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Review Article

From Palm Carotenoids to Respiratory Immune Programming: Retinoid Signaling, Antiviral Epithelial Defense, and the Context-Dependent Trade-Offs of Vitamin A

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Abstract

Red palm oil contains provitamin A carotenoids that may contribute to vitamin A adequacy, yet the relationship between dietary carotenoids and respiratory antiviral protection is neither direct nor uniformly beneficial. This critical qualitative literature review integrates evidence on palm-oil processing, carotenoid bioaccessibility, retinoid metabolism, respiratory epithelial defenses, dendritic-cell regulation, mucosal antibodies, and clinical supplementation outcomes. A thematic synthesis of peer-reviewed research published from 2020 to 2026 distinguishes nutritional deficiency correction from pharmacological alteration of retinoic acid signaling. Retinoids contribute to epithelial maintenance, immune-cell differentiation, and mucosal homeostasis, but effects vary according to receptor localization, infection stage, cellular context, and baseline vitamin A status. Evidence that selective retinoic acid signaling inhibition can improve host responses in an experimental respiratory syncytial virus model illustrates a mechanistic trade-off rather than a contradiction of nutritional sufficiency. Clinical reviews do not establish broad respiratory-infection prevention from indiscriminate vitamin A supplementation, and direct trials connecting red palm oil consumption with respiratory antiviral endpoints remain scarce. An integrated Nutritional–Retinoid–Respiratory Immunity framework identifies testable links between dietary inputs, conversion phenotypes, epithelial interferon responses, mucosal IgA, and clinically important disease outcomes. Future interventions should stratify participants by vitamin A status, characterize exposure, and evaluate safety alongside antiviral efficacy. Red palm oil should be investigated as a potential nutritional input, not represented as an established antiviral intervention.

Keywords: Red Palm Oil, Provitamin A Carotenoids, Beta-Carotene, Vitamin A, Retinoic Acid, Respiratory Viral Infection, Mucosal Immunity, Dendritic Cells, Interferon Signaling, Secretory Immunoglobulin A

Introduction

Background: respiratory infection, nutrition, and immune heterogeneity

Respiratory viral diseases remain a major cause of illness across the life course and have disproportionate consequences for infants, older adults, and people whose respiratory or immune systems are compromised. Respiratory syncytial virus (RSV) is particularly consequential in early childhood, however, the distribution of hospitalizations varies geographically and across seasons. Pandemic-associated changes in viral circulation also illustrate why apparent reductions in case counts need not signify a permanent biological decline in risk. For a nutritional intervention to be considered relevant, researchers must therefore specify whether it is intended to prevent infection, reduce symptom intensity, shorten viral shedding, prevent hospitalization, or facilitate recovery. These endpoints reflect different immunological processes and are not interchangeable. The population burden motivates research on host resilience, but does not authorize claims that a particular food or nutrient prevents respiratory disease (Cong et al., 2024, Mazur et al., 2024, Duan et al., 2025).

The airway immune system is more than a circulating collection of immune cells. Nasal and bronchial epithelial cells constitute an organized physical and biochemical frontier: ciliated cells move mucus, secretory cells contribute trapping and lubrication, and epithelial pattern-recognition systems detect viral invasion. Resident and recruited leukocytes interpret these local danger signals and balance viral elimination against tissue-preserving responses. In early infection, well-timed type I and type III interferons can restrict viral replication, excessively delayed or mislocalized inflammatory responses may add to pathology. The importance of timing is particularly evident in RSV and SARS-CoV-2 studies, in which protective signals and damaging inflammation can coexist. This complexity provides a rationale for studying nutrition in relation to clearly defined immune pathways rather than invoking a vague concept of strengthened immunity (Stanifer et al., 2020, Barnes et al., 2022, Savan and Gale, 2023). Cross-disciplinary nutritional immunology provides a useful interpretive boundary. Dietary adequacy can support epithelial differentiation and normal immune function without producing the same effect as a targeted antiviral drug, and susceptibility may differ by age and nutritional background. Reviews spanning respiratory virology and nutrition emphasize that host vulnerability, preventive supplementation, and treatment after symptom onset require separate evaluation. Consequently, studies of carotenoid-containing foods should prespecify both the intended population and the stage of infection at which an effect is expected (Govers et al., 2022, Stephensen and Lietz, 2021).

Red palm oil offers a scientifically interesting dietary exposure because its natural pigment fraction includes alpha- and beta-carotene, which can serve as precursors to vitamin A. Nevertheless, the designation palm oil obscures differences between carotenoid-rich red palm oil and highly refined or bleached

products whose pigment concentrations may be substantially reduced. The composition of any intervention depends on raw material, extraction, heating, processing, storage, and the particular formulation administered. Fatty-acid characteristics and accompanying lipophilic constituents may further influence the matrix. A nutritional study that merely records palm oil consumption, without identifying processing grade or analyzing carotenoid content, cannot rigorously assess whether the purported exposure actually supplies meaningful provitamin A. The food-science literature thus provides the first indispensable layer of the proposed causal chain (Madoromae and Lertcanawanichakul, 2025, Gao et al., 2023, Nainggolan and Sinaga, 2021).

The retinoid paradox and article contribution

Vitamin A is required for normal immune development, epithelial differentiation, and multiple responses to microbial challenge. Deficiency can disturb host defense, whereas adequate supply helps maintain tissue and immune homeostasis. Yet retinoic acid, an active metabolite, is not a simple accelerator of every antimicrobial response. As a ligand for nuclear receptors, it can reshape gene expression in a cell-type-dependent manner, under some conditions its regulatory or tolerogenic effects may limit inflammation, whereas in others they may constrain an antiviral response that would otherwise be advantageous. This distinction between nutritional adequacy and the direction of a specific signaling intervention is central to a balanced interpretation of the literature. The biological consequences of increasing dietary precursors cannot be inferred from an experiment that selectively disables a receptor in one immune-cell lineage (Amimo et al., 2022, Rao et al., 2025, Deka et al., 2024).

An especially informative challenge to linear reasoning comes from a 2024 RSV investigation reporting improved antiviral immunity and reduced infection-associated pathology after experimental inhibition of retinoic acid signaling in selected dendritic cells. That finding does not establish that vitamin A deficiency protects against RSV, and it does not test the respiratory effects of red palm oil. Instead, it reveals how local receptor signaling during an established infection can diverge from the long-term nutritional requirements of an intact immune system. The present review addresses this tension directly by integrating nutrient chemistry, cellular mechanisms, human trial findings, and research-design implications. It proposes an explicit Nutritional–Retinoid–Respiratory Immunity (NRRI) framework, where every link has a defined evidentiary status and potential confounders (Farazuddin et al., 2024, De Leeuw and Hammad, 2024).

Questions and boundaries

The analysis asks how red palm carotenoids become available to the body, how retinoic acid is generated, distributed, and sensed, how respiratory barriers and immune cells respond, why viral species and infection stages may alter those responses, and whether any of these mechanisms translate into meaningful human outcomes. It also asks what evidence would be required to assert an antiviral effect from a palm-specific intervention. Importantly, the review does not claim to quantify a pooled treatment effect, and it does not substitute selected experimental findings for clinical prevention evidence. Its objective is explanatory synthesis: to identify robust principles, genuine contradictions, and experimentally tractable gaps that can guide future work in food technology, immunology, and nutritional public health (Cheng et al., 2024, Zhang et al., 2021).

Literature Review: Conceptual and Theoretical Foundations

Dietary carotenoids, food matrices, and metabolic conversion

Carotenoids constitute a chemically diverse family of lipophilic pigments that must be released from food structures, incorporated into mixed micelles, absorbed by intestinal cells, and transported before their physiological effects can be considered. Alpha- and beta-carotene are relevant because they possess provitamin A activity, whereas not every carotenoid is a retinol precursor. Red palm oil differs from many leafy or fibrous carotenoid sources because the pigment is already dispersed in a lipid-rich matrix, but potential advantages in bioaccessibility still depend on dose, oxidation, digestion, and meal composition. Literature on carotenoid encapsulation and delivery demonstrates that improving apparent solubility or in vitro micellarization is a formulation outcome, not direct proof of superior vitamin A status or respiratory protection in humans (Saini et al., 2022, Molteni et al., 2022, González-Peña et al., 2023).

The chemistry of red palm oil is also inseparable from industrial practice. Heat, light, oxygen exposure, prolonged storage, and oil refining can change the concentration and chemical integrity of the carotenoid fraction. Red palm olein products developed for food applications may retain recognizable pigments and some antioxidants, yet shelf-life findings from a selected formulation cannot be extrapolated to every processed palm ingredient. Nanoliposomes and lipid-carrier systems offer technical strategies for delivering lipophilic compounds, and studies of palm-derived lipid mixtures illustrate the feasibility of manipulating carotenoid bioaccessibility. However, a laboratory demonstration of antioxidant capacity or digestive release must remain in the technological-evidence category until human absorption, retinol-related biomarkers, and relevant immune outcomes are directly tested (Alkandari et al., 2021, Rodsamai et al., 2025, Rohmah et al., 2022).

