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Review

Essential oil-loaded lipid nanoparticles for cancer therapy: current advances and limitations

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Abstract

Cancer is a major global public health concern. Despite advances in therapeutic strategies, its management remains challenging due to the limited number of effective treatment options. In this context, the exploration of novel therapeutic approaches has become increasingly important.

Essential oils (EOs) and their bioactive constituents have attracted increasing attention as natural products with diverse pharmacological properties, including notable anticancer activity. However, their clinical application is limited by their high volatility and physicochemical instability, which can compromise their therapeutic efficacy.

To address these limitations, the development of innovative delivery systems such as encapsulation within biocompatible lipid nanoparticles has emerged as a promising strategy to enhance their stability, improve bioavailability, and ultimately increase their therapeutic potential.

This review aims to summarize recent advances in lipid-based delivery systems for essential oils and highlight their potential in cancer therapy. Furthermore, current limitations as low stability, batch variability and scale-up processing are critically discussed. The future perspectives were settled, including the development of targeted and stimuli-responsive nanocarriers as well as strategies to facilitate clinical translation.

Keywords:

Essential oils, lipid, cancer, nanomedicine, phytochemicals, targeted delivery.

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Introduction

Nowadays, cancer is the leading cause of mortality worldwide, driven by population growth, aging, environmental exposure, and lifestyle-associated risk factors [1]. Although significant advances have been made in diagnosis and treatment, conventional chemotherapy drugs suffer from critical drawbacks, including poor aqueous solubility [2], cytotoxicity to healthy tissues, rapid clearance, and the emergence of multidrug resistance [3,4]. These challenges underscore the urgent need for innovative delivery systems that enhance therapeutic efficacy while minimizing off-target effects [5].

In this context, essential oils (EOs) have attracted significant attention as natural anticancer agents. They are complex mixtures of volatile phytochemicals extracted from medicinal plants, rich in terpenoids, phenylpropanoids [6], and phenolic compounds [7] [8]. EOs exhibit potent antitumor activities through several mechanisms, including induction of apoptosis [9], cell cycle arrest, inhibition of metastasis, and modulation of key signaling pathways such as PI3K [10], as well as downregulation of NF-κB, a transcription factor involved in anti-apoptotic processes [11]. For instance, carvacrol from *Origanum vulgare* and thymol from *Thymus vulgaris* demonstrate potent cytotoxicity against breast, colon, and lung cancer cell lines through reactive oxygen species (ROS) generation and mitochondrial disruption [12]. Despite their promising preclinical profiles, the clinical translation of EOs is severely hampered by inherent physicochemical limitations. EOs are highly hydrophobic, volatile, prone to oxidative degradation, and exhibit poor bioavailability due to rapid metabolism and limited systemic circulation [13]. These properties result in suboptimal pharmacokinetics, with therapeutic concentrations rarely sustained at tumor sites [14]. Traditional formulation strategies often fail to provide long-term stability or controlled release, leading to burst effects and reduced potency. Consequently, advanced nanocarrier systems are imperative to unlock the full therapeutic potential of EOs [15].

Lipid nanoparticles (LNs) including liposome, solid lipid nanoparticles, and nanostructured lipid carriers represent a versatile and biocompatible platform well suited for EOs encapsulation [16]. Composed of physiologically tolerated lipids, LNs feature a hydrophobic core that accommodates lipophilic payloads with high entrapment efficiency. Their nanoscale size (50-500 nm) enables passive tumor targeting via the enhanced permeability and retention (EPR) effect [17], while surface modifications such as PEGylation or ligand conjugation facilitate active targeting [18]. Moreover, LNs can provide sustained release profiles, protecting encapsulated drug or EOs from enzymatic degradation and enabling pH or enzyme-triggered release in the acidic tumor microenvironment [19]. The combination of EOs encapsulation within LNs has yielded remarkable anticancer outcomes in recent years. Chaouki et al. [20] reported an enhanced bioactivity of citral-loaded solid lipid nanoparticles (SLNs), with IC50 values of 18×10^{-5} M in MCF-7 breast cancer cells, attributed to improved cellular uptake and prolonged ROS-mediated apoptosis.

