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Immunomodulatory properties of palm oil derivatives in cancer immunotherapy: A systematic review of preclinical evidence

Abstract

Research efforts have increasingly explored natural bioactive compounds for their potential contribution to the regulation of immune mechanisms involved in cancer biology. Compounds derived from *Elaeis guineensis* contain several phytonutrients associated with antioxidant activity and immune signaling. However, current evidence on their immunomodulatory roles remains dispersed across experimental studies, highlighting the need for a systematic synthesis of preclinical findings. This study aims to synthesize existing evidence regarding the immunomodulatory properties of bioactive compounds derived from Palm Oil in experimental cancer models relevant to immunotherapy research. The analysis focuses on immune-related mechanisms, including cytokine regulation, immune cell activation, oxidative stress responses, and tumor microenvironment dynamics. The research employed a Systematic Literature Review following the PRISMA framework. Data were collected through structured searches in the Scopus database using predefined keywords. From an initial dataset of 400 records, a total of 31 preclinical studies were included after applying sequential filters related to relevance, publication year (2019–2025), language, and open-access status. The data were analyzed using qualitative thematic synthesis. The findings identified four main mechanisms: cytokine signaling modulation, activation of immune effector cells involved in tumor surveillance, antioxidant protection of immune cells, and regulation of tumor microenvironment pathways. Frequently studied compounds include Tocotrienols, Carotenoids, and Phytosterols. Overall, current preclinical evidence indicates that palm-derived phytonutrients interact with several immune-related pathways relevant to cancer immunology, while further experimental research is required to expand mechanistic understanding.

Keywords: palm oil derivatives, immunomodulation, cancer immunology, tocotrienols, systematic review

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Introduction

Across the world, cancer is widely recognized as a critical public health issue due to its substantial contribution to disease burden and death in both high-income and low- to middle-income regions. According to recent epidemiological assessments, the global burden of cancer includes more than 19 million new cases annually and close to 10 million related deaths, reflecting the ongoing impact of malignant diseases on health systems and public health infrastructure.[1] Although advances in early detection, targeted therapies, and precision medicine have improved clinical outcomes for certain cancer types, many malignancies continue to demonstrate resistance to conventional treatments such as chemotherapy, radiation therapy, and surgical intervention. These limitations have stimulated growing scientific interest in therapeutic strategies capable of harnessing the capacity of the human immune system to identify and remove malignant cells with greater effectiveness.[2]

Within this framework, immunotherapy has gained recognition as one of the most promising approaches in current oncology research. Immunotherapy strategies aim to stimulate or restore immune functions that can identify abnormal cells and suppress tumor progression. This approach has led to the development of several treatment strategies, including immune checkpoint inhibitors, therapeutic cancer vaccines, adoptive cellular therapies, and cytokine-based interventions.[3] These approaches operate by modulating immune signaling pathways, enhancing antigen presentation, or strengthening cytotoxic immune responses against tumor cells. Despite their transformative potential, current immunotherapeutic interventions still face several challenges, including heterogeneous patient responses, immune-related adverse effects, and the complex regulatory dynamics of the tumor microenvironment.[4] As a result, considerable attention has been directed toward identifying bioactive compounds capable of supporting or modulating immune responses in ways that complement existing immunotherapy strategies.

Bioactive molecules originating from plant sources are gaining significant attention in biomedical research owing to their varied pharmacological characteristics, particularly antioxidant, anti-inflammatory, and immunomodulatory activities. Numerous plant-derived phytochemicals have demonstrated the ability to influence cellular signaling pathways associated with immune regulation and tumor suppression. Such compounds may interact with immune cells, cytokine networks, and oxidative stress pathways that collectively shape immune responses within cancer-related biological environments.[5] As a consequence, phytochemicals are widely investigated as complementary or supportive agents within experimental oncology research. Their relatively broad biological activity profiles make them promising candidates for further investigation within the rapidly evolving field of immuno-oncology.

Among the various plant-derived sources of bioactive compounds, Palm Oil has received increasing scientific attention due to its rich composition of naturally occurring phytonutrients. Extracted primarily from the fruit of Elaeis guineensis, palm oil contains several lipid-soluble micronutrients with well-documented antioxidant and biological properties. These include compounds such

as Tocotrienols, Tocopherols, Carotenoids, and Phytosterols, which are known to participate in cellular protection mechanisms against oxidative stress and inflammatory damage. Of particular interest are tocotrienols, which have been widely investigated for biological activities that extend beyond their well-known antioxidant roles. Several experimental investigations have reported that tocotrienol-rich fractions derived from palm oil may influence cellular pathways related to inflammation, immune signaling, and apoptosis in tumor cells.[6]

Preclinical studies have increasingly explored how palm-derived phytonutrients may interact with immune-related biological pathways associated with cancer development. Evidence from experimental cellular systems and animal models suggests that certain palm-derived compounds may influence immune responses through mechanisms such as modulation of cytokine expression, enhancement of immune cell activity, and regulation of oxidative stress responses within tumor-associated environments.[7] In cancer immunotherapy studies, such mechanisms are particularly important because immune activation and immune regulation significantly affect treatment outcomes. Some laboratory studies have demonstrated that tocotrienols may affect inflammatory mediators such as interleukins and tumor necrosis factors, which are important regulators of immune signaling networks in tumor biology.[8] Additionally, carotenoids and other palm-derived antioxidants have been investigated for their potential ability to support immune cell function under oxidative conditions frequently associated with tumor progression.

Another aspect that has stimulated growing interest is the potential interaction between palm-derived phytonutrients and the tumor microenvironment. The tumor microenvironment is a multifaceted biological setting that includes cancer cells, immune populations, stromal structures, and signaling mediators, all of which collectively affect tumor growth and immune detection mechanisms. Several experimental investigations have reported that natural antioxidants may contribute to modifying oxidative stress levels, inflammatory signaling pathways, and immune cell infiltration patterns within tumor tissues.[9] Although these findings remain primarily within preclinical contexts, they suggest that naturally occurring bioactive compounds could play supportive roles in shaping immune-related responses relevant to cancer therapy research.

