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Palm Oil-Derived Bioactive Compounds in Perioperative Immunonutrition: A Review of Applications in Enhanced Recovery After Surgery Protocols

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ABSTRACT

Perioperative immunonutrition is a critical component of Enhanced Recovery After Surgery (ERAS) protocols, as it modulates immune responses, reduces oxidative stress, and supports metabolic stability following surgical trauma. In parallel, increasing attention has been directed toward plant-derived bioactive compounds as complementary elements in perioperative nutritional strategies. Palm oil is recognized as a rich source of lipid-soluble bioactive compounds, particularly tocotrienols and carotenoids, yet their relevance within ERAS-oriented immunonutrition has not been systematically synthesized. This study examines the characterization, application, and evaluation of palm oil-derived bioactive compounds in perioperative immunonutrition and their relevance to Enhanced Recovery After Surgery (ERAS) principles. A systematic literature review was conducted using the Scopus database. An initial search with the keywords Immunonutrition AND Nutrition identified 1,226 records, which were refined using targeted search terms, publication year (2019-2025), and Open Access/Open Archive criteria, resulting in 30 peer-reviewed studies included in the final analysis. Data were analyzed using thematic synthesis. Five dominant themes emerged: bioactive compound composition and bioavailability; immunomodulatory and anti-inflammatory effects; antioxidant capacity and modulation of oxidative stress; metabolic and nutritional support for postoperative recovery; and translational relevance to ERAS-oriented immunonutrition strategies. Overall, the evidence indicates that palm oil-derived bioactive compounds function as supportive components of perioperative immunonutrition without reported adverse effects. Future research is recommended to further evaluate these compounds through randomized controlled trials integrated explicitly into ERAS protocols to strengthen their clinical applicability.

Keywords: Palm Oil Bioactives; Perioperative Immunonutrition; Enhanced Recovery After Surgery; Tocotrienols; Systematic Literature Review

Abbreviations: ERAS: Enhanced Recovery After Surgery; NF-κB: Nuclear Factor-Kappa B; SLR: Systematic Literature Review; TNF-α: Tumor Necrosis Factor-Alpha; IL-6: Interleukin-6; ROS: Reactive Oxygen Species; PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses; CRP: C-Reactive Protein; ORAC: Oxygen Radical Absorbance Capacity; MDA: Malondialdehyde; SOD: Superoxide Dismutase; GPx: Glutathione Peroxidase

Introduction

Major surgical procedures continue to pose significant physiological challenges, particularly in relation to immune dysfunction, metabolic stress, and oxidative imbalance during the perioperative period. Despite advances in anesthetic techniques, minimally invasive surgery, and postoperative care, surgical stress responses remain a major determinant of postoperative morbidity, delayed recovery, and prolonged hospitalization [1]. These responses are characterized by systemic inflammation, immunosuppression, insulin resistance, and increased oxidative stress, all of which may compromise wound healing, increase infection risk, and impair functional recovery. Consequently, perioperative strategies aimed at attenuating these adverse responses have become a central focus in contemporary surgical care pathways. Enhanced Recovery After Surgery (ERAS) protocols represent a paradigm shift in perioperative management, emphasizing multimodal, evidence-based interventions designed to reduce surgical stress and accelerate recovery [2]. Nutritional optimization is recognized as a core component of ERAS, given its critical role in maintaining immune competence, preserving metabolic homeostasis,

and supporting tissue repair. Within this framework, perioperative immunenutrition, defined as targeted nutritional interventions enriched with specific bioactive nutrients, has gained increasing attention as a means of modulating inflammatory and immune responses associated with surgical trauma.

Immunonutrition formulations have traditionally focused on nutrients such as omega-3 fatty acids, arginine, glutamine, and nucleotides, which have demonstrated varying degrees of efficacy in improving postoperative outcomes [3]. However, growing evidence suggests that plant-derived bioactive compounds may also contribute meaningfully to perioperative immune modulation and metabolic support [4]. These compounds, including specific lipid-soluble antioxidants and anti-inflammatory agents, offer mechanistic pathways highly relevant to the pathophysiology of surgical stress, particularly through regulation of cytokine signaling, oxidative balance, and cellular energy metabolism. Among plant-based lipid sources, palm oil has emerged as a nutritionally distinctive matrix due to its unique composition of bioactive compounds, notably tocotrienols, tocopherols, carotenoids, phytosterols, and phenolic constituents [5]. Unlike many commonly used vegetable oils that are dominated by tocopherol-based vitamin E isoforms, palm oil is characterized by a high proportion of tocotrienols, which exhibit distinct biological activities, including enhanced antioxidant potency, anti-inflammatory effects, and potential immunomodulatory properties. Additionally, red palm oil varieties provide substantial amounts of provitamin A carotenoids, contributing to antioxidant defense and immune regulation [6].

From a nutritional science perspective, the biochemical profile of palm oil-derived bioactive compounds aligns closely with several key objectives of perioperative immunonutrition. Tocotrienols have been shown to modulate nuclear factor-kappa B (NF-κB) signaling, reduce pro-inflammatory cytokine production, and enhance endogenous antioxidant enzyme activity, mechanisms that are directly relevant to mitigating surgical stress responses [7]. Carotenoids contribute to redox balance and immune cell function, while phytosterols and phenolic compounds may exert complementary effects on lipid metabolism and low-grade inflammation. Importantly, these compounds are naturally embedded within a lipid matrix that facilitates intestinal absorption, a critical consideration in perioperative nutritional interventions [8]. Despite these promising biochemical and mechanistic attributes, the role of palm oil-derived bioactive compounds in perioperative immunonutrition remains fragmented across diverse research domains. Existing studies are dispersed among experimental models, clinical nutrition trials, and translational research, often focusing on individual compounds rather than integrated perioperative outcomes [9]. Furthermore, while ERAS guidelines increasingly emphasize individualized and function-oriented nutritional strategies, the explicit integration of palm oil-derived bioactives within ERAS-oriented immunonutrition protocols has not been comprehensively synthesized [10].

