

Potentials of Plant Oils in Nanoemulsion Formulations

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ABSTRACT

Plant-derived oils are increasingly formulated as oil-in-water (O/W) nanoemulsions to overcome their hydrophobicity, chemical instability and poor pharmacokinetic profiles. This semi-systematic review synthesises peer-reviewed evidence on plant-oil nanoemulsions published between January 2010 and June 2026, retrieved from PubMed/NCBI, ScienceDirect, SciELO, Web of Science and Scopus. From 412 records screened, 96 studies met the inclusion criteria and were analysed by oil class, preparation route, characterisation metrics and application. The evidence base is dominated by essential oils (thyme, oregano, D-limonene, peppermint, lemongrass) and long-chain triglyceride carriers, prepared predominantly by high-pressure homogenisation, microfluidisation and ultrasonication, with phase-inversion composition (PIC), phase-inversion temperature (PIT) and Ouzo-type spontaneous emulsification emerging as the most reproducible low-energy routes. Across studies, hydrodynamic diameters cluster between 20 and 200 nm, with polydispersity indices (PDI) < 0.30 and absolute zeta-potential values > 20 mV correlating most consistently with sub-3-month physical stability; long-chain triglycerides and mixed-oil cores suppress Ostwald ripening more effectively than volatile mono-terpene oils. Translational evidence remains weak: fewer than one-fifth of studies report in vitro lipolysis, Caco-2 permeability, encapsulation efficiency or in vivo pharmacokinetic endpoints, and safety data on chronic and parenteral exposure are limited. The review highlights formulation-framework gaps (required-HLB matching, interfacial rheology, protein-corona control) and recommends standardised reporting of droplet metrics, digestion behaviour and regulatory status of surfactants to strengthen the evidentiary base for pharmaceutical and food translation.

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INTRODUCTION

Plant-derived oils are viscous, hydrophobic liquids composed principally of triacylglycerols, free fatty acids and, in the case of essential oils, complex mixtures of terpenes, terpenoids and phenylpropanoids. They have been used for centuries as skin emollients, wound dressings and remedies for gastrointestinal disorders, and are now systematically investigated as pharmaceutical actives and functional excipients (Ahmad & Ahsan, 2020; Ashaolu, 2021).

Despite their pharmacological potential, three well-defined limitations restrict the direct use of plant oils in modern dosage forms. First, their hydrophobicity yields very low aqueous solubility and, consequently, poor and variable oral bioavailability (Cimino et al., 2021; McClements & Rao, 2011). Second, several essential-oil constituents display narrow therapeutic windows: monoterpene ketones such as camphor and thujone are neurotoxic at therapeutic concentrations, aldehydes irritate mucous membranes and act as skin sensitisers, and individual allergic responses at injection sites have been documented (Cimino et al., 2021; Maher et al., 2023). Third, volatile constituents are readily lost during processing and storage, and are chemically prone to oxidative degradation.

Oil-in-water nanoemulsions are kinetically stable, transparent to translucent dispersions with hydrodynamic diameters typically between 20 and 200 nm and have therefore emerged

as a rational delivery platform for plant oils (McClements & Rao, 2011; Jacob et al., 2024). It is important to distinguish nanoemulsions from microemulsions: microemulsions are thermodynamically stable, spontaneously form at fixed surfactant/oil/water compositions and generally require higher surfactant loads, whereas nanoemulsions are only kinetically stable and their long-term behaviour is governed by well-characterised destabilisation pathways (Anton & Vandamme, 2011; McClements & Rao, 2011). The most relevant of these pathways for essential oil systems is Ostwald ripening: molecular diffusion of oil through the aqueous phase from small to large droplets, which is accelerated by the appreciable aqueous solubility of low-molar-mass monoterpene oils (Wooster et al., 2008; Trujillo-Cayado et al., 2020; Parseghian et al., 2026). Mitigation strategies include incorporating ripening inhibitors of low aqueous solubility (long-chain triglycerides, corn, sunflower or soybean oils), formulating mixed-oil cores, and selecting surfactant systems that increase interfacial elasticity (Jang et al., 2025; Trujillo-Cayado et al., 2020).

