

From Palm Fraction to Pharmaceutical Platform: Palm Stearin, Palm Kernel Lipids, and Palm Oil Esters in Oral, Topical, and Targeted Nanomedicine—A Translational Review

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Abstract

Lipid nanocarriers have become important pharmaceutical technologies for improving the solubility, stability, controlled release, bioavailability, and tissue distribution of therapeutic compounds. Solid lipid nanoparticles and nanostructured lipid carriers are particularly attractive because their physicochemical properties can be tailored through lipid composition, crystallinity, interfacial engineering, and manufacturing conditions. Palm-derived materials, including palm stearin, palm-kernel-derived lipids, palm olein, and chemically modified palm oil esters, represent an underexplored source of functional pharmaceutical lipids. This qualitative literature review critically examines their potential as structural matrices, liquid lipid phases, or functional excipients in oral, topical, ocular, pulmonary, intranasal, and targeted drug-delivery systems. The analysis integrates recent evidence on lipid selection, polymorphism, nanoparticle manufacturing, drug loading, release kinetics, gastrointestinal and dermal transport, cellular uptake, safety, scale-up, Quality by Design, regulatory qualification, and sustainability. Palm-stearin/palm-olein systems demonstrate that feedstock-specific lipid composition can be manipulated to generate imperfect nanostructured matrices capable of protecting and improving access to lipophilic compounds. However, most palm-specific evidence remains preclinical or originates from nutraceutical and dermocosmetic applications. Human pharmacokinetics, comparative therapeutic studies, pharmaceutical-grade raw-material specifications, chronic toxicology, sterilization, manufacturing reproducibility, and regulatory pathways remain insufficiently developed. A translational roadmap is therefore proposed in which palm-derived lipids progress from chemically standardised feedstocks through Quality-by-Design formulation, mechanistic characterisation, disease-relevant pharmacology, comparative pharmacokinetics, toxicology, scalable manufacture, and ultimately human evaluation.

Keywords: Palm Stearin, Palm Kernel Lipids, Palm Oil Esters, Solid Lipid Nanoparticles, Nanostructured Lipid Carriers, Lipid Nanomedicine, Oral Drug Delivery, Topical Drug Delivery, Targeted Therapy, Pharmaceutical Translation

JEL Classification: L65; I15; O32; O33; Q56

Introduction

The pharmaceutical usefulness of a drug molecule is determined by more than intrinsic pharmacological activity. Numerous promising therapeutic compounds exhibit poor aqueous solubility, inadequate gastrointestinal dissolution, susceptibility to enzymatic or chemical degradation, limited epithelial permeability, rapid systemic elimination, or non-selective distribution to healthy tissues. These limitations can lower oral bioavailability, increase the required dose, generate pharmacokinetic variability, and contribute to dose-dependent toxicity. Nanocarrier technologies have consequently become important tools for changing how a therapeutic molecule interacts with biological barriers

without altering its fundamental molecular pharmacology. Among these technologies, solid lipid nanoparticles (SLNs) and nanostructured lipid carriers (NLCs) have received sustained attention because they combine a lipidic internal phase with nanometric dimensions, surfactant-mediated dispersion, and tunable drug-release behaviour [1-6].

SLNs consist predominantly of lipids that remain solid at physiological or ambient temperature. This architecture can protect incorporated molecules from chemical degradation and permit controlled release, but an extensively ordered crystalline lattice can constrain drug loading and promote expulsion of the payload

during lipid recrystallization or storage. NLCs were developed partly to address these limitations by combining solid and liquid lipids. Introducing a liquid component generates imperfections in the lipid matrix, reduces crystal order, and can create additional molecular accommodation sites for incorporated compounds. Consequently, NLCs frequently show higher loading capacity, lower risk of drug expulsion, and greater formulation flexibility than first-generation SLNs, although their performance remains highly dependent on formulation composition and processing history [3-10].

The lipid component of an SLN or NLC should not be considered an inert background material. Lipid chain length, degree of saturation, triglyceride composition, melting profile, polymorphism, miscibility with liquid lipids, compatibility with the payload, oxidation susceptibility, and interaction with surfactants can influence nanoparticle formation and therapeutic performance. Experimental work has demonstrated that even when particle sizes appear similar, differences in internal lipid organisation can modify stability and cellular uptake [8]. For example, showed that the location of liquid lipids within or near the surface of NLCs can affect their uptake by cells. Such observations strengthen the argument that rational nanocarrier design requires molecular-level control of lipid composition rather than optimisation of particle diameter alone.

This principle makes palm-derived lipids scientifically interesting. Palm oil fractionation produces chemically and physically distinct lipid streams rather than a single uniform material. Palm stearin is relatively enriched in higher-melting triglycerides and represents a logical candidate for the solid fraction of a lipid nanoparticle. Palm olein provides a more fluid lipid fraction that can disrupt ordered crystal packing when combined with a solid lipid. Palm-kernel-derived lipids are chemically differentiated by their relatively high content of medium-chain and lauric fatty acids, while esterification and other oleochemical modifications can generate palm-derived esters with different polarity, viscosity, spreading behaviour, and solvent characteristics. These attributes suggest that palm-derived materials could be engineered as pharmaceutical lipid matrices rather than considered solely nutritional or industrial commodities.

Direct evidence supporting this proposition is emerging but remains limited [12]. Investigated binary mixtures of palm stearin and palm olein in NLCs and demonstrated that the balance between solid and liquid palm fractions influences physical characteristics relevant to carrier performance. Subsequent work showed that β -carotene incorporated into palm-stearin/palm-olein NLCs achieved improved gastrointestinal bioaccessibility in an in vitro digestion model [13]. Palm stearin has also been incorporated into solid lipid nanoparticle systems designed to protect fucoxanthin, with improved stability and in vivo bioavailability being reported [14]. These studies originated primarily from food, nutraceutical, or bioactive-delivery research rather than conventional prescription pharmaceutical development, but the underlying physicochemical evidence is directly relevant to drug-delivery science.

Palm-derived bioactives create another research dimension. Tocotrienol-rich fractions originating from palm have been incorporated into NLC-based topical systems, including formulations investigated for photoprotection, anti-ageing effects, controlled release, and safety in human-derived cells or reconstructed skin models [15, 16]. These studies establish a useful proof of concept for a “bioactive-plus-carrier” paradigm in which palm-related bioactives can interact with advanced lipid delivery technologies. Nevertheless, the carrier in such studies is not necessarily itself entirely palm derived; therefore, therapeutic claims about a fully palm-based pharmaceutical platform must remain clearly differentiated from evidence regarding palm-derived payloads.

