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Palm oil consumption and glycemic control in type 2 diabetes mellitus: a systematic literature review

Abstract

The metabolic implications of palm oil consumption remain disputed because clinical reports frequently combine chemically distinct exposures, including refined palm oil, red or minimally refined palm oil, palm olein, isolated palmitic acid, and interesterified palm-based fats. This systematic review therefore reassessed the relationship between palm oil-related exposures and glycemic control in Type 2 Diabetes Mellitus (T2DM), with specific attention to insulin resistance, processing-related variation, short intervention windows, dietary-matrix confounding, and molecular mechanisms. The review followed PRISMA principles and used a structured synthesis of 36 eligible reports identified from a Scopus-based search for 2019–2026. In addition to direction-of-effect synthesis, the distribution of each study's primary analytical focus was quantified using proportions, Wilson 95% confidence intervals, and a chi-square goodness-of-fit test. Fasting-glucose studies represented 27.8% of the corpus, insulin-sensitivity or insulin-resistance studies 22.2%, comparative-fat studies 19.4%, HbA1c studies 16.7%, and bioactive-compound studies 13.9%; the distribution did not differ significantly from equal allocation across domains ($\chi^2(4)=2.06$, $p=0.726$). Direct clinical evidence did not establish a consistent independent effect of palm oil on fasting glucose or HbA1c, but certainty was constrained by short follow-up, small samples, heterogeneous products, and mixed dietary interventions. Mechanistic and preclinical evidence was more cautionary: palmitate can impair IRS-1/PI3K/Akt signaling through lipotoxic, inflammatory, and stress pathways, while interesterified palm oil has produced adverse adipose and metabolic responses in animal models. Conversely, red palm oil and tocotrienol-rich fractions retain bioactive compounds that are substantially reduced during refining and may modulate oxidative and inflammatory pathways. Evidence involving PPAR-α, PPAR-γ, FABP2, FFAR1, AMPK, NF-κB, and related targets remains predominantly preclinical and should not be treated as proof of clinical benefit or harm. Overall, the evidence is context-dependent and insufficient for a blanket conclusion that all palm oil forms are metabolically neutral or uniformly harmful.

Keywords: palm oil, palmitic acid, glycemic control, Type 2 Diabetes Mellitus, insulin resistance, interesterification, systematic review

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Loso Judijanto
IPOSS Jakarta, Indonesia

Correspondence: Loso Judijanto, IPOSS Jakarta, Indonesia

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Introduction

Type 2 Diabetes Mellitus (T2DM) is characterized by a progressive mismatch between insulin demand and insulin action, producing chronic hyperglycemia and increasing the risk of vascular, renal, neurological, and ocular complications. Glycemic management therefore depends not only on pharmacotherapy but also on dietary patterns that influence energy balance, ectopic lipid accumulation, inflammation, and tissue-specific insulin responsiveness. Although carbohydrate quantity and quality remain central to diabetes nutrition, the metabolic consequences of dietary fats have become increasingly important because fatty-acid composition can alter cellular lipid intermediates, membrane function, hormone secretion, and intracellular signaling.[1,2]

Palm oil is a major edible fat in household cooking, food manufacturing, and commercial food preparation. However, the label "palm oil" conceals substantial compositional variation. Crude or red palm oil retains carotenoids, tocopherols, tocotrienols, phytosterols, and other minor constituents; refined, bleached, and deodorized palm oil contains markedly lower concentrations of several heat- and processing-sensitive compounds; fractionation produces palm olein and palm stearin; and chemical or enzymatic interesterification rearranges fatty acids on the triacylglycerol backbone. These products should not be assumed to have identical biological effects.[3–5]

A second source of confusion is the frequent substitution of evidence about isolated palmitic acid for evidence about whole palm oil. Palmitic acid is the principal saturated fatty acid in palm oil, but palm oil also contains substantial oleic acid and other constituents whose metabolic actions may differ from those of palmitate delivered alone or within an experimental high-fat diet. Palmitate exposure has been associated with ceramide and diacylglycerol accumulation, activation of stress and inflammatory kinases, and attenuation of insulin-receptor-substrate and Akt signaling. Human skeletal-muscle evidence also indicates that palmitate-rich and oleate-rich dietary conditions can produce different insulin-sensitivity responses, supporting the need to distinguish fatty-acid-specific effects from food-level effects.[6,7]

Clinical findings are difficult to interpret because most interventions are short, products are incompletely characterized, and palm oil is usually consumed as part of a mixed meal rather than as an isolated exposure. Fasting glucose can change over days, whereas HbA1c integrates glycemia over approximately two to three months; trials shorter than this period are therefore poorly suited to estimating durable HbA1c effects. In addition, the effects of an oil depend on what it replaces, the amount of energy consumed, carbohydrate quality, cooking method, degree of oxidation, physical activity, body-weight change, and medication use. These dietary-matrix and substitution effects can either mask or exaggerate any independent contribution of palm oil.[8,9]