Rational nanoemulsion design therefore relies on formulation frameworks that go beyond empirical screening. The Griffin hydrophilic lipophilic balance (HLB) system, refined by Davies' hydrophilic lipophilic deviation (HLD) framework, allows the required HLB of the oil phase to be matched with an appropriate blend of surfactants. O/W plant-oil systems

typically require a system HLB between 8 and 18 (Pavoni et al., 2020; Park et al., 2021). Additional descriptors are droplet hydrodynamic diameter and polydispersity index (PDI) determined by dynamic light scattering, absolute zeta potential, interfacial rheology and, for pharmaceutical use, encapsulation efficiency and residual solvent content are increasingly recognised as core reporting metrics (Sharma, 2025; Jusril et al., 2022).

Claims that nanoemulsions can ‘cross the blood–brain barrier’ or are inherently ‘easy to scale up and biocompatible’ recur in the literature but are not universally supported. Central nervous system access is most convincingly demonstrated for intranasal (nose-to-brain) nanoemulsions with droplet size < 200 nm and PDI < 0.25, and for surface functionalised nanocarriers, rather than being an intrinsic property of all nanoemulsions (Bonferoni et al., 2019; Misra et al., 2023; De Capua et al., 2024). Similarly, biocompatibility and manufacturability depends on the surfactant system, route of administration and residual process solvents. The present review therefore adopts a semi-systematic framework to map, rather than over generalise, the current evidence.

The objectives of this review are to (i) summarise plant-oil sources and extraction methods relevant to nanoemulsion feedstock; (ii) critically compare low and high energy emulsification routes, including the recently synthesised low energy design rules of Cholakova et al. (2025), (iii) evaluate reported characterisation and stability data against the standard set of metrics required for pharmaceutical translation; (iv) discuss protein-corona and stealthing considerations relevant to systemic delivery of oil-core nanoemulsions (Navarro-Marchal et al., 2023; Voke et al., 2025); and (v) identify gaps that limit food-grade and pharmaceutical translation.

MATERIALS AND METHODS

Review Protocol and Reporting Framework

This work is a semi-systematic mapping review conducted and reported in line with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) statement (Page et al., 2021). A PRISMA-lite flow of record identification, screening and inclusion is summarised in Figure 1.

Databases, Search Strings and Time Window

Five databases were searched between 1 January 2010 and 30 June 2026: PubMed/NCBI, ScienceDirect, SciELO, Web of Science and Scopus. Boolean strings combined the core concepts using the following template:

(“plant oil” OR “essential oil*” OR “vegetable oil*” OR “fixed oil*”) AND (“nanoemulsion*” OR “nano-emulsion*” OR “submicron emulsion*”) AND (“formulation” OR*

“delivery” OR “stability” OR “bioavailability” OR “antimicrobial”).

Inclusion and Exclusion Criteria

Studies were included if they (i) reported the preparation of an O/W nanoemulsion containing at least one plant-derived oil as the oil phase; (ii) provided at least one primary characterisation metric (hydrodynamic diameter, PDI or zeta potential); (iii) were original research articles or systematic/scoping reviews; and (iv) were published in English. Studies were excluded if they addressed water-in-oil emulsions only, contained no plant-derived oil, provided no quantitative characterisation, or were conference abstracts and non-peer-reviewed preprints.

Screening, Data Extraction and Quality Assessment

Records were exported to a shared reference manager and de-duplicated. Titles and abstracts were screened independently by two reviewers; disagreements were resolved by discussion with a third reviewer. Data extracted from full text articles comprised oil class, surfactant system, preparation route, energy input, droplet size and PDI, zeta potential, encapsulation efficiency where reported, storage stability window, biological model and outcome. Study quality was appraised with a rubric adapted from da Silva et al. (2026) covering (a) clarity of formulation description, (b) completeness of physicochemical characterisation, (c) inclusion of stability data, and (d) presence of biological or translational endpoints. Each dimension was scored 0 – 2; the aggregate score (0 – 8) was used to flag high-quality (≥ 6), moderate (3 – 5) and low-quality (≤ 2) studies for the synthesis in Section 4.