This review provides a comprehensive analysis of EOs encapsulation in LNs for anticancer applications, including synthesis strategies, physicochemical characterisation, release kinetics, and antitumor mechanisms across diverse cancer types. We critically evaluate studies from the last decade, highlighting trends in EOs selection, LN optimization for stimuli-responsiveness, and emerging hybrid systems. EOs-LNs hold considerable promise to revolutionize natural product-based nanomedicine, bridging phytochemistry and oncology toward safer and more effective therapies.

Essential oil composition

Essential oils are volatile and semi-volatile complex mixtures of phytochemicals synthesized as secondary metabolites in aromatic plants. Their composition is highly diverse and may include hundreds of individual compounds [21]. Terpene derivatives are the predominant constituents, comprising monoterpene C_{10}, e.g., limonene, linalool, α-pinene, γ-terpinene) and sesquiterpenes (C_{15}, β-caryophyllene, α-humulene, δ-cadinene), alongside minor fractions of phenylpropanoids (e.g., eugenol, cinnamaldehyde), aliphatic aldehydes, and phenolic derivatives [22].

The composition of essential oils is influenced by plant species, genotype, geographical origin, climate, soil conditions, developmental stage, harvesting season, and the plant organ used [23]. Consequently, essential oils obtained from the same botanical species may exhibit distinct chemotypes characterized by different dominant compounds [24], which can markedly affect their pharmacological properties, safety profile, and therapeutic performance. For instance, Origanum vulgare EOs is dominated by carvacrol and thymol [25], while Artemisia herba-alba is characterized by a high content of cis-thujone (25.5%) [26].

EOs anti-cancer activities

Essential oils (EOs) exhibit anticancer properties arising from their selective cytotoxicity, antiproliferative activity, and antimetastatic effects [27]. EOs exert anticancer effects through multiple molecular and cellular mechanisms. One of the primary pathways is the induction of apoptosis, mediated by the activation of caspases enzymes, upregulation of pro-apoptotic proteins such as Bax, and downregulation of anti-apoptotic proteins such as Bcl-2, ultimately leading to programmed cell death [28]. EOs also inhibit cell proliferation by arresting the cell cycle at various checkpoints (G0/G1, S, or G2/M) and modulating signalling pathways involved in cell growth, including PI3K/Akt and MAPK [29]. Furthermore, EOs generate reactive oxygen species (ROS), inducing oxidative stress that selectively damages cancer cells [30]. They can further modulate critical signaling pathways such as NF-κB and p53, suppress tumor invasion and migration by inhibiting matrix metalloproteinases (MMPs), and reduce angiogenesis through downregulation of vascular endothelial growth factor (VEGF) [30,31].

Combination of Essential Oils and chemotherapeutic drugs

Recent studies have demonstrated that the combination of essential oils or their bioactive constituents with conventional chemotherapeutic agents can significantly enhance anticancer efficacy through synergistic mechanisms. Rosemary essential oil has been shown to potentiate the cytotoxic activity of 5-fluorouracil in colorectal cancer cells by promoting apoptosis and reducing cell migration [32]. Similarly, β-caryophyllene and d-limonene have been reported to enhance the activity of paclitaxel and docetaxel, respectively [33,34], leading to increased cancer cell inhibition at lower drug concentrations. Furthermore, nanoformulation strategies combining essential oils with chemotherapeutic drugs, such as gemcitabine-loaded lipid nanocarriers, have demonstrated improved drug delivery and enhanced cytotoxic effects [35].

Lipid nanoparticles

Lipid nanoparticles (LNPs) are a class of nanocarriers composed of physiological or biocompatible lipids with spherical matrices (50-1000 nm) classified primarily into solid lipid nanoparticles (SLNs), nanostructured lipid carriers (NLCs), liposomes, nanoemulsions, and lipid -polymer hybrid nanoparticles [36], each distinguished by their internal architecture and lipid composition [37].

