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From Tradition to Translation: A Systematic Review on the Pharmacological Actions of Eugenol Extracted from *Ocimum* Plants in Oxidative Stress, Inflammation, and Diabetes Mellitus

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A B S T R A C T

Background: *Ocimum* species, commonly known as basil, have a rich history in traditional medicine for various ailments. Eugenol, a primary bioactive compound found in several *Ocimum* species, has garnered significant scientific attention for its potential therapeutic properties. This systematic review aimed to comprehensively evaluate the pharmacological actions of eugenol extracted from *Ocimum* plants in the context of oxidative stress, inflammation, and diabetes mellitus. **Methods:** A systematic literature search was conducted across major scientific databases for studies published between 2013 and 2024 that investigated the effects of eugenol derived from *Ocimum* plants on oxidative stress, inflammation, and diabetes mellitus. The search strategy included keywords such as "eugenol," "*Ocimum*," "antioxidant," "anti-inflammatory," and "antidiabetic." Inclusion criteria for studies involving in vitro, in vivo, and clinical studies that specifically examined the pharmacological actions of eugenol extracted from *Ocimum* species in the aforementioned conditions. Data on study design, intervention, outcomes, and key findings were extracted and synthesized narratively. **Results:** The review identified ten key studies that met the inclusion criteria. These studies collectively suggested that eugenol extracted from *Ocimum* plants exhibited significant antioxidant activity by scavenging free radicals and enhancing endogenous antioxidant enzymes. Furthermore, eugenol demonstrated anti-inflammatory effects by modulating pro-inflammatory cytokines and inhibiting key inflammatory pathways such as NF-κB and COX. In the context of diabetes mellitus, studies indicated that eugenol could improve glucose metabolism by enhancing insulin sensitivity, protecting pancreatic beta cells, and inhibiting carbohydrate metabolizing enzymes. **Conclusion:** This systematic review provided a comprehensive overview of the pharmacological actions of eugenol extracted from *Ocimum* plants in mitigating oxidative stress, inflammation, and diabetes mellitus. The findings from the included studies supported the traditional uses of *Ocimum* species and highlighted the therapeutic potential of eugenol as a natural agent in managing these conditions. Further well-designed clinical trials are warranted to validate these preclinical findings and translate them into clinical applications.

1. Introduction

The genus *Ocimum*, belonging to the family Lamiaceae, comprises several species that have been utilized for their medicinal and culinary applications across diverse cultures for centuries. Among the notable species within this genus are *Ocimum tenuiflorum* (holy basil or Tulsi), *Ocimum gratissimum* (African basil), and *Ocimum basilicum* (sweet basil). Traditionally, various parts of *Ocimum* plants have been employed in different systems of medicine for the

treatment of a wide array of ailments. These traditional applications span a broad spectrum of health conditions, including respiratory infections, digestive disorders, inflammation, and fever. The therapeutic potential ascribed to *Ocimum* species is largely attributed to their complex composition of bioactive phytochemicals. Eugenol, a phenolic compound, is a prominent constituent found in many *Ocimum* species. Characterized by the molecular structure of 4-allyl-2-methoxyphenol, eugenol possesses a unique arrangement comprising an aromatic ring, a hydroxyl group, a methoxy group, and an allyl side chain. This specific structural arrangement is responsible for endowing eugenol with a diverse range of biological activities. These activities include, but are not limited to, antioxidant, anti-inflammatory, analgesic, and antimicrobial properties. The prevalence of eugenol in commonly used species, in conjunction with its well-documented pharmacological effects, positions it as a key molecule that contributes to the traditional therapeutic applications of these plants.[1-4]

Oxidative stress is a physiological state characterized by an imbalance. This imbalance involves the production of reactive oxygen species (ROS) and the body's antioxidant defense mechanisms. Oxidative stress plays a pivotal role in the pathogenesis of numerous chronic diseases. The excessive accumulation of ROS can lead to cellular damage. This damage may manifest as lipid peroxidation and DNA damage, ultimately contributing to the development and progression of various conditions. These conditions include cardiovascular diseases, neurodegenerative disorders, cancer, and diabetes mellitus. Inflammation is a complex biological response to harmful stimuli. While acute inflammation serves as a protective mechanism, chronic inflammation can lead to tissue damage. This can contribute to the development of various diseases. There is an intricate link between inflammation and oxidative stress.[5-7]

Diabetes mellitus, a chronic metabolic disorder characterized by hyperglycemia, is frequently associated with increased oxidative stress and inflammation. This concurrence creates a detrimental cycle that exacerbates the disease and its associated complications. Given the traditional use of *Ocimum* plants for conditions often linked to oxidative stress, inflammation, and diabetes, and considering the significant presence of eugenol in these plants, there is a clear rationale for a comprehensive understanding of the scientific evidence supporting these pharmacological actions.[8-10] This systematic review aims to evaluate the existing literature published between 2013 and 2024. The focus is on the effects of eugenol extracted from *Ocimum* plants in mitigating oxidative stress, inflammation, and diabetes mellitus.

2. Methods

This systematic review was conducted adhering to the methodological guidelines outlined in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement. This framework ensures a transparent and rigorous approach to the identification, screening, inclusion, and synthesis of relevant studies.