Despite the growing body of experimental studies examining the biological activities of palm-derived phytonutrients, the available literature remains widely dispersed across different biomedical disciplines, including nutritional science, molecular oncology, immunology, and pharmacology. Individual studies often focus on specific compounds, experimental models, or molecular pathways, making it challenging to obtain a consolidated understanding of how these bioactive substances may influence immune-related mechanisms within cancer research contexts.[10] Furthermore, variations in experimental design, compound dosage, and biological models used across different studies may lead to heterogeneous findings that require systematic synthesis to clarify overarching trends and research patterns.

For this reason, systematic synthesis of existing evidence is essential in order to provide a clearer overview of the current state of knowledge. The use of a Systematic Literature Review allows researchers to identify relevant studies, evaluate their methodological characteristics, and integrate findings within a transparent and reproducible analytical framework. By applying systematic search strategies and structured screening procedures, SLR studies help consolidate fragmented research evidence while minimizing bias in the selection and interpretation of scientific literature.[11,12] Within the context of palm-derived phytonutrients and cancer immunology research, such an approach is particularly valuable because it enables comprehensive mapping of experimental findings related to immunomodulatory mechanisms, antioxidant functions, and tumor-related biological pathways.

In response to this research gap, the present study systematically evaluates and integrates preclinical evidence on the immunomodulatory properties of palm oil derivatives in experimental cancer models linked to immunotherapy investigations. Specifically, this study analyzes peer-reviewed studies that explore how bioactive compounds derived from oil palm may influence immune-related biological processes, including cytokine regulation, immune cell activation, oxidative stress responses, and tumor microenvironment dynamics. This study aims to synthesize findings from various experimental investigations in order to provide an organized overview of the existing scientific evidence on palm-derived phytonutrients within cancer-focused immunological research.

To support the achievement of this objective, the study is directed by the following research questions:

RQ1: *What immunomodulatory mechanisms associated with palm oil–derived bioactive compounds have been reported in preclinical cancer research?*

RQ2: *How do palm-derived phytonutrients interact with immune-related pathways relevant to tumor development and immune response regulation within experimental cancer models?*

Addressing these questions provides a clearer understanding of how existing preclinical evidence characterizes the potential biological interactions between palm-derived bioactive compounds and immune mechanisms in cancer-related research contexts.

Literature review

Scientific interest in the interaction between natural bioactive compounds and immune-mediated cancer responses has expanded considerably in recent decades. Within contemporary oncology research, increasing attention has been directed toward naturally occurring phytochemicals capable of influencing immune signaling pathways that regulate tumor recognition, inflammatory responses, and cellular defense mechanisms. The growing field of Cancer Immunology explores how immune cells, cytokine networks, and molecular signaling systems interact with malignant cells. These interactions determine whether tumors evade immune detection or become targets for immune-mediated destruction. Understanding how bioactive compounds influence these pathways has therefore become a major research focus in the development of supportive or complementary strategies related to Cancer Immunotherapy.

Immunological foundations of cancer immunotherapy

The ability to recognize abnormal cellular changes and suppress malignant transformation is a fundamental role of the immune system. Under normal physiological conditions, immune surveillance mechanisms continuously monitor tissues for the presence of abnormal or transformed cells. The early elimination of potentially malignant cells is largely mediated by immune effectors such as cytotoxic T lymphocytes, NK cells, and macrophages. However, tumors may develop mechanisms that allow them to evade immune detection through alterations in antigen presentation, immune checkpoint signaling, and cytokine-mediated immunosuppression.[13,14]

Modern cancer immunotherapy seeks to overcome these immune evasion strategies by restoring or enhancing immune responses against tumor cells. A number of treatment modalities have been developed, including immune checkpoint inhibitors, adoptive T-cell therapies, cancer vaccines, and cytokine-mediated interventions. These therapies aim to reactivate immune cells that can target tumor antigens and suppress malignant cell proliferation. Despite significant clinical progress, not all patients respond equally to immunotherapy, and some tumors develop resistance mechanisms that limit treatment efficacy. These challenges have stimulated ongoing research exploring bioactive compounds capable of modulating immune responses and supporting immune-mediated tumor suppression.[15]

Immune signaling pathways are central to the success of immunotherapy approaches. Intercellular signaling within the immune system is partly regulated by cytokines such as IL-2, IL-6, IL-10, and interferon-gamma (IFN-γ), which also influence inflammatory activity in tumor environments. The relative balance of pro-inflammatory and anti-inflammatory cytokines can strongly influence both tumor development and immune system activity. Consequently, compounds capable of influencing cytokine expression and immune signaling pathways are frequently investigated as potential modulators of tumor-associated immune responses.[16]

Natural bioactive compounds in immunomodulatory research

Increasing scientific attention has been directed toward phytochemicals derived from plants owing to their diverse biological properties. Many plant-based compounds demonstrate antioxidant, anti-inflammatory, and immunomodulatory properties that may influence cellular signaling systems associated with disease development. In cancer research, phytochemicals are frequently investigated for their ability to regulate oxidative stress pathways, modulate immune cell activity, and influence tumor-related molecular mechanisms.[17]

Natural antioxidants represent an important class of compounds investigated in this context. The overproduction of reactive oxygen species (ROS) can promote oxidative stress, potentially resulting in DNA damage, mutational changes in cells, and tumor development. At the same time, oxidative stress may impair immune cell function by disrupting signaling pathways involved in immune activation. Antioxidant compounds derived from natural sources may help regulate oxidative balance and support immune cell functionality under conditions associated with tumor development.[18]

