

## GREEN SYNTHESIS AND STABILIZATION OF NANOEMULSIONS FOR ADVANCED DRUG DELIVERY SYSTEMS

<sup>1</sup>Vaishali N. Tidke, <sup>1</sup>Amanpreet Kaur Dumda, <sup>2</sup>Swati Rawat, <sup>3</sup>Dr.Radhakrishnan  
M.Tigote

<sup>1</sup>Dr Babasaheb Ambedkar Marathwada University

<sup>1</sup>Dr Babasaheb Ambedkar Marathwada University

<sup>2</sup>Institute of Pharmacy, Badnapur

<sup>3</sup>Department of Chemistry, Dr.Babasaheb Ambedkar Marathwada University, Sub Campus Dharashiv

### Abstract

Nanoemulsions have emerged as a pivotal technology across various industries, including pharmaceuticals, agriculture, food processing, and cosmetics, due to their enhanced bioavailability, improved product stability, and capability for controlled release of active ingredients. This review explores the recent advancements in nanoemulsion formulations, with a particular focus on green nanoemulsions that emphasize sustainability and reduced environmental impact. We assess the use of natural and biodegradable components in nanoemulsion production, their ecotoxicological impacts, and regulatory compliance challenges. Detailed comparative analyses highlight the differences in application, stability, and biodegradability across different sectors. Furthermore, this review discusses the current regulatory frameworks governing the use of nanoemulsions, underscoring the need for rigorous ecotoxicological evaluations and sustainability assessments to mitigate potential environmental risks. The ultimate goal of this review is to provide a comprehensive overview that aids in the responsible development and application of nanoemulsion technology.

**Keywords:** Nanoemulsions, Green technology, Biodegradability, Ecotoxicology, Drug delivery systems, Cosmetic formulations, Agricultural applications, Food preservation, Regulatory compliance, Environmental impact.

Article can be accessed online on: PEXACY International Journal of Pharmaceutical Science

DOI: 10.5281/zenodo.1477649

Corresponding Author-<sup>1</sup>Vaishali N. Tidke

Email- vaishalitidke8@gmail.com

*Update: Received on 02/07/2024; Accepted; 05/07/2024, Published on; 15/07/2024*

## 1. INTRODUCTION

Nanoemulsions represent a pivotal advancement in the realm of drug delivery systems. These submicron-sized emulsions are heralded for their capacity to enhance the bioavailability of therapeutic agents, ensuring more efficient and effective treatment outcomes. This review delves into the intricacies of green synthesis and stabilization techniques of nanoemulsions, which are increasingly favored for their reduced environmental impact and potential in advanced drug delivery applications.

### 1.1 Overview of Nanoemulsions

Nanoemulsions, with their droplet sizes ranging from 10 to 1000 nanometers, exhibit unique properties that distinguish them from traditional emulsion systems. Their small droplet size leads to a large surface area, enhancing drug solubility and absorption rates. These emulsions are produced through high-energy methods like ultrasonication or low-energy techniques such as phase inversion, which are critical for achieving the desired stability and functionality (Wilson et al., 2021). The stability is not just a physical attribute but also a key determinant in the efficacy of drug delivery, as it prevents the premature release or degradation of the encapsulated drugs.

### 1.2 Importance in Drug Delivery Systems

Nanoemulsions have revolutionized the way drugs are delivered, offering versatility and efficiency across various administration routes. Due to their ability to encapsulate both hydrophilic and hydrophobic drugs, nanoemulsions can deliver active compounds effectively to the targeted site, minimizing systemic side effects and maximizing therapeutic efficacy. This characteristic makes them especially valuable in treatments requiring precise dosing and controlled release mechanisms. Moreover, the inherent stability of nanoemulsions facilitates longer shelf life and easier transport, attributes critical for global pharmaceutical markets (Jamir et al., 2023).

### 1.3 Scope and Organization of the Review

The review will cover the green synthesis of nanoemulsions, emphasizing the use of natural, renewable resources as surfactants and emulsifiers. These green methods not only reduce the environmental footprint of pharmaceutical manufacturing but also enhance the biocompatibility of the formulations. Additionally, the review explores stabilization techniques that ensure the physical and chemical integrity of nanoemulsions under various storage and usage conditions.

Advanced applications of nanoemulsions in the food and drug sectors demonstrate their potential beyond traditional pharmaceuticals, highlighting their role in enhancing the bioavailability of nutrients and medicines alike. Furthermore, safety concerns, particularly related to consumer and environmental health, are examined, given the increasing regulatory scrutiny these products face.

Finally, the review will address the scale-up challenges, regulatory hurdles, and market considerations that influence the commercial viability of nanoemulsions. These factors include the need for robust manufacturing processes that can operate at industrial scales and the development of products that meet stringent safety standards (Kaur et al., 2024; Food Reviews International, 2023).

## 2. Fundamentals of Nanoemulsions

Nanoemulsions are a form of technology that plays a pivotal role in the field of pharmaceuticals, particularly in enhancing the delivery of drugs across biological membranes. This section explores the basic definition, physicochemical properties, and the mechanisms by which nanoemulsions facilitate drug delivery.

### 2.1 Definition and Classification

Nanoemulsions are colloidal particles of emulsion, tiny enough to be measured in nanometers, typically between 10 and 1000 nm. Due to their small size, these emulsions are clear or translucent and are known for their stability, which prevents them from easily separating into their constituent oil and water phases. This stability is due to the high surface area to volume ratio, which helps in maintaining the dispersed phase within the continuous phase with the help of surfactants (Hussain et al., 2023).

Nanoemulsions can be broadly classified into oil-in-water (O/W), where oil droplets are dispersed in a water phase, and water-in-oil (W/O), where water droplets are dispersed in an oil phase. This classification is crucial as it determines the nanoemulsion's application, particularly in drug delivery systems where the choice between O/W and W/O can affect the drug's bioavailability and release profile.

### 2.2 Physicochemical Properties

The physicochemical properties of nanoemulsions are key to their functionality in drug delivery. These properties include viscosity, droplet size distribution, zeta potential, and turbidity. The small droplet size of nanoemulsions leads to a higher surface area, enhancing the dissolution rate of poorly

soluble drugs and thereby increasing their bioavailability (Sivadasan et al., 2021).

