease of Manufacture:**

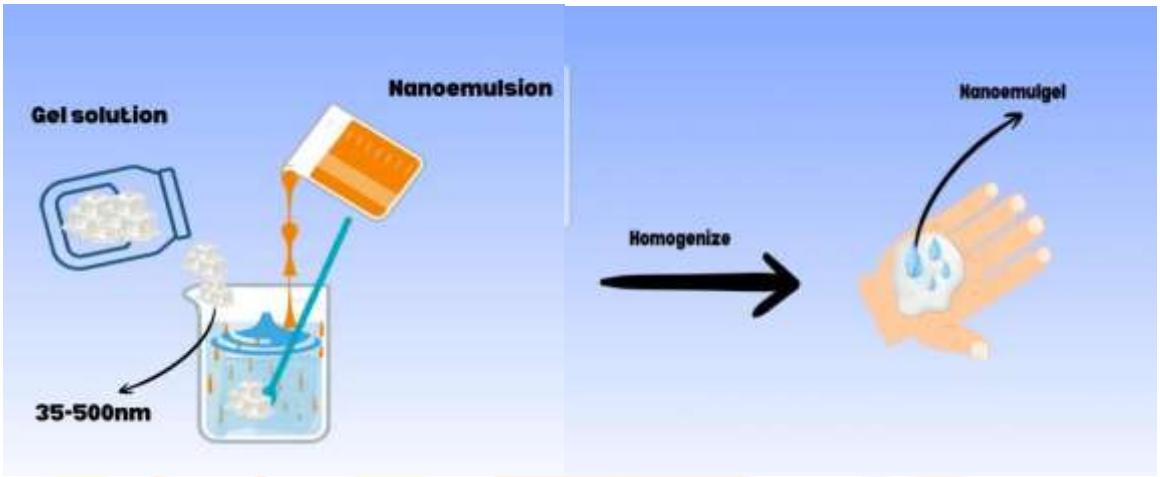
Nano emulsions need less surfactant than micro emulsions and can be made using methods that can be easily scaled up. Enhanced drug solubility and bioavailability.

Nano emulsions boost the dissolving ability of drugs that don't mix well with water, thereby improving how well the body can use them.

Disadvantage of Nanoemulsion Gel[18,19]

- ❖ Unsteadiness – Prone to separating into different layers or undergoing Ostwald ripening.
- ❖ Harmfulness – Possible danger from surfactants or Nano-sized materials.
- ❖ Production difficulties – Issues with making large amounts efficiently.
- ❖ Expense – High costs associated with machinery and other necessary materials.
- ❖ Thickness – Changes in thickness impact how well it spreads and how drugs are released.
- ❖ Keeping conditions – Vulnerable to changes in heat and moisture.

Figure 1: Mechanism of Drug Delivery Through the Skin Using Nanoemulsion Gels[20]



Nanoemulsion gels, also known as Nanoemulgels, improve the way medicine is delivered through the skin by using the tiny features of Nano emulsions along with the thick, sticky qualities of gels. This combination helps to break through the tough outer layer of the skin called the stratum corneum. The stratum corneum is made up of flat, dead skin cells trapped in a thick layer of fats, which makes it hard for drugs to get through. Nanoemulgels help to change this fatty layer by having surfactants and co-surfactants interact with the lipids between the skin cells. This process makes the lipids more fluid and rearranges them, which decreases the resistance to penetration. The very small size of the droplets, usually between 20 and 200 nanometers, ensures a large surface area that allows these droplets to closely contact the skin and helps them to enter more easily[21,22]. The oil part of the Nano emulsion serves as a storage place for fat-soluble medicines, helping them dissolve better and offering a source for gradual release. Surfactants boost absorption by lowering surface tension and making cell membranes more flexible, allowing easier drug movement. The gel structure provides additional benefits: it helps the product stay on the skin longer, improves sticking, and allows for controlled and steady drug release, which aids in consistent and lasting uptake[23].

Transdermal transport through Nanoemulgels happens in three main ways:

Intercellular (between cells): Improved absorption occurs when surfactants break apart lipid layers, which loosens the lipids found between cells and forms channels for permeation. Trans cellular (through cells): Tiny droplets move through cell membranes thanks to the smoothing effect of surfactants, which allows drug particles to flow through alternating water-loving and fat-loving areas of the skin cells. Appendageal (through skin features): Droplets can get into hair follicles, sweat glands, and other skin features, providing alternate paths that go around the thick outer skin layer. These processes are backed by laboratory and live studies. For example, it has been shown that Nano emulsion gels can wear away and disrupt the lipid structure of the outer skin layer, easing the barrier, boosting hydration, and improving occlusion, all of which lead to much better absorption through the skin. Studies using fluorescence have also indicated that compounds delivered by Nanoemulgels can settle in hair follicles and go deep into the outer skin layer, proving that appendageal routes enhance their effectiveness. A

thorough review of systems based on Nanoemulsions confirms their effectiveness for delivering substances through the skin. Such reviews highlight that Nanoemulsions and Nanoemulgels improve the solubility and availability of both water-loving and fat-loving drugs, enhance skin absorption through physical and chemical changes, and allow for controlled release without needing extra chemical enhancers[24,25].