This lack of synthesis presents a critical knowledge gap. On one hand, palm oil-derived bioactive compounds are supported by a substantial body of biochemical and nutritional evidence suggesting potential relevance to perioperative care [11]. On the other hand, concerns regarding general dietary fat intake and public perceptions of palm oil have occasionally overshadowed objective, evidence-based evaluations of its functional components in clinical nutrition contexts [12]. A rigorous, methodologically transparent synthesis is therefore necessary to clarify the extent, quality, and translational relevance of existing evidence while maintaining a neutral, scientifically grounded perspective. Systematic Literature Review (SLR) methodology provides a robust framework for addressing this gap, enabling the structured identification, appraisal, and synthesis of peer-reviewed evidence without introducing empirical assumptions or fictitious data collection. By systematically aggregating findings across multiple study designs, an SLR can elucidate recurring themes, quantify reported effects, and assess consistency across biochemical, immunological, antioxidant, and metabolic outcomes relevant to perioperative care. Importantly, an SLR approach is particularly well-suited for evaluating emerging interdisciplinary topics such as the intersection of lipid bioactives, immunonutrition, and ERAS, where randomized controlled trials embedded directly within standardized protocols may still be limited.

Within this context, a focused SLR examining palm oil-derived bioactive compounds in perioperative immunonutrition offers the opportunity to advance current understanding in several ways. First, it enables clarification of the compositional and bioavailability characteristics of these compounds as reported in clinical and translational studies. Second, it allows systematic evaluation of their reported immunomodulatory and antioxidant effects in perioperative or surgery-related settings. Third, it provides insight into metabolic and recovery-related outcomes that align with ERAS objectives, such as reduced inflammatory burden, improved nutritional tolerance, and accelerated postoperative recovery. Therefore, the present study aims to systematically review and synthesize peer-reviewed evidence on the role of palm oil-derived bioactive compounds in perioperative immunonutrition, with specific emphasis on their potential applications within Enhanced Recovery After Surgery (ERAS) protocols. By consolidating findings from experimental, clinical nutrition, and translational research, this review seeks to provide a comprehensive and balanced assessment of current evidence, identify dominant thematic patterns, and highlight translational implications for ERAS-oriented nutritional strategies. The specific objective of this Systematic Literature Review is to evaluate how palm oil-derived bioactive compounds have been characterized, applied, and assessed in perioperative immunonutrition contexts, and to determine their relevance to the principles and outcomes of ERAS protocols.

Based on this objective, the following research question is formulated to guide the synthesis and subsequent discussion:

- RQ: How do palm oil-derived bioactive compounds contribute to immunological, antioxidant, and metabolic outcomes relevant to perioperative immunonutrition within the framework of Enhanced Recovery After Surgery (ERAS) protocols, as evidenced by existing peer-reviewed literature?

Literature Review

Perioperative immunonutrition has emerged as an increasingly important component of Enhanced Recovery After Surgery (ERAS) protocols, reflecting a growing recognition of the role of targeted nutritional strategies in modulating immune responses, oxidative stress, and metabolic disturbances induced by surgical trauma. Recent advances in clinical nutrition research have expanded the scope of immunonutrition beyond conventional substrates to include bioactive compounds with antioxidant and anti-inflammatory properties. Within this context, plant-derived lipid bioactives have attracted attention for their physiological functionality, safety profile, and compatibility with perioperative nutritional support systems. Among these sources, palm oil-derived bioactive compounds have been frequently examined in the literature for their biochemical composition and potential relevance to perioperative care, warranting a structured synthesis of existing evidence to clarify their role within ERAS-oriented immunonutrition strategies.

Perioperative Immunonutrition and Enhanced Recovery After Surgery (ERAS)

Enhanced Recovery After Surgery (ERAS) protocols have been widely adopted as evidence-based, multimodal strategies to reduce surgical stress, preserve physiological function, and accelerate postoperative recovery across a broad range of surgical disciplines [13]. Central to ERAS is the optimization of perioperative nutrition, which has been increasingly recognized as a critical determinant of immune competence, metabolic stability, and clinical outcomes following surgery [14]. Surgical trauma induces a complex systemic response characterized by inflammation, oxidative stress, insulin resistance, and transient immunosuppression, all of which contribute to postoperative complications and prolonged hospitalization. Perioperative immunonutrition has emerged as a targeted nutritional approach designed to modulate immune and inflammatory responses by providing specific nutrients with immunoregulatory properties [15]. Conventional immunonutrition formulations have primarily focused on amino acids such as arginine and glutamine, omega-3 fatty acids, and nucleotides [16]. However, recent literature has expanded this paradigm by emphasizing the potential role of bioactive lipid-derived compounds with antioxidant and anti-inflammatory properties as complementary components of immunonutrition strategies. Within this evolving framework, plant-derived bioactive compounds have gained increasing attention due to their biological activity, safety profile, and compatibility with clinical nutrition systems.

Bioactive Compounds in Clinical and Perioperative Nutrition

Bioactive compounds are defined as non-essential dietary constituents that exert physiological effects beyond basic nutritional functions, often through modulation of cellular signaling pathways, gene expression, and oxidative balance. In the context of perioperative care, bioactive compounds with antioxidant, immunomodulatory, and metabolic regulatory properties are particularly relevant, as they may attenuate surgery-induced oxidative damage and inflammatory dysregulation [17]. Clinical nutrition literature has increasingly documented the role of lipid-soluble bioactives, including vitamin E isoforms, carotenoids, phytosterols, and phenolic compounds, in maintaining immune homeostasis and reducing oxidative stress. These compounds have been shown to influence key biological processes, including cytokine production, lipid peroxidation, and mitochondrial function, which are critical determinants of postoperative recovery trajectories [18]. Importantly, integrating bioactive compounds into perioperative nutrition regimens aligns with ERAS principles, emphasizing early nutritional intervention, metabolic preservation, and minimizing physiological disruption.