SLNs feature a solid lipid core of triglycerides such as Compritol or stearic acid stabilized by surfactants such as Tween 80 and Poloxamer 188, forming a hexagonal crystalline structure with lattice imperfections [38]. NLCs, considered second-generation lipid carriers, disrupt this crystallinity by blending solid lipids with liquid oils such as Miglyol® 812, yielding imperfect or amorphous matrices. They are generally classified into three subtypes : imperfect (oil-in-solid), amorphous (homogeneous blend), and multiple (oil-in-water compartments) [39].

Liposomes comprise unilamellar (small unilamellar vesicles, SUVs, ~30-100 nm; large unilamellar vesicles, LUVs, >100 nm) or multilamellar vesicles (MLVs) formed by phospholipid bilayers primarily phosphatidylcholine and cholesterol enclosing an aqueous core, thereby mimicking cell membranes and conferring superior biocompatibility and fusion [40]. Modern LNPs are typically composed of ionizable lipids (often representing ~40–60 mol%), helper phospholipids, cholesterol, and polyethylene

glycol (PEG)-lipids, assembled into a core–shell nanostructure [41]. In this architecture, ionizable lipids organize with aqueous payloads into inverse micellar domains within the particle core, while phospholipids and PEG-lipids contribute to surface stabilization. Such systems are particularly effective for encapsulating nucleic acids and lipophilic bioactives, including essential oil constituents. Their ionizable nature enables a near-neutral surface charge at physiological pH, followed by protonation in acidic endosomal compartments, promoting nanoparticle destabilization, membrane fusion, and efficient endosomal escape following cellular uptake.

Each LNP type exhibits distinct encapsulation behavior, release kinetics, stability profile, and biological performance, making formulation selection highly dependent on the intended therapeutic application [42]. Although SLNs offer good protection and controlled release their highly ordered crystalline matrix may limit drug loading and promote expulsion during storage. The incorporation of liquid lipids within NLCs generates a less ordered internal matrix, which increases loading capacity and reduces compound leakage during storage [43]. Liposomes differ structurally from SLNs and NLCs in that they are vesicular systems composed of one or more phospholipid bilayers enclosing an aqueous core; this amphiphilic architecture allows the simultaneous encapsulation of hydrophilic molecules within the aqueous compartment and lipophilic compounds within the lipid bilayer [44]. While SLNs and NLCs generally offer greater mechanical stability, liposomes provide a more biomimetic structure that facilitates membrane fusion. The final particle size of all three systems is often refined through extrusion or membrane filtration to ensure a narrow polydispersity index (PDI) suitable for clinical applications.

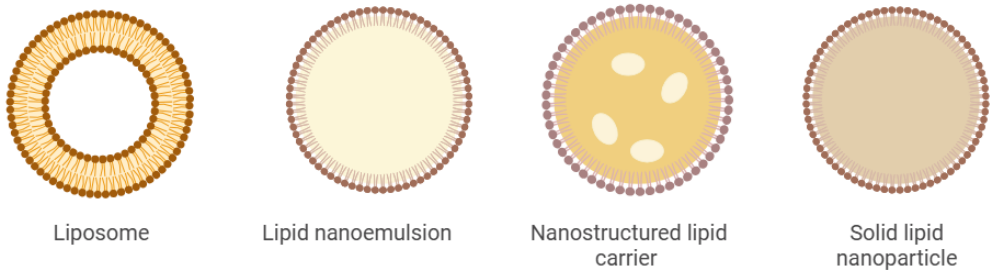

Figure 01. Schematic representation of major lipid nanoparticles (LNPs)

The selection of the optimal carrier have to be performed by the needed characteristics of the essential oil, the route of administration, and the desired therapeutic effect .Among lipid-based nanocarriers, NLCs appear to be the most promising vector for essential oil delivery due to their high encapsulation efficiency, reduced drug expulsion, and improved storage stability compared with conventional SLNs. Although liposomes exhibit excellent biocompatibility and clinical acceptance, their susceptibility to leakage and oxidation may compromise the long-term retention of volatile essential oil constituents. Nanoemulsions remain attractive because of their simple production and high loading capacity; however, their kinetic low stability limits long time storage. More recently, lipid nanoparticles and lipid–polymer hybrid nanoparticles have emerged as advanced delivery systems capable of combining high protection, controlled release, and active tumor-targeting strategies. Table 01 present a critical comparison between the different LNPs.