The evidence is also internally conflicting. Some clinical and observational reports describe little difference between palm oil and comparator vegetable oils, while preclinical studies identify palmitate-related lipotoxicity or adverse responses to interesterified palm oil. Conversely, studies of tocotrienol-rich fractions, red palm oil, or palm-fruit extracts report antioxidant, anti-inflammatory, or tissue-protective effects. These findings are not necessarily contradictory because they examine different exposures, doses, matrices, endpoints, and biological models. A rigorous synthesis must therefore separate direct clinical glycemic evidence from mechanistic plausibility and must avoid translating preclinical molecular findings into clinical claims without qualification.[10–12]

This review addresses the following research question: how do the form and processing of palm oil, its palmitic-acid content, the surrounding dietary matrix, and the duration and design of available studies influence reported glycemic outcomes and insulin-resistance mechanisms in people with T2DM or relevant metabolic models? The review has three linked objectives: to synthesize direct glycemic evidence, to quantify the distribution of the evidence base using inferential statistics, and to integrate clinical findings with processing-specific and molecular evidence while explicitly identifying uncertainty and limits to causal inference.

Literature review

Glycemic control and the metabolic relevance of dietary fat: Glycemic control is assessed through complementary indicators. Fasting plasma glucose and postprandial glucose characterize relatively short-term regulation, HbA1c reflects longer-term exposure, and fasting insulin, HOMA-IR, clamp-derived measures, or dynamic tolerance tests provide information about insulin action. These indicators are not interchangeable. A dietary intervention may alter postprandial hormone responses without changing HbA1c, or may improve glycemia indirectly through weight loss rather than through the fatty-acid source itself. Interpretation therefore requires alignment between the intervention duration, the biological time scale of the endpoint, and the metabolic characteristics of the population.

Dietary fatty acids influence metabolism through several levels of organization. At the whole-diet level, fats alter energy density, satiety, gastric emptying, and the replacement of carbohydrate or other fats. At the tissue level, fatty acids can be oxidized, stored, or converted to signaling lipids. At the cellular level, excess lipid intermediates can interfere with insulin signaling, while some unsaturated fatty acids and lipid-derived ligands activate nuclear or cell-surface receptors. This multilevel framework explains why the health effect of an edible oil cannot be predicted solely from the percentage of saturated fat.[1,8]

Palm oil forms, refining, fractionation, and interesterification: Crude palm oil and red palm oil are visually and compositionally distinct from refined palm oil because they retain a larger proportion of carotenoids and vitamin E-related compounds. Refining, bleaching, and deodorization improve color, flavor stability, and industrial functionality but reduce several minor bioactive constituents. Palm olein, the liquid fraction, and palm stearin, the higher-melting fraction, also differ in fatty-acid and triacylglycerol distribution. Consequently, evidence obtained from red palm oil, isolated tocotrienol-rich fractions, refined palm olein, or palm stearin should be reported under the specific product name rather than generalized to all palm oil.[4,12,13]

Interesterification is another distinct processing step. It redistributes fatty acids among stereospecific positions on glycerol and is used to modify melting behavior without partial hydrogenation. This process may alter digestion, chylomicron formation, postprandial incretin responses, tissue lipid handling, and inflammation even when the overall fatty-acid percentages remain similar. In a clinical meal study involving people with T2DM, interesterified palm olein altered the postprandial glucose-dependent insulinotropic polypeptide response, whereas a recent mouse study linked interesterified palm oil in a high-fat dietary context with white-adipose-tissue inflammation and broader metabolic disturbances.[11,14] These findings justify process-specific caution but do not establish that naturally structured palm oil has the same risk profile.

Palmitic acid, lipotoxicity, and insulin resistance: Palmitate can contribute to insulin resistance when supply exceeds oxidative and storage capacity. Excess intracellular palmitoyl-CoA may be directed toward diacylglycerol and ceramide synthesis, activating protein kinase C isoforms and stress kinases such as JNK and IKKβ. These signals promote inhibitory serine phosphorylation of insulin receptor substrate proteins, weaken PI3K/Akt signaling, reduce GLUT4 translocation in muscle and adipose tissue, and disturb suppression of hepatic glucose production. Palmitate can also provoke endoplasmic-reticulum stress, mitochondrial reactive-oxygen-species generation, and TLR4/NF-κB-linked inflammatory responses.[1,6,15]

Human evidence supports biological relevance but remains dependent on exposure context. Sarabhai et al.[7] showed that diets enriched in palmitate and oleate differentially modulated insulin sensitivity and skeletal-muscle metabolism, indicating that saturated and monounsaturated fatty acids are not metabolically interchangeable. Nevertheless, isolated palmitate experiments, high-fat rodent diets, and whole-food palm-oil interventions answer different questions. The adverse cellular effects of palmitate cannot be converted directly into a quantitative estimate of the effect of moderate palm oil consumption without considering dose, oleate content, energy surplus, and substitution food.

