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Molecular Mechanisms Underlying the Hypolipidemic Effects of Bioactive Compounds from Avocado (*Persea americana* Mill.) Peel: A Literature Review

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Abstract: Avocado peel (*Persea americana* L.) contains a number of bioactive compounds that have the potential to act as antihyperlipidemic agents. These compounds include polyphenols, flavonoids, triterpenoids, phytosterols, and phenolic acids, which are known to affect lipid metabolism through various molecular pathways. This review aims to identify the molecular mechanisms underlying the antihyperlipidemic effects of avocado peel extract. Relevant literature was obtained through searches in the PubMed, Scopus, and Web of Science databases using relevant keywords. Selected studies were analyzed based on the PICO (Population, Intervention, Comparison, Outcome) framework and summarized using the PRISMA methodology. The results of the review indicate that avocado peel extract has the potential to activate the AMPK pathway, regulate PPAR-α/γ, inhibit HMG-CoA reductase, and increase bile acid excretion. However, most of the evidence is limited to animal models and in vitro studies, and further research in humans is needed to confirm the efficacy and to elucidate more in-depth molecular mechanisms.

Keywords: Antihyperlipidemic; Avocado peel; Bioactive compounds; Dyslipidemia; HMGCoA

Introduction

Dyslipidemia is one of the main risk factors for cardiovascular disease, which remains the leading cause of death worldwide. According to a report by WHO (2018), cardiovascular disease causes more than 17 million deaths each year, most of which are related to uncontrolled lipid profiles. Elevated levels of total cholesterol, LDL, triglycerides, and decreased HDL accelerate the development of atherosclerosis and chronic inflammation, which ultimately trigger severe cardiovascular events (Ference et al., 2017). Although pharmacological therapies such as statins, fibrates, and PCSK9 inhibitors have been proven effective, their adverse effects, including hepatotoxic side effects, myopathy, and therapeutic resistance necessitate new, safer, and more accessible hypolipidemic therapy alternatives (Stroes et al., 2015).

In recent years, the development of natural materials as candidates for hypolipidemic therapy has increased significantly. One plant with great potential is the avocado (*Persea americana* Mill.), especially its peel, which is currently underutilized and considered agricultural waste. Phytochemical studies indicate that avocado peel is rich in bioactive compounds, such as flavonoids, phenols, terpenoids, and tannins (Brajawikalpa et al., 2020; Ibarra-Junquera et al., 2019). These compounds are reported to have antioxidant and anti-inflammatory activities that play a role in improving lipid profiles (Shahidi & Ambigaipalan, 2015).

Several in vivo studies have reported that avocado plant extracts can reduce LDL and triglyceride levels and increase HDL levels (Alhassan & Ahmed, 2016). In

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addition, several of their active compounds, especially flavonoids, have been shown to be able to modulate important molecules in lipid metabolism such as HMG-CoA reductase, PPARα, PPARγ, and influence the SREBP-1c and AMPK signaling pathways (Chen et al., 2025; Li et al., 2025). However, this evidence remains fragmented, and no scientific review has comprehensively integrated in vitro, in vivo, and in silico data to map the molecular mechanisms of the hypolipidemic effects of bioactive compounds in avocado fruit peel (Tovar et al., 2024).

On the other hand, in silico approaches, such as molecular docking and network pharmacology, have rapidly developed as important tools in understanding the mechanisms of action of natural compounds that are multitarget (Daina et al., 2019). These approaches are expected to map the interactions between bioactive compounds and molecular targets associated with lipid metabolism. However, the use of these approaches, especially for avocado fruit peel, is still very limited and has not been systematically explored.

Thus, a systematic review is needed to summarize and integrate all available experimental and computational evidence, to chart the molecular mechanisms of the hypolipidemic effects of bioactive compounds in avocado fruit peel.