Table 01. Comparison between different LNPs formulations

Carrier	Stability	Biocompatibility	Loading efficiency	Processing limitation	Suitability for EOs loading
SLN	High stability	Excellent; composed of physiological lipids	Low loading due to highly ordered crystal	Lipid crystallization may cause EOs products expulsion during storage	Moderate
NLC	Very high stability	Excellent	Higher loading capacity	More complex formulation complex optimization of lipid ratios; possible formulation variability	Excellent
Liposomes	Moderate phospholipid oxidation and leakage	Excellent Biocompatible, clinically validated	moderate	Limited physical stability, costly phospholipids, sterilization challenges, potential leakage during storage	Excellent
Nano emulsion	Moderate limited long-term stability	Excellent	Very high	simple preparation but requires relatively high surfactant concentrations	Excellent
Lipid polymers	Very high; combines lipid biocompatibility with polymer stability	Excellent	high controlled release,	Expensive ionisable lipids Multi-step preparation, scale-up complexity, batch-to-batch variability	Highly

Synthesis of Lipid nanoparticles

The synthesis of lipid nanoparticles encompasses a variety of "top-down" and "bottom-up" strategies designed to stabilize volatile essential oils (EOs) within a biocompatible framework. High-Pressure Homogenization (HPH) remains the industrial gold standard for producing Solid Lipid Nanoparticles (SLNs) and Nanostructured Lipid Carriers (NLCs); this method forces a hot lipid-oil-surfactant mixture through a narrow valve at extreme pressures, using shear stress and cavitation to achieve a uniform nanometric dispersion [45]. For laboratory-scale preparation, Ultrasonication is frequently employed, utilizing acoustic energy to fracture lipid globules, though it requires careful temperature control to prevent the degradation of heat-sensitive EOs.

In contrast, the synthesis of liposomes which feature a distinct aqueous core surrounded by a phospholipid bilayer is typically achieved through Thin-Film Hydration (the Bangham method) [46]. In this process, lipids and EOs are dissolved in an organic solvent and evaporated to form a thin film, which is subsequently hydrated with an aqueous buffer to trigger the self-assembly of vesicles. Other "bottom-up" techniques, such as Solvent Evaporation and Ethanol Injection, rely on the rapid diffusion of an organic phase into an aqueous phase to induce supersaturation and controlled precipitation.

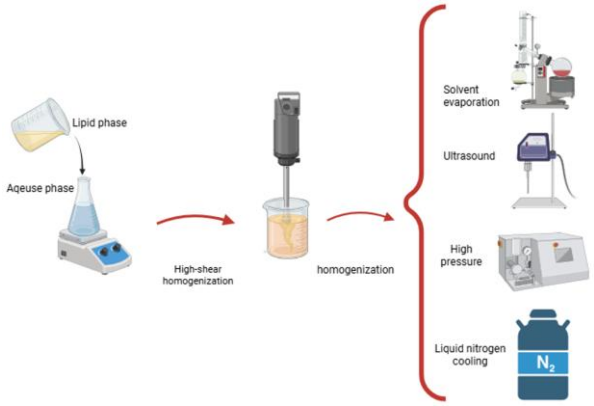

Figure 02. Schematic representation of major lipid nanoparticles (LNP) fabrication techniques

Characterisation of lipid nanoparticles

The characterisation of lipid nanoparticles is essential to evaluate their quality, stability, and suitability for drug delivery applications. Particle size and polydispersity index are commonly measured by dynamic light scattering, as they influence cellular uptake, biodistribution, and formulation homogeneity [47]. Zeta potential is determined to assess surface charge and colloidal stability, where higher absolute values generally indicate better dispersion stability. Morphological analysis is performed using transmission or scanning electron microscopy to observe particle shape and surface structure [48]. Encapsulation efficiency and drug loading capacity are measured to determine the amount of active compound successfully incorporated into the lipid matrix [49]. In addition, thermal and spectroscopic techniques such as differential scanning calorimetry and Fourier-transform infrared spectroscopy are used to study lipid crystallinity and possible interactions between the carrier and encapsulated compounds [50].