The central translational issue is therefore not whether palm lipids can be converted into nanoparticles. That question has largely been answered at the proof-of-concept level. The more demanding question is whether palm-derived lipids can be transformed into reproducible, pharmaceutical-grade, clinically credible delivery materials whose advantages are demonstrated against suitable reference formulations. Such translation requires evidence extending far beyond particle size, polydispersity index, zeta potential, and encapsulation efficiency. It requires reproducible chemistry, defined critical material attributes, mechanistic drug-release data, route-specific permeability studies, comparative pharmacokinetics, toxicology, stability, manufacturability, sterilisation where appropriate, Quality by Design (QbD), regulatory qualification, and eventually human trials [10-19]. Recent translational guidance for nanomedicines likewise emphasises rigorous physicochemical understanding, clinically relevant exposure, reproducibility, biocompatibility, scalable manufacturing, and early attention to regulatory requirements [19].

This review therefore evaluates palm stearin, palm-kernel-derived lipids, palm olein, and palm oil esters through a translational pharmaceutical lens. Its objectives are to explain how feedstock chemistry could determine nanocarrier behaviour; synthesise evidence concerning oral, topical, ocular, pulmonary, intranasal, and targeted delivery; examine therapeutic applications for poorly soluble, anti-inflammatory, antimicrobial, dermatological, and anticancer agents; identify deficiencies in safety and clinical evidence; and propose a pathway for transforming a promising palm-derived formulation into a clinically acceptable medicine.

Literature Review: Conceptual and Theoretical Foundations

Solid Lipid Nanoparticles and Nanostructured Lipid Carriers

Modern lipid nanoparticles occupy a continuum of structures rather than representing a single standardised architecture. In classical SLNs, a drug is dispersed or dissolved within a predominantly solid lipid matrix stabilised by surfactants. Depending on preparation conditions, the payload may be homogeneously dispersed, concentrated near the particle core, enriched toward the shell, or partly associated with the interface. This structural heterogeneity helps explain why apparently similar formulations can exhibit different burst-release profiles, encapsulation efficiencies, or storage behaviour [1-20].

NLCs deliberately introduce a liquid lipid into the solid matrix. The resulting reduction in crystalline perfection can improve payload accommodation and decrease the likelihood that recrystallisation will force the active ingredient out of the carrier. Reviews comparing SLNs and NLCs consistently identify drug loading, matrix organisation, physical stability, and release behaviour as critical distinctions between the two systems [3-21]. However, the common description of NLCs as simply “more disordered SLNs” is incomplete. The location of the liquid lipid, its miscibility with the solid phase, interfacial composition, and thermal history all contribute to final structure [8, 9].

Palm-Derived Lipids as Pharmaceutical Material Candidates

Palm stearin is especially suitable for conceptualization as an SLN or NLC solid phase because its relatively high melting fraction can remain structured under relevant storage and physiological conditions. Yet high crystallinity is a double-edged characteristic. An ordered matrix can provide mechanical and chemical stability but may leave insufficient accommodation space for a drug and may become progressively more ordered during storage, thereby increasing the risk of payload expulsion. Combining palm stearin with palm olein offers an intuitive materials-engineering strategy because the more fluid lipid fraction can create controlled lattice disorder.

The empirical work of is important for this reason. Rather than merely demonstrating nanoparticle formation, it showed that changing the palm-stearin/palm-olein ratio alters properties of the resulting nanostructured carrier [12]. Subsequently connected this architecture with functional gastrointestinal performance by showing improved β -carotene bioaccessibility during simulated digestion. These studies are not equivalent to evidence for therapeutic drug delivery in humans, but they validate the mechanistic proposition that palm-fraction composition can be manipulated to tune a lipid matrix [13].

Palm-kernel-derived lipids deserve separate consideration because they should not be treated as chemically interchangeable with mesocarp-derived palm oil. Their comparatively greater abundance of shorter and lauric fatty acids can alter melting

behaviour, enzymatic digestion, interfacial properties, and potential absorption pathways. Contemporary pharmaceutical research directly comparing standardised palm-kernel fractions with palm stearin in SLN/NLC systems remains limited. This scarcity is itself an important research gap: future studies should compare chemically characterised palm-kernel matrices, palm stearin, conventional pharmaceutical lipids, and mixed systems using identical payloads and manufacturing conditions.

Palm oil esters create still greater formulation flexibility. Esterification can alter polarity, spreading, solvent properties, viscosity, and interactions with skin lipids or hydrophobic drugs. Earlier oleochemical research established their value in cosmetic and topical systems, but the 2020–2026 literature contains substantially fewer high-quality pharmaceutical studies specifically identifying standardised palm oil esters as the dominant nano-carrier phase. Therefore, the translational literature should distinguish between direct evidence and chemical plausibility rather than extrapolating broadly from unrelated nanoemulsion oils.

Drug Incorporation, Crystallinity, and Release

Drug incorporation into lipid nanoparticles depends strongly on drug–lipid affinity. A lipophilic drug may partition into the internal lipid phase, whereas poorly compatible molecules may migrate to interfaces or crystallise separately. Differential scanning calorimetry, powder X-ray diffraction, spectroscopy, microscopy, and increasingly advanced scattering techniques are therefore required to determine whether the drug remains crystalline, becomes molecularly dispersed, or changes the organisation of the lipid matrix [10-23].

As shown conceptually in Figure 1, the relationship begins with the feedstock rather than with the finished nanoparticle. This framing makes the material-to-clinic sequence explicit and helps distinguish raw-material attributes from downstream product-performance outcomes. Figure 1 illustrates the proposed feedstock-to-clinic logic of palm-derived nanomedicine. The model emphasises that pharmaceutical performance emerges sequentially from feedstock composition, molecular organisation, formulation engineering, biological interaction, and translational validation rather than from nanosizing alone.