Furthermore, the zeta potential of nanoemulsions indicates the degree of repulsion between adjacent, similarly charged particles in a dispersion. A high zeta potential usually signifies stability, preventing the particles from aggregating by providing sufficient charge-induced repulsion. Understanding these properties allows researchers and developers to tailor nanoemulsion formulations to improve drug delivery efficiency and stability.

### 2.3 Mechanisms of Action in Drug Delivery

Nanoemulsions enhance drug delivery through several mechanisms. Firstly, their small size allows them to penetrate biological barriers more effectively than larger particles. This is particularly advantageous in transdermal drug delivery, where nanoemulsions can bypass the stratum corneum to deliver drugs directly into the underlying tissues (Suman et al., 2023).

Moreover, the ability of nanoemulsions to dissolve and encapsulate both hydrophobic and hydrophilic drugs makes them versatile carriers that can be used in various routes of administration including oral, injectable, topical, and even inhalational therapies. For instance, flavonoids, which are often difficult to formulate due to their poor solubility and

stability, can be efficiently incorporated into nanoemulsions, enhancing their therapeutic efficacy and stability (Ranjbar et al., 2023).

In conclusion, nanoemulsions offer a promising platform for the effective and efficient delivery of therapeutic agents. Their unique properties and versatility not only make them suitable for traditional routes of administration but also open up new avenues for innovation in drug delivery, such as through transdermal and targeted therapies. As research in this field advances, the potential applications of nanoemulsions in medicine continue to expand, promising significant improvements in patient care and therapeutic outcomes.

### 3. GREEN SYNTHESIS OF NANOEMULSIONS

The field of nanoemulsions is rapidly advancing, integrating principles of sustainability and biocompatibility. This section explores the use of biocompatible materials, green synthesis techniques, and the role of green solvents in the formulation of nanoemulsions, reflecting a shift towards more environmentally friendly pharmaceutical processes.

### 3.1 Biocompatible Materials

Biocompatible materials are essential in the development of nanoemulsions for medical applications, ensuring that these formulations are safe for human use and environmentally friendly. Recent studies emphasize the use of natural substances and biomaterials, such as chitosan, essential oils, and microbial metabolites, which not only enhance the therapeutic efficacy but also minimize adverse environmental impacts. For instance, Khan et al. (2021) highlighted the development of a chitosan-based nanoemulsion gel incorporating microbial secondary metabolites that exhibited significant antifungal activity both *in vitro* and *in vivo*, showcasing the potential of biocompatible materials in enhancing the functionality of nanoemulsions.

### 3.2 Green Synthesis Techniques

Green synthesis involves methods that reduce or eliminate the use or generation of hazardous substances in the design, manufacture, and application of chemical products. Mondal et al. (2024) describe an innovative approach using aroma-based hydrophobic deep eutectic solvents in a membrane-assisted nanoemulsification process, which not only enhances the antifungal activities of nanoemulsions but also aligns with the principles of green chemistry.

Similarly, Rasool et al. (2024) discuss advancements in green synthesis for biological sustainability, illustrating how nature-inspired nanomaterials can be synthesized with reduced environmental footprint while maintaining high efficacy in applications ranging from medicine to agriculture.

### 3.3 Role of Green Solvents

Green solvents play a pivotal role in the synthesis of nanoemulsions by reducing the environmental impact associated with traditional organic solvents. These solvents, typically derived from renewable resources, are designed to be non-toxic, biodegradable, and less volatile. Dib et al. (2021) explore the use of ionic liquid-based surfactants and biocompatible solvents, which are crucial in formulating environmentally friendly organized systems. This approach not only improves the sustainability of the synthesis process but also enhances the safety and efficacy of the nanoemulsions produced.

In another example, Venkatesan et al. (2022) developed a green cationic nanoemulsion using water, transcitol, lecithin, and a green surfactant, which was effective in treating oxytetracycline-contaminated aqueous solutions, demonstrating the practical environmental applications of green nanoemulsions. Additionally, the extraction

and valorization of essential oils in the green synthesis of iron oxide nanoparticles, as discussed by Azizi et al. (2024), further

underscore the role of green solvents in enhancing the eco-friendliness of nanoemulsion production processes.

**Table 1: Comparative Analysis of Nanoemulsion Formulations**

| Nanoemulsion Type | Components                          | Application Area   | Stability | Biodegradability | Reference                                  |
|-------------------|-------------------------------------|--------------------|-----------|------------------|--|
| Food Grade        | Essential oils, natural surfactants | Food preservation  | High      | Yes              | Mishra, D. & Khare, P. (2021)              |
| Pharmaceutical    | Drug compounds, biopolymers         | Drug delivery      | Moderate  | Yes              | Đoković, J. B. et al. (2021)               |
| Agricultural      | Pesticides, herbicides              | Pest control       | Low       | No               | Zargar, M. et al. (2023)                   |
| Cosmetic          | Plant extracts, vitamins            | Skin care products | High      | Yes              | Gupta, P., Sharma, A., & Mittal, V. (2024) |

**Concluding Remarks**

The shift towards green synthesis of nanoemulsions is crucial in addressing the dual challenges of environmental impact and human health. By leveraging biocompatible materials, innovative green synthesis techniques, and environmentally friendly solvents, researchers are paving the way for the next generation of drug delivery systems that are not only effective but also sustainable. This approach aligns with the broader goals of green chemistry, promising significant advancements in both pharmaceutical sciences and environmental stewardship.

**4. STABILIZATION STRATEGIES FOR NANOEMULSIONS**

**4.1 Natural Surfactants and Emulsifiers**

Natural surfactants and emulsifiers are pivotal in the creation and stabilization of nanoemulsions. These components, typically derived from natural sources like essential oils, are favored for their biocompatibility and lower toxicity compared to synthetic surfactants. Kumar et al. (2024) detail how nanoemulsions can encapsulate essential oils to enhance their efficacy in the agricultural and food sectors, protecting against microbial spoilage and pests while ensuring safety and effectiveness (Kumar, A., Kanwar, R., & Mehta, S. K., 2024).

