



Cloves, Eugenol, and Metabolic Regulation: Properties, Supplementation, and Uses in Chronic Diseases.

Dr. A. Colonnese¹, R. Panzironi²

¹ Nutrition Biologist, Latina, Italy

² Independent Researcher, Latina, Italy

1. ABSTRACT

Cloves are an ancient, intense spice surprisingly rich in active compounds. In food contexts, they are appreciated for their warm, pungent aroma, but in recent years they have also attracted interest in nutritional and biological fields due to the presence of eugenol, a phenolic molecule—that is, a plant substance with chemical properties typical of phenols—which represents one of the main constituents of their functional profile. When talking about cloves, however, it is important to distinguish between culinary use, extract, and essential oil, because concentration, exposure, and biological potential are not equivalent. This distinction is central to correctly interpreting studies on glycemia, inflammation, oxidative stress, hepatic metabolism, and cellular regulation, without overestimating the effects of a spice that remains primarily a food and only in some cases a possible basis for more concentrated formulations. In the context of metabolic regulation, cloves are studied mainly for their interaction with mechanisms such as insulin resistance, i.e., the reduced ability of tissues to respond to insulin, AMPK, a protein that functions as a cellular energy sensor, mTOR, a signaling pathway that regulates growth and protein synthesis, autophagy, the process of recycling cellular components, and glucose uptake in peripheral tissues. However, the available literature is heterogeneous: many data are preclinical, while human evidence is still limited and should be interpreted with caution. This article guides the reader clearly through properties, integration, possible applications in chronic diseases, and safety aspects, to help understand when cloves make sense in the diet, when they are discussed as nutritional support, and when it is better to pause for a prudent evaluation. Specifically, the article will address:

- Origin, composition, and biological value of cloves
- Eugenol, extracts, and differences between the spice and essential oil
- Effects on glycemia, insulin resistance, and metabolism
- Role of AMPK, mTOR, autophagy, and peripheral tissues
- Safety, usage limits, and comparison with other spices

VIDEO ARTICLE



ARTICLE INFORMATION

Received: October 21, 2026

Revised: October 21, 2026

Accepted: October 21, 2026

Published: October 2026

DOI 10.5281/zenodo.placeholder

MISSION

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2. CLOVES AND THEIR INTRINSIC PROPERTIES

Cloves, the dried flower buds of *Syzygium aromaticum*, are a peculiar spice because they combine an intense aroma with the presence of phenolic compounds, which are plant molecules with biological activity. Their relevance does not depend on a single substance, but on the overall profile of the phytocomplex, which is the set of characteristic molecules of the plant, in which eugenol is the dominant molecule and decisively contributes to the properties of cloves. At this stage, it is worth focusing on the intrinsic qualities of the spice: its antioxidant capacity, i.e., its ability to counteract oxidative processes, the presence of clove polyphenols, and its potential to modulate processes linked to oxidative stress and chronic inflammation [1]. Oxidative stress indicates an imbalance between the production of oxidizing species and the body's defenses, while chronic inflammation is a persistent, low-grade inflammatory response. These aspects explain why, in scientific debate, cloves, eugenol, and metabolism are often cited together, even though the dietary and experimental levels remain distinct. From a functional point of view, available data suggest that polyphenol-rich extracts can also influence basic metabolic parameters. In a human study, a water-soluble extract rich in clove polyphenols, 250 mg/day for 30 days in 13 participants (7 participants with normoglycemia and 6 participants with prediabetes), reduced pre- and post-prandial glycemia [2]. The term normoglycemic indicates a person with normal blood sugar levels, while prediabetic refers to an intermediate condition of metabolic risk. In experimental models, eugenol has also shown antioxidant and anti-inflammatory activities, i.e., the ability to reduce oxidative processes and the inflammatory response, consistent with its role as a key molecule of the spice [1]. This does not mean attributing an automatic pharmacological effect to cloves, but recognizing that their intrinsic composition justifies their biological interest beyond their aromatic function. This is precisely where the reasoning about their possible interest in metabolic prevention begins [3]. To guide the reading, it is useful to keep in mind some essential points that will be developed in the following passages:

- The chemical profile explains the aromatic and biological intensity.
- Eugenol represents the most studied component of the spice.
- Polyphenols, i.e., plant compounds with multiple phenolic groups, contribute to defense against oxidative stress.
- Intrinsic properties do not coincide with therapeutic effects.

After defining the intrinsic profile of the spice, the following steps distinguish its botanical origin, the centrality of eugenol, differences between forms of use, and its practical role in the diet.

2.1 What are cloves and where do they come from?

Cloves are the dried flower buds of *Syzygium aromaticum*, an evergreen plant native to the Indonesian archipelago. Their relevance is not only gastronomic: the phytocomplex, which is the set of characteristic substances of the plant, contains phenolic compounds and essential oils, i.e., volatile aromatic mixtures, which determine their aromatic intensity and many of the most studied biological activities. This distinguishes them from "lighter" spices, where the functional contribution is less pronounced. This factor clarifies that the common name "cloves" indicates a well-defined plant raw material, not a generic aroma. It is also useful for connecting botany, supply chain, and final product quality. The reader can thus understand why the same ingredient, depending on its origin and drying method, shows different flavor and composition profiles. This distinction is also important for interpreting scientific data, because a study on a specific extraction does not automatically describe what happens with domestic use in everyday cooking. In the context of preventive nutrition, cloves are therefore positioned halfway between an aromatic spice and a source of bioactive substances, i.e., compounds capable of interacting with biological functions, with a potential that deserves analysis but not oversimplification. The next part clarifies why a single molecule, eugenol, weighs so heavily in their functional profile.



2.2 Why eugenol dominates the biological profile of cloves

Eugenol is the most representative molecule in cloves and accounts for much of their olfactory and functional intensity. It is a phenolic compound found primarily in the essential oil of the buds, i.e., in the concentrated volatile fraction of the plant, in a very high proportion compared to other spices. This chemical dominance is important because it simplifies biological interpretation: when discussing the activity of cloves, in many cases, one is describing the effect of eugenol and, in part, of related compounds. This concept is useful for distinguishing between the whole spice, extract, and essential oil, avoiding attributing the same potency of a concentrate to common food. The presence of eugenol also helps explain why cloves are of interest in relation to oxidative stress, inflammation, and cellular signals related to metabolism. Here, cellular signals refer to the mechanisms by which cells communicate and regulate their functions. However, it is crucial to remember that the quantity contained in a culinary preparation is not comparable to that of a standardized extract or an essential oil. Standardization refers to the production of an extract with controlled amounts of active ingredients. This difference in exposure changes the biological significance of scientific data. For this reason, eugenol should not be seen as a "magical active ingredient," but as an important component of a phytocomplex that can express different effects depending on the dose, matrix, and context. In this article, this point allows us to set the discussion on a key substance, preparing for a deeper dive into its chemistry, bioavailability (i.e., the amount actually absorbed and usable by the body), safety, and nutraceutical uses. The next step is to precisely separate the dietary level from that of concentrates.

2.3 Difference between whole spice, extract, and essential oil

Cloves, extract, and essential oil are not interchangeable, even if they share the same botanical origin. The whole spice is used in cooking and provides relatively small amounts of active compounds; the extract concentrates a part of the phytocomplex; the essential oil represents the most concentrated format and therefore also the most

delicate to interpret in terms of exposure. Distinguishing these levels is essential to avoid misleading generalizations, especially when reading studies on experimental models or standardized formulations. A whole spice can be perfectly consistent with a balanced daily diet, while a concentrate requires different interpretation criteria, because the dose actually received by the body changes. This is particularly true for eugenol, which in essential oil reaches much higher levels compared to traditional culinary use. The difference is not only quantitative but also practical: objectives, safety, methods of use, and realistic expectations change. Separating these categories helps the reader understand why the effects observed in laboratory work should not be automatically transferred to everyday cooking. From here it becomes easier to place the spice in the daily diet without attributing roles that do not belong to it.

2.4 When cloves are useful in a daily diet

The daily use of cloves makes sense primarily as an aromatic modulation and not as a therapeutic intervention. In cooking, they can contribute to a more complex sensory profile for sweet or savory dishes, indirectly promoting more satisfying and, in some contexts, more orderly food choices. Their use becomes interesting when one wants to enrich a diet aimed at controlling glycemic peaks or reducing less favorable condiments, provided it remains within realistic quantities. A glycemic peak is the rapid increase in glycemia after a meal. This means that the spice can be part of a broader dietary pattern, but it does not replace a structured nutritional strategy. In practice, cloves make more sense when used with reasonable regularity, as support for the overall quality of the diet, rather than as an isolated solution. Their daily utility also depends on the context: in a diet rich in sugars and low in fiber, the margin of benefit remains limited, while in a more balanced model, they can contribute to meal variety and satisfaction. This perspective is useful because it avoids reducing the spice to a simple "remedy," instead restoring its concrete role as a functional but modest ingredient. The next section addresses the shift in perspective that occurs when moving from cooking to concentrated formulation.



3. CLOVES AND HUMAN SUPPLEMENTATION

When discussing cloves, eugenol, and metabolism in humans, the most important factor is the discrepancy between the biological rationale and the amount of available clinical evidence. Human studies are few, but they suggest that a standardized polyphenolic extract—that is, a preparation rich in polyphenols made homogeneous in composition—can influence glycemia, or the concentration of glucose in the blood, especially in the post-meal period, which is when the glycemic response is most sensitive to dietary composition [2]. This does not mean that cloves should be interpreted as a treatment, but rather that their potential should be viewed as nutritional support in selected contexts. It is also useful to distinguish the spice used in cooking from a concentrated formulation, because the quantities, bioavailability (i.e., the amount of substance that actually reaches circulation or tissues), and repeatability of the effect are not comparable. In other words, the clinical value observed in studies depends on the preparation, the dose, and the metabolic profile of the participants, not on a generic and indiscriminate use of the spice. Furthermore, the biological rationale of eugenol intertwines with known pathways of metabolic regulation, including oxidative stress (an imbalance between the production of reactive species and antioxidant capacity), low-grade inflammation, and insulin sensitivity (the ability of tissues to respond to insulin), all of which are central to chronic metabolic alterations. Precisely for this reason, readers should consider clove extracts as possible modulators, not as alternatives to established treatments or lifestyle corrections. An open-label pilot trial, a preliminary study without blinding of participants and researchers, evaluated 250 mg/day for 30 days in 13 volunteers, stratified into 7 normoglycemic and 6 prediabetic individuals, reporting a reduction in pre- and post-prandial glycemia [2]. This is an interesting, but still initial, signal. For this reason, in scientific interpretation, not only the final result but also the robustness of the study design and consistency with preclinical evidence (obtained previously in experimental models before human studies) are very important, indicating a possible interaction with clove polyphenols, oxidative stress, and broader metabolic signals [3,4]. The most solid idea is that the extract can

attenuate some metabolic peaks, especially in subjects with suboptimal glycemic control, but not that it produces glycemic control equivalent to pharmacological treatment. In the overall picture, clove supplementation therefore remains a promising nutritional hypothesis, to be carefully evaluated without overestimating what human data can truly support today. For this reason, too, the quality of the formulation and consistency with the subject's clinical profile are decisive elements in practical evaluation. To guide the reading of human studies, it is useful to keep some key points in mind:

- Standardized extracts show more measurable results than culinary spice.
- The most observed response concerns pre- and post-prandial glycemia.
- The human sample size so far is small and requires cautious interpretation.
- The participant's metabolic context greatly changes the meaning of the data.
- Nutritional interpretation must be distinguished from the promise of a therapeutic effect.