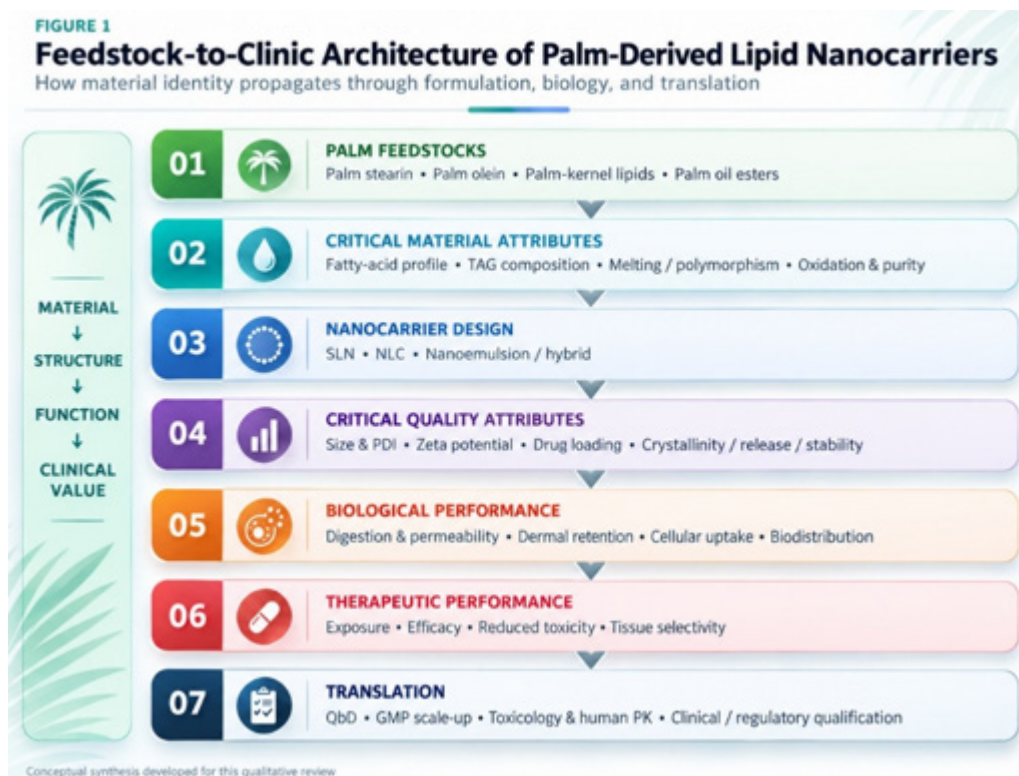


Figure 1: Feedstock-to-Clinic Architecture of Palm-Derived Lipid Nanocarriers

The major implication of Figure 1 is that changing the source or composition of a lipid can propagate effects throughout the development pathway. A change in triglyceride composition may alter melting and crystallization; altered crystallization may change payload distribution; payload distribution may change release; release may alter pharmacokinetics; and altered pharmacokinetics may determine clinical efficacy or toxicity. Consequently, raw-material specification is not merely a procurement issue but a pharmaceutical-development variable.

Method

This article employed a qualitative literature review (QLR) design. It was explicitly designed as an interpretive and translational review rather than a systematic literature review, bibliometric analysis, or meta-analysis. The purpose was not to produce an exhaustive count of all formulations or a pooled estimate of effect size. Instead, the review synthesized heterogeneous pharmaceutical, biochemical, nanotechnological, toxicological, and translational evidence to identify mechanisms, recurrent themes, evidence gaps, and development requirements relevant to palm-derived lipid nanocarriers.

Literature published primarily between 2020 and 2026 was prioritised. Literature searches were conducted iteratively across PubMed/MEDLINE, Scopus, Web of Science, ScienceDirect, SpringerLink, Wiley Online Library, ACS Publications, Taylor & Francis, and other peer-reviewed sources. Search concepts included combinations of “palm stearin,” “palm olein,” “palm kernel lipid,” “palm oil ester,” “solid lipid nanoparticle,” “nanostructured lipid carrier,” “lipid nanocarrier,” “nanoemulsion,”

“drug delivery,” “oral bioavailability,” “lymphatic transport,” “topical,” “transdermal,” “ocular,” “pulmonary,” “nose-to-brain,” “targeting,” “crystallinity,” “polymorphism,” “Quality by Design,” “scale-up,” “toxicity,” “stability,” and “pharmacokinetics.” Because the review was qualitative rather than systematic, searching was purposive and iterative rather than PRISMA-based or exhaustively protocolised.

Because direct pharmaceutical evidence involving palm-derived matrices remains limited, evidence was interpreted through four purposive layers. The first consisted of studies directly evaluating palm-derived lipid matrices, such as palm-stearin/palm-olein NLCs. The second incorporated palm-bioactive or palm-related formulations that provided transferable evidence concerning formulation, stability, safety, or topical delivery. The third consisted of high-quality contemporary SLN/NLC studies using non-palm lipids but addressing mechanisms relevant to oral, dermal, ocular, pulmonary, intranasal, or targeted delivery. The fourth consisted of translational literature involving QbD, manufacturing scale-up, stability, toxicology, and regulatory barriers.

Evidence was thematically coded into material selection, lipid structure, manufacturing, physicochemical properties, biological transport, therapeutic applications, safety, scale-up, regulation, and sustainability. Particular attention was paid to evidence maturity. A formulation displaying attractive particle size or encapsulation efficiency was not considered equivalent to a formulation with demonstrated pharmacokinetic or therapeutic superiority. The analytical hierarchy therefore distinguished formulation characterisation, in vitro biological activity, ex vivo

transport, animal pharmacokinetics, disease-model efficacy, toxicology, human pharmacokinetics, clinical efficacy, and regulatory readiness.

This methodological distinction is essential because lipid nanomedicine has generated a large volume of technically successful formulations whose clinical relevance remains uncertain. Reviews of manufacturing and translational challenges consistently identify reproducibility, scale-up, long-term stability, route-specific safety, and regulatory characterisation as persistent barriers [4-24].

Results: Thematic Findings

Theme 1: Feedstock Chemistry is a Functional Component of Nanocarrier Design

The literature supports the conclusion that lipid selection directly influences nanocarrier architecture. Lipid composition affects melting temperature, matrix viscosity during processing, drug solubility within the molten phase, recrystallization after cooling, surface organisation, and susceptibility to oxidation. The comparative literature on SLNs and NLCs therefore increasingly treats formulation composition as a determinant of biological performance rather than merely a manufacturing variable [7-25].

Palm stearin illustrates this principle particularly well. Its relative solidity can provide a structured matrix, while palm olein can serve as a disordering liquid phase [12]. Demonstrated that combining these fractions produces NLC systems in which composition influences physical behaviour [13]. Subsequently showed that β -carotene carried in such a system had enhanced in vitro gastrointestinal bioaccessibility [14]. Similarly incorporated palm stearin into a solid-lipid system protecting fucoxanthin and demonstrated improved stability and in vivo bioavailability. These findings collectively support palm stearin as more than an industrial fat fraction; it can function as a tunable structured lipid in nanoscale delivery matrices.