Phytochemicals capable of influencing immune signaling pathways may also affect the tumor microenvironment. Within the tumor microenvironment, cancer cells interact with immune cells, stromal structures, and multiple signaling mediators, forming a network that shapes tumor progression and immune responses. Modulation of oxidative stress, inflammatory signaling, and immune cell recruitment within this microenvironment represents a potential mechanism through which natural compounds may influence cancer-related biological processes.[19]

Palm oil as a source of bioactive phytonutrients

Among the various natural sources of bioactive compounds investigated in biomedical research, Palm Oil has attracted scientific interest due to its rich composition of lipid-soluble phytonutrients. Derived primarily from the fruit of Elaeis guineensis, palm oil contains a range of biologically active compounds known to possess antioxidant and metabolic properties. These include several members of the vitamin E family as well as carotenoid pigments and plant sterols that participate in cellular protection mechanisms.[20]

One of the distinctive features of palm oil is its substantial concentration of tocotrienols, a form of vitamin E compounds identified by their unsaturated isoprenoid side chains. Numerous studies have examined tocotrienols for their possible biological functions in cellular regulation, including modulation of inflammatory signaling pathways, antioxidant protection, and regulation of gene expression associated with cell survival and apoptosis.[21] Compared with other vitamin E forms, tocotrienols demonstrate distinctive molecular properties that may influence membrane interactions and cellular signaling systems involved in immune regulation.

Another group of compounds present in palm oil includes Carotenoids, which contribute to the characteristic reddish coloration of crude palm oil. Carotenoids serve as naturally occurring antioxidants that counteract reactive oxygen species, thereby protecting cells from oxidative stress–related damage. Furthermore, these molecules have been investigated for their potential contributions to immune regulation and inflammatory pathway modulation.[22]

In addition to tocotrienols and carotenoids, palm oil also contains Phytosterols, which are structurally similar to cholesterol but originate from plant sources. Phytosterols have been associated with various biological activities, including modulation of lipid metabolism and anti-inflammatory effects. Some experimental studies suggest that phytosterols may also influence immune signaling pathways, although the precise mechanisms remain an active area of investigation.[23]

Immunomodulatory mechanisms of palm-derived compounds

Several preclinical studies have investigated the potential immunomodulatory properties of palm-derived bioactive compounds in experimental cancer models. These investigations often focus on how tocotrienols and related phytonutrients influence immune cell activity, cytokine signaling, and oxidative stress pathways associated with tumor development. Evidence from cellular and animal studies suggests that these compounds may interact with multiple molecular targets involved in immune regulation.[24]

One proposed mechanism involves the regulation of cytokine production within immune cells. Experimental research indicates that tocotrienol-rich fractions may influence the expression of cytokines involved in immune activation and inflammatory signaling. Changes in cytokine profiles may alter immune cell communication and potentially enhance immune surveillance mechanisms that contribute to tumor recognition.[25]

Another mechanism involves modulation of oxidative stress responses. Reactive oxygen species generated during tumor development may disrupt immune cell function and contribute to inflammatory processes that support tumor growth. Antioxidant compounds present in palm-derived phytonutrients may help regulate oxidative balance within cellular environments, thereby supporting immune cell activity and maintaining physiological signaling processes.[26]

Research has also explored how tocotrienols may influence intracellular signaling pathways associated with inflammation and cell survival. Experimental studies have indicated that tocotrienols may interact with transcription factors including nuclear factor-kappa B (NF-κB), which is involved in controlling the expression of inflammatory genes. Modulation of NF-κB signaling pathways may

influence immune responses and tumor-related biological processes in experimental systems.[27]

Tumor microenvironment and immune response modulation

A key factor influencing how effectively the immune system responds to cancer cells is the tumor microenvironment. Within this microenvironment, interactions between tumor cells, immune cells, and signaling molecules create conditions that may either promote or inhibit immune-mediated tumor suppression. The presence of oxidative stress, inflammatory cytokines, and immunosuppressive signaling molecules can significantly affect the capacity of immune cells to recognize and eliminate malignant cells.[28]

Natural bioactive compounds capable of influencing these microenvironmental factors may contribute to shaping immune responses in experimental cancer models. Some preclinical studies suggest that palm-derived phytonutrients may affect immune cell infiltration patterns within tumor tissues, influence cytokine signaling networks, and regulate oxidative stress levels that affect immune cell functionality. Although these observations remain within laboratory-based research contexts, they highlight the potential biological interactions between palm-derived compounds and immune-related pathways.[29]

Need for systematic synthesis of preclinical evidence

Despite increasing interest in the biological activities of palm-derived phytonutrients, the available research remains dispersed across multiple scientific disciplines and experimental models. Individual studies frequently examine specific molecular pathways, compound concentrations, or cancer cell types, resulting in a fragmented understanding of the broader immunological implications. Differences in experimental conditions, biological models, and analytical methods further contribute to variability in reported findings.[30]

Consequently, a structured synthesis of the existing literature is necessary to consolidate current knowledge regarding the immunomodulatory properties of palm oil derivatives within cancer research contexts. Systematic evaluation of preclinical studies can provide a clearer understanding of recurring research themes, commonly investigated mechanisms, and areas where further investigation may be required. Such synthesis is particularly relevant in emerging research areas where experimental evidence is expanding rapidly but remains distributed across diverse fields of biomedical investigation.

Within this context, the present study employs a systematic literature review approach to evaluate preclinical evidence examining the interaction between palm-derived phytonutrients and immune-related biological pathways in cancer research. By integrating findings from multiple experimental studies, the review aims to provide a structured overview of how bioactive compounds associated with palm oil may influence immune signaling mechanisms relevant to cancer immunology while maintaining a balanced and evidence-based scientific perspective.