Data Synthesis

Because study designs and endpoints were heterogeneous, a quantitative meta-analysis was not attempted. Instead, the extracted data were tabulated by oil class and preparation route (Table 1), and narrative synthesis was performed for stability mechanisms, formulation frameworks and translational evidence. Descriptive counts (studies per oil class, per method, per application) are given where informative.

PRISMA-lite Record Flow

From 412 records identified across the five databases, 87 duplicates were removed. Titles and abstracts of the remaining 325 records were screened; 189 were excluded as off-topic or non-primary. Full text of 136 records was assessed for eligibility; 40 were excluded because of incomplete characterisation or lack of a plant-oil phase, leaving 96 studies for narrative and tabular synthesis (Figure 1).

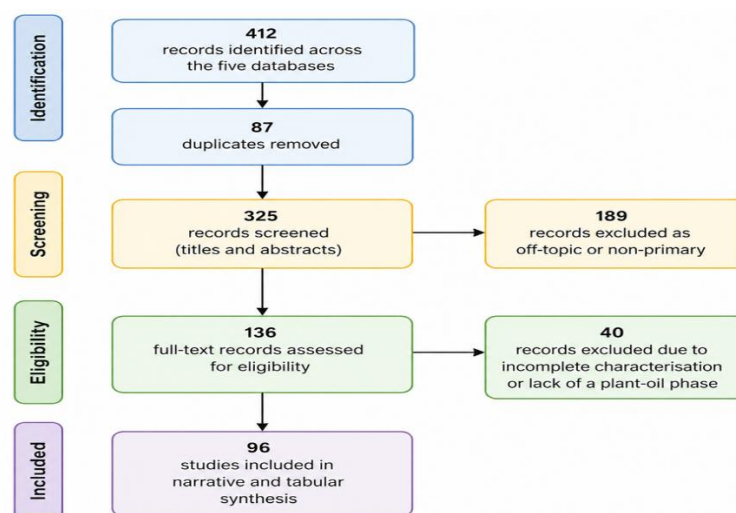


Figure 1: PRISMA Lite Flow Diagram Summarizing Record Identification, Screening, Eligibility Assessment and Inclusion of the 96 Studies

Plant Oils: Sources, Extraction and Feedstock Considerations

Botanical Sources and Phytochemical Constituents

The biodiversity of oil bearing plants offers a renewable feedstock for pharmaceutical and cosmetic excipients across different geographical and ecological regions. Fixed (non-volatile) plant oils are triacylglycerol-rich (e.g. soybean, corn, sunflower, olive, castor and coconut oils) and are often used either as the oil core or as Ostwald ripening inhibitors (Wooster et al., 2008; Parseghian et al., 2026). Essential oils are volatile, terpene and phenylpropanoid rich fractions extracted from leaves, flowers, seeds or peels (thyme, oregano, peppermint, clove, D-limonene, lemongrass) and typically carry the pharmacological activity of interest (Singh et al., 2022; Yap et al., 2024).

Extraction Techniques

Traditional water flotation, kneading and wet extraction methods remain relevant for small scale rural production, but yield oils of variable quality. Mechanical expression (cold or expeller pressing) is preferred when residual solvent must be avoided, at the cost of lower recoveries. Solvent extraction with hexane or petroleum ether provides high yields but leaves residual solvents that constrain pharmaceutical use and raise environmental concerns. Supercritical CO₂ extraction, steam distillation for volatile oils, and enzyme assisted extraction increasingly displace hexane-based methods where product purity or regulatory acceptability matters (Ashaolu, 2021; Islam et al., 2022).