Recent food-science research further distinguishes chemical retention from biological availability. Beta-carotene is susceptible to degradation and is poorly soluble in aqueous systems, encapsulation and other stabilisation strategies may protect the compound during processing or improve its dispersion. These engineering improvements, however, do not establish a predictable change in vitamin A stores or immune-cell retinoid signaling after ingestion. Translational studies should therefore quantify the carotenoid dose at preparation and consumption, measure relevant metabolites, and report stability-related losses rather than equating nominal product enrichment with physiological delivery (Zhao et al., 2024, Saini et al., 2022).

Conversion of provitamin A carotenoids to retinoids is regulated rather than automatic. Intestinal uptake, beta-carotene oxygenase activity, retinyl ester formation, liver storage, and retinol-binding protein transport together influence the relationship between intake and tissue availability. Genetic and phenotypic variation can modify this chain, while body composition, inflammation, and existing vitamin A stores may alter circulating markers. As a result, identical servings of a carotenoid-rich food can produce different changes in retinol activity equivalents or storage-related measures across participants. A responsible intervention should quantify the administered alpha- and beta-carotene, document habitual dietary intake, and evaluate baseline sufficiency. The distinction matters because a food-derived exposure may improve adequacy in one population without meaningfully changing homeostatically controlled retinoid signaling in another (Suzuki and Tomita, 2022, Rao et al., 2025).

The broader food literature reinforces why the physical presentation of pigments matters. Carotenoid concentrations differ among plant varieties and processing platforms, biofortification research is consequently concerned with delivering nutrients in usable forms

rather than maximizing pigment concentration alone. Dairy-based carriers show another approach to distributing carotenoids in food matrices, while general health reviews describe antioxidant and anti-inflammatory activities in a range of experimental settings. None of these findings, individually, demonstrates clinically meaningful antiviral efficacy. The relevant scientific lesson is methodological: source characterization, delivery technology, metabolic fate, and disease outcome must be investigated as distinct stages, with intermediary biomarkers connecting them only when validated. This principle also prevents the misleading impression that any antioxidant assay establishes superior host defense during respiratory infection (Morelli and Rodriguez-Concepcion, 2023, Conboy Stephenson et al., 2021, Crupi et al., 2023).

Retinoid homeostasis and nuclear-receptor biology

Within tissues, retinol may be oxidized to retinaldehyde and subsequently to retinoic acid, which interacts with retinoic acid receptors and their heterodimeric partners to regulate transcription. Intracellular binding proteins, local synthesis enzymes, receptor expression, and metabolic clearance constrain the intensity and location of signaling. These mechanisms make tissue exposure more difficult to interpret than a single dietary intake estimate. Retinoic acid is best conceptualized as a developmental and immunoregulatory signal that acts within a network of cytokines, transcription factors, and cell-state-dependent chromatin accessibility. Consequently, an effect observed in intestinal dendritic cells, a cancer-associated immune microenvironment, or circulating leukocytes is mechanistically informative but cannot simply be treated as equivalent to signaling in infected human airway epithelial cells (Bang et al., 2023, Wei et al., 2023, Joshi et al., 2023).

The gastrointestinal immune system provides a well-studied illustration of tissue-specific retinoid biology. Intestinal antigen-presenting cells can produce retinoic acid and contribute to the differentiation, localization, and regulatory behavior of lymphocytes. Recent work on the beta-catenin–Raldh2 axis shows that inflammatory signaling intersects with pathways capable of generating tolerogenic dendritic-cell phenotypes. Studies of B-cell class switching add another dimension, showing that local tissue environments influence antibody isotype selection and mucosal protection. These observations support the plausibility of retinoid-regulated mucosal immunity, but intestinal immune imprinting should be explicitly described as an analogy, not direct evidence of identical airway effects. The respiratory tract has distinct epithelial architecture, microbial exposure, immune-cell populations, and viral challenges (Bang et al., 2023, Deka et al., 2024, Fleming et al., 2022).

The mechanistic evidence for retinoic acid–dependent IgA class switching is particularly informative when its anatomical origin is kept explicit. Research synthesized by Bos et al. (2022) shows how retinoic acid influences B-cell differentiation in intestinal lymphoid tissues, including through direct and T-cell-mediated routes. Those findings support a testable mucosal-immunity mechanism, but they do not quantify antigen-specific IgA secretion in the human nose following a carotenoid-rich food intervention. A credible respiratory translation must measure airway samples and pathogen-specific antibody function rather than infer protection from intestinal results alone (Bos et al., 2022, Sinha et al., 2024).

Deficiency models help establish essentiality but are not sufficient to determine the optimum immune effect of supplementation above adequacy. Experiments involving vitamin A–deficient hosts have demonstrated impaired defense in non-respiratory infection systems, including altered neutrophil-mediated bacterial control and modified responses to intestinal viruses. Retinoid-associated modulation of inflammatory pathways has also been investigated during sepsis. Together these studies reveal a system capable of affecting both pathogen clearance and immunopathology across biological compartments. They should not be combined into a single numeric estimate of respiratory benefit. Instead, they justify experiments that directly compare deficiency, sufficiency, and higher exposure while observing the relevant airway cells and infection phases (Lokken-Toyli et al., 2024, Lee et al., 2023, Dolin et al., 2023).

Respiratory epithelial defense and interferon networks

Airway epithelial cells are metabolically active immune sentinels. Viral nucleic acids or replication intermediates stimulate sensors that initiate antiviral signaling and induce interferon-stimulated genes. Type III interferons are particularly relevant at epithelial surfaces because their receptor distribution is relatively restricted, type I interferons can exert broader effects. Nevertheless, host defense is spatially heterogeneous, and single-cell investigations demonstrate that different nasal epithelial subpopulations may initiate distinct antiviral programs. Chronic airway disease further changes the starting condition: RSV-exposed epithelial cells from people with asthma show response abnormalities concentrated in particular differentiated cell types. Nutritional effects should therefore be investigated against a realistic background of epithelial cell differentiation, inflammatory history, and tissue-specific interferon biology (Stanifer et al., 2020, Wang et al., 2025, Gay et al., 2024).

A frequent terminological misunderstanding must also be excluded: retinoic acid–inducible gene I, or RIG-I, is the name of a viral RNA-sensing protein and does not mean that supplying dietary vitamin A necessarily activates the antiviral sensor. Studies that pharmacologically stimulate RIG-I can demonstrate potent antiviral effects in experimental RSV systems, while investigations of aged lung epithelia have implicated impaired IRF1–RIG-I pathways in reduced viral defense. These results are important for describing antiviral recognition, but they are not evidence that increased retinoic acid ligand concentrations reproduce RIG-I agonism. Maintaining the distinction between a historical gene name and an active metabolic pathway is essential for protecting the article from an attractive but invalid mechanistic inference (Schwab et al., 2022, Li et al., 2025).

Dendritic cells, antibody specialization, and viral ecology

Respiratory dendritic-cell populations interpret epithelial alarm signals, capture antigen, migrate to lymphoid tissues, and influence T-cell differentiation. Conventional and plasmacytoid dendritic cells perform partially overlapping but distinguishable tasks, including antigen presentation and antiviral cytokine responses. Their output depends on the virus, the tissue of origin, and the inflammatory conditions at antigen encounter. A receptor-mediated shift that reduces inflammatory damage can be advantageous in one setting but detrimental in another if viral clearance requires stronger cellular immunity. Describing dendritic cells merely as an amplifier of immunity therefore ignores their regulatory functions and masks the question of whether an intervention changes host resistance, host tolerance, or both (De Leeuw and Hammad, 2024, Barnes et al., 2022).

Secretory immunoglobulin A is a central component of mucosal defense because antibody can act at the site where many respiratory viruses first interact with the host. Nasal and airway IgA may restrict attachment and support immune exclusion, but its protective effects depend on antigen specificity, affinity,

concentration, secretion, and sampling site. Mucosal IgA should not be conflated with serum IgG, a systemic antibody response and a local antibody response can follow different trajectories. Contemporary vaccine research highlights this separation by targeting mucosal immune induction directly. Vitamin A biology plausibly interacts with aspects of B-cell differentiation, although strong evidence about IgA regulation in the intestine cannot be assumed to demonstrate a corresponding causal relationship between red palm oil and protective respiratory IgA in humans (Sinha et al., 2024, Joseph, 2022, Zhou et al., 2025).

Frameworks of resistance, tolerance, and nutritional sufficiency

Three theoretical distinctions organize the interpretation. First, resistance refers to processes that restrict pathogen replication or eliminate infection, whereas disease tolerance refers to limiting tissue damage despite pathogen exposure. Second, chronic nutritional adequacy is an organism-level state, whereas receptor agonism or antagonism is a pathway-specific experimental perturbation. Third, immune markers such as interferon transcripts, IgA titers, or epithelial integrity are intermediate measures and should not automatically substitute for clinical endpoints. These distinctions explain how intervention A might improve epithelial maintenance while intervention B, which reduces retinoid signaling in one cell population during active infection, might also benefit the host. The apparent paradox dissolves once intervention level, timing, and outcome are stated precisely (Farazuddin et al., 2024, Amimo et al., 2022, Savan and Gale, 2023).

