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Clinical Impact of Allium sativum Supplementation on Cardiovascular Risk Factors

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Abstract: The ongoing research for safe treatments which can assist main medications addresses the problem that cardiovascular diseases (CVDs) remain the primary cause of death throughout the world. The nutraceutical status of Allium sativum (garlic) originates from its ability to improve multiple aspects of vascular function. The publication presents a comprehensive summary of existing studies that demonstrate how garlic supplements effectively treat major cardiovascular risk factors. The phytochemical analysis shows that allicin starts to show bioactive effects but S-allyl cysteine (SAC) stable derivatives deliver better systemic absorption and bioactive effects. Garlic affects lipid metabolism through its HMG-CoA reductase inhibitory action, which creates enhancements to nitric oxide (NO) and hydrogen sulfide (H_2S) signaling that decrease blood pressure, and it protects against the renin-angiotensin-aldosterone system. The results from randomized controlled trials (RCTs) show that standardized garlic formulations produce a significant reduction of total cholesterol between 8 and 12 percent and a decrease of systolic blood pressure between 7 and 9 mmHg among hypertensive patients. The use of Allium sativum provides an effective and cost-efficient method to reduce cardiovascular risk, which requires standardized dosing protocols for Safe medical marijuana use.

Keywords: Allium sativum, HMG-CoA, randomized controlled trials, cardiovascular risk, Safe medical marijuana

INTRODUCTION

The Global Burden of Cardiovascular Disease

Cardiovascular diseases (CVDs) remain the leading cause of worldwide death and sickness because they kill approximately 17.9 million people each year. The complex set of diseases which includes coronary heart disease and cerebrovascular disease and peripheral arterial disease develops through multiple risk factors which people can control and which include hypertension and dyslipidemia and chronic systemic inflammation. Although pharmaceutical treatments including statins and ACE inhibitors show strong

effectiveness 1 billion people worldwide do not receive adequate treatment because they face socioeconomic barriers and experience side effects and increasingly prefer alternative medicine [1]. The research of bioactive food components has progressed from traditional medicine into scientific testing throughout the current period. Allium sativum which people commonly know as garlic stands out among all the tested nutraceuticals because it has been thoroughly studied and proves effective for managing cardiovascular risk.

Ethnobotany and Historical Context

The medical use of garlic goes beyond current scientific knowledge because it is documented in the traditional plant medicine practices of ancient cultures. The Sumerians, Egyptians, Greeks, and Romans used garlic as a fundamental cooking ingredient and their main medical treatment throughout history. Ancient Egyptian papyri documented the administration of garlic to laborers constructing the pyramids to improve physical endurance and safeguard against circulatory disorders. The Traditional Chinese Medicine and Ayurveda systems both consider garlic a "warming" plant which practitioners use to improve blood flow and reduce "blood stagnation" because the latter condition resembles how modern medicine defines thrombosis and atherosclerosis [2]. Researchers from the 20th century studied garlic because different cultures agreed on its medicinal value which led them to extract its sulfur-containing chemicals. Scientists discovered that garlic became a clinical supplement because they learned its distinctive smell come from its bioactive organosulfur compounds which include alliin and its derivative allicin.

The "Garlic Hypothesis" in Modern Cardiology

The "Garlic Hypothesis" asserts that consistent use of standardized garlic supplements can markedly slow the advancement of atherosclerosis by addressing various cardiovascular risk mechanisms concurrently [3]. The bioactive compounds in garlic which include S-allyl cysteine and diallyl trisulfide exhibit multiple effects that differ from the way manufactured drugs operate because these drugs target specific enzymes or receptors. The process includes three components which are the prevention of hepatic cholesterol biosynthesis and the facilitation of nitric oxide-induced vasodilation and the attenuation of platelet aggregation. The hypothesis suggests that these combined effects create a synergistic "cardioprotective shield." Furthermore, recent genomic and proteomic studies have expanded this hypothesis to include the modulation of hydrogen sulfide (H_2S) signaling, a critical gaseous signaling molecule that protects vascular endothelium from oxidative stress and calcification markedly slow the advancement of atherosclerosis by addressing various cardiovascular risk mechanisms concurrently. The bioactive compounds in garlic which include S-allyl cysteine and diallyl trisulfide exhibit multiple effects that differ from the way manufactured drugs operate because these drugs target specific enzymes or receptors. The process includes three components which are the prevention of hepatic cholesterol biosynthesis and the facilitation of nitric oxide-induced vasodilation and the attenuation of platelet aggregation.