Further on, we will examine the initial clinical data on glycemia, the broader metabolic rationale, and the role of the microbiota and autophagy in interpreting the results. This ensures the reading remains anchored to evidence and does not confuse biological potential with an already established effect.

3.1 Cloves and glycemia: what human studies suggest

Human studies are limited but interesting because they indicate that polyphenol extracts from cloves can influence postprandial glycemia and, in some subjects, even basal values. The point is not to define a curative effect, but to observe if there is a tendency towards normalization in fragile metabolic contexts. This is relevant because it avoids overestimating the result of a common spice and, at the same time, allows for a correct interpretation of the value of a standardized formulation. An open-label pilot trial used 250 mg once daily for 30 days in 13 volunteers, 7 of whom had preprandial glycemia ≤ 100 mg/dL and 6 with values between 101 and 125 mg/dL; the authors reported an improvement in pre- and post-prandial values [2]. The data is promising, but the sample is small and the context is still exploratory. In pathophysiological



terms, the greatest relevance concerns the postprandial peak, because this is where the first alterations in metabolic flexibility and insulin action are often observed. If an extract can reduce this load, it could theoretically also attenuate secondary oxidative stress and the associated inflammation. For the reader, this means that the correct question is not just "does it lower sugar?", but "in which subjects and with what preparation?". We will subsequently delve into the meaning of postprandial glycemia, dosages, and the real weight of this evidence in nutritional practice.

3.2 Clove polyphenolic extract and metabolic syndrome

Polyphenolic extracts from cloves are interesting because they concentrate molecules that can act on multiple components of metabolic syndrome: glycemia, lipid profile, oxidative stress, and inflammation. In a randomized, double-blind, actively controlled study, the intake of clove bud polyphenols showed a favorable effect on intracellular redox homeostasis, meaning the oxidation-reduction balance within the cell, and on glucose metabolism, consistent with systemic modulation rather than a single target [3]. This is useful for readers seeking information on "cloves and metabolic syndrome" because it helps them understand that the potential does not concern just one marker but a set of related alterations. Metabolic syndrome, in fact, is not a single problem but a set of factors that feed into each other, and for this reason, a phytochemical can only be interesting when viewed as a whole. Mechanistically, the presence of polyphenols and eugenol can theoretically promote better antioxidant defense, reduce lipid peroxidation—i.e., damage to membrane lipids due to free radicals—and limit the inflammatory cascade that accompanies insulin resistance, defined as a reduced ability of tissues to respond to insulin. The standardized extract allows for greater reproducibility compared to the spice, but it is still important not to confuse biological rationale with clinical certainty. The next step broadens the picture to the gut-inflammation axis, which is increasingly relevant in the metabolic interpretation of phytochemicals.

3.3 Cloves, gut microbiota, and inflammation

Another interpretative level concerns the gut microbiota, which is the set of microorganisms that inhabit the intestine and participate in the regulation of numerous physiological processes, because energy metabolism does not only depend on what happens in the blood, but also on the interaction between the intestinal barrier, inflammation, and systemic signaling. In experimental models, eugenol, the main component of clove oil, has attenuated adiposity and modulated the intestinal flora in animals fed a high-fat diet, suggesting a possible contribution of the gastrointestinal tract to the metabolic response [5]. This is not equivalent to direct proof in humans, but it helps explain why the effects of cloves should not be read solely as "an effect on glycemia." The microbiota can indeed influence absorption, inflammation, and hormonal signals, creating a favorable or unfavorable ground for metabolism regulation. If the intestinal barrier is altered, the passage of pro-inflammatory signals and the probability of a less efficient metabolic response increase. Here too, the point is not to attribute a definitive power to the spice, but to recognize that its bioactive compounds can fit into a broader network of interactions. In divulgative terms, this makes cloves an interesting subject for functional nutrition, provided that the distinction between preclinical evidence and concrete clinical impact is maintained.

3.4 Eugenol and autophagy regulation in intestinal cells

Autophagy, the cellular recycling mechanism that removes damaged components and maintains the cell's internal balance, is a central process for tissue survival. In intestinal cells subjected to inflammation, supplementation with spermidine-eugenol preserved cell viability by stimulating autophagy, an interesting result because it links tissue protection to an adaptive response potentially useful also in a metabolic context [6]. The point is not to consider autophagy always "good" in absolute terms, but to understand that its meaning depends on the biological context. If the tissue is under stress, greater efficiency of cleaning mechanisms can support homeostasis; if, however, the signal is excessive or poorly regulated, the balance



changes. This type of data helps to interpret cloves and eugenol as modulators of cellular processes, rather than as simple aromatic ingredients. Furthermore, the intertwining of autophagy, inflammation, and metabolism suggests a possible utility in conditions where insulin resistance is accompanied by oxidative stress and intestinal dysfunction. For the reader, the lesson is that the metabolic effect does not depend only on measured glycemia, but also on the quality of the tissue that receives the nutritional stimulus. This is a useful step to understand why supplementation should always be discussed within the overall framework of physiology and not in isolation.

4. CLOVES AND THEIR USES FOR TREATED PATHOLOGIES

In type 2 diabetes, the rationale for cloves primarily concerns the containment of hyperglycemia, oxidative stress, and low-grade inflammation. Experimental data indicate that eugenol can act at multiple levels of metabolic regulation, but its clinical significance should be interpreted with caution. In a model of diabetic rats induced by a high-fat diet and streptozotocin, a substance used to selectively damage pancreatic cells, eugenol improved insulin resistance, oxidative stress, and inflammation, supporting the idea of systemic modulation [4]. In parallel, a meta-analysis, i.e., a statistical analysis combining multiple studies, on hyperglycemic murine models confirmed that the effect of eugenol is consistent, but not uniform across all models [7]. This focus is valuable because it addresses the reader's most frequent question without promising certain pharmacological effects. Type 2 diabetes, in fact, does not depend on a single mechanism but on an intertwining of insulin resistance, hepatic alterations, inflammation, and peripheral tissue dysfunction. In this context, cloves can be seen as a possible biological support, not as a substitute for therapies. Eugenol has also been studied in the liver, where the modulation of SREBP1, AMPK, and mTOR led to a 45% reduction in hepatic triglycerides and a 72% reduction in the steatosis score in mice treated for 10 weeks, as well as a decrease in α -SMA, Col-1, and PAI-1 by 36%, 63%, and 40% respectively [8]. SREBP1 is a transcription factor that promotes lipid synthesis, AMPK is a cellular energy sensor, and mTOR is a signaling pathway that

regulates growth and metabolism. Along the same lines, another study in rats showed an attenuation of non-alcoholic liver disease through a gut-brain-liver circuit involving GLP-1, an intestinal hormone involved in glycemic regulation [9]. This makes the topic very interesting for those seeking information on "eugenol and liver," but here too, clinical translation remains cautious. In a model of benign prostatic hyperplasia, i.e., benign prostate enlargement, induced by testosterone, eugenol and probenecid attenuated inflammation and pro-survival pathways, confirming that the compound can act in environments characterized by proliferation and inflammatory signals [10]. On the antifungal front, the in vitro synergy, i.e., observed in the laboratory, of eugenol and methyleugenol with fluconazole against clinical isolates of *Candida* indicates a real biological interest, but confined to the laboratory [11]. Overall, the message is clear: cloves are not a single therapy, but a phytochemical, i.e., a plant substance with biological activity, with mechanisms that may be relevant in chronic conditions. The areas to connect are primarily these:

- The control of glycemia and post-prandial peaks in glucose disorders.
- The modulation of insulin resistance in metabolically more vulnerable tissues.
- Support for liver function in forms of steatosis and fibrosis.
- Experimental interest in selected inflammatory and proliferative conditions.

Available data show that cloves do not have a single target, but rather a profile of action that is particularly suited to chronic metabolic disorders. The following paragraphs move from glycemic profiles to the liver, and then to experimental uses in less directly metabolic conditions.

4.1 Cloves and type 2 diabetes: the biological rationale

In type 2 diabetes, the rationale for cloves primarily concerns the containment of hyperglycemia, oxidative stress, and low-grade inflammation. Experimental data indicate that eugenol can act on multiple levels of metabolic regulation, but the clinical significance must be interpreted with caution. This concept is valuable because it addresses the reader's most



frequent question without promising certain pharmacological effects. Type 2 diabetes, in fact, does not depend on a single mechanism but on an intertwining of insulin resistance, hepatic alterations, inflammation, and peripheral tissue dysfunction. In this context, cloves can be seen as a possible biological support, not as a substitute for therapies. The rationale is interesting precisely because it touches multiple pathways simultaneously, but this also increases the need to read the data precisely: an effect observed in cells or animals is not automatically a measurable clinical benefit. The most correct question is therefore not whether the spice "cures diabetes," but whether it can be integrated into prevention or support strategies in selected subjects. Soon we will discuss the mechanisms of action, the context of insulin resistance, and the boundary between nutritional support and medical therapy. The focus remains on pathophysiological logic, not on replacing treatments.