Bioactive constituents and processing-dependent countervailing pathways: Palm-derived tocotrienols, tocopherols, carotenoids, phytosterols, and phenolic constituents may modulate oxidative and inflammatory pathways relevant to diabetic complications. Preclinical studies have reported effects on endothelial nitric-oxide bioavailability, retinal inflammation, angiogenesis, neural injury, and tissue oxidative status. Pilot clinical studies of tocotrienol-rich preparations have also examined diabetic nephropathy and retinopathy, although these interventions evaluate concentrated fractions rather than conventional refined cooking oil.[16–19]

The coexistence of palmitate-related lipotoxic pathways and antioxidant bioactives is one reason palm-oil evidence cannot be reduced to a single mechanism. The net response depends on the product's composition, dose, oxidation state, and metabolic context. Red or minimally processed palm oil may deliver substantially more carotenoids and tocotrienols than refined palm oil, whereas repeated heating or deep frying can generate oxidized products that introduce a different exposure. Thus, the product used in each study is a core effect modifier rather than a minor reporting detail.[4,20]

Molecular targets requested for mechanistic integration: Peroxisome proliferator-activated receptor alpha (PPAR-α) promotes hepatic and muscular fatty-acid oxidation, whereas PPAR-γ regulates adipocyte differentiation, lipid buffering, adipokine signaling, and insulin sensitivity. Fatty acids and their metabolites can act as ligands or modify the expression of these receptors, thereby shifting the balance between oxidation, storage, and lipotoxic spillover. Gamma-linolenic acid (GLA)-rich oils have been studied in obese KK-Ay mice for effects on hepatic lipogenesis, fatty-acid oxidation, and adipose-tissue gene expression.[21] However, GLA is not a characteristic

major fatty acid of palm oil. This evidence is therefore relevant as comparative mechanistic evidence about fatty-acid signaling, not as direct proof of a palm-oil effect.

Fatty acid-binding protein 2 (FABP2) participates in intestinal uptake and intracellular trafficking of long-chain fatty acids, potentially influencing postprandial lipid delivery and downstream insulin sensitivity. Free fatty acid receptor 1 (FFAR1/GPR40), expressed prominently in pancreatic β-cells and other tissues, senses medium- and long-chain fatty acids and modulates glucose-stimulated insulin secretion. These targets provide plausible links between fatty-acid structure, intestinal handling, and incretin or insulin responses, but receptor activation can be beneficial or maladaptive depending on concentration, exposure duration, and tissue context.[22,23]

Other relevant pathways include AMPK-mediated energy sensing; insulin receptor/IRS-1/PI3K/Akt/GLUT4 signaling; ceramide- and diacylglycerol-dependent protein kinase C activation; JNK and IKKβ/NF-κB inflammatory signaling; Nrf2-regulated antioxidant defenses; mitochondrial β-oxidation; and incretin pathways involving GIP and GLP-1. Palm-fruit extracts and tocotrienol-rich fractions have generated transcriptomic and tissue-level signals across some of these pathways, while palmitate and interesterified-fat models more often identify inflammatory or insulin-signaling impairment.[11,24,25] The mechanistic literature is therefore informative but heterogeneous and predominantly indirect for routine dietary intake in T2DM.

Sources of conflicting evidence: Conflicting trial results can arise from differences in participant phenotype, background medication, body-weight change, comparator oil, total energy intake, carbohydrate quality, meal structure, cooking practice, and adherence. A palm-oil intervention replacing butter is not equivalent to one replacing olive oil, and a controlled isocaloric feeding study is not equivalent to an observational estimate of household oil use. Similarly, a high-fat animal diet designed to induce metabolic dysfunction does not model moderate consumption within an energy-balanced human diet.

Duration is particularly important. Acute meal studies are suitable for postprandial glucose, insulin, GIP, or GLP-1 responses, but they cannot establish sustained HbA1c effects. Trials shorter than 12 weeks may also miss adaptation in body weight, hepatic fat, or insulin sensitivity. The present review therefore treats short-term, long-term, human, and preclinical evidence as separate layers and avoids a single pooled conclusion when biological and statistical exchangeability are absent.

Method

Review design and reporting framework: This review used a systematic literature review design aligned with PRISMA 2020 for identification, screening, eligibility assessment, and transparent reporting. Because the eligible evidence comprised heterogeneous clinical, observational, animal, and mechanistic studies, the synthesis also followed the principles of Synthesis Without Meta-analysis (SWiM), including explicit grouping of studies, structured direction-of-effect interpretation, and transparent justification when statistical pooling was not appropriate.[26,27]

Search strategy and study selection: The Scopus database was searched because it provides broad multidisciplinary coverage of nutrition, endocrinology, metabolism, food science, and biomedical research. The preliminary query palm oil AND diabetes returned 236 records. The search was then refined using the Boolean string: ("palm oil" OR "palm olein" OR "palm fat" OR "palm oil consumption" OR palmitate OR "interesterified palm oil") AND ("glycemic control" OR glycemic OR HbA1c OR "blood glucose" OR "fasting blood glucose" OR insulin OR "insulin resistance") AND ("type 2 diabetes mellitus" OR "type 2 diabetes" OR T2DM OR diabetes).

After removal of records that were clearly outside the review scope, 91 records underwent title and abstract screening. Application of the 2019–2026 priority period left 46 reports for full-text retrieval, and 10 reports could not be verified in full text under the review's accessibility rules. Thirty-six reports were included in the final evidence corpus. A small number of pre-2019 landmark sources were used only to explain established mechanisms or earlier clinical signals; they were not added to the quantitative evidence-map denominator. The use of full-text accessibility as an operational criterion is acknowledged as a possible source of availability bias.