The evidence is insufficient, however, to conclude that palm stearin is superior to pharmaceutical lipids such as glyceryl behenate, glyceryl monostearate, cetyl palmitate, or other commonly used matrices. Few studies have conducted controlled head-to-head comparisons using identical payloads, surfactants, processing conditions, and biological models. Future palm-specific pharmaceutical studies should therefore include conventional benchmark lipids. Without such comparisons, claims of superiority risk conflating successful nanoparticle fabrication with material advantage.

Theme 2: Controlled Crystalline Imperfection Can Improve Loading But Creates a Stability Trade-Off

A central rationale for NLC development is that deliberate crystalline imperfection can improve drug accommodation. The concept is particularly relevant to palm-derived mixtures because a high-melting palm-stearin fraction can theoretically be combined with palm olein or compatible palm-derived esters to create a less ordered matrix. NLC reviews consistently describe this solid/liquid design as an approach to increasing loading and

reducing drug expulsion compared with highly ordered SLNs [3-21].

Yet disorder is not automatically beneficial. Excess liquid lipid can reduce structural robustness, increase leakage, alter interfacial composition, or produce phase separation [8]. Showed that the distribution of liquid lipids within NLCs changes stability and cellular uptake, demonstrating that nominal composition alone cannot predict performance. In developing cannabidiol-loaded NLCs, similarly illustrated the importance of optimizing composition for encapsulation, release, and storage stability. The relevant design objective is therefore controlled—not maximal—matrix disorder [26].

Theme 3: Manufacturing History Becomes Part of the Medicine SLNs and NLCs can be prepared through high-pressure homogenization, ultrasonication, melt-emulsification, solvent injection, solvent diffusion, double emulsification, microemulsion techniques, and related approaches. Each method imposes a different thermal and mechanical history on the lipid phase. Demonstrated that solvent-injection parameters materially influence SLN/NLC characteristics. Likewise reviewed how production routes influence particle properties and suitability for different administration routes [4-23].

Hot processing may improve lipid fluidity and emulsification but can degrade thermolabile drugs. Ultrasonication is accessible at laboratory scale but energy distribution becomes difficult to reproduce when volume increases. High-pressure homogenization is among the more industrially attractive approaches but pressure, cycle number, inlet temperature, lipid concentration, and cooling conditions must be controlled. Double-emulsion strategies can broaden the range of payloads to include more hydrophilic molecules; for example, used a double-emulsion-related approach to co-load simvastatin and adenosine in NLCs for wound-healing applications [27].

These observations have a major implication for palm-derived systems. Two manufacturers using nominally identical palm stearin can produce different nanoparticle microstructures if homogenization intensity, cooling rate, lipid preheating, surfactant hydration, or storage conditions differ. Consequently, a pharmaceutical specification cannot be restricted to chemical identity of the lipid; it must incorporate the process variables that create the final solid-state structure.

Theme 4: Oral Delivery is a Particularly Compelling Application

Oral delivery of poorly water-soluble compounds represents one of the strongest use cases for lipid nanoparticles. Potential mechanisms include maintenance of the drug in a solubilized state, protection from gastrointestinal degradation, modification of mucosal interactions, enhanced dissolution, stimulation of bile-mediated solubilization, transport in mixed micelles, altered efflux, and in selected cases greater intestinal lymphatic transport [2]. Reviewed the ability of SLNs to improve oral absorption through multiple gastrointestinal transport pathways, while demonstrated that SLN formulation could enhance perme-

ability of a molecule relevant to multidrug-resistant tuberculosis management [28]. Further showed that an SLN-containing oral system could be engineered toward duodenal targeting and modified pharmacokinetic performance [29]. A recent review of oral lipid nanoparticles further highlights gastrointestinal solubilisation, epithelial transport, and selective lymphatic pathways as key mechanisms by which lipid-based carriers may improve the exposure of poorly bioavailable compounds [30].

NLCs can extend these advantages by improving loading of highly lipophilic molecules [31]. Applied a QbD-based strategy to atazanavir-loaded NLCs with attention to lymphatic targeting and bioavailability. showed that an NLC could protect phloretin under gastric conditions and produce sustained release behaviour. demonstrated that lipid and emulsifier selection affect digestion and performance of curcumin-containing solid lipid systems [32]. Collectively, these studies reinforce a key translational point: oral lipid nanocarriers should be evaluated not only by dissolution but by digestion-dependent colloidal transformation, intestinal transport, lymphatic exposure, and systemic

pharmacokinetics [23].

Palm-derived materials could be particularly relevant to this route because palm triglycerides are substrates for physiological lipolysis. The hypothesis is not that palm lipids automatically increase absorption but that their digestibility and fatty-acid composition may be engineered to influence the colloidal environment generated during intestinal digestion. This hypothesis should be tested experimentally through comparative digestion, micellization, epithelial transport, mesenteric lymph sampling where feasible, and pharmacokinetic studies.

Figure 2 summarises the proposed mechanisms by which a palm-derived oral nanocarrier could translate physicochemical formulation properties into increased systemic exposure. The figure also distinguishes digestion-mediated colloidal transformation from the less certain assumption that intact nanoparticles must cross the intestinal epithelium to generate a bioavailability benefit.