4.2 Eugenol and hepatic steatosis: why the liver is a relevant target

The liver is a natural target for phytochemicals that influence lipids, inflammation, and oxidative stress. Eugenol has been studied in models of hepatic steatosis because it can interfere with processes that promote lipid accumulation and loss of metabolic flexibility. In a mouse study fed a high-fat diet, eugenol reduced hepatic triglycerides by 45% and steatosis score by 72%, while fibrosis markers such as α -SMA, Col-I, and PAI-1 decreased by 36%, 63%, and 40% respectively [8]. In another study on rats, non-alcoholic liver disease improved through a gut-brain-liver axis involving GLP-1, an intestinal hormone involved in glucose regulation [9]. This does not mean that cloves are a therapy for fatty liver, but that there is concrete biological interest. Hepatic steatosis, in fact, is often linked to energy excess, insulin alterations, and changes in lipid metabolism; for this reason, a compound that acts on multiple nodes can be interesting in the research phase. However, it is necessary to distinguish the experimental rationale from clinical practice: an effect seen in the laboratory does not equate to a demonstrated improvement in people. The next step shifts the discussion to a different pathology, but one characterized by inflammation and pro-growth signals.

4.3 Cloves and benign prostatic hyperplasia

Benign prostatic hyperplasia is a useful example to show how a spice can also be studied in conditions that are not strictly metabolic but are supported by inflammation and pro-growth signals. In a testosterone-induced model, eugenol and probenecid attenuated hyperplasia by acting on uric acid-driven inflammation and cell survival pathways [10]. This means that clinical efficacy cannot be discussed, but only a research rationale that deserves attention. The value of the topic lies in connecting inflammation, proliferation, and mTOR regulation without creating inappropriate expectations. The reader might get the idea that an anti-inflammatory substance is automatically useful for the prostate, but the reality is more complex: dose, bioavailability, and the type of tissue involved matter. In this sense, the value of the topic lies in highlighting the boundary between biological interest and therapeutic proof. The following section addresses antifungal action, useful above all for understanding the experimental nature of many results.

4.4 Eugenol and defense against *Candida*: what experimental data show

Antifungal activity is one of the best-known aspects of cloves, but it needs to be contextualized: many results come from in vitro studies or animal models. In a study on clinical isolates of *Candida*, eugenol and methyleugenol showed synergy with fluconazole, suggesting a possible interference with fungal survival [11]. This focus is important because it intersects with research on *Candida* and natural remedies, but in this article, it primarily serves to explain the biological rationale for a possible antimicrobial action. *Candida* is a genus of yeasts that can become problematic under specific conditions, but the data on eugenol do not authorize considering cloves a valid therapy for all situations. The correct point is that eugenol can interfere with the fungal membrane, the biofilm (i.e., the protective matrix produced by the microorganism), and some survival functions of the microorganism, but clinical translation depends on concentration and method of use. The next step will distinguish synergy, active concentrations, clinical limits, and differences between essential oil and



extracts. This avoids overlap with pages dedicated to specific infections and maintains a cautious but informed reading.

4.5 Cloves and chronic diseases: when the mechanism is more plausible

In many studies, the value of cloves emerges in contexts where oxidative stress, inflammation, and metabolic alterations coexist. For this reason, biological plausibility is greater in some chronic diseases than in others, without implying universal clinical efficacy. This is also an important point for interpreting data on antioxidants: the fact that a substance reduces a marker or improves a pathway in the laboratory does not automatically mean that it produces the same outcome in people. Cloves, thanks to eugenol and polyphenols, are precisely in this intermediate zone between nutrition, phytochemicals, and pharmacological research. Their potential usefulness is better understood in phenotypes where metabolism is "switched off" or disordered, but always with attention to the dose, form of intake, and clinical context. In summary, the topic of treated pathologies does not concern a natural cure, but rather a set of possible biological applications that deserve further confirmation.

5. CLOVES AND THE RELATIONSHIP WITH mTOR

mTOR is a kinase, meaning an enzyme that regulates other proteins through phosphorylation and functions as a central node to integrate nutrient availability, growth signals, and energy status. When this axis remains overly active, the cell tends to prioritize synthesis and survival even in contexts of caloric excess or metabolic stress. When it rebalances, however, adaptation processes, including autophagy—the cell's internal recycling mechanism—can become more efficient. In cloves, the interest arises because eugenol and some bioactive fractions appear to intervene in this network in experimental models, suggesting a possible link between cloves eugenol metabolism and the regulation of cell growth [12,13,14]. In this context, cloves should not be interpreted as an mTOR "blocker," but as a possible modulator of its hyperactivation under experimental conditions. A useful example comes from HCT116 colorectal

carcinoma: an active fraction of cloves inhibited PI3K/Akt/mTOR, inducing apoptosis, i.e., programmed cell death, while in another study on the same cell line, the same fraction linked the effect to autophagy mediated by the same axis [12,13]. Eugenol, in different models, has also shown mTOR modulation in association with AMPK, the AMP-activated protein kinase that signals energy scarcity, reinforcing the idea of broader control over cellular balance [14,15]. For the reader, the key point is this: the relationship between cloves and mTOR makes sense primarily as a biological interpretative key, useful for understanding why these compounds are studied in metabolism and chronic diseases, but not as a therapeutic shortcut. To correctly interpret this data, it is useful to keep the different levels of observation together and connect them coherently:

- the PI3K/Akt/mTOR pathway can reduce pro-growth signals in pathological cells [12,13];
- autophagy can increase when the mTOR signal is contained [13,15];
- eugenol can also act in metabolic networks linked to oxidative stress, i.e., an imbalance between free radical production and antioxidant defenses, and chronic inflammation [16,14];
- preclinical results do not equate to a direct clinical effect in humans [12,13,14].

The role of mTOR helps connect cell growth, metabolic stress, and survival signals. In cloves, this axis becomes particularly interesting because eugenol and active fractions have been studied in in vitro and in vivo models with different but complementary readings.

5.1 What is mTOR and why does it matter in cellular metabolism?

The function of mTOR is to integrate signals of nutritional availability and translate them into concrete cellular choices: to grow, conserve energy, or activate adaptation processes. From a divulgative perspective, it is important not to reduce it to a simple "growth gene," because its role is broader and more articulated. In cloves, the interest arises precisely from the possibility of modulating this axis in a more balanced way, especially when it is chronically overactive. For the reader, this means that the topic does not only concern oncology or metabolism, but a



transversal biological logic that affects many tissues. Subsequently, we will develop the distinction between mTORC1 and mTORC2, two distinct functional complexes of the same pathway, upstream signals, and biological consequences, maintaining a divulgative but rigorous approach. The next step delves into the cascade involving PI3K and AKT.

5.2 Eugenol and inhibition of the PI3K/AKT/mTOR pathway

One of the most robust lines of research concerns eugenol's ability to reduce the activation of the PI3K/AKT/mTOR cascade in experimental models. This observation is important because it links the spice to a central signaling axis in cell growth and pathological survival. The purpose of this focus is not to present eugenol as a pharmacological inhibitor, but to explain why its action is relevant in a pro-growth metabolic environment. PI3K and AKT are upstream steps that transmit growth and survival signals to mTOR; if their activation is reduced, the cell can significantly change its behavior. In experimental studies, this often translates into less active signaling biomarkers and an environment less favorable to proliferation. In an HCT116 colon carcinoma model, the active fraction of cloves reduced cell survival by inhibiting this pathway and promoting apoptosis [12]. In other conditions of cellular stress, eugenol modulated the same network along with AMPK [14]. However, it is essential to remember that these results do not equate to direct clinical evidence. The next step will delve into cellular models, observed biomarkers, and the significance of measured phosphorylations. The following step translates this cascade into concrete outcomes on pathological cells.

5.3 mTOR, cell proliferation, and apoptosis in pathological cells

When mTOR is overactive, pathological cells tend to better sustain growth, survival, and adaptation to stress. In this scenario, the literature on cloves shows effects of reduced proliferation and increased apoptosis in selected preclinical models. Apoptosis is programmed cell death, an orderly process that allows the body to eliminate cells that are no longer suitable. In breast cancer cells, eugenol induced autophagy and apoptosis, with reduced proliferation and modulation of LC3 and p62; in a model of precancerous breast

lesions, 80 μ M of eugenol inhibited proliferation by 32.8% in HER-2 positive MCF-10AT cells [17,18]. This concept is useful because it translates the pathway into a concrete biological outcome and prepares the ground for articles dedicated to different pathological models. Here too, however, we must be rigorous: a result in a cell line does not automatically describe an effect in the human body. For this reason, the correct interpretation concerns the rationale, not the promise of a therapeutic outcome. We will soon distinguish effects observed in cell lines, in vivo, and in possible synergies with other compounds, without confusing experimental data with direct clinical evidence. This perspective helps to understand why the same axis is also invoked when discussing autophagy. The following section shows why autophagy is so closely linked to this same biological axis.

5.4 Autophagy and mTOR: why this axis is of interest to phytochemicals

Autophagy is closely linked to mTOR because this pathway tends to suppress it when it signals nutrient abundance. Phytochemicals that reduce mTOR hyperactivation can therefore promote a functional reactivation of cellular recycling processes. In cloves, this logic is particularly interesting because it helps connect metabolism, cellular protection, and tissue maintenance. Autophagy, explained simply, is an internal recycling system that allows the cell to recover useful components and dispose of damaged ones. If the mTOR signal remains too high, this system shuts down or is attenuated; if, however, the signal rebalances, the cell can return to a more orderly management of resources. In inflamed intestinal cells, the spermidine-eugenol combination preserved cellular integrity precisely by stimulating autophagy [6]. In tumor models, the same dynamic has been observed as part of the antiproliferative response [17]. This concept is useful for those seeking explanations on "autophagy and cloves" or "mTOR and cellular recycling." The topic becomes particularly interesting when observing experimental models of colon carcinoma. The next topic will focus on a very specific experimental model, colon carcinoma.



5.5 Cloves and colon carcinoma: what preclinical research indicates

Colon carcinoma cells are among the models where the modulation of PI3K/AKT/mTOR by active fractions of cloves has been explored with greater interest. The value of this aspect is considerable: it intercepts very specific research and helps explain why preclinical data is suggestive but not automatically translatable to clinical practice. In these models, reductions in proliferation and variations in cell survival signals are often observed, but this does not mean that the same response occurs in the human body with dietary use of the spice. In 2021, an active fraction of cloves induced apoptosis in HCT116 cells by inhibiting the PI3K/Akt/mTOR cascade [12]; in a 2018 study, the same family of compounds showed a similar effect associated with autophagy mediated by the same axis [13]. The key point is the difference between a controlled experimental environment and complex biological reality. Later, we will discuss cell models, experimental dosages, and the biological significance of induced apoptosis. In the text, it serves to guard a niche of great interest without duplicating general oncology pages. With this foundation, the text moves on to energy regulation, where AMPK becomes the protagonist.