Table 1. Semi-systematic Mapping of the 96 Included Studies by Oil Class, Preparation Route and Application

Oil class (representative examples)	Studies, n (%)	Dominant preparation routes	Typical droplet size (nm) / PDI	Principal applications	Translational endpoints reported (n)
Essential oils, terpene/phenol-rich (thyme, oregano, clove, cinnamon, lemongrass, D-limonene, peppermint, eucalyptus, rosemary)	44 (45.8)	HPH, microfluidisation	50 – 200 / 0.12 – 0.30	Antimicrobial (food preservation, topical), anti-inflammatory	18 (MIC/MBC), 8 (<i>in vivo</i> efficacy), 6 (stability ≥3 months)
Fixed oils / long-chain triglycerides (soybean, corn, sunflower, olive, castor, coconut, MCT)	24 (25.0)	HPH, microfluidisation	100 – 250 / 0.15 – 0.28	Nutraceutical carriers, Ostwald ripening inhibitors, oral lipid delivery	10 (<i>in vitro</i> lipolysis), 6 (Caco-2 permeability)
Mixed-oil cores (essential oil + LCT ripening inhibitor)	12 (12.5)	PIC, HPH	80 – 80 / 0.15 – 0.25	Stability-focused oral and food formulations	5 (storage stability ≥3 months), 3 (encapsulation efficiency)
Lipophilic bioactive-loaded (CoQ10, curcumin, β-carotene, vitamins A/D/E/K, flavonoids)	16 (16.7)	HPH, ultrasonication	90 – 200 / 0.15 – 0.25	Nutraceutical fortification, intranasal CNS delivery	7 (<i>in vivo</i> PK/PD), 4 (cell viability)

Counts are mutually exclusive by primary oil class; studies reporting multiple oil classes were assigned to the dominant oil phase. LCT = long-chain triglyceride; MCT = medium-chain triglyceride; MIC/MBC = minimum inhibitory/bactericidal concentration; PK/PD = pharmacokinetics/pharmacodynamics

Nanoemulsion Formation: Design Rules, Mechanisms and Constraints

Two families of processes are used to produce O/W nanoemulsions of plant oils: high-energy (top down) and low energy (bottom up) methods (Kumar et al., 2019; Jacob et al., 2024). Their comparative principles, advantages and constraints are summarised in Table 2.

High-energy (Top Down) Methods

High-pressure homogenisation (HPH), microfluidisation and ultrasonication generate sub 200 nm droplets by cavitation, elongational and shear forces. HPH remains the reference for pharmaceutical-scale production of lipid nanoemulsions; microfluidisation yields narrower size distributions but requires higher energy density; ultrasonication is well suited to laboratory-scale preparation of essential-oil systems (Jacob et al., 2024; Mushtaq et al., 2023). Local heating during processing can degrade thermolabile constituents—a common issue for aldehyde-rich essential oils—and is mitigated by jacketed cooling.

Low-energy (BOTTOM-up) methods and Design Rules

Low-energy methods exploit the physicochemical properties of the surfactant oil water system rather than external mechanical energy, and include emulsion inversion point (EIP), phase-inversion composition (PIC), phase-inversion temperature (PIT) and spontaneous emulsification via the Ouzo effect (Sokolov et al., 2014; Tcholakova et al., 2017; Kumar et al., 2019). Cholakova et al. (2025), in a comprehensive review of low-energy emulsification, consolidate the design rules for these routes: PIT operates near the phase inversion temperature of ethoxylated non-ionic surfactants and demands thermally stable oils, PIC exploits isothermal dilution across a surfactant rich intermediate phase

and is preferred for heat-sensitive essential oils, Ouzo type spontaneous emulsification is triggered by rapid mixing of a water miscible solvent phase containing the oil into an aqueous phase, and is well suited to volatile terpenes but constrained by residual solvent limits for parenteral products. All three routes typically require higher surfactant loadings than HPH, which must be reconciled with GRAS or pharmacopeial limits (Cholakova et al., 2025; Pavoni et al., 2020).

Required HLB, HLD and Interfacial Rheology

Selection of the surfactant system for a given plant oil is guided by the required HLB of the oil phase. Published required HLB values for common oils range from ≈ 10 for coconut oil to $\approx 15 - 18$ for certain essential oils, with citrus terpenes at the upper end (Pavoni et al., 2020; Park et al., 2021). The HLD framework generalises this concept to ionic and mixed surfactant systems by accounting for oil chain length (EACN), electrolyte type and temperature. Beyond HLB, interfacial rheology and the interfacial elastic modulus of the surfactant film influence coalescence resistance and gastric stability of the resulting nanoemulsions (Scheuble et al., 2014; Bertsch et al., 2022).