Methodology

The present study adopted a Systematic Literature Review design aligned with the PRISMA framework to promote transparency, reproducibility, and rigorous methodological standards. This review systematically sought, screened, and synthesized preclinical studies exploring the immune-regulating effects of bioactive compounds derived from oil palm, particularly Elaeis guineensis, in experimental cancer contexts associated with immunotherapy research. The SLR framework consisted of four sequential steps identification, screening, eligibility, and inclusion guided by established criteria covering database selection, keyword strategies, publication years, language restrictions, and open-access availability. Using a standardized protocol, all stages of the review including search strategy formulation, article screening, data extraction, and qualitative synthesis were systematically executed. This section is dedicated to the procedural implementation of the review and does not address conceptual discussions regarding immunological mechanisms or therapeutic approaches in cancer immunotherapy.

The PRISMA-guided workflow employed in this review is presented in Figure 1, highlighting the stepwise process of identifying, screening, assessing eligibility, and including studies. The search for relevant literature was carried out exclusively in Scopus to capture a comprehensive set of high-quality, peer-reviewed studies within the fields of biomedical and life sciences. In the identification stage, an initial exploratory search using the keyword combination *palm oil AND cancer* generated 400 records. To enhance analytical focus and contextual relevance, a more targeted Boolean search string was subsequently applied: *("palm oil" OR "Elaeis guineensis" OR "palm extract" OR "palm phytonutrients" OR "palm bioactive compounds" OR "palm oil component" OR "palm oil components") AND (tocotrienol OR tocotrienols OR carotenoid OR carotenoids OR phytosterol OR phytosterols OR "vitamin E") AND (cancer OR tumor OR tumour OR carcinoma OR neoplasm OR malignancy OR malignant OR metastasis OR metastatic OR immunotherapy OR immunomodulation OR immunomodulatory OR "immune response" OR immune OR immunity)*. This refinement resulted in the exclusion of 212 articles that did not align with the specific scope of the review, yielding 188 records for further evaluation.

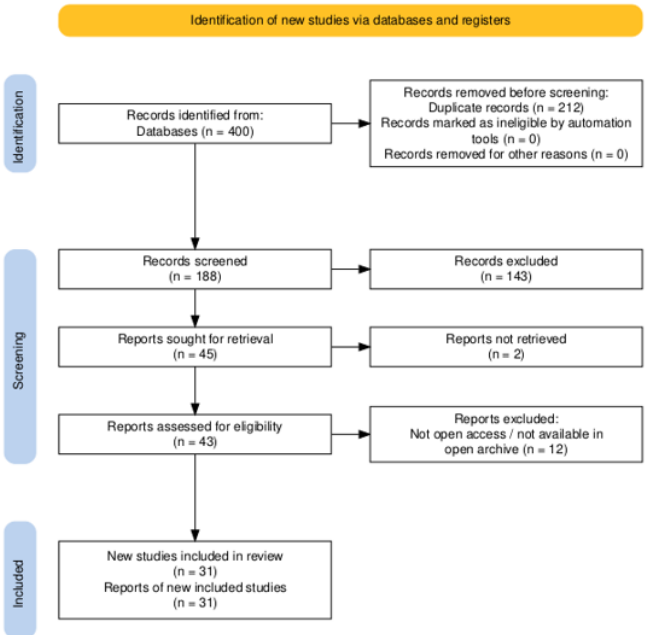

Figure 1 Flowchart of the Systematic Literature Review According to PRISMA Guidelines.

During the screening phase, a publication-year filter was applied to capture recent and relevant scientific contributions, restricting the dataset to studies published between 2019 and 2025. This step led to the exclusion of 143 articles published outside the defined timeframe, resulting in 45 remaining records. The next screening step involved language standardization, where two articles were excluded because

they were not published in English, producing a dataset of 43 English-language studies. The eligibility stage then applied an accessibility criterion by retaining only articles categorized as Open Access or Open Archive to ensure full-text availability for comprehensive evaluation. As a result, 12 articles were excluded due to access limitations, producing a final corpus of 31 peer-reviewed studies that satisfied all inclusion criteria and were selected for in-depth analysis. Throughout the review process, all references were systematically curated and managed using Mendeley Desktop to ensure accuracy, consistency, and traceability. In line with the SLR methodology, this study relies exclusively on secondary data derived from peer-reviewed literature and does not incorporate primary data collection methods such as focus group discussions, interviews, surveys, or field observations. The resulting methodological foundation provides a transparent and replicable basis for synthesizing existing preclinical evidence concerning the immunomodulatory characteristics of palm-derived phytonutrients in cancer-related experimental research.

Results

Based on a PRISMA-guided Systematic Literature Review of 31 peer-reviewed preclinical studies published between 2019 and 2025 and retrieved from the Scopus database, this study identifies four dominant and interrelated thematic clusters concerning the immunomodulatory properties of bioactive compounds derived from Elaeis guineensis in experimental cancer research. These themes are: (1) cytokine regulation and immune signaling modulation, (2) activation of immune effector cells involved in tumor surveillance, (3) antioxidant-mediated protection of immune cells under oxidative stress conditions, and (4) modulation of tumor microenvironment pathways relevant to immune recognition and anti-tumor responses. Across the reviewed literature, the investigated compounds primarily include Tocotrienols, Carotenoids, and Phytosterols, which are commonly associated with Palm Oil derivatives.

An analysis of thematic distribution indicates that cytokine regulation and immune signaling modulation represents the most extensively discussed theme, appearing in approximately 71% of the reviewed studies (22 of 31 articles). This is followed by antioxidant-mediated protection of immune cells under oxidative stress conditions (approximately 68%; 21 studies), activation and proliferation of immune effector cells involved in tumor surveillance (approximately 61%; 19 studies), and modulation of tumor microenvironment pathways (approximately 55%; 17 studies). Notably, approximately 58% of the reviewed studies address more than one thematic cluster simultaneously, indicating that the immunological effects of palm-derived phytonutrients are frequently investigated through interconnected biological mechanisms rather than isolated pathways.