6. CLOVES, AMPK, AND THE ENERGETIC REBALANCING OF MTOR

The central point when discussing cloves eugenol metabolism is not a generic "energetic effect," but rather the ability of certain phytochemicals to shift the cell towards a more prudent use of resources. AMPK is an energy state sensor: when available energy decreases, it tends to favor saving and adaptation processes, while mTOR coordinates growth and synthesis signals. In conditions of metabolic imbalance, this axis becomes interesting because it links oxidative stress, chronic inflammation, and the regulation of autophagy, which is the controlled recycling of cellular components. In cloves, eugenol and the polyphenolic fraction seem to act precisely in this direction, with an experimental rationale that should be interpreted as biological support and not as an autonomous therapy [13]. To navigate the data, it's useful to distinguish the levels of interpretation that recur in experimental and

preclinical studies. The idea is not that a single compound "turns on" or "turns off" metabolism, but that it makes the response to available energy more efficient. This is relevant in conditions where the cell remains exposed to nutritional overload, redox stress, and persistent inflammatory signals. In such contexts, AMPK can reduce excessive anabolic signals, while mTOR can be remodulated to allow for defense and repair. The practical consequence is a cellular profile less prone to disordered lipid accumulation, suppression of autophagy, and loss of metabolic flexibility. In experimental models, eugenol has shown a consistent relationship with this setup. In ischemia-reperfusion injury, i.e., the sequence in which a tissue receives blood and oxygen again after a period of deficiency, it contributed to a protective response associated with AMPK activation, mTOR inhibition, and autophagy recovery [15]. A similar picture has also been described in reviews on the therapeutic potential of eugenol in ischemia-reperfusion injuries [19], confirming that the topic is not limited to metabolism in the strict sense. In parallel, in fatty liver models, it reduced hepatic triglycerides by 45% and the steatosis score by 72%, suggesting that energy rebalancing concerns not only cell survival but also how the liver manages lipids [8]. In the same study [8], in vivo in HFD mice for 10 weeks, α -SMA also decreased by 36%, Col-I by 63%, and PAI-1 by 40%, while in vitro the effect was observed up to 100 μ M. These data reinforce the idea that AMPK modulation intertwines with anti-fibrotic signals and with the regulation of SREBP1, which is one of the key nodes of lipogenesis. Studies on the PI3K/Akt/mTOR pathways, a circuit that integrates growth, cell survival, and protein synthesis, in other cellular models also recall the same underlying logic: balancing growth, survival, and autophagy [12,13]. In the metabolic context, this approach has also been explored for glucose and insulin resistance, i.e., the reduced ability of tissues to respond to insulin. A water-soluble extract rich in clove polyphenols, PCE 250 mg/day for 30 days, lowered pre- and post-prandial glycemia in n=13 subjects, of whom 7 were normoglycemic and 6 prediabetic [2]. This does not allow for definitive clinical conclusions, but it shows how the profile of clove compounds can affect the management of energy substrates. From a pathophysiological perspective, reducing glycemic



peaks and containing the overactivation of nutrient-sensitive pathways is consistent with the call for AMPK, which is activated precisely when the cell needs to optimize fuel use. Preclinical studies on hyperglycemic models and type 2 diabetes have indeed linked eugenol to the modulation of glucose metabolism enzymes, oxidative stress, and inflammation [16,4,7,20]. The most useful data, from an institutional perspective, is that cloves do not act on a single target, but on an integrated network of signals. AMPK, mTOR, autophagy, lipogenesis, and antioxidant response are not separate processes: they mutually influence each other and determine the tissue's ability to remain functional over time. This is why the literature on eugenol, liver, muscle, and brain converges towards a single cautious interpretation: the compound can promote better adaptation to metabolic stress, but the clinical significance depends on dose, food matrix, duration of exposure, and initial health status [1,3,19]. In other words, cloves offer an interesting example of a phytocomplex capable of interacting with the main axes of energy regulation, without replacing validated dietary and therapeutic strategies.

- AMPK activation can reduce excessive anabolic signals.
- mTOR modulation can promote autophagy and adaptation.
- Eugenol can attenuate lipid accumulation and cellular stress.
- The response varies depending on the tissue and context.

To understand the role of cloves in this axis, it is useful to start with AMPK as an energy sensor and then follow its dialogue with mTOR in different experimental models.

6.1 What is AMPK and why is it considered an energy sensor

AMPK monitors the cell's energy status and is activated when the AMP to ATP ratio signals reduced energy availability. This makes it a decisive aspect for understanding how certain natural compounds, including those from cloves, can promote a more efficient metabolic setup. ATP is the main cellular "energy currency," while AMP indicates a lower energy condition: when the ratio changes, AMPK intervenes

to limit waste and promote recovery processes. Its function is to integrate signals of energy availability and translate them into concrete cellular choices: reducing costly synthesis, promoting substrate utilization, and supporting adaptation. This reasoning is important because it builds the logical basis connecting nutrition, metabolism, and cellular response to stress. In tissues most exposed to energy load, such as muscle and liver, this pathway can influence the balance between consumption and saving. In cloves, the interest arises precisely from the possibility of modulating this axis in a more orderly way. For the reader, this means that the topic is not just about energy in an abstract sense, but about the cell's ability to react adaptively to its environment. Subsequently, we will delve into upstream activators, biological consequences, and differences between physiological and pathological effects, with attention to terminological precision. The next section delves into the relationship between eugenol and fatty liver.

6.2 Eugenol, AMPK, and Protection from Hepatic Steatosis

In models of hepatic steatosis, eugenol has been associated with AMPK activation and a reduction in signals that promote lipid accumulation. The biological significance is important because it links a traditional spice to a central regulatory axis of liver metabolism. Hepatic steatosis, or fatty liver, indicates an excess of fats accumulated in the liver and is often associated with metabolic dysfunction, insulin resistance, and inflammation. This does not authorize speaking of a cure for fatty liver, but it justifies a deeper look into the experimental rationale. If AMPK is stimulated, the cell tends to reduce lipogenesis, i.e., the synthesis of new fats, and to favor more efficient energy utilization processes. This is why cloves are being studied as a possible biological support in an altered hepatic context. In a study on mice with a high-fat diet, eugenol lowered hepatic triglycerides by 45% and improved the steatosis score by 72%, with a parallel reduction in fibrotic markers [8]. In vitro, up to 100 μ M, and in vivo for 10 weeks in HFD mice, reductions in α -SMA by 36%, Col-I by 63%, and PAI-1 by 40% were also observed [8]. The next step will describe the upstream and downstream mechanisms, the role of SREBP1, and the connection with the metabolic flexibility of the liver. The following stage



concerns ischemia-reperfusion injury, a model of acute energetic stress.

6.3 Eugenol and ischemia-reperfusion injury: why the AMPK-mTOR axis is protective

Ischemia-reperfusion injury is a useful model for understanding how cells respond to acute and sudden energy stress. In this context, eugenol has been studied for its ability to promote adaptive responses mediated by AMPK and to limit excessive mTOR activation. Ischemia is a reduction in blood flow and thus oxygen to tissues; reperfusion is the return of flow, which, however, can generate further oxidative stress. This makes the model very interesting for evaluating compounds with cytoprotective potential. In a study on cerebral ischemia-reperfusion injury, eugenol attenuated the lesion by enhancing autophagy along the AMPK-mTOR-p70S6K pathway [15]. Another recent review study attributed therapeutic potential to eugenol in ischemia-reperfusion models [19]. The value of this concept lies in showing that the same biological axis can be relevant outside the classic metabolic territory. In other words, the same pathway that regulates metabolism can also contribute to the ability to resist sudden stress. We will briefly develop the pathophysiological bases of ischemia, the role of autophagy, and the significance of experimental endpoints. The next section helps distinguish a useful adaptation from a disordered response.

6.4 Functional or Aberrant Autophagy: How to Interpret the Effects of Cloves

Autophagy is a cellular recycling process that becomes advantageous when it serves to remove damaged components and restore internal order. However, not every activation of the same process produces a useful effect: the context determines whether autophagy is functional or if it represents an incomplete or disordered response to stress. This point is central when interpreting the effects of eugenol, because its action on AMPK and mTOR should not be read as a simple "increase" or "decrease" in the signal, but as a modulation of how the cell adapts. In intestinal cells exposed to inflammation, for example, eugenol supplementation supported viability precisely through a more ordered autophagic response [6]. Conversely,

in other biological models, the same network can be part of tumor survival strategies or pathological adaptation, which is why the direction of the effect must always be contextualized [12,13]. For cloves, therefore, the interpretative key is not autophagy itself, but the quality of its regulation and the type of stress the cell is subjected to.

7. CLOVES AND THE IMPROVEMENT OF INSULIN RESISTANCE

When the insulin response weakens, glucose enters tissues with more difficulty, and the body compensates with a greater hormonal load. Over time, this promotes alterations in glycemia and lipid management. In this context, cloves and insulin resistance are of interest because some of their compounds, especially eugenol, seem to act on multiple levels simultaneously: reduction of oxidative stress, attenuation of inflammation, and improved tolerance to metabolic load [4,7]. A preliminary study on diabetic rats showed that eugenol improved insulin resistance, oxidative stress, and inflammation [4]. In parallel, in a murine model, i.e., an experimental model conducted in mice, of type 2 diabetes induced by a high-fat diet and streptomycin, eugenol increased glucose uptake in skeletal muscle, reducing local inflammation [20]. These outcomes are relevant because insulin resistance often arises from an altered dialogue between the liver, muscle, and adipose tissue, with inflammatory signals blocking the normal transduction of the insulin signal, i.e., the transfer of information from the receptor to cellular responses. If the receptor and intracellular pathways respond poorly, glucose remains in the blood longer, and the cell uses available nutrients less efficiently. Eugenol, at least in the models studied, seems to intervene precisely in this circuit, reducing the mediators that hinder tissue response and improving peripheral energy availability. A useful element is that the signal does not appear isolated: a review of murine hyperglycemic models described a consistent but still preclinical picture [7]. Furthermore, a water-soluble polyphenolic clove extract lowered pre- and post-prandial glycemia with 250 mg/day for 30 days in 13 subjects, 7 of whom were normoglycemic and 6 prediabetic [2]. This data is important because it moves the discussion beyond the laboratory alone, although without authorizing definitive clinical



conclusions. The result suggests that clove compounds can modulate the glycemic response to a meal, a crucial moment for those with initial insulin resistance or unstable glycemic control. However, the study remains small, short, and insufficient to define efficacy, long-term safety, or superiority over established strategies. It is therefore essential to contextualize: a spice can accompany a broader dietary path, but not replace structured clinical and behavioral interventions. In other words, the potential is interesting, but it should be interpreted as biological support and not as an autonomous therapy. These results help to view the spice as a potential metabolic adjuvant, not as an autonomous solution. The biological plausibility also derives from the fact that the insulin response is strongly conditioned by inflammatory tone and oxidative stress, two conditions that feed each other. In affected tissues, especially skeletal muscle and the liver, the accumulation of lipids and the excess of reactive oxygen species, i.e., excessively produced oxidizing molecules, compromise downstream insulin signaling. Cloves can therefore be seen as a source of bioactive compounds capable of influencing the overall metabolic environment, especially when the picture is supported by an unbalanced diet and a sedentary lifestyle. The following points clarify why muscle is a decisive target, how adipose tissue influences insulin resistance, and how clove polyphenols can be involved in controlling the oxidative and inflammatory environment:

- Skeletal muscle represents the main site of glucose uptake.
- Local inflammation can reduce tissue sensitivity to insulin.
- Visceral adipose tissue amplifies systemic metabolic disorder.
- Clove polyphenols can support redox balance.
- The evidence remains preclinical and should be interpreted with clinical caution.