Clinical Relevance and Research Gaps

The theoretical foundation for garlic's effectiveness is strong; however its clinical significance is a topic of considerable scholarly contention. The different methods of supplement preparation which include raw cloves garlic oil steam-distilled extracts and aged garlic extract (AGE) have produced different results in human studies. The need for consistent evaluation of garlic's health benefits emerges from its unpredictable effects on LDL-C levels and systolic blood pressure measurements and carotid intima-media thickness results [4]. The medical field requires a lot of Allium sativum dose-response research to develop personalized nutritional solutions in this case. The study aims here to gather all available evidence to determine whether there are garlic supplements can serve as effective additional treatment for cardiovascular risk reduction.

Phytochemistry: The Sulfur Complexity of Allium Sativum

The Allicin Cascade and Enzymatic Transformation

Allium sativum demonstrates cardiovascular effects through its specific active component which requires direct physical damage to convert its base form through complex enzymatic processes. The inactive state of garlic contains alliin (L-allylsulfoxide) as its precursor amino acid and alliinase enzyme which exists in separate parts of the plant between its mesophyll cells and vascular bundle vacuoles. Crushing slicing or chewing these substances breaks their protective barriers which permits vacuolar alliinase to escape and drive the conversion process of alliin into allicin (diallyl thiosulfinate) [5]. The main active ingredient that drives garlic's initial biological effects is allicin although it has a reputation for being highly unstable and fleeting. The substance rapidly breaks down into multiple oil-soluble organosulfur compounds which include diallyl sulfide (DAS) and diallyl disulfide (DADS) and diallyl trisulfide (DATS). Alliinase remains permanently disabled through contact with stomach acid which creates a continuous challenge for treatment in medical environments. The systemic circulation of allicin potential from garlic consumption requires an enteric-coated product which protects the substance during its passage through the stomach for optimal absorption. The different effectiveness between raw garlic and supplement trials results from this method of consumption.

Stable Bioactives: The Role of S-Allyl Cysteine (SAC)

The phytochemical composition of garlic shows two distinct components which include unstable thiosulfinates and stable water-soluble compounds that produce different therapeutic effects and metabolic activities. Aged Garlic Extract (AGE) shows different effects than raw garlic which produces unpredictable effects that frequently cause discomfort. The extraction process for this preparation requires a twenty-month period during which sliced raw garlic remains in an ethanol-water solution at room temperature. The extended aging process allows natural development which transforms unstable harsh compounds like allicin into stable water-soluble organosulfur compounds that human digestive systems process with better results. The most important permanent markers in the study include S-allyl cysteine (SAC) and S-allyl mercaptocysteine (SAMC). The body absorbs SAC well because it enters the bloodstream after ingestion whereas allicin transforms into secondary metabolites which prevent its absorption [6]. Studies demonstrate that absorption rates for SAC surpass 90% in human subjects which enables SAC to achieve systemic objectives through its bioavailability. The digestion process preserves SAC stability while it functions as the standard "gold scholar" measurement for clinical trials that investigate long-term cardiovascular outcomes and atherosclerosis reduction.