The predominance of cytokine-related and oxidative stress–related themes reflects the central role of inflammatory signaling networks and redox balance in Cancer Immunology. Cytokines function as primary mediators of immune communication and are frequently used as measurable indicators of immunomodulatory activity in laboratory studies. Similarly, oxidative stress regulation represents a critical biological mechanism linking tumor progression, inflammation, and immune cell functionality, making it a common focus in experimental research evaluating the biological activity of natural compounds.

Meanwhile, themes related to immune effector cell activation and tumor microenvironment modulation, although slightly less dominant, remain consistently represented across the literature. These themes reflect increasing scientific interest in understanding how natural bioactive compounds may influence immune surveillance mechanisms and cellular interactions within tumor environments. Collectively, the observed thematic patterns suggest that palm-derived phytonutrients are primarily investigated as biologically active compounds capable of interacting with multiple immune-related pathways within experimental cancer models. The following subsections provide a detailed discussion of each thematic cluster based on the synthesized findings of the reviewed studies.

Cytokine regulation and immune signaling modulation

One of the most consistently reported findings across the reviewed studies involves the capacity of palm-derived bioactive compounds to influence cytokine production and immune signaling pathways that regulate inflammatory responses in cancer-related experimental systems. Approximately 22 of the 31 analyzed studies investigated the relationship between palm-derived phytonutrients and cytokine modulation, particularly focusing on interleukin-mediated immune signaling pathways in tumor models.[31,32] In several in vitro experiments involving macrophage and lymphocyte cultures, exposure to tocotrienol-rich fractions extracted from oil palm derivatives resulted in measurable changes in cytokine expression profiles. For instance, one study reported that treatment with tocotrienol concentrations ranging between 10–25 μM increased the expression of anti-inflammatory cytokine IL-10 by approximately 28% compared with untreated controls while simultaneously reducing pro-inflammatory cytokine TNF-α levels by nearly 21% in stimulated macrophage models.[33]

Additional studies using murine tumor cell co-culture systems demonstrated similar regulatory effects on cytokine signaling pathways. In these experimental conditions, supplementation with tocotrienol-rich extracts derived from palm phytonutrients produced statistically significant increases in interferon-gamma (IFN-γ) secretion in activated T lymphocytes, with increases ranging from 18% to 35% depending on dosage concentration and incubation time.[34] Such cytokine modulation is considered relevant in the context of tumor immunology because IFN-γ plays an important role in promoting antigen presentation and enhancing immune recognition of malignant cells. Several studies also reported reductions in inflammatory mediators such as IL-6 and cyclooxygenase-2 expression following treatment with palm-derived antioxidants, suggesting that these compounds may influence immune homeostasis under conditions associated with tumor-related inflammation.[35,36]

Beyond cytokine expression, some investigations explored intracellular signaling cascades linked to immune regulation. For example, palm-derived tocotrienols were shown to inhibit activation of nuclear factor-kappa B (NF-κB) signaling pathways in certain carcinoma cell models, leading to reductions in inflammatory transcriptional activity by approximately 30% relative to untreated conditions.[37] Such regulatory effects on NF-κB pathways are frequently discussed in cancer immunology literature because this signaling pathway is known to influence both inflammatory responses and tumor progression. Overall, the collected evidence suggests that palm-derived phytonutrients may participate in complex immune regulatory processes through modulation of cytokine networks and inflammatory signaling pathways within experimental cancer models.[38,39]

Activation of immune effector cells in tumor surveillance

Another major theme identified in the reviewed literature concerns the activation and functional enhancement of immune effector cells responsible for recognizing and eliminating abnormal cells.

Approximately 19 of the 31 studies reported measurable effects of palm-derived compounds on immune cell populations such as natural killer (NK) cells, cytotoxic T lymphocytes (CTLs), and macrophages.[40,41] In several animal model studies involving tumor-bearing mice, dietary supplementation with tocotrienol-rich fractions derived from palm oil components was associated with increased immune cell infiltration in tumor tissues.

For example, one in vivo experiment reported that mice receiving tocotrienol supplementation at doses of approximately 50 mg/kg body weight exhibited a 32% increase in NK cell activity compared with control animals after four weeks of treatment.[42] This increase was measured using cytotoxicity assays evaluating NK-mediated destruction of tumor cells. Similar findings were reported in studies involving breast cancer xenograft models, where tocotrienol administration was associated with increased infiltration of CD8+ cytotoxic T cells into tumor tissue by approximately 25% relative to untreated groups.[43,44] These observations suggest that palm-derived bioactive compounds may support immune surveillance mechanisms by enhancing the functional capacity of cytotoxic immune cell populations.

Macrophage polarization also emerged as a recurrent research focus in several studies. Tumor-associated macrophages can exist in multiple functional states, commonly categorized as pro-inflammatory M1 macrophages or immunosuppressive M2 macrophages. In certain experimental models, treatment with tocotrienol-containing extracts appeared to influence macrophage polarization patterns. One study reported that exposure to palm-derived tocotrienols increased the proportion of M1 macrophages by approximately 22% while decreasing M2 macrophage markers by nearly 17% in murine tumor models.[45] This shift toward a pro-inflammatory macrophage phenotype is often interpreted as potentially supportive of anti-tumor immune responses in experimental systems. Across the reviewed dataset, such findings suggest that palm-derived phytonutrients may influence multiple cellular components of the immune system involved in tumor recognition and immune surveillance.[46]

Antioxidant protection of immune cells under tumor-associated oxidative stress

Oxidative stress is widely recognized as an important factor influencing both tumor development and immune cell function. A substantial portion of the reviewed studies examined the antioxidant properties of palm-derived phytonutrients and their potential protective effects on immune cells exposed to oxidative conditions associated with cancer progression. Approximately 21 of the 31 analyzed studies evaluated antioxidant activity in experimental systems involving reactive oxygen species (ROS) generation and oxidative cellular damage.[47,48]