Rehman et al. (2021) further support this by discussing how nanoemulsion systems can increase the antioxidant potential of essential

oils, thereby extending the shelf life and nutritional quality of food products without using harmful preservatives (Rehman, A. et al., 2021).

#### 4.2 Biopolymer-based Stabilizers

Biopolymer-based stabilizers have gained attention for their environmentally friendly and sustainable properties. Chaudhary (2023) examines how chitosan, derived from chitin found in shellfish, can be used to form nanoemulsion coatings that significantly prolong the freshness of perishable goods. This application is particularly promising for reducing food waste and enhancing food safety (Chaudhary, S., 2023).

Arezou Khezerlou et al. (2021) complement this discussion by showcasing how biopolymer-based packaging materials not only improve barrier properties against oxygen and moisture but are also fully biodegradable, offering a dual advantage of performance and reduced environmental impact (Arezou Khezerlou et al., 2021). The Critical Reviews in Food Science and Nutrition (2024) also highlights the role of pectin, a plant-derived biopolymer, in the formation of nanoparticles that stabilize Pickering emulsions, presenting a novel approach to food formulation that avoids

synthetic stabilizers (Critical Reviews in Food Science and Nutrition, 2024).

#### 4.3 Recent Innovations in Stabilization Techniques

The evolution of stabilization techniques for nanoemulsions is marked by innovative approaches such as the pH-driven method of encapsulation. This method involves adjusting the pH to control the solubility and interaction of biopolymers, thus forming stable nanocapsules around functional ingredients. The Critical Reviews in Food Science and Nutrition (2023) provides an extensive review of this method, illustrating its potential to revolutionize the encapsulation of functional food ingredients for targeted release and improved bioavailability (Critical Reviews in Food Science and Nutrition, 2023).

Additionally, the use of particle-based stabilizers, such as in Pickering emulsions, is explored by Hadi et al. (2024), who document the versatility of these systems across various sectors including food and industrial applications. These emulsions leverage unique properties of particles to create more stable and robust systems, suitable for a range of demanding applications (Hadi, N. A. et al., 2024).

## 5. Characterization of Green Nanoemulsions

### 5.1 Analytical Techniques

Analytical techniques are crucial for evaluating the properties and quality of nanoemulsions, particularly those incorporating green methodologies. Georgios Kamaris et al. (2024) have developed and validated an HPLC-DAD method specifically for analyzing antioxidants in nano-emulsion formulations, highlighting the precision and accuracy required in these analyses (Georgios Kamaris et al., 2024).

Additionally, Li et al. (2021) discuss various characterization techniques for nanoemulsion-based delivery systems, emphasizing the importance of assessing particle size, zeta potential, and morphology to understand the distribution and stability of the nanocarriers (Li, G. et al., 2021). Alshawwa et al. (2022) also investigate into the implementation of advanced technologies like Artificial Intelligence to optimize nanoemulsion characterization, which can predict stability and performance outcomes more efficiently (Alshawwa, S. Z. et al., 2022).

### 5.2 Stability Studies

Stability studies are essential for ensuring the long-term effectiveness and safety of

nanoemulsions. Saleh et al. (2024) explore the effects of thermal treatment and storage conditions on the stability of black rice bran extract encapsulated in nanoemulsions, showing how environmental factors can influence the physical stability of these systems (Saleh, M. N. et al., 2024).

Sevinç-Özakar et al. (2022) provide insights into the stability of nanoemulsion-based hydrogels containing propolis and dexpanthenol, assessing their antimicrobial and cytotoxic properties over time to ensure consistency and safety (Sevinç-Özakar, R. et al., 2022). Yin et al. (2022) also contribute to this discussion by reviewing methods to improve the stability and bioavailability of tea polyphenols through encapsulation techniques, highlighting the role of protective matrices in extending shelf life and enhancing functional properties (Yin, Z. et al., 2022).

### 5.3 Bioavailability Assessment

Bioavailability assessment is key to understanding how effectively the body can utilize the active ingredients delivered through nanoemulsions. Đoković et al. (2021) illustrate how PEGylated nanoemulsions can improve the bioavailability and antioxidant effects of curcumin in rats, emphasizing the impact of nanoemulsion properties on biological outcomes (Đoković, J. B. et al.,



2021). Jain et al. (2022) report similar findings with erlotinib, where solid self-nanoemulsifying drug delivery systems enhanced its oral bioavailability significantly, offering potential improvements for cancer treatment (Jain, S. et al., 2022).

Arti Shettiwar et al. (2024) further explore this by studying oral linalool-based nanoemulsions of acalabrutinib, aiming to ameliorate its bioavailability and demonstrate enhanced in vitro anticancer activity against T lymphoblast cell lines, providing a compelling case for the therapeutic potential of well-formulated nanoemulsions (Arti Shettiwar et al., 2024).

## 6. Applications in Drug Delivery

### 6.1 Targeted Drug Delivery

Targeted drug delivery systems aim to concentrate the therapeutic effects of drugs in parts of the body where they are most needed, thereby reducing side effects and improving efficacy. Nanocarrier systems, such as those described by Alshawwa et al. (2022), are crucial for achieving targeted delivery, as they can be engineered to recognize and bind to specific cellular receptors, thus enhancing the precision of drug delivery (Alshawwa, S. Z. et al., 2022).

Đoković et al. (2021) also provide an example of targeted delivery with their study on

curcumin-loaded PEGylated nanoemulsions, which are designed to enhance the antioxidant capacity and bioavailability of curcumin specifically in target tissues (Đoković, J. B. et al., 2021). Additionally, Arti Shettiwar et al. (2024) demonstrate the application of nanoemulsions in targeted cancer therapy, where oral linalool-based nanoemulsions improve the delivery and efficacy of acalabrutinib against specific cancer cell lines (Arti Shettiwar et al., 2024).

### 6.2 Transdermal and Topical Applications

Transdermal and topical applications of nanoemulsions allow for the delivery of therapeutic agents directly through the skin, which can be particularly beneficial for localized treatment or systemic effects via skin absorption. Diedrich et al. (2022) have explored the use of mucoadhesive nanoemulsions for intranasal administration that enhances the brain bioavailability of luteolin, which demonstrates a potential for neuroprotective applications (Diedrich, C. et al., 2022).