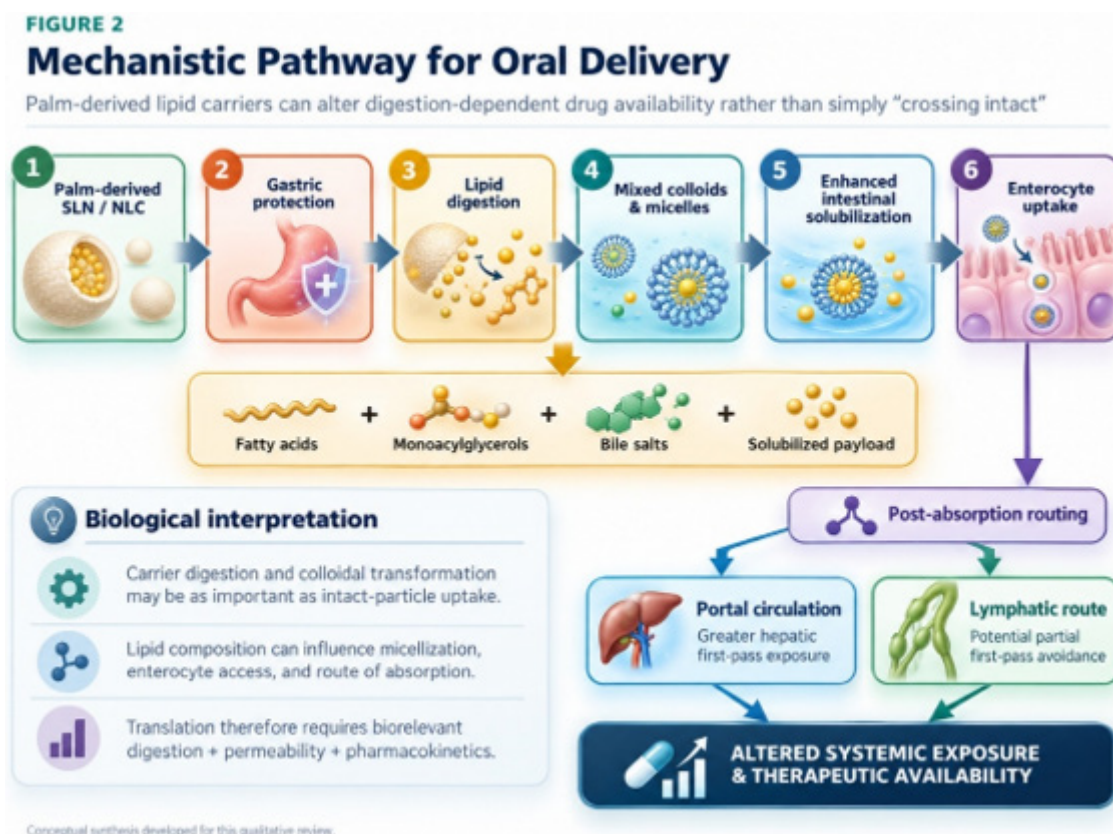


Figure 2: Mechanistic Pathway for Oral Delivery

Figure 2 illustrates that the oral advantage of lipid nanocarriers should not be understood as intact nanoparticles simply crossing the gastrointestinal epithelium. Some intact-particle uptake may occur, but the formulation can also function by controlling digestion and maintaining the drug within absorbable colloidal structures. This distinction matters when selecting palm-derived lipids because their fatty-acid and triglyceride compositions may influence digestive processing and therefore the physical state in

which a drug approaches the intestinal membrane.

Theme 5: Dermal and Topical Delivery has the Strongest Near-Term Translational Fit

Topical delivery is one of the most extensively investigated applications of SLNs and NLCs. Lipid nanoparticles can form an occlusive film, reduce transepidermal water loss, improve hydration of the stratum corneum, increase contact between for-

mulation and skin, provide local controlled release, and enhance follicular or epidermal deposition. Reviewed NLCs for transdermal administration, whereas emphasized their application to topical anti-inflammatory natural compounds [33, 34].

Numerous recent experimental studies strengthen this evidence [35]. Reported SLN-mediated dermal delivery of vitamin A. Incorporated curcumin NLCs into a hydrogel and demonstrated favourable topical-delivery characteristics [10-36]. Developed tacrolimus/thymoquinone co-loaded NLC gel for psoriasis and demonstrated sustained release and improved penetration characteristics. Evaluated riluzole NLCs for hyperproliferative skin disease, while investigated NLC-enriched hydrogels containing quercetin and omega-3 fatty acids [37, 38].

The wound-healing literature is similarly active. reported sustained release and improved healing-related outcomes from simvastatin-loaded NLCs [39]. Described curcumin-loaded NLCs with antioxidant, antimicrobial, and regenerative potential [40]. reviewed advances and persistent limitations of NLCs in wound healing, while showed that co-delivery strategies can be used to combine pharmacologically distinct agents within a topical lipid platform. These findings are relevant because local delivery may require lower systemic exposure than oral or parenteral nanomedicine, potentially reducing some translational barriers associated with systemic nanoparticle biodistribution [27-41].

Palm-related topical systems provide additional support. Investigated NLC formulations containing a tocotrienol-rich fraction and reported anti-ageing-related biological activity. Subsequently evaluated cytotoxicity, phototoxicity, irritation, photostability, and controlled release using human-derived cells and skin models. Although these are dermocosmetic rather than prescription-medicine applications, they demonstrate a translationally useful progression from formulation to biologically relevant safety testing [15, 16].

Theme 6: Ocular, Pulmonary, and Intranasal Delivery Broaden the Platform But Increase Complexity

The ocular surface presents rapid tear turnover, nasolacrimal drainage, epithelial barriers, and limited residence time. demonstrated that clarithromycin-loaded SLNs could be optimised for topical ocular therapy, illustrating how lipid carriers can increase drug residence and control release [42]. More broadly, NLC systems continue to be investigated as ocular formulations because they can be incorporated into gels or mucoadhesive systems, although sterility, ocular tolerability, clarity, particle-size reproducibility, and preservative compatibility become critical translation requirements.

Pulmonary administration introduces different constraints. Aerodynamic behaviour, nebulization or dry-powder processing, lung deposition, macrophage interaction, surfactant compatibility, and inhalation toxicology must be considered. Reviewed lipid nanocarriers for pulmonary glucocorticoid delivery, highlighting both the potential and the route-specific formulation variables [43]. Discussed NLCs in the context of lung-cancer

targeting, reflecting increasing interest in combining pulmonary and oncological delivery strategies [44].

Intranasal delivery is particularly attractive for CNS therapeutics because it may provide access to olfactory and trigeminal pathways while reducing dependence on conventional systemic transport across the blood-brain barrier. Applied QbD principles to rivastigmine-loaded NLCs for nose-to-brain delivery. Reviewed the role of liquid lipids in CNS-targeted NLCs, while synthesized pharmacokinetic and pharmacodynamic evidence concerning intranasal SLNs and NLCs. more broadly reviewed lipid carriers in relation to the blood-brain barrier. These studies show the technological possibilities available to palm-derived lipid matrices, but each new route adds route-specific safety and manufacturing requirements [45-48].

Theme 7: Cancer Delivery Illustrates Both the Promise and the Danger of Overclaiming Targeting

Cancer is a major application area for NLCs because many anticancer agents are hydrophobic, unstable, or highly toxic. reviewed chemotherapeutic delivery using NLCs, while demonstrated in vitro and in vivo evaluation of docetaxel-loaded ultrasmall NLCs. Examined SLNs and NLCs in glioblastoma therapy, where blood-brain barrier penetration and tumour selectivity are particularly challenging [49-51].

