

ICOPMAP SPECIAL EDITION

REVIEW

Microemulsion technology: Nanoparticle-based emulsion as a sustainable natural product formulation

Mikael Ham Sembiring , Arsyadi , Taufik Riadi 

Faculty of Military Pharmacy, Indonesia Defense University, Sentul, Bogor, Indonesia

Keywords

Essential oil
Microemulsion
Nanoparticle
Natural product
Sustainable technology

Correspondence

Arsyadi
Faculty of Military Pharmacy
Indonesia Defense University
Bogor
Indonesia
arsyadi064@gmail.com

Abstract

Natural products refer to chemicals or compounds from living creatures occurring naturally in the environment. Natural commodities, such as spices, herbs, and medical remedies, are often used as additions. Natural products have many advantages, such as their environmentally sustainable nature, compatibility with the skin, affordability, and widespread availability. Nevertheless, developing natural products has several challenges, such as limited options for ingredients, functional limitations of natural substances, considerations about stability and preservation, consumer perceptions and expectations, and the variability in the composition of natural products. Microemulsions are prevalent emulsions that incorporate nanoparticles. A microemulsion is a homogeneous, transparent liquid consisting of oil, water, and a surfactant, often combined with a cosurfactant. The use of microemulsions has been extensively observed in many chemical and pharmacological applications owing to their unique attributes, such as a significant interfacial area, little interfacial tension, and the ability to solubilise and deliver hydrophobic substances. Therefore, the present review paper aims to comprehensively analyse microemulsion technology and its applications as an environmentally friendly formulation for natural products. Here, we propose strategies and research on microemulsions to overcome problems in natural product formulations.

Introduction

Developing environmentally friendly formulations has emerged as a critical topic of discussion in various industries, including the cosmetics, personal care, and home care sectors. Increased consumer demand for environmentally and socially responsible goods drives this sustainability movement forward. Sustainable formulation ideas are becoming an increasingly important focus for businesses to align themselves with the most recent green trends and address the environmental effects of their goods (Marinho *et al.*, 2022). Conventional formulations often produce excessive waste or depend on non-renewable resources. Sustainable formulations emphasise the efficient use of resources, focusing on renewable ingredients, decreased energy usage, and limited

utilisation of hazardous compounds (Martins *et al.*, 2023).

Natural products are environmentally friendly substances that provide several benefits. Natural products are widely used in pharmaceuticals as a source for drug discovery and as lead compounds for drug development. Approximately 35% of the yearly worldwide pharmaceutical market comprises natural goods or their derivatives. This category mostly includes plant-derived compounds, accounting for 25% of the market, followed by microorganisms at 13% and animal sources at 3% (Najmi *et al.*, 2022).

Natural products are often used in the form of essential oils. Essential oils have complex combinations of volatile molecules obtained from plants. Essential oils have many benefits in pharmaceuticals, cosmetics, botany, and food and beverages (Irshad, *et al.*, 2020).

Most of the chemicals found in essential oils are terpenes, esters, aldehydes, ketones, alcohols, and phenols. Different plant types, growth conditions, harvest times, and the part of the plant used for extraction can all change the chemicals that make up essential oils (Dhifi *et al.*, 2016).

Microemulsion technology

According to Danielsson and Lindman (1981), a microemulsion is a system of water, oil, and an amphiphile, a single optically isotropic and thermodynamically stable liquid solution. The components of a microemulsion mixing system include air, oil, surfactant, and cosurfactant. Preconditioning using surfactants and cosurfactants lowers surface tension, resulting in thermodynamically stable microemulsions (Souto *et al.*, 2022). Because the size of the particles in microemulsions ranges from 10 nm to 100 nm, the microemulsions look visibly translucent.

Thermodynamic stability, visual clarity, enhanced lipophilic substance solubility, enhanced bioavailability of active compounds, and enhanced penetration ability are among the advantages of using microemulsions (Sharma *et al.*, 2020).

The use of high-frequency ultrasound has created microemulsions containing essential oils. In addition, several methods can be used in making microemulsions (Figure 1) (Racovita *et al.*, 2023):

- Method of phase inversion: This approach involves adding an extra dispersed phase to the surfactant system under temperature control, resulting in phase inversion. Drug and agrochemical particle size decreases during phase inversion, resulting in active release kinetics.
- Method of phase titration: This mechanism, known as spontaneous emulsification, may be shown using phase diagrams. The phase diagram helps analyse interactions between microemulsion components during mixing.