Composition of Nanoemulsion Gels

Oil phase

The oil part of oil-in-water (O/W) Nanoemulsions is very important for mixing fat-soluble medicines and creating the part that spreads out. Typical oils like isopropyl myristate, caprylic/capric triglycerides, castor oil, and oleic acid offer moisturizing benefits and help the medicine pass through the skin better, which increases how much of the drug can be used by the body[26].

Aqueous Phase

The aqueous phase, which is typically made up of clean water or buffer mixtures, acts as the main part in oil-in-water (O/W) Nano emulsions. It provides a space for mixing water-loving medicines, helping to keep them stable and evenly spread throughout the mixture, which is essential for successful medicine delivery[27].

Surfactants

Surfactants help keep oil-in-water Nanoemulsions stable by lowering the tension at the boundary between the oil and water layers. Non-ionic surfactants like Tween 80, Span 20, and Poloxamer 188 are favored because they are gentle on the skin and have low toxicity, which makes them suitable for delivering medications through the skin and into the body[28].

Co-surfactants

Co-surfactants such as propylene glycol, ethanol, and polyethylene glycol (PEG-400) boost the stability of Nanoemulsions by making the interfacial film more flexible. This improvement helps create uniform, tiny droplets, which results in better drug solubility, stability, and increased effectiveness in delivering drugs through the skin[29].

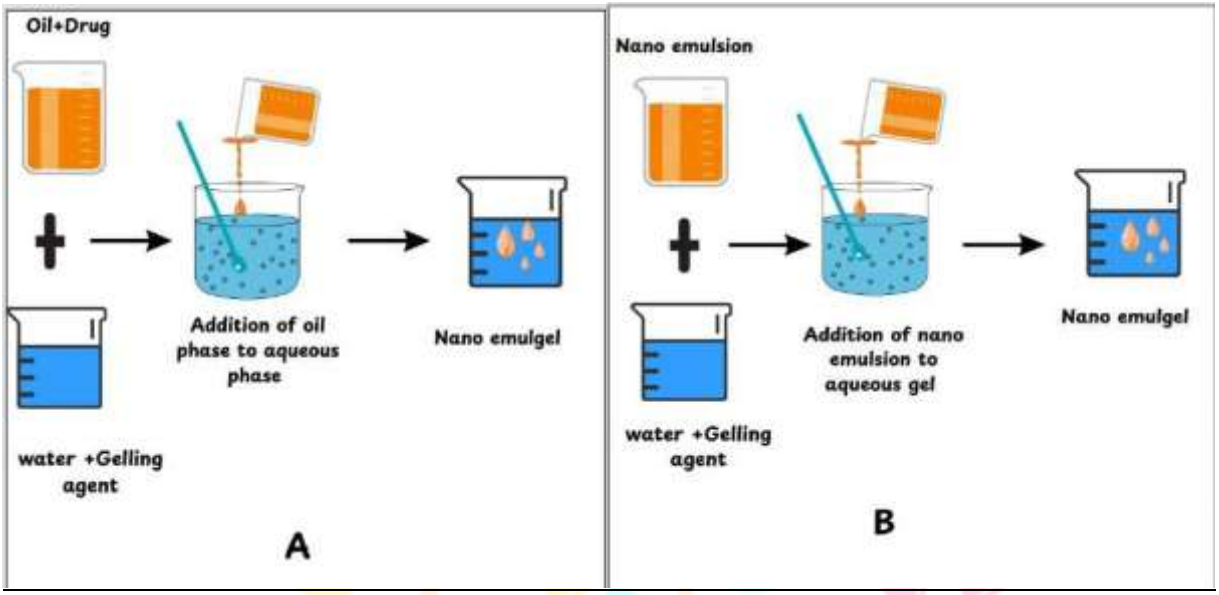
Gelling Agents

Substances such as Carbopol 940, xanthan gum, and hydroxypropyl methylcellulose (HPMC) are used to turn Nanoemulsions into gels. These gelling substances make the mixture thicker, help it stay on the skin longer, and create a nice, non-greasy feel, which improves the overall quality and makes it more acceptable for users[30].