Method: Critical Qualitative Literature Review

Review approach and epistemic boundaries

This article adopts a critical qualitative literature review (QLR), not a systematic literature review or meta-analysis. The purpose is to interpret mechanisms across food chemistry, nutritional physiology, immunology, virology, and clinical epidemiology and to develop a coherent conceptual explanation of apparently discordant results. A QLR is appropriate because the literature spans incomparable exposure types: red palm oil food matrices, purified carotenoids, vitamin A supplementation, retinoic acid receptor perturbations, animal infections, cell-culture experiments, and human respiratory outcomes. Pooling these designs into a common treatment effect would create false comparability. No exhaustive study capture, formal PRISMA flow, quantitative risk-of-bias score, or pooled estimate is claimed. The conclusions are therefore interpretive and hypothesis-generating rather than evidence of a single causal intervention effect.

Source identification and evidence appraisal

The literature was assembled through targeted searches of journal and scholarly indexing sources, including PubMed, PMC and journal publisher records, with attention to papers published between January 2020 and October 2026. Conceptual search families included red palm oil and carotenoid bioaccessibility, vitamin A and retinoic acid signaling, airway epithelium, interferons, and dendritic cells, RSV, influenza, and SARS-CoV-2, mucosal IgA, and vitamin A clinical trials. Selection privileged journal articles whose methods, target population, exposure, and measured outcomes were identifiable, while including selected reviews to connect mechanisms. Each included source was assigned a role in the synthesis rather than treated as equally capable of proving a nutritional–clinical causal pathway. Reporting this search logic supports transparency without implying systematic completeness. Database-specific search strings, query dates, and a reproducible study count were not retained, consequently, the selection is presented as purposive and the review makes no claim of exhaustive coverage.

Thematic coding and inferential safeguards

The selected evidence was coded into six intersecting themes: food composition and delivery, conversion and homeostasis, epithelial sensing, dendritic-cell regulation, mucosal adaptive immunity, and clinical supplementation or prevention. Studies were additionally classified by model and inference level: in vitro studies, non-human experiments, human observational or genetic analyses, interventional trials, and evidence syntheses. For each proposition, the review distinguishes a demonstrated finding from a plausible extrapolation and identifies which intermediate steps remain untested. Particular care was taken not to treat vitamin A and red palm oil as equivalent interventions, not to conflate RIG-I with dietary retinoic acid, and not to assign intestinal findings directly to the airway. Conflicting evidence was retained rather than resolved by preferentially citing positive results.

Quality, transparency, and limitations

Quality was considered through biological specificity, clarity of exposure measurement, independence of endpoints, and whether confounding or context had been addressed. Randomized human supplementation studies were prioritized for population-level preventive claims, while perturbation studies were prioritized for narrowly defined mechanisms. Reviews and meta-analyses were used to summarize broader evidence but not as substitutes for the underlying designs. Limits include the narrative nature of study selection, heterogeneity in vitamin A biomarkers, differing infection models, and sparse direct red palm oil–respiratory outcome investigations. The reference list is restricted to sources cited in this manuscript, each entry includes a DOI link for verification and access. The resulting synthesis should be read as a structured research argument, not as a clinical guideline.

Results: Thematic Findings

Theme one: red palm oil is a variable nutritional input, not a defined retinoid dose

The first thematic finding is that red palm oil can be a source of provitamin A carotenoids, but the available evidence does not support treating one unspecified serving as a reproducible pharmacological exposure. Variation in cultivar, extraction, fractionation, heat processing, and storage changes carotenoid delivery, while digestion and metabolic conversion add biological variation. Different formulations can produce comparable dietary mass with unequal beta-carotene availability. Product characterization must therefore precede claims about immune outcomes. Analytical data should be reported as carotenoid species and concentrations, together with processing conditions, rather than a generic statement that an intervention contains palm oil. Food technology work provides useful starting points for dose standardization, but it does not establish the amount of retinoic acid subsequently formed inside respiratory immune cells (Madoromae and Lertcanawanichakul, 2025, Rohmah et al., 2022, Rodsamai et al., 2025).

The wider carotenoid literature shows that the route from food to systemic exposure contains several bottlenecks. A fraction of dietary carotenoid may not enter intestinal micelles, absorbed carotenoid may remain unconverted, converted retinol may be stored or transported instead of producing an immediate increase in free retinoic acid. The possibility of changes in the intestinal microbiota or inflammation also complicates causal attribution in whole-food interventions. Emerging reviews describe interactions between carotenoids and immune processes, but many proposed benefits derive from antioxidant assays, animal experiments, or pathways measured outside the respiratory tract. Mechanistic enthusiasm is reasonable as a research premise, provided it is not presented as an observed reduction in human influenza, RSV, or

coronavirus infection (Rocha et al., 2023, Medina-García et al., 2025, Crupi et al., 2023).

Figure 1 summarizes the sequence of necessary biological transitions. The diagram intentionally uses multiple gates between a carotenoid-containing food and clinical outcomes because each gate can vary independently. It also shows where a proposed relationship may be modified by the background diet, genetic conversion phenotype, inflammatory state, and virus-specific immune requirements. Consequently, an epidemiological association between red palm oil intake and respiratory symptoms would be difficult to interpret without measuring at least some intervening nutritional and immunological states. Conversely, a change in plasma beta-carotene following feeding would demonstrate uptake but would not alone establish improved epithelial interferon responses or antiviral disease protection (Suzuki and Tomita, 2022, Gannon et al., 2025).

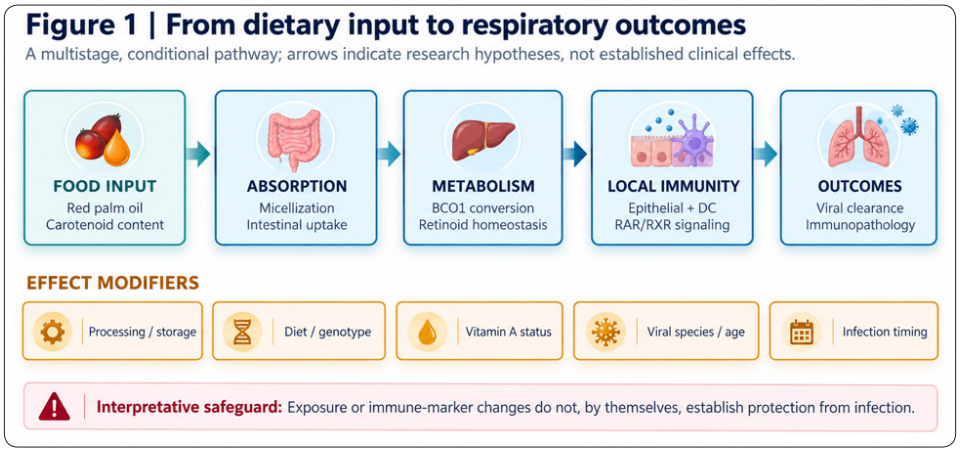


Figure 1: Conditional pathway from red palm carotenoid exposure to respiratory outcomes. Original conceptual synthesis

Figure 1 highlights two independent sources of uncertainty: chemical delivery and biological programming. Reliable food chemistry can validate the intake of provitamin A carotenoids, but it cannot establish which receptors operate in infected nasal or bronchial tissues. Similarly, identifying a receptor-associated transcriptional shift cannot tell us whether the patient will experience a lower infection rate. Directly linked exposure, biomarker, and clinical measurements are needed to test the entire sequence (Molteni et al., 2022, Farazuddin et al., 2024).

Theme two: epithelial integrity and antiviral signaling are related but distinct endpoints

The second finding concerns the need to separate normal epithelial maintenance from a virus-triggered antiviral program. Vitamin A participates in epithelial differentiation and tissue homeostasis, and impaired nutritional status may weaken the physiological context in which antiviral immunity operates. Yet epithelial integrity encompasses cell composition, mucus production, barrier permeability, and mucociliary function, none of these measures is identical to interferon induction. A respiratory virus is sensed through discrete receptor pathways that depend on viral genome characteristics, replication location, and cell-specific competence. The most direct evidence for epithelial antiviral protection must therefore combine exposure characterization with viral challenge, cellular phenotyping, and appropriate functional measures, ideally in differentiated human airway tissues. General conclusions from nutritional status should remain broader and less mechanistically specific (Amimo et al., 2022, Stanifer et al., 2020, Gay et al., 2024).

Epithelial interferon signaling also presents a timing problem. Responses generated before extensive viral replication may be protective, while sustained cytokine activation in already-injured tissue can have different consequences. Type III interferons are often discussed as relatively localized defenses at mucosal surfaces, but experimental context, dose, and timing still matter. Single-cell research further shows that the nasal epithelial compartment cannot be represented by a single average interferon value. If a palm-derived nutritional exposure is proposed to modify antiviral readiness, studies should determine whether changes occur in basal, secretory, or multiciliated cells and whether such changes reduce infectious virus rather than only shifting gene-expression signatures. Age and pre-existing airway inflammatory conditions need to be measured because they can alter the same readouts (Wang et al., 2025, Li et al., 2025, Stanifer et al., 2020).

The antiviral literature also documents a semantic trap that can inflate claims. The RIG-I name contains the phrase retinoic acid–inducible, yet RIG-I signaling is a viral-sensing pathway whose deliberate activation can restrict RSV in laboratory and animal models. Those experiments are not interchangeable with administering beta-carotene, retinol, or retinoic acid. They differ in molecular target, dose, delivery route, and likely distribution within the airway. Although a retinoid-dependent change in expression of antiviral sensors is conceivable in some contexts, the inferential chain would require direct demonstration. For a QLR intended to generate reliable hypotheses, the defensible statement is that retinoid biology and RNA-sensing biology may intersect in a complex network, it is not that carotenoid-rich palm oil has been shown to activate RIG-I-mediated protection (Schwab et al., 2022, Li et al., 2025).