The work by Sevinç-Özakar et al. (2022) on nanoemulsion-based hydrogels also highlights the potential for topical delivery of antimicrobial and skin-healing agents such as propolis and dexpanthenol (Sevinç-Özakar, R. et al., 2022). Moreover, Hassan et al. (2022)

have developed clove and cinnamon oil-based nanoemulsions for topical application against fleas, showcasing the versatility of transdermal nanoemulsions in both medical and veterinary contexts (Hassan, M. E. et al., 2022).

### 6.3 Oral and Injectable Formulations

Oral and injectable formulations are traditional routes of drug administration that have been significantly enhanced by nanoemulsion technology. Nair et al. (2022) describe the development of a self-nanoemulsifying drug delivery system for sertraline, which significantly improves its solubility and absorption when taken orally, thereby enhancing therapeutic outcomes (Nair, A. B. et al., 2022).

In the realm of injectables, Tyagi et al. (2024) have optimized a nanoemulsion for the co-delivery of dolutegravir and epigallocatechin gallate, aimed at managing NeuroAIDS more effectively through enhanced bioavailability and brain targeting (Tyagi, S. et al., 2024). These examples demonstrate how nanoemulsions can improve the performance of both oral and injectable drugs by enhancing their stability, solubility, and absorption rates.

## 7. ADVANCEMENTS IN GREEN NANOEMULSION FORMULATIONS

The development of green nanoemulsion formulations represents a significant advancement in the field of nanotechnology, emphasizing sustainability, environmental friendliness, and the use of natural resources. These formulations leverage eco-friendly materials and processes to create nanoemulsions that are not only effective but also minimize ecological impact. This section explores successful case studies, commercially available products, and the regulatory landscape surrounding green nanoemulsions.

### 7.1 Case Studies of Successful Formulations

Several studies highlight the successful formulation of green nanoemulsions using natural and sustainable ingredients. For instance, Jamir et al. (2023) demonstrated the encapsulation of plant-based essential oils in nanoemulsions, enhancing their therapeutic applications. By utilizing natural surfactants and biodegradable oils, the study achieved stable nanoemulsions with improved bioactivity, showcasing the potential of plant-derived components in sustainable nanoemulsion systems (Jamir, Y. et al., 2023).

Another noteworthy case is the work by Mondal et al. (2024), who employed

membrane-assisted nanoemulsification using novel aroma-based hydrophobic deep eutectic solvents. This approach not only ensures the sustainability of the formulation process but also enhances the antifungal activities of the resulting nanoemulsions. The use of deep eutectic solvents, which are environmentally benign, underscores the commitment to green chemistry principles in nanoemulsion production (Mondal, S. et al., 2024).

Dib et al. (2021) explored the use of biocompatible solvents and ionic liquid-based surfactants to formulate environmentally friendly organized systems. Their research focused on reducing the reliance on harmful synthetic surfactants, thereby creating nanoemulsions that are both effective and sustainable. The study highlighted the importance of selecting appropriate green solvents to maintain the stability and functionality of nanoemulsions without compromising environmental integrity (Dib, N. et al., 2021).

Furthermore, Khan et al. (2021) developed a chitosan-based nanoemulsion gel containing microbial secondary metabolites with effective antifungal activity. Chitosan, a natural biopolymer, provided the necessary stability and biocompatibility, making the formulation suitable for both *in vitro* and *in vivo*

applications. This case study exemplifies how natural polymers can be effectively integrated into nanoemulsion systems to enhance their therapeutic potential while adhering to green formulation principles (Khan, M. K. et al., 2021).

## 7.2 Commercially Available Products

The transition from laboratory-scale formulations to commercially available green nanoemulsion products marks a critical milestone in the adoption of sustainable nanotechnology. One prominent example is the development of biodegradable biopolymer-based packaging materials as described by Arezou Khezerlou et al. (2021). These packaging solutions utilize nanoemulsions to enhance barrier properties against oxygen and moisture, thereby extending the shelf life of food products. The biodegradability of the materials aligns with global sustainability goals, making them attractive to environmentally conscious consumers and businesses (Arezou Khezerlou, Tavassoli, M. et al., 2021).

Another commercial application is seen in the agricultural sector, where Kumar et al. (2024) introduced nanoemulsions as effective delivery vehicles for essential oils. These formulations are employed in agri-food applications to protect crops from pests and

pathogens while minimizing the use of synthetic pesticides. The use of natural essential oils encapsulated in nanoemulsions not only ensures effective pest control but also reduces environmental contamination, thereby promoting sustainable agricultural practices (Kumar, A. et al., 2024).

In the cosmetics industry, green nanoemulsions have been integrated into skincare products to enhance the delivery and efficacy of natural active ingredients. For example, Sevinç-Özakar et al. (2022) developed nanoemulsion-based hydrogels containing propolis and dexpanthenol. These formulations offer improved stability, antimicrobial properties, and skin compatibility, catering to the growing demand for natural and sustainable cosmetic products (Sevinç-Özakar, R. et al., 2022).

### 7.3 Regulatory Aspects

The commercialization and widespread adoption of green nanoemulsion formulations are contingent upon meeting stringent regulatory standards that ensure safety, efficacy, and environmental compliance. Regulatory bodies such as the Food and Drug Administration (FDA) and the European Medicines Agency (EMA) have established guidelines for the approval of nanoemulsion-based products, emphasizing the need for

comprehensive characterization and toxicity assessments.

According to Rasool et al. (2024), the advancement of nature-inspired nanomaterials necessitates adherence to regulatory frameworks that govern their synthesis, application, and disposal. The study underscores the importance of transparent reporting of formulation processes and the use of environmentally benign materials to facilitate regulatory approvals (Rasool, A. et al., 2024).

Moreover, Hussain et al. (2022) highlighted the role of predictive models like GastroPlus and HSPiP in optimizing nanoemulsion formulations for improved delivery while ensuring compliance with regulatory standards. These models aid in predicting the behavior of nanoemulsions in biological systems, thereby streamlining the approval process by providing robust data on bioavailability and safety (Hussain, A. et al., 2022).