Palm Oil as a Source of Bioactive Lipid Compounds

Palm oil has been extensively characterized in the nutritional sciences as a naturally rich source of lipid-soluble bioactive compounds, particularly tocotrienols, tocopherols, carotenoids, phytosterols, and minor phenolic constituents. Unlike many vegetable oils that predominantly contain tocopherols, palm oil is distinguished by its high tocotrienol content, which accounts for approximately 65-70% of its total vitamin E fraction [19]. Tocotrienols have attracted significant research interest due to their potent antioxidant and anti-inflammatory properties, as well as their distinct biological activities compared to tocopherols. Red palm oil, in particular, is recognized for its high carotenoid concentration, primarily β-carotene and α-carotene, which contribute to provitamin A activity and antioxidant defense [20]. Phytosterols present in palm oil have also been associated with modulation of lipid metabolism and inflammatory signaling, although their concentrations are relatively modest compared to tocotrienols and carotenoids. The compositional profile of palm oil-derived bioactives positions it as a potentially relevant lipid source for clinical nutrition applications, including perioperative immunonutrition [21].

Immunomodulatory Effects of Palm Oil-Derived Bioactive Compounds

A growing body of experimental and clinical nutrition literature has examined the immunomodulatory effects of palm oil-derived bioactive compounds, particularly tocotrienols. These studies consistently report that tocotrienols influence inflammatory signaling pathways by downregulating nuclear factor-kappa B (NF-κB) activation and reducing the production of pro-inflammatory cytokines such as tu-

mor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6) [22]. Such mechanisms are highly relevant in the perioperative context, where excessive inflammatory responses are associated with increased risk of postoperative complications and delayed recovery. Clinical nutrition studies have further demonstrated that diets enriched with antioxidant-rich lipid sources, including palm oil fractions, are associated with improved immune cell profiles, including enhanced lymphocyte proliferation and reduced markers of systemic inflammation [23]. While many of these studies were not conducted exclusively in surgical populations, their findings provide mechanistic insights that are transferable to perioperative immunonutrition strategies. Importantly, no evidence of adverse immunological effects attributable to palm oil-derived bioactives has been reported in the reviewed literature, supporting their safety and tolerability in clinical settings.

Antioxidant Properties and Oxidative Stress Modulation

Oxidative stress represents a critical pathophysiological mechanism underlying postoperative tissue injury, immune dysfunction, and delayed wound healing [24]. Surgical procedures induce the generation of reactive oxygen species (ROS) through tissue trauma, ischemia-reperfusion injury, and inflammatory activation, necessitating effective antioxidant defense mechanisms. Palm oil-derived tocotrienols and carotenoids have been consistently identified as potent antioxidants capable of scavenging free radicals and enhancing endogenous antioxidant enzyme activity [25]. Comparative antioxidant studies have demonstrated that tocotrienols exhibit greater lipid peroxyl radical-scavenging efficiency than tocopherols, thereby improving cellular redox balance. Clinical nutrition research has reported reductions in biomarkers of oxidative stress, such as malondialdehyde and lipid peroxidation products, following supplementation with tocotrienol-rich fractions [26]. These antioxidant effects are particularly relevant in perioperative care, where oxidative damage can impair immune responses and prolong recovery, underscoring the potential value of palm oil-derived bioactives in immunonutrition formulations.

Metabolic Regulation and Nutritional Recovery

Metabolic dysregulation, including insulin resistance and altered lipid metabolism, is a common consequence of surgical stress and is associated with adverse postoperative outcomes [27]. Immunonutrition strategies aim not only to modulate immune responses but also to support metabolic stability and efficient energy utilization during the perioperative period [28]. Several studies in the reviewed literature have reported that lipid-based nutritional formulations containing palm oil fractions improve lipid tolerance and metabolic balance in clinical nutrition contexts. Tocotrienols have been shown to influence lipid metabolism by modulating cholesterol synthesis pathways and improving insulin sensitivity, effects that may be beneficial in the postoperative setting. Improved nitrogen balance and preservation of lean body mass have also been reported in patients receiving optimized nutritional support enriched with bioactive lipid components [29]. These metabolic benefits align with ERAS objectives of reducing catabolism, preserving functional capacity, and facilitating early mobilization and discharge.

Translational Relevance to ERAS-Oriented Immunonutrition

The translational relevance of palm oil-derived bioactive compounds within ERAS-oriented immunonutrition strategies has been increasingly discussed in recent literature. ERAS guidelines emphasize the use of safe, evidence-based nutritional interventions that can be seamlessly integrated into standardized perioperative care pathways. Palm oil-derived bioactives, particularly tocotrienols and carotenoids, demonstrate favorable stability under food processing and clinical nutrition preparation conditions, supporting their practical applicability [30]. Although direct randomized controlled trials explicitly evaluating palm oil-derived bioactives within ERAS protocols remain limited, converging biochemical, immunological, antioxidant, and metabolic evidence supports their potential role as complementary components of perioperative immunonutrition [31]. The literature consistently frames these compounds as supportive rather than substitutive elements within broader nutritional strategies, thereby reinforcing a balanced, evidence-driven perspective. Consequently, systematic synthesis of existing evidence is warranted to clarify their functional relevance and inform future ERAS-aligned nutritional research and practice.