Method

This review adhered to the PRISMA guidelines (Page et al., 2021). A comprehensive search was conducted across PubMed, Scopus, and ScienceDirect databases using the keywords: "avocado peel", "hypolipidemic", "molecular mechanism", and "bioactive compounds". Inclusion criteria were (1) articles published between 2015–2025; (2) studies examining molecular mechanisms of hypolipidemic activity; and (3) studies involving avocado peel as the primary source of bioactives. Exclusion criteria included review articles lacking a mechanistic focus and inaccessible full texts. The review process involved identification, screening, eligibility, and inclusion stages as follows: article identification: Searches were conducted using the keywords “avocado peel,” “Persea americana,” “lipid metabolism,” “hypolipidemic,” and “bioactive compounds”; article screening, selection based on title and abstract, followed by full-text assessment; data extraction, collection of data from selected articles, including research model, extract dosage, type of bioactive compounds, molecular mechanisms, and effects on lipid metabolism; data synthesis, thematic analysis to identify the molecular pathways involved.

PICO analysis i.e., P (population), animal models (rats, mice) and cellular models (hepatocytes, intestinal cells), I (intervention), avocado peel extract or bioactive compounds from avocado peel (flavonoids, phytosterols), C (comparison) a control group or a group given conventional antihyperlipidemic therapy (e.g., statins), O (outcome), modification of lipid profile (decrease in total cholesterol, LDL-C, triglycerides, and increase in HDL-C); activation or inhibition of molecular pathways related to lipid metabolism (Motwani et al., 2013; White et al., 1986; Williamson et al., 2014).

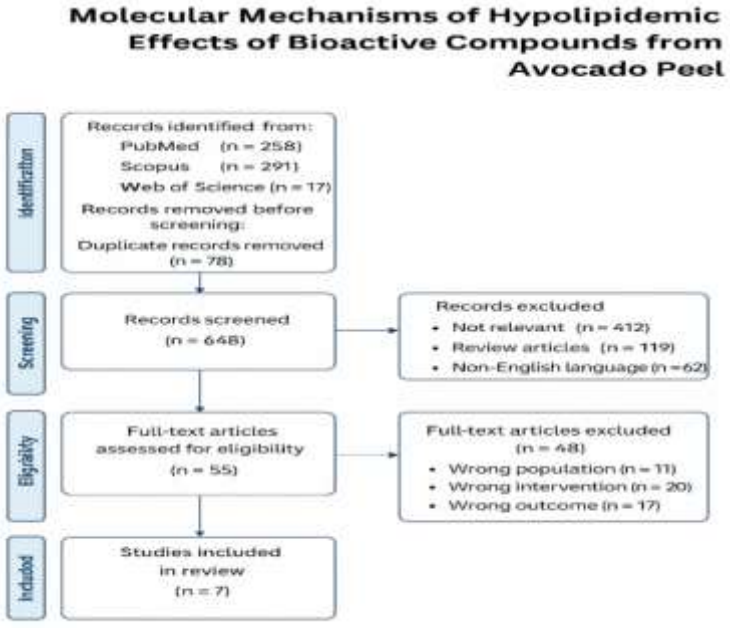
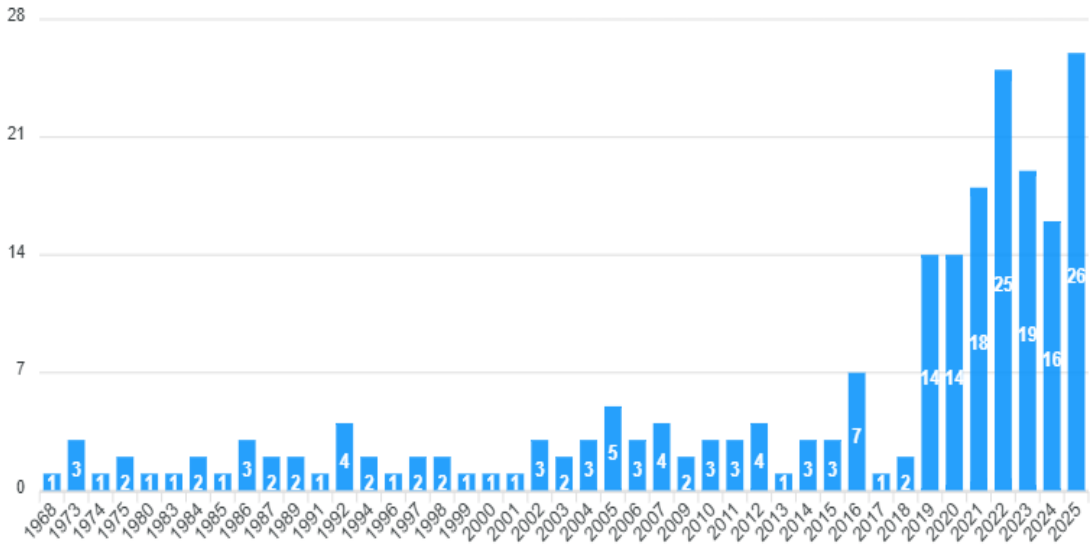