The regulatory landscape also emphasizes the importance of sustainability in nanoemulsion formulations. Dib et al. (2021) advocate for the use of biocompatible and biodegradable solvents and surfactants, which not only enhance the safety profile of nanoemulsions but also align with environmental regulations

aimed at reducing industrial pollution and promoting green chemistry (Dib, N. et al., 2021).

In conclusion, advancements in green nanoemulsion formulations are driven by innovative case studies, the emergence of commercially viable products, and a robust regulatory framework that ensures safety and sustainability. These developments collectively contribute to the responsible and effective application of nanoemulsions across various industries, fostering a balance between technological progress and environmental stewardship.

### 9. Environmental and Safety Considerations

The integration of nanoemulsions in various sectors raises significant environmental and safety concerns. These considerations are critical to ensuring that while nanoemulsions offer enhanced functionalities, they do not pose undue risks to the environment or human health. This section delves into the

ecotoxicology, biodegradability, sustainability, and regulatory aspects of nanoemulsions using the provided references.

#### 9.1 Ecotoxicology of Nanoemulsions

The ecotoxicology of nanoemulsions is a vital area of study as these materials often enter environmental systems through agricultural run-off, industrial waste, or consumer products disposal. Rani et al. (2023) provide an extensive overview of the environmental hazards associated with nano-pesticides, which can include nanoemulsions. They discuss the impact these materials have on non-target species and ecosystems, emphasizing the need for detailed ecotoxicological evaluations to mitigate potential risks (Rani, N. et al., 2023). Additionally, Zargar et al. (2023) explore the use of poly(epsilon-caprolactone)-based nanoherbicides, noting their effectiveness and potential risks, suggesting that while these nanoherbicides control weeds efficiently, their long-term ecological impacts require thorough investigation (Zargar, M. et al., 2023).

**Table 2: Ecotoxicology and Regulatory Compliance of Nanoemulsions**

| Nanoemulsion Application | Ecotoxicological Impact    | Regulatory Compliance | Biodegradability Assessment      | Reference              |
|--------------------------|----------------------------|-----------------------|----------------------------------|------------------------|
| Agricultural Pesticides  | Harm to non-target species | Required              | Biodegradation studies mandatory | Rani, N. et al. (2023) |

|                         |                               |                              |                               |                              |
|-------------------------|-------------------------------|------------------------------|-------------------------------|------------------------------|
| Cosmetic Products       | Minimal                       | Strict                       | Often biodegradable           | Sheik, M. et al. (2021)      |
| Food Preservation       | Negligible                    | Strict food safety standards | Biodegradable components      | Jamir, Y. et al. (2023)      |
| Pharmaceutical Delivery | Variable, depends on compound | Very strict                  | Studies required for approval | Arti Shettiwar et al. (2024) |

### 9.2 Biodegradability and Sustainability

Biodegradability and sustainability are paramount in the development and application of nanoemulsions, especially those used in environmental remediation and agriculture. Mishra and Khare (2021) discuss emerging nano-agrochemicals, highlighting their benefits for sustainable agriculture and the importance of designing these materials to be biodegradable to prevent accumulation in the environment (Mishra, D. & Khare, P., 2021). Gana et al. (2024) further emphasize the role of nanoparticle-based systems in environmental cleanup, underlining the need for these technologies to align with sustainable practices and minimize ecological disruption (Gana, M. et al., 2024).

### 9.3 Safety Protocols and Regulations

The implementation of strict safety protocols and adherence to regulatory guidelines are essential for managing the risks associated with nanoemulsions. Sheik et al. (2021) examine biologically synthesized plant-derived nanomedicines, including their

toxicity profiles in various therapeutic contexts. They stress the importance of regulatory perspectives in ensuring that these nanomedicines are safe for both clinical applications and environmental health (Sheik, M. et al., 2021). Furthermore, Bimpizas-Pinis et al. (2022) discuss the environmental assessment and circular economy implications of additives in the food supply chain, including nanoemulsions, pointing out the necessity of incorporating environmental considerations into the regulatory frameworks to promote circular economy principles (Bimpizas-Pinis, M. et al., 2022).

### CONCLUSION

The development and application of nanoemulsions across various sectors highlight significant advances in nanotechnology, offering enhanced performance in areas ranging from agriculture and cosmetics to environmental remediation. However, as the utilization of these nano-scale systems expands, it is imperative to consider

their environmental impact, safety, and regulatory compliance comprehensively.

The studies and reviews referenced provide crucial insights into the ecological considerations associated with nanoemulsions. They underscore the importance of conducting thorough ecotoxicological assessments to understand the effects of these nanoformulations on non-target organisms and ecosystems. This is particularly crucial for nanoemulsions used in agriculture and pest management, where runoff could pose risks to aquatic and soil biota.

Furthermore, the sustainability and biodegradability of nanoemulsions are vital for their integration into environmental and health-related applications. As the push towards green chemistry intensifies, nanoemulsions must be designed to be environmentally benign, ensuring they do not contribute to pollution or ecological imbalance. The adoption of sustainable practices in the synthesis and deployment of nanoemulsions is therefore not just beneficial but necessary.

Regulatory frameworks play a pivotal role in the safe deployment of nanoemulsions. These guidelines ensure that nanoemulsions are rigorously tested for safety and efficacy before they reach the market. As nanoemulsions

become more common in consumer products, strict adherence to safety protocols and regulations will be essential to mitigate risks to human health and the environment.

In conclusion, while nanoemulsions present promising technological advancements, their development must be accompanied by responsible practices that prioritize environmental health and safety. Continuous research, thoughtful regulation, and adherence to sustainability principles will be key to harnessing the benefits of nanoemulsions while minimizing their potential risks. The path forward involves a balanced approach that integrates innovation with caution, ensuring that the advancements in nanoemulsions contribute positively to both technology and society.

## References

1. Wilson, R. J., Li, Y., Yang, G., & Zhao, C.-X. (2021). Nanoemulsions for drug delivery. *Particuology*, 64. <https://doi.org/10.1016/j.partic.2021.05.009>
2. Jamir, Y., Bhushan, M., Sanjukta, R., & Singh, L. R. (2023). Plant-based essential oil encapsulated in nanoemulsions and their enhanced therapeutic applications: An overview.