Eligibility criteria: Eligible reports evaluated palm oil, red palm oil, palm olein, palm stearin, palm-derived bioactive fractions, interesterified palm-based fats, or palmitic-acid exposures relevant to glucose metabolism. Human studies included adults with T2DM, prediabetes, metabolic syndrome, obesity, or elevated metabolic risk when glycemic or insulin-related outcomes were reported. Preclinical studies were eligible when they directly investigated insulin signaling, glucose homeostasis, adipose inflammation, pancreatic responses, oxidative stress, or diabetic complications relevant to the review question.

Primary outcomes were fasting or postprandial glucose, HbA1c, fasting insulin, HOMA-IR, insulin-sensitivity measures, glucose tolerance, incretin responses, and molecular markers directly linked to insulin action. Studies focused exclusively on industrial processing, biomass, biofuel, engineering, antimicrobial production, or other non-metabolic outcomes were excluded from the analytic synthesis. Reviews and consensus papers were used for context but were not treated as independent effect estimates.

Data extraction, evidence grouping, and critical appraisal: For each included report, the extraction framework recorded study design, population or biological model, palm-oil form or fatty-acid exposure, comparator, intervention duration, dietary context, glycemic or insulin-related outcomes, direction of effect, and mechanistic pathways. To prevent double counting in the quantitative evidence map, each report was assigned to one primary analytical domain according to its main endpoint: fasting glucose, insulin sensitivity or insulin resistance, comparative dietary fats, HbA1c or longer-term glycemia, or palm-derived bioactive compounds.

Critical appraisal considered design-appropriate domains: randomization and allocation procedures for trials; confounding and exposure measurement for observational studies; model validity, allocation, blinding, and outcome completeness for animal studies; and selective reporting, product characterization, and indirectness across all designs. Formal composite quality scores were not created because the corpus contained different study types and several reports lacked sufficient detail for defensible numerical scoring. Instead, risk-of-bias concerns were integrated into the certainty and interpretation of each evidence domain.

Statistical analysis: The statistical unit for the evidence map was the included report. For each primary domain, the number and percentage of reports were calculated, and Wilson 95% confidence intervals were used because the domain counts were modest. A Pearson chi-square goodness-of-fit test evaluated whether the observed distribution across the five domains differed from equal allocation. Statistical significance was assessed at two-sided $p<0.05$. The chi-square analysis quantifies the structure of the evidence base; it is not an estimate of the clinical effect of palm oil.

Citation: Judijanto L. Palm oil consumption and glycemic control in type 2 diabetes mellitus: a systematic literature review. *J Diabetes Metab Disord Control.* 2026;13(2):97–104. DOI: 10.15406/jdmdc.2026.13.00319

A conventional meta-analysis of glycemic effect sizes was not performed because the reports did not provide a sufficiently exchangeable set of interventions, populations, comparators, outcome scales, time points, and variance estimates. Combining acute postprandial responses, HbA1c, HOMA-IR, animal glucose tolerance, and molecular endpoints would create spurious precision and violate the assumptions required for pooled inference. No missing standard deviations were imputed, and human and preclinical outcomes were not pooled. Clinical findings were instead synthesized by direction and context, with discordant evidence and risk-of-bias limitations reported explicitly (Figure 1).