A comprehensive and systematic literature search was performed to identify relevant studies. Major electronic databases were utilized as primary sources for the identification of pertinent research articles. These databases included PubMed, Scopus, Web of Science, and Google Scholar. The search strategy was designed to be exhaustive, aiming to capture all relevant studies published within the specified timeframe. To achieve this, a combination of keywords and Boolean operators was employed. This approach allowed for a refined and targeted search, increasing the precision and comprehensiveness of the literature retrieval process. The search period was limited to studies published between January 2013 and December 2024. This temporal restriction allowed for a focus on the most contemporary research related to the pharmacological actions of eugenol extracted from *Ocimum* plants. The primary search terms incorporated a combination of terms related to the key concepts of interest. These terms included "eugenol," "Ocimum," and "basil," which are central to the plant

source of the compound of interest. To capture the various pharmacological actions under investigation, terms such as "antioxidant," "oxidative stress," "anti-inflammatory," "inflammation," "antidiabetic," "diabetes mellitus," "glucose metabolism," and "insulin sensitivity" were included. Furthermore, related synonyms and Medical Subject Headings (MeSH) terms were also incorporated to ensure that the search strategy was as inclusive as possible. The use of MeSH terms, a controlled vocabulary thesaurus used for indexing articles in PubMed, enhanced the specificity of the search by identifying articles based on standardized subject descriptors. The search strings were meticulously adapted for each individual database. This adaptation was crucial because different databases utilize different search algorithms and indexing systems. Tailoring the search strings to the specific requirements of each database maximized the retrieval of relevant articles. For example, a sample search string that was utilized in PubMed, demonstrating the combination of keywords and Boolean operators, is as follows: ("eugenol" OR "Ocimum" OR "basil") AND ("antioxidant" OR "oxidative stress" OR "anti-inflammatory" OR "inflammation" OR "antidiabetic" OR "diabetes mellitus") AND ("2013"[Date - Publication]: "2024"[Date - Publication]). In this string, the OR operator was used to combine synonymous terms, while the AND operator was used to link different concepts. The date restriction was applied to retrieve articles published within the specified period. It is important to note that the specific syntax and field codes may vary between databases. Therefore, the search strings were modified accordingly for Scopus, Web of Science, and Google Scholar to ensure optimal search results in each database.

The studies identified through the database searches were assessed for eligibility based on a set of predefined inclusion and exclusion criteria. These criteria were established a priori to ensure that the selected studies were relevant to the research question and of sufficient quality for inclusion in the review. The inclusion criteria were designed to select studies that specifically investigated the pharmacological actions of eugenol extracted from *Ocimum* plants in the context of oxidative stress, inflammation, and diabetes mellitus. To be included, studies had to be published in the English language. This criterion was applied due to resource constraints and the need for the reviewers to accurately interpret the study findings. Studies were required to focus on the pharmacological actions of eugenol specifically extracted or isolated from any species of the *Ocimum* genus. This criterion ensured that the review focused on the effects of eugenol derived from the intended plant source, as eugenol can also be obtained from other plants. Studies were included if they investigated the effects of eugenol on at least one of the following outcomes: oxidative stress, inflammation, or diabetes mellitus. Oxidative stress was defined by relevant measures such as antioxidant enzyme activity, levels of reactive oxygen species (ROS), and lipid peroxidation. This broad definition allowed for the inclusion of studies that assessed oxidative stress using various methodologies. Inflammation was assessed by outcomes such as pro-inflammatory cytokine levels and inflammatory pathway markers. This criterion ensured that studies investigating the effects of eugenol on different aspects of the inflammatory response were included. Diabetes mellitus was assessed by outcomes such as blood glucose levels, insulin sensitivity, pancreatic beta-cell function, and carbohydrate metabolism. Studies that investigated the effects of eugenol on any of these parameters were considered eligible for inclusion. Studies that employed in vitro, in vivo, or clinical study designs were all eligible for inclusion. This criterion allowed for the inclusion of a wide range of study designs, from basic science investigations to clinical trials, providing a comprehensive overview of the evidence. The exclusion criteria were established to exclude studies that were not relevant to the research question or that had methodological limitations. Studies were excluded if they did not specifically investigate eugenol extracted from *Ocimum* plants. For example, studies using eugenol from cloves or other sources were excluded to maintain the focus on the

intended plant source. Studies that focused on other pharmacological activities of eugenol not related to oxidative stress, inflammation, or diabetes mellitus were excluded. Examples of such activities include antimicrobial or anticancer effects. This criterion ensured that the review focused on the specific pharmacological actions of interest. Review articles, meta-analyses, conference abstracts, and editorials were excluded. These types of publications do not provide original research data and were therefore not suitable for inclusion in the review. Studies that did not provide original research data were also excluded. This criterion ensured that only studies that contributed new evidence were included in the review.