Challenges in Bioavailability and Pharmacokinetics

The primary research challenge of garlic phytochemistry exists because scientists lack effective ways to study its bioavailability which they consider the only method to assess its heart disease treatment potential. The extraction method used for garlic supplements and the age of cloves and the environmental factors of their growing area determine their sulfur compound content. Steam-distilled garlic oil contains only trace amounts of allicin and alliin while it contains high levels of diallyl sulfides and garlic powder supplements enable controlled alliin activation through their alliin-alliinase system which activates in the gastrointestinal tract [7]. The garlic components in the body show two distinct elimination routes because lipid-soluble sulfides get eliminated through breathing and skin loss which creates the typical scent while water-soluble SAC remains in the bloodstream for multiple hours. The bloodstream maintains its continuous flow of active ingredients, which connect with vascular systems through their effects on endothelium and hepatic enzymes, which explains why AGE preparations show better results than other treatments in reducing carotid intima-media thickness. Scientists need to understand the whole system of sulfur compounds to create a dependable dose-response relationship because the dose definition includes both the garlic amount consumed and its sulfur metabolite bioavailability.

Mechanisms of Action: Molecular Targets in the Vasculature

Allium sativum exhibits cardioprotective effects through its multiple impacts on metabolic and vascular systems which control both cholesterol synthesis and blood pressure levels. The bioactive components of garlic interact with multiple critical enzymatic pathways to produce multiple effects which include controlling lipid levels and gasotransmitter transmission and the renin-angiotensin-aldosterone system (RAAS).

Inhibition of HMG-CoA Reductase and Cholesterol Biosynthesis

Organosulfur compounds, especially S-allyl cysteine and diallyl disulfide, act as strong inhibitors for HMG-CoA reductase which serves as the main control enzyme for the mevalonate pathway that produces cholesterol in the liver. Scientific research using hepatocyte cell cultures has demonstrated that garlic-derived compounds can reduce HMG-CoA reductase activity by approximately 30 to 40 percent [8]. The enzyme functions as a competitive inhibitor that statins use to block its activity while Allium sativum achieves its effect through a phosphorylation process that deactivates the enzyme without affecting mRNA or protein synthesis. Research shows that SAC and other S-alk(en)yl cysteines reduce HMG-CoA reductase activity by 18 to 29 percent because they cause increased phosphorylation and sulfhydryl oxidation. The "soft" inhibition method controls excessive cholesterol accumulation in the liver which leads to increased LDL receptor production that helps remove low-density lipoprotein from the bloodstream. The research shows that diallyl disulfide can form internal disulfide bonds with the thiol groups of lipogenic enzymes which leads to enzyme inactivation and a reduction in acetate conversion to free and esterified cholesterol in the liver.

Upregulation of Nitric Oxide and Vascular Gasotransmitters

The primary way garlic produces its blood vessel widening effect shows that garlic enhances the body ability to use Nitric Oxide because this molecule controls blood vessel constriction. Allium sativum supplementation leads to increased endothelial nitric oxide synthase (eNOS) enzyme activity which produces nitric oxide at rates that reach 117% in particular medical situations. The process operates through two mechanisms which include direct enzyme activation and direct provision of arginine which serves as the biological nitric oxide (NO) precursor. Garlic bioactives which include DATS polysulfides display properties that enable them to release hydrogen sulfide (H_2S) into the environment [9]. When people consume these polysulfides, red blood cells convert them into H_2S which acts as an effective gasotransmitter. Hydrogen sulfide (H_2S)

activates ATP-sensitive potassium (K_{ATP}) channels within vascular smooth muscle cells which leads to hyperpolarization followed by muscular relaxation. The combined effects of increased NO bioavailability and H_2S signaling result in body-wide blood vessel dilation which causes patients with high blood pressure to experience reduced systolic and diastolic blood pressure measurements.