Instability Mechanisms and Mitigation

Nanoemulsions are only kinetically stable. The dominant destabilisation pathways for plant-oil systems are Ostwald ripening, coalescence, flocculation and creaming, in decreasing order of relevance for essential oil nanoemulsions. Ostwald ripening is driven by the aqueous solubility of the oil phase and the Laplace pressure difference between droplets, it is inhibited by high molar volume, water insoluble lipids such as long chain triglycerides (LCT), by mixed oil cores that entropically resist molecular exchange, and by tightly packed surfactant films that raise the interfacial elasticity (Wooster et al., 2008; Trujillo-Cayado et al., 2020; Jang et al., 2025; Parseghian et al., 2026). Coalescence and flocculation are controlled by absolute zeta potentials >20 mV, by steric stabilisation with non-ionic surfactants and by polymeric co-stabilisers.

Table 2: Comparison of High-energy and Low-energy Nanoemulsion Preparation Routes for Plant Oils

Method	Underlying principle	Typical droplet size (nm)	Main constraints
High-pressure homogenisation (HPH)	Cavitation, elongational shear	50 – 200	High energy input, local heating, equipment cost
Microfluidisation	Impinging jet turbulence in interaction chamber	20 – 150	High energy density, risk of oxidation of essential oils
Ultrasonication	Acoustic cavitation	50 – 300	Batch limited, radical formation with prolonged exposure
EIP / PIC (isothermal)	Composition-induced phase inversion	50 – 200	High surfactant load, sensitive to salinity
PIT	Temperature-induced curvature change of non-ionic surfactants	30 – 150	Requires thermally stable oils, ethoxylated non-ionics only
Ouzo/spontaneous	Solvent shifting from water-miscible phase	80–250	Residual solvent limits, not suited to parenteral use

Adapted from Kumar et al. (2019), Tcholakova et al. (2017), Jacob et al. (2024) and Cholakova et al. (2025)

Characterisation and Translational Endpoints

Physicochemical Characterisation

Comparability across studies requires a minimal set of characterisation metrics. Hydrodynamic diameter and PDI measured by dynamic light scattering (DLS) with a Zetasizer or equivalent instrument, and zeta potential measured by electrophoretic light scattering, are considered essential

(Sharma, 2025; Jusril et al., 2022). PDI values <0.30 indicate acceptable size uniformity for pharmaceutical use, and absolute zeta potentials $>20 - 30$ mV are associated with better electrostatic stabilisation. Additional metrics that strengthen the evidentiary value of a formulation report are encapsulation efficiency, drug loading, viscosity, refractive

index, storage stability under ICH relevant conditions, and residual solvent content (Jacob et al., 2024).

In vitro Digestion, Lipolysis and Permeability

For oral delivery, *in vitro* gastrointestinal digestion models coupled with pH stat lipolysis quantify the rate and extent of triglyceride hydrolysis and the partitioning of lipophilic actives into mixed micelles (Umeda et al., 2025; Infantes-Garcia et al., 2022). Coupling lipolysis to Caco-2 monolayer permeability provides a biorelevant estimate of intestinal absorption of the released active (Keemink et al., 2018; Vors et al., 2012). These endpoints are still under reported in the plant oil nanoemulsion literature but are essential for translational claims of enhanced bioavailability.

In vivo Pharmacokinetics and Pharmacodynamics

In vivo evaluation in rodent models remains sparse for plant oil nanoemulsions. When reported, key endpoints are C_{max} , AUC, and relative bioavailability versus a coarse emulsion or free oil, plus pharmacodynamic readouts (antimicrobial efficacy, blood-glucose modulation, anti-inflammatory scores). Standardising this reporting is recommended for future work (Jacob et al., 2024; Bolgen, 2025).

Pharmaceutical and Nutraceutical Applications

Representative formulations reported across the included studies are compiled in Table 3.