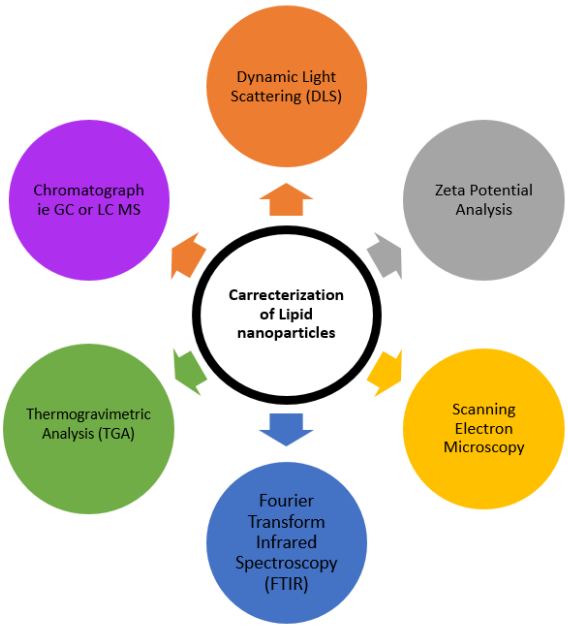

Figure 03. Schematic representation of Characterisation methods of lipid nanoparticles (LNP)

Anti-cancer activities of lipid nanoparticles loaded EOs

Several studies have investigated the anticancer activity of essential oil-loaded lipid nanoparticles; Table 02 summarizes the most recent research findings.

Table 02. Anti-cancer activities of lipid nanoparticles loaded EOs

Plant / EOs	LNP Type	Size (nm)	Cancer Target	Methodology & Model	Key Results	Reference
Rosa damascena	NLC	78.4	Breast	MDA-MB-231 cells	Induced superior apoptosis compared to free oil and cisplatin	[51]
Lavandula angustifolia	Liposomes	120	Breast	MCF-7 & SK-BR-3; (Bcl-2/Bax).	Downregulated Bcl-2; increased Caspase-3 expression 2-fold.	[52]
Croton argyrophyllus	SLN	185	Neuro blastoma	SH-SY5Y cells; DCFH-DA (ROS measurement).	Reduced oil toxicity to healthy cells; high antioxidant protection.	[53]
Foeniculum vulgare	SLN	55.4	Breast	MCF-7 Cell cycle analysis (Propidium Iodide).	Triggered significant sub-G1 arrest and DNA fragmentation.	[54]
Croton cajucara	NLC	38 –110	Lung	A549 & H1299; Cells ROS quantification.	Sustained intracellular ROS generation; improved terpene stability.	[55]
Satureja khuzistanica	SLN chitosan	279	Brreast	HFF and MCF-7 Cells	Inhibition of cancer cells by activating the internal pathway of apoptosis and cell cycle disruption	[56]
Zataria multiflora	SLN	176	melanoma	A-375 celles	Dose dependant anti proliferative effect	[57]
Ferula gummosa	Nano-emulsions	24	Colon	In vivo test and ht-29 cells	Concentration of 2,9 ug/ml Inhibited 50% of cancer cells	[58]
bergamot	Liposome	188	neuroblastoma	SH-SY5Y Cells	Bergamot EOs loaded liposomes outperform there non liposomal anti-cancer activities	[59]
Origanum glandulosum	Nano-Emulsion nanocapsule	20 - 34	Liver	HepG2 Cells	nanocapsules showed the strongest cytotoxic effect on liver cancer cell line Hep-G2 (54.93 µg/mL) in comparison to HD oil (73.13 µg/mL)	[60]

Although numerous investigations have reported promising anticancer effects of EO-loaded lipid nanoparticles, but most studies remain limited to in vitro experiments using a restricted number of cancer cell lines. Furthermore, experimental protocols vary considerably with respect to nanoparticle composition, essential oils concentration, exposure time, and biological endpoints, making direct

comparison between studies difficult. While several in vivo studies have demonstrated significant tumors growth inhibition, the majority of studies were conducted on xenograft mouse models that do not fully representative of the complexity of human tumors. Consequently, the current evidence, although encouraging, remains insufficient to predict therapeutic efficacy, highlighting the need for standardized preclinical evaluation and well-designed translational studies.