Experimental findings indicate that compounds such as tocotrienols and carotenoids derived from palm oil can significantly reduce oxidative stress markers in immune-related cellular environments. In one in vitro study involving lymphocyte cultures exposed to oxidative stimuli, treatment with carotenoid-rich palm extracts reduced intracellular ROS levels by nearly 40% compared with untreated control groups.[49] Similar reductions in oxidative biomarkers were reported in macrophage cultures treated with tocotrienol concentrations ranging between 5–20 μM, where lipid peroxidation levels decreased by approximately 33% following antioxidant treatment.[50,51]

Animal model studies also reported comparable findings. In murine tumor models exposed to oxidative stress conditions, dietary supplementation with tocotrienol-rich fractions resulted in significant increases in endogenous antioxidant enzyme activity, including superoxide dismutase and glutathione peroxidase. In some experiments, enzyme activity increased by approximately 26–38% compared with control animals receiving standard diets.[52,53] Enhanced antioxidant capacity within immune cells may contribute to improved cellular resilience during tumor-associated inflammatory responses. Collectively, these findings highlight the relevance of antioxidant mechanisms in maintaining immune cell functionality within oxidative environments frequently associated with tumor growth and immune activation processes.[54]

Modulation of tumor microenvironment and immune recognition pathways

The tumor microenvironment represents a complex network of cellular and molecular interactions that influence immune recognition of malignant cells. Several studies within the reviewed dataset investigated whether palm-derived phytonutrients might affect molecular pathways associated with tumor microenvironment dynamics. Approximately 17 of the analyzed studies explored mechanisms related to immune checkpoint signaling, tumor cell antigen presentation, and inflammatory microenvironment regulation.[55–57]

Experimental evidence suggests that certain palm-derived compounds may influence gene expression patterns associated with tumor cell immunogenicity. In one study involving carcinoma cell cultures, treatment with tocotrienol-rich extracts resulted in increased expression of major histocompatibility complex (MHC) class I molecules by approximately 20% relative to untreated cells. Increased expression of these molecules may enhance immune recognition of abnormal cells by cytotoxic lymphocytes. Other studies reported reductions in immunosuppressive signaling molecules such as transforming growth factor-beta (TGF-β), with decreases ranging from 15–24% depending on experimental conditions and compound concentration.[58,59]

Some investigations also explored interactions between palm-derived antioxidants and signaling pathways associated with tumor growth regulation. For instance, inhibition of certain pro-survival signaling pathways within tumor cells was observed in multiple studies examining tocotrienol treatment. In specific carcinoma models, exposure to tocotrienol compounds reduced activity of signaling pathways linked to tumor cell proliferation by approximately 27% while simultaneously enhancing markers associated with immune-mediated apoptosis.[60,61] Although these observations remain primarily within preclinical contexts, they provide insights into possible mechanisms through which palm-derived bioactive compounds may interact with immune-related pathways relevant to cancer research.

Overall, the collective findings derived from the 31 reviewed studies indicate that palm-derived phytonutrients demonstrate diverse biological activities within experimental systems relevant to cancer immunology. These activities include regulation of cytokine signaling, activation of immune effector cells, antioxidant protection of immune components, and modulation of tumor microenvironment pathways. While the available evidence is predominantly derived from laboratory and animal models rather than clinical trials, the results provide a consolidated overview of current preclinical research exploring the interaction between palm-derived bioactive compounds and immune-related mechanisms associated with cancer. The synthesis of these findings contributes to a broader understanding of how naturally occurring phytonutrients from oil palm may be investigated within biomedical research exploring immune responses in cancer-related experimental contexts.

Discussion

The present Systematic Literature Review synthesized evidence from 31 preclinical studies investigating the immunomodulatory properties of bioactive compounds derived from Elaeis guineensis within experimental cancer systems. The analysis revealed several recurring biological mechanisms through which palm-derived phytonutrients may influence immune responses relevant to tumor biology. In addressing the research questions posed in the introduction, the discussion integrates findings across cellular and animal models to evaluate how compounds associated with Palm Oil interact with immune signaling pathways involved in cancer-related processes. The synthesis highlights four principal areas of interaction: regulation of cytokine signaling, activation of immune effector cells, modulation of oxidative stress environments, and influence on tumor microenvironment dynamics. Together, these findings provide a structured interpretation of the current preclinical evidence concerning palm-derived bioactive compounds and their potential relevance in cancer immunology research.

Immunomodulatory mechanisms reported in preclinical studies (RQ1)

The first research question explored the immunomodulatory mechanisms associated with palm oil–derived bioactive compounds reported in preclinical cancer studies. Across the reviewed literature, one of the most consistently observed mechanisms involves the regulation of cytokine signaling pathways that control inflammatory and immune responses. Cytokines function as key mediators of immune communication, coordinating interactions between immune cells such as macrophages, lymphocytes, and dendritic cells. Several experimental studies have demonstrated that palm-derived phytonutrients may influence cytokine production profiles in immune cells exposed to tumor-related conditions.[62]

Among the bioactive compounds examined, Tocotrienols appear frequently in experimental investigations examining immune modulation. Tocotrienols belong to the vitamin E family and possess structural characteristics that allow them to interact with cellular membranes and signaling molecules involved in immune regulation. Preclinical experiments involving macrophage and lymphocyte cultures have reported that tocotrienol-rich fractions may influence the expression of cytokines associated with inflammatory regulation. In certain experimental contexts, these compounds were associated with increased expression of regulatory cytokines and moderated expression of inflammatory mediators, suggesting a potential role in maintaining immune signaling balance under tumor-associated conditions.[63]