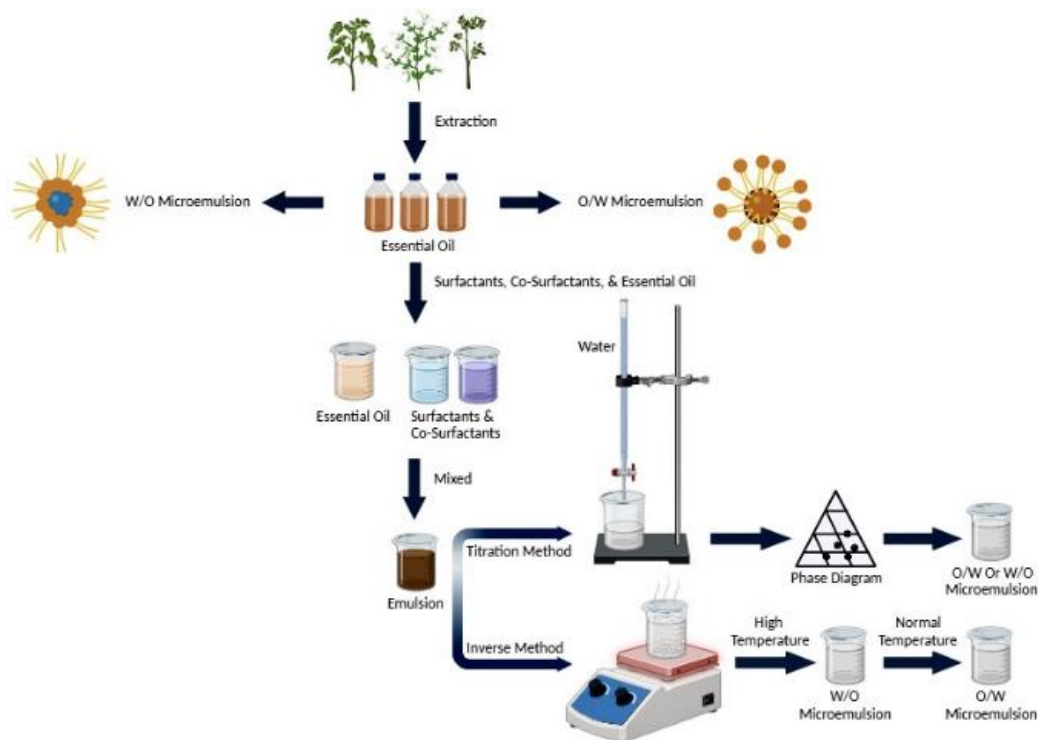


Figure 1: Essential oils are obtained by extracting the designated herbs. Subsequently, a comprehensive examination is conducted to determine the configuration of the desired microemulsion and whether it adopts the water-in-oil (W/O) or oil-in-water (O/W) composition. The selection of surfactant and co-surfactant should be predicated upon their safety and efficacy. Subsequently, a combination of surfactants, co-surfactants, and essential oils is blended inside a singular receptacle. Two distinct procedures are used in producing microemulsions: the titration method and the inverse approach. The titration approach does not use an inverse phase but utilises a phase diagram to ascertain the optimal combination of oil and surfactant. Conversely, the inverse method involves a phase inversion phenomenon occurring in the microemulsion due to temperature variation.

Application of microemulsion essential oil

Previous research has demonstrated the antimicrobial properties of peppermint, oregano, and rosemary essential oils when formulated as microemulsions. These oils are effective against *Escherichia coli* and *Listeria monocytogenes*, with minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) values 20-75% lower than the non-encapsulated essential oils (Dávila *et al.*, 2020). Microemulsions containing essential oils have shown notable efficacy in repelling insects, giving a viable and ecologically sustainable substitute for mosquito larvicides and agricultural pest control. Furthermore, Pavela *et al.* report that using microemulsions containing *Apiaceae* essential oils has shown efficacy as mosquito larvicides. These microemulsions have LC50 values ranging from 1.45 to 4.01 ml L⁻¹, indicating their potency in inducing larval death (Pavela *et al.*, 2019).