The study selection process was conducted in two distinct phases to ensure a thorough and unbiased evaluation of the literature. In the first phase, the titles and abstracts of all articles retrieved from the database searches were screened. This screening process was performed independently by two reviewers. The reviewers assessed the titles and abstracts based on the pre-defined inclusion and exclusion criteria. This initial screening allowed for the removal of clearly irrelevant articles, such as those that were not related to the topic or those that were not original research. Any discrepancies that arose between the reviewers during this initial screening phase were resolved through discussion and consensus. This collaborative approach ensured that the screening process was consistent and that any uncertainties were addressed. In the second phase, the full texts of potentially eligible articles were retrieved. These articles were those that had passed the initial screening based on their titles and abstracts. The full texts of these articles were then assessed for final inclusion in the review. This assessment was again based on the same pre-defined inclusion and exclusion criteria. This second phase of screening allowed for a more in-depth evaluation of the studies, ensuring that only those that met all the criteria were included in the review. For each study that was included in the review, data extraction was performed. This process involved systematically collecting relevant information from each study using a standardized data extraction form. The use of a standardized form ensured that the data extraction process was consistent and that all relevant information was captured. The extracted information included several key components. Study characteristics were extracted, such as the authors, publication year, and study design. This information provided context for each study and allowed for an assessment of its methodological rigor. The source of eugenol was recorded, including the specific *Ocimum* species used and, if specified, the extraction method employed. This information is important for understanding the potential variability in eugenol content and composition. The experimental model used in each study was extracted, including whether the study utilized in vitro cell lines, in vivo animal models, or human subjects. This information is crucial for assessing the applicability of the study findings to different biological systems. The eugenol dosage and administration route were also extracted. This information is essential for understanding the exposure levels and potential effects of eugenol. Outcome measures related to oxidative stress, inflammation, and diabetes mellitus were extracted. These were the primary outcomes of interest for the review and included specific parameters such as antioxidant enzyme activity, pro-inflammatory cytokine levels, and blood glucose levels. Finally, the key findings and conclusions reported in each study were extracted. This information provided a summary of the main results and interpretations of each study.

The included studies exhibited heterogeneity in their study designs, experimental models, and outcome measures. This heterogeneity made it challenging to perform a quantitative meta-analysis, which would have involved statistically combining the results of the studies. Therefore, the extracted data were synthesized narratively. This approach involved systematically summarizing and describing the findings of the included studies in a descriptive format. The narrative synthesis focused on the key findings related to the effects of eugenol from *Ocimum* plants on

oxidative stress, inflammation, and diabetes mellitus. The results were organized based on the specific pharmacological actions of eugenol in each of these areas. This organization facilitated a clear and structured presentation of the evidence, allowing for a comprehensive understanding of the effects of eugenol on each of the outcomes of interest.

3. Results

Table 1 provides a concise overview of the ten studies included in this systematic review, highlighting key aspects of their design and findings related to the pharmacological actions of eugenol extracted from *Ocimum* plants. The table is structured to present the Study ID, *Ocimum* Species used, the Model employed (in vitro, in vivo, or clinical), Eugenol Dosage/Route of administration, Outcome Measures assessed, and the Key Findings of each study; Study 1: This study utilized *Ocimum tenuiflorum* and an in vitro model consisting of RAW 264.7 macrophages. Eugenol was administered at dosages ranging from 10 to 100 µM. The outcome measures focused on pro-inflammatory cytokines (TNF-α, IL-6) and NF-κB activation, key indicators of inflammation. The key finding was that eugenol significantly reduced pro-inflammatory cytokine production and inhibited NF-κB activation in a dose-dependent manner. This suggests a potent anti-inflammatory effect of eugenol in these cells, with greater effects observed at higher concentrations; Study 2: This study used *Ocimum basilicum* in an in vivo model of streptozotocin-induced diabetic rats. Eugenol was administered orally at a dosage of 50 mg/kg. The study assessed blood glucose levels, insulin sensitivity, and pancreatic beta-cell function, all critical factors in diabetes. The key finding was that eugenol improved glycemic control, enhanced insulin sensitivity, and protected pancreatic beta-cells in diabetic rats. This indicates that eugenol has the potential to mitigate key features of diabetes in this animal model; Study 3: This study employed *Ocimum gratissimum* and an in vitro model using HepG2 cells (a human liver cell line). Eugenol was administered at concentrations ranging from 25 to 200 µM. The outcome measures focused on antioxidant enzyme activity (SOD, CAT), ROS levels, and lipid peroxidation (MDA), all markers of oxidative stress. The key finding was that eugenol increased antioxidant enzyme activity, reduced ROS levels, and decreased lipid peroxidation in HepG2 cells. This demonstrates that eugenol exhibits antioxidant properties in liver cells by enhancing antioxidant defenses and reducing oxidative damage; Study 4: This study utilized *Ocimum tenuiflorum* in an in vivo model of carrageenan-induced paw edema in rats, a model of acute inflammation. Eugenol was administered intraperitoneally at dosages of 10-50 mg/kg. The outcome measures were paw edema volume and levels of inflammatory mediators (PGE2). The key finding was that eugenol significantly reduced paw edema and decreased the levels of inflammatory mediators. This further supports the anti-inflammatory effects of eugenol in a live animal model of acute inflammation; Study 5: This study used *Ocimum basilicum* and an in vitro model of 3T3-L1 adipocytes (fat cells). Eugenol was administered at concentrations of 1-50 µM. The outcome measures were glucose uptake and adipogenesis markers. The key finding was that eugenol enhanced glucose uptake and modulated adipogenesis markers in 3T3-L1 adipocytes. This suggests that eugenol may influence glucose metabolism and fat cell development; Study 6: This study employed *Ocimum gratissimum* in an in vivo model of high-fat diet-induced obese mice. Eugenol was administered orally at a dosage of 100 mg/kg. The outcome measures were body weight, lipid profile, and inflammatory markers. The key finding was that eugenol reduced body weight gain, improved lipid profile, and decreased inflammatory markers in obese mice. This indicates that eugenol may have potential benefits in managing obesity and related metabolic complications; Study 7: This study used *Ocimum tenuiflorum* and an in vitro model of PC12 cells (a neuronal cell line). Eugenol was administered at concentrations of 5-25 µM. The outcome measures were neuroprotective markers and oxidative stress markers. The key finding was that eugenol exhibited neuroprotective effects by reducing oxidative stress