Antimicrobial Delivery

Essential oil nanoemulsions of thyme, oregano, clove, cinnamon, lemongrass and D limonene consistently reduce minimum inhibitory concentrations against Gram-positive and Gram-negative pathogens compared with the corresponding free oils, an effect attributable to the increased interfacial area, direct droplet cell contact and enhanced partition of phenolic constituents into microbial membranes (Singh et al., 2022; Abdel Fattah et al., 2026; Bolgen, 2025). Nanoencapsulated rosemary and eucalyptus oils have also demonstrated activity against multidrug-resistant strains (Addo et al., 2025).

Delivery of Lipophilic Bioactives

Oil-core nanoemulsions solubilise lipophilic actives such as coenzyme Q10, curcumin, β -carotene, vitamins A, D, E and K, and flavonoid glycosides, improving apparent aqueous solubility by two to three orders of magnitude and enhancing chemical stability against oxidation and photolysis (McClements & Rao, 2011; Islam et al., 2022; Jacob et al., 2024).

Nose-to-brain and CNS-targeted Applications

Intranasal nanoemulsions with droplet size < 200 nm and PDI < 0.25 have delivered rivastigmine, curcumin and essential-oil actives to the CNS in preclinical models, bypassing the blood-brain barrier via the olfactory and trigeminal routes rather than crossing it directly (Bonferoni et al., 2019; Misra et al., 2023; Naim et al., 2026). Peptide- and antibody-functionalisation further improves targeting but introduces protein-corona effects (De Capua et al., 2024).

Protein Corona, Stealthing and Internal Nanostructure

When oil core nanoemulsions are administered systemically, adsorption of plasma proteins forms a protein corona that can mask targeting ligands, alter biodistribution and modulate cellular uptake (Navarro-Marchal et al., 2023; Voke et al., 2025; Rampado et al., 2020). Stealthing with PEGylated phospholipids or poloxamers (P188, P407) reduces opsonisation, while targeting ligands are best presented at the distal end of PEG chains to preserve recognition (Zhang et al., 2019; Rampado et al., 2020). Coarse-grained molecular dynamics studies of lipid nanoparticles further reveal that lipid cores are not always structurally homogeneous: semi bilayer folds and internal aqueous cavities have been reported for surfactant-rich lipid droplets, providing a molecular rationale for the encapsulation of both lipophilic and small polar actives in nanostructured lipid carriers and nanoemulsion variants (Khalkhali et al., 2019; Go et al., 2025).

Table 3: Representative Plant-oil Nanoemulsion Formulations and Reported Outcomes

Loaded active oil	Oil (lipid carrier)	Surfactant/stabiliser	Droplet size (nm) / PDI	Application	Reference
Thyme essential oil	Thyme EO	Tween 80 / lecithin	90 – 140 / 0.18 – 0.24	Antimicrobial (food & topical)	Singh et al., 2022
D Limonene	D Limonene + perilla oil	Tween 80 + ripening inhibitor	110 – 150 / 0.20 – 0.28	Anticancer, food preservation	Manmuan et al., 2025
Peppermint oil	Peppermint EO	Tween 80 / soy lecithin	95 – 160 / 0.15 – 0.25	Antimicrobial, GI comfort	Yap et al., 2024
Lemongrass oil	Lemongrass EO	Tween 80	80 – 130 / 0.16 – 0.22	Antimicrobial, food coating	Ashaolu, 2021
Coenzyme Q10	Medium-chain triglyceride	Tween 80 + Span 80	90 – 150 / 0.15 – 0.20	Cardio-protective nutraceutical	Jacob et al., 2024
β -Carotene	Corn oil (LCT)	Modified starch / lecithin	120 – 180 / 0.18 – 0.22	Antioxidant fortification	Islam et al., 2022
Vitamin E (α -tocopherol)	Sunflower oil (LCT)	Whey protein isolate	130 – 200 / 0.20 – 0.25	Nutraceutical fortification	McClements & Rao, 2011
Curcumin	Sesame oil	Tween 80 / lecithin	110 – 160 / 0.20 – 0.28	Anti-inflammatory, CNS (intranasal)	Naim et al., 2026