Theme three: retinoic acid signaling can change the direction of dendritic-cell responses

The third and most conceptually important finding is that retinoic acid signaling has regulatory effects that depend on cell identity and disease conditions. Dendritic cells are capable of initiating adaptive responses, directing lymphocyte differentiation, and shaping inflammation, but these functions are not maximized by a single universal signaling state. Retinoid receptor expression and intracellular retinoic acid generation operate alongside pattern-recognition pathways, costimulatory signals, and cytokines. Under one set of conditions, a regulatory program may preserve tissue from damaging inflammation, under another, it may reduce the antiviral effector response needed for clearance. Any assertion about beneficial pathway modulation therefore requires explicit identification of the cell population, experimental perturbation, virus, timing, and measured benefit. The broad label immunomodulation is insufficient (De Leeuw and Hammad, 2024, Deka et al., 2024).

Farazuddin and colleagues provide the primary example of this conditionality. In a 2024 experimental RSV model, inhibiting retinoic acid signaling in dendritic cells improved selected measures of antiviral immunity and reduced infection-associated pathology. The intervention examined selected immune signaling states during infection, it was neither a human dietary trial nor an experiment demonstrating that vitamin A deficiency is advantageous. Its implication is that a receptor pathway may have inhibitory effects on a protective response in a defined context. This observation is compatible with the well-established need for vitamin A in normal development and physiological maintenance. The relevant scientific response is to map dose-response and cell-type specificity rather than force the two bodies of evidence into a uniform positive or negative judgment on vitamin A (Farazuddin et al., 2024, Amimo et al., 2022).

A further implication is that peripheral blood assays may inadequately reflect local airway dendritic-cell biology. Even within the lung, antigen-presenting populations vary across nasal tissue, bronchial mucosa, and distal airspaces. Circulating retinol concentrations cannot directly reveal receptor occupancy or transcriptional response within those compartments. In addition, an intervention that improves resistance by reducing infectious viral load might differ from one that primarily reduces inflammatory injury without changing viral replication. Future investigations must measure both, preferably at multiple intervals. Figure 2 illustrates how nutritional deficiency correction and selective retinoid pathway inhibition can produce effects that are not mutually exclusive and warns against regarding those different experimental manipulations as equivalent therapies (Farazuddin et al., 2024, De Leeuw and Hammad, 2024).

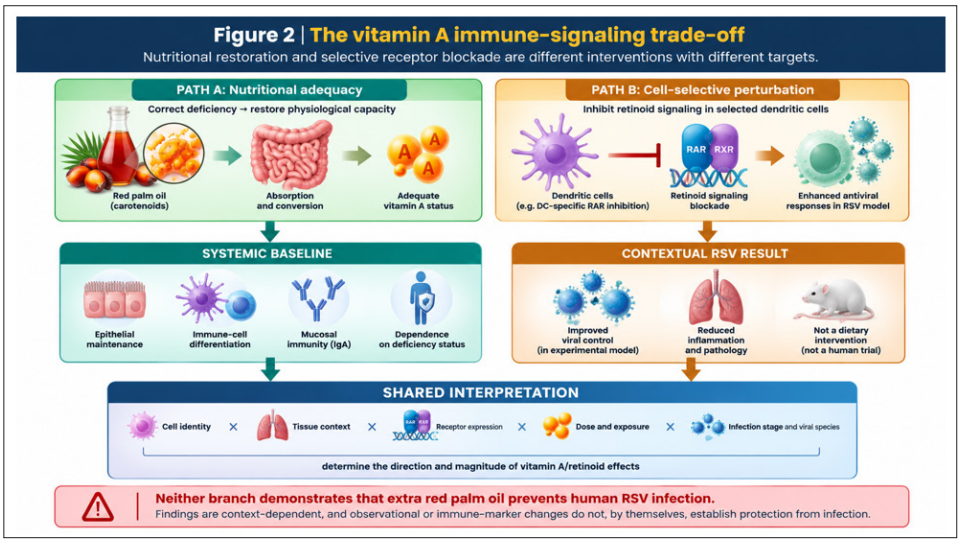


Figure 2: Reconciling nutritional vitamin A adequacy with selective retinoic acid receptor pathway inhibition. Original conceptual synthesis.

The two arms of Figure 2 should not be represented as competing clinical recommendations. Restoring nutritional sufficiency is an organism-level process that occurs over time, blocking a receptor in selected cells is an experimental manipulation of one regulatory node. The balance among viral clearance, interferon activity, T-cell polarization, and tissue damage may differ even when both interventions are relevant to vitamin A biology. This distinction explains why a deficiency correction benefit need not conflict with favorable experimental outcomes from selective signaling inhibition (Amimo et al., 2022, Farazuddin et al., 2024).

Theme four: mucosal antibodies provide a credible endpoint but not a palm-specific causal result

Secretory IgA is a plausible intermediate endpoint linking mucosal immune programming to respiratory protection. Its localization at the mucosal surface can make it relevant to events preceding systemic infection, while antigen specificity determines whether a measured response targets a particular respiratory virus. Reviews of mucosal IgA describe protective mechanisms and technical challenges involved in sampling, standardization, and functional interpretation. Evidence from long-term-care settings reveals variation in anti-influenza mucosal IgA across time, suggesting that a one-time nasal antibody measurement may not accurately capture an individual's stable protection. Such findings argue for prospective sampling and standardized methods rather than reliance on a single total-IgA assay (Sinha et al., 2024, Joseph, 2022, Hitchings et al., 2023).

A 2026 real-world influenza study investigated antigen-specific nasal IgA and viral infection outcomes, providing a more direct human setting for evaluating this proposed correlate of protection. The relevance to the present review lies in the outcome construct: nasal IgA is measured where infection begins, and the analysis distinguishes mucosal from systemic antibody responses. Yet the study did not test red palm oil or manipulate retinoid signaling. Consequently, it supports selection of a useful future immune endpoint without establishing that carotenoid intake will raise protective mucosal IgA. Literature on intestinal antibody class switching and emerging respiratory mucosal vaccines further indicates that local tissues strongly determine the nature of antibody immunity. Translating these insights requires experiments in the respiratory compartment itself (Bladh et al., 2026, Fleming et al., 2022, Zhou et al., 2025).

Theme five: viral species, age, and microbial ecology alter the meaning of immune effects

RSV, influenza, and SARS-CoV-2 differ in host-cell tropism, replication strategies, age-associated severity, and the relevant mix of protective immune responses. A result in one virus model cannot be transferred to another merely because all three infect the respiratory tract. Differences in mucosal pre-existing immunity, interferon kinetics, and the role of T-cell recruitment further complicate extrapolation. Reviews of SARS-CoV-2 have described substantial context dependence in the timing and functional effects of interferon responses, while work on RSV has emphasized epithelial and immunopathological interactions. The responsible

approach is to formulate pathogen-specific hypotheses within an overarching nutritional framework, rather than claim a single universal antiviral mechanism for red palm oil (Savan and Gale, 2023, Barnes et al., 2022, Mazur et al., 2024).

Host age and respiratory ecology add further heterogeneity. Young infants enter infection with developing immune systems and distinctive exposure histories, older adults may experience changes in epithelial sensing and adaptive responsiveness. The respiratory microbiome interacts with epithelial immunity and viral challenge, but it is neither identical to the intestinal microbiome nor necessarily modified by a food intervention in the same way. Reviews of microbiota–mucosal immunity interactions suggest useful explanatory pathways, although direct causal chains from palm carotenoid intake to respiratory microbial community change and antiviral benefit remain unproven. The possibility of an indirect nutritional effect through the gut–lung axis is therefore best presented as a candidate mechanism requiring simultaneous microbial, nutritional, and host immune measurements (Li et al., 2025, Cong et al., 2024, Wang et al., 2025).

Investigations of carotenoids in the context of emerging viral infections illustrate the distance between plausible biochemical activity and clinical benefit. Proposals based on redox balance, anti-inflammatory properties, or computational interactions with viral proteins can be valuable for prioritizing research, yet they have markedly lower causal relevance than a randomized trial testing a defined nutritional intervention against virologically confirmed infection. Similarly, avian infectious bronchitis experiments with vitamin A can offer information on immune physiology, but avian viral ecology and species-specific vitamin A metabolism limit direct inference to human influenza or RSV. These studies should be included in the synthesis as hypothesis-generating evidence and explicitly labeled to prevent model overextension (Lu et al., 2022, Khalil et al., 2021, Zhang et al., 2023).

Theme six: supplementation trials do not support indiscriminate vitamin A escalation

Human prevention evidence is more guarded than nutritional marketing claims often imply. A 2021 meta-analysis did not identify a consistent preventive benefit across vitamin A supplementation trials for acute respiratory infections and reported an increased incidence signal in some higher-exposure subgroups. A 2024 Cochrane review specifically considering acute upper respiratory tract infections in young children found evidence that did not establish a reliable preventive advantage from oral vitamin A supplementation. These publications concern vitamin A interventions rather than red palm oil, but they provide an important boundary: a presumed mechanistic benefit cannot override inconclusive or adverse clinical outcomes. Baseline deficiency status, dose, and formulation must be analyzed before extending findings to a nutrition policy (Zhang et al., 2021, Cheng et al., 2024).