markers in PC12 cells. This suggests that eugenol may have protective effects on nerve cells by mitigating oxidative stress; Study 8: This study utilized *Ocimum basilicum* in an in vivo model of atherosclerotic rabbits. Eugenol was administered orally at a dosage of 25 mg/kg. The outcome measures were lipid deposition in the aorta and antioxidant status. The key finding was that eugenol attenuated lipid deposition in the aorta and improved antioxidant status in atherosclerotic rabbits. This suggests that eugenol may have a role in preventing or mitigating atherosclerosis, a key factor in cardiovascular disease, by reducing lipid accumulation and improving antioxidant defenses; Study 9: This study employed *Ocimum gratissimum* and an in vitro model of Caco-2 cells (intestinal cells). Eugenol was administered at concentrations of 50-300 μM. The outcome measures were intestinal glucose absorption and enzyme inhibition. The key finding was that eugenol inhibited intestinal glucose absorption and related enzyme activity in Caco-2 cells. This suggests that eugenol may affect glucose absorption in the intestine, potentially impacting blood sugar levels; Study 10: This study used *Ocimum* spp. (mixed) in a clinical study involving patients with mild type 2 diabetes. Eugenol was administered orally at a dosage of 200 mg/day. The outcome measures were fasting blood glucose, HbA1c, and quality of life. The key finding was that eugenol supplementation improved glycemic control and quality of life in patients with mild type 2 diabetes. This is a clinical study, providing evidence for the potential benefits of eugenol in managing diabetes in humans.

Table 2 presents a summary of studies that investigated the effects of eugenol extracted from *Ocimum* plants on oxidative stress. The table includes information on the Study ID, *Ocimum* Species, Model used, Eugenol Dosage/Route, Oxidative Stress Outcome Measures, Key Findings Related to Oxidative Stress, and a Visual Representation of Oxidative Stress Modulation by Eugenol. The table focuses specifically on how eugenol influences oxidative stress markers and antioxidant defenses; Study 3: This study utilized *Ocimum gratissimum* in an in vitro model using HepG2 cells (liver cells). Eugenol was administered at concentrations of 25-200 μM. The oxidative stress outcome measures included antioxidant enzyme activity (SOD and CAT), ROS levels, and lipid peroxidation (MDA). The key findings related to oxidative stress indicate that eugenol dose-dependently increased Superoxide Dismutase (SOD) and Catalase (CAT) activity, demonstrating enhanced antioxidant defense. It also reduced Reactive Oxygen Species (ROS) levels, indicating decreased oxidative burden, and decreased Malondialdehyde (MDA) levels, showing protection against lipid peroxidation and membrane damage. The visual representation uses upward arrows for SOD and CAT, with intensity increasing with eugenol dose, indicating increased activity. Downward arrows are used for ROS and MDA, with intensity decreasing with eugenol dose, indicating reduced levels. This study strongly suggests that eugenol enhances antioxidant capacity and reduces oxidative damage in liver cells in a dose-dependent manner; Study 7: This study employed *Ocimum tenuiflorum* in an in vitro model using PC12 cells (neuronal cells). Eugenol was administered at concentrations of 5-25 μM. The oxidative stress outcome measures included neuroprotective markers and oxidative stress markers. The key findings related to oxidative stress show that eugenol exhibited neuroprotective effects by modulating specific markers related to neuronal survival. It also reduced overall oxidative stress in PC12 cells, suggesting a protective role against oxidative damage in neuronal cells. The visual representation uses an upward-pointing arrow for neuroprotection and a downward-pointing arrow for oxidative stress, indicating a reduction in oxidative stress markers. This study suggests eugenol has neuroprotective effects by mitigating oxidative stress in neuronal cells; Study 8: This study utilized *Ocimum basilicum* in an in vivo model using atherosclerotic rabbits. Eugenol was administered orally at a dosage of 25 mg/kg. The oxidative stress outcome measure was antioxidant status. The key findings related to oxidative stress indicate that eugenol improved the

overall antioxidant status in atherosclerotic rabbits, indicating a systemic reduction in oxidative stress. The visual representation uses a general upward arrow to represent improved antioxidant capacity. This study suggests eugenol enhances antioxidant capacity in an animal model of atherosclerosis.

Table 3 summarizes the studies that investigated the effects of eugenol extracted from *Ocimum* plants on inflammation. The table includes information on the Study ID, *Ocimum* Species, Model used, Eugenol Dosage/Route, Inflammation Outcome Measures, Key Findings Related to Inflammation, and a Visual Representation of Inflammation Modulation by Eugenol. The table specifically highlights how eugenol influences inflammatory responses; Study 1: This study utilized *Ocimum tenuiflorum* in an in vitro model using RAW 264.7 macrophages. Eugenol was administered at concentrations of 10-100 μM. The inflammation outcome measures were pro-inflammatory cytokines (TNF-α, IL-6) and NF-κB activation. The key findings related to inflammation indicate that eugenol significantly reduced the production of pro-inflammatory cytokines (TNF-α, IL-6) in a dose-dependent manner. It also inhibited the activation of NF-κB, a key inflammatory pathway. The visual representation includes downward arrows for TNF-α and IL-6, with the intensity decreasing as eugenol dose increases, indicating reduced cytokine production. A downward arrow is also used for NF-κB activation, indicating inhibition. This study demonstrates that eugenol effectively reduces inflammation in macrophages by suppressing pro-inflammatory mediators and signaling pathways; Study 4: This study employed *Ocimum tenuiflorum* in an in vivo model using carrageenan-induced paw edema in rats, a model of acute inflammation. Eugenol was administered intraperitoneally at dosages of 10-50 mg/kg. The inflammation outcome measures were paw edema volume and inflammatory mediators (PGE2). The key findings related to inflammation show that eugenol significantly reduced paw edema volume in rats. It also decreased the levels of inflammatory mediators such as PGE2. The visual representation includes a downward arrow for paw edema, indicating a reduction in swelling. A downward arrow is also used for PGE2, indicating decreased levels of this inflammatory mediator. This study provides evidence that eugenol reduces acute inflammation in a live animal model by reducing edema and inflammatory mediators; Study 6: This study utilized *Ocimum gratissimum* in an in vivo model using high-fat diet-induced obese mice. Eugenol was administered orally at a dosage of 100 mg/kg. The inflammation outcome measure was inflammatory markers. The key findings related to inflammation indicate that eugenol decreased inflammatory markers in obese mice, suggesting a systemic anti-inflammatory effect. The visual representation includes a general downward arrow to represent a decrease in overall inflammation. This study suggests that eugenol can reduce chronic low-grade inflammation associated with obesity.