More recent evidence continues this trajectory. Investigated indomethacin-loaded NLCs for anticancer applications, and compared lipid nanoparticle approaches for doxorubicin, reporting enhanced photostability and anticancer activity. Reviewed passive and active targeting approaches, including surface functionalization and stimulus-responsive systems [52-54].

However, nanoparticle accumulation in tumour tissue is not synonymous with clinically meaningful targeting. Smaller size, altered biodistribution, ligand attachment, or improved cellular uptake constitute mechanistic steps rather than proof of therapeutic selectivity. Targeting claims require direct demonstration of differential tissue exposure, preferably through quantitative biodistribution and pharmacokinetic analysis, followed by evidence that improved localisation produces a superior therapeutic index. For palm-derived carriers, cancer applications should therefore be considered a long-term opportunity rather than the first translational target.

Theme 8: Antimicrobial and Anti-Inflammatory Applications are Well Aligned with Local Delivery

Lipid nanoparticles can enhance the local concentration, stability, and sustained release of antimicrobial compounds. investigated eugenol-containing NLCs for topical activity against *Candida albicans*. reported multifunctional enzyme-responsive NLCs designed for bacterial-infection targeting. Reviewed lipid nanocarriers for skin infections and identified stability, manufacturing, and regulatory barriers despite substantial therapeutic promise [24-56].

Anti-inflammatory and dermatological applications are similar-

ly compatible with NLCs because localized therapy can reduce systemic exposure, and collectively illustrate how lipid systems can be adapted for inflammatory skin disorders, including combination therapy and sustained local release. This therapeutic area could represent a strategically realistic entry point for palm-derived matrices because topical administration permits detailed evaluation of local tolerability, dermal pharmacokinetics, and retention without immediately confronting the systemic biodistribution issues associated with intravenous nanomedicine [34-57].

Discussion and Analysis

The Central Finding: Palm-Derived Lipid Nanomedicine is Plausible, But Evidence Maturity is Uneven

The strongest conclusion from the literature is not that palm-derived nanocarriers have already been clinically validated. Rather, it is that the materials-science basis is credible, while the translational evidence remains incomplete. Palm-stearin/palm-olein NLCs demonstrate controllable matrix engineering, and palm-stearin-containing nanoparticles have improved the stability or bioaccessibility of model lipophilic compounds [12-14]. Palm-derived tocotrienol formulations further demonstrate the potential for biologically active palm constituents to be incorporated into sophisticated topical systems [15, 16].

At the same time, the broader NLC literature shows what will be required to move beyond proof of concept. Oral SLNs have been linked to altered absorption and targeted gastrointestinal delivery [2-29]. QbD has been successfully used to optimize complex NLC formulations [16-45]. Disease-specific animal or cell models exist for cancer, psoriasis, wounds, ocular infection, and other applications. Palm-specific studies have not yet progressed to comparable depth across all these domains.

Palm Stearin Should be Treated as a Pharmaceutical Material, Not Merely a Natural Lipid

The source of an excipient does not establish its pharmaceutical suitability. A lipid intended for food manufacture may be chemically safe for ingestion but still lack the narrow compositional specifications required for a reproducible nanomedicine. Pharmaceutical-grade palm stearin would need defined limits for fatty-acid composition, triglyceride distribution, free fatty acids, peroxide value, secondary oxidation products, moisture, metals, residual processing contaminants, microbial load where applicable, and thermal properties.

Crystallization deserves particular attention. The solid-state history of triglycerides can generate polymorphic transitions over time. A nanoparticle that initially exhibits desirable loading may reorganize during storage, potentially increasing crystal order and expelling the drug. Consequently, differential scanning calorimetry and X-ray diffraction should not be used solely as one-time characterisation tools immediately after formulation. They should form part of longitudinal stability testing. The broader literature demonstrates that stability depends on molecular mixing, surface organisation, lipid composition, and environmental conditions [8-26].

Palm Kernel Lipids Constitute a Separate Research Platform

A major conceptual error would be to use “palm-derived lipid” as if all such materials were interchangeable. Palm-kernel lipids have a substantially different fatty-acid composition from palm mesocarp oil. This difference can alter melting, digestion, oxidative behaviour, interfacial properties, and drug solubility. Therefore, palm-kernel-derived matrices should be developed as a separate platform and compared experimentally with palm stearin rather than blended into a generic palm-oil category.

Future studies should construct a compositional matrix in which standardised palm stearin, palm-kernel fractions, palm olein, and selected palm-derived esters are tested against reference pharmaceutical lipids. A model hydrophobic drug could be used to establish drug–lipid solubility, thermal compatibility, crystallization behaviour, nanoparticle formation, release, digestion, and cellular transport under identical processing conditions. Such a study would provide far more translational value than developing multiple unrelated formulations without comparators.

The Bioactive-Plus-Carrier Concept is Scientifically Attractive But Must be Tested Rigorously

Palm bioactives such as tocotrienols and carotenoids create an unusual opportunity: a palm-derived lipid carrier might eventually deliver another palm-derived compound. This could produce material compatibility, oxidative protection, or complementary biological effects. Evidence supporting tocotrienol-containing NLC topical formulations and β -carotene delivery makes the concept plausible [13-16].

Nevertheless, three different phenomena must be separated. Formulation synergy means that the carrier physically accommodates and protects the payload. Pharmacokinetic synergy means that the carrier increases exposure or tissue retention. Pharmacodynamic synergy means that the carrier or co-component contributes biological activity that enhances the drug’s therapeutic effect. The first does not prove the second, and neither proves the third. Future experiments should be designed with appropriate controls to distinguish these mechanisms.

Translational Success Requires Pharmacokinetics, Not Merely Release Curves

A recurring limitation in nanocarrier research is the assumption that sustained in vitro release indicates better clinical performance. Release testing is necessary but insufficient. For oral delivery, comparative studies should measure C_{max}, T_{max}, area under the concentration–time curve (AUC), absolute or relative bioavailability, variability among animals or participants, metabolite profiles, and, where mechanistically relevant, lymphatic transport. Demonstrated how pharmacokinetic endpoints can reveal effects that simple dissolution data cannot capture [29].

For topical systems, systemic plasma exposure may be less relevant than dermatokinetics. Tissue concentrations should be measured in the stratum corneum, viable epidermis, dermis, wound bed, or target lesion [11]. Demonstrated that NLC-based topical co-delivery can materially alter dermatokinetic exposure compared with conventional formulations. Such approaches are

valuable models for future palm-derived dermatological products.

For targeted systemic therapies, biodistribution is essential. Nanoparticles should be labelled or analytically traced to determine whether increased drug concentration at a target tissue results from the carrier, changed metabolism, altered protein binding, or nonspecific retention. Without such data, “targeted” becomes a formulation aspiration rather than a demonstrated pharmacological property.