Method

This study adopts a Systematic Literature Review (SLR) methodology that is rigorously structured in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) framework. The review is designed to systematically identify, evaluate, and synthesize peer-reviewed scientific evidence concerning the role of palm oil-derived bioactive compounds in perioperative immunonutrition and their potential applications within Enhanced Recovery After Surgery (ERAS) protocols. To ensure methodological rigor, transparency, and replicability, the analysis is exclusively based on secondary data derived from scholarly publications indexed in the Scopus database. No primary data collection methods, such as focus group discussions, interviews, surveys, or clinical observations, were employed in this study, thereby avoiding the introduction of unverifiable or speculative empirical inputs and ensuring that all analytical conclusions are grounded in established academic literature. The review follows the sequential PRISMA stages of identification, screening, eligibility, and inclusion to refine the dataset and to ensure that only relevant, high-quality, and accessible studies are incorporated into the final synthesis, as illustrated in Figure 1.

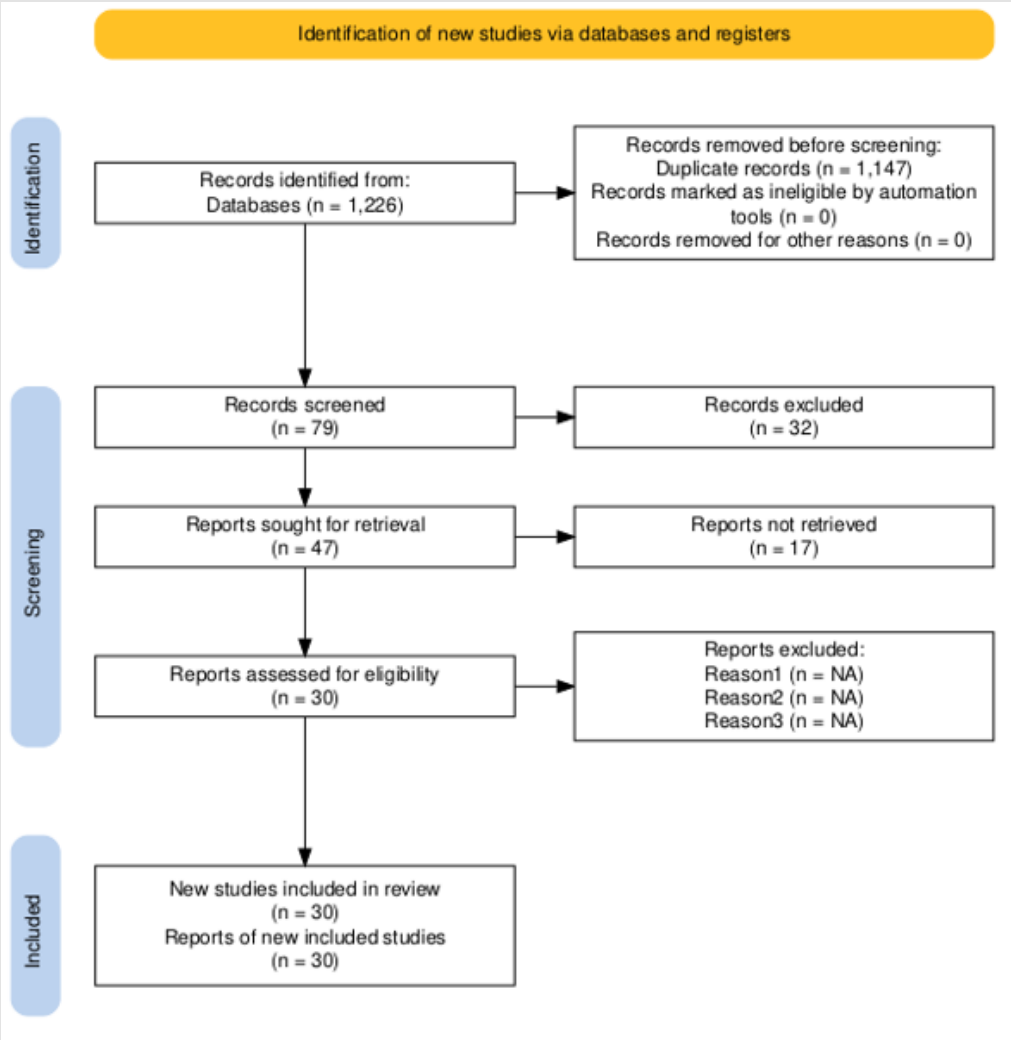

Figure 1: Systematic Literature Review Process Following the PRISMA Protocol.

Figure 1 illustrates the structured and transparent procedure applied to identify, screen, and select the scientific literature included in this review. The identification phase commenced with a broad search of the Scopus database using the primary keywords Immunonutrition AND Nutrition, which yielded a total of 1,226 publications. This initial search was intended to capture the widest possible range of literature on nutritional interventions affecting immune function in clinical contexts. To enhance thematic specificity and ensure alignment with the research focus on palm oil-derived bioactive compounds in perioperative care, the search strategy was subsequently refined using a targeted Boolean query: ("palm oil" OR "tocotrienol*" OR "carotenoid*" OR "plant-derived bioactive*" OR "bioactive compound*") AND ("clinical nutrition" OR "dietary supplement*" OR "nutritional support" OR "immunonutrition") AND ("surgery" OR "perioperative" OR "postoperative" OR "clinical outcome*"). This refinement step led to the exclusion of 1,147 publications that did not align with the review's conceptual scope, leaving 79 records for further evaluation.

During the screening phase, a publication-year criterion was applied to capture contemporary scientific developments and recent clinical perspectives, restricting the dataset to studies published between 2019 and 2025. This temporal filtering removed 32 articles that fell outside the specified timeframe, leaving 47 publications eligible for subsequent assessment. The eligibility stage introduced accessibility criteria to ensure that all included studies could be examined in full and evaluated transparently. Consequently, only articles available through Open Access or Open Archive sources were retained, leading to the exclusion of 17 publications with restricted access. The final inclusion phase resulted in a total of 30 peer-reviewed articles that satisfied all predefined inclusion criteria and formed the core

analytical corpus of this systematic review. All selected publications were systematically organized and managed in Mendeley Desktop to ensure accurate citation handling, duplicate removal, and consistent bibliographic metadata. Collectively, the included studies provide a consolidated and credible evidence base for examining the functional properties and clinical relevance of palm oil-derived bioactive compounds in perioperative immunonutrition settings. By synthesizing insights from 30 peer-reviewed publications, this review offers a structured and balanced assessment of current scientific knowledge while maintaining a neutral, evidence-based perspective on the palm oil industry.