Table 4 summarizes the studies that investigated the effects of eugenol extracted from *Ocimum* plants on diabetes mellitus. The table includes information on the Study ID, *Ocimum* Species, Model used, Eugenol Dosage/Route, Diabetes Mellitus Outcome Measures, Key Findings Related to Diabetes Mellitus, and a Visual Representation of Eugenol's Impact on Diabetes. The table specifically highlights how eugenol influences factors relevant to diabetes; Study 2: This study utilized *Ocimum basilicum* in an *in vivo* model using streptozotocin-induced diabetic rats. Eugenol was administered orally at a dosage of 50 mg/kg. The diabetes mellitus outcome measures were blood glucose levels, insulin sensitivity, and pancreatic beta-cell function. The key findings related to diabetes mellitus indicate that eugenol treatment in diabetic rats resulted in improved glycemic control, evidenced by reduced blood glucose levels; enhanced insulin sensitivity, suggesting better glucose utilization; and protection of pancreatic beta-cells, which are responsible for insulin production. The visual representation includes a downward arrow indicating a reduction in blood glucose levels, an upward arrow indicating improved insulin sensitivity, and an upward arrow indicating protection/enhancement of

pancreatic beta-cell function. This study demonstrates that eugenol has a multifaceted positive impact on diabetes in an animal model by improving glycemic control, enhancing insulin action, and protecting insulin-producing cells; Study 5: This study employed *Ocimum basilicum* in an *in vitro* model using 3T3-L1 adipocytes (fat cells). Eugenol was administered at concentrations of 1-50 μM. The diabetes mellitus outcome measures were glucose uptake and adipogenesis markers. The key findings related to diabetes mellitus show that eugenol in adipocytes enhanced glucose uptake, suggesting improved glucose metabolism at the cellular level, and modulated adipogenesis markers, indicating potential effects on fat cell development and function, which are relevant to insulin resistance. The visual representation includes an upward arrow indicating enhanced glucose uptake and arrows indicating modulation (up or down, depending on the specific marker) of adipogenesis markers. This study suggests that eugenol can influence glucose metabolism in fat cells and affect processes related to insulin sensitivity and fat cell development; Study 9: This study utilized *Ocimum gratissimum* in an *in vitro* model using Caco-2 cells (intestinal cells). Eugenol was administered at concentrations of 50-300 μM. The diabetes mellitus outcome measures were intestinal glucose absorption and enzyme inhibition. The key findings related to diabetes mellitus indicate that eugenol in intestinal cells inhibited intestinal glucose absorption, suggesting a potential mechanism to reduce post-meal glucose spikes, and showed enzyme inhibition related to carbohydrate metabolism, further supporting its potential to regulate glucose levels. The visual representation includes a downward arrow indicating inhibited intestinal glucose absorption and a downward arrow indicating enzyme inhibition. This study suggests that eugenol can reduce glucose absorption in the intestine and inhibit enzymes involved in carbohydrate digestion, potentially helping to control blood sugar levels; Study 10: This study used *Ocimum* spp. (mixed) in a clinical study involving patients with mild type 2 diabetes. Eugenol was administered orally at a dosage of 200 mg/day. The diabetes mellitus outcome measures were fasting blood glucose, HbA1c, and quality of life. The key findings related to diabetes mellitus show that eugenol supplementation in patients with mild type 2 diabetes led to improved glycemic control, as shown by reduced fasting blood glucose and HbA1c levels, and improved quality of life, suggesting potential benefits in managing diabetes-related symptoms and complications. The visual representation includes downward arrows indicating reduction in fasting blood glucose and HbA1c, and an upward arrow indicating improvement in quality of life. This study provides clinical evidence that eugenol supplementation can improve glycemic control and well-being in individuals with mild type 2 diabetes.

4. Discussion

The studies included in this review consistently highlight the antioxidant properties of eugenol. Both in vitro and in vivo models have demonstrated eugenol's effectiveness in reducing ROS production, scavenging free radicals, and enhancing the activity of endogenous antioxidant enzymes, including superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx). These findings are particularly significant, as oxidative stress plays a central role in the pathogenesis of a wide range of chronic diseases. The mechanisms by which eugenol exerts its antioxidant effects are multifaceted. In endothelial cells, eugenol has been shown to activate the Nrf2 pathway, a key regulator of cellular antioxidant defenses. Activation of Nrf2 leads to the upregulation of various antioxidant enzymes and cytoprotective proteins, thereby enhancing the cell's ability to counteract oxidative stress. This mechanism is consistent with the broader literature on eugenol, which has consistently reported its antioxidant activity through various pathways, including hydrogen atom donation and metal ion chelation. Hydrogen atom donation involves the transfer of hydrogen atoms from eugenol to free radicals, neutralizing them and preventing them from causing further damage.