Active Pharmaceutical Ingredient (API)

Medications, regardless of being water-loving or fat-loving, are blended into Nano emulsion gels according to how well they dissolve. These gels successfully transport drugs that do not dissolve well in water and are not easily absorbed by the body by increasing their solubility and promoting absorption through the skin, which leads to better availability in the body and improved treatment effectiveness[31].

Figure 2: **Types of Nanoemulsion Gel**[32]



Oil-in-Water (O/W) Nano emulsion Gels

In these formulations, tiny oil droplets with fat-soluble medications are mixed into a water-based solution. This Nanoemulsion is then added to a gel. O/W Nanoemulsion gels are preferred for use on the skin or for absorption through the skin because they have a light and non-oily feel and allow for better absorption into the skin[33] .

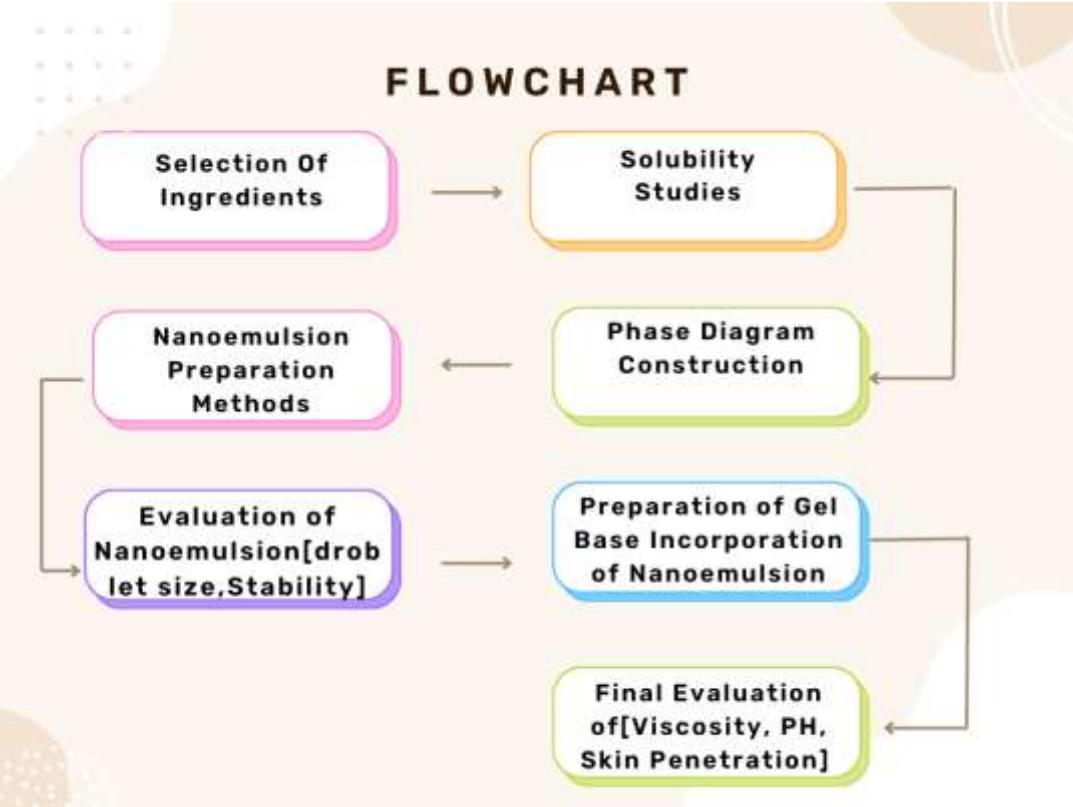
Water-in-Oil (W/O) Nano emulsion Gels

These are made up of tiny water droplets spread throughout a flowing oil layer, and then they turn into a gel. W/O Nanoemulsion gels are great for delivering water-loving medications, keeping the skin moist and creating a shield, which makes them helpful for dry or injured skin[34].

Bi-continuous Nanoemulsion Gels

These mixtures have oil and water working together, which helps dissolve both water-friendly and oil-friendly medicines. Bi-continuous gels are helpful for complicated products, particularly when it's important to load two drugs at once or improve how well they can be absorbed[35].