Targeting mechanism of lipid nanoparticles

Lipid nanoparticles achieve tumor targeting through both passive and active mechanisms that enhance drug accumulation at the diseased site while limiting systemic exposure [61]. Passive targeting primarily relies on the enhanced permeability and retention (EPR) effect [62], a hallmark of many solid tumors characterized by leaky vasculature, defective endothelial junctions (100–1000 nm), and impaired lymphatic drainage [63,64]. These features allow nanoscale carriers such as solid lipid nanoparticles (SLNs), nanostructured lipid carriers (NLCs), and liposomes to preferentially accumulate within tumor tissue following systemic administration [65]. Surface modification with polyethylene glycol (PEG) further prolongs circulation time by reducing opsonization and clearance by the mononuclear phagocyte system, thereby increasing the probability of tumor deposition [66,67]. In contrast, active targeting involves functionalization of the nanoparticle surface with specific ligands such as antibodies, peptides, aptamers, or small molecules as folic acid and transferrin that selectively bind to overexpressed receptors on cancer cells or tumor-associated endothelium [68]. This ligand–receptor interaction promotes receptor-mediated endocytosis, enhancing intracellular delivery of the encapsulated essential oils and improving therapeutic efficacy. Additionally, lipid nanoparticles can be engineered to respond to tumor-specific stimuli such as acidic pH, redox gradients, or enzymatic activity, enabling controlled drug release within the tumor microenvironment [69]. The combination of passive accumulation and active cellular targeting represents a synergistic strategy to maximize anticancer activity while minimizing off-target toxicity, making lipid-based nanocarriers highly promising platforms for precision oncology [70].

In vitro assay for cancer therapy investigation

The in vitro evaluation of anticancer activity of essential oil-loaded lipid nanoparticles commonly involves a combination of cytotoxicity, cellular uptake, mechanistic, and migration assays using established human cancer cell lines. Cell viability is typically assessed by colorimetric or fluorometric methods such as MTT, MTS, XTT, resazurin (Alamar Blue), or sulforhodamine B (SRB) assays, allowing determination of IC_{50} values and comparison with free essential oils or blank carriers [71–73]. Frequently used models include MCF-7 and MDA-MB-231 (breast cancer) [74], A549 (lung cancer), HeLa (cervical cancer), PC-3 (prostate cancer), HepG2 (liver cancer), and HT-29 or HCT116 (colorectal cancer) [75]. Selectivity is generally examined in parallel using non-tumoral cell lines such as fibroblasts or HEK293 cells [76]. Cellular internalization of fluorescently labeled nanoparticles is investigated by fluorescence microscopy, confocal laser scanning microscopy, or flow cytometry to confirm enhanced uptake relative to free oil [77,78]. Mechanistic studies often include apoptosis and necrosis quantification by Annexin V/propidium iodide staining, caspase-3/7 activation [79], mitochondrial membrane potential assays (JC-1 or Rh123), intracellular reactive oxygen species generation using DCFH-DA, DNA fragmentation, and cell-cycle analysis by flow cytometry [80]. Additional assays such transwell migration, colony formation, and spheroid penetration models are increasingly employed to evaluate anti-metastatic potential and effects in more physiologically relevant three-dimensional systems [81]. Collectively, these in vitro approaches consistently demonstrate that encapsulation of essential oils into lipid nanoparticles can enhance cytotoxic potency, improve cellular uptake, prolong intracellular retention, and potentiate apoptosis compared with non-encapsulated oils.