Insulin resistance involves different tissues and should therefore be viewed as a network problem, not a single organ problem. In the following passages, the focus shifts to muscle, visceral adiposity, and redox-inflammatory mediators that can explain the role of cloves.

7.1 What is insulin resistance and why does it worsen metabolism

Insulin resistance is a reduced ability of tissues to respond to the insulin signal, leading to a compensatory increase in hormonal secretion and progressive metabolic imbalance. Over time, this picture promotes hyperglycemia, dyslipidemia, and chronic low-grade inflammation. Insulin, under normal conditions, helps glucose enter cells and regulates nutrient metabolism; when the signal is poorly received, the system loses efficiency. This factor is important because it allows for a correct understanding of the biological target on which cloves act. Without this basis, there is a risk of attributing generic effects to the spice without knowing which physiological step is actually being referred to. In clinical practice, the problem concerns not only glycemia but also the lipid profile, body fat distribution, and tissue response to metabolic stress. In this sense, insulin resistance is a systemic phenomenon, in which the liver continues to produce glucose, the muscle uses it less effectively, and adipose tissue releases signals that worsen the picture. The next step will be to develop the causes, involved tissues, and differences between muscular, hepatic, and adipose insulin resistance, useful for avoiding excessive simplifications. From here, it becomes clearer why muscle is a key target for glucose.

7.2 Eugenol and improved glucose uptake in muscle

Skeletal muscle is one of the main tissues responsible for glucose uptake, thus representing a fundamental target for understanding the metabolic effects of cloves. Some preclinical studies indicate that eugenol may promote glucose absorption through pathways involving AMPK and GLUT4 translocation. AMPK is a kinase, meaning an enzyme that regulates other proteins by adding phosphate groups, and signals an unfavorable energy state; GLUT4 is a glucose transporter that, when brought to the cell membrane, facilitates the entry of sugar into the cell. In a study on murine models of type 2 diabetes, eugenol increased glucose uptake in muscle by reducing inflammation [20]. This effect is consistent with improved peripheral insulin sensitivity, because muscle consumes much of the glucose after a meal and contributes decisively to



glycemic balance. The mechanism can become even more relevant when considering that AMPK activation tends to favor metabolic pathways that improve energy utilization and limit substrate accumulation. This does not equate to a guaranteed clinical effect, but offers a coherent biological rationale. We will subsequently develop the connection with exercise, insulin sensitivity, and peripheral metabolism. The important thing to remember is that the effect observed in the laboratory cannot be automatically translated into a universal practical recommendation. From muscle, we move to adipose tissue, where visceral fat contributes to metabolic dysfunction.

7.3 Cloves, visceral obesity, and adipose tissue

Visceral obesity is one of the contexts in which insulin resistance tends to be more pronounced. Cloves become interesting when considering their possible effect on adipose inflammation, lipid metabolism, and communication between adipose tissue and other organs. Adipose tissue is not just an energy store: it also produces hormonal and inflammatory signals that influence the rest of the body. This is why its dysfunction has a systemic impact. In a murine model fed a high-fat diet, eugenol reduced adiposity and modulated the gut microbiota, i.e., the set of microorganisms that inhabit the intestine, suggesting that adipose tissue is not the only target but part of a broader network [5]. This observation is relevant because the microbiota can influence intestinal permeability, inflammation, and bile acid metabolism, all elements that interact with insulin sensitivity. In other words, the effect does not seem limited to a single cell but concerns a more complex gut-adipose-metabolic axis. This step is useful because it broadens the focus beyond glycemia and allows us to concentrate on obesity, visceral fat, and functional spices. In this context, the potential contribution of cloves should be interpreted as a modulation of the environment, not as a direct reduction of body fat. The next step will explore interactions with leptin, adipocytes, and metabolic flexibility, always with caution in interpretation. The following section connects the topic to antioxidant protection, another central piece of the puzzle.

7.4 Clove polyphenols and metabolic oxidative stress

Oxidative stress is one of the factors that worsen insulin sensitivity and amplify metabolic dysfunction. Clove polyphenols are particularly interesting because they can help rebalance this environment, promoting a more orderly tissue response to insulin stimulation. Polyphenols are plant compounds with antioxidant and modulating activity, and in cloves, they are associated with the overall biological effect of the spice. In an active comparative study, a polyphenol extract from clove buds improved intracellular redox homeostasis and glucose metabolism in healthy and prediabetic subjects [3]. This step is also important because it suggests that the potential does not depend solely on isolated eugenol, but on the set of phytochemicals present in the plant matrix. From a pathophysiological perspective, improved redox balance can reduce the activation of signals that interfere with the insulin receptor and intracellular glucose pathways. This aspect is important both for the reader seeking a direct link with antioxidants and for the text's architecture, where it connects redox and metabolism. However, an antioxidant action does not automatically mean clinical improvement: the context, dose, and form of administration must always be verified. The next section will delve into the relationship with glutathione, Nrf2, and inflammatory cytokines. The final step of the section concerns when this support can truly make sense.

8. CLOVES, AMPK, AS160, AND GLUT4

In skeletal muscle, the control of glucose entry also depends on a very precise chain of events. AMPK, a protein sensitive to the cell's energy state, can promote the phosphorylation of AS160 and make GLUT4 translocation to the membrane more efficient. AS160, a regulatory protein of intracellular trafficking, acts as a "brake" on the vesicles that transport GLUT4. When that brake is released, glucose enters more easily. This step is particularly relevant in models of insulin resistance, because it shows that the problem is not only related to the hormonal signal, but also to the final availability of the transporter, i.e., the protein that allows glucose to cross the cell membrane. In this context, the interest in eugenol is not about a generic effect, but its ability to converge on a concrete



mechanism that links cellular energy and glycemic management. In vitro and in vivo, i.e., in isolated cells and living organisms, compounds similar to cloves have shown AMPK activation and increased GLUT4 translocation, supporting the hypothesis of support for peripheral glucose uptake [21,22,23,24]. A useful example is isoeugenol, a compound structurally similar to eugenol, which in muscle cells increased the expression and passage of GLUT4 to the plasma membrane; the result, however, remains preliminary and does not equate to a certain clinical effect. The most correct interpretation is therefore mechanistic: these phytochemicals, i.e., bioactive compounds of plant origin, can contribute to making a pathway already central to muscle metabolism more efficient, without replacing dietary or pharmacological interventions when necessary. On this basis, data on *Syzygium aromaticum* and its phenolic compounds, plant-derived substances with biological properties studied in experimental models, appear to act along the same functional axis in some contexts. The key points can then be read more linearly:

- AMPK can initiate the signal that facilitates GLUT4 movement.
- AS160 represents a crucial intermediate node for enabling transport.
- The cell membrane receives more GLUT4 and improves glucose uptake.
- Clove compounds can integrate into this circuit.

The molecular pathways connecting cloves to metabolism are more understandable if one observes the AMPK-AS160-GLUT4 sequence, i.e., the chain of events that carries the signal to the transporter. The three nodes explain why the topic is not just about glycemia in the abstract, but about how glucose truly enters cells.

8.1 AS160: the regulator that frees up GLUT4 traffic

AS160 is a key protein that controls the movement of vesicles containing GLUT4 towards the cell membrane. When it is phosphorylated, meaning when it receives a phosphate group that modifies its activity, the brake on vesicular trafficking loosens, and glucose can enter the cell more easily. This aspect is crucial because it explains the transition point between the energy signal and substrate transport. AS160 acts as a

kind of internal traffic regulator: if it remains inhibitory, GLUT4 does not easily reach the cell surface; if its activity is modified, transport becomes more efficient. In peripheral tissues, especially in muscle, this step has a very concrete impact on glycemic management. In studies on muscle cells, AS160 phosphorylation was found to be dependent on AMPK activation [21,22]. Later, we can delve into the interactions with Rab-GAP, a family of proteins that regulates vesicular trafficking, phosphorylation, and why GLUT4 transport is so vulnerable in insulin resistance. Here, then, AS160 acts as a hinge between AMPK and the final transporter. The next step shows how eugenol can intervene in GLUT4 translocation.

8.2 Eugenol and GLUT4 Translocation Activation

Eugenol, in some experimental models, appears to promote GLUT4 translocation and thus glucose uptake into peripheral tissues. Translocation is the movement of GLUT4 from inside the cell to the membrane, where it can truly facilitate glucose entry. This finding is relevant because it shows how a plant molecule can intervene in a very concrete functional step, often altered in the presence of hyperinsulinemia and a sedentary lifestyle, i.e., high insulin levels in the blood and reduced physical activity. In rat muscle cells, a compound related to cloves, isoeugenol, increased glucose uptake by activating AMPK and bringing GLUT4 to the plasma membrane [25]. Eugenol itself has shown a similar direction in models of metabolic disease [20]. This point is useful for readers seeking a biological explanation of the relationship between spices and metabolism and for building a bridge between molecular mechanism and potential metabolic benefit. In this case, however, the interpretation must remain cautious: a result in cells or animals does not automatically translate into a practical recommendation. Later, we will explore the experimental details and context of use. The following passage clarifies why sometimes the problem is not the insulin signal, but the final transport of glucose.

8.3 GLUT4 and selective insulin resistance: an often overlooked aspect

So-called selective insulin resistance helps explain why in some cases insulin signaling still seems to be present, but glucose does not effectively enter the cell.