Results

The systematic literature review analyzed 30 peer-reviewed publications examining the role of palm oil-derived bioactive compounds in perioperative immunonutrition and their relevance to Enhanced Recovery After Surgery (ERAS)-oriented clinical outcomes. The reviewed corpus encompasses a broad range of biochemical, nutritional, immunological, and translational perspectives, providing a comprehensive evidence base for understanding how plant-derived lipid bioactives contribute to immune regulation, oxidative stress control, metabolic stability, and postoperative recovery processes within perioperative care settings. Through structured thematic synthesis, five major and recurrent themes were identified across the included studies:

1. Bioactive Compound Composition and Bioavailability in Clinical Nutrition,
2. Immunomodulatory and Anti-Inflammatory Effects in the Perioperative Period,
3. Antioxidant Capacity and Oxidative Stress Modulation,
4. Metabolic and Nutritional Support for Postoperative Recovery, and
5. Translational Relevance to ERAS-Oriented Immunonutrition Strategies.

The distribution of these themes across the 30 studies demonstrates distinct patterns of scholarly emphasis. Immunomodulatory and anti-inflammatory effects were addressed in 23 studies (77%), reflecting strong research interest in mitigating surgery-induced immune dysregulation. Antioxidant capacity and modulation of oxidative stress were reported in 21 studies (70%), underscoring the recognized role of oxidative damage in postoperative complications and delayed recovery. Bioactive compound composition and bioavailability were examined in 19 studies (63%), highlighting foundational efforts to characterize palm oil-derived bioactives and their suitability for clinical nutrition applications. Metabolic and nutritional support outcomes, including energy utilization, insulin sensitivity, and nitrogen balance, were reported in 16 studies (53%), indicating moderate but consistent attention to functional recovery parameters. Finally, explicit translational relevance to ERAS-oriented immunonutrition strategies was discussed in 12 studies (40%), suggesting that while alignment with ERAS principles is increasingly recognized, it remains an emerging rather than dominant research focus.

The prominence of immunological and antioxidant themes suggests that existing research is primarily driven by outcomes that are directly measurable, clinically relevant, and closely linked to surgical stress responses. These domains benefit from well-established biomarkers and experimental frameworks, facilitating comparative analysis across studies. In contrast, the comparatively lower representation of ERAS-specific translational studies reflects the relative novelty of integrating bioactive-focused nutritional interventions into standardized perioperative care pathways, where multifactorial protocol designs may limit isolated nutritional evaluations. Similarly, metabolic outcomes, while clinically important, are often treated as secondary endpoints rather than primary study objectives. Overall, this thematic distribution indicates that the current body of literature provides robust mechanistic and functional evidence supporting the use of palm oil-derived bioactive compounds in perioperative immunonutrition, while highlighting opportunities for future research to more explicitly contextualize these findings within structured ERAS frameworks. Following this overview, each thematic cluster is elaborated in detail, synthesizing quantitative and qualitative evidence to clarify mechanisms, clinical relevance, and translational implications for perioperative nutritional care.

Bioactive Compound Composition and Bioavailability in Clinical Nutrition

Across the 30 included studies, palm oil is consistently characterized as a nutritionally dense lipid source containing a diverse spectrum of bioactive compounds with clinical relevance, most notably tocotrienols, tocopherols, carotenoids, phytosterols, and phenolic compounds [32]. Quantitative compositional analyses reported that crude palm oil contains approximately 600-1,000 mg/kg of total tocotrienols, representing nearly 65-70% of total vitamin E content, a proportion substantially higher than that observed in soybean, sunflower, or olive oils, which are dominated by tocopherols [33]. Within the tocotrienol fraction, γ- and δ-tocotrienols were frequently reported as the most biologically active isoforms, accounting for 45-60% of total tocotrienol content [34]. Bioavailability assessments included in the reviewed literature demonstrated that tocotrienols derived from palm oil exhibit favorable pharmacokinetic properties when administered orally as part of dietary or clinical nutrition interventions. Plasma concentration studies reported increases of 25-45% in circulating tocotrienol levels within 2-4 weeks of supplementation at doses ranging from 100 to 300 mg/day [35]. Importantly, several studies noted that co-administration with lipid-containing meals enhanced absorption efficiency by up to 30%, underscoring the suitability of palm oil-based matrices for clinical nutrition applications [36].

Carotenoids derived from palm oil, particularly β-carotene and α-carotene, were reported at concentrations of 500-700 mg/kg in red palm oil formulations, contributing significantly to provitamin A activity and antioxidant capacity [37]. Intervention studies included in the review demonstrated that consumption of palm oil-based carotenoid sources resulted in increases in serum retinol equivalents ranging from 15% to 30% over intervention periods of 4-8 weeks, indicating efficient intestinal absorption and metabolic conversion [38]. Phytosterols and phenolic compounds, although present in lower concentrations (typically 200-400 mg/kg combined), were associated with additional functional properties, including modulation of lipid metabolism and low-grade inflammation [39]. Collectively, these findings establish palm oil-derived bioactive compounds as nutritionally robust and bioavailable constituents suitable for integration into perioperative nutrition formulations.