Figure 3: General Method of Preparation on a Nanoemulsion Gel[36,37,38,39]



Therapeutic Uses of Nanoemulsion Gels

Medications that reduce inflammation, like ibuprofen and ketoprofen, show better local benefits and fewer overall side effects when applied through skin creams made with Nano emulsions. This method helps the medicine soak into the skin more effectively, focusing on inflammation right at the source while lowering exposure to the stomach and the rest of the body[40]. Fungal treatments such as clotrimazole and ketoconazole, when made into gels or Nanoemulgels, help the medicine stay on the skin longer and target the infection better, which makes them more effective for treating fungal infections on the skin surface. These types of products enable the medicine to be released slowly and reach deeper into the skin, reducing the amount that enters the bloodstream and making it easier for patients to follow their treatment[41]. Antibacterial substances like chlorhexidine and silver nanoparticles, when added to gel products, greatly improve the healing of wounds and the prevention of infections. These gels provide long-lasting protection against germs, better stick to the skin, and work right where they are applied, making them very useful for treating infected wounds and lowering the growth of bacteria[42]. Anti-acne products like tretinoin and benzoyl peroxide, when made into tiny gel particles, help the medicine go deeper into the skin, decrease how often you need to use them, and lessen the irritation that often comes with regular products. These methods allow for steady release, better focus on the hair follicle and oil glands, and make it easier for patients to stick to their treatment[43]. Transdermal delivery of medications like propranolol and estradiol allows them to enter the bloodstream directly, skipping the liver's first-pass processing. This method enhances how much of the drug the body can use, keeps the amount of drug in the blood stable, lowers how often patients need to take the medicine, and decreases stomach-related side effects, making it ideal for extended use in treatment[44]. 5-Fluorouracil nano-gels improve the treatment of skin cancer by allowing for focused and controlled release of the medication right at the tumor locations. This specific method boosts the effectiveness of the treatment, lowers overall toxicity in the body, and lessens unwanted effects, presenting a hopeful option for effectively handling skin cancers[45] .

Table 1: **Herbal-based Nanoemulsion Gels: Types and the Application** [46,47,48,49,50,51,52]

TYPE OF NANOEMULGEL	HERBAL INGRIDIENTS	APPLICATION
Cur cumin	Cur cumin (Curcuma longa)	Anti-inflammatory, Antimicrobial.
Neem	Neem Oil (Azadirachta indica)	Antifungal, Antibacterial.
Triple Herbal	Cur cumin, Thymoquinone, Resveratrol	Psoriasis treatment.
Ginger	Ginger extract (Zingiber officinale)	Rheumatoid arthritis, Pain relief.
Myrrh Oil	Myrrh oil + Cur cumin	Anti-inflammatory.
Propolis	Propolis + Dexpanthenol	Antibacterial, Wound healing.
Cucumber	Cucumis melo var. agrestis extract	Antifungal, Enhanced skin permeability.

Herbal-Based Nanoemulsion Gels Benefits[53]

- **Enhanced Skin Penetration and Bioavailability**

Nanoemulsion gels help medicines pass through the skin better by making lipophilic herbal substances more soluble and easier to penetrate.

- **Improved Stability of Herbal Actives**

Nanoemulgels shield plant chemicals from breaking down (like due to light or oxygen), which helps them last longer.

- **Controlled and Sustained Drug Release**

These gels allow for a steady release of medication, which means users do not need to apply it as often and the treatment becomes more effective.

- **Potent Anti-inflammatory Effects**

Herbal Nanoemulgels that contain essential oils or plant extracts (such as clove and eucalyptus) have stronger anti-inflammatory benefits**.**

- **Antimicrobial and Antifungal Activities**

Mixes that include rosemary, clove, or Neem work better against germs and fungi than regular gels do.

- **Antioxidant and Anti-aging Properties**

Nano emulsion gels make antioxidants last longer and help them reach the skin, which is good for anti-aging and skin care.

- **Wound Healing Effects**

Using herbal oils that promote healing, like olive oil and St. John's wort, in Nanoemulsion gels helps the skin heal more quickly.

- **Analgesic and Anti-migraine Potential**

Chamomile nanoemulgels provide pain relief in the body and may assist with migraine treatment.

Conclusion

Nanoemulsion Gels: A New Way to Deliver Medicine Nano emulsion gels are a new and exciting method for delivering drugs, especially for applying on the skin or through it. They blend the benefits of Nanoemulsions-like better dissolving, greater ability to penetrate the skin, and controlled release of medication with the easy-to-use nature of gels. This combination provides better healing effects and makes it easier for patients to use the products. When these gels include natural ingredients like cur cumin, neem oil, ginger extract, or propolis, they take advantage of the health benefits from plants while addressing issues like poor dissolving in water and being

unstable. Their tiny droplet size, usually less than 200 nanometers, leads to improved absorption and effectiveness where it matters. Moreover, Nanoemulsion gels are not greasy, stable, and work well for long-term skin problems like infections, inflammation, psoriasis, and arthritis. In summary, herbal Nanoemulsion gels provide a natural, safe, and effective option compared to traditional skin treatments, helping to push forward eco-friendly nanotechnology in today's drug development. More studies and testing will improve their usefulness in healing.

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