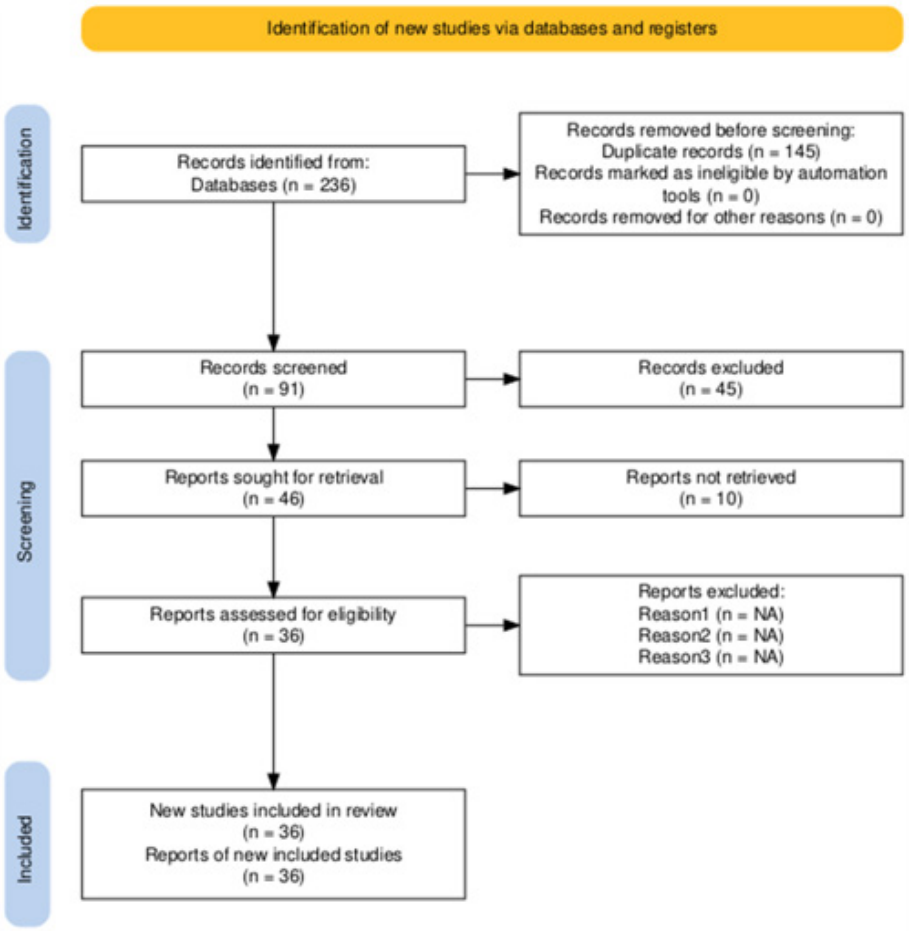

Figure 1 PRISMA-aligned identification, screening, and inclusion process used in the review.

Results

Study selection and evidence profile: The selection process retained 36 reports for the structured synthesis. The corpus included controlled and uncontrolled clinical interventions, observational studies, animal experiments, cell or tissue models, and studies of palm-derived bioactive fractions. This diversity expanded mechanistic coverage but reduced direct comparability. Direct long-term glycemic trials were less common than short-term metabolic, complication-focused, or preclinical studies.

The revised synthesis separates three evidentiary layers. The first consists of direct human glycemic outcomes, including fasting glucose, postprandial glucose, HbA1c, insulin, and incretin responses. The second consists of product- and process-specific evidence, particularly red or minimally refined palm oil, tocotrienol-rich fractions, repeated-heating exposures, and interesterified palm oil. The third consists of mechanistic evidence concerning palmitate, lipid signaling, oxidative stress, inflammation, and receptor or transcriptional targets. This separation prevents indirect mechanistic observations from being presented as equivalent to clinical outcomes.

Quantitative evidence MAP and inferential analysis: The primary-focus classification produced the distribution shown in Table 1. Fasting-glucose studies formed the largest category, but its confidence interval overlapped those of all other categories. The chi-square goodness-of-fit test was not significant, $\chi^2(4)=2.06$, $p=0.726$, indicating that the apparent numerical ranking of themes did not provide evidence that the corpus was disproportionately concentrated in one domain. This result also demonstrates why percentages should not be interpreted as a hierarchy of evidentiary strength.

Citation: Judijanto L. Palm oil consumption and glycemic control in type 2 diabetes mellitus: a systematic literature review. *J Diabetes Metab Disord Control.* 2026;13(2):97–104. DOI: 10.15406/jdmdc.2026.13.00319

Table 1 Quantitative distribution of the 36 included reports by primary analytical focus

Primary analytical focus	n	%	Wilson 95% CI
Fasting glucose	10	27.8	15.8–44.0
Insulin sensitivity/resistance	8	22.2	11.7–38.1
Comparative dietary fats	7	19.4	9.8–35.0
HbA1c/long-term glycemia	6	16.7	7.9–31.9
Palm-derived bioactives	5	13.9	6.1–28.7
Total	**36**	**100**	**—**

Note: The chi-square test evaluated the distribution of study focus, not treatment efficacy. CI, confidence interval.

Direct clinical glycemic evidence and the problem of short evaluation windows: Across the direct clinical evidence, no stable pattern showed that palm oil independently improved or worsened fasting glucose or HbA1c relative to all comparator fats. Several studies reported small or statistically non-significant differences, but many interventions simultaneously changed energy intake, carbohydrate quality, body weight, medication adherence, or physical activity. These co-interventions make it difficult to isolate the oil effect. The revised interpretation therefore replaces the earlier blanket statement of "neutrality" with the more defensible conclusion that direct evidence is inconsistent and of limited certainty.

Short evaluation windows were a recurrent limitation. Acute meal studies can detect postprandial glucose, insulin, or incretin responses, as illustrated by the altered GIP response to interesterified palm olein reported by Mo et al.[14], but they cannot establish sustained glycemic control. Pilot trials of palm-derived tocotrienol preparations in diabetes have primarily examined complications or intermediate biomarkers rather than sufficiently powered, long-duration HbA1c effects.[16,17] Even when HbA1c was measured, follow-up and sample size were often insufficient to distinguish a small oil-specific effect from ordinary variation or concurrent lifestyle change.

The direct evidence also varied in exposure definition. Some studies evaluated household palm-oil use, others used controlled meals, and others administered concentrated tocotrienol-rich fractions. These exposures cannot be merged as if they represented the same intervention. Looi et al.12 similarly emphasized heterogeneity across randomized trials of palm tocotrienol-rich fractions, reinforcing the need for product-specific interpretation.