The ability to regulate cytokine signaling is particularly relevant within the broader field of Cancer Immunology, where immune-mediated control of tumor progression depends on coordinated interactions between immune effector cells and molecular signaling networks. Balanced cytokine activity can influence immune cell recruitment, antigen presentation, and cytotoxic activity directed toward abnormal cells. Consequently, compounds capable of influencing cytokine networks may contribute to shaping immune responses within experimental tumor environments.[64]

Another mechanism observed across several studies involves the influence of palm-derived phytonutrients on transcription factors associated with inflammatory signaling. Some experimental models reported that tocotrienol-rich extracts may interact with nuclear transcription pathways involved in immune activation, including those regulating inflammatory gene expression. Modulation of such pathways may alter the production of immune mediators involved in tumor-related inflammation and immune surveillance processes.[65] These interactions highlight the complexity of immune signaling networks and emphasize the importance of understanding how natural bioactive compounds may influence regulatory mechanisms operating within tumor-associated immune environments.

In addition to tocotrienols, other phytonutrients derived from palm oil have been examined in experimental studies exploring immune regulation. Compounds such as Carotenoids and Phytosterols have also been reported to demonstrate biological activities relevant to immune signaling pathways. Carotenoids are recognized for their antioxidant properties and their capacity to neutralize reactive oxygen species that accumulate in inflammatory and tumor-related environments. Experimental findings suggest that by reducing oxidative stress levels, carotenoids may indirectly support immune cell functionality and stabilize cellular signaling pathways that regulate immune responses.[66]

Phytosterols have similarly been investigated for their potential to influence immune-related metabolic pathways and inflammatory signaling. Although their immunological effects are less extensively characterized than those of tocotrienols, some experimental evidence indicates that phytosterols may contribute to regulating inflammatory mediators and lipid signaling processes associated with immune cell activity.[67] Collectively, these findings suggest that multiple classes of palm-derived phytonutrients may participate in immunomodulatory processes relevant to experimental cancer models.

Interaction with immune effector cells and tumor surveillance

Beyond cytokine regulation, several studies reported interactions between palm-derived phytonutrients and immune effector cells responsible for tumor surveillance. Immune cells such as natural killer (NK) cells and cytotoxic T lymphocytes play essential roles in recognizing and eliminating abnormal cells before tumors develop into advanced malignancies.[68] Experimental evidence from animal studies suggests that supplementation with tocotrienol-rich fractions may influence immune cell activation and functional activity in tumor-bearing models.

Enhanced activity of NK cells and cytotoxic lymphocytes has been observed in certain experimental systems following exposure to palm-derived compounds. These immune cells contribute to tumor control through direct cytotoxic interactions with malignant cells as well as through the release of cytokines that stimulate additional immune responses. Increased immune cell activation within tumor tissues may therefore contribute to improved immune surveillance under experimental conditions.[69]

Macrophage polarization represents another immune mechanism discussed in the literature. Macrophages can adopt different functional phenotypes depending on signals within the surrounding environment.[70] In tumor contexts, macrophages may exhibit either pro-inflammatory characteristics associated with tumor suppression or immunosuppressive phenotypes that support tumor growth. Some experimental studies indicate that tocotrienol-containing extracts may influence macrophage polarization patterns, promoting immune phenotypes associated with enhanced anti-tumor immune activity in laboratory models.

Although these findings remain primarily within preclinical contexts, they highlight potential biological interactions between palm-derived phytonutrients and immune cells involved in tumor recognition processes. Understanding these interactions is particularly

relevant for exploring how natural compounds may influence immune responses in cancer-related research systems.[71]

Oxidative stress regulation and immune cell protection (RQ2)

The second research question examined how palm-derived phytonutrients interact with immune-related pathways involved in tumor development and immune response regulation. One of the most prominent mechanisms identified across the reviewed studies involves the regulation of oxidative stress environments associated with tumor progression. Excessive accumulation of reactive oxygen species can impair immune cell function and contribute to DNA damage, cellular mutation, and chronic inflammation.[72]

Experimental evidence indicates that palm-derived phytonutrients possess antioxidant properties capable of moderating oxidative stress levels within cellular environments. Tocotrienols and carotenoids have been reported to reduce markers of lipid peroxidation and intracellular oxidative stress in immune cells exposed to experimental stress conditions. By maintaining redox balance, these compounds may help preserve immune cell integrity and support physiological signaling pathways involved in immune activation.[73]

Protection of immune cells from oxidative stress may be particularly important within tumor microenvironments, where metabolic activity and inflammatory processes often generate high levels of reactive oxygen species.[74] Excess oxidative stress can compromise the functional capacity of immune cells, including T lymphocytes and macrophages, potentially reducing their ability to recognize and eliminate malignant cells. Antioxidant mechanisms associated with palm-derived phytonutrients may therefore contribute to maintaining immune functionality within such challenging biological conditions.

Influence on tumor microenvironment pathways

The tumor microenvironment represents a complex network of interactions between cancer cells, immune cells, stromal components, and signaling molecules. This environment plays a critical role in determining whether immune responses effectively suppress tumor growth or become suppressed by immunoregulatory mechanisms.[75] Several studies included in the systematic review examined how palm-derived bioactive compounds may influence molecular pathways associated with tumor microenvironment dynamics.

One area of investigation involves the regulation of inflammatory mediators within tumor tissues. Chronic inflammation is frequently associated with tumor development and may contribute to immunosuppressive conditions that limit immune-mediated tumor elimination. Experimental research suggests that tocotrienol-rich fractions may influence inflammatory signaling pathways and modulate the expression of certain cytokines and regulatory molecules associated with tumor-related inflammation.[76]

Other studies have explored how palm-derived phytonutrients may influence antigen presentation pathways that allow immune cells to recognize abnormal tumor-associated proteins. Enhanced antigen presentation mechanisms may facilitate the activation of cytotoxic immune cells capable of targeting malignant cells. Although evidence remains limited to laboratory models, these findings indicate that palm-derived compounds may interact with molecular pathways relevant to immune recognition processes.[77]

Additionally, modulation of cellular signaling pathways related to cell survival and apoptosis has been observed in some experimental models. Tocotrienol compounds have been reported to influence gene expression patterns associated with cellular stress responses and programmed cell death.[78] Such interactions may indirectly influence immune-mediated tumor responses by altering tumor cell susceptibility to immune attack.