A broader 2024 synthesis of randomized trials examining important clinical outcomes also challenges the assumption that additional vitamin A consistently improves survival or morbidity across heterogeneous populations. Interpretation requires care because population-wide supplementation programs, high-dose trials, deficiency correction, and short-term pharmacological exposure address different questions. A small pediatric vaccine-supplement trial conducted among children with relatively adequate baseline vitamin levels offers another caution against assuming that extra vitamin A produces uniformly stronger vaccine responses. Importantly, the vaccines assessed in that trial were not respiratory-virus vaccines, so its appropriate use here concerns saturation and baseline-status issues rather than an observed influenza or RSV effect. The synthesis therefore favors targeted adequacy over universal escalation (Bjelakovic et al., 2024, Patel et al., 2025).

The classification of participants as vitamin A sufficient or deficient is itself subject to error. Inflammation can lower circulating retinol and retinol-binding protein through the acute-phase response, potentially producing biomarker patterns that do not map cleanly onto liver reserves. Evaluations of biochemical testing describe the strengths and limitations of available indicators, while field investigations have illustrated a trade-off when adjusting serum retinol for inflammation. A trial that enrolls patients during an acute respiratory infection and uses a single retinol measurement may therefore misclassify baseline nutritional status. Future work should combine dietary assessment, longitudinal biomarkers, inflammatory markers, and validated tests appropriate for the population. Without careful classification, true benefits among deficient participants could be obscured by an apparent null average result or confounded by illness-related changes in biomarker concentrations (Gannon et al., 2025, Suri et al., 2021).

An important safety distinction also separates preformed vitamin A from dietary provitamin A carotenoids. The 2024 European Food Safety Authority appraisal assessed their different metabolic and toxicological profiles, retaining an adult tolerable upper intake level for preformed vitamin A while cautioning against routine supplemental beta-carotene beyond nutritional requirements. This assessment should not be read as a prohibition on customary carotenoid-containing foods, nor as approval for unrestricted concentrated extracts. Clinical intervention protocols should specify the chemical form, total exposure from all sources, participants' baseline status, and prespecified safety monitoring (EFSA NDA Panel, 2024, Stephensen and Lietz, 2021).

Genetic epidemiology offers a complementary but not definitive perspective. A 2024 Mendelian randomization analysis reported associations consistent with a possible protective relationship between genetically proxied retinol-related traits and COVID-19 susceptibility, while findings for severity and hospitalization were not uniformly aligned. Such work can help interrogate confounding, but its validity depends on instrumental-variable assumptions, population ancestry, and the biological specificity of the genetic proxies. It cannot determine the effect of a particular red palm oil formulation or guarantee that deliberate dietary supplementation will mimic lifelong genetic differences. Accordingly, these results add evidence about potential biological relevance while leaving the intervention question unresolved (Wang et al., 2024, Suzuki and Tomita, 2022).

Figure 3 summarizes the inferential ladder across food analytics, mechanistic experiments, human biomarkers, intervention studies, and clinical outcomes. The figure emphasizes a recurring conclusion: studies supporting the leftmost nutritional and molecular stages are substantially more developed than direct palm-specific respiratory clinical evidence. Progress requires bridging experiments that measure multiple stages of the pathway in the same participants, not only accumulating further independent demonstrations of antioxidant activity or general vitamin A immunology. The distinction is essential for a review that seeks to identify translational research opportunities without exaggerating the present state of clinical evidence (Rohmah et al., 2022, Farazuddin et al., 2024, Cheng et al., 2024).

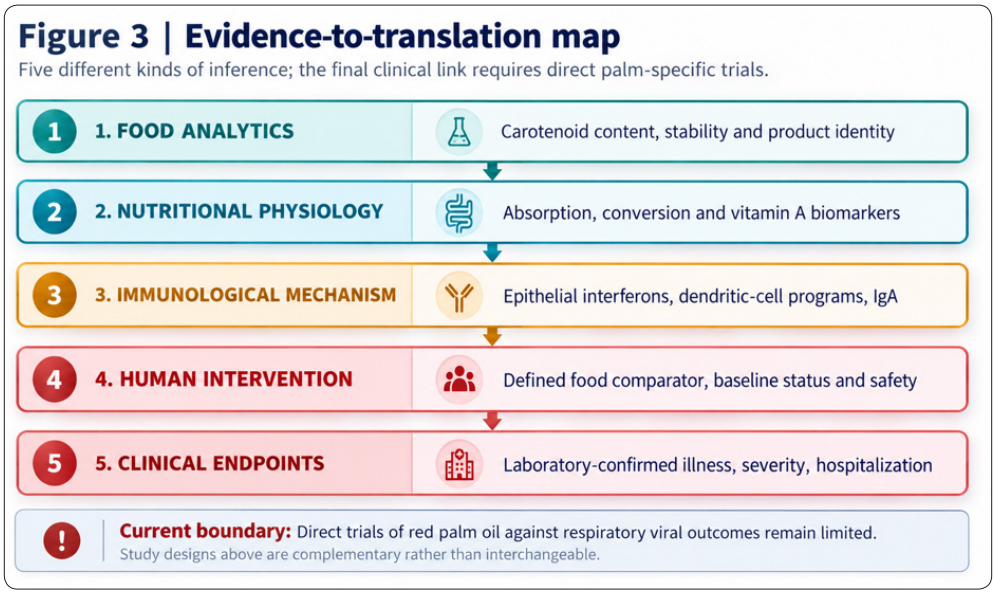


Figure 3: Evidence-to-translation map and the missing palm-specific respiratory clinical bridge. Original conceptual synthesis.

Figure 3 also differentiates strength of causal attribution from the number of publications at a given level. A sophisticated cell experiment may establish a receptor mechanism more convincingly than a large questionnaire, while a randomized intervention is better suited to estimating the effect of offering a food. Neither evidentiary form can replace the other without changing the scientific question. A future palm-specific respiratory trial would be most valuable if it incorporates standardized composition, verified nutrient-status change, and clinically meaningful antiviral measurements (Cheng et al., 2024, Gannon et al., 2025).

Discussion and Analysis

An integrated nutritional–retinoid–respiratory immunity framework

The NRRI framework treats carotenoid ingestion as an upstream and conditional input, rather than as a direct pharmacological command to respiratory immune cells. In the first stage, food composition and processing establish actual carotenoid exposure. In the second stage, absorption and metabolic conversion determine systemic handling and local tissue availability. In the third stage, a network of epithelial cells, dendritic cells, lymphocytes, and their signaling pathways reacts to the physiological environment. In the fourth stage, host resistance and tissue tolerance jointly shape clinically meaningful outcomes. Each arrow in this sequence is a hypothesis requiring distinct evidence. By separating them, the framework avoids causal shortcuts such as inferring fewer infections from improved antioxidant capacity or inferring benefit from an elevated total IgA concentration without antigen specificity (Saini et al., 2022, Rao et al., 2025, Sinha et al., 2024).

The framework also identifies important interactions rather than only a serial chain. Baseline vitamin A deficiency may make normal epithelial maintenance or immune-cell differentiation the limiting factor, in which case nutritional correction could reasonably improve physiological competence. In a sufficient person undergoing a particular acute infection, the limiting factor might instead be the balance of dendritic-cell receptor signaling, interferon timing, and immunopathology. In that context, raising dietary carotenoids need not intensify the desired response, while experimentally inhibiting a particular receptor in a particular cell type might have a favorable effect. This is not a paradox once the intervention, target compartment, and endpoint are clearly distinguished. It is a demonstration of immunological conditionality (Farazuddin et al., 2024, Amimo et al., 2022, De Leeuw and Hammad, 2024).

The trade-off between pathogen resistance and tissue protection

Antiviral research frequently privileges reduced viral load as an intuitive marker of benefit. However, patients suffer from both infectious replication and the host response to infection. A manipulation can improve symptoms by reducing inflammatory damage without dramatically changing viral quantity, conversely, a stronger antiviral response can be accompanied by greater tissue injury. Retinoid signaling operates within immune circuits capable of influencing both sides of this trade-off. The appropriate endpoint architecture should therefore combine infectious titers or molecular viral measurements with barrier assessments, cytokine profiling, histopathology in preclinical studies, and clinical severity in human research. Only then can a nutrient or signaling intervention be described as improving resistance, tolerance, or both (Barnes et al., 2022, Farazuddin et al., 2024, Stanifer et al., 2020).

The relative value of immune activation also changes over time. Before exposure, normal tissue differentiation and immunological readiness may be desirable. During viral entry, prompt epithelial sensing and localized interferon signaling can be important. During established infection, cell-mediated clearance, cytokine control, and tissue repair must occur in sequence. During recovery, persistent inflammatory signaling may become harmful. A single assessment taken at the peak of infection can miss this trajectory and make beneficial early immune priming appear neutral or a transient inflammatory response appear uniformly adverse. Longitudinal approaches are consequently needed to determine whether nutritional adequacy alters the timing, rather than merely the magnitude, of defensive processes (Savan and Gale, 2023, Gay et al., 2024, De Leeuw and Hammad, 2024).