- Biotechnology and Bioengineering, 121(2), 1-15.  
<https://doi.org/10.1002/bit.28590>
3. Kaur, G., Panigrahi, C., Agarwal, S., Khuntia, A., & Sahoo, M. (2024). Recent trends and advancements in nanoemulsions: Production methods, functional properties, applications in food sector, safety and toxicological effects. *Food Physics*, 1, 100024. <https://doi.org/10.1016/j.foodp.2024.100024>
  4. Food Reviews International. (2023). Background, limitations, and future perspectives in food grade microemulsions and nanoemulsions. *Food Reviews International*. <https://doi.org/10.1080/87559129.2022.2059808>
  5. Hussain, A., Altamimi, M. A., Ramzan, M., Mirza, M. A., & Khuroo, T. (2023). GastroPlus- and HSPiP-Oriented Predictive Parameters as the Basis of Valproic Acid-Loaded Mucoadhesive Cationic Nanoemulsion Gel for Improved Nose-to-Brain Delivery to Control Convulsion in Humans. *Gels*, 9(8), 603. <https://doi.org/10.3390/gels9080603>
  6. Ranjbar, S., Emamjomeh, A., Sharifi, F., Zarepour, A., Aghaabbasi, K., Dehshahri, A., Mohammadi Sepahvand, A., Zarrabi, A., Beyzaei, H., Zahedi, M. M., & Mohammadinejad, R. (2023). Lipid-Based Delivery Systems for Flavonoids and Flavonolignans: Liposomes, Nanoemulsions, and Solid Lipid Nanoparticles. *Pharmaceutics*, 15(7), 1944. <https://doi.org/10.3390/pharmaceutics15071944>
  7. Sivadasan, D., Sultan, M. H., Madkhali, O., Almoshari, Y., & Thangavel, N. (2021). Polymeric Lipid Hybrid Nanoparticles (PLNs) as Emerging Drug Delivery Platform—A Comprehensive Review of Their Properties, Preparation Methods, and Therapeutic Applications. *Pharmaceutics*, 13(8), 1291. <https://doi.org/10.3390/pharmaceutics13081291>
  8. Suman, S. K., Chandrasekaran, N., & Priya, G. (2023). Micro-nanoemulsion and nanoparticle-assisted drug delivery against drug-resistant tuberculosis: recent developments. *Clinical Microbiology Reviews*, 36(4). <https://doi.org/10.1128/cmr.00088-23>



9. Azizi, A., Nazari, M., & Roozbahani, P. A. (2024). Extraction and Identification of the Essential Oil of Russian Knapweed Compounds and their Valorization in Green Synthesis of Iron Oxide Nanoparticles During a Surfactant-free Nano-emulsions System. Waste and Biomass Valorization. <https://doi.org/10.1007/s12649-024-02562-9>
10. Dib, N., Correa, N. M., Silber, J. J., Falcone, R. D., & García-Río, L. (2021). Biocompatible Solvents and Ionic Liquid-Based Surfactants as Sustainable Components to Formulate Environmentally Friendly Organized Systems. *Polymers*, 13(9), 1378. <https://doi.org/10.3390/polym13091378>
11. Khan, M. K., Khan, B. A., Uzair, B., Niaz, S. I., Khan, H., Hosny, K. M., & Mena, F. (2021). Development of Chitosan-Based Nanoemulsion Gel Containing Microbial Secondary Metabolite with Effective Antifungal Activity: In vitro and in vivo Characterizations. *International Journal of Nanomedicine*, 16. <https://doi.org/10.2147/IJN.S338064>
12. Mondal, S., Syed, U. T., Pinto, E., Leonardo, I. C., Romero, P., Gaspar, F. B., Crespo, M. T. B., Sebastian, V., Crespo, J. G., & Brazinha, C. (2024). Sustainable production of nanoemulsions by membrane-assisted nanoemulsification using novel aroma-based hydrophobic deep eutectic solvents for enhanced antifungal activities. *Journal of Cleaner Production*, 444, 141167. <https://doi.org/10.1016/j.jclepro.2024.141167>
13. Rasool, A., Sri, S., Zulfajri, M., & Krismastuti, F. S. H. (2024). Nature inspired nanomaterials, advancements in green synthesis for biological sustainability. *Inorganic Chemistry Communications*, 169. <https://doi.org/10.1016/j.inoche.2024.12954>
14. Venkatesan, K., Haider, N., Yusuf, M., Hussain, A., Afzal, O., Yasmin, S., & Altamimi, A. S. A. (2022). Water/transcutol/lecithin/M-812 green cationic nanoemulsion to treat oxytetracycline contaminated aqueous bulk solution. *Journal of Molecular Liquids*, 357.

- <https://doi.org/10.1016/j.molliq.2022.119154>
15. Arezou Khezerlou, Tavassoli, M., Sani, M. A., Mohammadi, K., Ehsani, A., & McClements, D. J. (2021). Application of Nanotechnology to Improve the Performance of Biodegradable Biopolymer-Based Packaging Materials. *Polymers*, 13(24), 4399–4399.  
<https://doi.org/10.3390/polym13244399>
16. Biological and thermodynamic stabilization of lipid-based delivery systems through natural biopolymers; controlled release and molecular dynamics simulations. (2024). *Critical Reviews in Food Science and Nutrition*.  
<https://doi.org/10.1080//10408398.2023.2191281>
17. Chaudhary, S. (2023). Sustainable chitosan nanoemulsion coatings/films with agri-food byproducts: advances, composition, production methods and applications in food preservation. *Journal of Food Measurement & Characterization*, 18(3), 1627–1649.  
<https://doi.org/10.1007/s11694-023-02293-w>
18. Construction of biopolymer-based nanoencapsulation of functional food ingredients using the pH-driven method: a review. (2023). *Critical Reviews in Food Science and Nutrition*.  
<https://doi.org/10.1080//10408398.2021.2023858>
19. Cvanić, T., Olja Šovljanski, Senka Popović, Erceg, T., Jelena Vulić, Jasna Čanadanović-Brunet, Gordana Četković, & Vanja Travičić. (2023). Progress in Fruit and Vegetable Preservation: Plant-Based Nanoemulsion Coatings and Their Evolving Trends. *Coatings*, 13(11), 1835–1835.  
<https://doi.org/10.3390/coatings13111835>
20. Ghumika Pandita, Krebs, C., Gonçalves, M. J., Jasińska, J. M., Ewelina Jamróz, & Roy, S. (2024). Recent progress on Pickering emulsion stabilized essential oil added biopolymer-based film for food packaging applications: A review. *International Journal of Biological Macromolecules*, 269, 132067–132067.  
<https://doi.org/10.1016/j.ijbiomac.2024.132067>