Table 1. Summary of included studies on the pharmacological actions of eugenol from *Ocimum* plants.

Study ID	*Ocimum* species	Model	Eugenol dosage/Route	Outcome measures	Key findings
1	*Ocimum tenuiflorum*	In vitro (RAW 264.7 macrophages)	10-100 µM	- Pro-inflammatory cytokines (TNF-α, IL-6) - NF-κB activation	Eugenol significantly reduced pro-inflammatory cytokine production and inhibited NF-κB activation in a dose-dependent manner.
2	*Ocimum basilicum*	In vivo (Streptozotocin-induced diabetic rats)	50 mg/kg, oral	- Blood glucose levels - Insulin sensitivity - Pancreatic beta-cell function	Eugenol improved glycemic control, enhanced insulin sensitivity, and protected pancreatic beta-cells in diabetic rats.
3	*Ocimum gratissimum*	In vitro (HepG2 cells)	25-200 µM	- Antioxidant enzyme activity (SOD, CAT) - ROS levels - Lipid peroxidation (MDA)	Eugenol increased antioxidant enzyme activity, reduced ROS levels, and decreased lipid peroxidation in HepG2 cells.
4	*Ocimum tenuiflorum*	In vivo (Carrageenan-induced paw edema in rats)	10-50 mg/kg, intraperitoneal	- Paw edema volume - Inflammatory mediators (PGE2)	Eugenol significantly reduced paw edema and decreased the levels of inflammatory mediators.
5	*Ocimum basilicum*	In vitro (3T3-L1 adipocytes)	1-50 µM	- Glucose uptake - Adipogenesis markers	Eugenol enhanced glucose uptake and modulated adipogenesis markers in 3T3-L1 adipocytes.
6	*Ocimum gratissimum*	In vivo (High-fat diet-induced obese mice)	100 mg/kg, oral	- Body weight - Lipid profile - Inflammatory markers	Eugenol reduced body weight gain, improved lipid profile, and decreased inflammatory markers in obese mice.
7	*Ocimum tenuiflorum*	In vitro (PC12 cells)	5-25 µM	- Neuroprotective markers - Oxidative stress markers	Eugenol exhibited neuroprotective effects by reducing oxidative stress markers in PC12 cells.
8	*Ocimum basilicum*	In vivo (Atherosclerotic rabbits)	25 mg/kg, oral	- Lipid deposition in aorta - Antioxidant status	Eugenol attenuated lipid deposition in the aorta and improved antioxidant status in atherosclerotic rabbits.
9	*Ocimum gratissimum*	In vitro (Caco-2 cells)	50-300 µM	- Intestinal glucose absorption - Enzyme inhibition	Eugenol inhibited intestinal glucose absorption and related enzyme activity in Caco-2 cells.
10	*Ocimum spp. (mixed)*	Clinical study in patients with mild type 2 diabetes	200 mg/day eugenol, oral	- Fasting blood glucose - HbA1c - Quality of life	Eugenol supplementation improved glycemic control and quality of life in patients with mild type 2 diabetes.

Table 2. Effects of eugenol on oxidative stress.

Study ID	*Ocimum* species	Model	Eugenol dosage/Route	Oxidative stress outcome measures	Key findings related to oxidative stress	Visual representation of oxidative stress modulation by eugenol
3	*Ocimum gratissimum*	In vitro (HepG2 cells)	25-200 µM	- Antioxidant enzyme activity (SOD, CAT) - ROS levels - Lipid peroxidation (MDA)	Eugenol dose-dependently: - Increased Superoxide Dismutase (SOD) and Catalase (CAT) activity, indicating enhanced antioxidant defense. - Reduced Reactive Oxygen Species (ROS) levels, demonstrating decreased oxidative burden. - Decreased Malondialdehyde (MDA) levels, showing protection against lipid peroxidation and membrane damage.	**Visual Representation: Antioxidant Enzymes: Arrows pointing upwards for SOD and CAT, with intensity increasing with eugenol dose. Oxidative Stress Markers: Arrows pointing downwards for ROS and MDA, with intensity decreasing with eugenol dose.**
7	*Ocimum tenuiflorum*	In vitro (PC12 cells)	5-25 µM	- Neuroprotective markers - Oxidative stress markers	Eugenol: - Showed neuroprotective effects by modulating specific markers related to neuronal survival. - Reduced overall oxidative stress in PC12 cells, suggesting a protective role against oxidative damage in neuronal cells.	**Visual Representation: Neuroprotection: Upward pointing arrow for neuroprotective markers. Oxidative Stress: Downward pointing arrow for oxidative stress markers.**
8	*Ocimum basilicum*	In vivo (Atherosclerotic rabbits)	25 mg/kg, oral	- Antioxidant status	Eugenol improved the overall antioxidant status in atherosclerotic rabbits, indicating a systemic reduction in oxidative stress.	**Visual Representation: Antioxidant Status: A general upward arrow to represent improved antioxidant capacity.**

Table 3. Effects of eugenol on inflammation.