Implications for interpreting palm oil's nutritional and health claims

It is scientifically legitimate to characterize carefully processed red palm oil as a potentially useful food-based source of provitamin A carotenoids. It is not yet legitimate to market it as a proven respiratory antiviral prophylactic on the basis of retinoid receptor biology, IgA research, or cell-culture assays involving unrelated

carotenoid formulations. Red palm oil interventions need compositional quality control, characterization of culinary use and total dietary energy, and attention to competing nutritional sources. Moreover, the health implications of a food cannot be reduced to a single micronutrient: an intervention may replace other fats or foods, thereby affecting intake patterns beyond carotenoids. Research designs should use appropriate comparators to distinguish carotenoid-specific effects from the lipid vehicle, substitution effects, and improvements in the broader diet (Gao et al., 2023, Alkandari et al., 2021, González-Peña et al., 2023).

Food policy implications are similarly conditional. In communities with vitamin A inadequacy, culturally acceptable, safe sources of provitamin A may contribute to dietary diversification when assessed within established nutrition programs. Yet producing carotenoid-rich oil does not automatically guarantee accessibility, intake, absorption, or clinical benefit. Public health assessment should incorporate dietary diversity, affordability, exposure measurement, safety, equity, and locally relevant nutritional indicators. This reasoning does not replace existing vitamin A deficiency programs, infant feeding guidance, or vaccination initiatives. It instead locates a potential palm-derived food product inside a broader nutrition system in which adequacy is a legitimate objective and infection-prevention claims require direct clinical evidence (Madoromae and Lertcanawanichakul, 2025, Suzuki and Tomita, 2022, Bjelakovic et al., 2024).

Translating mechanisms into an experimentally tractable program

A first research phase should prioritize standardized analytical characterization. Investigators can quantify alpha- and beta-carotene and record storage stability, lipid composition, processing methods, and the carotenoid content of the delivered intervention at the point of consumption. A second phase should test bioaccessibility under controlled digestive conditions and validate findings through human postprandial and longer-term nutritional measures. Genetic or phenotypic markers relevant to conversion may be incorporated where appropriate. These stages are indispensable because downstream immunological experiments cannot confidently attribute outcomes to a specific carotenoid dose if the intervention remains chemically undefined. Modern lipid-delivery research offers useful tools, but technical gains in dispersion or micellarization should be confirmed with biologically meaningful markers before clinical trials (Rohmah et al., 2022, Molteni et al., 2022, Rodsamai et al., 2025).

A third phase should employ differentiated primary human nasal and bronchial epithelial cultures, including air–liquid interface systems and airway organoids, to examine barrier differentiation, mucociliary properties, viral replication, interferon release, and cell-specific gene expression. Studies should compare deficiency-like and sufficient metabolic conditions where experimentally valid, while carefully distinguishing retinol exposure from retinoic acid receptor agonism or antagonism. Coculture with relevant dendritic-cell populations could clarify how epithelial alarm signaling translates into antigen presentation and antiviral T-cell responses. RSV and influenza should be investigated separately rather than combined into a generic respiratory-virus endpoint, variant and model characteristics must be stated. An especially informative design would test whether altered retinoid availability changes the same immune-cell pathways identified by selective receptor perturbation experiments (Gay et al., 2024, Wang et al., 2025, Farazuddin et al., 2024).

A fourth phase should establish a prospective clinical trial among participants whose vitamin A status has been characterized before infection season. A food-based, compositional-matched red palm oil intervention could be compared with a carotenoid-poor oil matrix, with attention to equal energy intake, blinding feasibility, habitual diet, and adequate follow-up. Randomization would reduce confounding from socioeconomic conditions, diet quality, and health behavior. Laboratory-confirmed symptomatic respiratory infection should be considered a primary efficacy endpoint if prevention is claimed, disease duration and severity, healthcare utilization, and potential adverse effects would be relevant secondary outcomes. Respiratory antibody profiles, nasal epithelial sampling, and validated retinoid biomarkers could form mechanistic substudies. An ethics-reviewed trial would require dose justification and monitoring rather than simply assuming food-derived carotenoids are risk-free at any concentration (Cheng et al., 2024, Zhang et al., 2021, Gannon et al., 2025).

The most informative stratification variables include baseline vitamin A status, age, dietary pattern, chronic respiratory disease, relevant metabolic or absorption disorders, and prior vaccination or infection. Biomarker collection should anticipate acute-phase confounding rather than treating low retinol observed during illness as unequivocal evidence of antecedent deficiency. Serial nasal samples would allow measurement of antigen-specific IgA before and after verified infections, while blood measurements could quantify systemic responses without substituting for mucosal samples. Preplanned analyses should test effect modification rather than merely report pooled averages. Such precision-nutrition approaches could establish whether any benefit is restricted to nutritional vulnerability, a particular age group, or a defined immunological phenotype. They might equally demonstrate that the hypothesized antiviral pathway is not clinically consequential, an outcome that would still be valuable (Suri et al., 2021, Bladh et al., 2026, Hitchings et al., 2023).

Distinguishing evidence levels and avoiding translational overreach

An evidence hierarchy is necessary but not sufficient because different study types answer different questions. Cell experiments can identify candidate pathways, but often use concentrations or conditions not achieved through food consumption. Animal experiments permit controlled infection and tissue sampling but may differ from humans in viral susceptibility and retinoid handling. Observational human data can describe associations but remain vulnerable to confounding, reverse causation, and nutritional measurement error. Genetic approaches offer separate inferential tools with their own assumptions. Randomized human trials are especially important for determining whether offering a defined food or supplement reduces clinical respiratory outcomes. None of these categories alone is superior for every mechanism, but causal claims should be matched to the design actually employed (Wang et al., 2024, Zhang et al., 2023, Patel et al., 2025).

This distinction is crucial when reviewing the broader vitamin A literature. Studies of intestinal norovirus, bacterial infection, sepsis, or cancer immunology may demonstrate that retinoid pathways can alter inflammation or immunity, yet their tissue and disease contexts differ from respiratory viral challenge. The appropriate contribution of those studies is to identify possible shared regulatory motifs and candidate biomarkers. Their use as direct evidence for prevention of RSV or influenza would be a category error. Even apparently relevant discussions of COVID-19 and dietary carotenoids often synthesize preclinical pathways rather than controlled nutritional clinical trials. The review therefore favors a transparent phrase such as mechanistic plausibility over established clinical protection whenever no linked human intervention has been demonstrated (Lee et al., 2023,

Lokken-Toyli et al., 2024, Wei et al., 2023, Lu et al., 2022).

Safety, ethical interpretation, and clinical relevance

Vitamin A exists in multiple dietary and supplemental forms with different metabolic constraints and safety profiles. Excessive preformed vitamin A intake is not equivalent to ordinary ingestion of carotenoid-containing foods, but neither observation supports unlimited supplementation or use of concentrated extracts without dose assessment. Individuals with particular life-stage, hepatic, or clinical considerations may require professional dietary guidance. For research, safety must be defined in advance and recorded alongside biomarkers of benefit. A positive immune-marker result should not justify high-dose exposure if clinical outcomes are unchanged or if unwanted effects appear. The supplementation literature reinforces that greater provision is not automatically safer or more effective among nutritionally adequate groups (Zhang et al., 2021, Bjelakovic et al., 2024, Rao et al., 2025).

Safety interpretation also depends on formulation and context. Higher intakes of preformed retinol carry risks that cannot be assigned indiscriminately to ordinary food-derived carotenoids, yet supplemental beta-carotene has its own evidence base and requires particular caution in populations at elevated risk. A food intervention should report dietary substitution and the total vitamin A contribution rather than describe an oil serving as a pharmacological retinoid dose. These distinctions help prevent conclusions about the safety or efficacy of one chemical form from being generalized to another (EFSA NDA Panel, 2024, Govers et al., 2022).

Nutrition research must also avoid displacing established respiratory prevention measures. Immunization strategies, including evolving RSV preventive approaches, have demonstrated clinically relevant protection through mechanisms that cannot be equated with carotenoid supplementation. Early real-world evaluations of nirsevimab have provided information about reduced RSV-associated hospitalization among infants, illustrating the importance of direct clinical outcomes. Nutrition may complement vaccination, public health infrastructure, and access to care, but it should not be described as a substitute for them. Claims that red palm oil can strengthen antiviral defense need to specify whether they refer to correction of deficiency, changes in a biomarker, reduced infection frequency, or reduced severity, otherwise they risk overstating the significance of molecular observations (Moline et al., 2024, Moe et al., 2024, Mazur et al., 2024).

Research priorities and falsifiable hypotheses

The NRRI framework generates four falsifiable predictions. First, a chemically standardized red palm oil intervention should change selected vitamin A adequacy markers more clearly in participants with low baseline intake than in already sufficient participants. Second, changes in nutritional biomarkers will not necessarily correlate linearly with nasal interferon responses because tissue and infection-stage regulation intervene. Third, associations between dietary carotenoid exposure and antigen-specific nasal IgA, if present, should be examined separately from serum antibody and total IgA, using virus-specific measures. Fourth, controlled experiments altering retinoid availability should not be assumed to reproduce selective dendritic-cell receptor blockade during RSV challenge. Each prediction could be disproved by carefully designed studies, and none asserts established antiviral efficacy in advance (Farazuddin et al., 2024, Gannon et al., 2025, Bladh et al., 2026).