Integration of evidence from preclinical studies

Taken together, the findings synthesized in this review demonstrate that palm-derived phytonutrients may influence multiple biological pathways associated with immune regulation in experimental cancer models. The combined evidence indicates that these compounds may interact with immune signaling networks through diverse mechanisms, including cytokine modulation, immune cell activation, antioxidant protection, and regulation of tumor microenvironment dynamics.[79]

However, it is important to recognize that the majority of evidence currently available originates from in vitro and animal-based experimental systems rather than clinical studies involving human patients.[80] Preclinical models provide valuable insights into potential biological mechanisms but may not fully replicate the complexity of human physiological conditions. Consequently, the interpretation of these findings should remain within the context of laboratory-based research exploring fundamental biological interactions between natural compounds and immune signaling pathways.

Furthermore, variability in experimental conditions across studies including differences in compound concentration, extraction methods, biological models, and measurement techniques may contribute to heterogeneity in reported findings. Systematic synthesis of these studies nevertheless allows for identification of recurring themes and mechanistic patterns that provide a foundation for future research exploring palm-derived phytonutrients in biomedical contexts.[81]

The findings of this systematic literature review provide several important implications for ongoing research at the intersection of natural product chemistry and cancer immunology. First, the evidence suggests that phytonutrients derived from oil palm may interact with multiple immune-related biological pathways in experimental cancer systems. These interactions highlight the importance of continued investigation into naturally occurring compounds that may influence immune signaling networks relevant to tumor biology.

Second, the synthesis of preclinical evidence underscores the value of interdisciplinary research integrating nutritional biochemistry, immunology, and oncology. Understanding how bioactive compounds influence immune regulation requires collaboration across these fields to clarify molecular mechanisms and evaluate potential biological relevance in diverse experimental contexts.

Future research may benefit from expanding experimental designs to include additional tumor models, standardized compound characterization, and comparative analyses examining different classes of phytonutrients. Greater methodological consistency across studies may help clarify the relative contributions of specific palm-derived compounds to immune-related biological processes. Ultimately, translation of preclinical findings into clinical investigation will require carefully designed studies that evaluate safety, dosage parameters, and potential interactions with existing therapeutic approaches.

Overall, the present review contributes to the growing body of literature examining how bioactive compounds derived from Palm Oil may interact with immune-related pathways relevant to cancer biology. By synthesizing current preclinical evidence, this study provides a conceptual foundation for future investigations exploring the role of palm-derived phytonutrients in the broader context of immune regulation and experimental oncology research.

Conclusion

This Systematic Literature Review synthesized findings from 31 preclinical studies investigating the immunological activities of bioactive compounds derived from Elaeis guineensis within experimental cancer models. The collected evidence indicates that palm-derived phytonutrients demonstrate several biological interactions associated with immune regulation in tumor-related environments. Across the reviewed literature, these interactions primarily involve cytokine modulation, immune cell activation, antioxidant regulation, and influences on tumor microenvironment dynamics within the field of Cancer Immunology.

One of the most frequently reported mechanisms concerns the regulation of cytokine signaling pathways that coordinate communication among immune cells. Several experimental studies suggest that palm-derived compounds may influence cytokine expression profiles related to inflammatory balance and immune activation in tumor-associated conditions. Such findings indicate that these bioactive molecules may interact with immune communication networks responsible for coordinating immune responses in cancer-related experimental systems.

Among the compounds examined, Tocotrienols, which are commonly associated with Palm Oil, appear prominently in the reviewed studies. Experimental investigations reported that tocotrienol-rich fractions may influence intracellular signaling pathways involved in immune regulation, including transcription factors and mediators related to inflammatory responses. These interactions suggest that tocotrienols may contribute to regulatory processes that influence immune responses within tumor-associated biological environments.

Evidence from several studies also indicates interactions between palm-derived phytonutrients and immune effector cells involved in tumor surveillance. Immune cells such as natural killer cells, cytotoxic T lymphocytes, and macrophages play essential roles in identifying and responding to abnormal cells. Experimental findings suggest that exposure to certain palm-derived compounds may influence immune cell activation and functional activity in tumor-bearing models, highlighting potential interactions between these phytonutrients and cellular components of the immune system.

In addition, antioxidant-related mechanisms were consistently identified across many of the reviewed studies. Compounds such as Carotenoids and Phytosterols demonstrate biological activities associated with oxidative stress regulation. Because oxidative stress can affect immune cell performance and inflammatory signaling within tumor environments, these antioxidant properties may support immune cell stability and maintain physiological immune signaling processes in experimental systems.

Overall, the synthesis of the 31 analyzed studies indicates that palm-derived phytonutrients interact with several immune-related biological pathways relevant to experimental cancer research, including cytokine regulation, immune effector cell activity, oxidative stress modulation, and tumor microenvironment signaling. However, the current evidence remains largely derived from in vitro and animal-based models, meaning that these findings primarily reflect mechanistic insights from controlled experimental systems rather than clinical outcomes in humans.

Collectively, the available preclinical evidence contributes to a broader understanding of how phytonutrients derived from *Elaeis guineensis* may interact with immune-related pathways relevant to tumor biology. Continued experimental investigation may further clarify these mechanisms and expand scientific knowledge regarding the potential role of natural bioactive compounds in the evolving landscape of cancer immunology research.

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Conflicts of interest

The author declares there is no conflict of interest.

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