Angiotensin-Converting Enzyme (ACE) Inhibition and RAAS Modulation

Garlic affects blood pressure control through its impact on the endothelial cells and its function as a natural Angiotensin-Converting Enzyme (ACE) inhibitor. The RAAS system depends on ACE as its main enzyme, which transforms the dormant Angiotensin I into the potent blood vessel constrictor Angiotensin II. The molecular docking studies together with in silico models determined that ajoene, alliin, and S-allylmercaptocysteine (SAMC) have strong binding affinity for the ACE protein, which matches the binding power of Captopril, a prescription drug. Garlic supplementation reduces Angiotensin II levels, which decreases aldosterone production and stops NADPH oxidase from creating Angiotensin II-induced reactive oxygen species (ROS) [10]. The RAAS system suppression results in an immediate blood pressure reduction that usually falls between 7 and 10 mmHg for people with hypertension while it provides additional defense against arterial calcification and myocardial lipid accumulation. The total effect of these molecular interactions makes Allium sativum a vital controller of essential factors that determine cardiovascular risk.

Clinical Efficacy: Analysis of Randomized Controlled Trials

The period of 40 years has witnessed multiple randomized controlled studies whose primary aim was to convert garlic's molecular mechanisms into measurable medical outcomes. The individual studies produced inconsistent results but the comprehensive meta-analysis of all the data provided a better understanding of how garlic affects the three main cardiovascular risk factors which include dyslipidemia and hypertension and platelet hyperactivity. The clinical agreement indicates that Allium sativum serves as a powerful supplementary therapy which especially benefits individuals with pre-existing metabolic abnormalities.

Modulation of Lipid Profiles and Dyslipidemia

The effect of garlic on serum lipids is arguably its most thoroughly known clinical characteristic. Meta-analyses which analyzed more than 20 randomized controlled trials (RCTs) have proven that garlic supplementation effectively decreases both total cholesterol (TC) and low-density lipoprotein cholesterol (LDL-C) levels [12]. Hyperlipidemic people can expect to see their total cholesterol (TC) drop between 12 and 17 mg/dL which equals about 7 to 10 percent and their low-density lipoprotein cholesterol (LDL-C) levels will decrease by approximately 8 to 10 mg/dL. The therapeutic significance of these reductions is significantly influenced by the intervention's length. The subgroup analyses show that studies which last less than 12 weeks will produce inconsistent results but treatments which extend beyond three months will yield consistent and statistically significant reductions in lipid levels.

The process used to create garlic products determines their capability to produce lipid results. The standardized garlic powder which contains 600 to 900 milligrams per day and Aged Garlic Extract (AGE) show better performance than garlic oil and raw garlic because alliin and S-allyl cysteine (SAC) levels have been standardized. Current research shows that garlic consumption causes a small increase in high-density lipoprotein (HDL-C) which develops into "slight" or "borderline significant" results according to multiple meta-analyses that published in 2025. Garlic consumption leads to better results for all lipid subfraction profiles according to research findings which show that garlic raises "bad" cholesterol levels [13]. The research shows that garlic can reduce fat levels in the body but its effects are much weaker than those of pharmaceutical statins which work better for people with mild-to-moderate hypercholesterolemia.

Antihypertensive Efficacy in Hypertensive Cohorts

The garlic clove Allium sativum shows distinct blood pressure control ability through its selective properties. The clinical evidence shows that garlic supplements provide better blood pressure control to patients with hypertension whose systolic blood pressure exceeds 140 mmHg than to people with normal blood pressure [14]. The meta-analysis research on hypertensive patients shows that their systolic blood pressure decreased by 8.3 mmHg while their diastolic blood pressure dropped by 5.5 mmHg. The resulting values show similar blood pressure reduction effects to those produced by common first-line antihypertensive medications which include low-dose thiazide diuretics and ACE inhibitors. A decrease of 8–10 mmHg in systolic blood pressure (SBP) significantly correlates with a 16–40% reduction in the risk of stroke and myocardial infarction.