Figure 1. PRISMA analysis results

Result and Discussion

A total of 648 studies were initially identified (records identified from PubMed, Scopus, and Web of Science). After removing duplicates (78 studies) and applying the inclusion criteria, seven articles were selected for full analysis. The selected studies utilized in vitro (HMGCoA reductase, HepG2 and Caco-2 cell lines), in vivo (rat models), and in silico (molecular docking) methods (Figure 2).



Based on the results of the annual keyword searches shown in Figure 3, there has been a significant increase in the number of publications over time. In the period from 1968–2018, the occurrence of keywords was still relatively low and stable. Entering the years 2019–2021, the number of publications began to increase gradually, indicating the emergence of initial interest in this research topic. A much sharper growth trend has been seen since 2022, with the biggest surge occurring in 2025. This increase shows that research topics related to these keywords have become increasingly relevant and have received a lot of attention in recent years, thereby reinforcing the urgency and value of this SLR research.

Discussion

The increase in the prevalence of dyslipidemia as a major risk factor for cardiovascular disease has prompted the search for alternative natural-based therapies. In this context, the use of agricultural waste, such as avocado peel (Persea americana), has begun to attract attention due to its high content of bioactive compounds. Avocado peel is known to be rich in phenolic compounds, flavonoids, triterpenoids, and phytosterols, which have the potential to act as natural hypolipidemic agents (Robin et al., 2024). The table of article review results can be seen in Table 1.

Table 1. Table of article review results

Research Title	Research Location	Author	Insight	Theory Used Research	Research Methods	Result Research	Limitations	Correlation with Your Research
Lipid Digestibility and Polyphenols Bioaccessibility of Oil-in-Water Emulsions Containing Avocado Peel and Seed Extracts	Spanyol (University of Lleida)	(Velderrain-Rodríguez et al., 2021)	Avocado peel extract increases FFA release in emulsions, but decreases flavonoid bioaccessibility	O/W emulsion bioaccessibility of phenolic compounds	UPLC-MS/MS, *in vitro* digestion model	LMP + avocado peel extract increases lipid digestibility, but decreases flavonoid bioaccessibility	The study was limited to *in vitro* simulations, not *in vivo*	Demonstrating that phenolic compounds from avocado peel affect lipid metabolism