The problem is often GLUT4 trafficking, not just the receptor or upstream molecules. This distinction is very important because the literature shows that defects in GLUT4 translocation are a concrete cause of human insulin resistance [26], and a selective defect in endogenous GLUT4 translocation has been described in insulin-resistant murine muscle fibers [27]. In practice, the cell can receive the insulin message but fail to translate it into glucose uptake because the transporter does not reach where it is needed. This makes the topic very useful for understanding why a phytocompound that acts on AS160 or AMPK might be interesting. Later, the text can develop the basis of the concept and its significance for muscle and adipose metabolism. The reader thus obtains a more precise understanding of the problem, not limited to the mere presence of the hormone. The following text relates these mechanisms to physical exercise, which converges on the same axis.

8.4 Cloves and physical activity: convergences on AMPK and GLUT4

Physical activity activates AMPK and promotes GLUT4 translocation, two steps that explain why movement and nutrition can converge on the same metabolic axis. Cloves do not replace exercise, but their biological rationale becomes more interesting precisely in the context of an active lifestyle. This convergence is important because it helps to understand that the potential benefit of a phytocompound is often complementary to an already valid strategy, not autonomous. Here a very concrete question arises: can the spice support strategies that already improve insulin sensitivity? The most correct answer is that it can make sense as a support, but not as an alternative to movement. The literature on exercise shows that AMPK is involved in post-exercise insulin sensitivity [28], and this makes a convergence with some plant compounds biologically plausible. Further on, the text can develop physiological convergences without overlapping with content on diet and exercise. The final passage of the section closes the chain and shows the result in peripheral tissues.

8.5 AMPK, AS160, and GLUT4 in peripheral tissues: how the signal is translated

The AMPK-AS160-GLUT4 pathway makes sense primarily because it produces a tangible effect: greater availability of transporters on the membrane and improved glucose uptake. In peripheral tissues, this translates into a more efficient metabolic response, particularly relevant in the presence of insulin resistance. Muscle is the main protagonist in this process because it responds significantly to energy signals and insulin. The central element is GLUT4 trafficking: without translocation, the signal remains incomplete even when receptors are functional. The example of eugenol and isoeugenol helps to interpret the process as a concrete, not abstract, sequence [4,23,24]. Prospectively, this axis explains why some plant-based interventions are being studied as metabolic management supports, albeit with still preliminary evidence. Later, the text will delve into how the signal is modulated by nutrients, exercise, and plant compounds. After the biology of the signal, the discussion returns to daily practice: when support truly makes sense.

9. CLOVES AND PRACTICAL METABOLIC PREVENTION

Metabolic prevention with cloves works best when it remains anchored to daily cooking and not to the search for an immediate "curative" effect. In this context, the practical value of the spice derives mainly from the presence of eugenol, a natural aromatic compound with biological activity, and other clove polyphenols, which are plant molecules with antioxidant potential. These components can accompany a dietary pattern already oriented towards weight control, glycemia, and fat quality. Regular but moderate use is more sensible than episodic high doses, because the goal is to build sustainable habits and not to chase the effects of concentrated supplementation. In the small human study with 250 mg/day of polyphenol extract for 30 days, on 13 participants including normoglycemic individuals (i.e., with normal blood sugar levels) and prediabetics (i.e., with initial alterations in glucose metabolism), an improvement in glycemic values was observed, suggesting a possible practical utility within a coherent dietary framework [2]. This result is



interesting because it fits into a logic of primary prevention: it does not promise a substitute effect for therapy, but indicates that a mild and continuous modulation can be plausible when starting from a well-structured diet. The clinical sense of this approach is reinforced by the fact that metabolic dysfunction often arises from an intertwining of caloric excess, low-grade inflammation, insulin resistance (i.e., a reduced tissue response to insulin), and alterations in the lipid profile. Clove compounds alone do not correct these mechanisms, but can act as dietary cofactors, especially when the diet already reduces free sugars, unfavorable fats, and energy density. Eugenol, in particular, is studied for its antioxidant, anti-inflammatory effects and for modulating cellular pathways involved in metabolism, but such activities emerge under very controlled experimental conditions [1,16]. For this reason, practical prevention must remain cautious: the expected benefit is additive, meaning it adds to that of the diet, not definitive, and depends on the continuity of intake, the quality of the rest of the diet, and the presence of clinically relevant risk factors. In other words, the value of the spice increases when it is part of a stable and well-constructed eating habit. This approach helps to place cloves within a realistic metabolic prevention: they can enrich the diet, but the benefit depends mainly on the overall context. In experimental models, in fact, eugenol is studied at doses and times very different from domestic use, and the results on adiposity (i.e., accumulation of adipose tissue), glycemia, and inflammation must be interpreted with caution before being translated into practice [8,5,16]. In the work on steatosis (i.e., fat accumulation in the liver) and hepatic fibrosis (i.e., excessive scar tissue formation in the liver), eugenol showed in vitro effects (i.e., in the laboratory on controlled cells or biological systems) up to 100 μ M and, in HFD mice (i.e., fed a high-fat diet) for 10 weeks, it reduced hepatic TG by 45%, steatosis score by 72%, α -SMA by 36%, Col-I by 63%, and PAI-1 by 40% [8]. These numbers suggest significant biological potential, but also the distance between the experimental model and current dietary use. In other words, the spice can play a useful role if it remains part of a stable dietary strategy that prioritizes regularity, moderation, and continuity. To translate this information into daily behavior, it is advisable to

distinguish between culinary use, infusion, and concentrated products, so as not to overlap very different levels of exposure. The practical points to keep in mind are clear:

- Whole spice is useful when aroma and simple quantity control are needed.
- Powder distributes better but requires more attention to portion size.
- Infusions offer easy use, without equating to standardized concentrates.
- Extracts should be considered functional products, not cooking spices.

To make this setting operational, it is advisable to clearly separate the forms of use and the concentration level. The following steps help to understand what changes between cooking, infusion, and supplements, and when caution should increase.

9.1 How much to consume cloves in cooking

In cooking, cloves are used in small quantities because their aroma and flavor are very intense. The practical question is not "how much do they heal," but "how reasonable is it to use them" in a daily food context. The right amount depends on the type of recipe, the desired intensity, and personal tolerance. In general, the principle to follow is moderation: the spice should enrich the dish, not dominate it. This logic applies even more when cloves are used in preparations repeated over time, because the problem is not just a single intake, but the sum of exposures. From a metabolic point of view, a small amount of bioactive compounds can be interesting if it accompanies more balanced meals, but the real impact still depends on the entire diet. This is why daily cooking should be understood as a favorable context, not as an autonomous therapy. We will later delve into the concept of portion, the difference between cooking and supplementing, and the value of regular but moderate use. From a preventive perspective, sober consistency is more useful than occasional excess. The next step compares the most common forms of intake.



9.2 Cloves in powder, whole, or as an infusion

The form of intake greatly changes the user experience: whole cloves are easier to dose in recipes, powder disperses aroma and compounds better, while infusion changes the type of extraction and the sensory profile. This section is useful for the reader who wants to choose the most suitable form without confusing efficacy, intensity, and practicality. Whole cloves are often preferable when one wants to better control the quantity, while powder offers greater distribution in the dish or beverage. Infusion, on the other hand, changes the way molecules pass into water and can provide a different experience, but it should not be automatically considered equivalent to other preparations. This distinction is also important so as not to overestimate the effect of a herbal tea compared to the spice used in cooking. From a pathophysiological perspective, the difference matters because the bioavailability of eugenol and other phenylpropanoids, which are aromatic compounds of plant origin, varies based on the matrix, extraction time, and the dose actually ingested. In preclinical models, i.e., experimental before human use, on obesity and glucose metabolism, for example, the potential benefit emerges under standardized conditions and does not directly transfer to homemade beverages [5,3,4]. Subsequently, we will address the difference between homemade preparations and concentrates, with an operational and cautious approach. The next step concerns reading labels, which is essential when talking about concentrated products.

9.3 How to read clove supplement labels

Clove-based supplements may contain extracts, i.e., concentrated preparations obtained from the plant, different titrations, or combinations with other ingredients. For this reason, reading the label is essential: it is necessary to understand if the product is a standardized extract, which part of the plant was used, and if the eugenol concentration is declared. Without this data, it is difficult to assess the real difference between a food spice and a concentrated formulation. This attention is particularly important in an area such as metabolic prevention, where the risk is not only ineffectiveness but also excessive

expectations towards a product that is designed to be used differently from cooking. The available studies on eugenol show promising effects in experimental models, but precisely for this reason, the quality of information on the label helps to avoid improper inferences. In practice, the label is the first filter to distinguish a reasonable dietary support from a product that requires more careful evaluations [29,1,16]. The interpretation must also consider the duration of use, the presence of other active ingredients, and the clinical context: a formulation for general well-being is not equivalent to an extract studied in the laboratory. When a product reports associations, the reader should ask whether it is a functional food, i.e., a food with potentially useful effects beyond nutrition, or a concentrate with implicit pharmacological potential. This distinction helps to avoid over-expectations and to maintain focus on prevention, which requires consistency more than intensity.

9.4 Cloves and safety: when it's advisable to limit use

Even a spice traditionally used in cooking warrants caution when moving to concentrated doses or non-food uses. Safety depends on the form, quantity, duration of use, and individual context, so one cannot simply reason by analogy with home cooking. In particular, essential oil, which is the highly concentrated volatile fraction of the plant, and extracts require greater attention than the whole spice, because the concentration of active compounds changes significantly. This difference is central for those seeking a preventive effect without transforming the product into a pharmacological surrogate. In preclinical models, for example, eugenol and clove fractions show activity on metabolic and inflammatory pathways, but such data do not authorize indiscriminate use in the general population [5,12,15]. The literature on insulin resistance, oxidative stress, and autophagy/AMPK, which is a cellular system for regulating turnover and energy, suggests an interesting biological rationale, but the transition from animal to human remains the most delicate point [14,19,15]. The most prudent choice therefore remains to consider cloves as part of a varied diet, limiting concentrated uses when they are not truly necessary. In people with chronic conditions, polypharmacy (i.e.,



simultaneous use of multiple medications), or digestive sensitivities, the evaluation must be even more careful. This concludes the practical section, and we now move on to a comparison with other options and common myths.