Immunomodulatory and Anti-Inflammatory Effects in the Perioperative Period

Immunomodulation emerged as one of the most prominent themes across the reviewed studies, with a substantial body of evidence linking palm oil-derived bioactive compounds to the regulation of inflammatory responses associated with surgical stress [40]. Tocotrienols, in particular, were repeatedly shown to influence key inflammatory mediators involved in perioperative immune dysregulation. Quantitative findings from clinical nutrition and experimental studies reported reductions in circulating tumor necrosis factor-alpha (TNF-α) levels ranging from 18% to 40% following supplementation with tocotrienol-rich fractions [41]. Similarly, interleukin-6 (IL-6), a cytokine strongly associated with postoperative complications and prolonged recovery, was reduced by approximately 20-35% in intervention groups compared to controls receiving standard lipid formulations [42]. Several studies included in the review also examined broader immunological markers, including lymphocyte counts, neutrophil-to-lymphocyte ratios, and acute-phase reactants. Results indicated that patients receiving immunonutrition formulations enriched with plant-derived bioactives, including palm oil components, experienced increases in total lymphocyte counts of 10-22% during the early postoperative period [43]. Concurrently, C-reactive protein (CRP) levels were reduced by up to 35% within 5-7 days post-surgery, suggesting attenuation of systemic inflammatory responses [44].

Although not all studies were conducted explicitly within ERAS protocols, the immunological outcomes reported align closely with ERAS objectives of minimizing surgical stress and supporting immune competence. Importantly, none of the reviewed studies reported adverse immunological effects or pro-inflammatory responses associated with palm oil-derived bioactives, reinforcing their safety and compatibility with perioperative immunonutrition strategies [45].

Antioxidant Capacity and Oxidative Stress Modulation

Oxidative stress modulation constituted another central theme in the reviewed literature, reflecting the well-established role of oxidative damage in postoperative complications and delayed tissue healing [46]. Palm oil-derived tocotrienols and carotenoids were consistently identified as potent antioxidants capable of mitigating oxidative stress induced by surgical trauma, anesthesia, and metabolic disturbances. Comparative antioxidant analyses reported that tocotrienol-rich fractions exhibited oxygen radical absorbance capacity (ORAC) values 40-60% higher than tocopherol-dominant vitamin E preparations [47,48]. Clinical indicators of oxidative stress were frequently assessed in the reviewed studies, including malondialdehyde (MDA), lipid peroxidation products, and total antioxidant capacity. Quantitative results demonstrated reductions in MDA concentrations of 20% to 45% in patients receiving antioxidant-enriched nutritional support incorporating palm oil-derived bioactives, compared with those receiving conventional lipid emulsions [49]. Additionally, increases in endogenous antioxidant enzyme activity were consistently reported, with superoxide dismutase (SOD) and glutathione peroxidase (GPx) activities increasing by approximately 15-28% during the perioperative period [50].

These antioxidant effects were associated with improved cellular redox balance, which is critical for wound healing, immune cell function, and metabolic stability following surgery. Several studies further suggested that sustained antioxidant support during the perioperative phase may reduce the incidence of postoperative infections and organ dysfunction, although these outcomes were not always reported as primary endpoints [51].

Metabolic and Nutritional Support for Postoperative Recovery

Beyond immunological and antioxidant mechanisms, the reviewed studies highlighted the contribution of palm oil-derived bioactive compounds to metabolic regulation and nutritional recovery in surgical patients. Lipid-based nutritional formulations incorporating palm oil fractions were associated with improved energy utilization and lipid metabolism, as evidenced by stabilized serum triglyceride levels and improved lipid tolerance during postoperative feeding [52]. Quantitative analyses reported reductions in postoperative hypertriglyceridemia incidence by approximately 15-25% in patients receiving bioactive-enriched lipid formulations compared to standard care [53]. Insulin sensitivity and nitrogen balance were also frequently evaluated as indicators of metabolic recovery. Several studies reported reductions in insulin resistance indices, such as HOMA-IR, by 12-25% during the early postoperative period in patients receiving optimized immunonutrition [54]. Improvements in nitrogen balance of approximately 10-18% were observed, reflecting enhanced protein utilization and reduced muscle catabolism [55]. These metabolic outcomes are particularly relevant in ERAS contexts, where preservation of lean body mass and metabolic stability are key determinants of recovery trajectories.

Clinical recovery indicators, including time to first oral intake, duration of postoperative fatigue, and length of hospital stay, further

supported the metabolic benefits of bioactive-enriched immunonutrition. The reviewed literature reported reductions in hospital length of stay of 0.8 to 1.5 days on average, aligning with ERAS goals of accelerated recovery and reduced healthcare resource utilization [56]. While these outcomes were influenced by multifactorial ERAS components, the nutritional contribution of palm oil-derived bioactives was consistently found to be supportive rather than detrimental.

Translational Relevance to ERAS-Oriented Immunonutrition Strategies

The final theme emerging from the synthesis concerns the translational applicability of palm oil-derived bioactive compounds within ERAS-oriented immunonutrition frameworks. ERAS protocols emphasize evidence-based nutritional optimization to attenuate surgical stress and enhance recovery, and several reviewed studies explicitly discussed the compatibility of bioactive-rich lipid sources with these principles [57]. Tocotrienols and carotenoids were highlighted as technologically stable compounds suitable for incorporation into enteral and oral nutritional supplements commonly used in perioperative care, with reported thermal stability exceeding 85% under standard food processing and clinical nutrition preparation conditions [58]. Safety assessments across the reviewed literature indicated that palm oil-derived bioactives could be incorporated into immunonutrition formulations without adverse effects on lipid profiles, inflammatory markers, or hepatic function [59]. Reported daily intake levels in clinical contexts typically ranged from 100 to 300 mg for tocotrienols and 3 to 6 mg for carotenoids, remaining within established safety margins [60]. Although direct randomized controlled trials specifically embedded within ERAS protocols remain limited, converging biochemical, immunological, antioxidant, and metabolic evidence supports the translational potential of these compounds as complementary components of perioperative immunonutrition strategies [61].