Safety Must be Route-Specific and Formulation-Specific

The description of plant-derived lipids as biocompatible should not be interpreted as evidence that every nanoparticle containing them is safe. Toxicity can arise from surfactants, particle concentration, degradation products, oxidation products, residual solvents, surface charge, impurities, or interactions with immune and epithelial cells. An excipient safely consumed as food may behave differently when deposited in the lung, injected intravenously, applied repeatedly to damaged skin, or delivered intranasally.

The most appropriate toxicological program therefore depends on administration route. Topical products require irritation, sensitization, phototoxicity where relevant, repeated-use tolerability, and evaluation of systemic absorption [16]. Provide a useful model by evaluating NLC formulations in human cell and reconstructed skin systems. Pulmonary systems require lung-cell and inhalation toxicology; ocular products require irritation and corneal compatibility; intranasal CNS formulations require evaluation of nasal mucosa and neurological safety; systemic formulations demand a far more extensive program addressing immune activation, organ distribution, hematological effects, and repeated-dose toxicity.

Quality by Design Should be the Organizing Strategy for Palm-Derived Nanocarriers

Traditional formulation optimisation often changes one variable at a time. This approach is poorly suited to lipid nanoparticles because composition and processing variables interact. QbD offers a more appropriate framework by linking the quality target product profile (QTPP), critical material attributes (CMAs), critical process parameters (CPPs), and critical quality attributes (CQAs). Reviewed QbD application to lipid nanoparticles and nanoemulsions, while demonstrated its use in rivastigmine NLCs. Further emphasized the value of risk-based nanocarrier optimisation for industrial robustness. More recent QbD-focused evidence for oral lipid nanoparticles confirms that QTPP definition, risk-based identification of CMAs and CPPs, and design-of-experiments approaches can improve process understanding and support scalable product quality [15-59].

For a palm-stearin NLC, CMAs could include fatty-acid profile, triglyceride composition, iodine value, melting range, peroxide value, liquid-lipid ratio, surfactant identity, surfactant purity, and drug–lipid solubility. CPPs could include lipid-melting temperature, phase-mixing rate, homogenization pressure, number of homogenization cycles, sonication energy, cooling rate, and drying conditions. CQAs could include particle size, PDI, zeta potential, payload content, free drug, crystallinity, polymorphic state, release profile, oxidation, sterility or microbial limits, and redispersibility.

Figure 3 presents a QbD framework specifically adapted to palm-derived lipid nanocarriers, linking variable agricultural and oleochemical feedstocks to clinically meaningful pharmaceutical quality. It shows how material attributes and process parameters should be connected prospectively to CQAs, design-space definition, manufacturing control, and product reproducibility.

FIGURE 3
Quality-by-Design Framework for Palm-Derived Nanomedicine
Linking raw-material variability to clinically meaningful product quality



Figure 3: Quality-by-Design Framework for Palm-Derived Nanomedicine

Figure 3 illustrates that QbD is particularly valuable for palm-derived materials because biological feedstocks exhibit intrinsic variability. Rather than attempting to eliminate every compositional difference, manufacturers can define a material and process design space within which variability remains compatible with final product performance. The central regulatory question is therefore whether a variation in palm lipid composition changes a clinically relevant quality attribute.

Scale-up is a Major Translational Bottleneck

A laboratory formulation produced by probe sonication in tens of millilitres does not automatically define an industrial process. Scale-up changes energy distribution, mixing time, thermal gradients, cooling, shear history, and opportunities for contamination. Reviewed scale-up methods for SLNs and emphasised the need to maintain nanoparticle quality during increasing production volume. Similarly described manufacturing approaches and their route-specific implications [4-18].

High-pressure homogenization is especially attractive for lipid nanoparticles because it is established at industrial scale. Nevertheless, a palm-stearin formulation may behave differently during high-pressure processing from a laboratory sonication process because crystallisation begins as the homogenised material cools. The pharmaceutical development programme must therefore define not only pressure and cycle count but also inlet temperature, cooling profile, hold time, and batch geometry.

Drying may also become necessary for oral or long-term-stable products. Lyophilization and spray drying can improve physical stability but introduce new stressors that promote aggregation or polymorphic transformation. Cryoprotectant selection, reconstitution behaviour, and particle-size recovery should therefore be treated as CQAs rather than secondary formulation details.

Sterilization and Microbiological Control Require Route-Specific Solutions

Parenteral and many ocular products must be sterile. Traditional terminal sterilization can destabilize lipid nanoparticles by heat, radiation, or chemical exposure. Sterile filtration may be possible for sufficiently small and robust systems but can alter concentration, retain particles, or be impractical if aggregation occurs. Consequently, aseptic processing may ultimately be required for some palm-derived nanomedicines.

This requirement raises the quality threshold dramatically. Pharmaceutical-grade lipid must be combined with low-bioburden manufacturing, validated cleaning, controlled environments, sterile excipients, validated hold times, and container-closure compatibility. These considerations reinforce the argument that translation is primarily a manufacturing and quality problem after the fundamental formulation science has been established.

Regulatory Qualification Should Focus on Material Identity and Product Function

Regulatory evaluation of palm-derived lipid nanoparticles would involve both the excipient and the finished nanomedicine.

A material may have a history of safe dietary exposure without a corresponding history of pharmaceutical use via a specific administration route. Therefore, the amount, duration, administration route, impurity profile, nanoscale presentation, and interaction with the drug all influence the required evidence. Contemporary regulatory reviews similarly identify nanotoxicology, material complexity, manufacturing consistency, and the lack of fully harmonised regulatory pathways as persistent obstacles to clinical translation [60].

The most efficient regulatory strategy may initially involve topical or oral applications in which constituent lipids have a favourable safety history. More complex parenteral and targeted applications should follow only after the platform has accumulated robust pharmaceutical and toxicological evidence. This staged progression mirrors the broader translational evolution of nanocarrier technology and reduces the risk that technologically ambitious formulations fail because the underlying material platform was insufficiently characterised. This staged approach is consistent with broader translational frameworks that recommend integrating product characterisation, exposure, safety, manufacturability, and regulatory planning from early development rather than treating them as late-stage requirements [19].

Sustainability can be an Advantage Only When Demonstrated
Palm-derived materials are often described as renewable, but renewability is not equivalent to sustainability. Agricultural land use, fertilizer, mill operations, refining, fractionation, transport, energy consumption, coproduct allocation, methane management, certification, and traceability can materially change life-cycle performance. Life-cycle analyses of palm-oil processing demonstrate that environmental outcomes depend strongly on system boundaries and production practices [61-63].