Palmitic acid and insulin resistance: The relationship between palmitic acid and insulin resistance is supported by mechanistic and human evidence, but effect magnitude depends on energy balance, tissue, and comparator fatty acid. Palmitate can increase ceramide and diacylglycerol production, activate PKC, JNK, and IKKβ/NF-κB signaling, and inhibit the IRS-1/PI3K/Akt/GLUT4 axis. These changes reduce insulin-stimulated glucose uptake and can amplify inflammatory and oxidative stress. Sarabhai et al.[7] provided direct human evidence that palmitate- and oleate-enriched diets differentially modulate skeletal-muscle insulin sensitivity, supporting fatty-acid-specific biological effects.

Nevertheless, the evidence does not justify treating palmitic acid and palm oil as synonymous exposures. Palm oil contains oleic acid and minor constituents, and the metabolic response to a mixed oil depends on dose and substitution. A high-palmitate experimental diet delivered in caloric excess tests a different hypothesis from moderate palm-oil intake replacing another fat in an isocaloric diet. The revised manuscript therefore uses palmitate evidence to explain plausible pathways and risk conditions, not to calculate an unqualified clinical effect for palm oil.

Interesterified palm oil and processing-specific concerns: Evidence on interesterified palm-based fats raises a distinct process-specific concern. In mice consuming a high-fat diet, interesterified palm oil was associated with inflammatory changes in white adipose tissue and broader metabolic disturbances.[11] In people with T2DM, an acute controlled-meal study found that interesterified palm olein reduced the postprandial GIP response relative to a comparator condition.[14] The latter finding is physiologically relevant because GIP participates in nutrient-stimulated insulin secretion, but an acute hormonal response cannot establish chronic glycemic harm.

Interesterification changes triacylglycerol structure rather than simply changing the percentage of palmitic acid. Physicochemical studies show that enzymatic interesterification modifies melting and structural characteristics of palm-olein-based fats.[5] The health implications may therefore reflect stereospecific fatty-acid position, digestion kinetics, postprandial lipid transport, and the surrounding high-fat matrix. The current evidence warrants further clinical testing but is insufficient to generalize the animal findings to all interesterified products or to non-interesterified palm oil.

Unrefined, red, and refined palm oil are not interchangeable: Red palm oil and minimally processed palm oil retain carotenoids and tocotrienols at concentrations not representative of refined, bleached, and deodorized commercial oil. Studies of rice cooked with red palm oil have evaluated glycemic response within a specific starch–lipid food matrix, while studies of isolated tocotrienol-rich fractions have focused on antioxidant, inflammatory, retinal, vascular, or neurological outcomes.[13,18,28] Such findings cannot be used as direct evidence that refined palm oil improves glycemic control.

Conversely, evidence concerning refined or repeatedly heated palm oil should not automatically be applied to red palm oil. Refining reduces several minor constituents, and repeated frying introduces oxidation products and thermal degradation that may dominate the biological response. The appropriate interpretation is therefore product-specific: unrefined or red palm oil may have a more bioactive-rich profile, refined oil has greater compositional standardization but fewer retained pigments and antioxidants, and repeatedly heated or structurally modified oils represent additional exposures requiring separate evaluation.[4,20]

Dietary-matrix confounding and conflicting trial evidence: The dietary matrix was a major confounder across the evidence base. Mixed meals differ in carbohydrate amount, glycemic index, fiber, protein, energy density, and physical form; each can influence gastric emptying and postprandial glucose independently of the cooking oil. Physical activity performed after a high-fat, high-carbohydrate meal can also modify acute autonomic and metabolic responses in people with T2DM.9 Observational comparisons are further confounded by socioeconomic factors, food access, cooking methods, total caloric intake, and adiposity.

The comparator determines the apparent direction of effect. Replacing an animal fat rich in saturated fatty acids may yield a different outcome from replacing an oil rich in monounsaturated or polyunsaturated fatty acids. Likewise, results from red palm oil in a rice matrix, palm oil used for deep frying, and palm olein in a controlled test meal should not be combined without stratification. The conflicting evidence therefore reflects genuine heterogeneity rather than a simple failure to reach consensus. A causal conclusion requires

trials that standardize the matrix, maintain energy balance, specify the palm-oil fraction and processing history, and use a biologically adequate duration.

Molecular targets and preclinical signaling pathways: Table 2 integrates the molecular and processing-specific evidence requested by the reviewer. The table deliberately distinguishes direct palm-oil evidence from comparative fatty-acid evidence and identifies where translation to human T2DM remains uncertain.

Table 2 Mechanistic and processing-specific evidence relevant to glycemic control and insulin resistance