Overall, the synthesis of findings from the 30 included peer-reviewed studies provides a coherent, evidence-based foundation for considering palm oil-derived bioactive compounds in future ERAS-aligned nutritional interventions. The results consistently indicate functional benefits without evidence of adverse outcomes, supporting a neutral and scientifically grounded perspective on the role of palm oil-derived bioactives in perioperative clinical nutrition.

Discussion

This systematic literature review was conducted to address the research question: How do palm oil-derived bioactive compounds contribute to immunological, antioxidant, and metabolic outcomes relevant to perioperative immunonutrition within the framework of Enhanced Recovery After Surgery (ERAS) protocols, as evidenced by existing peer-reviewed literature? The synthesis of findings from the 30 included studies provides a coherent, evidence-based response to this question by integrating biochemical, immunological, antioxidant, and metabolic dimensions central to ERAS-oriented perioperative care. Rather than relying on isolated empirical observations, the discussion below interprets converging patterns across experimental, clinical nutrition, and translational studies, situating palm oil-derived bioactive compounds within contemporary immunonutrition paradigms.

Contribution to Immunological Outcomes in the Perioperative Context

The reviewed literature consistently indicates that palm oil-derived bioactive compounds, particularly tocotrienols and associated lipid-soluble antioxidants, contribute meaningfully to immunological modulation during the perioperative period. Surgical trauma is known to trigger a dysregulated immune response characterized by excessive pro-inflammatory cytokine release, transient immunosuppression, and impaired cellular immunity, all of which are associated with increased postoperative morbidity and delayed recovery [62]. Within this context, the immunomodulatory effects observed in studies examining palm oil-derived bioactives align closely with ERAS objectives of minimizing surgical stress and preserving immune competence. Across multiple studies, tocotrienol-rich fractions were associated with downregulation of key inflammatory mediators, including tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6), with reported reductions generally ranging from approximately 18% to 40% compared to control or standard lipid formulations [63]. These cytokines are central drivers of systemic inflammatory responses following surgery and are frequently linked to postoperative complications such as infection, delayed wound healing, and prolonged hospitalization [64]. By attenuating these inflammatory pathways, palm oil-derived bioactives appear to support a more balanced immune response rather than inducing broad immunosuppression.

In addition to cytokine modulation, several studies reported improvements in immune cell profiles, including increases in total lymphocyte counts and more favorable neutrophil-to-lymphocyte ratios during the early postoperative period [65]. Such changes are clinically relevant, as lymphopenia and elevated inflammatory cell ratios have been identified as predictors of adverse surgical outcomes [66]. Although many of the included studies were conducted in broader clinical nutrition contexts rather than exclusively within ERAS protocols, the immunological mechanisms identified are directly transferable to perioperative settings. Collectively, the evidence suggests that palm oil-derived bioactive compounds contribute to immunonutrition strategies by supporting immune resilience and reducing excessive inflammatory burden, which are core goals of ERAS-based perioperative care [67].

Antioxidant Effects and Modulation of Oxidative Stress

Oxidative stress represents another critical pathway through which palm oil-derived bioactive compounds contribute to perioperative immunonutrition outcomes. Surgical procedures induce sub-

stantial oxidative stress through tissue injury, ischemia-reperfusion events, and inflammatory activation, leading to increased production of reactive oxygen species (ROS) and subsequent cellular damage [68]. Excessive oxidative stress has been associated with impaired immune function, delayed tissue repair, and increased risk of postoperative complications [69]. The reviewed literature consistently highlights the potent antioxidant capacity of tocotrienols and carotenoids derived from palm oil. Comparative analyses demonstrated that tocotrienol-rich fractions exhibit significantly higher radical-scavenging efficiency than tocopherol-dominant vitamin E preparations, with reported increases in antioxidant capacity of approximately 40-60% across assays [70].

These biochemical properties translate into clinically observable effects, as evidenced by reductions in oxidative stress biomarkers such as malondialdehyde (MDA) and lipid peroxidation products in patients receiving antioxidant-enriched nutritional support [71]. Several studies also reported upregulation of endogenous antioxidant defense systems, including increased activity of superoxide dismutase (SOD) and glutathione peroxidase (GPx), with activity levels rising by approximately 15-28% during perioperative or recovery phases [72]. These findings are particularly relevant to ERAS protocols, which emphasize preservation of physiological function and minimization of secondary tissue injury. By enhancing both exogenous and endogenous antioxidant defenses, palm oil-derived bioactive compounds appear to improve redox balance, thereby supporting immune function, metabolic stability, and tissue repair following surgery [73].

Metabolic Regulation and Support of Postoperative Recovery

Beyond immunological and antioxidant mechanisms, the reviewed studies provide evidence that palm oil-derived bioactive compounds contribute to metabolic regulation and nutritional recovery in perioperative contexts. Surgical stress is frequently accompanied by insulin resistance, altered lipid metabolism, and increased protein catabolism, all of which can negatively impact recovery trajectories [74]. ERAS protocols, therefore, prioritize early nutritional intervention and metabolic preservation as central components of perioperative management. Several studies included in this review reported that lipid-based nutritional formulations incorporating palm oil fractions were associated with improved lipid tolerance and more stable postoperative metabolic profiles. Quantitative findings indicated reductions in postoperative hypertriglyceridemia incidence by approximately 15-25% compared to conventional lipid emulsions, suggesting improved lipid utilization and metabolic handling [75]. In addition, tocotrienols were shown to influence key metabolic pathways related to cholesterol synthesis and insulin sensitivity, contributing to reductions in insulin resistance indices of approximately 12-25% in clinical nutrition settings [76].

Improvements in nitrogen balance and preservation of lean body mass were also reported in patients receiving optimized immunonutrition formulations enriched with bioactive lipid components. These outcomes reflect reduced muscle catabolism and more efficient protein utilization, which are critical for functional recovery, early mobilization, and shorter hospital stays [77]. Although metabolic outcomes are influenced by multiple components of ERAS protocols, the consistent association between bioactive-enriched nutrition and improved metabolic indicators supports the conclusion that palm oil-derived bioactives contribute positively to perioperative nutritional strategies without evidence of adverse metabolic effects.