A credible pharmaceutical sustainability claim would therefore require comparison with the lipid that palm-derived material is intended to replace. For example, if palm stearin substitutes a synthetic or animal-derived lipid, the relevant analysis is not simply the carbon footprint of palm stearin but the cradle-to-gate or cradle-to-grave difference between alternative excipient supply chains at equivalent pharmaceutical function.

Sustainability may also interact with quality. Pharmaceutical production requires additional purification, testing, documentation, and possibly segregation of feedstock. These steps may increase environmental burdens while improving safety and reproducibility. Therefore, pharmaceutical-grade life-cycle assessment should reflect the actual purification and quality-control process rather than using generic food-grade palm-oil datasets.

A Staged Translational Roadmap is Required

The accumulated evidence suggests that palm-derived nanocarriers should progress through a staged development model. Figure 4 integrates the principal translational requirements identified in this review.

Figure 4 represents the proposed translational roadmap from

palm feedstock qualification to clinical medicine. Advancement should be evidence-gated: failure to demonstrate reproducible composition, clinically meaningful pharmacokinetic improve-

ment, or acceptable safety should prevent premature progression.



Figure 4: Translational Roadmap for Palm-Derived Lipid Nanocarriers

Figure 4 illustrates that the roadmap deliberately places human evaluation after comparative pharmacokinetics, disease-relevant efficacy, and manufacturing qualification. This sequence prevents the common translational error of advancing a formulation because it has attractive physicochemical characteristics without demonstrating that those characteristics generate a clinically relevant advantage.

Priority Indications for Translation

Not every therapeutic application should be pursued simultaneously. A rational prioritisation framework should consider formulation advantage, clinical need, route complexity, toxicological burden, and the feasibility of demonstrating local or systemic exposure.

First-Priority Opportunities include topical dermatological and wound-healing products. The existing NLC literature is substantial, local exposure is measurable, and systemic risk may be lower than for parenteral applications [27-41].

Second-Priority Opportunities include poorly soluble oral medicines and bioactives. Palm-derived triglyceride matrices have a mechanistic connection to gastrointestinal digestion, and palm-stearin NLC evidence already demonstrates improved bio-

accessibility of lipophilic molecules [13]. Comparative pharmacokinetic studies would be the critical next step.

Third-Priority Opportunities include ocular and intranasal delivery. These routes provide important therapeutic advantages but require stronger local tolerability, sterility, mucosal-safety, and device-performance evidence [42-47].

Longer-term applications include systemic cancer targeting and pulmonary therapy because they impose more complex requirements involving biodistribution, immune interactions, inhalation or systemic toxicology, sterile manufacturing, and clinically meaningful targeting [42-53]. These higher-risk indications should therefore follow, rather than precede, platform qualification in routes where local exposure and tolerability can be demonstrated more directly.

Research Agenda

Several high-value research questions emerge from this review. Together, they define a research agenda that moves beyond proof-of-concept formulation toward comparative, mechanism-based, and clinically relevant evaluation.

First, standardised palm fractions should be compared direct-

ly with conventional pharmaceutical lipids. Such experiments should use the same drug, surfactants, manufacturing conditions, and analytical methods.

Second, detailed lipidomics or triglyceride profiling should be connected to nanoparticle solid-state behaviour. Rather than treating palm stearin as a single material, studies should identify which compositional parameters predict melting, drug incorporation, and stability.

Third, studies should investigate whether palm-kernel-derived lipids create distinct advantages in digestion or membrane interaction. This question is insufficiently addressed by contemporary pharmaceutical literature.

Fourth, palm oil esters should be revisited using modern pharmaceutical standards, including QbD, high-resolution characterisation, ex vivo skin models, pharmacokinetics, and long-term stability. Priority should be given to studies that compare chemically defined palm-derived esters with established pharmaceutical lipid excipients under otherwise identical formulation conditions.

Fifth, translational studies should include benchmark comparators. A palm-derived NLC should be compared not only with free drug but also with a well-established NLC based on conventional pharmaceutical lipids.

Sixth, long-term stability must be connected to matrix restructuring. Changes in DSC, XRD, particle size, free-drug fraction, oxidation, and release should be followed simultaneously.

Seventh, toxicological testing should evaluate the complete formulation rather than the lipid alone. Surfactants and degradation products can dominate tolerability.

Eighth, sustainable sourcing should be integrated into pharmaceutical specifications. Traceability, certification, and life-cycle data can become part of raw-material qualification, especially if environmental performance is used as a product-development rationale.

Conclusion and Future Directions

Palm-derived lipids represent a scientifically plausible but incompletely developed platform for advanced drug delivery. Palm stearin offers a structured solid phase; palm olein can introduce controlled crystalline disorder; palm-kernel-derived lipids provide a chemically distinct medium-chain- and lauric-rich platform; and palm oil esters may expand formulation flexibility toward liquid-lipid, nanoemulsion, and topical systems. The available evidence demonstrates that palm fractions can be engineered into nanoscale carriers and can protect or improve access to lipophilic bioactive compounds.

The principal challenge is no longer simply demonstrating that a nanoparticle can be prepared. The central challenge is demonstrating that a palm-derived formulation is reproducible, stable,

safe, manufacturable, and therapeutically superior or otherwise clinically advantageous relative to existing alternatives. Particle size and encapsulation efficiency are necessary characterisation endpoints but cannot substitute for comparative pharmacokinetics, tissue exposure, disease-relevant efficacy, repeated-dose toxicology, scale-up, and regulatory-quality manufacturing.

The most credible near-term strategy is therefore a staged translational program. Palm-derived feedstocks should first be converted into tightly characterised pharmaceutical materials. Formulation development should then proceed through QbD, comparative physicochemical studies, mechanistic transport research, pharmacokinetics, route-specific toxicity, and scalable manufacturing. Topical and poorly soluble oral therapies appear to offer particularly realistic first indications, while pulmonary, CNS, parenteral, and actively targeted oncology applications should be considered later-stage opportunities.

A successful research program would transform the question from whether palm oil can be used in nanoparticles to whether precisely defined palm-derived molecular fractions can satisfy the same pharmaceutical, clinical, regulatory, and sustainability standards demanded of any advanced therapeutic delivery technology. That transition—from commodity lipid to standardised pharmaceutical platform—is the defining opportunity for palm-derived nanomedicine.

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