Research Title	Research Location	Author	Insight	Theory Used Research	Research Methods	Result Research	Limitations	Correlation with Your Research
Computational Identification of Natural Compounds as Potential Inhibitors for HMG-CoA Reductase	India	(Athista et al., 2023)	Identification of food compounds capable of inhibiting HMG-CoA reductase through molecular docking	HMG-CoA reductase inhibitor theory	Virtual screening, molecular docking	Several natural compounds from foods show high affinity for target enzymes	Not yet tested *in vitro* or *in vivo*	Explaining the main molecular targets of the hypolipidemic effect, relevant to compounds from avocado peels
Persea americana Peel: A Promising Source for Mitigation of Cardiovascular Risk in Arthritic Rats	Mesir	(Mohamed et al., 2025)	Avocado peels extracted with 2:1 EtOH, IL-6, IL-1β, TNF-α increases IL-10, and lowers cardiovascular risk	Gut–joint axis, expression of cytokine inflammation	*In vivo* pada tikus RA, RT-PCR, 16S rRNA sequencing, docking	APE lowers inflammatory markers and plasma lipids, improves gut microbiota composition	Specific to the RA model; not focused on the general population	Demonstrating the systemic effects of bioactive compounds in avocado skin, including hypolipidemic effects
The Pulp, Peel, Seed of *Persea americana* as Sources of Bioactive Phytochemicals with Cardioprotective Properties: A Review	Polandia	(Olas, 2024)	Avocado peels contain compounds such as flavonoids, procyanidins, and triterpenoids, which have cardioprotective potential	Stress oxidative and antiinflammation theory	Narrative review based on PubMed, Scopus	Avocado peel contains compounds that have the potential to reduce cholesterol, inflammation, and platelet aggregation	Does not present new experimental data	Reinforcing the importance of bioactive compounds in avocado peels for cardiovascular health
Bioactive Properties of *Persea americana* Peel Extract and Their Role in Hypercholesterolemia Management	Portugal	(Teixeira et al., 2025)	Avocado peel extract inhibits cholesterol permeation and is safe	Inhibition of cholesterol permeation, antioxidants	*In vitro* (Caco-2, HepG2), analysis fitokimia	Pyridoxine-O-hexoside reduces cholesterol absorption in the intestines	Only *in vitro* testing, not yet clinical	Supporting molecular mechanisms in inhibiting cholesterol absorption
Avocado (*Persea americana*) Peel: A Promising Source of Bioactive Compounds	Nigeria	(Oke et al., 2025)	Avocado peels are rich in polyphenols, procyanidins, quercetin,	Phytochemicals and natural molecular mechanisms	Literature review and exploration of industrial	Emphasizing the pharmacological potential of avocado skin in functional	Has not yet tested specific *in vivo* or molecular development of hypolipid	Confirming the potential of bioactive compounds in

Research Title	Research Location	Author	Insight	Theory Used Research	Research Methods	Result Research	Limitations	Correlation with Your Research
			and catechins, which have hypolipidemic and anti-inflammatory properties		application	formulations	emic agents	avocado peels
Hypolipidemic Effect of Avocado Peel Extract in Rats with Dyslipidemia	Indonesia (FK UNSWAGATI Cirebon)	(Brajawikalpa et al., 2020)	Avocado peel extract significantly reduces LDL and triglycerides in dyslipidemic rats	Herbal-based interventions	*In vivo* experiments on Sprague Dawley rats	Significant reduction in LDL at a dose of 300 mg/200 g body weight	Not evaluating the molecular mechanism	Immediately providing the hypolipidemic effect of avocado peel

Brajawikalpa et al. (2020) showed that avocado peel extract was able to significantly reduce LDL and triglyceride levels and increase HDL levels in animal models with dyslipidemia. These effects occurred in a dose-dependent manner, reinforcing the indication of the presence of active compounds that play a role in modulating lipid metabolism. However, the study did not elaborate on the molecular mechanisms underlying these hypolipidemic effects, opening up room for further exploration.

In line with this, research by Mohamed et al. (2025) developed a nutraceutical formulation from avocado peel and evaluated its effects on arthritic rats with high cardiovascular risk. The results showed that administration of avocado peel nutraceutical (APN) not only reduced lipid parameters such as total cholesterol and LDL, but also decreased the expression of inflammatory genes such as TNF-α, IL-6, IL-1β, and increased the expression of IL-10, both in the liver and spleen. This finding provides preliminary evidence that the hypolipidemic effects of bioactive compounds in avocado peel may be mediated by interrelated inflammatory and oxidative stress pathways. Furthermore, the gut–joint axis approach used in the study emphasizes the interconnection between gut microbiota, the immune system, and lipid metabolism, broadening the molecular perspective of avocado peel's effects on cardiovascular health.