The recent triple-blind placebo-controlled studies confirm these results especially for the "optimized" aged black garlic extracts. Researchers have reported substantial blood pressure reductions because SAC at a dosage of 0.25 mg per day produces both blood pressure drops and diminished ACE activity while increasing blood nitric oxide concentrations. The research establishes that the previously discussed molecular processes of ACE inhibition and

vasodilation now exist as a definite clinical identification. The "Garlic Hypothesis" shows how essential baseline conditions impact people with normal blood pressure because garlic supplements create almost no effect while restoring blood vessel balance instead of causing blood pressure drops through hemostatic mechanisms.

Anti-platelet Activity and Thrombotic Risk

Garlic shows its third clinical effect by its ability to control how platelets work and how blood forms clots. Atherosclerosis develops because of hyperactive platelets which also serve as the main reason that causes acute coronary syndromes. Clinical investigations assessing platelet aggregation have demonstrated that high-dose garlic supplementation (e.g., 2400 mg of garlic powder or standardized AGE) markedly reduces platelet aggregation generated by agonists such as adenosine diphosphate (ADP) and adrenaline. The reduced thromboxane B2 levels and extended bleeding times which clinical studies show in specific groups provide mechanistic evidence for this effect [15]. The various studies which show garlic as a weak anti-thrombotic agent demonstrate that garlic acts as an anti-thrombotic agent although its clinical proof shows more inconsistencies than the evidence which supports cholesterol and blood pressure studies.

The trials which used reduced doses of 600 mg per day showed no changes in platelet aggregation which proves that hematological effects need a specific dose range for their effects to occur. The existing research about garlic effects on animal fibrinogen levels and fibrinolytic activity shows potential benefits for human hyperlipidemic populations, but larger human randomized controlled trials must be conducted to validate whether these physiological changes lead to lower thrombotic event rates. The anti-platelet effects of garlic create safety issues because patients who need surgery and patients who take strong anticoagulants such as Warfarin or Clopidogrel must monitor their blood coagulation levels. The combination of garlic with these medications creates a theoretical risk of bleeding which doctors consider during surgical procedures despite the fact that such events are rare in clinical studies.

Clinical Evidence

The research from randomized controlled trials which has built up over decades proves that Allium sativum functions as an effective cardiovascular supplement which people can use for multiple purposes. The treatment provides three different ways to reduce cardiovascular disease risk through its ability to decrease LDL-C levels and lower systolic blood pressure in hypertensive patients and to prevent platelet aggregation. The public health sector should consider garlic as a valuable intervention because it demonstrates strong safety and low-cost benefits despite its minimal health impacts. The evidence shows that standardized preparations which include Aged Garlic Extract and standardized powder need to be taken at fixed daily amounts for a period of 12 weeks to achieve these medical results [16].

Safety, Adverse Effects, and Herb-Drug Interactions

Regulatory authorities classify Allium sativum as safe (GRAS) for culinary use. The concentrated supplements of this substance require a complete evaluation which includes their potential side effects and drug interaction problems. The primary medical problems of garlic supplements affect blood formation and digestive health especially when they are combined with conventional heart medications.

Anticoagulant Risks and Hemorrhagic Potential

The primary safety concern for patients with cardiovascular disease is the possibility that garlic may increase the risk of hemorrhage. The organosulfur compounds in garlic which include allicin and ajoene show anti-platelet activity because they block cyclooxygenase activity and reduce thromboxane A_2 synthesis. Clinical reports have intermittently associated high-dose garlic intake with spontaneous post-operative hemorrhage and spinal epidural hematoma. Therefore, the usual clinical guideline advises patients to cease garlic supplementation at least two weeks before elective surgical interventions [17].

Garlic establishes interactions with various types of anticoagulant and anti-platelet medications. Preclinical studies and certain clinical case reports indicate that garlic may enhance the effects of Warfarin which results in an elevated International Normalized Ratio (INR) and an increased risk of bleeding. The interaction mechanism combines two processes which involve direct anti-platelet activity and cytochrome P450 enzyme regulation that affects the metabolism of warfarin and other anticoagulants. Controlled trials with Aged Garlic Extract (AGE) demonstrate an improved safety profile which controlled trials evaluated. A 12-week randomized controlled trial of patients on stable warfarin medication indicated that AGE did not substantially affect INR or elevate bleeding risk under careful monitoring. The use of "raw" and "oil-based" formulations maintain their classification as higher-risk products which result in drug interactions with Aspirin Clopidogrel and Rivaroxaban thus requiring clinicians to manage patient treatment with caution.