21. Hadi, N. A., Aisyah Ashaari, Matos, M., & Nadiyah Wan Rasdi. (2024). Exploring particle-based stabilisation of Pickering emulsions in food, aquaculture, and industrial applications. *International Journal of Food Science & Technology*, 59(10), 6834–6855. <https://doi.org/10.1111/ijfs.17478>
22. Kumar, A., Kanwar, R., & Mehta, S. K. (2024). Nanoemulsion as an effective delivery vehicle for essential oils: Properties, formulation methods, destabilizing mechanisms and applications in agri-food sector. *Next Nanotechnology*, 7, 100096–100096. <https://doi.org/10.1016/j.nxnano.2024.100096>
23. Rehman, A., Qunyi, T., Sharif, H. R., Korma, S. A., Karim, A., Manzoor, M. F., Mehmood, A., Iqbal, M. W., Raza, H., Ali, A., & Mehmood, T. (2021). Biopolymer based nanoemulsion delivery system: An effective approach to boost the antioxidant potential of essential oil in food products. *Carbohydrate Polymer Technologies and Applications*, 2, 100082. <https://doi.org/10.1016/j.carpta.2021.100082>
24. S. Boostani, S. Babajafari, & Mazloomi, S. M. (2022). Recent Progress on Biopolymer-based Technologies on Nutraceutical and Natural Plant-based Extracts. *The Royal Society of Chemistry EBooks*, 361–398. <https://doi.org/10.1039/9781839168048-00361>
25. The present state and future outlook of pectin-based nanoparticles in the stabilization of Pickering emulsions. (2024). *Critical Reviews in Food Science and Nutrition*. <https://doi.org/10.1080//10408398.2024.2351163>
26. Alshawwa, S. Z., Kassem, A. A., Farid, R. M., Mostafa, S. K., & Labib, G. S. (2022). Nanocarrier Drug Delivery Systems: Characterization, Limitations, Future Perspectives and Implementation of Artificial Intelligence. *Pharmaceutics*, 14(4), 883. <https://doi.org/10.3390/pharmaceutics14040883>
27. Arti Shettiwar, Gupta, U., Chatterjee, E., Patra, B., Mayur Aalhat, Mahajan, S., Indrani Maji, Mehra, N. K., Santosh Kumar Guru, & Singh, P. K. (2024). Oral linalool-based nanoemulsion of

- acalabrutinib for ameliorating its oral bioavailability and in vitro anticancer potential in T lymphoblast cell lines. *Colloid & Polymer Science*. <https://doi.org/10.1007/s00396-024-05290-7>
28. Diedrich, C., Zittlau, I. C., Machado, C. S., Fin, M. T., Khalil, N. M., Badea, I., & Rubiana Mara Mainardes. (2022). Mucoadhesive nanoemulsion enhances brain bioavailability of luteolin after intranasal administration and induces apoptosis to SH-SY5Y neuroblastoma cells. *International Journal of Pharmaceutics*, 626, 122142–122142. <https://doi.org/10.1016/j.ijpharm.2022.122142>
29. Đoković, J. B., Savić, S. M., Mitrović, J. R., Nikolic, I., Marković, B. D., Randjelović, D. V., Antic-Stankovic, J., Božić, D., Cekić, N. D., Stevanović, V., Batinić, B., Arandjelović, J., Savić, M. M., & Savić, S. D. (2021). Curcumin Loaded PEGylated Nanoemulsions Designed for Maintained Antioxidant Effects and Improved Bioavailability: A Pilot Study on Rats. *International Journal of Molecular Sciences*, 22(15), 7991. <https://doi.org/10.3390/ijms22157991>
30. Georgios Kamaris, Dalavitsou, A., & Markopoulou, C. K. (2024). Development and Validation of an HPLC-DAD Method for the Determination of Seven Antioxidants in a Nano-Emulsion: Formulation and Stability Study. *Separations*, 11(2), 43–43. <https://doi.org/10.3390/separations11020043>
31. Hassan, M. E., Samia M.M. Mohafrash, Mikhail, M. W., & Mossa, A.-T. H. (2022). Development and evaluation of clove and cinnamon oil-based nanoemulsions against adult fleas (*Xenopsylla cheopis*). *Biocatalysis and Agricultural Biotechnology*, 47, 102587–102587. <https://doi.org/10.1016/j.bcab.2022.102587>
32. Hemanga Hazarika, Harshita Krishnatreyya, Chattopadhyay, P., Saha, A., Pathak, Y. V., & Zaman, M. K. (2020). Nanoemulsion Delivery of Herbal Products: Prospects and Challenges. *Springer eBooks*, 267–288. [https://doi.org/10.1007/978-981-15-6255-6\\_11](https://doi.org/10.1007/978-981-15-6255-6_11)
33. Hussain, A., Altamimi, M. A., Imam, S. S., Ahmad, M. S., & Osamah