Velderrain-Rodríguez et al. (2021) raised another important issue, namely the bioaccessibility and bioavailability of bioactive compounds in avocado skin and seeds in oil-in-water emulsion systems. They showed that adding avocado peel extract to low-methoxyl pectin-based emulsions increased the release of free fatty acids during in vitro digestion, which is an indicator of improved lipid digestibility. In addition, the peel extract also affects the release profile of flavonoids and phenolic compounds, which are very important in the context of the bioeffectiveness of these compounds in the gastrointestinal tract. Although this study did not directly investigate the effects on blood lipid parameters, it provides a strong basis that the active compounds in avocado peel play a role in improving lipid metabolism through increased release and absorption in the intestine.

The in silico research by Athista et al. (2023) makes an important contribution to understanding the potential molecular mechanisms involved in the hypolipidemic effects of natural bioactive compounds. They conducted virtual screening of compounds from natural foods to identify compounds that can inhibit the enzyme 3-hydroxy-3-methylglutaryl-coenzyme A reductase (HMG-CoA reductase), a key enzyme in cholesterol biosynthesis. The results showed that a number of compounds from natural food sources had high binding affinity to the active site of the enzyme, similar to the mechanism of action of statins. Although this study did not include specific compounds from avocado peel, the methodology used can be applied to test compounds such as β-sitosterol, quercetin, and catechin, which are known to be contained in avocado skin as identified in other studies.

Furthermore, a review by Olas (2024) highlights various bioactive compounds contained in avocados, including the pulp, seeds, and skin. Compounds such as oleic acid, phytosterols, and flavonoids have been shown to have cardioprotective effects through mechanisms such as antioxidants, anti-inflammation,

and platelet aggregation inhibition. This study provides an in-depth understanding of the biological pathways that may be involved in the hypolipidemic effects, although it does not explicitly focus on avocado skin. Nevertheless, these findings can be used as a reference for evaluating similar compounds derived from the skin in experimental studies.

Teixeira et al. (2025) developed an aqueous extract from avocado peel and evaluated its effectiveness in reducing cholesterol permeability through a Caco-2 cell model, which simulates absorption in the human intestine. The results showed that this extract significantly inhibited cholesterol permeability and exhibited high antioxidant activity in the HepG2 model. This indicates that bioactive compounds from avocado peel can modulate lipid absorption through their effect on intestinal epithelial permeability (Bhuyan et al., 2019; Salazar-López et al., 2021; Zuñiga-Martínez et al., 2021), which is an important mechanism in the management of dyslipidemia. The study also found a new compound, pyridoxine-O-Hex, in avocado peel extract that may have a bioactive role, although further study is needed.

A review by Oke et al. (2025) compiled various research results on the bioactive compound content of avocado peel and its potential in functional applications. They mentioned that avocado peel contains various compounds such as (epi)catechin, procyanidins, and chlorogenic acid, which have antioxidant, anti-inflammatory, and antimicrobial capacities. This study emphasizes that avocado peel has a rich and diverse compound profile, making it a potential candidate for functional food-based hypolipidemic interventions. However, this study is narrative in nature and does not experimentally elaborate on the molecular effects of these compounds on lipid metabolism (Han, 2016; Pawlak et al., 2015).

Conclusion

Avocado peel bioactives exhibit promising hypolipidemic effects via multiple molecular mechanisms, including HMGCR inhibition, transcriptional modulation (PPAR-α/SREBP-1c), and intestinal cholesterol transport suppression. These findings support the potential development of avocado peel-based functional foods or nutraceuticals. Further clinical research is needed to confirm efficacy and safety.

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Author Contributions

Conceptualization, Suwahyuni M. and Nanik S methodology, Suwahyuni; software, Sapto Y; validation, Suwahyuni.,Nanik S.; formal analysis, Suwahyuni M.; investigation, Suwahyuni M.; resources, Sapto Y.; data curation, Suwahyuni M.; writing—original draft preparation, Suwahyuni M.; writing—review and editing, Suwahyuni, Nanik S.; visualization, Nanik Y; supervision, Suwahyuni M.; project administration, Suwahyuni M.; funding acquisition, Sapto Y. All authors have read and agreed to the published version of the manuscript.

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Conflicts of Interest

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