Issue	Representative evidence	Principal pathway or observation	Interpretive limitation
Palmitic acid and insulin resistance	Sarabhai et al.[7] ;Palomer et al.[6]	Ceramide/DAG accumulation; PKC, JNK and IKKβ activation; weaker IRS-1/PI3K/Akt/GLUT4 signaling	Isolated palmitate or palmitate-rich diets are not equivalent to whole palm oil in an energy-balanced diet.
Interesterified palm oil	Mo et al.[14] ; Martins et al.[11]	Altered postprandial GIP in T2DM; adipose inflammation and metabolic disturbance in mice	Acute human physiology and high-fat animal models do not establish long-term clinical harm.
Red/unrefined versus refined palm oil	Nurdin et al.[13] ; Zainal et al.[4] ; Looi et al.[12]	Differences in carotenoids, tocotrienols, antioxidant capacity and food-matrix behavior	Bioactive-rich fractions cannot be generalized to refined commodity oil.
PPAR-α and PPAR-γ	Ide[21]; Leow et al.[24]	Fatty-acid oxidation, adipocyte lipid buffering, transcriptional control and insulin sensitivity	GLA evidence is comparative and indirect because GLA is not a major palm-oil fatty acid.
FABP2 and FFAR1	Hotamisligil and Bernlohr[22] ; Kimura et al.[23]	Intestinal fatty-acid trafficking and long-chain-fatty-acid sensing linked to insulin secretion	Target engagement does not predict net clinical effect without dose, tissue and duration information.
Other signaling pathways	Wu et al.[15] ; Sadikan et al.[19] ; Rusli et al.[25]	AMPK, NF-κB, Nrf2, oxidative stress, inflammation, insulin-receptor signaling and metabolomic changes	Predominantly preclinical; indirectness and model-specific effects lower certainty.

Risk of bias and certainty of the evidence: The principal threats to certainty were short follow-up, small samples, incomplete product characterization, co-interventions, and indirectness from animal or cell models. Observational studies were vulnerable to residual confounding, while clinical trials often lacked adequate duration for HbA1c and did not consistently report allocation, adherence, or background medication changes. Preclinical studies provided stronger mechanistic control but lower direct applicability to routine human diets.

Taken together, certainty was low for an independent effect of conventional palm oil on long-term glycemic control, low-to-moderate for palmitate-related mechanisms of insulin resistance, and low for chronic harms of interesterified palm oil because the human evidence was acute and the adverse metabolic evidence was primarily animal-based. Evidence for benefits of red palm oil or tocotrienol-rich fractions was also low-to-moderate and product-specific. These ratings support cautious, conditional conclusions rather than a universal safety or hazard claim.

Discussion

Interpretation of the direct clinical evidence: The revised synthesis indicates that current clinical evidence is insufficient to establish a consistent, independent effect of palm oil on fasting glucose, HbA1c, or insulin resistance in T2DM. This conclusion is more cautious than the original characterization of the evidence as generally neutral. A null or small difference in a short, heterogeneous trial may reflect low statistical power, an unsuitable endpoint, a weak exposure contrast, or confounding by weight and dietary change. Absence of a consistent effect should therefore be interpreted as uncertainty rather than proof of equivalence.

The quantitative evidence map adds inferential structure but does not replace an effect-size meta-analysis. The non-significant chi-square result shows that the 36 studies were distributed without a statistically dominant thematic focus; it does not indicate that palm oil has no glycemic effect. This distinction is important because evidence-map statistics describe the literature, whereas clinical meta-analysis estimates intervention effects. A pooled clinical estimate would require sufficiently similar products, comparators, durations, populations, and outcome reporting, conditions not met by the present corpus.

Reconciling palmitate-related mechanisms with whole-oil evidence: Palmitate-related insulin resistance is biologically plausible and supported by converging evidence. Excess palmitate can promote lipid intermediates, inflammatory kinases, endoplasmic-reticulum stress, mitochondrial dysfunction, and impaired insulin signaling. The human skeletal-muscle findings of Sarabhai et al.[7] strengthen the relevance of fatty-acid quality. However, dose and metabolic context determine whether these pathways are activated; palmitate consumed within energy balance and alongside oleate may not reproduce the exposure achieved in cellular or high-fat animal models.

This distinction explains why apparently neutral clinical comparisons can coexist with adverse mechanistic findings. Whole palm oil is not pure palmitate, and clinical comparator oils may differ in multiple fatty acids, minor compounds, and culinary uses. Furthermore, an observed effect may result from the displaced food rather than the added oil. Future trials should therefore specify the replacement nutrient and use compositional analysis rather than relying on the generic label "palm oil."

Interesterification, refining, and product-specific interpretation: The reviewer's concern about interesterified palm oil is supported by emerging evidence, but the risk signal is process-specific. Interesterification may alter the stereospecific distribution of palmitate and thereby change digestion and postprandial physiology. The animal evidence of adipose inflammation and the acute human evidence

of altered GIP justify targeted long-term trials that compare natural and interesterified structures under matched fatty-acid composition. Until such studies are available, these findings should prompt caution without being generalized to all palm oils.

The same principle applies to refining. Red palm oil and tocotrienol-rich fractions retain bioactive compounds that may counter oxidative and inflammatory stress, but concentrated fractions are not nutritionally equivalent to refined cooking oil. Refined oil, in turn, is not equivalent to repeatedly heated oil. Product identity, minor-component profile, thermal history, and oxidation status should be treated as mandatory reporting variables. Failure to distinguish them is a major source of inconsistency and an avoidable limitation in future evidence synthesis.