Deeper research proves the penetration-enhancing effects of clove oil, peppermint oil, and tea tree oil microemulsion, which may be attributed to the terpenic components present in these oils (Thakur *et al.*, 2021). Specific terpene components, such as limonene, menthol, carvone, and thymol, have minimal systemic toxicity and excellent skin penetration-

boosting qualities. In addition to these, because of their ability to increase penetration, fatty acid esters, such as ethyl oleate and isopropyl myristate, and monounsaturated fatty acids, such as oleic acid, have also been widely used for the hydrophobic phase of Microemulsion production. This finding underscores their therapeutic potential and suggests their use as vehicles for drug delivery (Ait-Touchente *et al.*, 2023).

The composition of the essential oil obtained from *Lavandula angustifolia* Mill. Consists of many compounds, such as linalool, linalyl acetate, geraniol, and β -caryophyllene. The microemulsion oil derived from *Lavandula angustifolia* exhibited notable antibacterial effects against *Klebsiella pneumoniae*, MRSA, and *Staphylococcus aureus*. The MIC measurements for these bacteria were determined to be 32, 16, and 16 $\mu\text{g/mL}$, respectively. However, the microemulsion oil showed little effectiveness against *Proteus mirabilis*. The recently produced formulation of nano-gold and nano-*Lavandula angustifolia* demonstrated complete eradication of pre-existing *P. mirabilis* biofilm. The MIC and minimum biofilm eradication concentration (MBEC) values for this formulation were determined to be 8 and 16 g/mL, respectively (Figure 2) (Fadel *et al.*, 2023).

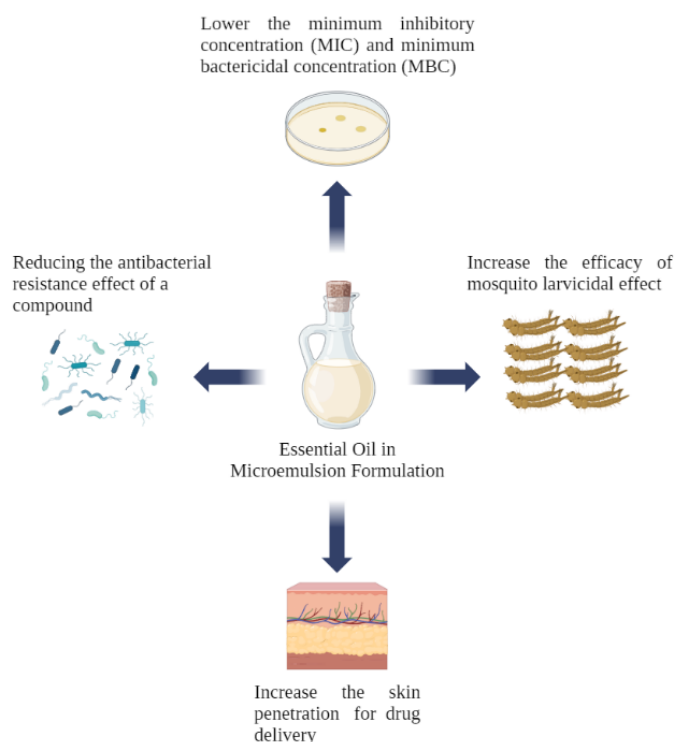


Figure 2: Microemulsions containing essential oils have shown efficacy in preventing bacterial resistance, reducing minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC), enhancing the anti-larval activity against mosquitoes, and improving the skin penetration of chemicals

Conclusion

Microemulsion technology allows for particle size reduction from 100 nm to 400 nm. Thermodynamically stable microemulsions may be produced, and this approach can decrease surface voltage. Furthermore, using microemulsion technology for vegetable essential oils may improve the antibacterial effect, boost the killing impact against mosquito larvicides, and increase active chemical absorption. It can also be used as an agricultural pest management method.

Acknowledgement

Figure 1 & Figure 2 were made with BioRender.com.

Source of funding

This research received no external funding.

Conflicts of Interest

The authors declare no conflict of interest.