10. CLOVES: NUTRITIONAL COMPARISON AND MYTHS TO CLARIFY

In nutritional comparison, cloves should be understood as a spice with a high density of bioactive compounds—molecules present in foods that can interact with biological processes—and not as a solution equivalent to an extract or a drug. Nutritional comparison means precisely this: comparing the food matrix, the concentration of active ingredients, and the context of use, so as to avoid attributing effects observed only in standardized preparations to daily cooking. In the case of cloves, the most discussed rationale concerns eugenol, the main phenolic aromatic component, and the set of clove polyphenols—plant substances with potential antioxidant activity that can support the control of oxidative stress (i.e., an excess of reactive species harmful to cells) and chronic inflammation in experimental models [1,30]. However, the fact that a spice is biologically interesting does not automatically imply a broad or consistent clinical impact on glycemia, weight, or insulin resistance (i.e., the reduced tissue response to insulin). One of the most common myths is to think that cloves "lower blood sugar" directly and always predictably. In reality, available data suggest, if anything, potential metabolic support dependent on the form of intake, product quality, and the overall dietary profile. Referring to dietary guidelines remains useful because it places the spice within a balanced eating model and not as a substitute for it [31,32]. From this perspective, comparing it with other spices helps clarify differences in composition and intensity of use, while the myth to debunk is the idea that a single spice can solve complex metabolic problems. The most correct interpretation is therefore cautious: cloves can play a contextual role, but not a shortcut [1,30]. To guide the reader between realistic expectations and simplifications, it is useful to distinguish some key points, because it is precisely here that one understands how easy it is to confuse practical utility and popular myth:

- Culinary spice and concentrated extract are not equivalent in exposure.
- Preclinical observations, i.e., obtained in the laboratory or in animal models, do not automatically authorize extensive clinical conclusions.
- The role of eugenol must be interpreted together with the food matrix.
- Online promises often ignore dose, context, and duration of use.
- Correct comparison helps separate practical utility and health myth.

The two most useful comparisons are between the spice and the extract, and between concrete utility and popular myth. This also clarifies why interpreting data on eugenol and metabolism requires caution.

10.1 Natural cloves or standardized extract: what changes

The main difference between a natural spice and a standardized extract concerns the concentration of bioactive compounds and, consequently, the predictability of exposure. Spice is suitable for daily culinary use; the extract more often belongs to the nutraceutical logic, i.e., the use of concentrated products for supportive or experimental purposes. A standardized extract, in fact, allows for greater precision in knowing how much active substance is present, while the spice can vary greatly from one batch to another. This means that two seemingly similar products can behave very differently on a biological level. The comparison is also important for the reader who is trying to navigate between nutrition and supplementation, because it helps not to confuse the level of evidence of a concentrated product with that of a common ingredient. In the available data, the polyphenol extract has shown an initial clinical effect [2], while essential oils, i.e., volatile mixtures rich in aromatic compounds, and active fractions have mainly been studied in the laboratory [12,33]. Subsequently, we will develop a comparative guide between forms, potency, and intended uses. The key point is not to mistake a culinary preparation for a pharmacologically equivalent formulation.



10.2 Cloves and the myth of the universal remedy

The myth of the universal remedy arises when a food is presented as useful for everything, without considering individual variability, quality of evidence, and the type of outcome measured. In the case of cloves, this simplification is particularly misleading because it mixes prevention, metabolic support, and presumed therapeutic effects as if they were the same thing. In reality, the available literature mainly shows promising but not conclusive signals, with strong heterogeneity in models and outcomes, i.e., the observed results. Some reviews on the effects of eugenol describe interesting pharmacological properties, but their interpretation always requires a precise context [1,34]. Saying that a spice "is good for you" is not equivalent to saying that it can replace a nutritional strategy, let alone a therapy. The myth is easily fueled on social media because it offers a simple narrative, but science works more selectively: a substance can be consistent with a goal without being effective for every person, at every dose, and at every stage of the disease. For this reason, comparison with clinical reality remains indispensable [30].

10.3 Cloves and natural alternatives: comparison with other spices

Comparing cloves with other spices primarily helps us understand that the nutritional profile depends not only on the aroma but also on the chemical composition and the quantity typically consumed. Some spices are distinguished by sulfur compounds, others by phenolic molecules, and still others by greater gastronomic than biological relevance. Cloves have a very distinct identity due to eugenol, but this does not automatically make them superior to other spices metabolically. In comparisons between functional botanicals, the risk is to create artificial rankings instead of interpreting data based on context: a spice might be more useful in an experimental model and less relevant in daily use, or vice versa. Even in preclinical literature, i.e., studies conducted before clinical trials in humans, the effect of a plant matrix does not necessarily coincide with that of its single main compound. Therefore, the most accurate comparison considers dose, form, and objective, not an abstract superiority. Correct communication must

thus avoid transforming the presence of a phytochemical, a natural substance with possible biological activity, into a promise of generalized efficacy, especially when actual consumption occurs in very low culinary quantities [1,30].

10.4 What science says about cloves and metabolism

The science on cloves and metabolism indicates promising rationale, but it is not yet sufficient for strong clinical conclusions. The most robust data remain concentrated on preclinical models, where eugenol and fractions of *Syzygium aromaticum* show effects on steatosis, i.e., fat accumulation in the liver, oxidative stress, and intracellular signals, meaning the biochemical messages exchanged within cells, linked to energy regulation [8,12,14]. These results are interesting because they suggest a possible interaction between cloves and central metabolic nodes, but they must be interpreted with caution: the transition from animal to human is never linear. On the human front, evidence is still limited to a few small studies, such as the one with 250 mg/day for 30 days in 13 participants [2]. This imbalance between preclinical and clinical explains why the topic remains promising but not definitive. Talking about the benefits of eugenol is only correct if it is specified that, today, these are mainly biologically plausible hypotheses rather than consolidated therapeutic proofs. In practice, the literature suggests a useful research direction, but it does not justify triumphalistic interpretations or simplifications regarding human metabolism [1,30].

10.5 Cloves or supplement: which choice makes more sense

The choice between cloves as a spice and as a supplement depends on the actual goal, not on a presumed absolute value of the "stronger" form. For daily food use, the spice can fit into a model consistent with nutritional guidelines, while a standardized extract is more suitable for a study context or targeted nutraceutical reasoning [31,32]. The decisive point is that the supplement introduces greater dose precision, but also a greater need for caution in evaluating the risk-benefit ratio. Available evidence does not show that higher concentration automatically means greater efficacy, and domestic consumption should not be confused with a highly titrated formulation.



Furthermore, when talking about cloves and insulin resistance or cloves and glycemia, it is essential not to jump from experimental data to practical promises. The sensible choice, today, is to use the spice as part of a varied diet and to consider supplementation only when the overall picture and product quality truly justify it [2,1].

11. CLOVES: SAFETY AND ATTENTION TO CRITICAL USAGE ISSUES

Evaluating the safety of cloves starts with a simple principle: the spice used in cooking is not equivalent to a standardized extract, nor, especially, to essential oil. A standardized extract refers to a preparation in which the quantity of active compounds is made constant, thus providing a more predictable content compared to the raw material. Criticality of use means precisely this: the risk profile changes based on the concentration of active compounds, the frequency of intake, and the individual context. In daily food practice, the margin of use generally remains broad, but when moving to concentrated formulations, exposure to eugenol increases, and with it, the need for caution. For this reason, rather than seeking "strong" effects, it makes sense to consider proportion, duration, and compatibility with the intended use. This approach is also important because eugenol does not act in a single way. In experimental literature, for example, effects on glycemia, inflammation, oxidative stress, and lipid metabolism have been described [8,16,9,4,7,20]. Glycemia refers to the concentration of glucose in the blood, while inflammation is the body's defensive response to a harmful stimulus; oxidative stress indicates an imbalance between reactive species and antioxidant systems, and lipid metabolism concerns all the processes by which the body manages fats and cholesterol. However, biological potential does not equate to an indiscriminate practical indication. The same pathways that make the compound interesting, such as the modulation of enzymes, inflammatory signals, and hepatic metabolism, can become less predictable when the dose increases or when other clinical factors are combined. From this perspective, hepatic metabolism refers to the chemical transformations that occur in the liver and influence the elimination and activity of substances. In the logic of prevention, therefore, safety is not a separate issue from efficacy: the two

dimensions are evaluated together, with attention to the form of intake and the person's profile. A useful piece of information for guidance is that, in the available clinical study, a water-soluble extract rich in clove polyphenols was administered at 250 mg/day for 30 days to 13 subjects, 7 of whom were normoglycemic and 6 prediabetic, with a favorable effect on pre- and post-prandial glycemia [2]. Polyphenols are plant compounds known for their antioxidant activity, while prediabetic refers to people with blood glucose levels higher than normal but not yet in the diabetic range. This information helps to avoid inappropriately equating food doses with supplement doses. The result should be read as a signal of interest, but also as an example of measured use, limited in time and in a small sample. Precisely for this reason, the data cannot be transferred to scenarios of prolonged self-medication. On the experimental side, clove essential oil showed hypoglycemic activity in STZ diabetic rats at 20 mg/kg BW, with a significant reduction in glycemia and total cholesterol and with an IC₅₀ against α -amylase of 298.0 ± 2.75 μ g/mL [33]. Essential oil refers to the concentrated and volatile aromatic fraction of the plant, while STZ indicates streptozotocin, a substance used to induce diabetes in animal models; α -amylase is an enzyme that contributes to starch digestion, and IC₅₀ represents the concentration required to achieve 50% of the observed inhibitory effect. However, the biological potency observed in animal models does not coincide with a sufficient safety profile for free use. From a cautious perspective, cloves remain interesting as a food, but concentrated formulations should be considered carefully, especially if the goal is prolonged use or in fragile individuals. Before extending the reasoning to practice, it is useful to distinguish the points that make this topic central:

- The actual dose varies greatly between spice, extract, and essential oil.
- Tolerability also depends on the duration of exposure.
- People undergoing therapy require greater caution.
- Concentrated uses should not be confused with food uses.

In the final part of the article, the focus shifts from biological effects to the safest conditions of use. The following points clarify when caution is sufficient and when, instead, the concentrated form requires more



careful evaluation.

11.1 Cloves and safety of use in daily diet

In normal food consumption, cloves are used in small quantities, which limits overall exposure to eugenol and other aromatic constituents. Safety, however, does not depend solely on the absolute quantity: frequency, duration, and individual sensitivity also matter. Sporadic use in cooking has different implications than daily and repeated intake, especially when the spice becomes part of a "do-it-yourself" health strategy. In terms of public communication, it is important to avoid a common misconception: natural does not automatically mean free of side effects. For this reason, the most reasonable criterion remains moderation, i.e., use consistent with diet and not with disproportionate therapeutic expectations. Within the framework of the relationship between cloves, eugenol, and metabolism, safety is therefore a contextual issue even more than an ingredient issue. A realistic approach also helps not to overestimate the possible benefits of clove polyphenols when consumed outside a balanced dietary model. Furthermore, available data on glycemia and metabolism often derive from controlled experimental conditions [2,16,3], while in daily life, variables such as meal composition, dietary adherence, and potential comorbidities come into play. The correct evaluation, therefore, does not concern only the single food, but its inclusion in the overall dietary profile.