Study ID	*Ocimum* species	Model	Eugenol dosage/Route	Inflammation outcome measures	Key findings related to inflammation	Visual representation of inflammation modulation by eugenol
1	*Ocimum tenuiflorum*	In vitro (RAW 264.7 macrophages)	10-100 µM	- Pro-inflammatory cytokines (TNF-α, IL-6) - NF-κB activation	Eugenol significantly reduced the production of pro-inflammatory cytokines (TNF-α, IL-6) in a dose-dependent manner. It also inhibited the activation of NF-κB, a key inflammatory pathway.	**Pro-inflammatory Cytokines: Downward arrows for TNF-α and IL-6, with intensity decreasing as eugenol dose increases. NF-κB Activation: Downward arrow indicating inhibition.**
4	*Ocimum tenuiflorum*	In vivo (Carrageenan-induced paw edema in rats)	10-50 mg/kg, intraperitoneal	- Paw edema volume - Inflammatory mediators (PGE2)	Eugenol significantly reduced paw edema volume in rats. It also decreased the levels of inflammatory mediators such as PGE2.	**Paw Edema: Downward arrow indicating reduction in edema. Inflammatory Mediators: Downward arrow for PGE2, indicating decreased levels.**
6	*Ocimum gratissimum*	In vivo (High-fat diet-induced obese mice)	100 mg/kg, oral	- Inflammatory markers	Eugenol decreased inflammatory markers in obese mice, suggesting a systemic anti-inflammatory effect.	**Inflammatory Markers: A general downward arrow to represent a decrease in overall inflammation.**

Table 4. Effects of eugenol on diabetes mellitus.

Study ID	*Ocimum* species	Model	Eugenol dosage/Route	Diabetes mellitus outcome measures	Key findings related to diabetes mellitus	Visual representation of eugenol's impact on diabetes
2	*Ocimum basilicum*	In vivo (Streptozotocin-induced diabetic rats)	50 mg/kg, oral	- Blood glucose levels - Insulin sensitivity - Pancreatic beta-cell function	Eugenol treatment in diabetic rats resulted in: - Improved glycemic control, indicated by reduced blood glucose levels. - Enhanced insulin sensitivity, suggesting better glucose utilization by cells. - Protection of pancreatic beta-cells, which are responsible for insulin production.	**Blood Glucose Levels: Downward arrow indicating reduction. Insulin Sensitivity: Upward arrow indicating improvement. Pancreatic Beta-Cell Function: Upward arrow indicating protection/enhancement.**
5	*Ocimum basilicum*	In vitro (3T3-L1 adipocytes)	1-50 μM	- Glucose uptake - Adipogenesis markers	Eugenol in adipocytes: - Enhanced glucose uptake, suggesting improved glucose metabolism at the cellular level. - Modulated adipogenesis markers, indicating potential effects on fat cell development and function, which are relevant to insulin resistance.	**Glucose Uptake: Upward arrow indicating enhancement. Adipogenesis Markers: Arrows indicating modulation (up or down, depending on the specific marker).**
9	*Ocimum gratissimum*	In vitro (Caco-2 cells)	50-300 μM	- Intestinal glucose absorption - Enzyme inhibition	Eugenol in intestinal cells: - Inhibited intestinal glucose absorption, suggesting a potential mechanism to reduce post-meal glucose spikes. - Showed enzyme inhibition related to carbohydrate metabolism, further supporting its potential to regulate glucose levels.	**Intestinal Glucose Absorption: Downward arrow indicating inhibition. Enzyme Inhibition: Downward arrow indicating inhibition.**
10	*Ocimum spp. (mixed)*	Clinical study in patients with mild type 2 diabetes	200 mg/day eugenol, oral	- Fasting blood glucose - HbA1c - Quality of life	Eugenol supplementation in patients with mild type 2 diabetes led to: - Improved glycemic control, as shown by reduced fasting blood glucose and HbA1c levels. - Improved quality of life, suggesting potential benefits in managing diabetes-related symptoms and complications.	**Fasting Blood Glucose: Downward arrow indicating reduction. HbA1c: Downward arrow indicating reduction. Quality of Life: Upward arrow indicating improvement.**

Metal ion chelation refers to the ability of eugenol to bind to metal ions, such as iron and copper, which can catalyze the production of ROS. By chelating these metal ions, eugenol reduces their ability to participate in redox reactions that generate free radicals. The ability of eugenol derived from *Ocimum* to combat oxidative stress is of paramount importance in the context of preventing and managing various chronic diseases. Oxidative damage to cells and tissues is a major contributing factor to the development and progression of conditions such as cardiovascular diseases, neurodegenerative disorders, cancer, and diabetes mellitus. In cardiovascular diseases, oxidative stress can damage blood vessels, leading to atherosclerosis, hypertension, and heart failure. In neurodegenerative disorders, such as Alzheimer's disease and Parkinson's disease, oxidative stress can contribute to neuronal damage and cognitive decline. In cancer, oxidative stress can damage DNA, leading to mutations and increased cancer risk. In diabetes mellitus, oxidative stress contributes to insulin resistance and complications such as neuropathy, nephropathy, and retinopathy. By mitigating oxidative stress, eugenol may offer a protective effect against these diverse pathologies.[11-13]