A research roadmap should also address reporting quality. Studies would benefit from preregistered primary endpoints, disclosure of carotenoid analysis, detailed dietary records, transparent adverse-event reporting, and explicit separation of planned subgroup analyses from exploratory findings. Collaboration between palm-oil chemists, analytical nutrition laboratories, virologists, mucosal immunologists, and clinical trialists would reduce the common problem of highly developed analysis at one biological level coupled with missing evidence at adjacent levels. Economic and sustainability questions, including cost, accessibility, and trade-offs with alternative dietary sources, could then be evaluated without turning the immunological hypothesis into an industrial advocacy claim. The strongest future contribution would be a coherent experiment that travels across several steps of the same biological pathway (Alkandari et al., 2021, Patel et al., 2025, Zhou et al., 2025).

Conclusion and Future Directions

Substantive conclusions

The evidence supports a clear distinction between the importance of vitamin A sufficiency and the assertion that greater retinoid signaling always improves respiratory antiviral immunity. Red palm oil can supply provitamin A carotenoids if the product is appropriately processed and its composition established, but the conversion of this dietary input into immune outcomes is subject to multiple physiological gates. Airway epithelial defense, dendritic-cell regulation, interferon kinetics, and virus-specific antibody protection constitute interacting rather than uniformly aligned systems. Current studies establish essential components of these systems without demonstrating a complete causal chain from red palm oil consumption to prevention of human respiratory viral infections.

Clinical and public health recommendations

Correction of vitamin A inadequacy remains a defensible nutritional objective, but indiscriminate supplementation should not be promoted as a universal antiviral intervention. Clinical applications must consider baseline status, dose, safety, age, underlying disease, and the pathogen-specific endpoint under study. Public health communication should identify the difference between food-based nutritional adequacy and claims of infection prevention. Appropriate vaccination, clinical care, and established respiratory prevention practices remain essential components of a comprehensive strategy. A palm-derived nutritional intervention should be assessed as a potential complement within that strategy only after suitable evidence has been generated.

Methodological conclusions and priority research agenda

The proposed NRRI framework provides a structured route for testing the unresolved pathway. Priority work should analyze the actual carotenoid exposure in red palm oil, establish conversion and biomarker responses, assess differentiated human airway models, investigate retinoid signaling in defined immune-cell populations, and then conduct controlled trials with laboratory-confirmed respiratory endpoints. Future studies should prespecify nutritional-status strata, assess antigen-specific mucosal IgA, monitor epithelial interferon responses, distinguish resistance from tissue tolerance, and measure safety. The immunological trade-offs of vitamin A should be approached as a central empirical question, not as an obstacle to be explained away.

Final synthesis

Palm carotenoids provide a scientifically plausible nutritional entry point into a much wider retinoid–mucosal immune network. The decisive issue is not whether vitamin A has immunological effects, but when, where, and for whom particular retinoid-dependent processes support respiratory defense or alter inflammatory risk. A critical qualitative review can clarify this conceptual landscape

while acknowledging that the pivotal palm-specific human antiviral evidence is still missing. The most responsible conclusion is therefore conditional: nutritional adequacy deserves attention, cell-specific receptor biology requires careful experimental interpretation, and clinical claims should follow directly measured outcomes rather than precede them.

References

1. Alkandari, S. et al. (2021) Pilot scale production of functional foods using red palm olein: Antioxidant, vitamins stability and sensory quality during storage, Saudi Journal of Biological Sciences, 28(10), pp. 5547–5554. https://doi.org/10.1016/j.sjbs.2021.06.032.
2. Amimo, J.O. et al. (2022) Immune Impairment Associated with Vitamin A Deficiency: Insights from Clinical Studies and Animal Model Research, Nutrients, 14(23), 5038. https://doi.org/10.3390/nu14235038.
3. Bang, Y.-J. et al. (2023) Vitamin A: a key coordinator of host-microbe interactions in the intestine, BMB Reports, 56(3), pp. 133–139. https://doi.org/10.5483/BMBRep.2023-0005
4. Barnes, M.V.C., Openshaw, P.J.M. and Thwaites, R.S. (2022) Mucosal Immune Responses to Respiratory Syncytial Virus, Cells, 11(7), 1153. https://doi.org/10.3390/cells11071153
5. Bjelakovic, G. et al. (2024) Effects of primary or secondary prevention with vitamin A supplementation on clinically important outcomes: a systematic review of randomised clinical trials with meta-analysis and trial sequential analysis, BMJ Open, 14, e078053. https://doi.org/10.1136/bmjopen-2023-078053.
6. Bladh, O. et al. (2026) The role of mucosal IgA in protection against influenza A H1N1 virus infection in a real-world setting, eBioMedicine, 129, 106359. https://doi.org/10.1016/j.ebiom.2026.106359.
7. Bos, A., van Egmond, M. and Mebius, R. (2022) The role of retinoic acid in the production of immunoglobulin A, Mucosal Immunology, 15, pp. 562–572. https://doi.org/10.1038/s41385-022-00509-8
8. Cheng, X. et al. (2024) Oral vitamin A supplements to prevent acute upper respiratory tract infections in children up to seven years of age, Cochrane Database of Systematic Reviews, 2024, CD015306. https://doi.org/10.1002/14651858.CD015306.pub2.
9. Conboy Stephenson, R., Ross, R.P. and Stanton, C. (2021) Carotenoids in Milk and the Potential for Dairy Based Functional Foods, Foods, 10(6), 1263. https://doi.org/10.3390/foods10061263.
10. Cong, B. et al. (2024) Changes in the global hospitalisation burden of respiratory syncytial virus in young children during the COVID-19 pandemic: a systematic analysis, The Lancet Infectious Diseases, 24(4), pp. 361–374. https://doi.org/10.1016/S1473-3099(23)00630-8
11. Crupi, P. et al. (2023) Overview of the Potential Beneficial Effects of Carotenoids on Consumer Health and Well-Being, Antioxidants, 12(5), 1069. https://doi.org/10.3390/antiox12051069.
12. De Leeuw, E. and Hammad, H. (2024) The role of dendritic cells in respiratory viral infection, European Respiratory Review, 33(172), 230250. https://doi.org/10.1183/16000617.0250-2023.
13. Deka, A. et al. (2024) Non-canonical NF-κB signaling limits the tolerogenic β-catenin-Raldh2 axis in gut dendritic cells to exacerbate intestinal pathologies, The EMBO Journal, 43(18), pp. 3895–3915. https://doi.org/10.1038/s44318-024-00182-6.
14. Dolin, H. et al. (2023) Retinoic Acid-Induced Regulation of Inflammatory Pathways Is a Potential Sepsis Treatment, Infection and Immunity, 91(4), e00457-22. https://doi.org/10.1128/iai.00457-22.
15. Duan, Q. et al. (2025) Global outbreaks of respiratory syncytial virus infections from 1960 to 2025: a systematic review and meta-analysis, eClinicalMedicine, 86, 103352. https://doi.org/10.1016/j.eclinm.2025.103352.
16. EFSA NDA Panel (2024) Scientific opinion on the tolerable upper intake level for preformed vitamin A and β-carotene, EFSA Journal, 22(6), e8814. https://doi.org/10.2903/j.efsa.2024.8814.
17. Farazuddin, M. et al. (2024) Inhibiting retinoic acid signaling in dendritic cells suppresses respiratory syncytial virus infection through enhanced antiviral immunity, iScience, 27(7), 110103. https://doi.org/10.1016/j.isci.2024.110103
18. Fleming, A., Castro-Dopico, T. and Clatworthy, M.R. (2022) B cell class switching in intestinal immunity in health and disease, Scandinavian Journal of Immunology, 95(2), e13139. https://doi.org/10.1111/sji.13139
19. Gannon, B.M. et al. (2025) Selected laboratory-based biomarkers for assessing vitamin A deficiency in at-risk individuals, Cochrane Database of Systematic Reviews, 2025, CD013742. https://doi.org/10.1002/14651858.CD013742.pub2.
20. Gao, Z. et al. (2023) Chemical–Physical Properties of Red Palm Oils and Their Application in the Manufacture of Aerated Emulsions with Improved Whipping Capabilities, Foods, 12(21), 3933. https://doi.org/10.3390/foods12213933
21. Gay, A.C.A. et al. (2024) Airway epithelial cell response to RSV is mostly impaired in goblet and multiciliated cells in asthma, Thorax, 79(9), pp. 811–821. https://doi.org/10.1136/thorax-2023-220230.
22. González-Peña, M.A. et al. (2023) Chemistry, Occurrence, Properties, Applications, and Encapsulation of Carotenoids—A Review, Plants, 12(2), 313. https://doi.org/10.3390/plants12020313
23. Govers, C., Calder, P.C., Savelkoul, H.F.J., Albers, R. and van Neerven, R.J.J. (2022) Ingestion, immunity, and infection: Nutrition and viral respiratory tract infections, Frontiers in Immunology, 13, 841532. https://doi.org/10.3389/fimmu.2022.841532
24. Hitchings, M.D.T. et al. (2023) Dynamics of Anti-influenza Mucosal IgA Over a Season in a Cohort of Individuals Living or Working in a Long-term Care Facility, Journal of Infectious Diseases, 228(4), pp. 383–390. https://doi.org/10.1093/infdis/jiad029.
25. Joseph, J. (2022) Harnessing Nasal Immunity with IgA to Prevent Respiratory Infections, Immuno, 2(4), pp. 571–583. https://doi.org/10.3390/immuno2040036
26. Joshi, M. et al. (2023) Modulatory role of vitamins A, B3, C, D, and E on skin health, immunity, microbiome, and diseases, Pharmacological Reports, 75(5), pp. 1096–1114. https://doi.org/10.1007/s43440-023-00520-1
27. Khalil, A. et al. (2021) Carotenoids: Therapeutic Strategy in the Battle against Viral Emerging Diseases, COVID-19: An Overview, Preventive Nutrition and Food Science, 26(3), pp. 241–261. https://doi.org/10.3746/pnf.2021.26.3.241
28. Lee, H. et al. (2023) Chemokine CCL6 Plays Key Role in the Inhibitory Effect of Vitamin A on Norovirus Infection, Journal of Microbiology, 61(5), pp. 579–587. https://doi.org/10.1007/s12275-023-00047-3
29. Li, S. et al. (2025) IRF1-RIG-I signaling defects in the aged alveolar epithelial cells may contribute to decreased pulmonary antiviral immune responses, Mechanisms of Ageing and Development, 224, 112037. https://doi.org/10.1016/j.mad.2025.112037
30. Li, X. et al. (2025) The intricate interplay among microbiota, mucosal immunity, and viral infection in the respiratory tract, Journal of Translational Medicine, 23, 488. https://doi.org/10.1186/s12967-025-06433-2
31. Lokken-Toyli, K.L. et al. (2024) Vitamin A deficiency impairs neutrophil-mediated control of Salmonella via SLC11A1 in mice, Nature Microbiology, 9, pp. 727–736. https://doi.org/10.1038/s41564-024-01613-0.
32. Lu, L.W. et al. (2022) The landscape of potential health