11.2 Clove essential oil: why it requires caution

Essential oil concentrates a much higher proportion of volatile compounds than the spice, and this substantially alters the exposure profile. It is useful for the reader to remember that a concentrated formulation is not simply a "stronger version" of the culinary product, but a preparation with different usage and tolerability considerations. Experimental literature shows relevant biological activities even at low doses: in STZ diabetic rats, 20 mg/kg BW of essential oil reduced glycemia and total cholesterol, with an inhibitory effect on α -amylase documented by an IC_{50} of $298.0 \pm 2.75 \mu\text{g/mL}$ [33]. These results explain why essential oil is studied, but do not authorize considering it suitable for home self-management. In

particular, unguided or repeated use can amplify critical issues compared to simple food use. The reason is physiological: when concentration increases, the probability of interactions with metabolic and enzymatic pathways already engaged by drugs, diet, or inflammatory state increases. Therefore, if the goal is nutritional prevention, the spice in cooking remains the most prudent reference; concentrated extracts and essential oils, on the other hand, require a more rigorous evaluation of dose and context.

11.3 Cloves and possible interactions: when to seek advice

When considering cloves, one must take into account not only the product but also the person consuming it. Pharmacological therapies, digestive fragility, liver conditions, pregnancy, and other clinical contexts may warrant a consultation with a healthcare professional. The point is not to create alarm, but to avoid the mistake of applying the same consumption rule to everyone. This is even more true for concentrated formulations, where the higher availability of eugenol can make tolerability less predictable compared to culinary use. In a scientific reading of safety, the advice is not to give up the spice, but to incorporate it into a proportionate framework compatible with the individual's profile. Even studies on metabolic effects do not replace this evaluation, because efficacy data does not automatically coincide with appropriateness of use. For this reason, the correct question is not whether cloves "work," but in what form, at what dose, and for which people their use is truly sensible. Caution is particularly useful for individuals taking multiple herbal products together, because the sum of intakes can increase overall exposure without the consumer realizing it. In the presence of chronic diseases, the safest choice is to discuss use with your doctor, to avoid unnecessary overlaps or unrealistic expectations.

11.4 Common mistakes in using cloves

The most frequent mistakes concern overestimating the effect, using excessive doses, confusing the spice with the extract, and expecting an aromatic substance to replace broader dietary interventions. Another common misconception is thinking that if a product has been studied in the laboratory or in animal models, it can be directly replicated in daily practice.

In the case of cloves, this risk is particularly relevant because the concentration of active compounds varies greatly between different forms of use. The reference to possible effects on glycemia and metabolism should also be interpreted with caution: signs of scientific interest do not eliminate the need for measurement, especially when talking about prolonged or concentrated use. The key point, therefore, is to avoid

both excessive enthusiasm and prejudiced rejection. Safety comes from proportion, product quality, and consistency between objective and form of use. From this perspective, supplementation should be seen as a possible support, not as a therapeutic shortcut. If the use is dietary, the reference remains the spice in normal quantities; if it is extractive or essential, stricter criteria for selection, dosage, and supervision are needed.

12. QUADRO COMPARATIVO E SINTESI DELLE EVIDENZE

The following table summarizes the most important concepts that emerged in the article, to immediately distinguish between food use, extracts, and cautionary aspects.

Quadro comparativo

Concept	What it means	Practical implication
Whole spice	Culinary raw material with moderate concentration of active compounds	Suitable for daily use in small quantities
Standardized extract	More concentrated preparation with more predictable content	More useful for studies or supplementation, with greater caution
Essential oil	Highly concentrated form of eugenol and other volatile compounds	Not equivalent to the spice, requires greater attention

This summary reorders only the sources already present in the doilist, to show where the evidence is strongest, where it remains preliminary, and which results are repeated most consistently.

Sintesi delle evidenze scientifiche

Publication Year	Area Studied	What Studies Indicate	Main Limitation	Level of Evidence
2022	Metabolic Syndrome and Glucose Metabolism	Evidence indicates that a polyphenol extract from cloves can promote redox balance and glucose management.	Limited human sample and finite duration comparison.	Clinical trials [3]
2019	Pre- and Post-prandial Glycemia	Studies suggest a reduction in glycemia with a water-soluble polyphenol-rich extract in healthy and prediabetic volunteers.	Open pilot study with a very small sample size.	Clinical trials [2]
2014	Hepatic Steatosis and Fibrosis	Evidence indicates that eugenol can modulate AMPK and mTOR, with favorable effects on lipid accumulation and fibrosis in animal models.	Clinical transferability not yet demonstrated.	Observational studies [8]

2022	Microbiota and Adiposity	Studies suggest a possible reduction in adiposity and modulation of the microbiota in murine models fed a high-fat diet.	Results obtained only in animals.	Observational studies [5]
2023	Autophagy and Intestinal Cells	Evidence indicates that the spermidine-eugenol combination can preserve cell viability by stimulating autophagy in an intestinal model.	Cellular and non-clinical model.	Preliminary evidence [6]
2021	PI3K/Akt/mTOR and Apoptosis	Studies suggest that an active fraction of cloves can modulate PI3K/Akt/mTOR and promote apoptosis in colon carcinoma cells.	In vitro oncological context, not directly applicable to metabolic clinical practice.	Preliminary evidence [12]
2024	AMPK, oxidative stress and experimental toxicity	Evidence indicates that eugenol can remodel AMPK/p-AKT/mTOR in an animal model of acrylamide toxicity.	Specific toxicological and non-human metabolic model.	Preliminary evidence [14]

13. SINTESI EDITORIALE E CONCLUSIONI

EDITORIAL REVIEW OF THE EVIDENCE

Overall, the literature shows a fairly consistent line: clove compounds, especially eugenol and polyphenol fractions, are associated with favorable signals on glucose metabolism, oxidative stress, and certain cellular pathways that regulate adaptation and growth. The picture is stronger in experimental models, but not without initial human signals. This makes a real nutritional interest plausible, especially when the spice is seen as part of a broader dietary strategy and not as an isolated solution.

The main limitation is the imbalance between studied mechanisms and available clinical confirmations. Many results come from cells or animals, with concentrated preparations and controlled conditions that do not reflect domestic use. Even in the few human studies, samples are small and follow-up is short. Furthermore, spice, extract, and essential oil are not equivalent, so practical translation must remain cautious.

FINAL CRITICAL NOTE

The strongest part of the bibliography concerns the biological rationale, not clinical confirmation. This creates a significant gap between what is observed in the laboratory and what can truly be supported in human practice. Many results are obtained with cells, animals, or highly concentrated fractions, i.e., under conditions far from the daily use of the spice. Furthermore, positive outcomes are not uniform across dose, matrix, and experimental context: in some conditions, the signal appears consistent, in others, it is more uncertain or depends on concentrations difficult to translate to the diet. The literature on autophagy, mTOR, and energy regulation is also fascinating, but often originates in oncological, toxicological, or acute stress models, not in studies dedicated to human metabolic prevention. The evidence linking cloves to insulin resistance, steatosis, and glycemia is therefore plausible, but not yet robust clinically. For this reason, the most correct interpretation remains cautious: the compound is interesting, the mechanism is credible, but practical translation requires broader confirmations, better samples, and longer studies. The difference between



spice, extract, and essential oil also remains a critical point, because concentration profoundly changes exposure and thus the meaning of the result. In summary, the available material allows for a solid scientific interpretation on a mechanistic level, but does not authorize clinical shortcuts or generalized conclusions.

CONCLUSIONS AND EDITORIAL SUMMARY

Cloves hold an interesting position as both a traditional spice and a source of bioactive compounds. Their composition, dominated by eugenol and enriched with polyphenols—plant compounds with antioxidant activity—explains why they have been studied in relation to glycemia, insulin resistance, oxidative stress, inflammation, and the regulation of cellular pathways like AMPK and mTOR. From an editorial and scientific perspective, the strongest point is not the idea of a miraculous effect, but the presence of a coherent biological rationale. This rationale emerges particularly when the literature observes the behavior of standardized extract or eugenol in controlled models, where signals are seen regarding glucose metabolism, energetic flexibility, autophagy, and nutrient response. At the same time, a correct interpretation requires not confusing different levels of evidence. The whole spice used in cooking is not equivalent to an extract, and an extract is not equivalent to an essential oil. This distinction is central to metabolic prevention because it changes the dose, bioavailability—the amount of substance actually absorbed and usable by the body—and the meaning of the data. When discussing nutrition, real benefits almost always arise from incorporating a food into a coherent dietary pattern, not from a single isolated ingredient. In this sense, cloves can play a useful supporting role, especially in enriching the diet with interesting plant compounds, but they should not be presented as a shortcut or a substitute for established dietary or clinical approaches. Another important aspect concerns the link between metabolism and cellular physiology. The literature on eugenol, AMPK, mTOR, and autophagy shows that phytochemicals—biologically active components of plant origin—can interact with very broad networks, capable of influencing how tissue uses energy, responds to stress, and maintains homeostasis, meaning internal functional balance. This makes the

topic relevant for those studying prevention, liver function, control of energy substrates, and overall dietary quality. However, the best results remain preliminary at the human clinical level, and therefore the most serious message is one of balance: interest, yes; overinterpretation, no. From a nutritional perspective, cloves fit well into the idea of a varied diet rich in spices, vegetables, and minimally processed foods. Within this framework, they can contribute to the quality of the aromatic profile and the overall functional density of the meal, while concentrates require more cautious language and more rigorous evaluation. It is precisely this dual identity, culinary and biological, that makes them a useful topic for readers seeking reliable content on metabolism and prevention. Future in-depth analysis can naturally connect to other topics on the site, from glycemic regulation to functional nutrition, always maintaining the same criterion: starting from data, distinguishing forms of use, and prioritizing scientific coherence.

Aggiornato al 21/10/2026. Questo contenuto riflette una sintesi divulgativa delle evidenze scientifiche al momento della pubblicazione e non sostituisce il parere medico.

14. TRANSPARENCY AND SCIENTIFIC RESPONSIBILITY

Artificial Intelligence was used solely as a tool for editorial and documentary support. All content, interpretations, bibliographic citations and conclusions have been verified, reviewed and approved by the author, who assumes full scientific responsibility for them.

The manuscript was also subjected to independent peer review prior to publication.

To ensure the greatest transparency, the complete history of the article, including the dates of submission, revision, acceptance and publication, as well as information on the peer review process, is available on the dedicated Article History page.

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