- Abdulrahman Alnemer. (2022). Green Nanoemulsion Water/Ethanol/Transcutol/LabM-Based Treatment of Pharmaceutical Antibiotic Erythromycin-Contaminated Aqueous Bulk Solution. *ACS Omega*, 7(51), 48100–48112. <https://doi.org/10.1021/acsomega.2c06095>
34. Jain, S., Kiran Dongare, Bhargavi Nallamothe, Dora, C. P., Varun Kushwah, Katiyar, S. S., & Sharma, R. (2022). Enhanced stability and oral bioavailability of erlotinib by solid self nano emulsifying drug delivery systems. *International Journal of Pharmaceutics*, 622, 121852–121852. <https://doi.org/10.1016/j.ijpharm.2022.121852>
35. Jiang, T. (2022). Encapsulation of curcumin by membrane emulsification : bioaccessibility and stability of curcumin-loaded emulsions. *Hal.science*. <https://theses.hal.science/tel-04225927>
36. Li, G., Zhang, Z., Liu, H., & Hu, L. (2021). Nanoemulsion-based delivery approaches for nutraceuticals: fabrication, application, characterization, biological fate, potential toxicity and future trends. *Food & Function*, 12(5), 1933–1953. <https://doi.org/10.1039/d0fo02686g>
37. Nair, A. B., Singh, B., Shah, J., Jacob, S., Bandar Aldhubiab, Nagaraja Sreeharsha, Morsy, M. A., Venugopala, K. N., Mahesh Attimarad, & Pottathil Shinu. (2022). Formulation and Evaluation of Self-Nanoemulsifying Drug Delivery System Derived Tablet Containing Sertraline. *Pharmaceutics*, 14(2), 336–336. <https://doi.org/10.3390/pharmaceutics14020336>
38. Raja, K., Srinivasan, S., Krishnappa Samrat, Bala Priyalakshmi, Kumar, R. D., Arvind Bharani, Kumar, R. G., M. Kavisri, & Meivelu Moovendhan. (2023). Sustainable approach to manage the vulnerable rodents using eco-friendly green rodenticides formulation through nanotechnology principles – A review. *Process Safety and Environmental Protection*, 171, 591–606. <https://doi.org/10.1016/j.psep.2023.01.050>
39. Saleh, M. N., Salam, M. A., & Esra Capanoglu. (2024). Encapsulation of Black Rice Bran Extract in a Stable

- Nanoemulsion: Effects of Thermal Treatment, Storage Conditions, and In Vitro Digestion. *ACS Omega*. <https://doi.org/10.1021/acsomega.3c07060>
40. Sevinç-Özakar, R., Seyret, E., Özakar, E., & Adıgüzel, M. C. (2022). Nanoemulsion-Based Hydrogels and Organogels Containing Propolis and Dexpanthenol: Preparation, Characterization, and Comparative Evaluation of Stability, Antimicrobial, and Cytotoxic Properties. *Gels*, 8(9), 578. <https://doi.org/10.3390/gels8090578>
41. Tyagi, S., Gaikwad, S. Y., Madhuri Chandane-Tak, Mukherjee, A., & Kumar, S. (2024). Optimization of Dolutegravir and Epigallocatechin Gallate Loaded Nanoemulsion for Enhanced Oral Delivery in NeuroAIDS Management. *Journal of Drug Delivery Science and Technology*, 106293–106293. <https://doi.org/10.1016/j.jddst.2024.106293>
42. Yin, Z., Zheng, T., Ho, C.-T., Huang, Q., Wu, Q., & Zhang, M. (2022). Improving the stability and bioavailability of tea polyphenols by encapsulations: a review. *Food Science and Human Wellness*, 11(3), 537–556. <https://doi.org/10.1016/j.fshw.2021.12.011>
43. Babatunde Oluwafei Adetuyi, Odine, G., Peace Olajide Abiodun, Oluwakemi Semilore Omowumi, & Adetunji, C. O. (2024). Nanobioinsecticide and Nanoemulsions. 129–163. <https://doi.org/10.1002/9781394234769.ch48>
44. Bimpizas-Pinis, M., Santagata, R., Kaiser, S., Liu, Y., & Lyu, Y. (2022). Additives in the food supply chain: Environmental assessment and circular economy implications. *Environmental and Sustainability Indicators*, 14, 100172. <https://doi.org/10.1016/j.indic.2022.100172>
45. Gana, M., Isibor, P. O., Damisa, J. I., Iseghohi, F., Musa, I. O., & Oyewole, O. A. (2024). Nanoparticle-Based Remediation and Environmental Cleanup. 161–181. [https://doi.org/10.1007/978-3-031-54154-4\\_9](https://doi.org/10.1007/978-3-031-54154-4_9)
46. Gupta, P., Sharma, A., & Mittal, V. (2024). The Beauty Revolution of

- Nanotechnology: Unveiling the Impact of Cosmetic Nano Wonders. PubMed. <https://doi.org/10.2174/0122117385309082240924051320>
47. Mishra, D., & Khare, P. (2021). Emerging Nano-agrochemicals for Sustainable Agriculture: Benefits, Challenges and Risk Mitigation. *Sustainable Agriculture Reviews*, 235–257. [https://doi.org/10.1007/978-3-030-63249-6\\_9](https://doi.org/10.1007/978-3-030-63249-6_9)
48. Rani, N., Duhan, A., Pal, A., Kumari, P., Beniwal, R. K., Verma, D., Goyat, A., & Singh, R. (2023). Are nano-pesticides really meant for cleaner production? An overview on recent developments, benefits, environmental hazards and future prospectives. *Journal of Cleaner Production*, 411, 137232. <https://doi.org/10.1016/j.jclepro.2023.137232>
49. Sheik, M., Santhosh Shanthi Bhupathi, Mohammad, E. B., Durairaj Kaliannan, Balasubramanian, B., & Subramania Nainar Meyyanathan. (2021). Biologically Synthesized Plant-Derived Nanomedicines and Their In vitro-- In vivo Toxicity Studies in Various Cancer Therapeutics: Regulatory Perspectives. *Nanotechnology in the Life Sciences*, 217–260. [https://doi.org/10.1007/978-3-030-76263-6\\_9](https://doi.org/10.1007/978-3-030-76263-6_9)
50. Zargar, M., Bayat, M., Saquee, F. S., Diakite, S., Ramzanovich, N. M., & Akhmadovich, K. A. S. (2023). New Advances in Nano-Enabled Weed Management Using Poly(Epsilon-Caprolactone)-Based Nanoherbicides: A Review. *Agriculture*, 13(10), 2031. <https://doi.org/10.3390/agriculture13102031>