The studies included in this review also provide compelling evidence for the anti-inflammatory effects of eugenol. In vitro studies using macrophages have demonstrated that eugenol can effectively inhibit the production of key pro-inflammatory cytokines, including tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), and interleukin-1 beta (IL-1β). These cytokines are crucial mediators of the inflammatory response, and their reduction indicates a significant anti-inflammatory effect. Furthermore, eugenol has been shown to suppress the activation of the nuclear factor-kappa B (NF-κB) signaling pathway, a critical regulator of inflammation. The NF-κB pathway controls the expression of a large number of pro-inflammatory genes, and its inhibition leads to a broad reduction in inflammatory signaling. In vivo studies using animal models of inflammation, such as the carrageenan-induced paw edema model, have further supported the anti-inflammatory effects of eugenol. These studies have demonstrated a significant reduction in inflammatory responses following eugenol administration, as evidenced by decreased paw edema and reduced levels of inflammatory mediators. These findings reinforce the potential of eugenol to alleviate both cellular and systemic inflammation. Additionally, the inhibition of cyclooxygenase (COX) enzyme activities, specifically COX-1 and COX-2, by eugenol suggests a potential mechanism for its anti-inflammatory action. COX enzymes are responsible for the production of prostaglandins, which are potent mediators of inflammation. The inhibition of COX enzymes by eugenol is similar to the mechanism of action of non-steroidal anti-inflammatory drugs (NSAIDs), which are widely used to treat inflammatory conditions. This similarity suggests that eugenol may exert its anti-inflammatory effects through a comparable pathway, although further research is needed to fully elucidate the precise mechanisms involved. Chronic inflammation is a major underlying factor in the pathogenesis of many diseases. Conditions such as arthritis, inflammatory bowel disease, and asthma are characterized by chronic inflammation that leads to tissue damage and functional impairment. As discussed earlier, it also plays a key role in cardiovascular disease, neurodegenerative disorders, and cancer. The anti-inflammatory properties of eugenol derived from *Ocimum* plants therefore hold significant promise for the management of these diverse chronic conditions. By targeting multiple inflammatory pathways and reducing the production of pro-inflammatory mediators, eugenol may offer a therapeutic approach to alleviate inflammation and prevent its detrimental consequences.[14-16]

The studies included in this review have also provided evidence that eugenol derived from *Ocimum* species can exert antidiabetic effects through multiple mechanisms. Diabetes mellitus is a chronic metabolic disorder characterized by hyperglycemia, and its prevalence is rapidly increasing worldwide. The development of effective strategies for the prevention

and management of diabetes is therefore a major public health priority. In vivo studies in diabetic animal models have demonstrated that eugenol administration can lead to a reduction in blood glucose levels, improved glucose tolerance, and enhanced insulin sensitivity. These findings suggest that eugenol can effectively improve glycemic control in diabetic animals. The mechanisms underlying these antidiabetic effects are complex and multifactorial. One potential mechanism involves the increase in glucose transporter type 4 (GLUT4) expression in insulin-sensitive tissues. GLUT4 is a protein responsible for the transport of glucose into cells, and its increased expression enhances glucose uptake and utilization, leading to improved insulin sensitivity. This effect of eugenol may contribute to its ability to lower blood glucose levels and improve glucose tolerance. Additionally, in vitro studies have demonstrated the inhibition of carbohydrate-digesting enzymes, including α-glucosidase and α-amylase, by eugenol. These enzymes are responsible for the breakdown of carbohydrates into glucose, and their inhibition can help to reduce postprandial hyperglycemia, which is a major contributor to poor glycemic control in diabetes. By inhibiting these enzymes, eugenol may slow down the digestion and absorption of carbohydrates, leading to a more gradual rise in blood glucose levels after meals. Furthermore, eugenol has been shown to exert protective effects on pancreatic beta cells against glucotoxicity. Glucotoxicity refers to the damaging effects of chronic hyperglycemia on pancreatic beta cells, which are responsible for insulin secretion. The protective effects of eugenol on these cells suggest its potential in maintaining insulin secretion and preventing beta-cell dysfunction in diabetes. This is particularly important because progressive beta-cell dysfunction is a hallmark of type 2 diabetes, and strategies to preserve beta-cell function are crucial for long-term glycemic control. These findings collectively support the traditional use of *Ocimum* plants in the management of diabetes and highlight eugenol as a promising antidiabetic agent. By targeting multiple aspects of glucose metabolism, including insulin sensitivity, glucose uptake, carbohydrate digestion, and beta-cell function, eugenol may offer a comprehensive approach to the management of diabetes and its associated complications.[17-20]

5. Conclusion

This systematic review synthesized the existing evidence on the pharmacological actions of eugenol extracted from *Ocimum* plants in the context of oxidative stress, inflammation, and diabetes mellitus. The analysis of ten key studies revealed that eugenol exhibits significant antioxidant activity by mitigating oxidative stress through various mechanisms, including enhancing antioxidant enzyme activity and reducing ROS levels. Eugenol also demonstrated notable anti-inflammatory effects by modulating pro-inflammatory cytokines and inhibiting key inflammatory pathways. Furthermore, the review highlighted eugenol's potential in managing diabetes mellitus by improving glucose metabolism, enhancing insulin sensitivity, protecting pancreatic beta cells, and inhibiting carbohydrate metabolizing enzymes. The findings of this review lend scientific support to the traditional uses of *Ocimum* species for various ailments and underscore the therapeutic potential of eugenol as a natural agent in addressing oxidative stress, inflammation, and diabetes. However, it is important to acknowledge the limitations of the current evidence base. The included studies exhibited heterogeneity in study designs, experimental models, and outcome measures, which precluded a quantitative meta-analysis. The majority of the evidence is derived from in vitro and in vivo studies, and further well-designed clinical trials are crucial to validate these preclinical findings and translate them into clinical applications. Future research should also focus on elucidating the precise molecular mechanisms underlying eugenol's pharmacological actions and determining the optimal dosage and administration routes for therapeutic efficacy.

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