In-vivo assay for cancer therapy investigation

The in vivo evaluation of anticancer efficacy of lipid nanoparticles is primarily conducted in murine tumor models to assess therapeutic performance, biodistribution, systemic safety, and translational potential under physiological conditions [82]. Commonly used models include xenograft systems

generated by subcutaneous implantation of human cancer cell lines [83] such as MCF-7, MDA-MB-231, A549, HeLa, PC-3, and HepG2 in immunodeficient mice, as well as syngeneic models in immunocompetent mice to investigate tumor–immune interactions . Following intravenous, intraperitoneal, oral, or intratumoral administration, antitumor activity is generally determined by measuring tumor volume progression, tumor weight at sacrifice, survival rate, and inhibition percentage relative to untreated controls or free essential oil formulations [84]. Histopathological analyses of excised tumors commonly evaluate necrosis, mitotic index, angiogenesis, and apoptosis using hematoxylin–eosin staining, TUNEL assay, Ki-67, caspase-3, Bax/Bcl-2, and CD31 immunohistochemistry. Biodistribution studies using fluorescent, radiolabeled, or magnetic tracers frequently demonstrate enhanced tumor accumulation of lipid nanoparticles through prolonged circulation and passive targeting via the enhanced permeability and retention effect [85].

In vivo evaluation of anticancer activity of lipid nanoparticles also includes comprehensive safety assessment through hematological parameters [86], serum biochemical markers (ALT, AST, creatinine, urea), and histological examination of major organs such as liver, kidney, spleen, heart, and lung to detect systemic toxicity [87].

Translational Potential and Limitations of Essential

Despite their therapeutic promise, (EOs)-loaded lipid nanoparticles face significant limitations and challenges that hinder clinical translation [88]. Key hurdles include poor physical stability due to EOs volatility and lipid phase transitions, leading to drug expulsion during storage, low encapsulation efficiency for highly hydrophobic EOs, and batch-to-batch variability from polymorphic transitions [89]. Large-scale production [90], reproducibility across industrial bioreactors, supply chain constraints for GMP-grade lipids/cholesterol, and cost-effective sterilization without compromising EOs integrity. Safety concerns encompass potential cytotoxicity from surfactant overload as Tween 80 and Span 80 [91], also incomplete biodegradation yielding fatty acid metabolites, long-term immunogenicity of PEGylated surfaces [92].

Nevertheless, critical gaps persist. While in vitro and ex vivo data abound, robust in vivo pharmacokinetics, biodistribution studies, and long-term safety profiles remain scarce. Formulation challenges, including lipid-EOs interactions leading to polymorphic transitions or drug expulsion during storage, demand optimization. Furthermore, standardization of EOs composition given batch-to-batch variability and clinical-grade scalability represent hurdles to translation. Few reviews have holistically integrated the chemical engineering of EOs-LNPs systems with their anticancer pharmacology, leaving a void in guiding future innovations [93]. The translation of essential oil-loaded lipid nanoparticles from laboratory research to clinical application presents both significant opportunities and notable challenges. These nanosystems have demonstrated improved stability, bioavailability, tumor targeting, and anticancer efficacy compared with free essential oils, highlighting their potential as innovative therapeutic platforms. However, their clinical development remains constrained by issues such as variability in essential oil composition, limited standardization, formulation instability, large-scale manufacturing difficulties, and insufficient long-term safety data. Addressing these challenges through standardized production processes, comprehensive toxicological studies, and well-designed clinical trials will be essential for realizing the full therapeutic potential of EO-loaded lipid nanoparticles in cancer therapy.

Conclusion

Essential oil-loaded lipid nanoparticles represent a promising frontier in cancer therapy, effectively bridging the potent anticancer properties of natural volatile compounds with advanced delivery systems to enhance bioavailability, targeting specificity, and therapeutic efficacy.

These versatile carriers ranging from solid lipid nanoparticles and nanostructured lipid carriers to biomimetic liposomes overcome key limitations of free essential oils while minimizing the toxicity associated with conventional chemotherapeutics.

Despite ongoing challenges related to scalability, long-term stability, and regulatory validation, their demonstrated ability to induce apoptosis, reverse multidrug resistance, and act synergistically with

standard drugs positions them as a promising and greener alternative in precision oncology. Looking ahead, focused efforts on clinical translation, standardized formulation protocols, and personalized targeting strategies will be essential to fully unlock their therapeutic potential in addressing the global cancer burden.

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