benefits of carotenoids as natural supportive therapeutics in protecting against Coronavirus infection, Biomedicine & Pharmacotherapy, 154, 113625. https://doi.org/10.1016/j.biopha.2022.113625.
33. Madoromae, H. and Lertcanawanichakul, M. (2025) Red Palm Oil: Nutritional Composition, Bioactive Properties, and Potential Applications in Health and Cosmetics: A Narrative Review, Molecules, 30(22), 4402. https://doi.org/10.3390/molecules30224402.
34. Mazur, N.I., Caballero, M.T. and Nunes, M.C. (2024) Severe respiratory syncytial virus infection in children: burden, management, and emerging therapies, The Lancet, 404(10458), pp. 1143–1156. https://doi.org/10.1016/S0140-6736(24)01716-1.
35. Medina-García, M. et al. (2025) Carotenoids and Their Interaction with the Immune System, Antioxidants, 14(9), 1111. https://doi.org/10.3390/antiox14091111.
36. Moe, S.S., Wong, S. and Kolber, M.R. (2024) Preventing respiratory syncytial virus in infants, Canadian Family Physician, 70(10), e155. https://doi.org/10.46747/cfp.7010e155
37. Moline, H.L. et al. (2024) Early Estimate of Nirsevimab Effectiveness for Prevention of RSV-Associated Hospitalization Among Infants Entering Their First RSV Season, Morbidity and Mortality Weekly Report, 73(9), pp. 209–214. https://doi.org/10.15585/mmwr.mm7309a4
38. Molteni, C., La Motta, C. and Valoppi, F. (2022) Improving the Bioaccessibility and Bioavailability of Carotenoids by Means of Nanostructured Delivery Systems: A Comprehensive Review, Antioxidants, 11(10), 1931. https://doi.org/10.3390/antiox11101931.
39. Morelli, L. and Rodriguez-Concepcion, M. (2023) Open avenues for carotenoid biofortification of plant tissues, Plant Communications, 4(1), 100466. https://doi.org/10.1016/j.xplc.2022.100466.
40. Nainggolan, M. and Sinaga, A.G.S. (2021) Characteristics of fatty acid composition and minor constituents of red palm olein and palm kernel oil combination, Journal of Advanced Pharmaceutical Technology & Research, 12(1), pp. 22–26. https://doi.org/10.4103/japtr.JAPTR_91_20
41. Patel, N. et al. (2025) Randomized Controlled Clinical Trial of Pediatric Pneumococcus and Hepatitis A Vaccinations With or Without a High-Dose Oral Vitamin A Supplement, Biomolecules, 15(4), 540. https://doi.org/10.3390/biom15040540.
42. Rao, S. et al. (2025) Vitamin A and Its Related Diseases, Food Science & Nutrition, 13(7), e70630. https://doi.org/10.1002/fsn3.70630.
43. Rocha, H.R. et al. (2023) Carotenoids Diet: Digestion, Gut Microbiota Modulation, and Inflammatory Diseases, Nutrients, 15(10), 2265. https://doi.org/10.3390/nu15102265
44. Rodsamai, T. et al. (2025) Design and Bioanalysis of Nanoliposome Loaded with Premium Red Palm Oil for Improved Nutritional Delivery and Stability, Foods, 14(4), 566. https://doi.org/10.3390/foods14040566.
45. Rohmah, M., Rahmadi, A. and Raharjo, S. (2022) Bioaccessibility and antioxidant activity of β-carotene loaded nanostructured lipid carrier (NLC) from binary mixtures of palm stearin and palm olein, Heliyon, 8(2), e08913. https://doi.org/10.1016/j.heliyon.2022.e08913.
46. Saini, R.K. et al. (2022) Carotenoids: Dietary Sources, Extraction, Encapsulation, Bioavailability, and Health Benefits—A Review of Recent Advancements, Antioxidants, 11(4), 795. https://doi.org/10.3390/antiox11040795.
47. Savan, R. and Gale, M. (2023) Innate immunity and interferon in SARS-CoV-2 infection outcome, Immunity, 56(7), pp. 1443–1450. https://doi.org/10.1016/j.immuni.2023.06.018
48. Schwab, L.S.U. et al. (2022) Retinoic Acid–Inducible Gene I Activation Inhibits Human Respiratory Syncytial Virus Replication in Mammalian Cells and in Mouse and Ferret Models of Infection, Journal of Infectious Diseases, 226(12), pp. 2079–2088. https://doi.org/10.1093/infdis/jiac295.
49. Sinha, D. et al. (2024) Unmasking the potential of secretory IgA and its pivotal role in protection from respiratory viruses, Antiviral Research, 223, 105823. https://doi.org/10.1016/j.antiviral.2024.105823.
50. Stanifer, M.L. et al. (2020) Importance of Type I and III Interferons at Respiratory and Intestinal Barrier Surfaces, Frontiers in Immunology, 11, 608645. https://doi.org/10.3389/fimmu.2020.608645.
51. Stephensen, C.B. and Lietz, G. (2021) Vitamin A in resistance to and recovery from infection: Relevance to SARS-CoV-2, British Journal of Nutrition, 126(11), pp. 1663–1672. https://doi.org/10.1017/S0007114521000246.
52. Suri, D.J. et al. (2021) Inflammation Adjustments to Serum Retinol and Retinol-Binding Protein Improve Specificity but Reduce Sensitivity when Estimating Vitamin A Deficiency Compared with the Modified Relative Dose-Response Test in Ghanaian Children, Current Developments in Nutrition, 5(8), nzab098. https://doi.org/10.1093/cdn/nzab098.
53. Suzuki, M. and Tomita, M. (2022) Genetic Variations of Vitamin A-Absorption and Storage-Related Genes, and Their Potential Contribution to Vitamin A Deficiency Risks Among Different Ethnic Groups, Frontiers in Nutrition, 9, 861619. https://doi.org/10.3389/fnut.2022.861619.
54. Wang, H. et al. (2024) Retinol and retinol binding protein 4 levels and COVID-19: a Mendelian randomization study, BMC Pulmonary Medicine, 24, 206. https://doi.org/10.1186/s12890-024-03013-w.
55. Wang, X. et al. (2025) Single-cell transcriptomics reveals a compartmentalized antiviral interferon response in the nasal epithelium of mice, Journal of Virology, 99(3), e01413-24. https://doi.org/10.1128/jvi.01413-24.
56. Wei, C.-H. et al. (2023) A novel retinoic acid receptor-γ agonist antagonizes immune checkpoint resistance in lung cancers by altering the tumor immune microenvironment, Scientific Reports, 13, 14907. https://doi.org/10.1038/s41598-023-41690-5.
57. Zhang, L. et al. (2023) Effect of oral vitamin A supplementation on host immune response to infectious bronchitis virus infection in specific pathogen-free chicken, Poultry Science, 102(7), 102701. https://doi.org/10.1016/j.psj.2023.102701
58. Zhang, Y. et al. (2021) Excessive Vitamin A Supplementation Increased the Incidence of Acute Respiratory Tract Infections: A Systematic Review and Meta-Analysis, Nutrients, 13(12), 4251. https://doi.org/10.3390/nu13124251
59. Zhao, T., He, X., Yan, X., Xi, H., Li, Y. and Yang, X. (2024) Recent advances in the extraction, synthesis, biological activities, and stabilisation strategies for β-carotene: A review, International Journal of Food Science & Technology, 59(4), pp. 2136–2147. https://doi.org/10.1111/ijfs.16986
60. Zhou, M. et al. (2025) Novel vaccine strategies to induce respiratory mucosal immunity: advances and implications, MedComm, 6(2), e70056. https://doi.org/10.1002/mco2.70056.

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