References

Ait-Touchente, Z., Zine, N., Jaffrezic-Renault, N., Errachid, A., Lebaz, N., Fessi, H., & Elaissari, A. (2023). Exploring the versatility of microemulsions in cutaneous drug delivery: Opportunities and challenges. *Nanomaterials*, **13**(10), 1688. <https://doi.org/10.3390/nano13101688>

Dhifi, W., Bellili, S., Jazi, S., Bahloul, N., & Mnif, W. (2016). Essential oils' chemical characterization and investigation of some biological activities: A critical review. *Medicines*, **3**(4), 25. <https://doi.org/10.3390/medicines3040025>

Dávila-Rodríguez, M., López-Malo, A., Palou, E., Ramírez-Corona, N., & Jiménez-Munguía, M. T. (2020). Essential oils microemulsions prepared with high-frequency ultrasound: Physical properties and antimicrobial activity. *Journal of Food Science and Technology*, **57**, 4133–4142. <https://doi.org/10.1007/s13197-020-04449-8>

Danielsson, I., & Lindman, B. (1981) The definition of microemulsion. *Colloids Surf.*, **3**, 391–392. [https://doi.org/10.1016/0166-6622\(81\)80064-9](https://doi.org/10.1016/0166-6622(81)80064-9)

Fadel, B. A., Elwakil, B. H., Fawzy, E. E., Shaaban, M. M., & Olama, Z. A. (2023). Nanoemulsion of *Lavandula angustifolia* essential oil/gold nanoparticles: Antibacterial effect against multidrug-resistant wound-causing bacteria. *Molecules*, **28**(19), 6988. <https://doi.org/10.3390/molecules28196988>

Irshad, M., Subhani, M. A., Ali, S., & Hussain, A. (2020). Biological importance of essential oils. *Essential Oils-Oils of Nature*, **1**, 37–40. <http://dx.doi.org/10.5772/intechopen.87198>

Marinho, V. H., Neves, F. B., Jimenez, D. E., Oliveira, F. R., Santos, A. V. T., Ferreira, R. M., ... & Ferreira, I. M. (2022). Development of an environmentally friendly formulation of silk fibroin combined with fatty acid from *Astrocaryum murumuru* Mart. effective against *Aedes aegypti* larvae. *Journal of Drug Delivery Science and Technology*, **75**, 103626. <https://doi.org/10.1016/j.jddst.2022.103626>

Martins, A. M., & Marto, J. M. (2023). A sustainable life cycle for cosmetics: From design and development to post-use phase. *Sustainable Chemistry and Pharmacy*, **35**, 101178. <https://doi.org/10.1016/j.scp.2023.101178>

Najmi, A., Javed, S. A., Al Bratty, M., & Alhazmi, H. A. (2022). Modern approaches in the discovery and development of plant-based natural products and their analogues as potential therapeutic agents. *Molecules*, **27**(2), 349. <https://doi.org/10.3390/molecules27020349>

Pavela, R., Benelli, G., Pavoni, L., Bonacucina, G., Cespi, M., Cianfaglione, K., ... & Maggi, F. (2019). Microemulsions for delivery of Apiaceae essential oils—Towards highly effective and eco-friendly mosquito larvicides? *Industrial Crops and Products*, **129**, 631–640. <https://doi.org/10.1016/j.indcrop.2018.11.073>

Racovita, R. C., Ciuca, M. D., Catana, D., Comanescu, C., & Ciocirlan, O. (2023). Microemulsions of nonionic surfactant with water and various homologous esters: Preparation, phase transitions, physical property measurements, and application for extraction of tricyclic antidepressant drugs from aqueous media. *Nanomaterials*, **13**(16), 2311. <https://doi.org/10.3390/nano13162311>

Sharma, A., Dubey, S., & Iqbal, N. (2021). *Microemulsion formulation of botanical oils as an efficient tool to provide sustainable agricultural pest management*. Nano-and Microencapsulation-Techniques and Applications. IntechOpen. <https://doi.org/10.5772/intechopen.91788>

Souto, E. B., Cano, A., Martins-Gomes, C., Coutinho, T. E., Zielińska, A., & Silva, A. M. (2022). Microemulsions and nanoemulsions in skin drug delivery. *Bioengineering*, **9**(4), 158. <https://doi.org/10.3390/bioengineering9040158>

Thakur, D., Kaur, G., Puri, A., & Nanda, R. (2021). Therapeutic potential of essential oil-based microemulsions: reviewing state-of-the-art. *Current Drug Delivery*, **18**(9), 1218–1233. <https://doi.org/10.2174/1567201818666210217161240>