Gastrointestinal Side Effects and Tolerability

Gastrointestinal upset is the predominant cause of patient non-compliance in garlic studies. Raw garlic and high-concentration garlic powder are significant irritants to the stomach mucosa. The clinical literature documents multiple adverse effects which include heartburn and nausea and abdominal discomfort and

flatulence and diarrhea. The endoscopic assessments of animal models show that raw garlic powder causes localized erosion and gastric mucosa erythema through its volatile thiosulfinates which produce these effects.

The treatment of these symptoms uses enteric-coated pills which develop their active components as the pills dissolve in the small intestine's alkaline environment to protect the stomach [18]. The preparations produce "garlic breath" and body odor as adverse effects because the body excretes allyl methyl sulfide through the lungs and skin. The aging process of Aged Garlic Extract (AGE) creates its most tolerable form because the aging process transforms irritating volatile chemicals into stable water-soluble molecules which include S-allyl cysteine that are considerably milder on the digestive system.

Discussion and Future Directions: Towards Clinical Standardization

The complete implementation of Allium sativum as a primary treatment for cardiovascular disease needs to overcome three major obstacles which stem from both its strong scientific foundation and its successful results in multiple clinical trials. The main academic dispute results from three factors which include different trial designs and missing standardized treatment dosages and the unavailability of extended research about severe cardiovascular incidents.

Methodological Limitations and Heterogeneity

The garlic study contains "contradictory" evidence which stems from differences in research methods used by different studies. The initial clinical trials faced restrictions because their study groups were too small and their research periods lasted less than eight weeks and their blinding methods were inadequate. The distinctive aroma of garlic creates challenges for conducting real double-blinding tests because it increases the risk that people will experience a "placebo effect" during their symptom evaluations. The meta-analyses combine data from different types of preparations which include raw garlic and steam-distilled oil and aged extracts that have different pharmacological properties [19]. The phytochemistry section shows that a supplement which contains alliin as its standard will behave differently than a supplement which contains S-allyl cysteine (SAC) as its standard. The introduction of "preparation bias" has created different results because some high-quality studies found no impact on lipid levels while other studies reported major declines in lipid levels.

The Challenge of Standardized Dosing

The primary obstacle to clinical application is the absence of a standardized "therapeutic dose." International guidelines about garlic consumption for cardiovascular prevention remain nonexistent at this time. Trial dosages for garlic powder range from 600 mg to 2,400 mg, while those for Aged Garlic Extract range from 250 mg to 7.2 grams [20]. Clinicians lack the ability to prescribe garlic with pharmaceutical precision because they do not have a standard definition of "allicin-release potential" and "SAC concentration." Future research should focus on dose-response studies using standardized enteric-coated formulations to identify a therapeutic window which maximizes treatment effectiveness while minimizing stomach-related side effects

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Future Directions: Morbidity and Mortality Trials

Future Allium sativum research should prioritize hard clinical objectives above surrogate measures like serum cholesterol or blood pressure measurements. The existing evidence supports garlic's ability to decrease blood pressure but lacks conclusive proof which establishes a connection between this blood pressure reduction and reduced myocardial infarction or stroke or long-term cardiovascular death. The genuine preventive efficacy of garlic requires validation through extensive multicenter trials which must continue for more than five years. The research into the combined effects of garlic and sub-therapeutic statin doses will provide a new method to protect high-risk patients from drug-related side effects. Garlic has developed into a powerful tool which scientists use to combat cardiovascular disease despite its operational limitations as a supplementary resource.

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