Molecular targets and the limits of translation: PPAR-α, PPAR-γ, FABP2, and FFAR1 provide a coherent mechanistic framework linking fatty-acid handling to glucose regulation. PPAR-α favors oxidation, PPAR-γ supports adipose storage and insulin sensitivity, FABP2 influences intestinal long-chain-fatty-acid trafficking, and FFAR1 links fatty-acid sensing to glucose-stimulated insulin secretion. These targets interact with AMPK, insulin-receptor/IRS/PI3K/Akt signaling, inflammatory kinases, and oxidative-stress responses. Their inclusion strengthens biological interpretation by moving beyond generic theoretical assumptions.

At the same time, the evidence must be correctly attributed. GLA-rich oils can influence PPAR-related and lipid-metabolism genes in obese mice, but GLA is not a major palm-oil constituent. Similarly, transcriptomic changes induced by water-soluble palm-fruit extract or tissue protection from tocotrienol-rich fractions do not demonstrate that ordinary refined palm oil engages the same targets at dietary doses. Mechanistic plausibility should generate hypotheses and inform biomarkers, not substitute for clinical outcome evidence.

Trial duration, dietary matrices, and confounding: Short intervention periods remain one of the most important limitations. HbA1c requires an observation window long enough to capture erythrocyte exposure, while changes in liver fat, body weight, and insulin sensitivity may evolve over months. Acute studies remain valuable for mechanistic endpoints, but their conclusions must be restricted to the measured postprandial period. Future clinical trials should last at least 12–16 weeks when HbA1c is a primary outcome and longer when durability or safety is the central question.

Dietary matrices require equally careful control. Trials should use matched energy, carbohydrate quality, fiber, protein, and meal timing; specify cooking temperature and reuse of oil; monitor body weight and medication; and report the comparator nutrient explicitly. Factorial or crossover designs may help separate oil type from meal composition. Without such controls, conflicting results will continue because the measured response reflects the whole meal and behavior pattern rather than the oil alone.

Clinical, public-health, and research implications: For clinical practice, the evidence does not support treating a single edible oil as the dominant determinant of glycemic control. Energy balance, carbohydrate quality, body-weight management, physical activity, medication adherence, and the overall dietary pattern remain more directly actionable. Nevertheless, people with T2DM may reasonably be advised to avoid excessive intake of saturated-fat-rich, repeatedly heated, or highly processed fat matrices and to favor dietary patterns rich in minimally processed foods, fiber, and unsaturated-fat sources, while recognizing that direct evidence comparing specific palm-oil products remains incomplete.[2,8]

For researchers and industry, the priority is product characterization. Trials should report fatty-acid composition, triacylglycerol structure, free-fatty-acid content, oxidation markers, carotenoids, tocopherols and tocotrienols, refining history, interesterification method, dose, and culinary use. Core outcomes should include fasting and postprandial glucose, HbA1c, fasting insulin or validated insulin-sensitivity measures, body weight, liver-fat or lipid intermediates where feasible, inflammatory biomarkers, and adverse events. This would permit future meta-analysis and prevent the current problem of pooling chemically non-equivalent exposures.

Strengths and limitations: This revision strengthens the review by removing repetitive statements, separating direct clinical evidence from preclinical mechanisms, quantifying the distribution of study focus, and explicitly analyzing palmitic acid, interesterified palm oil, refining, dietary matrices, conflicting trial evidence, and reviewer-specified molecular targets. The use of Wilson confidence intervals and a chi-square test adds inferential analysis without overstating what the heterogeneous data can support.

Several limitations remain. The review relied primarily on one bibliographic database and an accessibility criterion that may introduce selection bias. The included studies were heterogeneous and often inadequately reported, preventing a defensible pooled clinical effect estimate. The evidence map assigns one primary theme per report and therefore simplifies multi-outcome studies. Some mechanistic conclusions depend on preclinical models, and the absence of standardized product descriptions limits exposure comparability. These constraints reduce certainty and should be considered when interpreting the conclusions.

Conclusion

The available evidence does not justify a universal conclusion that palm oil is either glycemically neutral or uniformly harmful. Direct clinical findings are inconsistent and constrained by short follow-up, small samples, heterogeneous products, and confounding from the wider dietary matrix. The quantitative evidence map describes how the literature is distributed but does not establish an intervention effect, and the current study-level data are not sufficiently comparable for a valid pooled meta-analysis.

Mechanistic evidence supports a relationship between excess palmitic-acid exposure and insulin resistance through lipid-intermediate accumulation, inflammatory signaling, cellular stress, and impairment of the IRS-1/PI3K/Akt/GLUT4 pathway. Interesterified palm oil warrants specific attention because animal evidence and acute human physiology suggest possible metabolic effects that may differ from those of naturally structured palm oil. Red or minimally refined palm oil and tocotrienol-rich fractions also differ materially from refined palm oil because they retain bioactive constituents with potential antioxidant and anti-inflammatory actions.

Future research should use long-duration, adequately powered trials that distinguish refined, red, fractionated, repeatedly heated, and interesterified products; standardize the food matrix and replacement nutrient; and report both clinical glycemic outcomes and mechanistically informative biomarkers. Until such evidence is available, interpretation should remain product-specific, context-dependent, and explicit about the difference between direct clinical outcomes and preclinical molecular plausibility.

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Conflict of interest

The author declares that there is no conflict of interest.

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