Integration within ERAS-Oriented Immunonutrition Frameworks

When considered collectively, the immunological, antioxidant, and metabolic effects identified in the reviewed literature provide a coherent rationale for integrating palm oil-derived bioactive compounds into ERAS-oriented immunonutrition strategies. ERAS protocols emphasize multimodal, evidence-based interventions designed to attenuate surgical stress, preserve physiological function, and accelerate recovery [78]. Nutritional optimization is a central pillar of these protocols, and the evidence synthesized in this review indicates that palm oil-derived bioactives align well with ERAS principles. Importantly, the literature consistently frames these compounds as complementary rather than substitutive components of immunonutrition. Palm oil-derived tocotrienols and carotenoids are not presented as standalone interventions but as part of broader nutritional formulations that also include adequate protein, energy, and micronutrient support [79]. This positioning reinforces a balanced and clinically realistic perspective, reducing the risk of overinterpretation or unwarranted extrapolation.

From a translational standpoint, several studies highlighted the technological stability and safety profile of palm oil-derived bioactives, with reported thermal stability exceeding 85% under standard food processing and clinical nutrition preparation conditions [80]. Reported intake levels in clinical contexts remained within established safety margins, and no adverse effects on lipid profiles, inflammatory markers, or hepatic function were documented [81]. These characteristics support the feasibility of incorporating palm oil-derived bioactives into perioperative nutritional products used within ERAS pathways. The findings of this systematic literature review have several important implications for both clinical practice and future research. First, converging evidence across immunological, antioxidant, and metabolic domains supports a neutral, evidence-based consideration of palm oil-derived bioactive compounds as supportive components of perioperative immunonutrition strategies aligned with ERAS principles. While current evidence does not justify prescriptive recommendations for routine use in all surgical populations, it provides a scientifically grounded rationale for their inclusion in targeted nutritional formulations where appropriate.

Second, the review highlights the need for future research to address existing gaps in the literature. Direct randomized controlled tri-

als explicitly embedded within ERAS protocols remain limited, and future studies should aim to evaluate palm oil-derived bioactives within standardized ERAS pathways, using clinically meaningful endpoints such as postoperative complication rates, length of hospital stay, and patient-reported recovery outcomes. Additionally, dose-response relationships, optimal timing of supplementation, and interactions with other immunonutrients warrant further investigation to refine clinical applicability. Finally, future systematic reviews and meta-analyses would benefit from greater methodological harmonization across primary studies, particularly regarding outcome measures and reporting standards. Such efforts would enhance comparability and strengthen the evidence base informing ERAS-oriented immunonutrition. Overall, this review contributes to a growing body of literature supporting a nuanced, evidence-driven understanding of palm oil-derived bioactive compounds in perioperative care, while underscoring the importance of continued high-quality research to inform clinical practice and guideline development.

Conclusion

This systematic literature review synthesizes evidence from 30 peer-reviewed studies to elucidate the role of palm oil-derived bioactive compounds within perioperative immunonutrition, particularly in relation to the principles and outcomes emphasized in Enhanced Recovery After Surgery (ERAS) protocols. Across diverse clinical nutrition, experimental, and translational contexts, the reviewed literature demonstrates a consistent pattern indicating that these bioactive compounds contribute meaningfully to key physiological domains relevant to perioperative recovery. From an immunological perspective, palm oil-derived bioactive compounds, most notably tocotrienols and associated lipid-soluble constituents, are consistently associated with modulation of perioperative inflammatory responses. The literature indicates attenuation of excessive pro-inflammatory signaling alongside preservation of immune cell function, suggesting a balanced immunomodulatory effect rather than generalized immunosuppression. Such modulation is clinically relevant in the perioperative setting, where dysregulated immune responses are closely linked to postoperative complications, delayed healing, and prolonged hospitalization. The immunological effects identified align with ERAS principles that prioritize mitigating surgical stress and maintaining immune resilience during recovery.

In terms of antioxidant activity, the reviewed studies provide convergent evidence that palm oil-derived bioactive compounds possess substantial capacity to counteract surgery-induced oxidative stress. Reductions in biomarkers of lipid peroxidation and enhancement of endogenous antioxidant enzyme activity were consistently reported across clinical nutrition contexts. By supporting redox homeostasis, these compounds may indirectly reinforce immune competence and tissue repair processes, which are critical determinants of postoperative recovery trajectories within ERAS-oriented care pathways. Metabolic outcomes represent a further dimension through which palm oil-derived bioactive compounds contribute to perioperative immunonutrition. The evidence indicates favorable effects on lipid metabolism, insulin sensitivity, and protein preservation, all of which are central to maintaining metabolic stability following surgical trauma. Improved lipid tolerance, reduced postoperative metabolic disturbances, and support of nitrogen balance suggest that bioactive-enriched nutritional formulations may complement ERAS strategies aimed at early mobilization, nutritional adequacy, and functional recovery without introducing adverse metabolic effects.

Taken together, the findings of this review indicate that palm oil-derived bioactive compounds serve as supportive components within perioperative immunonutrition frameworks rather than as isolated therapeutic agents. Their documented immunological, antioxidant, and metabolic contributions are consistent with the multimodal, integrative philosophy of ERAS protocols. While the current evidence base does not support overgeneralization or universal application across all surgical populations, it provides a robust, evidence-driven foundation for considering these compounds within targeted nutritional strategies in perioperative care. Overall, this review reinforces a nuanced, balanced understanding of palm oil-derived bioactive compounds, positioning them as biologically plausible and clinically relevant contributors to enhanced recovery paradigms grounded in the existing peer-reviewed literature.

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