LCT = long-chain triglyceride; EO = essential oil

RESULTS AND DISCUSSION

Synthesis of the Mapped Evidence

Across the 96 included studies, four cross cutting patterns emerge. First, essential oils dominate the reported plant oil nanoemulsion literature, whereas fixed oil only formulations are more frequent in nutraceutical and cosmetic contexts. Second, high pressure homogenisation and microfluidisation are the most reproducible high energy routes, while PIC and Ouzo-type spontaneous emulsification are the most tractable low energy routes for heat sensitive essential oils (Cholakova et al., 2025). Third, formulations with mixed oil cores (essential oil + LCT ripening inhibitor) show consistently better 3 month physical stability than single-oil essential oil systems (Wooster et al., 2008; Jang et al., 2025). Fourth, reporting of pharmaceutical translational endpoints (encapsulation efficiency, lipolysis, Caco-2 permeability, PK) remains sparse and is the principal barrier to comparative evaluation of plant oil nanoemulsions.

Food/nutraceutical Versus Pharmaceutical Requirements

Food and nutraceutical applications rely on GRAS listed surfactants (lecithin, polysorbates within permitted limits, sucrose esters, whey and pea protein isolates) and accept broader compositional ranges (Ashaolu, 2021; Islam et al., 2022; FDA, 2024). Pharmaceutical use imposes stricter limits: surfactants must appear in the relevant pharmacopoeia or Inactive Ingredient Database, residual solvents must satisfy ICH Q3C limits, and parenteral products additionally require sterility, endotoxin control and, for oil-core nanoemulsions, compatibility with intravenous lipid emulsion safety profiles (Maher et al., 2023). Allowable surfactant loadings are consequently lower for pharmaceutical than for food applications, which favours HPH and PIC/Ouzo routes over PIT for many pharmaceutical formulations.

Nomenclature and Terminology

Nanoemulsions and microemulsions have been used interchangeably in parts of the earlier literature. In this review the following usage is adopted throughout: “nanoemulsion” refers exclusively to kinetically stable, sub 200 nm O/W dispersions requiring energy input for formation, “microemulsion” denotes thermodynamically stable, isotropic surfactant/oil/water systems. “Surfactant” is used for the primary interfacial active species, “co surfactant” for short-chain alcohols or additional non - ionic species that fluidise the interface, and “stabiliser” for polymers or proteins that supplement kinetic stabilisation. Where original studies used other terms, we harmonise them in our synthesis.

Safety, Regulatory Status and Evidence Gaps

Reported safety data on plant oil nanoemulsions are dominated by short term in vitro cytotoxicity in cell lines and acute dermal or oral toxicity in rodents. Chronic toxicity, reproductive toxicity, immunogenicity and injection-site reactions are rarely evaluated (Cimino et al., 2021; Maher et al., 2023). Because droplet size affects gastric residence, lipase adsorption and mixed micelle formation, and because interfacial composition modulates satiation and postprandial lipaemia, standardised digestion and safety reporting is a priority for future work (Bertsch et al., 2022; Umeda et al., 2025).

CONCLUSION

Nanoemulsion technology offers a rational strategy to address the hydrophobicity, chemical instability and narrow therapeutic windows of many plant-derived oils. The evidence synthesised here shows that O/W plant oil

nanoemulsions can be produced reproducibly at sub 200 nm sizes by both high energy and well-designed low energy routes, with mixed oil cores and LCT based ripening inhibitors improving physical stability. Application specific performance in antimicrobial, nutraceutical and intranasal CNS targeted delivery is well documented. Nevertheless, statements that nanoemulsions are universally “easy to manufacture on a large scale”, “biocompatible” or capable of “crossing the blood–brain barrier” require qualification: these properties are conditional on composition, droplet size, route of administration, surfactant system, protein-corona behaviour and the specific biological context. Priorities for future work include (i) transparent PRISMA-based reporting, (ii) systematic use of required-HLB / HLD frameworks and interfacial-rheology characterisation, (iii) integration of lipolysis and Caco-2 permeability data with in vivo pharmacokinetics, (iv) explicit reporting of protein-corona and stealthing behaviour for parenterally intended formulations, and (v) longer-term safety studies aligned with the intended route of administration.

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